Diabetes Mellitus

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Synonyms:
Sugar diabetes

Disease description:
Diabetes mellitus (DM) results when there is either absolute or relative insulin deficiency resulting in hyperglycemia. **Absolute insulin deficiency** occurs with loss or malfunction of 75-80% of the pancreatic beta cells. **Relative insulin deficiency** is associated with insulin resistance, where the insulin secreted is less effective.

CLASSIFICATIONS

There are three classifications of DM:
1. Type I DM is comparable to insulin dependent diabetes mellitus (IDDM) in humans. It is characterized by beta cell destruction leading to absolute insulin deficiency. This usually occurs via cell-mediated autoimmune processes and is associated with multiple genetic predispositions and poorly defined environmental factors. It results in low basal insulin concentrations with impaired insulin secretion following a glucose load. Treatment requires insulin injections. ***Type I DM is the most common form of DM in dogs.***

2. Type II DM is similar to non-insulin dependent diabetes (NIDDM) in humans and is characterized by an impaired ability to secrete insulin as well as insulin resistance. ***Type II DM currently is thought to account for the majority of cases of feline DM.*** Triggering causes include obesity, genetics, and insular amyloid deposition. Some cases can be managed with dietary therapy and oral hypoglycemics, while others require insulin.

3. Type III DM is a condition whereby medications or concurrent insulin antagonistic diseases (hyperadenocorticism, acromegaly, diestrus) interfere with insulin action and cause glucose intolerance, which can lead to DM. It is similar to impaired glucose tolerance in humans and is initially characterized by hyperinsulinemia. This type of DM may resolve or become overt depending on the underlying disease process.

PATHOPHYSIOLOGY

Insulin is an anabolic hormone that promotes glucose uptake by cells, increases fat and protein synthesis, and promotes glycogenesis and inhibits GNG in the liver.

Insulin deficiency results in lipolysis with increased fatty acid and ketone body production, protein catabolism, hyperglycemia due to decreased glucose uptake and increased gluconeogenesis, and decreased tissue utilization of glucose, fatty acids, and amino acids.

CLINICAL SIGNS

Common clinical signs of DM include polyuria (hyperglycemia results in glycosuria and a resultant osmotic diuresis), polydipsia, polyphagia, and weight loss although some animals will still be obese upon presentation. Variable degrees of dehydration are often present. Cataract formation is common in dogs with DM, but rare in cats. Cats may have icterus due to concurrent hepatic lipidosis and/or pancreatitis but icterus is not common in dogs unless they have pancreatitis. Cats may also develop a peripheral neuropathy characterized by plantigrade stance to the pelvic limbs; such neuropathies are rare in dogs.

Diabetes mellitus has been associated with immune suppression, retinopathy, hypertension, hypotension, and proteinuria. [4, 11, 13]

DIAGNOSIS

Normal blood glucose (BG) is 80 - 120 mg/dl. The diagnosis of DM is based on persistent fasting hyperglycemia of usually > 200 mg/dl. If the BG is between 120 - 200 mg/dl, consider stress, post-prandial hyperglycemia, and excess diabetogenic hormones.

Hemogram results may show a stress leukogram and variable increases in WBC's due to concurrent infection.

Chemistry changes often include elevated liver enzymes (ALT, AST, SAP) secondary to hepatic lipidosis or pancreatitis. Hyperlipidemia and hypercholesterolemia are due to increased lipolysis and decreased lipogenesis. Amylase and lipase may be elevated with concurrent pancreatitis. Electrolytes are often abnormal in the diabetic ketoacidotic patient.

Urinalysis should show glucosuria, which occurs when the blood glucose exceeds 180-225 mg/dL. Urine should be routinely evaluated in the diabetic to monitor for urinary tract infection, ketonuria and glomerular disease. Significant ketonuria in association with systemic illness suggests diabetic ketoacidosis; ketonuria may also occur with anorexia.

