Management of Diabetes Mellitus
Insulin Therapy
Cynthia Ward, VMD, PhD, DACVIM
College of Veterinary Medicine, University of Georgia

Diabetes mellitus is a common endocrinopathy in dogs in cats. Dogs usually get Type 1 or the insulin-dependent form. This occurs from loss of pancreatic beta cells such that adequate amounts of insulin are not produced and secreted. Cats usually get Type 2 or the non-insulin dependent form of diabetes mellitus. This occurs as a result of insulin-resistance, often from obesity. The pancreatic beta cells are forced to produce increasing amounts of insulin to overcome the resistance, resulting in ultimate loss of function in the cells. Additional loss results from direct glucose toxicity of the beta cells. Cats also get a “transient” diabetes mellitus a syndrome in which insulin requirements diminish or cease to be necessary after initial treatment. This is probably due to correction of a pathological condition causing insulin resistance. This is also known as diabetic remission. Definitions of feline diabetic remission vary widely between published studies, and the practitioner should be aware of these differences before evaluating the efficacy of insulin types.

DIAGNOSIS. Diabetes mellitus is relatively easy to diagnose. Clinical signs include polyuria/polydipsia, weight loss, persistent or recurrent urinary tract infections, weakness and muscle wasting, cataracts (dogs), and peripheral neuropathies (cats). Diagnosis can be made by recognition of appropriate clinical signs, and demonstration of persistent hyperglycemia and glucosuria. One confounding factor to this diagnosis is stress. Stress, alone, can cause hyperglycemia, that can be high enough to be cause spill over into the urine and glucosuria. Should the clinician have any doubt of whether hyperglycemia and glucosuria are due to diabetes mellitus, s/he should check a serum fructosamine level. This value gives the average of the blood glucose over the preceding 2-3 weeks. If elevated, then diabetes mellitus can be diagnosed. If not elevated, then the hyperglycemia/glucosuria was probably due to stress.

Initial evaluation will decide how intensively the patient should be managed as diabetic treatment is begun. If the animal is eating and drinking normally and is well hydrated, there is no reason to hospitalize him/her while insulin therapy is initiated. If the animal is ketotic, acidic, hyperosmolar, or dehydrated, s/he should be admitted to the hospital and stabilized before long term insulin therapy is instituted. The most common concurrent diseases seen with diabetes mellitus include: urinary tract infections, concurrent endocrinopathies such as Cushing’s disease, hypothyroidism, and hyperthyroidism, pancreatitis, infections, and pregnancy.

Initial evaluation of the diabetic animal should include a complete physical examination, CBC, chemistry profile, urinalysis, and T4 (cats). A urine culture should be considered even if urinalysis and sediment parameters are normal since up to 35% of urinary tract infections can be clinically silent in animals with dilute urine. Abdominal imaging may be pursued if clinically indicated. Concurrent medical conditions should be addressed aggressively so that the diabetes mellitus can be more easily controlled.

TREATMENT. Diabetes mellitus can be frustrating, expensive, and time-consuming for owners to treat. Because veterinary patients do not live as long as humans, veterinarians do not have to worry about keeping blood glucose within the tight range required for human diabetic management. Our goals of therapy, therefore, can be less rigorous, thereby alleviating some of
the burden to our clients. Our goals of therapy should be correction of clinical signs, control of concurrent diseases, and avoidance of emergency situations such as hypoglycemia, ketosis, and hyperosmolality. It is beneficial to have an in depth discussion with the owner as to the time and effort s/he can realistically commit for diabetic control for the pet. It is important to establish a good rapport with diabetic owners since they will be asked to provide invasive (injections) and time-consuming (glucose monitoring) care for their pets. We want owners to be honest about what they can and can’t do. Often the veterinary technician can make owners feel more comfortable and more willing to admit problems they will have with diabetic care.

Stable cats with blood glucoses less than 400 mg/dl can be treated initially with a diet change. Cats are very carbohydrate intolerant, and a low carbohydrate diet can result in euglycemia in some cats. Prescription diets are recommended; however, if the owners can’t or won’t commit to these diets, commercial diets can be used. Canned diets tend to be lower in carbohydrates and some websites include carbohydrate data on specific diets. Because of the deleterious effects of a hyperglycemic environment on the cat pancreas, diet change alone should not be tried for more than 2 weeks. If the cat has not become euglycemic over that time period, then insulin therapy should be instituted.

The optimal diet for diabetic dogs is one high in insoluble fiber. This diet slows glucose absorption from the gut and postprandial hyperglycemia. Unlike cats, dogs will not usually revert to euglycemia as a result of a food change and insulin therapy should be initiated immediately after the diagnosis of diabetes mellitus is made.

