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# Retinopathy in Greyhound dogs: Prevalence, fundoscopic, and histopathological findings

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## Abstract

**Objectives:** To determine the prevalence of retinal lesions and describe the fundoscopic findings of retinopathy in Greyhound dogs in the Manawatu/Whanganui region of New Zealand. To examine possible associations between sex, age, and racing variables with retinopathy in the study population. To describe retinal histologic findings in seven Greyhounds with retinopathy in New Zealand.

**Methods:** Two hundred Greyhound dogs from the Manawatu/Whanganui region of New Zealand underwent fundoscopy and fundic photography to identify and score the degree of retinopathy. Associations between retinopathy and age, sex, as well as racing variables, were examined. Histologic examination of the retina was undertaken on the eyes of seven Greyhounds from the Manawatu and Canterbury regions previously diagnosed with retinopathy by fundoscopy.

**Results:** Fifty dogs (25.1%) were identified with retinopathy of varying degrees of severity. In at least one eye, 7.5% of dogs had mild retinopathy, 11.6% moderate retinopathy, and 6.0% severe retinopathy. Males were more likely to be affected in both eyes and with moderate or severe grades, than females. Increasing age was not associated with increased prevalence of retinopathy, nor increased grade of severity. Retinal histology identified multifocal retinal detachment in 5 of the 7 cases examined and other common lesions included choroidal necrosis and outer to full-thickness retinal atrophy in the absence of significant inflammation.

**Conclusions:** Retinopathy is prevalent in Greyhounds in the Manawatu/Whanganui region of New Zealand, but more research is required to elucidate the etiopathogenesis. Consideration should be made to include mandatory eye health examination in racing Greyhound dogs.

**KEYWORDS**

chorioretinitis, greyhound, retinal degeneration, retinal detachment, retinopathy, working dog retinopathy

## 1 | INTRODUCTION

Limited reports describe fundic lesions in Greyhounds. A series of 10 cases of focal to generalized retinal degeneration in young, male Greyhounds was described in Australia,[1] and seven of 100 retired racing Greyhounds in the United States were identified with lesions consistent with chorioretinal degeneration.[2] In New Zealand, similar fundic lesions have been reported in working farm dogs[3,4] and were associated with ocular larval migrans in one report.[4] Focal to multifocal retinopathy has been described in other breeds for which the etiology is not elucidated[5,6] and X-linked inheritance has been proposed in Border Collies.[7] The proportions of affected dogs in the populations studied ranged from 12% to 39%.[3–5,7] Further investigation to improve our understanding of the prevalence and pathogenesis of retinal disease in Greyhounds is important to improve both animal welfare and potentially racing performance and safety. In the present study, we sought to determine the prevalence of and describe the fundoscopic features of retinopathy in a subset of the Greyhound population of the Manawatu/Whanganui region. We also described the retinal histologic findings of seven Greyhounds with retinopathy. Secondary aims were to identify any possible associations between age, sex, racing variables, and parentage with retinopathy in this population that could be explored if required in future research.

## 2 | METHODS

Ethical approval for fundoscopy and fundic photography of 200 Greyhound dogs in the Manawatu/Whanganui region was obtained from the Massey University Animal Ethics Committee (protocol 18-117), and all procedures were performed in accordance with The Code of Ethical Conduct for the Use of Live Animals for Research, Testing and Teaching and the New Zealand Animal Welfare Act 1999. No dogs were euthanized as part of this study nor were owners advised that euthanasia should be considered. However, if any Greyhounds that had been diagnosed with retinopathy within, or outside of, the study died or were euthanized for any reason, owners were advised of the option to contact their veterinarian to have eye and brain tissue collected from the dogs at post-mortem for diagnostic histopathology.

The prevalence study participants comprised 160 dogs from 16 training kennels in the Manawatu/Whanganui region of New Zealand, and 40 dogs from a local Greyhound rehoming organization that rehomes ex-racing Greyhounds from around New Zealand. Movement of Greyhound dogs between kennels occurs throughout New Zealand, as well as the importation of some dogs from overseas. All dogs in the prevalence study resided in the Manawatu/Whanganui region at the time of examination, however, some dogs had previously lived in other locations. Greyhound trainers volunteered access to their training kennels and each training facility provided approximately 10 dogs of a range of ages and racing statuses to be examined. Prior random selection of participants was not practical as the dogs registered to the facilities differed from the dogs available for examination, either due to the dog's physical location or due to trainer choice. Three animals were excluded from examination due to detection of advanced keratitis that would obstruct fundic examination. One animal was examined but was subsequently excluded from the statistical analysis due to keratitis obstructing the fundic view in one eye.

Information was collected from the Greyhound Racing New Zealand database for each dog including birth date, age, racing performance, and pedigree. Trainers were questioned on their use of anthelmintics at their facilities, with data collected on the types of internal and external anti-parasitic treatments, and the frequency of their use.

The menace response and palpebral reflex were assessed, followed by the dazzle and pupillary light reflexes using a pen torch (Coast HP3R, Coast, Coast Products, Inc., Portland, OR, USA). In 147 dogs, chromatic red and blue pupillary light reflexes were assessed with a 200 kcd/$m^2$ light intensity torch (Melan-100®; BioMed Vision Technologies, Ames, IA, USA). Pupillary light reflexes were considered complete and normal if the pupil diameter constricted to approximately one third of the corneal diameter or less, in response to the light sources described above. Following examination of ocular reflexes, one drop of tropicamide 1% (Mydriacyl Eye Drops, Alcon Laboratories, Auckland, New Zealand) was applied to each eye to achieve mydriasis and facilitate fundic examination. Any dog that was scheduled to race in the following 48 h was excluded from the tropicamide application due to concerns regarding prohibited substance swabbing.

The fundus of each dog was examined with an indirect ophthalmoscope (Scanoptics SO-2700, Adelaide, Australia) and a 20-dioptre handheld lens (Scanoptics, Adelaide, Australia). All examinations were conducted by a single ophthalmology resident (PP) of the Australian and New Zealand College of Veterinary Scientists. The method described by O'Connell et al.[3] was used to detect retinopathy, which involves the assessment of seven features of retinal degeneration. As retinal degeneration and its features exist as a spectrum of disease, we modified O'Connell's method by scoring the extent of the features from zero to three based on clinical judgment (Table 1). A score of zero was normal, one was mildly affected, two was moderately affected and three was severely affected.