Disease description in this species:

Effects of gestation and diestrous

If DM is diagnosed in a bitch during either pregnancy or diestrus, it probably should be classified as being comparable to human gestational DM. If DM persists after the pregnancy or diestrus ends, then it should be reclassified as Type I or another specific type of DM.

ETIOLOGY IN DOGS

In dogs, DM generally thought to be an immune mediated disease with gradual destruction of beta cells. The progression from normal, to glucose intolerant, to DM, is generally slow so that most islets (over 90%) are lost before diabetes occurs. Other factors include genetic predisposition, chronic pancreatitis, and medication-induced DM (glucocorticoids and megestrol acetate).

Genetic predisposition to DM is most common in the following breeds: German Shepherd dogs, Schnauzers, Beagles, and Poodles. Golden Retrievers and Keeshonds are more prone to juvenile DM. Gender is a factor in dogs with females being 3 times more likely to develop DM than males. Generally, DM occurs in middle aged dogs (six to nine years) but can also occur earlier for specific breeds, particularly the Golden Retriever and Keeshond.

Laboratory Profile:

Sodikoff's Laboratory Profiles of Small Animal Diseases: Diabetes Mellitus, Insulin-Dependent
Sodikoff's Laboratory Profiles of Small Animal Diseases: Hepatopathy, Reactive

Etiology:

Diabetogenic hormones
Epinephrine
Estrus
Glucagon excess
Glucocorticoids
Growth hormone
Obesity
Pancreatitis
Pregnancy
Progesterone
Stress

Breed predilection:

None, no breed signalment

Diagnostic procedures:	Diagnostic results:
Hemogram (complete blood count)	ANEMIA Hemoconcentration or polycythemia
Serum chemistry	Alanine aminotransferase (ALT) increased Alkaline phosphatase (ALP) increased

	Aspartate aminotransferase (AST) increased Azotemia/uremia Blood urea nitrogen (BUN) increased Creatinine increased Hyperbilirubinemia, bilirubin increased Hypercholesterolemia Hyperglycemia Hypernatremia Hypokalemia Hypophosphatemia Ketosis, ketones increased Lipidemia, lipids increased
Urinalysis	Glucosuria, glycosuria Ketonuria Proteinuria, albuminuria Pyuria, increased white blood cells Urine specific gravity decreased
Radiography of abdomen	Renomegaly
Blood pH measurement	Blood pH increased, alkalosis Blood/serum bicarbonate decreased, metabolic acidosis
Blood pressure measurement	Hypertension (>160/100 mmHg) Hypotension
Fructosamine assay on serum	Fructosamine assay increased
Ocular examination	Aqueous lipemic Cataract, lens opacity Hyphema, blood anterior chamber eye Retinal hemorrhages
Ultrasonography of abdomen	Abdominal mass internal

Treatment/Management/Prevention:

GOALS

1. The goals are to reduce or eliminate the clinical signs of persistent hyperglycemia, avoid insulin-induced hypoglycemia, and prevent or retard the development of cataracts and other diabetic complications.

2) For the diabetic dog, the ideal glucose level is between 90 and 200 mg/dl for most of the day with the lowest glucose nadir occurring halfway between the two daily injections of insulin.

SPECIFIC for Uncomplicated DM dog

1) Begin using one of the following intermediate acting (NPH or Lente) insulins at 0.5 U/kg q 12 hours.

- Porcine lente insulin (Vetsulin is the US brand manufactured by Intervet and Caninsulin is the European/Australian brand). The structure of porcine lente insulin is identical to canine insulin. It consists of 30% amorphous zinc insulin and 70% crystalline zinc insulin. The amorphous component has a peak activity within 4 hours, and duration of effect for 7-8 hours. The crystalline component has a peak around 10-11 hours. According to the manufacturer, these kinetics may allow once-daily dosing in some dogs, however one study demonstrated that most dogs required twice-daily administration for adequate control. The concentration of Vetsulin and Caninsulin is 40 U/ml (U-40).

