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Emergency Patients - An Organ Approach Mini Series

Session Two: Nursing Care of the Endocrine Emergency Patient

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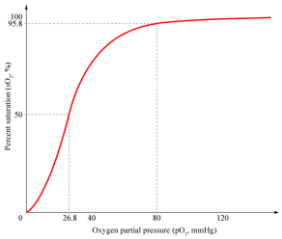
Blood Gas Analysis

Within the vascular system, oxygen is either bound to haemoglobin or dissolved in the plasma. The vast majority of the oxygen (98%) is carried in association with haemoglobin in the red blood cells. Haemoglobin molecules are able to carry large quantities of oxygen to tissues with each molecule of haemoglobin able to carry up to four molecules of oxygen.

Both arterial blood gas analysis and pulse oximetry are techniques used to evaluate the ability of the lungs to deliver oxygen to systemic arterial blood, but the information they provide is not equivalent.

Pulse oximetry measures the percentage of haemoglobin saturated with oxygen (SaO2). Arterial blood gas analysis measures the amount of oxygen dissolved in the plasma (expressed as the partial pressure of oxygen or PaO2). The relationship between PaO2 and SaO2 is not linear; the oxygen-haemoglobin dissociation curve the curve is sigmoid in shape. If the curve is shifted to the left, this indicates that the haemoglobin has a higher affinity for oxygen and thus a higher saturation for a given PaO2. The opposite is true if the curve is shifted to the right. Such shifts occur as a result of changing physiological conditions such as temperature, acid-base status and levels of 2,3-diphosphoglycerate in erythrocytes. This means it is not possible to accurately predict the SaO2 from the PaO2 and vice versa.



Oxygen-haemoglobin dissociation curve

Blood gas analysis

Blood gas analysis gives us information about both pulmonary function and acid-base status and is essential in order to make a diagnosis, provide treatment and monitor the progress of patients with either respiratory or metabolic abnormalities. Acid-base status can be evaluated on arterial (ABG) or venous (VBG) samples. In order to evaluate oxygenation, however, an arterial sample is mandatory. Four key pieces of information are provided from the ABG: partial pressures of both oxygen (PaO2) and carbon dioxide (PaCO2), blood pH and bicarbonate concentration (HCO3). It is vital to know the normal values in order to evaluate samples accurately (Table 1).

Value	Normal	Abnormal	
pH	7.35-7.45	<7.35 Acidosis	>7.45 Alkalosis
PaO2	>90mmHg	75-89mmHg Mild hypoxia	<75mmHg Severe hypoxia
PaCO2	35-45mmHg	<35mmHg Alkalosis	>45mmHg Acidosis
HCO3	18-24 mEq/l	<18mEq/l Acidosis	>24mEq/l Alkalosis

Table 1: Normal arterial blood gas values.

Assessing ventilation.

PaO2 (measured in mmHg or kPa) is an accurate reflection of the ability of the lungs to transfer oxygen to the blood. A low PaO2 represents hypoxaemia and can initiate hyperventilation. The SaO2 (pulse oximeter) measures the percentage of haemoglobin actually carrying oxygen, which is why 95-100% is normal. These two values are crucial to optimize the oxygen concentration delivered during mechanical ventilation.

PaCO2 (in mmHg or kPa) indicates the effectiveness of alveolar ventilation. Alveolar ventilation determines PaCO2: hyperventilation results in a decreased PaCO2 (hypocapnia), whereas hypoventilation increases PaCO2 (hypercapnia). Changes in ventilation may occur in patients with primary pulmonary disease, central nervous system (CNS) impairment, or may occur as a compensatory change in patients with metabolic disturbances.

Assessing Acid-Base Status

Changes in ventilation may occur as a response to a metabolic disorder causing an abnormal pH. Respiratory compensation occurs when the body attempts to correct an acidosis or alkalosis by altering ventilation in order to either increase or decrease the level of CO2 within the body. For example, a decrease in the blood pH and HCO3 indicate a primary metabolic acidosis; in response, the respiratory rate would increase in order to reduce the PaCO2 and therefore try and self-correct the imbalance.

Metabolic assessment

Serum bicarbonate levels provide information about the metabolic aspect of acid-base balance. HCO3 is controlled by renal retention and excretion; this can be accurately measured in either venous or arterial samples. An increase in HCO3 results in a metabolic alkalosis, whilst an abnormally low HCO3 results in a primary metabolic acidosis. Primary metabolic acid-base disorders are predominantly corrected by treating the underlying disease.

The kidneys respond to respiratory acid-base disturbance by retaining or excreting increased amounts of HCO3. This compensatory response occurs far more slowly than respiratory changes.

