PURINA Pro Club®

Golden Retriever Update

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Golden Retriever Ichthyosis May Be Underdiagnosed Due to Seborrhea Similarity

When a scaling skin disorder first showed up in Golden Retrievers in the 1990s, it was frequently misdiagnosed as seborrhea, a condition that also causes scaling and dandruff. More than a decade later, veterinary specialists began studying the disorder and realized it is specific to Golden Retrievers. More recently, geneticists identified the causative mutation and developed a direct DNA test to identify affected and carrier dogs.

Fortunately, Golden Retriever ichthyosis is seldom severe. The disorder is named for the Greek word ichthys, meaning fish, because it looks like fish scales. Breeders sometimes refer to the condition as "puppy dandruff" since puppies usually outgrow signs of flaky skin as they mature, although ichthyosis also occurs in adult dogs. Research in Goldens led to the discovery that the disorder is similar to one of the human autosomal recessive congenital ichthyoses (ARCI).

An ongoing survey conducted by the Orthopedic Foundation for Animals in conjunction with the Golden Retriever Club of America (GRCA) reports that ichthyosis accounts for 0.2 percent of skin disorders in the breed. "Overall, this is a very low percentage," says Rhonda Hovan, the GRCA research facilitator. "The percentage of affected Goldens in this survey probably does not reflect how many dogs have the disease, especially if the diagnosis is based on physical signs alone. It is likely that mild cases go undetected or ignored. It also is possible that ichthyosis is inadvertently diagnosed as seborrhea, which accounts for 0.9 percent of skin disorders."

An Inherited Congenital Disorder

Cindy Williamson of Harford County, Md., who breeds Golden Retrievers under the Lycinan prefix, describes unknowingly breeding litters with ichthyosis since 1992. "It was not diagnosed then as ichthyosis," she says. "The veterinarian suggested it was 'walking dandruff,' which is caused by mites, but the puppies outgrew the condition and quit showing signs by 8 weeks of age. We called the puppies 'peelers' because of their flaky skin. We didn't think much about it because it went away and never persisted into adulthood."

Ichthyoses are a diverse group of hereditary, usually congenital, diseases characterized by faulty formation of the outer layer of the epidermis, the stratum corneum, with resultant scaling.[2,3,4] Skin biopsies have revealed two types of ichthyoses: epidermolytic ichthyosis (EI) and nonepidermolytic ichthyosis (NI).

Golden Retrievers develop the NI type, which also occurs in American Bulldogs and Jack Russell Terriers though in a more serious, yet not common, form. Among the breeds that develop EI are Norfolk Terriers, Rhodesian Ridgebacks and Labrador Retrievers.

A University of Pennsylvania study of 46 Golden Retrievers diagnosed with ichthyosis from January 2004 to January 2007 found that all the dogs had mild to moderate dry scaling with variable hyperpigmentation on their abdomens. Large, loose scales ranging from soft white to gray were described as looking like snowflakes.

"The dogs looked like walking snow globes," says Elizabeth Mauldin, D.V.M., associate professor of pathology and dermatology at the University of Pennsylvania School of Veterinary Medicine. "We documented that the dogs suffered from a primary disorder of cornification, the process of making scale in natural skin turnover. We determined that a skin biopsy can be used to diagnose the disorder."

The 46 dogs in the study consisted of 25 females and 21 male Golden Retrievers. Twenty-two dogs had skin lesions when they were younger than 1 year of age; three dogs developed the disorder between 1 and 2 years of age; and 13 dogs were older than 2 years of age. The age of onset was unknown for eight dogs.

The wide age distribution reflects the subtle nature of the phenotype.[2] The challenge of determining an exact age of onset is difficult as mild scaling could have been overlooked. Hereditary ichthyosis is often present at birth, but it is not uncommon for signs to develop later in adulthood.

"All the dogs had strikingly similar histopathologic changes consisting of mild to moderate hyperkeratosis, or thickening of the outer layer of skin, and an absence of epidermal hyperplasia, which is the proliferation of normal cells, and dermal inflammation," Mauldin explains. "Environmental factors including nutrition, supplements, humidity, estrous cycle, and other skin conditions likely impacted the degree of scale formation."

Electron microscopic analysis of the skin of five affected dogs compared with two normal control dogs showed crystalline structures in the outer layer of skin, the stratum corneum. Pedigree analysis of 14 dogs indicated that Golden Retriever ichthyosis is an autosomal recessive condition in which a dog inherits a copy of the mutated gene from both its sire and dam.

