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DIABETES MELLITUS (DM) IN DOGS AND CATS

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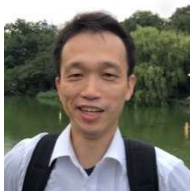

Diabetes mellitus (DM) is a heterogeneous group of diseases with multiple etiologies characterized by hyperglycemia resulting from inadequate insulin secretion, inadequate insulin action or both[*1].

Pathogenesis

When considering the clinical signs of DM in dogs and cats, analyzing what causes the signs is important. The structure of DM pathogenesis is shown in Fig. 1. DM is caused by underlying diseases. Underlying diseases for DM in dogs and cats differ and these are summarized in Fig. 2. DM has direct symptoms of hyperglycemia which may cause various complications.

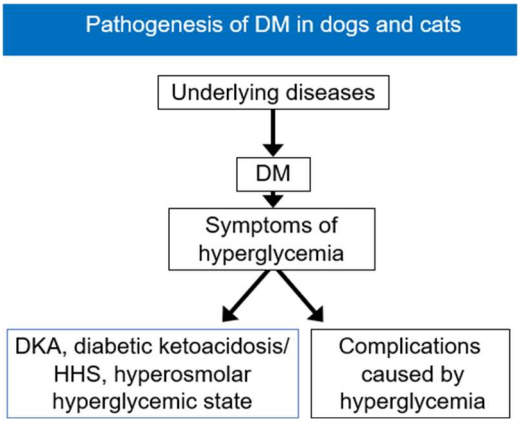

Fig. 1 Pathogenesis of DM in dogs and Cats

Main underlying diseases for DM

Dog	Cat
Immune-mediated insulitis	Islet amyloidosis
Pancreatitis	Obesity
Hyperadrenocorticism	Pancreatitis
Diestrus-induced	Acromegaly
Drug	
Infection	
Concurrent illness	

Fig. 2 Underlying diseases for DM

Fig. 3 shows the clinical signs directly caused by hyperglycemia in DM dogs and cats. If DM becomes severe, Diabetic Ketoacidosis (DKA) or Hyperosmolar Hyperglycemic State (HHS) may develop.

Clinical signs directly caused by hyperglycemia in DM dogs and cats

- PUPD	- ↑ GLU (even in the fasting status)
- Weight loss	- ↑ TCHO
- Dehydration	- ↑ TG
- Glycosuria	- ↑ ALT, ALP (typically <500 U/L)
	- ↓ Na
	- ↑ K

PUPD: Polyuria and polydipsia

Fig. 3 Clinical Signs caused by Hyperglycemia

Clinical signs of DKA

- Clinical signs of DM
  +
- Hyperglycemia
- Ketonuria
- Severe dehydration and acidosis ⇒
  - Vomiting, lethargy, shock, etc…
  - Lactic acidosis
  - Prerenal azotemia (BUN, CRE↑)
  - Hyper viscosity ⇒ thrombosis
  - ↑Aldosterone ⇒ ↓K
  - ↑Catecholamine, metabolic stress
    ⇒ ↑Lipolysis, WBC, insulin resistance

Fig. 4 Clinical Signs of DKA

In addition to hyperglycemia and ketonuria, severe problems like vomiting, lethargy, shock, lactic acidosis, prerenal azotemia, hyper viscosity, hyperaldosteronemia, hypercatecholaminemia, metabolic stress can occur as the clinical signs of DKA (Fig 4). For HHS, aside from the clinical signs of general DM, there are characteristic clinical signs of HHS that are related to severe dehydration. Severe dehydration reduces neurological activity. Then, lethargy, depressed, comatose, etc… may occur. In blood chemical examinations, GLU is over 600 mg/dL, hyperosmolality is over 400 mOsm/kg, and ketoacidosis is not observed. Sodium and potassium concentrations are very variable (Fig 5).

