

Approach to the diagnosis of seizures

Part 1: Epileptic and non-epileptic seizures

Prof. Dr. med. vet. **Dorothea Schwartz-Porsche**

Klinik und Poliklinik für kleine Haustiere der Freien Universität Berlin, Germany



*Dorothea Schwartz-Porsche,
Small Animal Clinic and
Polyclinic of the Free
University of Berlin, Germany.*

Table 1
Classification of non-epileptic seizures

Non-epileptic seizures are pathological events that recur suddenly, are of short duration, disappear just as quickly, and are of non-epileptic etiology

Syncope

- Cardiac arrhythmias
- Congenital heart diseases
- Cardiomyopathies

Episodic weakness

- Metabolic in origin
 - hypoglycemia, Addisonian crisis, etc
- Myasthenia gravis
- Polymyopathy, polyneuropathy

Narcoleptic seizures

Cataplectic seizures

Attacks of vertigo

- vestibular symptoms

Recurring attacks of pain

Table 2
Classification of epileptic seizures

Partial (focal, local) seizures

- Simple partial seizures
 - With motor signs
 - With somatosensory or special-sensory symptoms
 - With autonomic symptoms or signs
 - With psychic symptoms
- Complex partial seizures
 - Simple partial onset followed by impairment of consciousness
 - With impairment of consciousness at onset

Partial seizures evolving to secondarily generalized seizures

Generalized seizures (convulsive or nonconvulsive)

- Absence seizures
- Myoclonic seizures
- Clonic seizures
- Tonic seizures
- Tonic-clonic seizures
- Atonic seizures

Unclassified epileptic seizures

From Commission on Classification and Terminology of the International League against Epilepsy. Proposal for Revised Clinical and Electroencephalographic Classification of Epileptic Seizures (*Epilepsia* 1981; 22: 489–501).

KEY POINTS

- Episodic events or non-epileptic seizures and epileptic seizures occur frequently in dogs and cats.
- Non-epileptic seizures have very diverse causes.
- Epileptic seizures are based on paroxysmal, bioelectric functional disturbances of the brain. They can be of both cerebral and extracerebral etiology and have to be differentiated diagnostically from each other.
- The term 'epilepsy' is only used for seizures that recur chronically, have their primary origin in the brain, and are not caused by progressive or still active brain diseases.
- Extracerebral seizure disorders and progressive or still active brain diseases must be distinguished diagnostically from epilepsy.
- Epilepsy is divided into three types: idiopathic, symptomatic, and cryptogenic.





Figure 1 Focal seizure on right side of the face, with cheek and eyelid affected. Symptomatic epilepsy with multifocal and secondary generalized seizures. Castrated male cat. Age at onset: 1.5 years.

Videoprint captured with digital imaging.



Figure 3 Focal seizure in right thoracic limb, spreading to pelvic limb and passing over to a complex partial seizure with impairment of consciousness and salivation. Ectopic ependymoma in the area of the left cerebral hemisphere. Male wire-haired Dachshund, 4.3 years old.

Videoprint captured with digital imaging.



Figure 2 Focal seizure in left thoracic limb. Unknown etiology. Female long-haired Dachshund, 3 years old.

Videoprint captured with digital imaging.

INTRODUCTION

Seizures can present a considerable diagnostic challenge since, although quite frequent, they are only rarely seen by the veterinarian. In addition, there are other seizures or episodic events that emerge repeatedly and suddenly, last for a short time, and then disappear just as quickly (1, 2, 3). These non-epileptic seizures (Table 1), which have various causes, can be easily confused with epileptic seizures (1, 4), so making a diagnosis is difficult. Further, the epileptic seizures themselves have a variety of causes that have to be differentiated diagnostically.

EPILEPTIC SEIZURES

Epileptic seizures are the clinical manifestation of paroxysmal, bioelectric functional disturbances of the brain, caused by excessive paroxysmal electric discharges of systems of neurones (1, 3, 5–7). The discharges are the result of a biochemical imbalance in neurotransmitter activity (2, 5, 6) and/or disrupted intracellular energy metabolism, as well as of altered membrane properties (5, 6).

These paroxysmal discharges can occur in circumscribed regions of the brain or simultaneously in both hemispheres. Depending on the extent and location of the discharges, more or less severe impairment of consciousness, motor and vegetative functions (autonomic), sensory perception, or behavior can occur (4, 5). This means that the appearance of epileptic seizures can vary. They are divided into focal, generalized, and non-classifiable seizures (Table 2), a classification (5, 7) borrowed from human medicine (8).

