The geographic form of retinal dysplasia in dogs is not always a congenital abnormality

Dolores M. Holle,* Mary E. Stankovics,* Carolyn S. Sarna* and Gustavo D. Aguirre†
*The Seeing Eye Inc., Morristown, NJ 07963, USA, †James A. Baker Institute for Animal Health, College of Veterinary Medicine, Cornell University, Ithaca, NY 14853-6401, USA

INTRODUCTION
Retinal dysplasia in dogs is a defect of retinal differentiation. The generalized form is characterized by detachment from the retinal pigment epithelium of the abnormally developed retina at birth, or during the first 6 weeks of life, the time period when the retina undergoes the major period of postnatal retinal maturation.1 The disease has been reported as an inherited trait in the Labrador Retriever,2 Sealyham,3 Yorkshire4 and Bedlington5 Terriers. The focal/multifocal form is characterized by a wide spectrum of ophthalmoscopically visible abnormalities ranging from retinal folds present singly or in multiples, to larger plaque-like lesions which consist of ophthalmoscopically visible clusters of retinal folds present in the tapetal or nontapetal regions. Nonsyndromic focal/multifocal retinal dysplasia is recognized as a familial trait in the American Cocker Spaniel,6 as an autosomal recessive disorder in the English Springer Spaniel,7 and in multiple other breeds, e.g. the Puli, Cavalier King Charles Spaniel and Golden Retriever (8 and G. D. Aguirre, unpublished). Syndromic retinal dysplasia is present in the Labrador Retriever and Samoyed breeds where it represents nonallelic oculoskeletal disorders.9–11 Homozygous affected dogs exhibit short-limbed dwarfism and a constellation of ocular changes which, in the most severe form, are characterized by complete retinal detachment and cataracts. Heterozygous dogs have lesions limited to the retina, and consist of unilateral or bilateral focal/multifocal dysplastic changes.11–13

Ophthalmologic examinations carried out through the Canine Eye Registry Foundation (CERF) program have been promoted as a means of reducing the incidence of inherited ocular diseases in pure-bred dogs by identifying affected dogs early in life, and encouraging their withdrawal from breeding. In general, this program, as well as those in effect in several other countries, has been very effective in its goal, even when the exact mode of inheritance of a given disease is not known. For disorders such as retinal dysplasia, which is believed to represent a congenital abnormality of retinal differentiation, early CERF screening of dogs, usually at 6–8 weeks of age, has been encouraged. However, we have recently become aware that many dogs examined at this age are ophthalmoscopically normal, yet are diagnosed with
retinal dysplasia when re-examined at an older age. To examine the congenital nature of the geographic form of focal/multifocal retinal dysplasia, we carried out a retrospective analysis of the medical records of dogs produced in a closed colony of service dogs who receive very thorough ophthalmologic examinations early in their life, and later, when they return for training. Our findings indicate that, in most cases, the geographic form of retinal dysplasia is not visible before dogs are 10 weeks of age.

**MATERIALS AND METHODS**

**Dogs**

Medical records were reviewed from all dogs produced by The Seeing Eye, Inc. between October 1991 and September 1998, and which had a diagnosis of geographic retinal dysplasia coded. Thirty-five dogs were identified in the five different breeds or interbreed crosses that comprise the breeding and production program: Golden Retrievers ($n=9$), German Shepherds ($n=9$), Labrador Retrievers ($n=12$), Labrador Retriever/Golden Retriever cross ($n=4$) and German Shepherd/Labrador Retriever cross ($n=1$). Further examination of the medical records identified a subset of 23 dogs (Table 1) in which the results of at least two complete ophthalmic examinations were documented, the first before 10 weeks of age, and the second when the dog was a young adult (see below).

All dogs used in this study were the progeny of breeding stock of proven excellent working ability, and none of the parents were affected with retinal dysplasia (focal, multifocal or generalized), or any other ocular disorder which was inherited or potentially inherited. The Labrador Retrievers, German Shepherds and Golden Retriever cross-bred dogs were bred and raised at the breeding facility of The Seeing Eye, Inc. in Mendham, NJ, USA. These dogs received their first general physical and ophthalmic examination between 5 and 6 weeks of age. The pure-bred Golden Retrievers were raised in a satellite breeding facility of The Seeing Eye, Inc. located in Oklahoma, USA. These pups received their first complete physical and ophthalmic examination on arrival at The Seeing Eye, Inc., between 8 and 9 weeks of age. Thereafter, all the puppies were placed in a home environment, and not examined further until they were $\approx 1.5$ years of age unless they were returned to The Seeing Eye, Inc. because of an unrelated medical problem.

