

# IDIOPATHIC EPILEPSY

## (SEIZURE DISORDER OF UNKNOWN CAUSE)

### BASICS

#### OVERVIEW

- “Idiopathic” is the medical term for a disease or disorder of unknown cause; “epilepsy” is a brain disorder, in which the animal has sudden, recurring attacks, with or without loss of consciousness
- “Idiopathic epilepsy” is a brain disorder characterized by recurrent seizures in the absence of structural brain lesion; it is age-related and assumed to have a genetic basis

#### GENETICS

- Dogs—genetic in many breeds; familial (runs in certain families or lines of animals) susceptibility reported for the beagle, keeshond, Belgian Tervuren, golden retriever, Labrador retriever, vizsla and Shetland sheepdog.
- Polygenic recessive mode of inheritance suggested in the Bernese mountain dog and Labrador retriever; autosomal recessive trait proposed in the vizsla and Irish wolfhound; partially penetrant autosomal recessive trait in the English springer spaniel; genetic cause suspected in the Finnish spitz

#### SIGNALMENT/DESCRIPTION of ANIMAL

##### *Species*

- Dogs and rarely cats

##### *Breed Predispositions*

- Beagles, all shepherds (German shepherd dog, Australian shepherd, Belgian Tervuren), boxers, cocker spaniels, collies, border collies, dachshunds, golden retrievers, Irish setters, Irish wolfhound, keeshonden, Labrador retrievers, poodles (all sizes), St. Bernards, Shetland sheepdogs, Siberian huskies, English springer spaniels, Welsh corgis; wire fox terriers

##### *Mean Age and Range*

- Range—6 months to 5 years of age
- Prevalence—10 months to 3 years of age

##### *Predominant Sex*

- Males are more likely to have idiopathic epilepsy than females in the Bernese mountain dog

#### SIGNS/OBSERVED CHANGES in the ANIMAL

- Seizures may be generalized from onset, or have a short aura (focal onset) with rapid generalization of seizure activity; an “aura” is a sensation that precedes a seizure—for example, the animal appears frightened, dazed, seeks attention, or hides
- Presence of an aura is frequent, preceding the generalized seizure activity
- Seizures are mainly focal (that is, involve localized areas of the brain) in the Finnish spitz
- Seizures—most occur while the patient is resting or asleep; often at night or in early morning; frequency tends to increase if left untreated; affected animal falls on its side, becomes stiff, chomps its jaw, salivates profusely, urinates, defecates, vocalizes, and paddles with all four limbs in varying combinations; seizure activity is of short duration (30 to 90 seconds)
- Behavior following the seizure (known as “post-ictal behavior”)—periods of confusion and disorientation; aimless wandering, compulsive behavior, blindness, pacing; frequent increased thirst (known as “polydipsia”) and increased appetite (known as “polyphagia”); recovery immediate or may take up to 24 hours following the seizure
- Dogs with established epilepsy may have cluster seizures at regular intervals of 1 to 4 weeks; particularly evident in large-breed dogs
- No asymmetry in movements should be observed during seizure, such as twitching more pronounced on one side, limb contractions on one side, circling just before or after the seizure
- Physical examination findings generally are normal; patients usually have recovered by time of presentation to the veterinarian

#### CAUSES

- Unknown cause (idiopathic)
- Genetic in some breeds

#### RISK FACTORS

- Known epilepsy in the parents

### TREATMENT

## HEALTH CARE

- Initiate treatment at the second generalized seizure, or if sudden (acute) cluster seizures or sudden (acute) repeated or prolonged seizure activity (known as “status epilepticus”) occur
- Inpatient—seizure disorder requires constant monitoring; cluster seizures (more than 1 seizure/24 hours) repeated or prolonged seizure activity (status epilepticus); treat early and aggressively
- Outpatient—recurrence of isolated seizures
- Other treatments: acupuncture, vagal nerve stimulation, transcranial magnetic motor stimulation

## ACTIVITY

- Avoid swimming, to prevent drowning

## DIET

- Most dogs on long-term (chronic) medications to control seizures (known as “antiepileptic drugs” or “anticonvulsants”) become overweight; monitor weight closely; add a weight-reducing program as necessary
- Potassium bromide (KBr) treatment to control seizures—patients should have steady levels of salt in their diets to maintain therapeutic levels of KBr in the serum; an increase in salt causes an increase in bromide excretion preferentially over chloride, with subsequent decreased serum KBr levels; alternatively, a decreased salt content leads to increased KBr serum levels
- If the epileptic dog treated with potassium bromide (KBr) requires a diet change, take into consideration salt content difference
- Avoid salty treats in dogs treated with potassium bromide (KBr)

## MEDICATIONS

Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive.

