

# VACUOLAR HEPATOPATHY

## (DISORDER CHARACTERIZED BY THE PRESENCE OF CAVITIES [VACUOLES] WITHIN LIVER CELLS)

### BASICS

#### OVERVIEW

- “Vacuolar” refers to vacuoles; “vacuoles” are small cavities within cells—the cavities are surrounded by a membrane and they contain various substances (such as fluids, storage products, or waste products)
- “Hepatopathy” is the medical term for a disorder or disease of the liver
- Vacuolar hepatopathy—reversible change in the liver cells of dogs; associated with accumulation of glycogen in clear cavities within liver cells; “glycogen” is the material that serves as the carbohydrate storage or reserve of the body, which is broken down readily into glucose (sugar)
- Development of the clear cavities (vacuoles) containing glycogen often is secondary to steroid treatment; increased levels of steroids in the body (either produced by the adrenal glands [known as “spontaneous hyperadrenocorticism” or “spontaneous Cushing’s disease”] or through administration of steroid-containing medications [known as “iatrogenic hyperadrenocorticism” or “iatrogenic Cushing’s disease”]); enlargement of the adrenal glands (known as “adrenal hyperplasia”) leading to release of adrenal sex hormones [especially progesterone]; or long-term (chronic) illness of other systems
- Condition leads to high alkaline phosphatase (ALP) activity as seen on blood tests, often without signs of liver insufficiency; “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
- In some animals, vacuolar hepatopathy is associated with the presence of lipids (compounds that contain fats or oils) in the clear cavities—may occur in animals with high levels of lipids in their blood for unknown reason (so called “idiopathic hyperlipidemia”); lipid with glycogen—diabetes mellitus (“sugar diabetes”)

#### SIGNALMENT/DESCRIPTION of ANIMAL

##### **Species**

- Dogs; rarely cats

##### **Breed Predispositions**

- Breeds susceptible to increased levels of steroids produced by the adrenal glands (hyperadrenocorticism or Cushing’s disease), such as the miniature poodle, dachshund, boxer, Boston terrier
- Enlargement of the adrenal glands with increased levels of adrenal sex hormones (sex-hormone adrenal hyperplasia) and increased levels of lipids (compounds that contain fats or oils) in the blood (hyperlipidemia)—Scottish terrier
- Increased levels of lipids (compounds that contain fats or oils) in the blood (hyperlipidemia)—miniature schnauzer

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

- Middle-aged to old dogs—more than 75% of dogs with increased levels of steroids produced by the adrenal glands (spontaneous hyperadrenocorticism) are older than 9 years of age; long-term (chronic) inflammation or tumors
- Dogs of any age—vacuolar hepatopathy subsequent to steroid administration (known as “iatrogenic vacuolar hepatopathy”)
- Young dogs or cats—genetic increased levels of lipids (compounds that contain fats or oils) in the blood (hyperlipidemia)
- Puppies or kittens—disease in which fats and lipids (compounds that contain fats or oils) accumulate in the liver (known as “juvenile hepatic lipidosis”)

#### SIGNS/OBSERVED CHANGES in the ANIMAL

- Signs often related to effects of steroids or other generalized (systemic) illnesses causing stress
- Rarely, signs of liver disease or failure; however, liver failure can occur with severe, long-term (chronic) vacuolar hepatopathy
- Signs related to high levels of steroids—increased urination (known as “polyuria”) and increased thirst (known as “polydipsia”); increased appetite (known as “polyphagia”); hair loss (known as “alopecia”); abdominal distention; muscle weakness; panting; sluggishness (lethargy); fragile skin; bruising
- Enlargement of the adrenal glands with increased levels of adrenal sex hormones (sex-hormone adrenal hyperplasia)—similar signs to those of high levels of steroids, but may be fewer and less severe; hair loss (alopecia) with darkened skin (known as “hyperpigmentation”) is least common; some dogs have no signs and only finding is chronically high 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
- Enlarged liver (known as “hepatomegaly”)
- Other signs relate to the underlying disease

#### CAUSES

- Steroid administration
- Increased levels of steroids produced by the adrenal glands (hyperadrenocorticism or Cushing’s disease)

- Enlargement of the adrenal glands with increased levels of adrenal sex hormones (sex-hormone adrenal hyperplasia)—over-production of various steroid hormones (especially progesterone)
- Generalized (systemic) diseases associated with stress—examples include severe dental disease; inflammatory bowel disease (IBD); long-term (chronic) inflammation of the pancreas (known as “pancreatitis”); generalized cancer (especially lymphoma; “lymphoma” is a type of cancer that develops from lymphoid tissue, including lymphocytes, a type of white-blood cell formed in lymphatic tissues throughout the body); long-term (chronic) infections (urinary tract, skin); low levels of thyroid hormone (known as “hypothyroidism”); errors of lipid (compound that contains fats or oils) metabolism, leading to lipid or glycogen accumulation

