



Update

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Exocrine Pancreatic Insufficiency May Have Complex Inheritance Pattern

"Izzy" had lost one-third of her body weight. Despite a voracious appetite, the 1-year-old Spanish Water Dog dropped to 27 pounds in four months. Owner Olesia Kennedy went from feeding two cups of food daily to eight cups.

"She was still losing weight," says Kennedy, of Georgetown, Ind. "It seemed like no matter what I did, nothing helped. It was awful to watch my beloved companion fading away."

A fecal test for bacterial infection came back negative, yet Izzy continued to decline, going from having a few loose stools to constant diarrhea. "I frantically called the veterinarian and said something is seriously wrong with my dog," Kennedy recalls.

Kennedy's veterinarian suggested testing for exocrine pancreatic insufficiency (EPI). Within a week, the results of the blood test came back positive for the disease.

EPI is a disorder in which the pancreas fails to produce an adequate amount of digestive enzymes. Without those enzymes, food is not properly digested and absorbed. No matter how much food is ingested, a dog with EPI can literally starve to death.

Signs of EPI include weight loss, ravenous appetite, diarrhea, eating feces, vomiting, gas, changes in temperament, and loose, foul-smelling stool. In many cases, signs of the condition — which can strike at any age — do not appear until as much as 90 percent of the pancreas is destroyed.

There is no cure for EPI, but the disease can be successfully managed. Treatment, however, is lifelong.

About 8,000 dogs worldwide are diagnosed with EPI every year, says Jörg M. Steiner, Dr.med.vet., Ph.D., director of the Gastrointestinal Laboratory at Texas A&M University. About 800 cases are diagnosed in his laboratory every year.

The list of affected breeds is long, says David A. Williams, Vet.M.B., Ph.D., chairman of the Department of Veterinary Clinical Medicine at the University of Illinois College of Veterinary Medicine. "I stopped counting in the late 1980s when the breed count diagnosed

through my laboratory went well past 100," he says. "While certain breeds have an above-average occurrence, essentially all breeds are at risk. The disease is known to be prevalent in German Shepherd Dogs, Rough-Coated Collies and Chow Chows."

Shortage of Digestive Enzymes

The pancreas is a glandular organ located under the stomach that produces and secretes digestive enzymes. Acinar cells in the pancreatic tissue produce amylase to digest carbohydrates, lipase to digest fats, and trypsin and other proteases to digest proteins. These enzymes are secreted into the small intestine to help break down food into smaller parts so nutrients can be absorbed through the intestinal wall. An insufficiency of these enzymes causes nutrients to remain in the gastrointestinal tract undigested and pass in the feces.

The most common cause of EPI in dogs is pancreatic acinar atrophy (PAA) in which the acinar cells decrease in number and function. Though little is known about the cause of PAA, researchers believe the condition is genetically inherited. PAA usually develops between 6 months and 6 years of age. German Shepherd Dogs represent the majority of the cases identified in several studies.

EPI also can develop due to chronic pancreatitis, or inflammation of the pancreas. The pancreas synthesizes all the major digestive enzymes, but repeated bouts of pancreatitis can destroy acinar cells that synthesize these enzymes. Risk factors for chronic pancreatitis include high-fat diets and some anti-seizure and cancer drugs, Steiner says. In some cases, chronic pancreatitis may be an inherited condition.

In rare cases, EPI results from pancreatic cancer or pancreatic hypoplasia. Pancreatic hypoplasia is a congenital condition in which the exocrine pancreas does not fully develop.

Amy Vose has bred and owned German Shepherd Dogs for 33 years, but she had never heard of EPI until after her obedience champion "Dulcimer" (OTCH LuJon's Dulcimer of Ashmead, UDX) had her second litter in 1992. Vose kept a female puppy she named "Sassafras" and sold the other nine puppies.

"When the puppies were about 1 year old, I received a phone call from one of the buyers," says Vose, of Paw Paw, Ill. "The woman's male puppy had started losing weight inexplicably and was finally diagnosed with EPI. I was extremely shocked and heartsick."

Contacting everyone who bought a

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A Web Site With a Mission

Olesia Kennedy bought her Spanish Water Dog "Izzy" to start a breeding program. Those plans changed when Izzy developed exocrine pancreatic insufficiency (EPI) at age 1.

Two years ago, Kennedy started the Web site www.epi4dogs.com to raise awareness of EPI. The site offers comprehensive information about the disease and includes before- and after-treatment photographs, the latest research findings and a list of affected breeds. Fundraising items also are featured.

Visitors can share their experiences with EPI, ask questions and find emotional support through the site's discussion forum. "It is very helpful to talk with others also dealing with EPI," Kennedy says. "This is why I created the EPI forum."

Researchers and EPI dog owners frequently contribute information on the popular Web site. "The site now averages approximately 10,000 hits a month, which indicates to me that EPI is much more widespread than anyone ever thought," Kennedy says. "More and more breeds are being diagnosed with EPI. About half our visitors own German Shepherd Dogs with EPI, and half own other breeds. Hopefully, the Web site provides information that helps people realize there are many choices when dealing with EPI."

Exocrine Pancreatic Insufficiency

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puppy, Vose encouraged them to have their dogs tested. Though Dulcimer did not have EPI, six of her puppies did, including Sassafras.

Vose was able to turn that tragedy into hope. When she learned that researchers at Texas A&M University were working to find a genetic link to pancreatic insufficiency in German Shepherd Dogs, she coordinated the donation of more than 80 blood samples from Dulcimer's progeny.

