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Endocrine Emergencies Online 'Mini Series'

Session 3: Endocrine Emergencies In Cats

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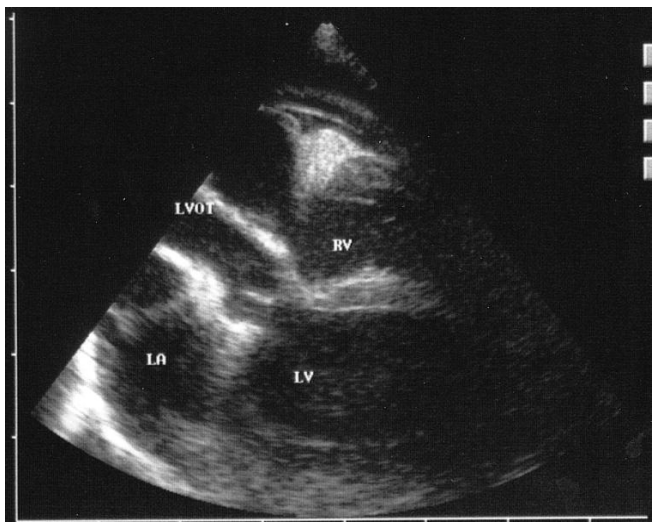


Endocrine Emergencies

Study Notes – Session 3: Feline Endocrine Emergencies

Introduction

General indicators of endocrine emergencies in cats

Crisis event may be acute or peracute in onset BUT

Usually prior history of waxing and waning vague illness

- Inappetence or polyphagia
- PU/PD
- Weight changes
- Intermittent GIT signs
- Lethargy

Signs may indicate multisystemic disease

Weakness or collapse is a common presenting feature

Although an uncommon emergency, feline endocrine emergencies will be encountered periodically. Cats are more frequently presented with apparent acute onset of disease than dogs due to their ability to hide and accommodate progressive organ dysfunction. Endocrine emergencies present a diagnostic challenge as relatively few practices have the ability to measure hormones in house so the diagnosis has to be presumptive based on the history and changes in routine haematologic and biochemical parameters and on imaging

Outline

- Diabetic crises
    - Diabetic ketoacidosis
    - Hyperglycaemic hyperosmolar syndrome (non-ketotic hyperosmolar diabetes)
    - Neurologic and pain syndromes associated with diabetes
    - Insulin overdose
- Hyperthyroid collapse
    - Thyroid storm
    - Hypertension
    - Cardiomyopathy
    - Post-thyroidectomy hypocalcaemia
- Hyperaldosteronism (Conn's syndrome)
    - Hypokalaemic muscle weakness
    - Hypertension
- Acromegaly
- Rare endocrinopathies presenting as emergencies in cats
    - Insulinoma
    - Hyperadrenocorticism
    - Phaeochromocytoma
    - Hypoadrenocorticism

- Hypocalcaemia (covered in taster session)

Diabetic crises

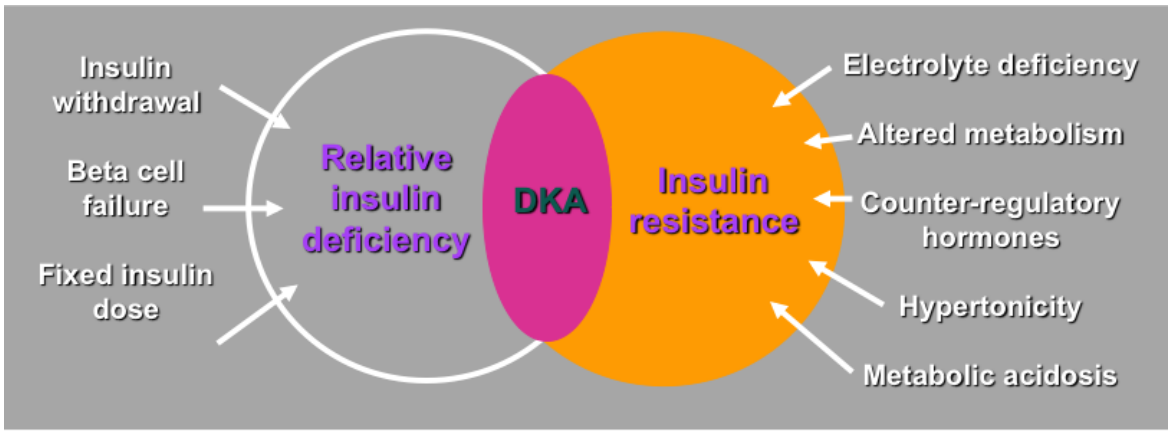
Diabetes is the most common endocrinopathy in cats and will also be the cause of the majority of endocrine emergencies seen in practice. Feline diabetes is, however significantly different from canine diabetes in a number of important aspects that can subtly affect the way diabetic emergencies present

1. Cats more frequently have a form of type II diabetes i.e. a significant component of end organ resistance to insulin and glucose toxicity impeding the ability of the pancreas to produce insulin.
2. Cats have a much higher constitutive production of glucose from proteins in the liver.
3. Amino acids are more potent secretagogues of insulin than glucose.
4. Post-prandial increases in glucose tend to be less marked.
5. Transient diabetes is common; in a recent study 85% of newly diagnosed diabetic cats were transient with aggressive management.

Diabetic ketoacidosis and hyperglycaemic hyperosmolar syndrome

Pathophysiology, diagnosis and treatment of diabetic ketoacidosis was reviewed in session 2 and is essentially similar in cats (Fig. 1). However there are a number of points of subtle difference that are highlighted below. Lack of insulin production does not seem to be an important factor in the development of DKA in cats (or dogs).

