Evaluation of potential risk factors for development of primary angle-closure glaucoma in Bouviers des Flandres

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OBJECTIVE  
To evaluate potential risk factors for development of primary angle-closure glaucoma (PACG) in Bouviers des Flandres.

DESIGN  
Prospective, observational study.

ANIMALS  
98 Bouviers des Flandres.

PROCEDURES  
All dogs underwent slit-lamp biomicroscopy, indirect ophthalmoscopy, gonioscopy, applanation tonometry, streak retinoscopy, and A-scan, B-scan, and high-resolution ultrasonography. Iridocorneal angles and degree of pectinate ligament dysplasia sheeting were graded, and an angle index was mathematically derived for each eye on the basis of these values. Ciliary clefts evaluated by high-resolution ultrasonography were classified as open, narrow, or closed. Owners were contacted by telephone 7 to 9 years after the initial examination to determine whether dogs had a subsequent diagnosis of PACG. Relationships between previously recorded variables and the development of PACG were evaluated by logistic regression methods. Available pedigrees were reviewed to assess genetic relationships among affected dogs.

RESULTS  
9 of 92 (9.8%) dogs with follow-up information available developed PACG. An angle index ≤ 1 and presence of a narrow or closed ciliary cleft in 1 or both eyes were each significantly associated with development of PACG. Odds of developing PACG for dogs with an angle index ≤ 1 (indicating marked reduction in outflow capacity through the iridocorneal angle), a narrow or closed ciliary cleft in ≥ 1 eye, or both findings were 13, 20, and 28 times those for dogs that did not have these findings, respectively. All dogs that developed PACG shared 1 common male sire or grandsire.

CONCLUSIONS AND CLINICAL RELEVANCE  
Several anatomic factors were significant risk factors for development of PACG in this population of dogs. Results also suggested a genetic component for the disease. (J Am Vet Med Assoc 2017;250:60–67)
dogs are brought in for evaluation late in the course of the disease and, therefore, blindness, enucleation, or a globe salvage procedure are common outcomes even with state-of-the-art care. Therefore, there is a need for diagnostic modalities that allow for the earlier identification of the underlying anatomic and physiologic disturbances in at-risk dogs and for new treatment modalities directed at correcting these disturbances before the disease becomes advanced.

Several breeds of dogs, including the Bouvier des Flandres (commonly termed Bouvier) in Europe and the United States, are affected by PACG. In Bouviers des Flandres, the prevalence of PACG appears to have increased from 0.83% from 1984 to 1993 to 1.31% between 1994 to 2002. Primary angle-closure glaucoma in this breed is associated with PLD, in which development of the iridocorneal angle is arrested, resulting in the persistence of large sheets of dysplastic tissue or thick, broad-based pectinate strands covering varying amounts of the trabecular meshwork and deeper structures of the iridocorneal angle. Large sheets of tissue can be punctuated by variably sized perforations (described as flow holes) that permit aqueous humor to enter the trabecular meshwork and eventually the ciliary cleft before exiting the eye. The deeper tissues of the iridocorneal angle may or may not be normal. In 1 study in The Netherlands, PLD was present in 60 of 80 (75%) otherwise ophthalmically normal Bouviers des Flandres and in 43 of 43 eyes of Bouviers des Flandres with PACG, whereas it was found in 27 of 72 (38%) otherwise ophthalmically normal dogs of this breed examined in Switzerland. In the study performed in The Netherlands, all Bouviers des Flandres with PACG had PLD; however, only a small fraction of dogs with PLD are expected to develop glaucoma.

The high prevalence of PLD but much lower frequency of PACG with PLD in Bouviers des Flandres strongly suggests that PLD is an important risk factor for PACG in this breed, but that alone it is insufficient to cause glaucoma except in the extremely rare instance in which the iridocorneal angle completely fails to develop and the dog is born with glaucoma (congenital glaucoma). This indicates that PLD is only 1 component in the pathogenesis of PACG and that other risk factors for PACG must be present. These risk factors appear to be of sufficient importance that their absence can prevent PACG, suggesting that by gaining a better understanding of these risk factors, it may be possible to identify novel treatments that could be more effective than existing approaches.

