2023 AAHA Selected Endocrinopathies of Dogs and Cats Guidelines

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ABSTRACT

Canine and feline endocrinopathies reflect an endocrine gland disease or dysfunction with resulting hormonal abnormalities that can variably affect the patient's wellbeing, quality of life, and life expectancy. These guidelines provide consensus recommendations for diagnosis and treatment of four canine and feline endocrinopathies commonly encountered in clinical practice: canine hypothyroidism, canine hypercortisolism (Cushing's syndrome), canine hypoadrenocorticism (Addison's disease), and feline hyperthyroidism. To aid the general practitioner in navigating these common diseases, a stepwise diagnosis and treatment algorithm and relevant background information is provided for managing each of these diseases. The guidelines also describe, in lesser detail, the diagnosis and treatment of three relatively less common endocrinopathies of cats: feline hyperaldosteronism, feline hypothyroidism, and feline hyperadrenocorticism. Additionally, the guidelines present tips on effective veterinary team utilization and client communication when discussing endocrine cases. (*J Am Anim Hosp Assoc* 2023; 59:■–■. DOI 10.5326/JAAHA-MS-7368)

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These guidelines were prepared by a task force of experts convened by the American Animal Hospital Association. This document is intended as a guideline only, not an AAHA standard of care. These guidelines and recommendations should not be construed as dictating an exclusive protocol, course of treatment, or procedure. Variations in practice may be warranted based on the needs of the individual patient, resources, and limitations unique to each individual practice setting. Evidence-guided support for specific recommendations has been cited whenever possible and appropriate. Other recommendations are based on practical clinical experience and a consensus of expert opinion. Further research is needed to document some of these recommendations. Drug approvals and labeling are current at the time of writing but may change over time. Because each case is different, veterinarians must base their decisions on the best available scientific evidence in conjunction with their own knowledge and experience.

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ACTH (adrenocorticotropic hormone); ACTHST (adrenocorticotropic hormone stimulation test); ADH (adrenal-dependent hyperadrenocorticism); ALP (alkaline phosphatase); ALT (alanine aminotransferase); CKD (chronic kidney disease); CS (Cushing's syndrome); DOCP (desoxycorticosterone pivalate); FHT (feline hyperthyroidism); fT4 (free thyroxine); fT4ed (free thyroxine by equilibrium dialysis); HA (hypoadrenocorticism); HAC (hyperadrenocorticism); ^{131}I (radioactive iodine); LDDST (low-dose dexamethasone suppression test); PDH (pituitary-dependent hyperadrenocorticism); PHA (primary hyperaldosteronism); SHT (systemic hypertension); T3 (triiodothyronine); T4 (thyroxine); TSH (thyroid-stimulating hormone); TT4 (total thyroxine concentration); UCCR (urine cortisol-to-creatinine ratio)

Introduction

Veterinary clinicians routinely encounter and are expected to manage various endocrinopathies in their canine and feline patients. Most commonly, these conditions include canine hypothyroidism, canine hypercortisolism (Cushing's syndrome), canine hypoadrenocorticism (Addison's disease), and feline hyperthyroidism (FHT). Canine and feline diabetes mellitus is not discussed in these guidelines but is addressed in previously published guidelines.[1] These endocrinopathies can be overt or have minimal clinical impact, especially in early-stage disease. Diagnosis relies on a recognition of clinical signs or physical examination abnormalities, careful compilation of the patient's history, interpretation of hormone concentration assays, and exclusion of comorbidities that can complicate an accurate diagnosis. Early intervention in endocrinopathy cases avoids the severe syndromes that can impact the patient's quality of life and cause secondary organ damage and mortality. The guidelines are designed to provide practitioners with a practical, stepwise approach to the diagnosis and treatment of the four most common canine and feline endocrinopathies.

The guidelines introduce each endocrinopathy by providing a definition and clinical profile of the disease. In addition to the four principal diseases described in the guidelines, three less common feline endocrinopathies are also discussed: feline hyperaldosteronism, feline hypothyroidism, and feline hyperadrenocorticism. The guidelines are not intended to cover all endocrinopathies that affect dogs and cats, but to provide a foundation for accurate recognition and diagnosis and effective clinical management of the most common endocrine-related morbidities. Practitioners will benefit from consulting the abundant literature to gain additional clinical perspectives on each disease.

The guidelines discuss the four principal endocrinopathies using an innovative, categorical approach to diagnosis based on clinical presentation, as previously described in the *2016 AAFP Guidelines for the Management of Feline Hyperthyroidism*.[2] This approach evaluates the patient's clinical presentation as determined by the attending veterinarian, combined with the patient's medical history as reported by the client. The clinical presentation of each disease is summarized in a table, which also includes the next steps for diagnosis and treatment. Accompanying the table is a more detailed, referenced narrative specific to each disease. The table is a prescriptive, quick-reference tool, whereas the narrative provides useful contextual background for making informed clinical decisions.

The most successful veterinary practices recognize the importance of engaging the owner in the management of a pet's health. The dialog with the client should involve the entire practice team. Accordingly, these guidelines also include a section on practice team and client considerations. When all those involved in the patient's wellbeing are well informed and engaged, better adherence to treatment recommendations and improved case outcomes is expected.

Canine Hypothyroidism

Overview

Hypothyroidism is most commonly an acquired condition of adult dogs characterized by primary failure of the thyroid gland to produce adequate amounts of thyroxine (T4) and triiodothyronine (T3). Pathogenesis commonly involves immune-mediated destruction of functional thyroid tissue (thyroiditis) or idiopathic thyroid atrophy, which may represent end-stage thyroiditis.[3] Well-documented breed associations support a genetic susceptibility, with a selection of commonly affected breeds including English setters, Doberman pinschers, Rhodesian ridgebacks, and golden and Labrador retrievers.[4–7] Disruption of other portions of the thyroid axis are rarely reported as causes of hypothyroidism, such as reduced secretion of pituitary thyroid-stimulating hormone (TSH) or hypothalamic thyrotropin-releasing hormone.[8] Congenital hypothyroidism resulting from inherited genetic defects or abnormal thyroid gland development have been rarely reported in dogs.[9–11]

Diagnostic Testing and Monitoring

Clinical signs of canine hypothyroidism often manifest in middle age, with a mean age at diagnosis reported to be 6.8 yr.[12] Signs may be subtle and slowly progress over months to years. Dermatologic abnormalities occur frequently and often include truncal nonpruritic alopecia, "rat tail" appearance, poor coat quality, seborrhea, hyperpigmentation, and recurrent pyoderma.[6] Other commonly reported clinical signs include lethargy, mental dullness, exercise intolerance, obesity or unexplained weight gain, and heat-seeking behaviors. Less commonly reported associations include facial nerve paralysis, vestibular disease, and polyneuropathy.[13]

Abnormalities on initial biochemical screening are nonspecific, with a fasted hypercholesterolemia, hypertriglyceridemia, and mild nonregenerative anemia most commonly found.[14] Hypothyroid dogs are expected to have a total thyroxine concentration (TT4) below the laboratory reference range; a result in the upper half of the reference range generally excludes the condition. If clinical suspicion of hypothyroidism is high in a patient with a TT4 below or in the lower end of the reference interval, evaluation of free T4 (fT4) and TSH concentrations is warranted. Although equilibrium dialysis is preferred for fT4 testing (fT4ed), it is not essential, and assay availability should be confirmed with the laboratory. Definitive hypothyroidism diagnosis is characterized by TT4 and fT4 concentrations below the reference interval with a TSH concentration above the reference interval; however, ~20–40% of dogs with overt hypothyroidism will

TABLE 1

Summary of Categorical Approach to Diagnosing Suspected Canine Hypothyroidism

GROUP 1	GROUP 2	GROUP 3
Classic clinical HT	**No HT signs with low TT4**	**Possible HT with normal TT4**
Clinical Presentation:		
• Clinical HT • Low TT4	• No clinical HT • Low TT4	• Clinical HT • Normal TT4
Next Steps:		
↓	↓	↓
• Measure fT4 and TSH to confirm diagnosis • Treat with supplementation • Monitor levels 4 weeks after starting medication or dose adjustments until controlled, and then every 6 to 12 months	• Review history & medications • Evaluate for NTD • Monitor for clinical signs, retest as indicated	• Evaluate for NTD • Perform fT4ed, TSH, +/- anti-T4 autoABs • Treat with supplementation if indicated • Monitor levels 4 weeks after starting medication or dose adjustments until controlled, and then every 6 to 12 months

Anti-T4 autoABs, anti-thyroxine auto-antibodies; fT4, free thyroxine level; fT4ed, free thyroxine level by equilibrium dialysis; HT, hypothyroidism; NTD, nonthyroidal disease; TSH, thyroid-stimulating hormone level; TT4, total serum thyroxine level.

have TSH concentrations within the reference range.[15,16] Therefore, having two of the three hormone concentrations indicative of hypothyroidism is enough to support the diagnosis in a patient with compatible clinical or biochemical abnormalities. An isolated TT4 below the reference interval should not be the only criteria used to diagnose hypothyroidism. Practitioners must consider that reduction of TT4 concentrations can occur secondary to patient breed, advancing age, and administration of certain medications, such as prednisone, as well as during periods of illness or stress.[17,18] Severe illness can also suppress fT4 concentrations, further mimicking a hypothyroid state; therefore, thyroid testing should ideally be performed following clinical stabilization or disease recovery when possible, to maximize the diagnostic accuracy of results.[19]

Therapy

Treatment involves oral hormone replacement using levothyroxine sodium at a starting dosage of 0.02 mg/kg twice daily. In obese patients, dose calculations should be based on estimated lean body weight. Veterinary approved medications should be used and given on an empty stomach. If given with food, higher doses of supplementation may be needed to overcome reductions in bioavailability and dose monitoring should be performed in a nonfasted state so results accurately reflect the patient's response. Clinical signs typically improve rapidly once therapy is started; however, dermatologic abnormalities may be slower to resolve.

