



2019 WINTER MEETING

Sunday, February 10, 2019
Burlington Hilton Hotel

Patty Lathan, DVM, DACVIM

Associate Professor of Small Animal Internal Medicine
Mississippi State University
Lathan@cvm.msstate.edu

UPDATES IN ENDOCRINOLOGY

Generously sponsored by:



HOLD THE DATE!

VVMA SUMMER MEETING

Friday, June 21, 2019
Burlington Hilton Hotel
6 CE Credit Hours

Small Animal Topic TBD by your survey responses!

Bovine Topic TBD by your survey responses!

We listen to YOU! Please complete and return the survey in your registration packet to determine topics and speakers!

Thanks for being a VVMA Member!

We are pleased to welcome the following members who joined since our 2018 Summer Meeting

Charley Abernathy – BEVS
Ashley Ackert – Green Mountain Vet. Hospital
Dana Ames – West Mountain Animal Hospital
*Lauren Blume – Peak Veterinary Referral Ctr.
Shannon Bradley – Essex Veterinary Center
Earl Brady – Cold Hollow Veterinary Services
Adrian Flanders – Fitzgerald Animal Hospital
*Miranda Fritz – Mountain View Animal Hospital
*Jeanne Harding
Brian Hurley – Gardner Animal Care Center
Krista Jones
Andrew Koenitzer – Ark Veterinary Hospital
Kayla Miner – Affectionately Cats

Kathryn Miller – West River Valley Vet. Services
Nicole Poppenger – Animal Hospital of Hinesburg
Matthew Reimert – East Haven Veterinary Service
*Michael Romp – Vermont Air National Guard
Nicholas Sherman – Essex Veterinary Center
Allaire Smith-Miller
Lainie Springer – BEVS
Mallory Sullivan – BEVS
Kathereen Tamburello – Newport Vet. Hospital
Jaclyn Torzewski – VT-NH Veterinary Clinic
Elisabeth Zenger – BEVS
Courtney Zwahlen – Peak Veterinary Referral Ctr.

Congratulations new VVMA Life Members!

Life members are veterinarians who have been state VMA-dues paying members for thirty-five (twenty of which must be Vermont VMA membership years). Life members are exempt from Association dues but retain all privileges of membership. They also receive reduced registration rates at VVMA CE programs. Thank you to the following members who reached Life Member status this year. We appreciate your long-time commitment to the VVMA!

Steven Carey – Retired
*David Lamb – Vermont Equine Medical
Barbara LeClair – Riverbend Veterinary Clinic

*Chris Mangini – Retired
Steve Wadsworth – Northwest Veterinary Associates

*** Attending this 2019 Winter Meeting!**



88 Beech Street Essex Jct., VT 05452
802-878-6888 office
www.vtvets.org
kathy@vtvets.org

VVMA Mission:

Promoting excellence in veterinary medicine, animal well-being and public health through education, advocacy and outreach.

VVMA Vision:

To be the preeminent authority on veterinary medicine and animal well-being in Vermont.

VVMA Values:

Integrity, Service, Dedication, Compassion,
Inclusivity, Visionary Thinking, Life-Long Learning

For questions or more information on the VVMA, contact Executive Director Kathy Finnie.

2019 Winter Meeting Exhibitors

Thank you for your support of our Meeting!

Boehringer-Ingelheim Sponsor of Dr. Kurt Selberg	Kara Kirchherr Paige Willson	kara.kirchherr@boeringer-ingelheim.com page.willson@boeringer-ingelheim.com
Burlington Emergency & Vet. Specialists	Whitney Durivage Brenna Mousaw	whitbier@bevsvt.com b.mousaw@bevsvt.com
Christian Veterinary Mission	Dr. Amy St. Denis	amystdenis@myfairpoint.net
Dechra Sponsor of Dr. Patty Lathan	Lauren Baker Scott Rowe	lauren.baker@dechra.com scott.rowe@dechra.com
Eastern States Compounding Pharmacy	Kim Johnson	kimberley@easternstatesrx.com
Elanco Animal Health Sponsor of VVMA Reception	Elizabeth Hall	elizabetholsonhall@elanco.com
Ethos – Peak Veterinary Referral Ctr.	Linda Story	lstory@ethosvet.com
Haun Specialty Gases	Jamie Badger Erik Eliason	jbadger@thehaunedge.com eeliason@thehaunedge.com
Henry Schein Animal Health	Martha Rose Jazz Heath	mrose@henryscheinvet.com jheath@henryscheinvet.com
Hill's Pet Nutrition	Dr. Andrew Hagner	Andrew_hagner@hillspet.com
Idexx Sponsor of Dr. Armell De Laforcade	Colin Dudnake Bob Lynch Carmelita Castellon	Colin-dudnake@idexx.com robert-lynch@idexx.com Carmelita-castellon@idexx.com
K-Laser	Barry Levine	blevine@k-laser.com
Merry Xray	Jon Nealy Chuck Gilroy	jon.nealy@merryxray.com chuck.gilroy@merryxray.com
MWI Veterinary Supply	Danielle Preece	dpreece@mwianimalhealth.com
Nestle Purina PetCare Company	Lauren Koron	lauren.koron@purina.nestle.com
Patterson Veterinary Supply	George White Art Yanke	george.white@pattersonvet.com art.yanke@pattersonvet.com

Phibro Animal Health
Sponsor of Dr. Mike Hutjens

Seth Johnson

seth.johnson@pahc.com

Purina Animal Nutrition

Kelsey Bornt
Rusty Suher

kbornt@landolakes.com
hdsuher@landolakes.com

Universal Imaging

Michael McElhinney

mmcelinney@universalimaging.com

VetCor

Bryan Brackett

bbrackett@vetcor.com

VetriScience Laboratories

Kelley Lucarell
Patti Rosenberg

klucarell@foodsciencecorp.com
prosenberg@foodsciencecorp.com

Thank you also to

- CareCredit for sponsoring Wendy Myers' presentation
- Zoetis for sponsoring Sunday morning's break



SAME GREAT TEAM. BRAND NEW, ULTRAMODERN LOCATION.

WE ARE RELOCATING OUR HOSPITAL IN
MARCH 2019, RIGHT DOWN THE STREET:
1417 MARSHALL AVENUE • WILLISTON, VT



17,000 sq ft • 13 exam rooms • 3 high-tech surgery suites • CT/MRI units • 60+ experienced and compassionate team members

**We are Vermont's only specialty and 24/7 emergency
animal hospital, providing a level of advanced care
you simply won't find anyplace else in the state.**

NOTES

Treatment of Canine Hyperadrenocorticism

Patty A Lathan, VMD, MS, DACVIM

Mississippi State University, Starkville, MS, USA

Adrenal Tumor

Treatment of adrenal tumors depends on the presence of metastasis and invasion of adjacent structures. Ideally, ATs are surgically removed. However, if the mass is surgically non-resectable due to the invasiveness of the tumor, an unsuitable anesthetic candidate, or owner choice, medical therapy may be attempted. Mitotane and trilostane have both been used in these cases. Due to its adrenocorticolytic mechanism of action, mitotane may be preferable if metastasis is present. However, survival times between patients treated with mitotane and trilostane do not appear to be different (Helm 2011).