In addition to a genetic predisposition to PLD, other risk factors for PACG appear to include female sex (with an approx 2:1 frequency, compared with that in males), increasing age (although PLD is present at birth, glaucoma typically does not develop until the dog is middle-aged or older), stressful or exciting situations, and dim light. Results of a study in ophthalmically normal Beagles revealed that female dogs had a smaller angle opening distance than did males, which could partially explain the predisposition to PACG in females. Among people, predispositions for PACG have been identified in females (with a similar 2:1 frequency, compared with that in males) and in some races. Compared with findings for normal emmetropic individuals, a shallow anterior chamber, hypermetropia (so-called far-sightedness), and shorter axial length of the eye or a thicker, more anteriorly positioned lens have also been associated with PACG in human patients. Additional risk factors that have not been previously identified in people or dogs may also be present.

The purpose of the study reported here was to prospectively evaluate potential risk factors, including ocular anatomic relationships, in a large population of Bouviers des Flandres for association with development of PACG in this breed.

**Materials and Methods**

**Dogs**

Bouviers des Flandres were identified for potential enrollment with the aid of members of the Bouvier Health Foundation (a part of the American Bouvier des Flandres Club). Health Foundation members recruited members of the breed club through direct conversations, notifications at breed club shows or meetings, and digital and print media disseminated to its members. The dogs were of various bloodlines and pedigrees in the Midwest, Southwest, and West Coast regions of the United States. All dogs with or without a familial history of PACG were eligible for study inclusion. Dogs with prior history of PACG in 1 eye were eligible provided they had 1 intact, unaffected eye. Because the intent of the study was to identify potential risk factors that could be associated with eventual onset of PACG, the owners of dogs that were subjectively believed to be at risk for development of PACG (on the basis of the breeders’ knowledge of the presence of severe PLD, PACG, or both in related dogs) were encouraged to participate by Bouvier Health Foundation members in an effort to increase the likelihood of including dogs that would subsequently develop PACG. Seventy-one dogs enrolled in the study had been included in a previous report on the refractive states of eyes in dogs of various breeds. The study was approved by the Institutional Animal Care and Use Committee, and owners provided informed consent for evaluation of their dogs.

**Procedures**

Initial examinations were performed at the University of Wisconsin Veterinary Medical Teaching Hospital and at a privately owned veterinary ophthalmology practice in El Cerrito, Calif, between May 1, 2004, and March 31, 2006; all dogs but 1 were evaluated before the end of July 2005. Examination included streak retinoscopy, gonioscopy, indirect ophthalmoscopy, slit-lamp biomicroscopy, and A-scan, B-scan, and 20 MHz-high-resolution ultrasonography.
(performed with the probe at the 12:00 position according to a clockface analogy). Pupil dilation was achieved by topical application of a 1% tropicamide ophthalmic solution.\textsuperscript{2} Intraocular pressures were measured by means of applanation tonometry\textsuperscript{3} before and after pupil dilation. The eyes evaluated for study purposes were not being treated with antiglaucoma drugs at the time of the examination.

The 360° gonioscopic appearance of the iridocorneal angle was visually evaluated by 1 board-certified ophthalmologist (PEM) using a 3-mirror pediatric lens\textsuperscript{3} and a slit-lamp biomicroscope.\textsuperscript{4} Iridocorneal angle width (as observed on gonioscopy) and the extent of PLD sheeting were scored separately according to a scheme described by Ekesten and Narfström.\textsuperscript{8} An angle index was calculated from the scores assigned to a scheme described by 1 board-certified veterinary ophthalmologist (EB) graded all eyes. Grading was as follows: the iridocorneal angle was scored (closed = 0, very narrow = 1, mildly narrowed = 2, open = 3, and wide open = 4) according to the criteria of Ekesten and Narfström.\textsuperscript{8} For scoring PLD, the portion of the iridocorneal angle (for 360°) affected by sheeting was visually estimated (eg, 10% affected = 0.1). The angle index was then calculated as follows: iridocorneal angle score \( X \) (1 – PLD score). For example, if the iridocorneal angle was mildly narrowed and 80% of the iridocorneal angle was sheeted because of PLD, the angle index was calculated as \( 2 \times (1 - 0.80) = 0.40 \). With this scheme, the maximal angle index value was 4.0 and the minimum value was 0. Therefore, an eye with an iridocorneal angle score of 2 and PLD sheeting affecting 80% of the circumference of the iridocorneal angle would have 0.4/4 or 10% of the estimated outflow capacity of a fully open iridocorneal angle with no PLD sheeting.

