

# AAHA Diabetes Management Guidelines for Dogs and Cats

## Special Report

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### Introduction

Diabetes mellitus (DM) is a treatable condition that requires a committed effort by veterinarian and client. This document provides current recommendations for the treatment of diabetes in dogs and cats. Treatment of DM is a combination of art and science, due in part to the many factors that affect the diabetic state and the animal's response. Each animal needs individualized, frequent reassessment, and treatment may be modified based on response.

In both dogs and cats, DM is caused by loss or dysfunction of pancreatic beta cells. In the dog, beta cell loss tends to be rapid and progressive, and it is usually due to immune-mediated destruction, vacuolar degeneration, or pancreatitis.<sup>1</sup> Intact females may be transiently diabetic due to the insulin-resistant effects of the diestrus phase. In the cat, loss or dysfunction of beta cells is the result of insulin resistance, islet amyloidosis, or chronic lymphoplasmacytic pancreatitis.<sup>2</sup>

Risk factors for both dogs and cats include insulin resistance caused by obesity, other diseases (e.g., acromegaly in cats, hyperadrenocorticism in dogs), or medications (e.g., steroids, progestins). Genetics is a suspected risk factor, and certain breeds of dogs (Australian terriers, beagles, Samoyeds, keeshonden<sup>3</sup>) and cats (Burmese<sup>4</sup>) are more susceptible.

Regardless of the underlying etiology, diabetic dogs and cats are hyperglycemic and glycosuric, which leads to the classic clinical signs of polyuria, polydipsia (PU/PD), polyphagia, and weight loss. Increased fat mobilization leads to hepatic lipidosis, hepatomegaly, hypercholesterolemia, hypertriglyceridemia, and increased catabolism. Eventually, hyperketonemia, ketonuria, and ketoacidosis develop and result in progressive compromise of the animal.

### Diagnostic Criteria and Initial Assessment

#### *Presentation*

In this document, the authors describe different approaches to the animal depending on the level of hyperglycemia and severity of the clinical signs. Animals with DM may be presented with a variety of signs that are dependent, in part, on the time interval between onset of hyperglycemia and the client seeking veterinary help; the severity of hyperglycemia; presence and severity of ketonemia; and the nature and severity of concurrent disease, such as pancreatitis. Clinical signs of PU/PD do not develop until the blood glucose (BG) concentration exceeds the renal tubular threshold for spillage of glucose into the urine. In dogs and cats, glycosuria typically develops

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when the BG concentration exceeds approximately 200 mg/dL and 250 mg/dL, respectively.

Clinical signs of DM are not generally present in dogs and cats with persistent fasting BG concentrations above the reference range but below the concentration that results in glycosuria (i.e., BG between the reference upper limit to 200 mg/dL in dogs and between the reference upper limit to 250 mg/dL in cats). BG concentrations in these ranges may occur for several reasons, including stress hyperglycemia (in cats), presence of an insulin-resistant disorder (e.g., obesity, hyperadrenocorticism), in association with medication (e.g., glucocorticoids), or as part of the early stage of developing DM.

Dogs and cats that are in the early stage of developing DM are classified as subclinical diabetics. Subclinical diabetics often appear healthy, have a stable weight, and are usually identified when routine laboratory work is performed for other reasons. A diagnosis of subclinical diabetes should only be made after stress hyperglycemia has been ruled out and hyperglycemia persists despite identification and correction of insulin-resistant disorders. Reassessing the BG at home or measuring serum fructosamine concentration may help differentiate between stress hyperglycemia and subclinical DM and help determine if further action is needed.

Clinical DM is diagnosed on the basis of persistent glycosuria and persistent hyperglycemia (>200 mg/dL in the dog and >250 mg/dL in the cat). Documentation of an elevated serum fructosamine concentration may be necessary to confirm the diagnosis in cats.<sup>5</sup>

Animals with clinical diabetes manifest PU/PD, polyphagia, and weight loss. Some animals present with systemic signs of illness due to diabetic ketoacidosis (DKA), such as anorexia, dehydration, and vomiting. Additional problems may include lethargy, weakness, poor body condition, cataracts (in dogs), and impaired jumping ability and abnormal gait (in cats).

### Assessment

The initial evaluation of the diabetic dog and cat should:

- Assess the overall health of the animal (history, physical examination, medications, diet).
- Identify complications associated with the disease (e.g., cataracts in dogs, peripheral neuropathy in cats).
- Identify concurrent problems often associated with the disease (e.g., urinary tract infections, pancreatitis).
- Identify conditions that may interfere with response of the diabetic to treatment (e.g., hyperadrenocorticism, hyperthyroidism, renal disease).
- Evaluate for risk factors such as obesity, pancreatitis, insulin-resistant disease, diabetogenic medications, and diestrus (in the female dog).

