

How do you solve a problem like diabetes?

Ciara Feeney, Companion Animal Technical Advisor with Intervet, has carried out several practice, clinical club and CPD meetings discussing the management of diabetes mellitus. Here, she presents a number of frequently asked questions and problem clinical cases described by veterinary practitioners over the past 12 months.

Diabetes mellitus (DM) is one of the most frequently diagnosed endocrine diseases in dogs and cats. Regardless of the cause, DM is associated with insulin deficiency, which may be totally or partially due to insulin resistance (e.g., in cases of obesity). In general, the prognosis is good provided that it is diagnosed at an early stage, treated adequately and there is good owner compliance. The overall objective in treating a diabetic patient is to have a happy pet and a happy owner. This is achieved by eliminating the clinical signs so that the animal has a normal thirst, appetite, frequency and amount of urination and a stable weight. The aim is not to achieve a specific blood glucose concentration but rather to have the owner describe their diabetic pet as “doing well”.

Successful management relies upon drug treatment (insulin or oral hypoglycaemic therapy) and diet, but without a compliant owner the patient will not do well. As a technical advisor, I am often asked for advice on the management of these cases. The following are some of the issues which I have dealt with over the past 12 months.

How much and how often?

If a veterinary practitioner has diagnosed a new case he or she often wants to know what dosage of which insulin they should use and how often the insulin should be administered.

Commercial insulins are categorised by onset, duration and intensity of action after subcutaneous administration.

In Ireland there are four licensed insulin preparations:

- Lente pork U-40 insulin (Caninsulin, Intervet)
- Regular beef U-100 insulin (Insuvet Neutral, Schering Plough Animal Health)
- Lente beef U-100 insulin (Insuvet Lente, Schering Plough Animal Health)
- PZI beef U-100 insulin (Insuvet Protamine Zinc, Schering Plough Animal Health)

However, at the time of going to press, Caninsulin is the only commercially available product on the Irish market.

Cats

Traditionally, it has been considered that up to 70% of diabetic cats will require insulin while the remainder can be managed by proper weight control, correct diet and/or oral hypoglycaemic drugs such as glipizides. However, more recent data suggest that glipizide-stimulated insulin secretion can accelerate the loss of functional β cells (Nelson, 2003). Instead, early treatment of such cats with a small dose of insulin seems to have a protective effect and may increase the chances of completely weaning the cat

off insulin therapy. The general starting dose for insulin for a new feline diabetic patient is 0.25-0.5 units/kg or 1-3 units/cat administered in two doses per day to achieve best glycaemic control and minimise hypoglycaemia (Scott-Moncrieff, 2007). The dose should be adjusted in steps of 1 IU. Following adjustment, evaluation should not take place before a week in cats (unless there has been a hypoglycaemic episode).

Dogs

Apart from a condition such as dioestrous diabetes, where the diabetes may be reversible, all dogs with DM will require insulin therapy. Dosage is weight-dependent and the attending veterinary practitioner should follow the directions in the product data sheet. The available lente pork insulin is licensed for once-a-day administration. Approximately 70% of dogs will stabilise on this regime but the rest may need twice-daily administration.

In dogs, dose adjustment should be managed in steps of 10%. As with cats, evaluation should not take place before the new dosage has been given for a period unless there has been a hypoglycaemic episode. In the case of dogs, this period is three days.

I want to do things legally

If a practitioner has previously stabilised diabetic animals on human insulin, and now wants to use a licensed veterinary product, how do they switch over? It is difficult to have general guidelines regarding conversion from one type of insulin to another but, in most cases, it is not necessary to go back to an initial stabilisation protocol. I recommend the following four steps:

- 1) Initially reduce the dose by 10-20% compared with the previous insulin.
- 2) Ask the owner to monitor the animal closely for signs of hypoglycaemia during the first 12-24 hours after the first injection has been given.
- 3) Give the reduced dose for a period of five to seven days and ask the owner to monitor for clinical signs of DM. It would be particularly useful if water intake could be monitored.
- 4) Re-assess the animal after these five to seven days; ideally a blood glucose curve is made.

Remember to ensure that owners only use the correct syringes as human insulin is U-100 insulin and the commercially available insulin in Ireland is U-40 insulin.

The case of the over-eager client

A practitioner has been treating a newly-diagnosed diabetic

for the past month but the dog is not stabilising. What should they do? In this, an actual case, a long discussion with the client was key. It transpired that the vet had taught the client to home-monitor blood glucose concentrations. However, the client was a medical nurse and was changing the dosage of the insulin every day depending on the blood glucose results.

