

Diabetes Mellitus in dogs and cats^a

INTRODUCTION

Diabetes mellitus is a frequently occurring disorder. Frequencies vary from 1 out of 100 to 1 out of 500 in both dogs and cats. In this paper the clinical presentation, treatment and some difficulties of diabetes mellitus in dogs and cats are discussed.

HOW DO WE DIAGNOSE DIABETES MELLITUS?

Normal fasting plasma glucose values are 3.9-5.0 mmol/l in dogs and 3.4-5.7 mmol/l in cats and renal threshold for plasma glucose in most dogs is about 10 mmol/l and in cats 15 mmol/l. Diabetes mellitus is the condition of persistent or permanent hyperglycaemia, with plasma glucose values well above the renal threshold (usually 20 mmol/l or more) and hence glucosuria.

It is important to differentiate a transient hyperglycaemia from true diabetes mellitus. Transient hyperglycaemia may occur during stress in cats, such as in any severe illness, but rarely in dogs. It can also occur in both dogs and cats in uraemia, in acute pancreatitis, and rarely as an idiopathic condition. In uraemia, hyperglycaemia is due to insulin resistance and it is sometimes difficult to differentiate between this combination and diabetic ketoacidosis. In cases with prolonged hyperglycaemia (true diabetes mellitus) fructosamine levels will be elevated (above 400 $\mu\text{mol/l}$) Urine measurements should always be crosschecked with a plasma measurement. Renal glucosuria (i.e., glucosuria without hyperglycaemia) can be caused by decreased resorption of glucose in the proximal tubule. This occurs in the Fanconi syndrome and following damage to the proximal tubule (e.g., by outdated tetracycline or heavy metals such as cadmium, lead, thallium, etc.).

ETIOLOGY

In human medicine a distinct differentiation between a type 1 and type 2 DM is made. In type 1 DM no insulin is present either due to a congenital or acquired absence of beta-islets. It is called an Insulin Dependent Diabetes Mellitus (IDDM). Type 2 DM is a disorder in which there is still insulin production but due to an insulin resistance it cannot function properly. It will not seldom develop into a type 1 DM. It is also called a Non-insulin Dependent Diabetes Mellitus (NIDDM). Type 2 occurs most in dogs. The DDx of type 1 DM would be an originally type 2 case, a congenital absence of islets or an immune mediated destruction or amyloidosis. Seldom an infection or pancreatitis is the cause. In type 2 cases it would be progesterone, Cushing, GH excess, hyperthyroidism (seldom) and obesity (rare).

In dogs the most frequent cause of potential diabetes and clinical diabetes mellitus or the prolonged or repeated exposure to progesterone or progestagens and hence these disorders occur most often in middle-aged and older female dogs that have had repeated exposure to progesterone in normal oestrous cycles, and in those that have had repeated injections of progestagens to prevent oestrus. The prolonged secretion of progesterone in the canine oestrous cycle stimulates increased secretion of growth hormone, which causes peripheral resistance to the action of insulin. This results in hyperglycaemia, which stimulates the beta cells to increase the secretion of insulin. Very high blood levels of insulin may result, but insulin action continues to be inhibited by excess growth hormone. If the dog is sterilized soon enough (2-4 weeks), the decrease in growth hormone (within 1 week) removes the insulin resistance and the beta cells may recover. If not, the beta cells undergo complete exhaustion and degeneration, and permanent insulin deficiency results.

Recovery of beta cell function is sometimes possible even when clinical diabetes mellitus is already present, if progesterone is removed by ovariohysterectomy and the hyperglycaemic stimulation of the beta cells is reduced by insulin therapy, allowing the beta cells to rest. The chance of complete recovery from diabetes is usually excellent, sometimes even without insulin therapy, if ovariohysterectomy is performed within no more than 2-3 weeks after the onset. Complete recovery is sometimes possible even when diagnosis and ovariohysterectomy are delayed by a month or more after onset of the pu/pd, but this requires very well regulated insulin therapy for weeks or months. When diabetes mellitus has been caused by use of a progestagen, recovery of beta cell function may still be possible if correct insulin therapy is started promptly and beta cell exhaustion is prevented by

^a Grotendeels gebaseerd op de endonotes van dr. B. Belshaw. Destijds universitair medewerker UKG, Utrecht. Thans dierenarts te ruste & Mandigers P.J.J. (2000) Diabetes Mellitus in dogs and cats. "Der Alte Hund – die alte Katze" Arbeitstagung Österreichische Gesellschaft der Tierärzte – 25 November 2000, Vienna Austria, p 27-31

very good regulation of plasma glucose until the effect of the progestagen disappears (hence a few months). During the first few weeks, extreme insulin resistance can be encountered.

