

Diabetes Mellitus in the Dog and Cat with Special Emphasis on Feline Diabetes

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General Overview

The vast majority of dogs have insulin-dependent (type 1) diabetes mellitus. In 90% of the cases the cause is linked to autoimmune destruction of the beta cells or pancreatitis. Secondary diabetes from chronic insulin resistance and subsequent beta cell burnout (e.g., with Cushing's disease, acromegaly, and diestrus) accounts for approximately 10% of canine diabetics.

In approximately 80-95% of cases, feline diabetes mellitus is similar to type 2 diabetes in humans. Both are characterized by an absolute or relative insulin deficiency coupled with insulin resistance. The other 5-20% of affected cats have other specific causes of their diabetes such as pancreatitis or pancreatic cancer, acromegaly, Cushing's syndrome, or hyperthyroidism. The majority of diabetic cats are between 10 and 13 years and only 5-40% of diabetic cats with presumed type 2 diabetes can be controlled without insulin.

Type 2 diabetes is the result of impaired insulin secretion and insulin action (decreased insulin sensitivity or insulin resistance). Diabetic cats are 6 times less sensitive to insulin than normal cats. As insulin sensitivity decreases more insulin is required to produce the same glucose lowering effect. Eventually this hyperinsulinemia cannot be sustained by the beta cells and overt diabetes develops.

What causes of insulin resistance in the cat?

- Obesity. In one study cats that gained more than 40% of their body weight had a 50% decrease in insulin sensitivity.
- Physical inactivity. Physical inactivity and confinement has been shown to predispose to diabetes in Burmese cats.
- Gender. Neutered male cats have twice the risk of developing diabetes than female cats.
- Drugs. Certain drugs such as glucocorticoids and progestins cause insulin resistance.
- Glucose toxicity: Persistently high blood glucose levels decrease insulin sensitivity.
- Genetic, dietary, and evolutionary factors. In humans insulin sensitivity and insulin resistance is genetically determined. This may also be true in cats. Insulin resistance may provide a survival advantage in wild cats fed a high protein, high fat, low carbohydrate diet. Modern day cats eat excess calories, are physically inactive, develop obesity, and have changed from diets with relatively low carbohydrates to high carbohydrate diets. These diets lead to greater postprandial hyperglycemia. In inherently insulin resistant animals the additional demands of a high carbohydrate diet may likely predispose to increased insulin secretion and beta cell exhaustion.

What causes of impaired insulin secretion in the cat

-The hormone amylin (islet amyloid polypeptide- IAPP) is the building block of amyloid. Amylin is secreted by the beta cells together with insulin. Islet amyloid deposition potentially leads to permanent beta cell loss. Cats with higher amylin concentrations tend to have higher amyloid deposition in the pancreas than cats with lower concentrations. In some diabetic cats 80-90% of the beta cell volume has been replaced by amyloid.

-Pancreatitis. This leads to variable loss of beta cells.

-Glucose and lipid toxicity. Glucose toxicity is defined as impaired insulin secretion resulting from chronic hyperglycemia . It is often reversible in as little as 5 weeks after lowering elevated glucose concentrations. Elevated fatty acids can also cause the same phenomenon. Therefore, it is important to lower blood glucose and lipid concentrations as soon as possible to reverse the glucose/lipid toxicity and facilitate beta cell recovery. However, this process can take as long as 1 to 12 weeks.

Concurrent disease

As part of a diabetic workup it is important to identify and treat other underlying diseases that may interfere with diabetic control. These diseases/disorders include dental disease (especially in cats), feline hyperthyroidism, pancreatitis, hyperlipidemia, Cushing's disease, canine hypothyroidism, acromegaly, renal failure and or pyelonephritis, and diestrus in the dog.

Goals of therapy

The goal of therapy in the diabetic dog and cat are different. The goal in the dog is diabetic control (remission is rare) while the goal in the cat is diabetic remission.

Treatment principles

The mainstay of therapy in both dogs and cats is insulin plus the proper choice of diet. When choosing a diet for the diabetic patient ask the question "is there concurrent disease or is the pet obese?" For example, obese dogs or dogs with concurrent pancreatitis and/ or hyperlipidemia benefit from low fat diets while diabetic dogs without concurrent disease can be managed feeding a good quality adult maintenance dry dog food.

