Feline Diabetes: Initial Management

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Profile

DEFINITION

DM is an increasingly common endocrine disorder in cats. It occurs as the result of β-cell loss with decreased insulin secretion and/or peripheral insulin resistance.

GENETIC IMPLICATIONS

Burmese cats have a four-fold risk for DM compared with domestic shorthair cats; otherwise, purebred cats tend to be at decreased risk for DM.

INCIDENCE/PREVALENCE

Recent studies have shown an increase in prevalence rates in academic institutions from 8 cases per 10,000 cats in 1970 to 123 cases per 10,000 cats in 1999. A recent survey of private practices showed a prevalence rate of 1 in 180 cases.

SIGNALMENT

In a recent study, age was the strongest risk factor for DM in cats. Cats from 10 to 15 years of age were 49 times more likely to develop DM than were cats younger than 1 year of age ($P < 0.001$). Male cats were at higher risk than females ($P < 0.001$). A significant correlation was found between weight and gender. For example, compared with male cats weighing 5 or fewer pounds, the risk for DM increased significantly with increasing weight class ($P < 0.001$). No such increase was observed in female cats. When controlling for weight and age, no significant increased risk for DM was found in neutered cats compared with intact cats.

CAUSES/RISK FACTORS

The most common cause is islet-associated amyloidosis. Drug-induced insulin resistance (glucocorticoids, progestins), acromegaly, hyperadrenocorticism, and pancreatitis may also result in DM.

Risk factors include increasing age, male gender, weight greater than 5 pounds in male cats, and being a mixed-breed cat.

CLINICAL SIGNS

The most common clinical signs are PU/PD, polyphagia, and weight loss. A history of obesity or prior obesity with recent weight loss is also common. Rarely, cats may present initially with a plantigrade stance (diabetic neuropathy).

Photo courtesy of FunnyPoP.com

Polydipsia is a common clinical sign of DM, which occurs more frequently in obese male cats.

Diagnosis

DEFINITIVE

A definitive diagnosis can usually be made by demonstration of persistent hyperglycemia and glycosuria. This may be difficult in some cats because of stress-induced hyperglycemia; however, this disorder can be distinguished easily from DM by measurement of serum fructosamine levels. With chronic hyperglycemia (> 2 weeks), fructosamine levels are elevated, whereas the acute hyperglycemia seen with stress has no effect on fructosamine levels.

DIFFERENTIAL DIAGNOSIS

The most common differentials include hyperthyroidism, renal disease, IBD, intestinal lymphoma, and liver disease. See the Diagnostic Tree, pages 24-25, for a complete list of differentials for PU/PD.

LABORATORY FINDINGS

Persistent hyperglycemia, glycosuria, increased liver enzymes (particularly with concurrent hepatic lipidosis and/or pancreatitis), decreased urine specific gravity, and urinary tract infections.

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DM = diabetes mellitus; PU/PD = polyuria/polydipsia; IBD = inflammatory bowel disease

Treatment

See Aids & Resources for comprehensive reviews on long-term management of diabetic cats. In this review, we will focus on the initial management of cats with DM.

DIET

Recent evidence and a review of nutritional requirements support low-carbohydrate, high-protein diets for feline DM. Cats appear to be relatively carbohydrate-intolerant and have higher protein and lower carbohydrate requirements than dogs. Use of high-protein, low-carbohydrate diets (we most commonly use Hill's feline m/d [canned or dry] or Purina DM [canned or dry]) is associated with lowered insulin requirements and even remission of DM in cats with recent-onset of disease. In one study, nine cats were evaluated, and insulin requirements were decreased in eight of the nine cats when transitioned from a high-fiber diet to a high-protein diet. Insulin injections were stopped altogether in three cats. Results of regression analysis indicated that exogenous insulin could be reduced by over 50% with no loss of glucose control, as measured by serum fructosamine. Renal function should be monitored closely in cats with preexisting or emerging renal disease, as the effects of high-protein diets on progression of renal disease in diabetic cats has yet to be studied.