Ovariohysterectomy appears to be helpful in these cases also.

The next most common cause is glucocorticoid excess, in both males and females, due to Cushing's disease or corticosteroid administration. Glucocorticoid excess causes hyperglycaemia via increased gluconeogenesis (the production of glucose from noncarbohydrate sources, chiefly protein). If the hyperglycemic stimulus is prolonged, the beta cells can undergo exhaustion and degeneration, resulting in permanent diabetes mellitus. This is an important distinction from diabetes caused by progesterone or progestagens: clinical diabetes caused by corticosteroid excess is almost never reversible. Fasting hyperglycaemia is found in about one-half of the dogs with Cushing's disease and clinical diabetes mellitus is found in about 10% by the time the Cushing's disease is diagnosed.

Diabetes mellitus is also caused by repeated use of short-acting corticosteroids (e.g., prednisone) and particularly by the injection of long-acting corticosteroids (even a single injection in some cases).

MANAGEMENT OF DIABETES MELLITUS

It has been known for more than 30 years that oral medications used in the treatment of some forms of diabetes in man, are ineffective in dogs and cats. The mechanism of these drugs is to increase insulin secretion but the cause of most cases of diabetes mellitus in dogs is excessive stimulation of insulin secretion, leading to exhaustion and then death of the beta cells. Hence such drugs are not only ineffective but are also contraindicated.

Ovariohysterectomy

If diabetes began during the luteal phase of the estrous cycle, rather than due to progestagen injections or glucocorticoid excess, and clinical signs have been present for no more than three weeks, immediate ovariohysterectomy may result in complete reversal without insulin therapy or after only a short period of insulin therapy. If the dog still has a good appetite and is not dehydrated or uremic, ovariohysterectomy before starting regulation is definitely advantageous. Even if the diabetes is not completely reversed by this prompt action, removing the stimulus to growth hormone-induced insulin resistance makes regulation easier. Trying to regulate the dog before surgery is usually counterproductive, for if there is growth hormone-induced insulin resistance, 2-3 weeks or more of treatment may be required before plasma glucose is satisfactorily lowered and stable. During this time the dog will continue in unregulated diabetes and its suitability for surgery may be made worse, not better.

Caninsulin®

The mixture of 30% amorphous and 70% crystalline zinc insulin has two phases of action. The amorphous zinc insulin reaches its peak effect at about 3 hours after s.c. injection and its total useful effect lasts not more than 6-8 hours. The crystalline zinc insulin has a slower onset, has its maximum effect between 7 and 12 hours and then gradually decreases in effect over the remainder of 20 to 24 hours. Feeding is synchronized with the two phases of action and in most dogs the plasma glucose level is satisfactory over most of the 24-hour period. The treatment schedule allows the dog to be under observation by the owner during the period (afternoon) when hypoglycaemia is most likely to occur if the insulin dose is too high. Note: "NPH insulin" does not have the same biphasic activity curve and is not suitable for the method of treatment described in these notes.

Caninsulin® should be stored in the refrigerator. It should be mixed thoroughly but gently before the dose is withdrawn: do not shake vigorously. The expiration date on the label should be observed.

Diet

The diet is as important as the administration of insulin in the successful treatment of diabetes. It must be constant in composition and amount from meal to meal and from day to day, in order for a constant dose of insulin to be achieved. Even if the dog has always been fed a mixed diet, the most reliable way to be certain that the diet is constant is to use a commercial food.

Treatment Schedule

The daily schedule is based on the two phases of action of the mixture of 30% amorphous and 70% crystalline zinc insulin. The first meal is given with the insulin injection in the morning and the second meal is given 7 ½ hours later. A typical daily schedule is to give the insulin injection and first meal at 8.30 and second meal at 16.00. The schedule can begin earlier (e.g., meals at 7.00 and 14.30) or later (e.g., meals at 13.00 and 20.30), the insulin injection always being given with the first meal.

Discussion Before Starting Treatment

Diabetes in dogs and cats is insulin-dependent and cannot be treated by diet alone or by oral medications.