Pituitary-Dependent Hyperadrenocorticism

Possible treatment modalities for PDH include hypophysectomy, medical (mitotane or trilostane), and radiation therapy. Since hypophysectomy is only performed in very limited locations (and I have no experience with it), it will not be discussed further in these notes.

The goal of medical therapy is to decrease cortisol secretion from the adrenal cortex, thus decreasing the changes associated with HAC. The goal of radiation therapy is to shrink a pituitary tumor, either because of current neurologic signs of a macroadenoma, or to help prevent growth of the tumor. Traditional radiation therapy does NOT usually decrease cortisol secretion, so medication must be used in addition.

Medical Therapy

Mitotane and trilostane are the drugs currently recommended for medical treatment of PDH. Deprenyl and ketoconazole have also been recommended in the past. Deprenyl increases dopamine concentrations in the intermediate lobe, which decreases ACTH secretion from that lobe. However, since the majority of pituitary tumors in dogs (80-85%) arise from the anterior lobe, and dopamine does not affect ACTH secretion from the anterior lobe, the efficacy of deprenyl is less predictable and more controversial than the efficacy of mitotane and trilostane. Ketoconazole inhibits the synthesis of cortisol; however, due to its side effects and lesser efficacy, it is no longer a drug of choice for PDH.

Mitotane is a chemotherapeutic drug that induces adrenocorticolysis. Management of PDH using mitotane consists of two different phases—induction and maintenance. During the induction phase, mitotane is usually given for 7-10 days at a dose of 50 mg/kg/day, divided. When the dog shows any decrease in clinical signs (drinking, urinating, appetite) or signs of cortisol deficiency (vomiting, diarrhea, lethargy), the dog is given an ACTH stimulation test. The recommended target post-stimulation cortisol concentration range is 2-5 µg/dL. Once induction is complete (achieved the recommended post-stim cortisol), the maintenance phase may be initiated. The dog is given about 50 mg/kg/week, divided. The more the dose is divided (2, 3, or 4 times per week), the less likely the patient is to have side effects associated with

drug administration itself. An ACTH stimulation test is performed 1 month after starting the maintenance phase, then once every 3 months, and when clinical signs of HAC or hypoadrenocorticism appear.

Mitotane is usually selective in that it only destroys the *zona fasciculata* and *reticularis* of the adrenal cortex. Thus, most side effects are due to cortisol deficiency. However, at higher doses, and in patients that are more sensitive to it, mitotane can also destroy the *zona glomerulosa*. In these cases, the patient may turn into a glucocorticoid and mineralocorticoid-deficient Addisonian. It is IMPERATIVE that owners follow dosing and testing instructions closely, and contact you if the dog shows any signs of hypoadrenocorticism, such as lethargy, inappetance, vomiting, or diarrhea. Whereas HAC is chronic in nature, hypoadrenocorticism can be rapidly fatal. If in doubt, the owner should discontinue mitotane therapy until able to contact a vet. Owners may be given prednisone to use in case of an emergency.

Trilostane is an enzyme inhibitor that decreases production of cortisol, and, to a lesser extent, aldosterone and other steroids. Based on its mechanism of action, it should not cause adrenal necrosis in the same way as mitotane, but trilostane can still lead to Addisonian crisis due to hypocortisolemia. Additionally, trilostane has been reported to cause idiosyncratic adrenal necrosis in dogs (resulting in both glucocorticoid and mineralocorticoid deficiency), although this is rare. Survival times for PDH patients treated with trilostane and mitotane are similar (approximately 2 years) (Barker EN 2005). However, in my experience, if a veterinarian has little experience using either mitotane or trilostane, trilostane is easier to learn to use.

There is no induction phase involved with the administration of trilostane. Dogs are started on 2-3 mg/kg totally daily dose (SID or divided and given BID), and seen for a recheck 10-14 days later. During rechecks, it is important to assess the clinical signs of the patient based on the owners' assessment of how much the dog is drinking, urinating, and eating. Any lethargy, diarrhea, vomiting, or refusal to eat should also be noted. Although the ACTH stimulation test has been used to assess treatment efficacy for the past two decades, recent evidence suggests that a pre-pill cortisol concentration correlates with clinical signs at least as well as an ACTH stimulation test. However, ACTH stimulation tests are still sometimes necessary, particularly if the patient is showing any signs of illness consistent with Addison's disease.

The pre-pill cortisol is measured from blood taken just prior to the time that the morning pill is administered. If the patient is well-controlled and the pre-pill cortisol is >1.4 ug/dL, continuing on the current dose is probably safe. However, if the value is <1.4 ug/dL, or the dog is showing any signs of illness, an ACTH stimulation test is indicated. If the patient is not clinically controlled (still polyuric, polydipsic, and/or polyphagic), and the pre-pill cortisol is >3.0 ug/dL, it is likely safe to increase the dose by 10-20%, and recheck in 2-4 weeks. If the pre-pill cortisol is <3.0 ug/dL, I recommend performing an ACTH stimulation test prior to increasing the dose.

An ACTH stimulation test can be used either instead of using pre-pill cortisol monitoring, or in addition to pre-pill cortisol monitoring. The test should be started 3-4 hours post-pill to assess cortisol levels at peak inhibition. Thus, the pill should be given in the morning if the dog is on SID dosing. The target post-stimulation cortisol concentration for a well-controlled dog is 2-6 ug/dL, but this MUST be interpreted in light of clinical signs. This range is flexible, depending

on clinical response; a dog that has been on trilostane for 6 months and is doing well with a post-stimulation value of 1.6 µg/dL may be fine, whereas a dog that has GI signs with a post-stimulation value of 2.1 µg/dL may need his dose decreased. Similar holds true at the upper end of the range.

Of note, the effects of a given dose of trilostane often increase even after the first two weeks of therapy. For example, if a dog is on 30 mg once daily and has a post-ACTH stimulation cortisol value of 9 ug/dL at 14 days, this may decrease to 5.5 ug/dL two weeks later, even if the dog is on the same dose. Thus, if the 14 day post-stim cortisol is <10 ug/dL following initiation of trilostane, I usually wait to increase the dose until after the next ACTH stimulation test two weeks later. Depending on those ACTH stim results, the trilostane dose may be increased or decreased by 10-20%.

Each time the trilostane dose is changed, a baseline cortisol and/or ACTH stimulation test should be run about 10-14 days later. After the appropriate dose is determined, the dog should return for monitoring (assessment of clinical signs AND pre-pill cortisol +/- ACTH stimulation test) two weeks later, 3 months later, and then every 3-6 months. The dose of trilostane may need to be increased, as patients seem to get more resistant to it with time.

Additionally, adrenocortical necrosis is possible at any point during therapy. It MUST be stressed that owners still need to be cautioned that this drug can also lead to disastrous consequences if appropriate monitoring is not followed.

Dogs seem to get regulated more quickly on twice-daily dosing. Some dogs aren't as well-controlled on once-daily trilostane dosing, likely because the duration of efficacy of trilostane is variable, from 10-18 hrs. In these dogs, the dose may be divided and given BID. Dogs on the BID protocol generally need a lower total daily dose than those on SID dosing, and their clinical signs are often better controlled. Because of the increased efficacy of trilostane based on ACTH stimulation tests, some authors prefer to start patients on BID dosing (1-2 mg/kg BID).