- NPH (Isophane) Insulins (Humulin N manufactured by Eli Lilly or Novolin N manufactured by Novo Nordisk) are crystalline suspensions of recombinant human insulin with protamine and zinc resulting in an intermediate-acting insulin with a slower onset of action and a longer duration of activity than that of regular insulin. Most are available as 100 units/ml (U-100).

2) After the first insulin injection, the blood glucose concentrations should be monitored 2 to 3 times within a 4-12 hour period to ensure that hypoglycemia does not occur at the dose used.

3) Make sure that the owner is counseled on insulin handling, injection technique, and monitoring of clinical signs that would indicate either hypoglycemia or inadequate control of DM. Clients should be encouraged to keep a chart of pertinent information about the pet such as daily insulin dose and timing, feeding schedule, urine dipstick results, appetite, etc. You may find this Insulin Administration Guide by Dr. Brooks handy for clients. Insulin syringes are calibrated in units and it is preferable to use U-40 syringes for U-40 insulin; and U-100 syringes for U-100 insulin. But here is link to a chart for using U-40 syringes with U-100 insulin.

4) If hypoglycemia did not develop during the first injection, then give the patient at least one week on this dose before making any adjustments as long as the patient is eating and not showing any signs of hypoglycemia.

5) A blood glucose curve should be done 7–10 days after insulin is started or anytime after the dose is changed. To perform the curve, have the owner bring the dog to the clinic when it opens, and take an initial glucose sample, then have owner feed the dog its regular food, and observe the owner administer insulin to assess their injection technique. Then take blood samples at 2 hour intervals for next 12 hours. The disadvantage to this technique is that some dogs won't eat as they normally would when they are in a clinic environment.

Thus an alternative is have the owners feed and give insulin as they normally do at home in the morning, then bring the animal into the clinic within an hour of the injection and start the curve then. If you need to assess the owner's injection technique, then have them administer saline as a test.

Click here to view a handout by Dr. Linda Fleeman on glucose curve interpretation.

Click here to view an on-line glucose curve generator. Note that the time of sampling spreads over 2 days.

6) Current nutritional guidelines for Type I diabetic dogs suggest that any balanced diet is reasonable as long as the dog is fed the same amount of the same diet at the same times each day. Daily caloric requirements for maintaining ideal body weight should be calculated and fed. However, dogs with poor body condition need to be fed more calories. Dogs with recurrent bouts of pancreatitis should avoid high fat diets.
Ideally the dog should be fed prior to the insulin injections so that maximal insulin activity is present when maximal post-prandial glucose is being absorbed from the gut. Treats should be avoided during the day. For dogs used to large meals daily, divide the caloric requirements in half and feed in association with the twice daily insulin injection. For dogs used to eating several small meals a day, spread the calculated caloric requirements out over the day similar to what would be done for a cat.

7) Regular dipstick monitoring for urine glucose may help reduce the risk of hypoglycemia because persistent negative results may indicate subclinical hypoglycemia.

Special considerations:

Click here to view a conversion chart for blood glucose concentration from mmol/L to mg/dl.

INSULIN OVERDOSAGE

Factors that could lead to insulin overdosage include incomplete mixing of insulin suspensions, administration of insulin at irregular intervals, inappetence, excessive exercise, and increased insulin sensitivity associated with the end of diestrus or treatment of concurrent disease such as hyperadrenocorticism.

Care must be taken when dispensing insulin syringes to owners to ensure that there is no confusion regarding dosing. For example, the graduations on many 1-mL insulin syringes are equal to 2 units, while graduations on most 0.5-mL insulin syringes are 1 unit.

Graduations on syringes designed for use with 100 units/ml insulin preparations represent a different volume from graduations on syringes designed for use with 40 units/ml insulin preparations, and this may also lead to dosing errors.

