Monitoring Diabetics
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Owners should be instructed to monitor urine glucose and ketones once weekly in dogs and daily in cats undergoing diet (low carbohydrate) and insulin therapy. Insulin therapy should be evaluated once weekly by serial blood glucose curves, assessment of body weight and resolution of clinical signs for approximately one month. Long-term insulin therapy should be monitored by serum fructosamine or glycosylated hemoglobin concentrations. Adjustments to insulin dosage should be made in increments of 0.5-3 units/dog (depending on the size of the dog) at the time of these evaluations. Once adequate insulin therapy has been established, assessment of diabetic control should be made every 3-6 months depending the degree of diabetic control.

Urine Glucose Monitoring

Urine glucose is a measure of trends in blood glucose, and should not be used alone to adjust insulin dosages. Urine glucose monitoring may be performed at home by owner, is not affected by stress, and may indicate insulin-induced hyperglycemia (Somogyi effect). In dogs, urine is collected with a long-handled cup holding device or a flat pie tin in female dogs. Urine glucose should decrease to trace or one plus with appropriate therapy. Consistently high urine glucose indicates the need for blood glucose evaluation. Decrease urine monitoring to once weekly or biweekly in well-regulated diabetics.

It is vitally important that the client monitor the urine sugar in order to determine when the cat is ready to go off insulin. This is best accomplished using the Glucotest system which allows the client to “wean” the cat off of insulin. Glucotest is a home urine glucose monitoring system for cats marketed with Purina DM. The packets can be sprinkled in the litter pan using premium clumping litter and read at the owners convenience on a daily basis. Using this method of monitoring and treating diabetes in the cat, approximately 70% of cats can be managed with little or no insulin.

Protocol for monitoring urine glucose after hanging to a low carbohydrate diet
1. Change the diet to Purina DM.
2. Feed the prescribed amount in two equal meals twice daily.
3. Give the prescribed amount of insulin twice daily subcutaneously. The ideal place for insulin injection is on the abdomen, but the lower back and sides of the chest and abdomen are also acceptable.
4. OR your veterinarian may prescribe an oral hypoglycemic agent such as glyburide.
5. Monitor urine sugar using the GLUCOTEST system. As the urine sugar drops, you will see less color change on the strips. When the urine sugar becomes negative for 2 days in a row, decrease the insulin by the following schedule:
   a. 2 units insulin twice daily starting dose
   b. negative urine glucose x 2 days, decrease to 1 unit twice daily
   c. negative urine glucose x 2 days, decrease to 1 unit once daily
   d. negative urine glucose x 2 days, off insulin completely
6. INSULIN dosages should NEVER be increased based on urine sugar.
7. Visit your local veterinarian for check-ups (fructosamine, chemistry profile) once monthly.
Glucose Monitors