Definitions

Acid – A substance that can donate hydrogen ions (H+)
Base – A substance that can accept hydrogen ions (H+)
Acidosis – refers to processes in the body that result in increased acidity (decrease pH)
Alkalosis – refers to processes in the body that result in decreased acidity (increase pH)
Acidaemia/alkalaemia – describes the actual pH of the blood. Acidaemia is present if the pH is <7.4 and alkalaemia is present if the pH is >7.4
Buffers – systems that offer immediate cushioning (buffering) to sudden changes in pH
Respiratory acid – Carbon dioxide (CO2)
Metabolic acid – body acids that cannot be converted to a gas (lactic acid, ketones, glycolic acid, acetoacetic acid)
Base excess – a measurement used to assess the metabolic contribution to an acidosis or alkalosis. A positive value indicates an excess of base (metabolic alkalosis) and a negative value indicates a deficit of base (metabolic acidosis)
pH - Determines the acid-base status by measuring hydrogen ions (H^+).
$PaCO_2$ - the partial pressure of CO2 dissolved in arterial blood as the result of cellular metabolism, and is a direct reflection of the adequacy of alveolar ventilation. $PaCO_2$ is controlled through the lungs via either hyper- or hypo-ventilation and changes can occur within minutes. Measured in mmHg or kPa.

PaO2 – the partial pressure of oxygen dissolved in arterial blood, representing the lungs' ability to oxygenate blood. A decrease in PaO2 is defined as hypoxaemia. Measured in mmHg or kPa.

FiO2 – Fraction of inspired oxygen is the measured concentration of oxygen delivered to the patient. Room air is 21% (FiO2=0.21).

Step by step blood gas analysis

As previously stated, the body functions best at a pH of 7.4. Any physiological event that causes a change in blood pH is called a *primary disorder*. A primary disorder will stimulate a compensatory response in an attempt to restore the pH to normal.

Step 1. Examine the PaO2 and determine if the patient is hypoxaemic – administer oxygen if necessary!

Step 2. Examine the pH. If the pH is <7.35 an acidaemia exists; if the pH is >7.45 an alkalaemia exists

Step 3. Is there a respiratory component? Examine the PaCO2. If it is high or low, a respiratory component exists (could be primary or secondary/compensatory); if it is normal, no respiratory component is present.

Step 4. Is there a metabolic component? Examine the $HCO3^{-}$, if it is high or low, a metabolic component exists (could be primary or secondary/compensatory); if it is normal, no metabolic component is detected. If the $HCO3^{-}$ is high, a metabolic alkalosis exists; if low, a metabolic acidosis exists.

Step 5. Determine which component is the primary disorder. In simple acid-base disturbances, the primary disorder is the component that has changed in the same manner as the pH. If an acidaemia exists, the primary disorder will be the component that corresponds to an acidosis. For example, if the pH and the $HCO3^{-}$ are low, the primary disorder is metabolic (a metabolic acidosis). Conversely, if the pH is low, and the pCO2 is elevated (respiratory acidosis), the primary disorder is respiratory. If both the metabolic and respiratory components have changed, in the manner of the pH, then a mixed acid-base disturbance exists.

Step 6. Determine if there is a compensatory response. Compensatory responses will cause the component to move in an opposite manner from the pH. That is, if an acidaemia exists, the compensatory response to an acidaemia would be an alkalosis. Thus, a compensatory response to an acidaemia wound be an elevated $HCO3^{-}$, or a decreased pCO2; a compensatory response to an alkalaemia would be a decreased $HCO3^{-}$ or increased pCO2. For example, if the pH $HCO3^{-}$ and pCO2 are low, then a primary metabolic acidosis with respiratory compensation exists. If the pH is low, and the $HCO3^{-}$ and pCO2 are high, a primary respiratory acidosis, with metabolic compensation exists.

Step 7. Always remember the body can never fully compensate to a normal pH, and it will never over-compensate.

Treating acid-base disorders

Acid-base disorders are best treated by addressing and correcting the underlying problem. Occasionally, however, intervention to directly adjust pH must be initiated, usually if the pH becomes life-threatening.

