Sweet success: Managing the difficult diabetic patient

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Management of diabetes mellitus in small animals can be challenging; however, the application of a systematic method of dietary and pharmaceutical (insulin, oral hypoglycemics) interventions coupled with practical monitoring strategies can result in improved patient care and client satisfaction. This article will cover the management of newly diagnosed and complicated cases of diabetes in cats and dogs.

Feline diabetes mellitus

Diagnosis of feline diabetes mellitus

Feline diabetes is most often type 2 in nature and is one of the most common endocrinopathies of the cat. Middle-aged to older, male cats with a history of obesity are most at risk. Clinical signs of type 2 diabetes mellitus are subtle and progressive over a period of months to years until blood glucose rises above the renal threshold, which is quite high in the cat, and polyuria/polydipsia ensues. Obesity combined with fasting or postprandial hyperglycemia may be the only clinical sign of early type 2 diabetes mellitus. Cats affected with diabetic neuropathy will have trouble jumping onto high surfaces such as counters and beds because the hind limbs are usually affected. As blood glucose concentrations exceed the renal threshold (which may be as high as 350 mg/dl in some cats), polyuria and secondary polydipsia become the primary clinical signs. Weight loss begins to occur as a result of insulin resistance and insulin deficiency with calories lost in glucose-laden urine.

In cats, physical examination findings of uncomplicated diabetes mellitus are typically nonspecific. The most common physical examination findings in cats are lethargy and depression, dehydration, unkempt haircoat; hepatomegaly, and muscle wasting. Plantigrade rear limb stance resulting from diabetic neuropathy is observed in approximately 10% of diabetic cats in previous studies. However, recent evidence suggests that diabetic cats can have a variety of clinical signs suggestive of diabetic neuropathy including pain on palpation of distal extremities, hypersensitivity, gait abnormalities, and palmigrade stance. Based on electromyogram (EMG), nerve biopsy, and nerve conduction studies, all diabetic cats have some degree of diabetic neuropathy at the time of presentation.

A diagnosis of diabetes mellitus should be based on the presence of clinical signs compatible with diabetes mellitus and evidence of fasting hyperglycemia and/or glycosuria. Common clinopathologic features of diabetes mellitus in cats include fasting hyperglycemia, hypercholesterolemia, increased liver enzymes (ALP, ALT), neutrophilic leukocytosis, proteinuria,
increased urine specific gravity, azotemia, and glycosuria. Many cats are susceptible to stress-induced hyperglycemia in which the serum glucose concentrations approach 300 to 400 mg/dL. Serum fructosamine is formed by glycosylation of serum protein such as albumin. The fructosamine concentration in serum is directly related to blood glucose concentration. However, because albumin has a shorter life span than hemoglobin has, fructosamine concentrations reflect more recent (one to three weeks) changes in serum glucose concentrations than glycosylated hemoglobin does. Measuring serum fructosamine concentrations in cats may be of benefit when trying to distinguish early or subclinical diabetes mellitus from stress-induced hyperglycemia. One study of 17 normal cats showed that transient glucose administration (1 g/kg 50% glucose solution, intravenously) did not increase serum fructosamine concentrations. In the same study, it was noted that 50% of sick cats showed mild increases in serum fructosamine concentrations consistent with subclinical to mildly clinical diabetes mellitus even when the serum glucose concentrations were in the normal or near normal range. This finding suggests that subclinical type 2 diabetes mellitus is probably much more common than previously believed and that obese cats with increased serum fructosamine levels should be followed carefully for evidence of developing diabetes mellitus. In cats, normal fructosamine concentrations are 283 ± 32 μmol/L.