Not curable, ichthyosis is treated with moisturizers and emollients to provide palliative care. "Corticosteroids, such as prednisone, do not improve skin condition and actually worsen the skin barrier," explains Mauldin. "This further impairs the body's natural defenses and puts a dog at risk for secondary bacterial and possibly yeast infections."

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Breeders Can Test Golden Retrievers for Ichthyosis

A direct DNA test to help identify Golden Retrievers that are carriers, affected or normal for ichthyosis is available through Antagene, a diagnostic testing laboratory in La Tour-de-Salvagny, France. Ichthyosis is a scaling skin disorder with an autosomal recessive inheritance.

The $120 genetic test can be performed from a cheek swab or blood sample. Samples from Golden Retrievers in the U.S. should be sent to Optigen, a diagnostic testing laboratory in Ithaca, N.Y., which extracts the DNA and ships it to Antagene for DNA testing. Results are available in three to four weeks.

The GRCA Health & Genetics Committee recommends prebreeding testing primarily for dogs that have clinical signs of ichthyosis and for dogs that have close relatives known to be carriers, affected or have clinical signs.

Golden Retriever Ichthyosis

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Two other studies were simultaneously performed on ichthyosis in Golden Retrievers. The studies, which took place in England[3] and France,[4] concluded similar clinical and histopathological results. Thus, the three studies led to the hypothesis of an autosomal recessive transmission mode.

DNA Discovery Aids Understanding

The discovery of the causative mutation for Golden Retriever ichthyosis was made in 2010 by a group of French geneticists led by Catherine André, Ph.D., head of the Canine Genetics team at CNRS/University of Rennes. The project was funded by CNRS and the European Commission under the LUPA initiative that brought together genomic experts at university and private laboratories to study the genetics of dogs and learn more about human diseases. A genomewide association study of 40 affected dogs and 40 unrelated healthy ones allowed them to identify a genomic region on canine chromosome 12.

The researchers used candidate gene sequencing in 12 affected and 12 healthy Goldens to identify the mutation in the PNPLA1 (patatin-like phospholipase) protein. They found a homozygous insertion-deletion, or indel, mutation in PNPLA1 that leads to a premature stop codon and then an altered protein in the affected dogs.

"We considered PNPLA1 to be a promising candidate gene," André says. "This premature stop codon causes a loss of 74 amino acids in the C-terminal region, affecting enzyme activity and potentially lipid droplet binding, of the PNPLA1 protein."

The research was confirmed by sequencing 320 Golden Retrievers, consisting of 120 affected and 200 unaffected healthy dogs. All the affected dogs were homozygous for the mutation, about 30 percent, and the healthy ones were either homozygous for the normal allele, about 30 percent, or heterozygous, about 40 percent, which is consistent with an autosomal recessive mode of inheritance.

The mutation was not found in 180 healthy dogs representing the other four retriever types: Labrador Retriever, Flat-Coated Retriever, Curly Coated Retriever, and Chesapeake Bay Retriever. Nor was the mutation found in 300 healthy dogs of 25 other breeds.

"The data support the causative nature of the mutation in Goldens, as well as the specific founder effect in the breed," André explains. "The indel introduced a frameshift and thus a premature stop codon in the open reading frame of the gene, which led to a loss of 74 amino acids in the highly conserved C-terminal region of the PMPLA1 protein."

The geneticists applied information from the Golden genetic model to human research. "We screened the PNPLA1 gene in humans affected with ARCI," says André. "The research translated well from Goldens to humans through collaborations with Dr. Judith Fisher, a specialist of human ichthyoses from the Institute of Human Genetics at Freiburg University in Germany. Mutations in the PNPLA1 gene were identified in two human families affected by ARCI. This was the first evidence for the involvement of PNPLA1 in ichthyosis in dogs and humans."

Random sampling of 500 Golden Retrievers in France further supports the autosomal recessive inheritance and the mutation frequency as follows:

- Forty percent of dogs are carriers that inherit one copy of the mutated allele. Though they will not be affected, they transmit the mutated allele to 50 percent of their offspring.
- Thirty percent are affected, inheriting two copies of the mutated allele and passing one mutated allele on to 100 percent of their offspring. Many affected dogs do not show signs of disease, while others develop mild to moderate disease.
- Thirty percent are normal. They inherit two copies of the normal allele, and their offspring cannot get the disease even if the other parent is affected or a carrier.

André notes that thus far all affected Golden Retrievers have the same mutation. She believes the disease is less prevalent in Golden Retrievers in the U.S. compared to those in France and other European countries, where the frequency of the mutation now reaches about 50 percent.