### ***Phenobarbital and Potassium Bromide (KBr)***

- Phenobarbital requires 12 to 15 days of treatment to reach steady levels in the serum; potassium bromide (KBr) requires 3 to 4 months of treatment to reach steady levels in the serum and levels vary with salt concentration in diet; in dogs predisposed to epilepsy that is not responsive to medical treatment, both drugs may be initiated at once, in which case, the combine treatment may produce a beneficial and synergistic effect
- Phenobarbital—traditional first-line drug; evaluate serum levels 12 to 15 days after onset of treatment and after changes in dosage; evaluate levels again 4 weeks after initiation of treatment; increase dosage if needed and recheck levels every two weeks until optimal therapeutic range is reached
- Potassium bromide (KBr)—alternative first-line drug; may be added to treatment for patients started on phenobarbital that continue to have seizures at a frequency of more than one every 8 to 12 weeks

### ***Diazepam***

- To treat ongoing seizures; dogs with cluster seizures or repeated or prolonged seizure activity (status epilepticus)
- Inpatient treatment—administer diazepam intravenously
- Reinstate medications administered by mouth (oral medication) as soon as possible; the oral dosage of phenobarbital and/or potassium bromide (KBr) may be increased as directed by your pet’s veterinarian, if the serum drug levels before emergency treatment were inadequate
- Outpatient treatment—for dogs known to have cluster seizures, as directed by your pet’s veterinarian

### ***Other Drugs***

- With the use of multiple drugs (known as “polypharmacy”) to control seizures, initiate add-on medications gradually to avoid sedation
- Levetiracetam or gabapentin; both drugs are well tolerated, safe to add to phenobarbital and potassium bromide (KBr) and have generic formulation available
- Zonisamide; well tolerated; safe to add to phenobarbital and potassium bromide (KBr); high cost; not available in Canada
- Felbamate; not readily available in Canada
- Clorazepate; clonazepam

## FOLLOW-UP CARE

### **PATIENT MONITORING**

- Serum drug levels—essential to monitor therapeutic levels of drugs in the blood
- Phenobarbital—measure 2 and 4 weeks after initiating therapy; adjust oral dose as needed; repeat until the optimal serum levels are reached; with long-term (chronic) administration of phenobarbital, monitor blood work (complete blood count [CBC], serum chemistry profile, and drug levels) every 6 to 12 months to evaluate potential side effects and serum levels of the drugs
- Potassium bromide (KBr)—elimination rate depends on concentration of salt in the food; measure serum levels (along with phenobarbital levels) 4 to 6 weeks after initiating treatment
- Carefully monitor older dogs with kidney insufficiency that are on potassium bromide (KBr) treatment

- If the epileptic dog treated with potassium bromide (KBr) requires a diet change, take into consideration salt content difference and monitor accordingly

#### **PREVENTIONS AND AVOIDANCE**

- Abrupt discontinuation of medication(s) to control seizures may precipitate seizures
- Avoid salty treats in dogs treated with potassium bromide (KBr)

#### **POSSIBLE COMPLICATIONS**

- Phenobarbital-induced high serum alkaline phosphatase (“alkaline phosphatase” is a normal enzyme found in several types of cells, including liver cells; increased levels of alkaline phosphatase may indicate abnormal liver function)—occurs frequently; may be an early sign of liver toxicity, but is of less concern if another liver enzyme (alanine aminotransferase [ALT]) on the blood work is within the normal range
- Phenobarbital-induced liver toxicity—occurs after long-term (chronic) treatment with serum phenobarbital levels in the middle to upper therapeutic range; may be subtle in onset; the only biochemical abnormality may be a decrease in albumin (a protein in the blood, that is produced by the liver)
- Higher incidence of inflammation of the pancreas (known as “pancreatitis”) in patients treated with phenobarbital and/or potassium bromide (KBr); once pancreatitis develops, recurrence is frequent
- Phenobarbital: rare decreased production of blood cells by the bone marrow (known as “bone-marrow suppression”) with severe low neutrophil count (neutrophils are a specific type of white-blood cell that fight infection; low neutrophil count is known as “neutropenia”) and generalized bacterial infection (known as “sepsis”) may develop early in the course of treatment; if occurs, discontinue drug as directed by your pet’s veterinarian
- Unexpected hyperexcitability may result with phenobarbital treatment; if occurs, discontinue drug as directed by your pet’s veterinarian
- Potassium bromide (KBr)—patient may be unsteady while managing stairs