**TABLE 1** Number of affected and not affected eyes with each feature of retinopathy and breakdown of severity of affectation.

| | Not affected (%) | Affected (%) | Mild (%) | Moderate (%) | Severe (%) |
|---|---|---|---|---|---|
| Focal tapetal hyper-reflectivity | 354 (88.9) | 44 (11.1) | 5 (11.4)* | 31 (70.4)* | 8 (18.2)* |
| Melanotic foci | 359 (90.2) | 39 (9.8) | 17 (43.6)* | 14 (35.9)* | 8 (20.5)* |
| Generalized tapetal hyper-reflectivity | 353 (88.7) | 45 (11.3) | 20 (44.4)* | 16 (35.6)* | 9 (20.0)* |
| Generalized discoloration | 348 (87.4) | 50 (12.6) | 10 (20.0)* | 27 (54.0)* | 13 (26.0)* |
| Retinal vascular attenuation | 372 (93.5) | 26 (6.5) | 7 (26.9)* | 17 (65.4)* | 2 (7.7)* |
| Optic nerve head atrophy | 382 (96.1) | 16 (4.0) | 8 (50.0)* | 7 (43.8)* | 1 (6.3)* |
| Tapetal depigmentation | 383 (96.2) | 15 (3.8) | 10 (66.7)* | 4 (26.7)* | 1 (6.7)* |
| Overall severity by total score. | 330 (82.9) | 68 (17.1) | 24 (35.3)* | 27 (39.7)* | 17 (25.0)* |
| Overall severity by holistic grade | 330 (82.9) | 68 (17.1) | 23 (33.8)* | 29 (42.6)* | 16 (23.5)* |

*Note*: Parentheses represent the percentage of eyes in that category out of total eyes (398). In affected eyes, the severity of changes for each feature is represented in mild, moderate, and severe grades, with the number of eyes in each grade shown. Parentheses with asterix (*) represent the percentage of eyes in that grade out of total eyes affected by that feature.

The scores of individual features were combined to give a total score, which was translated into an overall grade of mild, moderate, or severe. A total score of 1–3 received a grade of mild, 4–9 moderate, and 10 or higher severe. In addition to scoring and combining each feature, a holistic grade of the fundus from normal to severe was assigned. This holistic grade correlated well with the total scores and subsequent grades of the individual features. Additional findings such as vitreal degeneration, punctate retinal hemorrhage, or cataract were noted. Dogs with these additional findings would still obtain a score of zero if none of the seven referenced features were present.

Each fundus was imaged with the ClearView® retinal camera (Opti-brand Ltd, Fort Collins, Colorado, USA), and a written description of the fundoscopic appearance was recorded. All fundic images were reviewed by a registered Veterinary Ophthalmologist (AI).

Retinal histology was performed on the eyes of seven Greyhounds that had a prior ophthalmoscopic diagnosis of retinopathy and were euthanized at their owner's request, with eye samples collected post-mortem for diagnostic purposes. One of the seven dogs had been a participant in the prevalence study. Diagnosis of retinopathy was made by the primary investigator in four cases from the Manawatu/Whanganui region (three of which were examined as part of veterinary clinical work, not in a research setting). The three cases from Canterbury were diagnosed with retinopathy by another ophthalmologist, and subsequently, fundic images were taken of these three dogs under ethical approval from the Lincoln University Animal Ethics Committee (protocol 2121-31) and in accordance with the New Zealand Animal Welfare Act 1999, Section 100. The fundic images obtained from these dogs were reviewed by the study investigators to confirm the lesions were consistent with those seen in the Manawatu/Whanganui dogs.

Dogs were euthanized by registered veterinarians at the owner's request. Following euthanasia, both eyes from each dog were removed by the veterinarian for histopathologic examination, along with the whole brain in six dogs. The eyes were fixed whole in Bouin's or Davidson's solution for 24–48 h before being immersed in ethanol for up to 72 h. Each eye was sectioned sagittally through the optic nerve, processed for histopathology, and sections at varying depths were stained with hematoxylin and eosin (HE). The brain was fixed whole in 10% formalin and sections incorporating the optic chiasm, lateral geniculate nucleus, and visual cortex were processed routinely for histopathological examination. All examinations were performed by the same pathologist (HH). In addition, slides from the four dogs from the Manawatu/Whanganui were submitted for review to Comparative Ophthalmology Laboratory of Wisconsin.

## 2.1 | Statistics

Sex and age differences in retinopathy presence and score were compared via two-way tables using the Fisher exact test for two-by-two tables and the chi-square test for larger tables. Confidence intervals were calculated from the binomial distribution.

The association between the retinopathy measures and racing performance measures, along with other potentially confounding effects was examined via logistic regression. The association between total score of retinopathy and normal vs abnormal pupillary light reflex scores (red PLR, blue PLR, and white PLR) was examined in two-way tables. Analysis of the grade of severity within the abnormal dogs was not possible as there were too few samples at each severity level for the model to have enough power to detect significant differences between

them. As the right and left eye reflexes were highly correlated, (correlation value between the left and right white PLR = 0.8315073, $p < 2.2^{e-16}$) the score for each eye was combined into a single binary value (normal in both eyes vs abnormal in at least one eye). The significance of the association between the total score and each of the reflexes was tested using the Fisher exact test for two-by-two tables and correlation tests. Associations between retinopathy occurrence and parentage were investigated using a generalized linear mixed model, with either sire or dam fitted as a random effect. Statistical analyses were performed on Genstat for Windows 21st Edition software (Version 21.1, VSN International, Hemel Hempstead, UK).

## 3 | RESULTS

A total of 200 dogs were examined with 199 dogs undergoing bilateral fundic examination. Ages ranged from 4 months to 12 years, with a mean age of 3.3 years. There were 83 females and 117 males. Race status included 125 active racing dogs, 35 unraced dogs, and 40 dogs at a rehoming agency. There were 42 dogs that had not raced, 31 dogs with 1–25 starts, 40 dogs with 25–45 starts, 43 dogs with 46–75 starts, and 44 dogs that had more than 75 starts. In total, 68 eyes (17.0%) in 50 (25.1%) dogs had identifiable retinal lesions. There were 18/199 (9.0%) dogs affected bilaterally, and 32/199 (16.1%) affected unilaterally, with right and left eyes affected in equal numbers (34 dogs each). There was no significant difference detected in lesion score between left and right eyes overall. Of the 50 affected dogs, 40 dogs had disparate severity between eyes. Figure 1 represents the asymmetric distribution. In at least one eye, 15/199 (7.5%) dogs were mildly affected (Figure 2), 23/199 (11.6%) moderately affected (Figure 3), and 12/199 (6.0%) severely affected (Figure 4).

