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Endocrine Emergencies Online 'Mini Series'

Session 2: Insulin Trouble and Hypothyroidism In Dogs

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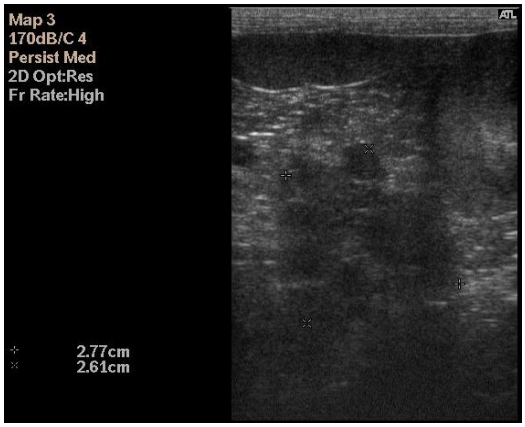


Endocrine Emergencies

Study Notes – Session 2: Canine insulin issues and hypothyroidism

Introduction

General indicators of emergencies associated with insulin abnormalities or thyroid disease

Crisis event may be acute or peracute BUT usually chronic, non-specific signs have been present particularly weight and appetite change, exercise intolerance, weakness (table 1).

Table 1 – Key historical signs associated with insulin abnormalities and thyroid disease.

Hyperglycaemia	*Hypoglycaemia*	*Hypothyroidism*
Previous PU/PD Lethargy Anorexia Adipsia Vomiting and diarrhoea Hyperventilation	Collapse Seizures Muscle weakness Ataxia	Obtundation → stupor → coma Hypothermia Bradycardia Hypoventilation

Outline

Diabetic ketoacidosis

- Review of pathophysiology of DKA
- DKA presentation and diagnosis
- Treatment of DKA emergencies
- Other diabetic emergencies
    - Hyperglycaemic, hyperosmolar syndrome
    - Diabetic cataracts
    - Diabetic neuropathy

Hypoglycaemia

- Insulin overdose
- Insulinoma
    - Presentation and diagnosis
    - Emergency treatment

Thyroid disease

- Review of thyroid anatomy and physiology
- Myxoedema
- Hyperthyroidism
- Thyroid carcinoma

Diabetic emergencies

Diabetes is the most common endocrinopathy in dogs and the most common cause of endocrine emergencies. Classification of diabetes in dogs does not fit easily into the human nomenclature however broadly canine diabetes falls into the three main groups

- Type I (insulin dependent) diabetes due to a failure of pancreatic β-cells
    - Most common form of diabetes in dogs associated with immune-mediated destruction of β-cells
    - Significant genetic and therefore breed predispositions and reduced risk for examples
        - Predisposition – Schnauzers, Bichon Frise, Samoyed, miniature and toy poodle, Lhasa apso, cairn and Yorkshire terriers
        - Reduced risk – GSD, Boxer, Doberman, Labrador, English Springer and Cocker Spaniels, Rottweiler, Collie
- Type II (non-insulin dependent or insulin resistant) diabetes
- Type III (intercurrent disease)

Diabetic ketoacidosis

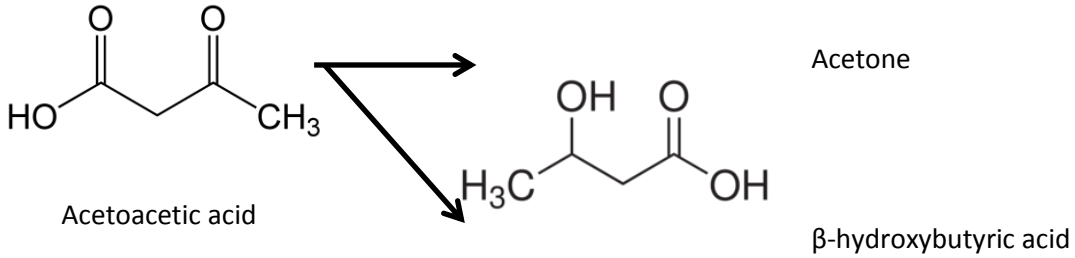
DKA should be distinguished from diabetic ketosis that can be present intermittently in many diabetic dogs especially those with poorly stable DM. Specific management of the ketosis is rarely required and should resolve with improved diabetic control.

