



Yorkshire Terrier

Update

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Researchers Seek Candidate Genes for Protein-Losing Enteropathy

Researchers at Cornell University School of Veterinary Medicine in Ithaca, N.Y., are working to find candidate genes that predispose Yorkshire Terriers to protein-losing enteropathy (PLE), a potentially fatal condition in which dogs lose significant protein into their gastrointestinal system.

While genetics are likely to play a role in determining which dogs are predisposed to developing PLE, environmental factors, such as enteric (intestinal) bacteria or food intolerance or allergy, may contribute as well. The extent to which environmental factors influence the disease is not fully known.

In Yorkshire Terriers, PLE is widely attributed to lymphangiectasia, a condition in which the lymph vessels become dilated and disrupt the normal flow of lymph throughout the body. Recent studies have showed extensive cystic dilatation of the intestinal crypts (mucosal glands of the epithelial lining of the small intestine) also may contribute to PLE. One study showed that Yorkies have a tenfold greater risk of

developing lymphangiectasia than other breeds.

Recognizing the widespread occurrence of PLE in the breed, the Yorkshire Terrier Club of America and the Yorkshire Terrier Club of America Foundation recently helped fund an AKC Canine Health Foundation grant that supports the Cornell University research. The researchers' ongoing efforts to collect DNA samples from affected and normal dogs are instrumental to the success of the study.

"Our goal is to identify a gene change or set of changes that predispose a dog to PLE," says lead investigator Nate Sutter, Ph.D., assistant professor of medical genetics. "The evidence that PLE has a genetic component primarily rests on the observation that some breeds — such as Yorkies — are at an elevated risk for the disease. The simplest explanation is that at-risk breeds have one or more genetic factors that confer risk."

Ultimately, once a genetic marker is identified and the causative mutation for PLE is discovered, a DNA test

can be developed that would identify affected dogs and thus provide a diagnostic tool for the disease. Currently, the only definitive test to detect and distinguish between different causes of PLE is an intestinal biopsy that is expensive, requires general anesthesia and carries some health risks.

The severity of PLE varies among individual dogs and may be related to differences in genetic expression of the disease. Some dogs show no clinical signs, yet die quickly. Others exhibit serious manifestations, but with proper disease management do well. Diarrhea, anorexia, vomiting, lethargy, weight loss, edema (swelling) or ascites (fluid in the abdominal cavity), and respiratory difficulty from fluid in the chest are not uncommon signs in dogs with PLE.

Other at-risk breeds for PLE are Basenji, Chinese Shar-Pei, Norwegian Lundehund and Soft-Coated Wheaten Terrier. The genetic basis for the disease may vary by breed. Besides lymphangiectasia, conditions that can

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Managing a Lifelong Condition

Protein-losing enteropathy associated with lymphangiectasia and crypt cysts is a fatal condition in as many as half or more Yorkshire Terriers, experts estimate. Most diagnosed dogs receive lifelong therapy. Some dogs never improve despite therapy, while others continue to live a normal, active life. Here are stories of the journeys of owners whose Yorkshire Terriers were diagnosed with PLE.

Liz Youngblood of Seattle was pleased when her 7 1/2-year-old Yorkie, "Taffy," responded well to medications given to help reduce the signs of PLE. "In the beginning, Taffy was well enough to play and enjoy herself," she says.

Not long afterward, diarrhea and fluid on the abdomen returned. "Then, Taffy began struggling to breathe," says Youngblood. "We had the fluid drained off several times, but it always came back."

The fluid-draining procedure was painful and put Taffy at risk for peritonitis, or inflammation of the membranes lining the abdomen. After seven months, Youngblood made the difficult decision to have Taffy euthanized.

Pancreatitis was the initial diagnosis given Denise Fallon's Yorkie, "Winnie," who had lost her appetite and frequently vomited. After two weeks on a bland diet, Winnie continued to weaken. Fallon, of Mechanicsburg, Pa., was referred to a veterinary teaching hospital, where

the specialist recommended an intestinal biopsy to determine definitively whether Winnie had PLE.