Treatment monitoring is initiated 4 wk after starting supplementation unless signs persist in the face of therapy or signs of iatrogenic hyperthyroidism develop. Monitoring includes TT4 assessment, with the blood sample obtained 4–6 hr after medication administration ("post-pill") to check the peak serum concentration. Dose adjustments are performed as needed monthly until the post-pill serum TT4 concentration is in the upper half or slightly above the laboratory's reference range, or within the range for dogs receiving supplementation if provided by the laboratory. If an elevated TSH concentration was present at diagnosis, it should return to the reference range following treatment; however, confirming TSH normalization is not required and adds additional cost to monitoring. Once control is achieved, twice-daily dosing can be continued indefinitely with TT4 monitoring performed every 6–12 mo. Alternatively, after several months of twice-daily dosing, patients can possibly be transitioned to once-daily medication administration. A serum sample is obtained at the time the medication is due ("pre-pill"). A trough TT4 concentration >1.5 mcg/dL suggests the dose is likely adequate for once-daily administration. Pre-pill TT4 concentrations <1.5 mcg/dL warrant either continuation of twice-daily dosing or increasing the once-daily dose by at least 50% and assessing a month later. Both pre- and 4–6 hr post-pill monitoring would be necessary at this visit to ensure

the dose increase avoids iatrogenic hyperthyroidism and provides sufficient 24 hr hormone replacement.

Clinical Tips

- Certain breeds and active working dogs are known to have thyroid hormone concentrations that are below standard laboratory reference ranges in the absence of thyroid disease. Therefore, it is essential to consider the patient's breed and purpose when presented with abnormal thyroid hormone concentration results. This is especially important in sighthounds, such as greyhounds or salukis.[20–22]
- Although uncommon, circulating autoantibodies against thyroxine (T4) can cross-react with the TT4 assay, causing an artificially high reported result. A free T4 by equilibrium dialysis (fT4ed) or quantification of circulating autoantibodies may be warranted any time a normal dog is found to have an elevated TT4 concentration or in patients with clinical or biochemical abnormalities suggesting hypothyroidism but a TT4 concentration within reference range.[5,23]

Categorical Approach to Diagnosis Based on Clinical Presentation

Hypothyroidism is one of the most common endocrinopathies of the dog, and a clear-cut diagnosis can be made when the signalment and presentation of symptoms are classic and are supported by appropriate endocrine test results. However, the guidelines authors acknowledge that hypothyroidism is commonly overdiagnosed owing to the nonspecific nature of the signs, as well as the challenges that arise with the interpretation of thyroid function testing.

GROUP 1: DOGS WITH CLASSICAL SIGNS OF HYPOTHYROIDISM AND A LOW TT4

Clinical Presentation

- Signalment: middle-aged dogs and breed predisposition (beagles, golden retrievers, Doberman pinschers, Great Danes).[13]
- Group 1 dogs have one or more signs of hypothyroidism, most commonly including indications of decreased basal metabolic rate (weight gain without historical increase in appetite, cold intolerance or heat seeking, exercise intolerance, lethargy) and dermatological changes (alopecia, seborrhea, dry coat and skin, hyperpigmentation, myxedema, or recurrent pyoderma or otitis externa).
- Other systems that may be affected are cardiovascular (bradycardia) and neurologic, with signs related to the peripheral nervous system (i.e., facial nerve paralysis), vestibular and central nervous systems (ataxia, seizures, obtundation), and polyneuropathy (weakness).[7] Megaesophagus has been diagnosed in dogs with hypothyroidism, but there is little evidence of a causative linkage.[13]
- Assess for consistent laboratory abnormalities such as hypercholesterolemia and hypertriglyceridemia (ideally on a fasted sample). A mild nonregenerative anemia may also be present.

Next Steps

- Submit additional thyroid testing to document a subnormal fT4 and/or an elevated TSH concentration to confirm diagnosis.
- Approximately 20–40% of dogs with hypothyroidism have a low TT4 and low fT4 but a normal TSH concentration.[15,16] However, this scenario could also indicate nonthyroidal illness, so additional testing such as assessing for the presence of antithyroid autoantibodies or a TSH response test can be run to help confirm diagnosis, although these tests may be cost-prohibitive for some clients.[24]
- Initiate treatment with twice-daily levothyroxine supplementation (ideally on an empty stomach to maximize absorption).
- Monitor therapy based on clinical improvement and serial TT4 testing. Assess a TT4 level 4–6 hr post morning pill 4 wk after starting medication or after dose adjustments until control is achieved, then every 6–12 mo as indicated.
- Consider monitoring TSH level until normalized if it was elevated at initial diagnosis (refer to treatment and monitoring section above).

GROUP 2: DOGS WITH NO CLINICAL SIGNS OF HYPOTHYROIDISM AND A LOW TT4

Clinical Presentation

Group 2 dogs have no symptoms of hypothyroidism and a decreased TT4 on routine laboratory screening.

Next Steps

- It is critical to consider the dog's signalment, such as age and breed, before proceeding with additional testing for hypothyroidism. Clinically normal dogs of certain breeds such as greyhounds, Alaskan sled dogs (particularly when racing), shar peis, salukis, and deerhounds are routinely reported to have TT4 concentrations that are lower than established laboratory reference ranges. The guidelines task force recommends using breed-specific reference ranges when interpreting hormone levels in these breeds, especially if no clinical signs are present.[25]
- Review current and previous medications. Drugs such as phenobarbital, clomipramine, toceranib phosphate, glucocorticoids, and sulfonamides are reported to lower TT4 and/or fT4 concentrations; TSH may be increased or within the reference range, depending on the mechanism of the effect on thyroid function. These changes are reversible in most cases once the medications are discontinued.[18,26,27]
- Investigate for nonthyroidal illness if the dog is sick. Euthyroid sick syndrome can decrease circulating thyroid hormone concentrations, with preferential impact on TT4. In severe illness, fT4 is also impacted. TSH may be subnormal or within the reference range.[19] Ideally, further thyroid testing should be delayed until clinical illness has resolved and the dog is clinically well.
- Review symptoms of hypothyroidism with owner and consider measurement of fT4 and TSH levels if symptoms develop.
- Monitor for development of clinical signs.

GROUP 3: DOGS WITH CLINICAL SIGNS OF HYPOTHYROIDISM AND A NORMAL TT4

Clinical Presentation

Group 3 dogs have a similar clinical presentation to Group 1 dogs, but the TT4 does not confirm hypothyroidism.

Next Steps

- Investigate for other causes of clinical presentation by reviewing history with client and pursuing additional diagnostics.
- Perform an fT4ed with TSH and consider additional testing to rule out thyroiditis, specifically assessing for the presence of antithyroid autoantibodies. Dogs with thyroiditis can have antibodies that falsely elevate TT4 levels because of cross-reactivity of the T4 autoantibodies. Signs of hypothyroidism can develop slowly over time in some of these dogs.[3]
- A TSH response test could be considered if the TT4 or fT4 concentrations are in the low-normal reference range and the patient lacks circulating antithyroid antibodies.
- Dogs should be treated with supplementation if the diagnosis is confirmed, and therapy is monitored as described for Group 1. However, if the TT4 concentration was within reference range at diagnosis owing to the presence of T4 autoantibodies, an fT4ed is the preferred test to accurately monitor therapy.

Canine Hypercortisolism (Cushing's Syndrome)

Overview

Cushing's syndrome (CS) refers to clinical signs associated with excessive glucocorticoid exposure, including polyuria, polydipsia, polyphagia, and panting. It can be caused by endogenous oversecretion of cortisol or by exogenous administration of glucocorticoids (iatrogenic etiology). Naturally occurring CS can be adrenocorticotropic hormone (ACTH) dependent (85%) or ACTH independent (15%). The vast majority of cases of ACTH-dependent CS are caused by a pituitary tumor (pituitary-dependent hypercortisolism, PDH), and most cases of ACTH-independent CS are caused by adrenal tumors (adrenal-dependent hypercortisolism, or ADH). Other causes, including ectopic ACTH secretion and food-dependent hypercortisolism, will not be discussed here.

Diagnostic Testing and Monitoring

All diagnostic tests for Cushing's syndrome have limitations and can yield false-positive results when performed in patients with concurrent nonadrenal illness or stress.[28] Therefore, proper patient selection is essential before testing and likely impacts diagnostic accuracy more than which specific test is selected. Practitioners should only test patients when clinical suspicion of CS is high (i.e., the presence of two or more clinical or biochemical abnormalities suggesting CS). Additionally, attempts should be made to stabilize or resolve any known comorbidities (such as diabetes mellitus) before pursuing CS testing when possible.[29]

TABLE 2

Clinicopathologic Findings That Can Occur with Cushing's Syndrome

Increased alkaline phosphatase
Hypercholesterolemia
Mild hyperglycemia
Dilute urine (specific gravity <1.020)
Proteinuria
Stress leukogram (mature neutrophilia, lymphopenia, eosinopenia, monocytosis)
Thrombocytosis
Erythrocytosis
Systemic hypertension

The low-dose dexamethasone suppression test (LDDST) is the preferred diagnostic test of the guidelines panel members. False positives can occur with stress or nonadrenal illness such as uncontrolled diabetes.[30,31] Results of the LDDST may also differentiate between PDH and ADH.

Low-Dose Dexamethasone Suppression Test Technique

1. Draw a serum sample for baseline cortisol measurement.
2. Administer 0.01 mg/kg of dexamethasone IV (if dexamethasone sodium phosphate is used, calculate dose using a concentration of 3 mg/mL, instead of 4 mg/mL as listed on the bottle).[32]
3. Collect serum samples for cortisol measurement at 4 and 8 hr.

Test results are interpreted as follows:

- Refer to laboratory's diagnostic cutoffs for interpretation. The values below are used as examples only.
- Assess the 8 hr result. Cortisol >1.4 mcg/dL is consistent with a diagnosis of CS; continue with differentiation.
  - If the 8 hr cortisol concentration is between 1.0 and 1.39 mcg/dL but clinical suspicion for CS is high, consider performing an ACTH stimulation test (ACTHST) or repeating the LDDST in 2–3 mo.