DKA pathophysiology

DKA develops as a results of inadequate or, in the case of newly diagnosed DM, no insulin treatment. However not all dogs with DM develop DKA

- Contributory factors to development of DKA
    - Excess diabetogenic hormones
        - Glucagon, growth hormone, glucocorticoids
    - Fasting leads to increased hormone secretion
    - Dehydration leads to a further reduction in the ability to excrete glucose and H^+ ions
- Hyperglucagonemia
    - Primarily responsible for ketonemia
    - Insulin deficiency with glucagon excess results in peripheral lipolysis leading to increased plasma fatty acid concentrations

Under normal circumstances plasma fatty acids form acetyl coenzyme A in the liver and enter the triglyceride or citric acid cycle being metabolized to protein, glucose or glycogen. If glucagon levels are high plasma fatty acids form acetoacetyl coenzyme A that is metabolised to acetoacetic acid and thence to acetone and β-hydroxybutyric acid (ketones) (Fig. 1).



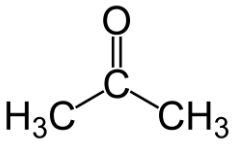


Figure 1 – metabolism of acetoacetic acid

Ketone metabolism

Ketones are metabolized by many tissues as they serve as a short-term source of energy when glucose levels entering the cell are insufficient.
BUT in cases where production greatly exceeds utilization, metabolic acidosis and osmotic diuresis due to ketonuria occurs leading to dehydration, electrolyte depletion, vomiting and diarrhoea. The dehydration and hypovolaemia can lead to prerenal azotaemia and hyperosmolality. Derangements are progressive and will eventually result in death if not treated.

DKA presentation

Not all dogs with DKA will present as emergencies; cases will have a similar presentation to DM i.e. PU/PD, polyphagia, weight loss. In one study of 221 newly diagnosed diabetics, 15% had DKA. Of these 15%, 23 had concurrent disease.

- 20% UTI
- 20% HAC
- 15% acute pancreatitis
- 5% neoplasia
- 5% hypothyroid
- 5% other

Severe DKA signs are usually rapid in onset presenting with lethargy, anorexia, adipsia, vomiting and diarrhoea.

Physical examination

Generally non-specific signs associated with dehydration, acidosis and azotaemia – depression, dehydration, weakness, tachypnoea, abdominal pain, acetone breath (individual sensitivity to detecting acetone is variable). Other clinical signs due to secondary diseases (as above) may also be present.

DKA diagnosis

DKA will usually be suggested by a standard blood screen for emergency patients showing hyperglycaemia that is usually marked. Other common haematologic and biochemical abnormalities include

- Leucocytosis and haemoconcentration
- Pre-renal azotaemia
- Whole body potassium depletion but serum potassium can be normal to increased due to acidosis or AKI

- Rarely severe life-threatening hypokalaemia
- Hyponatraemia due to diuretic-associated loss
- Hypophosphataemia – urinary loss vs. cellular shift

Definitive diagnosis requires presence of hyperglycaemia with acidosis and ketonemia or ketonuria.

Acidosis

It is difficult to assess acid-base status without being able to measure plasma pH; to some extent it can be assumed in dogs with high BG and ketonuria whose osmolality is normal.

Some DKA cases will show a marked acidosis seen as a low pH (<7.15), low bicarbonate and large negative base excess. pCO_2 will tend to be low in an attempt to compensate.

Acidosis can have profound effects on serum potassium and phosphorus levels (Fig. 2) giving a false impression of whole body changes.

Figure 2 – Effects of acidosis and its correction on plasma and cellular ions

Ketosis

Hand held ketometer (measure β-hydroxybutyrate) are widely available and inexpensive and give an opportunity to measure blood ketone levels to assess ketonemia rather than relying on ketonuria. There is a reasonable correlation between handheld meters and laboratory analysis of blood ketone levels however the precise reference ranges and cut-off points will vary with the meter used and as yet wide experience of their utility in general practice is lacking. In man β-HB levels often far exceed acetoacetic acid.

Suggested cut-off points (MediSense Optium, Abbott Laboratories, Oxon, UK)

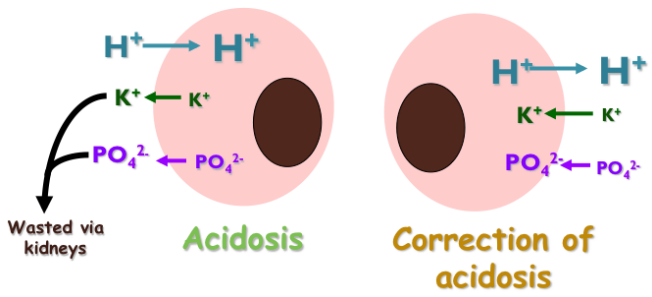
- Low cut-off around 2.3mmol/L has high sensitivity
- High cut-off around 4.5mmol/L had high specificity

The presence of ketosis does not of itself make a diagnosis of DKA (see hyperglycaemic, hyperosmolar syndrome).