Radiation Therapy

As mentioned above, radiation therapy can be used to treat neurologic signs secondary to a pituitary macroadenoma. Radiation is also indicated to treat moderately-sized pituitary tumors to prevent them from causing clinical signs later. Radiation does NOT predictably control the secretion of cortisol; this must be achieved with one of the aforementioned medications.

Clearly, the financial, emotional, and time commitments associated with radiation therapy prevent the vast majority of owners from pursuing it. However, CT/MRI should be offered to owners of all dogs with PDH that would consider radiation therapy. As our experience with treatment of HAC increases, patients are living longer, and this extended life span gives the macroadenomas time to grow and cause clinical signs of neurologic disease. One study (Bertoy EH, et al. JAVMA 208:1268,1996) showed that 50% of dogs with PDH had visible tumors at the time of diagnosis. Of these, 25% died within the next year. Of the 50% of the dogs with microadenomas, 40% had macroadenomas a year later. Radiation therapy can shrink and/or inhibit growth of the tumors.

References

Helm JR, et al. A comparison of factors that influence survival in dogs with adrenal-dependent hyperadrenocorticism treated with mitotane or trilostane. *J Vet Intern Med* 2011; 25:251-260.

Barker EN, et al. A comparison of the survival times of dogs treated with mitotane or trilostane for pituitary-dependent hyperadrenocorticism. *J Vet Intern Med* 2005; 19:810-815.

Bertoy EH, et al. One-year follow-up evaluation of magnetic resonance imaging of the brain in dogs with pituitary-dependent hyperadrenocorticism. *J Am Vet Med Assoc* 1996; 208:1268-1273.

Macfarlane L, Parkin T, Ramsey I. Pre-trilostane and three-hour post-trilostane cortisol to monitor trilostane therapy in dogs. *Vet Rec* 2016.

Updates for the Management of Canine Hypoadrenocorticism

Patty Lathan, VMD, MS, DACVIM

Mississippi State University

Starkville, MS, USA

Hypoadrenocorticism (“Addison’s disease”) is an uncommon disease in dogs. However, because of the potential for acute death in dogs with severe acid/base and electrolyte abnormalities, and the excellent prognosis with treatment, prompt diagnosis is crucial.

BACKGROUND

The adrenal cortex is divided into 3 different layers. In order of outermost to innermost, they are the *zona glomerulosa*, *zona fasciculata*, and *zona reticularis*. Only the *zona glomerulosa* can make aldosterone, while the *z. fasciculata* and *reticularis* are responsible for the production of cortisol. Cortisol’s function is primarily catabolic, in that it stimulates the breakdown of fat, muscle, and glycogen for use in gluconeogenesis. It’s one of the four “anti-insulin” hormones that protect the body from hypoglycemia.

Cortisol secretion is regulated by the hypothalamic-pituitary-adrenal axis (HPAA). Physiologic, psychologic, and/or emotional stress initially stimulates the hypothalamus to secrete CRH (corticotrophin releasing hormone). CRH then stimulates the pituitary gland to release adrenocorticotrophic hormone (ACTH) into systemic circulation. When ACTH reaches the adrenal cortex, it stimulates the synthesis of cortisol.

As with other endocrine axes, the synthesis of cortisol is controlled by feedback inhibition. Cortisol itself inhibits further release of CRH and ACTH. Thus, when an abundance of cortisol is present in the body, that cortisol prevents additional stimulation of cortisol secretion in normal animals.

Aldosterone is a mineralocorticoid that stimulates the resorption of sodium, chloride, and water; and excretion of potassium, from the distal renal tubules. A deficiency in aldosterone can lead to hyponatremia, hypochloremia, hypovolemia, and hyperkalemia. Secretion of aldosterone is controlled by the renin-angiotensin-aldosterone (RAS) system. Note that physiologic doses of ACTH do NOT appear to play a significant role in the regulation of aldosterone synthesis; therefore, pituitary pathology resulting in ACTH deficiency should not result in aldosterone deficiency.

ETIOLOGY

In dogs, Addison’s is most commonly caused by adrenocortical failure, usually secondary to immune-mediated destruction of >90% of the adrenal cortex. Most patients exhibit signs of both cortisol and aldosterone deficiency. Neoplastic, infectious, and inflammatory infiltration of both adrenal cortices may also result in combined deficiency. Secondary hypoadrenocorticism due to ACTH deficiency results in isolated cortisol deficiency. Iatrogenic administration of exogenous glucocorticoids is the most common cause of secondary hypoadrenocorticism; however, pituitary neoplasia or trauma, in addition to idiopathic causes, may also result in secondary hypoadrenocorticism.

In patients with “atypical” hypoadrenocorticism clinical signs of cortisol deficiency occur without concurrent electrolyte abnormalities. The etiology of atypical Addison’s is unclear; ACTH deficiency has been ruled out in most cases. It may be the result of partial immune-mediated destruction of the adrenal cortex, sparing the zona glomerulosa. Alternatively, some dogs with aldosterone deficiency may compensate via an unknown mechanism. Although some have speculated that atypical hypoadrenocorticism is simply an early manifestation of “typical” hypoadrenocorticism, many patients never lose their ability to secrete aldosterone.

CLINICAL PRESENTATION AND CLINICOPATHOLOGIC ABNORMALITIES

Clinical presentation of hypoadrenocortical patients varies from patients with chronic “failure to thrive” (ADR) and/or gastrointestinal signs (anorexia, vomiting, diarrhea, melena, etc.), to patients that present acutely in hypovolemic shock. Both groups of patients may have a history of improvement with fluid administration and/or glucocorticoid therapy.

Physical examination findings can also vary from almost normal to hypovolemic shock. Hyponatremia and hyperkalemia are the classic laboratory findings in dogs. However, these findings may be absent early in the disease process, and in dogs with atypical hypoadrenocorticism. Additionally, atypical Addisonians rarely present in hypovolemic shock; however, excessive gastrointestinal blood loss can lead to hypovolemic shock in these patients.

Regurgitation may be seen in rare Addisonian patients with megaesophagus, and seizures have also been reported secondary to hypoglycemia. Polyuria and polydipsia occur infrequently in dogs with hypoadrenocorticism; the mechanism is unknown.

Additional laboratory abnormalities may include azotemia, hypoglycemia, hyponatremia, hypocholesterolemia, hypercalcemia and metabolic acidosis (decreased tCO₂/bicarbonate). Hypoadrenocorticism should be considered in patients that present for signs of hypoglycemia (such as seizures) and hypercalcemia. Because most patients also have a specific gravity <1.030, azotemic patients can be incorrectly diagnosed with primary renal failure. In these cases, the patient’s history and rapid response to fluid therapy should increase suspicion of hypoadrenocorticism.