Figure 1 – Factors leading to DKA in cats



Presentation

Risk factors

- Mean age of DKA cats is 9 (2-16 years) tended to be newly diagnosed diabetics compared to HHS with a mean age 12.6 ± 3.2 years with greater likelihood of already being treated for DM
- Concurrent disease in 90% of DKA cats
    - Hepatic lipidosis, CKD, acute pancreatitis, infection and neoplasia
    - HHS cases – CKD, CHF and infection

Clinical signs

DKA - Most commonly PU/PD, lethargy, inappetence, anorexia, vomiting and weight loss

Less common - underweight, dehydrated, icterus and hepatomegaly

HHS – Commonly - ataxia, weakness, respiratory problems, neurologic signs (circling, pacing, unresponsive)

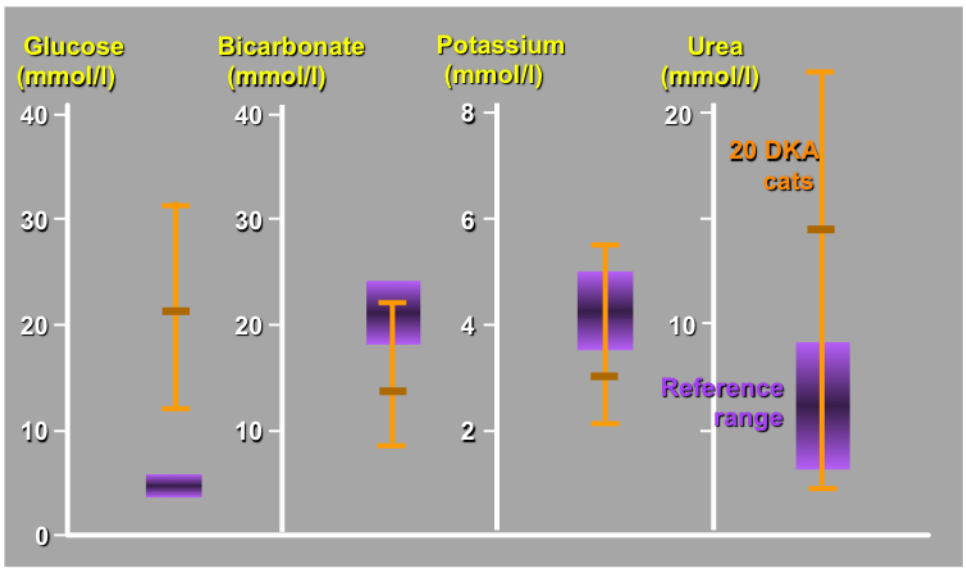
Less common - overweight, moderate to severe dehydration, respiratory compromise and hypothermia

Clinical pathology

Haematologic and biochemical changes have the features of most cats with DM.

- DKA cases (Figure 2) in addition are acidotic with ketonuria; Heinz bodies are common. Ketonemia will also be present although ketometers seem less able to distinguish between ketosis and DKA than in dogs.
- HHS cases show severe osmotic diuresis with marked hyperosmolality, azotaemia and variable sodium amounts. Anaemia is uncommon although this may reflect haemoconcentration.
- Unlike dogs, hyperphosphataemia is more commonly seen in cats than hypophosphataemia as in people and dogs; however this does not mean that hypophosphataemia will not occur with therapy.
- Hypomagnesaemia in DKA seems common although of uncertain clinical significance.
- Sodium levels can be difficult to assess as hyperglycaemia can draw fluid into the extracellular space causing pseudohyponatraemia. Corrected sodium values are sometimes used to try and guesstimate true sodium levels.
    - 'Corrected sodium' – increase serum Na^+ by 1.5mmol/L per 5mmol/L increase in glucose

Figure 2 – Biochemical changes in 20 cats with DKA



Treatment of DKA and HHS

The principles and aims of treatment are the same as for dogs

- Manage fluid balance
- Manage electrolytes and phosphorus
- Provide insulin and a carbohydrate substrate
- Correct acidosis
- Identify and treat precipitating causes and concurrent disease

American diabetes association guidelines are to treat with 0.9% saline for the first hour in patients with DKA and HHS and then use 0.45% saline if corrected sodium is high or within reference range. No studies have been conducted in cats to test the value of this approach.

Outcome

70% of DKA cats survived to discharge with median duration of hospitalisation of 5 days; 40% had recurrent episodes

HHS seems to carry a worse prognosis with only 35% surviving to discharge

Diabetic neuropathy

Diabetic neuropathy with plantigrade stance seems more common in cats than dogs but is rarely cause for emergency presentation. In rare cases diabetic cats can present in severe apparent spinal pain, cause is unknown but resolves with control of hyperglycaemia.

Insulin overdose

Insulin overdose will occur for similar reasons to those in dogs. Due to the low dose often given to cats the risks of the owner misreading the syringe or misunderstanding the dose rate is perhaps higher; using insulin pens can be considered but it is important for the owner to understand how to recognise that the cartridge in the pen is empty.

Treatment of a hypoglycaemic crisis is similar to that in dogs although cats can be harder to dose with oral glucose or sugars; Glucogel is particularly valuable in these cases. 5g of glucose(½ tube of Glucogel) is sufficient for most cats.

Cats may be more prone to relative insulin overdose as transient diabetes, variations in the level of insulin resistance and glucose toxicity are more prominent features of their disease making variation in the dose of insulin required more likely over time.