TABLE 3

Clinical Signs Associated with Naturally Occurring Cushing's Syndrome

Polyuria (± worsened incontinence, urinary accidents, and/or nocturia)
Polydipsia
Pot-bellied appearance
Polyphagia
Excessive panting
Dermatopathy
Muscle weakness or wasting

- If the 8 hr result was consistent with a diagnosis of CS, then assess for evidence of partial suppression; if any criteria are present, the result is consistent with PDH.
  - 4 hr cortisol concentration is <1.4 mcg/dL.
  - 4 or 8 hr cortisol concentration is <50% of the baseline concentration.
  - Up to 35% of dogs with PDH do not fulfill at least one of these criteria; therefore, failure to observe suppression does NOT confirm ADH. If differentiation is still desired, abdominal ultrasound and/or an endogenous ACTH concentration can be pursued.
- Relevant considerations:
  - Samples should be collected in a manner consistent with laboratory recommendations. Fasting is generally not required, but excessive lipemia may affect results. If lipemia is present, seek laboratory guidance for interpretation.
  - Glucocorticoid withdrawal before testing should be 2 wk for short-acting glucocorticoids, whereas up to 4 wk may be required following use of longer-acting glucocorticoids (such as triamcinolone).[33–35]

The ACTHST appears to be less impacted than the LDDST by stress and nonadrenal illness, particularly diabetes.[29,30] The ACTHST should also be considered if the LDDST does not support a diagnosis of hypercortisolism but clinical suspicion remains high, to confirm iatrogenic CS, and to monitor CS therapy. The testing procedure is detailed in the ACTH Stimulation Technique box, with results interpreted as follows:

1. Refer to laboratory's diagnostic cutoffs for interpretation. Values indicated here are used as examples only.
2. If the 1 hr post-ACTH cortisol exceeds 22 mcg/dL, this is consistent with CS.
3. If the ACTHST returns with both the pre- and stimulated cortisol in ranges that mimic hypoadrenocorticism, this is consistent with iatrogenic CS, and additional investigation into glucocorticoid exposure is warranted. This pattern may also be seen in dogs with ADH; an LDDST should be performed if iatrogenic hypercortisolism is excluded.

Relevant considerations for the ACTHST are as follows:

1. False-positive results can occur in dogs that are chronically or moderately stressed or have nonadrenal illness but are less common than with LDDST.[30]
2. This test lacks sensitivity in dogs with adrenal tumors, leading to false-negative results in up to 41% of dogs with ADH.[36] If the stimulated cortisol concentration is below the diagnostic cutoff and clinical suspicion of CS remains high, an LDDST should be performed.
3. See "Relevant Considerations" for LDDST, above.

The urine cortisol-to-creatinine ratio (UCCR) test is highly sensitive but poorly specific, leading to a large number of false positives, particularly in dogs with polyuric conditions. It is most appropriately used to exclude hypercortisolism in patients with a low clinical suspicion of CS, such as an asymptomatic dog with an alkaline phosphatase (ALP) elevation. To minimize the risk of false-positive results, urine samples are best collected in a nonstressed, home environment.[37] A low value (based on the laboratory's diagnostic cutoff) almost always rules out the disease.

Therapy

Adrenalectomy is the preferred therapy for ADH. However, clients may decline this option because of cost, potential complications, and comorbidities. Mitotane is an adrenocorticolytic drug that was previously the primary treatment option for PDH and is still preferred by some clinicians. Please see Behrend for more information.[38] Trilostane is FDA approved for treatment of PDH and ADH. Although labeled to be administered once daily, there are several peer-reviewed references that have found that twice-daily use may be preferable.[39–41] The FDA-approved dose is 2.2–6.7 mg/kg/day, but it has been commonly used at lower doses such as 2–3 mg/kg/day. Several members of the guidelines task force use a starting dosage of ~1 mg/kg twice per day, dependent on the FDA-approved commercially available capsule sizes.

Monitoring requires close attention to clinical signs and cortisol testing. There are many published monitoring and testing protocols; there is no universal consensus on one protocol.[42] The ACTHST has historically been used for monitoring mitotane and trilostane therapy, but more recent research shows that ACTH-stimulated cortisol has poor correlation with clinical signs in dogs treated with trilostane.[43,44] As the ACTHST is the only definitive diagnostic test for diagnosis of hypoadrenocorticism, the primary role for its use in monitoring treatment of naturally occurring CS is to rule out oversuppression of cortisol production. Because CS is a highly variable disease, clinician judgment and discretion are important in deciding on a specific monitoring protocol. There is consensus among the guidelines

TABLE 4

Summary of Categorical Approach to Diagnosing Suspected Canine Hypercortisolism (Cushing's Syndrome)

GROUP 1	GROUP 2	GROUP 3	GROUP 4
Classic clinical CS	**Clinicopathologic abnormalities without clinical signs**	**Clinical signs without clinicopathologic abnormalities**	**Sick patients that may have CS**
Clinical Presentation:			
• Clinical signs and clinicopathologic findings consistent with CS	• Obtain thorough history with specific questions about potential clinical signs and steroid exposure • If clinical signs are identified, go to Group 1, Next Steps (LDDST) • If clinical signs are not identified, go to Next Steps for Group 2	• Obtain thorough history with specific questions about potential steroid exposure	• Address the presenting clinical signs and underlying cause of acute illness
Next Steps:			
↓	↓	↓	↓
• Perform LDDST. If confirmatory, consider tests to differentiate between PDH and ADH, and treat accordingly. If not confirmatory, perform ACTHST • If ACTHST is not confirmatory, consult with or refer to a specialist	• Repeat testing to confirm clinicopathologic abnormalities • Consider alternative differential diagnoses if abnormalities exist • Endocrine testing is not necessary • A UCCR may be performed to rule out CS if desired by client or veterinarian	• If CS is strongly suspected, specific endocrine testing is recommended • If CS is not strongly suspected or is not confirmed, consider other differential diagnoses for the clinical signs	• Do not perform endocrine testing until 2–4 weeks following resolution of acute illness • If acute illness is unlikely to resolve without addressing CS, consider consultation with or referral to a specialist

ACTHST, adrenocorticotropic hormone stimulation test; ADH, adrenal-dependent hyperadrenocorticism; CS, Cushing's syndrome; LDDST, low-dose dexamethasone suppression test; PDH, pituitary-dependent hyperadrenocorticism; UCCR, urinary cortisol:creatinine ratio.

panel that the protocols and testing guidance described below have been effective. Initial response is assessed at 2 wk, then 1 mo later, and then every 3–6 mo. Clinical signs are the primary indicator of whether the patient is controlled or needs a dose adjustment.

Measurement of cortisol concentrations (before pill or following ACTHST) is recommended to help determine whether it is safe to continue with the current dose or to adjust the dose. Pre-pill cortisol testing involves obtaining a sample for cortisol measurement before the morning pill. The ACTHST should be done 3–5 hr after trilostane administration, with a lower dose of synthetic ACTH (1 mcg/kg IV) being acceptable for monitoring.[45] Timing of when the ACTHST is started following trilostane administration should be consistent between visits.

The primary purpose of the first recheck at 2 wk following initiation of trilostane treatment is to ensure cortisol is not becoming too low. Therefore, at the first 2 wk recheck following trilostane initiation, the guidelines authors do not usually recommend increasing the dose but may decrease the dose. After the first month of treatment, necessary dose increases are typically by 25–50% based on commercially available capsule sizes. Owners should not give trilostane if the dog is not feeling well. The guidelines task force does not routinely recommend, but recognizes, that patients are sometimes on unequal doses twice daily. Cortisol monitoring should always be performed following the higher dose. For example, if a patient is receiving 40 mg and 30 mg, an ACTHST should be performed after the 40 mg dose.

Clinical Tips

- A follow-up client questionnaire (available at aaha.org/endocrine-disease under the Resource tab) is a useful instrument for the client to complete at presentation of the patient. Answers to this questionnaire and follow-up questions about clinical signs are the primary determinants of whether the patient needs a dose adjustment.
- Cortisol measurements help determine whether the current dose is appropriate or if dose adjustment is needed for a patient.

Categorical Approach to Diagnosis Based on Clinical Presentation

In the past, patients have been diagnosed with CS based on classic clinical signs (polyuria, polydipsia, polyphagia, panting, and dermatologic abnormalities), clinicopathologic abnormalities (increased ALP and cholesterol, stress leukogram, thrombocytosis, urine specific gravity <1.020, and proteinuria), and definitive diagnostics (LDDST or ACTHST). However, as awareness of CS has increased, clinical suspicion has also increased in patients with more ambiguous presentations that may lack some of the classic clinical signs or clinicopathologic abnormalities. The purpose of the information in this section of the guidelines is to help the practitioner navigate the diagnostic pathway in patients with various presentations.

GROUP 1: CLINICAL SIGNS AND CLINICOPATHOLOGIC FINDINGS CONSISTENT WITH CUSHING'S SYNDROME

Clinical presentation

These are the dogs with classic signs and clinicopathologic abnormalities expected with CS (Tables 2 and 3).

Next Steps

- Minimum database should include complete blood count, serum biochemistry, and urinalysis. Consider assessing blood pressure, urine culture, and urine protein:creatinine ratio.
- Specific endocrine testing should be performed. The guidelines panel recommends an LDDST as a routine first step. If the LDDST confirms CS, consider differentiation between PDH and ADH (if not differentiated by the LDDST) and appropriate therapy.
- Differentiation between PDH and ADH is helpful because it helps direct therapeutic options and provides the owner with prognostic information. However, if the owner has no intention of pursuing adrenalectomy if an adrenal tumor is identified, patients can be treated with trilostane without knowing whether the dog has PDH or ADH.
- Diagnostics that help differentiate PDH from ADH include LDDST, abdominal ultrasound, and endogenous ACTH concentration.
- Computed tomography of the head may be performed in dogs with PDH if the dog has signs compatible with a macroadenoma or if the owner would pursue radiation therapy or hypophysectomy.
- In patients with ADH, abdominal computed tomography is usually pursued before adrenalectomy.
- If the LDDST is not confirmatory, perform an ACTHST. If the ACTHST is confirmatory, consider differentiation and therapy. If the ACTHST is not confirmatory, consider referral to a specialist.
- Note that endocrine diagnostics should not be performed within 2 wk of administration of short-acting glucocorticoids (oral, otic, or ophthalmic) or within 4 wk of receiving long-acting glucocorticoids.[33–35]

GROUP 2: DOGS WITH NO CLINICAL SIGNS, BUT WITH CLINICOPATHOLOGIC ABNORMALITIES SUGGESTIVE OF CUSHING'S SYNDROME

Clinical presentation

Group 2 dogs are those for whom the owners report no clinical signs consistent with CS but have one or more compatible clinicopathologic abnormalities (Table 2).