Patients exposed to cortisol often exhibit neutrophilia and lymphopenia (“stress leukogram”). In the absence of cortisol, such as with hypoadrenocorticism, patients may be predicted to have neutropenia, lymphocytosis, and eosinophilia. In fact, these specific changes don’t occur very frequently in Addisonian patients. However, a number of Addisonians do have a “lack of a stress leukogram,” meaning that they do not have neutrophilia or lymphopenia. In a clinically ill patient, the findings of normal neutrophil and/or lymphocyte counts, with or without eosinophilia, are unexpected, and may raise suspicion of hypoadrenocorticism.

ADDITIONAL DIAGNOSTICS

In cases of moderate to severe hyperkalemia, an ECG may reveal spiked T-waves, absent p-waves, increased P-R interval, and/or bradycardia. Other basic diagnostic findings in hypoadrenocortical dogs are non-specific. Thoracic radiographs may reveal microcardia

(consistent with hypovolemia) or megaesophagus. Abdominal ultrasound may reveal small adrenal glands.

DEFINITIVE DIAGNOSIS

Definitive diagnosis relies on results of an ACTH-stimulation test in both typical and atypical Addisonians. Post-stimulation cortisol samples of $<2 \mu\text{g/dL}$ are consistent with hypoadrenocorticism, although rare patients may have stim results between 2 and $3 \mu\text{g/dL}$. Steroids given days prior to the test may blunt the response, and it is not uncommon for a dog with a history of recent glucocorticoid administration to have a post-stimulation cortisol of $2.5 - 5.0 \mu\text{g/dL}$. Most synthetic glucocorticoids (including prednisone and methylprednisolone) will interfere with the cortisol assay itself, and may cause a falsely elevated cortisol result. However, dexamethasone does not interfere with the cortisol assay, and may be given prior to or during the ACTH stimulation test, if necessary.

BASELINE CORTISOL—FOR RULE-OUT PURPOSES ONLY!

Although definitive diagnosis of Addison's requires an ACTH stimulation test, the disease can be RULED-OUT by checking baseline cortisol values. If the baseline cortisol is $>2 \mu\text{g/dL}$, the dog does not have hypoadrenocorticism (there are exceptionally RARE cases that could have a value from $2-3 \mu\text{g/dL}$). If the baseline cortisol is $<2 \mu\text{g/dL}$, an ACTH stimulation test MUST be run to confirm the diagnosis. The baseline cortisol is most useful in patients without electrolyte abnormalities that may be suspected of atypical hypoadrenocorticism because of chronic GI signs. Since it does not require the purchase of synthetic ACTH, it is much less expensive than the ACTH stimulation test.

TREATMENT—TYPICAL HYPOADRENOCORTICISM

Treatment of hypoadrenocorticism depends on the presentation of the patient. If they present in hypovolemic shock ("Addisonian crisis"), diagnosis is usually unknown initially, and treatment is generally similar to that for any patient in hypovolemic shock. The first priorities in stabilizing a patient in Addisonian crisis are to correct the hypovolemia and the hyperkalemia, since these conditions are most likely to be fatal if not treated immediately. Although 0.9% NaCl is recommended because of its sodium content, isotonic crystalloids such as Normosol-R and Lactated Ringer's Solution may also be used. Hypoglycemic patients should be treated with dextrose.

If the dog is moderately hyperkalemic, the hyperkalemia will likely be corrected with fluid therapy alone. However, if the hyperkalemia is severe ($>8.5 \text{ mEq/L}$) or causing ECG changes, additional therapy may be warranted. A 10% solution of calcium gluconate ($0.5-1.5 \text{ mL/kg}$, or 2 to 10 mL/dog) may be administered intravenously over 10 to 15 minutes while monitoring for ECG changes associated with hypercalcemia. Although the effect is almost immediate, it lasts for only about 10 to 30 minutes. This treatment is cardioprotective and does NOT lower the potassium concentration. Simultaneous intravenous administration of dextrose (1 g/unit of insulin) and regular (R) insulin (0.2 U/kg) will decrease potassium levels within 15 to 30 minutes. A 5% dextrose solution in 0.9% sodium chloride should be administered after insulin treatment to alleviate hypoglycemia.

Glucocorticoids should be given to a patient during the crisis. Dexamethasone, 0.2 mg/kg, may be given initially. Although this dose is lower than recommended in some drug resources, it is equivalent to approximately 1.5 mg/kg of prednisone and is more than adequate. This dose is often given twice the first day, and then cut in half for the next two days. As soon as the patient is eating, he may be given oral prednisone. While in the hospital, the patient needs more than the normal physiologic dose (~0.2 mg/kg/day); approximately 1 mg/kg/day is commonly used. The dog may go home on an increased dose of 0.5 mg/kg/day for a couple of days, and then be tapered to around 0.1 – 0.3 mg/kg/day. This dose is adjusted based on the clinical signs of the dog (activity level, appetite, gastrointestinal signs), combined with the avoidance of side effects from the prednisone, such as PU/PD. The author frequently tapers to doses lower than 0.1 mg/kg (such as 0.05 mg/kg), especially in large dogs, based on clinical signs and side effects. Note that once an ACTH stimulation test confirms naturally-occurring hypoadrenocorticism, it does not need to be repeated and is not used in monitoring prednisone dose.

Following confirmation of hypoadrenocorticism, the dog should also be started on a mineralocorticoid replacement. The author's preference is desoxycorticosterone pivalate (DOCP). The label dose is 2.2 mg/kg, q25-28d, but recent studies and experience show that lower doses may be acceptable, particularly in large dogs. I usually start no higher than 1.5 mg/kg. Although the first dose may be given IM in case dehydration impedes SQ absorption, subsequent doses can usually be given SQ. Electrolyte values should be checked 14 days after injection to assess the dose, and immediately prior the next injection (25-28d) to assess duration of activity. Dose and frequency should then be modified based on these electrolyte values. Electrolytes should be rechecked every 3-6 months following dose stabilization.

Two FDA-approved DOCP formulations are available—Percorten-V[®] (Elanco) and Zycortal[®] (Dechra). The only differences between the two formulations are a different preservative is used in each, and that Zycortal[®] is labeled for SQ administration, while Percorten-V[®] is labeled for IM administration. In 1995, a study (McCaben, et al, *JAAHA*) established that Percorten-V[®] may be administered SQ, and there's no reason to believe that Zycortal[®] could not be administered IM, if necessary.

It is **IMPERATIVE** that owners be cautioned not to try to space out or skip DOCP injections without the advice of a veterinarian for financial reasons. This almost always leads to an Addisonian crisis eventually, which risks the patient's life and increases overall cost of treatment. Alternatively, fludrocortisone may be used as a mineralocorticoid supplement. It is oral and initially given at 0.02 mg/kg/d. It also has some corticosteroid activity. However, patients should be stabilized (ie, consistently normal electrolytes during rechecks) using a combination of fludrocortisone and prednisone. Then the prednisone dose can be tapered to the lowest effective dose. Approximately 50% of Addisonian dogs managed with fludrocortisone do not require long-term prednisone supplementation.

Management of a chronic Addisonian involves the administration of prednisone and a mineralocorticoid, as described above. Additional glucocorticoids, 2-3 times the normal dose, should be given when the dog is stressed, such as prior to veterinary visits (even for DOCP injections), or when there are visitors to the home.