**Examination procedure**

A complete ophthalmic examination was performed following pupillary dilatation with $1\%$ tropicamide (Mydriacyl 1%, Alcon Laboratories, Ft. Worth, TX, USA). The anterior segment was examined with a hand-held Kowa SL-5 or SL-14 biomicroscope (Kowa Company, Ltd, Japan), and the fundus was examined with a Keeler binocular indirect ophthalmoscope (Keeler Instruments, Broomall, PA, USA) and a Volk 2.2 pan-retinal fundus lens. In selected cases, fundus photography was performed with Kodachrome 25 film (Eastman Kodak Company, Rochester, NY, USA) and a Kowa RC-2 fundus camera (Kowa Company, Ltd, Japan) used directly, or indirectly through the Volk 2.2 or Nikon 20 diopter lenses. All the studies were made in full compliance with the ARVO Resolution on the Use of Animals in Ophthalmic and Vision Research.

**RESULTS**

The geographic retinal dysplasia lesions found in the affected dogs were clinically indistinguishable among the three pure-bred and two cross-bred lines examined. In the tapetal zone, the lesions appeared as thickened circular plaques of retinal tissue, i.e. circinate retinal lesions. They were usually darker, and altered the normal tapetal reflectivity; retinal folds were present around the margins of the plaques, and, in some cases, within its center (Fig. 1A–H). These plaques were generally present in the posterior pole and equatorial regions of the superior fundus, usually associated with the major retinal vessels. In one case, the major superior retinal vein was disassociated from the arterioles, and the geographic retinal dysplastic lesion was associated with the former (Fig. 1F). If there was retinal thinning as a

<table>
<thead>
<tr>
<th>Breed</th>
<th>No. of dogs</th>
<th>First examination</th>
<th>Second examination (previously normal dogs)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Age</td>
<td>Normal</td>
</tr>
<tr>
<td>Labrador Retriever</td>
<td>7</td>
<td>5–6 w.</td>
<td>7</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td>7</td>
<td>8–9 w.</td>
<td>7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Labrador Retriever ×</td>
<td>4</td>
<td>5–6 w.</td>
<td>3</td>
</tr>
<tr>
<td>Golden Retriever</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>German Shepherd</td>
<td>4</td>
<td>5–6 w.</td>
<td>4</td>
</tr>
<tr>
<td>German Shepherd ×</td>
<td>1</td>
<td>5 w.</td>
<td>1</td>
</tr>
</tbody>
</table>

Age: w., weeks; m. months.
Figure 1. Fundus photographs of German Shepherds (A–E, J) and Labrador Retrievers (F–I) in the study with different lesions characteristic of the geographic form of retinal dysplasia. Where applicable, arrowheads identify the affected region of the fundus, and the asterisk marks the focal hyperreflective zone located in the center of the dysplastic lesion in one dog (G, H). Figures A, C, E, F, and G are wide-field views taken through the Volk 2.2 or Nikon 20 diopter lenses and digitally enlarged; figures B, D, H, I, and J represent views of the fundus taken directly with the fundus camera.
result of the retinal dysplasia, focal hyper-reflectivity was evident on examination (Fig. 1G,H). If located in the nontapetal fundus, the lesions appeared as circular gray to white plaques. They usually contained prominent retinal folds, and were located in the immediate peripapillary region, or along the horizontal retinal vascular arcades located nasally or temporally (Fig. 1I,J).

Thirty-five dogs were diagnosed affected with retinal dysplasia between October 1991 and September 1998. Of these, six dogs were littermates: two Golden Retrievers, two German Shepherds, and two Labrador Retrievers. As detailed records were not available in all 35 dogs to indicate that the initial eye examination results were normal, we excluded 12 dogs from the study. Sixteen of the remaining 23 dogs (Labrador Retriever, German Shepherd, Labrador Retriever/Golden Retriever cross, German Shepherd/Labrador Retriever cross) were examined initially between 5 and 6 weeks of age (Table 1). Only one dog out of these 16 animals, a Labrador Retriever/Golden Retriever cross, had a geographic retinal dysplasia lesion on initial ophthalmologic examination. With the exception of three Labrador Retrievers which also showed retinal folds at the initial examination between 5 and 6 weeks of age, all of the remaining dogs were normal. The location of the retinal folds present in these three dogs was not correlated with the subsequent appearance of the geographic lesions. The seven pure-bred Golden Retriever dogs were not examined until 8–9 weeks of age, and they were normal at that time. Two were identified as affected at 5 and 11 months, respectively, when they were examined at The Seeing Eye, Inc. for unrelated medical problems, while the remaining five dogs were diagnosed as affected when examined between 14 and 19 months of age.

The distribution of the geographic retinal dysplastic lesions was variable, although in all cases they were unilateral, and in 22 of 23 cases they represented single isolated lesions. One Labrador Retriever had two distinct lesions located in the tapetal and the nontapetal zones of the right eye. Labrador Retrievers had lesions mainly in the
right eye, although this was likely to be a spurious sampling result because lesions were distributed almost equally between the right and left eyes in the other breeds. In general, however, dogs with single lesions tended to have them in the tapetal region (17 vs. 5). In only two cases were the lesions located sufficiently in the far peripheral region of the superior quadrant that they could have been missed when the eye examination was performed in a young puppy. In the remaining dogs, the geographic lesions were located in the posterior pole or equatorial regions, areas that are readily visible when examining the fundus with a binocular indirect ophthalmoscope. Details are presented in Table 2.

