Researchers Seek Alternative Treatment for Feline Diabetes Mellitus

"S

midgen," a handsome male Champagne Mink Tonkinese, almost didn’t survive to his 12th birthday. Unbeknownst to owner Carol Grove, Smidgen was suffering from a life-threatening condition, ketoacidosis, related to feline diabetes. Grove didn’t even realize her cat had diabetes. "I noticed Smidgen was drinking a lot of water and was really hungry all the time," says Grove of Harrah, Okla. "In fact, he was becoming obese, so I put him on a diet. Now I know I should have been watching his water intake and urination."

Frequent water intake and urination are signs of diabetes mellitus, the second most common feline endocrine disease after hyperthyroidism. Though most often diagnosed in older, overweight, neutered male cats, diabetes can affect cats of any age, sex or breed. Experts report the incidence of feline diabetes is increasing, with one in 200 to 250 cats affected. Likewise, diabetes is increasing in people, with 24 million Americans believed to have the disease. Over several months in 2008, Smidgen’s undiagnosed diabetes worsened, and his weight dropped from 12 to 7 pounds.

"One day Smidgen was just laying there. He smelled like fingernail polish," Grove recalls. "It scared me, so I rushed him to the veterinarian. Smidgen was in the hospital eight days while he was treated for ketoacidosis."

A condition that requires emergency veterinary care, ketoacidosis occurs when sugar can no longer be used as a fuel source, requiring the body to use fat instead. Ketones, which are byproducts of fat breakdown, build up in the body causing weakness, dehydration and severely low potassium and phosphate levels. Affected cats must be stabilized with intravenous (IV) fluids, electrolytes and insulin. Close monitoring at a veterinary hospital is essential to recovery.

"Cats with ketoacidosis are basically starving to death despite eating because they can’t use the food without sufficient insulin to drive nutrients into the cells," says Letrisa Miller, D.V.M., who treated Smidgen at The Cat Clinic in Norman, Okla. "Instead of metabolizing glucose for energy, their bodies break down tissue for nourishment. Toxic ketones form in the process. One of the major ketones that cats produce is aceton, a primary ingredient of nail polish."

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Though Smidgen was close to comatose, and possibly death, when he arrived at The Cat Clinic, he eventually recovered. The now 13-year-old Tonkinese thrives on a high protein, low carbohydrate diet. He also receives twice-daily insulin injections.

"Most of the diabetic cats that are difficult to regulate have chronic pancreatitis or a concurrent condition, in which excessive growth hormone interferes with insulin, that waxes and wanes, or they have changes in their diet or exercise that impacts their insulin requirements," says Miller. "Fortunately, cats with well-regulated diabetes can live normally. About 25 percent of cats revert to not needing insulin, although some may need insulin again in the future."

An estimated 80 to 90 percent of cats with diabetes suffer from Type 2 diabetes. Often related to obesity, this type of diabetes is associated with amyloidosis, a condition in which high blood sugar causes amyloid proteins to build up in the pancreas, eventually leading to irreversible damage. Type 2 feline diabetics may or may not require insulin, and cats may revert from one state to the other. In contrast, Type 1 diabetes is almost always insulin-dependent. It is characterized as an autoimmune disease in which a cat’s immune system attacks the pancreas.

Daily insulin injections, often part of a diabetic cat’s treatment protocol, can be challenging due to fluctuations in establishing and monitoring proper dosage. Periodic blood testing and interpretation by a veterinarian are needed to determine blood sugar levels and proper insulin requirements. Stress, infection or other illness can influence insulin dosage.

Alternatives to Insulin Injections
Researchers at the University of Illinois College of Veterinary Medicine in Urbana-Champaign are investigating an alternative treatment for diabetic cats so potentially owners may not have to give daily injections. "Diabetes

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Feline Diabetes Mellitus continued from page 1

treatment can be frustrating for owners,” says Chen Gilor, D.V.M., DACVIM, a research fellow.

“Most cats need injections of insulin twice a day,” he says. “For some owners, that presents a hard commitment. Additionally, a cat can have side effects from receiving too much or too little insulin. We are looking for a way to make treatment easier.”

Gilor and co-investigator Thomas Graves, D.V.M., Ph.D., DACVIM, associate professor, are studying gastro-intestinal (GI) hormones called incretins that are produced and released into the blood by the intestine in response to food. They aim to learn how incretins affect insulin production and glucose absorption in cats.

**Exenatide is one of a new class of drugs known as incretin mimetics because they mimic the effects of incretins.** Exenatide may provide an alternative treatment in cats as it already is doing in humans with type 2 diabetes.

“We believe incretin-based drugs can control and possibly someday cure diabetes,” Gilor says.

