# Oculopatie Ereditarie in Italia nel Pinscher e nello Schnauzer

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# SOMMARIO

- Introduzione
- Descrizione delle Malattie osservate più frequentemente nelle nostre razze in Italia
- Presentazione nuove malattie (PRA Gigante e Nano) con relativi test genetici
- Comparazione dati Italiani (Panel ECVO italiano e panel FSA) vs. dati esteri (Panel ECVO – D,S,A,DK,NO-, Svezia, Finlandia, USA)
- Visita oculistica e certificazioni presenti in Italia
- Condotta d'allevamento consigliata rispetto alle Malattie riscontrate più frequentemente in Italia
- Eventuali domande

# Malattie Oculari

- *Congenite* :(per definizione presenti alla nascita) spesso ***ereditarie*** o con predisposizione di razza;
- *Non congenite (acquisite)*: ***ereditarie*** (per definizione malattie di sviluppo, compaiono dopo la nascita);
- *(Acquisite non ereditarie)*.

# Malattie Oculari ereditarie

- "*Hereditary Eye Diseases*" (KP-HED);

- Known HED: (K-HED), di provata ereditarietà, ovvero è stata identificata la **mutazione** genetica ed esiste un test genetico disponibile (sono ancora pochi e non per tutte le malattie);

- Presumed HED: (P-HED), di presunta (ma non certa) ereditarietà, perchè non è stata ancora identificata la mutazione genetica e non è quindi disponibile un test genetico affidabile.

# **Quando** una malattia può essere considerata ereditaria in una determinata razza?

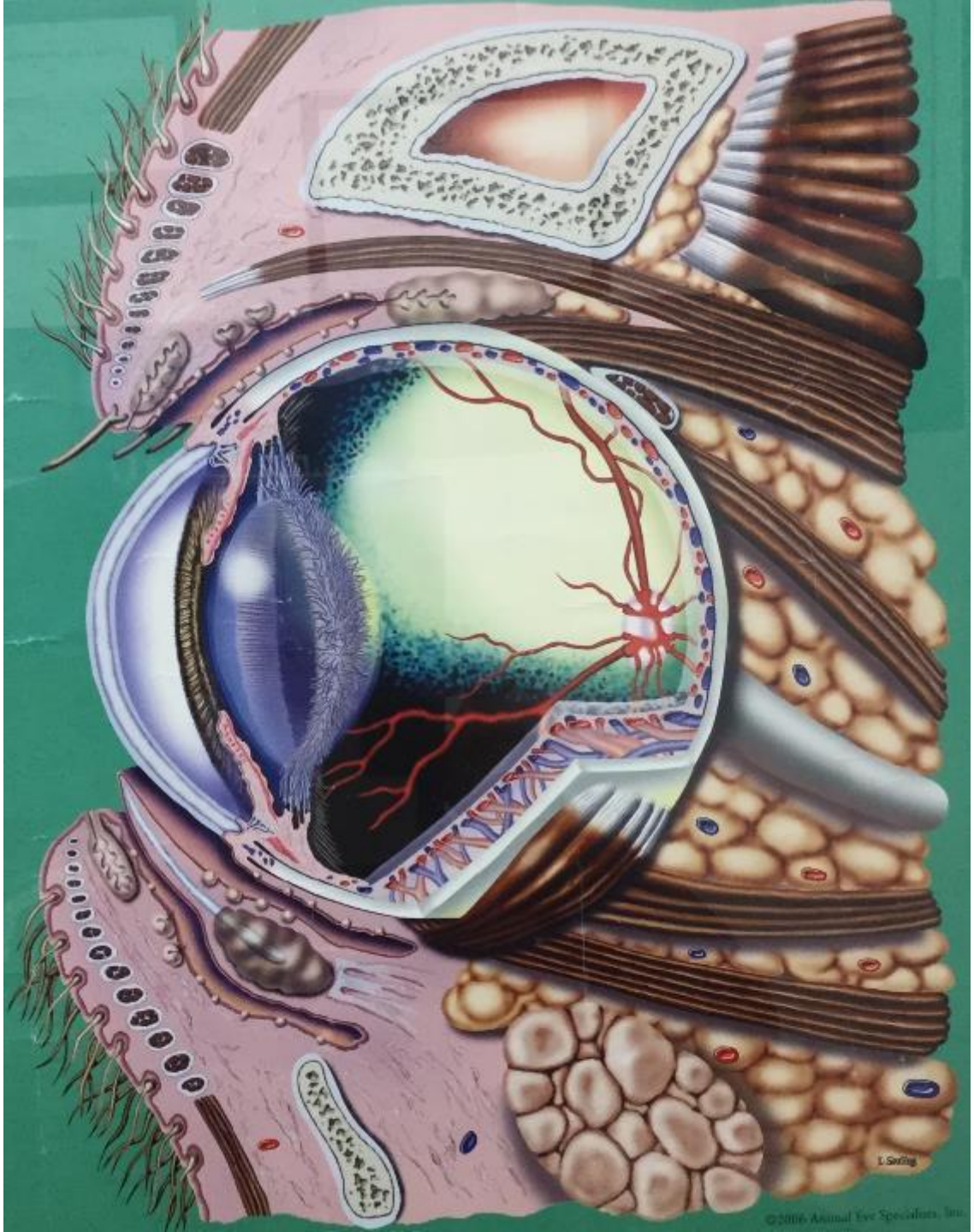
- **Quando la frequenza in quella razza è più alta che in altre;**
- **Quando la frequenza aumenta nella medesima razza;**
- **Quando la frequenza è più grande in soggetti imparentati;**
- **Quando ha aspetto e localizzazione particolari;**
- **Quando ha età di insorgenza e progressione particolari;**
- **Quando è uguale a patologie dimostrate ereditarie in altre razze;**
- **Quando si suppone una base genetica, ma non è stata individuata la mutazione.**

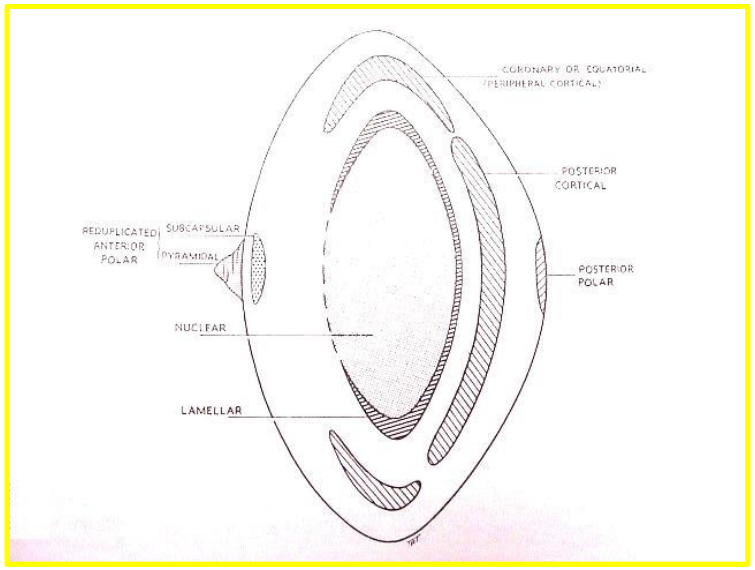
# **Perché** attuare un programma di prevenzione e controllo della malattie oculari ereditarie?

- **Per ridurre l'incidenza di malattie oculari gravi e spesso invalidanti;**
- **Per migliorare il benessere dei nostri animali;**
- **Per fornire maggior garanzia agli acquirenti;**
- **Per migliorare il "pool" genetico di razza;**
- **Per elevare la qualità dei soggetti allevati;**
- **Per bloccare la diffusione di malattie oculari gravi ed emergenti.**

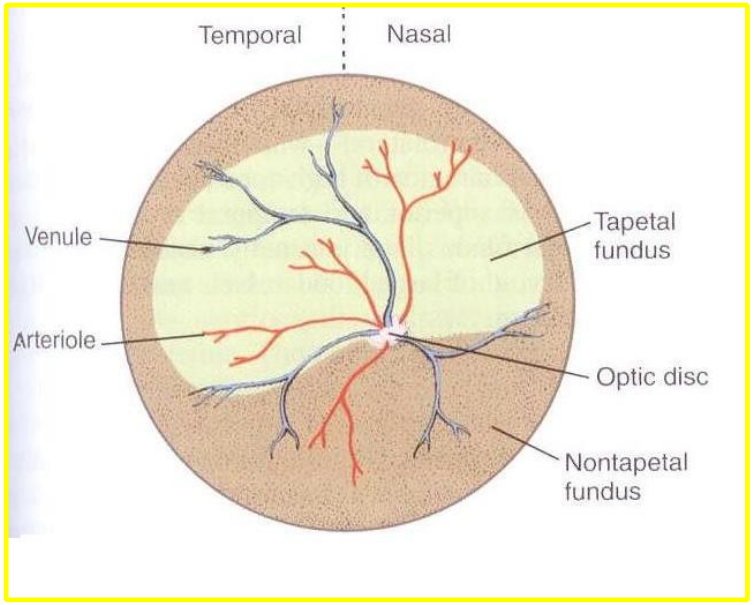
# **Come** attuare un programma di prevenzione e controllo della malattie oculari ereditarie?

- **Sottoporre a visita oculistica specialistica tutti i soggetti (adulti) destinati alla riproduzione (esame da ripetere annualmente);**
- **Associare alla visita la richiesta di esecuzione di test specifici genetici disponibili per ogni razza presso laboratori accreditati (una volta sola nella vita);**
- **Non riprodurre i soggetti affetti (anche se di pregio!) e, per alcune patologie gravi, anche i figli di tali soggetti;**
- **Sterilizzare ( o comunque NON utilizzare) i soggetti malati.**



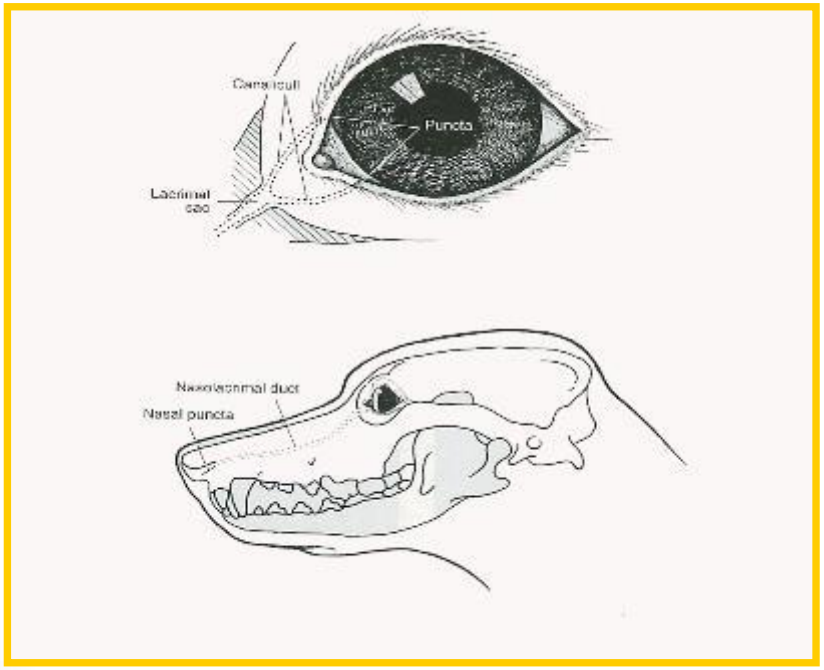


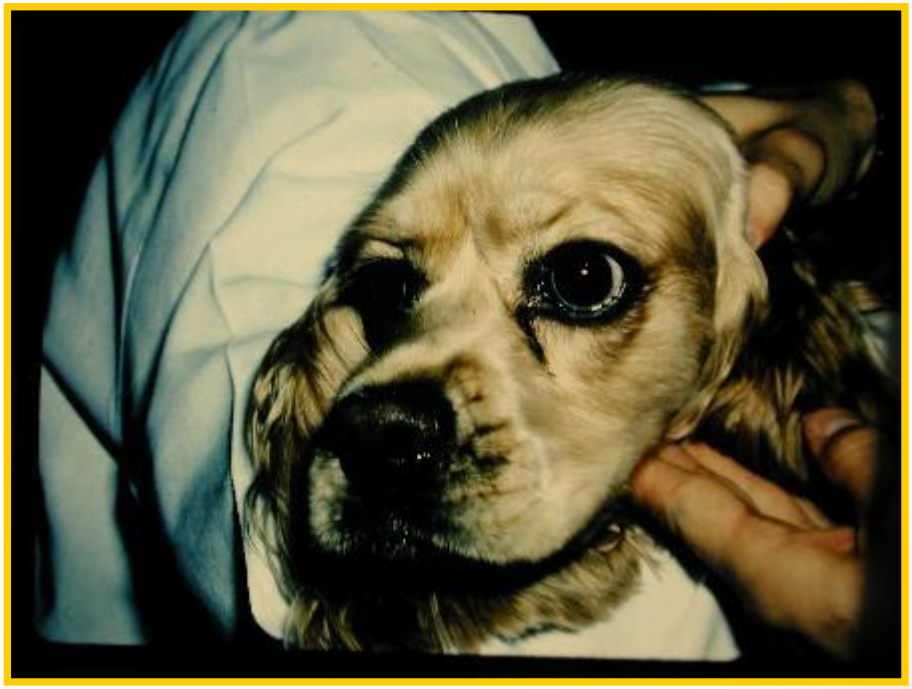

Cristallino (Lente)