She is hopeful that ongoing research will help identify and clarify the role of the PNPLA1 protein in normal and affected dogs. "This is a big concern for breeders," André says. "Some dogs are so mildly affected they are considered clinically unaffected, but if they are bred, they will spread the disease."

Realizing Breeding Implications

A direct DNA test now is available for determining if a Golden Retriever carries the PNPLA1 mutation or is affected by the scaling disorder, although the DNA test cannot predict which affected dogs will actually show clinical signs. Margret Casal, Ph.D., D.V.M., associate professor of medical genetics at the University of Pennsylvania School of Veterinary Medicine, cautions that a positive ichthyosis test should not discourage breeders. "Breeders should not remove affected or carrier dogs from the gene pool," she says. "This would reduce genetic diversity and create a super bottleneck."

The best approach is to gradually reduce the mutation over six or seven generations, Casal advises. "You should consider the entire dog — all his or her qualities and characteristics. An affected or carrier dog that has much to contribute should be bred, although you should avoid breeding two affected dogs. Instead, breed outstanding affected or carrier dogs to clear dogs. This provides a choice of dogs to progressively decrease the frequency of the PNPLA1 gene mutation."

The GRCA Health & Genetics Committee endorses this approach. It also echoes Casal's caution regarding unnecessarily reducing the genetic diversity that is so vital for long-term breed health, Hovan says.

Golden Retriever breeder Gayle Watkins of Cold Spring, N.Y., who breeds under the Galyan prefix, concedes that she has not been too concerned about ichthyosis since it appears so mildly in most Golden Retrievers. A recent litter of seven affected puppies made her think twice.

"We had DNA testing performed on the dam when she was pregnant," Watkins says. "Both she and the sire tested positive. After this happened, I realized how upset prospective buyers can become about buying puppies with a known flaw."

Two of the puppies had moderate to severe flakes, or dandruff. Scales could be seen when the hairs on their coat were parted. "When the puppies were 19 weeks old, the signs had disappeared, and eventually, there were no clinical signs," she says.

Once the genetic test was offered, Williamson tested the sire and dam of a recent litter that produced a puppy with lightly, flaking dandruff. Both the sire and dam came back as carriers. "The dam was bred three times before the DNA test was available," she says. "What's more, all three sires were carriers. I've always placed puppies with dandruff into pet homes, so while I don't have any affected dogs at my kennel, I have plenty of carriers."

Watkins worries that as DNA tests become available for milder conditions, breeders will be forced to avoid producing dogs with any diseases. "We are going to be pushed into making poor decisions for the breed, such as removing dogs from the gene pool for minor conditions," she says. "Fortunately, ichthyosis does not affect a dog's ability to hunt, retrieve, swim or participate in all kinds of activities. It is so important to not lose dogs with great qualities. A DNA test can be helpful as long as we use smart breeding." ■

[1] Grall A, et al. PNPLA1 mutations cause autosomal recessive congenital ichthyosis in golden retriever dogs and humans. *Nature Genetics.* 2012(Jan15);44(2):140-147.

[2] Mauldin EA, et al. The clinical and morphologic features of nonepidermolytic ichthyosis in the golden retriever. *Veterinary Pathology.* 2008(Mar); 45(2):174-180.

[3] Cadiergues MC, et al. Cornification defect in the golden retriever: clinical, histopathological, ultrastructural and genetic characterisation. *Veterinary Dermatology.* 2008:19;120-129.

[4] Guaguère E, et al. Clinical, histopathological and genetic data of ichthyosis in the golden retriever: a prospective study. *Journal of Small Animal Practice.* 2009:50(5);227-235.

Purina appreciates the support of the Golden Retriever Club of America and particularly Rhonda Hovan, the GRCA research facilitator, in helping to identify topics for the *Purina Pro Club Golden Retriever Update* newsletter.

Purina ONE beyOnd Packaging Now Has Weight Circles

Purina ONE beyOnd brand dog food, the super-premium natural food plus vitamins and minerals introduced in 2011, now includes Weight Circles on the packaging. Starting in January 2013, *Purina Pro Club* will no longer accept UPC codes for Purina Point credit.

Purina ONE beyOnd has a value of 11 points per pound, the same as other *Purina ONE* products. The *Purina ONE beyOnd* portfolio includes: Chicken & Whole Oat Meal Recipe, with real white meat chicken as the No. 1 ingredient and accented with carrots, tomatoes and apples, and Lamb & Whole Barley Recipe, with real lamb as the No. 1 ingredient and accented with blueberries, sweet potatoes and spinach. Both have a 26 percent protein to 17 percent fat ratio and are made without corn or wheat, added fillers or artificial preservatives. They offer complete and balanced nutrition for adult dogs.