Glucose monitors designed for home monitoring in human beings, are inexpensive, accurate, rapid, and require only a drop of blood. Although reasonably accurate in the blood glucose range of 4-12.5 mmol/L, these glucose monitors are designed to read lower than the actual value as glucose approaches the hypoglycemic range. Factors that affect accuracy of these monitors include altitude, oxygen therapy, patient hematocrit, shock, dehydration, severe infection, and out of date or improperly stored test strips. Whole blood glucose concentrations are lower than serum glucose and the manufacturer should be consulted about the suitability of these monitors for canine patients. Recently, a veterinary glucose monitor has been developed and marketed as the Abbott AlphaTRAK. As shown in Fig 1 below, the AlphaTRAK has the highest correlation to clinical laboratory sample analysis of glucose. The Bayer Ascensia Contour and the Roche Accu-Chek Advantage are both excellent human monitors, but fall short of the accuracy of the Abbott product. See Table 1 for a comparison of veterinary and human glucose monitors.
<table>
<thead>
<tr>
<th></th>
<th>AlphaTRAK</th>
<th>Bayer Ascensia Contour</th>
<th>Accu-chek Advantage</th>
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</thead>
<tbody>
<tr>
<td><strong>Ease of Use</strong></td>
<td>Easy</td>
<td>Easy</td>
<td>Easy</td>
</tr>
<tr>
<td><strong>Precision</strong></td>
<td>Most consistent</td>
<td>Very consistent</td>
<td>Very consistent</td>
</tr>
<tr>
<td><strong>Time</strong></td>
<td>20 sec</td>
<td>15 sec</td>
<td>15 sec</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td>± 2%</td>
<td>&gt; 20%</td>
<td>± 20%</td>
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<tr>
<td><strong>Cost</strong></td>
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<td>$70</td>
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<tr>
<td><strong>Good for pets</strong></td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td><strong>Blood (µl)</strong></td>
<td>1</td>
<td>0.6</td>
<td>1</td>
</tr>
<tr>
<td><strong>Pros</strong></td>
<td>Veterinary designed and tested</td>
<td>Rated in top 3 in consumer reports</td>
<td>Rated in top 3 in consumer reports</td>
</tr>
<tr>
<td><strong>Cons</strong></td>
<td>Access through vets only</td>
<td>Human</td>
<td>Human</td>
</tr>
<tr>
<td><strong>Maker</strong></td>
<td>Abbott Labs</td>
<td>Medisense</td>
<td>Roche</td>
</tr>
<tr>
<td><strong>% incorrect decision</strong></td>
<td>2-4%</td>
<td>20-25%</td>
<td>20%</td>
</tr>
</tbody>
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Blood Glucose Curve
- Take initial blood sample
- Feed same amount and type of food
- Feed and give insulin at the same time
- Have owner administer insulin
- Assess owners injection technique
- Take blood samples at two hour intervals for 12 hours

Ideal Blood Glucose Curve
The ideal blood glucose curve is characterized by three features. (Figure 1)

♦ The ideal glucose curve has a glucose nadir (lowest blood glucose concentration on the curve) between 4-6 mmol/L

♦ The time of the glucose nadir indicates peak insulin action. The nadir should occur approximately halfway through the dosing interval. For example, if insulin is being given every 12 hrs, the nadir should fall 5-6 hrs after the dose.

♦ The glucose differential is the difference between the glucose nadir and the blood glucose concentration prior to the next insulin dose.

The glucose differential should be less than 5 mmol/L in dogs without cataracts and less than 7.5 mmol/L in dogs with cataracts or cats.
The duration of insulin action is related to the both the time of the glucose nadir and the absolute concentration of the glucose nadir. One cannot make a determination of insulin duration unless the target glucose nadir concentration (80-120 mg/dl) has been achieved. If the glucose nadir occurs approximately halfway through the dosing interval, the duration of action of insulin should be adequate.

**Problems identified on the blood glucose curve**

It is very rare to obtain a perfect glucose curve in a single patient. In fact, blood glucose curves are good for identifying trends in blood glucose during the day in dogs and not at all helpful in cats. Generally, blood glucose curve problems can be differentiated by the characteristics of the curve and the insulin dosage (per dosing interval). If the patient is receiving > 2.2 U/kg of insulin per dose, insulin resistance should be investigated. Causes of insulin resistance in dogs include hypothyroidism, hyperadrenocorticism, acromegaly, estrus, drug therapy, and infections. If the animal is receiving < 2.2 U/kg per dose, the blood glucose curve will usually be indicative of one of the following: insufficient dosage of insulin, short duration of action of insulin, insulin-induced hypoglycemic hyperglycemia (Somogyi effect), insulin overlap or prolonged insulin action. Corrective actions include, respectively, increasing the insulin dose, changing to a longer acting insulin or twice daily insulin regimen, reduction of the insulin dose by 25%, or changing to a shorter duration insulin or insulin mixture (30% regular, 70% NPH). Causes of hyperglycemia and hypoglycemia in diabetic dogs and cats are listed in Table 1.

