Insulin dependent diabetes mellitus (IDDM) is a diabetic state in which endogenous insulin secretion is never sufficient to prevent ketone production. Type 1 diabetes mellitus is a diabetic state in which insulin secretion may be reduced or absent and which is readily corrected by exogenous insulin. Most dogs suffer from a syndrome similar to Type 1 diabetes or IDDM which is thought to have an autoimmune basis in both dogs and man. (1) Canine diabetes remains a common endocrine disease affecting from one in 100 to one in 500 dogs. Dogs suffering from diabetes mellitus range in age from 4-14 years with a peak incidence at 7-9 years.(1) In dogs, females are twice as likely to develop diabetes than are males.

Canine diabetes mellitus is an immune-mediated disease caused by complex interactions between genes and the environment. The disease affects many breeds of dog, including mixed breeds, and susceptibility varies greatly. Researchers suspect that genetic mutations may differ among breeds. Commonly affected breeds include poodles, dachshunds, miniature schnauzers, beagles, puliks, and pugs, Cairn terriers and miniature pinschers.(1) In some breeds, the risk is high. Experts say Australian Terriers are 32 times more likely to develop diabetes mellitus than mixed-breed dogs. Samoyeds, another high-risk breed, are 12 times more likely to develop diabetes.

In humans, the two most important genetic determinants of type 1 diabetes are the major histocompatibility complex (MHC) and insulin region genes. The MHC genes, also known as the human leukocyte antigen (HLA) system, are a group of genes found on the cell surfaces of chromosome 6 that code for protein and help determine immune responsiveness. A similar association has been seen in dogs.

Pathogenesis of clinical signs: IDDM

Hyperglycemia, caused by insulin deficiency, results primarily from impaired glucose utilization; however, increased hepatic gluconeogenesis and glycogenolysis by the liver contributes to hyperglycemia. Decreased peripheral utilization of glucose leads to accumulation of glucose in the serum; as the renal threshold for glucose is exceeded, osmotic diuresis ensues. Progressive dehydration results in the classic clinical signs of diabetes such as polyuria with compensatory polydipsia. Impaired glucose utilization by the hypothalamic satiety center combined with loss of calories in the form of glycosuria causes polyphagia and weight loss, respectively. Insulin is anabolic; therefore, insulin deficiency leads to protein catabolism and contributes to the clinical signs of weight loss and muscle atrophy. With insulin deficiency, the hormone-sensitive lipase system which is normally suppressed by insulin, becomes activated. As a consequence of this increased lipase activity, adipose tissue is broken down at an accelerated rate into nonesterified fatty acids. The unrestrained lipolytic activity of hormone sensitive lipase results in the clinical signs of weight loss in a previously obese or overweight animal.

Most diabetic dogs with the classic clinical signs of polyuria and polydipsia. Polydipsia was the most common clinical sign of diabetes mellitus in dogs (93%).(2) Polyuria on the other hand, was observed in only 77% of dogs) Dramatic and rapid weight loss in an animal with a good or even ravenous appetite will often alert the owner to seek veterinary advice. Weight loss is observed more commonly in dogs (62%)
19% of dogs exhibited polyphagia as a clinical sign of diabetes mellitus. In dogs, progressive polyuria, polydipsia and weight loss develops relatively rapidly usually over a period of several weeks. Another common presenting complaint of diabetes mellitus in dogs is acute onset of blindness caused by bilateral cataract formation.

In dogs, the most common physical examination findings are dehydration (48%) and muscle wasting or thin body condition (44%). About 35% of cats and 20% of dogs are obese upon initial examination; obese diabetic animals are more likely to suffer from non-insulin dependent diabetes mellitus. Hepatomegaly is observed in diabetic dogs (17%). Cataracts are observed in approximately 40% of diabetic dogs.

**Ketoacidotic, Hyperosmolar or Complicated Diabetes Mellitus: Pathophysiology and Clinical Signs**

Lipid metabolism in the liver becomes deranged with insulin deficiency and non-esterified fatty acids are converted to acetyl-CoA rather than being incorporated into triglycerides. Acetyl-CoA accumulates in the liver and is converted into acetoacetyl-CoA and then ultimately to acetoacetic acid. Finally, the liver starts to generate large amounts of ketones including acetoacetic acid, beta-hydroxybutyrate and acetone. As insulin deficiency culminates in DKA, accumulation of ketones and lactic acid in the blood and loss of electrolytes and water in the urine results in profound dehydration, hypovolemia, metabolic acidosis and shock. Ketonuria and osmotic diuresis caused by glycosuria results in urinary sodium and potassium loss which exacerbates hypovolemia and dehydration. Nausea, anorexia and vomiting, caused by stimulation of the chemoreceptor trigger zone via ketonemia and hyperglycemia, contribute to the dehydration caused by osmotic diuresis. Dehydration and shock lead to prerenal azotemia and a decline in GFR. Declining GFR leads to further accumulation of glucose and ketones in the blood. Stress hormones such as cortisol and epinephrine contribute to the hyperglycemia in a vicious cycle. Eventually severe dehydration may result in hyperviscosity, thromboembolism, severe metabolic acidosis, renal failure, and finally death.

The most common historical findings in dogs with diabetic ketoacidosis are anorexia (61%), weakness, depression, and vomiting. Physical examination findings may include shock, depression, tachypnea, dehydration, weakness, vomiting, and occasionally, a strong acetone odor on the breath.

In dogs, a diagnosis of diabetes mellitus should be based on the presence of clinical signs compatible with diabetes mellitus and evidence of fasting hyperglycemia and glycosuria. Common clinicopathologic features of diabetes mellitus in dogs include: fasting hyperglycemia, hypercholesterolemia, increased liver enzymes (ALP, ALT), neutrophilic leukocytosis, proteinuria, increased urine specific gravity and glycosuria. Common clinicopathologic findings in diabetic ketoacidosis include all of the above plus azotemia, hyponatremia, hyperkalemia, hyperlipasemia, hyperamylasemia, ketonemia, regenerative or degenerative left shifts, hyperosmolality, ketonuria, bacteriuria, hematuria and pyuria.

Glycosylated hemoglobin is formed by an irreversible, non-enzymatic binding of glucose to hemoglobin. As plasma glucose concentrations increase, hemoglobin glycosylation increases proportionately. Normal glycosylated hemoglobin (mean+/−SD) values are: 2.95 ± 0.15% in dogs. Serum fructosamine is formed by glycosylation of serum protein such as albumin. The concentration of fructosamine in serum is directly related to blood glucose concentration. However, due to the shorter lifespan of albumin
compared with hemoglobin, fructosamine concentrations reflect more recent (1-3 weeks) changes in serum glucose concentrations. Normal fructosamine concentrations in dogs are 254±42 µmol/L.

References