Only weeks after the first signs of PLE, Winnie died of peritonitis following the intestinal biopsy procedure. "It was probably a result of the disease causing changes that weakened the intestinal walls," Fallon says.

"Chloe," a 12-year-old Yorkshire Terrier owned by Jane Downey of Columbus, Ohio, continues to thrive despite having been diagnosed with PLE when she was 9 years old. "I have to work hard to keep Chloe's weight down with a strict diet," Downey says. "She loves to get into the other dogs' food bowls, so it's a constant struggle. If she overeats, she gets bloated."

Another long-lived Yorkshire Terrier diagnosed with PLE is "Martha," a retired conformation champion belonging to Stephanie Ruiz of Orange County, Calif. Martha was diagnosed at age 9 and today is 15. "When we were still working on a diagnosis, we tried several diets for Martha, but none seemed to help," Ruiz says.

Once Martha was definitively diagnosed with PLE, the veterinarian prescribed medications to help manage signs of the disease. "The key for us is consistently following the veterinarian's instructions regarding diet and medications," says Ruiz. "Martha's protein level is normal, and she has lived longer than any Yorkie we have ever owned."

Researchers Seek Candidate Genes

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lead to PLE are inflammatory bowel disease, intestinal lymphoma and fungal infections such as histoplasmosis.

Dogs with PLE lose protein from the body through the intestines. Normally the intestines absorb dietary protein from food during the digestive process, but the reverse happens in dogs with PLE. In these dogs, the protein is released into the intestines and lost in feces.

Signs of a Similar Condition

Chronic occasional vomiting was common in Julie Fritz-Rubert's 4 1/2-year-old Yorkshire Terrier, "Phoebe." When the dog vomited six times in one day, she became concerned. A few days later, the dog's abdomen appeared bloated. "I took Phoebe to the veterinarian, who suspected she had gastroenteritis but ran blood work to be sure," says Fritz-Rubert of Sacramento, Calif.

The blood test showed that Phoebe had low levels of albumin and globulin, consistent with PLE. The veterinarian recommended an intestinal biopsy to determine definitively whether Phoebe had lymphangiectasia or another cause of PLE. The biopsy confirmed that Phoebe had mild to moderate lymphangiectasia.

The lymph vessels in Phoebe's body were dilated due to pressure from inflammation. The lymph vessels in the intestines, called lacteals, were not able to absorb dietary fat because of increased intralymphatic pressure with subsequent malabsorption of fat and other nutrients such as fat soluble vitamins. With the loss of nutrients, particularly protein and fat, Phoebe had begun to lose weight.

Disease management focused on reducing inflammation in the intestinal mucosa and fluid accumulation in the abdomen. A corticosteroid, prednisone, was prescribed for the inflammation, and an immunosuppressive medication, azathioprine, was given to control overaggressive immune responses.

Dogs diagnosed with PLE may be given medications such as tylosin or metronidazole, which also help to modulate bacteria that may promote inflammation and reduce the risk of bacteria being transferred into the body through the impaired gut. Low-dose aspirin helps to reduce the risk of thromboembolism, a blood-clotting disorder that is common in dogs with PLE, and a low-dose diuretic may be given to reduce intra-abdominal fluid.

Veterinarians often recommend feeding a low-fat diet enriched with medium-chain triglycerides rather than the long-chain triglycerides found in most dietary fat. The shorter chain triglycerides may be absorbed directly into the bloodstream, bypassing the lymph system.

Even with medications and a special diet, Phoebe's abdomen was enlarged for about six weeks. "We could tell she didn't feel well," Fritz-Rubert says. "At

first, she didn't eat well, even with the prednisone. We could see she was wasting away and was losing muscle mass. We could see the bones in her shoulders and feel her spine. We were so afraid we would lose her."

After a couple of weeks, the veterinarian increased Phoebe's prednisone. "It was like magic," says Fritz-Rubert. "Within five days, Phoebe went from weighing 7 pounds to 5 pounds, and she lost 4 inches around her belly. The weight loss was because her ascites improved."

