

Diabetes Mellitus in Dogs and Cats

David Bruyette, DVM, DACVIM
VCA West Los Angeles Animal Hospital
Los Angeles, CA

Diabetes mellitus is a common endocrine disorder in dogs and cats. Recent data has shed light on the pathogenesis of the disorder in cats and has highlighted the role of diet and oral hypoglycemic therapy. In the majority of cases, the most appropriate therapy in both dog and cats includes the administration of insulin. We will discuss the role of the various insulin preparations currently available and develop a logic approach to the initial and long term management of diabetes.

The key to successful management of the diabetic patient lies in close communication with the pet owner and prompt recognition and treatment of concurrent disorders.

Key facts

1. Insulin is still the mainstay of therapy in the majority of dogs and cats with diabetes mellitus.
2. Diet is an important part of diabetic management especially in obese patients.
3. Oral hypoglycemics may be helpful in lieu of or in combination with insulin to improve glycemic control.
4. Auto-immune disease, pancreatitis and amyloidosis are the most common causes of diabetes in dogs and cats.

Successful management of the diabetic patient involves many factors. An understanding of dietary therapy, insulin preparations, oral hypoglycemic agents and management of concurrent illness, are all required to optimize glycemic control. The goals of therapy are to control clinical signs, prevent or slow the progression of cataracts, avoid hypoglycemia and maintain ideal body weight. The challenge is to address these concerns while attempting to help the owners deal with a time consuming, expensive and chronic medical condition.

Diabetes Mellitus in dogs and cats results from a decrease in insulin secretion from the beta cells of the pancreas and/or a decrease in insulin action. There are three classifications of diabetes:

Type I diabetes is comparable to insulin dependent diabetes mellitus (IDDM) in humans. It results in low basal insulin concentrations with impaired insulin secretion following a glucose load. Treatment requires insulin injections. It is the most common form of diabetes in dogs.

Type II diabetes is similar to non-insulin dependent diabetes (NIDDM) in humans and is managed with dietary therapy and oral hypoglycemic. It causes normal to increased basal insulin concentrations with decreased secretion following a glucose load. Insulin may or may not be required for animals with Type II diabetes.

Type III diabetes is seen most commonly in *hormonally-induced* diabetes in dogs and cats and is similar to impaired glucose tolerance (IGT) in humans. Diabetogenic hormones (epinephrine, cortisol, glucagon and growth hormone) or medications interfere with insulin action and cause glucose intolerance, which can lead to diabetes.

Etiology and signalment

Canine

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

Genetic predisposition to diabetes is most common in the following breeds: German Shepherd dogs, Schnauzers, Beagles, and Poodles. Golden Retrievers and Keshonds are more prone to juvenile diabetes.

Gender is a factor in dogs with females being three times more likely to develop diabetes than males. Generally, diabetes occurs in dogs in middle age (6-9 years) but can also present earlier for specific breeds, particularly the Golden Retriever and Keeshond.

Feline

The most common causes of diabetes in cats are obesity, pancreatitis and most commonly, amyloidosis of the pancreatic beta cells. There appears to be very little gender predisposition to this disease in cats, although it is slightly more common in males than females. As with dogs, the onset of diabetes in cats occurs most often in middle age.

Clinical signs

The clinical signs of diabetes include PU/PD (polyuria and polydipsia) from hyperglycemia, resulting in glycosuria and a resultant osmotic diuresis. Polyphagia and weight loss is common although many animals will still be obese upon presentation. In addition to the polyphagia, there may be variable degrees of dehydration especially in the cat. Cataract formation is very common in dogs with diabetes, but rare in cats. Cats often present with icterus as a result of concurrent hepatic lipidosis and/or pancreatitis. Icterus is not common in dogs unless they have pancreatitis. Cats may also exhibit a plantigrade stance (peripheral neuropathy) that is directly related to the severity and duration of hyperglycemia. Clinical neuropathies do occur in dogs, but are extremely rare.

Differential diagnoses include: hyperthyroidism (in cats), gastrointestinal lymphoma, hepatic disease, renal disease, pancreatitis, hyperadrenocorticism, and acromegaly.

