



## **GOLDEN RETRIEVER PIGMENTARY UVEITIS**

### **Late-Onset Inherited Eye Disease May Cause Blindness**



# GOLDEN RETRIEVER PIGMENTARY UVEITIS RESEARCH

## INCLUDES RISK SCORE MODEL TO AID EARLY TREATMENT

Breeding healthy Golden Retrievers is an important goal. When a successful dog is bred multiple times and then develops an inherited disease later in life, it is worrisome. Will the dog's offspring develop the disease or carry the gene(s) that causes the illness? This scenario has played out many times in Golden Retrievers that developed the eye condition pigmentary uveitis.

First described in 1996 by the American College of Veterinary Ophthalmologists' Genetics Committee,<sup>1</sup> the disorder has been diagnosed exclusively in Golden Retrievers and Golden Retriever cross-breeds, thus it is commonly referred to as Golden Retriever pigmentary uveitis (GRPU). A late-onset, progressive disease, GRPU typically occurs in dogs 8 to 9 years of age and older after they have been bred.

The inability to identify affected dogs during their reproductive years has contributed to the widespread penetrance of GRPU in Golden Retrievers across the U.S. and Canada. Initially, about 45 percent of dogs eventually went blind due to secondary glaucoma. However, with early detection and treatment, this number has decreased to about 17 percent, says Wendy M. Townsend, DVM, MS, DACVO, associate professor of veterinary ophthalmology at Purdue University.

Based on clinical data, 23.9 percent of dogs greater than 8 years of age that Dr. Townsend has examined are affected. "Due to the late onset of GRPU, a dog may be bred multiple times or produce multiple generations before being diagnosed," says Dr. Townsend, a Golden





IMAGES COURTESY OF DR. WENDY M. TOWNSEND, PURDUE UNIVERSITY

**From left: 1) In this severely affected GRPU eye, the white wispy fibrin-like material within the eye increases the risk for glaucoma, and the brown areas that look like sprockets on a gear show posterior synechia, where the iris adheres to the lens. 2) The classic radial pigment of GRPU that looks like spokes on a wheel is evident in this eye. 3) The multiple uveal cysts seen in this eye increase the risk for GRPU.**

Retriever enthusiast who began studying the disorder in 2005 while at Michigan State University. Her commitment to learning more about GRPU is reflected in her overseeing eye clinics at the annual Golden Retriever Club of America (GRCA) National Specialty.

GRPU is often a bilateral disease affecting both eyes. The distinguishing sign is radial pigment on the anterior lens capsule, or the front surface of the lens of the eye. "Radial pigment looks like spokes on a wheel where pigment is deposited in a circular pattern," she explains. "A lot of tiny cataracts may be present on the lens, though these do not typically threaten vision. Glaucoma, on the other hand, is painful and may cause loss of vision. Fibrinous material builds up behind the iris where fluid needs to flow, which is a big risk factor for glaucoma."

Fluid-filled uveal cysts may develop from the iris or ciliary body, which make up the vascular lining of the eye. Dr. Townsend says about 30 percent of Golden Retrievers develop uveal cysts, more than any other breed, though not all dogs with uveal cysts develop GRPU. In a study by researchers in Canada, [57 percent of dogs with uveal cysts developed GRPU](#). However, the exact role of cysts in the development and disease progression of GRPU is not known.

"About 58 percent of Golden Retrievers with multiple uveal cysts at the first

examination develop pigmentary uveitis compared with 10 percent of dogs with solitary cysts and 1 percent of those with no cysts," says Dr. Townsend. "Uveal cysts can be difficult to see without dilation and special equipment as they could be tucked behind the iris, the colored part of the eye. These cysts start appearing at around ages 4 to 6.

"In the early stages of GRPU, dogs are not in pain and their eyes look relatively normal," Dr. Townsend explains. "Most owners are not likely to recognize the eye disease. Some may notice a bit of redness over the white part of the eye, though it is inconsistent and potentially things such as dry eye, irritants and even corneal ulcers can cause redness."

The lead investigator of three GRPU studies funded by the [AKC Canine Health Foundation \(CHF\)](#) with support from the [Golden Retriever Foundation](#)<sup>®</sup>, Dr. Townsend aims to identify affected dogs earlier to help reduce disease incidence and potentially lead to improved treatments to prevent or delay the progression of the disease. Dr. Townsend's research grants have focused on:

- Developing a genetic risk model that can be used to score an individual dog's risk for GRPU ([CHF Grant No. 02569-MOU](#), from March 1, 2019, to Aug. 31, 2022)
- Characterizing the composition and source of amorphous material within





the eyes of affected dogs that blocks fluid flow and results in glaucoma and determining if all affected Golden Retrievers have this material within their eyes (CHF Grant No. 02590-A, from Feb. 1, 2019, to June 30, 2022)

- Conducting a genome-wide association study to identify a chromosomal region associated with GRPU (CHF Grant No. 2061, from Jan. 1, 2014, to June 30, 2018)

John Cotter, president of the Golden Retriever Foundation, says, "Pigmentary uveitis is a challenging eye disease partly because of the age at which it occurs after a dog may have produced

several litters. Obviously, it is a detrimental health issue in affected dogs. We have really been trying to stamp this out and support Dr. Townsend in her effort to find a resolution."

