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Diabetes mellitus (DM) is a common endocrine disorder, with an incidence of between 1 in 100 to 1 in 500 dogs. The majority of dogs with diabetes mellitus will be successfully stabilised and will remain stable for long periods of time. However a significant minority will either become unstable again or will be difficult to stabilize from the outset. The most common cause for instability is failures in the daily management of the patient. Problems associated with insulin resistance and Somogyi effects are quite rare. When investigating instability always start by checking the daily routine and equipment supplied to the owner, before embarking on a search for complex causes of instability. This paper will focus on diabetic management and the causes of insulin resistance.

**Goal of diabetic management**

The main goal is the elimination of owner-observed clinical signs by limiting blood glucose fluctuations and maintaining near-normal blood glucose levels. These are achieved through:

- Proper insulin administration
- Dietary therapy
- Exercise
- Avoidance or management of concurrent inflammatory, infectious, neoplastic or hormonal diseases

**Insulin therapy**

Insulin is classified according to its promptness, duration and intensity of action.

**Short acting insulin:** This is represented by the crystalline insulin “Actrapid”ä. It is used chiefly in the management of DKA. It may be given by any route. It has a rapid onset of action (minutes) and a short duration of effect (hours) and is very potent.
**Intermediate acting insulin:** These are represented by “Protophane”â. They are used mainly in the management of canine DM on a twice daily basis given subcutaneously. They have an intermediate duration of effect in dogs (lasting 6-8 hours usually) and are moderately potent.

**Long acting insulin:** This is represented by “Ultratard”â. This is occasionally used in the management of feline DM. It has a long duration of effect (usually between 12 and 18 hours). It is the least potent of all the insulins.

**Veterinary insulin:** The only insulin registered for veterinary use is “Caninsulin”â. It is regarded as an intermediate acting insulin in cats (usually needing twice daily administration) and a longer acting insulin in dogs (frequently once daily usage is sufficient). Generally this is the insulin that most veterinary patients are started on. It comes in a convenient strength of 40 IU per ml.

**Different species of insulin:** Human insulins are either porcine, bovine or recombinant human. Dogs generally respond better to porcine insulin and cats to bovine insulins. Combinations exist and the recombinant human technology is becoming more and more popular. Caninsulinâ is porcine.

There are many “recipes” out there for the management of diabetic dogs and cats. It is important that the protocol one decides to use is scientifically defendable and effective and that one becomes familiar with whatever products you use. The greatest majority of diabetics will be relatively easy to manage.

**Initial insulin treatment of the diabetic dog:**
Intermediate insulins are the initial insulins of choice (Monotardâ, Protophaneâ, Caninsulinâ). These are given twice daily (12 hrly with feeding at each injection) in the case of Monotardâ and Protophaneâ and once daily in the case of Caninsulinâ (with twice daily feeding). The starting dose is usually around 0.25 to 0.5 IU /kg per dose. This dose is kept up for a period of around a week and glycaemic control is then assessed.

**Initial adjustment of insulin therapy:**
The goal after the first visit (during which diagnostic evaluation occurs and the insulin treatment is initiated) is not to establish the ideal insulin dose. This will take anything from 4 – 8 weeks. The owner has a lot to learn and get used to after this first visit. The patient needs time to equilibrate to the insulin given and the metabolic derangements will slowly begin to reverse. Insulin dose should not be adjusted without a blood glucose curve. Adjustment of the dose (if done in the home environment) should not occur for at least a week following initiation of treatment. The dose will need adjustment if the owner continues to complain of clinical signs or examination of the patient’s condition deems it necessary (e.g. ongoing weight loss).

**Generating the serial blood glucose curve:**
Blood glucose should be measured every 1 – 2 hours for as many hours of the day as possible (ideally 24 hrs, but preferably not less than 12). It should always include the nadir (lowest blood glucose) and the peak blood glucose level and be constructed around at least one injection and feeding – preferably both injections (in the case of twice daily injections). This is usually done in hospital, although some owners can be taught to do this in the home environment. Hospitalization is stressful and may make reading the curve impossible in nervous dogs. Hand-held blood glucose machines are useful for these determinations. Keep in mind that they are programmed to read blood glucose lower than it actually is, at the low end of the scale (to prevent missing
hypoglycaemia in human patients).

You never get the information you need to properly adjust insulin dose on only one or two blood glucose levels in a day and even less so on urine dipstick information. The ideal curve keeps glucose between 5.5 and 11 mmol/l and not below 4.5 mmol/l in the dog. This may not be achievable and despite a poor curve some animals do well – in cases like this, believe the owner and the clinical examination, rather than the curve information.

**Interpretation of the serial blood glucose curve:**

There are 3 important questions to be considered when evaluating a glucose curve:

1. Is the patient insulin sensitive? I.e. does the insulin dose have any glucose lowering effect? If insulin is ineffective one should consider under-dosage or reasons for resistance. Insulin resistance should be considered if the dose used is more than 2 IU /kg /dose in the dog.
2. What is the lowest point to which the glucose drops (the glucose nadir)? Ideally the nadir should be between 5.5 and 7 mmol/l. If it is higher than 9 mmol/l the dose should be increased and if it is lower than 4.5 mmol/l it should be decreased. Insulin doses should not be changed by more than 25% at a time and not more frequently than weekly.
3. What is the insulin’s duration of effect? Frequency of administration should not be changed until an acceptable nadir is achieved. Duration of effect is defined as the time from insulin injection until blood glucose increases to beyond 12 – 14 mmol/l.