Retina

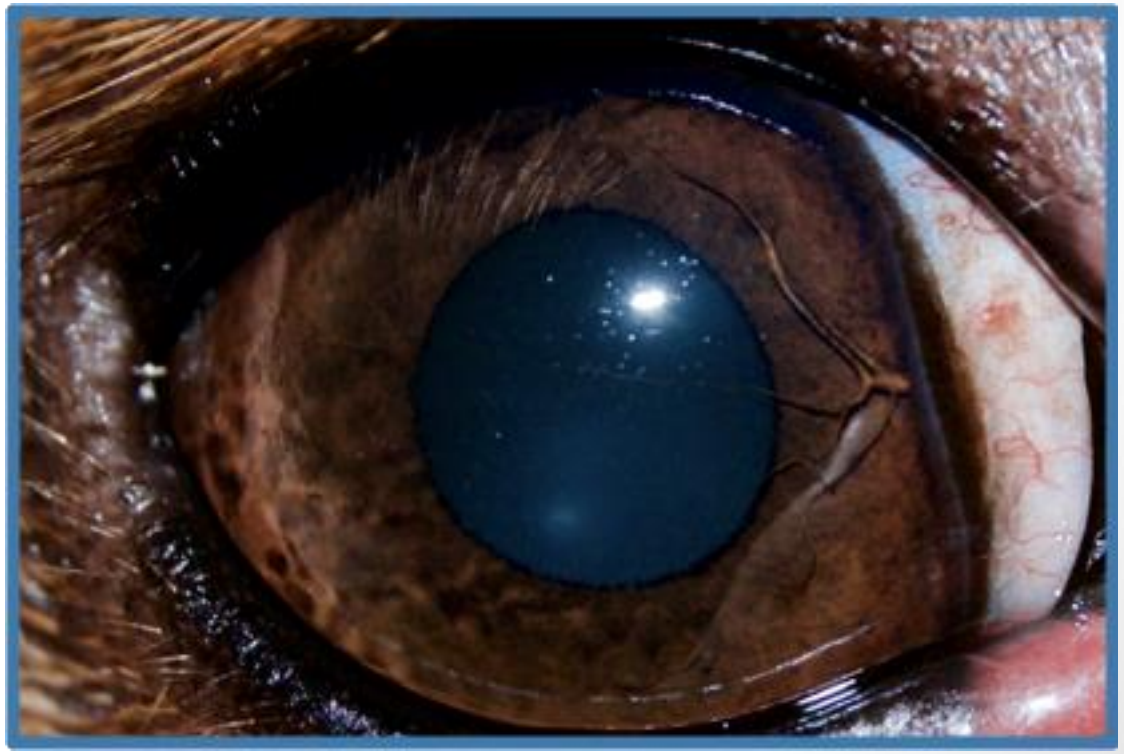
# Atresia punto lacrimale



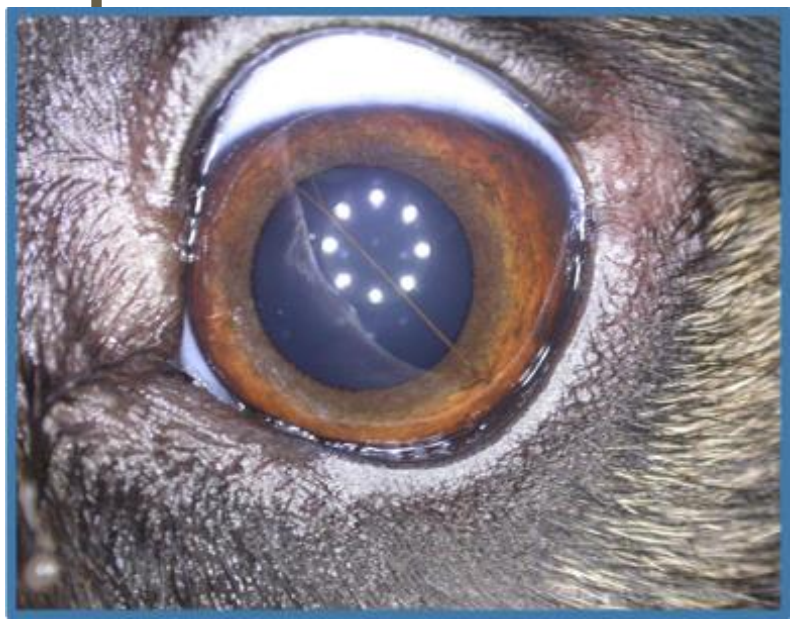



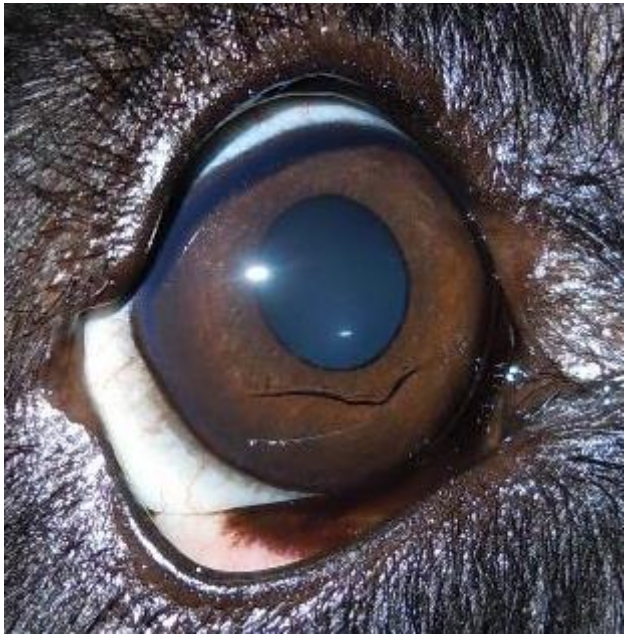
# Persistenza Membrana Pupillare (PPM)

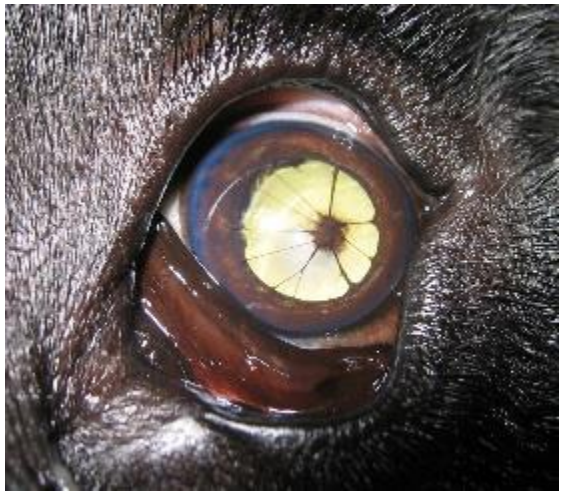
- Alta incidenza (>2-6 sett);
- Da segni clinici inosservati fino a gravi deficit visivi!
- **PPM iride-iride**;
- PPM iride-cornea;
- PPM iride-lente.

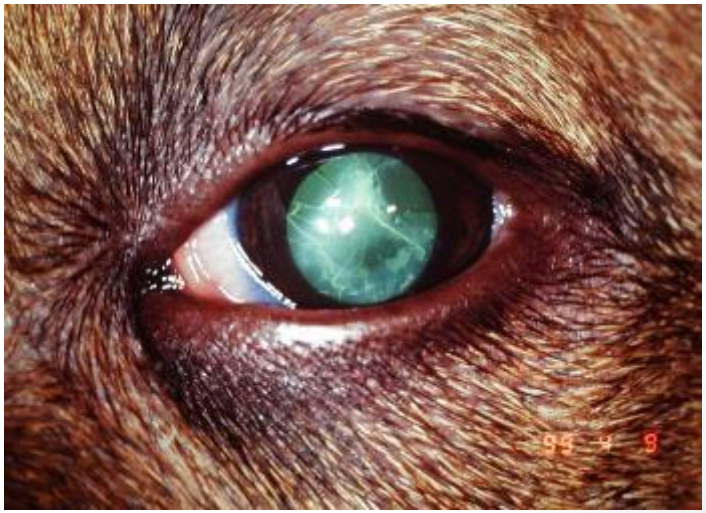


# PPM-Persistenza Membrana Pupillare









# Cataratta (ereditaria)

- Nel cane spesso cataratte genetiche; molte razze colpite, età variabile; evolutive e non evolutive; sempre **esclusione** dalla riproduzione!;
- 160 razze con sospetta ereditarietà (tratto autosomico recessivo semplice);
- solo un gene identificato (**HSF4**).

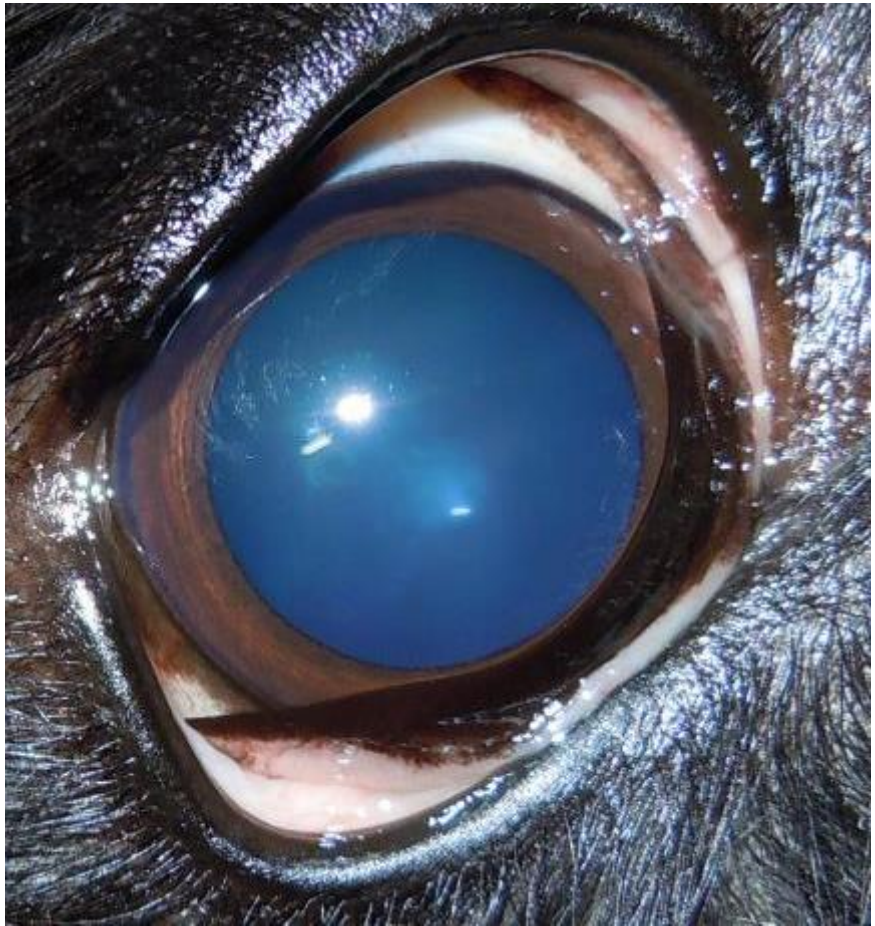
- Nell'*uomo* la maggior parte delle cataratte ereditarie sono *congenite*, mentre nel cane compaiono prevalentemente in età giovanile o adulta.

# Ereditarietà: HSF4

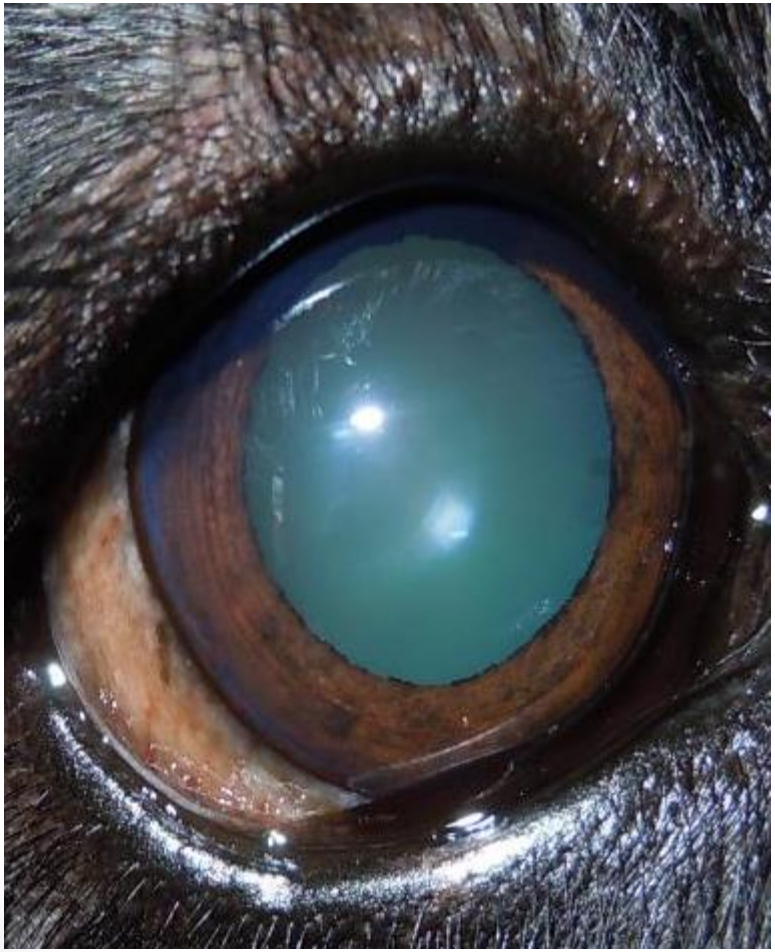
- **Staffordshire Bull Terrier**: autosomico recessivo;
- **Boston Terrier**: autosomico recessivo (f. giovanile);
- **Bouledogue Francese**: autosomico recessivo (?);
- Test genetico disponibile (HSF4-1);
- **Pastore Australiano**:  test genetico disponibile (HSF4-2)
- **“””NON ESISTONO TEST GENETICI PER LA CATARATTA PER SCHNAUZER E PINSCHER””**
- **Non riprodurre soggetti malati!**