Diabetes mellitus in an adult male dog or in a female which was previously ovariohysterectomized is almost always due to glucocorticoid excess. If not related to administered corticosteroids, it almost certainly indicates spontaneous Cushing's disease, which will also require diagnostic tests and treatment. Regulation of the diabetes will be imperfect until Cushing's disease has been treated. Female dogs, regardless of the cause of the diabetes, should be ovariohysterectomized. Otherwise, moderate to severe insulin resistance will occur during the luteal phase of each succeeding oestrous cycle. If the diabetes in a female has been caused by Cushing's disease alone, ovariohysterectomy should be delayed until the Cushing's disease has been treated, since the patient will then be in a better state for surgery. However, if the diabetes began during the luteal phase of oestrus, with or without Cushing's disease, prompt ovariohysterectomy is almost always beneficial to regulation.

Starting Treatment

A safe starting dose of Caninsulin is 1 unit per kg body weight. A small addition can be made to this, namely, add 1 extra unit for dogs under 10 kg, add 2-3 extra units for dogs of 10-20 kg, and add 4 extra units for dogs over 20 kg. It is best to use the 40 IU/ml syringes. The syringe can be kept in the refrigerator with the insulin and can be used for 5-7 days.

Some dogs do not eat the morning meal immediately if their appetite is depressed by hyperglycaemia. The full calculated dose of insulin should be injected and the food should be taken away if it is not eaten in an hour or so. After a few days the dog will adapt to the schedule. After regulation is achieved, it is better to give the food first and then, as the dog is eating, to give the insulin injection. If the dog has vomited in the previous 24 hours, wait for 15-20 minutes before giving the insulin, to be certain that the meal is not vomited also. After regulation has been achieved, if the first meal is refused or only a small amount is eaten (often the first sign of an illness), or if food is being withheld because of surgery, diarrhoea or vomiting, one-third of the dog's usual dose of insulin should be given. This will avoid unnecessary hyperglycaemia and yet be safe.

On the first day of treatment the owner feeds the dog and injects the insulin at the same time, at 8.30. The uneaten food should be removed after one hour, at both meals. The dose is increased by about 10% each day until the afternoon plasma glucose level is 6-8 mmol/l. If there has been a rather large decrease in one day (e.g., from 20 mmol/l or more to around 12 mmol/l), continue the same dose for another day. When plasma glucose has been lowered to 6-8 mmol/l, it should be checked one more day and then about one week later, to be certain that regulation is stable.

The owner should then check urine glucose in the morning, before the insulin injection and first meal. If this remains only a trace positive, the dose of insulin remains the same, but if it becomes more positive, the dose should be adjusted by measuring plasma glucose.

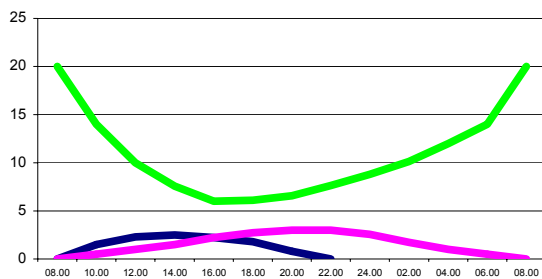
Satisfactory regulation can usually be achieved within 5-7 days and occasionally in only 2-3 days, but there may be some resistance to insulin during the beginning of treatment, so that several 10% increases have to be made. The resistance can decrease suddenly and afternoon plasma glucose can unexpectedly be found to be as low as 2-3 mmol/l. When this occurs, the dog should be fed immediately and an extra meal should be given at 18.00. On the following day the dose should be decreased by 20% and plasma glucose should be measured again in the afternoon. It is unwise to increase the dose unless plasma glucose can be measured on the same afternoon, to monitor the effect.

In Cushing's disease, 2-4 units/kg may be required, but doses above 4 units/kg may be reached in insulin resistance caused by progestagen injections.

Attempting to avoid measurements of plasma glucose by advising the owner to adjust the dose to maintain slight glucosuria at all times will almost certainly guarantee that the dog will become totally blind from rapidly developing cataracts and it will also increase the risk of urinary tract infections.

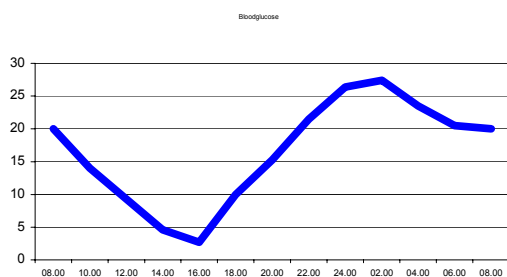
When the dose of insulin is correct, plasma glucose is just above the renal threshold in the morning and hence morning urine glucose is slightly positive. Plasma glucose will decrease to 6-8 mmol/l before the afternoon meal. During the night the action of insulin gradually decreases and plasma glucose rises to just above the renal threshold by the next morning.

