

# Providing Care for Diabetic Veterinary Patients

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Diabetes mellitus (DM) is a relatively common disease in dogs, cats, and humans and develops as a result of a dysregulation of blood glucose. Its prevalence in dogs and cats is between 1:400 to 1:500. It may arise from either a decreased or absolute loss of insulin secretion from pancreatic  $\beta$ -cells or from the development of insulin resistance at the tissue level. Diabetes mellitus may arise because of genetic susceptibility, infectious diseases, pancreatitis, the effects of drugs, or immune-mediated pancreatic  $\beta$ -cell destruction.

## Feline Diabetes

In cats, the most common form of primary diabetes is clinically and pathologically similar to human non-insulin-dependent diabetes mellitus (NIDDM), which is also referred to as type 2 diabetes mellitus. This type of diabetes results from impaired  $\beta$ -cell function with resulting insufficient insulin response to increased

blood glucose levels. DM in cats usually develops in middle-aged animals (age range, 7-10 yrs), neutered males (1.5 times more likely), and obese animals (more than 6.8 kg). As in humans, DM in cats can be managed effectively with proper diet, weight reduction, adequate exercise, and treatment with oral antidiabetic agents. However, cats with diabetes will eventually require exogenous insulin administration, and many veterinarians choose to treat all newly diagnosed diabetic cats with insulin injections. Secondary diabetes may also develop in cats. Growth hormone secreting pituitary tumors and administration of megestrol acetate may induce glucose intolerance in cats. These types of DM can usually be resolved with early diagnosis and correction of the precipitating factors.

## Canine Diabetes

Dogs with primary diabetes are clinically and pathologically similar to humans with type I DM (insulin-dependent diabetes mellitus). Although in humans, this type of diabetes usually develops during preteen and teenage years, diabetes develops in dogs when they are middle-aged or older. Risk factors for the development of diabetes in dogs include female gender (2 times greater risk than males), middle age (range, 7-9 yrs), and genetic predisposition (miniature pinschers, poodles, miniature schnauzers, dachshunds, beagles, and keeshonds). Secondary diabetes in dogs may develop during estrus (heat) or as a result of Cushing's syndrome, acromegaly, or pancreatitis or from prolonged treatment with glucocorticoids or progesterone-like drugs. As with secondary diabetes mellitus in cats, complete resolution can be achieved with early diagnosis and the correction of underlying factors.

## Clinical Signs of Disease

The clinical signs of diabetes mellitus in dogs and cats are similar to those found in humans. Cats typically present with a history of polyuria, polydipsia, and weight loss and will progress to peripheral neuropathy and chronic gastrointestinal problems if untreated. Dogs will present with a history of polyuria, polydipsia, and weight loss and often are diagnosed after the acute onset of blindness as a result of cataract formation.

## Diagnosis

The diagnosis of DM in dogs and cats is very similar to that for humans. Laboratory evaluation of blood and urine are useful in diagnosing diabetes in dogs and cats. A persistent fasting blood glucose level of more than 200 mg/dL and the presence of glucose in the urine support the diagnosis of DM in both dogs and cats. Serum glycosylated hemoglobin and fructosamine levels are also useful in diagnosis because they represent blood glucose concentrations over the previous 60 to 90 days and 14 days, respectively.

Those values are particularly useful in cats because even a normoglycemic cat can “spike” a blood glucose level of more than 300 mg/dL in response to a stressor such as being restrained for a blood test.

## Complications

Complications from DM can occur if the disease is not treated in dogs and cats. The classic signs of diabetic ketoacidosis (DKA) are a persistent fasting blood glucose level of more than 200 mg/dL, ketonemia, hyperosmolality (more than 305 mOsm/L), and metabolic acidosis. Other signs may include dehydration, anorexia, depression, vomiting, and diarrhea. Hypokalemia can develop because of the extracellular shift of potassium as well as from potassium losses caused by gastrointestinal complications.

Other complications of diabetes mellitus are related to long-term hyperglycemia. Cataracts (but not diabetic retinopathy) frequently develop in diabetic dogs. Ocular manifestations of diabetes rarely develop in cats, but neuropathy is common. Cats usually pre-

sent with a retrograde plantar stance. Constipation may also be a manifestation of long-term diabetic neuropathy. Dogs may exhibit evidence of neuropathy by a history of progressive symmetric paresis, depressed spinal reflexes, and muscle atrophy. DM may also alter immune function, and the risk of development of infectious disease may be increased. Urinary tract infections are the most commonly reported infection in the diabetic animal.

## Treatment Strategies

The treatment goal for dogs and cats with DM is to keep blood glucose concentrations between 100 and 200 mg/dL. This is usually accomplished by means of subcutaneous administration of insulin; however, some cats can be successfully maintained with oral glipizide. It is important to note that all diabetic cats will eventually need treatment with insulin; however, oral therapy may buy the owner some time in adjusting to the idea of administering daily injections of insulin to his or her pet. Traditionally, DM in dogs and cats has been managed with beef, pork, or beef/pork sources of in-

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ulin because of the similarity of those insulins in those species and the decreased risk of antigenicity. Increasing antigenicity among insulins may also decrease the duration of activity of the insulin. Cat insulin differs from pork insulin by only 1 amino acid, and pork origin insulin is the ideal insulin for cats. Dog insulin is identical to pork insulin and differs from beef and human insulin by only 1 and 2 amino acids, respectively. Unfortunately for dogs and cats, the advent and success of recombinantly generated human insulin has eliminated the need for animal-source insulins in the treatment of diabetic humans. Pork- and beef-source insulins will eventually be unavailable, and human insulin will remain as the only treatment option commercially available for animals.