The physical examination of the diabetic dog or cat can be relatively normal or may reveal dehydration, weight loss, dull coat, cataracts, or abdominal pain (if concurrent pan-

creatitis is present). A sweet odor may be noted on the breath if the animal is ketotic. Some cats with long-standing hyperglycemia may have a plantigrade stance secondary to a peripheral neuropathy.

Laboratory assessment should include the items in Table 1. Typical findings include a stress leukogram and increased glucose, cholesterol, and triglyceride concentrations.

Dogs often show increased alkaline phosphatase and alanine aminotransferase activity. In the cat, the stress leukogram and increases in alkaline phosphatase are variable. Cats with increased liver enzymes may have concurrent liver disease or pancreatitis and should be evaluated further.<sup>6</sup>

Dogs and cats with DKA may show very elevated BG concentrations, alterations in liver enzyme activity and electrolyte concentrations, azotemia, and decreased total carbon dioxide secondary to metabolic acidosis, osmotic diuresis, and dehydration.<sup>7,8</sup>

The urinalysis will reveal the presence of glucose and may reveal the presence of protein, ketones, bacteria, and/or casts. A urine culture should always be performed in glycosuric animals, as infection is commonly present.

If thyroid disease is suspected in a dog, it is best to perform thyroid testing after diabetes is stabilized because of the likelihood of euthyroid sick syndrome. All cats >7 years of age with weight loss and polyphagia should be tested for hyperthyroidism, as diabetes and hyperthyroidism cause similar clinical signs and can occur concurrently.

### Treatment

The mainstay of treatment for clinical DM in both species is insulin, along with diet modification. However, insulin treatment is not indicated in dogs and cats with subclinical disease, unless hyperglycemia worsens and glycosuria is noted.

Veterinarians use a variety of insulin products, but only two are presently approved by the Food and Drug Administration (FDA) for use in dogs and cats. One of these is a **porcine lente** product (porcine zinc insulin suspension) that is approved for both dogs and cats.<sup>9</sup> If available, the authors' recommendation is to use this product in dogs. The other FDA-approved insulin is a longer-acting product (human recombinant **protamine zinc** insulin [PZI]) and is currently approved for use in cats.<sup>10</sup> For the majority of diabetic cats, insulin glargine (not veterinary approved) and PZI have appropriate duration of action.

Although bovine PZI is available from compounding pharmacies, its use is not recommended because of concerns about production methods, diluents, sterility, and the consistency of insulin concentration between lots. In addition, bovine insulin causes antibody production in dogs, which may impact control of DM.<sup>11</sup>

### Initial Treatment and Monitoring of the Cat

#### Management of the cat with subclinical DM

##### Overall goals of treatment

- Prevent the onset of clinical DM.
- Address obesity and optimize body weight.

**Table 1****Recommended Diagnostic Testing for Animals With Suspected or Confirmed Diabetes Mellitus**

<b>Test/Procedure*</b>	<b>Initial Workup and Regular Monitoring</b>	<b>If Ill/Troubleshooting, Consider These in Addition</b>
CBC	Dog, Cat	
Serum biochemical analysis + electrolytes	Dog, Cat	
Urinalysis <i>with culture</i>	Dog, Cat	
T4	Cat	
Blood pressure	Cat	
Serum progesterone	Dog (intact female)	
Fructosamine	Dog, Cat	
FeLV/FIV	Cat, if status unknown	
Thyroid panel (T4/FT4 ± TSH)		Dog, Cat
TLI		Dog, Cat
PLI		Dog, Cat
Adrenal function testing		Dog, Cat
Cobalamin/folate		Cat
Abdominal ultrasound		Dog, Cat
Abdominal radiographs		Dog, Cat
Chest radiographs		Dog, Cat

\* CBC=complete blood count; T4=thyroxine; FeLV/FIV=feline leukemia virus/feline immunodeficiency virus; FT4=free thyroxine; TSH=thyroid-stimulating hormone; TLI=trypsin-like immunoreactivity; PLI=pancreatic lipase immunoreactivity.

- Reverse or mitigate other causes of insulin resistance.
- To obtain normal BG concentrations without need for insulin.<sup>12</sup>

Cats with subclinical DM may attain euglycemia without the use of insulin. Begin management with diet change. Evaluate and manage body weight, identify and cease any existing diabetogenic drug therapy, and correct concurrent insulin-resistant disease. Perform a recheck examination with urine analysis and BG measurement every 2 weeks. If clinical DM occurs despite dietary intervention, initiate insulin therapy.