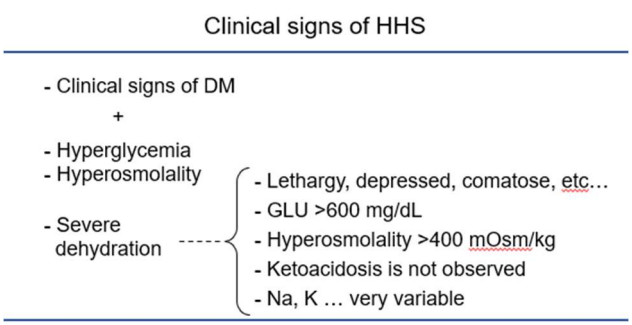

Fig. 5 Clinical Signs of HHS

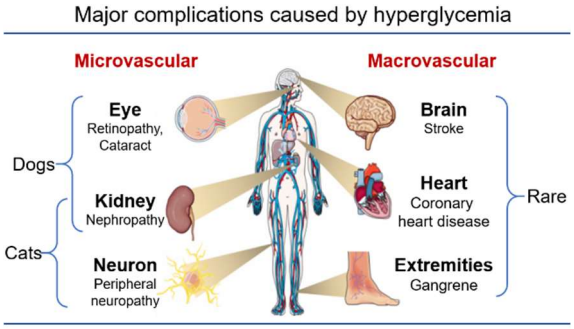

Fig. 6 Major complications caused by Hyperglycemia

Fig 6. Shows the major complications caused by hyperglycemia in humans[*2]. Hyperglycemia has glucotoxicity which causes various vascular to be damaged. Retinopathy, and cataracts for eyes, nephropathy for kidneys, and peripheral neuropathy for neurons are some of the microvascular damages. On the other hand, stroke for the brain, coronary heart disease for the heart, gangrene for the extremities are macrovascular damages that may occur. Interestingly, the prevalence in dogs and cats are different from those in humans. Eye and kidney damages can be seen in dogs, and kidney and neuron damages can be seen in cats. However, macrovascular damages are rare in these animals.

Diagnosis of DM

The diagnosis of DM in dogs and cats are a little bit variable between guidelines, but generally DM is diagnosed by these 3 points[*3]. 1: Appropriate clinical signs such as polyuria/polydipsia (PUPD), polyphagia, and/or weight loss. 2: Persistent fasting hyperglycemia such as over 200 mg/dL for dogs, >250-300 mg/dL for cats. 3: Persistent glycosuria. When all these 3 points are observed, the animal is diagnosed with DM. Caution must be taken when testing cats for Hyperglycemia, as cats can become hyperglycemic due to stress. Countermeasure and alternatives are shown in Fig. 7. Measuring fructosamine (FRT) or glycated albumin (GA) instead of glucose can be an alternative for this situation.