"We are still trying to understand the mode of inheritance of this disease," Dr. Townsend says. "In the meantime, it is important for dogs to have annual eye examinations starting at age 2 in which the eyes are dilated and examined by a board-certified veterinary ophthalmologist to catch the disease early and to potentially slow disease progression, relieve pain and maintain vision."

### TREATMENT & VISION LOSS STUDY

In the first study to compare treatment types on the progression of GRPU to glaucoma and vision loss, Dr. Townsend followed 29 Golden Retrievers diagnosed with the disorder in at least one eye from 2011 to 2018. Published in November 2020 in *Veterinary Ophthalmology*, the Canine Health Foundation-funded research (CHF Grant No. 02569-MOU and Grant No. 2061) involved performing at least two eye examinations on each dog at a minimum of six months apart. The hypothesis was that treatment with a topical corticosteroid would significantly slow disease progression compared to treatment with a topical non-steroidal anti-inflammatory drug (NSAID) ophthalmic preparation.

"At each visit, we recorded the dogs' visual status, signs of glaucoma and treatment protocol. We assigned a GRPU score from 0 to 6 based on the degree of pigmentation on the anterior lens, degree of posterior synechia, in which the iris adheres to the lens, presence of fibrinous material in the anterior chamber, and glaucoma," says Dr. Townsend. "At the first eye examination, all the dogs had vision, but by the second exam, nine of the 29 dogs had lost vision. Secondary glaucoma accounted for vision loss in seven dogs.

"We used ultrasound biomicroscopy to take images of the anterior segment

## GOLDEN RETRIEVER FOUNDATION SUPPORTS RESEARCH OF PIGMENTARY UVEITIS & FUNDS OFA EYE REGISTRATIONS OF DOGS 8 YEARS OF AGE & OLDER

The important link between the [Golden Retriever Foundation® \(GRF\)](#) and research of the inherited eye disease Golden Retriever pigmentary uveitis (GRPU) is helping to advance knowledge about this inherited, painful and potentially blinding eye disease that occurs exclusively in North American bloodlines.

GRPU was first described in 1996, and by happenstance, GRF was founded the next year to fund projects that further the welfare of the breed. The lead investigator of multiple studies funded by the [AKC Canine Health Foundation](#) with support from GRF, Dr. Wendy Townsend of Purdue University, a board-certified veterinary ophthalmologist, is working to recognize GRPU, a late-onset disorder, in dogs before their reproductive years.

John Cotter, president of GRF, says, “GRPU in the beginning was mostly seen in conformation bloodlines, but lately dogs coming from perfor-

mance lines have been affected as well. We are thankful for the research of Dr. Townsend and our ability to partner with her in helping to educate breeders and owners while working to understand what causes the disease and how to reduce its prevalence.”

In an ongoing effort to help build a reliable GRPU database, GRF funds the registration fee for the [Orthopedic Foundation for Animals \(OFA\)](#) [Companion Animal Eye Registry \(CAER\)](#) examination for dogs 8 years and older. The goal is to encourage annual examinations even for dogs that have never been used in a breeding program and for the results to be included in the public database. A dog’s date of birth exempts the owner from paying the registration fee.



of the eyes to check for uveal cysts that are part of GRPU. We found that all the dogs had more than four cysts per field when imaging both eyes. A proportional odds model helped us determine whether the topical steroid or topical non-steroidal ophthalmic preparation changed the dogs’ GRPU scores.”

Four factors were evaluated: treatment, age of the dogs, days between exams, and the interaction of these factors. “Although the dogs’ treatment did not affect changes in their GRPU score, we found that the time between examinations was a significant factor in disease progression,” Dr. Townsend says. “Eyes receiving topical steroids had the greatest increase in GRPU scores, but these dogs also had a longer time between exams, so time was the key factor. Only three eyes did not receive topical therapy.”

Ultimately, the eight-year observational study affirmed the need to diagnose pigmentary uveitis in Golden Retrievers in earlier stages via yearly eye exams. “Breeders and owners should ideally have annual ophthalmic examinations on their Golden Retrievers,” Dr. Townsend

says. “This allows for recognizing at-risk dogs so they can be monitored closely and receive proper treatment for glaucoma and other secondary conditions that may threaten their vision. The goal is to prolong vision.”

### TREATMENT CHALLENGES & BREEDING RECOMMENDATIONS

Among the most challenging aspects of GRPU is understanding the pathogenesis of the disease. This impacts treatment, though standard of care involves giving veterinarian-prescribed topical or systemic anti-inflammatory medications often with medications to control inflammation and glaucoma, if present.