#### *Diet therapy goals and management*

- Optimize body weight with appropriate protein and carbohydrate levels, fat restriction, and calorie control.
  - Weigh at least monthly and adjust intake to maintain optimal weight.
  - Management goal of weight loss in obese cats: 1% to 2% loss per week<sup>13</sup> or a maximum of 4% to 8% per

month (hepatic lipidosis risk is minimized with the recommended high-protein diet).

- Minimize postprandial hyperglycemia by managing protein and carbohydrate intake.
- Feed a high-protein diet (defined as >45% protein metabolizable energy [ME]) to maximize metabolic rate, improve satiety, and prevent lean muscle-mass loss.<sup>14-17</sup>
  - This is necessary to prevent protein malnutrition and loss of lean body mass.
  - Protein normalizes fat metabolism and provides a consistent energy source.
  - Arginine stimulates insulin secretion.
- Limit carbohydrate intake.<sup>18-21</sup>
  - Dietary carbohydrate may contribute to hyperglycemia and glucose toxicity in cats.
  - Provide the lowest amount of carbohydrate levels in the diet that the cat will eat.
  - Carbohydrate levels can be loosely classified as ultralow (<5% ME), low (5% to 25% ME), moderate (26% to 50% ME), and high (>50% ME).<sup>22</sup>

- Portion control by feeding meals.<sup>23,24</sup>
  - Allows monitoring of appetite and intake.
  - Essential to achieve weight loss in obese cats.
- Canned foods are preferred over dry foods. Canned foods provide:
  - Lower carbohydrate levels.
  - Ease of portion control.
  - Lower caloric density; cat can eat a higher volume of canned food for the same caloric intake.
  - Additional water intake.<sup>25-28</sup>
- Adjust diet recommendations based on concurrent disease (e.g., chronic kidney disease, pancreatitis, intestinal disease).

### Management of the cat with clinical DM

In addition to diet therapy, insulin treatment is required for cats with clinical DM.

#### Overall goals of treatment

- Minimal to no clinical signs.
- Owner perceives good quality of life and is satisfied with treatment.
- Avoid or improve complications, specifically DKA and peripheral neuropathy.
- Avoid symptomatic hypoglycemia.

#### Management

- Feeding meals four times daily is ideal to prevent clinical hypoglycemia for cats on insulin. Timed feeders are useful for cats that require multiple meals per day to manage weight and control calories. Use of insulin glargine may reduce the need for timed feedings, as long as home monitoring of BG is being done. (See Insulin therapy in the cat.)
- Free-choice feeding is acceptable for underweight cats on insulin therapy.
- The sick diabetic, ketotic cat should be hospitalized to initiate aggressive therapy. If unable to provide 24-hour care, refer to an appropriate emergency or specialty hospital.
- Adjunct therapy includes environmental enrichment, particularly for obese cats.<sup>29</sup>
- Oral hypoglycemic drugs, combined with diet change, are only indicated if owner refuses insulin therapy or is considering euthanasia.<sup>30</sup> These agents are not considered appropriate for long-term use.

### Insulin therapy in the cat

The insulin preparations with the appropriate duration of action in most diabetic cats are glargine (U-100) or the veterinary-approved human **protamine zinc** insulin (PZI U-40).<sup>31</sup>

This panel does not recommend the veterinary-approved **porcine zinc (lente)** insulin suspension as the initial treatment for the cat, because its duration of action is short and control of clinical signs is poor.<sup>32</sup> This insulin should be reserved for cats in which other insulin choices have not yielded satisfactory results.

Judicious dosing is recommended initially, given that diet change may alter food intake and impact the response to insulin. Likewise, with ongoing therapy and reversal of glucotoxicity, the pet's response to insulin will improve with time.<sup>17</sup> Use caution in increasing the insulin dose too soon. Increases should only be made once food intake has stabilized and only if clinical signs have not improved after 1 week of therapy.

Most cats are well regulated on insulin at 0.5 U/kg *q* 12 hours, with a range of 0.2 to 0.8 U/kg.<sup>15,33</sup> The panel recommends a starting dose of 0.25 U/kg *q* 12 hours, based on an estimate of the cat's **lean** body weight. This equates to 1 U *q* 12 hours in an average cat. Even in a very large cat, the starting dose of insulin should not exceed 2 U per cat *q* 12 hours.

