HOUSE & JACKSON
VETERINARY HOSPITAL

CUSHINGS SYNDROME

What is Cushing's Syndrome?

Cushing's Syndrome is also known as hyperadrenocorticism (HAC). It is a disorder caused by excessive production of steroids by the adrenal glands; "spontaneous" denotes lack of apparent cause.

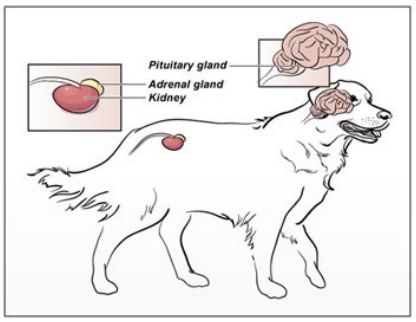
Spontaneous hyperadrenocorticism is a hormonal disorder; it can involve problems in the pituitary gland (the "master gland" of the body), in which case the pituitary gland "directs" the adrenal glands to produce excessive amounts of steroids—this type is known as "pituitary-dependent hyperadrenocorticism" or PDH, or it can involve problems in the adrenal gland itself (benign tumours or cancer), in which the adrenal glands produce excessive amounts of steroids on "their own" and not under the control of the pituitary gland.

"Iatrogenic" hyperadrenocorticism or Cushing's syndrome results from the use of medications containing steroids; the medications can be given by mouth or by injection, or can be applied topically to the skin, ears, or eyes; the signs of iatrogenic Cushing's syndrome usually are related to the dose of steroids and length of treatment, but some dogs are very sensitive to steroids and may show signs with normal doses of steroids or relatively short length of treatment; "iatrogenic" refers to changes induced by the medication itself, the changes generally are unfavourable.

In both types of hyperadrenocorticism, clinical signs are due to deleterious effects of elevated circulating steroid concentrations on multiple organ systems.

How Common is Cushing's Syndrome?

It is common in the following breeds of dog; Poodles, Dachshunds, Boston Terriers, German Shepherd Dogs, and Beagles in comparison to other breeds of dog. There is no increased likelihood for either sex for pituitary-dependent hyperadrenocorticism in dogs; possible increased likelihood that female dogs will have adrenal tumours that produce excessive steroids. Hyperadrenocorticism very rarely can be seen in dogs as young as 1 year of age and is generally a disorder of middle-aged to old dogs; pituitary-dependent.



What are the main causes?

- Pituitary-dependent hyperadrenocorticism—benign tumour (known as a "pituitary adenoma") most common; cancer (known as a "pituitary adenocarcinoma") rare
- Adrenal gland itself (not under control of pituitary gland)—benign tumour (known as "adrenal adenoma") or cancer (known as "adrenal carcinoma")
- Iatrogenic hyperadrenocorticism due to administration of steroid-containing medications

Clinical Signs

- Severity varies greatly, depending on duration and severity of steroid excess
- In some cases, the physical presence of cancer in the pituitary gland (leading to pituitary-dependent hyperadrenocorticism [PDH]) or the adrenal gland itself contributes to signs
- Excessive urination (known as "polyuria") and increased thirst (known as "polydipsia"); increased appetite (known as "polyphagia"); sagging abdomen due to weakened abdominal muscles (known as "pendulous abdomen"); increased panting; enlarged liver (known as "hepatomegaly"); hair loss; darkening of the skin (known as "hyperpigmentation"); thin skin; muscle weakness; obesity; sluggishness (lethargy); loss of muscle mass (known as "muscle atrophy"); "blackheads" (known as "comedones") on the skin; bruising; loss of size or tissue of the testicles (known as "testicular atrophy"); lack of heat cycles in female dogs (known as "anoestrus"); calcium deposits in the skin (known as "calcinosis cutis"); facial nerve paralysis.

Treatment

Healthcare

Dictated by the severity of clinical signs, the pet's overall condition, and any complicating factors (such as diabetes mellitus ["sugar diabetes"], blood clots to the lungs [known as "pulmonary thromboembolism"]).

