Anaesthesia for patients with endocrine diseases

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As the number of geriatric patients in the veterinary population increases, the number of patients with concurrent diseases, including endocrinopathies, will be more prevalent.

These patients may live with these conditions for many years and may require anaesthesia for unrelated issues in this time.

Understanding the pathophysiology of the endocrinopathy, and the clinical syndromes associated with it, will enable the clinician to pre-empt problems that may occur.

Where possible, treatment for the endocrinopathy should be initiated before anaesthesia and surgery. This will improve function and, hopefully, decrease the likelihood of morbidity.

Thyroid

Hypothyroidism

Table 1. Anaesthetic choices for hyperthyroid patients	
Premedication	
Acepromazine plus opioid	● Acepromazine will produce a degree of vasodilation, so take care with blood pressure and hypothermia. ● The combination may not be adequate for more fractious patients. ● Protection of the myocardium versus arrhythmias. ● Opioid must be adequate for the planned procedure.
Medetomidine plus opioid	● Low-dose medetomidine: 0.002mg/kg to 0.005mg/kg may have an adequate sedative effect as a premedication. ● Will decrease heart rate. ● Blood pressure will increase initially, so avoid in hypertensive patients.
Ketamine plus midazolam	● Ketamine will increase heart rate and cardiac work; avoid in patients with heart disease. ● Ketamine undergoes a degree of renal metabolism in the cat.
Opioid alone	● Butorphanol 0.1mg/kg to 0.4mg/kg may be adequate to allow venous cannulation. ● Full agonist opioids, such as methadone, are required for a more invasive procedure. ● Minimal cardiovascular effects. ● May not be adequate sedation to allow restraint.
Alfaxalone plus opioid	● Variable degree of sedation 2mg/kg to 3mg/kg alfaxalone. ● Appears to maintain heart rate.
Induction of anaesthesia	
Propofol	● Administer slowly to effect. ● Hypotension may occur. ● Smooth induction and recovery.
Alfaxalone	● Administer slowly to effect. ● Hypotension may occur. ● Stormy recoveries may occur, especially after short anaesthetics with little or no premedication.
Inhalational agents	● May lead to stressful induction of anaesthesia – catecholamine release. ● Isoflurane resented more than sevoflurane. ● Will require rapid endotracheal intubation. ● Not recommended as a first choice and should be reserved for those patients where other chemical restraint is not possible.
Maintenance of anaesthesia	
Inhalational agents	● Most common choice. ● Minimal metabolism, so recovery rapid. ● Rapid change in anaesthetic plane. ● Sevoflurane and isoflurane may lower blood pressure.
Injectable agents	● Require metabolism of drugs to a greater extent than inhalational agents.

Table 1. Anaesthetic choices for hyperthyroid patients.

Hypothyroidism results from decreased secretion of thyroid hormones and a consequent slowing of metabolism affecting multiple systems.

The physiological effects of hypothyroidism are:

- obesity
- lethargy
- hypothermia
- reduced drug metabolism
- bradycardia
- hypotension

Of particular interest to the anaesthetist is the possible impaired cardiac contractility.

In general, these patients may require lower doses of sedatives and anaesthetic agents, and should be closely monitored from premedication to recovery. They may also be more likely to become hypothermic and take longer to reach normal temperature, because of the suppressed level of metabolism.

Laryngeal paralysis has been associated with hypothyroidism. An increased inspiratory effort, often with an inspiratory stridor, may indicate its presence. The clinician should be ready for a difficult endotracheal intubation and may wish to evaluate laryngeal function at the time of anaesthetic induction.

If laryngeal paralysis is suspected, but not being surgically corrected, the patient should be closely monitored during recovery for upper airway obstruction.

Where possible, patients should be actively warmed from the time of premedication and be closely monitored during recovery until they return to normal body temperature.

Treatment should be initiated before anaesthesia and surgery. This will improve function and, hopefully, decrease the likelihood of morbidity.

Hyperthyroidism

Hyperthyroidism is most common in cats and some owners may elect for a surgical treatment. However, it is important to stabilise thyroid function before general anaesthesia, as cardiovascular function may be severely compromised.

The physiological effects of hyperthyroidism are:

- hypertrophic cardiomyopathy
- poor body condition score
- increased potential for catecholamine release
- possible underlying renal insufficiency
- hypertension
- nervous/aggressive behaviour
- tachypnoea
- vomiting

Hypertrophic cardiomyopathy is the most common cardiac disease that occurs secondary to hyperthyroidism in cats. They may exhibit gallop rhythm, tachycardia and, sometimes, pleural effusion. Hypertrophic cardiomyopathy is often reversible when treatment is started.

