

## Collie Eye Anomaly in Switzerland

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### Abstract

In this retrospective study, the results of 3'527 eye examinations in 6 different breeds affected with Collie Eye Anomaly (CEA) over a period of 8 years (1999–2007) are described. CEA was divided into three main ophthalmoscopic features, a) choroidal hypoplasia (CRH), b) CRH and coloboma and c) coloboma alone. Of the 101 Smooth Collies 8.9% showed signs of CRH, whereas 36.9% of Rough Collies were affected with CRH, 2.8% with CRH and coloboma and 0.38% with coloboma alone. Choroidal hypoplasia was present in 13.1%, CRH and coloboma in 1.8% and coloboma alone in 0.2% of the Shetland Sheepdogs. Only one Australian Shepherd dog had CRH, while 0.7% of the Border Collies were affected with CRH. None of the Nova Scotia Duck Tolling Retrievers were affected with CEA. There were no statistically significant differences in the occurrence of CEA between males and females, nor was there any relation between coat colors. Significant differences could be shown between dogs younger or older than 8 weeks at first examination. CEA was more often diagnosed in dogs younger than 8 weeks within the Rough Collie and Shetland Sheepdog.

Keywords: Collie eye anomaly, choroidal hypoplasia, coloboma, collies

### Collie Augenanomalie (CEA) in der Schweiz

In dieser retrospektiven Studie werden die Resultate von 3'527 Augenuntersuchungen über einen Zeitraum von 8 Jahren (1999–2007) bei 6 Rassen bezüglich Collie Eye Anomaly (CEA) beschrieben. Dabei wurde zwischen den drei wichtigsten Erscheinungsformen, a) choroidale Hypoplasie (CRH), b) CRH und Kolobom sowie c) Kolobom alleine unterschieden. Von 101 Kurzhaar (Smooth) Collies zeigten 8.9% eine CRH. Hingegen war die Befallsrate der Langhaar Collies mit 36.9% CRH, 2.8% CRH und Kolobom und 0.38% an Kolobom alleine erkrankten Hunden wesentlich höher. Beim Shetland Sheepdog zeigten 13.2% der Hunde eine CRH, 1.8% die Kombination CRH und Kolobom und 0.2% nur ein Kolobom. Eine Australian Shepherd Hündin hatte CRH, während 0.7% der Border Collies eine CRH zeigten. Kein Fall von CEA wurde beim Nova Scotia Duck Tolling Retriever diagnostiziert. Die statistische Auswertung der Resultate zeigte bei keiner der untersuchten Rassen gesicherte Unterschiede bezüglich des Geschlechts oder der Fellfarbe. Hingegen waren signifikante Unterschiede zwischen Hunden zu erkennen, die bei der ersten Untersuchung jünger beziehungsweise älter als 8 Wochen waren. CEA wurde bei den Rough Collies und den Shetland Sheepdogs vermehrt bei jüngeren Tieren diagnostiziert.

Schlüsselwörter: Collie Augenanomalie, choroidale Hypoplasie, Kolobom, Collies

### Introduction

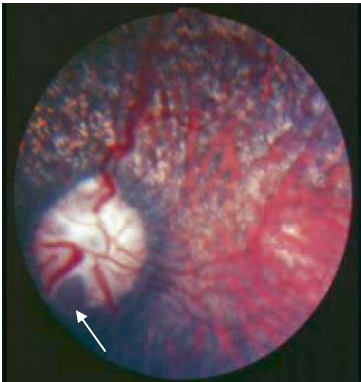
Collie Eye Anomaly (CEA) is a congenital, hereditary canine ocular disorder affecting the Smooth and Rough Collie, Border Collie, Shetland Sheepdog, Lancashire Heeler, Australian Shepherd and Nova Scotia Duck Tolling Retriever (Barnett, 1969; Roberts, 1969; Rubin, 1969; Blogg, 1970; Barnett, 1979; Bedford, 1982a; Bierkas, 1991). The

pleomorphic syndrome involves a failure of the development of the posterior segment of the optic vesicle. The ophthalmoscopic changes consist of focal hypoplasia or absence of the tapetum and a focal lack of pigment of the retinal pigmented epithelium allowing the visualization of abnormal choroidal blood vessels (choroidal