<u>Metabolic acidosis</u>

Causes:
Diabetic ketoacidosis
Renal insufficiency
Excessive lactic acid production
Exogenous toxins (ethylene glycol)
Diarrhoea

Acidaemia should be treated with intravenous sodium bicarbonate, but only when the pH is less than 7.05. To calculate the amount of sodium bicarbonate to administer it is necessary to firstly calculate the bicarbonate deficit:

Bicarbonate deficit = Bodyweight (kg) x 0.3 x Base Excess

Administer ¼ of the bicarbonate deficit intravenously over 5-10 minutes, and then re-check the patient's pH. If the pH returns to a more acceptable range >7.2, discontinue bicarbonate administration and continue treating the underlying disorder. There are potentially several adverse complications associated with the administration of sodium bicarbonate. The most common are:

1. Rebound alkalaemia
2. Hypernatremia
3. Hypokalaemia – rapid correction of the pH drives potassium intracellularly. This is most important with severe metabolic acidosis secondary to DKA. This is an advantage when treating severe hyperkalaemia and acidosis secondary to urethral obstruction.
4. Seizures secondary to hypocalcaemia. If there is a rebound alkalaemia, this will cause increased protein binding of calcium, which lowers ionized calcium.
5. Paradoxical CSF acidosis. Increasing plasma HCO_3 can increase $PaCO_2$. Increased amounts of CO_2 can then cross the blood-brain barrier readily and lower the pH of the CSF.

Respiratory acidosis (hypoventilation)

The most common cause of respiratory acidosis is respiratory depression caused by the following:
1. Drugs - general anaesthetics,
opioids etc.
2. Central nervous system trauma
3. Space occupying lesions in the brain
4. Respiratory disease/trauma – pneumothorax, airway obstruction, pulmonary oedema etc.

Treatment depends on the underlying cause and the severity of the hypercapnia. Acute, severe respiratory acidosis usually requires intubation and positive pressure ventilation.

Metabolic alkalosis

The most common causes of metabolic alkalosis are:

1.Vomiting (loss of H^+ in the stomach contents)
2. Hyperadrenocorticism
3. Exogenous steroid therapy
4. Potassium depleting diuretic therapy leading to hypokalaemia and 'contraction alkalosis'
5. Bicarbonate therapy

It is very rare for any patient to require the administration of acid to correct a severe metabolic alkalaemia (pH >7.8). Nearly all patients will respond when 0.9% saline is administered because it is an acidifying solution.

Respiratory alkalosis (Hyperventilation)

Respiratory alkalosis is the result of hyperventilation. The most common causes in animals are pain, fever and anxiety. Other conditions include CNS disorders, exogenous drug administration and overzealous ventilation. Treatment is based on identification and treatment of the underlying cause.

Endocrine Physiology

In animals and humans, we have both the endocrine and exocrine systems. The endocrine system is a series of organs that act in tandem within the body to cause or maintain bodily functions. It is a very complex system which we will only touch on in this section. It is comprised of glandular organs or tissue that secretes hormones or precursors directly into the bloodstream (also referred to as "ductless" glands). Organs that are part of the endocrine system include: the thyroid gland, parathyroid gland, adrenal glands, central nervous system (CNS), gastrointestinal tract, pancreas, kidney, and the reproductive organs. Below is a short list of the more familiar products excreted by some of the glands of the endocrine system:

Thyroid gland

- triiodothyronine (T3)
- tetraiodothyronine (T4)

Parathyroid gland

- parathyroid hormone (PTH)

Hypothalamus, Pituitary (posterior and anterior)

- oxytocin
- antidiuretic hormone (ADH)
- adrenocorticotropic hormone (ACTH)
- and others

Adrenal Gland

- Cortex- corticosteroids
    - glucocorticoids: cortisol
    - mineralocorticoids: aldosterone)
- Inner medulla
    - catecholamines
        - epinephrine
        - norepinephrine
    - dopamine

Gastrointestinal Tract

- cholecystokinin (CCK)
- secretin
- gastrin

Pancreas

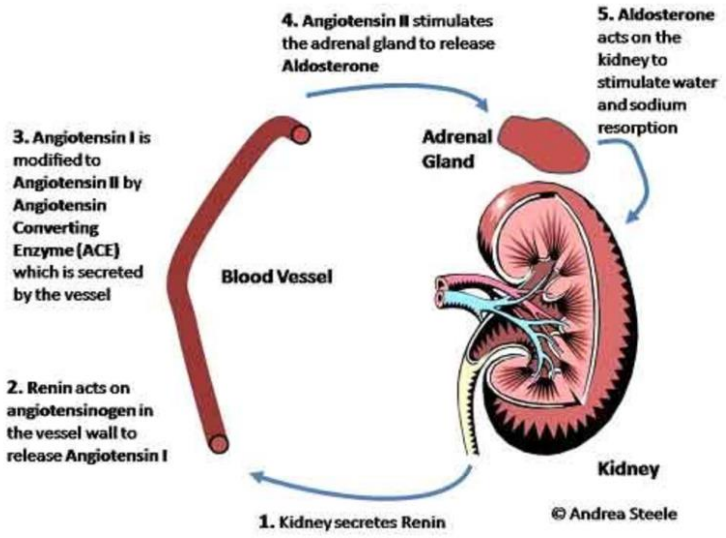
- insulin
- glucagon
- somatostatin

Kidney

- erythropoietin
- calcitriol
- renin (an enzyme)

It is important not to confuse the endocrine system with the exocrine system. In some cases, organs have both endocrine and exocrine functions, as an example, the exocrine pancreas secretes amylase and lipase, two enzymes directly into the digestive system, via the pancreatic duct. The endocrine pancreas (specifically the Islets of Langerhans) secretes insulin and glucagon directly into the blood stream without a duct.