When the patient has been treated for hyperthyroidism, it may show signs of renal insufficiency (due to decreased glomerular filtration rate) and renal perfusion, so renal parameters and urine-specific gravity should be evaluated after stabilisation of the thyroid disease.

Patients may also experience hypertension, which should be evaluated pre and post-treatment for thyroid disease. Treatment should be initiated for hypertension that does not resolve with stabilisation of thyroid disease prior to general anaesthesia.

A few cases may require anaesthetising or sedating with uncontrolled hyperthyroidism; the owner should be informed of the risks involved, which may include worsening of cardiac function and death.

Assuming the patient has been adequately stabilised and renal parameters are within normal limits, the anaesthetic plan should be tailored to the individual patient and procedure (**Table 1**). General considerations to be aware of include:

- Hypothermia – due to decreased body mass index, these patients are likely to develop hypothermia. Measures should be taken from the time of the premed to maintain heat and actively warm the patient. Preheating may help to decrease the initial loss of heat during anaesthesia. The ability to do this may depend on the patient. Continuing active heating during the preparation time will also help mitigate some heat loss due to clipping and prepping of the surgical area. Simple actions, such as wrapping feet with bubble wrap, may also help minimise heat loss.
- Temperament – even with stabilisation, these patients may be more fractious than usual; gentle, stress-free handling is essential for a smooth anaesthetic period. Adequate chemical restraint may be needed to allow cannulation of a vein and induction of anaesthesia.
- Cardiac function – one aim of anaesthesia should be to minimise cardiac work. Avoiding catecholamine release (stress) or drugs such as ketamine, which stimulate the sympathetic system, is desirable.

Unstable hyperthyroidism

Table 2. Suggested protocol for glucocorticoid supplementation during surgery in dogs with adrenal insufficiency. (Johnson and Norman, 2007)

Minor surgery	Major surgery
Preoperatively – either hydrocortisone 4mg/kg to 5mg/kg, dexamethasone 0.1mg/kg to 0.2mg/kg or prednisolone sodium succinate 1mg/kg to 2mg/kg.	Preoperatively – either hydrocortisone 4mg/kg to 5mg/kg, dexamethasone 0.1mg/kg to 0.2mg/kg or prednisolone sodium succinate 1mg/kg to 2mg/kg.
Immediately postoperatively – either hydrocortisone 4mg/kg to 5mg/kg, dexamethasone 0.1mg/kg to 0.2mg/kg or prednisolone sodium succinate 1mg/kg to 2mg/kg.	Immediate postoperatively – either hydrocortisone 4mg/kg to 5mg/kg, dexamethasone 0.1mg/kg to 0.2mg/kg or prednisolone sodium succinate 1mg/kg to 2mg/kg.
Postrecovery – back to normal maintenance regime.	Postrecovery three days – either prednisolone/ prednisone 0.5mg/kg twice daily, cortisone/ hydrocortisone 2.5mg/kg twice daily or dexamethasone 0.1mg/kg once daily for three days. Day four – back to normal regimen.

Table 2. Suggested protocol for glucocorticoid supplementation during surgery in dogs with adrenal insufficiency. (Johnson and Norman, 2007).

Many patients with unstable hyperthyroidism may be difficult to handle, which can make performing diagnostic tests a challenge. The considerations taken for stable hyperthyroid patients remain valid and the aim of sedation or anaesthesia is to maintain cardiovascular function to as close to normal as possible.

An echocardiogram to assess cardiac function may be an advantage, if it is possible, to allow

appropriate anaesthetic planning.

If a hypertrophic obstructive cardiomyopathy exists, evidence suggests using medetomidine to slow the heart rate and allow a more effective contraction (Lamont et al, 2002).

However, without echocardiography, it is wise to avoid the use of alpha-2 agonists in patients experiencing cardiac symptoms due to hyperthyroidism. The main aim is to keep heart rate about similar to the resting heart rate to maintain cardiac output.

Adrenal glands

Stress response to anaesthesia and surgery

The “stress response” is the body’s way of dealing with noxious stimuli; this system activates during anaesthesia and surgery.

An impaired endocrine system may influence the stress response to anaesthesia and surgery, changing the risks associated with both of these.