#### **EXPECTED COURSE AND PROGNOSIS**

- Treatment for life
- Some dogs are well controlled with the same drug and dosage for years; others remain poorly controlled despite the use of multiple medications (polypharmacy)
- Medication(s) to control seizures (antiepileptic treatment)—decreases frequency, severity, and length of seizures; perfect control rarely achieved
- In many young, large-breed dogs, seizures may continue despite adequate treatment
- Lack of response to treatment may develop
- Patient may develop repeated or prolonged seizure activity (status epilepticus) and die

#### **KEY POINTS**

- Animals usually do not die after a seizure; however, severe cluster seizures and repeated or prolonged seizure activity (status epilepticus) are life-threatening emergencies requiring immediate veterinary medical attention
- Prevent the patient from injuring itself on surrounding objects during a seizure
- Keep a calendar of the seizures noting date, time, length and severity of the seizures, as an objective way to assess response to treatment
- Once treatment is instituted, the patient will require medication for life in most cases

### **(LOW LEVELS OF THYROID HORMONE)**

#### **BASICS**

##### **OVERVIEW**

- Clinical condition that results from inadequate production and release of thyroid hormone by the thyroid gland
- Characterized by a generalized decrease in metabolism

##### **GENETICS**

- No known genetic basis for the inheritance of primary hypothyroidism in dogs
- Familial (runs in certain families or lines of animals) inflammation of the thyroid gland characterized by the presence of lymphocytes (condition known as “lymphocytic thyroiditis”) has been reported in individual colonies of borzois, beagles, and Great Danes; “lymphocytes” are a type of white-blood cell that are formed in lymphatic tissues throughout the body; lymphocytes are involved in the immune process

##### **SIGNALMENT/DESCRIPTION of ANIMAL**

###### ***Species***

- Dogs and rarely cats

###### ***Breed Predislection***

- Primary acquired (condition that develops sometime later in life/after birth) hypothyroidism is more common in medium- to large-sized dogs
- Breeds reported to have increased likelihood of developing primary acquired hypothyroidism as compared to other dog breeds include the golden retriever, Doberman pinscher, Irish setter, Great Dane, Airedale terrier, Old English sheepdog, dachshund, miniature schnauzer, cocker spaniel, poodle, and boxer

#### **Mean Age and Range**

- Most common in middle-aged dogs (4 to 10 years of age)

#### **Predominant Sex**

- No definitive predominant sex has been identified in affected dogs; however, castrated male dogs and spayed female dogs appear to be at increased risk of developing hypothyroidism

#### **SIGNS/OBSERVED CHANGES in the ANIMAL**

- Most common signs—sluggishness (lethargy); inactivity; mental dullness; weight gain; hair loss or excessive shedding; lack of hair regrowth following clipping; dry or lusterless hair coat; excessive scaling (accumulations of surface skin cells, such as seen in dandruff); darkened skin (known as “hyperpigmentation”); recurrent skin infections; and cold intolerance
- Uncommon signs—generalized weakness, incoordination, head tilt, facial paralysis, seizures, and infertility
- Clinical signs develop slowly and are progressive