Figures 2–5 show examples of the major fundoscopic aspects identified and the number and percentage of dogs affected by each aspect is represented in Table 1. Well-circumscribed focal (Figures 2B, 3C,D, 4A, 5A,B), multifocal (Figure 2A), or geographic regions of tapetal hyper-reflectivity were identified frequently often with melanotic foci within the center or near to the lesions (Figures 3D, 4A–D, 5A,B). Striking vermiform melanotic lesions were seen in 5 eyes of 3 dogs (Figure 6A,B). Ill-defined, heterogenous discoloration of the tapetal fundus and generalized tapetal hyper-reflectivity were also identified frequently (Figure 2C,D). Optic nerve head atrophy, retinal vascular attenuation, and non-tapetal changes including apparent retinal thinning and/or depigmentation

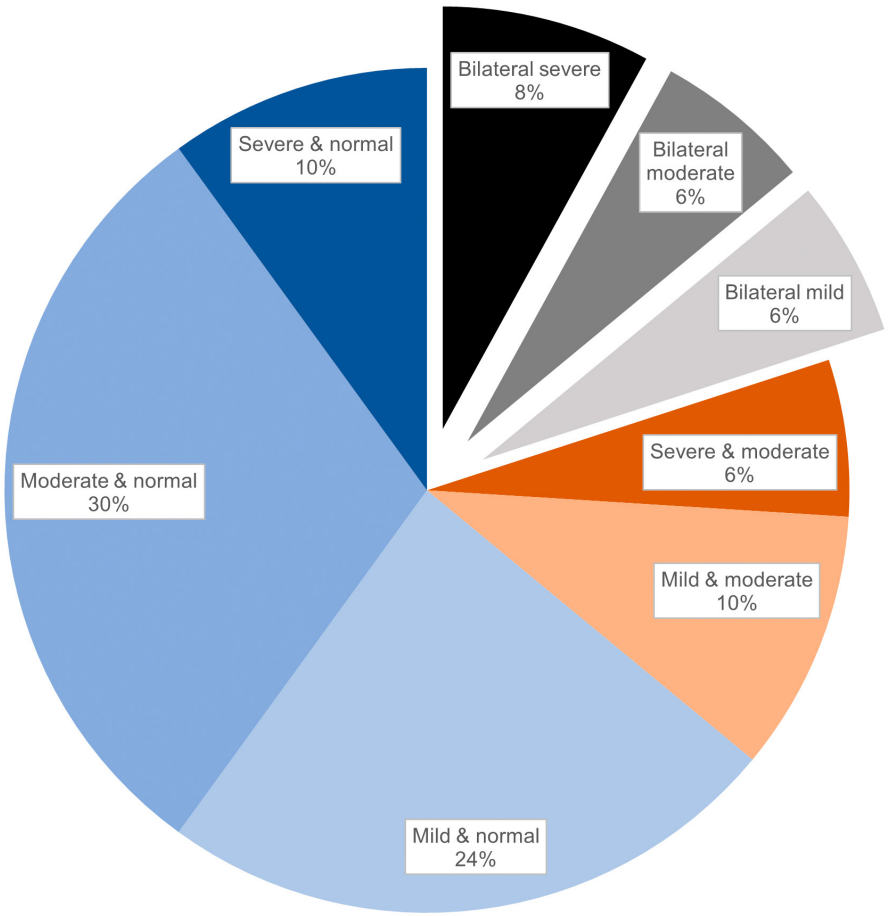



**FIGURE 1** Comparison of retinopathy grade between eyes of affected dogs indicating disparate severity. Blue segments indicate unilateral disease. Exploded segments indicate dogs with the same grade of disease in both eyes.

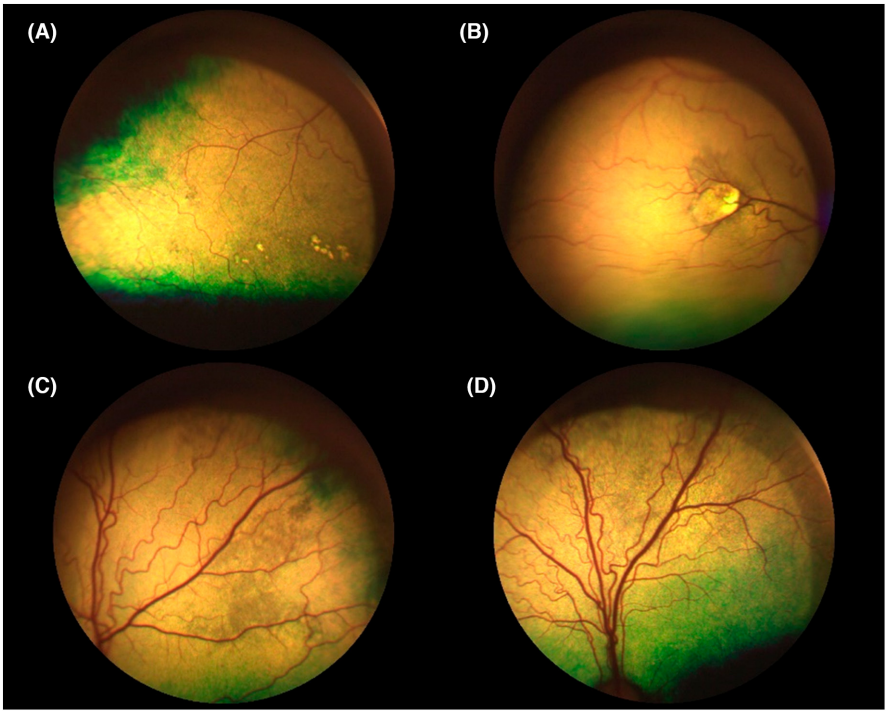



**FIGURE 2** Fundic photographs demonstrating features of mild retinopathy. (A) Mild retinopathy with scattered focal hyper-reflective lesions pictured. (B) Mild retinopathy with focal hyper-reflective lesion and surrounding discoloration. (C and D) Mild retinopathy with heterogenous discoloration.

