Peer Reviewed

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Feline Diabetes Mellitus

PROFILE

Definition

- Diabetes mellitus (DM), classified as type I or type II, is a treatable condition caused by complete or relative insulin deficiency.
- Most diabetic cats have type II, characterized by β-cell dysfunction and peripheral insulin resistance.
  - Type I diabetes, uncommon in cats, results from immunologic destruction of β cells, leading to complete insulin insufficiency.
- Reversion to noninsulin-dependent diabetic mellitus (NIDDM) state is more likely with type II diabetes, as some causes of peripheral insulin resistance are reversible and islet cell dysfunction is variable in these cases.

Systems

- In uncomplicated DM, urinary and immune systems are most commonly affected.
- Long-standing, uncontrolled DM can lead to complications (eg, polyneuropathy, hepatic disease [hepatic lipidosis], bacterial infections).

Prevalence

- Up to 1% of cats in the United States and Australia are affected.

Signalment

- Burmese cats are overrepresented in Australia, New Zealand, and the UK.[1,2]
- Most cats are diagnosed ≥7 years of age.[3,4]
- Males are more frequently affected.[4]

Causes

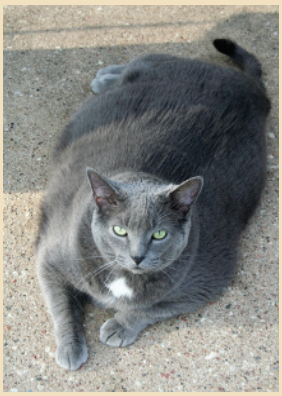
- Multiple causes of peripheral insulin resistance have been identified (see **Causes of Insulin Resistance in Cats**, next page):
  - Obesity.
  - Concurrent disease.
  - Diet.
  - Drugs.
- Direct β-cell loss can be secondary to chronic amyloid deposition or pancreatitis but does not cause DM; instead, conditions that lead to β-cell loss may increase susceptibility to DM when faced with peripheral insulin resistance.

Risk Factors

- Risk factors for DM include obesity, male gender, advanced age, and renal transplantation.[3-5]

CONTINUES

DM = diabetes mellitus, NIDDM = noninsulin-dependent diabetes mellitus



CAUSES OF INSULIN RESISTANCE IN CATS

- Obesity
- Chronic pancreatitis
- Bacterial infection
- Kidney disease
- Hyperthyroidism
- Heart disease
- Neoplasia
- Hyperadrenocorticism
- Acromegaly
- Glucocorticoid or progestogen administration

Pathophysiology

- Insulin deficiency results in hyperglycemia by causing uninhibited hepatic glucose production, impaired glucose tissue entry, and accelerated protein and lipid catabolism.
- Persistent hyperglycemia results in glycosuria when the renal tubular threshold for glucose excretion exceeds 200–300 mg/dL in cats.
- Ultimately, endothelial damage, immunosuppression, and glucose toxicity (ie, negative effects of chronic hyperglycemia) occur.
- Glucose toxicity initially suppresses insulin secretion (reversible), but eventually can cause permanent β-cell loss, thereby perpetuating diabetic disease.
- Increased proteolysis can lead to muscle wasting and poor wound healing.
- As accelerated lipid catabolism persists, hepatic lipidosis develops; ketoacidosis can occur secondary to enhanced ketone body production.

Signs

History

- Patients with DM may have a history of polyuria, polydipsia, polyphagia, weight loss, lethargy, lack of grooming, and/or plantigrade posture.

Physical Examination

- Lackluster coat.
- Obese despite history of weight loss.
- Hepatomegaly.
- Signs of polyneuropathy (eg, plantigrade posture, pelvic limb weakness).
- Findings related to concurrent disease or diabetic ketoacidosis (DKA).

DIAGNOSIS

Definitive Diagnosis

- Based on clinical signs, history, and documentation of persistent hyperglycemia and glycosuria.
  - Stress hyperglycemia can complicate diagnosis, suggesting consideration of serum fructosamine measurement.
    - Normal serum fructosamine is 200–360 µmol/L.
    - Diabetic levels are frequently >400 µmol/L.
- For evaluation of persistent glycosuria, owners may collect urine for glucose strip testing or use Glucotest (glucotest.com) flakes in litter box.