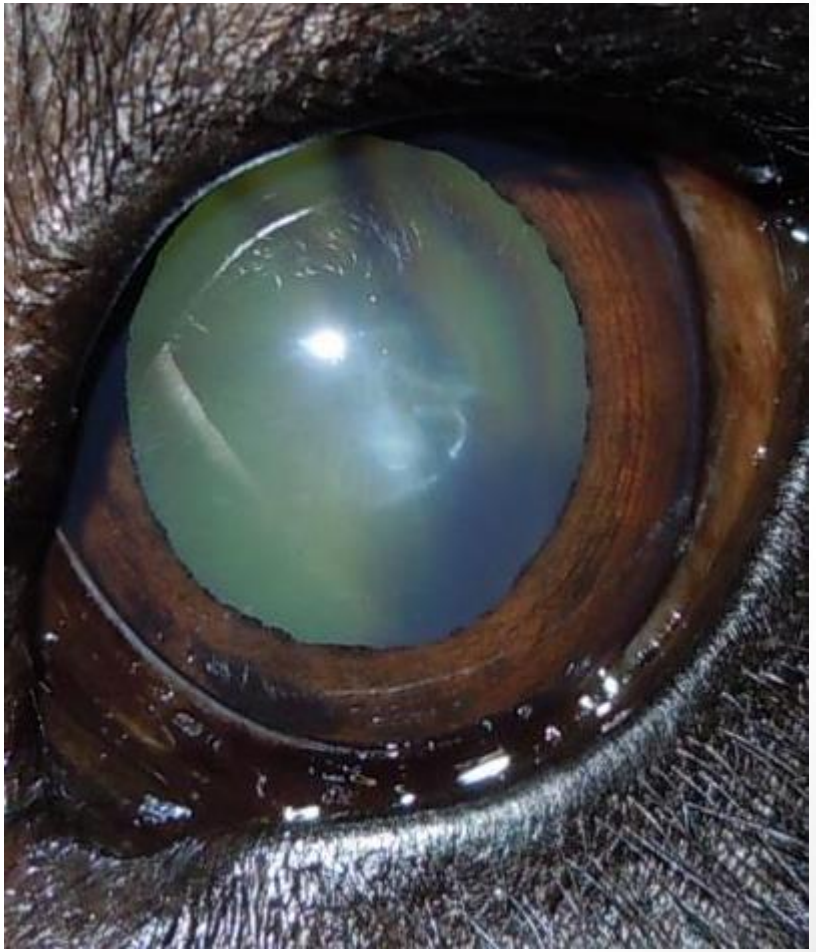
# CATARATTA

CATARATTA SUBCAPSULARE POLARE POSTERIORE. SCHNAUZER MEDIO

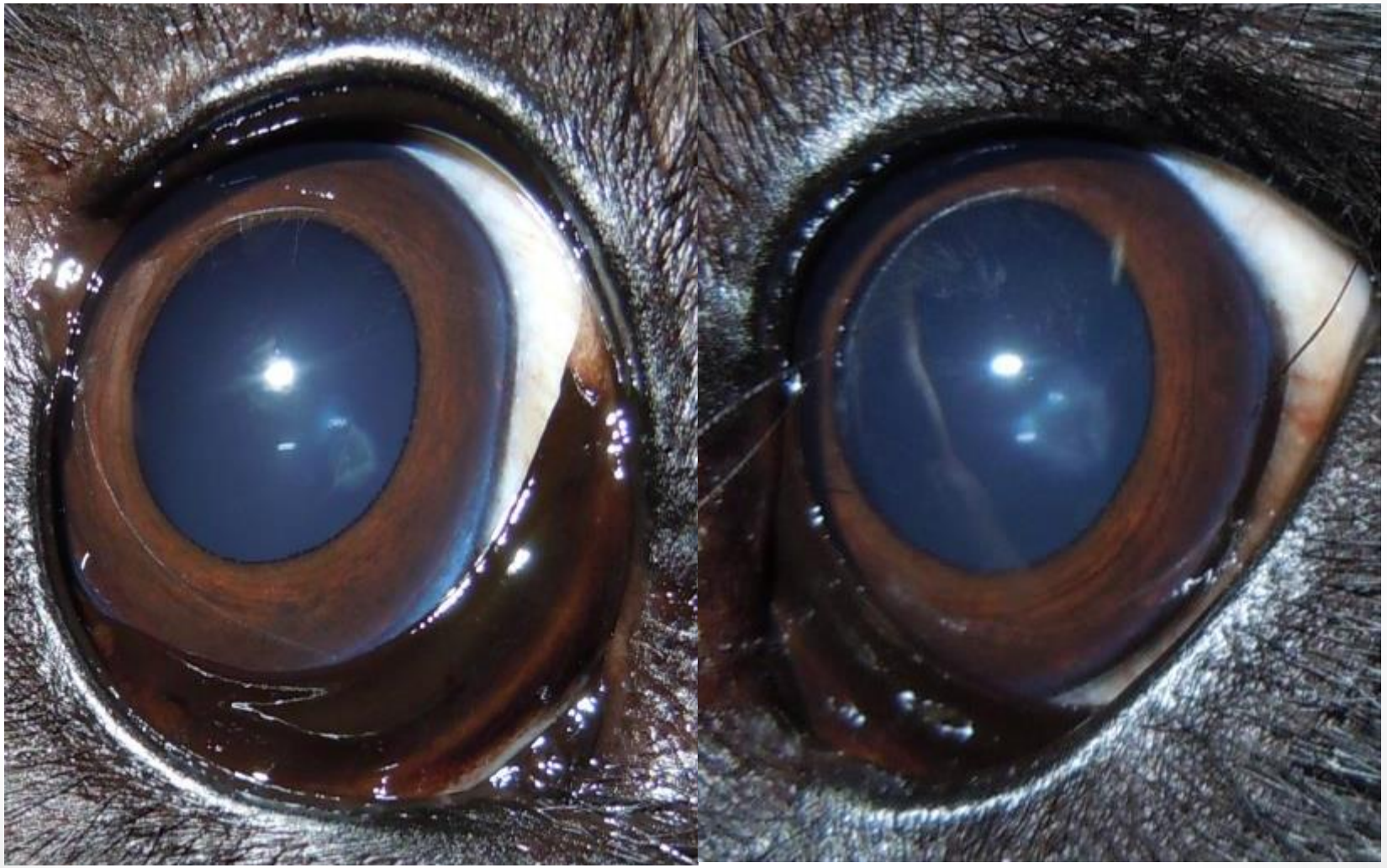


# Cataratta subcaps. Pol. Post. OU; Riesenschnauzer





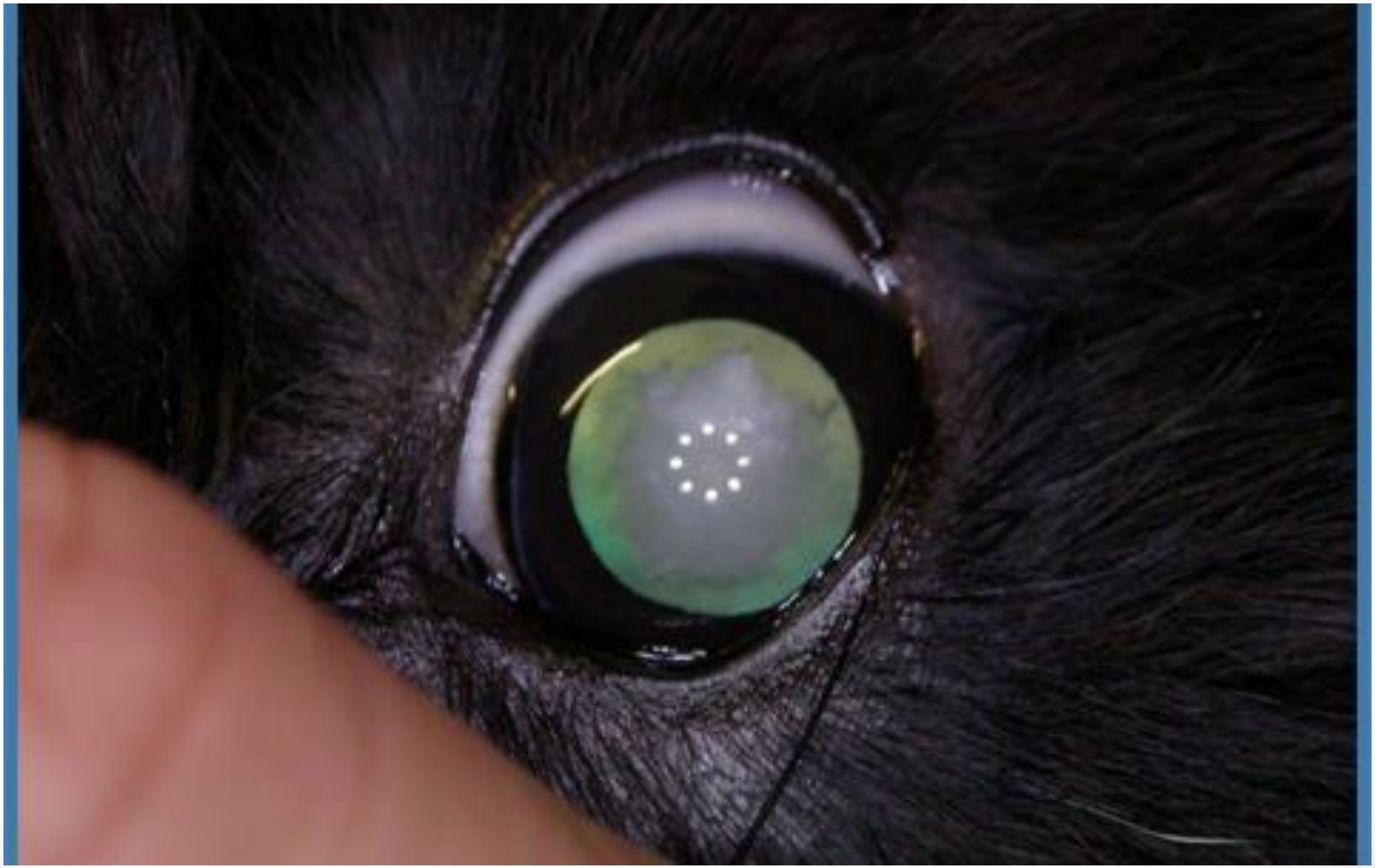
# Cataratta subcaps. Pol. Post. OU; Riesenschnauzer



# Cataratta (Congenita)

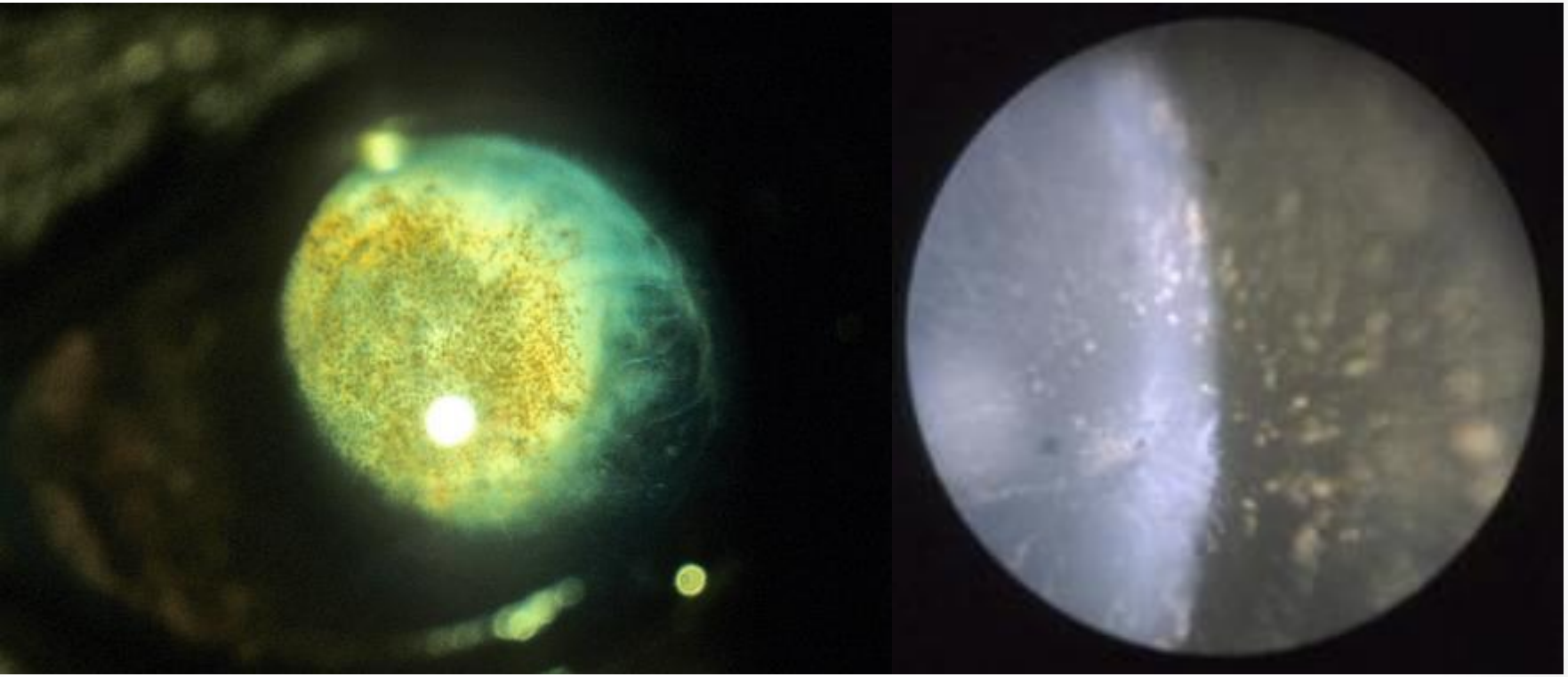
- *Definizione*: Opacità della lente;
- *Diagnosi*: tra la nascita e le 8 sett. di vita;
- *Localizzazione*: opacità nucleare fetale (non evolutiva); a volte anche corticale anteriore e posteriore (unilaterale o bilaterale, evolutiva).

# Cataratta congenita Schnauzer Nano

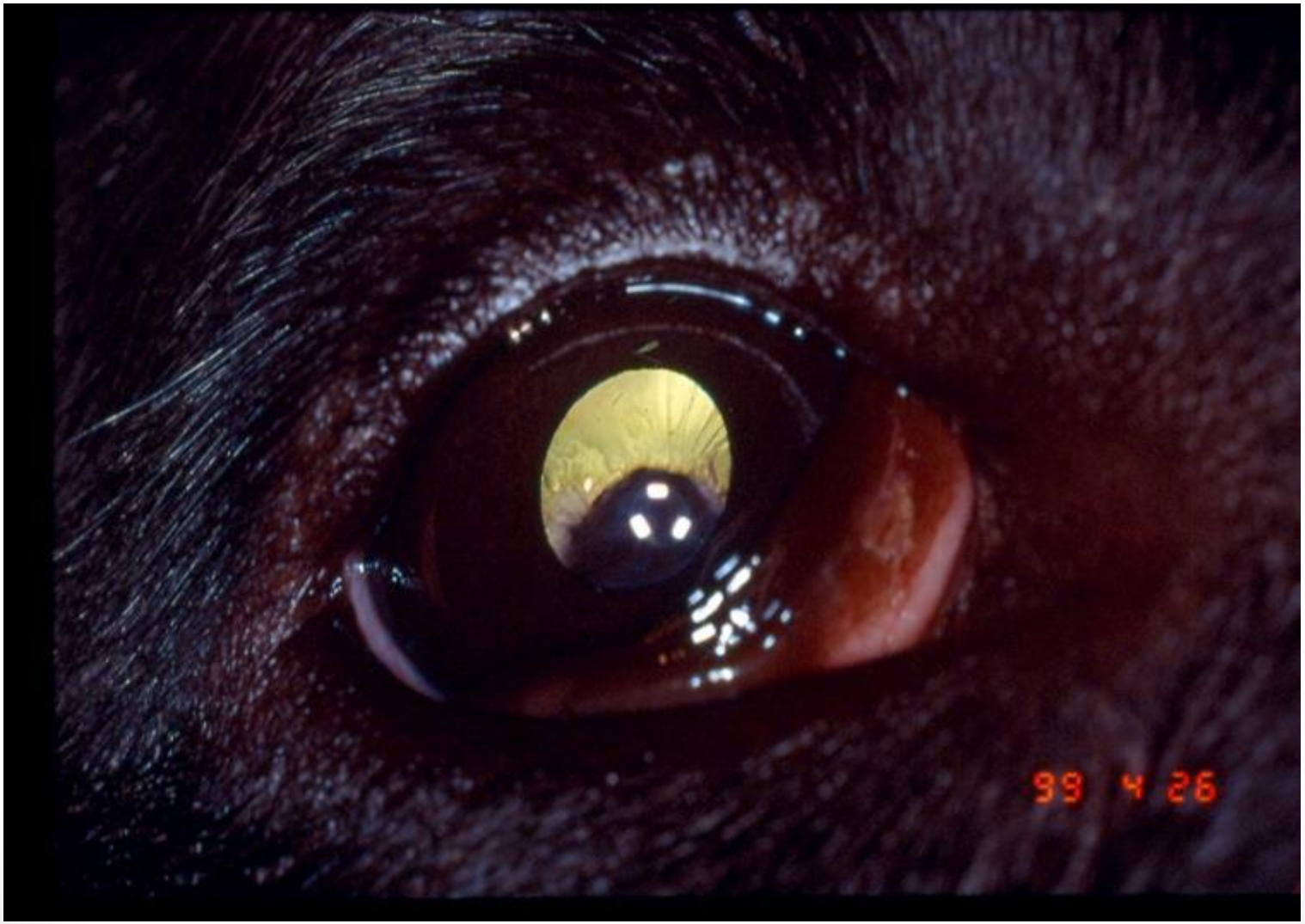


- ***Schnauzer nano***: ereditarietà recessiva;
- Opacità nucleare o subcapsulare posteriore bilaterale (*rapidamente evolutiva*), spesso associata a microftalmo (lieve).