<u>Presentation</u>

Risk factors

- Neutered male cats >12 years old (normal diabetic population!)
- Heavier cats >5.8kg
- Higher insulin doses >6iU/dose

Common signs

- Lethargy, dullness and anorexia
- Seizures
- Recumbency
- Shaking
- Vomiting
- Ataxia

<u>Treatment in the practice</u>

- Immediate IV access and 0.5-1g/kg glucose (1-2ml 50% glucose/kg) over 5-10 minutes.
    - If immediate IV access not possible give Glucogel
- Continue on 5% glucose saline for at least the next 24 hours. Initially monitor the blood glucose every 30-60 minutes.
- If there has been a massive overdose of insulin dose (especially in the practice) or non-responsive hypoglycaemia consider glucagon.

Glucagon (GlucaGen Hypokit)

- Effect in 30 min
- Persists for about 90 min
- Initially give a 50 ng/kg bolus IV then
- CRI at 10–15 up to 40ng/kg/minute
    - 1mg vials with prefilled syringe containing water for injection

- Inject reconstituted 1mg into 1 litre of 5% dextrose (0.9% saline if 5% dextrose not available) to make a 1µg/ml solution.
  - Give 0.05ml/kg of solution as IV bolus
  -

Hyperthyroid crises

Thyroid adenomas or adenomatous hyperplasia account for the vast majority of hyperthyroidism in cats. The distinction between these pathological changes is difficult to make and it is suggested that all such cases represent hyperplastic change. Carcinomas of the thyroid are often endocrinologically active in cats (unlike dogs) and are responsible for around 1-3% of all cases of feline hyperthyroidism and can involve both lobes. Both follicular and papillary carcinomas are reported and are of particular importance in view of the implications for treatment and prognosis. Over 70% of hyperthyroid cases are bilateral; in reality most cases are likely to be bilateral but at presentation only one gland appears grossly abnormal at surgical exploration. This view is supported by radioactive thyroid scans which show that although only one gland may appear abnormal on gross examination both glands may be affected. Furthermore in a high proportion of cats which have undergone unilaterally thyroidectomy there is a recurrence of hyperthyroidism resulting from abnormalities of the remaining gland. The cause of hyperthyroidism remains controversial although there is renewed interest in the role of fluctuating iodine intake. A variety of goitrogens are also present in commercial cat food and the environment including phthalates, resorcinol, polyphenols, polychlorinated biphenyls and soybean.

General clinical features of hyperthyroidism

Cats presenting with hyperthyroid emergencies will have a background history supportive of hyperthyroidism, typical features of hyperthyroidism in cats are described below.

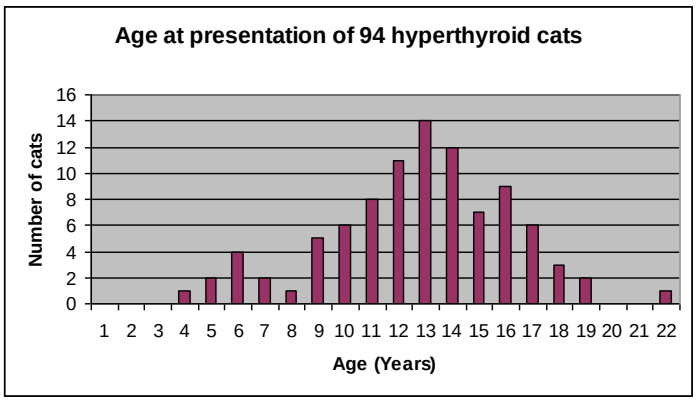


Figure 3

Signalment

- Mean age at presentation is 12-13 years (Fig. 3)
- <5% of cats are <8 years old
- No sex predilection
- Some studies have suggested Siamese and Himalayan cats may have a decreased risk

Presenting clinical signs and physical examination changes (Table 1)

Presentation is often delayed with the majority of cats showing clinical signs for 6-12 months as many of the signs are those associated with 'good health' such as good appetites and high levels of activity. Other owners accept many of the changes as a normal sign of ageing in their cat.

Diagnosis

Based on the history, physical appearance and examination, the presence of hyperthyroidism will be suspected in most cases. The key issue in cats presenting as an emergency is whether their hyperthyroidism is relevant to their emergency presentation. In those cats where the diagnosis is less clear, routine haematology and biochemistry tends to show

- Increased PCV, haemoglobin, red cell count and MCV (40-50%)
- Stress leucogram
- Elevated liver parameters (>90% of hyperthyroid cats have at least one of ALT, ALP, AST or LDH raised)

- Increase in ALP has been correlated with the magnitude of T_4 and can act as a surrogate marker in emergency cases.
- Hyperphosphataemia in the absence of azotaemia (40%)
- Reduced ionised calcium (50%)
- Azotaemia (20%)

Urinalysis also tends to show some changes; although SG can range from 1.009-1.050, the urine is generally less concentrated than expected. UTI is present in around 12% of cats. Trace ketonuria is found in some non-diabetic hyperthyroid cats that can present a diagnostic dilemma as blood glucose will be mild to moderately elevated

Table 1 – Presenting features and physical examination findings in hyperthyroid cats

Frequency (% of cats) of owner observations		*Physical examination*	
Weight loss	90	Palpable goitre	90
Polyphagia	60	Underweight	70
PD/PU	50	Tachycardia (>240bpm)	50
Hyperactivity	40	Hyperactive/difficult to examine	50
Gastrointestinal sign	40	Skin changes	35
Poor coat quality	35	Small kidneys	25
Respiratory signs	25	Hyperthermia	15
Inappetence	15	Gallop rhythm	15
Lethargy	10	Easily stressed	10
Weakness	10	Dehydrated/cachexic appearance	10
Tremor/seizure, heat intolerance, haematuria, neck ventroflexion	<10	Also – aggressive, premature cardiac beats, increased nail growth, depressed/weak, neck ventroflexion	10 1 → 8

T_4 estimation

If available in-house may give a negative or equivocal result in emergency presentations even where hyperthyroidism is responsible as the metabolic stress may be driving the level down hence results need to be interpreted with care and should not deter the clinician form considering hyperthyroidism as the cause of the presentation.