Traditionally ketosis is measured by looking for urinary ketones.

URINALYSIS

- Glycosuria – usually ++++
- Ketonuria - dipstick react with acetone and acetoacetate so can underestimate the level of ketosis
  - Differential diagnosis of positive urinary ketone reaction
    - Out of date sticks
    - Fasting
    - Glycogen storage disease
    - Persistent fever
    - Persistent hypoglycaemia
    - Low carbohydrate diet
- USG poorly reflects true renal concentration due to effects of high levels of glucose on specific gravity; urine osmolality is a more accurate measure.



- Urine should also be submitted for sediment analysis and culture as around 20% of DKA cases are also likely to have a UTI.

Serum osmolality

DKA can have profound effects on serum osmolality due to dehydration and sodium wastage. Although not immediately available in-house estimation by calculation can help drive appropriate therapy. To this end, some in-house machines do calculate osmolality although the algorithm used may vary. A wide variety of algorithms have been published but the below is a relatively simple formula that gives clinically valuable results for decision making; reference range for serum/plasma osmolality in the dog is 290-310 mOsm/kg.

Osmolality ≅ 1.86 (Na^++ K^+) + glucose + urea +10

Examples
DKA dog : K – 4.8; Na – 130; glucose 32.5; urea 18.2
Calculation 1.86(4.8 + 130) + 32.5 + 18.2 + 10 = 311.4

If sodium not depleted and especially if AKI may be markedly hyperosmolar – HNKD
Calculation 1.86(6.5 + 145) + 55 + 40 + 10 = 356.8

Treatment of severe DKA

Inappropriate therapy can hasten a patient's death so it is essential that each patient is assessed individually and has their own treatment plan formulated. Prior to therapy commencing (or as soon afterwards as possible) blood samples for diagnostics should be taken. DKA is a dynamic situation hence frequent monitoring of physical and biochemical parameters is crucial.

Aims of therapy

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

Fluid therapy

Appropriate fluid therapy is the mainstay of DKA treatment. Preferably more than one large bore catheter should be placed. In patients that are severely dehydrated with circulatory collapse this can be challenging; start with a small catheter and as circulation is restored insert a 2nd large catheter at another site.

Then :-

- Estimate dehydration
- Estimate likely fluid losses –remember that the glycosuria means that osmotic diuresis will persist
    - Place a urinary catheter – ins and outs
- Choose fluids based on baseline electrolytes, acid-base and osmolality calculation. In general 0.9% NaCl or Hartmann's with added potassium, phosphorus and glucose as required is appropriate.
    - If the patient is hyperosmolar hypotonic saline may be required (<0.45% NaCl) - mix half a bag of 0.9% NaCl with half a bag of 5% dextrose.

- Assess response
    - Clinical status, urine output, bodyweight, central venous pressure if available and a central line has been fitted.

If high fluid rates are being used, repeat electrolytes, phosphorus, acid-base, urea & glucose in 2 hours as these can change dramatically through cellular shifting and renal excretion.

Fluid rate

IVFT should aim to meet hourly demands + replace 50% of the estimated deficit over 2-4 hours and the remainder of the deficit within 24 hours.

Example - 8kg diabetic miniature poodle with DKA Estimated 10% dehydrated = 800ml deficit Replacement requirement 100-200/hour Osmotic diuresis means producing 5ml/kg/hr urine Insensible losses @ 1ml/kg/hr Total fluid requirement = 148-248ml/hr (9=15 x maintenance!)

It is essential to monitor urine output especially in DKA cases with marked azotaemia as acute kidney injury may have occurred (be occurring) and is likely if urine output is low (<2ml/kg/hr). High fluid rates in these patients can lead to volume overloading.

Electrolyte balance

Sodium levels will be managed by fluids and kidneys alone. Due to electrolyte shifting associated with acidosis (Fig. 2) high serum potassium may still reflect a whole body deficit associated with renal wasting (unless patient has AKI) hence potassium supplementation of the fluids is required. Potassium supplementation of the fluids should be based on plasma levels and fluid rate. It is the total amount of potassium that is being given that matters not the fluid concentration. In general potassium supplementation to the patient should not exceed 1mmol/kg/hour.