Next Steps

- The first step in managing these patients is to thoroughly probe the patient's history, with specific questions about water intake, urination habits, worsened incontinence, or nocturia. Potential administration of glucocorticoids, including ophthalmic or otic preparations, should also be ruled out.
- Repeat testing to confirm persistence of previous abnormalities.
- If no clinical signs of CS are identified, consider alternative differentials for clinicopathologic abnormalities, and pursue appropriate diagnostics. For example, for an increased ALP concentration, abdominal imaging may be performed.
- Specific endocrine testing is not necessary unless or until clinical signs of CS are present.
- A UCCR test may be considered if the veterinarian or client is highly motivated to rule out the diagnosis of CS. Note that the UCCR test is a very sensitive but nonspecific test. Although a negative result makes CS very unlikely, a positive result does not confirm the presence of CS.

GROUP 3: DOGS WITH CLINICAL SIGNS SUGGESTIVE OF CUSHING'S SYNDROME WITHOUT CLINICOPATHOLOGIC ABNORMALITIES

Clinical presentation

Clinical signs in Group 3 dogs may include polyuria, polydipsia, polyphagia, excessive panting, and dermatopathy (Table 3).

Next Steps

- Carefully question the owner to rule out administration of glucocorticoids that could cause CS.
- If clinical suspicion of CS is low, monitor the patient's progression or change in clinical signs. A UCCR test can be considered to rule out CS.

- If clinical suspicion is high, specific endocrine testing is recommended. In patients without significant comorbidities (such as diabetes mellitus), an LDDST is recommended.
- If CS is confirmed, consider differentiation (see GROUP 1). If CS is not confirmed, consider other differential diagnoses for the specific clinical signs.
- If CS is still strongly suspected, ACTHST and/or consultation with a specialist may be pursued.

GROUP 4: SICK PATIENTS PRESENTING WITH SIGNS AND/OR CLINICOPATHOLOGIC FINDINGS CONSISTENT WITH CUSHING'S SYNDROME

Clinical presentation

Group 4 dogs are patients that may have CS but whose presenting signs must be addressed before pursuing diagnostics for CS. Note that hypercortisolism does not cause anorexia, vomiting, or diarrhea. Patients in this category may include:

- Dogs in whom the presenting signs are due to a disease process that is unrelated to CS (e.g., acute gastroenteritis)
- Dogs with presenting signs caused by a comorbidity associated with CS (e.g., pulmonary thromboembolism, gall bladder mucocele, or diabetic ketoacidosis)
- Dogs with signs of an enlarging macroadenoma (decreased appetite, behavior change, or other neurologic signs). In these cases, the macroadenoma is causing the presenting signs; hypercortisolism is not.

Next Steps

- Address the presenting clinical signs and underlying cause of the acute illness.
- Do not perform specific endocrine testing for CS until the acute illness is managed or controlled. Acute illness causes stress that can lead to false-positive results, particularly with the LDDST. Additionally, because CS is not causing the presenting clinical signs, diagnosis and treatment of CS will not immediately ameliorate the presenting clinical signs.
- If relevant, treatment of diabetes mellitus should not be delayed in dogs with suspected CS.
- The guidelines task force recommends, if possible, waiting at least 2–4 wk after improvement of the acute illness to test for CS.
- If the acute or chronic illness is unlikely to resolve or improve without addressing the possible underlying CS, consider consultation with a specialist to discuss the need for and timing of specific endocrine testing.

Canine Hypoadrenocorticism (Addison's disease)

Overview

Hypoadrenocorticism (HA), or Addison's disease, describes a spectrum of conditions resulting in deficiencies of important adrenal hormones (i.e., cortisol and aldosterone). HA usually results from direct adrenocortical injury (primarily autoimmune disease) although the rapid withdrawal of adrenal suppressive medications (steroids), pituitary surgery, or cancer sporadically result in ACTH deficiency. The variable clinical signs correspond to a loss of the vital functions of cortisol in maintaining metabolism, immunity, and gastrointestinal health and of aldosterone in maintaining sodium and volume status. Recent studies suggest up to 25–30% of patients with HA have normal electrolytes (i.e., "atypical" HA).[46–48]

The clinical signs of HA can occur in dogs of any age or breed. Most dogs are diagnosed in middle age, with a female predisposition inconsistently reported. Commonly affected breeds include the standard poodle, Portuguese water dog, and Great Dane. Often, sudden signs of volume depletion (shock) predominate in "typical" HA (cortisol deficiency with aldosterone deficiency), although the atypical form (clinical signs reflecting cortisol deficiency without electrolyte

TABLE 5

Diseases with a Similar Clinical Presentation to Hypoadrenocorticism

Conditions with similar clinical presentation to classic HA
• Acute kidney injury • Severe gastrointestinal disease
Diseases with a similar clinical presentation to atypical HA
• Severe gastrointestinal disease • Hepatic dysfunction

HA, hypoadrenocorticism.

TABLE 6

Conditions That Biochemically Resemble Hypoadrenocorticism (Pseudo-Addisonian Conditions)

Whipworms
Third spacing of fluids
Chronic gastrointestinal disease
Renal failure
Hepatic failure
Reperfusion injury
Acidosis
Artifact (thrombocytosis, hemolysis)

TABLE 7

Laboratory Changes That Can Occur with Hypoadrenocorticism

CLINICAL CHEMISTRY	CBC	URINALYSIS
• Hyperkalemia • Hyponatremia • Na:K ratio <27 • Hypochloremia • Acidemia • ALT elevation • Hypoalbuminemia • Hypocholesterolemia • Azotemia • Hypercalcemia	• Anemia • Absent stress leukogram (± eosinophilia, lymphocytosis)	• Urine specific gravity <1.030

ALT, alanine aminotransferase; CBC, complete blood count.

derangements) is more often chronic. Atypical HA is characterized by vomiting, lethargy, anorexia, and diarrhea; hypoalbuminemia and/or hypocholesterolemia are common laboratory findings.[49] The presence of a lymphopenia makes cortisol deficiency extremely unlikely.[50]

Diagnostic Testing and Monitoring

The diagnosis relies on confirming cortisol deficiency by means of an ACTHST. A sodium-to-potassium ratio <27 is suggestive, although sodium and/or potassium concentrations are within the reference range in nearly one in four cases of HA, and many other disorders can impact the sodium-to-potassium ratio.[49,51] Aldosterone measurement is available through multiple laboratories and can be used to further determine adrenal function if appropriate.[52]

The finding of a baseline or "resting" serum cortisol >2 mcg/dL rules out HA with nearly 100% confidence, assuming that the patient has not received exogenous glucocorticoids known to cross-react with the cortisol assay (such as prednisone).[53] However, most dogs with a baseline cortisol <2 mcg/dL do not in fact have hypoadrenocorticism, so this finding is not sufficient to establish the diagnosis. The diagnosis is confirmed by a post-ACTH stimulation cortisol value <2 mcg/dL or below the laboratory-specific diagnostic cutoffs (see box, ACTH Stimulation Technique). Reference ranges derived from healthy pets are not the same as diagnostic cutoffs, which are developed by sampling dogs with HA. Measurement of endogenous ACTH, specifically the cortisol-to-endogenous ACTH ratio, or a UCCR are promising sensitive and specific tests for dogs with primary adrenocortical injury, although this test is not yet routinely performed.[54–58]

Therapy

For cortisol deficiency, a small daily dose of glucocorticoids is recommended. Many dogs require doses <0.1 mg/kg/day of prednisone or prednisolone, and 0.25 mg/kg/day should be enough to manage all clinically stable dogs with HA long term. Other glucocorticoids are acceptable, and the dose should be calculated on a prednisone-equivalent basis. The daily dose should be doubled or tripled before known stressful events.

Dose should be further adjusted based on clinical signs and side effects. Dose should be increased when a dog shows clinical signs of Addison's disease, such as anorexia, lethargy, vomiting, diarrhea, hematochezia, and melena. Dose should be decreased when the dog has side effects of glucocorticoid administration including polyuria/polydipsia, polyphagia, panting, muscle wasting, elevated ALP, or hair loss.

Patients with hyperkalemia and/or hyponatremia require mineralocorticoid supplementation. The labeled dose of desoxycorticosterone pivalate (DOCP) is 2.2 mg/kg given intramuscularly or subcutaneously, but research has demonstrated efficacy with lower doses.[59,60] Starting doses of 1.1–1.5 mg/kg may be appropriate in most cases.[61,62]

The dose and the dosing interval are determined by electrolyte monitoring. Check electrolyte levels 10–14 days after injection and again 25 days after injection. If hyperkalemia or hyponatremia are persistent, the dose is typically increased. If electrolytes are normal, the dose may be gradually decreased with monitoring. If the dose is already low, extending the dosing interval to 28–30 days is reasonable.[60] If DOCP cannot be used, consideration can be given to using fludrocortisone.

ACTH Stimulation Technique

1. Collect a baseline serum cortisol sample. The patient may need to be fasted to avoid lipemia.
2. Inject cosyntropin (5 mcg/kg intramuscularly or IV up to 250 mcg per dog) and collect a second serum sample 1 hr later.
   a. A 1 mcg/kg dose of cosyntropin has been shown equivalent to a 5 mcg/kg dose of cosyntropin for most dogs suspected of HA.[63]
   b. A 1 mcg/kg dose of cosyntropin has been shown appropriate for *monitoring* of dogs with Cushing's syndrome being treated with trilostane or mitotane but is *not* reliable for the diagnosis of Cushing's syndrome.[45]
   c. The absorption of compounded ACTH-depot ("gel") may be delayed from the intramuscular space. Thus, samples for cortisol should be collected at both 1 and 2 hr after injection.
3. The cost of the cosyntropin can be decreased by using lower doses when appropriate and by freezing the reconstituted product in small aliquots.[64]
   a. Using an aseptic technique, reconstitute the ACTH solution for injection as instructed on the package (1 mL NaCl for a 250 mcg/mL solution).
   b. With a tuberculin syringe, draw up 0.1–0.2 mL aliquots. Draw up an additional 0.1 mL of air to provide space for expansion during freezing. Store at 20°C for up to 6 mo.
   c. At the time of use, thaw one or more syringes in the palm of a gloved hand. The solution will quickly liquefy. Expel the small air bubble from the hub before use and double-check drug volume.
   d. Once thawed, use or discard the solution. Do not refreeze.