TREATMENT—ATYPICAL HYPOADRENOCORTICISM

Treatment of atypical hypoadrenocorticism includes glucocorticoid replacement and supportive therapy. Depending on the presentation, patients with more chronic signs may be managed at home, whereas patients with more significant gastrointestinal signs will need hospitalization. The physiologic dose of prednisone is thought to be 0.1- 0.25 mg/kg, and stressed patients need between 2 and 10 times this dose. At diagnosis, I typically start these patients at about 1 mg/kg of prednisone per day to account for the stress of illness and hospitalization (or hospital visits). (If parenteral therapy is necessary, I use 0.10-0.15 mg/kg dexamethasone, as it has 7-8 times the glucocorticoid activity as prednisone.) This dose is slowly decreased so that the patient is receiving the physiologic dose of prednisone within a few days of returning home. Dose is adjusted based on the clinical signs. If the dog becomes PU/PD, the dose is decreased. If gastrointestinal signs increase, or the dog is lethargic overall, the dose is increased. Additionally, the prednisone dose must be increased if the patient experiences stress—such as a vet visit, houseguests, increased exercise (such as hunting), or unrelated illness.

Supportive therapy may include intravenous fluids, gastroprotectants, blood transfusion (if GI blood loss is severe), dextrose administration, etc., depending on the clinical presentation of the patient.

PROGNOSIS

The prognosis for good quality of life is excellent with prompt treatment of typical hypoadrenocorticism. Even hunting dogs can return to normal activity (with adjustment of prednisone dose), and patients have a normal life expectancy. Dogs with atypical hypoadrenocorticism also have a great prognosis, and some (approximately 10%, based on experience) develop mineralocorticoid deficiency following initial diagnosis. Thus, measurement of electrolytes one week, 1 month, and then every 3-6 months following diagnosis is recommended.

MONITORING DIABETIC DOGS & CATS: FOCUSING ON THE WHOLE PATIENT IN CLINIC & AT HOME

*Patty A. Lathan, VMD, MS, DACVIM
Mississippi State University
Mississippi State, MS, USA*

INTRODUCTION

Diabetes mellitus (DM) is the second most frequently diagnosed endocrine disorder in cats and dogs, with an incidence of at least 1 in 400. Whereas the pathophysiology of most cases of canine DM appears to most closely resemble that of human type 1 DM, most cases of feline DM are now believed to be more analogous to human type 2 DM. However, in contrast to people, recently diagnosed diabetic cats almost always require insulin therapy. As in people, there is probably a genetic predisposition to the development of dysfunctional beta cells and insulin resistance in cats. Multiple concurrent and inter-related processes then contribute to the eventual development of clinical DM in cats, including insulin resistance, amyloid deposition, and glucose toxicity.

SIGNALMENT AND CLINICAL SIGNS

DM is generally a disease of older cats, and males are predisposed. Middle-aged female dogs are predisposed, with higher incidence in miniature schnauzers, bichon frises, miniature poodles, and Samoyeds. Polyuria and polydipsia are the most frequent clinical signs. Weight loss and muscle wasting are also common, and may be accompanied by polyphagia, although polyphagia is less common in diabetic cats than dogs. Physical examination often reveals dehydration and poor, unkempt fur. Hindlimb weakness and/or plantigrade stance (“dropped hocks”), in addition to the client complaint of impaired jumping, occur in some diabetic cats with diabetic neuropathy. Diabetic cataracts develop within 6 months in most dogs, but are rare in diabetic cats. Patients with diabetic ketoacidosis exhibit various clinical signs, depending on the underlying cause.

DIAGNOSIS

Diagnosis of diabetes mellitus relies on the demonstration of persistent hyperglycemia and glucosuria, with clinical signs of DM. Unfortunately, this is not as straight-forward in cats as in dogs, due to stress hyperglycemia (SH). Blood glucose concentrations (BGs) in stressed, non-diabetic cats, are usually less than 250 mg/dL, although values greater than 400 mg/dL have been documented in sick, non-diabetic cats. BGs in untreated diabetic cats, however, are usually above 350 mg/dL, but some diabetic cats may have BGs as low as 200 mg/dL.

Differentiation between SH and DM in cats is achieved by a combination of the presence of clinical signs consistent with DM, glucosuria, repeat BG measurement, and fructosamine concentration. Owners of inside cats can usually identify PU/PD in their pets by the fact that they’re soaking the litter box, so the lack of this historical finding decreases the likelihood of DM. Almost all cats with DM have glucosuria (as long as the BG is persistently >250-280 mg/dL), whereas cats with SH rarely do. The absence of clinical signs and glucosuria is most consistent with stress hyperglycemia, whereas the presence of clinical signs and glucosuria is most consistent with DM. If a BG is rechecked a few hours later, it typically normalizes in cats

with SH. The fructosamine concentration, which correlates with BGs over the previous 2-3 weeks, should be assessed if the diagnosis is unclear. A high fructosamine concentration is consistent with DM, whereas cats with SH should have normal values.

In summary:

Most cats with DM: PU/PD, weight loss, BG>350 mg/dL at diagnosis, glucosuria, increased fructosamine

Most cats with SH: Not PU/PD, BG<250 mg/dL, no glucosuria, normal fructosamine

TREATMENT

The goals of treating diabetes include improvement of the patient's (and owner's) quality of life, control of clinical signs, avoidance of complications from diabetes (such as diabetic neuropathy) and from over-treatment with insulin (hypoglycemia), and diabetic remission (in cats). Proper treatment includes identifying and treating or eliminating any cause of insulin resistance (infection, obesity, etc.), dietary management, and insulin therapy.

Diet

Although large controlled studies are lacking, a high protein, low carbohydrate diet is generally recommended in diabetic cats. Canned food is ideal, as these diets are usually lower in carbohydrate content and are more filling due to the added water content. Several prescription diets have been formulated to meet low carbohydrate specifications (including Hill's m/d, Purina DM, and Royal Canin DS 44 dry). Given the higher caloric density of dry foods, the canned foods usually have lower carbohydrate contents and are preferred in obese patients. Weight loss cannot be over-emphasized, as obesity promotes insulin resistance. Obese cats are four times more likely to develop DM in the first place! Weight loss of 1-2% body weight per week should be achieved using food restriction. Exceptions to the use of low carbohydrate, high protein diets include patients with chronic renal failure and, potentially, patients with chronic pancreatitis.

Although high fiber diets have been recommended in dogs, they are not ideal for all diabetics. High fiber diets tend to cause weight loss, which is undesirable in dogs that are underweight or at an ideal body weight. In these dogs, a high quality maintenance dog food with a moderate fiber content is preferred.

Insulin Therapy

Newly-diagnosed cats should be treated with twice daily insulin injections (unless DKA is present) for best regulation and diabetic remission rate. Glargine (Lantus®), PZI (ProZinc®) and lente (Vetsulin®) insulins are all viable options. Glargine and PZI insulins appear to result in slightly higher remission rates than lente insulin. However, given the significant price differences, lente insulin is a practical option for owners with financial limitations. NPH is available, but is not recommended in cats due to short duration of action. The use of compounded PZI insulin is also not recommended. Although most cats will need twice daily injections, glargine is the insulin of choice if twice-daily therapy is not possible.