The high-resolution ultrasonographic appearance of the ciliary cleft at the 12:00 position was graded as open, narrow, or closed (Figure 1). Clefts were scored as open if the inner and outer leaves of the ciliary body were divergent and the uveal meshwork within the cleft had the expected abundant amounts of relatively hypoechoic spaces (ie, spaces of Fontana) separated by relatively thin hyperechoic fibers representing the uveal trabeculae and ciliary muscle fibers. A cleft was judged narrow if the leaves of the ciliary body were parallel or convergent, leaving fairly compact and relatively hyperechoic tissue within the cleft. The cleft was scored as closed if it was not perceptible. For consistency, one board-certified veterinary ophthalmologist (EB) graded all clefts.

A-scan high-resolution ultrasonography was used for measurement and recording of the axial length of the anterior chamber; the lens, the vitreous, and the eye as a whole. B-scan ultrasonographic images were qualitatively evaluated for grossly visible abnormalities.

Between August 1 and September 1, 2013, 7 to 9 years after the initial examinations were performed, 1 author (AJD) attempted to contact all owners of study dogs by telephone to determine which animals had developed any ocular disorders consistent with glaucoma in 1 or both eyes during the interval following the initial examination if authors were not already aware that the dog had developed PACG. A dog was considered to have developed PACG (as opposed to another ocular disorder) if it had the previously described clinical signs of PACG (eg, acute onset of episcleral injection, corneal edema, pupil dilation, optic disc cupping, and vision impairment). The IOP typically exceeded the upper limit for the tonometer that was used, although occasionally, IOP-lowering medication had been administered by the breeder or the referring veterinarian prior to IOP measurement and IOP at the initial examination was within the normal range. However, every dog previously treated with IOP-lowering drugs that had IOP within the reference range on initial evaluation had primary glaucoma as evidenced by vision loss, optic disc cupping, and no other causes of secondary glaucoma. For all dogs with PACG, the diagnosis was made by a veterinarian. At the time follow-up information was obtained, multigenerational pedigree analysis was performed for all dogs that had follow-up information available. Pedigrees were obtained from the owners or breeders and were examined to identify familial relationships among affected dogs by 2 of the authors (AJD and PEM).

**Statistical analysis**

The primary response variable was new development of glaucoma in 1 or both eyes between the initial (baseline) examination and the time of last telephone follow-up. Covariates included data collected on the basis of dog (age, sex, previous enucleation of 1 eye because of preexisting PACG, and owner data) and eye (categorical ciliary cleft status [open, narrow, or closed], refractive error, IOP before and after pupil dilation, ultrasonographic measurements, and sheet-adjusted iridocorneal angle index). For all analyses of covariates assessed on a per-eye basis, a covariate was derived on a per-dog basis: for dogs with 2 eyes at baseline (some dogs had a previous enucleation of 1 eye), mean values for both eyes were calculated for continuous covariates and categorical covariates were analyzed as mean counts and assessments of findings for \( \geq 1 \) eye. For dogs with PACG in 1 intact eye on initial examination, findings for the glaucomatous eye would have been excluded from the data set because the study was focused on finding factors associated with new development of PACG. However, no such dogs were included in the study. Association of the primary response variable with covariates was assessed and ORs with 95% confidence intervals, and associated \( P \) values were calculated via logistic regression of response against each covari-
ate with an adjustment for age at the time of baseline data collection. The limited number of dogs that had newly diagnosed glaucoma during the study period precluded more sophisticated multivariate modeling. In cases where unconditional logistic regression led to degenerate estimates, exact conditional logistic regression was used to calculate confidence intervals (but point estimates were not reported). Evidence of clustering by owner of patients with newly diagnosed glaucoma was assessed via a \( \chi^2 \) test.