Differential diagnosis

There is a limited differential list for the polyphagic, thin cat

- Hyperthyroidism
- Diabetes mellitus
- Inflammatory bowel disease
- Lymphocytic cholangitis
- Drugs
- EPI

Emergency presentations

There are a number of potential emergency presentations of hyperthyroid cats

- Collapse associated with dehydration and cachexia
- Thyroid storm (thyrotoxicosis)
- Heart failure and apathetic hyperthyroidism

- Hypertensive crises (see hyperaldosteronism)
- Hypocalcaemia following thyroidectomy (taster session)
- Medication side effects
- Neuromuscular disease

Collapse

Cats that have severe hyperthyroidism particularly where this has been long standing will sometimes present when a minor additional stress e.g. a period of vomiting and diarrhoea leads to a failure of their organ reserve capacity. Typically these cats will be significantly cachexic, dehydrated, hypothermic and azotaemic. Approach to these cases will be generally careful rehydration having assessed cardiovascular capacity and renal function for evidence of acute kidney injury (AKI), slow passive warming and management of other signs e.g. vomiting followed by nutrition and control of their hyperthyroidism.

Thyroid storm

Thyroid storm is a syndrome described in human medicine to define a multi systemic disorder resulting from organ exposure to excessive levels of thyroid hormone. This form of acute thyrotoxicosis can be life-threatening and is a significant cause of mortality in human emergency rooms. Thyrotoxicosis is a term used to describe any condition in which there is an excessive amount of circulating thyroid hormone whether from excess production and secretion from an overactive thyroid gland, leakage from a damaged thyroid gland, or from an exogenous source; in veterinary cases this is almost exclusively associated with hyperfunctioning thyroid gland. Although discussed in the veterinary literature, case series as a clinical entity have not been described.

Thyroid hormone excess

Although, one would expect circulating thyroid hormones to be increased in patients with thyroid storm, there is no difference between serum thyroid hormone levels in these patients and in more stable hyperthyroid patients in human medicine. This results in the diagnosis being made primarily based on clinical signs. In fact it is likely to be rapid and acute increases in circulating thyroid hormone that precipitate the crisis hence thyroid storm can be associated with radioactive iodine therapy and thyroid surgery that damage the thyroid gland causing release of hormone or following abrupt cessation of anti-thyroid medication resulting in the rapid rise of serum thyroid hormone levels. As 99% of plasma thyroid hormone is bound, non-thyroidal illness that alters binding of thyroid hormones to their carriers could be lead to rapid alteration of free thyroid hormone without changing the total level.

Further infection, sepsis, hypoxemia, hypovolaemia and lactic or ketoacidosis can lead to increased intracellular responses to thyroid hormone.

Hyperactivity of the sympathetic nervous system

Thyroid hormones can alter tissue sensitivity to catecholamines, at the cell surface receptor as well as the intracellular signalling levels, and this increased sensitivity may result in the clinical signs seen during thyroid storm of apparent catecholamine excess. In addition, many of these clinical signs are controlled by β-adrenergic blockade.

Precipitating events

Common events that may precipitate thyroid storm in feline hyperthyroid patients may include infection, severe other non-thyroidal illness, radioactive iodine therapy, abrupt withdrawal of antithyroid medication, thyroid surgery, vigorous thyroid palpation, stress and administration of stable iodine compounds.

Clinical Signs

Thyroid storm is the acute exacerbation of clinical signs of thyrotoxicosis; but diagnosis is based upon the prevalence of 4 major clinical signs.

- Fever
- CNS effects from mild agitation to seizures or coma
- GI-hepatic dysfunction ranging from vomiting/diarrhoea and abdominal pain to unexplained jaundice
- Cardiovascular effects including sinus tachycardia, atrial fibrillation and congestive heart failure.

Clinical signs are associated with the major organ dysfunction

- Arrhythmia especially gallop rhythm
- Crackles or dullness in the lung fields indicating pulmonary oedema or pleural effusion,
- Retinopathies
- Tachypnoea and hyperthermia
- Absent limb motor function secondary to thromboembolic disease
- Severe, acute muscle weakness and ventroflexion of the neck associated potentially with hypokalaemia or thiamine deficiency
- Sudden death may also occur

Diagnosis

Specific clinical signs are not different form other cats with hyperthyroidism. Laboratory changes are also similar although hyperbilirubinaemia, hypokalaemia tend to be more marked.

Treatment

Treatment of thyroid storm is aimed at controlling the four major problematic areas:

1) Reduce the production/secretion of thyroid hormones,
2) Counteract the peripheral effects of thyroid hormones,
3) Systemic support,
4) Identify and eliminate the precipitating factor.

Reduction in the production or secretion of new thyroid hormones

Standard anti-thyroid therapy will block new formation (use higher end of dose range). Stable iodine compounds such as potassium iodide can be used to prevent further secretion of formed hormone and can also decrease the synthesis rate of thyroid hormone. They must be given 1 hour after carbimazole/methimazole administration since a large load of iodine will initially stimulate thyroid hormone production. Potassium iodide may be given at 25 mg PO q8hr. Lipid-soluble radiographic contrast agents such as, iopanoic acid, may be given at 100 mg PO q12hr; it can be given IV if oral route is not available. It has the additional advantages of blocking peripheral conversion of T_4 to T_3, blocking T_3 binding to its receptor, and inhibiting thyroid hormone synthesis.

