Chapter 42

Endocrine Disease

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Introduction

Endocrine disease is more often a factor influencing anesthetic management than a disease directly requiring anesthesia for medical or surgical intervention. Patients with endocrine disease–induced derangements of homeostasis require that anesthetic management be designed to take into account the appropriate physiological support, perioperative monitoring, and selection of medications to reduce the risks associated with sedation, anesthesia, and analgesia. Recognition of physiological derangements typical of specific endocrine diseases provides the framework for customizing anesthesia for individual patients. Endocrinopathies often increase the requirements for intervention, particularly for physiological support.

Diabetes Mellitus

Insulin is essential for normal cellular function. The effects of insulin on normal cellular function include (a) inhibition of glycogenolysis, (b) inhibition of gluconeogenesis, (c) inhibition of lipolysis, (d) stimulation of glucose uptake into cells, (e) stimulation of potassium transport into cells, and (f) suppression of ketogenesis.[1]

Carbohydrate, protein, and fat metabolism are all affected with an insulin deficiency. Glucose uptake is decreased, especially in fat and muscle. Also, control of hepatic gluconeogenesis is lost, with the resultant hyperglycemia leading to osmotic diuresis. Muscle tissue undergoes catabolic metabolism for energy, and protein synthesis is inhibited, resulting in muscle wasting. Acetyl coenzyme A and ketone bodies are produced for energy. Lipolysis is inhibited with a resultant accumulation of ketone bodies causing osmotic diuresis and metabolic acidosis. Prolonged hyperglycemia and ketonemia can lead to (a) metabolic acidosis, (b) dehydration, (c) circulatory collapse, (d) renal failure, and/or (e) coma and death.[1]

Diabetes mellitus should be suspected in any patient with the following clinical signs: (a) a recent history of polyuria, polydipsia, weight loss, or rapid onset of cataracts; (b) dehydration, weakness, collapse, mental dullness, hepatomegaly and/or muscle wasting; and/or (c) increased rate and depth of respiration and breath with a sweet acetone odor. Diabetes mellitus occurs more frequently in female dogs and male cats. These clinical signs should alert the clinician to the possibility of diabetes mellitus.

The presence of glucose with or without ketones in the urine, along with resting blood glucose of greater than 250 mg/dL with hyperketonemia, is a common finding. Electrolyte and renal function tests may be altered (especially hypokalemia) and serum alkaline phosphatase may be increased due to hepatic fatty infiltration. Severe metabolic acidosis (a pH of less than 7.1) should be treated with sufficient sodium bicarbonate to return pH to 7.2.

A patient with diabetes mellitus should be stabilized and regulated prior to anesthesia. The anesthetic protocol is probably not as critical as the adjunct support during and after anesthesia and surgery. The key to the anesthetic management of a diabetic is to use preanesthetic and anesthetic agents that will result in the shortest anesthetic recovery time with the least amount of drug hangover. Drugs that can be antagonized (narcotics, α_2-agonists, and benzodiazepine tranquilizers) or are readily eliminated from the patient (propofol, etomidate, and inhalant anesthetics) should be considered. The goal is to get the patient awake as soon as possible so that the patient can resume its normal feeding schedule.

The procedure should be scheduled early in the morning after the administration of the patient's normal dose of insulin or one-half of the usual dose.[2] Preoperative and serial intraoperative and postoperative blood glucose levels should be determined. Ideally, the blood glucose should be maintained between 150 and 250 mg/dL. During the procedure, 2.5% to 5% dextrose in a balanced electrolyte solution should be administered to prevent hypoglycemia.[3] An intraoperative fluid rate of 11 to 15 mL $\cdot$ kg^{-1} $\cdot$ h^{-1} is usually adequate. Depending on the blood glucose values, measured hourly, the dextrose drip may need to be continued following the procedure. Avoid blood glucose extremes and lower any marked elevations of blood glucose to a rate not to exceed 75 to 100 mg/dL per hour. As soon as a postoperative patient starts eating, it is probably not necessary to continue the dextrose in the

intravenous fluids. Close monitoring of the patient should be continued, because the stress of anesthesia and surgery may cause a diabetic to decompensate. A return home and resumption of the normal regulation pattern is desired as soon as possible. The use of corticosteroids may also cause decompensation and should be avoided unless absolutely necessary.

Diabetes Insipidus

If anesthesia is needed before correction of electrolyte abnormalities, it becomes essential to continue with diuresis. Oral water deprivation can be very deleterious for cerebral function and blood pressure, so water should not be withdrawn from these patients. Generous intravenous fluid therapy is indicated to avoid hypertonic encephalopathy. Serum sodium concentration should be monitored, and appropriate fluids administered to prevent it from rising to more than 160 mEq/L. The fluid of choice is 5% dextrose in water as needed, or half-strength (0.45%) saline with 2.5% dextrose may be used if a more isotonic solute is desired. Metabolism of the dextrose provides free water and thereby reduces plasma sodium. Chronic hypernatremia should be corrected slowly, at rate not to exceed 12 mEq for first 24-h period, with correction achieved over 72 h. Rapid-onset hypernatremia (occurring within less than 24 h) can be carefully treated more rapidly.