In the diabetic cat, the highest rate of diabetic remissions is associated with insulin treatment plus a low carbohydrate diet such as canned Purina DM or Hills m/d. The low fat high fiber diets (e.g. Hills w/d or r/d) are also associated with diabetic remission, but the remission rates are much lower. While some cats will respond to oral hypoglycemics, insulin therapy is preferred. It has been suggested that insulin therapy plus the low carbohydrate diet more rapidly reverses glucose toxicity which leads to beta cell repair and diabetic remission.

Dietary modification in the diabetic cat

Dietary recommendations for diabetic cats has changed in the past few years as more research data has become available. Traditionally high fiber diets have been recommended to blunt postprandial hyperglycemia and increase peripheral insulin sensitivity. Interestingly, only one study on the effects of high fiber on diabetic cats has

been published. In this study a high fiber diet was compared to a low fiber diet. While mean blood glucose concentrations were lower, the two diets had different concentrations of macronutrients making comparisons difficult. There has been no comparison between high fiber and moderate fiber diets which is typical of most commercial cat foods.

The ideal concentration of protein, fat, carbohydrate and fiber to feed diabetic cats is currently unknown. Cats have a much longer period of postprandial hyperglycemia than dogs or humans. Peak glucose concentration occurs 6-12 hours after eating and do not return to normal until 14-24 hours. In addition, postprandial blood glucose concentration varies greatly depending on the carbohydrate content of the food. For example, in healthy diets of 47% carbohydrate resulted in 25-30% higher glucose concentrations than a diet of 25% carbohydrate (healthy cats). Initial data from diabetic cats suggests that low carbohydrate, high protein diets result in better glycemic control, reduced insulin requirements and increased rates of diabetic remission. Whether a very low carbohydrate, high fat diet is superior to a moderate carbohydrate diet, moderate fat diet has not been investigated.

Amount of food

Obese cats should be fed 70% of their maintenance requirements (60 kg/kg/day). A 1-2% loss of weight per week is ideal. Weight loss improves insulin sensitivity and may reduce insulin requirements. Underweight cats should be fed ad libitum until an ideal body weight is achieved. Similar guidelines should be followed for canine diabetics.

Time of feeding

Because postprandial hyperglycemia lasts much longer in cats and most insulins have their peak effect 4-10 hours after injection it is recommended to feed diabetic cats twice daily at the time of insulin injection (accept for the severely underweight cat). Twice daily feeding at the time of insulin injection is also advocated for diabetic dogs.

All Those Insulins: Is There a Best Insulin for the Treatment of Diabetes Mellitus in Dogs and Cats?

One of the most common questions asked related to treating diabetes mellitus is “which is the best insulin”? There is no best insulin as glycemic control may vary from patient to patient. For example, a hyperlipidemic diabetic Miniature Schnauzer may do better using an insulin mixture (70/30 NPH-Regular) given BID as compared to NPH BID whereas another diabetic hyperlipidemic schnauzer may be controlled relatively well using lente insulin BID rather than NPH or an insulin mixture BID. In some diabetic cats adequate diabetic control can be achieved using human NPH or porcine lente BID whereas with others optimal glycemic control is best achieved using PZI or glargine insulin.

Insulin Therapy for Diabetic Cats

Insulin therapy remains the preferred initial and long-term treatment of choice for diabetes in the cat.

What type of insulin and how often should it be administered? In general, therapy for uncomplicated diabetes mellitus should be initiated with either a long-acting insulin preparation (PZI or glargine insulin) given once to twice daily or an intermediate-acting insulin (lente or NPH) given twice daily. In some diabetic cats, hyperglycemia can be adequately controlled with once-daily administration of PZI or glargine insulin but most will require twice daily administration of these long-acting insulins for optimal diabetic regulation. Because intermediate-acting insulins have a shorter duration of action than the long-acting insulins, once daily administration would rarely, if ever, satisfactorily control hyperglycemia in cats with diabetes.

What source of (animal or human) should be used? There are many different sources of commercial insulins. NPH is recombinant human origin and lente (Vetsulin) is porcine insulin. Glargine insulin is a recombinant human insulin while PZI is only available as beef-pork insulin. Since cat insulin is most similar to beef insulin, this may be the insulin of choice (combination beef-pork is 90% beef insulin) although glargine insulin appears to be equally, if not more effective. However, the other insulin preparations (pork or human) also work well in most cats. Once a cat is stabilized on one source of insulin, the same type of insulin should be continued. If a change in insulin is contemplated, it is important to realize that different types and brands of insulin may have different pharmacological properties necessitating insulin dosage adjustments.