Results

The cohort of dogs examined at baseline included 98 dogs (36 males and 62 females; median age, 4.3 years [range, 0.3 to 13.9 years]) that belonged to 30 owners. At baseline, 4 (4.1%) dogs had prior enucleation of 1 eye because of PACG, and 1 dog had undergone enucleation of 1 eye for secondary glaucoma related to trauma. No dogs had intact, PACG-affected eyes at the initial examination.

Follow-up was available for 92 of 98 (93.9%) dogs. During the intervening 7- to 9-year period, 9 of 92 (9.8%) dogs had developed PACG. Anatomic factors that were significantly associated with development of PACG in the (baseline) age-adjusted logistic regression analyses were summarized (Table 1). Identification of a narrow or closed ciliary cleft in 1 or both eyes by high-resolution ultrasonography (\( P = 0.006 \)), presence of PLD in 1 or both eyes (\( P = 0.002 \)), and an angle index (mean of both eyes eyes) \( \leq 1 \) (\( P = 0.018 \))
Anatomic factors significantly associated with development of PACG for 92 of 98 Bouviers des Flandres that were enrolled in a prospective, observational study to evaluate potential risk factors for the disease in this breed and for which long-term follow-up information was available.

Table 1—Anatomic factors significantly associated with development of PACG for 92 of 98 Bouviers des Flandres that were enrolled in a prospective, observational study to evaluate potential risk factors for the disease in this breed and for which long-term follow-up information was available.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Proportion (%) of dogs with factor</th>
<th>Proportion (%) of dogs without factor</th>
<th>Age-adjusted OR (95% confidence interval)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of PLD (any degree)*</td>
<td>9/56 (16)</td>
<td>0/36 (0)</td>
<td>NA (2.3–∞)</td>
<td>0.002</td>
</tr>
<tr>
<td>Angle index ≤ 1</td>
<td>8/39 (21)</td>
<td>1/53 (2)</td>
<td>13 (1.6–111)</td>
<td>0.018</td>
</tr>
<tr>
<td>Narrow or closed ciliary cleft†</td>
<td>8/33 (24)</td>
<td>1/57 (2)</td>
<td>20 (2.3–172)</td>
<td>0.006</td>
</tr>
<tr>
<td>Angle index ≤ 1 and narrow closed cleft†</td>
<td>7/16 (44)</td>
<td>2/74 (3)</td>
<td>28 (4.9–156)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

The ORs (adjusted for age at the time of initial examination) represent the odds for subsequent development of PACG among dogs for which the described factor was present, compared with those for dogs in which it was absent, on initial examination. To determine the angle index, iridocorneal angles were scored as closed = 0, very narrow = 1, mildly narrowed = 2, open = 3, and wide open = 4. PLD was scored by visually estimating the portion of the iridocorneal angle (for 360°) affected by sheeting (eg, 10% affected = 0.1). The angle index was then calculated for each eye as iridocorneal angle score X (1 – PLD score); the mean of both eyes (when applicable; ie, for dogs that had not undergone a previous enucleation prior to the initial examination) was used for analysis. Follow-up was obtained 7 to 9 years after the initial examination by telephone contact with owners if the authors were not already aware that the dog had developed PACG; all dogs that developed PACG had the diagnosis made by a veterinarian.

*Factor present in 1 or both eyes. †Data were not available for 2 dogs.

NA = Not applicable (unconditional OR estimates were degenerate; exact conditional logistic regression was used to calculate a confidence interval only).

were each significantly associated with new development of PACG between the times of initial examination and follow-up. There was a doubling of PACG odds for each 0.20-unit decrease (95% confidence interval, 0.11 to 0.47; P = 0.003) in angle index. Additionally, every dog that developed PACG had extensive PLD in which sheeting affected ≥ 50% of the iridocorneal angle circumference and often the entire iridocorneal angle circumference.

Prior PACG at the time of initial study examination was a risk factor for new development of PACG in the contralateral eye. All 4 dogs with prior PACG (in 1 enucleated eye) at the initial examination eventually developed PACG in the other eye, whereas PACG developed in 1 or both eyes of 5 of 88 (6%) dogs that did not have PACG in either eye at the baseline examination (95% confidence interval of the OR, 1.4 to ∞; P = 0.017 in the age-adjusted analysis).

