One of the most common questions asked by practitioners about treating diabetes mellitus is which is the “best” insulin to use in dogs and cats? Unfortunately, this question is difficult to answer. In diabetic dogs or cats, glycemic control may vary greatly from patient to patient. All insulin types currently on the market have the potential to work well in some diabetic animals but not in others. Which insulin is ultimately the most effective in the individual diabetic dog or cat is not predictable at time of initial diagnosis. The veterinarian’s role is to identify which type of insulin works best in the individual diabetic dog or cat being treated. Success with insulin therapy requires knowledge of currently available insulin preparations. This includes the insulin’s intended use, its potency and duration of effect, as well as the potential impact of species of insulin origin on diabetic control.

Available insulins can be categorized as short-acting, intermediate-acting or long-acting. At this time, available short-acting insulins include regular crystalline (Humulin R, manufactured by Eli Lilly), insulin lispro (Humalog, manufactured by Eli Lilly), and insulin aspart (Novolog, manufactured by Novo Nordisk). Regular crystalline insulin (U-100 concentration) is a recombinant human insulin, whereas insulin lispro and insulin aspart are insulin analogs. In human patients with diabetes, insulin lispro and insulin aspart are generally considered the insulin of choice for control of postprandial blood glucose concentrations. The role, if any, of these insulin analogs for the treatment of diabetes in dogs or cats is unclear at this time.

Currently, the only intermediate-acting insulins that are available are recombinant human NPH (neutral protamine Hagedorn) and porcine Lente insulin (Vetsulin/Caninsulin). All available NPH insulins are now crystalline suspensions of recombinant human insulin with protamine and zinc. No animal source NPH insulins are available. These human NPH insulins are still available as either Humulin N (manufactured by Eli Lilly) or Novolin N (manufactured by Novo Nordisk). Both are available only in a U-100 insulin concentration. Porcine Lente insulin is a purified pork Lente insulin consisting of 30% amorphous zinc insulin and 70% crystalline zinc insulin. The concentration of Vetsulin/Caninsulin is 40 U/ml (U-40). The structure of porcine Lente insulin is identical to that of canine insulin. The amorphous component has a peak activity within 4 hours, and duration of effect for 7-8 hours. The crystalline component has a peak around 10-11 hours. According to the manufacturer, these kinetics may allow once-daily dosing in some dogs; however, one study demonstrated that most dogs required twice-daily administration for adequate control. We recommend twice daily administration of NPH and Lente insulins in dogs.

Long-acting insulins include PZI, glargine insulin and detemir insulin. An animal origin PZI insulin is no longer being manufactured. A recombinant human PZI, ProZinc (BVI) is available and approved for use in cats in the U.S. The concentration is 40 U/ml (U-40). PZI is also available as a compounded product. We do not recommend using compounded PZI, however, because the potency can vary from batch to batch and regulation could be more difficult. Detemir insulin is a human recombinant insulin analog available as Levemir (manufactured by Novo Nordisk). It differs from other insulins because it has been genetically modified, by having an acylated fatty acid chain added to the insulin molecule which slows SQ absorption and enables reversible binding to plasma proteins resulting in slow release from plasma proteins. In a recent small study of dogs poorly controlled with NPH or Lente insulin, it was effective in achieving adequate glucose control in most patients. The dose is much lower than other insulin preparations which can limit its use in very small dogs. It is probably the second choice to NPH or Lente in most cases. Glargine insulin is a human
recombinant insulin analog available as Lantus (manufactured by Sanofi Aventis). It differs from other insulins because it has been genetically modified, by replacing an asparagine with glycine and adding 2 arginine amino-acids to the c-terminal end of the molecule. This alters the pH solubility (isoelectric point) of the molecule, so that it is soluble at a pH 4 but insoluble at neutral pH (e.g., in the body). When glargine insulin is injected into the skin, it precipitates because of the pH change and forms insoluble microcrystals, which are slowly absorbed into the circulation. This constant release of small amounts of insulin prevents major peaks and troughs from developing. In people, insulin glargine is intended to provide basal insulin levels over an extended period when administered once daily. In a preliminary study involving healthy cats, most of the pharmacokinetic and pharmacodynamic properties (i.e., onset of action, glucose nadir, time for blood glucose concentration to return to baseline, mean daily blood glucose concentration) were similar for insulin glargine and PZI. Although there are only a few small studies of the use of this product in dogs, it may be useful as a longer-acting insulin in patients for which NPH or Lente insulins and detemir insulin have proven inadequate to provide adequate glycemic control with 2 daily injections.

Current recommendations regarding the initial insulin of choice for treating diabetic dogs are based on personal experience and vary between clinicians. Some veterinarians prefer human NPH insulin, while others favor porcine Lente insulin. Studies comparing the efficacy of recombinant human NPH versus porcine Lente insulin have not been reported, but both appear effective in most diabetic dogs. We generally prefer Vetsulin if cost is not a factor. NPH can be effective in many cases and we recommend a starting dosage for NPH insulin of approximately 0.25-0.4 U/kg, administered BID. Initiating treatment with twice daily insulin administration will make it easier to establish diabetic control with fewer problems associated with hypoglycemia or development of the Somogyi phenomenon. Although there is very little information about the use of insulin glargine (Lantus) or PZI (ProZinc) in dogs, they may be useful as longer-acting insulins in patients for which NPH, Lente or detemir insulins have failed to provide adequate glycemic control.