When the dose of insulin is too low, plasma glucose remains above the renal threshold and thus there



is glucosuria and pu/pd during the entire day and night.

When the dose of insulin is much too high, signs of hypoglycaemia develop in the afternoon, usually between noon and the time of the afternoon meal, and can result in convulsions if not corrected.



When the dose of insulin is too high but plasma glucose decreases at a slower rate, the dog may be unusually hungry and anxious, or may be unusually lethargic and dull. When plasma glucose is lowered to about 3 mmol/l, the glucose deficiency in the brain triggers the release of epinephrine, followed by glucagon, cortisol and growth hormone. The effects of epinephrine and glucagon are the most important, for they both stimulate the release of glucose from glycogen stores, thereby raising plasma glucose rapidly. Since the diabetic cannot secrete insulin when the rise in plasma glucose

exceeds the normal range, moderate to severe hyperglycaemia results. This hyperglycaemic rebound following hypoglycaemia is the Somogyi effect. Plasma glucose usually exceeds the renal threshold within two or three hours and can reach 20-30 mmol/l during the evening and night. Urine glucose is negative during the day but becomes increasingly positive during the evening, causing pu/pd, and is strongly positive by the next morning.

If the Somogyi effect is not understood and the same dose of insulin is repeated, the same response will occur and may be more pronounced. When the effect is very pronounced, the night-time hyperglycaemia can carry over into the morning until the next dose of insulin takes effect. This results in continuing glucosuria for some hours after insulin has been given. As a result, there can be enough glucose in the bladder to give a strongly positive urine glucose in the afternoon at the same time that the dog is again in severe hypoglycaemia. Measuring urine glucose, rather than plasma glucose, can lead to potentially fatal errors, since morning urine glucose can be positive either because the dose of insulin is too low or because it is too high.

HYPOGLYCEMIA

Before the first dose of insulin is administered, the owner should have a box of Dextropuur (powdered glucose) at home and should know the amount that is equivalent to about 1 gram per kg of the dog's weight. Hypoglycaemia can occur in any diabetic dog, during initial regulation or even after months of good regulation. It can be caused by over dosage of insulin, by failure to eat or by vomiting of food, by unusual excitement or physical activity, or it can occur without any obvious explanation. It is most likely to occur during the 3-4 hours before the second meal, but can occur at any hour of the day or night.

Simply giving glucose is not enough, for the excessive action of insulin will continue. Glucose administration will raise plasma glucose for about 30-60 minutes and hence food must also be given to generate a continuing input of glucose. As a general rule, when signs of hypoglycaemia occur in the afternoon, food should be given at two-hour intervals until 20.00 or 22.00, unless pu/pd and glucosuria occur, indicating that plasma glucose is above 10 mmol/l.

Unexpected hunger and mild anxiety develop when plasma glucose is reduced to around 3 mmol/l. As glucose is decreased to 2 mmol/l or less, there is increasing anxiety, confusion and disorientation, with ataxia and stumbling or falling in the rear legs. Then muscle spasms begin, soon followed by grand mal convulsions with extreme excitability. Even if the dog is rescued from this severe degree of

hypoglycaemia by the administration of glucose, mild to moderately severe permanent brain damage can result. To avoid this risk, the owner must be instructed that hypoglycaemia must be treated immediately, at home, and that time spent in telephoning or coming to the veterinarian may be fatal for the dog. Hence the owner must overcome panic and immediately administer glucose orally, continuing until the dog is able to take food. Hypoglycaemic convulsions can be quite frightening and the owner must be given adequate instructions. A 10-ml disposable plastic syringe should be provided to aid in giving glucose solution orally even if the dog is convulsing and biting.

PROBLEMS IN REGULATION

In uncomplicated diabetes the dose of insulin at which stable regulation is achieved is usually between 1 and 2 units/kg. If diabetes began during the luteal phase of oestrus and regulation is attempted before ovariohysterectomy, the dose may well exceed 2 units/kg. Following ovariohysterectomy, a marked reduction in the dose should be expected. Plasma glucose should be checked on the morning after ovariohysterectomy and the instructions under the heading Ovariohysterectomy should be followed.