What dose of insulin should be used? When initiating therapy with an intermediate- or long-acting insulin, it is best to start with a relatively low dose (0.25 to 0.5 U/kg/day) and slowly increase the dose as needed. Most insulins are available in concentrations of 100 U/ml (U-100 insulin). However, PZI is available only in concentrations of 40 U/ml (U-40 syringes are available from the manufacturer). When using U-100 insulin, low-dose syringes (0.3 and 0.5 ml capacity U-100 insulin syringes) may be helpful for accurate dosing in cats with very low insulin requirements.

The Use of PZI Insulin in Cats

Protamine zinc insulin (PZI) is a long-acting preparation of beef/pork-source insulin used to treat diabetes mellitus in the cat. PZI (PZI Vet) is available from Idexx Pharmaceuticals., Greensboro, NC as a 40 U/ml preparation. 40 U/ml insulin syringes are provided. Compounded PZI preparations are available from pharmacists at the request of veterinarians. These preparations have provided inconsistent glycemic control in diabetic cats and are not recommended.

Based on a multicenter study with 67 diabetic cats, 90% of these cats had good control based on owner observation and serum fructosamine levels. Seventy-five percent of previously treated ‘hard-to-regulate’ cats did well on PZI. The absorption kinetics, glucose nadirs, and duration of action of PZI is variable. In general, most cats require PZI twice daily. However, the blood glucose nadir occurred 9 hours or longer after PZI

administration in 25% of cats, suggesting that once a day administration of PZI may be effective for controlling hyperglycemia in a small percentage of cats.

The initial recommended dosage is 1 U/cat/injection. Subsequent increases in the PZI dosage should be based on owner perception of their cat's response to treatment, urine glucose readings, changes in physical examination and body weight, and the results of blood glucose and serum fructosamine measurements.

Insulin glargine

Insulin glargine is a new long-acting synthetic insulin analogue that has shown encouraging results in recent clinical studies. After subcutaneous injection in humans, this insulin forms a microprecipitate in the subcutaneous tissue and is slowly released throughout the day with no pronounced peak effect (so-called "peakless" insulin). Although in healthy cats a peak occurs at 16 hours with significant glucose suppression for up to 24 hours. Preliminary studies of insulin glargine in healthy and diabetic cats suggest that twice daily administration provides optimal glycemic control. The starting dose is 0.25 to 0.5 U/kg given twice daily.

A recent clinical study showed that treatment with glargine results in higher remission rates than PZI and lente insulins in diabetic cats (Marshall R and Rand J. JVIM abstract, 2005; 19:425). Twenty-four newly diagnosed diabetic cats were treated with glargine, PZI, or lente insulin. (There were 8 cats in each group) and fed a low carbohydrate, high protein diet (Purina DM canned). Insulin was initially given at 0.5 U/kg SC if the blood glucose was > 360 mg/dl and 0.25 U/kg if the blood glucose was < 360 mg/dl. Insulin dose was then adjusted based on serial glucose curves and water intake. At diagnosis there was no statistical difference between treatment groups with regard to age, body condition score, body weight, and initial fructosamine concentrations.

Mean 12-hour glucose concentrations at 4 weeks was significantly lower for the glargine treated cats (239 mg/dl) than PZI and lente (343 mg/dl and 553 mg/dl respectively). Fructosamine concentrations were also significantly lower than at diagnosis for the glargine treated cats (343 and 553 umol/L) but not for PZI (469 and 570 umol/L) or lente (465 and 574 umol/L).

All 8 cats treated with glargine went into diabetic remission within 4 months of starting treatment while 3 cats treated with PZI and 2 cats treated with lente went into diabetic remission. Of the 7 cats treated with glargine that remain alive, 6 remain in remission (mean remission time 13 + 3.5 months). No cats in the glargine treated group developed clinical hypoglycemia.

In conclusion, glargine resulted in higher remission rates than PZI and lente in newly diagnosed diabetic cats. It is postulated that improved glycemic control with glargine resulted in better reversal of B-cell glucose toxicity and higher diabetic

Recommendations for Using Glargine In Diabetic Cats

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These instructions for using glargine are based on a small number of cats, and caution should be exercised with the insulin until it has been used in a larger number of cats. Because glargine is very long-acting, there is the potential for prolonged hypoglycemia if overdosed.