**Management of newly diagnosed diabetic cats**

The management of newly diagnosed feline diabetic patients includes first and foremost attention to diet (Table 1). Initial studies using a canned high-protein/low-carbohydrate diet and the starch blocker acarbose have shown that 58% of cats were able to discontinue insulin injections and those with continued insulin requirements could be regulated with a much lower dosage (1 U b.i.d.) Comparison of canned high-fiber/moderate-carbohydrate diets versus low-carbohydrate/low-fiber diets showed that cats fed low-carbohydrate diets were almost twice as likely to discontinue insulin injections. Feeding newly diagnosed diabetic cats a canned low-carbohydrate, high-protein diet, such as Purina Veterinary Diets OM Dietetic Management, will result in the highest remission rates. For cats that refuse to eat canned food, Purina OM dry combined with acarbose (12.5 mg b.i.d. with 1000) is another alternative. Studies have shown that compared with PZI and Lente insulins, glargine insulin is associated with the highest remission rates. Yet veterinarians often balk at the cost of this human recombinant insulin. One strategy to reduce the cost of this insulin and to improve the administration technique is to use an insulin injector pen. The cost of the 3-cc cartridge and pen is about one-tenth the cost of a 10-cc bottle of glargine insulin. Another

### Table 1. Nutrient (Macro) Composition of Feline Therapeutic Diets for Diabetes Mellitus

<table>
<thead>
<tr>
<th>Food Form</th>
<th>Protein</th>
<th>Carbohydrates</th>
<th>Fat</th>
<th>Crude Fiber</th>
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<tbody>
<tr>
<td>Hill's Prescription Diet</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Feline wet</td>
<td>Canned</td>
<td>52.8</td>
<td>15.7</td>
<td>19.4</td>
</tr>
<tr>
<td>Feline dry</td>
<td>Dry</td>
<td>51.1</td>
<td>15.1</td>
<td>21.8</td>
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<tr>
<td>Purina Veterinary Diets</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OM Dietetic Management</td>
<td>Canned</td>
<td>53.4</td>
<td>4.5</td>
<td>32.9</td>
</tr>
<tr>
<td>DM Dietetic Management</td>
<td>Dry</td>
<td>579</td>
<td>14.9</td>
<td>179</td>
</tr>
<tr>
<td>Royal Canin Veterinary Diet</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetic</td>
<td>Dry</td>
<td>46.1</td>
<td>25.3</td>
<td>12.0</td>
</tr>
<tr>
<td>Diabetic</td>
<td>Canned</td>
<td>57.3</td>
<td>15.3</td>
<td>16.4</td>
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</table>
option would be to use PZI insulin, which is associated with a lower remission rate (70%) but is easier
to administer and less costly. In either case, in my experience, an
initial dosage of 2 U per cat twice
daily has not been associated with
hypoglycemia. For owners who
prefer to give oral medication,
glucizide,a sulfonylurea antidiabetic
agent, has been used to successfully
treat diabetes mellitus in cats at a
dosage of 2.5 mg twice daily when
combined with a high-protein, low-
carbohydrate diet.

Monitoring newly diagnosed
and treated feline diabetics can be
challenging. I prefer to use a slow
method of remission induction using
urine glucose monitoring at home
coupled with periodic (every three
weeks) serum chemistry, urinalysis,
and fructosamine monitoring. An
algorithm for monitoring with serum
fructosamine is shown in Figure 7.
The owner must agree to not increase
the insulin dosage based on urine
sugar, and to only decrease the
dosage if the urine glucose becomes
negative. Owners are not encouraged
to monitor cats using blood

glucose testing because the stress of a new
diet, administration of insulin, and
altered home routine make home

fructosamine curves difficult to interpret. Continuous glucose monitors may be
more effective in determining if
the cat is going into remission or if hypoglycemia is occurring.

Complicated feline diabetes
One of the most common
reasons for a cat to fail to go into
diabetic remission is a concurrent
endocrinopathy. In cats, the
most common endocrinopathy
associated with diabetes mellitus is
hypersomatotropism. Patients

should be suspected in male cats
that do not go into remission or
that require increasing dosages of
insulin to control their diabetes.
Other clinical signs of acromegaly
include stridor and increased

interdigital spaces. Diagnosis is
achieved by measuring insulin-like
growth factor 1 concentrations.