Hypoglycemia from Insulinoma

Monitoring and supplementation of blood glucose are required in patients with an insulinoma. Acute hypoglycemia must be recognized and treated effectively with dextrose. If there is no response to intravenous dextrose, a glucagon infusion may be useful. In postoperative patients, there is a risk of acute pancreatitis after surgical removal of the insulinoma. These patients may be maintained non per os for 1 to 2 days after surgery to help reduce the risk of acute pancreatitis. Continued monitoring of blood glucose is necessary to recognize potential hyperglycemia and hypoglycemia in the perioperative period. These patients may become insulin dependent.

Hyperparathyroidism

Preoperative management requires decreasing the serum calcium before anesthesia and surgery. It is important to evaluate renal status and stabilize or treat accordingly. After parathyroid (or thyroid) removal, there is risk of acute hypoparathyroidism. These animals require repeated monitoring for hypocalcemia during the first 48 h after surgery and appropriate management.

Hypoparathyroidism

Hypoparathyroidism occurs less often than hyperparathyroidism and is often diagnosed in patients after surgery to remove either the thyroid or parathyroid glands. Close monitoring of blood calcium is indicated. Rarely, preparturient eclampsia is present in bitches requiring Caesarean section. Treat hypocalcemia with calcium gluconate until signs abate and serum calcium is at safe level, greater than 7 mg/dL.

Hypoadrenocorticism (Addison's Disease)

Hypoadrenocorticism is a deficiency in aldosterone and/or glucocorticoids that results from adrenal cortex dysfunction. As with diabetics, patients with hypoadrenocorticism should be stabilized and regulated prior to anesthesia and surgery when possible.

Hypoadrenocorticism can be caused either by diseases, destruction of the adrenal glands, or by decreased corticotropin (adrenocorticotropic hormone [ACTH]) secretion. Primary idiopathic hypoadrenocorticism is the most common cause of hypoadrenocorticism in dogs and may be immune mediated. Other diseases that may destroy the adrenal glands include systemic mycosis, metastatic tumors, hemorrhagic infarction, amyloidosis of the cortices, canine distemper, and glucocorticoid therapy for certain disorders that might cause a selective deficiency of cortisol caused by negative feedback inhibition of the hypothalamic-pituitary-adrenal axis.[4]

Decreased ACTH secretion can cause secondary hypoadrenocorticism. Adrenocorticotropic hormone directly stimulates glucocorticoid secretion and is secreted by the anterior pituitary gland. Decreased ACTH secretion may develop with diseases or tumors of the pituitary gland or with decreased secretion of corticotropin-releasing factor (CRF) owing to hypothalamic lesions. Prolonged negative feedback from exogenous corticosteroid therapy can cause glucocorticoid deficiency while maintaining adequate mineralocorticoid secretion.

The clinical signs of hypoadrenocorticism will depend on the particular adrenal hormone (aldosterone or glucocorticoids) most affected by the disease. The primary function of aldosterone is to stimulate absorption of sodium in the distal renal tubules and promote potassium excretion. Aldosterone deficiency produces hyponatremia and hyperkalemia. Hyponatremia with concurrent water loss can produce lethargy, nausea, impaired cardiac output, hypovolemia, hypotension, and/or impaired renal perfusion. Hyperkalemia will produce muscle weakness, decreased cardiac conduction, and excitability and bradycardia.

Glucocorticoid deficiency can result in significant physiological abnormalities. Cortisol stimulates gluconeogenesis, increases blood glucose, enhances extravascular fluid movement to the intravascular compartment, stabilizes lysosomal membranes, and counteracts the effects of stress. Cortisol depletion impairs renal excretion of water and energy metabolism, decreases stress tolerance, and can cause anorexia, vomiting, and/or diarrhea. Cortisol depletion rarely produces electrolyte imbalances.[4]

Hypoadrenocorticism should be suspected in any dog with a history of anorexia, vomiting, diarrhea, and lethargy when clinical findings are muscle weakness, dehydration, and bradycardia. Electrolyte imbalance may be suggestive of hypoadrenocorticism. Serum sodium levels are often less than 135 mEq/L, and serum potassium levels may be greater than 5.5 mEq/L. The sodium-potassium ratio may be less than 25:1 (normal is 33:1).