DISCUSSION

Control of inherited diseases, whether they affect the eye or other target organs, relies on the accurate identification of affected animals early in life, not only prior to their use in breeding programs, but also before owners and breeders invest a significant amount of resources in training or finishing the dog in the show ring. For those conditions such as retinal dysplasia where the mode of inheritance is known, at least for some breeds, identification of affected dogs provides information on the potential genotype of the parents, thus influencing breeding decisions based on the clinical status of the progeny. For this reason, organizations representing the veterinary ophthalmology and eye registry communities have promoted the early examination of puppies at risk for retinal dysplasia.

Over the past several years, one of the authors (G.D.A.) has been surprised to find many dogs affected with focal/multifocal retinal dysplasia, either in the form of folds or geographic lesions, when examined at 1–1.5 years of age, even though these dogs were normal when examined as puppies. The location of most of these lesions in the posterior pole and equatorial retinal regions indicated that these abnormalities would have been readily recognized, if present, during the initial ophthalmologic examination. To establish if the 5–10 weeks of age time period is the appropriate age to recommend ophthalmic examinations in pups at risk for retinal dysplasia, we carried out a retrospective study in a closed breeding colony of service dogs whose ocular disease status is closely monitored at different points of their life. We selected as a clinical end point the geographic form of retinal dysplasia because it is more easy to evaluate, usually occurs as single isolated lesions, and is not subject to the genetic, temporal and phenotypic variabilities found with retinal folds.

Our results indicate that within the five pure-bred and cross-bred lines of dogs that make up our breeding and production program, the geographic form of retinal dysplasia is rarely diagnosed (1 of 23) in dogs before 9 weeks of age. As the standard operating procedures for The Seeing Eye, Inc. do not call for repeat ophthalmic examinations before the dogs are returned for training at ≈ 1.5 years of age, our records do not indicate the earliest age at which a definitive diagnosis can be made, and dogs that are phenotypically normal will remain so. Three dogs were found to be affected when examined before the final examination scheduled at ≈ 1.5 years. Two were Golden Retrievers with geographic lesions noted at 5 and 11 months of age, and one was a Labrador Retriever/Golden Retriever cross-bred found affected at 6 months.

Our finding that the geographic retinal dysplasia lesions were unilateral in all dogs that were part of this study was surprising because most inherited retinal diseases in dogs are bilateral even though they are not necessarily symmetrical. In order to address the question of laterality of the geographic lesion, we queried the CERF database program for a breakdown of this diagnosis by eye affected. Unfortunately, even though the diagnostic categories in the CERF form require identification of the eye affected, this information is not available for retrieval (CERF, personal communication). However, a review of the ophthalmology examination records of one of the authors (G.D.A.) indicated that in most cases geographic retinal dysplasia is a unilateral rather than bilateral disease.

Based on these results, we would recommend that dogs at risk for the geographic form of retinal dysplasia receive more than one examination in order to unequivocally establish the retinal dysplasia phenotype. An initial ophthalmic examination between 5–9 weeks of age can only determine the presence and severity of retinal folds, or the presence of other ocular abnormalities that become manifest in the congenital or perinatal period. A second examination should be performed between 6 months and 1 year of age. Until additional information becomes available, we also would recommend an examination at 1.5 years. In our experience, we have not found any dogs that were normal at this age that subsequently developed the geographic lesions characteristic of retinal dysplasia.

Table 2. Distribution of geographic retinal dysplasia by eye and region

<table>
<thead>
<tr>
<th></th>
<th>Labrador Retriever</th>
<th>Golden Retriever</th>
<th>Labrador Retriever × Golden Retriever</th>
<th>German Shepherd</th>
<th>German Shepherd × Labrador Retriever</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left eye</td>
<td>Tapetal</td>
<td>4 *</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Nontapetal</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right eye</td>
<td>Tapetal</td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>Nontapetal</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Tapetal and Nontapetal</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Geographic retinal dysplastic lesions located in the far periphery in one dog.
ACKNOWLEDGMENTS
The authors are grateful to Cathy Faas and the staff of The Seeing Eye, Inc. for assisting with the medical record collection and retrieval, and Kathleen Weeks and Jill Czarnecki of the James A. Baker Institute for help with medical records and illustrations, respectively. This study was supported in part by the Inherited Eye Disease Research Fund of the Baker Institute.

REFERENCES
8 American College of Veterinary Ophthalmologists, Genetics Committee. Ocular Disorder Presumed to be Inherited in Purebred Dogs. 2nd edn. American College of Veterinary Ophthalmologists 1996.