INSULIN THERAPY: Insulin is a small peptide hormone that has a highly conserved amino acid sequence throughout different mammalian species. This allows for the use of human-based insulins in veterinary species. Insulin is secreted in a stable hexomeric form stabilized by a zinc molecule in the middle. The hexomer needs to be broken down to a monomer before it can bind to the insulin receptor and activate cells. In considering insulin therapy, the practitioner should be aware of the source of the insulin (animal, human recombinant DNA, human sequence mutated), the type of the insulin or how it is made into a repository form, and the concentration (U-40, U-100, U-300).

Regular insulin is available as a human recombinant insulin in 100 U/ml (U-100) form. It is the stabilized hexomeric form of insulin, and therefore, not precipitated or mutated. It may be used intravenously, intramuscularly, and subcutaneously. Regular insulin is used to treat unstable or dehydrated diabetics. Effective protocols for IM intermittent therapy or continuous rate IV infusion are available in any emergency medicine handbook.

Protamine Zinc Insulin (ProZinc®) is human recombinant insulin. It is precipitated with protamine zinc and is stable in suspension. It should be rolled gently to mix. ProZinc® is formulated at a concentration of 40 U/ml; therefore dosing can be easier in smaller animals like cats. The 0.3 ml syringes can be used so that half units can be easily measured. ProZinc® is approved by the FDA for veterinary use; therefore, company support of the product is readily available for veterinarians. This is a great insulin in cats and also is effective in dogs.

Vetsulin® is a purified porcine insulin that has an identical amino acid sequence to canine insulin. It is a mixture of ultralente and semilente insulins and is precipitated with zinc to form a suspension. To keep the ratio of semilente to ultralente consistent, it must be shaken vigorously.
before use. VetPensR containing VetsulinR are available for convenient dosing by owners. These pens may be measured for accurate ½ unit dosing. VetsulinR is approved for veterinary use by the FDA and company support is readily available for veterinarians. This should be a first pick for dogs and is also effective in cats.

NPH (neutral protamine hagedorn) is a recombinant human insulin. It is distributed by several manufacturers under names such as Humulin N® (Eli Lilly) and Novolin N® (Novo Nordisk). A generic version is also available. It is a crystalline suspension of human recombinant insulin with protamine and zinc added. The concentration of NPH is 100 U/ml. This is the most inexpensive insulin on the market and may work in some dogs. It has a short duration of action in cats that can remain hyperglycemic for significant portions of the day. Thus, NPH is not recommended as a long term insulin in cats (unless the owners want to give 3-4 injections daily to their cat).

Glargine (LantusR) is a long-acting human mutated insulin available as a U-100 and U-300. It is stable at pH 4.0 but forms crystals at pH 7.0 when injected under the skin. Insulin adsorbs off the crystals and is released into the blood stream. It is marketed to give 24 hour basal control of insulin circulation. In humans, glargine is often used in a basal-bolus pattern with injection of another insulin preparation at meal times. LantusR pens are available but are only adjustable in 1U increments and have relatively short injection needles. This is a great insulin in cats and will also work in dogs.

Detemir (LevemirR) is a similar insulin to glargine in its use in human diabetes mellitus. It is a mutated human insulin with fatty acid side chains added so that it can bind to albumin after being injected under the skin. It is also available as a prefilled pen with the caveats of the LantusR pen. This is a fabulous insulin in dogs especially as a “rescue” insulin. It may also be used in cats.

Lispro (NovalogR) and Aspart (HumalogR) are two mutated human recombinant insulins that are used to manage human diabetes mellitus along with the longer acting glargine and detemir insulins. They are available as U-100 insulins. These insulins work extremely quickly because they are already in monomeric form and do not need to be broken down from the normal insulin hexamers. Their onset of action is rapid (5-15 minutes) and their duration of action is approximately 1 hour. Their use has been limited in veterinary medicine.

The starting dose of insulin should be: 0.25 U/kg for cats and 0.5 U/kg for dogs, except for detemir in dogs that should be started at a lower dose of 0.25 U/kg. Most dogs and cats will need insulin twice per day. If owners are only able to give insulin once per day, consider VetsulinR or LevemirR in dogs and ProZincR or LantusR in cats. Dogs and cats should be fed twice a day when insulin is given. A small amount of food should be presented, and the animal’s appetite noted. Insulin should then be given. If the pet does not eat normally, half the dose of insulin should be given. Many owners give insulin while the animal is eating. This makes the insulin injection a pleasant experience for the pets and easier for owners to treat the animal. Some cats prefer to nibble food throughout the day. These grazers can often be well managed by allowing them free choice eating with insulin injections twice per day. Care should be taken to ensure that the cats are not receiving more than their caloric needs since extra weight should be avoided.
Exercise is beneficial to diabetics and serves to lower insulin requirements and provide better glycemic control. Daily walking for dogs and cat play can be effective ancillary treatments for diabetes mellitus. Average time for initial diabetic control is 4-6 weeks.