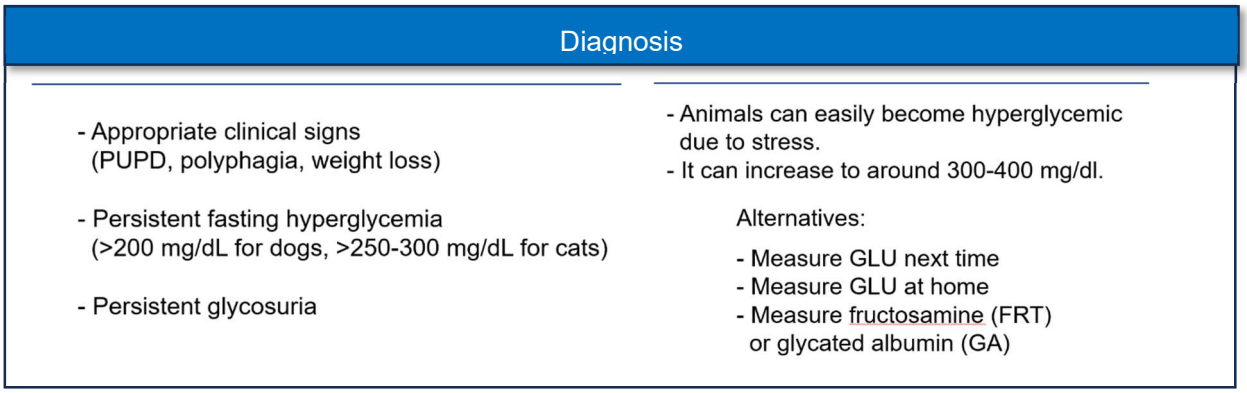

Fig. 7 Diagnosis of DM and cautionary point when testing for Hyperglycemia

Treatment and Monitoring

In treating DM in dogs and cats, one must consider the following treatments: treatment of the underlying disease, dietary therapy, and insulin treatment.

Dietary therapy for DM dogs and cats is summarized in Fig. 8. DM dogs are not mainly type 2 DM. So carbonate restriction in dogs is milder than that in cats. In general, low-fat + high-fiber food such as glucose-balance diet and other diabetic prescription foods should be used. Avoid saccharides, propylene glycol, and corn syrup to minimize the postprandial hyperglycemia. DM cats are similar to type 2 DM. So low carbohydrate + high protein food such as glucose-balance diet, and other diabetic prescription foods are better than other foods. If the cats are obese, correction of obesity is the most beneficial step. In the early stages of DM, sometimes dietary changes alone can be enough to effectively control blood glucose levels. Feeding method is also important. Maintain consistency in the meals, for instance, same timing, same contents, and same amount. Eat slowly to prevent postprandial hyperglycemia. Frequent feeding is also one option.