Diagnosis

Diagnosis involves testing for persistent fasting hyperglycemia, with fasting blood glucoses greater than 200mg/dl. Clinicians also will need to rule out transient hyperglycemia that may be due to: post-prandial hyperglycemia; diabetogenic hormones (endogenous or exogenous); and stress hyperglycemia. Stress hyperglycemia can be a problem in cats due to the release of epinephrine when stressed or handled.

Laboratory abnormalities include

- Hemogram
 - Non-specific
 - Signs of dehydration
- Biochemistry profile
 - Hyperglycemia
 - Increased in SAP and ALT
 - Increased in bilirubin (usually in cats)
 - Hepatic lipidosis
 - Pancreatitis
- Urinalysis
 - Glycosuria
 - Renal threshold for glucose
 - Canine 180-220mg/dl
 - Feline 240-300 mg/dl
 - Ketonuria
 - Up to 40% of patients will have positive urine cultures in the absence of an active urine sediment.

Treatment

The number one cause of death in diabetic dogs and cats is not the disease itself, rather, it is the owner's frustration with the disease. This is an extremely important point to remember when treating diabetic animals. Good communication with the pet owner is perhaps the most important component of managing the disease.

It is recommended that clinicians schedule a 30-minute appointment with the client at the time of discharge before sending the diabetic patient home for the first time. During this appointment, clinicians should thoroughly discuss the care required for the patient. Include the following instructions in that discussion: how to give the animal injections; how to store insulin, what types of food to feed and how often; how to recognize the signs of hypoglycemia and how to react to this condition. Also include information on what clinical signs to look for in terms of monitoring water intake and urine production. The client should be given written instructions for use as a reference once they are caring for the patient at home. It is essential that the clinician and veterinary staff strive to educate the caregiver and motivate them to get involved in the care of their diabetic pet.

The goals of treatment include elimination of the clinical signs of diabetes, prevention or slowing of cataract formation and resulting blindness, prevention of potentially dangerous hypoglycemia, and prevention and/or treatment of concurrent illness.

Therapy for diabetes centers on four main areas: Treatment of concurrent illness (i.e., urinary tract infections, pyoderms, etc.); oral hypoglycemic agents; insulin therapy, and dietary management.

Concurrent illness

Monitoring for concurrent illness is very important in effectively managing diabetic dogs and cats. Clinicians must effectively recognize and treat the other disorders because the concurrent illness will impact the diabetic regulation and many common diseases have similar clinical signs to diabetes mellitus. Even simple problems such as UTI's and pyoderms can result in activation of stress hormones and result in insulin resistance.

Insulin therapy

There has been a considerable amount of confusion over the various insulin preparations that are available. In general, animal origin insulins are being discontinued as the desire and ability to treat people with human derived insulin preparations has progressed.

There is concern that animals receiving human insulin will develop antibodies resulting in decreased insulin activity and/or effectiveness. Dogs receiving any insulin product that is not derived from pork may make antibodies. However, studies have shown that those antibodies do not interfere with the glucose control. In fact, dogs that made antibodies against insulin had a longer duration of insulin action, which actually enhanced the effect of the insulin rather than decreased its efficacy. A recent study in cats showed that 13% developed anti-insulin antibodies. None of the cats showed signs of insulin resistance.

The options with human insulin include ultra short acting, short acting, intermediate acting, and long-acting insulins. The short acting insulins are primarily used for ketoacidosis, and therefore, are not covered in this article. The intermediate acting insulins are classified as either NPH or Lente. It is important to note however, that even though they are classified as intermediate, they do not behave the same way in the dog or cat. Lente is actually a mixture of semi-lente and ultra lente, which results in a bimodal onset of actions. This is helpful in some patients because it helps block post-prandial hyperglycemia. Conversely, a lente insulin is not recommended for use in an animal that does not develop post prandial hyperglycemia. It is recommended that NPH be used in the majority of dogs and cats with diabetes and it is also understood that most patients will require two injections a day to achieve glycemic control.