INSULIN RESISTANCE

Insulin resistance should be suspected if the insulin dosage is > 1.5 U/kg and blood glucose concentration is > 300 mg/dl.
1) Hyperadrenocorticism: Either endogenous or exogenous

2) Hypothyroidism and obesity can induce an insulin resistant state
3) Hyperthyroidism
4) Acromegaly
5) Severe hyperglycemia
6) Insulin metabolized too quickly
7) Infection, or concurrent illness
8) Obesity
9) Pancreatitis
10) Poor insulin absorption
11) Antigenic insulin or insulin components
12) Administration of progestational compounds
13) Stress
14) Renal disease
15) Hepatic disease
16) Pheochromocytoma
17) Neoplasia

FRUCTOSAMINE

The fructosamine test may be a valuable parameter for the diagnosis and the metabolic control of diabetes mellitus in dogs and cats. The concentration of fructosamine in serum reflects the average blood sugar concentration over the preceding two to three weeks. The fructosamine assay is based on the ability of ketoamine-linked glucose residues on glycated serum proteins to reduce nitroblue tetrazolium.[8] Your laboratory will have values for fructosamine concentrations that indicate poor to good control.

Other conditions that alter protein metabolic pathways may interfere with the use of fructosamine in diabetic monitoring. In hyperthyroidism, protein turnover is increased, therefore, results of the fructosamine test must be interpreted cautiously in hyperthyroid patients.[9]

GLUCOMETERS

Glucose meters should be compared to commercial laboratory results before relying on them. Glucose meters register lower glucose levels in order to protect the human diabetic from over dosing with insulin. And using whole blood will yield results that are about 10-15% lower than actual reading because mechanical dilution by the RBCs displaces serum. Thus using serum or plasma gives a more accurate reading. The AlphaTrak by Abbott (Veterinary) is accurate for animals and closer to serum readings than most human glucose meters. Some have noted that serum glucose values are higher than those found at outside laboratories on same sample. And you have to make sure you key in the cat or dog code before you test the sample. See these interesting VIN message folder discussions on glucometers!

RETINOPATHIES, NEUROPATHIES, AND NEPHROPATHIES

Diabetic retinopathy, nephropathy, and neuropathy occur infrequently in small animals. The pathogenesis of these disorders is most likely multifactorial; metabolic alterations secondary to the hyperglycemic state, and microvascular changes seen with diabetes have both been implicated. One study in diabetic dogs evaluated the perineurium and found significant abnormalities. [10] Current treatment consists of aggressive control of the hyperglycemia.

Diabetic gastroparesis is an autonomic neuropathy seen in people with DM; the condition either does not occur in animals or is infrequently diagnosed. Signs in people may include bloating of abdomen, nausea, and vomiting, particularly hours after ingesting a meal. The condition may be diagnosed with abdominal ultrasound hours after ingestion of a meal. There is minimal gastric contractions and food still in the stomach. Treatment depends on glycemic control and administering prokinetic medications.[15]

POLYENDOCRINOPATHIES

Polyendocrinopathies can be present and influence the treatment of the patient. If overlapping clinical signs are present with other endocrinopathies, further testing should be performed to rule in or out hyperadrenocorticism or hypothyroidism.[9]

References:

1) Feldman EC, Nelson RW: Diabetes mellitus. Canine and Feline Endocrinology and Reproduction, 2nd ed.