In some cases, we have a single endocrine gland with two functions; good examples are the adrenal glands, which are divided into two completely different tissues, the cortex and the medulla. The cortex secretes the corticosteroids (easy to remember, think "cortico-" for cortex) aldosterone (think steroids) and cortisol (think "cort-"), while the medulla secretes the catecholamines epinephrine and norepinephrine.
In many cases, the release of one hormone causes the release of another from a different organ, which may cause further release of a hormone of compound to elicit a specific function within the body. Let's consider one such related system:



Since the endocrine system is so closely linked with multiple organs being involved in the desired responses, it is easy to see why dysfunctions in an endocrine organ can cause such widespread chaos within the body.

Common types of dysfunction we recognize are under or overproduction of hormones (i.e. hypo or hyperthyroidism). In general, the body has mechanisms to prevent the over or underproduction of hormones (or other secreted products) through what are termed "***feedback mechanisms***". Feedback mechanisms sense the levels of hormones circulating in the blood and tell the organ to increase or reduce production. In most cases, the body uses what is termed "negative feedback control" which is likened to a thermostat: The temperature goes down; the thermostat senses this and turns on the heating.

Once the temperature is back in its normal range, the thermostat turns off the heat. The same thing happens every day in our bodies, with many different hormones and hormone systems.
Feedback mechanisms are vital to maintaining the ideal levels of each of our hormones. In most cases, the feedback mechanisms arise from neural tissue, and this system is often referred to as the neuroendocrine system. Most of this neural tissue is located within the **hypothalamus**, which you could call the "master switchboard" and it sends signals to its partner, the **pituitary gland**, which is often referred to as the "master gland".

The **pituitary gland** is attached to the hypothalamus by a thin stalk and is a bi-lobed gland. It is divided into the ***adenohypophysis*** (anterior lobe) and a ***neurohypophysis*** (posterior lobe). The adenohypophysis is responsible for the production and secretion of seven different hormones in response to commands from the hypothalamus:

- Thyroid Stimulating hormone (TSH)
- Adrenocorticotropic hormone (ACTH)
- Follicle Stimulating hormone (FSH)
- Luteinizing hormone (LH)
- Prolactin (PRL)
- Growth hormone (GH)
- Melanocyte-stimulating hormone (MSH)

The posterior pituitary acts as the distribution centre for hormones produced within the hypothalamus. The primary hormones that are released by the posterior pituitary are oxytocin and vasopressin (aka antidiuretic hormone-ADH).
This leads to the concept of Primary or Secondary causes of endocrine dysfunction. An example of this is primary hyperadrenocorticism vs. secondary hyperadrenocorticism. ***Primary*** *hyperadrenocorticism*, as the name implies is caused by a dysfunction in the **adrenal gland** itself, while ***secondary*** *hyperadrenocorticism* is caused by a dysfunction in the **pituitary gland**.

Common Endocrine Disorders in Veterinary Patients
So, now that we have covered some basic anatomy and physiology of the endocrine system, we need to discuss some of the disorders that we commonly see in veterinary patients. We have already alluded to some of them with the examples given, but here is a list of disorders:

- Hyperadrenocorticism (Primary or Secondary)
- Hypoadrenocorticism
- Hyperthyroidism
- Hypothyroidism
- Diabetes Mellitus
- Diabetic Ketoacidosis
- Diabetes Insipidus
- Hyperglycemic, Hyperosmolar Syndrome
- Hyperparathyroidism
- Hypoparathyroidism

Of these, several are considered to be "emergencies" or "critical", while others are typically managed by basic medicine. I will obviously spend more time talking about those that fall into the ECC categories!!

Hyperadrenocorticism

Hyperadrenocorticism is commonly known as "Cushing's Disease"; however that is a misnomer when used to describe **primary** hyperadrenocorticism, which should be described as "Cushing's Syndrome". As already mentioned, Primary hyperadrenocorticism is caused by a dysfunction in the adrenal gland, while secondary hyperadrenocorticism is caused by a dysfunction in the pituitary gland. Both primary and secondary hyperadrenocorticism produce the same derangements: elevated levels of cortisol circulating in the blood. There is also **iatrogenic** hyperadrenocorticism, which is caused by excessive, long-term use of corticosteroids (specifically glucocorticosteroids).