Basic information

- Insulin glargine must not be diluted or mixed with anything because the prolonged action is dependent on its pH.
- Insulin glargine should be kept refrigerated to prolong its life.
- Insulin glargine has a shelf-life of 4 weeks once opened and kept at room temperature. Opened vials stored in the refrigerator can be used for > 6 months.
- If using an insulin pen, the manufacturer recommends that the pen and cartridge be kept at room temperature and not refrigerated. This is to reduce the changes in volume of insulin dispensed associated with changes in temperature.
- When performing a blood glucose curve, samples probably only need to be taken every 4hrs over 12 hr in many cats (i.e. 0h [before morning insulin], 4h, 8h and 12h after morning insulin)
- Dose changes should be made based on pre-insulin glucose concentration, nadir (lowest) glucose concentration, daily water drunk, and urine glucose concentration.
- Better glycemic control is achieved with twice daily dosing rather than once daily
- More accurate dosing may be achieved using 0.3ml U-100 insulin syringes

Starting Cats On Glargine

- If blood glucose concentration $\geq 360\text{mg/dL}$ (20mmol/L) begin glargine at an initial dose of 0.5U/kg ideal body weight twice daily (BID)
- If blood glucose concentration $< 360\text{mg/dL}$ (20mmol/L) begin at 0.25U/kg ideal body weight BID
 - Perform a 12hr glucose curve with samples taken every 4hrs
 - DO NOT increase dose for the first week.
 - Decrease dose if biochemical or clinical hypoglycemia occurs
 - It is suggested that cats stay in hospital for 3 days to check the initial response to insulin, or home glucose curves are obtained for the first 3 days
 - Recheck at 1, 2, 3 and 4 weeks after the cat is sent home, and then as required.

- Many cats have negligible glucose lowering effect in the first 3 days (do not increase dose), although by day 10 after beginning insulin, most cats have good glycemic control.
- Until experience is gained in ketoacidotic cats, these should be treated initially with a shorter acting insulin.

ADJUSTING INSULIN DOSE

1. Indications for increasing the dose of glargine

- If pre-insulin glucose conc. is ≥ 360 mg/dL (20mmol/L), then increase dose by 0.5U/injection

AND / OR

- If nadir glucose conc. is > 180 mg/dL (10mmol/L) then increase dose by 0.5U/injection

2. Indications for maintaining the same dose

- If pre-insulin glucose conc. ≥ 240 - < 360 mg/dL (≥ 15 - < 20 mmol/L)

AND / OR

- if nadir glucose conc. 90-180mg/dL (5-10mol/L)

3. Indications for decreasing the dose of glargine

- If pre-insulin glucose conc ≤ 180 mg/dL (≤ 10 mmol/l) decrease 0.5U
- If nadir glucose conc < 54 mg/dL (< 3 mmol/l) decrease 1U
- If clinical signs of hypoglycemia develop, then reduce dose by 50%

4. Insulin dose may be maintained or decreased depending on the water intake, urine glucose, clinical signs and length of time the cat has been treated with insulin

- If pre-insulin glucose conc. 198 - 252 mg/dL (11 - 14 mmol/L)
- If nadir 54 - 72 mg/dL (3 - 4 mmol/l)

Determining if the cat is in remission

After a minimum of 2 weeks of insulin therapy, if the pre-insulin blood glucose is < 200 mg/dL (12mmol/L) insulin should be withheld and a 12hr glucose curve performed. If at the next due dosing time the blood glucose is > 200 mg/dL (12mmol/L) then insulin can be administered at 1U BID. If blood glucose is ≤ 200 mg/dL then continue to withhold insulin and discharge with a follow-up visit in 1 week.

Some cats may have a pre-insulin glucose concentration below 12mmol/L within 2 weeks, but insulin therapy should be maintained for a total of 2 weeks to give beta cells a better chance at recovery from glucose toxicity. Use 0.5-1U BID or once daily until insulin is withdrawn

Urine glucose

With the long duration of action of glargine, there should be minimal periods when blood glucose is >14mmol/L (240mg/dL) for cats treated for more than 2 to 3 weeks, and hence well controlled cats should almost always be 0 or 1+ for urine glucose. A value 2+ or greater likely indicates that an increase in dose is required.