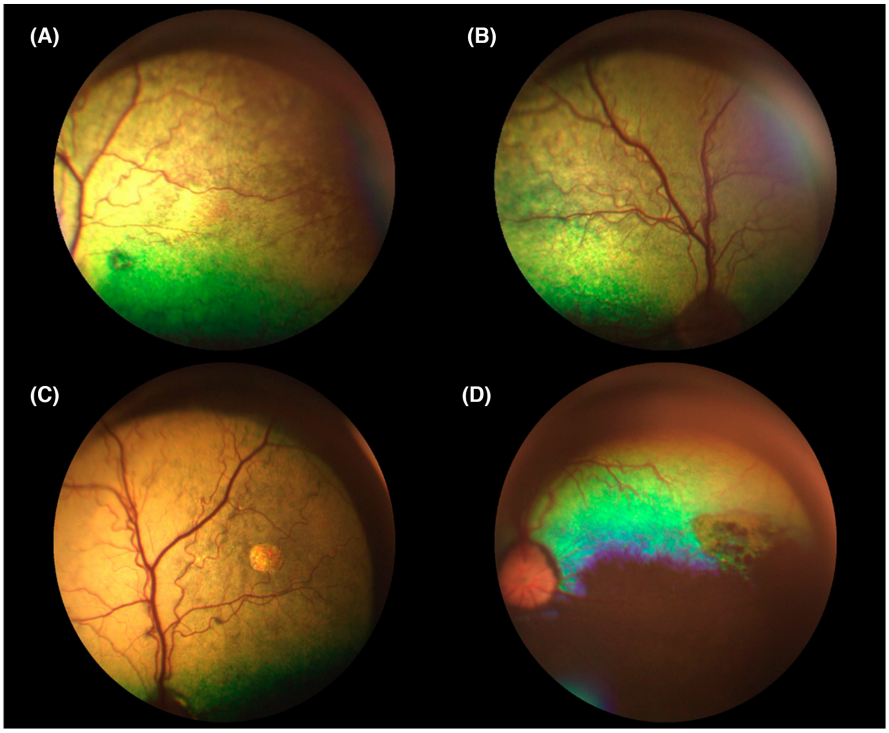



**FIGURE 3** Fundic photographs demonstrating features of moderate retinopathy. (A and B) Moderate retinopathy with heterogenous discoloration pictured. Discrete hyper-reflective region shown in A. (C) Moderate retinopathy with heterogenous discoloration and discrete hyper-reflective lesion pictured. (D) Moderate retinopathy with larger hyper-reflective lesion with melanotic foci within the center.

were identified less commonly. In some animals, an "end-stage fundus" (Figure 4D) was apparent by generalized, advanced retinal atrophy, with or without melanotic foci. Additional findings included punctate retinal hemorrhages (8 eyes), vitreal degeneration (17 eyes), incipient cataract (8 eyes), and iris atrophy (8 eyes). Regions of tapetal hypo-reflectivity and retinal separation were identified in one animal (Figure 6B).

There was no significant difference in the number of males and females affected with retinopathy ($p = .088$, Fisher exact test). However, significantly ($p = .04$) more males had bilateral retinopathy (15/117 males, 12.8%) compared to females (3/82 females, 3.7%). Males were also significantly ($p = .002$) more likely to have moderate to severe retinopathy (29/117, 24.8% males vs. 6/82, 7.2% females.) There was a significant difference in the presence

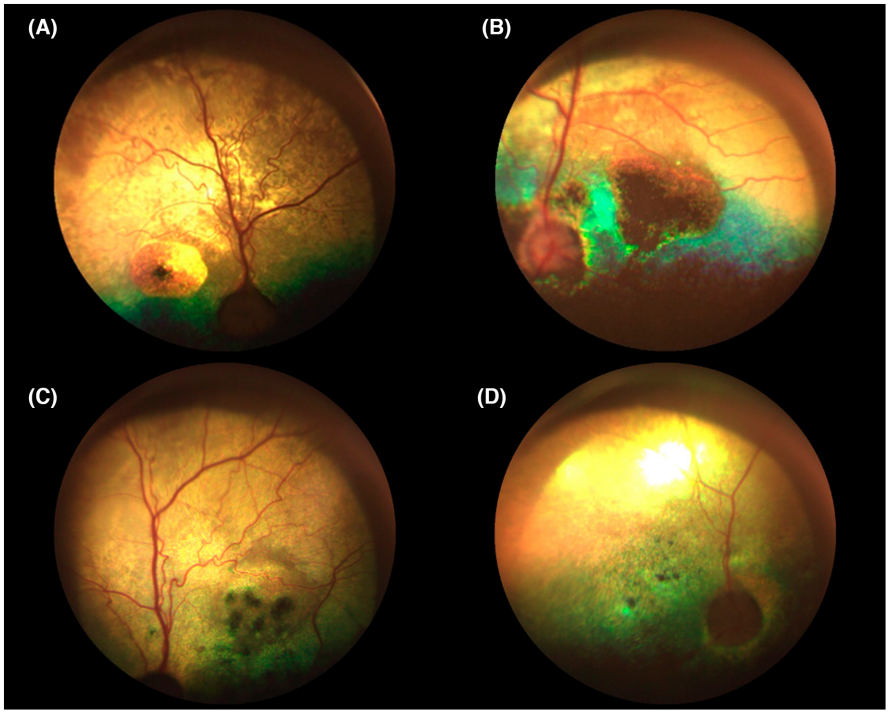
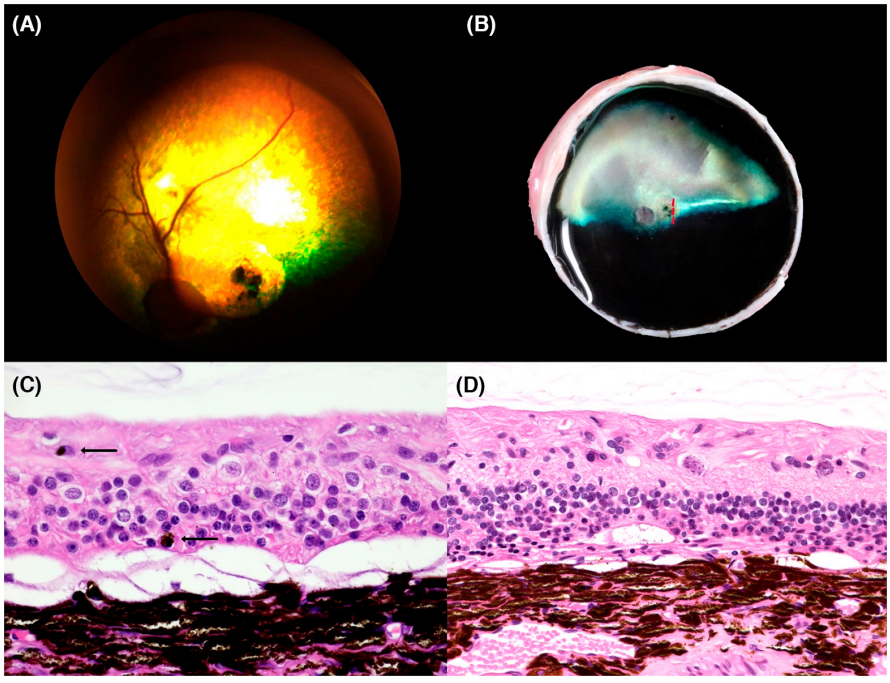