Differential Diagnosis

- Hyperthyroidism, chronic kidney disease, and exocrine pancreatic insufficiency can result in classic complaints (eg, polyuria, polydipsia, polyphagia, weight loss).
- Stress hyperglycemia must be considered in a hyperglycemic cat.
- Concurrent diseases (eg, pancreatitis, renal failure, infection) may complicate the diagnosis.

Laboratory Findings

- Mild anemia.
- Hypercholesterolemia.
- Hypertriglyceridemia.
- Mild increases in serum alanine transaminase (ALT) and alkaline phosphatase (ALP).
- Less common findings:
  - Trace to small amounts of ketones in urine.
  - Evidence of urinary tract disease (pyuria, hematuria, bacteriuria) on urinalysis.
  - Nonspecific hepatic changes seen via abdominal imaging.

Postmortem Findings

- Hepatic lipidosis.
- Pancreatic amyloid deposits.
- Concurrent disease.

TREATMENT

Inpatient or Outpatient

- Healthy diabetics ± minimal ketonuria can be managed on outpatient basis.
- Hospitalization may be required with DKA or concurrent disease.

ALP = alkaline phosphatase, ALT = alanine transaminase, DKA = diabetic ketoacidosis, DM = diabetes mellitus, NIDDM = noninsulin-dependent diabetes mellitus

Nutritional Aspects

- Dietary therapy may minimize postprandial blood glucose fluctuations.
- Diets should be palatable to ensure predictable consumption.
- A consistent feeding schedule is more important than timing between insulin administration.
  - Owners may feed q12h, at time of insulin administration, or small amounts throughout the day.
- The ideal dietary composition is debatable, as low-carbohydrate/high-protein and high-fiber/low-fat (and occasionally adult-maintenance) diets can result in good glycemic control when used with insulin.[6]
  - Low-carbohydrate diets result in higher remission rates.[7,8]
  - Both diets can induce remission.
- Dietary glycemic control is not different in insulin-dependent cats.
- Overweight cats require a weight-reduction program, as obesity is a reversible cause of insulin resistance.
- Compared with dry foods, canned foods are generally preferred, as they typically have a lower carbohydrate content.

Alternative Therapy

- Few insulin alternatives are available.
- Although most diabetic cats are insulin-dependent, there is higher NIDDM incidence in cats than dogs.
- Oral hypoglycemic agents may be considered for diabetic cats; however, studies evaluating their efficacy are sparse.

Clinical Remission

- Up to 60% of cats enter diabetic remission with insulin and dietary therapy.
  - Remission may not be permanent (median, 11 months).[9]
  - Approximately 30% of cats in remission will revert to a diabetic state and require reinstitution of insulin therapy.[9,10]
  - Remission rates increase in cases with good glycemic control within 6 months of diagnosis.[9]

Client Education

- Treatment is lifelong; owners should be prepared for complications or remissions.
- At-home insulin therapy, dietary management, and careful monitoring are cornerstones of successful management.
  - Insulin administration.
  - Insulin storage.
  - Syringe sizes and use (U-40 vs U-100).
- Weight reduction (if necessary) and consistent diet and feeding schedule facilitate glycemic control.

MEDICATIONS

Drugs/Fluids

- Short-acting insulin (eg, regular insulin) is primarily used in the hospital for clinically ill diabetics or DKA cases, as increased potency increases risk for hypoglycemia.
- Long-acting insulin, the mainstay of therapy, should be administered immediately after diagnosis.
- Common insulin choices for cats are human recombinant types:
  - Protamine zinc insulin (PZI) (ProZinc, prozinc.us).[11]
    - Only insulin FDA approved for cats.
    - U-40 syringe.
  - Insulin glargine (Lantus, lantus.com).[12]
    - In conjunction with a low-carbohydrate/high-protein diet, may comparatively increase likelihood for diabetic remission.[12]
    - U-100 syringe.
  - Neutral protamine Hagedorn (NPH) insulin (duration short in cats).
    - U-100 syringe.
  - Lente insulin (Vetsulin, vetsulin.com) is currently unavailable.
- PZI and glargine result in similar glycemic control and can induce remission.[10]
- Insulin should be administered q12h rather than q24h, as duration of effect is often unpredictable and shorter than expected in cats.
- Hypoglycemia can occur with insulin therapy.