In some cases, it may be appropriate to initiate the stress response by administering steroids at the time of anaesthesia and surgery, allowing a physiological response to noxious stimuli (discussed more in the hypoadrenocorticism section).

Hypoadrenocorticism (Addison’s disease)

Hypoadrenocorticism is caused by a deficiency of aldosterone and, to a certain extent, glucocorticoids. The physiological effects are:

- hyponatraemia
- hyperkalaemia – cardiac arrhythmias may result from this
- hypovolaemia and hypotension
- pre-renal azotaemia
- poor tolerance to stress

Stabilising these patients prior to general anaesthesia is essential, especially with respect to potassium levels and the possible secondary cardiac arrhythmias. When preparing to anaesthetise a patient being treated for hypoadrenocorticism, take a blood sample to check electrolytes are within normal limits.

Assuming all is normal, the patient can be admitted as per routine on the day of the surgery and any medication should be continued as usual. Anaesthesia premedication and induction can be carried out as normal.

One factor to take into consideration is the patient's ability to mount an effective stress response in the face of anaesthesia and surgery. The author will often supplement the patient with exogenous steroids. The amount administered depends on the perceived severity of the stress – for example, major or minor surgical procedures (**Table 2**).

Hyperadrenocorticism (Cushing's disease)

Figure 1. A dog with hyperadrenocorticism. Notice the pot-bellied appearance that may impact on ventilation, especially when placed in dorsal recumbency.

Cushing's disease is characterised by an overproduction of glucocorticoids. This excess steroid can lead to muscle weakness, redistribution of fat to the cranial abdomen, generalised neuropathies and coagulation abnormalities (**Figure 1**). Problems related to this disease, their impact on anaesthesia and their possible solutions are listed in **Table 3**.

These patients are at higher risk of pulmonary thromboembolism due to the altered coagulation function. Early mobilisation after surgery may help reduce clot development, so adequate analgesia is essential. However, it is probably prudent to avoid NSAIDs as they may be synergistic with the high levels of circulating steroids present in these patients.

Maintaining adequate perfusion is essential during anaesthesia, so monitoring blood pressure is desirable. Low doses of acepromazine (0.005mg/kg to 0.01mg/kg IV or IM) may allow some vasodilation without causing hypotension. This, combined with an opioid, may allow stress-free handling.

Medetomidine should be avoided in hypertensive patients, as it will produce an initial hypertension. It may be helpful at anaesthesia induction to administer supplemental oxygen for five minutes beforehand, in an effort to reduce the incidence of hypoxaemia.

Pancreas

Insulinoma

Although unlikely to perform surgery to remove a pancreatic mass in general practice, clinicians may have to sedate or anaesthetise a patient with a suspected insulinoma when making a diagnosis.

Table 3. Physiological effects of hyperadrenocorticism

Clinical change	Body system affected	Effect during anaesthesia	Action
Muscle weakness	Respiratory	Hypoventilation, especially in combination with inhalational agents.	Monitor ventilation. Intermittent positive pressure ventilation may be necessary.
Pot-bellied appearance (**Figure 1**)	Respiratory	Cranial abdominal fat and enlarged liver may push on diaphragm, decreasing ability to flatten, and lead to hypoventilation.	Monitor ventilation. Intermittent positive pressure ventilation may be necessary.
Hypertension	Cardiovascular, renal and CNS	Blood pressure autoregulation curve pushed to the right.	Stabilise blood pressure prior to anaesthesia or maintain higher than normal blood pressure.
Hypercoagulability	Cardiovascular and respiratory	Thromboembolism more likely in perioperative period.	Stabilise condition prior to anaesthesia.
Diabetes	Endocrine	May have refractory hyperglycaemia.	Stabilise diabetes and Cushing's disease before anaesthesia and surgery.

Table 3. Physiological effects of hyperadrenocorticism.

Insulinomas produce excess insulin, thereby making the patient hypoglycaemic. Hypoglycaemia may be controlled by small frequent meals, sometimes with additional steroid therapy. Preoperative preparation should, therefore, be carefully considered.

Minimise preoperative fasting in an effort to reduce the likelihood of hypoglycaemia. If it does occur, bolus administration of glucose should be avoided as this can lead to increased insulin release and, therefore, a rebound hypoglycaemia. Instead, a slow increase in glucose should be initiated using 2.5% to 5% glucose solutions. The author often supplements Hartmann's solution with glucose to deliver a balanced electrolyte solution (see diabetes section).