**DIET and EXERCISE**

The goals of dietary therapy in diabetes mellitus for both cats and dogs are to provide sufficient calories to maintain ideal body weight and correct obesity or emaciation, to minimize post-prandial hyperglycemia, and to facilitate ideal absorption of glucose by timing meals to coincide with insulin administration. Caloric intake should be 60-70 Kcal/kg/day for smaller dogs and 50-60 Kcal/kg/day for larger dogs. Obese animals should have their body weight reduced gradually over a period of 2-4 months by feeding 60-70% of the calculated caloric requirements for ideal body weight. Underweight animals should be fed a high-caloric density food based on caloric intake for optimum body weight. Once ideal body weight is reached, the animal may be switched to a high fiber diet. Table 2 lists the fiber and caloric content of some commercially available dog foods. The feeding schedule should be adjusted to the insulin therapy.

Micronutrients may be added to the diet to improve glucose control in some dogs. Compounds containing the transition metals, vanadium and chromium, have been shown to have insulinomimetic properties when administered to diabetic rodents. A recent USDA study of 180 human patients with NIDDM found that administration of 1,000 µg of chromium picolinate once daily resulted in amelioration of the classic signs of diabetes and normalization of blood levels of hemoglobin A1c. Current research indicates that transition metals bypass the insulin-receptor and activate glucose metabolism within the cell. Unlike insulin, vanadium and chromium do not lower blood glucose concentrations in normal animals.
One of the newer approaches to managing diabetes mellitus in dogs combines the use of micronutrients, such as chromium, with nutritional components such as starch blends, carboymethyl cellulose and fermentable fiber blends. (Iams, Glucose-control) Barley and sorghum are used to blunt the post-prandial rise in blood glucose, adjust postprandial insulin to appropriate levels, and to help blunt glucose surge. Fermentable fibers, such as FOS, beet pulp and gum arabic, increase short chain fatty acids from the large intestine which in turn increases glucogon like peptide-1 secretion and activity. GLP-1 is necessary for normal insulin secretion and for normal timing of insulin secretion after eating. L-carnitine is used to promote weight loss in overweight diabetic dogs and carboymethylcellulose delays gastric emptying further blunting the glucose surge that occurs after feeding.

The cat is an obligate carnivore and as such is unique among mammals in its insulin response to dietary carbohydrates, protein and fat. The feline liver exhibits normal hexokinase activity but glucokinase activity is virtually absent. Glucokinase converts glucose to glycogen for storage in the liver and is important in “mopping” up excess post-prandial glucose. Normal cats are in fact similar to diabetic humans because glucokinase levels drop precipitously with persistent hyperglycemia in human beings suffering from type 2 diabetes mellitus. Amino acids, rather than glucose, are the signal for insulin release in cats. In fact, a recent publication demonstrated more effective assessment of insulin reserve in cats using the arginine response test rather than a glucose tolerance test. Another unusual aspect of feline metabolism is the increase in hepatic gluconeogenesis seen after a normal meal. Normal cats maintain essential glucose requirements from gluconeogenic precursors (i.e. amino acids) rather than from dietary carbohydrates. As a result, cats can maintain normal blood glucose concentrations even when deprived of food for over 72 hrs; furthermore, feeding has very little effect on blood glucose concentrations in normal cats. In summary, the cat is uniquely adapted to a carnivorous diet and is not metabolically adapted to ingestion of excess carbohydrate. When type 2 diabetes occurs in cats, the metabolic adaptations to a carnivorous diet become even more deleterious leading to severe protein catabolism; feeding a diet rich in carbohydrates may exacerbate hyperglycemia and protein wasting in these diabetic cats. In fact, in human beings with type 2 diabetes, the first recommendation is to restrict excess dietary carbohydrates such as potatoes and bread and to control obesity by caloric restriction. Furthermore, human beings with type 2 diabetes mellitus have been shown to have improved glycemic control and improvement in nitrogen turnover during weight loss when a low–energy diet (high protein) was combined with oral hypoglycemic therapy. A low-carbohydrate, high-protein diet which is similar in fact to a cat’s natural diet (mice) may ameliorate some of the abnormalities associated with diabetes mellitus in the cat. Initial studies using a canned high protein/low carbohydrate diet (Hill’s feline growth) and the starch blocker acarbose have shown that 58% of cats discontinue insulin injections and those with continued insulin requirements could be regulated on a much lower dosage (1U BID). Comparison of canned high fiber vs low carbohydrate diets showed that cats fed low carbohydrate diets were 3 times more likely to discontinue insulin injections.