I thoroughly advocate the education of clients to home-monitor but it is always the responsibility of the attending veterinary practitioner to advise on changes in dosage. Monitoring of diabetic pets can be performed in a number of different ways. A monitoring plan should be tailored to each pet owner depending on their abilities. This could include:

- Water intake
- Appetite
- Frequency of urination
- Weight
- Blood glucose concentrations
- Urinalysis

(I believe that urine monitoring should not be used as a basis to change insulin dosage – see ‘Too much insulin?’ below. Urine monitoring, however, can be a quick and easy way to test for ketones.)

Serial blood glucose curves (Figure 1) are an excellent way to identify the cause of inadequate regulation. The blood tests are generated at home as this minimises stress and allows the pet to follow his/her normal daily routine. Twenty-four-hour blood glucose curves can then be easily generated. In my experience, most owners of diabetic pets will be willing to carry out this procedure over a weekend on a two-hourly basis. However, the attending veterinary practitioner should be satisfied that there is full owner compliance and good injection technique before requesting this.

In practice, generating a 24-hour blood glucose curve



Figure 2: Marginal ear vein technique (van de Maele *et al.*, 2005). Photo: A. Schulze, c/o Intervet Germany.

is only practical in a hospital situation where there is a member of staff on duty round the clock. Alternatively, a 12-hour blood glucose curve could be generated during the day if the client is unable or unwilling to carry out the procedure.

The marginal ear vein, which is easily recognised in dogs and cats, is a good point from which to take blood (Figure 2). Hair can be clipped in long-haired animals. A stable background can be created with the use of a cylindrically shaped object (e.g., bandage roll). The vein is punctured with a needle or lancet and a sufficient drop of blood can be obtained. A portable glucometer can then be used to give a blood glucose concentration within 30 seconds. Afterwards, pressure is applied to the punctured site to avoid excessive bleeding.

Too much insulin?

After two months, you have a dog that is still losing weight and drinking excessively: what do you do? In this case, a 7.7kg, eight-year-old female neutered West Highland

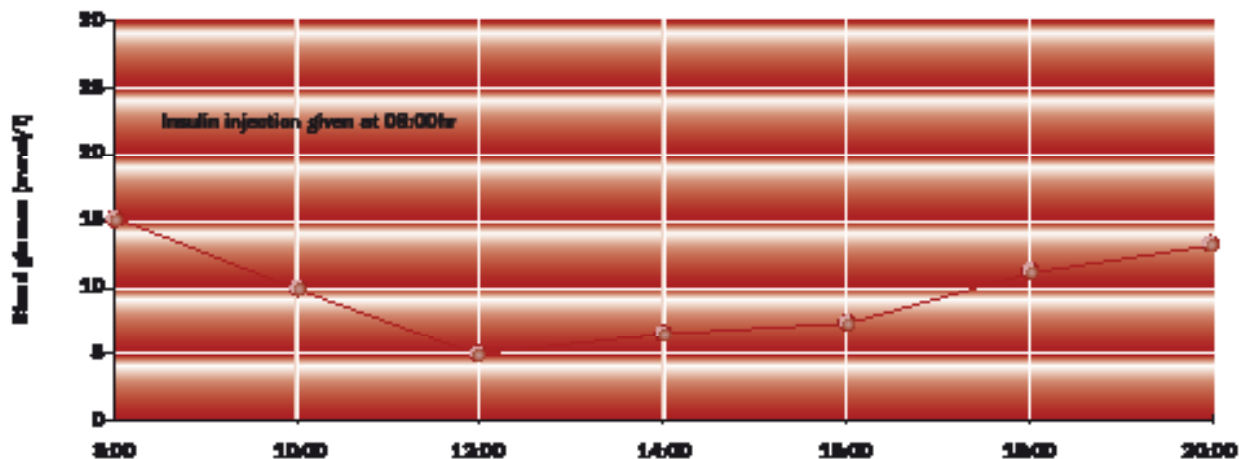


Figure 1: Ideal blood glucose curve in a treated diabetic dog (taken over 12 hours). Insulin was administered at 08:00hr. Normal blood glucose in non-diabetic dogs ranges from 3.5 to 6.1 mmol/l. The renal threshold is 10 mmol/l. A stable diabetic dog maintains a blood glucose range of 5–12 mmol/l for most of a 24-hour period.