Example - 8kg diabetic miniature poodle with DKA estimated 10% dehydrated (page 5) Amount of potassium given will depend on the speed with which fluid deficits is corrected Moderate amount of potassium added to fluids e.g. 40mmol/L 50% of deficit over 4 hours – (40 x 0.148)/8 = 0.74mmol potassium/kg/hr 50% of deficit over 2 hours – (40 x 0.248)/8 = 1.24mmol potassium/kg/hr

Managing phosphorus

Often forgotten in DKA patients, unmanaged hypophosphataemia can cause severe complications resulting in haemolytic anaemia if phosphate drops below approximately 0.5mmol/L. Supplementation should be started once phosphate falls below 0.6mmol/L

- Dose rate 0.01-0.03mmol/kg/hr
    - Options
        - Intravenous potassium phosphate (Fresenius Kabi 100mmol/500ml)
        - Foston - 2.5mmol/mL [approx.]

Insulin therapy

Reducing BG is important but rapid reduction can lead to profound electrolyte, acid-base and osmolality changes; hyperglycaemia *per se* is not life threatening so the aim is to SLOWLY decrease BG to <15mmol/L over the first 8 hours of treatment. Insulin should be given IM or IV as SC will probably be ineffective due to poor cutaneous circulation.
The author prefers IM administration as it is less complicated and less prone to error in the midst of a DKA crisis. A loading dose of 0.2iU/kg of neutral insulin should be given followed by 0.1iU/kg neutral insulin q1-2hr
If IV CRI is to be used it should be given via a separate syringe driver as this allows changes in IVFT rate without changes rate insulin is administered or necessitating a new bag of fluid to be made up.

- Dilute insulin in 0.9% saline to a standard concentration e.g. 0.5iU/ml and alter rate (table 3) of administration to alter dose of insulin given.
- Hypoglycaemia is potentially a greater risk than using IM therapy.

Table 3 – Suggested administration rates (ml) of a 0.5iU/ml solution of insulin according to bodyweight and BG level

BG (mmol/L)	5kg dog	10kg dog	20kg dog	30kg dog
>15	1-2	2-4	4-8	6-12
12-15	1	2	4	6
9-12	0.75	1.5	3	4.5
6-9	0.5	1	2	3
<6	Stop	Stop	Stop	Stop

Managing insulin therapy

- Monitor blood glucose hourly
    - Aim to decrease BG by <5mmol/L/hr
- Once insulin below 15mmol/L move to q4-6hr administration
- Move to longer acting insulin when patient alert and ketosis resolved (can take 48 hours to occur).

<u>Glucose therapy</u>

As glucose levels fall the risk of hypoglycaemia increases and glucose should be added to the infusion solution (table 4). As insulin effects will last longer than glucose will persist in the circulation, glucose therapy should continue for at least 2 hours after insulin therapy has been stopped.

Table 4 – Suggested rates of glucose inclusion to IVFT with change in BG

BG (mmol/L)	% glucose in fluids	ml of 50% glucose to 1L
>15	0	0
12-15	2.5	5
9-12	2.5	5
6-9	5	10
<6	5	10

Managing acid-base disturbances

Acidosis is can be profound with a pH <7.0 is a being a poor prognostic indicator for survival. In general, the kidneys are good at sorting out acidosis so where possible IVFT alone should be used. However if the acidosis is profound (pH < 7.20 and/or bicarbonate <11mmol/L), bicarbonate may be required. Bicarbonate is available as 8.4% $NaHcO_3^-$ solution that is equivalent to 1mmol/ml of bicarbonate. There are two approaches to therapy; the author prefers to give a standard amount and monitor the response as despite the formulae that are available, the true effect of adding bicarbonate to the system can be difficult to predict.

Give 0.5-1mmol/kg of sodium bicarbonate over 20 minutes slow IV regardless of level of acidosis

- This level is also safe is acidosis cannot be measure but is assumed to be present and severe enough to warrant therapy

- Calculated dose (in mmol) = Bodyweight (kg) x 0.4 x (12-patient bicarbonate)

As with BG, it is important to correct acidosis slowly due to the potential adverse effects of rapid correction

- Metabolic alkalosis
- Paradoxical cerebral acidosis
  - Correction of acidosis generates CO_2
  - Most of CO_2 removed by lungs
  - Some diffuses across BBB and recombines with water to produce H^+ ions

    $H_2O + CO_2 \leftrightarrow H_2CO_3 \leftrightarrow H^+ + HCO_3^-$
  - Progressive worsening neurologic signs despite therapy
- Rapid falls in potassium and phosphate to life-threatening levels