Clinical Tips

- Clients as well as veterinary health care professionals can learn to administer subcutaneous injections. Once a stable dose and dosing interval are achieved, monthly DOCP injections may be administered by someone other than the veterinarian.
- Other health care team members may serve as the primary client educators regarding symptoms of illness and side effects.
- Routine biannual health care visits are still encouraged.

Categorical Approach to Diagnosis Based on Clinical Presentation

Although some dogs with hypoadrenocorticism present with typical physical examination and laboratory abnormalities, making diagnosis relatively straightforward, other cases may have a vague or atypical presentation. The clinical signs or laboratory findings associated with hypoadrenocorticism can mimic several other diseases, making diagnosis challenging. The guidelines panel has organized clinical presentations into four groups to aid in diagnosis.

GROUP 1: CLASSIC CLINICAL DISEASE

Clinical Presentation

Group 1 dogs present with chronic or episodic clinical signs and laboratory abnormalities consistent with hypoadrenocorticism.

Next Steps

If suspicion for disease is high, an ACTHST should be performed to confirm diagnosis. If suspicion for disease is low, a resting cortisol could be performed. If the resting cortisol is <2 mcg/dL, an ACTHST should be performed to diagnose hypoadrenocorticism. If the resting cortisol is >2 mcg/dL, other differentials for these clinical and laboratory abnormalities should be pursued.

Once the diagnosis of hypoadrenocorticism is confirmed, appropriate treatment(s) and monitoring should be instituted. For patients with classic clinical disease, treatment generally consists of both mineralocorticoid and glucocorticoid supplementation.

GROUP 2: NO CLINICAL SIGNS, BUT WITH CLASSIC LABORATORY ABNORMALITIES

Clinical Presentation

Group 2 dogs present without clinical signs of disease and have laboratory derangements on routine laboratory work, which include hyperkalemia and/or hyponatremia. Additional laboratory abnormalities may be present (Table 7).

Next Steps

In these cases, the owner should be requestioned as to the presence of associated clinical signs including questions related to gastrointestinal health (appetite and stool), energy, and water intake. If upon deeper analysis there are still no clinical signs of hypoadrenocorticism, other causes of laboratory changes such as spurious causes should be ruled out (Table 6). If the blood sample was run on serum, consider reevaluation of plasma because serum potassium levels can be artificially high due to potassium release from platelets during clot formation.[65] If no clinical signs are present and spurious causes have been excluded, monitor clinical signs and repeat the laboratory testing as indicated.

If laboratory abnormalities are persistent or progressive, or upon deeper analysis clinical signs are present, either a resting

TABLE 8

Summary of Categorical Approach to Diagnosing Suspected Canine Hypoadrenocorticism

GROUP 1	GROUP 2	GROUP 3	GROUP 4
Classic clinical HA	**Biochemical changes suggestive of HA**	**Addisonian crisis**	**Atypical presentation**
Clinical Presentation:			
• Clinical HA • Hyperkalemia ± hyponatremia • ± other typical laboratory abnormalities	• No clinical HA • Hyperkalemia ± hyponatremia	• Hypovolemic shock • ± historical HA	• Chronic or episodic clinical HA • No electrolyte imbalances
Next Steps:			
↓	↓	↓	↓
• Resting cortisol or ACTHST • If resting cortisol <2 mcg/dL, proceed with ACTHST • If resting cortisol >2 mcg/dL, rule out HA and investigate other causes of clinical findings	• Reinvestigate for presence of clinical signs (directed history taking) • Look for other causes of laboratory changes • If no definitive findings, monitor for clinical signs and repeat laboratory tests as indicated • If clinical HA upon repeated investigation, consider resting cortisol or ACTHST • If no other causes of laboratory changes identified and laboratory changes persist or progress, consider resting cortisol or ACTHST	• Stabilize patient • Monitor electrolytes and PCV/TP • Provide supportive care • Perform resting cortisol or ACTHST • If resting cortisol <2 mcg/dL, proceed with ACTHST • If >2 mcg/dL, exclude HA and pursue other differentials	• Perform resting cortisol • If <2 mcg/dL, proceed with ACTHST • If >2 mcg/dL, exclude HA and pursue other differentials

ACTHST, adrenocorticotropic hormone stimulation test; HA, hypoadrenocorticism; PCV, packed cell volume; TP, total protein.

cortisol should be considered to exclude this disease or an ACTH stimulation test (ACTHST) could be performed.[52] If a resting cortisol test is chosen and results are <2 mcg/dL, an ACTHST should be performed to confirm the diagnosis.

GROUP 3: ADDISONIAN CRISIS

Clinical Presentation

Group 3 dogs present in hypovolemic shock with or without historic episodic signs consistent with hypoadrenocorticism. This is the most serious and life-threatening manifestation of hypoadrenocorticism and typically presents as hypovolemic shock accompanied by severe hyperkalemia and hyponatremia. Other laboratory abnormalities may be seen (Table 7).

Next Steps

Immediate stabilization should be implemented, with IV fluids being the cornerstone of therapy. Treatment should target correcting hypovolemia and hypotension. Specific therapy to correct hyperkalemia, hypoglycemia, and acidosis may be required. Gastrointestinal support including early enteral nutrition should be implemented as needed.

Once stable, these patients may need to be transferred to a facility that provides 24 hr care to provide continued support. Frequent monitoring of electrolytes is required. The guidelines task force recommends daily packed cell volume monitoring as these patients can become severely anemic following rehydration.[66]

Once stable, perform a baseline cortisol test to rule out this diagnosis, or, if suspicion for disease is high, perform an ACTHST to

confirm diagnosis. In some cases, administering a single dose of a steroid before testing is required for stabilization. Dexamethasone (0.1 mg/kg IV) is the steroid of choice because it does not interfere with the cortisol assay.[66] Consider aldosterone measurement. Mineralocorticoids can be started once the patient is stable, there is a confirmed diagnosis, and sodium is >130 mEq/dL.

GROUP 4: CLINICAL SIGNS WITH NONSPECIFIC LABORATORY ABNORMALITIES (ATYPICAL PRESENTATION)

Clinical Presentation

Group 4 dogs present with chronic or episodic clinical signs without the characteristic findings associated with classic hypoadrenocorticism. Because signs of canine hypoadrenocorticism can mimic many other diseases, patients may present with episodic clinical signs that could be consistent with this disease without the hallmark laboratory findings of hyperkalemia or hyponatremia (Table 6).

Next Steps

When signalment and clinical signs are consistent with hypoadrenocorticism (e.g., episodic gastrointestinal signs after periods of stress, polyuria/polydipsia) or if there are other suggestive laboratory findings (Table 7), a resting cortisol should be performed. If the resting cortisol is <2 mcg/dL, an ACTHST should be performed. If the resting cortisol is >2 mcg/dL, other differentials should be considered. If hypoadrenocorticism is diagnosed, consider testing for aldosterone deficiency as many of these patients have hypoaldosteronism, even with normal electrolytes.[51] Appropriate treatment and monitoring should be instituted based on diagnosis.

Feline Hyperthyroidism

Overview

The management of FHT has been covered extensively in other publications, notably the *2016 AAFP Guidelines for the Management of Feline Hyperthyroidism*.[2] Much of the information in the 2016 AAFP guidelines remains applicable today. This discussion of FHT will serve to highlight certain key points and present recent findings related to the disease.

FHT is an extremely common endocrinopathy in cats, resulting from excessive circulating levels of T4 and T3. These excess hormone levels are most often caused by benign adenomatous hyperplasia of one or both thyroid glands and create a state of increased metabolism. Thyroid carcinoma is a rare FHT etiology, present in fewer than 3% of cats at the time of initial diagnosis.[67] Although FHT is typically diagnosed in cats older than 10 yr, elevated T4 levels in younger cats may be found more often as annual blood screening becomes more commonplace. It is important to note that T4 levels naturally decrease with age. A senior or geriatric cat with high normal T4 values according to the reference laboratory may actually be hyperthyroid. Following trends on annual screenings should reveal T4 levels either static or dropping. Elevation over time with development of clinical signs warrants further confirmation testing, even if the T4 level is technically within the laboratory's normal range.

Diagnosis and Monitoring

The classic presentation of FHT (also known as Group 1 in the 2016 AAFP guidelines and in Table 8) is a cat that is losing weight, eating voraciously, and hyperactive. Many cats, however, do not have these classic signs and can be assigned to one of the other five diagnostic groups. Cats with elevated T4 levels on basic blood screens may be minimally symptomatic or asymptomatic. Regardless of the cat's clinical presentation, a repeatedly elevated T4 level requires treatment to prevent progression of the disease and subsequent secondary organ damage.