Partial seizures

The clinical signs of partial seizures point to the activation of a limited system of neurones (2, 4). They are generally the result of congenital or acquired focal brain lesions (3, 5, 7, 9) which may have occurred long before the first seizure. They can be divided into

simple and complex partial seizures (3, 5, 7, 9), which may both generalize secondarily (3, 5), with both hemispheres being drawn into the epileptic discharges. This can happen so quickly that it is not possible to recognize the partial origin (3, 5).

Simple partial seizures occur without impairment of consciousness. They are manifest as partial motor, somatosensory, autonomic, or psychic phenomena. They are not frequent among animals, but, when they occur, motor signs are usually seen (5, 9) – e.g., twitching of individual groups of muscles or tonus or clonus of an extremity (Figures 1 and 2), with this activity occurring contralaterally to the lesion (4). The non-motor signs are rarer or are not recognized as seizures (4, 5, 7, 9).

Complex partial seizures can arise out of simple partial seizures; they are accompanied by an impairment of consciousness. Animals suffering from this type of seizure seem confused and are often restless. During the seizure they do not react adequately and present with short-lived disturbances in behavior (such as an absent stare, unmotivated barking and howling, licking and chewing movements) as well as salivation and occasional fly-catching movements (Figure 3) (2, 4, 5, 7, 9). In cats, which frequently suffer from this type of seizure, it often evolves into status epilepticus (10, 11), most showing unilateral twitching of the face (11) and not infrequently an aggressive defensive behavior (10).

Generalized seizures

Primary generalized seizures are based on synchronous, paroxysmal discharges in both cerebral hemispheres. They show no initial focal signs. These seizures are usually accompanied by a complete loss of consciousness. In dogs and cats one mainly sees tonic-clonic seizures (3–5), but other types of primary generalized seizures also occur (Table 2).

Absences, in human beings, are characterized by a short loss of consciousness, typical EEG patterns, and age-dependence. They may be accompanied by mild motor and/or vegetative signs. They occur very rarely, or are uncommonly observed, in animals (2–4).

Myoclonic seizures are characterized by sudden muscular twitching, giving the impression that the animal has been startled. They can appear individually or in quick sequence and may progress into tonic-clonic seizures. This type of seizure can be seen in Lafora's disease (myoclonic epilepsy), a storage disease of Basset Hounds that emerges at an advanced age (12).

Clonic seizures are characterized by rhythmic muscle contractions without a tonic component. They are rare in dogs but not uncommon in cats (5, 10).

Tonic seizures, with and without a total loss of consciousness,



Videoprint captured with digital imaging.

Figure 4 Primary generalized tonic-clonic seizure, tonic phase. Idiopathic epilepsy. Male English Springer Spaniel. Age at onset: 2.3 years.



Videoprint captured with digital imaging.

Figure 6 Mild generalized seizure (twitching of the facial muscles, mydriasis, salivation). Lymphosarcoma (only the brain was affected). Castrated male cat, 1.8 years old.



Videoprint captured with digital imaging.

Figure 5 Primary generalized tonic-clonic seizure, tonic phase. Symptomatic (post-traumatic) epilepsy. Female cat. Age at onset: 6 months.

occur mainly in dogs. There is only an intense increase in tone of all skeletal muscles that causes a tonic extension of the head and extremities. They can show a changing, phase-like intensity and last from a few minutes to several hours (5, 13, 14).

Tonic-clonic seizures are the most frequent form seen in both dogs and cats (3–5, 10), making up about 80% of the epileptic seizures in dogs and 60% of those in cats (5, 10). They are usually accompanied by a complete loss of consciousness. In this form of seizure it is often impossible to distinguish between primary and secondary generalization, and therefore both types will be described together.

The course of a seizure can vary considerably among animals but is always the same for a given animal (5). The seizure can be divided into two, three, or four stages (prodroma, aura, ictus, and postictal stage), although the first two are often not clearly distinguished from each other in the literature and these two stages can be absent or they can vary greatly in severity and appearance.

A **prodromal stage** can precede the seizure and last from several hours to several days (5, 14). The animals show slight changes in character or behavior (reduction in play, increased barking, clinging, light withdrawal), which can usually be recognized only by their owner.

An **aura** is not present in many animals, and the seizure begins suddenly without any warning (primary generalization). Some animals, on the other hand, become restless and fearful – they tremble, whine, seek protection, or withdraw. Others begin to snuffle around, salivate, or vomit. Cats often run around hectically. These signs can last from several seconds to several minutes, rarely longer. Some authors interpret them as belonging to the prodromal stage (5, 7, 14); others designate them as aura (2, 4–6, 15) and, of the latter,

one group of researchers claims that they are focal seizures that generalize secondarily (15). Others do not interpret the above-mentioned signs in this manner but only the focal motor activity that emerges at the start of a seizure (4, 14).