Review of the pedigrees for the 9 dogs that developed PACG during the study period revealed a common ancestor (a male dog that was either the sire or grandsire of the affected dogs; the dams were 5 different bitches). However, this dog had also sired a number of other dogs (≥ 27) in the study that did not develop PACG during the study period. The common ancestor was not known to have developed glaucoma; however, the dog had not been examined as part of the study and had no public Canine Eye Registry Foundation examination record available. The 9 dogs that developed new cases of PACG belonged to 7 of 30 owners, with evidence of clustering by owner for affected dogs (χ² test; P = 0.047).

The proportion of dogs that developed PACG during the study period did not differ significantly (OR, 1.0; 95% confidence interval, 0.21 to 4.0; P = 0.88 in age-adjusted analysis) between males (3/33 [9%]) and females (6/59 [10%]), and there was no association between development of PACG and age at the initial examination (logistic regression analysis; P = 0.41). The IOPs before and after pupil dilation at the start of the study and the difference in IOP between the 2 measurements also had no significant association with this outcome (P > 0.20 for all comparisons in the age-adjusted analysis). However, although predilation IOP was assessed for 91 of 92 (98.9%) dogs (including all dogs that developed PACG during the study), postdilation IOP was not assessed in ≥ 1 eye for 6 dogs, including 4 of the 9 dogs that subsequently developed a new case of PACG during the study, limiting the power to detect any association.

There was no significant (P = 0.81 in the age-adjusted analysis) association between development of PACG and refractive error at the initial examination, although the dogs in the study were relatively hyperopic, with a mean ± SD refractive error of 0.6 ± 0.8 D (expected value for emmetropic eyes is 0 D). There also was no significant (P > 0.05 for all comparisons by age-adjusted analysis) association between development of PACG and A-scan ultrasonographic measurements (axial length of the anterior chamber, lens, vitreous, and of the eye as a whole).

Discussion

In the present study, several risk factors for PACG were identified for a population of Bouviers des Flandres. These included a narrow or closed ciliary cleft in 1 or both eyes, a severely reduced capacity for aqueous humor outflow through the iridocorneal angle as estimated by the angle index (ie, an angle index ≤ 1,
which equates to < 25% of normal outflow capacity as observed with a goniolens), any degree of PLD (all affected dogs had severe PLD with sheeting affecting at least 50% of the iridocorneal angle circumference), and previously diagnosed PACG leading to enucleation of the contralateral eye. All affected dogs in this study shared a common sire or grandsire, suggesting a genetic component, although the study was not designed to explore this further. Diagnostic evaluations at the time of initial examination that were not found to be predictive for subsequent development of PACG included IOPs before and after dilation of the pupil; the degree of change in IOP following pupil dilation; A-scan ultrasonographic measurements including anterior chamber depth, axial lens thickness, and axial length of the eye; refractive state of the eye; and the presence of abnormalities on qualitative evaluation of B-scan ultrasonographic images. It is possible that with a larger population of dogs or with repeated measurements over time, 1 or more of these factors would be found to have a statistical association with development of PACG.

It is important to note that the factors associated with PACG in this study were typically present at a single examination time point many months or years prior to development of PACG (although the exact intervals were not obtained owing to follow-up limitations). The ability to identify dogs at risk for the disease at such a time increases the opportunity for therapeutic intervention before IOP increases and the cascade of impediments to aqueous humor outflow and the anatomic and molecular pathways that lead to optic nerve degeneration have become irreversible. Although it is unclear whether prophylactic therapy of eyes at risk for PACG is effective, there have been several studies which have evaluated the efficacy of prophylactic treatment in eyes at high risk for developing PACG (ie, the fellow normotensive eye in dogs with unilateral PACG). A prospective controlled clinical trial examining the efficacy of such prophylactic treatment for the normotensive eye in dogs with unilateral PACG. A prospective controlled clinical trial examining the efficacy of such prophylactic treatment for the normotensive eye in dogs with unilateral PACG found that dogs treated by topical ophthalmic administration of 0.25% demecarium bromide solution and 0.3% gentamicin-0.1% betamethasone solution once daily or 0.5% betaxolol hydrochloride ophthalmic suspension twice daily developed PACG significantly (p < 0.0001 and p = 0.0002, respectively) later (median, 31 months from time of initial diagnosis of PACG in the initially affected eye) than did untreated control dogs (median, 8 months). Results of a retrospective clinical case series indicated that, among dogs of breeds predisposed to PACG, those that received any prophylactic treatment for the unaffected eye developed the condition in that eye significantly later (median of 10 months from the time of onset in the initially affected eye) than dogs that received no prophylactic treatment (median of 5 months). Findings of another retrospective clinical case series also suggested that any form of prophylactic preventative treatment (eg, dorzolamide, brinzolamide, or latanoprost) was associated with an increase in the time to onset of PACG from the median of 5 to 8 months (reported in the literature) to a median of 19.2 months. Finally, a retrospective case series that lacked a control group and evaluated only dogs for which prophylactic treatments failed found no difference in the median time to medical treatment failure (defined as the second eye developing PACG) for dogs that received various antiglaucoma drugs alone or in combination with antiinflammatory treatment. Taken together, the results of the aforementioned studies suggest that prophylactic antiglaucoma treatment of the normotensive eye in dogs with unilateral PACG is likely beneficial. However, it is unclear whether such effects occur in dogs with a narrow or closed ciliary cleft, an angle index ≤ 1, or both, with no signs of overt PACG in the contralateral eye. Prophylactic treatment for such eyes, especially if closely related dogs have developed PACG, is worthy of investigation.