**FIGURE 4** Fundic photographs demonstrating features of severe retinopathy. (A) Severe retinal degeneration with generalized discoloration, hyper-reflectivity, and vascular attenuation. Discrete hyper-reflective zone with melanotic foci (B) Severe retinopathy with large melanotic foci, vascular attenuation, generalized discoloration and hyper-reflectivity, and optic atrophy shown. (C) Severe retinopathy with hyper-reflective lesion with associated melanotic foci, vascular attenuation, and generalized hyper-reflectivity and discoloration shown. (D) Severe "end-stage" retinopathy with severe generalized tapetal hyper-reflectivity and vascular attenuation multifocal melanotic foci shown.

**FIGURE 5** Correlation between fundic, gross, and microscopic findings in a 3.5-year-old Greyhound. Series of fundus photograph (A), gross (B), and histology (C and D) of a severe retinopathy showing a melanotic foci adjacent to the optic disc. (C) Histology from the edge of the melanotic foci indicated by the red line in image B, shows marked retinal atrophy with loss of identifiable retinal layers. Cells containing brown pigment consistent with melanin are present in the retina (arrows). (D) Histology away from the pigmented lesion, showing generalized atrophy of outer retinal layers.




of retinopathy ($p = .008$) between dogs under 1 year of age and the rest of the population (0/19, 0% under 1 year vs. 50/181, 28% over 1 year), although one dog under one was identified with 3 punctate retinal hemorrhages in one eye. There was no significant difference between the age groups 1–3, 4–5, and 6+ years in the presence of ($p = .943$) or score ($p = .619$) of retinopathy. The distribution of ages and severity of retinopathy is represented in Figure 7.

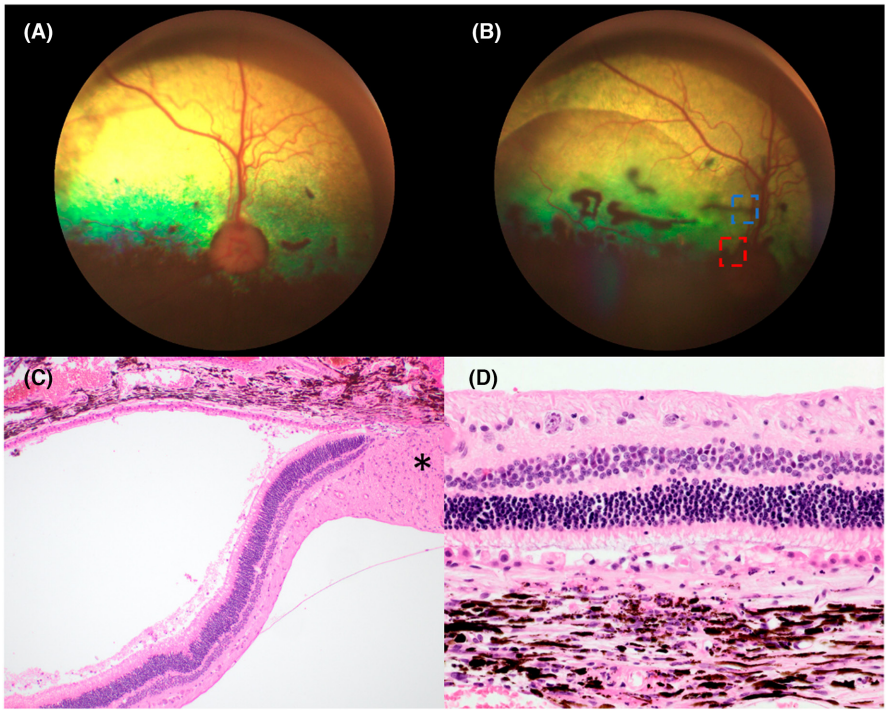



**FIGURE 6** Repeated fundic images from the right eye of a 5-year-old greyhound showing progression of melanotic foci and development of partial retinal detachment over a period of 4 weeks, and the corresponding microscopic appearance of these lesions. (A) Right eye at first presentation picturing vermiform melanotic foci. (B) Right eye at second presentation (4 weeks later) showing increased vermiform melanotic foci and partial retinal detachment. (C) Histology of the right eye in the region of the red box in image (B) showing extensive retinal detachment adjacent to the optic disc (*). (D) Histology of right eye in the region of melanotic foci outlined by the blue box in image (B). There is choroidal necrosis, with melanin pigment and hemorrhage extending into the adjacent tapetum, which is also necrotic. The retina is detached, and the retinal pigment epithelium cells are hypertrophic.

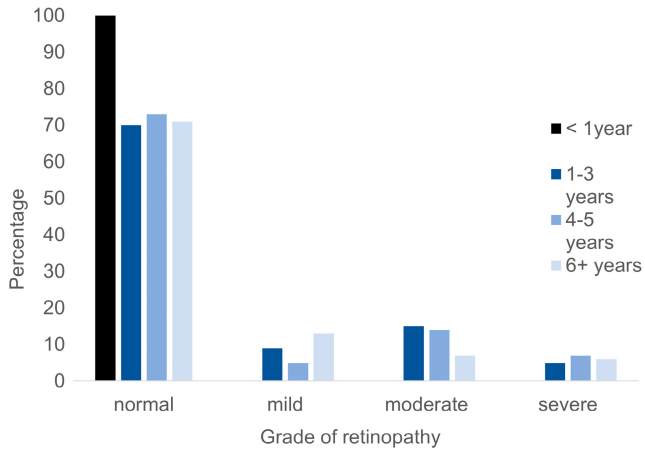



**FIGURE 7** Percentage of age groups in different grades of retinopathy showing a similar prevalence of each grade in age groups over one year. Dogs under one were not affected.