EXERCISE

Exercise should be kept constant in diabetic animals. The owners should be instructed to walk the animal daily and avoid intermittent episodes of strenuous exercise, such as racing or
hiking. Increasing exercise in obese diabetic animals will reduce insulin resistance and improve glycemic control.

Hypoglycemia

Clinical signs of hypoglycemia in diabetics are initially consistent with epinephrine release to counter the hypoglycemia. Nervousness, anxiety, vocalization, muscle tremors, ataxia, and pupillary dilatation should alert the owner to the possibility of hypoglycemia. At this point, the animal should be offered food and the owner should seek veterinary advice. Late in the course of hypoglycemic shock the animal may become recumbent, comatose or seizure. If access to a vein is not readily available or if the owner is administering therapy, 50% dextrose (Karo syrup, pancake syrup) may be applied to the mucous membranes of the mouth using a large syringe. One should caution the owner to pour the syrup on the gums from a reasonable distance from the animal’s teeth to prevent accidental injury from biting. The owner should transport the animal to a veterinarian as soon as possible. At the veterinary office, treatment should consist of administration of a slow IV bolus of 50% dextrose (0.5 g/kg diluted 1:4). Thereafter in animals suffering from hypoglycemia of any cause, a continuous infusion of 5% dextrose should be administered until the animal can be fed. Many animals that experience insulin overdose will suffer cerebral edema and temporary blindness or behavior changes; often these signs are temporary and resolve after several weeks or months. Endogenous glucose stores may have been depleted by the insulin overdose and it may take several days for hyperglycemia to recur. In these cases, insulin therapy should be discontinued until hyperglycemia recurs.

Monitoring Diabetes Mellitus with Glycated Blood Proteins: Glycosylated Hemoglobin and Serum Fructosamine

Glycosylated blood proteins are indicative of mean glucose concentrations in serum over an extended period of time. Glycated blood proteins may be used to monitor long-term insulin therapy; these proteins are particularly useful in monitoring diabetic cats that may be stressed by hospitalization and serial blood glucose curves. As plasma glucose concentrations increase, hemoglobin glycosylation increases proportionately. Normal glycosylated hemoglobin (mean+/−SD) values are: 2.9 ± 0.15% in dogs. Serum fructosamine is formed by glycosylation of serum protein such as albumin. The concentration of fructosamine in serum is directly related to blood glucose concentration. However, due to the shorter lifespan of albumin compared with hemoglobin, fructosamine concentrations reflect more recent (1-3 weeks) changes in serum concentrations. Fructosamine concentrations less than 400-450 mg/dl are associated with good to excellent diabetic control, whereas serum fructosamine of 450-550 mg/dl indicates fair to good control, serum fructosamine greater than 550 mg/dl indicates poor glycemic control. Relative changes in serum fructosamine may be more helpful than absolute values in some cases.
Algorithm: Monitoring with serum fructosamine

Measure glucose (BG mg/dl) and fructosamine (FR mmol/L)

FR < 400
BG < 180
Excellent control

FR > 400
BG < 180
Owner non-compliance

FR < 400
BG < 60
Over regulation

FR < 400
BG > 180
Stress induced hyperglycemia

FR > 400
BG > 180
Poor control