Dogs should also be treated with twice daily insulin injections, using a moderate acting insulin. Lente (Vetsulin®) and NPH (Neutral protamine Hagedorn, either Humulin N® or Novolin N®) are

most frequently used for first-line therapy (0.25 – 0.5U/kg BID). Most of my canine patients are started on lente insulin. Glargine and detemir have also been evaluated for use in dogs, and detemir is useful when the duration of lente or NPH is too short. Remember that detemir is more potent in dogs than in cats or people, so a starting dose of 0.1 U/kg BID is recommended.

MONITORING

There are several methods available for monitoring diabetic patients, including assessment of clinical signs, blood glucose curves (BGCs in clinic and at home), continuous blood glucose monitoring (specifically the FreeStyle Libre), fructosamine concentrations, and urine glucose measurement.

Clinical Signs

Since the primary goal of treating a diabetic patient is to control clinical signs, clinical signs should always be considered when assessing diabetic control. A stable diabetic patient should have normal water intake (<60 mL/kg/day) and urination, “normal” energy level, and a stable weight. Although weight loss is recommended in obese animals, it is preferably delayed until at least moderate diabetic control is achieved. Water intake directly correlates to blood glucose concentrations, and having the owner measure (and log) daily water intake gives them a way to be active in the management of their pet. Additionally, owners can assess urination by recording how many urine clumps are in a cat’s litterbox, or how many times a dog asks to go out during the day (and the middle of the night!). Cell phone apps are now available to help owners log daily water intake, food consumption, signs of illness, and at home BGC measurements, including Merck’s PetDiabetes App and the RVC Pet Diabetes App. Both apps allow the owner to email information directly to the veterinarian. The patient’s weight should be recorded and assessed at each veterinary visit. Note that all other monitoring modalities should be interpreted in light of the patient’s clinical signs and weight.

Blood Glucose Measurements

Blood glucose curves in clinic or in the hospital, and continuous blood glucose monitoring, are options for measuring blood glucose in diabetic patients.

Blood Glucose Curves

Traditionally, blood glucose curves have been used to help identify clinically-undetectable hypoglycemia, and can help determine an insulin’s duration of action. If the duration of activity is too short, that patient may benefit from a longer-acting insulin. BGCs are also helpful in determining whether it is safe to increase the patient’s insulin dose when clinical signs are present. They are particularly important when initially arriving at an insulin dose and when clinical signs return. Curves **MUST** be interpreted in light of clinical signs, such as PU/PD, polyphagia and weight loss. Disadvantages of BGCs include the inability to identify hypoglycemia during the hours or days in which a curve is not performed (ie, in the middle of the night, when more hypoglycemic events occur), inconsistent correlation with clinical signs, and the effects of stress hyperglycemia in cats.

When BGCs are done in the clinic, I prefer to check BGs prior to insulin administration and then every two hours throughout the day, and every hour if the BG is less than 150 mg/dL. However, it is more important for owners to follow their normal schedule than it is to get a pre-insulin BG reading (unless hypoglycemia is suspected). For example, if the owner typically feeds the pet at 6 am and gives insulin immediately after, they should continue with this schedule and the first sample will be taken as soon as the pet arrives at the clinic. I generally recommend that the patients be fed at home if there is any concern that the pet (especially cats) will not eat at the clinic.

The first BGC has been recommended 1-2 weeks after initiating insulin therapy. I do not recommend increasing the insulin dose based on “spot glucose checks” alone, as this may lead to insulin-induced hyperglycemia (similar to the Somogyi effect), and result in inappropriate insulin dose increases. However, if the patient is started on the low end of the starting dose range for insulin (0.25 U/kg BID in dogs, or 1 U/cat BID), and the owner reports no improvement in clinical signs, the insulin dose can be increased up to the high end of the starting dose range (0.5 U/kg BID in dogs, or 2 U/cat BID) without a full BGC. A BGC is then recommended prior to increasing the dose further.

In a well-regulated pet, BGs stay below the renal threshold for glucose throughout the day (180 mg/dL in dogs and 250-280 mg/dL in cats), but above approximately 100 mg/dL. Lower BGs (down to 80 mg/dL) are sometimes acceptable in cats, particularly during the first 3-6 months while trying to achieve remission. Lower values in the clinic are concerning since stress hyperglycemia in the clinic may mask hypoglycemia that occurs at home.

Remember to consider the clinical signs in each pet, in light of the BGC. For example, if the owners report that the dog’s clinical signs are well-controlled at home (normal water intake and urination) and the dog’s weight is increasing, yet BG values range between 200 mg/dL and 300 mg/dL in the clinic, the insulin dose does not need to be increased.

At-home Glucose Curves

A much less stressful alternative to in-hospital glucose curves is at-home glucose curves performed by owners. These are ideal because they give us a more realistic idea of normal daily BGs in cats that experience SH, and are often less stressful for the pet and the owner (especially when the patient hates going to the clinic, resulting in owner guilt). Additionally, even if the owners don’t routinely perform full BGCs on their pets, knowing how to obtain BG readings at home can help them identify hypoglycemia when suspected.

Sites for obtaining BG samples in cats include the marginal ear vein or inner pinna, and the edge of a non-weightbearing paw pad. In dogs, the inner pinna, gums, and elbow callus may be used.

Owners must still be instructed to contact the veterinarian regarding insulin dose adjustments. Except for occasional BGs assessed to r/o hypoglycemia, most owners should be instructed not to perform glucose curves more than about once weekly. (Some owners DO get overly zealous about measuring BGs!)

Although BGCs can help identify hypoglycemia, episodes of hypoglycemia often occur in the middle of the night/early morning, when samples are not typically obtained. Thus, sometimes a patient has high BG measurements during the day and undetected hypoglycemia at night, resulting in poor diabetic control. One clue that this is happening may be that the patient's clinical signs were better controlled on a lower dose of insulin. One way to determine if this is happening is to decrease the pet's insulin dose and reassess clinical signs. Alternatively, an overnight BGC could be performed. Additionally, a continuous blood glucose monitoring system (CBGM) such as the FreeStyle Libre can be used.

Continuous Blood Glucose Monitoring System (CBGM); FreeStyle Libre

The FreeStyle Libre (FSL) is a CBGM system that measures BG every 15 minutes for up to 14 days. Sensors are easily placed, even in less agreeable patients, and generally as affordable as a BGC (late 2018: reusable reader--\$85; 14-day sensor--\$65). The FSL must be purchased from a human pharmacy, with a prescription required; veterinarians have not, to my knowledge, been able to obtain them directly from the manufacturer yet (our pharmacist tried at the MSU-CVM). A 2016 paper (Corradini et al, JVIM) reported successful use of the FSL in dogs. We have been using them instead of traditional BGCs and also in hospitalized DKA patients (following rehydration). They appear to be accurate for the most part, but we have identified discrepancies with the AlphaTrak in specific patients. There is no study in cats yet, but we have used them in several patients thus far, and they are particularly helpful in "stressed" patients in which a BGC is impossible without harm to the pet or staff. There's no question that more studies must be performed to assess the accuracy of the FSL. However, we have used the FSL to monitor multiple diabetics thus far, with positive results. A video for placement of the sensor on a dog can be found here:

<https://www.youtube.com/watch?v=ytkcjpdxkY>

Note that the sensor used in this video is different than the 14 day sensor that we currently use. The 14 day sensor starts reading 1 hour after placement.