Canine patients

Newly diagnosed patients

1. Vetsulin (porcine origin lente): A zinc, porcine, intermediate acting insulin. Canine and porcine insulin have an identical amino acid sequence thereby eliminating the theoretical complication of anti-insulin antibodies and their effect on glycemic control. The suggested, initial starting dose is 0.5 units/kg BID. This insulin is only available at a concentration of 40 iu/ml (U-40) so please make sure that proper insulin syringes are provided to the owner. Re-assessment of clinical signs and a serial blood glucose curve should be performed 1 week after starting therapy. For additional information see: www.vetsulin.com.
2. Humulin N or Novolin N; These are both intermediate acting, human origin insulins. Suggested starting doses are 0.5 units/kg BID. Re-assessment of clinical signs and a serial blood glucose curve should be performed 1 week after starting therapy.
3. Glargine: To date, no information on the use of glargine in the dog is available (see discussion below regarding glargine and cats)

Transitioning canine patients

- If you have canine patients currently taking Humulin L lente insulin, I would switch them to either Vetsulin or Humulin N. The initial dose of Vetsulin or Humulin N will remain the same with re-assessment of clinical signs and a serial blood glucose curve performed 1 week after changing insulin preparations.

Feline patients

Newly diagnosed patients

1. Insulin glargine (Lantus): Glargine is a modified, recombinant, long acting insulin analog. A study presented at ACVIM in 2005 showed a very high rate of remission (8/8 in remission within 4 months with 6/7 still in remission at 1 year) in feline diabetics with the use of glargine and a low carbohydrate-high protein diet. The recommended starting dose is 0.5 units/kg BID if the fasting blood sugar is greater than 360 mg/dl and 0.25 units/kg BID if the initial fasting blood glucose is less than 360 mg/dl. For additional product information see: www.lantus.com. Glargine highlights:
 - a. Should not be diluted or mixed as this will affect pH
 - b. Should be kept refrigerated. Once open the vial has a shelf life of 4 weeks at room temperature. I would discard any remaining insulin after 8 weeks of refrigeration pending further clinical data.
2. PZI: As with dogs we only recommend the use of PZIR from BI.
3. Humulin N and Novolin N: Similar to PZI with remission rates of 40-50 % when used with a low carbohydrate-high protein diet. Starting doses are generally 1-3 units/cat once a day.
4. Vetsulin: Again similar to PZI and Humulin N with remission rates of 40-50 % when used with a low carbohydrate-high protein diet. Starting doses are generally 1-3 units/cat once a day.

Transitioning feline patients

- If you have patients currently taking either Humulin L or Humulin U, I would switch them to either Vetsulin or Humulin N. The initial starting dose will remain the same with re-assessment of clinical signs and a serial blood glucose curve performed 1 week after changing insulin preparations. If you wish to transition them to glargine, I would follow the dosage recommendations as outlined above under newly diagnosed patients. It is important to note that remission rates will be much lower with glargine and a low carbohydrate-high protein diet in long standing diabetic patients (cats with diabetes for more than 6 months) than in newly diagnosed patients.

With the recent introduction of the AlphaTrak Blood Glucose Monitoring System (Abbott) we have the ability to very accurately measure blood glucose concentrations in both dogs and cats using very small quantities of blood. This will allow both veterinarians and pet owners to obtain very reliable results in both the hospital and home setting. This information can then be used to make informed decisions regarding the management of diabetic patients. These decisions impact the type and dose of insulin selected, the frequency of insulin administration, aid in the assessment of glycemic control, help in preventing hypoglycemic episodes and monitor for remission of diabetes especially in feline patients.

Glycemic control can be evaluated in a numbers of ways. Owner assessment of clinical signs (polyuria, polydipsia, weight gain or loss), progression of diabetic cataracts (dogs), presence of peripheral neuropathy (cats), and episodes of hypoglycemia are often the best indicators of glycemic control. Changes in insulin dosage or documenting remission of diabetes, is best determined by blood glucose measurement. Recognizing that the measurement of blood glucose concentrations can be problematic in the hospital setting (especially in cats as a result of stress induced hyperglycemia) recent work has evaluated the practicality and value of at home blood glucose monitoring in dogs and cats. At home blood glucose monitoring is essential in the management of human patients with diabetes given that a number of the complications associated with long term diabetes are directly related to persistent hyperglycemia. While diabetic retinopathy, nephropathy, painful neuropathies and cardiovascular disease are rare in our veterinary patients, adequate glycemic control is required to eliminate clinical signs and decrease morbidity and mortality in dogs and cats. Control of clinical signs does not require the restoration of euglycemia but rather involves keeping the blood glucose levels below renal threshold for the majority of the day. Renal threshold for glucose is 180 mg/dl in the dog and approximately 280 mg/dl in the cat. It is very important that we remember the owners of diabetic dogs and cats are being asked to do a great deal to help in the management of their pet's chronic illness and we need to do whatever we can to make the clients job easier while at the same time taking steps to assure maximal diabetic control.