# PHPV/PHTVL 1° GRADO



# PHPV/PHTVL 2°-6° GRADO

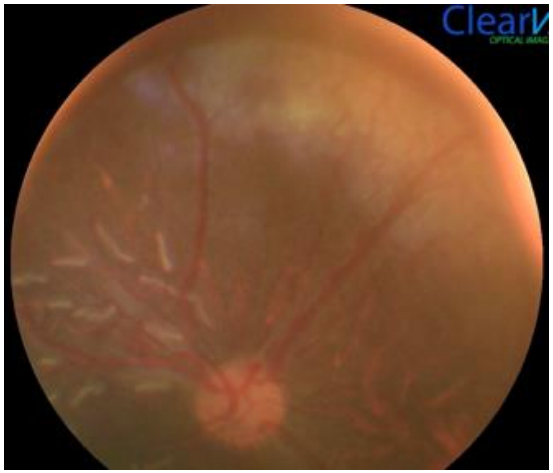


# Displasia Retinica

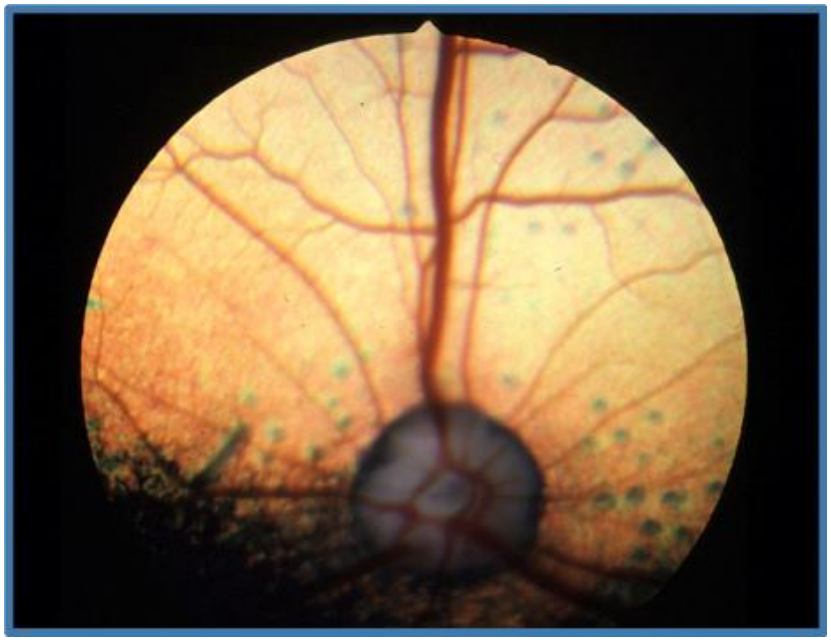
- Anomala differenziazione retinica durante il suo sviluppo con proliferazione di alcuni suoi elementi; formazione di “rosette” (rosettes) con/senza “pieghe” (folds);
- Tre forme cliniche;
- Ereditarietà in molte razze;

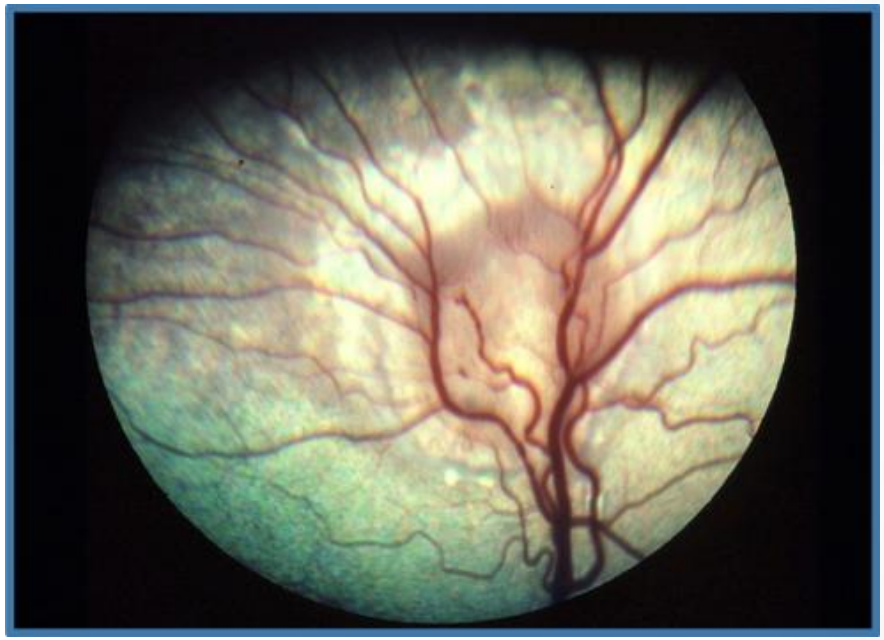
# Displasia Retinica

- “Retinal folds”: strie bianche o grigie singole o multiple, rotonde, ovali, triangolari, lineari o curvilinee, a V o Y uni o bilaterali, zona tappetale o non tappetale (displasia focale o multifocale; 30 razze);
- “Forma geografica”: area irregolare con zone retiniche più sottili insieme a zone di retina più spessa (displasia geografica; 11 razze);
- “Forma totale o completa” (displasia retinica completa con distacco o “non attacco”).

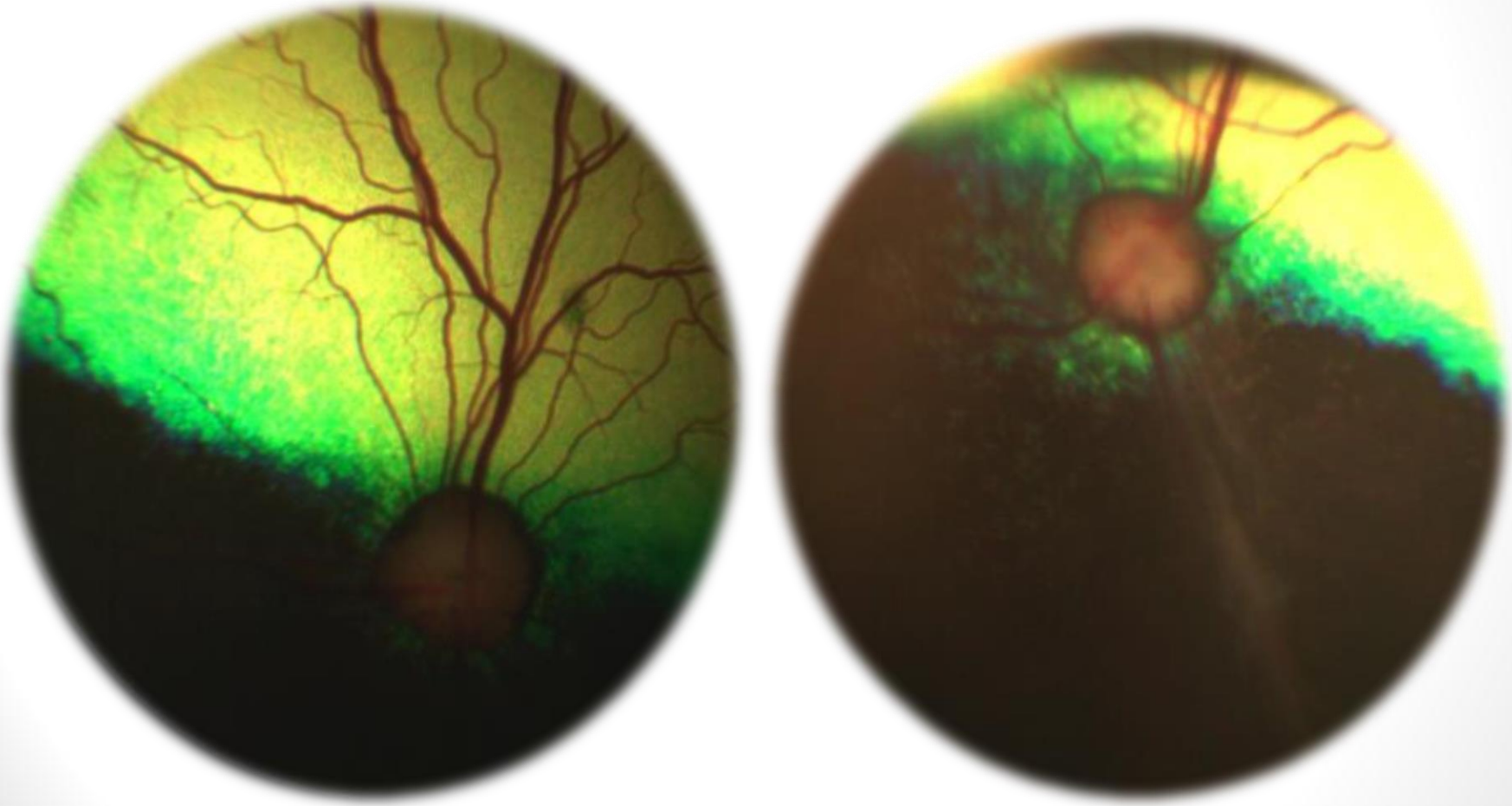


# Displasia Retinica MF/Geografica

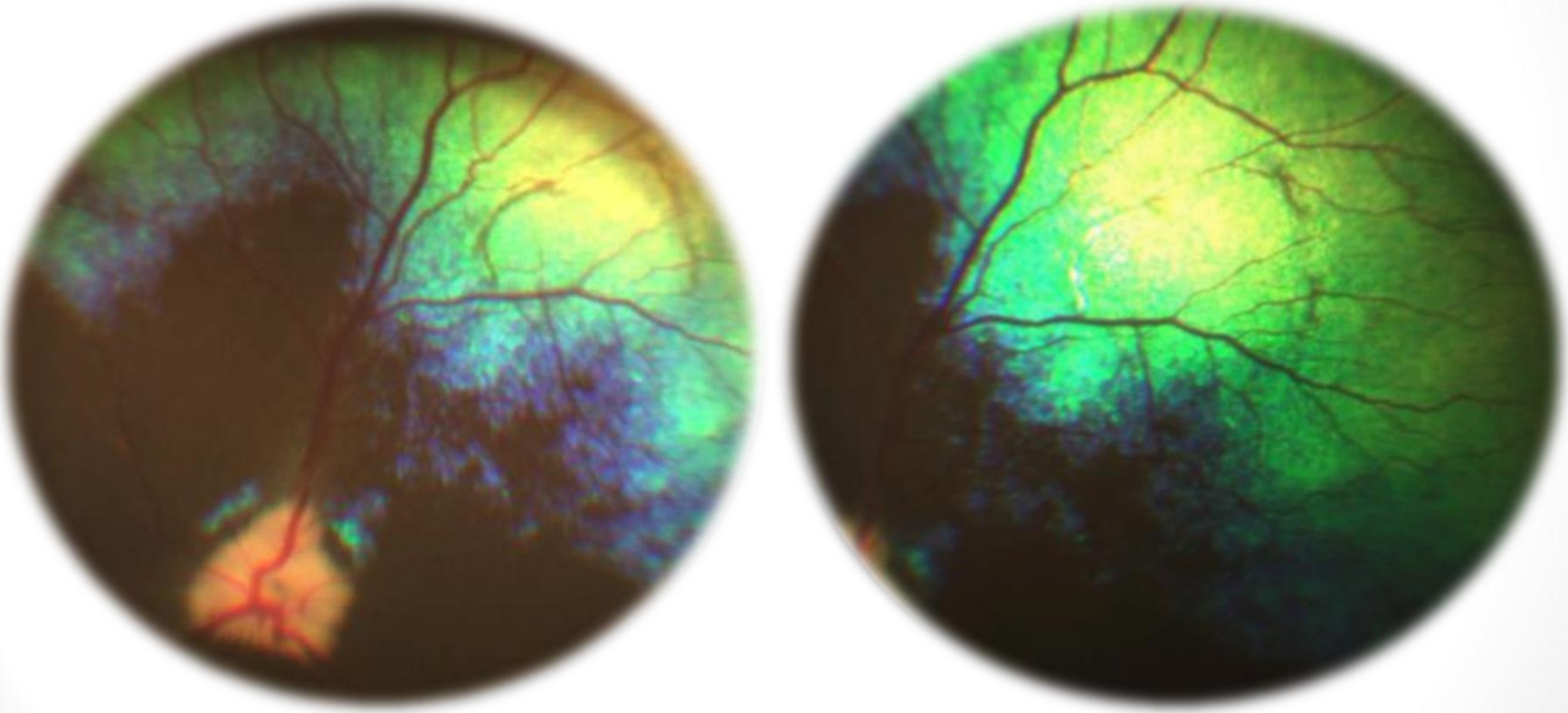




# Displasia Retinica MF, Riesenschnauzer



# Displasia Retinica Geografica, Zwergpinscher



# Displasia retinica

- Forme **ereditarie** (più comuni);
- *Test genetico* per alcune forme (RD-OSD); “”QUESTO TEST E’ INUTILE PER LE NOSTRE RAZZE; QUINDI **NON ESISTONO TEST GENETICI PER LE RAZZE SCHNAUZER E PINSCHER**””

Veterinary Ophthalmology (2004) 7, 3, 151–158

# Inherited retinal dysplasia and persistent hyperplastic primary vitreous in Miniature Schnauzer dogs

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**Abstract**

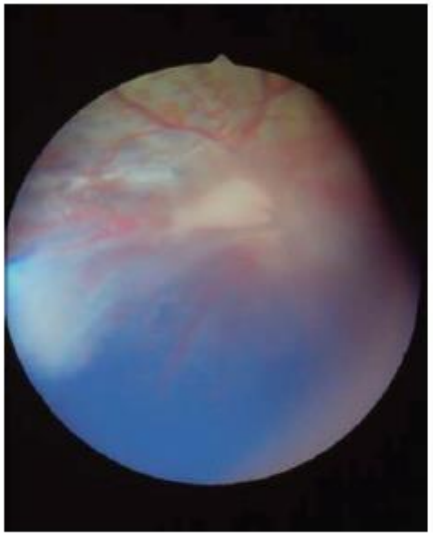
The objectives of this study were to define the clinical syndrome of retinal dysplasia and persistent primary vitreous in Miniature Schnauzer dogs and determine the etiology. We examined 106 Miniature Schnauzers using a biomicroscope and indirect ophthalmoscope. The anterior and posterior segments of affected dogs were photographed. Four enucleated eyes were examined using routine light microscopy and scanning electron microscopy. A pedigree was constructed and related dogs were test-bred to define the mode of inheritance of this syndrome. Congenital retinal dysplasia was confirmed in 24 of 106 related Miniature Schnauzer dogs. Physical and postmortem examinations revealed that congenital abnormalities were limited to the eyes. Biomicroscopic, indirect ophthalmoscopic, and neuro-ophthalmic examinations confirmed that some of these dogs were blind secondary to bilateral retinal dysplasia and detachment (nonattachment) ($n = 13$), and the remainder had generalized retinal dysplasia ($n = 11$). Fifteen of these dogs were also diagnosed with unilateral ($n = 9$) or bilateral ($n = 6$) persistent hyperplastic primary vitreous. Nutritional, infectious, or toxic etiologies were not evident on physical, postmortem, light microscopic, or transmitting and scanning electron microscopic examination of four affected Miniature Schnauzers. We examined the pedigree and determined that an autosomal recessive mode of inheritance was most likely. Three test-bred litters including those from affected parents, carrier and affected parents, and carrier parents confirmed this mode of inheritance. This study confirms that retinal dysplasia and persistent hyperplastic primary vitreous is a congenital abnormality that is inherited as an autosomal recessive condition in Miniature Schnauzers.