Exenatide is one of a new class of drugs known as incretin mimetics because they mimic the effects of incretins. Exenatide may provide an alternative treatment in cats as it already is doing in humans with type 2 diabetes. Similar to natural incretin, exenatide boosts insulin secretion from the pancreas. Exenatide has less side effect than insulin, principally weight gain and hypoglycemia. “People are usually treated with exenatide or insulin,” explains Gilor. “However, some people are treated with both if one is not enough. Exenatide is injected twice daily — in the same way insulin is given to cats.”

Prolonged high blood sugar, called hyperglycemia, eventually destroys pancreatic beta cells. “Some researchers theorize an abnormal incretin response can occur many years before diabetes develop and may contribute to high glucose levels in the blood and urine, causing organ damage before clinical signs appear,” Gilor says.

Gilor and Graves are working on two overlapping research studies. In one, they are analyzing blood sugar levels in 10 healthy, non-diabetic cats given oral glucose, IV glucose, and exenatide prior to IV glucose. This study is funded by the Winn Feline Foundation (www.winnfelinehealth.org), a nonprofit organization that supports feline health research, and the Companion Animal Grant Program of the University of Illinois.

In the second study, they are evaluating the effects of fatty acids and amino acids on diabetic cats. Funding sources at the University of Illinois are supporting this research. Gilor notes that the diabetic cats in the studies are fed Purina Veterinary Diets® DM Dietetic Management® brand Feline Formula, which is specially made for cats with diabetes mellitus.

“People typically see diabetes as a disease where there’s simply not enough insulin in the body,” Gilor says. “We believe GI hormones may play a role in development of the disease in cats and definitely in treatment.”

“In the pancreas, beta cells of the islets of Langerhans produce insulin to regulate blood glucose. The incretin hormones augment insulin secretion three- to fourfold, triggering more insulin secretion after meals. This incretin effect can be shown by charting glucose curves. This is done by measuring glucose and insulin concentrations in the blood and comparing them between sugar ingestion and IV sugar administration.”

Insulin secretion is controlled primarily by blood glucose concentration. The pancreas increases insulin production and secretion in direct proportion to elevations of blood glucose. After a meal, digested nutrients — glucose, fatty acids and amino acids — stimulate incretin secretion. Incretins, in turn, change the sensitivity of the pancreas to the prevailing blood glucose concentrations.

Under the influence of incretins, more insulin is produced and secreted for any given elevations in blood glucose. Thus, in comparison to IV administration, an elevation of blood glucose that is caused by ingestion of sugar is associated with relatively more insulin secretion and more effective glucose metabolism. An important role of incretins is preparing the pancreas to anticipate insulin needs. “These GI hormones tell the pancreas it is going to get a lot more sugar soon, because the body is digesting sugar. It tells the pancreas to be prepared and create more insulin,” explains Gilor. “Some research indicates that incretins may even tell the pancreas to make more beta cells. This theory holds promise in providing a way to cure diabetes.”

Gilor and Graves are planning a clinical trial to test the effect of exenatide in treating diabetic cats. Their initial research shows that exenatide requires less intravenous glucose to duplicate the oral glucose curve. “We perceive that the process of delivering glucose to the tissues in cats is less effective with IV administration and more effective when it goes through the GI tract,” Gilor says.

Preliminary results indicate that exenatide duplicates the incretin effect “to some extent” in healthy cats. Though the effect is small in healthy cats, it may be greater in diabetic cats and thus warrants further study, he says.

The second part of the research — evaluation of the effects of fatty acids and amino acids on diabetic cats — could provide the most telling information about incretins. “Theoretically, the most pronounced incretin effect should be with fatty acids,” Gilor says. “We are working on a screening test to show if fats, proteins or carbohydrates have the biggest influence on insulin levels in diabetic cats. Then we potentially could treat them by modifying their diet.”

Managing Feline Diabetes

Though the exact etiology of diabetes in cats is not known, veterinarians do know that a therapeutic diet is a crucial part of effective treatment.

**Obesity in cats is contributing to an increase in cases of feline diabetes mellitus, according to P. Jane Armstrong, D.V.M., M.S., M.B.A., professor of internal medicine at the University of Minnesota College of Veterinary Medicine.**

Obesity increases the risk of developing feline diabetes three- to fivefold,” Armstrong told attendees of the Central Veterinary Conference last August in Kansas City. “Given that the prevalence of obesity in cats between 5 and 11 years old in the U.S. is over 40 percent, the high prevalence of feline diabetes is understandable.”

Age, weight, gender and sexual status are risk factors for diabetes, but age is the greatest consideration, Armstrong says. “Diabetes usually affects cats 6 years of age and older, but most often those between the ages of 9 and 13. Young cats rarely are affected,” she says.