CONTINUES

A consistent feeding schedule is more important than timing between insulin administration.

FOLLOW-UP

Patient Monitoring

- Clients should monitor for changes:
  - Polyuria.
  - Polydipsia.
  - Appetite.
  - Weight.
  - Hypoglycemia (eg, disorientation, wobbliness, tremors, seizures).
  - Signs of concurrent disease (eg, pollakiuria, stranguria, hematuria, anorexia, vomiting, skin infections, weakness).

Complications

- Iatrogenic hypoglycemia.
- DKA and severe electrolyte abnormalities (uncontrolled diabetics).
  - Can be fatal, particularly in presence of severe pancreatitis.
- Polyneuropathy (from chronic hyperglycemia) frequently resolves with good glycemic control.

Future Follow-up

- Twelve-hour blood glucose curves (BGCs) should be performed q10–14days from each insulin dose adjustment until patient appears healthy and blood glucose is relatively controlled.
  - BGC measurements should be 100–300 mg/dL.
- Fructosamine measurements:
  - For cats experiencing stress hyperglycemia.
  - For cats with good glucose control based on the initial BGC.
  - For fractious cats in which BGCs are difficult to perform.
- Owners can be taught to perform at-home BGCs (AlphaTrak, alphatrakmeter.com).
  - May minimize stress hyperglycemia.
    - However, at-home BGCs may not represent significantly lower stress hyperglycemia than clinic-generated curves.[13,14]
  - Advantage of at-home glucose monitoring includes the ability to frequently monitor cats that are difficult to regulate.
- Once well-controlled, BGCs and/or fructosamine may be performed q3–6mo or more, based on owner observations (eg, changes in polyuria, polydipsia, appetite, weight).
- Urine cultures should be performed regularly (eg, q3–6mo) regardless of whether the urinalysis suggests infection.[15]

Tx AT A GLANCE

- Long-acting insulin should be administered immediately after diagnosis.
- Insulin should be administered q12h rather than q24h.
- Concurrent dietary and medical therapy is often best.

Two Dietary Options

- Low-carbohydrate/high-protein diet.
- High-fiber/low-fat diet.

Two Medical Options

- PZI (0.25 Units/kg SC q12h after a meal).
- Insulin glargine (0.25 Units/kg SC q12h after a meal).

IN GENERAL

Relative Cost

- Diagnostic workup for uncomplicated DM: $$
- Treatment and follow-up care for uncomplicated DM: $$–$$$ monthly
- Diagnostic workup for complicated DM: $$$$–$$$$$
- Treatment and follow-up care for complicated DM: $$$–$$$$$

Cost Key

$ = up to $100	$$$$ = $501–$1000
$$ = $101–$250	$$$$$ = more than $1000
$$$ = $251–$500	

Prognosis

- Fair with diligent care and monitoring.
- Can be stabilized with appropriate treatment, although diabetic remission may result in a waxing/waning course of disease.
- Dependent on owner commitment, ease of glycemic control, and possible concurrent diseases.
- Many cats can do well for months to years with diligent care.

Prevention

- Minimizing circumstances for insulin resistance (eg, obesity, inactivity).
  - Not all obese cats become diabetic, and many diabetic cats are of normal size.

Future Considerations

- More studies to evaluate the impact of diet on diabetic control are necessary.
- Remission studies directly comparing insulin types would be valuable.
- Given the changing insulin market, continued investigation into alternative insulin types for diabetic cats is important.

See **Aids & Resources**, back page, for references & suggested reading.

BGC = blood glucose curve, DKA = diabetic ketoacidosis, DM = diabetes mellitus, NIDDM = noninsulin-dependent diabetes mellitus, NPH = neutral protamine Hagedorn, PZI = protamine zinc insulin