Presence of a narrowed or closed ciliary cleft at the 12:00 position identified by high-resolution ultrasonography was found to be a significant (P = 0.006) predictor for PACG in dogs of the present study months or years prior to its onset. The overall prevalence of glaucoma in Bouviers des Flandres in North America is on the order of 0.8% to 1.3%, but in our study, 8 of 33 (24%) dogs with a narrow or closed ciliary cleft in 1 or both eyes developed PACG, whereas this was found for only 1 of 57 (2%) dogs without ciliary cleft abnormality. The odds of developing PACG in dogs with a narrow or closed cleft were 20 times those of dogs that did not have this feature. This finding was likely attributable to the fact that collapse of the ciliary cleft may have a greater impact on aqueous humor outflow capacity than does PLD; in 1 study of 4 Bouviers des Flandres with PLD, total outflow capacity as measured by tonography was considered normal, suggesting that PLD alone may create minimal resistance to outflow, provided that there are flow holes that allow aqueous humor to access the ciliary cleft. Complete or partial collapse of the ciliary cleft, however, may create a substantially greater impediment to outflow and may be indicative of previous episodes of PACG resulting in compression of the uveal meshwork. Examination of regions of the iridocorneal angle other than that at the 12:00 position by high-resolution ultrasonography or more detailed morphometric analysis of the ciliary cleft may have increased our ability to identify abnormalities of this structure in the present study, but these regions were difficult to consistently acquire images from fully conscious, large-breed dogs, and detailed morphometric analysis of the ciliary cleft is not readily feasible in a clinical setting. Nevertheless, a simple and rapid classification scheme (open, narrow or closed) for characterizing the appearance of the ciliary cleft at the position evaluated readily identified dogs at risk for development of PACG.

The presence of PLD and the calculated angle index, which partially reflected the severity of PLD as...
well as the width of the iridocorneal angle, were also significant predictors for subsequent development of PACG in dogs of the present study. As found in a study from The Netherlands, all dogs that developed PACG in our study had severe PLD, with sheeting affecting 50% to 100% of the iridocorneal angle circumference. However, although PLD has been shown to be a risk factor for glaucoma, most animals with PLD do not develop PACG. We developed the angle index in this study to better capture the capacity for outflow of aqueous humor through the iridocorneal angle, taking into account the degree of angle opening and the degree of PLD (sheeting). Although the angle index was a subjective estimate of outflow capacity through the iridocorneal angle, and the pectinate ligament might not be a limiting factor for the flow of aqueous through the iridocorneal angle, there was a doubling of odds of new glaucoma for each 0.20-unit decrease in the angle index. This indicates that reduction in the capacity for outflow through the iridocorneal angle is related to development of PACG and that the overall appearance of the iridocorneal angle is an important component of this predictive tool. The observation that the presence of anomalies in the iridocorneal angle is associated with development of PACG is also consistent with findings in previous studies. It is important to recognize, however, that the appearance of the iridocorneal angle is dynamic, considering that eyes with various forms of PLD, angle narrowing, or both ultimately develop a gonioscopically closed iridocorneal angle at the time of onset of PACG. Results of a European study of Flat-Coated Retrievers suggested that PLD may be a progressive disorder even in the absence of an overt increase in IOP; however, further investigation is required to determine whether similar processes occur in breeds other than the Flat-Coated Retriever.