Blood glucose monitoring

Reliability of the AlphaTrak system depends of course on proper use. Please review the materials supplied with your system to ensure optimal performance. We will review a number of important points here that should be followed by veterinarians, technicians and pet owners. Following these easy steps will help ensure accurate test results.

1. Insert the top of the test strip into the meter until it stops. Note: The butterfly is at the bottom of the strip and should face up.
2. Press the "m" button to power on the meter.
3. Check/adjust the code number using the "m" button to scroll down and the "c" button to scroll up. The code number on the display must match the CODE DOG or CODE CAT on the side of the test strip vial.
4. Wait for blood drop and test drip symbol to appear on screen.
5. Obtain a blood sample from the pet (See below). Dispose of lancet in biohazard sharps container. The owner should be disposing of insulin needles and lancets in a similar manner.
6. Gently touch only 1 sample area of the test strip to the blood sample (sample size is only 0.3 ul). Make sure to apply the blood to the side of the test strip. Do not put blood on the top or bottom of the strip. The meter will beep when it has an adequate sample.
7. Wait for result. The test is complete when the blood glucose concentration is shown on the display screen.

Monitoring of blood glucose concentrations should be done in the following situations and may be performed in the clinic or preferably at home by the pet owner:

1. One week after initiating insulin treatment or changing insulin dosage.
2. At any time hypoglycemia is suspected.
3. At any time a change in clinical status is observed. For instance, return of pu/pd, weight loss, cataract progression, etc.

In general, we are interested in obtaining blood samples at the following times to assess glycemic control:

1. Pre-prandial and pre insulin
2. Every 2 hours (dogs; cats on NPH, lente or ultralente) or 4 hours (cats on glargine or PZI) post prandial/insulin
3. Samples should be obtained for 12 hours or until the nadir (lowest glucose concentration) is observed. It is rare that a curve will need to be performed for a full 24 hours.

Obtaining at home blood glucose samples

Most pet owners can be taught and are in fact eager to learn how to obtain blood samples at home. Obviously if the pet is too fractious or will not tolerate blood collection other methods of assessing glycemic control will have to be employed (clinical signs, fructosamine levels, urine glucoses, etc).

Dogs

The easiest location seems to be the oral buccal mucosa (similar to performing a buccal mucosal bleeding time (BMBT)). Before starting glucose testing on a diabetic dog at home, have the owner run through a mock scenario to get the dog accustomed to the procedure. A lot of the "ease" of home testing depends on a calm and pleasant atmosphere and patient.

To do an actual test, have the pet lie on its side on the floor. Roll back the upper lip and gently wipe the buccal mucosa dry with facial tissue. Then using an AlphaTrak sterile lancet, stick the buccal mucosa close to the lip edge. Wait a couple of seconds for a spot of blood to appear gently massaging the area if necessary to produce a large enough drop. Apply the blood drop to the test strip as outlined above. After a reading is obtained, the result is recorded and positive reinforcement provided.

Other sites that may also work in dogs include the foot pads, calloused areas and a shaved area in the skin near the dorsal tail head. The site that is ultimately chosen will inevitably depend on the individual preferences of the pet and the owner.

Cats

In cats the lateral ear veins seem to work the best although we have also had success with the carpal and tarsal pads. For the ear veins and pads do not wash the site or apply alcohol prior to using the lancet as it can make obtaining a sample very difficult. The site can be wiped with an alcohol swab following sample collection.

To see the lateral ear vein, look carefully around the outer (haired) edge of the ear. Shining a flashlight from under the ear increases its visibility even on dark haired cats. It is much easier to get blood from a warm ear than from a cold one so gently massing the ear or applying a warm cloth or heated rice sock will help dilate the vessel. Have a folded tissue or gauze pad, the AlphaTrak lancet, and the AlphaTrak meter ready. Use the lancet to prick the ear near the vein. If you hit the vein directly you easily obtain a large enough sample. Remember you only need a 0.3 ul of blood. Put the tissue underneath the ear so you do not prick yourself and contaminate the blood sample. You may need to prick more than once to get enough blood and gentle massage around the site will also encourage the blood to form at the surface. Apply the blood drop to the test strip as outlined above. After a reading is obtained, the result is recorded and positive reinforcement provided. After you have done a series of tests in the same area it becomes slightly swollen and it appears easier to obtain a sample.