#### Initiating insulin therapy

##### Outline of initial approach

- Initiate insulin therapy with PZI or insulin glargine at a starting dose of 1 U per cat *q* 12 hours.
- The decision to monitor BG on the first day of insulin treatment is at the discretion of the veterinarian.
- The goal of monitoring is solely to identify hypoglycemia. The insulin dose should **not** be increased based on first-day BG evaluation.
  - If monitoring is elected, measure BG every 2 to 3 hours for cats on PZI and every 4 hours for those on insulin glargine, for 10 to 12 hours following insulin administration.
  - Decrease insulin dose by 0.5 U if BG is <150 mg/dL any time during the day.
  - Treat as an outpatient and plan to reevaluate in 7 days regardless of whether BGs are monitored on the first day.
  - Immediately reevaluate if clinical signs worsen; if clinical signs suggest hypoglycemia; or if lethargy, anorexia, or vomiting is noted.

##### Precautions and details

- Home monitoring of BG is ideal and strongly encouraged to obtain the most accurate interpretation of glucose relative to clinical signs.<sup>34</sup> Most owners are able to learn to do this with a little encouragement, and interpretation of glucose results is much easier for the clinician. See Table 2 for web links to client educational materials.
- The pressing concern for cats at this stage is identifying impending hypoglycemia, since cats often do not show overt signs until the BG is dangerously low.
- Use extreme caution when interpreting a "high BG" in the cat. It is important to discern between stress hyperglycemia and hyperglycemia that needs treatment. Use all laboratory findings and the clinical examination when evaluating response to insulin.
- Be aware that chronic insulin overdose may not only result in clinical hypoglycemia (seizures, coma), but also the development of sustained hyperglycemia and insulin ineffectiveness following secretion of insulin antagonists (catecholamines, glucagon, cortisol, growth hormone) that combat hypoglycemia.<sup>35</sup>

**Table 2****Web Links for Staff and Client Education**

<b>Title</b>	<b>URL</b>
AAHA/AAFP Feline Life Stage Guidelines	<a href="http://www.aahanet.org">www.aahanet.org</a> and <a href="http://www.catvets.com">www.catvets.com</a>
ACVIM referral resources	<a href="http://www.acvim.org">www.acvim.org</a>
University of Queensland diabetes information for veterinarians	<a href="http://www.uq.edu.au/ccah/index.html?page=41544&amp;pid=42973">http://www.uq.edu.au/ccah/index.html?page=41544&amp;pid=42973</a>
Canine diabetes site for owners	<a href="http://www.caninediabetes.org">www.caninediabetes.org</a>
Washington State University client information	<a href="http://www.vetmed.wsu.edu/ClientEd/diabetes.aspx">http://www.vetmed.wsu.edu/ClientEd/diabetes.aspx</a>
Winn Feline Foundation information on cats	<a href="http://www.winnfelinehealth.org/Health/Diabetes.html?gclid=CK3R9__T8p4CFQklswodAhcdLA">http://www.winnfelinehealth.org/Health/Diabetes.html?gclid=CK3R9__T8p4CFQklswodAhcdLA</a>

- In-clinic blood glucose curves (BGCs) are more likely to be affected by stress hyperglycemia than BGCs generated at home. Veterinarians should be cautious of high glucose results and subsequent overzealous increases in dose.
- Regardless of the approach, it is important to remember that a BGC performed at the time insulin is initiated was intended mainly to detect and avoid dangerous hypoglycemia.

**Ongoing Monitoring of the Cat**

Monitoring strategies may be influenced by persistence or resolution of clinical signs. The pressing concern for the newly diagnosed and treated cat is the development of hypoglycemia in individuals that may quickly go into remission. Cats on long-acting insulin may not show overt signs of hypoglycemia until the BG is dangerously low, so it is important to identify impending hypoglycemia by home glucose testing whenever possible.

If BG monitoring is not possible, close attention and documenting changes in clinical signs are imperative. Likewise, urine glucose testing using glucose-detecting crystals in the litter can be helpful for detecting diabetic remission.<sup>17</sup>

**Ongoing home monitoring for all cats**

- Log food, water, and appetite daily.
- Log insulin dose daily.
- Note any signs suggestive of hypoglycemia; contact veterinarian if persistent.
- Periodically test urine, looking for negative glycosuria (suggestive of hypoglycemia or diabetic remission) or positive ketonuria (suggestive of substantial hyperglycemia).

**At 1 week after initiating insulin treatment**

- If clinical signs have improved, and no ketonuria is present:
  - Continue present insulin dose.
  - Introduce home monitoring if not already done.