The **ictus**, which is the actual seizure or seizure core, begins suddenly or develops out of a focal seizure. When it begins, suddenly, there is an abrupt increase in tone of all skeletal muscles and a short-lived apnea and loss of consciousness, which cause the animal to fall down or over onto one side (**Figures 4 and 5**). Symmetric orofacial movements can precede the tonic phase (5, 7, 13). The tonic phase itself is characterized by stretching of the forelegs and opisthotonus, but one also may see tonic flexion of the head, neck, and extremities (emprosthotonus). With the increase in muscle tone the hind legs are drawn in, frequently beginning with a tonic bending before stretching. The mouth can be wide open, but it can also be shut tight. The pupils are dilated and staring. Clonic convulsions are superimposed on the tonic phase or start during them. Very severe jerking, thrashing of the jaws, heavy salivation, urination, and defecation may occur. The clonic phase can be followed by running and rowing movements, or such movements can occur at interludes during the clonic phase. The actual ictus lasts from several seconds to several minutes (4, 5, 7).

In the **postictal stage** following the seizure, only a few dogs will remain lying down or exhausted or sink into a deep sleep; most animals get up after several seconds or minutes. In contrast, cats often remain motionless for a long time (10). At first the animals are disoriented, wandering around restlessly; they seem deaf and blind and do not react to a voice or show only a delayed reaction. As they gradually return to normal, many show increased hunger and thirst. The postictal phase can last a few minutes to several hours, sometimes even days (2, 4, 5, 7, 14).

In addition to these typical tonic-clonic seizures, there are less severe ones that are not accompanied by a complete loss of consciousness (5, 14, 16). Depending on the intensity of the seizures, these are also designated as generalized motor or mild generalized seizures (11) or as major or minor motor seizures (5). In cats they are seen in a very mild form: the cat freezes suddenly, does not react and shows an extreme mydriasis, light salivation, and fine, symmetrical, frequent twitching of the eyelids, chaps, and whiskers (10, 11) (**Figure 6**). These seizures are reminiscent of the absences in human beings.

Atonic seizures are characterized by a sudden loss of muscle tone. To my knowledge this has only been described once in an animal (2).

Non-classifiable seizures

This category comprises all seizures that do not fit into the classification scheme or that cannot be classified due to insufficient information (8).

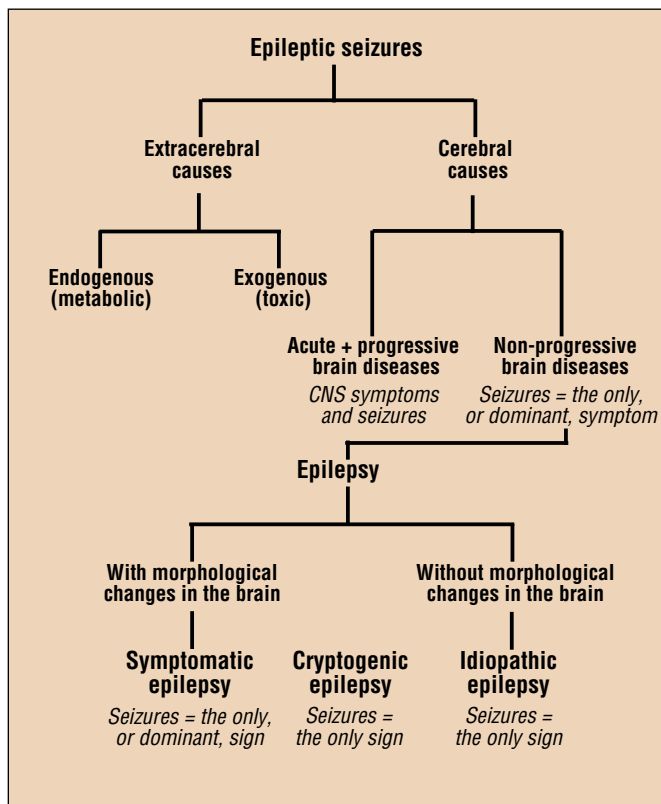


Figure 7 Diagram of epileptic seizures.

EPILEPTIC SEIZURE DISORDERS

Epileptic seizures can occur in both cerebral and extracerebral diseases. Depending on the location of the cause, two groups are distinguished – seizures or seizure disorders of primary extracerebral and primary cerebral origin (3, 5, 7, 10). In the former, the cause can be endogenous (metabolic) or exogenous (toxic); in the latter, a distinction is made between still active or progressive brain diseases on the one hand and non-progressive brain diseases (3, 5, 7, 10) on the other (Figure 7).

The causes of **extracerebral seizures** (Table 3) alter brain metabolism and therefore the electrophysiological activity of the brain. The whole brain is affected and primary generalized seizures are triggered (5–7, 11). However, in the case of damage to the brain due to metabolic products (portosystemic shunt) or a severe hypoglycemia, brain lesions can arise which can then cause focal seizures.