FEEDING SCHEDULE

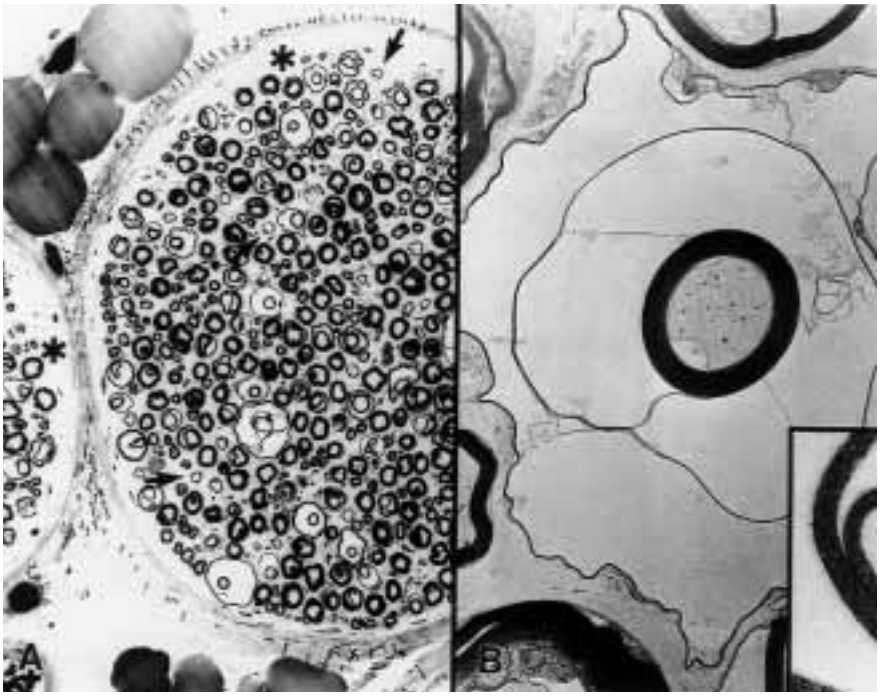
In human diabetics, numerous small meals throughout the day, compared with larger, less frequent meals, minimize glucose fluctuation and optimize glycemic control. Although this strategy has also been recommended for diabetic cats and follows this species' natural feeding pattern of eating 10 to 20 small meals a day, a recent study showed that ad libitum feeding resulted in significantly higher insulin concentrations than once-daily feeding. This suggests that ad lib feeding could increase demand for insulin secretion on the β-cells and may contribute to hyperinsulinemia and β-cell exhaustion in susceptible cats. Thus, once-daily feeding may be advantageous in cats predisposed to impaired glucose tolerance or diabetes. Additional studies are needed to determine the optimal feeding strategy (ad lib vs meal fed) for cats with DM. For initial management of uncomplicated cases of DM in normal-weight or obese cats, dietary therapy alone may be attempted for 2 to 3 weeks. If no improvement in clinical signs is noted, then adding insulin and/or oral hypoglycemic agents should be considered.

A plantigrade stance in a cat with diabetic neuropathy

INSULIN

Insulin is the most effective therapy for feline DM and should be used before oral hypoglycemic agents are considered. Many types of insulin are available and effective for cats with DM. The intermediate-acting insulins (lente and NPH) are most commonly used. Both types usually require twice-daily dosing to optimize glycemic control. Lente insulin may be preferable to NPH in cats that develop postprandial hyperglycemia. Longer-acting insulins, such as ultralente, PZI, and glargine, are also used for cats with DM. Up to 25% of cats may have difficulty absorbing human origin ultralente insulin (Humulin-U—Eli Lilly & Co, Indianapolis, IN) after subcutaneous administration. For this reason, many prefer to use PZI. Recently, PZI was approved by the U.S. Food and Drug Administration for use in cats (PZI Vet—Idexx Laboratories, Westbrook, ME) and is preferred to compounded forms of PZI. Despite use of these so-called long-acting insulins, most cats still require twice-daily dosing to obtain adequate glycemic control. Recently, insulin glargine (Lantus—Aventis Pharmaceuticals, Bridgewater, NJ) was evaluated in cats.