The same general procedure is followed when using the larger carpal or tarsal pads.

Using the information derived using at home or in hospital glucose monitoring

The data obtained with at home blood glucose monitoring in conjunction with clinical signs is used to adjust the dose of insulin and to monitor for remission of diabetes. We will look at scenarios for both cats and dogs. The recommendations for cats are based on our experience as well as the data generated by Dr Jacqui Rand at the University of Queensland.

Cats

1. Cats on Glargine and PZI Insulins
 - a. If the preinsulin blood glucose concentration is > 360 mg/dl and/or the nadir blood glucose (PZI) or 4 hour (glargine) post blood glucose concentration is > 180 mg/dl the dose of insulin is increased by 0.5 to 1 unit BID.
 - b. If the preinsulin blood glucose concentration is 270 to 360 mg/dl and/or the nadir glucose (PZI) or 4 hour (glargine) post blood glucose concentration is 90 - 180 mg/dl the dose of insulin is maintained.
 - c. If the preinsulin blood glucose concentration is 190 - 270 mg/dl and/or the nadir glucose (PZI) or 4 hour (glargine) post blood glucose concentration is 54 - 90 mg/dl use the nadir, clinical signs and the next preinsulin glucose concentration to determine if the dose is decreased or maintained.
 - d. If the preinsulin blood glucose concentration is < 180 mg/dl and/or the nadir blood glucose (PZI) or 4 hour (glargine) post blood glucose concentration is < 54 mg/dl the dose of insulin is decreased by 0.5 to 1 unit BID. If the total insulin dose is already 0.5 – 1 unit BID, stop the insulin and check for diabetic remission.
2. Cats on NPH, Lente or Ultralente Insulins
 - a. If preinsulin blood glucose is < 210 mg/dl withhold insulin and check for diabetic remission.
 - b. If preinsulin blood glucose is 234 - 288 mg/dl total insulin dose should not be higher than 1 unit BID.
 - c. If nadir blood glucose is < 54 mg/dl insulin dose should be reduced by 50%.
 - d. If nadir blood glucose is 54 - 90 mg/dl dose should be reduced by 1 unit BID.
 - e. If nadir blood glucose is 91 - 162 mg/dl insulin dose should remain the same.
 - f. If nadir blood glucose is > 180 mg/dl insulin dose should be increased by 1 unit BID.

Dogs

1. Dogs on NPH or Lente Insulins
 - a. If the preinsulin blood glucose concentration is > 360 mg/dl and/or the nadir blood glucose concentration is > 180 mg/dl the dose of insulin is increased by 25%.
 - b. If the preinsulin blood glucose concentration is 270 to 360 mg/dl and/or the nadir blood glucose concentration is 90 - 180 mg/dl the dose of insulin is maintained.
 - c. If the preinsulin blood glucose concentration is 190 - 270 mg/dl and/or the nadir blood glucose concentration is 54 - 90 mg/dl use the nadir, clinical signs and the next preinsulin glucose concentration to determine if the dose is decreased (50%) or maintained.
 - d. If the preinsulin blood glucose concentration is < 180 mg/dl and/or the nadir blood glucose concentration is < 54 mg/dl the dose of insulin is decreased by 50%.

The use of the AlphaTrak Blood Glucose Monitoring System both in the clinic and at home will greatly improve our ability to assess glyemic control and improve insulin therapy. In conjunction with close observation of clinical signs, at home glucose monitoring should go a long way towards improving the quality of life of diabetic pets and their owners.

Summary

Diabetes mellitus is a common endocrine disorder in both the dog and the cat. An understanding of the pathogenesis of diabetes is crucial to understanding how to best manage the disease in both dogs and cats. Diet is playing an even larger role in the management of diabetes in cats. While oral hypoglycemic agents may have a place in both dogs and cats, the mainstay in treatment remains exogenous insulin administration.

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