Diabetic cats are totally unpredictable in their glycemic response to exogenous insulin. There is no single type of insulin which will effectively control hyperglycemia in all diabetic cats, even with twice daily administration. Current recommendations regarding the initial insulin of choice for treating diabetic cats are based on personal experiences and vary between clinicians. Most clinicians prefer ProZinc or glargine insulin, whereas others use detemir insulin and a few Lente or NPH as the initial insulin. It is important to remember that the response to insulin is always unpredictable, and that individual cats respond individually to any or all insulin preparation. For this reason, it is important to be conservative when selecting insulin doses, either initially or when switching a cat from one type of insulin to another. Although Lente and NPH insulin are consistently and rapidly absorbed following subcutaneous administration in cats, the duration of effect of Lente (and especially NPH) can be considerably shorter than 12 hours, resulting in inadequate control of hyperglycemia despite twice a day administration. Although these insulins may be adequate in some cats, they usually produce too short a duration of action for optimal blood glucose control in cats. This commonly leads to poor glycemic control and/or induction of the Somogyi phenomenon. It must be remembered, however, that the response to Lente or NPH insulin is variable. There may be cats in which these intermediate-acting insulin preparations have a longer action, making one of them suitable for BID dosing. In general, longer-acting insulin preparations, such as ProZinc or glargine insulin, are best in diabetic cats. Currently, our preference for the initial treatment of newly-diagnosed diabetes in cats is ProZinc or glargine insulin administered at an initial dose of 0.25 U/kg administered twice a day. Generally, the initial starting dose should not exceed 3 U/cat BID. In general, the dose should not be increased in the first week, and in some cats, the dose needs to be reduced during the first week of treatment. In some cats, glargine appears to have little glucose lowering effect in the first 3 days. It is important that the dose is not increased during this time, because increasing the dose without monitoring can result in clinical hypoglycemia. Because the majority of diabetic cats require insulin twice a day and to provide the best control of blood sugar and increase the chances of remission,
we prefer to start with a twice a day therapy. Subsequent increases in the insulin dosage should be based on owner perception of their cat's response to treatment, urine glucose readings, changes in physical examination and body weight, and the results of blood glucose and serum fructosamine measurements. It is recommended that close monitoring and adjustment of dose occur in the few months of treatment, because many cats will achieve diabetic remission within this time. The duration of effect of insulin glargine appears quite variable, with the glucose nadir occurring as soon as 4-6 hours and as late as 18-22 hours after administration. Insulin glargine works well when given once or twice a day in some diabetic cats and does not work very well in other cats. As with other insulin preparations, the glycemic response to glargine is always unpredictable, and each cat treated with this insulin, as with any insulin, must be carefully monitored and evaluated to judge the cat's response. Preliminary studies have shown that detemir insulin can be comparable to ProZinc and glargine in diabetic cats and may be a suitable choice in some cases. Regardless of the insulin chosen, diabetic cats should be placed on a low carbohydrate, high protein diet (unless contraindicated by concurrent disease) to increase the chances of diabetic remission. Some long-term diabetic cats appear to be better managed on a moderate carbohydrate/high fiber diet. Recent investigations are assessing the use of GLP analogs for treatment of feline diabetes.

When it comes to managing diabetes, good outcomes depend on regular monitoring. The results of monitoring can guide sound medical decisions and contribute to efficacy of treatment and quality of life for your patients. Older pets are often more frequently diagnosed with diabetes, which will then require lifelong treatment and management with long-term medications and/or special or restricted diets. Therefore, once the disease is diagnosed, implementing a monitoring program that includes regularly scheduled diagnostic testing tailored to the individual patient is crucial to judge the efficacy of treatment plans. Frequent communication between the veterinary healthcare team is critical to the successful care of a diabetic patient, as are regularly scheduled recheck examinations, during which clinical signs and body weight are assessed. Therapy of the diabetic patient is monitored by assessing clinical response, evaluating blood glucose curves and determining fructosamine concentrations. Evaluation of clinical improvement or lack thereof is crucial for evaluating response to therapy. In addition, periodic monitoring of urine glucose levels by the owner can provide valuable additional information. Serial blood glucose curves are used concurrently with fructosamine levels to monitor the effectiveness of insulin therapy. Blood glucose curves can provide valuable information relating to how well the insulin dose is working in that patient, including duration of insulin action, blood glucose nadir and presence or absence of rebound hyperglycemia. They are, however, potentially impacted by the stress of travel, hospitalization and multiple blood collections, especially in the feline patient. In these cases, home glucose monitoring is preferred. Determination of fructosamine levels has come to be an integral part of the monitoring of insulin therapy of diabetes mellitus in both dogs and cats. Recheck evaluations, fructosamine levels and BG curves are determined every 2–4 weeks during the initial regulation of the diabetic patient and then every 3–6 months during long-term management. Whether or not to alter the dosage of insulin is determined by evaluating the fructosamine level in conjunction with the patient’s clinical signs and results of the blood glucose curve. Lastly, underlying or concurrent disease states that complicate diabetes management or cause insulin resistance should be addressed if possible; examples include hyperadrenocorticism and acromegaly.