Purina ONE beyOnd dog food comes in 3.5, 15 and 26 pound package sizes. *Purina ONE beyOnd* is sold at pet specialty, grocery and mass retail stores. For information, visit *www.purinaonebeyond.com*. To talk to a pet adviser, call 1-866-PURINA (1-866-787-4621) from 7 a.m. to 7 p.m. Central time Monday through Friday.

Pro Club Dog Food Checks Change to Match New Packaging Sizes

One of the benefits of being a member of *Purina Pro Club* is receiving dog food checks to offset the costs of *Purina* brand dog food. The $7 dog food checks now can be used toward the purchase of any 14-pound or larger bag of *Purina* brand dog food. New packaging sizes for *Purina* brand dog foods prompted the change.

Purina Points accrue when members submit Weight Circles, the colored circles on packages of *Purina* brand dog food. Weight Circle submissions are processed as Purina Points that can be redeemed for items from the *Pro Club* Member Rewards Brochure, online at *www.purinaproclub.com*, or for *Purina* dog food checks. Members should submit a minimum of 250 pounds worth of Weight Circles in one submission.

Pro Club members may order any quantity of checks in multiples of 10 checks, using their Purina Points. A set of 10 *Purina* brand dog food checks can be ordered for 7,000 Purina Points. A limit of one check can be used per bag. Members should allow three to five weeks for processing and delivery of checks.

How to Reach *Purina Pro Club*

To view your Purina Point balance, *Pro Club* members should visit *www.purinaproclub.com* or call 1-877-PRO-CLUB (1-877-776-2582) between 7 a.m. and 5 p.m. Central time Monday through Friday.

Purina dog food checks expire in one year and cannot be reissued. Members should protect dog food checks like cash. Purina is not responsible for replacement in the event of loss, theft or destruction after issuance.

When submitting Weight Circles, *Pro Club* recommends that you mail them by certified first-class mail or other traceable delivery method. This helps to ensure proof of delivery in the event *Pro Club* does not receive your Weight Circles. *Pro Club* is not responsible for Weight Circles not in its possession.

Reminders from Pro Club

Pro Club members should be aware of the following:

- *Purina Pro Club* is not a program for institutional organizations, such as rescue groups, humane societies or animal shelters.
- Any retail sale or purchase — including Internet transactions — of Purina and *Purina Pro Club* materials is a violation of program terms and conditions. This includes, but is not limited to, the selling or buying of Puppy Starter Kits and weight circles.
- *Pro Club* is not responsible for fraudulent weight circles. Submitting fraudulent weight circles is a violation of the *Pro Club* program terms and conditions.
- Purina reserves the right to terminate membership or remove or disqualify earnings for any violation of account or program terms.

11th Annual National Dog Show Will Be Broadcast on Thanksgiving Day

"The National Dog Show Presented by Purina," hosted by the Kennel Club of Philadelphia, will be broadcast on NBC from noon to 2 p.m. Central time on Thanksgiving, Nov. 22, following the "Macy's Thanksgiving Day Parade."

In its 11th year, The National Dog Show, which features Group and Best in Show judging, has become an American Thanksgiving Day tradition with about 20 million people tuning in. Co-hosts John O'Hurley, of "Seinfeld" and "Dancing with the Stars" fame, and David Frei, of the Westminster Kennel Club and an expert analyst, have provided commentary since the program began in 2002.

Held at the Greater Philadelphia Expo Center at Oaks, The National Dog Show is filmed during the Saturday, Nov. 17 Kennel Club of Philadelphia Dog Show. Judging Best in Show is Vicki L. Abbott of McKinney, Texas.

One of only five benched dog shows held in this country, the Kennel Club of Philadelphia and its predecessor clubs have presented dog shows since 1879. Today, the show draws more than 4,000 entries on Saturday and Sunday and more than 100,000 spectators.

Purina-Sponsored Dog Shows* | November 2012 to January 2013

Event	Date	Location
Bulldog Club of America National Specialty	Nov. 19-24	Costa Mesa, CA
American Brittany Club National Specialty	Nov. 23-25	Fort Smith, AR
Lone Star Winter Classic & Texas Kennel Club Dog Show	Dec. 6-9	Dallas, TX
Holiday Cluster & Malibu Kennel Club Dog Show	Dec. 7-10	Costa Mesa, CA
Cleveland Crown Classic Dog Shows	Dec. 13-16	Cleveland, OH
Kennel Club of Palm Springs Dog Show	Jan. 3-6	Indio, CA
Land O'Lakes Kennel Club Dog Show & Cluster	Jan. 4-6	St. Paul, MN
Florida Gulf Coast Cluster	Jan. 10-11, Jan. 13-15, Jan. 18-20	Ocala, FL

* This table lists some, but not all, upcoming Purina-sponsored dog shows.