Identifying and treating precipitating factors

Most DKA patients will have other issues; identifying these issues will help long term management but may be of limited value short term. Once stabilization is under way, consider -

- Abdominal ultrasound, thoracic radiographs
- IV antimicrobials to treat UTI
- Evaluating patient for HAC of limited value in acute phase

Prognosis

With good management the prognosis for DKA dogs is good, however, severe cases that present late in the course of their disease can die despite intensive support.
Results from a large study of DKA dogs

- 70% of dogs survived to be discharged
- Median hospitalization was 6 days
- Negatively survival factors
    - Lower ionized calcium
    - Lower haematocrit
    - Lower venous blood gas
    - Larger base deficit

Other potential diabetic emergencies

Hyperglycaemic hyperosmolar syndrome [HHS] (Non-ketotic hyperosmolar DM)

HSS is an unusual but severe complication to DM; cases show severe hyperglycaemia and azotaemia resulting in marked hyperosmolality causing CNS depression, lethargy, hypovolaemia. Cases present with severe dehydration, depression, weakness and shock. Calculated osmolality will depend on plasma sodium that can be anywhere from low to high. Levels that are normal to elevated reflects substantial cellular dehydration. Due to the effects of hypovolaemia and hyperglycaemia on sodium levels, formulae to calculate corrected sodium have been advocated but the clinical utility of this calculation is unclear although it may serve to highlight the degree of free water deficit.

- 'Corrected sodium' – increase serum sodium by 1.5mmol/L for every 5mmol/L increase in glucose
    - Na^+ 135; glucose 45mmol/L = Corrected Na^+ 148.5mmol/L

Treatment

- Careful choice of fluids and rate to prevent cerebral oedema
    - Even if sodium is high, sodium containing fluids are required; initially ≥ 0.45% sodium
- Slow reduction of glucose at 3-5mmol/hr
- Re-establish urine output to > 2ml/kg/hr
- Regular (initially every 1-2 hours) monitoring of electrolytes, glucose, urea, (phosphate)
- Hourly assessment of level of consciousness & mentation in case cerebral oedema occurs.

Diabetic cataracts

Rarely an emergency situation but can develop very quickly (over days) most commonly follow an episode of poor diabetic control. Some dogs will become depressed, lethargic and disorientated precipitating urgent appointment.
Management

- Short term - ? Sedation, anxiolytic drugs
- Long term cataract removal

Diabetic neuropathy

Measurable reduction in nerve function is common in diabetes but clinically apparent disease is unusual. Results in a distal, symmetrical neuropathy that occurs secondary to un/poorly controlled DM.
Clinical signs much less common in dogs compared to cats

- Initially involve the pelvic limbs.
- Plantigrade stance, progressive paraparesis, hyporeflexia, and muscle atrophy (esp. distally).
- Thoracic limbs eventually become involved.

Diagnosis

- Electrophysiological abnormalities (axonal degeneration and demyelination).

Treatment

- Early, aggressive therapy to improve diabetic control
    - Majority show significant neurological improvement
    - Many returning to normal although resolution may take weeks to months.

Hypoglycaemia

Hypoglycaemia can result from a variety of disease states, most commonly associated with an excess of insulin. Less commonly hypoglycaemia will be associated with decreased production or drug-induced. The most common cause on most biochemical screens is a delayed separation of serum or plasma resulting in white cell metabolism of glucose.

- Decreased glucose production
    - Severe liver disease – toy breeds
    - Hormonal – hypoadrenocorticism, GH deficiency, hypopituitarism
    - Fasting, malnutrition, pregnancy, extreme exercise
    - Sepsis
- Drug-induced – rare e.g. β-blockers, amitriptyline

Insulin overdose

Robust procedures should be in place in practice to prevent overdose of insulin being given to hospitalised patients. Even so mistakes will and do occur most commonly due to misreading the prescribed dose. Similarly mistakes can also be made by clients particularly following a dose change. To some extent this can be lessened by the use of insulin pens.

Common causes of insulin overdose

- Using 40iU/ml syringes with 100iU/ml insulin
- New insulin bottle – if the previous insulin supply has been damaged and is much less effective leading to significant increase in dose, when a new bottle is started this can lead to a relative overdose.
- Insulin given and patient refusing to eat
- Insulin dose high due to resistance that now has resolved – e.g. increased dose given associated with a UTI that is then treated with antibacterials, post-seasonal diabetes.

Insulin overdose should always be suspected in a collapsed diabetic patient; if there is any doubt glucose should be given (e.g. patient still at home) until BG can be measured.