INSULIN RESISTANCE

Uraemia can cause insulin resistance in addition to a decreased and unpredictable appetite. In any diabetic patient in which unexplained problems of this kind begin to develop, plasma creatinine should be measured and the diet changed if necessary. The insulin resistance is usually not severe and it disappears within 1-3 days when i.v. fluids are given for forced diuresis, or about one week when only dietary protein restriction is required.

Apparent insulin resistance can occur as a result of inactivation of the insulin in the bottle being used. This can be caused by vigorous shaking of the bottle to mix the insulin before withdrawing the dose each day, or lack of refrigeration, but it sometimes occurs without discovery of the cause. The result is an apparent increase, usually sudden and quite severe, in the insulin dose requirement. Until the owner and/or the veterinarian thinks of trying a fresh bottle of insulin, the patient's pu/pd and hunger will cause increasing problems.

Insulin resistance characterized by a shortened period of insulin action as well as a higher insulin dose requirement occurs very infrequently in dogs. In such patients, Caninsulin and similar preparations of amorphous and crystalline zinc insulin act for about 12 rather than 24 hours. Initially, the abrupt onset of pu/pd and glucosuria every evening may be misinterpreted as the Somogyi effect, but lowering the dose of insulin in response to this results in pu/pd and glucosuria during the day as well. It is only by measuring plasma glucose every 2 hours from the time of insulin injection until late in the evening that it is found that 1) plasma glucose does not decrease below the level of 3 mmol/l which is necessary to trigger the hyperglycemic reactions and hence 2) the evening hyperglycaemia is not a compensatory rebound (Somogyi effect) and hence 3) in this dog the duration of action of the insulin is only about 12 hours. Since the total action is shorter, both of the two peaks of insulin action are also earlier and shorter. The treatment which has been found satisfactory in these cases is as follows:

1. Divide the total daily amount of food into three equal meals. Give the first meal and dose of insulin early in the morning and the second meal 5-5½ hours later. Adjust the morning dose by measuring plasma glucose just before this meal.

2. Give the third meal 11-12 hours after the first, together with a second dose of insulin which is one-half of the morning dose. If in doubt, the second dose of insulin can be evaluated by measuring plasma glucose 3-4 hours later. Another (4th) meal is not usually required, but the owner should be alert to the possibility of occasional signs of hypoglycaemia late in the evening and then a snack or small meal can be given. For this reason it is better to start the daily program earlier, the three meals being given at, for example, 7.00, 12.30 and 18.30.

3. In cases seen thus far, the 2:1 relationship between the morning and the evening doses of insulin has been fairly dependable. If clinical signs and/or plasma glucose measurements indicate the need for a change in either dose, then it is usually correct to change both, maintaining the 2:1 proportion. The total daily amount of insulin usually exceeds 2 units/kg. It is fortunate that these patients are rare, for they present twice the number of possible complications as other diabetics. In any diabetic, the insulin requirement can change from time to time, but in these patients the first indication of a decreased requirement can be a hypoglycaemic episode during the night. Although more attention is required, treatment can be as satisfactory as in any other diabetic. We have not encountered a similar phenomenon in cats.

Antibodies against insulin can cause insulin resistance in man, but this appears to be a rare problem in the dog.

TIPS

1. Teach the owner to give the insulin injections subcutaneous on the lower half of the side of the body, not on the top or in the neck.
2. Most dogs and cats show less discomfort and awareness of the injection if it is given while they are eating. If there is still a reaction to the injection, the needle may be dull: try changing the syringe and needle at shorter intervals. Use a different injection site every day.
3. Strict avoidance of between-meal snacks is important in the beginning, to establish the correct dose of insulin. Later the owner can discover what snacks the dog can tolerate without disturbing regulation. Small pieces of fruit or raw vegetable or a bone to chew will have no significant effect, nor in most cases will a small cookie before going to bed.
4. The owner should always be prepared for unexpected hypoglycaemia and always carry sugar (preferably glucose) and a small portion of food in a plastic sandwich bag, in the auto, pocket or purse, when travelling or walking with the dog. It is better to give some extra food before going for an unusual walk (e.g., in the woods), out of the dog's normal daily routine, than to have to try to correct hypoglycaemia in the middle of the walk. With experience, the owner will learn how much is appropriate.

DIABETES MELLITUS IN THE CAT

ETIOLOGY

There is no recognized clinical syndrome of potential diabetes mellitus in cats, comparable to that in dogs, and the onset of clinical diabetes is usually without warning: the cat simply develops pu/pd, for which glucosuria and hyperglycaemia are found to be the cause. If veterinary examination is delayed, weight loss develops in spite of polyphagia. The clinical signs bear some resemblance to those of hyperthyroidism in cats, but the accent is reversed: polyphagia and weight loss usually predominate in hyperthyroidism while pu/pd predominates in diabetes mellitus, at least initially.