There was no significant association between the number of dogs with retinopathy and their racing status ($p = .964$), stakes ($p = .421$), or the number of racing starts ($p = .353$).

Off-label use of ivermectin (8 of 16 trainers), fenbendazole (five trainers), and triflumuron/imidacloprid (10 trainers) were reported. Use of on-label praziquantel/pyrantel pamoate or praziquantel/pyrantel pamoate/febantel was administered by 11 trainers. Other commercial anti-parasiticides were used less commonly. Frequency of administration of anthelmintics was more than once every 3 months (10 trainers), 3-6 monthly (four trainers), and "as needed" basis (one trainer).

There were no significant differences between sires or between dams in the number of affected dogs. Although some training facilities did have more affected dogs than others, the number of dogs per facility was too small to determine any significance or to interpret husbandry differences between properties.

Dogs with retinopathy had significantly ($p = .05$) more red PLR deficits (21/36 dogs, 58.3%) compared to normal dogs (42/111 dogs, 37.8%). Similarly, dogs with retinopathy had significantly ($p = .02$) more white PLR deficits (16/50 dogs, 32%) than normal dogs (23/149 dogs, 15.4%). A similar trend was seen for blue PLR deficits with 9/36 (25.0%) dogs with retinopathy having a blue PLR deficit versus 13/110 normal dogs (11.8%), but the difference did not reach significance ($p = .107$). The menace response was absent in one eye that had severe retinal lesions.

### 3.1 | Pathology

The seven dogs that underwent histopathological examination of their eyes were aged between 1.6 and 5 years old at the time of euthanasia and all were intact males. Fundoscopic findings in these dogs were consistent with those described in the prevalence study. One dog was included in the prevalence study and subsequently had a second fundoscopic examination performed prior to euthanasia 4 weeks later; on initial examination (Figure 6A) there were vermiform melanotic foci, tapetal hyper-reflectivity, vascular attenuation, and multifocal pinpoint hyporeflective lesions. Progression of disease was identified at the second examination with hemorrhages in the non-tapetal fundus and increased vermiform melanotic change as well as a partial retinal detachment (Figure 6B).

Histologically, all seven dogs had normal areas of retinal architecture (Figure 8A) interspersed with focal to multifocal outer retinal necrosis and atrophy, and occasional focal areas of full-thickness retinal atrophy (Figure 8B–D). Lesions were not symmetrical, with two dogs having extensive retinal atrophy in the right eye, with only a single focus of outer retinal atrophy in the left eye in the sections examined. Four of the dogs had focal or multifocal areas of retinal detachment (Figures 6C and 8B,C) that were bilateral in three and unilateral in one dog. The areas of retinal detachment involved both the tapetal and non-tapetal retina and were often associated with atrophy of photoreceptor segments, hypertrophy of the retinal pigmented epithelium (RPE), subretinal accumulation of variable amounts of pale eosinophilic fluid (Figure 8C), and small numbers of macrophages and detached free floating retinal pigment epithelial cells (Figures 6D and 8D). Two of the dogs with microscopic retinal detachment also had bilateral multifocal to focally extensive areas of choroidal necrosis (Figures 6D and 8B,D) that were infiltrated by a small number of neutrophils, and these areas were accompanied by atrophy of the retina adjacent to them. In one of these dogs, the areas of choroidal necrosis corresponded with vermiform melanotic foci on fundic examination, and melanin pigment from the necrotic chordoid was present in the adjacent damaged tapetum (Figure 6D). Two of the seven dogs had melanotic foci within hyper-reflective lesions seen on fundic examination and gross dissection of the eye. Histologically, these melanotic foci were areas of retinal atrophy with occasional round to polygonal cells containing brown granules in their cytoplasm (melanin) (Figure 5C). Infiltration

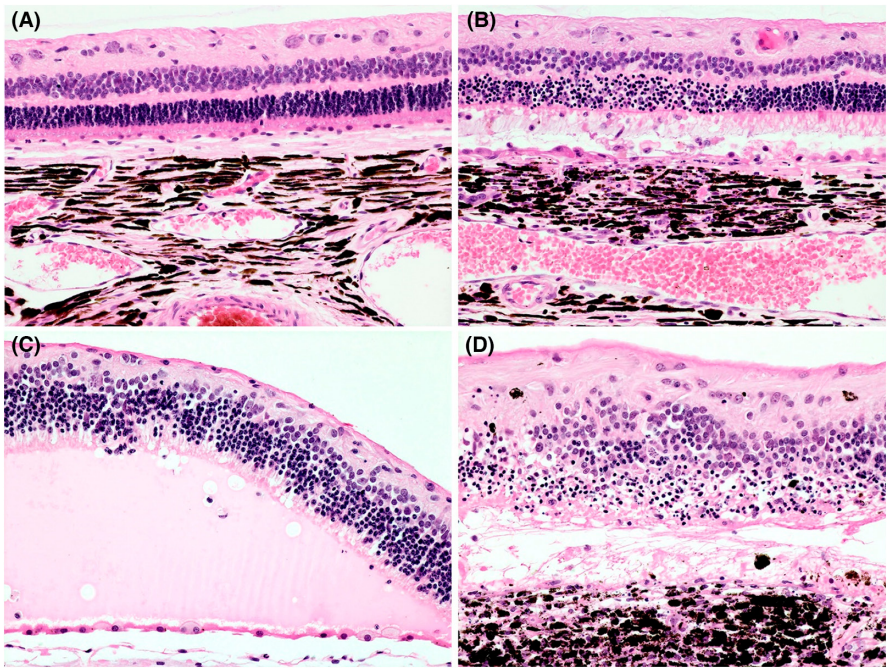



**FIGURE 8** Retinal histology from 2 greyhounds demonstrating the range of microscopic lesions seen in affected dogs. (A and B) Photomicrographs of the retina and choroid of the right eye in a 5-year-old male entire Greyhound who was a participant in the prevalence study (same dog as shown in Figure 6). Areas of normal retinal architecture (A) are interspersed with multifocal areas of retinal detachment with hypertrophy of the retinal pigmented epithelium and choroidal and outer retinal necrosis (B). HE stain, 200× magnification. (C and D) Photomicrographs of the retina and choroid of the left eye in a 1.6-year-old male entire Greyhound. There are focally extensive areas of retinal detachment (C) with accumulation of proteinaceous fluid and rare macrophages in the subretinal space. There is hypertrophy of retinal pigmented epithelial cells and atrophy of the adjacent retina. In other regions, there is severe choroidal and retinal necrosis (D). HE stain, 200× magnification.