Activity

No alteration of activity necessary

Diet

Usually no need to alter diet; use appropriate diet if dog also has diabetes mellitus (sugar diabetes)

Surgery

Surgical removal of the pituitary gland (known as "hypophysectomy")—described in veterinary literature, but generally not available in the United States

Surgical removal of both adrenal glands (known as "bilateral adrenalectomy") not used for treatment of pituitary-dependent hyperadrenocorticism in dogs

Surgery is the treatment of choice in dogs with adrenal adenomas (benign tumors of the adrenal gland) and small carcinomas (cancer of the adrenal gland), unless the pet is a poor surgical risk; appropriate personnel and facilities are required as this is a technically demanding surgery and intensive postoperative management is required.

Depending on status of the pet, medical control of hyperadrenocorticism may be desirable prior to surgery, if possible.

What medications are available?

Trilostane

Trilostane (Vectoryl) is the treatment of choice for canine pituitary and adrenal dependent hyperadrenocorticism. Trilostane can suppress aldosterone (another hormone produced by the adrenal gland; involved in sodium and potassium regulation in the body) secretion, causing a sudden change in sodium and potassium regulation (known as an "Addisonian crisis"), which requires immediate medical treatment; fortunately, the low levels of aldosterone generally resolve within 48–72 hours of discontinuation of drug administration, but low levels of weeks' to months' duration or even permanently have been reported.

Can be used to treat adrenal tumours and will control clinical signs, at least temporarily, but is not the drug of choice; for adrenal tumours, mitotane is the drug of choice, as it is truly chemotherapeutic and may kill tumour cells.

Other Treatment—Radiation Therapy

Radiation therapy is required for dogs with large, benign pituitary tumours (known as "pituitary macro adenomas").

Decreases in secretion of the pituitary hormone (known as ACTH) that directs the adrenal gland to produce steroids, thus decreasing serum steroid concentrations levels, may take several months; meanwhile, control signs of hyperadrenocorticism with previously described drugs.

Possible Complications

- High blood pressure (known as "hypertension")
- Presence of protein in the urine (known as "proteinuria")
- Recurrent infections
- Stones in the urinary tract (known as "urinary calculi") frequently composed of calcium oxalate
- Diabetes mellitus (also known as "sugar diabetes")
- Blood clots in the lungs (known as "pulmonary thromboembolism")
- Nervous system signs secondary to the presence of a large tumour in the pituitary gland (pituitary macro adenoma)

Expected Course & Prognosis

- Periodic bloodwork (such as complete blood count [CBC] and serum biochemistry profile as well as specific tests for adrenal gland function)
- Untreated hyperadrenocorticism—generally a progressive disorder, with a poor prognosis
- Treated pituitary-dependent hyperadrenocorticism—usually a good prognosis; median survival time for a dog with PDH treated with mitotane or trilostane is approximately 2 years; at least 10% survive 4 years; dogs living longer than 6 months tend to die of causes unrelated to HAC
- Dogs with large, benign pituitary tumours (macro adenomas) and nervous system signs—poor-to-grave prognosis; dogs with macro adenomas with no or mild nervous system signs—fair-to-good prognosis with radiation and medical therapy
- Dogs with benign adrenal-gland tumours (adrenal adenomas)—usually a good-to-excellent prognosis; dogs with small adrenal-gland cancers (carcinomas) that have not metastasized have a fair-to-good prognosis
- Dogs with large adrenal-gland cancers (carcinomas) and/or with widespread spread (metastasis)—generally a poor-to-fair prognosis, but impressive responses to high doses of mitotane are seen occasionally
- If using medical therapy, lifelong therapy required
- If adverse reaction trilostane occurs—discontinue drug, give prednisone, and have veterinarian revaluate next day; if no response to prednisone is noted within a few hours of administration, veterinarian should evaluate immediately
- **Perform ACTH- Stimulation blood test at 10 days, 1 months, 3 months and every 6 months, following initial diagnosis and after each dose adjustment.**