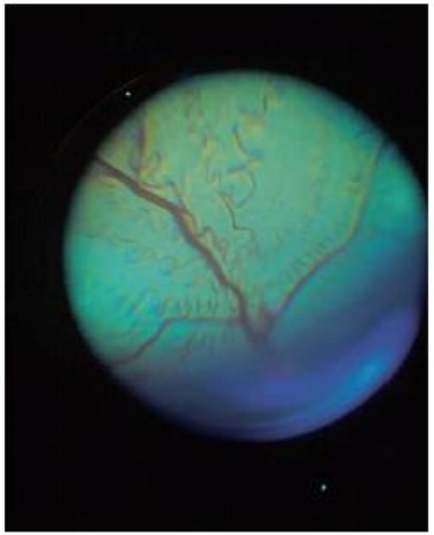
**Key Words:** inherited retinal dysplasia, Miniature Schnauzer, persistent hyperplastic primary vitreous, retinal detachment

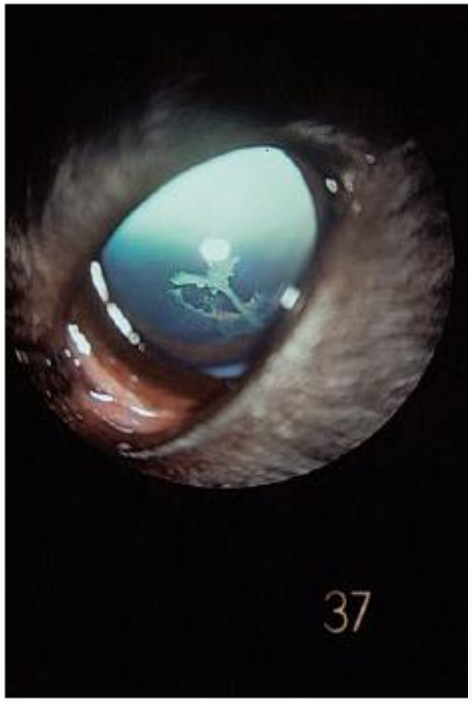
## INTRODUCTION

Retinal dysplasia is a common clinical syndrome in dogs. The clinical manifestations include single, multiple, or generalized gray retinal folds in the tapetal or nontapetal fundus.[1] Retinal dysplasia has been morphologically categorized as single folds, geographic, and generalized forms, and the latter two may be associated with retinal detachment.[2] Retinal dysplasia is a congenital lesion, although a developmental form of geographic retinal dysplasia has been recently proposed.[3] The pathogenesis of retinal dysplasia is complex and four developmental types have been proposed:[4] (i) a hyperplastic extension of retina into abnormal sites away from the retinal pigment epithelium (RPE); (ii) within the retina that is detached from the RPE; (iii) within the retina over regions devoid of RPE, i.e. colobomas; and (iv) within the retina *in situ* by a process which may involve the entire retina or a portion of it with no evidence of detachment from the RPE.[4] Inherited retinal dysplasia in English Springer Spaniels has been the most thoroughly investigated of all the dog breeds. Whiteley reported an incomplete retinal differentiation, disruption of the outer limiting membrane, and formation of multiple rosettes within the nuclear and plexiform layers between days 45–50 of gestation in English Springer Spaniels.[5] Multiple etiologies for retinal dysplasia have been identified in animals, including viruses and toxins, although most retinal dysplasia in dogs is inherited.[6–8]









# PRA

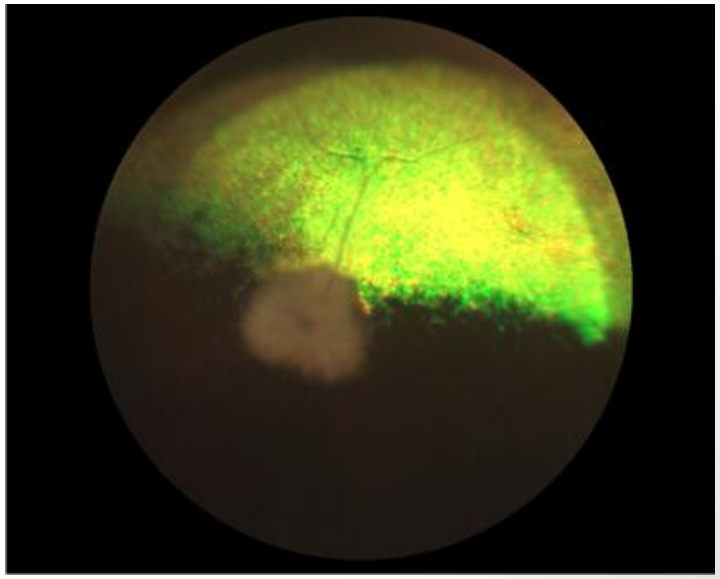
- Progressive retinal atrophy: termine generico che comprende le **degenerazioni retiniche ereditarie**
- Malattie descritte in più di 100 razze canine (quadri clinici simili, ma diversa trasmissione, insorgenza e patogenesi);
- **PRA**: malattie di sviluppo (displasie) e malattie degenerative dei fotorecettori; quasi sempre cecità totale, **sempre esclusione** dalla riproduzione (soggetti malati, genitori e figli!);
- Per alcune forme in alcune razze sono disponibili i **test genetici**

# PRA

- Insorgenza precoce:

- Iniziale arresto di sviluppo dei fotorecettori, seguito da rapida degenerazione (displasia dei fotorecettori, es. rcd);

- Trasmissione autosomica recessiva;
- Alterazioni oftalmoscopiche precoci.



# PRA (PRCD) OPTIMAL SELECTION/OPTIGEN

- Insorgenza tardiva:

- RIESENSCHNAUZER
- *Progressive Rod-cone Degeneration* (prcd): notevole variabilità nell'età di comparsa, nella progressione, nel grado e nella sede delle lesioni retiniche tra e nelle razze colpite;
- Rappresentano le forme più comuni;
-
- **Degenerazione** (tardiva) prima dei bastoncelli e poi dei coni;
- Di solito alterazioni oftalmoscopiche tardive;
- 27.27% portatori
- Geneticamente a rischio di sviluppare la malattia 2.27%

- Trasmissione autosomica recessiva.

# PRA (PRCD)

- ***Prcd (PRA)***: tratto autosomico recessivo;

- ***Soggetto "Normale"***: OMOZIGOTE (due geni normali);
- ***Soggetto "Portatore"***: ETEROZIGOTE (un gene normale e uno malato);

- ***Soggetto "Affetto"***: OMOZIGOTE MUTANTE (due geni malati).
- TEST PER RIESENSCHNAUZER OFFERTO DA OPTIGEN (VETOGENE)/OPTIMAL SELECTION

genes

MDPI

Article

# Whole Genome Sequencing of Giant Schnauzer Dogs with Progressive Retinal Atrophy Establishes *NECAP1* as a Novel Candidate Gene for Retinal Degeneration

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Received: 15 April 2019; Accepted: 17 May 2019; Published: 21 May 2019

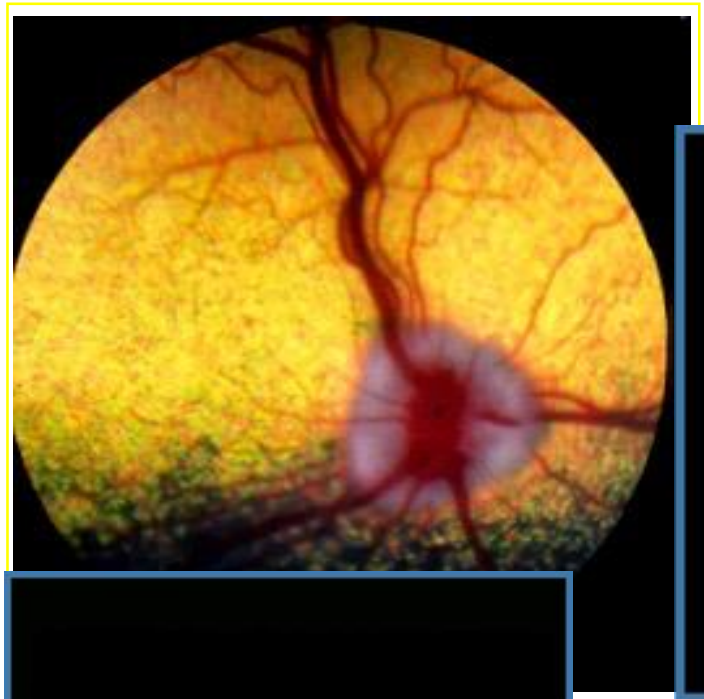

**Abstract:** Canine progressive retinal atrophies (PRA) are genetically heterogeneous diseases characterized by retinal degeneration and subsequent blindness. PRAs are untreatable and affect multiple dog breeds, significantly impacting welfare. Three out of seven Giant Schnauzer (GS) littermates presented with PRA around four years of age. We sought to identify the causal variant to improve our understanding of the aetiology of this form of PRA and to enable development of a DNA test. Whole genome sequencing of two PRA-affected full-siblings and both unaffected parents was performed. Variants were filtered based on those segregating appropriately for an autosomal recessive disorder and predicted to be deleterious. Successive filtering against 568 canine genomes identified a single nucleotide variant in the gene encoding NECAP endocytosis associated 1 (*NECAP1*): c.544G>A (p.Gly182Arg). Five thousand one hundred and thirty canids of 175 breeds, 10 cross-breeds and 3 wolves were genotyped for c.544G>A. Only the three PRA-affected GS were homozygous (allele frequency in GS, excluding proband family = 0.015). In addition, we identified heterozygotes belonging to Spitz and Dachshund varieties, demonstrating c.544G>A segregates in other breeds of German origin. This study, in parallel with the known retinal expression and role of *NECAP1* in clathrin mediated endocytosis (CME) in synapses, presents *NECAP1* as a novel candidate gene for retinal degeneration in dogs and other species.

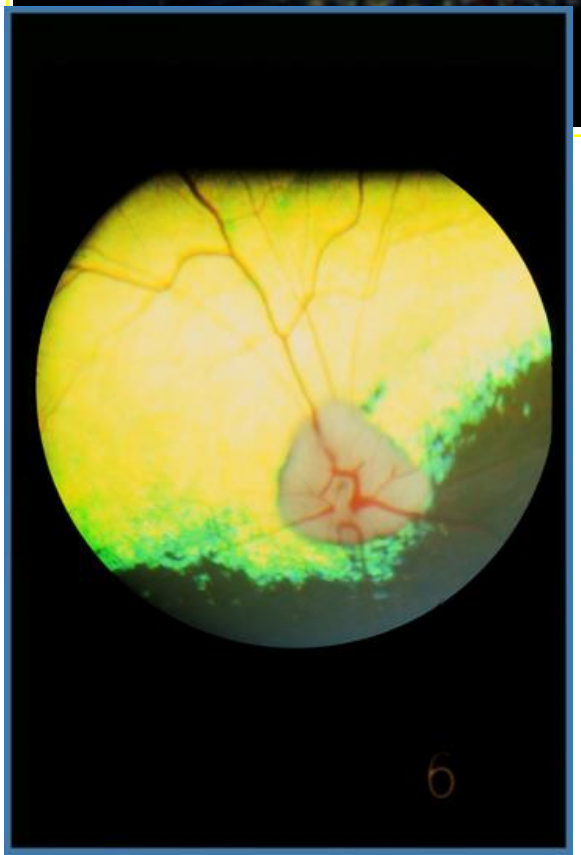
**Keywords:** canine; dog; progressive retinal atrophy; PRA; retinal degeneration

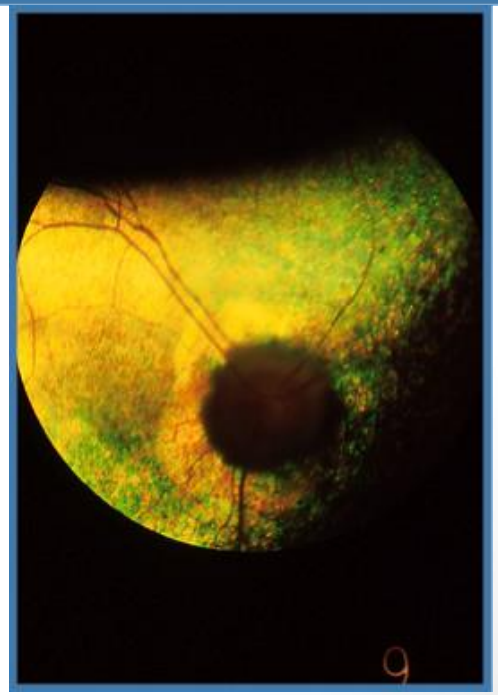
# PRA (NECAP1) AHT

- 3/7 manifestarono PRA a 4 anni di età
- Autosomica recessiva (madre e padre non affetti ad 8 e 11 anni , rispettivamente)
- Analizzati 5130 cani di 175 razze, 10 meticci e 3 lupi, inclusi 322 Riesenschnauzer
- Solo i 3 RS affetti erano omozigoti, entrambe i genitori erano eterozigoti
- 6 altri Riesenschnauzer eterozigoti identificati nella popolazione studiata
- Identificati soggetti eterozigoti  in Spitz e Bassotti (quindi  il gene segrega in altre razze di origine Tedesca)

# PRA





# PRA Type A

ORIGINAL ARTICLE

## Photoreceptor Dysplasia: An Inherited Progressive Retinal Atrophy of Miniature Schnauzer Dogs

Charles J. Parshall[1], Milton Wyman[2], Susan Nitroy[2], Gregory Acland[3], Gustavo Aguirre[3]*

A progressive retinal atrophy (PRA) affecting Miniature Schnauzer dogs is reported. Of the 287 individuals (148 female, 139 male) comprising the study population, 66 (23 percent) were affected (33 female, 33 male) and 221 animals (115 female, 106 male) were phenotypically normal. There was no sex predilection for the disease. Results of histologic and electroretinographic studies indicate that the disease is a new and different type of PRA, characterized by unique morphologic and functional deficits during rod and cone development. Accordingly, the disease has been termed photoreceptor dysplasia. Clinically, and particularly ophthalmoscopically, diagnosis is only practicable in very late stages of the disease. Electroretinography, however, can provide evidence of the disease in dogs at least as young as 8 weeks of age. Pedigree analysis and test-mating studies conclusively establish that inheritance is autosomal recessive. The gene symbol ***pd*** (for photoreceptor dysplasia) is assigned. (*Progress in Veterinary & Comparative Ophthalmology*, Vol. 1, No. 3, 1991, pp. 187-203; Key words: dog, electroretinography, photoreceptor dysplasia, progressive retinal atrophy.)