Primary Hyperadrenocorticism is not as common as secondary, and has been linked genetically to such breeds as: Labrador Retrievers, German Shepherd Dogs and Toy Poodles, and is usually caused by adrenal tumours.

Secondary Hyperadrenocorticism is the most common form of the disease, and has been associated with breeds such as Terriers, Poodles, Dachshunds and Boxers. It is usually caused by pituitary tumours.

Signs of hyperadrenocorticism can take several months to years to develop and include thin skin and haircoat, distended belly, polyuria/polydipsia, and muscle weakness.
Rarely is hyperadrenocorticism considered an emergency case, although we often see patients, most notably diabetics and pancreatitis patients that are also "cushingoid" which may or may not have been previously diagnosed. Cushingoid patients can complicate other disease processes, as these patients are often slow to heal or may have coagulopathies.

Hypoadrenocorticism

Hypoadrenocorticism is also known as "Addison's Disease" after the doctor who discovered it, Thomas Addison in 1855 in humans.
Hypoadrenocorticism can also be of primary or secondary causes. Primary hypoadrenocorticism is caused by dysfunction of the adrenal gland resulting in deficiencies in both gluco- and mineralocorticosteroids (cortisol and aldosterone), while secondary hypoadrenocorticism results from lack of stimulation of the adrenal cortex, resulting in deficiency in glucocorticosteroids (cortisol) only. Hypoadrenocorticism can be an incidental finding, or a patient can present in a full-out crisis. Primary hypoadrenocorticism is the most common form of this disease, and it is far more prevalent in dogs than it is in cats. On occasion, we can see iatrogenic hypoadrenocorticism when a patient is administered excessive doses of mitotane, a drug commonly used to treat hyperadrenocorticism.
In dogs, there has been a genetic link to certain breeds, including the Labrador Retriever, Standard Poodles, Portuguese Water Dogs, Great Danes and Rottweilers, and more commonly affects females.

Addison's disease has been called the "Great Pretender", as its signs can be very vague and mimic many other diseases. When a patient presents in an Addisonian Crisis, it is usually in shock, which can appear as either hypovolemic shock or distributive shock. Let's refresh ourselves on the characteristics of hypovolemic and distributive shock:

Hypovolemic Shock:

- caused by acute ***intravascular volume*** depletion
- patient has a decrease in "preload"
- low preload causes decreased cardiac output (CO)
- the body responds with vasoconstriction (to minimize the volume of circulating blood required to keep pressures adequate) and increased heart rate
- vasoconstriction causes cool to cold limbs
- patients have a decreased mentation due to poor perfusion to the brain

Distributive Shock:

- have a normal to increased cardiac output
- ***decreased systemic vascular resistance*** (SVR) "flabby vessels"
- low mean blood pressure
- often have warm limbs (since vasoconstriction is not occurring)
- hyperemic mucous membranes
- bounding pulses (these are often very remarkable, considering the mean pressure is often quite low)
    - Because of lack of vasoconstriction, systolic pressures are often higher than one would expect, and diastolic pressures are often very, very low.

We have said that with primary hypoadrenocorticism, we have a decrease in both gluco- and mineralocorticosteroids. Let's look at the function of each of these:

Glucocorticosteroids:

- stimulate appetite
- maintain sense of "well-being"
- maintain calcium homeostasis
- maintain blood pressure
- protect the body against the negative effects of stress
- have anti-inflammatory effects
- gluconeogenesis
-

Mineralocorticosteroids: act on the renal tubules to:

- promote reabsorption of sodium and water
- promotes excretion of potassium

So, when the adrenal gland is not making sufficient corticosteroids, we see the following:

Lack of Mineralocorticoids:

- the kidneys excrete more water, leading to dehydration
- the kidneys fail to reabsorb sodium, leading to hyponatremia

- the kidneys fail to excrete potassium, leading to hyperkalemia
- azotemia due to dehydration

Lack of Glucocorticoids:

- depression
- anorexia
- vomiting/diarrhea
- weight loss
- moderate hypoglycaemia

The shock reaction is precipitated by dehydration and hyponatremia. Hyperkalemia can become quite severe, resulting in bradycardia and atrial standstill. Often the patient in shock has a lower heart rate than expected given their condition. This bradycardia can be a key finding in the initial stages of diagnostics. Hypoglycemia is also a common finding in these patients, requiring dextrose supplementation.