Concurrent disease may cause the serum T4 level to be lower than expected in a cat suspected to be hyperthyroid. In these cases, a fT4 will be helpful to confirm the diagnosis. For cats that fall into Groups 4 or 6 that may be considered early or subclinically hyperthyroid, there may be some benefit to measuring TSH levels before deciding on treatment options. Cats with detectable serum TSH concentrations (≥0.03 ng/mL) are at much higher risk for development of ^{131}I-induced hypothyroidism.[68] A commercially available feline TSH test was recently released; however, the canine TSH test is a reasonable alternative.[69,70] A measurable TSH level may make a cat more susceptible to hypothyroidism following radioactive iodine treatment. Waiting until TSH declines to an unmeasurable level may be beneficial.[68,70] TSH levels are not sensitive for initial diagnosis of hyperthyroidism and must be used in conjunction with elevated T4 or fT4 levels.[70]

Therapy

Left untreated, FHT will eventually be fatal. Hyperthyroidism affects multiple organ systems. Until FHT is corrected, management and assessment of comorbidities cannot be accurately assessed. Options for treatment include radioactive iodine, oral antithyroid medication, surgical removal of the adenomatous thyroid gland, and an iodine-deficient therapeutic diet. The treatment of choice is radioactive iodine (^{131}I), which will provide a cure in more than 95% of cases. Radioactive iodine avoids anesthesia, requires no ongoing medication administration, and does not require the cat to have a restrictive diet. Radioactive iodine may be used as an initial treatment for stable hyperthyroid cats, even in the presence of some concurrent diseases. Cats with elevated N-terminal pro-B-type natriuretic peptide levels and mild heart disease will likely benefit from having the hyperthyroid state corrected. Cats with mild renal changes (IRIS stage 1) can

TABLE 9

Summary of Categorical Approach to Diagnosing Suspected Feline Hyperthyroidism*

GROUP 1	GROUP 2	GROUP 3	GROUP 4	GROUP 5	GROUP 6
Classic clinical disease	**Possible FHT with probable NTD**	**Enlarged thyroid without clinical FHT**	**Subclinical FHT**	**Clinical FHT with confirmed NTD**	**Clinically normal**
Clinical Presentation:					
• Clinical FHT • Elevated T4	• Clinical FHT • Normal T4	• No clinical FHT • Normal T4 • Enlarged thyroid gland	• No overt clinical FHT but some PE findings suggestive of FHT • Elevated T4	• Clinical FHT • Elevated T4 • One or more concurrent diseases	• No clinical FHT • No palpable nodule • Elevated T4
Next Steps:					
↓	↓	↓	↓	↓	↓
• Consider and recommend treatment options for FHT	• T4 with fT4ed assays 2–4 weeks after initial exam • Evaluate for NTD • Consider T3 suppression or thyroid scintigraphy	• Monitor clinical signs • Repeat T4 assay in 6 months	• Repeat T4 assay in 2 weeks • If elevated, treat for FHT • If T4 is normal, reevaluate in 6 months	• Treat for FHT • Institute appropriate management of concurrent diseases	• Confirm T4 • If normal, monitor clinical signs and repeat T4 in 6 months • If elevated, treat for FHT

FHT, feline hyperthyroidism; fT4ed, free thyroxine measured by equilibrium dialysis; NTD, nonthyroidal disease; PE, physical examination; T3, triiodothyronine; T4, total serum thyroxine concentration.

*Carney HC, Ward CR, Bailey SJ, et al. 2016 AAFP Guidelines for the Management of Feline Hyperthyroidism. *J Feline Med Surg*. 2016;18(5):400-416, copyright ©2016 by SAGE Publications. Reprinted by Permission of SAGE Publications. Access the AAFP Guidelines for Management of Feline Hyperthyroidism and additional resources at catvets.com/hyperthyroidism.

also be treated with ^{131}I without a therapeutic medication trial first.[2] Note that cats with normal renal and symmetric dimethylarginine values may develop abnormalities after the hyperthyroidism is corrected, and a normal symmetric dimethylarginine cannot be used to predict renal function after hyperthyroid resolution.[71] Iatrogenic hypothyroidism is a risk of ^{131}I, so ensuring the TSH concentration is nondetectable before referral may be ideal.[70]

Important Note

- The AAHA guidelines task force recommends for AAFP groups 4 and 6, the practitioner should consider checking TSH prior to ^{131}I treatment and postponing if measurable (>0.03 ng/mL) to help avoid creating iatrogenic hypothyroidism.[70]

Unfortunately, radioactive iodine treatment may not be available to all practitioners. Thyroidectomy may be curative, but it includes the risk of anesthetizing a cat with potential cardiac compromise. The parathyroid glands are at risk of being damaged during thyroidectomy even by skilled surgeons. Infrequently, there may be ectopic thyroid tissue that is not easily surgically removed that will continue to be overactive. Before surgical intervention, the cat should be medically stabilized.

An iodine-deficient diet is commercially available by prescription and is effective for many cats in controlling hyperthyroidism. Depending on the degree of initial elevation of the T4 level, some cats may take several months to become regulated.[72] For the therapeutic diet to be effective, cats must not be allowed access to any other food, including other pets' foods and human food, as well as items that they may hunt and eat outdoors. In some cats, the T4 level

will fail to normalize even after prolonged periods of exclusively feeding the restrictive diet. It has been shown that feeding the iodine-deficient diet to nonhyperthyroid cats in the household is not harmful if it is not possible for owners to feed separate diets in multi-cat homes.[72]

Medical management with methimazole is a common and effective way of controlling hyperthyroidism. To minimize potential adverse effects, methimazole should be started at a low dose and titrated up to the dose needed to maintain T4 levels between 1.0 and 2.5 mcg/dL. Dosing of 1.25–2.5 mg every 24 hr for the first week of treatment, increasing to 2.5–5 mg every 12–24 hr, will help minimize side effects, although adverse effects including vomiting, bone marrow dyscrasias, and skin excoriations can occur up to several months after initiating therapy. Gastrointestinal side effects may be mitigated by using a transdermal preparation of methimazole; however, all other adverse drug effects require discontinuation and selection of a different treatment method. Methimazole doses will need to be adjusted over time because the drug does not affect the growth of the adenomatous hyperplasia. Avoidance of hypothyroidism is imperative and requires periodic veterinary monitoring.

Clinical Tips

- For many practitioners, it has become commonplace for pet owners to do their own research when a diagnosis is made and subsequently propose alternative therapies. For cats with FHT, there is no effective homeopathic remedy despite the availability of products claiming to be effective.[73] Clients should be advised to pursue traditional treatments for this disease.
- If initial regulation is with methimazole, T4 monitoring should occur every 2–4 wk until the goal levels are reached. Complete blood count, chemistry profiles, and urinalysis will provide information on potential bone marrow dyscrasias, development or progression of azotemia, resolution of any liver enzyme changes, and any other issues that may have been concealed by the hyperthyroid state.
- Blood samples for T4 measurement may be taken at any time during the day after methimazole administration. There is no need to schedule sampling for a specific time after medication administration.[68]
- Once the patient has been regulated, a physical examination and minimum database should be performed at least every 6 mo and more frequently if there are significant comorbidities.

Categorical Approach to Diagnosis Based on Clinical Presentation*

GROUP 1: CLASSIC CLINICAL DISEASE

Clinical Presentation

Cats with uncomplicated clinical hyperthyroidism and elevated T4. These are cats with one or more clinical signs consistent with FHT that have an elevated T4 and no identifiable concurrent disease. T4 is above the laboratory reference interval in FHT cases.

Next Steps

The AAFP Guidelines Panel recommends that reference laboratory testing be utilized for diagnosis and monitoring of FHT so that precise serum hormone levels can be followed throughout treatment and to avoid quality control discrepancies. Ideally, for purposes of consistency, monitoring should be performed at the same reference laboratory. If in-clinic testing is performed for geriatric screening and significant changes are noted in thyroid hormone levels, obtain confirmatory testing at a reference laboratory.

Complete blood count (CBC) findings are generally unremarkable, although macrocytosis may be present. Cats with marked anemia may suffer from a comorbidity and further work-up should be performed. Serum chemistry findings often include elevated serum alanine transferase (ALT) or alkaline phosphatase. Serum ALT levels can be markedly elevated.

If liver enzymes do not normalize after successful treatment for FHT, further diagnostic work-up is warranted. Azotemia may suggest dehydration or underlying renal failure. Urinalysis results are variable, although the urine specific gravity may be less than 1.030 due to primary polydipsia or inability to concentrate the urine due to hyperthyroidism.

Management of Group 1 cats consists of treatment for their hyperthyroid disease.

GROUP 2: POSSIBLE FHT WITH PROBABLE NON-THYROIDAL DISEASE

Clinical Presentation

Cats with clinical hyperthyroidism and normal T4. Cats in this category have clinical signs suggestive of FHT along with T4 within the laboratory reference interval.

Next Steps

The AAFP Guidelines Panel recommends the following approaches for Group 2 cats:

- Further testing for FHT should consist of T4 and fT4 assays measured 2–4 weeks after the initial blood screening. A T4 value in the upper half of the reference interval combined with an elevated fT4 supports a diagnosis of hyperthyroidism.

- If the T4 and fT4 are both within the reference interval, the cat should be evaluated for non-thyroidal disease.
- If no concurrent illness is found and FHT is still suspected, further testing is warranted, including triiodothyronine (T3) suppression testing, serum TSH concentration in conjunction with T4 and fT4ed, or thyroid scintigraphy.

NOTE: *Common conditions with signs similar to FHT*: Certain classic signs of hyperthyroidism (polydipsia, polyuria, weight loss in the face of a good appetite) have similarities with the following morbidities that are plausible differential diagnoses:

- Diabetes mellitus
- Gastrointestinal malabsorption, maldigestion
- Gastrointestinal neoplasia, especially lymphosarcoma

GROUP 3: ENLARGED THYROID GLAND WITHOUT CLINICAL FHT

Clinical Presentation

Cats without clinical hyperthyroidism, T4 within the reference interval, but with enlarged thyroid gland(s).

Next Steps

Monitor clinical signs in these cats and repeat a serum T4 assay in 6 months.

GROUP 4: SUBCLINICAL FHT

Clinical Presentation

Cats without overt clinical hyperthyroidism but with an elevated T4 and with some physical exam findings suggestive of hyperthyroidism.

Next Steps

Repeat the T4 test in 1–2 weeks. If serum T4 is still elevated, treat the cat for FHT. While no data exist for the best way to manage Group 4 cats, the consensus of the Panel is to treat these cats for hyperthyroidism. If a repeat T4 is normal, then re-evaluate the patient in 6 months with a complete physical exam and a T4 assay.

GROUP 5: CLINICAL FHT WITH CONFIRMED NON-THYROIDAL DISEASE

Clinical Presentation

Cats with clinical hyperthyroidism confirmed by elevated T4, and one or more concurrent diseases.

Next Steps

Hyperthyroid cats are commonly middle-aged or older and often have concurrent diseases. But because FHT is a serious disease that can result in rapid deterioration of the patient, the Panel recommends the treatment of all diagnosed cats, including those animals with comorbidities. Appropriate monitoring and careful management of concurrent diseases will optimize the patient's health.