Generalized progressive retinal atrophy (PRA) is a clinical diagnostic category that groups together a variety of hereditary degenerative retinal diseases in domestic animals (primarily in the dog). Although an increasing number of specific diseases within this category have been defined in several canine breeds, the diverse forms of PRA in the dog share certain clinical features.[1-6] Foremost among these similarities are a consistent ophthalmoscopic appearance of the retinal disease process, and an inexorable deterioration of retinal structure and function, leading to loss of vision. Furthermore, in all canine forms of PRA studied to date, the inheritance pattern has been autosomal recessive.[1,2,4,6,7,10] Dissimilarities in manifestation of the disease, particularly among breeds, indicate that separate entities are grouped under the PRA rubric. These dissimilarities include differences in the age of emergence of clinical signs; in pathophysiology (dysplasia vs. degeneration); in the relative degree to which rod or cone cells are affected; and in biochemical abnormalities, such as deficiency of cyclic

**cGMP-PDE**, cyclic guanosine monophosphate phosphodiesterase; ***erd***, early retinal degeneration; ERG, electroretinography; **ONL**, outer nuclear layer; ***pd***, photoreceptor dysplasia; **PRA**, progressive retinal atrophy; ***prcd***, progressive rod-cone degeneration; ***rcd1***, rod cone dysplasia type 1; ***rcd2***, rod-cone dysplasia type 2; ***rd***, rod dysplasia.

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# PRA Type A SCHNAUZER NANO

- **Type A PRA o XLPRA2 : nella popolazione di S.N. si è rivelato una mutazione molto rara nella razza  probabilmente perchè ormai eradicata o presente in bassissima frequenza. NON ha senso ora testare per questo gene**
- **It soon became clear that Type A PRA was an extremely rare disorder in the breed; in the 17 years the test has been available, not a single case of the disease was found out of 375 samples tested.**
- **Carriers < 1%**
- **Geneticamente a rischio** <1%
- **Cecità notturna  già a 6-7 settimane e cecità a 2 anni di età**

G3 Genes | Genomes | Genetics

INVESTIGATION

# Complex Structural *PPT1* Variant Associated with Non-syndromic Canine Retinal Degeneration

**Leonardo Murgiano,*,†,2 Doreen Becker,*,†,‡ Dina Torjman,* Jessica K. Niggel,* Ausra Milano,† Cheryl Cullen,§ Rui Feng,** Fan Wang,†† Vidhya Jagannathan,†† Sue Pearce-Kelling,† Martin L. Katz,§§ Tosso Leeb,‡‡ and Gustavo D. Aguirre*,2**

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**ABSTRACT** Rod and cone photoreceptors are specialized retinal neurons that have a fundamental role in visual perception, capturing light and transducing it into a neuronal signal. Aberrant functioning of rod and/or cone photoreceptors can ultimately lead to progressive degeneration and eventually blindness. In man, many rod and rod-cone degenerative diseases are classified as forms of retinitis pigmentosa (RP). Dogs also have a comparable disease grouping termed progressive retinal atrophy (PRA). These diseases are generally due to single gene defects and follow Mendelian inheritance. We collected 51 DNA samples from Miniature Schnauzers affected by PRA (average age of diagnosis ~3.9 ±1 years), as well as from 56 clinically normal controls of the same breed (average age ~6.6 ±2.8 years). Pedigree analysis suggested monogenic autosomal recessive inheritance of PRA. GWAS and homozygosity mapping defined a critical interval in the first 4,796,806 bp of CFA15. Whole genome sequencing of two affected cases, a carrier and a control identified two candidate variants within the critical interval. One was an intronic SNV in *HIVEP3*, and the other was a complex structural variant consisting of the duplication of exon 5 of the *PPT1* gene along with a conversion and insertion (named $PPT1_{dcl}$). $PPT1_{dcl}$ was confirmed homozygous in a cohort of 22 cases, and 12 more cases were homozygous for the CFA15 haplotype. Additionally, the variant was found homozygous in 6 non-affected dogs of age higher than the average age of onset. The *HIVEP3* variant was found heterozygous (n = 4) and homozygous wild-type (n = 1) in cases either homozygous for $PPT1_{dcl}$ or for the mapped CFA15 haplotype. We detected the wildtype and three aberrant *PPT1* transcripts in isolated white blood cell mRNA extracted from a PRA case homozygous for $PPT1_{dcl}$, and the aberrant transcripts involved inclusion of the duplicated exon 5 and novel exons following the activation of cryptic splice sites. No neurological signs were detected among the dogs homozygous for the $PPT1_{dcl}$ variant. Therefore, we propose $PPT1_{dcl}$ as causative for a non-syndromic form of PRA ($PRA_{PPT1}$) that shows incomplete penetrance in Miniature Schnauzers, potentially related to the presence of the wild-type transcript. To our knowledge, this is the first case of isolated retinal degeneration associated with a *PPT1* variant.

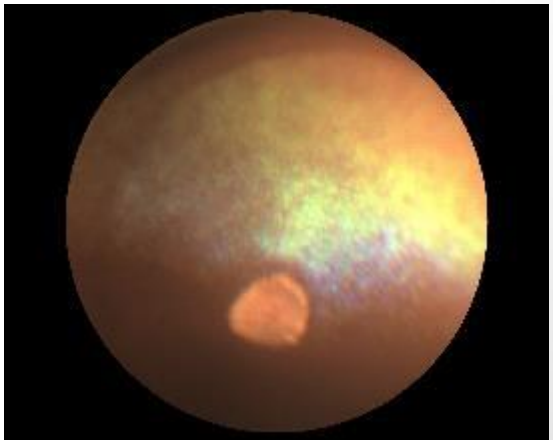
**KEYWORDS**
progressive retinal atrophy
PRA
complex variant
retinal degeneration
whole genome sequencing
dog
palmitoyl protein thioesterase

# PRA Type B SCHNAUZER NANO (OPTIGEN)

- **TYPE B PRA (PRA*PPT1*): nuova variante che spiega numerosi casi di PRA nello S.N. (offerta da Optigen)**
- **This genetic variant accounts for 63% of Miniature Schnauzers affected with retinal degeneration in which the Type A form of the disease has been excluded, which indicates that at least one additional retinal disease locus exists in the breed.**
- **Soggetti omozigoti per questa variante hanno l'86% di probabilità di sviluppare la malattia ; comunque il 14% degli omozigoti per questo gene non sviluppa la malattia entro i 7 anni forse per "penetranza" incompleta del gene o perchè la variante in oggetto è un marker genetico che si trova solo vicino alla vera mutazione causale**
- **Ereditarietà autosomica recessiva**

# PRA SCHNAUZER NANO

- **The average age of the affected dogs was 3.961 years of age. In fact, seven dogs were older, with clinical disease not diagnosed until 4.5-6.5 years of age.**
- **Di 76 cani con PRA il 55% erano omozigoti per il Tipo B**
- **Dei rimanenti 45%, l'11% erano eterozigoti e il 34% erano clear per il Tipo B**
- **Questo significa che esiste ALMENO una ulteriore forma di PRA (oltre A e B) presente nella razza. Quindi:** *esistono anche soggetti con mutazioni diverse (sono affetti, ma con test negativo!) (al contrario possibile anche cani con test positivo, ma senza sviluppo della malattia!).*



# Comparazione Italia-Panel ECVO (D,A,O,DK,N)

**Italia Riesenschnauzer**
**2013/2019 ECVO, 2014/2018 FSA**

- 27 esaminati (14 affetti) 51.8%
- 2 atresia punto lacrimale 7.4%
- 9 cataratte (5 subcaps pol post) 33.3%
- 2 PHPV/PHTVL 1° grado 7.4%
- 5 displasia retinica mf/geografica 18.5%
- 1 PRA 3.7%

**Panel ECVO Riesenschnauzer**

- 840 esaminati (178 affetti) 21%
- 2 atresia punto lacrimale 0.23%
- 67 cataratte (polare posteriore) 7.9%
- 7 PHPV/PHTVL 1°grado 0.83%
- 11 displasia retinica mf/geografica 1.3%
- 15 PRA 1.78%

# Comparazione Italia-Panel Svedese

**Italia Riesenschnauzer 2013/2019 ECVO, 2014/2018 FSA**

- 27 esaminati (14 affetti) 51.8%
- 2 atresia punto lacrimale 7.4%
- 9 cataratte (5 subcaps pol post) 33.3%
- 2 PHPV/PHTVL 1° grado 7.4%
- 5 displasia retinica mf/geografica 18.5%
- 1 PRA 3.7%

**Panel Svedese Riesenschnauzer 2010/2015**

- 43 esaminati (7 affetti) 16.2%
- 3 Cataratte 6.97%
- 1 Displasia retinica 2.32%
- 1 PRA 2.32%

# Comparazione Italia-Panel Finlandese

**Italia Riesenschnauzer 2013/2019 ECVO, 2014/2018 FSA**

- 27 esaminati (14 affetti) 51.8%
- 2 atresia punto lacrimale 7.4%
- 9 cataratte (5 subcaps pol post) 33.3%
- 2 PHPV/PHTVL 1° grado 7.4%
- 5 displasia retinica mf/geografica 18.5%
- 1 PRA 3.7%

**Panel Finlandese ECVO Riesenschnauzer 2014/2019**

- 284 esaminati (40 affetti) 14%
- 16 atresia punto lacrimale 14.08%
- 3 cataratte (2 posteriore polare) 1.05%
- 7 PHPV/PHTVL 1°grado 2.46%
- 11 Displasia retinica mf/geografica 3.8%

# Comparazione Italia-USA

**Italia Riesenschnauzer**
**2013/2019 ECVO, 2014/2018 FSA**

- 27 soggetti esaminati (14 affetti) 51.8%
- 2 atresia punto lacrimale 7.4%
- 9 cataratte (5 subcaps pol post) 33.3%
- 2 PHPV/PHTVL 1° grado 7.4%
- 5 displasia retinica mf/geografica 18.5%
- 1 PRA 3.7%

**Riesenschnauzer USA 2014-2018**

- 379 soggetti esaminati (82 affetti) 21.6%
- 1 atresia punto lacrimale 0.3%
- 20 cataratte (5 corticale posteriore) 5.3%
- NO PHPV/PHTVL
- 7 displasia retinica mf/geografica 1.8%
- NO PRA

# Comparazione Italia-Panel ECVO (D,A,O,DK,N)

**Italia Zwergschnauzer**
**2013/2019 ECVO, 2014/2018 FSA**

- 177 esaminati (62 affetti) 35%
- 7 atresia punto lacrimale 3.95%
- 13 cataratte (5 corticale posteriore) 7.34%
- 7 displasia retinica mf/geografica 3.95%

**Panel ECVO Zwergschnauzer**

- 2508 esaminati (466 affetti) 18.5%
- 8 atresia punto lacrimale 0.31%
- 101 cataratte (57 corticale) 4.02%
- 3 displasia retinica mf/geografica 0.11%
- 38 PRA 1.5%

# Comparazione Italia-Panel Svedese

**Italia Zwergschnauzer 2013/2019 ECVO, 2014/2018 FSA**

- 177 esaminati (62 affetti) 35%
- 7 atresia punto lacrimale 3.95%
- 13 cataratte (5 corticale posteriore) 7.34%
- 7 displasia retinica mf/geografica 3.95%

**Panel Svedese Zwergschnauzer 2010/2018**

- 1683 esaminati (157 affetti) 9.3%
- 1 atresia punto lacrimale 0.059%
- 58 cataratte (26 corticale e post.polare) 3.44%
- No displasia
- 13 PRA 0.77%

# Comparazione Italia-Panel Finlandese

**Italia Zwergschnauzer 2013/2019 ECVO, 2014/2018 FSA**

- 177 esaminati (62 affetti) 35%
- 7 atresia punto lacrimale 3.95%
- 13 cataratte (5 corticale posteriore) 7.34%
- 7 displasia retinica mf/geografica 3.95%

**Panel Finlandese ECVO Zwergschnauzer 2014/2019**

- 902 esaminati (183 affetti) 20.2%
- 14 atresia punto lacrimale 1.55%
- 17 cataratte 1.88%
- 1 displasia retinica 0.11%
- 4 PRA 0.44%

# Comparazione Italia-USA

**Italia Zwergschnauzer**
**2013/2019 ECVO, 2014/2018 FSA**

- 177 esaminati (62 affetti) 35%
- 7 atresia punto lacrimale 3.95%
- 13 cataratte (5 corticale posteriore) 7.34%
- 7 displasia retinica mf/geografica 3.95%

**Zwergschnauzer USA 2014-2018**

- 5843 soggetti esaminati (741 affetti) 13.5%
- 2 atresia punto lacrimale 0.034%
- 244 cataratte 4.2%
- 3 PHPV/PHTVL 0.1%
- 6 displasia retinica mf/geografica 0.1%
- 8 PRA 0.1%

# Comparazione Italia-Panel ECVO (D,A,O,DK,N)

**Italia Schnauzer 2013/2019 ECVO, 2014/2018 FSA**

- 21 soggetti esaminati (4 affetti) 19%
- 1 PPM iride-iride 4.76%
- 3 cataratte (2 corticale post, 1 subcaps pol post) 14.2% (NERI)

**Panel ECVO Schnauzer**

- 398 soggetti esaminati (48 affetti) 12%
- 2 PPM 0.5%
- 22 cataratte (7 corticale, 4 posteriore polare) 5.5%
- 2 PRA 0.5%

# Comparazione Italia-Panel Svedese

**Italia Schnauzer 2013/2019 ECVO, 2014/2018 FSA**

- 21 soggetti esaminati (4 affetti) 19%
- 1 PPM iride-iride 4.76%
- 3 cataratte (2 corticale post, 1 subcaps pol post) 14.2% (NERI)

**Panel Svedese Schnauzer 2010-2017**

- 10 soggetti esaminati (6 affetti) 60%
- 1 PPM 10%
- 3 cataratte (2 corticale) 30%
- 1 PRA 10%

# Comparazione Italia-Panel Finlandese

**Italia Schnauzer 2013/2019 ECVO, 2014/2018 FSA**

- 21 soggetti esaminati (4 affetti) 19%
- 1 PPM iride-iride 4.76%
- 3 cataratte (2 corticale post, 1 subcaps pol post) 14.2% NERI

**Panel Finlandese ECVO Schnauzer 2014/2019**

- 151 soggetti esaminati (13 affetti) 8.6%
- 3 cataratte (1 corticale, 1 polare post) 1.98% NERI

# Comparazione Italia-USA

**Italia Schnauzer 2013/2019**
**ECVO, 2014/2018 FSA**

- 21 soggetti esaminati (4 affetti) 19%
- 1 PPM iride-iride 4.76%
- 3 cataratte (2 corticale post, 1 subcaps pol post) 14.2% NERI

**Schnauzer USA 2014-2018**

- 657 soggetti esaminati (105 affetti) 15.9%
- 2 PPM (1 iride-iride, 1 iride –cornea) 0.4%
- 37 cataratte 5.6%

# Comparazione Italia-Panel ECVO (D,A,O,DK,N)

**Italia Zwergpinscher 2013/2019 ECVO, 2014/2018 FSA**

- 41 soggetti esaminati (9 affetti) 21.9%
- 4 PPM (1 iride-iride, 3 iride lente) 9.75%
- 1 cataratta (corticale polare posteriore) 2.43%
- 1 Displasia retinica mf/geografica 2.43%
- 2 PRA 4.87%
- NO LL ???