of large numbers of melanin-containing cells was seen multifocally within areas of atrophic retina in the non-tapetal region (migration of retinal pigment epithelial cells, Figure 8D). All dogs had normal numbers of ganglion cells (except in completely atrophic foci) and normal optic nerve architecture, and no vascular lesions were identified with Periodic Acid-Schiff staining. No infectious organisms were visible in any sections, and brain sections examined from six of the dogs identified no abnormalities.

## 4 | DISCUSSION

This study demonstrates that retinopathy is a common finding in Greyhounds in the Manawatu/Whanganui region of New Zealand, with 50 of 199 (25.1%) dogs identified with retinal lesions. The fundic appearance in affected dogs is similar to the fundic findings previously described in 10 Greyhounds in Australia[1] and retired Greyhounds in the United States of America at a lower prevalence of 7/100 (7%).[2]

In our study, there was a spectrum of severity from mild focal lesions, to multifocal or geographic lesions, to diffuse and severe or "end-stage" retinal atrophy. The changes seen are consistent with inactive chorioretinitis/chorioretinal degeneration but are not specific changes and can be associated with a wide range of etiologies,[8] which may represent more than one disease process occurring in this population. The melanotic foci, commonly termed pigment aggregations, are thought to occur due to the proliferation of the retinal pigment epithelium (RPE) or alternatively focal tapetal or RPE damage.[9] Microscopically, these focal lesions in the tapetal region were associated with choroidal and tapetal damage with the spread of melanin from the choroid, or the migration of small numbers of pigmented cells into the retina. In the non-tapetal regions, there were larger aggregations of pigmented cells (RPE) in areas of marked retinal atrophy, demonstrating that pigmented fundic lesions may be associated with more than one underlying microscopic lesion.

Dogs under 1 year of age were not identified with retinopathy, and the degree or presence of retinopathy was not significantly different between the older age groups. These findings indicate a possible acquisition of retinal lesions between the ages of 1 and 3 years, rather than progressively throughout the dogs' lifetimes. Previously described cases of retinal degeneration in Greyhounds were documented in dogs examined between the ages of 18–36 months, although visual impairment had been noted from 12 months of age in some of these dogs.[1] The disease is asymmetric, and some dogs had severe but unilateral disease. Repeated retinal insults may occur, as on histology the stage of chronicity of different lesions varied within the same eye and the same dog. Repeated examinations over time are required to properly characterize the evolution of this retinopathy, elucidate age of onset, and determine if the severe retinal atrophy seen in some dogs is the result of damage from a single severe insult, acquisition of multiple insults, or continuous degeneration over time.

The range of lesions seen share some fundoscopic and microscopic similarities to those described in working farm dogs in New Zealand, who have been reported to have a similar high prevalence of retinopathy (39% in 1987, 24% in 2010).[3,4] Historically, the working farm dog retinopathy has been attributed to ocular larval migrans as a small number of dogs in the 1987 study had larval remnants visible on ocular histology.[4] Ocular larval migrans in dogs has also been reported in Border Collie dogs with retinopathy,[10] and larval migration has been reported to be associated with asymmetric multifocal inflammatory and degenerative retinal lesions in both humans and dogs in a disease termed Diffuse Subacute Unilateral Neuroretinitis (DUSN).[9] Given these findings in other breeds, and that Greyhounds are reported to have a high prevalence of intestinal parasitism and antibodies to larval antigens[11] compared to urban dogs, parasite larval migration could be considered as a potential cause of the identified retinal lesions in Greyhounds. Larval remnants were not identified histologically and it should be noted that the choroidal lesions seen in the Greyhound samples differ from those described in the working farm dogs with larval migrans; choroidal necrosis was a feature in the Greyhounds in the absence of choroidal fibrosis, whereas fibrosis without necrosis is described in the farm dogs.[4] In addition, microscopic retinal detachment appeared to precede retinal degeneration in the eyes examined histologically in our study, and inflammation appeared to be minimal, which differs from what is described with ocular larval migrans and other infectious diseases. As ocular tissue samples for histology were available for only seven dogs, the lack of supportive evidence does not preclude ocular larval migrans or other infectious agents as possible etiologies. Greater numbers of histologic examinations with additional histopathologic stains, bleaching of the choroid, and the use of immunohistochemistry markers for inflammatory cells would help to highlight and characterize any retinal and choroidal inflammation associated with the lesions in Greyhounds, as well as any infectious organisms.

Alternatively, the predominance of degenerative lesions on retinal histology and lack of active chorioretinitis on fundic examination in the present study could suggest that this retinopathy is a form of inherited retinopathy. Although the "end-stage" fundoscopic appearance may be phenotypically similar to advanced progressive retinal atrophies such as Progressive Rod Cone Degeneration,

Greyhound retinopathy appears to be distinct. The prevalence and severity of lesions in Greyhounds did not increase with age and the disease was asymmetric and heterogenous in appearance. In the present study, males were more likely to have bilateral retinopathy and were more likely to have moderate or severe grades of retinopathy compared to females. A more striking predominance of males affected with retinopathy is reported in some other breeds.[3,5,7,12] An X-linked trait can result in male predominance and was proposed for a similarly appearing retinopathy identified in Border Collies.[7] There were no significant differences between individual sires or dams in the number of affected offspring in the study, and no clear pattern of inheritance despite some affected dogs being from the same litter. However, a full pedigree analysis on a larger cohort of dogs would be required to investigate any inherited relationship further. An inherited basis for Canine Multifocal Retinopathy (CMR) has been shown in the Australian Shepherd, Mastiff-derived breeds, and Coton du Tulear, and is associated with mutations in the *BEST1* gene.[13–15] Typically in CMR, multifocal bullous retinal detachments occur within the first 4 months of life and progress until 12 months of age, with some lesions subsequently becoming hyper-reflective areas of retinal degeneration after several years.[13,14] Greyhound retinopathy appears distinct from CMR as, although retinal detachment was a histological finding in the Greyhounds examined in the present study, macroscopic retinal detachment was present fundoscopically in only one animal and no bullae or detachments were present in the juvenile dogs examined. CMR appears to have a younger age of onset but a slower progression than Greyhound retinopathy, and has not been described to cause generalized retinal atrophy or the hyper-reflective lesions with melanotic foci that are seen in the Greyhounds and described in other working dog retinopathies. Despite these distinctions, it would be worthwhile performing genetic testing for CMR mutations and other known heritable retinal diseases in this population of Greyhounds with retinopathy.