Insulin-induced hypoglycaemia (Somogyi overswing)

Insulin-induced hypoglycaemia is probably a relatively common phenomenon and accounts for a significant number of unstable diabetics. Excess insulin dose causes BG to drop below the reference range. This process can happen very rapidly (10-20 minutes) making it difficult to document in some patients using standard glucose curves.
Following hypoglycaemia, gluconeogenic hormonal environment leads to apparent insulin resistance for up to 2-3 days. BG measurements made during this period when counter-regulatory hormones are high tend to suggest insulin resistance so dose is increased creating and ever lowering nadir until a hypoglycaemic crisis occurs.

Managing a hypoglycaemic crisis associated with insulin overdose

Hypoglycaemia will cause rapid irreversible brain damage. Aggressive early treatment is therefore essential; oral glucose can be absorbed through the buccal and oesophageal mucosa. All owners of diabetic dogs on insulin should be aware of the clinical signs of hypoglycaemia – tremors, disorientation, visual disturbance, behavioural changes, weakness , ataxia, collapse and seizures

Patient at home

- Give glucose, honey, Ribena concentrate, Lucozade, jam, sugar water and bring to surgery immediately – equivalent of about 1g/kg
    - Make sure that these are not low sugar preparations
- Ideally all owners with diabetic dogs should have glucose tablets (about 50g/tablet) or Glucogel (Hypostop) (10g/tube or 30g/bottle) at home and be aware of what dose to give (0.5-1g/kg).

At surgery

- 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

Insulinoma

Insulinomas are the most common tumour of the pancreas in dogs and are usually functional. Some will have abnormal enzyme expression e.g. hexokinase resulting in an abnormal glucose sensitivity and an excessive insulin secretory response to glucose loading. This is why giving potential insulinoma cases large amounts of glucose of big meals can worsen their hypoglycaemic problems. Insulinomas will often produce other hormones as well including glucagon, somatostatin, growth hormone, IGF-1, gastrin, pancreatic islet polypeptide. Despite their apparent benign histology (usually reported as well differentiated adenomas with low mitotic rate) they usually malignant phenotype in dogs. Metastases are to regional lymph nodes and liver but rarely the lung.

Classification

WSAVA classification

- Stage I – pancreas only (T1N0M0)
- Stage II – pancreas + LN (T1N1M0)
- Stage III – pancreas + LN + distant metastasis (T1N1M1)

Markers of survival and/or disease free interval have been shown to be tumour size and Ki67 index (proliferation marker).

<u>Presentation</u>

Older dogs with a median age 9-10 years although a relatively large range (3-15); no sex predilection.

- Primarily medium and large breed dogs although WHWT seem predisposed

Golden retrievers, GSD, pointers, setters, boxers

Clinical signs

Are the result of neuroglycopenia (inadequate glucose in the nervous system), initially they may be episodic occurring particularly after exercise, fasting or a large meal. Reported duration of clinical signs is very variable from 1 day to 3 years.

- Weakness (75%)
- Ataxia (40%)
- Collapse (80%)
- Disorientation, visual disturbance, behavioural changes (40%)
- Seizures (95%) → coma → death

Some of signs commonly associated with hypoglycaemia are actually the result of increased production of counter-regulatory hormones particularly catecholamines.

- Tremors (40%), hunger (15%) and nervousness

Emergency presentation

Cases usually present collapsed or seizuring with an unremarkable physical examination

- Tonic clonic seizure
- Muscle weakness
- Weight gain
- Post ictal signs

Tetraparesis is a rare presentation associated with a polyneuropathy. Examination reveals decreased or absent appendicular reflexes.

Diagnosis

Can be complicated and difficult to establish in patients with vague signs but requires demonstration of low glucose in the face of a normal to raised insulin level. However, in the emergency situation, typical signs of hypoglycaemia with low blood glucose (see page 10 for differential diagnosis of hypoglycaemia). If insulinoma is suspected, a serum sample for measuring insulin levels should be taken where possible prior to administering glucose.

Emergency treatment

- Slow glucose bolus 0.5g/kg over 20-30 minutes

NB can cause marked insulin release resulting in limited response or even worsening of hypoglycaemia

- Followed by 2.5-5% dextrose solution IV as a CRI until signs of hypoglycaemia are resolved and glucose is ≈ 3mmol/L or higher.

Hypotonic solutions are not normally appropriate and glucose should be added to 0.9% saline (see table 4 page 7)

- If patient fail to respond to IV glucose then

Dexamethasone – 0.1mg/kg IV q12hr
Somatostatin analogue (octreotide) 10-20µg/kg SC q8hr
CRI glucagon – 5-13ng/kg/min
Can increase insulin release

In addition the effects of the hypoglycaemia may require management

Seizure management

- Diazepam is the first choice due to its rapid onset of action.