Inhibition of peripheral effects of thyroid hormone

Inhibition of β-adrenergic receptors with propranolol given initially IV (0.02 mg/kg over 1 minute) is preferred. Oral propranolol has poor bioavailability in cats and atenolol is probably a better choice for oral therapy. Propranolol has been shown to inhibit the peripheral conversion of T_4 to T_3, although this effect happens slowly. In acute situations, the short acting β_1 blocker, esmolol, may be used intravenously at a loading dose of 0.5mg/kg IV over 1 minute; followed by a CRI of 10-200 mcg/kg/minute.

Systemic Support

Crystalloid IVFT is usually indicated with potassium supplementation. Addition of glucose as a 5% solution should be considered as well as B_1 supplementation to address potential thiamine deficiency. Management

of heart failure (see below) and arrhythmias may be necessary. As thromboembolism is a potential sequelae, anticoagulation therapy should be considered e.g. low dose aspirin (20mg/cat PO q72h), clopidogrel (18.75mg.cat PO q24hr) or low molecular weight heparin (dalteparin 100U/kg SC q6hr). Anti-hypertensive therapy may be necessary with amlodipine (0.625-1.25mg/cat q12-24hr) depending on whether propranolol is also being given. Thyroid storm in man can result in relative adrenal insufficiency due to increased cortisol clearance. No such studies have been undertaken in feline patients and the use of glucocorticoid therapy in patients with thyroid storm is controversial.

Identification of precipitating factors

Once the patient is stable review of the case is beneficial to exclude exciting events associated with thyroid manipulation or abrupt changes in therapy. If none are present, urine culture should be undertaken along with other investigations to look for underlying disease.

Prognosis

Thyroid storm in man has a significant mortality rate. Thyroid storm is not as well a defined syndrome in feline medicine, although acute manifestations of thyrotoxicosis result in a syndrome that can be considered feline thyroid storm. As in man, it is anticipated that early recognition and aggressive treatment of feline thyroid storm will improve survival.

Heart failure and apathetic hyperthyroidism

Apathetic hypothyroidism is reported in 10% of hyperthyroid cats although clinical experience in primary care practice would suggest that it is less common than this. Cats are inactive and inappetent with an increased rate of weight loss. Such cases in man indicate atrial fibrillation and congestive heart failure (CHF). In cats they tend to be those that are hypotensive in CHF and frequently moderately azotaemic. Often their cardiac hypertrophy has progressed to a more dilated form with significant reduction in myocardial contractility.

Diagnosis

Can be challenging in the acute presentation as the typical signs and routine clinical pathology changes can be associated with a number of diseases including primary heart disease although the weight loss is usually more profound than expected. Goitre is however usually palpable and hyperthyroidism can be assumed. However primary treatment of the hyperthyroidism is not indicated until management of CHF has been initiated giving time for T_4 to be checked.

Therapy

Standard therapy for CHF is appropriate with diuresis. Managing hypotension can be critical and positive inotropes (dobutamine or pimobendan) may be necessary. Cases are often also significantly dehydrated due to their hyporexia and careful attention needs to be paid to their fluid balance to ensure that AKI is not initiated and there is sufficient venous return to cause ventricular filling.

Hypocalcaemia post thyroidectomy

The major potential complication of bilateral thyroidectomy is hypocalcaemia associated with hypoparathyroidism. This risk can be minimised by careful surgical technique but the risk is present to some degree following all bilateral thyroidectomies. This complication most often arises between one and three days of thyroidectomy but clinical signs of hypocalcaemia can develop in some cats within eight hours of surgery and not until five days following surgery in others. A mild hypocalcaemia (<2.2mmol/L) is a consistent postoperative feature but clinical signs develop in only a minority of these cases. Signs are more likely to develop with severe hypocalcaemia (<1.8 mmol/L) but the degree of hypocalcaemia is not an entirely reliable predictor of development of clinical signs. Blood calcium should be measured once or twice daily for four days following thyroidectomy and then at intervals determined by the degree of hypocalcaemia; ionised calcium is preferred as it is more biologically relevant but is not essential. If blood

calcium drops below 1.8 mmol/L (ionised calcium <0.9mmol/L) or if clinical signs develop, treatment should be begun immediately. This policy leads to treatment of some cats which would not have developed clinical signs. The first signs of hypocalcaemia are general agitation and hyperaesthesia. This rapidly progresses to tonic muscular spasms with opisthotonus. Signs of hypocalcaemia develop very quickly and death may follow rapidly without treatment. The above approach therefore avoids the risk of a hypocalcaemic crises arising when the cat is not being observed.