- If a spot check on the BG is possible, assess for hypoglycemia at 6 to 8 hours following insulin administration.
  - If BG is <150 mg/dL, either decrease insulin dose to 0.5 U *q* 12 hours, consider dosing *q* 24 hours, or suspend insulin treatment and wait for clinical signs and glycosuria to recur before restarting insulin at 0.5 U *q* 12 hours.
- If clinical signs have persisted or worsened:
  - Evaluate client compliance and dosing technique (see Client Education).
  - If adherence is good, consider increasing the dose to 2 U *q* 12 hours.
  - If the cat is ketonuric, has developed peripheral neuropathy, or does not have a good appetite, evaluate for DKA and rule out complicating disease (e.g., pancreatitis) that may be worsening the diabetic state.

**During the first month after initiating insulin treatment**

- In-clinic (only if home monitoring is not possible)
  - Every 1 to 2 weeks:
    - Spot checks of BG at 6 to 8 hours following insulin administration.
      - Decrease insulin dose if BG is <150 mg/dL.
      - Cautiously increase insulin dose if clinical signs persist or worsen or ketonuria is noted. Do not exceed 3 U per injection.
    - Urinalysis (to detect glycosuria, ketonuria, or infection).
    - Consider BGC if clinical signs persist or worsen and insulin dose is at 3 U per injection.
- Home
  - Weekly:
    - Spot checks of BG at 6 to 8 hours following insulin administration (more often if hypoglycemia is suspected).

- Increase dose if necessary based on BG results.
- Urine dipsticks for glucose and ketones (particularly useful if BG measurements are not possible).
- Every 2 weeks:
  - Perform BGC (see protocol for BGC).
  - Utilize urine dipstick or litter glucose-detecting crystals.
  - Adjust insulin as discussed previously.
  - Consider insulin overdose and/or possible diabetic remission if three consecutive negative urine glucose results are obtained.
  - If ketones or persistently high urine glucose are noted, a clinic evaluation is in order; consider the need for dose increase.

#### ***At 1 month after initiating insulin treatment***

- In-clinic examination recommended for all cats:
  - Thorough history, physical examination, weight, and urinalysis.
  - Measure fructosamine unless detailed home-monitoring records are available.
  - Additional laboratory analysis if indicated by examination [Table 1].
  - Adjust insulin **if** needed; insulin dose should not be increased more than 1 unit at a time.
  - The cat must be reevaluated if clinical signs persist at 3 U *q* 12 hours. Consider problems with insulin duration or action, concurrent conditions, or medications causing insulin resistance. The majority of cats on insulin glargine or PZI do not need >3 U of insulin *q* 12 hours to control diabetes.

#### ***Long-term monitoring of insulin treatment***

- Advise clients to monitor and record the following:
  - Daily: Clinical signs, food/water intake, insulin dose.
  - Weekly: Body weight.
  - Monthly: BG spot checks (twice monthly if practical).
    - If on insulin glargine, evaluate BG prior to insulin administration and at 8 hours following.
    - If on PZI, evaluate BG prior to insulin administration and 3, 6, and 9 hours later.
  - Twice monthly: Urine glucose and ketones.
    - If urine glucose is consistently negative, consider diabetic remission.
- In-clinic:
  - Any items listed above that client cannot perform.
  - If the cat is doing well, don't make changes based on increased BG measurements alone, especially if measured at the clinic.
  - Every 3 months: Examination, including weight.
  - Every 3 to 6 months: Serum fructosamine concentration.
    - If at the lower end of the reference range or below the reference range, consider chronic hypoglycemia and diabetic remission.
    - Consider monitoring BG or urine glucose at home, or decrease insulin dose and recheck in 4 weeks.

- If BG is consistently <150 mg/dL or urine is persistently negative for glucose, or both, consider decreasing the insulin dose, switching treatment to *q* 24 hours, or stopping insulin and monitoring response. In cats, glucose toxicity suppresses beta cell function, and with control of hyperglycemia and resolution of glucose toxicity, the remaining beta cells become functional again and start secreting insulin.
- Every 6 to 12 months: Full laboratory analysis [Table 1].

#### ***Initial Treatment and Monitoring of the Dog***

##### ***Management of the dog with subclinical DM***

- Investigate and address causes of insulin resistance
  - Obesity.
  - Medications.
  - Intact female in diestrus.
  - Hyperadrenocorticism.
- Initiate diet therapy to limit postprandial hyperglycemia.
- Evaluate closely for progression to clinical DM.
- Subclinical diabetes is not commonly identified in the dog. Most dogs in the early stages of naturally acquired diabetes (i.e., not induced by insulin resistance, *per se*) quickly progress to clinical diabetes and should be managed (using insulin) as described in that section.