0.5-1mg/kg IV or PR repeated if necessary or CRI @ 0.5-1mg/kg/hr (appropriate giving sets as diazepam is absorbed onto some plastics used for giving or extension sets)

- Pentobarbital if diazepam is ineffective but takes 20 minutes before a CNS response is evident.

12mg/kg IV
Additional 3mg/kg IV q20min if required (maximum of two doses)

- Anaesthesia and CRI of propofol

Cerebral hypoxia and oedema

- Maintain circulating BP – saline, colloid but do not over hydrate
- Adequate ventilation – short term hyperventilation will decrease ICP
- Elevate head by 15-30^0 to facilitate venous drainage
- Furosemide and mannitol

Prognosis

Surgical removal offers the best long-term solution unless gross metastasis identified on imaging (ultrasound).

- 80% of tumours are solitary in pancreatic limb
- Occasionally no discrete mass is visible – these can be associated with very small tumours or beta-cell hyperplasia
- Around 50% cases have metastases at surgery

Median survival surgical cases in reported studies is 12-14 months.

- Stage I better – 50% remaining euglycemic at 14 months
- Young dogs have poorer survival than older dogs (appear to have more aggressive tumours)
- Patients that achieve postoperative euglycaemia or that are hyperglycaemic survive longer.

One more recent study suggested longer median survival times that the above.

- 2 years surgery alone
- 3 ½ years surgery + prednisolone
- 6 months medical therapy alone (usually due to the fact that gross metastasis had been identified and surgery considered inappropriate.

Thyroid disease

Thyroid emergencies are very rare in dogs particularly compared to cats.

Hypothyroidism

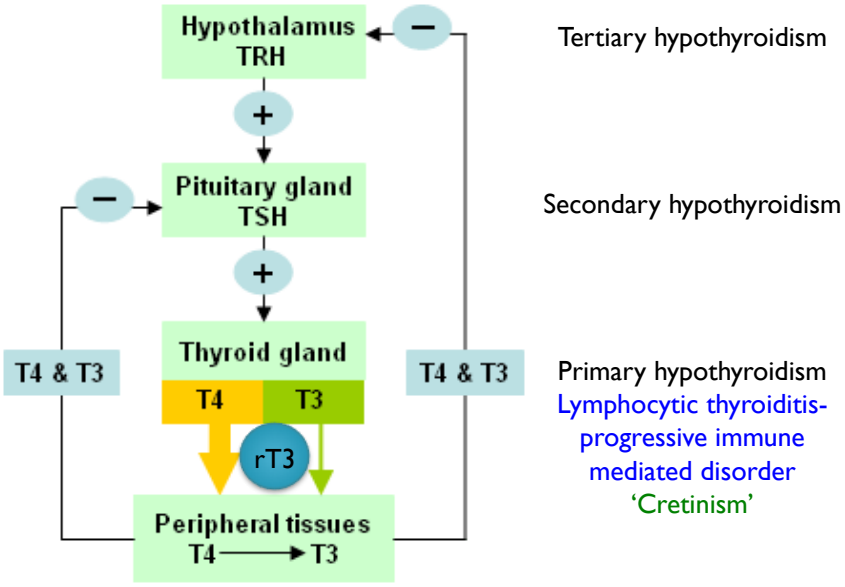
Hypothyroidism is the second most common endocrinopathy. Usually presenting as a slowly progressive disease associated with metabolic issues or dermatologic changes caused by low circulating thyroid hormone. Rarely hypothyroid crises will occur and even in those cases, despite the acute presentation, dogs will have had a previous history that is compatible with hypothyroidism.

Anatomy and physiology

Thyroid hormone is produced in the follicular cells of the thyroid gland where iodine is combined with tyrosine residues on thyroglobulin to produce precursor hormone. Thyroxin (T_4) is the major secretory product and is de-iodinated to T_3 or rT_3 mainly in the periphery. T_3 is 3-5x more biologically active than T_4. In plasma 99% of thyroid hormone is plasma bound and inactive.

Regulation of thyroid hormone production
Regulation of thyroid hormone levels occurs via the hypothalamic-pituitary-thyroid axis. The type of hypothyroidism will depend on the level the HPT axis at which failure occurs (Fig 3).