There are a limited number of ways that you can respond to try and correct glucose curves that demonstrate poor control. These include:

1. Change the insulin dose to affect the nadir.
2. Change the frequency of insulin dosage to affect the duration of effect.
3. Eliminate causes of insulin antagonism.
4. Ensure that the owner is storing, drawing up and injecting the correct volume (this is still one of the most common problems with DM control).

**Glycosylated haemoglobin (Hb) and fructosamine:**

Proteins left in the presence of high glucose concentrations will glycate with time (a CHO will attach to the protein). The glycated protein becomes a marker of blood glucose concentrations during the circulating life span of the protein. Glycation takes a relatively long time to occur and is permanent once it has happened (hence the glycated protein circulates until the protein has been cleared – i.e. for the life span of the red cell in the case of glycosylated Hb. The concentration of a glycated protein thus becomes a reflection of the average glucose control over a long time. Glycosylated Hb will reflect the previous 4 – 8 weeks of control and fructosamine the previous 1 to 3 weeks. These measures may be used in lieu of blood glucose curves – especially in cats that develop stress hyperglycaemia easily or in dogs that do not tolerate blood glucose curves. The assays are freely available and cost effective.

**Dietary therapy should be aimed at:** correcting obesity, maintaining consistency in timing of feeding and caloric consent and minimizing post-prandial glycaemic swings.

**Dietary fiber and complex carbohydrates (CHO):** High fiber, complex CHO diets are ideal as they slow glucose
absorption, minimize post-prandial glucose fluctuations and promote weight loss. It is more important to get a diabetic eating than to have it eating the perfect diet. High fiber diets are often not all that palatable and time for gradual adaptation should be allowed. A diabetic patient may be obese and needs to lose weight to achieve ideal weight, but should not be thin. Thin diabetics will need to gain weight. Obesity induces a state of insulin resistance. Some fat cats’ diabetic state will spontaneously resolve once their weight is corrected and fat dogs are certainly a lot more difficult to control. There are no firm recommendations regarding protein content and a low restricted fat diet is usually recommended.

**Feeding schedule:** Feeding must be regular, scheduled and always the same amount. ROUTINE is the key to managing diabetic animals. Traditionally feeding occurs twice daily with injections, i.e. food in the gut should be providing glucose to the blood at the same time that the injected insulin has its peak effect.

**Exercise:** Regular scheduled exercise helps glycaemic control through weight management and enhanced insulin sensitivity.

**Complications of insulin therapy:**

**Hypoglycaemia**

This occurs with sudden increases of insulin dose, sudden inappetance, strenuous exercise or using insulin twice a day when the duration of effect overlaps slightly and the previous injection has additive effects on the later injection. Clinical signs include weakness, shivering, tachycardia and ultimately seizures (due to neuroglycopaenia). Treatment must be prompt and can be per os or IV.

**Somogyi over-swing phenomenon**

This results from a normal physiologic response to hypoglycaemia induced by excessive insulin. When the blood glucose drops to below 3.3 mmol/l or falls very quickly (note: it’s not only the level it falls to, but also the rate at which it falls), several important protective hormones are released (the “diabetogenic” hormones). These are catecholamines, cortisol, growth hormone and glucagons. In fact glucose levels will often rise above normal levels, subsequent to their release. The animal persists with its diabetic signs, because it spends the majority of the 24-hour cycle with high glucose levels. The clinician’s “knee jerk” response (a response based on clinical signs alone without glucose curve information) is to raise the insulin dose. This results in an even more severe drop, and even more vigorous endocrine response and an even higher over-swing hyperglycaemia. The correct action to take in these cases is to reduce the dose of insulin.

**Short duration of insulin effect**

The objective of any treatment plan is to keep blood glucose below renal threshold for as much of the day as possible (20 hours or more). Correction involves increasing the frequency of insulin dosage (to twice a day if it is only being used once daily) or to use an insulin with longer duration of effect. Caninsulina can be used safely twice daily in cats, but in dogs this should be instituted carefully, because after several days of twice daily use, the effects of the first dose in the day may not have completely waned by the time the second is given and this may have an additive effect and induce hypoglycaemia several days into the program.
Insulin resistance

**Definition:** For most diabetic dogs adequate control can be achieved with a dose of around 1 IU /kg once or twice daily. Resistance should be suspected if the dose goes above 2 IU /kg /dose. The most common cause of this is poor technique on the part of the owner.

**Causes of poor response include:**

**Obesity**

Reversible insulin resistance occurs because of down regulation of receptors. Fiber content and caloric density of the diet should be attended to correct this.

**Administration techniques and insulin activity problems**

Ensure that you observe the person who injects the insulin so that it is given properly. Insulin needs to be kept in the fridge (not freezer) and being a protein, must not be shaken vigorously. Warming and shaking inactivate it. Mark the syringe with a piece of tape, watch the owners draw up the correct amount and ensure you see them inject it correctly. Let them practice with saline several times.

**Impaired insulin absorption**

Remind the owner to vary the injection site, because large granulomas which delay absorption can develop at repeatedly used injection sites.

**Circulating insulin-binding antibodies (VERY RARE)**

The insulins used are of bovine, porcine or recombinant human origin and as such, anti-insulin antibodies may develop. If this is suspected, change the species of insulin origin.

**Concurrent diseases causing insulin resistance**

In dogs, Cushing’s disease, bacterial infections, organ insufficiency, di-oestrus and hypothyroidism should be considered important causes of insulin resistance.

**Further reading:**
2. Feldman and Nelson’s Canine and feline endocrinology and reproduction 2004, 3rd edition, Elsevier science, USA