Fructosamine

Fructosamine concentrations can also be used to help monitor glucose regulation. They are most useful in cats with stress hyperglycemia, in which BGC results do not coincide with apparent clinical control. Trends are generally more helpful than individual values. Obtaining a value when the patient is well-controlled and then rechecking every 3-6 months may give some indication of glycemic control. However, fructosamine concentrations should be interpreted with caution, as insulin-induced hyperglycemia (Somogyi effect) may also result in increased concentrations. Additionally, fructosamine concentrations can only give an idea of whether the patient is regulated or not; they do not reveal the cause of dysregulation, and a BGC is often needed for more information. As with BGCs, fructosamine concentrations should be interpreted in light of clinical signs.

Urine glucose

Urine glucose measurements can be used to determine whether a cat has come out of diabetic remission and also to indicate when hypoglycemia may be present. Negative glucosuria mean that the blood glucose is consistently below the renal threshold for glucose. Since this is 250-280 mg/dL in cats, a negative urine glucose measurement does not confirm hypoglycemia. However, since the renal threshold for glucose is lower in dogs, a negative measurement is

more suspicious for hypoglycemia, and BGs should be checked. I find it useful to have owners of diabetic cats that are in remission check the urine glucose weekly initially, to confirm that insulin is no longer needed. I do not routinely have owners check the urine glucose in dogs unless I am concerned about hypoglycemia (eg, I've made an insulin dose adjustment and am concerned about hypoglycemia, or BGs during the day are high and I am concerned that the dog is hypoglycemic at night). Measuring urine glucose can be confusing for owners, as it is sometimes difficult for them to understand that positive urine glucose is to be expected in dogs, and that we are concerned about negative urine glucose. Regardless, it is imperative that they understand not to increase the insulin dose based on urine glucose measurements.

Getting to the Bottom of PU/PD

Patty Lathan, VMD, MS, DACVIM

Mississippi State University

Starkville, MS, USA

Polydipsia and polyuria can be particularly frustrating for clients AND veterinarians. Although some cat owners are unaware of the problem (especially in multiple cat households), most owners of PU/PD dogs are made acutely aware by the number of times the dog wakes them up in the middle of the night, or by the amount of urinary accidents they must clean up. There are many, many potential causes of PU/PD. The most common causes are diabetes mellitus, chronic kidney disease, hyperadrenocorticism (dogs), and hyperthyroidism (cats). Most causes can be identified with a minimum data base and a few other diagnostics. It should be noted that primary central diabetes insipidus is a very rare condition, and that the use of a water deprivation test is rarely required in the workup of PU/PD, and can be dangerous.

Polyuria is defined as urine production >50 mL/kg/d, while polydipsia is defined as drinking >100 mL/kg/day. However, in most cases, quantification of urine output is not necessary for diagnosis of the cause, but may be used to monitor progression. I do like to have clients measure water intake prior to any therapeutic actions so that we can follow the trend to assess efficacy (or lack thereof).

Prior to proceeding towards a workup for PU/PD, it is imperative to obtain a good history, including how long the patient has been PU/PD, any change in eating habits, weight loss, drug/diet history, and differentiation between pollakiuria (frequent urination) and polyuria (urinating large amounts of urine). Physical examination may also help point towards the underlying cause (anal gland masses are suggestive of anal sac adenocarcinoma, which may cause hypercalcemia and PU/PD). Historical and physical exam findings might also help identify a patient with pyometra.

Following history and physical examination, the minimum data base for a patient with PU/PD includes a complete blood count, serum biochemistry, urinalysis, and urine culture. Total T4 is also recommended in cats. Not only will these diagnostics help identify the most common

causes of PU/PD, but they will help identify concurrent disease. Serum chemistry may reveal renal disease, hypercalcemia, electrolyte abnormalities (suggestive of hypoadrenocorticism or dehydration), signs of liver disease, and potentially values suggestive of hyperadrenocorticism. Urinalysis is imperative in ALL patients with PU/PD. It may identify glucosuria (suggestive of diabetes mellitus, Fanconi's syndrome, or proximal renal tubular disease) or an active sediment, suggestive of a urinary tract infection (including pyelonephritis). Urinalysis will also help determine whether the patient is hyposthenuric, isosthenuric, or hypersthenuric. Most cases of PU/PD are associated with isosthenuria. If a patient is hypersthenuric, lower urinary tract disease is likely to be causing pollakiuria, not polyuria. Although most lower urinary tract infections do not cause PU/PD, pyelonephritis can, but may not cause an active sediment on urinalysis due to dilution.

If the minimum data base (MDB) does not reveal the cause of PU/PD (note: urinalysis and culture are critical!!), additional diagnostics are necessary based on additional clinical signs and any other abnormalities found on MDB. These may include a liver function test (such as bile acids), Leptospiriosis serology, abdominal imaging to help identify renal disease (such as pyelonephritis, which does not always result in a positive cystocentesis-derived urine culture), and diagnostics for hyperadrenocorticism. SDMA (symmetric dimethylarginine) is often measured when non-azotemic renal disease is suspected, since SDMA can detect as early as 40% loss of renal function, and azotemia does not occur until there is 75% loss of renal function. Remember that hyperadrenocorticism is one of the most common causes of PU/PD in dogs, and PU/PD may be the only obvious clinical sign. Thus, especially in an older dog, diagnostics for Cushing's should almost always be performed prior to considering primary central diabetes insipidus. If, and only if, all other causes of PU/PD have been ruled out, the clinician may be left with differentiating primary central diabetes insipidus from primary polydipsia.

The cause of primary polydipsia is unknown, but in my experience, it occurs in some anxious dogs or dogs that were recently acquired as strays, and become PU/PD over time following less activity or boredom. If minimum data base findings are within normal limits, the diagnosis of primary polydipsia is possible. Additionally, a sodium at the bottom of or below the reference

range can be suggestive of primary polydipsia. Some dogs with primary polydipsia drink less when in a new environment, such as a veterinary clinic. One easy way to identify some of these patients is to have the owners bring the dogs in the morning and check a urine specific gravity. If it is hyposthenuric, put the dog in a kennel with **free choice water**. Monitor water intake throughout the day, and then check a urine specific gravity at the end of the day. Lack of increase does not exclude the diagnosis, but if the specific gravity has increased to greater than 1.020, primary polydipsia is very likely. We have diagnosed several primary polydipsia patients this way.

If a patient does not concentrate when placed in a different environment, and **all of the other differentials for PU/PD have been ruled out**, testing must be performed to distinguish between primary polydipsia (PP) and primary central diabetes insipidus (DI). Note that primary central DI is rare and that abnormal presentations of many of the diseases listed above are more common than primary central DI. Also remember that patients with complete central DI have a specific gravity of less than 1.006. One clue that helps differentiate DI from PP is the sodium concentration. Dogs with DI are likely to have sodium concentrations in the upper end of the reference range (free water deficit), whereas dogs with PP are more likely to have sodium concentrations in the bottom end of the reference range (free water excess).