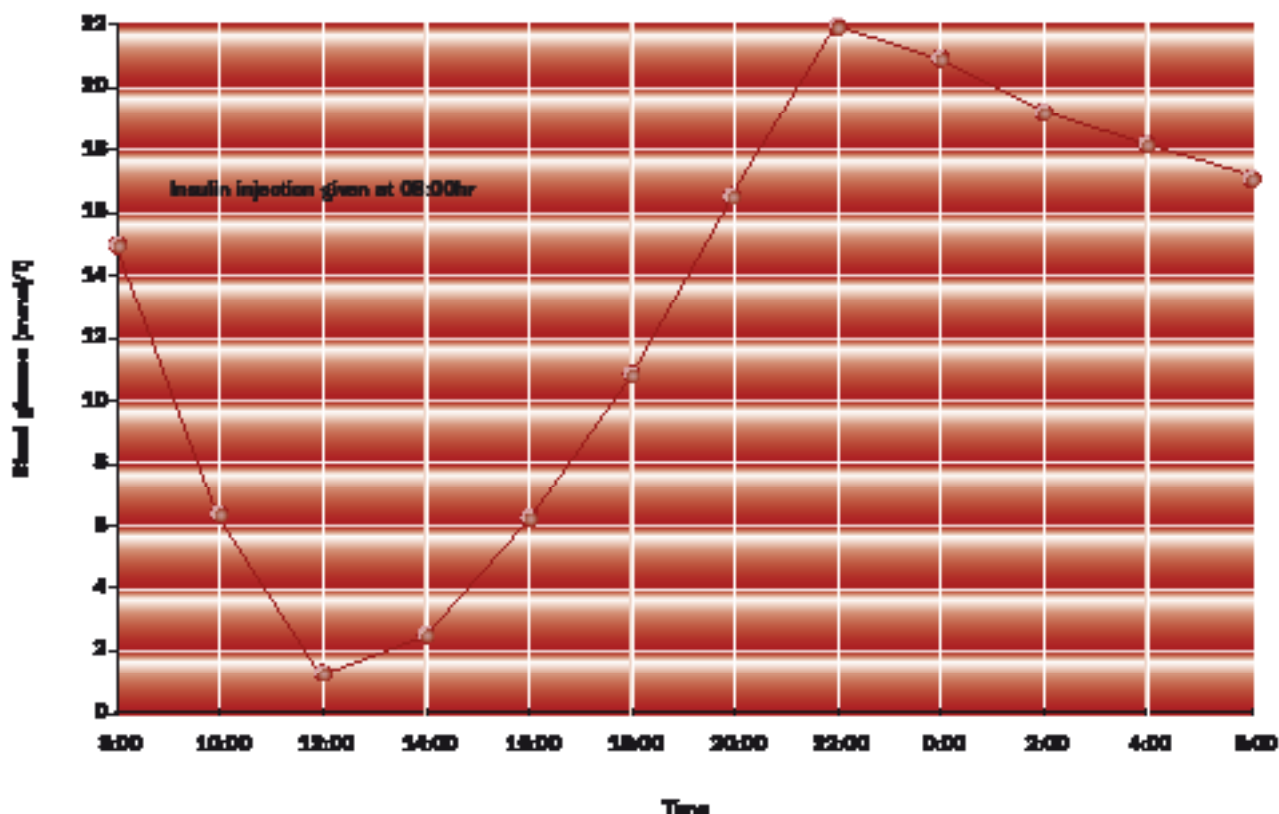


Figure 3: A 22-hour serial blood glucose curve in a canine diabetic revealed a hyperglycaemia response known as the 'Somogyi effect'.

white terrier was receiving 14 IU in the morning and 8 IU in the evening. This dosage was based on the fact that there had been glucose in her urine every day for the past two months. The dog was admitted for a 22-hour serial blood glucose curve (Figure 3), which revealed a hyperglycaemia known as the 'Somogyi effect'.

An insulin dose that is too high may bring about the Somogyi effect or rebound hyperglycaemia. This can also be produced if blood glucose concentrations fall too rapidly. The moment that the Somogyi effect, a life-saving response, is triggered is very individual to each animal.

The body attempts to counteract the decline in the blood glucose concentration through a chain of reactions:

- The blood glucose concentration falls rapidly or approaches hypoglycemia (a blood glucose concentration of less than 5 mmol/l) following the injection of insulin. The animal can become hungry and either restless or lethargic.
- In response to a declining blood glucose concentration in the CNS, adrenaline and (subsequently) cortisol, glucagon and growth hormone are released.
- These hormones bring about an increase in the blood glucose concentration (through gluconeogenesis, release of glucose from hepatic glycogen and increased peripheral resistance to insulin).