Philadelphia, WB Saunders 1996 pp. 339-391.
2) Greco DS: Diagnosis of Diabetes Mellitus in Cats and Dogs. Vet Clin North Am Small Anim Pract 2001 Vol 31 (5) pp. 845-53.
3) Fall T, Hamlin HH, Hedhammar A, et al: Diabetes mellitus in a population of 180,000 insured dogs: incidence, survival, and breed distribution. J Vet Intern Med 2007 Vol 21 (6) pp. 1209-16.
4) Struble AL, Feldman EC, Nelson RW, et al: Systemic hypertension and proteinuria in dogs with diabetes mellitus. J Am Vet Med Assoc 1998 Vol 213 (6) pp. 822-825.
5) Kimmel S, Ward C, Henthorn P, et al: Familial insulin-dependent diabetes mellitus in Samoyed dogs. J Vet Int Med 2002 Vol 38 (3) pp. 235-238.
6) Beam S, Correa MT, Davidson MG.: A retrospective-cohort study on the development of cataracts in dogs with diabetes mellitus: 200 cases. Vet Ophthalmol 1999 Vol 2 pp. 169-72.
7) Melendez L, Lorenz M: Canine Diabetes Mellitus. Western Veterinary Conference 2002.
8) Reusch CE, Liehs MR, Hoyer M, et al: Fructosamine. A new parameter for diagnosis and metabolic control in diabetic dogs and cats. J Vet Intern Med 1993 Vol 7 pp. 177-182.
9) Hess RS, Ward CR: Diabetes mellitus, hyperadrenocorticism, and hypothyroidism in a dog. J Am Anim Hosp Assoc 1998 Vol 34 (3) pp. 204-207.
10) Ghani M, Malik RA, Walker D, et al: Perineurial abnormalities in the spontaneously diabetic dog. Acta Neuropathol 1999 Vol 97 (1) pp. 98-102.
11) Munana KR: Long-term complications of diabetes mellitus, Part I: Retinopathy, nephropathy, neuropathy. Vet Clin North Am Small Anim Pract 1995 Vol 25 (3) pp. 715-30.
12) Dahme E, Hafner A, Reusch C, Schmidt P: Diabetic neuropathy in dogs and cats--a bioptic electron microscopic study. Tierarztl Prax 1989 Vol 17 (2) pp. 177-88.
13) Johnson CA, Kittleson MD, Indrieri RJ: Peripheral neuropathy and hypotension in a diabetic dog. J Am Vet Med Assoc 1983 Vol 183 (9) pp. 1007-9.
14) Steiss JE, Orsher AN, Bowen M: Electrodiagnostic analysis of peripheral neuropathy in dogs with diabetes mellitus. Am J Vet Res 1981 Vol 42 (12) pp. 2061-4.
15) Takeda M, Mizutani Y, Yamano M, et al: Gastric emptying in diabetic gastroparetic dogs: effects of SK-951,a novel prokinetic agent. Pharmacology 2001 Vol 62 (1) pp. 23-28.
16) Stenner VJ, Fleeman LM, Rand JS: Comparison of Lente, Glargine, and Protamine Zinc Insulin Preparations in Dogs. Australian College of Veterinary Scientists Science Week 2003.
17) Bruyette D: Diabetes Mellitus: Treatment Options. World Small Animal Veterinary Association World Congress Proceedings 2001.
18) Fleeman LM, Rand RS: Management of canine diabetes. Veterinary Clinics of North America. Small Animal Practice 2001 Vol 31 pp. 855-880.
19) Greco DS: Monitoring Diabetics. Atlantic Coast Veterinary Conference 2002.
20) Sirosi M: Monitoring Insulin Therapy. ACVIM Proceedings 2003.
21) Fleeman LM: What to Feed Diabetic Dogs: An Evidence-Based Approach. ACVIM 2003.
22) Kimmel SE, Michel KE, Hess RS, et al: Effects of insoluble and soluble dietary fiber on glycemic control in dogs with naturally occurring insulin-dependent diabetes mellitus. J Am Vet Med Assoc 2000 Vol 216 (7) pp. 1076-1081.
23) Nelson RW, Robertson J, Feldman EC, et al: Effect of the a-glucosidase inhibitor acarbose on control of glycemia in dogs with naturally acquired diabetes mellitus. J Am Vet Med Assoc 2000 Vol 216 (8) pp. 1265-1269.

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If you have any questions about a specific case or about this disease, please post your inquiry to the appropriate message boards on VIN.

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