

Diabetes Mellitus

- Understand the expected clinical signs and clinicopathological abnormalities caused by insulin deficiency in a diabetic patient.

Clinical Signs of Diabetes include polyuria, polydipsia, polyphagia, and weight loss

Physical exam findings may be unremarkable or have evidence of weight loss (not always thin, could have gone from a BCS of 7/9 to 5/9). There may be hepatomegaly due to a vacuolar hepatopathy and dogs often get diabetic cataracts. Cats may have a diabetic neuropathy with a plantigrade stance.

In veterinary medicine, diabetes is a spectrum between insulin deficiency and insulin resistance. Dogs typically have an absolute insulin deficiency which is similar to the human “Type 1” form while cats often have relative insulin dysfunction/deficiency which is more similar to the human “Type 2” disease.

Renal Glucose Thresholds

Dogs: ~180mg/dL

Cats ~270mg/dL

Insulin Overview

- Insulin is secreted by B cells of the islet of Langerhans in the pancreas. The most prominent function is to promote the uptake of glucose by cells which is done through the glucose transporters (GLUT-4) on the surface of muscle and adipose tissue. Insulin is an anabolic hormone and facilitates the uptake of amino acids in muscle promoting protein synthesis. It inhibits the synthesis of glucose in the liver and promotes the synthesis of triglycerides in adipose tissue. It also leads to increased glycogen deposition by increasing its synthesis and inhibiting its degradation. Glycogen is stored glucose in the body.

DM in Dogs	DM in Cats
Prevalence ~ 0.5% Females > Males; middle-aged to geriatric Schnauzers Absolute insulin deficiency Immune destruction of B-cells Cataracts typically develop within a year in 80% of cases	Prevalence ~1% B-cell loss/dysfunction in combination with insulin resistance (~75% of cases) May be comparable to type-II diabetes in humans Weight loss and diet can minimize insulin requirements and can result in remission in 10-30% of cats Insulin is usually required at the time of diagnosis for the best chance of remission Risk factors: obesity, male, geriatric, sedentary lifestyle, Burmese cats

Laboratory Findings

CBC	Chem	UA
Generally unremarkable Increased HCT if dehydrated Increased WBC with concurrent infection/inflammation	Fasting hyperglycemia Elevation in liver enzymes (vacuolar hepatopathy and pancreatitis) Hyperlipidemia (increased cholesterol and triglycerides) due to a decrease in lipoprotein lipase Pre-renal azotemia if dehydrated Electrolyte abnormalities (hyponatremia)	Glucosuria Possible ketonuria Possible bacteriuria

Glycosylated Proteins

- Fructosamine (albumin/globulin/etc.) ~2-3 weeks
- Hb-A1c (RBC): ~ 2-3 months (70 days in cats and 110 days in dogs)

Pancreatic physiology

Alpha	Beta	Delta	Epsilon	PP/"F"
Glucagon GLP-I	Insulin Amylin (75% of the islets)	Somatostatin	Ghrelin	Pancreatic Polypeptide

Glucose homeostasis

Cortisol, glucagon, epinephrine, growth hormone, and meals all increase BG while insulin and exercise decrease BG

Insulin Resistance

Obesity, hyperlipidemia, inflammation (pancreatitis), infection, endocrinopathies, diestrus, cardiac and renal disease

Hypersomatotropism in cats

~25% of cats also have hypersomatotropism which is an increase in growth hormone leading to severe insulin resistance and DM. IGF-1 is a proxy for growth hormone and is the test of choice. Hypersomatotropism is a biochemical diagnosis whereas acromegaly is a clinical dx based on a phenotypic appearance.

- **Understand the components of treatment of DM (diet and exercise, oral hypoglycemics, insulin, and other therapies)**

Treatment

Insulin

*need to shake if in suspension form, this can alter the insulin concentration!!!

- Degludec
 - U100 and U200
 - Available in a pen and vial
 - Amino acid modifications
 - Long lasting
 - For use in dogs and cats
 - Longest-acting insulin in people
- Glargine (Toujeo)
 - U300 (slower onset of action due to a smaller surface area)
 - Pen form
 - Amino acid modification
 - Long lasting
 - For use in dogs and cats

Starting dose

- Dogs
 - 0.25 u/kg SQ q12h
- Cats
 - 1u SQ q12h

Once-daily starting dose

- Dogs
 - 0.4 u/kg SQ q24h
 - ~60-80% of dogs are controlled q24
- Cats
 - 2u SQ q12h
 - ~50-60% of cats are controlled q24

Diet (refer to Dr. Larsen's lecture)

Exercise (not as successful with cats)

Oral anti-hyperglycemics (SGLT-2 inhibitors)

These either promote insulin secretion, increase insulin sensitivity, decrease glucose absorption from the GIT or increase glucosuria

SGLT2 inhibitors inhibit glucose reabsorption in the kidneys and increase glucosuria. They are nice because they block glucose reabsorption but not all of it and therefore they cannot make the animal hypoglycemic!

SGLT-2 Inhibitors

Bexacat (bexaglifloxin)	Senvelgo (velaglifoizin)
FDA-approved anti-hyperglycemic for cats Only labeled for cats > 3kgs that are not on insulin Augment glucosuria which lowers BG and reduces glucose toxicity to beta cells and allows them to recover At risk for euglycemic DKA which may be missed Home ketone monitoring is CRITICAL 15mg tablet: 1 po q24h	FDA-approved anti-hyperglycemic for cats No weight minimum (can't be on insulin) Augment glucosuria which lowers BG and reduces glucose toxicity to beta cells and allows them to recover At risk for euglycemic DKA which may be missed Home ketone monitoring is CRITICAL 15mg/ml solution: 1mg/kg po q24h

GLP-1 Agonists

Used weekly in humans, studied monthly in cats

GLP-1 = endogenous hormone secreted from GI epithelium after a meal

- Potentiates insulin and inhibits glucagon as BG increases
- Slows gastric emptying (nausea) which decreases appetite and can lead to weight loss
- May stimulate beta cell proliferation
- Minimal effect with normal BG

Optimizing treatment!

- Minimize insulin errors
 - Consistent day-to-day diet
 - Exercise
 - Ideal body weight
 - Address comorbidities that cause insulin antagonism
- Understand the various monitoring options (clinical signs, fructosamine, continuous glucose monitoring) and their advantages and disadvantages**
- Clinical signs (PUPD, PP, Weight loss)
 - Fructosamine or Hb-A1c
 - CGM
 - Urine glucose/ketone strips, at-home BG/ketone monitoring
 - Inpatient glucose curve, no longer recommended due to stress in-hospital

Remission

Cats can go into remission since they are often insulin resistant. This can be done with lifestyle changes such as weight loss and exercise. Remission is uncommon in dogs since they are usually insulin deficient.