Westminster Best in Show Dogs Remembered for their Achievements, Ambassador Roles

The recent passing of three Westminster Kennel Club Best in Show winners has left a void in the hearts of their owners and dog enthusiasts around the world. "J.R.," "Stump" and "Rufus" will be remembered for the records they set but also for how they endeared all who knew them.

Owner-handler Scott Sommer of Houston lost his beloved house dogs, J.R. and Stump, over six days in September. J.R. (CH Special Times Just Right), the Bichon Frise who won the Garden in 2001, died Sept. 20 at 15 years of age. On Sept. 26, Stump (CH Clussexx Three D Grinchy Glee), the Sussex Spaniel who at age 10 became the oldest Westminster winner in 2009, passed away at 13 years of age.

After retiring as show dogs, J.R. and Stump had a daily ritual of taking a 10-minute ride with Sommer to the boarding/show kennel where they lived when they were being campaigned. Stump would get out of the car, walk into the kennel and take his place in the first run — the same that was his when being shown. J.R. liked to sit on a grooming table, where he would bark hello to all who entered.

The top-winning Bichon in breed history, J.R. won the Garden as a 3-year-old. Sommer continued to show the Bichon at select shows, and J.R. captured his 101st show at the first AKC National Championship. Best known for his bouncy, energetic temperament, J.R. also had a calm, empathetic side that came out when Scott took him to visit patients at children's hospitals.

Stump, the 2004 Sporting Group winner at the Garden, came out of retirement to win Westminster, his 51st Best in Show and a first for the rare English breed. Though Stump was entered for Westminster, it was not until the Wednesday before that Sommer decided to bring him due to concerns that he was older and would have to fly in the cargo section because he was too large to meet the size requirement to fit under the seat. On the return trip from New York, Stump flew first class with Sommer.

Barbara and Tom Bishop of Holmdel, N.J., lost their beloved Rufus (CH Rocky Top's Sundance Kid), the 2006 Westminster winner, Aug. 9 at 12 years of age. The first Colored Bull Terrier to win the Garden, Rufus accumulated 35 Bests in Show, including "The National Dog Show Presented by Purina" and the Morris and Essex Kennel Club Dog Show. A dynamic show dog and the most successful Colored Bull Terrier of all time, Rufus went on to became a therapy dog and breed ambassador.

Preceding the passing of these Westminster champions, "James" (CH Felicity's Diamond Jim), the English Springer Spaniel who won the Garden in 2007, died in May 2011 at 11 years old. Owned by Teresa and Allen Patton of Fairfax Station, Va., and handled by Kellie Fitzgerald of Bear, Del., James later visited children at cancer centers and Ronald McDonald houses with Teresa Patton. He became the only canine celebrity to be recognized by the Alzheimer's Association as a Champion for Alzheimer Awareness.

J.R., Stump, Rufus and James, along with "Uno," the Beagle and "Sadie," the Scottish Terrier, helped christen the Purina Event Center at Purina Farms in Gray Summit, Mo., in August 2010. Along with their owners and handlers, these Westminster Best in Show winners walked the red carpet and were the first dogs to enter the facility. Their names are engraved on brick pavers lining the Walk of Champions going into the building.

Purina joins the owners of these special dogs in commemorating their lives. Their accomplishments and their shining personalities will be remembered for many years to come. ■

Purina-Sponsored Sporting Events* | November to December 2012

Event	Date	Location
NGSPA Pheasant Championship	Nov. 1 to Conclusion	Queenstown, MD
Kentucky Open Shooting Dog Championship	Nov. 6 to Conclusion	Richmond, KY
Retriever National Open Championship	Nov. 10-17	Montgomery, TX
English Springer Spaniel National Amateur Championship	Nov. 12	Ogden, UT
Southern Championship	Nov. 12 to Conclusion	Holly Springs, MS
American Brittany Club National Championship	Nov. 23-25	Booneville, AR
English Springer Spaniel National Open Championship	Nov. 24-28	Pinckneyville, IL
UKC Battle of the Breeds	Dec. 7-8	Ada, OK

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

PURINA Pro Club Golden Retriever Update

Your Purina Points Summary

Points Available Through October 31, 2012

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

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