Several months after Phoebe was diagnosed with PLE, good news came

How to Contribute to PLE Genetic Research

Breeders and owners of Yorkshire Terriers can contribute DNA samples to help advance genetic research at Cornell University School of Veterinary Medicine to identify candidate genes that cause protein-losing enteropathy (PLE). The researchers are requesting samples from affected dogs of all ages and from older, healthy dogs.

For information about the criteria to qualify and how to submit samples and pedigree and clinical information, please contact Dr. Kenneth Simpson at kws5@cornell.edu or 607-253-3567, or Dr. Nate Sutter at sutterlab@cornell.edu.

on a veterinary visit. "It turned out Phoebe had gained too much weight," Fritz-Rubert says. "Her big belly was due to fat, not fluid as we had feared."

Not only had Phoebe gained weight, but her albumin and globulin levels were normal. The toy dog regained muscle mass and began feeling good, even playing. Phoebe continues to take a small dose of prednisone and is fed a low-fat diet and low-fat treats. She also continues to take the immunosuppressive medication, azathioprine, which clearly states on the label: Give medicine every other day, forever.

Surveying the Dog's Genome

Once a dog is diagnosed with protein-losing enteropathy, the condition usually requires lifelong disease management. The ability to recognize affected dogs sooner and begin preventive care sooner may offer a better prognosis. Should a DNA test one day become available to determine dogs that carry the PLE-associated gene mutation, breeders will have a tool to potentially reduce disease incidence in their litters.

Sutter, the Cornell University researcher leading the genetics study of PLE in Yorkshire Terriers, is working with Kenneth Simpson, professor of small animal medicine who specializes in gastroenterology. Though their initial grant was completed last May, the research still is in the early stages, with no indication whether PLE has

an autosomal recessive or dominant inheritance pattern.

"Many Yorkshire Terriers with PLE succumb to the disease despite aggressive therapeutic intervention," Simpson says. "The reasons for a good response versus a poor response are not clear."

In the future, once sufficient numbers of samples are collected, the team plans a genomewide association scanning that will help them to identify regions of genes that vary among affected and healthy Yorkies. "This genetic assay provides genotypes from roughly 170,000 SNP (single nucleotide polymorphism) markers," Sutter explains. "These markers occur all over the dog genome and give us a nice survey picture of an individual dog's genome."

"Each SNP marker on the chip has two allele forms. If we find a SNP marker allele, or form, in affected dogs that is not present in healthy dogs, we could have a correlation between the genotype and the disease phenotype. Since we know the genomic location for each SNP, we could then look at the location, or locus, in the genome for clues about the disease."

Next, the researchers will zero in on that locus to make a finer grained map showing differences and to help identify the location more precisely. "Only after that step is completed will we be in a position to create a DNA test to help breeders gauge the risk for disease," Sutter says.

As the research continues, the goal is to collect 100 samples of DNA from affected dogs and healthy controls. "We need to collect DNA samples, pedigrees and clinical data from Yorkies with and without disease," says Sutter.

Phoebe's DNA will be included in the study. Fritz-Rubert became an advocate for supporting the genetic research while learning about the disease through Phoebe. "I probably have spent about \$4,000 in medications and veterinary visits for Phoebe," she says. "The emotional toll has been just as costly."

When she found an online forum (<http://www.savelouie.com/phpBB3/>) for people whose dogs suffer from PLE, Fritz-Rubert welcomed the comfort of sharing her experiences with others. "I discovered this while Phoebe was in the hospital," she says. "I have learned so much from reading other people's stories. We have lost lots of dogs to this, and each one breaks my heart." ■

Purina appreciates the support of the Yorkshire Terrier Club of America and particularly Mary Trimble, president of the YTCA Foundation, in helping to identify topics for the *Purina Pro Club Yorkshire Terrier Update* newsletter.