Common comorbidities associated with FHT:

- Thyrotoxic heart disease
- Hypertension
- Retinopathy
- CKD
- Gastrointestinal disease, malabsorption, cobalamin deficiency
- Insulin resistance

GROUP 6: CLINICALLY NORMAL

Clinical Presentation

Cats with no clinical signs of hyperthyroidism and no palpable thyroid nodule but with an elevated T4 on screening lab test.

Next Steps

Because falsely elevated T4 values may occur, repeat the T4 test preferably using radioimmunoassay or chemiluminescent enzyme assay.[74,75] If the T4 is now normal, monitor the cat and retest T4 every 6 months, or sooner if clinical signs develop. If the T4 is elevated, treat for FHT.

Less Common Feline Endocrinopathies

Three feline endocrinopathies are encountered in clinical practice with a lesser frequency than the other feline diseases discussed in these guidelines: feline hyperaldosteronism, feline hypothyroidism, and feline hyperadrenocorticism. This section provides general overviews of these less prevalent but still important endocrinologic diseases of cats.

Feline Hyperaldosteronism

The adrenal gland is the primary producer of the hormone aldosterone, which is responsible in part for sodium and potassium homeostasis. Feline primary hyperaldosteronism (PHA) is most commonly caused by a unilateral adrenocortical adenoma, with malignant adenocarcinomas reported less commonly.[76]

Cats with PHA are typically middle-aged to older cats. Presenting signs are typical of increased potassium loss/hypokalemia and retained sodium. Hypokalemia, usually less than 3 mEq/L, will lead to progressive muscle weakness. The owner may notice reluctance to jump, abnormal gait (plantigrade stance), lethargy, or cervical ventroflexion. Because the cats are considered mature to senior, owners often perceive clinical signs to be normal aging changes. Sudden blindness due to retinal detachment is a consequence of persistent systemic hypertension (SHT) and may or may not be noticed by the

TABLE 10

Key Factors in Managing Feline Primary Hyperaldosteronism

Presentation
• Hypokalemia, frequently under 3 mEq/L, which may not respond well to supplementation. • Systemic hypertension that may be difficult to control. • Serum sodium concentrations are usually normal. • Plasma aldosterone levels are elevated. • Abdominal ultrasound or other imaging may show adrenal mass.
Therapeutic Recommendations
• Control hypertension. • Supplement potassium. • Use aldosterone receptor blocker. • Consider surgical removal of the adrenal tumor.
Diagnostic Red Flags for Hyperaldosteronism
• Hypokalemia with no obvious cause, which may not respond well to supplementation. • Hypophosphatemia +/- metabolic alkalosis despite azotemia. • Hypertension that is difficult to control with standard doses of medications. • Hypertension without concurrent cardiac or thyroid disease.
Take-Home Messages for Practice Team Members
• Signs of PHA can be subtle in the early stages. • Blood pressure measurement should be a standard of care for adult cats at least annually, and any time a middle-age to older cat presents with nonspecific clinical signs.

PHA, primary hyperaldosteronism.

owner. Hypertension before this catastrophic stage may cause nonspecific changes in behavior such as lethargy, hiding, and irritability.

Physical examination findings in cats with PHA may be related to hypokalemia, systemic hypertension, or both. Muscle weakness and atrophy may be present. Chronic kidney disease (CKD) is a frequent comorbidity and can exacerbate the clinical impact of PHA. Minimum database and Doppler blood pressure measurement should be performed on cats with suspected PHA. Diagnostic imaging with abdominal ultrasound (or cross-sectional imaging) may reveal an adrenal mass. Ultrasound evaluation may reveal a unilateral adrenal mass, up to 5 cm in diameter, but in some cases the adrenal glands may appear normal.[77] Plasma aldosterone testing is currently the most readily available and reliable laboratory diagnostic tool, and a single very high value may be confirmatory. More complex testing may be needed in equivocal cases. Blood and urine changes consistent with CKD may also be present and must be addressed.

Confirmation of unilateral or bilateral disease is important, as it will influence treatment decisions.[74] Surgical removal of the affected adrenal gland is the treatment of choice for unilateral disease but may not always be an option.[78] Affected cats need to be stabilized medically before surgical intervention. Medical treatment is focused on resolution of the hypokalemia and SHT. Potassium supplementation, usually with potassium gluconate, is necessary, and higher-than-standard doses may be required to restore normal serum potassium concentrations. The aldosterone receptor blocker spironolactone at 1–2 mg/kg given twice daily should be used to help control hypokalemia. SHT must be corrected. Amlodipine administered at 0.625–1.25 mg per cat per day is an effective and affordable calcium channel blocker that is frequently used for SHT.

Feline Hypothyroidism

Although naturally occurring hypothyroidism in cats occurs rarely compared with its incidence in dogs,[79] it is occasionally reported in this species. A single low T4 level should be interpreted in light of the entire clinical picture because nonthyroidal illness can lead to reductions of serum T4 levels. The magnitude of serum T4 suppression is proportionate to the severity of the underlying disease. Final interpretation of thyroid function should be made when any nonthyroidal illness is stabilized, as well as in relation to the cat's clinical presentation.

TABLE 11

Clinical Signs of Feline Hypothyroidism

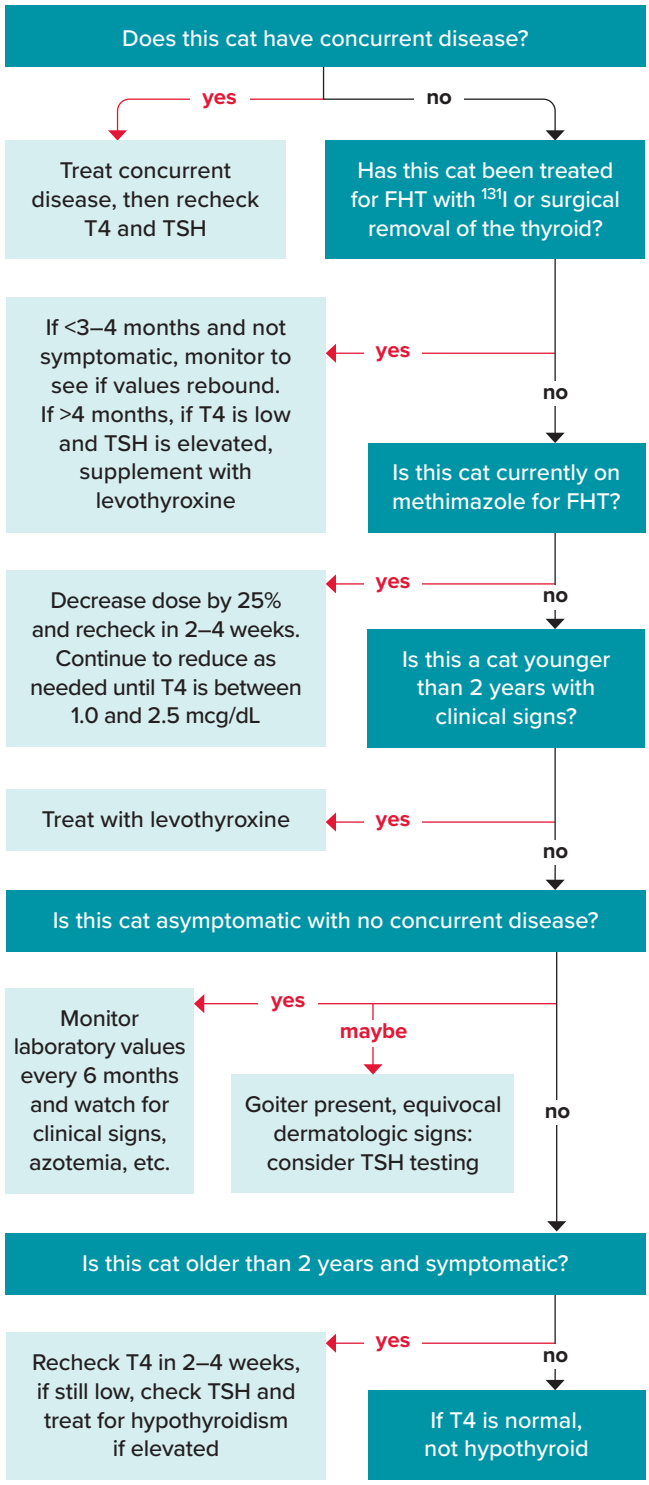
Congenital Disease
• Slow growth rate • Short limbs • Broad head • Lethargy • Constipation • Mental dullness • Retained deciduous teeth • Gingival overgrowth • Retained kitten hair coat
Iatrogenic or Adult-Onset Disease
• Lethargy • Weight gain, obesity • Seborrhea, poor haircoat • Poor regrowth of hair • Inappetence • Bradycardia

Clinical signs of feline hypothyroidism are shown in Table 11. Congenital hypothyroidism is usually identified in cats younger than 1 yr of age and most frequently in kittens younger than 8 mo. Affected kittens are usually stocky, with shorter limbs and a broader-than-usual head and neck. Lethargy, constipation, retained deciduous teeth, abnormal hair coat, and thickened gingiva are common findings.[76]

Diagnosis of hypothyroidism requires demonstration of a low serum T4 (<0.8 mcg/dL) and elevated TSH concentrations. Demonstration of low serum fT4 levels may also suggest hypothyroidism. A commercially available feline-specific TSH test was recently released; however, the historically used canine TSH test will also be elevated in cats with hypothyroidism.[68] In contrast to hypothyroidism in dogs, cats with naturally occurring hypothyroidism are more likely to be azotemic.[80] Figure 1 shows a diagnostic and treatment algorithm for deciding if a low T4 indicates a patient has feline hypothyroidism.

Treatment of hypothyroidism in cats is straightforward and similar to treatment in dogs. Levothyroxine sodium is recommended, with an initial dose range of 0.05–0.1 mg daily. The dosage is adjusted to target T4 levels between 1.0 and 3.0 mcg/dL; however, clinical signs may persist for 2–3 mo before responding to treatment.

Adult-onset hypothyroidism, although rare, may in fact be underdiagnosed in cats.[81] Even if that proves to be true, it is still an



FHT, feline hyperthyroidism; T4, thyroxine; TSH, thyroid-stimulating hormone level.