**Panel ECVO Zwergpinscher**

- 1259 soggetti esaminati (236 affetti) 18.7%
- 72 PPM (67 iride-iride, 15 iride-lente) 5.71%
- 47 cataratte ( 35 corticale, 9 post polare) 3.73%
- No displasia
- 5 PRA 0.39%
- 5 LL 0.39%

# Comparazione Italia-Panel Svedese

**Italia Zwergpinscher 2013/2019 ECVO, 2014/2018 FSA**

- 41 soggetti esaminati (9 affetti) 21.9%
- 4 PPM (1 iride-iride, 3 iride lente) 9.75%
- 1 cataratta (corticale polare posteriore) 2.43%
- 1 Displasia retinica mf/geografica 2.43%
- 2 PRA 4.87%
- NO LL ???

**Panel Svedese Zwergpinscher 2010-2018**

- 574 soggetti esaminati (174 affetti) 30.3%
- 6 PPM 1.04%
- 24 cataratte (11 corticale, 6 polare posteriore) 4.18%
- No displasia
- 5 PRA 0.87%
- NO LL

# Comparazione Italia-Panel Finlandese

**Italia Zwergpinscher 2013/2019 ECVO, 2014/2018 FSA**

- 41 soggetti esaminati (9 affetti) 21.9%
- 4 PPM (1 iride-iride, 3 iride lente) 9.75%
- 1 cataratta (corticale polare posteriore) 2.43%
- 1 Displasia retinica mf/geografica 2.43%
- 2 PRA 4.87%
- NO LL ???

**Panel Finlandese ECVO Zwergpinscher 2014/2019**

- 425 soggetti esaminati (23 affetti) 5.4%
- 2 PPM iride-iride 0.47%
- 9 cataratte (4 corticali, 4 posteriore polare) 2.11%
- 1 Displasia retinica mf 0.23%
- NO PRA
- NO LL
- 6 PHPV/PHTVL (4 1°grado, 2 2°-6° grado) 1.41%

# Comparazione Italia-USA

**Italia Zwergpinscher 2013/2019**
**ECVO, 2014/2018 FSA**

- 41 soggetti esaminati (9 affetti) 21.9%
- 4 PPM (1 iride-iride, 3 iride lente) 9.75%
- 1 cataratta (corticale polare posteriore) 2.43%
- 1 Displasia retinica mf/geografica 2.43%
- 2 PRA 4.87%
- NO LL ???

**Zwergpinscher USA 2014-2018**

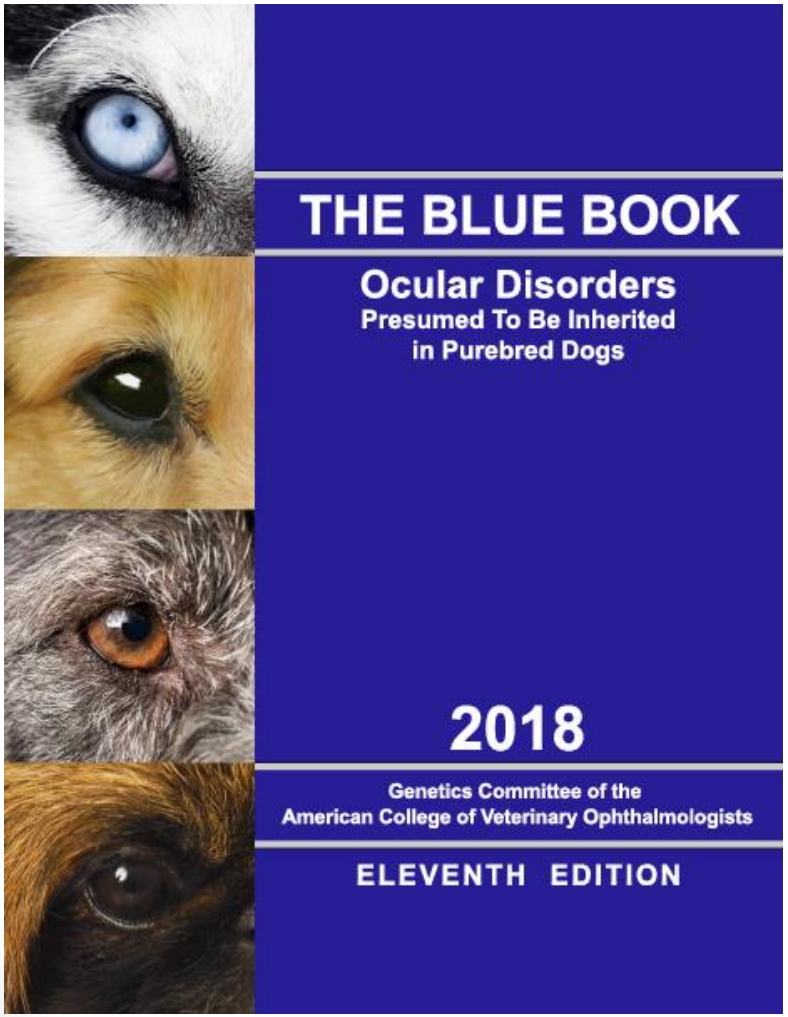
- 209 soggetti esaminati (64 affetti) 30.6%
- 6 PPM 2.9%
- 16 cataratte 7.7%
- 1 Displasia retinica mf 0.5%
- NO PRA
- NO LL

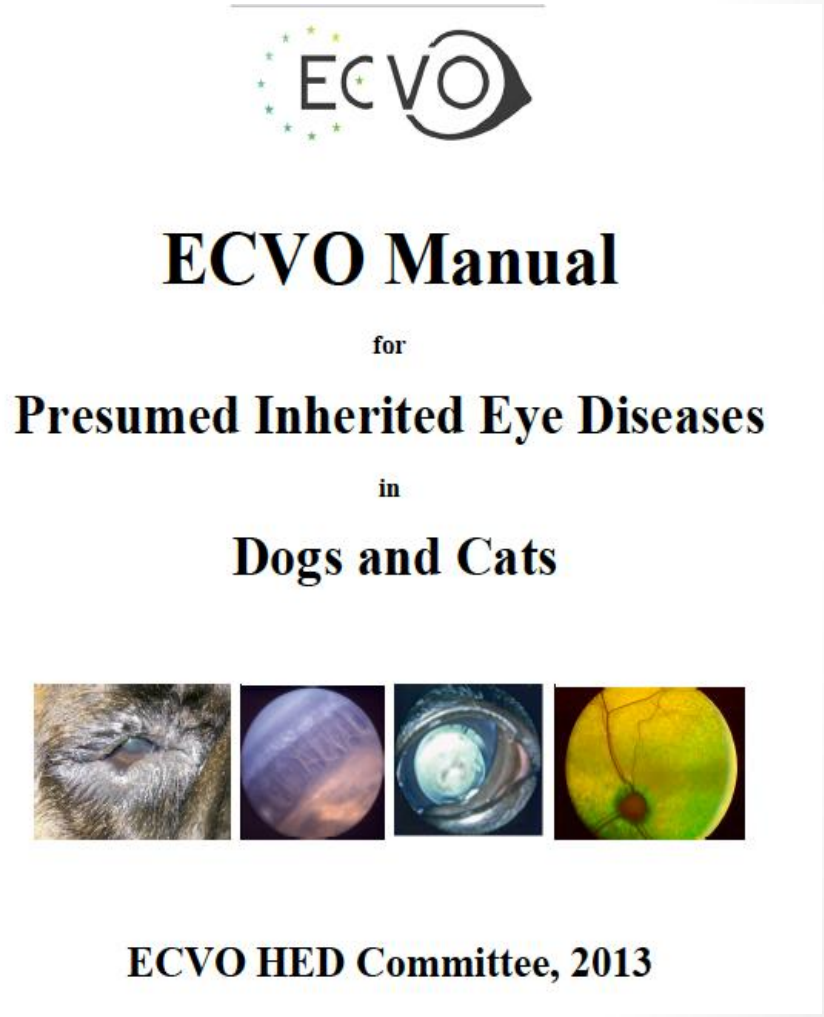
**Come** indagare le Malattie oculari

Lampada a fessura

Oftalmoscopia indiretta

**Quali** Riferimenti? (ECVO Manual 2017 (www.ecvo.org)/ ACVO Blue Book 2018)



# Chi?

- ***Diplomati ECVO***: con certificazione internazionale ECVO (attualmente 5 in Italia);
- ***Accreditati FSA***: con certificazione nazionale FSA (attualmente 30 in Italia);
- ***Abilitati ESE***: con certificazione internazionale ECVO (attualmente nessuno in Italia);
- ***Accreditati ENCI***: con certificazione ENCI (attualmente 8 in Italia).

FSA
Fondazione Salute Animale

FSA- Fondazione Salute Animale (Animal Health Foundation) via Trecchi 20 26100 Cremona, Italia

# *CERTIFICATO DI VISITA OCULISTICA PER LA DIAGNOSI DELLE MALATTIE OCULARI DI PROVATA O PRESUNTA ORIGINE EREDITARIA NEL CANE*

*OFFICIAL CERTIFICATE OF EYE EXAMINATION FOR THE DIAGNOSIS OF PROVEN OR PRESUMED INHERITED EYE DISEASES IN DOGS*

**VISITA OCULISTICA DEL:** _____ **CERTIFICATO N°** _____ **ESAMINATORE Dott.**_____ **n° aut FSA**_____

**CANE/*DOG***

**Nome/***Name*_____ **Razza/***breed*_____

**Sesso/***sex*_____ **Nato il/***date of birth*_____ **Colore/***color*_____ **Microchip** _____

**Tatuaggio/***tattoo* _____ **Test DNA**_____ **no** __ **si/***yes* __ **Data/***date* _____ **Risultato/***result*_____

**Esaminato/***checked* __ **Data/***date* _____ **Risultato/***result*: **esente/***unaffected* ___ **affetto/***affected* ___ **non def-sosp/***undet.-susp.* ___

**PROPRIETARIO / *OWNER***

**Proprietario / owner**_____

**Indirizzo / *address***_____

**Visita, protocollo obbligatorio: Midriatico** __ **Oftalmoscopia indiretta** __ **Biomicroscopia binoculare > 10x** __ **Esame pre-dilatazione x razza** __

**Altre indagini: Esame pre-dilatazione** __ **Oftalmoscopia diretta** __ **Gonioscopia** __ **Tonometria** __ **Altro**_____

## Risultati per le malattie ritenute congenito/ereditarie

| | Esente* | Non definito** | Affetto*** | |
|---|---|---|---|---|
| 1. Mem. Pupil. Persistens (PPM) | ☐ | ☐ | ☐ | iride☐ lente☐ cornea☐ laminar☐ |
| 2. Pers. Hyp.T. Vas.L./Pr. Vit. (PHTVL/PHPV) | ☐ | ☐ | ☐ | grado 1☐ gradi da 2 a 6☐ |
| 3. Cataratta (congenita) | ☐ | ☐ | ☐ | cort☐ post pol☐ ant pol☐ sut☐ punct☐ nucl☐ |
| 4. Retina: displasia (RD) | ☐ | ☐ | ☐ | (multi)focale☐ geografica☐ totale☐ |
| 5. Ipoplasia n.o./ Micropapilla | ☐ | ☐ | ☐ | |
| 6.Collie Eye Anomaly (CEA) | ☐ | ☐ | ☐ | ipoplasia coroide☐ coloboma☐ altro☐ |
| 7. Altro _____ | ☐ | ☐ | ☐ | |
| 8. Anomalie L. Pectinatum | ☐ | ☐ | ☐ | fibrae latae☐ laminae☐ occlusio☐ |

## Risultati per le malattie ritenute ereditarie

| | Esente* | Sospetto*** | Affetto*** | |
|---|---|---|---|---|
| 9. Entropion/trichiasi | ☐ | ☐ | ☐ | |
| 10. Ectropion/macroblepharon | ☐ | ☐ | ☐ | |
| 11. Distichiasi/ciglia ectopiche | ☐ | ☐ | ☐ | |
| 12. Distrofia corneale | ☐ | ☐ | ☐ | epiteliale☐ stromale☐ endoteliale☐ |
| 13. Cataratta (non congenita) | ☐ | ☐ | ☐ | cort☐ post pol☐ ant pol☐ sut☐ punct☐ nucl☐ |
| 14. Lussazione primaria lente | ☐ | ☐ | ☐ | |
| 15. Degenerazione retinica (PRA) | ☐ | ☐ | ☐ | |
| 16 Altro _____ | ☐ | ☐ | ☐ | |

N.B. [illegible], non è permanente ma il cane deve essere rivalutato ogni 12 mesi

**Non affetto, non si evidenziano alterazioni caratteristiche di oculopatie ereditarie ***Affetto, si evidenziano tali alterazioni*
***Si osservano alterazioni che potrebbero dipendere da una oculopatia ereditaria ma non sono del tutto patognomoniche. Riesaminare l'animale a distanza di_____mesi*
*****Vi sono alterazioni di lieve entità, si sospetta l'inizio di un'oculopatia ereditaria. Riesaminare l'animale a distanza di _____mesi*