Purina Pro Plan Takes Main Stage at National Pheasant Fest & Quail Classic

Tips from top professional trainers of retrieving, flushing and pointing breeds are among the featured activities planned at the National Pheasant Fest & Quail Classic Feb. 17 to 19 at the Kansas City (Mo.) Convention Center. *Purina Pro Plan* is the national dog food sponsor of the annual event that draws more than 20,000 people.

The professional trainers, who are Purina consultants, will hold seminars on the Main Stage of the Bird Dog Bonanza area. Tom Dokken of Dokken's Oak Ridge Kennels in Northfield, Minn., will offer retriever training tips. Rick Smith of Cozier, Va., who developed the Silent Command System of dog training, and his cousin, Ronnie Smith, will present guidelines on training pointing and flushing breeds.

Bob West, Director of Purina's

Sporting Dog Group, will emcee panel discussions in which the trainers will answer questions from attendees.



"We are excited to invite our Purina consultants to this event and to share their expertise on conditioning and training dogs," West says. "At the Purina booth, we will have experts on hand to discuss nutrition and care for hardworking dogs."

The largest trade show in the country for pheasant and quail hunters

and bird dog enthusiasts, the event will feature wildlife conservation, upland game bird hunting and wildlife habitat management and restoration. About 30 sporting dog breeds are expected to be represented by breed clubs and trainers on Bird Dog Alley.

Purina and *Pro Plan* was named in early 2011 as the national dog food sponsor of Pheasants Forever and Quail Forever, the largest nonprofit organization in the country dedicated to upland habitat conservation and one in which seven of 10 members own dogs. The agreement renewed Purina's more than two decades' support of Pheasants Forever, which was founded in 1982 by avid pheasant hunters and conservations. Quail Forever was launched in 2005. ■

2011 Pro Plan Champions Cup Standings

Dog	Breed/Variety	Points Earned*
GCH Casablanca's Thrilling Seduction	Black Cocker Spaniel	315
GCH Palacegarden Malachy	Pekingese	228
GCH Saks Hamelot Little Drummer Boy	Bichon Frise	174
GCH Cragsmoor Buddy Goodman	Skye Terrier	171
GCH Winfall Brookwood Styled Dream	Boxer	167
GCH Banana Joe Van Tani Kazari	Affenpinscher	166
GCH Starline's Chanel	Whippet	151
GCH Northgates As You Like It	Pharaoh Hound	140
GCH Babheim's Captain Crunch	German Shepherd Dog	132
GCH Szumeria's Wildwood Silver Six Pence	Kuvasz	117

*Points earned through November 30, 2011.

Purina-Sponsored Sporting Events January to March 2011*

Event	Date	Location
United Kennel Club (UKC) Grand American	Jan. 6 - 7	Orangeburg, SC
U.S. Complete Shooting Dog Association (USCSDA) National Open Championship	Jan. 12 - 15	Cheraw, SC
Continental Championships	Jan. 16 - 28	Greenville, FL
National Bird Hunters Association (NBHA) Invitational Championship	Jan. 20 - 23	Oneonta, AL
UKC Winter Classic and Purina Coonhound Awards	Jan. 27 - 28	Albany, GA
All-American Foxhound Championship	Feb. 3 - 5	Grenada, MS
NBHA National Amateur Championship	Feb. 10 - 12	Wheatstone, MO
National Championship	Feb. 13 - 26	Grand Junction, TN
National Pheasant Fest & Quail Classic	Feb. 17 - 19	Kansas City, MO
UKC Southeastern Treeing Walker Days	Feb. 23 - 25	Salisbury, NC
National German Shorthaired Pointer Association (NGSPA) National Championship	Feb. 24 - Mar. 4	Booneville, AR
NBHA National Open	Feb. 29 - Mar. 4	Cheraw, SC
USCSDA Futurity	Mar. 7 - 8	Sandland Wildlife, West End, NC
American Kennel Club Brace Beagle Southern Federation	Mar. 9 - 14	Rock Springs, GA
American Hunting Basset Association (AHBA) World Hunt	Mar. 16 - 17	Lynville, IN
Mid-America Brace Gundog Federation (MAB) All-Age National Run-Off	Mar. 24 - 25	Booneville, IN
NBHA Futurity	Mar. 26 - 29	Nashville, TN

*This table lists some, but not all, upcoming sporting events sponsored by Purina.