Insulin Therapy in Dogs

In general, most dogs can be managed successfully with human NPH or lente insulin. The advantage of lente over NPH is a more consistent duration of action. For example, in some patients the duration of action of NPH can be as short as 8 hours. The new porcine lente (Vetsulin: Intervet) is now available as a U-40 preparation. The theoretical advantage of this insulin in dogs is that the structure of porcine insulin is identical to dog insulin, although past studies in normal dogs have shown that porcine and human lente have similar pharmacokinetic properties. This insulin may prove advantageous for treating small dogs where accurate dosing of small doses of insulin are required and dogs with poor glycemic control being treated with NPH or lente. The starting dose of insulin, whether lente or NPH, is 0.25 to 0.5 U/kg given twice daily.

Oral Hypoglycemics

Most oral hypoglycemics improve and release and/or sensitivity of insulin and therefore may be clinically useful with Type 2 feline diabetics. Oral hypoglycemics are not recommended for Type 1 diabetics (the dog).

Sulfonylureas (glipizide; Glucotrol®). Oral hypoglycemics are often used, together with diet, to control hyperglycemia in human patients with NIDDM. The oral hypoglycemic agent most commonly used in cats is glipizide. When used in combination with dietary therapy, glipizide administered orally at a dosage of 5 mg BID seems to be somewhat effective in controlling hyperglycemia in some cats with uncomplicated diabetes mellitus (and suspected NIDDM). Glipizide is a sulfonylurea that works primarily by stimulating pancreatic beta-cells to synthesize insulin and enhance insulin secretion. In a study of 50 cats with previously untreated diabetes mellitus, improvement in diabetic control was observed in 22 cats (44%) treated with glipizide. However, in 3 of the responders glipizide control waned over time and in 6 of the responders the diabetes was transient (possibly insulin or diet therapy alone would have been effective?). Side effects in cats administered glipizide include vomiting, anorexia, hypoglycemia, and hepatopathy. The efficacy of treatment of oral hypoglycemics should be evaluated with home monitoring of urine glucose and ketone concentrations, as well as weekly serial blood glucose curves. If hypoglycemia or normoglycemia develops, the glipizide should

be discontinued. The glipizide may be reinstated if the hyperglycemia recurs, although the dose should be lowered if hypoglycemia was noted with prior treatment. If the cat does not respond to glipizide (e.g., pre-insulin blood glucose values > 300 mg/dl after 1 to 2 months of therapy), becomes ill or ketoacidotic, or develops adverse side effects, the glipizide should be discontinued and insulin therapy should be started. Overall, the trial use of glipizide is a feasible alternative to insulin therapy, especially in diabetic cats of owners who are unable or unwilling to administer insulin. Other sulfonylureas that some veterinarians have used with anecdotal success with once daily administration are glibenclamide (Micronase) and glimepiride (Amaryl) dosed at 0.625 mg and 1 to 2 mg per cat respectively.

Transition metals (vanadium and chromium). These heavy metals mimic the actions of insulin by presumably increasing insulin sensitivity. The dose of vanadium is 0.2 mg/kg/cat once daily with food. Vanadium can be purchased at health food stores as vanadyl sulfate (10 mg vanadyl sulfate is equivalent to 1.85 mg elemental vanadium). Vanadium acts like an “oral insulin” and appears to be most effective. In cats with uncomplicated diabetes mellitus that are easy to control with low doses of exogenous insulin. Adverse effects are anorexia and vomiting.

Alpha-glucosidase inhibitors (acarbose tablets; Precose®). Acarbose is an oral alpha-1 glucosidase inhibitor for use in NIDDM in man. Acarbose reversibly inhibits enzymatic breakdown of starches in the intestinal lumen. In diabetic patients this enzyme inhibition results in delayed glucose absorption and a lowering of postprandial hyperglycemia. Because its mechanism of action is different, the effect of acarbose to enhance glycemic control is additive to that of sulfonylureas or exogenous insulin when used in combination. However, some cats with mild diabetes require only acarbose (and dietary therapy) to control hyperglycemia. The dose of acarbose is 12.5 to 25 mg/cat given with meals. Side effects in people include flatulence and soft stools.

Thiazolidinediones. These agents increase insulin sensitivity by stimulating a gene to produce more insulin-controlled proteins that in turn remove glucose from the bloodstream. In a limited number of diabetic cats previously treated with exogenous insulin, concurrent administration of troglitazone (100 mg/cat once daily) significantly lowered insulin requirements. However, until further efficacy, safety and dosage studies are completed, troglitazone can only be cautiously recommended for the treatment of diabetes at this time.

