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Treatment of Diabetes Mellitus in Dogs and Cats

Diabetes mellitus results when insulin production is reduced or abolished (secretory defect) or when insulin action at target tissues is impaired (insulin resistance).

The metabolic defects of diabetes primarily include hyperglycemia and hyperlipidemia, although electrolyte abnormalities, dehydration, ketosis, and metabolic acidosis may develop with severe insulin deficiency when treatment is delayed. Prompt and effective treatment of diabetes is necessary to prevent catastrophic metabolic complications, but treatment of diabetes is associated with complications as well, some of which can be life-threatening.

Types of Complications

The complications associated with diabetes mellitus fall into two general categories: those that arise from untreated diabetes and those that develop during treatment for diabetes (**Table 1**). The emergency management of complicated diabetes has been reviewed in detail¹ and is not addressed here. This article focuses on the causes and treatments of complications that develop in dogs and cats during treatment of diabetes mellitus.

Complications associated with diabetes treatment may be classified as acute or chronic.

Acute complications are those directly related to insulin administration and can occur in new and established diabetics. Chronic complications occur when diabetes therapy is in the maintenance phase and usually result from poorly controlled diabetes.

Acute complications

Hypoglycemia: Insulin-induced hypoglycemia is a severe and potentially life-threatening complication of diabetes treatment. Under some circumstances, insulin therapy can precipitate hypoglycemia as well as exacerbate or promote hypophosphatemia, hypokalemia, and hypovolemia. Hypoglycemia in established diabetics may occur after pharmacologic insulin doses or accidental insulin overdose. In any circumstance, unrecognized or untreated hypoglycemia

can cause significant morbidity and may be fatal in some patients.² In some poorly regulated diabetic patients, chronic subclinical hypoglycemia or episodic bouts of clinical hypoglycemia may occur. The latter situations largely reflect problems with diabetic management that require reevaluation of the insulin therapy protocol.

Hypophosphatemia: In diabetic dogs and cats, hypophosphatemia usually develops after insulin treatment has begun and is caused by rapid insulin-mediated cellular uptake of phosphorus. Severe hypophosphatemia (phosphorous levels < 1.0 mg/dl) causes hemolysis, which can be life-threatening. Decreased serum phosphorus impairs adenosine triphosphate generation and reduces 2,3-diphosphoglycerate concentrations in red cells, which leads to red cell fragility and reduced oxygen delivery. Massive hemolysis can develop when serum phosphate falls below the critical level needed to maintain red cell integrity. Hypophosphatemia may also cause varying degrees of rhabdomyolysis, ileus, and encephalopathy.³

Hypokalemia and hypomagnesemia: These may be noted at diagnosis or develop during the treatment of ketoacidosis and other complicated forms of diabetes. Total-body potassium and magnesium may be depleted in diabetics because of reduced dietary intake and increased renal and gastrointestinal losses. During diabetes treatment, fluid diuresis promotes renal loss of potassium and magnesium, and insulin treatment can precipitate or exacerbate hypokalemia and hypomagnesemia by promoting cellular water and solute uptake.^{4,5}

Table 1. Complications of Treatment of Diabetes Mellitus

Acute

- Hypoglycemia
- Hypophosphatemia
- Hypokalemia
- Hypovolemia

Chronic

- Persistent hyperglycemia
- Cataracts
- Neuropathy
- Weight gain
- Episodic hypoglycemia
- Susceptibility to infection

continues

Chronic complications

Persistent hyperglycemia: Persistent hyperglycemia may be one of the most prevalent complications of diabetes. When due to ineffective insulin therapy, it is associated with persistent clinical signs of diabetes. Chronic hyperglycemia places the patient at risk for glucose toxicity and other chronic diabetic complications, such as cataract formation, neuropathy, malnutrition, and susceptibility to infection. Additionally, patient quality of life may be perceived as unacceptable, leading to premature or unnecessary euthanasia. Ineffective insulin therapy in established diabetics causes poor glycemic control and can lead to the development of severe metabolic complications, such as ketoacidosis.

Cataract formation: Diabetic cataract formation is common in dogs, and may be more common in cats than previously believed (Figure 1). Cataracts result from deranged glucose metabolism in the diabetic lens. Chronic hyperglycemia impairs glycolytic pathways and leads to increased sorbitol and fructose production in the lens. Sorbitol and fructose exert osmotic forces that draw water into the lens, causing swelling and rupture of the lens filaments and ultimately cataract formation.⁶ Secondary lens-induced uveitis is an additional ocular complication of cataract formation.