Incorporating medetomidine into the anaesthetic protocol may have some advantages, as it is an insulin antagonist and will help increase glucose levels during sedation and anaesthesia (Guedes and Rude, 2013). Monitoring blood glucose approximately every 60 minutes to 90 minutes during the perioperative period will help pre-empt any hypoglycaemic episodes.

If anaesthesia for pancreatectomy is performed, blood glucose should be measured regularly postoperatively.

Hyperglycaemia and hypoglycaemia may occur after insulinoma removal. Reports exist of propofol increasing the likelihood of pancreatitis. The mechanism of this is not entirely understood, but may

be related to the large lipid load administered.

Pancreatitis can also result from surgical handling of the pancreas, disruption of the blood supply and hypotension during surgery.

Diabetes

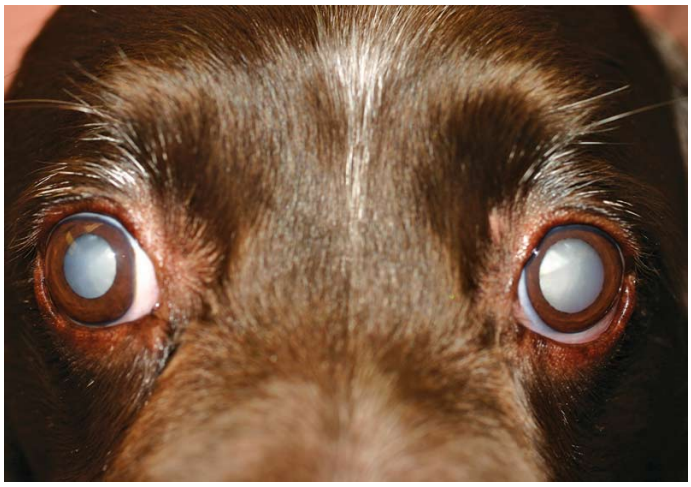

Figure 2. Mature diabetic cataracts.

The reasons for diabetic patients requiring general anaesthesia vary – from management of the underlying condition (for example, ovariohysterectomy) to unrelated reasons, such as anaesthesia to perform surgery for tumour removal (**Figure 2**).

Unless it is a life-threatening emergency, anaesthesia should only be performed on patients that have had their diabetes stabilised. Patients that have not been stabilised may be ketoacidotic with severe metabolic dysfunction (**Table 4**).

Notable effects

Diabetes effects of particular importance to anaesthesia are:

- Decreased oxygen transport – glucose interferes with the interaction between haemoglobin chains and may alter oxygen saturation of haemoglobin.
- Autonomic dysfunction:
- – Hypothermia due to a decreased ability to produce vasoconstriction.
- – Decreased ability to regulate blood pressure leading to a greater incidence of hypotension (this may be due to a lack of vasoconstriction and decreased vagal control of the heart).
- – Blunting of the effects in response to atropine.
- Gastrointestinal effects leading to possible delayed transit of food through the

gastrointestinal tract.

Hypoglycaemia effects

Hypoglycaemia can cause irritability, seizures, bradycardia, hypotension and respiratory failure.

All can be masked by general anaesthesia and sedation; therefore, blood glucose should be monitored during the procedure.

Diabetic patients may also be more susceptible to the effects of hypoglycaemia at higher glucose levels than a healthy patient, though the exact levels have not been established in canine and feline patients.

Anaesthesia for stable diabetic patients

It is useful to have a checklist or “crib sheet” to follow when admitting diabetic patients. Questions to include are:

- Recent history of hypoglycaemic episodes, or whether the patient has been “off colour”.
- Has insulin been administered today? If so, how much?
- What is the normal insulin regime? What type of insulin and how often is it administered?
- Details about the feeding regime, type and regularity of feeding. If the patient is being hospitalised overnight, ask the owner to bring in the patient’s food.
- Check if any food has been given today.
- Is the patient on other medication – for example, NSAIDs?

Even if a patient is stabilised with regard to its diabetes, it is very common anaesthesia and surgery will lead to a short period of destabilisation. Returning the patient to its normal regime as quickly as possible is the main aim.

Patients receiving once-daily insulin

There are no hard rules for patients receiving once-daily insulin, but it is more practical and logical to perform surgery in the morning to allow minimal disruption of the regime. Ask the owner to feed the pet as normal the night before, but withhold food and insulin in the morning. **Panel 1** is the protocol used in the author’s clinic.