No significant relationship was found between racing status and the presence of retinopathy in the present study, but associations between physical exertion and retinopathy have been proposed in several dog breeds including working German Shepherds,[6] and Border Collies and Borzois.[12] Some dogs that never raced were identified with retinopathy, however, Greyhounds may undertake significant exercise in training from around 13 months of age before becoming eligible to race from 18 months in New Zealand. Therefore, if an association with exercise exists, there is potential to acquire disease whilst remaining classed as un-raced, which would warrant further investigation. In Border Collies and Borzois, it has been suggested that microhemorrhage arising from athletic stress is involved in the development of multifocal retinal lesions, as the authors identified a break in the laminar separation of the retina and underlying structures, with focal retinal degeneration,[12] similar to what was seen in on histopathology in our Greyhounds. The microscopic lesions seen in the present study also share some features with central serous chorioretinopathy (CSCR) in humans, as micro-rips in the RPE and sub-retinal fluid accumulation and detachments are a feature of CSCR. Further, stress and catecholamines are thought to play a role in the pathogenesis of CSCR[16] and there is potential for high adrenaline secretion and sympathetic stimulation associated with training and racing in Greyhound dogs. Due to practical limitations, the present study lacks the supporting diagnostics of optical coherence tomography (OCT) or fluorescein angiography required to speculate further that CSCR and greyhound retinopathy could be analogous.

Ivermectin toxicosis could be considered as a possible cause of acquired retinal lesions in Greyhounds as this drug has been associated with transient retinal edema and partial retinal separation/detachment.[17] Eight of the training facilities in the present study reported the use of off-label anti-parasitic treatments including the administration of ivermectin, but many of the dogs with retinopathy had never been treated with ivermectin or related macrocyclic lactones, making this drug unlikely to be a sole cause of the lesions observed. More data is required to determine whether anthelmintics or other agents used as treatments for helminths or other diseases could be implicated in Greyhound retinopathy.

Most of the eyes in affected dogs retained a positive menace response, which is unsurprising as this test is considered a crude indication of vision. It is expected that increased severity of retinopathy on fundoscopic examination would translate to greater visual impairment, but the degree of visual impairment is difficult to quantify. Pupillary light deficits were identified in many animals with normal fundic examinations, which may be explained by high levels of circulating adrenaline inhibiting the pupillary light reflex, highlighting the fact that the pupillary light reflexes can be highly variable between animals and any reduction must be interpreted with caution at the individual animal level. Although measured subjectively, there were significantly more pupillary light deficits to both red and white light in dogs with retinopathy, supporting that the altered retinal form had a detectable effect on the retinal function. Further quantification of retinal function in all grades of severity with full field and multifocal electroretinography is indicated in future investigations as an objective measure of retinal function and to provide more information on the retinal layers affected.

A limitation of this study is selection bias due to the lack of random selection of participants. Another potential

source of bias is that dogs with impaired vision could be more likely to have poor performance or behavioral issues and be removed from a training facility. These biases may have impacted the representation of the true prevalence of the retinopathy. As Greyhounds may move between training facilities over their racing lives, and there were low numbers of dogs at each training facility, interpretation of differences between training facilities and husbandry factors in this cross-sectional study was not possible. This study was also limited by the lack of diagnostic investigation other than histopathology. Investigations were not attempted either due to a lack of access to the required equipment and/or the practical limitations of anesthetizing dogs involved in competitive racing, but additional testing will be important in the further characterization of this retinopathy. Fluorescein angiography (FA) has been used to document retinal and choroidal vascular changes in dogs with retinal disease and is useful to identify attenuated or neovascular circulation, vessel filling defects, blood-ocular barrier integrity, and attenuation of overlying structures.[18] Superior visualization of the choroidal vasculature may be obtained with indocyanine green angiography (ICGA) and the technique can be used to complement FA.[19] FA and ICGA would be helpful in the characterization of Greyhound retinopathy to assess the retinal and choroidal circulation and could help to assess the integrity of the tight junctions between RPE cells in areas of retinal detachment, as has been done for Great Pyrenees and Coton du Tulear dogs with CMR.[13,14] OCT allows high-resolution images of the retina and optic nerve head to be obtained non-invasively.[20] In future studies, OCT should be considered to enable the characterization of the retinal lesions in vivo, and it would be particularly useful in longitudinal studies.

This study confirms that retinopathy is prevalent in Greyhound dogs in the Manawatu/Whanganui region of New Zealand. Common fundic examination findings in affected dogs include focal to multifocal regions of tapetal hyper-reflectivity, generalized tapetal hyper-reflectivity, melanotic foci, and heterogenous discoloration of the tapetal fundus. Assessment of visual reflexes supports the conclusion that the identified fundic changes translate into altered retinal function. Males are more likely to be bilaterally and more severely affected compared to females and no dogs under 1 year of age had retinopathy. This retinopathy has important implications for Greyhound eye health and racing performance. Visual deficits associated with retinopathy may impact a Greyhound's quality of life and soundness to race and therefore ocular examination of racing Greyhounds is indicated. The etiopathogenesis of Greyhound retinopathy remains undetermined, but multifocal retinal detachment, choroidal necrosis, and outer retinal necrosis are features on histology. Further research employing genetic testing and pedigree analysis, ERG, OCT, FA, and ICGA, additional histologic examinations, and longitudinal studies will be important to understand risk factors and progression of retinopathy in Greyhounds and potentially other dog breeds that develop similar retinal lesions.

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