Purina Pro Plan Sponsors the 2012 Westminster Kennel Club Dog Show

New in 2012 at the Westminster Kennel Club Dog Show, dog handlers and enthusiasts arriving for the 136th annual show will notice signature purple *Purina Pro Plan* banners decorating Madison Square Garden in New York City.

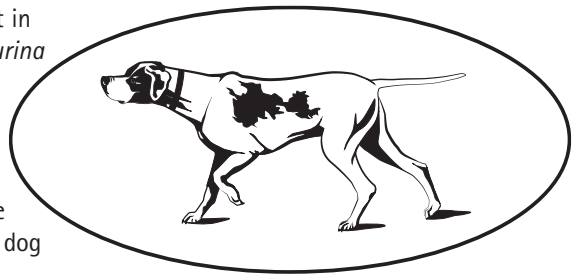
As the official pet food sponsor of the prestigious dog show, *Pro Plan* will reach out to the dog fancy and millions of people watching the televised program live on USA Network. Purina and the Westminster Kennel Club announced the multi-year sponsorship agreement last June.

"Westminster is a marquee dog show well known around the world," says Candy Caciolo, Purina Portfolio Director of Specialty, Breeder and Pet Acquisition. "Many Westminster win-

ners, including the last five Best in show winners, have been fed *Purina Pro Plan* brand dog food, so it's fitting for Purina to partner with this distinguished kennel club."

A longtime supporter of the dog fancy, Purina sponsors more than 100 all-breed and specialty dog shows a year. In 2010, Purina unveiled the Purina Event Center, a \$15 million, 84,000-square-foot indoor dog show facility in Gray Summit, Mo., where six Westminster Best in Show winners, along with their owners and handlers, participated in the Grand Opening.

Purina's support of the fancy contributed to the decision by the Westminster Kennel Club to choose Purina as the sponsor of its dog show. "Purina



was selected due to its stature in the pet industry and visibility at dog shows," says David Frei, Director of Communications for Westminster. "Purina will be a very active partner, not just during the dog show but year-round."

Founded in 1877, the Westminster Kennel Club Dog Show is the oldest organization in the country dedicated to the sport of purebred dogs. The 2012 dog show will be held Feb. 13 and 14. ■

Purina-Sponsored Dog Shows January to March 2012*

Event	Date	Location
Kennel Club of Palm Springs Dog Show	Jan. 5 - 8	Indio, CA
Land O'Lakes Cluster	Jan. 6 - 8	St. Paul, MN
Florida Classic Cluster I & II	Jan. 12 - 22	Brooksville, FL
Orange Empire Kennel Club Dog Show	Jan. 27 - 30	San Bernardino, CA
Cherokee Rose Cluster	Feb. 2 - 5	Atlanta, GA
Westminster Kennel Club Dog Show	Feb. 13 - 14	New York City, NY
Foothills Dog Show Circuit	Feb. 17 - 19	Spartanburg, SC
Rocky Mountain Cluster	Feb. 17 - 20	Denver, CO
International Kennel Club (IKC) of Chicago Dog Show	Feb. 23 - 26	Chicago, IL
Fiesta Cluster	Mar. 2 - 5	Scottsdale, AZ
Belle City Cluster	Mar. 3 - 4	Purina Event Center Purina Farms Gray Summit, MO
March Madness Cluster	Mar. 22 - 25	Edison, NJ
Fort Worth Cluster	Mar. 23 - 25	Fort Worth, TX

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PURINA Pro Club Yorkshire Terrier Update

Point balance may not reflect current account activity. For your detailed account activity, go to www.purinaproclub.com

Your Purina Points Summary
Points Available Through November 30, 2011



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