“The diagnostic challenge lies not in identifying severely affected eyes but with determining the minimum threshold of clinical findings to make a diagnosis,” Dr. Townsend says. “We know that radial pigment is seen on the anterior surface of the lens of the eye of all affected dogs. We also know that glaucoma occurs in 30 to 36 percent of eyes affected by GRPU, and cataracts

## OFA UPDATES BREEDER OPTION CODES FOR UVEAL CYSTS

The [Orthopedic Foundation for Animals \(OFA\)](#) revamped its classification of uveal cysts in July 2021 based on research showing the correlation between multiple uveal cysts and the development of Golden Retriever pigmentary uveitis (GRPU). The coding, which is used by board-certified veterinary ophthalmologists when performing OFA Companion Animal Eye Registry (CAER) examinations, is intended to help reduce the incidence of GRPU.

The recommendation to update the classification came from Wendy M. Townsend, DVM, MS, DACVO, a board-certified veterinary ophthalmologist who has studied GRPU since 2005, and the Golden Retriever Club of America (GRCA) Health & Genetic and Breeder Education committees. The late Cathie Turner of Sylmar, California, past chair of the GRCA Breeder Education Committee, was instrumental in helping to advance the Breeder Code Option revisions. She also coordinated [a 2021 educational webinar for GRCA in which Dr. Townsend shared insights about GRPU](#).

The revised reporting will enable breeders to avoid breeding dogs likely to develop GRPU and allow them to review ancestors and close relatives for multiple uveal cysts or GRPU. For dogs having an OFA eye report prior to July 2021, breeders

can review the actual eye exam form to help fill in important information not previously provided. It also will aid owners in monitoring dogs at risk of developing the eye disorder.

Previously, all uveal cysts were lumped together under Breeder Option Code D1. The new Breeder Option Codes are:

D1: Uveal Cyst (unspecified)

D1a: Free-Floating Uveal Cyst

D1b: Single Uveal Cyst

D1c: Multiple Uveal Cysts



Annual eye examinations starting at age 2 are among the recommended tests for Golden Retrievers to be eligible for Canine Health Information Center (CHIC) certification. OFA, working with GRCA, also recommends screening tests for hip dysplasia, elbow dysplasia and cardiac disease for all breeding stock. Dogs meeting these basic health screening requirements will be issued CHIC numbers.

Note that for CHIC certification, a dog's testing results do not need to be normal but must be made public so that responsible breeders can make informed breeding decisions. A dog also must be permanently identified via a microchip or tattoo to qualify for a CHIC number.

occur in 37 to 43 percent of eyes depending on the study."

[Although GRPU appears to have an inflammatory component](#), minimal inflammation is seen in eyes affected by the disorder. "Whether this reflects the lack of inflammation in the disease process or control of the inflammation by topical medications is hard to know, as most dogs receive topical anti-inflammatory medications," says Dr. Townsend.

"I generally start dogs on treatment with a topical NSAID, which works like an aspirin for the eye," she says. "Adjunctive therapy may include glaucoma medication if needed. Some dogs with glaucoma may require surgical enucleation, or removal of the eye, and these dogs have a great quality of life."

Breeding of dogs from bloodlines having multiple uveal cysts and of dogs showing radial pigment indicating GRPU is discouraged. Due to the increased risk of developing GRPU for dogs with multiple uveal cysts, the Orthopedic Foundation for Animals (OFA) now reports single versus multiple uveal cysts on the OFA Companion Animal Eye Registry (CAER) exam results. (See "OFA Updates Breeder Option Codes for Uveal Cysts" above)

"Unfortunately, even conscientious breeders who regularly screen their dogs for health clearances and study the health history of potential breeding partners have produced GRPU in their bloodlines," Dr. Townsend says. "Dogs should not be bred if they do





not pass the OFA eye exam because ultimately they could produce affected dogs having this painful condition.”

When clinical cases of GRPU were first described in Golden Retrievers in the Northeastern U.S., [a pedigree review indicated a common ancestry and suggested a founder effect in which a popular sire may have proliferated the disorder throughout the gene pool](#). More recently, it was suggested that GRPU has [an autosomal dominant inheritance with incomplete penetrance, explaining why some dogs but not all are affected and why some have more severe cases than others](#). Dr. Townsend speculates that a polygenic mode of inheritance could explain the pedigree.

Her research aims to determine the genetic risk for individual dogs to develop GRPU via gene sequencing and analysis of RNA expression. “If we could develop a risk score for GRPU, that would allow dogs to be treated sooner and potentially delay or reduce disease progression,” she says. “I also hope we can learn more about the fibrinous material that is seen in severely affected dogs so we will know how to treat them better.”

In the meantime, annual eye examinations by a board-certified veterinary

ophthalmologist and close monitoring of dogs showing early signs of GRPU may help save their vision. Likewise, breeders should study OFA CAER vertical pedigree records of dogs being considered for breeding and their ancestors to avoid using at-risk bloodlines.

To help provide breeders with as much important pedigree data as possible, the GRCA Code of Ethics states: “Dogs that produce offspring should continue to have ophthalmology examinations on a yearly basis for their lifetime, and if the findings permit recertification, the results should continue to be recorded in an approved database.”

As GRF president John Cotter says, hopefully, one day GRPU will be stamped out. ■

<sup>1</sup> Genetics Committee of the American College of Veterinary Ophthalmologists. Ocular Disorders Presumed to be Inherited in Purebred Dogs. Phoenix, AZ. 1996;2nd ed.

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