Treatment

An Addisonian crisis should be treated very aggressively with intravenous fluid therapy (IVFT) to correct the hypovolaemia and subsequent hypotension (0.9% NaCl, initial 30-90 ml/kg IV bolus over 15 minutes, then 2-3 times maintenance depending on clinical response). Glucocorticoids are administered in the form of injectable dexamethasone 0.5-1.0 mg/kg IV (or hydrocortisone). TIP: dexamethasone is the only glucocorticoid which does not interfere with the AcTH stimulation test! Patients will be severely acidotic, so sodium bicarbonate is indicated if IVFT fails to correct the pH. Hypoglycaemia should be treated with a 50% dextrose bolus or CRI as needed. Treatment of severe hyperkalaemia includes glucose with neutral insulin to increase cellular uptake of potassium, and/or calcium gluconate to stabilize the cardiac myocytes. Most patients become over following 12-72 hours.
Maintenance therapy includes fludrocortisone acetate (Florinef) at 0.02 mg/kg/day PO, as a mineralocorticoid supplement. Dose ranges may vary wildly between individuals and response can be monitored using weekly blood electrolyte concentrations (ideally patients should have Na:K >27). Glucocorticoid supplementation is indicated initially and during times of stress, but is used long term in less than 50% of patients. Prednisolone at 0.25 mg/kg PO BID is used initially, then the dose is tapered over 3-4 weeks until it is discontinued.

Prognosis

Excellent with ongoing monitoring and good owner compliance.

Hyperthyroidism

Hyperthyroidism results from excessive circulating thyroxine (T4) and triiodothyronine (T3) because of thyroid dysfunction.
While most common in cats, hyperthyroidism has been described in dogs, most typically secondary to thyroid carcinoma.

In cats, typical signs include weight loss, tachycardia, polyphagia, polyuria, polydipsia, nervousness, irritability, G.I. signs, and a poor hair coat. Occasionally they may be anorexic or lethargic. Patients often present with tachycardia and a heart murmur, gallop, or arrhythmia, and often have a palpable thyroid nodule.
While rarely an emergency situation, cats can present in what is called a "**thyroid storm**". This is characterized by severe tachycardia, open-mouthed breathing, hypoxia, and a panicked disposition. These cats are often confused with primary respiratory diseases, and need to be handled similarly with minimal stress. Dogs will occasionally present in this same situation, however it is most likely due to an overdose in thyroid medication for hypothyroidism.

Diabetes Mellitus

Diabetes Mellitus (DM) is another endocrine diseasethat rarely falls into the ECC category. Typically, these dogs and cats are managed medically and often as outpatients.
DM occurs when the patient either does not produce enough insulin, or is resistant to the insulin that they do produce. Insulin is a very important hormone that has activity on maintaining glucose homeostasis, fatty acid synthesis, and movement of many ions into and out of cells. In glucose homeostasis, insulin stimulates the conversion of glucose to glycogen, the storage form of glucose stored in the liver. Insulin also stimulates the uptake and utilization of glucose by specific cells of the body.
Similarly to humans, we can see Type I or Type II DM, **Type I** is when there is insufficient insulin produced because the beta cells of the Islets of Langerhans have been destroyed. This process can be the result of an immune mediated process or be idiopathic. In **Type II** DM, patients have developed insulin resistance, meaning essentially that they need more and more insulin to do the job.
Often in dogs and cats we simply group them into **Insulin Dependent Diabetes Mellitus** (IDDM), and **Non-insulin Dependent Diabetes Mellitus** (NIDDM). Cats are more likely than dogs to be NIDDM, and are often treated with hyperglycemic drugs that help to reduce insulin resistance. Most dogs are IDDM, meaning that they require insulin treatments.

Occasionally we may see hypoglycemia or hypoglycemic seizures following an overdose of insulin. Patients will normally be treated with an IV bolus of dextrose, followed by careful glucose monitoring and dextrose CRI as necessary.
I'm not going to talk too much more about uncomplicated DM, but I would like to discuss the "emergency form" of DM referred to as Diabetic Ketoacidosis.

Diabetic Ketoacidosis (DKA)
DKA occurs when a patient with DM is severely uncontrolled, often in cases where DM has not yet been diagnosed. Diagnosis of DM is often made on presentation of a DKA patient.
As already mentioned, one of insulin's major functions is to modulate glucose levels in the body. In doing so, it has to fight against other hormones whose function is to increase glucose levels, termed hyperglycemic or diabetogenic hormones.
Common examples of these hormones include: glucagon, catecholamines, estrogen, and cortisol. So, in a DKA patient, not only do we have a deficiency of insulin, we may have normal or increased levels of diabetogenic hormones. Increased levels are usually caused by other disease processes, such as neoplasia, or hyperadrenocorticism.