Biguanides. Metformin is the most commonly used biguanide and is one of the widely used oral hypoglycemic agents for the treatment of type 2 diabetes in humans. . It inhibits hepatic gluconeogenesis and glycogenolysis and increases peripheral insulin sensitivity. Studies in cats, however, have not been encouraging, particularly as a sole agent and it is difficult to make recommendations for its use. .

Monitoring diabetic control in dogs and cats

Response to treatment is best evaluated in a number of ways and no individual modality should be used as the sole parameter to adjusting therapy. A combination of owner assessment, clinical signs and changes in body weight and water intake are often the best indicators of glycemic control. Measurement of serum fructosamine and serum glucose curves can be useful for long-term monitoring and urine glucose measurements can be valuable in detecting diabetic remission in the cat. Initially diabetic cats are evaluated every 1-4 weeks until the clinical signs of the diabetes has resolved.

The insulin dose in newly diagnosed diabetic cats often needs to be increased over the first few weeks and frequently has to be decreased after several weeks of treatment. This decrease is likely due to the resolution of glucose toxicity leading to improved insulin sensitivity and insulin secretion. The majority of cats stabilize in 1-4 months, although occasionally it can take longer than 6 months.

Diabetic remission

In the past, up to 15% of diabetic cats would go into complete remission. Since the use of low carbohydrate diets, diabetic remission has increased to over 50%. Diabetic remission, if it occurs, is usually within 1 to 4 months following good glycemic control. Remission may be recognized initially only by a sudden hypoglycemic event (weakness, seizures) in a previously well controlled cat or it may occur gradually. Urine glucose monitored regularly at home is useful in detecting reduced insulin requirements. Diabetic remission in the dog is rare, but occasionally occurs following treatment for Cushing's disease and ovariohysterectomy.

Avoiding insulin overdosage: "Over interpreting" the glucose curve

Daily glucose fluctuations.

The intraday blood glucose following insulin administration can be quite variable in diabetic cats from day to day. In some dogs and cats the nadir blood glucose can vary as much as 100 mg/dl on consecutive days after administration of the same dose of insulin. Therefore, because of intraday variation the results of serial blood glucose determinations should always be interpreted conservatively and always in conjunction with other variables such as water intake, body weight, and serum fructosamine, and urine glucose readings

Diagnostic approach to the unregulated diabetic

Typically, the problem diabetic has a low body condition score, increased water intake (>100 ml/kg/day), polyphagia, a poor hair coat and is on an excessive dose of insulin (>1.5 U/kg/injection) and has a glucose nadir >180 mg/dl or is hypoglycemic. The most common causes of poor control are an excessive insulin dose (which includes a miscalculated dose), poor insulin absorption (commonly seen with glargine and PZI), and

short duration of action of insulin (e.g., 2-3 hours with NPH or lente or 6 hours with PZI or glargine)

An orderly practical approach to the poorly controlled diabetic is the following:

- First, rule out an insulin administration problem or outdated or old insulin
- Perform a glucose curve.
- If pu/pd and high doses of insulin (>1.5 U/kg/injection) have little effect on the blood glucose or the duration of action is too short lower the dose of insulin to 0.5 U/kg per injection for 2 weeks
- If no improvement, check the duration of action of insulin following an insulin dose of 0.5 U/kg
- In the cat, if glucose nadir is 2-3 hours (usually with lente or NPH) switch to glargine or PZI. If on once a day PZI or glargine and the glucose nadir is < 6 hours switch to twice daily administration.
- If the cat is on PZI or glargine and there is little response to insulin switch to lente or NPH. Lack of response to the longer acting insulins is often due to poor absorption.
- If there is a poor response to NPH or lente and the dog or cat remains unregulated check for Cushing's disease, acromegaly, hyperthyroidism, and causes of inflammation such as periodontal disease.

Treating and evaluating fractious cats

Most fractious cats can be successfully treated and monitored using water intake as a guide. Insulin is administered at 1 U per cat twice daily and daily water intake is monitored. In general, water intake $< 20-40$ ml/kg/day (fed canned food) and <70 ml/kg/day (fed dry food) correlates with good glycemic control and the insulin dose should not be changed. Water intake > 100 ml/kg/day indicates poor diabetic control and an adjustment in insulin dose is required. This dose is increased by 1 U per injection weekly until the water intake is < 70 ml/kg/day (dry food) or $< 20-40$ ml/kg/day (wet food).