Table 2 – Calcium supplementation for cats

Compound	Per cent elemental calcium	Multiplication factor for elemental calcium requirement	Forms
Calcium carbonate	40%	2.5	Most are available as tablets, chewable tablets or capsules. Some liquid forms are available. Some general calcium supplements e.g. Collocal D contain very small amounts of calcium
Calcium citrate	21%	5	
Calcium gluconate	9%	11	
Calcium lactate	13%	7.5	
Calcium oleate	7%	14	

Table 3 - Vitamin D supplements available for use in cats

Generic	Forms	Daily Dose Rate	Time to maximal effect	Duration of toxicity
Vitamin D_2 (ergocalciferol)	Capsules – 25 & 50000 U Oral syrup – 8000 U/ml Injectable 50000 U/ml	4000-6000 U/kg/day	5-21 days	1-18 weeks
Dihydro-tachysterol	Oral solution – 0.25mg/ml	Initially 0.02-0.03mg/kg/day Maintenance 0.01-0.02 mg/kg q24-48hrs	1-7 days	1-3 weeks
Alfacalciferol (Alfacalcidol)	Capsules – 0.25-1mg Solution – 2mg/ml Injectable – 2mg/ml	0.05mg/kg q24hr for 3-4 days then 0.1-0.25mg/kg q24hr	1-4 days	1-14 days
Vitamin D_3 (calcitriol)	Capsules – 0.25, 0.5mg Injectable – 1.0mg/ml	10-15ng/kg/q12hr for 3-4 days then 2.5-7.5ng/kg q12hr	1-4 days	1-14 days

Therapeutic approach

If blood calcium falls below 1.8 mmol/L but no clinical signs are evident 50-100mg of elemental calcium daily and vitamin D orally (table 2 and 3). The most convenient preparations are One Alpha™ suspension (Leo Pharmaceuticals) and Rocaltrol™ (Roche – 0.25 μg capsules). This treatment is adjusted according to subsequent blood calcium estimations the objective being to maintain concentrations within the low normal range. In some cases considerably higher dosages of calcium and vitamin D are required in the short-term (for the first week or so). If severe clinical signs of hypocalcaemia develop with muscular tetany up to 2-4 ml/kg of 2.5% calcium gluconate is given slowly intravenously. Further calcium may be given

intravenously to effect (to control muscular spasms but avoiding bradycardia) but with great care. Calcium can then be given as a CRI (2.5ml/kg of 10% calcium gluconate every 6-8 hours) or 10-20ml of the same solution administered subcutaneously and oral supplementation begun. Severely affected cats should be monitored carefully after resolution of signs following intravenous calcium as signs may recur quickly. Excessive supplementation should be avoided since hypercalcaemia may result in various complications such as metastatic calcification particularly of the renal tubules leading to nephrogenic diabetes insipidus. In most cases supplementation can be gradually reduced over time. Lack of access to rapid calcium estimations is a severe limiting factor in the short-term management of cats undergoing thyroidectomy. Prophylactic treatment is unsatisfactory since the dosage requirements and length of treatment needed are so variable and over-supplementation is potentially dangerous. Previous attempts to provide prophylactic treatment have proved unsuccessful

Outcome

A report of a large series of cases has shown that calcium and vitamin D supplementation can be withdrawn in nearly all cats that have shown hypoparathyroidism following thyroidectomy. Even if the parathyroids are inadvertently removed ectopic parathyroid tissue has been reported to be present in up to 50% of cats located in the mediastinum, pericardium or peri-tracheal area. Revascularisation of damaged or remnant parathyroid tissue may also account for the re-establishment of calcium homeostasis. In cases where the parathyroid glands have been accidentally removed at surgery then reimplantation in the muscle layers during closure has been recommended.

In a study of normal cats undergoing bilateral thyroid-parathyroidectomy treatment (calcium supplementation) was required for a median of 11 days (range 1-40 days) to maintain blood calcium at an acceptable level and avoid clinical signs of hypocalcaemia. PTH concentrations remained very low or undetectable throughout the monitoring period (of 90 days). It was concluded that cats are able to maintain blood calcium in the absence of significant PTH concentrations - although the PTH assay used in this study may not have been optimal.

Other post-thyroidectomy complications

Rarely laryngeal paralysis due to laryngeal nerve damage and haemorrhage will occur following thyroidectomy.

Medication side effects

Up to 20% of cats show side effects to methimazole or carbimazole; in general these are mild and transitory resolving with a reduction in dose or cessation of anti-thyroid medication. Most cats will show side effects within 4-6 weeks of starting medication. Rarely severe side effects will occur and these include

- Vomiting
- Severe pruritus and excoriation of the head and neck
- Bleeding diathesis (hypocoaguable state – probably indicates DIC)
- Jaundice
- Severe haematologic abnormalities
    - Agranulocytosis – neutrophil count $<2x10^9$/L associated with sepsis
    - Thrombocytopenia associated with epistaxis and oral bleeding
    - Haemolytic anaemia

Neuromuscular disease

Hyperthyroidism can cause neuromuscular signs in the cat, particularly involving the muscle, which can result in generalized weakness muscle atrophy, ventral neck flexion, fatigue, muscle tremors, and gait disturbances. CNS signs (forebrain) can include restlessness, irritability, aimless wandering, circling,

abnormal sleep/wake patterns and seizures that can be the result of hypertensive encephalopathy in some instances.

Hyperaldosteronism (Conn's syndrome)

Excess aldosterone production can be primary or secondary in origin. Secondary hyperaldosteronism results from increased stimulation of RAAS usually as a compensatory mechanism to hyponatraemic hypovolaemia such as chronic use of diuretics. Reduced renal perfusion secondary to CRD can also increase aldosterone levels.

Primary hyperaldosteronism (PHA) has been reported in 34 cats associated with adrenal adenoma/carcinoma, MEN and hyperplasia. Bilateral neoplasia is reported.