Few studies exist into the optimal insulin regime around the time of anaesthesia. One study investigated the use of full-dose insulin, compared to a quarter of the usual dose, and found both regimes resulted in unpredictable blood glucose levels. The full dose of insulin only gave marginal benefits over the reduced insulin dose (Kronen et al, 2001).

Patients receiving twice-daily insulin

Table 4. Physiological effects of diabetes mellitus and ketoacidosis

Diabetes mellitus
• loss of blood glucose homeostasis • polyuria/polydipsia • ketoacidosis • weight loss
Diabetic ketoacidosis
• dehydration • compromised renal function • hypovolaemia • vomiting • metabolic acidosis • anorexia • sodium deficiency • CNS depression • total body potassium deficit • underlying serious illnesses

Table 4. Physiological effects of diabetes mellitus and ketoacidosis.

Patients receiving twice-daily insulin can be anaesthetised in the morning or afternoon with minimal effect on their diabetic management.

Morning surgery

For morning surgery, use the same regime as for patients receiving once-daily insulin, until the end of surgery. When the surgery is finished, the patient should be encouraged to eat when safe. Blood glucose should be measured if the patient does not eat, particularly when peak insulin activity is expected. The aim is to try to return to a normal regime as soon as possible, to be able to administer the evening insulin dose.

Afternoon surgery

Preoperative fasting can be limited to six hours for anaesthesia for afternoon surgery (Savvas et al, 2009). It is important to try to time the anaesthesia so it is six hours after the last meal – either move the morning feeding and insulin forward a little, or delay anaesthesia.

Ask owners to feed as normal and give the usual dose of insulin in the morning. There is no need to perform a blood glucose if the patient has eaten well that morning, unless there has been a recent history of hypoglycaemic episodes.

Perform blood glucose at the time of induction of anaesthesia and every 30 minutes to 60 minutes thereafter.

If blood glucose has been within normal limits during surgery, feed when the usual schedule dictates and carry on insulin therapy as usual.

General considerations

Considerations for anaesthesia and surgery include:

- Start IV fluids plus glucose (2.5% to 5%) if blood glucose is greater than 5mmol/L, otherwise Hartmann’s solution would be indicated at the time of surgery (Table 5).
- – To make up a 5% solution of glucose, add 50ml of 50% glucose to 500ml Hartmann’s solution or sodium chloride.
- – Avoid 5% dextrose solutions as they are just metabolised to free water and are not a balanced electrolyte solution.
- Pre-anaesthetic medication should be tailored to the patient’s temperament and the procedure. Ideally, choose drugs with a minimal hangover effect to allow a more rapid recovery from anaesthesia, which, in turn, allows the patient to eat earlier and restart insulin.
- – Acepromazine 0.005mg/kg to 0.01mg/kg IM.
- – Opioids such as methadone 0.2mg/kg to 0.4mg/kg or buprenorphine 0.02mg/kg IM or IV.
- – Medetomidine acts as an insulin antagonist, so be aware blood glucose is likely to increase after administration. Generally, it is better to reserve this drug for fractious animals that cannot be sedated with other drugs.
- – Ketamine/midazolam in cats gives a good degree of sedation with minimal cardiovascular

effects. An opioid will need to be added to this combination to provide longer duration analgesia.

- Induction of anaesthesia – it is important to use the drugs you are most comfortable with. Anecdotal evidence shows propofol may be associated with an increased risk of pancreatitis, though this is not a clearly defined risk. It may be an advantage to use alfaxalone in patients with pre-existing pancreatitis, as a further episode may have a deleterious effect on diabetic stability.
- Maintenance of anaesthesia – the choice of agent for maintaining anaesthesia is unlikely to have a marked outcome on the patient in terms of their diabetes management. Important things to ensure are:
- – Normotension: maintain mean arterial blood pressure between 60mmHg and 100mmHg or systolic blood pressure at 100mmHg to 150mmHg. This will help to maintain blood flow to the pancreas and other vital organs.
- – Oxygen levels: delivering oxygen to tissues is important to maintain cellular health and depends on cardiac output and arterial blood oxygen content. Because these are difficult to measure in practice, blood pressure and haemoglobin oxygen saturation are used as an indicator. The most common complication reported in one study was moderate and severe hypotension (hypotension was defined as mean arterial blood pressure greater than 55mmHg in this study; Oliver et al, 2010). This may have been due to hypovolaemia secondary to hyperglycaemia and osmotic diuresis.
- Analgesia – a multimodal approach will help decrease the dose requirements for anaesthetic agents and minimise the effects on blood pressure. Using drugs from several groups of analgesics is also likely to decrease the doses used of each individual drug and, potentially, decrease the side effects – such as sedation – that may be seen with drugs such as opioids. The groups of drugs that can be used include:
- – Opioids: these are often our first line of treatment for surgical pain, but they can cause a degree of sedation, nausea and dysphoria – particularly if the patient is not very painful. It is prudent to avoid opioids more likely to induce emesis and nausea, such as morphine, and use drugs that do not have these effects, such as methadone or buprenorphine. The titration of opioids to clinical effect is important to minimise side effects, particularly if multiple groups of drugs are administered.
- – NSAIDs: these drugs are also commonly used in patients undergoing surgery and are useful for treating inflammatory pain.
- – Local anaesthetics: these can be used to perform nerve or regional blocks to reduce or obliterate the transmission of painful stimuli from the surgical site to the spinal cord. Lidocaine can also be administered systemically as a continuous rate infusion, particularly for visceral and neurological pain.
- – Ketamine: at sub-anaesthetic doses, ketamine elicits significant analgesia – particularly in relation to neuropathic pain.

