

HYPERADRENOCORTICISM OR CUSHING'S DISEASE IN DOGS

(EXCESSIVE LEVELS OF STEROIDS IN THE BODY)

BASICS

OVERVIEW

- “Spontaneous” hyperadrenocorticism (“HAC”) or Cushing’s disease 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 tumors 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 disease 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 disease 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 unfavorable
- In both types of hyperadrenocorticism, clinical signs are due to the deleterious effects of the elevated circulating steroid concentrations on multiple organ systems

SIGNALMENT/DESCRIPTION of ANIMAL

Species

- Dogs

Breed Predispositions

- Poodles, dachshunds, Boston terriers, boxers, and beagles reportedly are at increased risk as compared to other breeds

Predominant Sex

- No increased likelihood for either sex has been identified for pituitary-dependent hyperadrenocorticism (PDH) in dogs; possible increased likelihood that female dogs will have adrenal tumors that produce excessive steroids

Mean Age and Range

- Hyperadrenocorticism (HAC) is generally a disorder of middle-aged to old animals; pituitary-dependent hyperadrenocorticism (PDH) very rarely can be seen in dogs as young as 1 year of age

SIGNS/OBSERVED CHANGES in the ANIMAL

- Severity varies greatly, depending on the 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”); enlarged liver (known as “hepatomegaly”); hair loss; sluggishness (lethargy); muscle weakness; lack of heat cycles in female dogs (known as “anestrus”); obesity; loss of muscle mass (known as “muscle atrophy”); “blackheads” (known as “comedones”) on the skin; increased panting; loss of size or tissue of the testicles (known as “testicular atrophy”); darkening of the skin (known as “hyperpigmentation”); calcium deposits in the skin (known as “calcinosis cutis”); facial nerve paralysis; thin skin; bruising

CAUSES

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

RISK FACTORS

- Poodles, dachshunds, Boston terriers, boxers, and beagles reportedly are at increased risk, as compared to other breeds

TREATMENT

HEALTH CARE

- Dictated by the severity of clinical signs, the patient'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
- Surgical removal of both adrenal glands (known as "bilateral adrenalectomy") not used for treatment of pituitary-dependent hyperadrenocorticism (PDH) 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 patient is a poor surgical risk or the client refuses surgery; appropriate personnel and facilities are required as this is a technically demanding surgery and intensive postoperative management is required
- Depending on patient status, medical control of hyperadrenocorticism (HAC) may be desirable prior to surgery, if possible

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.

Mitotane

- **Mitotane** (also known as "*o,p'*-DDD" or "Lysodren®") remains the drug of choice for medical management of both pituitary-dependent hyperadrenocorticism (PDH) and adrenal tumors in dogs; it selectively destroys the steroid-secreting cells of the adrenal gland
- Inadequate levels of aldosterone (another hormone produced by the adrenal gland; involved in sodium and potassium regulation in the body) are possible secondary to mitotane therapy; if occurs, likely patient will have permanent complete adrenal-gland insufficiency; treatment for inadequate or too low levels of steroids produced by the adrenal glands (known as "hypoadrenocorticism" or "Addison's disease") should be initiated

***l*-Deprenyl**

- ***l*-Deprenyl** (also known as "selegiline hydrochloride" or Anipryl®) may be used as an alternative treatment for pituitary-dependent hyperadrenocorticism (PDH); it decreases secretion of the pituitary hormone (known as "ACTH") that directs the adrenal gland to produce steroids, thus decreasing serum steroid concentrations; not recommended for treatment of PDH in dogs with concurrent illnesses, such as diabetes mellitus
- Effectiveness of the drug in treating PDH is questionable; one study found 20% efficacy and another found it to be ineffective
- Adverse effects (such as lack of appetite [anorexia], sluggishness [lethargy], vomiting and diarrhea) are uncommon and usually mild; disadvantages include the need for lifelong daily administration and the expense of the medication

Ketoconazole

- **Ketoconazole** inhibits enzymes responsible for steroid production; indicated for dogs unable to tolerate mitotane at doses necessary to control hyperadrenocorticism (HAC); may be useful for control of clinical signs in dogs with adrenal tumors; effective in approximately 50% or fewer cases; adverse effects include lack of appetite (anorexia), vomiting, diarrhea, sluggishness (lethargy), and liver disease

Trilostane

- Trilostane (Vetoryl®) is approved for use in Europe and available in the United States by special application to the federal Food and Drug Administration (FDA) for compassionate use license—your pet's veterinarian will need to contact the FDA; efficacy for treatment of pituitary-dependent hyperadrenocorticism (PDH) is high, comparable to mitotane; survival of dogs with PDH is the same for dogs treated with mitotane or trilostane
- 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 to 72 hours of discontinuation of drug administration, but low levels of weeks' to months' duration has been reported
- Can be used to treat adrenal tumors and will control clinical signs, at least temporarily, but is not the drug of choice; for adrenal tumors, mitotane is the drug of choice, as it is truly chemotherapeutic and may kill tumor cells

Other Treatment—Radiation Therapy

- Consider radiation therapy for animals with large, benign pituitary tumors (known as "pituitary macroadenomas")

- 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; control signs of hyperadrenocorticism (HAC) with previously described drugs in the interim

FOLLOW-UP CARE

PATIENT MONITORING

- Response to therapy
- Periodic blood work (such as complete blood count [CBC] and serum biochemistry profile as well as specific tests for adrenal gland function)

EXPECTED COURSE AND PROGNOSIS

- Untreated hyperadrenocorticism (HAC)—generally a progressive disorder, with a poor prognosis
- Treated pituitary-dependent hyperadrenocorticism (PDH)—usually a good prognosis; median survival time for a dog with PDH treated with mitotane or trilostane is approximately 1.9 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 tumors (macroadenomas) and nervous system signs—poor to grave prognosis; dogs with macroadenomas with no or mild nervous system signs—fair to good prognosis with radiation and medical therapy
- Dogs with benign adrenal-gland tumors (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

KEY POINTS

- If using medical therapy, lifelong therapy required
- If adverse reaction to mitotane or trilostane occurs—discontinue drug, give prednisone, and have veterinarian reevaluate next day; if no response to prednisone is noted within a few hours of administration, veterinarian should evaluate immediately