Though a genetic marker for EPI has not been identified, several studies previously indicated that PAA is an autosomal recessive disease. This means that affected dogs inherit a copy of the gene mutation from both their sire and dam.

Results from a study published in the *Journal of Veterinary Internal Medicine* in the March/April 2010 issue and performed at the University of Helsinki in Finland cast doubt on that theory. Researchers mated two German Shepherd Dogs with EPI and tracked the litter of six puppies throughout their lives. If EPI was indeed an autosomal recessive condition, all offspring of the two affected dogs would be affected with the disease. During the 12-year study, only two of the six puppies developed PAA.

"That study clearly shows that it's not autosomal recessive," Steiner says.

EPI now is believed to have a more complex mode of inheritance, says Leigh Anne Clark, Ph.D., assistant professor of genetics and biochemistry at Clemson University. "EPI may result from mutations in multiple genes or from both genetic and environmental factors," she says.

Clark is studying the genetic variations between 100 healthy German Shepherd Dogs and 100 EPI-affected German Shepherd Dogs — two of which are from Dulcimer's family. "If we can identify the gene or major gene causative for EPI, we will be able to develop a genetic test," Clark says. "Breeders could then determine which dogs are at risk for developing EPI and thus make informed breeding decisions."

Until then, Clark, Steiner and Williams advise against breeding dogs with EPI or repeating matings that produced affected dogs. "The only way to decrease prevalence of the disease is by not breeding affected dogs," Steiner says.

Complicated Disease to Diagnose

Veterinarians sometimes have difficulty diagnosing EPI because signs of the disease mirror those of other health issues. "The clinical signs are much more variable than most veterinarians realize, especially in the early stages of the disease before there is extreme weight loss," Williams says. "The disease was formerly under-

diagnosed in dogs with the disease and overdiagnosed in dogs without the disease."

That situation improved considerably when a blood test for EPI was developed in England in the early 1980s. The canine trypsin-like immunoreactivity (cTLI) test was brought to the United States in 1985 when Williams made it available to veterinarians through university laboratories. Since the early 1990s, the test also has been available to veterinarians through commercial companies.

The cTLI test measures the amount of trypsinogen, an enzyme produced by the pancreas and converted into

Signs of Exocrine Pancreatic Insufficiency

- Weight loss
- Malnourished, thin or emaciated appearance
- Voracious appetite
- Chronic or intermittent diarrhea
- Eating feces or nonfood items
- Voluminous and frequent foul-smelling, yellowish, greasy stools with a watery to cow-pie consistency
- Gas (burping or flatulence)
- Rumbling digestive sounds
- Abdominal discomfort
- Dry, dull or brittle coat

trypsin, in the blood. Dogs with EPI have low levels of trypsinogen. The test costs less than \$100, and results are available in less than a week.

"With the advent of the serum cTLI test, there is simply no excuse for not testing suspect cases early, long before the classical signs of extreme weight loss and ravenous appetite become apparent," Williams says.

Along with the cTLI test, Steiner suggests testing cobalamin (vitamin B12) and folate levels since dogs with EPI often have low levels of cobalamin and high levels of folate. Performing the cTLI and cobalamin and folate blood tests together can save time and money.

This combination indicates small intestinal bacterial overgrowth (SIBO), a condition in which bad bacteria thrive on undigested food in the small intestine. SIBO can be treated with antibiotics. Cobalamin deficiency should be treated with injections of B12, a vitamin that is necessary for almost all cell functions, from normal neurological function to digestion and absorption of food.

EPI cannot be cured, but it can be managed and the prognosis is good. "Dogs having EPI can be treated with enzyme supplements that allow them to properly digest their food and live normal lives," Clark says.

Pancreatic enzyme supplements are available in tablet, capsule or powder form. Given before a meal or mixed with food, the supplements contain amylase, lipase, proteases and other pancreatic enzymes that replace the naturally occurring digestive enzymes depleted by EPI. The monthly cost of supplements is estimated at \$60 to \$100.

Most EPI dogs also require diet modification, including reducing fiber or grain. Many veterinarians recommend feeding several small meals a day and increasing the normal recommended amount until a dog reaches his or her target weight.

After their condition stabilizes, dogs still should be tested periodically, Williams says. "Cobalamin deficiency and other complications can occur years after the initial diagnosis of EPI even though classical signs of weight loss and diarrhea are well controlled by enzyme replacement," he says.

Some dogs stabilize quickly, while others require trying different combinations of supplements and food in varying amounts until the correct balance is achieved. Williams advises owners to keep a treatment log of each combination, and work closely with a veterinarian.

"EPI is generally a manageable disease, but some cases require a little extra effort to get the best results," Williams says. "With the right balance, most EPI dogs can live a full and wonderful life."

Izzy and Sassafras are two examples. Once her condition was managed, Sassafras went on to become an unofficial therapy dog for children with emotional and behavioral troubles at the junior high school where Vose works. She lived for 11 years after her diagnosis.

Izzy's condition stabilized in about three months, allowing her to return to pet therapy work at a local residence for senior citizens. She eventually gained back the weight she'd lost and then some, tipping the scale at 48 pounds and leading Kennedy to put her on a diet last summer.

Izzy, now 5 years old, "can do anything any dog can do," Kennedy says. "Most days, I forget that there is even anything wrong with her." ■

Send Us Your Questions

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