Anaesthesia for patients with diabetic ketoacidosis

Table 5. Addition of 50 per cent glucose to Hartmann's solution

Glucose solution required	1L Hartmann's solution	500ml Hartmann's solution
2.5 per cent	50ml of 50 per cent glucose	25ml of 50 per cent glucose
5 per cent	100ml of 50 per cent glucose	50ml of 50 per cent glucose

NB. Remove the amount to be added from the bag.

Table 5. Addition of 50% glucose to Hartmann's solution.

In ketoacidotic patients, the anaesthetic risk is high; therefore, stabilisation prior to anaesthesia is vital.

In the rare cases where surgical intervention or anaesthesia cannot be delayed, consider the following points:

- electrolyte levels: hyperkalaemia and hyponatraemia
- metabolic acidosis
- renal function compromise

Cardiovascular collapse can occur secondary to severe dehydration, due to diuresis and fluid deprivation, and/or myocardial depression, due to severe metabolic acidosis. Rapid correction of diabetic ketoacidosis can result in cerebral oedema.

Fluid therapy

Fluid therapy should be tailored to any blood results and the clinical condition of the patient.

Hyperkalaemia correction before anaesthesia is important and a balanced electrolyte solution can help this. A 2010 study showed sodium chloride or Hartmann's solution could be used to rehydrate cats with hyperkalaemia due to urethral obstruction, but Hartmann's was more effective at treating acidosis (Cunha et al, 2010).

This could be extrapolated to indicate using Hartmann's solution in diabetic ketoacidosis may be more sensible as it will help to alleviate the acidosis and electrolyte disturbances. In addition, appropriate insulin therapy should be started and monitored.

Panel 1. Protocol for patients on once-daily insulin

- Place an IV cannula and measure blood glucose.
- Administer insulin:
  - Blood glucose lower than 5mmol/L – no insulin.
  - Blood glucose 5mmol/L to 11mmol/L – quarter usual insulin dose.
  - Blood glucose greater than 11mmol/L – half usual insulin dose.
- Monitor blood glucose at the beginning of anaesthesia and then every 30 minutes to 60 minutes afterwards.
- Offer food and encourage to eat as soon as possible and safe after recovery.
- Administer half the usual insulin dose when the patient has eaten and monitor the patient clinically for the rest of the day. A blood glucose measurement at the time of peak effect can also be performed.

Panel 1. Protocol for patients on once-daily insulin.

Cardiovascular stability should be achieved before anaesthesia, as with other critical conditions, but monitoring this can be problematic.

Parameters that can be objectively measured are:

- heart rate and the effect of a bolus of crystalloid fluids on heart rate
- blood pressure
- central venous pressure
- urine output (remember hyperglycaemic patients may present osmotic diuresis)

Subjective assessments of cardiovascular status are:

- pulse assessment
- mucous membrane colour
- capillary refill time

If the patient is not adequately stabilised, the metabolic acidosis present will result in an increased effect of anaesthetic agents. Induction agents should be given slowly to effect and depth of anaesthesia should be monitored closely.

The patient will also be more susceptible to the effects of hypoxaemia, so pre-oxygenation may be advisable and the airway should be rapidly secured.

Where possible, end-tidal carbon dioxide should be monitored and, if greater than 45mmHg, intermittent positive pressure ventilation should be started to avoid worsening of the pre-existing acidosis.

- Some drugs in this article are used under the cascade.

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