Structural changes in the brain (Table 4) can give rise to partial or primary generalized seizures (3, 5, 7, 10, 11), depending on the type of disorder – focal, multifocal, or diffuse.

Epilepsies

Only seizures that have their primary origin in the brain and do not originate in an active or progressive brain disease are considered to be epilepsy or belong to epilepsies which are chronically recurrent (3, 7, 10, 13). Epilepsy can be divided on the basis of etiology into two (5, 7, 10, 11) or three (17) groups: idiopathic (primary, true), symptomatic (acquired, secondary), and cryptogenic (Figure 7). Since this classification is not always adhered to, confusion can arise. For example, recurring seizures of extracerebral etiology are in part classified as epilepsy (6), which makes little sense from the perspective of treatment and prognosis. Progressive brain diseases are also not always clearly distinguished from epilepsy (2, 4, 6), although clinically this distinction is of great importance (5, 7).

An **idiopathic epilepsy** is not preceded or occasioned by any other disease (17). There are no morphological changes in the brain

Table 3
Etiology of extracerebral epileptic seizures

Metabolic disturbances

Hypoxia
congenital and acquired cardiac diseases
respiratory disturbances

Hypoglycemia
excess insulin
increased glucose consumption
insufficient glucose supply

Hepatoencephalopathy
portosystemic shunt
severe liver diseases

Hypocalcemia
hypoparathyroidism
chronic renal diseases

Electrolyte disturbances

Hypothyroidism

Hyperlipemia, etc.

Intoxication

organophosphates, carbamates
chlorinated hydrocarbons
rodenticides, herbicides
heavy metals (esp. lead)
various plants, etc.

Table 4
Etiology of cerebral epileptic seizures caused by primary brain diseases (structural changes in the brain)

Space-occupying lesions

neoplasia
cysts

Cranial traumata

hemorrhages
scars

Meningitis and/or encephalitis

viruses: distemper, FIP, FeLV, etc.
bacteria: various types
fungi: cryptococcosis, etc.
protozoa: toxoplasmosis

Hydrocephalus

acquired
congenital

Malformations

Vascular disorders

Degenerative changes

Storage diseases

Pre-, peri- and postnatal brain lesions

and there is no known or suspected etiology, except for a possible genetic disposition (7, 18) that leads to a functional imbalance between inhibition and excitation. This form of epilepsy manifests itself in synchronous, paroxysmal discharges in both hemispheres. The resulting seizures are generalized and symmetrical from the outset. The epileptic seizures themselves are the only clinical sign, with the affected animal being completely normal between attacks. Neither the history, the description of the seizure, the neurological examination, the analysis of the cerebrospinal fluid, the EEG, nor any imaging technique indicates a morphological change in the brain.

Idiopathic epilepsy occurs most frequently in species with a low seizure threshold, as in man and dogs (5). Almost all canine breeds are affected, including mongrels. In the literature, the prevalence ranges between 0.5% and 5.7% (3, 5, 16, 18), increasing considerably with increased inbreeding (4, 18, 19). The high incidence in certain breeds is an indication that the disease is of genetic origin or at least that there is a genetically determined predisposition (2, 5, 7, 14, 16, 18, 19). For several breeds the genetic disposition has been proven (7, 14, 16, 18, 19). It is unlikely that there is a uniform mode of inheritance (18), since the appearance of the seizure varies too greatly among breeds (5). It must be assumed that different genes or gene complexes with variable penetrance are responsible (18). For Golden and Labrador Retrievers, a multi-factorial, autosomal recessive mode of inheritance has been demonstrated (14, 16). In the literature, idiopathic epilepsy is described as occurring in 40–80% of epileptic dogs (5, 11); the prevalence is much lower in cats (3, 5, 7, 11).

Symptomatic epilepsy originates in a congenital or acquired brain disorder that is no longer active but leaves the brain in a seizure-prone state (7, 13, 18). Here the seizures are also the sole, or predominant, symptom. Since focal lesions frequently occur in the brain, focal seizures can also occur and can generalize more or less quickly.

The term **cryptogenic epilepsy** is employed when it can be assumed from the seizure event (a partial onset) that there must be a focus of discharge – i.e., a structural change in the brain. None of the clinical procedures employed, however, can reveal such a focus and the cause of the seizure remains undetermined (17). The

presence of partial and secondary generalized seizures, together with negative clinical and neurological findings, has been described for Golden and Labrador Retrievers and has been classified as idiopathic epilepsy (14, 16). An epileptic focus in the motor cerebral cortex is suspected (14), but so far no neuropathological investigations have been carried out. The origin might be embryonic migration defects of genetic origin (20, 21), but so far there has been only one report of microdysgenesis in dogs (22).

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