Peripheral neuropathy: Distal symmetric



Cataract in a dog: Cataracts are a common and frustrating complication of diabetes, especially in dogs. In many dogs, cataracts are present when diabetes is diagnosed. In others, cataracts form after insulin therapy is initiated. Unfortunately, although glycemic control minimizes cataract formation, even dogs with reasonably well-controlled diabetes often develop cataracts that interfere with vision.

polyneuropathy has been described in diabetic dogs and cats. Clinically, the pelvic limbs are more commonly affected than the thoracic limbs. Affected animals demonstrate pelvic limb weakness, abnormal postural reactions, and depressed tendon reflexes.⁷ Diabetic cats with polyneuropathy assume a plantigrade stance characterized by dropped tarsi and gait abnormalities. The pathophysiology that underlies the development of neuropathy is unknown but may involve altered polyol metabolism and glucose toxicity.

Susceptibility to infection: Evidence suggests that diabetes causes immune suppression in dogs and cats, as it does in humans. Several studies have identified diabetes as a risk factor for bacterial and fungal urinary tract infections in dogs and cats.^{8,9} Emphysematous cystitis caused by infection with gas-forming bacteria occurs more often in diabetic dogs (Figure 2). Similarly, many clinicians feel that diabetic animals have a higher incidence of urinary, reproductive, and skin infections than nondiabetics and that infections may be more difficult or take longer to clear in diabetic patients.

Prevention of Complications

Prevention of complications in treated diabetics is facilitated by anticipation of common problems and a close veterinarian–pet owner relationship. Regular veterinary care that includes careful monitoring of glycemic control and proper dietary management is essential to minimize or prevent diabetic complications, but the vital role of client education for prevention of diabetic complications cannot be understated.

Maintain adequate glycemic control:

Chronic hyperglycemia is associated with the development of diabetic complications. Thus, adequate control of blood glucose is probably the single most important goal for prevention of chronic diabetic complications. Proper blood glucose control requires close patient monitoring by the owner at home and by periodic veterinary evaluations. Diabetic monitoring can take many forms depending on the patient, the owner, and the veterinarian. A simple at-home monitoring program might be limited to obser-



A portion of an abdominal radiograph showing emphysematous cystitis in a diabetic dog. The urinary bladder has a mixed air and soft-tissue density due to the accumulation of air within the bladder wall. Urinary culture confirmed infection with *Escherichia coli*, which is a common organism associated with this disorder in dogs.

vation with instructions to report the appearance of clinical signs or other concerns to the veterinarian. A more involved program might involve having the owners perform urine monitoring for glucose and ketones or keep a diary of pertinent details about the pet. Several recent studies showed the feasibility of at-home blood glucose monitoring for companion animals, which has led to alternative strategies for at-home glucose monitoring for certain pets.^{10,11}

Recommendations for veterinary monitoring also vary. Most diabetic dogs and cats should be evaluated by a veterinarian at least twice a year, although 3 to 4 times per year may be appropriate for some patients. Physical and laboratory assessments are performed at each visit. Laboratory evaluations helpful for assessing diabetic control include the serum fructosamine level and glucose curve assessment.

Client education: Client education is an essential part of diabetes therapy. For successful management, owners must be taught the basic principals of glucose control and insulin administration. It is important that they also be taught to look for clinical signs of poor glucose control and insulin overdose and learn to perform diabetic “first aid” should an adverse complication arise. Properly educated and motivated owners can help prevent or reduce morbidity associated with diabetic management.

Treatment of Complications

Hypoglycemia: Clinical signs of hypoglycemia after insulin administration are a relatively common adverse effect of diabetes treatment and often occur while the patient is at home with the owner.¹² Feeding the pet a small meal or rubbing corn syrup on the gingiva can be done at home by the owner and may be all that is needed to treat mild hypoglycemia. Moderate or severe hypoglycemia usually requires veterinary attention. Intravenous infusion of a 50% glucose solution (0.5 g glucose/ml) is the emergency treatment of choice. Glucose is administered at 0.5–1.0 g/kg body weight (1–2 ml/kg of the 50% solution). The 50% solution is typically diluted 1:4 (to make a 10% solution) before injection to minimize the discomfort associated with intravenous injection of concentrated glucose.¹²