Hypoadrenocorticism is confirmed by measuring serum corti-

sol. Determination of plasma cortisol levels is the most accurate method of diagnosing hypoadrenocorticism, and resting plasma cortisol is often less than 10 μg/mL. Plasma cortisol will not significantly increase in response to exogenous ACTH administration in hypoadrenocorticism patients. Prednisolone replacement therapy must be withheld for 1 to 2 days before testing, but dexamethasone can be used without causing interference with the radioimmunoassay for cortisol.[4]

Diagnostic testing that may be helpful in confirming the diagnosis of hypoadrenocorticism includes the complete blood count (CBC), blood urea nitrogen (BUN), and electrocardiogram (ECG). The CBC reflects dehydration, and decreased cortisol will sometimes cause eosinophilia and lymphocytosis. BUN may be elevated by prerenal uremia or renal failure. The ECG may show evidence of hyperkalemia. In severe hyperkalemic cardiotoxicity, therapy may be warranted with calcium gluconate, sodium bicarbonate, insulin, and dexamethasone.

The anesthetic protocol used in the patient with hypoadrenocorticism is not as critical as the medical management prior to anesthesia. A patient with hypoadrenocorticism must be stabilized. The treatment objectives are (a) to correct the dehydration and treat hypovolemic shock if present, (b) to return renal function to normal, (c) to correct electrolyte imbalances, and (d) to supply glucocorticoids.[5] In an Addisonian crisis, priorities are the patient's pH, hypotension, ECG complexes and rhythm, and the correction of hyponatremia, hyperkalemia, and any hypoglycemia.

Addisonian patients have decreased stress tolerance. The key to their perioperative management is to provide adequate intravenous fluid volume replacement and to provide exogenous glucocorticoids. A balanced electrolyte solution should be administered intraoperatively at a rate of 15 to 22 $mL \cdot kg^{-1} \cdot h^{-1}$. The rate may be adjusted depending on the patient's physiological status. The fluid rate may be decreased postoperatively to approximately 90 $mL \cdot kg^{-1} \cdot day^{-1}$. Again, this rate can be adjusted depending on a patient's physiological status.

Glucocorticoids should be given concomitantly with initiation of the anesthetic regimen. Preoperatively, 2 to 4 mg/kg of dexamethasone can be given intravenously or subcutaneously. Intraoperatively, a rapid-acting glucocorticoid such as prednisolone sodium succinate (Solu-Delta-Cortef) at a dose of 11 to 22 mg/kg should be administered intravenously and repeated as necessary. Postoperatively, additional glucocorticoids are given as needed. Patients with hypoadrenocorticism should be closely monitored for signs of hypotension and shock.

Hyperadrenocorticism (Cushing's Syndrome)

Although a common endocrine disease, hyperadrenocorticism is less problematic for successful anesthetic care than is hypoadrenocorticism. Patients with an excess of adrenal hormones will be predisposed to infection and poor wound healing. Most cats with hypoadrenocorticism are also diabetic. There is increased risk of pulmonary thrombosis and of thrombosis at other sites during the perioperative period.

Blood pressure monitoring and support are important for patients with hypoadrenocorticism because they are prone to hypertension. Preanesthetic evaluation should include baseline arterial blood pressure measurement. Patients with underlying hypertension should have blood pressure supported, if necessary, to prevent anesthetic-associated hypotension. Chronic hypertension predisposes patients to failures of autoregulatory control of tissue perfusion at reduced blood pressures that would be better tolerated by normotensive patients.

Pulmonary alveolar calcification is occasionally recognized on thoracic radiography with hypoadrenocorticism. This might cause hypoxemia from impaired perfusion, but is usually an incidental finding. A more commonly encountered problem related to the respiratory depression is impaired intraoperative ventilation. Many patients with hypoadrenocorticism have a large pendulous abdomen, which can impair ventilation during anesthesia. Monitoring ventilation with end-tidal carbon dioxide, pulse oximetry, and/or arterial blood-gas analysis is warranted.

When hyperadrenocorticism has been successfully treated, patients should have some functional adrenocortical reserve and thereby still be able to withstand the stresses of anesthesia and surgery. Adrenocortical reserve is indicated by a post-ACTH stimulation value of 3 to 10 μg/dL. Otherwise, these patients should be managed as having an iatrogenic adrenocortical insufficiency requiring glucocorticoid supplementation. Newer methods for medical management of pituitary gland–dependent and adrenal gland–dependent hyperadrenocorticism hold promise for more effective treatment and superior retention of adequate adrenocortical function.

Pheochromocytoma

Patients with pheochromocytoma are usually considered to be at very high anesthetic risk. The best approach to anesthetizing a patient with a pheochromocytoma is the preoperative monitoring and management of arterial blood pressures and cardiac function. Cardiac arrhythmias, particularly tachyarrhythmias, require diligent ECG monitoring. Stabilization of patients can require prolonged medical management, most often using phenoxybenzamine, a long-acting α-adrenergic antagonist, prior to anesthesia and surgery to lower and control arterial blood pressure adequately. Extreme hemodynamic instability is commonly a problem in these patients, especially if prior stabilization is inadequate. Even with prior stabilization, close attention to blood pressure and cardiac monitoring are imperative.