Confirmation of a pituitary adenoma
may be made using MRI or CT. If a
cat is diagnosed with acromegaly,
the options for treatment include

radiation treatment of the pituitary
tumor or cryohypophysectomy/
hypophysectomy. New medical
treatment for acromegaly may
become available in the future, but
at present, it is very expensive.

The second most common
endocrinopathy found in diabetic
cats is hyperthyroidism, about
10% of diabetic cats may have
current hyperthyroidism. Because
of the wide fluctuations in
serum thyroid concentrations,
hyperthyroid cats will be difficult
to manage. However, permanent
treatment of the hyperthyroidism
using iodine-131 (131I) will result in
remission in about 50% of the
cases.

Finally, diabetic cats with
concurrent hyperadrenocorticism
may be particularly difficult to
manage. Hyperadrenocorticism
should be suspected in female
cats with insulin-resistant diabetes
mellitus, persistent polydipsia and
dysuria, alopecia, and fragile skin.

Diagnosis can be suspected on
the basis of a lack of suppression

Figure 1. Interpretation of blood glucose and serum fructosamine measurements to monitor diabetic dogs and cats.

<table>
<thead>
<tr>
<th>FR &lt; 400</th>
<th>FR &gt; 400</th>
<th>FR &lt; 400</th>
<th>FR &lt; 400</th>
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<tbody>
<tr>
<td>BG &lt; 180</td>
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<td>BG &lt; 60</td>
<td>BG &gt; 180</td>
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</table>

ExcellenT Control Owner Noncompliance Over Regulation Stress-induced Poor Control
during a low-dose dexamethasone suppression test, urinary excretion of glucocorticoids, and/or elevated precursors of endogenous ACTH concentrations.²³²⁷

Renal complications of diabetes mellitus are common in human diabetics and may also be common in cats.²⁸ The earliest sign of diabetic nephropathy is microalbuminuria followed by concurrent renal disease in order to prevent dehydration and secondary renal damage.

Diabetic cats often have concurrent gastrointestinal disease, such as oral disease, pancreatitis, inflammatory bowel disease, and cholangitis.²⁸ Some of these gastrointestinal signs may originate as a result of suppressed immune function (periodontitis); autonomic diabetic neuropathy (vomiting diarrhea); or possibly as a result of concurrent pancreatitis, cholangitis, or inflammatory bowel disease. Careful attention to diet (low-carbohydrate Purina Veterinary Diets™ DM Dietetic Management® or Purina Veterinary Diets™ EN Gastroenteric™ Feline Formula), good oral health, the addition of probiotics (e.g. FortiFlora® Feline Probiotic Nutritional Supplement), and judicious use of antibiotics and steroids (for pancreatitis) may all help when managing a cat with concurrent gastrointestinal disease and diabetes.²⁸

**Canine diabetes mellitus**

**Diagnosis of diabetes mellitus in dogs**
Insulin-dependent diabetes mellitus is a diabetic state in which endogenous insulin secretion is never enough to prevent ketone production. Type 1 diabetes mellitus is a diabetic state in which insulin secretion may be reduced or absent and which is readily corrected by exogenous insulin. In dogs, type 1 diabetes is caused by autoimmune destruction of the beta cells (genetic disorder related to hypothyroidism), and Type 1b (mature onset diabetes of the young) is a non-immune destruction of islets caused by pancreatitis or an unknown cause.³

Dogs that have diabetes mellitus range in age from 4 to 14 years, with a peak incidence at 7 to 9 years. A genetic basis for diabetes mellitus type A is suspected in Samoyeds, Keeshonden, Labrador retrievers, and various terriers (Australian, Tibetan, Cairn). Other breeds commonly affected are miniature and toy poodles, dachshunds, beagles, pulks, miniature schnauzers, and miniature pinschers. Most dogs with diabetes mellitus present with the classic clinical signs of polyuria and polydipsia.³ Weight loss and polyphagia are commonly observed in dogs. Dogs with diabetes mellitus are also commonly presented with acute onset of blindness caused by bilateral cataracts. In dogs, dehydration and muscle wasting or thin body condition are the most common physical examination findings. Hepatomegaly is usually observed, and cataracts are observed in about 40% of diabetic dogs.³