Presentation

Signalment

Middle aged to older cats

Presentation

- Hypokalaemic polymyopathy – muscle weakness and head ventroflexion
    - Less commonly limb stiffness, dysphagia and collapse
    - Mild and episodic → sudden and acute onset
- Hypertensive retinal detachment and acute onset blindness
    - Other signs of severe hypertensive disease are possible but not, as yet, reported
- Occasional additional signs of hyperprogesteronism – similar signs to hypercortisolaemia

Emergency presentation

Usually due to severe hypokalaemia or hypertensive crisis causing intraocular or intracranial bleeding or retinal detachment.

Diagnosis

- Hypokalaemia often present but degree is variable and persists despite supplementation
- Elevated creatine kinase
- Elevated fractional excretion of potassium
- Hypertension
- Elevated basal aldosterone in the face of a low-normal plasma renin activity
    - An Aldosterone to renin ratio (ARR) in healthy cats of 0.3–3.8 has been published. No breed differences were found but ARRs in neutered cats and cats > 5 years old were significantly higher (due to low renin activity) than in intact cats and cats < 5 years old respectively.
- Adrenal mass on radiography, ultrasound or advanced imaging – NB pulmonary metastasis is reported so the thorax should be evaluated.

Diagnosis of PHA in the face of chronic renal disease can be difficult as aldosterone levels can be significantly elevated and incidental adrenal masses do occur.

Treatment

Hypokalaemic crisis

Immediate treatment with potassium may be necessary with some cats requiring very high doses of IV and then oral potassium (up to 6mmol PO q 12hr). Care must be taken with rapid fluid infusion as this can initially have a dilutional effect on serum potassium levels especially in cases that are also acidotic driving potassium back into the cells resulting in severe depression, collapse and potential death associated with cardiac arrhythmia. Some clinicians advocate administering oral potassium to cats with a serum potassium

of <2.0mmol/L prior to intravenous therapy. The author feels that this can be difficult and stressful to such cases worsening weakness and the possibility of cardiac arrhythmia due to catecholamine release and would use potassium supplemented fluids (120mmol/L) to deliver 1mmol/kg of potassium over the first two hours i.e. twice maintenance fluid.

Once the patient is able to take oral medication spironolactone should be started at 2-4mg/kg PO q24hr.

Hypertensive crisis

Although treatment of hypertension with amlodipine is appropriate for most hypertensive cats (0.625mg PO q24hr → 1.25mg q12hr) in a crisis situation where there is active bleeding or on going retinal detachment more aggressive reduction in blood pressure may be necessary although risks over benefits should be discussed with the owner as the hypertension is likely to have been chronic. Attempts at acute reduction in blood pressure mandate continuous blood pressure and ECG monitoring during the procedure. Options include

- Hydralazine acting as a direct arteriodilator has been most widely used at 2.5mg/cat SC usually resulting in reduction in blood pressure within 15 minutes.
    - Reflex tachycardia can occur and may require treatment with a β-adrenergic blocker.
- Where hydralazine is unavailable other options include propranolol - 0.02-0.06mg/kg slow IV over 1 minute.
    - Propranolol is available as a 1mg/ml solution – can be diluted in saline for accurate administration.
- Nitroprusside can be used but is unavailable in most practices are requires careful titration to effect with a CRI.

<u>Long term management and prognosis</u>

Adrenalectomy for unilateral masses – specialist surgical procedure

- Medical stabilisation prior to surgery
- High perioperative mortality of around $^{1}/_{3}^{rd}$ of cases is reported
- Invasion of the vena cava is common

Prognosis

- Medically managed – reported 7-30 months
- Surgically treated – 8/17 alive at 1 year 2/17 alive at 3 years

Acromegaly

Acromegaly (AM) is an uncommon endocrinopathy but is being increasingly recognised with the increased awareness of presentation and availability of advanced imaging. 18/56 diabetic cats that were screened had IGF-1 levels >1000ng/ml and of these 17 had evidence of an intracranial pituitary mass (although of itself this is not conclusive proof of a functioning tumour). The number of non-diabetic cats that are acromegalic is unknown. Unlike dogs, marked soft tissue and skeletal changes do not appear to be as prominent in cats and the majority of acromegalic cats present with signs indicative of DM (table 4).

Table 4 - Top 10 clinical signs of feline acromegaly

Sign	Assignment (DM or AM)
PU	DM
PD	DM
Polyphagia possibly extreme	DM ± AM
Weight gain	AM
Upper respiratory stridor	AM
Broad facial features	AM
Prognathia inferior	AM
Abdominal enlargement/organomegaly	AM
Clubbed paws	AM
Neurologic signs	AM

Diagnosis

Routine haematology and biochemistry show features consistent with DM although as a group AM cats had higher BG and proteins. Measurement of feline growth hormone is not widely available so insulin-like growth factor 1 (IGF-1) is used as a surrogate. Values over 1000ng/ml are considered suggestive of AM but IGF-1 does showed significant fluctuation and some cats with unstable DM do have IGF-1 levels >1000 without having AM. Advanced imaging (CT or MRI) to demonstrate a pituitary mass is considered sufficient for diagnosis but rare cases have been seen when these cats are do not have AM.

Emergency presentation

Most cats are seen as insulin-resistant diabetics. They will sometimes present with DKA as emergencies. Most cats managed medically with high-dose insulin will have hypoglycaemic crises as GH secretion fluctuates and hence the degree of insulin resistance so on occasions they can receive a significant insulin overdose.

Therapy

Standard treatment for DKA or hypoglycaemic crisis is appropriate. Long term medical management is difficult and somatostatin analogues that have been used successfully in man have been disappointing. Currently radiotherapy or hypophysectomy offer the best long term outcomes although post-procedural complications can be high.