Surges in blood pressure and tachyarrhythmias are treated as they occur. Propranolol or esmolol may be useful in controlling tachyarrhythmias, but it is important to provide effective α-adrenergic blockade before initiating ß-adrenergic blockade. For any adrenal gland surgery, there is very significant potential for intraoperative blood loss. This is particularly true for tumors involving the right adrenal gland because of proximity to the posterior vena cava. Cross-matched blood should be available, along with colloidal fluids, for immediate volume resuscitation.

After removal of the affected adrenal gland, acute and dramatic drops in endogenous catecholamine levels may occur. This

may be manifested as sudden and profound hypotension and bradycardia, especially in the presence of α-adrenergic and ß-adrenergic blockade. Intravenous inotropic (e.g., dobutamine) and pressor (e.g., ephedrine or phenylephrine) support should be immediately available to treat hypotension rapidly.

Hypothyroidism

Untreated and inadequately treated hypothyroid patients have reduced metabolic rates and may more slowly recover from sedation or anesthesia. Any anesthetic drug should be used in low doses and ideally should require minimal or no metabolism or can be readily antagonized. Opioids, low doses of tranquilizers, propofol, and inhalants are the preferred preanesthetic and anesthetic drugs.

Hypothyroid patients are often obese and may suffer from anemia. Obesity may cause ventilatory problems under anesthesia that are caused by the excess amounts of abdominal and intrathoracic fat. Assisted or controlled ventilation may be necessary in these patients to keep them adequately ventilated. Moderate anemia may occur in hypothyroid patients. If the anemia is significant, blood transfusion should be considered prior to anesthesia and surgery.[6] In severe cases of hypothyroidism (myxedema hypothyroidism), hypothermia and bradycardia may complicate anesthesia. These should be corrected slowly. Support with corticosteroids, levothyroxine, and respiratory support may be necessary.

Hyperthyroidism

Patients with thyroid adenomas, adenomatous hyperplasia, or adenocarcinomas may exhibit evidence of hyperthyroidism. Several factors may place these patients at higher anesthetic risk.[7] A thyroid tumor may place mechanical pressure on the trachea, causing a partial obstruction and interfering with respiration. The surgical site may be highly vascular, and this can lead to excessive bleeding.

Hyperthyroid patients may rarely develop a *thyroid storm* during the procedure as a result of excessive thyroid hormone production. This is precipitated by catecholamine release and is characterized by an increased heart rate, increased blood pressure, cardiac dysrhythmias, elevated body temperature, and shock. Hyperthyroid patients often have increased metabolic rates, making them more prone to developing hypoxemia. Oxygen and glucose demand and carbon dioxide production are increased. Hyperthyroid patients may be more prone to heart failure. They have an increased heart rate and myocardial oxygen consumption.

Because of their increased metabolic rate, hyperthyroid patients may rapidly metabolize anesthetic drugs. Adequate oxygenation must be provided because of the increased oxygen consumption and demands of the patient. Intubation may be difficult if the tumor is compressing the trachea. Preanesthetic and anesthetic agents that decrease catecholamine response and myocardial irritability are preferred. Low doses of acepromazine or an α_2-agonist can be used as a preanesthetic in hyperthyroid patients. Acepromazine decreases myocardial irritability, and it blocks α-adrenergic receptors and thus may help counteract hypertension. An opioid can be combined with acepromazine because opioids generally slow heart rate and decrease myocardial oxygen consumption.

Anesthesia may be induced with low-dose thiopental, propofol, etomidate, or an inhalant by mask using isoflurane or sevoflurane. Inhalant induction alone may be stressful in some patients, worsening the overall cardiovascular status. Cardiovascular and respiratory parameters should be monitored closely and ventilation controlled when necessary. A 2.5% to 5% dextrose drip can be administered to meet increased glucose demands.

Cats with thyrotoxic cardiomyopathy, and particularly those with hyperthyroidism and concurrent hypertrophic cardiomyopathy, should be managed so as to reduce heart rate and optimize ventricular filling.[8,9] The use of dissociative anesthetics and anticholinergics is avoided to help insure that a lower heart rate is maintained. Sevoflurane (or even halothane) is preferred over isoflurane so as to reduce heart rate and myocardial work. The use of acepromazine is avoided to prevent the reduction in preload and ventricular filling. By maintaining preload, ventricular filling, and diastolic interval, both myocardial blood flow and ventricular function are improved. Preanesthetic medication with an opioid such as buprenorphine and a benzodiazepine such as midazolam is followed by inhalant induction with sevoflurane. Intravenous induction with etomidate, propofol, or thiopental is acceptable in less severe cases.

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