Persistent hypoglycemia is best addressed by constant-rate glucose infusion or by administration of glucagon. A constant-rate infusion of glucose is prepared by adding 5% to 10% glucose to a balanced electrolyte solution. After an initial bolus injection to restore euglycemia, the glucose infusion is initiated at 10 to 20 ml/kg per hour. The infusion rate may have to be titrated to reach the desired endpoint of euglycemia. The total dose of glucose needed before euglycemia is restored is difficult to predict. In a study of dogs and cats with insulin overdose, median values have been reported to be greater than 1 g glucose/kg, but individual patients required as much as 20 g/kg.¹²

Glucagon infusion has been reported as an effective therapy for hypoglycemia caused by canine insulinoma but may also be helpful in cases of insulin overdose.¹³ A constant-rate infusion of glucagon is prepared by first reconstituting 1 mg of injectable glucagon with the diluent supplied by the manufacturer and adding it to 1 L 0.9% sodium chloride (final concentration of infusion solution is 1000 ng/ml). The initial constant-rate infusion is set at 5 to 10 ng/kg per minute, although the rate can be titrated as needed.

Hypophosphatemia: Phosphorous deficiency is treated with intravenous phosphorous supplementation. Potassium phosphate, which contains 3 mmol phosphate/ml, is added to compatible intravenous fluids. The recommended dose for phosphorous supplementation is 0.01 to 0.03 mmol/kg per hour, although higher replacement rates are needed in some dogs and cats.³

Hypokalemia: In hospitalized patients, hypokalemia is corrected by the addition of potassium chloride to intravenous fluids. Intravenous supplementation of potassium chloride should be based on the serum potassium level (Table 2), and the rate of potassium supplementation should not exceed 0.5 mEq/kg per hour. Contraindications for potassium supplementation include hyperkalemia of any cause, and it should be avoided in cases of acute renal failure where urine production is subnormal. Occasionally, hypokalemia will persist in diabetic dogs and cats, especially those with concurrent chronic renal failure. Chronic hypokalemia in stable patients can be treated by using oral potassium supplements added to daily meals.¹

Hypomagnesemia: Available magnesium supplements for intravenous use include magnesium chloride (9.25 mEq Mg²⁺/g) and magnesium sulfate (8.13 mEq Mg²⁺/g). Magnesium-containing solutions must be diluted in 5% dextrose in water (D5W solution; maximum concentration 20%) for intravenous administration. The dosage is up to 1 mEq/kg per day given by constant-rate infusion. Care must be taken to ensure that the magnesium solutions are compatible with any crystalloid fluid preparations and drugs the patient may be receiving.¹⁴

Persistent hyperglycemia: No single treatment strategy will be effective for all cases of persistent hyperglycemia.¹⁵ Often, persistent hyperglycemia results from ineffective insulin replacement therapy, but physiologic insulin resistance is responsible in some cases. Regardless of cause, the treatment goal is to reestablish blood glucose control. Glycemic control may be readily reestablished if the problem is due to a compliance or management problem or is

Table 2.
Intravenous Potassium Chloride Supplementation

Serum Potassium Level (mEq/L)	Potassium Chloride to Add (mEq/L)
> 3.5	20
3.0–3.5	30
2.5–3.0	40
2.0–2.5	60
< 2.0	80

caused by an inappropriate choice of insulin. Determining the cause of persistent hyperglycemia may be more difficult if the problem is due to true insulin resistance, which is typically suspected when the patient is receiving at least 2.2 U/kg of insulin per dose. An algorithm for approaching persistent hyperglycemia is presented in the **Diagnostic Tree** on page 39.

Cataracts: The preferred treatment for cataracts is surgical removal of the affected lens. If lens-induced uveitis is present, ocular inflammation should be controlled by using topical glucocorticoid or nonsteroidal antiinflammatory drug preparations before lensectomy.⁷ If retinal pathology is present, electroretinography should be performed before cataract removal.⁷ Cataract removal is a highly specialized procedure, and referral to a veterinary ophthalmologist or qualified veterinary surgeon is recommended.

Neuropathy: Unfortunately, there is no specific treatment for diabetic neuropathy. Clinical improvement in nerve function, posture, and gait is observed in some affected animals when strict glucose control is imposed, suggesting that glucose toxicity may play a role in the development of neuropathy.⁷ ■

See Aids & Resources, back page, for references, contacts, and appendices.
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