##### ***Diet therapy***

Evaluate and recommend an appropriate diet that will correct obesity, optimize body weight, and minimize postprandial hyperglycemia. Dogs with DM can do well with any diet that is complete and balanced, does not contain simple sugars, is fed at consistent times in consistent amounts, and is palatable for predictable and consistent intake.

Dietary considerations include:

- The use of diets that contain increased quantities of soluble and insoluble fiber or that are designed for weight maintenance in diabetics or for weight loss in obese diabetics.<sup>36,37</sup>
  - May improve glycemic control by reducing postprandial hyperglycemia.
  - May help with caloric restriction in obese dogs undergoing weight reduction.
  - In underweight dogs, the priority of dietary therapy is to normalize body weight, increase muscle mass, and stabilize metabolism and insulin requirements. Underweight dogs should be fed a high-quality maintenance diet or a diabetic diet that has mixed fiber and is not designed for weight loss.
- Modify the diet based on other conditions (e.g. pancreatitis, kidney disease, gastrointestinal disease) and needs of the dog.

##### ***Adjunctive treatment***

- Initiate a consistent, moderate daily exercise program to help promote weight loss and lower BG concentrations secondary to increased glucose utilization. Exercising

twice daily after feeding is ideal to minimize postprandial hyperglycemia.

- Oral sulfonylurea drugs work by stimulating insulin secretion and are not effective in the dog.

### ***Management of the dog with clinical DM***

Treatment of clinical DM in the dog always requires exogenous insulin therapy. The U-40 pork lente (porcine zinc insulin suspension) has been the first-choice recommendation for dogs. The duration of action is close to 12 hours in most dogs, and the amorphous component of the insulin helps to minimize postprandial hyperglycemia.<sup>38</sup> However, according to the FDA, that product has recently had “problems with stability,” and while the manufacturer is “working with FDA on resolving this issue, supplies may be limited” (<http://www.fda.gov/AnimalVeterinary/NewsEvents/CVMUpdates/ucm188752.htm>; accessed 4/14/2010). If it again becomes consistently available, it will remain a great option for dogs. In the meantime, diabetic dogs should be started on a different insulin.<sup>39</sup>

When porcine zinc insulin is not available, U-100 human recombinant Neutral Protamine Hagedorn (NPH) insulin is a good initial alternative, although its duration of action is often <12 hours in many dogs.<sup>40</sup>

As a third option, human PZI is likely to be a better choice for dogs than is insulin glargine. There are no studies showing effective use of either of these products in dogs, however, glargine would likely require concurrent use of a short-acting insulin due to its slow release from subcutaneous tissues.

### ***Overall goals of treatment***

- Resolve PU/PD.
- Optimize weight, activity level, and body condition.
- Avoid hypoglycemia.
- Avoid DKA.
- Minimize complications (e.g. urinary tract infections, cataracts).
- Owner-perceived good quality of life and owner satisfaction with treatment.

### ***Initiating insulin therapy***

#### **Outline of initial approach**

- Administer the first insulin dose (0.25 U/kg) and feed in the morning.
- Perform BGC with samples every 2 hours for at least 8 and preferably 12 hours, or until the nadir can be determined.
- If BG remains >150 mg/dL, send dog home and repeat BGC in 1 week.
- If BG becomes <150 mg/dL, decrease the next dose by 10% to 25% rounded to the nearest unit based on dog body weight and severity of glucose nadir. If possible, hospitalize dog to monitor response to the lower dose.
- Repeat BGC in 1 week (or sooner if concerns for hypoglycemia exist based on results of initial BGC).