In the present study, 1 male dog was the sire or grandsire of all 9 dogs that ultimately developed PACG. This dog had also produced a large number of offspring without PACG and was not known to have the condition, although this could not be verified with medical records. The profound degree of relatedness among affected dogs suggested a genetic component to development of PACG in this population of Bouviers des Flandres, which was in agreement with results of studies that suggested genetic factors play a critical role in the etiopathogenesis of PACG in other breeds, including Flat-Coated Retrievers, Samoyeds, and Great Danes. Although findings in 1 study from Switzerland suggested a recessive type of inheritance pattern for PLD in Bouviers des Flandres, the inheritance pattern is complex, and further studies are needed to elucidate the exact role genetics play in the development of PACG in this breed. The significant ($P \approx 0.047$) clustering by owner of new cases of PACG found in our study was also likely attributable to the tendency of breeders to retain closely related dogs in their kennels.

The Bouviers des Flandres in the present study were typically hyperopic (mean $±$ 0.6 ± 0.8 D), which was in agreement with results of a study by Kubai et al that included dogs of 90 breeds or types (and some of the same dogs enrolled in our study). In people, hyperopia has been shown to be a risk factor for PACG. We found no association between refractive error at the initial examination and the development of PACG in dogs of our study, although serial examinations might have revealed a change in refractive state with age if these had been performed. Serial refraction measurements may be of value in dogs predisposed to PACG, considering that episodic increases in IOP can gradually stretch an eye, increasing its axial length and gradually shifting the eye from a hyperopic or emmetropic state to a relatively myopic state. This so-called myopic shift could have confounded the findings in the present study, because some dogs might have been examined early in the course of developing the disorder (and been hyperopic), whereas others could have been first examined at a later stage and had transient episodes of increased IOP and a myopic shift.

Acknowledgments

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The authors declare that there were no conflicts of interest. Presented in abstract form at the 45th Annual American College of Veterinary Ophthalmologists Conference, Fort Worth, Tex, October 2014.

Footnotes

a. Bausch & Lomb Inc, Tampa, Fla.
b. Tono-Pen, Reichert Technologies, Depew, NY.
c. Haag-Streit USA, Mason, Ohio.
d. Kowa SL-2 slit-lamp biomicroscope, Kowa American Corp, Torrance, Calif.

References


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**From this month’s AJVR**

**Effectiveness of manual bladder expression in paraplegic dogs**
Darren R. Carwardine et al

**OBJECTIVE**
To determine the effectiveness of manual bladder expression in paraplegic dogs by comparing urine volumes measured by use of intermittent catheterization and ultrasonography.

**ANIMALS**
36 paraplegic dogs.

**PROCEDURES**
93 measurements of bladder volume were collected for the 36 dogs. Residual urine volume was determined by use of intermittent urethral catheterization and estimated by use of ultrasonography.

**RESULTS**
Manual bladder expression voided a mean of 49% of urine from the bladder in this population of dogs. There was no correlation ($R^2 = 0.06$) between the effectiveness of manual bladder expression and body weight. Ultrasonographic estimation of bladder volume had good correlation ($R^2 = 0.62$) with bladder volume determined by use of intermittent bladder catheterization but clinically unacceptable variation for predicting actual bladder volume (mean difference, 22 mL; 95% confidence interval, –96 to 139 mL).

**CONCLUSIONS AND CLINICAL RELEVANCE**
Manual bladder expression was ineffective at completely emptying urine from the bladder of paraplegic dogs, but the effectiveness of the procedure was not affected by body weight. Manual bladder expression would likely be a useful procedure to prevent increases in pressure within the bladder. Ultrasonographic estimation of bladder volume could be a useful predictor of actual bladder volume, but it was susceptible to wide variations among dogs, and results should therefore be interpreted with caution. (*Am J Vet Res* 2017;78:107–112)