#### **Dogs**

##### *Skin Abnormalities—Very Common*

- Symmetrical loss of hair on both sides of the trunk (known as “bilaterally symmetrical truncal alopecia”) that spares the head and extremities—common
- Hair loss (known as “alopecia”) is usually non-itchy, unless a secondary bacterial infection of the skin (known as a “secondary pyoderma”) or other itchy inflammation of the skin (known as “pruritic dermatitis”) also is present
- Hairs are removed from the hair follicles easily
- Hair loss (alopecia) occurs in areas of friction
- Hair loss (alopecia) often initially involves the flank area, base of the ears, tail (rat tail) and friction areas (such as under the front legs, lower chest, abdomen and neck, and under the collar)
- Early in the disease course, hair loss (alopecia) may be in multiple locations and not symmetrical; lesions may have irregular margins
- Darkened skin (hyperpigmentation) and increased thickness of the skin are common, particularly in friction areas
- Excessive scaling of the skin (known as “seborrhea”)—common; can be generalized, in multiple locations, or localized
- Dull, dry coat
- Secondary superficial bacterial infection of the skin (pyoderma) occurs occasionally; deep pyoderma is less common
- Accumulation of mucopolysaccharides in the skin can lead to nonpitting edema (known as “myxedema”), particularly in the facial area; this produces the classic “tragic” expression associated with hypothyroidism
- Inflammation of the outer ear (known as “otitis externa”) may be seen

##### *General/Metabolic Abnormalities—Very Common*

- Sluggishness (lethargy), mental dullness
- Weight gain
- Mild decrease in body temperature (low body temperature known as “hypothermia”)

##### *Reproductive Abnormalities*

- Infertility and prolonged interval between heat or estrus cycles (known as “anestrus”) in females
- Inappropriate white discharge that looks like milk from the nipples (known as “galactorrhea”) in sexually intact bitches; a “bitch” is a female dog

##### *Abnormalities Involving the Nervous System and/or Muscular System—Uncommon*

- Generalized weakness; dogs may have a stiff, stilted gait
- Other nervous system findings may include decreased reflexes (known as “hyporeflexia”), head tilt, facial paralysis, and a wobbly, incoordinated or “drunken” appearing gait or movement (known as “ataxia”)
- A secondary muscle disease (known as a “myopathy”) usually is present in dogs with hypothyroid-related disease of many nerves (known as a “polyneuropathy”)
- Some hypothyroid dogs develop generalized muscle disease (myopathy) without coexistent nervous system involvement; these dogs present for generalized weakness
- Seizures have been reported rarely in hypothyroid dogs with marked increase in levels of lipids (a group of compounds that contain fats or oils) in the blood (known as “hyperlipidemia”)
- Paralysis of the larynx or voice box (known as “laryngeal paralysis”); enlargement of the esophagus (the tube running from the throat to the stomach; condition known as “megaesophagus”); and Horner’s syndrome (condition in which one pupil is small or constricted, the eyelid droops, and the eyeball is withdrawn into the socket) have been associated with hypothyroidism, but it is unknown if hypothyroidism causes these signs

##### *Abnormalities of the Eyes*

- Lipid (compound that contains fats or oils) deposits in the cornea; the “cornea” is the clear outer layer of the front of the eye
- Lipemia retinalis (condition in which the blood vessels in the back of the eye [retina] appear pink rather than normal red; pink color is caused by whitish lipids mixing with the blood)

## **Cats**

- Rare
- Unkempt appearance; matting of hair; non-itchy, excessively dry scaling of the skin (known as “seborrhea sicca”); hair loss of the ears (known as “pinnal alopecia”)
- Sluggishness (lethargy)
- Obesity

## **Congenital (Present at Birth) Hypothyroidism—Cretinism**

- Mental dullness/retardation, sluggishness (lethargy), inactivity
- Disproportionate dwarfism (large, broad head with short neck and limbs); shortened lower jaw (mandible); protruding tongue; delayed eruption of deciduous or baby teeth
- Constipation/obstipation—particularly in cats
- Low body temperature (hypothermia)
- Retention of puppy coat, progressive hair loss on the sides of the trunk (truncal alopecia) in dogs

## **CAUSES**

- Inflammation of the thyroid gland characterized by the presence of lymphocytes (lymphocytic thyroiditis)
- Wasting away or decrease in size of the cells in the thyroid for unknown cause (so called “idiopathic thyroid atrophy”)
- Congenital (present at birth) thyroid disease
- Disease of the pituitary gland; the “pituitary gland” is the master gland of the body—it is located at the base of the brain; it controls many other glands in the body
- Dietary iodine deficiency; iodine is necessary for production of thyroid hormone
- Cancer
- Secondary to medication or treatment (known as “iatrogenic disease”)

## **RISK FACTORS**

- Neutering may slightly increase risk of developing primary hypothyroidism
- Surgical removal of the thyroid (known as “thyroidectomy”)

## **TREATMENT**

### **HEALTH CARE**

- Outpatient

### **DIET**

- Reduced-fat diet until body weight is satisfactory and serum thyroid hormone (T<sub>4</sub>) concentrations are normal

## **MEDICATIONS**

Medications presented in this section are intended to provide general information about possible treatment. The treatment for a particular condition may evolve as medical advances are made; therefore, the medications should not be considered as all inclusive.