A diagnosis of diabetes mellitus should be based on the presence of clinical signs compatible with diabetes mellitus and evidence of fasting hyperglycemia and glycosuria.³ Common clinicopathologic features of diabetes mellitus in dogs include fasting hyperglycemia, hypercholesterolemia, increased liver enzymes (ALP, ALT), neutrophilic leukocytosis, proteinuria, increased urine specific gravity, bacteriuria, and glycosuria.³

**Management of canine diabetes mellitus**
For diabetic dogs, the protein content of the diet should be
normal or increased, particularly if the dog is obese. Higher protein formulations may also benefit underweight diabetic dogs with significant muscle wasting or those experiencing concurrent exocrine pancreatic insufficiency. A moderately carbohydrate-restricted diet (<30% metabolizable energy [ME]) is recommended, and meals should have consistent carbohydrate content (Table 2). Low glycemic index carbohydrates such as sorghum and barley are recommended. Readily absorbed carbohydrates such as rice and corn syrup have high glycemic indices and should be avoided. Foods with high sugar content (semi-moist foods) should not be used to improve the palatability of food prescribed for diabetic dogs. Diets with moderate dietary fiber content are recommended for diabetic dogs, especially those that are overweight (crude fiber maximum 10% to 15% dry matter).

Exercise, if prescribed and regular, may reduce insulin requirements in dogs. The owners should be instructed to walk the dog daily and avoid intermittent episodes of strenuous exercise, such as racing or hiking.

Human recombinant insulin is the most available insulin preparation on the market and is perfectly acceptable as insulin therapy for all dogs. Intermediate-acting insulin (NPH/Lente) or long-acting glargine is administered twice daily in dogs, at a starting dosage of 0.4 to 0.5 U kg \(^{-1}\). In dogs, the long-acting insulin PZI is administered once or twice daily at 0.8 to 0.9 U kg \(^{-1}\). Detemir insulin is dosed at 0.1 to 0.2 U kg \(^{-1}\) twice daily in dogs and may be the insulin of choice for larger dogs. To mimic the physiologic release of insulin, insulin should ideally be given with each meal. If the animal does not eat, the insulin dosage can be reduced (usually by one-half) or skipped entirely and the animal evaluated by the veterinarian to determine the cause of the anorexia.

In general, the client should be instructed to monitor the insulin effect and gross regulation of hyperglycemia by noting changes in appetite, attitude, body condition, etc.
For diabetic dogs, the protein content of the diet should be normal or increased, particularly if the dog is obese. Higher protein formulations may also benefit underweight diabetic dogs with significant muscle wasting or those experiencing concurrent exocrine pancreatic insufficiency.
EPI is usually subtle; intermittent anorexia and hypoglycemia is more commonly seen than diarrhea or steatorrhea. Treatment with exogenous pancreatic enzymes is recommended if EPI is identified. Hyperlipidemias are commonly seen in diabetic dogs and may be a consequence of diabetes mellitus, pancreatitis, hypothyroidism, or hereditary hyperlipidemic syndromes (e.g., miniature schnauzers). Dietary fat restriction (< 12% on a dry matter basis or < 30% ME) is recommended for diabetic dogs with concurrent chronic pancreatitis or persistent hypertriglyceridemia (miniature schnauzers). Foods with a high fat content should not be given to improve the palatability of food prescribed for diabetic dogs. Instead, the low-carbohydrate, low-fat food may be made more palatable with agents such as warm low-fat chicken or beef broth.

**Conclusion**

The diagnosis and management of diabetes mellitus in cats and dogs is an important aspect of the practice of small animal internal medicine. The purpose of this article was to share some of my experiences in regulating diabetic animals. Clear direction, expectations, and follow-up about the care of their diabetic pet will help reduce owners’ stress and improve the quality of life for these patients."
References

34. Fleeman LM, Rand JS, Markwell PJ. Lack of advantage of high-fibre, moderate-carbohydrate diets in dogs with...