### **Precautions and details**

- Most dogs are well controlled on insulin at 0.5 U/kg *q* 12 hours, with a range of 0.2 to 1.0 U/kg.<sup>14,41</sup> The authors recommend a starting dose of 0.25 U/kg *q* 12 hours, rounded to the nearest whole unit.
- Feed equal-sized meals twice daily at the time of each insulin injection. Maintain a schedule to achieve a consistent amount of food at the same time, and thus consistent insulin needs.
- A critical initial goal of treatment is avoidance of symptomatic hypoglycemia, which may occur if the dose is increased too aggressively.
- Be cautious with adjustments until the dog and client are used to their new regimen (diet, insulin, etc). With stabilization of BG levels, reversal of hyperglucagonemia, and reduction in hepatic gluconeogenesis, insulin sensitivity is likely to improve during the first month of therapy. Once the routine is set, then adjustments in insulin can be made to maximize benefit and minimize risk.
- If problems attaining diabetic control persist despite adjusting the insulin dose, and the duration of effect of the insulin is found to be inappropriate (e.g., <10 hours or >14 hours), consider a different insulin type.
- In contrast with cats, diabetic remission does not occur in dogs with naturally acquired diabetes. Hypoglycemia in dogs results from excess insulin caused by an insulin overdose, excessive exercise, or inappetence, and not from diabetic remission.
- Tailor treatment and monitoring to the individual case, using a combination of in-clinic evaluation and phone consultation. Monitoring of BG can be done in the clinic, at home, or both.
- Strenuous and sporadic exercise can cause severe hypoglycemia and should be avoided.
- Note that the BGC in established cases differs slightly from the initial protocol.

### ***Ongoing Monitoring and Treatment of the Dog***

Always tailor the monitoring and treatment to the dog. See Client Education for links to how-to videos and information.

#### ***During first month after initiating insulin***

- Weekly (every 7 to 10 days):
  - Recheck examination and BGC.
  - Adjust insulin (as listed under Interpretation of the Glucose Curve).
  - Continue until clinical signs are controlled, body weight is trending toward optimal, and results of BG testing suggest control (see section on BGCs).

#### ***Long-term monitoring***

- Tailor monitoring to the dog. Focus on weight, history, physical examination, and client observations regarding thirst, urine output, energy level, and behavior.<sup>42</sup> Treat the dog, not the BG results. Always repeat the BGC 2 weeks after any insulin dose adjustment.

- In-clinic
  - Every 3 months:
    - Examination, including weight and ocular examination.
    - Measure BG.
    - Measure fructosamine if the dog is doing well clinically and if a spot-check glucose (prior to dose and at anticipated nadir) is satisfactory. If fructosamine concentration is abnormal, proceed with BGC.
    - Perform a BGC if the examination or clinical history suggests any problems, if the fructosamine level is abnormal, or if the insulin dose has recently been adjusted.
  - Every 6 months:
    - Full laboratory work, including urinalysis and urine culture [Table1].
- At home
  - Advise clients to monitor and record the following:
    - Daily: Clinical signs, food/water intake, insulin dose.
    - Weekly: Body weight.
    - Monthly: Home BGC.

### Indications, Method, and Interpretation of the BGC in the Dog and Cat

BGCs are part of the long-term monitoring plan. Create a BGC when:

- PU/PD persists.
- Signs of hypoglycemia are reported.
- 2 weeks after any change in insulin dose.
- Clinical history or physical examination suggests poor control (weight loss, neuropathy, etc.).

Use results to measure the nadir and to calculate the average BG over a roughly 12-hour period (average equals sum of all measurements divided by number of measurements). The BGC is the optimal way to assess:

- Duration of insulin action; the ideal duration is 12 (10-14) hours.
- The glucose nadir (to avoid hypoglycemia); approximately 8 hours postinjection is ideal.
- The average BG concentration throughout the day (indicates overall glycemic control).

#### Protocol for BGC in Established Diabetic Cases

Initial BG measurements are performed as described under Initial Treatment. This is the protocol for the BGC in established diabetic animals.

If the BGC is performed at home, have client measure BG before insulin or food is given. In free-fed cats, measure BG before insulin is given.

#### Dogs

1. Feed and administer insulin as usual.
  - a. Feeding at home ensures that pet eats all of its food.

2. Once food is consumed, transport pet to hospital for the duration of the day or continue BGC at home.
3. Test BG every 2 hours until next dose of insulin.
  - a. Repeat BG within 1 hour if any glucose value is <100 mg/dL.

#### Cats

1. At-home monitoring is strongly encouraged, as results are more reliable.
2. On PZI: Measure BG every 2 hours until next dose of insulin.
3. On insulin glargine: Measure BG prior to dose, 4 and 8 hours following insulin administration, and prior to next dose.

#### Target results<sup>43</sup>

- Nadir: 80 to 150 mg/dL.
- Time of nadir: 8 hours after insulin injection (a nadir may not be easily identified if using insulin glargine).
- Average BG <250 mg/dL; ideally no single BG >300 mg/dL.