- Levothyroxine is the treatment of choice; it is a thyroid (T<sub>4</sub>) replacement hormone; also known as “L-thyroxine”
- Adjust dosage on the basis of serum thyroid hormone (T<sub>4</sub>) concentration from blood obtained after giving the thyroid replacement medication and clinical response to therapy; initially, use a veterinary name-brand product
- If the patient responds to therapy, once-daily therapy can be tried; however, some patients require medication every 12 hours
- Different brands of L-thyroxine frequently have different absorption from the intestines; the dosage may change if the brand is changed
- Therapy with synthetic liothyronine (T<sub>3</sub>) is not indicated or recommended in the vast majority of hypothyroid dogs
- Liothyronine (T<sub>3</sub>) therapy is indicated only if a dog fails to achieve a normal serum T<sub>4</sub> concentration following appropriate therapy with at least two different brands of L-thyroxine, which probably indicates a lack of intestinal absorption—liothyronine is absorbed almost completely from the gut

## **FOLLOW-UP CARE**

### **PATIENT MONITORING**

- Check serum thyroid hormone (T<sub>4</sub>) levels after 1 month of therapy
- Determine peak serum thyroid hormone (T<sub>4</sub>) concentrations 4 to 8 hours after L-thyroxine administration
- Serum thyroid hormone (T<sub>4</sub>) concentrations should be in the normal range or mildly increased; keep peak serum T<sub>4</sub> concentrations at or below 5µg/dl (64 nmol/L)
- Patients on once-daily therapy that do not respond to therapy and have a normal or high peak T<sub>4</sub> concentration should have their pre-pill T<sub>4</sub> concentration (trough T<sub>4</sub>) assessed; if the trough T<sub>4</sub> concentration is low, twice-daily therapy is indicated

- Following initial normalization of serum T<sub>4</sub> values, check them yearly, or sooner if clinical signs of hypothyroidism or thyrotoxicosis (in which animal has signs of excessive thyroid hormone in the body; signs may include nervousness, weight loss, hyperactivity, and increased appetite) develop
- Recheck serum thyroid hormone (T<sub>4</sub>) concentrations 1 month after any change in dosage or brand of L-thyroxine being administered

#### **PREVENTIONS AND AVOIDANCE**

- Proper treatment prevents disease recurrence

#### **POSSIBLE COMPLICATIONS**

- Prolonged administration of a high dosage of L-thyroxine can cause excessive levels of thyroid hormone (known as “iatrogenic hyperthyroidism”)
- Clinical signs of thyrotoxicosis (excessive thyroid hormone in the body) include panting; increased appetite (known as “polyphagia”); weight loss; increased urination (known as “polyuria”) and increased thirst (known as “polydipsia”); anxiety; and diarrhea

#### **EXPECTED COURSE AND PROGNOSIS**

- Dogs treated for primary hypothyroidism have an excellent prognosis; life expectancy is normal
- Mental alertness and activity levels usually increase within 1 to 2 weeks after initiation of therapy
- Skin abnormalities slowly resolve over 1 to 4 months, as do nervous system deficits that are secondary to hypothyroidism
- Reproductive abnormalities resolve more slowly
- If significant clinical improvement does not occur within 3 months of initiation of therapy, with serum T<sub>4</sub> levels in the normal range, the diagnosis of hypothyroidism may be incorrect
- Patients with hypothyroidism may have a poor prognosis, if condition is secondary to a tumor or destructive process affecting the pituitary gland or hypothalamus

#### **KEY POINTS**

- Dogs with primary hypothyroidism respond well to treatment with oral synthetic thyroid hormone (levothyroxine or L-thyroxine)
- The appropriate dosage for L-thyroxine varies between individuals because of differences in gastrointestinal absorption of the medication and hormone metabolism
- Treatment is lifelong
- Most clinical and laboratory abnormalities resolve over a few weeks to a few months
- Occasionally, skin abnormalities worsen transiently during the first month of therapy