I do not like water deprivation tests because they can be unsafe for the patient unless they are monitored very closely (weights and electrolytes), and because they make the patients miserable. I prefer the desmopressin response test when I have a high suspicion of primary central diabetes insipidus. Desmopressin (DDAVP) is a synthetic analogue of vasopressin; it has less vasopressor activity than vasopressin. I use the version that is designed as a nasal inhaler for use in people, but have a pharmacist sterilely place it in a dropper bottle for ocular use. Compounded DDAVP drops can also be used. I start with one drop twice a day and monitor for response. A positive response is achieved when the USG reaches 1.020. The major risk of a DDAVP response test is overhydration of a patient that actually has primary polydipsia, which can lead to severe hyponatremia. Thus, electrolyte concentrations should be monitored closely in patients suspected of having primary polydipsia.

“Other” Feline Endocrinopathies

Patty Lathan, VMD, MS, DACVIM

Associate Professor, Mississippi State University

Email: lathan@cvm.msstate.edu

Feline Hyperadrenocorticism

Feline hyperadrenocorticism (HAC) shares many similarities with canine hyperadrenocorticism, but there are also some important differences. HAC is less common in cats than in dogs, and treatment is often more complicated. Most cases (80%) are caused by excess adrenocorticotropic hormone (ACTH) release from the pituitary gland; approximately 20% are due to adrenal tumors. Affected cats are usually older and, unlike in dogs, most cats (90%) have concurrent diabetes mellitus.

Uncontrolled diabetes mellitus and thin, fragile skin, are the most common reasons that veterinarians investigate the diagnosis of feline Cushing's. History and physical exam may reveal changes typical of DM, such as PU/PD, polyphagia, weight loss, poor grooming, and a plantigrade stance. If the cat is not diabetic, polyphagia and weight gain may be noted. Feline HAC is the top differential in a cat with thin, fragile skin, so torn skin may be the reason for presentation. Skin wounds in Cushingoid cats are notoriously difficult to treat, and the skin often dehisces after suturing (until the HAC is under control).

Diagnosis of feline HAC requires a minimum data base to rule out other differential diagnoses (CBC, serum biochemistry, urinalysis, and culture), endocrine testing, and abdominal ultrasound. CBC and serum chemistry are usually unremarkable. A stress leukogram is present in about half of the patients, but the ALP and ALT are only increased in approximately 20% of cats with HAC, a significant variation from dogs with the disease. Urine specific gravity is decreased in about 40%.

The ACTH stimulation test and the low dose dexamethasone suppression test (LDDST) are most often used for confirmation of hyperadrenocorticism (screening tests), but are less reliable than in dogs. The ACTH stimulation test has a sensitivity of only 50% in cats, so it is not routinely recommended. For the LDDST, a dose of 0.1 mg/kg dexamethasone is used. Note that this is 10 times the dose typically recommended for use in dogs. Cortisol is measured from serum samples obtained prior to and 4 and 8 hours following dexamethasone administration. Results are interpreted based on laboratory recommendations. The LDDST is reportedly 96% sensitive for the diagnosis of HAC in cats.

Differentiation of PDH from AT may require a combination of testing, including abdominal ultrasound and endogenous ACTH concentrations.

Treatment of cats with HAC depends on the underlying cause. Ideally, adrenalectomy is pursued in cats with adrenal tumors; however, stabilization prior to surgery may allow for better wound healing. Trilostane has been used to successfully treat cats with HAC. Using twice daily dosing is ideal in cats with concurrent DM.

Hyperaldosteronism

Primary hyperaldosteronism (PHA) is due to excessive aldosterone production by the adrenal cortex, usually leading to clinical signs associated with hypokalemia and/or systemic hypertension. Adrenocortical tumors have been implicated most frequently in cats, but idiopathic adrenal hyperplasia is likely more common than reported, since histopathological diagnosis is not obtained in these cats that are treated medically.

Aldosterone is the most important mineralocorticoid in dogs and cats, and it works on the kidneys to promote sodium and water reabsorption, and potassium and acid excretion. It is under the control of the renin-angiotensin-aldosterone system (RAAS). Decreased renal perfusion stimulates renin production, which stimulates angiotensin production, and, eventually, aldosterone synthesis. Hyperkalemia directly stimulates aldosterone secretion.

In addition to hypokalemia and hypertension, some cats with PAH develop renal disease. The reason for this is unclear. However, PHA should be ruled out in all azotemic cats with hypokalemia and/or hypertension, but this can be a challenge.

Middle-aged to older cats are predisposed to PHA, and the most common clinical signs include those associated with hypokalemia (hypokalemic myopathy) and hypertension (ocular changes). PU/PD, weight loss, and a palpable abdominal mass may also be present.

The diagnostic workup for PAH in cats includes measurement of blood pressure, CBC, serum biochemistry, urinalysis, imaging, and hormone testing. The plasma aldosterone concentration is most widely used for confirmation.

Treatment is initially aimed at controlling hypertension and hypokalemia, and the patient is stabilized prior to adrenalectomy. Spironolactone is a competitive aldosterone receptor antagonist and can help control both hypertension and hypokalemia. Amlodopine, a calcium channel blocker, is given to control hypertension.

Feline Acromegaly

Acromegaly is caused by a pituitary adenoma in cats. Although it was once thought to be a rare finding in diabetic cats, more recent studies suggest that it is more common, occurring in up to 25-30% of cats with diabetes mellitus. It is rarely diagnosed in non-diabetic cats.

The most common first indication of acromegaly is insulin resistance, with insulin doses sometimes reaching over 20 units BID. Although the classic presentation is of an insulin resistant cat that has lost weight and then starts gaining weight, and has an enlarged head, not all cats with acromegaly fit this clinical picture, particularly if diagnosed earlier in the course of the disease.

Clinical signs of acromegaly include those associated with diabetes, such as PU/PD and polyphagia. Weight loss usually occurs due to the diabetes initially, but growth hormone's anabolic effects eventually lead to weight gain. Physical examination may reveal a broad forehead (especially when compared to previous pictures of the cat), prognathia inferior, cranial organomegaly, murmur, large paws, and stridor. Owners may not initially report that their cat has been snoring, but will often confirm this upon direct questioning.

Diagnosis of acromegaly relies upon consistent clinical signs and physical exam findings in a diabetic cat. Although growth hormone analysis is ideal, it is not currently commercially available in the US. IGF-1 (insulin like growth factor-1) is a hormone produced by the liver and chondrocytes following stimulation by GF. IGF-1 is responsible for some of the anabolic effects of acromegaly, and an increased concentration is consistent with acromegaly. Identification of a pituitary tumor via CT or MRI, in conjunction with consistent clinical signs and increased IGF-1 concentration, provides definitive diagnosis.

Treatment of acromegaly may include radiation therapy, hypophysectomy (only available in a few highly specialized clinics), and medical therapy. For clients that don't have access to radiation therapy or hypophysectomy, attempting to control clinical signs by increasing insulin dose and monitoring blood glucose concentration is the only alternative.