DM = diabetes mellitus; PZI = protamine zinc insulin; PU/PD = polyuria/polydipsia



A cross-section of nerve with characteristic myelin ballooning seen with diabetic neuropathy

Glargine is considered a peakless insulin in humans and is used at night to supplement mealtime injections of regular insulin. Studies in cats have shown that, unlike humans, cats do experience a peak after glargine administration, and the effect of this type of insulin is similar to that of ultralente and PZI. It is more expensive than ultralente or PZI and due to its low pH, may cause pain on injection.

ORAL HYPOGLYCEMIC AGENTS

Oral hypoglycemics should be considered a second-tier treatment for cats with DM. Extensive reviews on oral hypoglycemics can be found in Aids & Resources. These agents should only be used in patients whose owners decline insulin treatment (although many will warm to the idea of insulin injections after attempting chronic oral medication) or if adequate glycemic control is not obtained with diet and insulin alone. The most commonly used oral agents in cats include the sulfonylureas (glipizide, glimepiride) and α-glucosidase inhibitors (acarbose). The use of the sulfonylureas as single agents is associated with a 50% short-term efficacy rate that decreases to 15% after 6 to 12 months. This may reflect further deposition of amyloid in beta cells and a progression to insulin-dependent DM. Although acarbose has been associated with gastrointestinal side effects, recently its use (12.5 mg PO Q 12 H) in conjunction with a high-protein diet and exogenous insulin was shown to significantly improve glucose control in cats with few side effects. Thus, acarbose may be considered as an adjunct to diet and insulin in cats with poor glycemic control.

ALTERNATIVE THERAPY

The insulinomimetic compounds chromium and vanadium have not been shown to be beneficial in management of feline DM; thus, routine use is not recommended.

PREVENTION

It seems that the best way to help prevent feline DM is to prevent obesity. The use of high-protein/low-carbohydrate diets may play a role in reducing the incidence of obesity in the pet population.

Follow-Up

During initial management, evaluate the patient at the end of the first week of therapy (diet alone or diet with insulin) and if glycemic control is acceptable, every 3 to 4 months thereafter. If initial glycemic control is inadequate, evaluate the pet weekly until glycemic control is achieved.

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FELINE DIABETES INITIAL MANAGEMENT

PATIENT MONITORING

The best patient monitoring tool is assessment of clinical signs. The goal is to reduce or eliminate PU/PD, polyphagia, and weight loss. A further goal is to maintain normal body weight, as obesity contributes to insulin resistance. Animals with adequate control of clinical signs will have obtained adequate glycemic control. Due to the inherent variability and difficulties with obtaining serial blood glucose curves in cats, it may be more prudent to use a combination of clinical signs and fructosamine measurements to assess the degree of glycemic control. Alternatively, measurement of blood glucose levels at home may provide meaningful information.

COMPLICATIONS

Hypoglycemia, neurologic signs (neuropathy), pancreatitis, cataracts (rare); most commonly, persistence of clinical signs.

In General

RELATIVE COST

Depends on ease of regulation and the appearance of concurrent illnesses. Owners may spend $200 to $600/year managing the cat with DM.

PROGNOSIS

No good long-term studies on prognosis in cats exist, but the most common cause of death in both dogs and cats appears to be related to owner frustration with long-term management of a chronic disease.

FUTURE CONSIDERATIONS

Additional work is being performed on the cause of amyloidosis and antiamyloidotic medications, the role of novel oral hypoglycemic agents (including oral insulin), and optimal prevention of feline obesity.

See Aids & Resources, back page, for references, contacts, and appendices.

Initial Tx at a Glance

Uncomplicated DM in normal-weight or obese cats

- **Dietary therapy alone for 2 to 3 weeks. Use of high-protein, low-carbohydrate diet is associated with lowered insulin requirements and even remission of diabetes in cats with recent-onset DM.**
- **Insulin. Twice-daily intermediate-acting insulins (lente and NPH) are most commonly used.**

Second-Tier Treatment

Oral hypoglycemic agents (e.g., glipizide, glimepiride, acarbose) should only be considered if owners decline insulin treatment or if adequate control is not obtained with diet and insulin alone.