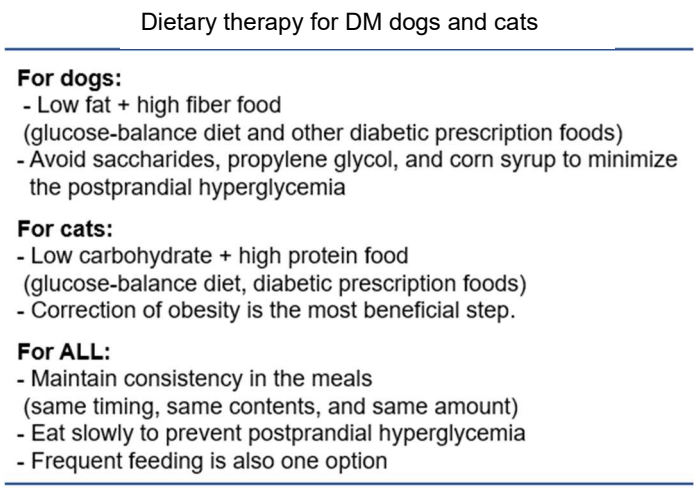

Fig. 8 Dietary Therapy for DM dogs and cats

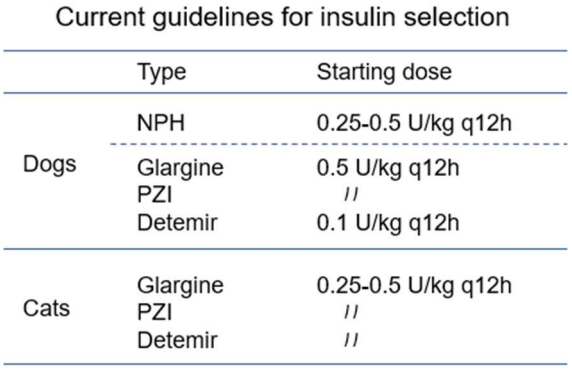

Fig. 9 Guidelines for insulin selection

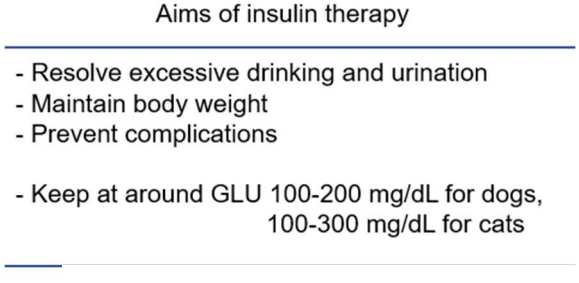

Fig. 10 Aims of Insulin Therapy

The current guidelines for insulin selection are shown in Fig 9[*4]. For dogs, it is recommended to start with NPH at this dose. Next, consider glargine, PZI, and detemir. There is no specific recommendation as to which one to start with for cats. There are three goals of insulin therapy (Fig. 10[*5,6]). Eliminate excessive drinking and urination. Maintain body weight. Prevent complications. To achieve these, GLU should be kept at around 100-200 mg/dL for dogs and 100-300 mg/dL for cats. One reason for the difference between dogs and cats is that the kidneys have different urinary glucose outflow thresholds.

Monitoring glucose is important in treating DM. Invasive blood glucose device and patch-type continuous glucose measuring device (CGMS) are tools to help monitor glucose. Fig. 11 shows an example of CGMS data. The red arrows indicate the timing of feeding and insulin administration. The Y axis of the graph ranges from 0 to 350 mg/dL. The vertical axis shows the gray zone from 100 to 160, but this is software for humans, so this area is inevitably gray. As the days go by, from days 3, 4, and 5, you can see that blood sugar management is gradually getting better. Use this device wisely to manage glucose levels in dogs and cats.

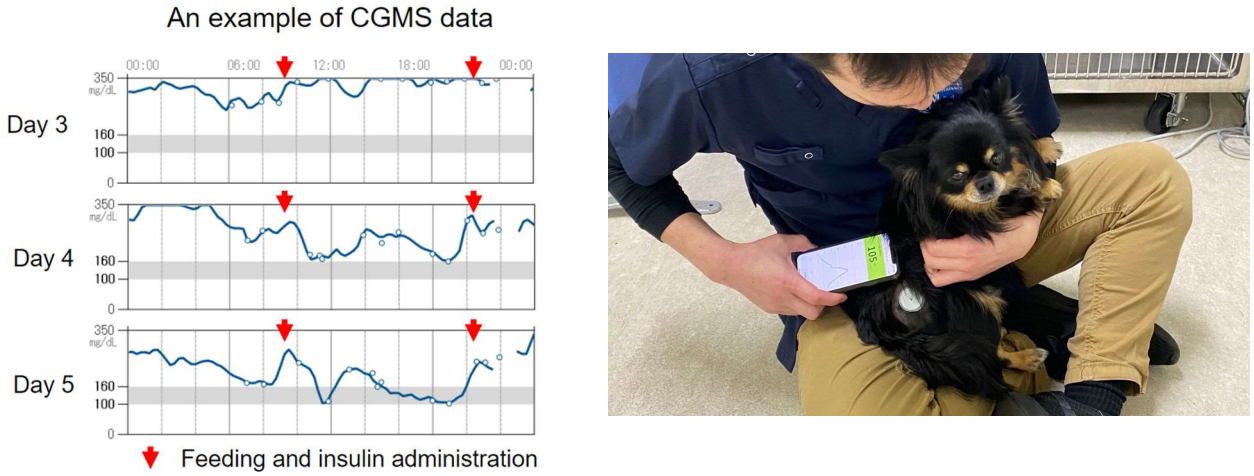

Fig. 11 Monitoring of glucose by Continuous Glucose Monitoring System (CGMS)

Reference:

*1 Vet J. 2022; 289: 105910.

*2 https://www.diabetesdaily.com/

*3 J Am Anim Hosp Assoc 54:1–19, 2018.

*4 Vet Med Res Rep. 2015; 6: 129-142

*5 J Feline Med Surg 17:235–250, 2015.

*6 J Am Anim Hosp Assoc 54:1–19, 2018.

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