The insulin of choice in dogs is neutral protamine Hagedorn (NPH) insulin. NPH insulin has an onset of action in 0.5 to 3 hours and has an expected duration of between 8 and 24 hours. Although animal-source NPH insulins can be dosed once daily in dogs, the human recombinant NPH must usually be dosed twice daily. Maintenance doses of NPH insulin in

dogs are usually 0.4 to 0.7 U/kg/dose.

Protamine zinc insulin (PZI) has historically been the insulin of choice for diabetic cats. PZI has an onset of action of 1 to 3 hours, peaks at 4 to 10 hours, and has a duration of activity of 12 to 30 hours. This allows for once-daily dosing in most cats. PZI was removed from the human market in 1991 but recently became available again as an approved veterinary product (PZI, Blue Ridge Pharmaceuticals, Greensboro, NC). In the interim, compounding pharmacists were able to supply PZI through adsorption of zinc onto the regular insulin molecule. The veterinary-approved PZI insulin is only produced in a 40-U/mL concentration. Because U-40 insulin syringes are difficult to obtain and the veterinary-approved product has been sporadically available, some veterinarians have chosen to continue prescribing compounded PZI insulin for diabetic cats. NPH insulin may also be used in cats, but it has a very erratic pattern of activity. NPH peaks at 1.5 to 6 hours and has a very short duration of activity of 4 to 10 hours. All cats treated with NPH insulin will require twice-daily dosing for good control.

Another insulin used in cats is ultralente insulin, which has an onset of action of 1 to 4 hours in cats and a duration of 12 to 24 hours. Most cats must receive twice-daily injections of ultralente to achieve control. Unfortunately, the absorption of the ultralente insulin is erratic in cats, and ~20% of cats will not respond to therapy, even with twice-daily dosing. In that case, lente insulin may be tried, because it is better absorbed. Lente insulin has an onset of activity of 0.5 to 3 hours with a duration of 6 to 12 hours in cats and must be given twice daily. Doses of insulin for cats are usually 0.2 to 0.5 U/kg/dose, but doses as high as 2 U/kg may be required. Sometimes, doses as low as 1 unit are required for cats. Insulin diluting fluids are available from the manufacturers and may facilitate the administration of lower doses. These fluids do contain cresol and phenol in small amounts, which may be harmful if used long-term in cats. I prefer to attempt dosing with undiluted insulin initially and then to resort to dilution only after the client has proven that he or she is unable to regulate the cat on undiluted insulin.

For owners who are not yet willing to administer daily injections of insulin to their cats, oral glipizide may be initially useful in controlling diabetes in ~25% to 50% of cats. This second-generation oral sulfonylurea is indicated in nonobese, stable cats with non-complicated diabetes. The most commonly reported adverse effect is gastrointestinal upset, which can be avoided by concurrent administration with food. Some animals may also become icteric, but this resolves upon discontinuation of the drug. Glipizide stimulates insulin secretion from pancreatic  $\beta$ -cells, but in time, those cells will eventually fail to be stimulated to produce insulin. Owners electing this method of therapy should be frequently reminded that oral therapy eventually fails in all diabetic cats and that insulin must be administered at some point to control the disease successfully in their pet. Because administering oral medication can cause a stress-induced increase in blood glucose in the animal treated, the



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compounding pharmacist can play a valuable role in providing a palatable dosage form that facilitates nonstressful administration to diabetic cats. Compounding semimoist treat bases should be avoided, because those products contain high levels of simple sugars that may complicate diabetic control. Diabetic animals are better maintained on diets that contain high fiber (more than 15%), high complex carbohydrates (more than 50%), and low fat (less than 20%).

Diabetic blood glucose monitoring aids designed for humans are not appropriate for pets, but pharmacists can instruct owners in the importance of blood glucose monitoring by the veterinarian. Urine monitoring for glucose and ketones can be accomplished by the owner with the use of dipstix (Ketodiastix,<sup>®</sup> Bayer Corporation, Elkhart, Ind) designed for humans. The owner can be instructed to catch urine from his or her dog as it urinates and then to proceed according to product instructions. Cats may not be as willing as dogs to donate a urine sample, and cat owners can be instructed to collect a urine sample by replacing cat litter with styrofoam packing material or some other non-

absorbent substrate. After the cat has urinated in the litter box, the owner can test the urine for glucose and ketones according to the dipstix product label. All owners should be instructed to contact a veterinarian immediately if ketones are detected. Animals routinely spilling glucose into their urine should be reevaluated by a veterinarian as soon as possible.

When equipped with an understanding of the pathophysiologic differences in diabetes that occur in different species, pharmacists can play a valuable role in providing diabetic care and monitoring for both human and animal patients. By working with veterinarians, pharmacists can acquire this understanding, which enables them to provide pharmacologic treatments for cats and dogs and to educate pet owners about the importance of diet, exercise, and monitoring in the management of diabetes in animals. ■

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