Figure 3 – Forms of hypothyroidism in relation to the hypothalamic-pituitary-thyroid axis



Clinical signs associated with low thyroid hormone production

Common signs are associated with metabolic, dermatologic or neuromuscular changes (table 5). It is neurologic and occasionally neuromuscular issues that most commonly lead to emergency presentations.

- Myxoedema coma
- Generalised weakness and tetraparesis
- Central signs – seizures, ataxia, circling
- Megaoesophagus and secondary aspiration
    - Association between disease but no direct causation
- Haemostatic defect
- (Heart failure)

Table 5 – Clinical manifestations of hypothyroidism.

Common manifestations			Rare manifestations
Metabolic	Dermatologic	Neuromuscular	
Lethargy Mental dullness Reduced exercise tolerance Weight gain Heat seeking	Dry and greasy Symmetric hair loss Scaling Dull, bleached and brittle hair Recurrent infection Hyperpigmentation Black heads		Neurologic disease Cardiovascular Reproductive GIT Ophthalmic Behavioural Skeletal

Diagnosis

Diagnosis of hypothyroidism is not always straight forward particularly in cases with subtle and non-specific metabolic signs. In the emergency situation access to estimating T_4 may be limited

and cTSH requires samples to be sent to an external facility. Indications that there is perturbation of the HPT-axis are usually present on routine blood tests but these changes are non specific.

- Hyperlipidaemia - hypercholesterolaemia present in more than 75% of hypothyroid dogs
- Non-regenerative anaemia (<50%)
    - Mild hypercalcaemia
    - Elevated CK

Myxoedema

Myxoedema is not uncommon in moderate to severe hypothyroid dogs but is rarely of clinical importance. Myxoedema is caused by the accumulation of mucopolysaccharides and hyaluronic acid in the dermis secondary to the metabolic derangements associated with hypothyroidism. Accumulation due to an imbalanced production and degradation of mucopolysaccharides and hyaluronic acid resulting in skin thickening and a 'tragic' expression seen as thickened lips and forehead with drooping eyelids.

Myxoedematous coma

Occurs when existing myxoedema is complicated by an additional stressor such as disease or anaesthesia.

CLINICAL SIGNS

- Obtundation, stupor, or coma
- Hypothermia often without appropriate shivering
    - Rectal temperature may as low as 25^0C
- Bradycardia
    - Heart rate may be as low as 20-30 bpm
- Hypotension
- Hypoventilation

MANAGEMENT

As myxoedematous coma is a life threatening condition, urgent therapy is required and as such diagnosis at the time is often presumptive.

- Gentle passive warming
- Intravenous fluids and BP support with care as impaired free water excretion
- Intravenous liothyronine sodium
    - 1.5µg/kg q4-12hr
    - Liquid levothyroxine sodium at 60-100µg/kg q12hr given by orogastric tube

Prognosis is guarded and depends on the initial response to treatment.

Hyperthyroidism and thyroid carcinoma

Hyperthyroidism is very rare in dogs compared to cats with the vast majority being caused by thyroid adenocarcinomas; functioning adenomas are rare. Thyroid adenocarcinomas occur in older dogs (median age 9-11 years) with golden retrievers, beagles, Boxers and Huskies amongst others being over-represented. Presentation is usually because a palpable mass in the area of the

thyroid has been found by the owners. By the time of presentation, metastatic disease is common. Thyroid status is variable with 60% euthyroid; 30% hypothyroid; 10% hyperthyroid.
At presentation, functional thyroid adenocarcinomas tend to be smaller than non-functional tumours (20-50mm in diameter) likely to be due to earlier presentation associated with their biological activity.

- Similar clinical signs to cats
- May present as emergencies

Excessive panting
Weakness
Shivering

Non-functional thyroid carcinomas
Occasionally present as emergencies

- Laryngeal paralysis and aspiration pneumonia
- Dyspnoea due to tracheal compression
- Acute haemorrhage due to vascular invasion

Conclusions

DKA is the most common canine endocrine emergency that is likely to be seen in first opinion practices. As most are undiagnosed diabetics DKA should be considered as a potential cause for collapsed, dehydrated dogs with GIT signs appropriate treatment carries a good prognosis for recovery. AS DKA, hypoadrenocorticism and insulin excess can all cause glucose abnormalities it emphasise the importance of mandatory glucose estimation in all emergency cases. Although an uncommon cause of seizuring, failure to recognise hypoglycaemic seizuring will result in a poor response to anti-seizure medication and, if uncorrected, death of the patient. Crises associated with thyroid disease are very rare, signs of myxoedema are usually present prior to additional stress leading to myxoedematous coma.