#### Action plan: If nadir is

- <80 mg/dL, decrease insulin approximately 25% in dogs and 0.5 U per injection for cats or decrease to *q* 24 hours dosing if on 1 U *q* 12 hours.
- >150 mg/dL, increase insulin.
  - Cats: 0.5 to 1 U per injection based on severity of hyperglycemia.
  - Dogs: 10% to 20% to nearest unit.
- 80 to 150 mg/dL, and
  - Average glucose is <250 mg/dL: no change.
  - Average glucose is >250 mg/dL:
    - Glucose nadir ≤6 hours after insulin, change to a longer-acting insulin.
    - Glucose nadir ≥10 hours after insulin, change to a shorter-acting insulin. Consultation with a specialist on suitable insulin choices is advisable at this time.

#### Troubleshooting of the Dog and Cat

The “uncontrolled diabetic” is one with poor control of clinical signs. This may include hypo- and hyperglycemic pets, those with insulin resistance (decreased responsiveness to the insulin, defined by >1.5 U/kg per dose), or those with frequent changes (up or down) in insulin doses. Any dog or cat with persistent BG >300 mg/dL despite receiving >1.5 U/kg per dose should be reevaluated [Table 1], as insulin resistance or insulin overdose causing the Somogyi response is likely.

1. Rule out client and insulin issues first.
  - a. Observe client’s administration and handling of insulin, including type of syringes used.
  - b. Assess insulin product and replace if out of date or if the appearance of the insulin changes (i.e., becomes flocculent, discolored, or—in the case of glargine—cloudy).

2. Review diet and weight loss plan.
3. Perform a BGC (at home for cats).
4. Perform laboratory analysis [Table 1].
  - a. Repeat basic laboratory testing.
  - b. Conduct additional testing to evaluate for endocrine disease, infection, pancreatitis, and neoplasia.
  - c. Rule out causes of continued insulin resistance (obesity, steroid use).
5. Consult with a specialist if you are unable to regulate your animal. This paper does not go into detailed management of the challenging diabetic or the animal with DKA.

### Client Education

Give clients a realistic idea of the commitment involved, along with positive encouragement that it is possible to manage this disease. Provide access to trained veterinary support staff and helpful web links. Stress the importance of appropriate nutrition and weight management. Table 2 provides web resources for education of staff and clients. Inform clients about the following:

#### *Insulin Mechanism, Administration, Handling, and Storage*

- Explain how insulin works and its effects on glucose.
- Roll, don't shake, bottles (PZI, lente/zinc insulin, NPH).
- Wipe bottle stopper with alcohol prior to inserting syringe needle.
- Do not freeze.
- Do not heat; avoid prolonged exposure to direct sunlight.
- Recommend storage in refrigerator for consistency in environment.
- Recommend new bottle if insulin changes in appearance or becomes out of date.
- Refer to package insert for instructions about shelf life after opening.

#### *Types of Syringes*

- Always use a U-40 insulin syringe with U-40 insulin and a U-100 insulin syringe with U-100 insulin.
- 0.3 and 0.5 mL insulin syringes are best to facilitate accurate dosing, especially in cats and dogs getting <5 U per dose.
- Syringes are for single use.
- Do not use "short" needles. A standard 29-g, half-inch length needle is recommended.

#### *Troubleshooting and Action*

- If the pet does not eat:
  - Educate owners to measure BG, to not administer insulin, and to contact veterinarian.
- Help clients with recognition and treatment at home for low BG.
  - Signs include lethargy, sleepiness, strange behavior, abnormal gait, weakness, tremors, and seizures.
  - If conscious, feed high-carbohydrate meal (e.g., rice/chicken, regular diet with added corn syrup).

- If pet is poorly responsive or has tremors, rub 1 to 2 teaspoons of corn syrup onto gum tissue. Feed if animal responds within 5 minutes; otherwise, take to veterinarian.
- Home BG monitors should be veterinary-approved products calibrated for dogs and cats.<sup>44</sup>
- Dosing increases to be made only after consulting with doctor. Client is empowered to decrease or skip an insulin dose if hypoglycemia is noted.

### Summary

Management of the diabetic animal requires commitment and excellent communication between veterinarian and client about the treatment, follow-up appointments, associated costs, and home care. Diabetes is a dynamic disease, and successful management requires frequent client education and communication with the veterinary team. With appropriate client commitment, monitoring, and a firm understanding of the variables that are within our control, DM can be well managed.

Important differences exist between the development of canine and feline DM, and understanding these differences will help predict management success. The recommendations made in this manuscript are intended to guide medical decisions and treatment choices, with the recognition that within each animal, variations in response will exist and no two cases are alike. In difficult-to-manage cases, you may consider consulting with or referring to an internal medicine specialist.

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