The resultant hyperglycaemia produces polyuria and polydipsia. This can easily be misinterpreted as a result of an inadequate dose of insulin. If the morning polyuria

is thought to be the result of an insufficient insulin dose and a higher dose is given, the problem will be aggravated and an even more pronounced Somogyi effect will follow. Eventually, the counter-regulatory mechanisms become exhausted, resulting in severe hypoglycaemia.

Hyperglycaemia due to a Somogyi effect can sometimes persist for as long as three days after a single hypoglycaemic episode. As a result, blood glucose concentrations do not always normalise within a few days after lowering the insulin dose.

Although the attending veterinary practitioner should be highly suspicious if the dosage of insulin is exceeding 2 IU/kg, a blood glucose curve is the only diagnostic tool that can be used to detect a Somogyi effect. Either of the following blood glucose curves indicates the Somogyi effect:

- Hypoglycaemia (low nadir) followed by rebound hyperglycaemia.
- A rapid decrease in blood glucose with an adequate nadir, followed by rebound hyperglycaemia.

The insulin dosage should be immediately reviewed, often resulting in a decrease of the dosage by more than half. In the case highlighted above, the insulin was reduced to 9 IU once-daily. The client was asked to monitor the dog's water intake. The dog is now doing well, with stable weight and normal thirst, on this dosage.

How many problems can one dog have?

In another case, a veterinary practitioner was concerned about a seven-year-old, 5kg male Pomeranian which was not stabilising on 7 IU of insulin twice a day. The vet was advised to generate a serial blood glucose curve which revealed that the dog was suffering from the Somogyi effect. The dosage of insulin was reduced to 6 IU once-daily. The dog did well for a month until he was presented for excessive thirst.

The blood glucose curve at this stage was acceptable for a diabetic patient. However, there was blood in the urine. Radiographs of the abdomen were taken and revealed a large urinary calculus which was surgically removed and the appropriate dietary changes were made. The dog continued to recover well from surgery. However, six weeks later, he again presented with excessive thirst. Urinalysis revealed a specific gravity of 1.009. Everything else was normal. An ACTH stimulation test was performed again at this stage and a diagnosis of Cushing's was made. Underlying disease must always be considered if a pet is not stabilising.

"To spay or not to spay?"

'Tiny' (a 10kg, eight-year-old entire female terrier cross) was diagnosed with DM in September 2006. The attending veterinary practitioner reported that she had never really "done well" and had a variable weight and excessive thirst. In January 2007 she came into season and was presented thereafter in a ketoacidotic state. She recovered after intensive treatment. However, the dog still continued to drink excessively and have a fluctuating weight. The decision was then made to spay her. Since the surgery, her weight is normal for her size and breed and her thirst is no longer excessive. It is advised that entire females should be spayed as soon as possible after diagnosis of DM.

'Ruath' (a 22kg, nine-year-old, entire female red setter) was diagnosed with DM. She was spayed six weeks after the diagnosis. Two months after the surgery she presented with excessive thirst while receiving 28 IU insulin per day. The attending veterinary practitioner generated a serial blood glucose curve which revealed the Somogyi effect. The dosage of insulin was dropped to 10 IU daily and the dog did well for two weeks but again presented with excessive thirst. It transpired that the dog went into diabetic remission after ovariohysterectomy. In this case, the diabetes was secondary to dioestral diabetes, which was reversible.

Long term maintenance of diabetic patients

Due to their shorter life span, diabetic dogs seem to develop fewer long term complications than human diabetics. The maintenance of optimal blood glucose concentrations can, however, help to minimise these further. After a diabetic animal has been stabilised successfully, routine checks should be carried out around three- to six-month intervals. Careful monitoring and control during maintenance is

important to limit the long term complications associated with diabetes, which can be associated, in turn, with prolonged hyperglycaemia, including cataracts, retinopathy and neuropathy.

Conclusion

The prognosis for a diabetic animal depends to a large extent on the level of confidence, knowledge and dedication of the owner. These factors can be influenced favourably by the attitude of the veterinary practice as a whole. The quality of information and level of support offered by both veterinary practitioners and veterinary nurses can make a very significant difference to the long term outcome for our diabetic patients.

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