These other disease processes are often enough to cause a patient to become severely uncontrolled, and develop into a DKA.
So, what exactly happens in DKA? Essentially the deficiency in insulin allows the diabetogenic hormones to win the battle, so to speak. They stimulate the liver to release more and more glucose, which would normally be moved into the cells for utilization, however with the insulin deficiency this does not happen.
This results in a high circulating glucose (hyperglycemia). Furthermore, the insulin deficiency causes a change in fatty acid metabolism, and instead of converting them to triglycerides, the fatty acids undergo an oxidation process, resulting in ketones. The three ketones are acetone, acetoacetic acid, and β-hydroxybutyric acid (notice the "acid" in the names of these ketones...this is key).
In summary, the beginning stages of a DKA are:

1. deficiency of insulin
2. excess of diabetogenic hormones
3. change in fatty acid metabolism resulting in the formation of ketones

Once all of this has occurred, DKA will progress as the hyperglycemia and excess ketones worsen. Glucose and ketones will be excreted by the kidneys resulting in the urine becoming **hyperosmotic**. The hyperosmotic urine causes water to be drawn through the kidneys in an effort to dilute the hyperosmotic fluid. This is termed ***osmotic diuresis***, and causes the patient to lose water, sodium and potassium in the urine, thus becoming very dehydrated with substantial electrolyte abnormalities. With increased ketogenesis, the blood becomes more and more acidic, leading to a profound metabolic ***acidosis.*** The body's buffer, HCO3 is gradually used up as the acidosis progresses. In late stages, the patient will begin to breathe very deeply with a normal to very slow rate, in order to lower blood CO2 and compensate for the acidosis (although this can rarely be done completely). This breathing pattern is referred to as ***Kussmaul Respirations***, and is a characteristic of diabetic coma.

When these patients present as an emergency, they are severely dehydrated, profoundly acidemic, often very depressed or non-responsive. Ketones, a fruity odour may be evident on the breath; blood gases will reveal several abnormalities including *hyperglycemia*, *severe metabolic acidosis*, *hyponatremia*, *hypokalemia*, *hypophosphatemia*, and other *electrolyte derangements*.

DKA can be precipitated by factors such as insufficient insulin therapy, bacterial infections and drugs that affect insulin action. Concurrent disease or steroid administration is identified in over 70% of cases presenting with DKA.
Common concurrent disorders found in dogs with DKA include urinary tract infections, hyperadrenocorticism, cardiac failure, renal failure and drug therapies (steroids or progestagens). In cats inflammatory bowel disease, hyperthyroidism, asthma and pancreatitis are common concurrent disorders which can precipitate DKA.

Clinical findings:

- Sick animal
- Dehydration (due to osmotic diuresis and vomiting/diarrhoea)
- Tachycardia
- Depressed demeanour
- Vomiting/diarrhoea/anorexia

Clinicopathological findings:

- Hyperglycaemia
- Glycosuria
- Ketonuria/ketonaemia
- Metabolic acidosis
- Often azotaemic
- Electrolyte abnormalities
- Neutrophilia +/- left shift

Treatment

The goal of therapy is to: 1) correct dehydration and restore intravascular volume,
2) normalise blood glucose levels,
3) correct electrolyte and acid-base abnormalities.

Restoration of Fluid Volume Deficit

The fluid volume deficit is a result of decreased circulating volume secondary to hyperglycemia and induced osmotic diuresis (due to glucose and ketones in the urine). Fluid loses may be also due to vomiting and lack of fluid intake.Within twelve to twenty four hours of initiating therapy our desired outcome is to return the patient to a normovolemic state as evidenced by a normal blood pressure, normal heart rate, normal CVP, balanced ins and outs, good urine production, normal skin turgor and pink and moist mucous membranes. Preferably, a central venous catheter is placed so that periodic blood samples can be obtained and so that central venous pressure measurements can be taken to help guide fluid therapy.
The initial fluid type to administer is dictated by electrolyte status. Because many DKA patients are hyponatremic, 0.9 % saline is often the fluid of choice. DKA patients are typically potassium depleted and administered fluids should be potassium enriched. Fluid rates and volumes are dependent upon severity of dehydration, maintenance needs and abnormal ongoing losses (vomiting, diarrhea and diuresis). Caution should be exercised if hypotonic sodium solutions are utilized. Too much free water puts the patient at risk for the development of cerebral oedema.