Neutered or spayed cats are nearly twice as likely to develop diabetes than are intact cats, and males are one and half times at greater risk than are females.
Feline Diabetes Mellitus
continued from page 2

part of effective treatment. Such diets offer high protein, low carbohydrate nutrition that helps reduce sugar in the bloodstream. Weight loss is particularly beneficial in treating obese diabetic cats. Weight loss coupled with a therapeutic feline diabetes diet is often effective in controlling the disease and eliminating the need for daily insulin.

LATER SIGNS OF DIABETES INCLUDE:
- PROGRESSIVE WEIGHT LOSS, VOMITING AND DIARRHEA;
- CONTINUED WEAKNESS AND LETHARGY, LOSS OF APPETITE;
- PANTING; SWEET SMELLING BREATH LIKE FINGERNAIL POLISH;
- AND COMA DUE TO KETOACIDOSIS.

“Cats that have their diabetes controlled either through diet or diet plus insulin injections can live good, long lives, sometimes a normal life span,” says Vicki Thayer, D.V.M., a feline practitioner and president-elect of Winn Feline Foundation. “If the diabetes is uncontrolled, cats are also more susceptible to infections, primarily urinary tract infections.”

Early diagnosis of diabetes is important. Signs include increased thirst (polydipsia); increased urination (polyuria); sticky urine (indicating glucose); increased appetite; lethargy and frequent napping; dull, flaky coat or dandruff; and weakness in the hind limbs progressing to a flat-footed hind gait (diabetic neuropathy). These signs may be taken by owners at home under less stressful situations,” she says. Later signs of diabetes include: progressive weight loss; vomiting and diarrhea; continued weakness and lethargy; loss of appetite; panting; sweet-smelling breath like fingernail polish; and coma due to ketoacidosis.

Unlike many owners, Grove never worried about giving Smidgen insulin injections. As a breeder, she was used to vaccinating cats. She did worry about taking blood from his ear for frequent blood tests requested by the veterinarian.

“I was nervous at first and didn’t like the blood testing anymore than he did,” Grove says. “When he’s quiet and lies around, I know something’s wrong.”

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Have comments about Purina Pro Club Update? Send them to us at: Purina Pro Club Update, c/o Editor, Nestlé Purina PetCare, 2T Checkerboard Square, St. Louis, MO 63164 or via e-mail at today@breeder@purina.com.
The nutritional needs of cats change as they grow and develop from kittens to adults to seniors. The Purina Pro Plan canned cat food line was developed to provide optimal nutrition for cats of all life stages.

The Pro Plan canned cat food portfolio features 26 formulas. Besides foods for healthy kittens, adults and seniors, the line includes four formulations for cats with special nutritional needs. Across the portfolio, Pro Plan canned cat foods are made with real meat, poultry or fish. All were developed to help bolster a cat’s immune, digestive and skin and coat systems, while also providing optimal energy and excellent palatability.

The Pro Plan canned cat food line includes several varieties for healthy adults. Among them are Beef & Chicken Entrée, Chicken & Liver Entrée, Ocean Whitefish & Salmon Entrée, and Sardines & Tuna Entrée. There are varieties available in gravy, chunky or ground forms. All are specially formulated to provide the energy and nutrition needed by healthy adult cats.

Pro Plan Selects canned cat food — which includes one kitten formula and six for healthy adults — are formulated with a unique combination of natural ingredients plus vitamins and minerals. All are formulated without corn, wheat or animal by-products, and no artificial colors or flavors have been added. Pro Plan Selects also provide antioxidants and omega-6 fatty acids.


As cats age, their nutritional needs change. Pro Plan makes canned cat foods specially developed to meet the needs of senior cats. These formulas are highly digestible and provide the nutrients needed to support strong bones and healthy joints. Pro Plan Chicken & Beef Entrée and Salmon & Tuna Entrée are specially made for senior cats.

Pro Plan offers four canned formulations for cats with special nutritional needs. The line includes: Pro Plan Hairball Management Chicken & Liver Entrée to help minimize hairballs; Indoor Care Salmon & Rice Entrée for indoor cats; Urinary Tract Health Formula Chicken Entrée to help lower urinary pH; and Weight Management Turkey & Rice Entrée for overweight or less active cats.

In addition to the Pro Plan Selects kitten formula, Pro Plan has three other canned kitten foods: Chicken & Liver Entrée, Ocean Whitefish & Tuna Entrée, and Salmon & Ocean Fish Entrée. These kitten foods are specially developed to provide optimal nutrition and help bolster the immune, digestive and skin and coat systems of growing kittens.

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