FIGURE 1

Decision Tree for Feline Hypothyroidism Diagnosis and Treatment.

extremely uncommon problem. Treatment should only be considered for cats with repeatable laboratory abnormalities and clinical signs consistent with hypothyroidism, such as lethargy, poor hair coat, and obesity. Confirmation of decreased serum T4 on more than one occasion, along with elevated TSH levels, is required to establish the diagnosis.

Iatrogenic hypothyroidism is caused by overdosing with antithyroid drugs such as methimazole, surgical removal of the thyroid glands, or ^{131}I treatment. Once patients have been stabilized on methimazole, monitoring at least every 6 mo will ensure proper thyroid control and avoidance of hypothyroidism. When treating with ^{131}I, consideration should be given to the T4 and TSH levels and the ^{131}I should be dosed appropriately.[82] Failing to recognize and address iatrogenic hypothyroidism can contribute to decreased renal function.[83] Maintaining T4 levels between 1.0 and 2.5 mcg/dL is ideal, and treatment should be initiated for patients with T4 values $<$1.0 mcg/dL and an elevated TSH level. Additionally, cats with T4 levels within the reference range but an elevated TSH who develop a new or progressive azotemia may benefit from methimazole dose reduction or levothyroxine supplementation if surgically or ^{131}I treated.

Feline Hyperadrenocorticism/Hypercortisolism

Hyperadrenocorticism (HAC), also referred to as hypercortisolism or Cushing's syndrome, is an infrequent diagnosis of cats. Similar to dogs, cats usually have pituitary-dependent HAC, and the hormonal mechanism of action is the same as in dogs. Clinical signs are due to the excess circulating glucocorticoid levels. Cats seem to be rarely negatively affected by chronic use of exogenous glucocorticoids, so the incidence of iatrogenic Cushing's syndrome in cats is much less frequent compared with dogs.[84]

HAC usually affects middle-aged to older cats, with the majority having concurrent diabetes mellitus that may be considered difficult to regulate. It is important to note that most difficult diabetic cases do not have HAC, and other causes of poor diabetic regulation should be pursued first. Clinical signs of HAC in cats are often nonspecific and include weakness, abdominal distension, and dermatological issues such as fragile skin and failure to regrow hair. Cats with concurrent diabetes mellitus are usually polyuric, polydipsic, and polyphagic, but these signs reflect persistent hyperglycemia rather than CS per se. Weight loss, lethargy, and gastrointestinal signs are possible but uncommon.

A minimum database will most commonly show hyperglycemia and glucosuria. Changes that are common in canine HAC are not as predictable in feline patients. Alkaline phosphatase levels are usually normal in cats who lack the steroid-induced isoenzyme, and hypercholesterolemia may be present. A stress leukogram is present in only half of feline cases. Definitive diagnosis in cats may be challenging, with the most reliable diagnosis coming from the LDDST. It is important to note that dexamethasone dosing for cats is greater than the effective canine dose. Cats must be dosed at 0.1 mg/kg dexamethasone IV.[82] The interpretative criteria are similar to those used in dogs, with a lack of suppression at 4 or 8 hr after administration confirming the diagnosis of HAC. UCCR testing may also be used for initial screening. At least two morning samples should be collected at home by the owner and submitted for evaluation.[85] A positive result from UCCR testing should be followed up with an LDDST, but a negative result likely rules out the diagnosis of HAC. An ACTH stimulation test is not recommended as a diagnostic tool in cats because of its poor sensitivity to detect feline HAC compared with the other available testing.[85]

Differentiation testing to determine if the HAC is caused by a pituitary tumor or adrenal tumor can be considered, as adrenalectomy may be curative in cats with unilateral adrenal tumors. Radiation therapy may be beneficial in cats with PDH.

Medical treatment with trilostane is the mainstay of HAC treatment in cats, with a recommended dosing of ~1 mg/kg given two to three times daily with food.[83] The licensed product may be reformulated if doses significantly less than 5 mg per dose are needed. The goal of treatment for feline HAC is control of clinical signs, and strict monitoring of cortisol levels may not be critical for treatment success. Improvement of weight, polyuria/polydipsia, polyphagia, and overall quality of life are the primary treatment goals. Laboratory monitoring with CBC, biochemical profiles, and urinalysis 7–14 days after starting trilostane and every 3–4 mo thereafter is recommended. If cortisol monitoring is pursued, the UCCR testing and ACTH stimulation test have been most commonly used to ensure trilostane is not leading to hypocortisolism. Final decisions on dosing, however, should be based on clinical assessment of the cat by both the veterinarian and the owner, the status of any concurrent disease, and the prevention of hypocortisolism.

Clinical Tips

- Poorly regulated diabetes in cats usually has an etiology other than HAC.
- Compared with the canine dose for LDDST, a higher dexamethasone dose is needed in cats: 0.1 mg/kg of dexamethasone is consistently effective in suppressing healthy cats but not cats with HAC.[86]
- Three-times-a-day dosing of trilostane may be needed to reach therapeutic doses with standard capsule sizes.
- Reformulation of the licensed product may be required for smaller doses.

- Clinical evaluation of the cat and any concurrent diseases may be more important than targeted monitoring of adrenal function.

The Team Approach

From initial patient presentation to long-term management, the pet owner interacts with every veterinary health care team member. Embracing a team-based approach can help establish clients' trust, promote communication and compliance, and improve overall patient care and quality of life.

Receptionists and client-service coordinators are often the first interaction the pet owner will have with the veterinary practice. Developing communication resources and telephone triage skills will help the nonclinical staff determine appropriate scheduling for ill patients and those requiring ongoing monitoring with timed testing or even potentially life-threatening situations.

The patient history that is obtained by the credentialed veterinary technician or veterinary assistant plays an essential role in veterinary case management for endocrinopathies. The patient history focuses on the pet's health from the point of view of the pet owner, which is invaluable as this information cannot be wholly determined by physical examination and diagnostic test results alone. An accurate history is helpful in determining the duration and severity of clinical signs, developing a problem list or prioritizing differentials, and monitoring a patient's response to therapeutic interventions. For example, knowing the likelihood of toxin exposure may help the veterinarian assess a patient in a hypoadrenocortical crisis, when the possibility of an acute kidney injury may confound the diagnosis.

Communication tips on how to take a quality patient history:

- Encourage the use of a pet owner questionnaire.
- Standardized history taking may promote continuity of care and monitoring of trends.
- Templates can be tailored for different situations—wellness, sick visits, ongoing monitoring for chronic diseases, etc.
- Address clients in a clear and courteous manner.
- Speak respectfully and avoid using medical jargon or slang.
- Start with open-ended questions.
- Establish the presenting complaint and pet owner's concerns with questions such as, "Can you describe to me what happened?" or "What brings you in today?"
- Endeavor not to interrupt the pet owner, as valuable information may be missed.
- After identifying the presenting complaint, progress to more focused closed-ended questions to clarify the situation, such as, "How long has this been happening?" or "How often does this occur?"
- Allow for pauses.
- Let the client gather their thoughts. Try not to rush them to fill the silence.
- Practice positive nonverbal communication. Use open body postures, direct eye contact, and head nodding.
- Engage in reflective listening.
    - After the client finishes talking, reflect on what was heard and ask if the situation has been understood correctly. For example, "Annabelle vomited five times since yesterday; is that correct?"
- Express empathy.
    - When talking to pet owners, the veterinary health care team should be able to understand the owner's situation and be able to communicate that to them. For example, "I know you care for Simon, and I understand this can be overwhelming."

In addition to acquiring a patient history from the owner regarding the presenting complaint, one must also inquire about the general status of the pet (including diet) and past pertinent medical history and obtain an accurate medication history. When asking about medications, one must be clear to specifically ask about preventives, over-the-counter medications, supplements or nutraceuticals, and any topical medications. Owners often only think of oral prescription medications and may not think to divulge important information, such as the use of topical exogenous corticosteroid products.

Clear communication with the pet owner and the veterinary team facilitates ongoing care and monitoring. Without proper communication and established protocols, scheduling something as simple as an ACTHST can be problematic if the owner, client-service coordinator, credentialed veterinary technician, or veterinary assistant does not know when an ACTHST should begin after trilostane administration. Additionally, one must remember that dose adjustments are not made in a diagnostic vacuum. Clinical signs and physical examination are equally important factors in successful ongoing patient management.

As these patients visit the veterinary practice more frequently for monitoring, prioritizing patient comfort and reducing stress will go a long way in building the veterinary health care team's relationship with the pet and their owner. Not only will low-stress visits reinforce pet owner compliance for timely follow-up, but they will also encourage more reliable diagnostic results as stress can influence many endocrine-related diagnostics. For example, using devices such as butterfly catheters for ACTHST and LDDST to facilitate both obtaining a baseline sample and administering the appropriate medication with a single venipuncture has the benefit of reducing stress and minimizing discomfort and vessel trauma when compared with repeated venipuncture events.

Another example of prioritizing patient comfort to support consistent diagnostic values to monitor trends is blood pressure measurement. The *2018 ACVIM Consensus Statement: Guidelines for the*

Identification, Evaluation, and Management of Systemic Hypertension in Dogs and Cats includes a helpful protocol for accurate blood pressure measurement in small animal patients.[87]

Regardless of the endocrinopathy, the veterinary health care team is instrumental in educating the pet owner. For successful management, the client should have a basic understanding of the disease, the clinical signs, adverse events, long-term goals, and recommendations regarding treatment and ongoing care.

Conclusion

Canine and feline practitioners will inevitably encounter the endocrinopathies discussed in these guidelines. The clinical signs of these diseases are typically nonspecific and often highly variable and in some cases can be iatrogenic in origin. Early-stage disease can be subclinical. Adding to the complexity of endocrine disease is the possibility of comorbidities, some of which can be secondary to advancing age, as in the case of canine hypothyroidism and hypercortisolism and feline hyperthyroidism. Collectively, these factors place a premium on diagnostic testing and an accurate patient history to arrive at a diagnosis and effective treatment plan. Careful treatment monitoring is indicated in endocrinopathy management, including noting the presence or resolution of clinical signs, trends in endogenous hormone levels, and therapeutic dose adjustments. The guidelines are intended to help practitioners logically deconstruct the ambiguous presentations that often characterize endocrine diseases. The algorithm tables included in the guidelines are designed to enable practitioners to quickly work through a diagnostic and treatment progression to address these often-challenging cases.

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