#### **RISK FACTORS**

- Treatment with steroid-containing medications
- Breeds at risk for increased levels of steroids produced by the adrenal glands (hyperadrenocorticism or Cushing’s disease), such as poodles, dachshunds, Boston terriers, and beagles
- Breeds at risk for increased levels of lipids (compounds that contain fats or oils) in the blood (hyperlipidemia), such as miniature schnauzers, Shetland sheepdogs, beagles

### **TREATMENT**

#### **HEALTH CARE**

- Outpatient—common for underlying disease

#### **ACTIVITY**

- Normal

#### **DIET**

- Fat restriction for cases with increased levels of lipids (compounds that contain fats or oils) in the blood (hyperlipidemia) or inflammation of the pancreas (pancreatitis)
- Cautious calorie restriction for obese animals, as directed by your pet’s veterinarian

#### **SURGERY**

- Depends on underlying conditions
- Adrenal gland masses may be removed surgically in some patients
- Pituitary gland masses may be removed surgically, but only by surgeons experienced in the procedure; pituitary gland masses may be better treated with radiation

### **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.

- Depend on the underlying disease
- Increased production of steroids by the adrenal glands secondary to stimulation from the pituitary gland (known as “pituitary-dependent hyperadrenocorticism”) or enlargement of the adrenal glands with increased levels of adrenal sex hormones (sex-hormone adrenal hyperplasia)—usually treated medically once diagnosis confirmed; treatment may include op<sup>3</sup>-DDD (Lysodren®), ketoconazole, or trilostane; 1-deprenyl usually ineffective; op<sup>3</sup>DDD (Lysodren®) preferred for sex-hormone adrenal hyperplasia; melatonin appears to be ineffective for treating sex-hormone adrenal hyperplasia
- Management of generalized (systemic) inflammatory disorders that necessitate the use of medications to decrease the immune response (known as “immunosuppressive drugs”) or medications to decrease inflammation (known as “anti-inflammatory drugs”)—use multiple medications to avoid or minimize steroid exposure in patients with signs of vacuolar hepatopathy; medications selected may include metronidazole (for treatment of inflammatory bowel disease); chemotherapeutic drugs used to decrease the immune response (such as azathioprine, chlorambucil, cyclophosphamide); and other immunosuppressive drugs (such as mycophenolate, cyclosporine)
- Cancer—chemotherapy or radiation, as appropriate
- Dental disease—antibiotics and dentistry
- Infection/inflammation of the kidney (known as “pyelonephritis”); long-term (chronic) inflammation of the skin (known as “dermatitis”); or other infectious disorders—long-term (chronic) antibiotic treatment, based on bacterial culture and sensitivity tests; other appropriate medications
- Low levels of thyroid hormone (hypothyroidism)—supplemental thyroid hormone

### **FOLLOW-UP CARE**

### **PATIENT MONITORING**

- Enlarged liver (hepatomegaly)—feeling the abdomen and liver during physical examination (known as “abdominal palpation”); X-rays or ultrasound examination; blood work (serum biochemical profile to evaluate improvement of liver enzyme levels)
- Adrenal gland function—**ACTH**-stimulation test, to determine response of the adrenal gland
- Cancer—physical examination and diagnostic imaging (X-rays, ultrasound examination, computed tomography [CT or CAT scan], magnetic resonance imaging [MRI])
- Control of infection—repeat bacterial cultures
- Increased levels of lipids (compounds that contain fats or oils) in the blood (hyperlipidemia)—assess presence of lipids visible in the blood (known as “gross lipemia”); measure triglycerides and cholesterol levels

### **PREVENTIONS AND AVOIDANCE**

- Limit steroids for treatment of confirmed conditions that require steroid therapy
- When steroids are necessary, use alternate-day therapy (if possible) with prednisone; titrate steroids to lowest effective dose (as directed by your pet’s veterinarian)

### **POSSIBLE COMPLICATIONS**

- Numerous complications related to the effects of steroids and associated conditions are possible; discuss possible complications with your pet’s veterinarian

### **EXPECTED COURSE AND PROGNOSIS**

- Most patients do not have signs of liver disease, despite high alkaline phosphatase; however, progressive liver disease (hepatopathy) leading to widespread (diffuse) nodule formation and liver failure may occur in long-term (chronic) vacuolar hepatopathy in patients only showing long-term (chronic) markedly high alkaline phosphatase levels; “alkaline phosphatase” is a normal enzyme found in several types of cells, including liver cells
- Blood work and liver abnormalities associated with vacuolar hepatopathy are completely reversible before liver nodules form

### **KEY POINTS**

- Vacuolar hepatopathy—reversible change in the liver cells of dogs; associated with accumulation of glycogen in clear cavities within liver cells; “glycogen” is the material that serves as the carbohydrate storage or reserve of the body, which is broken down readily into glucose (sugar)
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