Reduction of Serum Glucose Concentration

Regular crystalline insulin is recommended for the treatment of DKA. Insulin therapy willdecrease blood glucose by driving glucose into the cells providing the cells with this energysource, rather than ketone producing fatty acids. In addition, potassium is driven into the cells resulting in a decrease in serum potassium levels and unmasking a total body potassium deficit.
Insulin protocols include the intermittent intramuscular (IM) technique, and the continuous low dose IV infusion technique.
In the IM technique, insulin is administered every 2 hours based upon the blood glucose level while adjusting the dose up or down depending on the rate of declining glucose levels. Once the blood glucose approaches normal levels the hourly IM insulin dose can be changed to the subcutaneous route and administered every four to six hours.

When the patient is eating and drinking, and is not vomiting the regular insulin may be switched to a longer acting form of insulin.
In the continuous low dose IV infusion technique, the regular insulin dose is diluted in 250 mL of 0.9 % saline. The insulin infusion is piggybacked on to the primary fluid line and administered with a fluid infusion pump. Insulin binds to glass and plastic, so, the first 50 mL of the infusion should be discarded. The ultimate goal is essentially the same as the IM technique.
Initially blood glucose concentration is checked every one to two hours. Blood glucoseconcentration should decline by 50 - 100 mg/dl/hr.3 The patient should be monitored forhypoglycemia. It is characterized by lethargy, depression, ataxia, weakness, seizures, and coma.

Electrolyte and Acid-Base abnormalities

Once insulin therapy is started, potassium is driven back into cells and serum levels will drop, leading to the risk of hypokalaemia. Aggressive fluid therapy will also dilute serum potassium, so supplementation is likely to be required.
In the absence of electrolyte measurements clinical signs and ECG monitoring may be utilised. Clinical signs of hypokalemia include severe muscle weakness, cervical ventroflexion and arrhythmias. Clinical signs of hyperkalemia include bradycardia, weakness and neuromuscular paralysis. Ketones are acids, which are buffered by bicarbonate in the extracellular fluid. With the excessive ketone production and with a bicarbonate deficit metabolic acidosis develops. Decreased tissue perfusion may also be a contributing factor to the development of the metabolic acidosis. The initiation of insulin and fluid therapy will contribute to the correction of the acid base abnormalities. The use of sodium bicarbonate to correct metabolic acidosis is controversial.

Additional therapy:
1. Antimicrobials (many have UTIs)
2. Gut protectants (ranitidine/famotidine/cimetidine, sucralfate)?
3. Anti-emetics (maropitant, metoclopramide)
4. Identify and treat concurrent illness (e.g. UTI, pancreatitis)
5. Bicarbonate only considered if pH<7.1 and unresponsive to fluid therapy
6. Magnesium- hypomagnesaemia can lead to hypokalaemia which is unresponsive to supplementation. In such cases magnesium should be supplemented (0.75-1MEq/kg/24hrs)

Monitoring:
1. Check electrolytes every 6-8hours initially and adjust potassium as required
2. Check phosphate levels every 6-8hours (not required for first 12hrs)
3. Check blood glucose q2-4hrs until stabilized

Diabetes Insipidus (DI)
DI is not very common but patients may present as extremely dehydrated and hypernatremic. It is condition in which the hypothalamus fails to produce enough antidiuretic hormone (ADH), aka vasopressin. With a drop in circulating ADH, the kidneys fail to resorb water, causing the patient to become extremely polyuric. This triggers polydipsia as well.

If water is freely available, many patients can compensate by drinking more for some time, however if water is restricted (as owners may start to do in an effort to reduce the polyuria), the polyuria can cause the patient to become extremely dehydrated in a very short time. Patients may be extremely hypernatremic and must be treated with extreme caution. The hypernatremia is likely a chronic issue, and reducing the hypernatremia quickly with fluid therapy can lead to tragic results. We will discuss fluid therapy of the hypernatremic patient in the real time session.
DI is often seen as a result of a head trauma, with damage to the hypothalamus. It can also be caused by a brain tumour. Treatment of DI involves not only correcting the dehydration, but also providing exogenous ADH, which is usually done in the form of DDAVP (desmopressin) eye drops.

Hyper/Hypoparathyroidism

Hypoparathyroidism is a condition in which the parathyroid glands fail to produce enough parathyroid hormone (PTH), resulting in imbalance in calcium, phosphorus and Vitamin D. Notably, the patient will have hypocalcemia, hyperphosphatemia and reduced vitamin D production.
Conversely, hyperparathyroidism is associated with high PTH, resulting in hypercalcemia, and hypophosphatemia.
Emergency treatment is more commonly indicated for hypocalcemia associated with hypoparathyroidism, and the patient may arrive with tremors or seizures, tetany, ataxia and tachycardia and is normally treated initially with calcium gluconate infusion. Once the calcium level is stabilized, vitamin D supplementation, and oral calcium can maintain the patient.