Rare endocrinopathies

A number of endocrine disease are rarely seen in cats despite being common or relatively common in dogs. Emergency presentations can occur usually associated with the metabolic effects of the endocrine disease

Hyperadrenocorticism

HAC in cats is significantly less common than in dogs; PU/PD and polyphagia are not a feature of HAC but of the concurrent DM that accompanies > 80% of HAC cases in cats.

Aetiology 75% pituitary dependent adenoma (carcinoma rare) and 25% adrenal neoplasia (adenoma $^{2}/_{3}^{rd}$ and adenocarcinoma $^{1}/_{3}^{rd}$)

Iatrogenic cases – most commonly seen as dermatologic change

Clinical presentation

Signalment Mid to old aged, mixed breed cats, possible female bias

Clinical signs (table 5)

- Insulin resistant DM
- Skin fragility and bruising
- Poor coat with alopecia (asymmetric)
- Pot belly and muscle wasting
- Pigmented skin
- Key clinical pathology
    - Glycosuria and hyperglycaemia
    - Urine SG > 1.020 (cf dog)
    - Proteinuria rare
    - Hypercholesterolemia
    - Mild increase in ALT
    - Cats do not have an inducible isoenzyme of ALP
    - Hepatomegaly associated with vacuolar hepatopathy
    - Adrenomegaly on ultrasound useful as a positive finding

Historical findings	*Physical examination*	*Laboratory changes*
PU/PD (90%)		Hyperglycaemia (95%)
Increased appetite	Pot belly (85%)	Glycosuria
Hair loss	Alopecia	Hypercholesterolemia
Weight gain	Obesity	Increased ALT
Weakness/lethargy	Muscle wasting	Increased ALKP
Weight loss		
	Skin fragility	
	Pyoderma	
	Hepatomegaly	
	Seborrhea	

Prevalence	>75%	50-75%	25-50%	<25%

Table 5- Frequency of presenting signs in feline hyperadrenocorticism

Emergency presentations

Diabetic ketoacidosis

See page **

Skin tearing

Skin fragility is not typical of canine HAC but does occur more frequently in cats associated with the catabolic effects of hypercortisolaemia. This can result in spectacular skin tearing after only minor trauma (including scruffing) and the potential for life-threatening overwhelming sepsis similar to burns victims. In such cases, irrigating and then dressing the wound is critical, tacking the torn skin back into place, preventing self trauma and providing antibacterial cover. In the longer term managing the HAC is important with medical therapy being the initial choice due to poor surgical wound healing

Treatment

Medical - trilostane currently the best first choice medical therapy at 30-60mg/kg q24hr

Radiation - limited case reports of use with PDNAC with neurologic signs

Surgery - adrenalectomy may still represent the best option at this present time; but needs to be bilateral for PDHAC cases. Surgical complications are common; facilities for intensive post-operative management

should be available. Adrenal adenocarcinomas tend to be locally invasive and commonly involve the vena cava or aorta, making full surgical resection difficult. The extent of invasion is difficult to assess with preoperative imaging. Hypophysectomy- available at a few centres, surgical risks are relatively high but reducing with experience.

Insulinoma

Very rarely reported in cats. Presentation is similar to dogs so potential present with weakness, collapse, seizuring and coma. 6 cases are reported in the literature affecting older cats (12-17 years); 5/6 were male and 3/6 Siamese. Diagnosis and treatment is the same as for dogs although it is important to use an RIA assay that has been validated for measuring feline insulin.

Phaeochromocytoma

Very rarely reported as an ante mortem diagnosis in cats. More cases are reported at PM; the low diagnostic rate may be the result of a low index of suspicion, the vague and often episodic nature of the clinical signs, and the lack of easy diagnostic tests. Emergency presentation is likely to be that of severe systemic hypertension, and may include congestive heart failure, pleural effusion and hypertensive retinopathy. Diagnostic suspicion is raised by the presence of an adrenal mass confirmation requires demonstration of raised circulating or urinary catecholamines. Treatment is similar to dogs blocking the effects of excessive catecholamines with α- and β-adrenergic blockers (phenoxybenzamine and propranolol/atenolol).

Hypoadrenocorticism

Nearly 50 cases of hypoadrenocorticism are reported in cats. Presentation of crisis is similar to dogs, although one cat presented due to severe hypoglycaemia. However, it remains a rare endocrinopathy; in a report of 49 cats with low sodium:potassium ratio none had hypoadrenocorticism. This likely reflects that hyperkalaemia of other causes e.g. lower urinary tract obstruction or AKI is relatively common in cats. Index of suspicion would be higher in cases presenting with low sodium (as this is less common in cats) and hypoglycaemia (as most cats under metabolic stress will be hyperglycaemic). Diagnosis and treatment is similar to dogs.

Hypocalcaemia

Mild-moderate hypocalcaemia can be present associated with a number of endocrine emergencies such as DKA and hyperthyroidism where it is often associated with a poorer outcome. Hypocalcaemia post thyroidectomy is discussed on page 9-10. Primary hypocalcaemia associated with hypoparathyroidism is a rare presentation; management is the same as for post-thyroidectomy cases. Diagnosis is based on a low PTH in the presence of hypocalcaemia – samples for PTH should be taken prior to calcium or vitamin D therapy and require blood to be placed in cooled EDTA tubes spun immediately and the EDTA plasma frozen (about 1ml) and transported frozen for analysis.

Conclusions

Although uncommon, feline endocrine emergencies particularly diabetic ketoacidosis will present from time to time. Actively looking for endocrine disease will increase the number of cases diagnosed and, as the majority of endocrine emergencies in cats respond favourably to treatment, improve the success rate with feline emergencies.