The ddx of DM in cats is in type 2 DM among other stress (probably number 1), obesity, progesterone, GH, hyperthyroidism, Cushing's disease in type and in type 1 among others amyloidosis. Amyloid may be found in the islets of Langerhans, but may be a consequence rather than a cause of the degeneration. Diabetes occurs most often in middle-aged or older cats (5-12 years) and apparently more often in castrated males. Since there is no known relation between endogenous progesterone and the development of diabetes in the cat, there is no indication for ovariohysterectomy, in contrast to the dog.

There have been a few documented cases of diabetes mellitus in cats caused by a growth hormone-producing pituitary tumour, with very high plasma levels of growth hormone and thus diabetes with very severe insulin resistance, as well as acromegaly. Diabetes mellitus also develops in cats being treated with megestrol acetate. The diabetes may stop if the megestrol acetate is stopped permanently and correct insulin therapy is started. Spontaneous Cushing's disease is rare in cats but diabetes mellitus is usually the first recognized clinical sign. The excessive use of corticosteroids can result in diabetes mellitus in cats as it does in dogs. Extreme obesity causes insulin resistance and in rare cases this can be the primary cause or a contributing cause of diabetes in cats. Uraemia also causes insulin resistance but this does not cause diabetes. Congenital diabetes mellitus does occur in cats but apparently even less frequently than in dogs.

In 30 to 50% of the cases, the insulin requirement begins to decrease spontaneously after 2-3 months of well-regulated treatment and then stops completely, following which the disease may or may not recur. The risk of recurrence will be reduced by a low-carbohydrate, yet complete, diet. Diabetes developing in extremely obese cats may disappear after a few weeks or months of effective insulin therapy and adequate reduction of the obesity. Begin regulation on a weight reduction diet alone per day and adjust the dose of insulin to this.

In spite a few unusual problems, diabetes mellitus is usually easier to regulate in cats than in dogs, the insulin requirement remains much more stable after initial regulation, and there are fewer and less serious unexpected episodes of hypoglycaemia. The stability of diabetes in most cats is fortunate, for urine glucose cannot be checked at will, as it can in dogs, and in a few cats the collection of blood samples is difficult without an extremely capable assistant.

MANAGEMENT OF DIABETES MELLITUS

Clinical diabetes mellitus in cats can only be treated with insulin. Oral medications are as ineffective and as strongly contraindicated in cats as they are in dogs.

Caninsulin®

The insulin preparation used in the routine treatment of diabetes in cats is the same as that used in dogs. Its two phases of action are approximately the same as in the dog and it is stored, handled and administered in the same manner.

Diet

The diet must be constant in composition and amount. It is best to use a commercial diet. The owner should determine the amount of (canned or canned plus dry) food from memory, weigh it on a scale, and thereafter give the same amount daily, divided into equal (weighed) meals. There is no strict need to give food twice daily. The effect of the food on plasma glucose is considerably less than in dogs. However, the cat can be trained to eat twice daily; this is preferred.

Treatment Schedule

The daily schedule is exactly as described for the dog, with one big exception. It might be best to treat the cat twice daily. The dose to use is 0.25 IU/kg BID in a cat less than 4 kg bodyweight and 0.5 IU/kg BID in a cat of more than 4 kg. All other items said for the dog also apply for the cat.

Explaining Treatment to the Owner

Treatment and its explanation to the owner are less complex for the cat than for the dog.

Ovariohysterectomy is not required and the possibility of Cushing's disease is far lower, as is the risk of developing cataracts. Other aspects of the explanation of treatment to the owner are the same as for the dog. After regulation is achieved initially by measurements of plasma glucose, most owners of cats can maintain quite good regulation by use of random measurements of urine glucose and clinical signs. The use of morning urine glucose measurements alone is as unreliable in the cat as in the dog, and failure to understand the Somogyi effect can lead to severe and potentially fatal insulin over dosage.

Hypoglycaemia

The causes, clinical signs and treatment of hypoglycaemia are the same as in the dog and should be explained in the same way. A small bottle of 50% glucose (10 g glucose in 20 ml water) can be kept in the refrigerator and 2 ml given orally will be adequate in most cats in the event of severe hypoglycaemia. A disposable 5-ml syringe should be provided for this purpose.