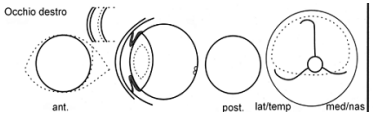
**MALATTIA N°**_____ **Gonioscopia: anomalia L. Pectinatum lieve** __**moderata** __ **grave**__

**DESCRIZIONE DEL QUADRO CLINICO**_____

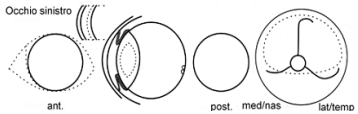
_____

**Nota: affetto da** _____**basi ereditarie non definite in questa razza**

Occhio destro




Occhio sinistro




**DICHIARAZIONE DEL PROPRIETARIO** Dichiaro che: a) i dati sopra riportati sono corretti e si riferiscono al mio cane esaminato in data odierna b) autorizzo FSA a tenere e conservare nel proprio archivio copia del certificato e utilizzarlo a scopo scientifico-epidemiologico c) ai sensi dell'art. 13 D. Lgs 30 Giugno 2003, n. 196, consento il trattamento dei dati personali riportati su questo certificato, nei limiti indicati dalla legge

**Data**_____

**Firma del proprietario**
**od chi ne fa le veci** _____

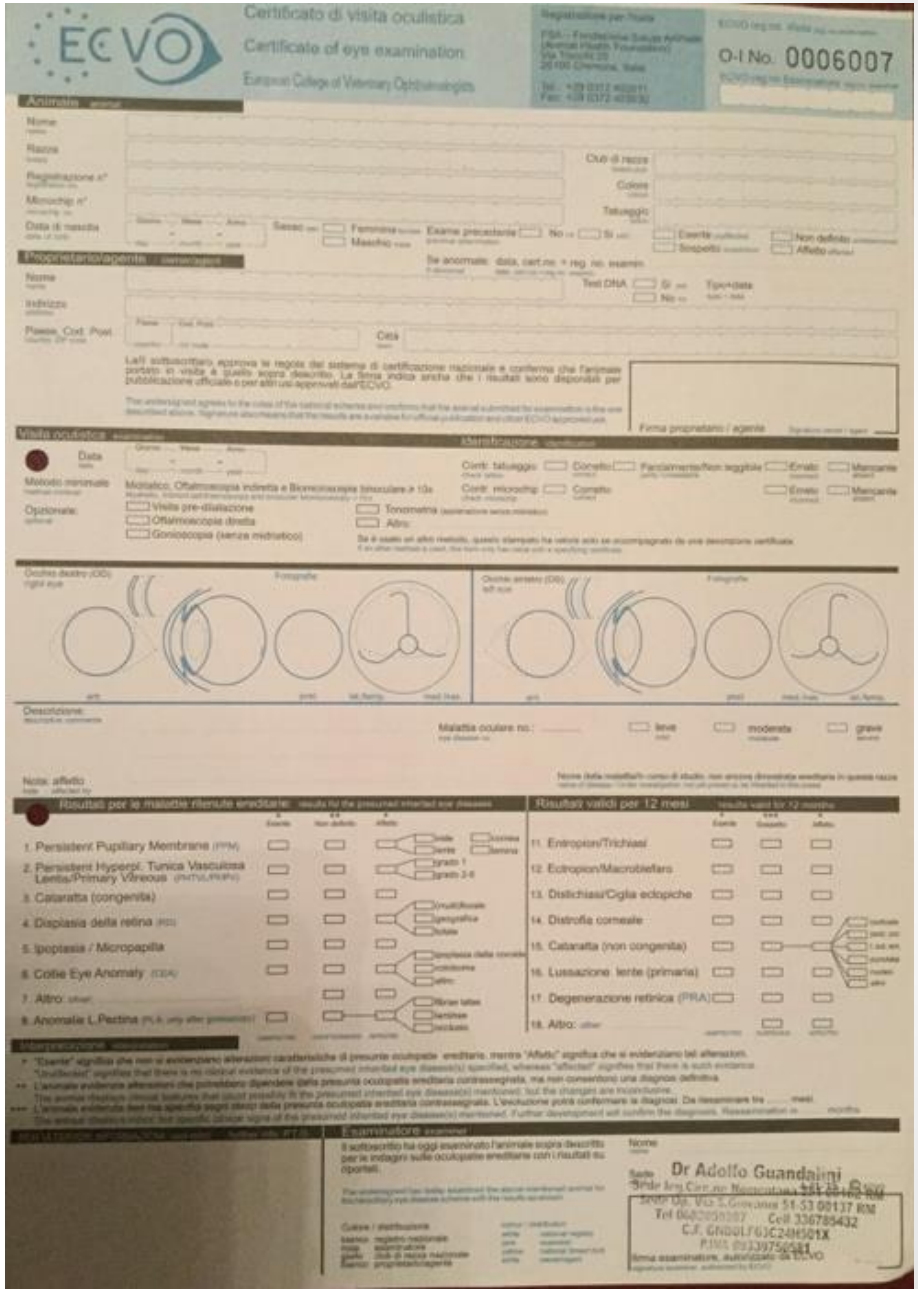
**DICHIARAZIONE DEL VETERINARIO** Confermo che il cane ha il microchip-tatuaggio n°_____ indicato sul Certificato genealogico e che da questa visita effettuata secondo il protocollo FSA è stato dichiarato: **esente/** *unaffected* __ **affetto/** *affected* __ **non definito/** *undetermined* __ **sospetto/** *suspicious* __ da malattie oculari di provata o presunta origine ereditaria/*by proven or presumed inherited eye diseases*

**Data**_____

**Firma e timbro del certificatore**_____

Questo certificato è stato redatto in base alle attuali conoscenze scientifiche e facendo riferimento alle liste delle oculopatie ereditarie o presunte tali pubblicate dall'European e American College of Veterinary Ophthalmologists. Lo stato di "**affetto**" determina l'esclusione dalla riproduzione per alcune malattie oculari ma non per tutte (vedasi indicazioni per ciascuna razza). **Non si autorizza la diffusione di informazioni pubblicitarie con riferimenti al nome del medico veterinario certificante**.

***Registrazione FSA: pratica FSA/HED n.*_____ *Data:* _____ *Timbro FSA***



# Quando?

- Nei soggetti ***Riproduttori***: visite effettuate a 1 anno di età e ripetute annualmente fino ai 6-7 anni;

- **Nei soggetti non Riproduttori, tre volte nella vita (1,3,7 anni di età)**;

# Condotta di Allevamento Riesenschnauzer

- VET ADVICE (CAP. 8 Manuale ECVO)

atresia punto lacrimale 7.4%- OPTIONAL

cataratte 33.3%- NO BREEDING from the affected animal

PHPV/PHTVL 1° grado 7.4%- OPTIONAL

Displasia retinica mf/geografica 18.5%- OPTIONAL (?) DA DISCUTERE

PRA 3.7%- NO BREEDING from the affected animal, its parents or offsprings

# Condotta di Allevamento Zwergschnauzer

- VET ADVICE (CAP. 8 Manuale ECVO)

atresia punto lacrimale 3.95%- OPTIONAL

cataratte 7.34%- NO BREEDING from the affected animal

displasia retinica mf/geografica 3.95%- OPTIONAL

PRA - NO BREEDING from the affected animal, its parents or offsprings

# Condotta di Allevamento Schnauzer

- VET ADVICE (CAP. 8 Manuale ECVO)

PPM iride-iride 4.76%- OPTIONAL

Cataratte 14.2%- NO BREEDING from the affected animal

PRA - NO BREEDING from the affected animal, its parents or offsprings

# Condotta di Allevamento Zwergpinscher

- VET ADVICE (CAP. 8 Manuale ECVO)

  PPM iride-iride - OPTIONAL, iride-lente - NO BREEDING from the affected animal 9.75%

  Cataratta 2.43% - NO BREEDING from the affected animal

  Displasia retinica mf/geografica 2.43% - OPTIONAL

  PRA 4.87% - NO BREEDING from the affected animal, its parents or offsprings

  LL - NO BREEDING from the affected animal, its parents or offsprings

A cosa servono i certificati ed i test genetici?

1) allevamento “sano”; beneficio per CANI, Allevatori e Proprietari
2) “movimento” internazionale di cani; adeguamento a standard più elevati di lavoro
3) studi epidemiologici

*Veterinary Ophthalmology* (2017) 1–6 DOI:10.1111/vop.12542

## Epidemiology of ocular disorders presumed to be inherited in three small Italian dog breeds in Italy

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**Abstract**

*Objective* To describe the prevalence and the types of eye disorders that are known or presumed to be inherited (KP-HED) in three small Italian dog breeds.

*Animals* Three small Italian dog breeds: Maltese, Bolognese, and Italian Greyhound.

*Procedures* All dogs of the breeds selected for this prospective observational study that underwent a complete ophthalmic examination between 1994 and 2015 were included. General and proportional KP-HED prevalence with 95% confidence intervals were reported.

*Results* Three hundred and six of 462 dogs were affected by at least one KP-HED (66.2%; 95% CI: 61.8%–70.4%). In the entire population, the five most common KP-HED were cataract ($n$ = 122; rate on the total number of KP-HED: 31.4%), entropion ($n$ = 56; 14.4%), keratoconjunctivitis sicca ($n$ = 33; 8.5%), retinal dysplasia ($n$ = 24; 6.2%), and persistent pupillary membrane (iris to iris) ($n$ = 21; 5.4%). The most common KP-HED in each breed were cataracts in the Maltese (35.1%) and in the Bolognese (24.2%), and presentation of vitreous in the anterior chamber in the Italian Greyhound (46.7%).

*Conclusions* Clinicians should be aware of KP-HED that commonly affect three small Italian dog breeds. Breed standards should be reconsidered, and breeding programs should be directed at limiting such disorders.

**Key Words:** cataract, hereditary, known and presumed-hereditary eye diseases, PIED, selection, vitreous degeneration

### INTRODUCTION

Inherited eye diseases significantly impair vision in humans and animals.[1–4] As of 2015, 278 genes and loci have been associated with retinal disorders in humans.[5] The identification and characterization of inherited eye disorders are critical for the diagnosis, prevention, and treatment of such disorders.[6,7]

Several inherited and presumed to be inherited eye disorders have been described in purebred dogs.[2,8–11] Until the genetic basis of an ocular disorder is properly defined, ocular disorders that are suspected to have a genetic basis are defined as 'known and presumed-hereditary eye diseases' (KP-HED). An ocular disorder is defined as 'presumed to be inherited' when 1: it is observed more frequently in one breed compared with other breeds; 2: its incidence increases in a breed; 3: it is observed more frequently within related dogs of a certain breed; 4: it has a characteristic appearance and location; 5: it has a characteristic age of onset and course of progression; and 6: it is similar to an entity which has been proven to be inherited in other breeds.[10]

Italy is homeland of sixteen dog breeds.[12] These include three small-sized breeds: Italian Greyhound [Fédération Cynologique Internationale (FCI) code: 200], which standard has been definitively accepted in 1956 and is included in the group 10, section 'Short-haired Sighthounds', Maltese [FCI code: 65], accepted in 1955, and Bolognese [FCI code: 196], accepted in 1956.[12] Both these two latter breeds are included in group 9, 'Companion and Toy Dogs' under the section 'Bichons and related breeds'.[12] Scientific knowledge about KP-HED in these breeds is limited. The 2017 publication of the Hereditary Eye disease (HED) Committee of the ECVO reports data on the



*Veterinary Ophthalmology* (2017) 20, 5, 420–426 DOI:10.1111/vop.12442

## Epidemiology of ocular disorders presumed to be inherited in three large Italian dog breeds in Italy

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The authors disclose any financial interests with companies that manufacture products that are the subject of the present research or with companies that manufacture competing products.

**Abstract**

*Objective* To describe the epidemiology and the types of eye disorders that are presumed to be inherited (PIED) in three large Italian dog breeds.

*Animals* Three large Italian dog breeds: Neapolitan Mastiff (FCI code: 197), Maremma Sheepdog (FCI code: 201), and Italian Corso dog (FCI code: 343).

*Procedures* All dogs that underwent a complete ophthalmic examination between 1992 and 2012 were included in this prospective observational study. The prevalence of eye disorders with 95% confidence intervals was reported for presumed healthy dogs and for dogs referred to a veterinary center for an ophthalmic consultation. Univariate and multivariate logistic regression techniques were used to generate odds ratios.

*Results* Of 605 dogs examined during the study period, 351 dogs were affected by at least one PIED (58%; 95% CI: 54–62%). The prevalence of PIED was significantly lower in dogs presented for ophthalmic examination (53.8%) as compared to presumed healthy dogs (62.2%)(OR: 1.4; 95% CI: 1.02–1.9; $P$ = 0.037). Also after multivariate adjustment for the period of observation, the odds of Neapolitan Mastiff (92.1%; OR: 21.4; 95% CI: 11.1–41.4) and of Cane Corso (57.7%; OR: 2.5; 95% CI: 1.7–3.6) suffering a PIED were greater than the Maremma Sheepdog (35.4%). The most common PIED in each breed were entropion (24.3% of all the PIED) in the Neapolitan Mastiff, ectropion (36.6%) in the Corso dog, and cataract (27.9%) in the Maremma Sheepdog.

*Conclusions* Clinicians should be aware that three large Italian dog breeds frequently suffer PIED. Bread standards should be reconsidered, and breeding programs should be directed at limiting such disorders.

**Key Words:** breed, ectropion, entropion, epidemiology, inherited, predisposition

### INTRODUCTION

Inherited eye diseases significantly impair vision in humans and animals.[1–4] As of 2015, 278 genes and loci have been associated with retinal disorders in humans.[5] The identification and characterization of inherited eye disorders are critical for the diagnosis, prevention, and treatment of such disorders.[6,7]

Several inherited and presumed to be inherited eye disorders have been described in pure-bred dogs.[2,8–11] Until the genetic basis of an ocular disorder is properly defined, ocular disorders that are suspected to have a genetic basis are defined as 'presumed to be inherited eye disorders' (PIED). An ocular disorder is defined as 'presumed to be inherited' when it is (i) observed more frequently in one breed compared with other breeds; (ii) observed more frequently within related dogs of a certain breed; (iii) with characteristic appearance and location; (iv) with characteristic age of onset and course of progression; and (v) similar to an entity which has been proven to be inherited in other breeds.[10]

Italy is the homeland of sixteen dog breeds.[12] These include three large-size breeds: the Neapolitan Mastiff [Fédération Cynologique Internationale (FCI) code: 197], the Maremma Sheepdog [FCI code: 201], and the Italian Corso dog [FCI code: 343].[12] Scientific knowledge about

# Conclusioni

- Importanza della **prevenzione** e della diagnosi precoce;
- Importanza delle **visite** oculistiche e dei **tests** genetici (l'uno non esclude l'altro); Possono esserci **mutazioni diverse** per la stessa malattia!;
- Per moltissime patologie **non esiste** ancora il test genetico!;
- Importanza nella **collaborazione** tra veterinari ed allevatori; **Unione** di intenti, fiducia e serietà reciproca!

# DOMANDE ?