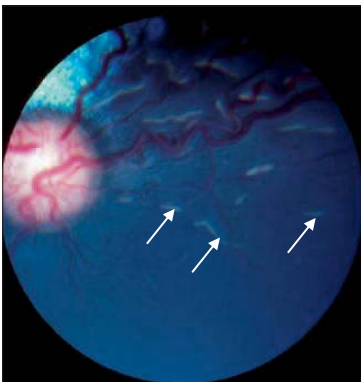
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**Figure 1:** Choroidal hypoplasia. Temporal to the optic disc choroidal vessels exhibit abnormalities in form and distribution and the white scleral tissue is visualized behind the abnormal choroid giving the lesion a whitish appearance.



**Figure 2:** Choroidal hypoplasia/coloboma. The optic disc or adjacent area colobomas are caused by ectasia of the cribriform plate or the peripapillary sclera. The papillary lesions are often seen as gray or pink indentations.



**Figure 3:** Retinal folds. They are located in the neurosensory retina of the neonate, which arise because of the unequal growth of the sclera, the choroid, and the retinal layers. The folds are seen as linear or circular, grayish or white configurations.

hypoplasia, CRH, Fig. 1) and colobomas of the optic disc or adjacent areas. Colobomas are seen as gray or pink depressions or excavations, which can severely distort the area of the disc. Typically, colobomas are located in the six o'clock position of the optic disc (Fig. 2). Less frequent manifestations of the anomaly are partial or complete retinal detachments, retinal folds (Fig. 3) and intraocular hemorrhages, which are usually associated with large colobomas. Choroidal hypoplasia does not impair vision, but dogs with large colobomas involving the optic papilla may exhibit visual deficits. Complete blindness is the result of retinal detachment and intraocular hemorrhage. CEA is usually bilateral but not always symmetrical

(Roberts, 1969; Barnett, 1979; Bedford, 1982b; Bierkas, 1991; Bedford, 1998; Rampazzo et al., 2005). By three months of age the puppy fundus changes from its blue tapetal color to the adult green-yellow appearance. At the same time minor chorioretinal changes can be masked by the development of more pigment in the RPE, in which case affected animals are classified as so called „go normal“ animals (Bedford, 1982b).

Various studies have been published about the inheritance of CEA (Roberts, 1969; Yakely, 1972). A simple autosomal recessive trait is postulated with a nearly 100% penetrance for CRH (Lowe et al., 2003) and a separate trait or a polygenic transmission is suspected for coloboma by Wallin-Hakanson (Wallin-Hakanson et al., 2000a, b). Parker showed with sequence analysis that all affected breeds share a homozygous 7.8-kb deletion in the gene NHEJ1 of chromosome 37 (Parker et al., 2007). A specific mutation-based DNA test has been discovered (Optigen, 2005). The objective of this study was to evaluate the results of 3'533 eye certifications by veterinary ophthalmologists in Switzerland between 1999 and 2007.

## Animals, Material and Methods

### Animals

Six different breeds including Smooth and Rough Collie, Shetland Sheepdog, Border Collie, Australian Shepherd dog and Nova Scotia Duck Tolling Retriever were examined by 5 veterinary ophthalmologists in Switzerland. A total of 3'533 dogs were examined between 1999 and 2007, including 101 Smooth Collies, 786 Rough Collies, 720 Shetland Sheepdogs, 1248 Border Collies, 571 Australian Shepherd dogs and 107 Nova Scotia Duck Tolling Retrievers. All coat colors, genders and age groups were represented. The dogs were presented by their breeders or owners for eye examinations as part of the breeding program at various ages.

### Examination and group formation

The ophthalmologic examination was performed in a dark examination room before and after pharmacologic dilatation of the pupils with 0.5% Tropicamide drops and was limited to slit-lamp biomicroscopy and indirect ophthalmoscopy. Dogs were divided into two groups according to the age at first examination. Group A8 included animals younger than 8 weeks, group B8 animals older than 8 weeks. In a second and third step groups A/B7 and A/B6 were generated accordingly. These groups were chosen because around 6 to 8 weeks the ophthalmoscopic appearance of the fundus could mask mild chorioretinal changes. The goal of this study was to define the best age of the puppies at their first examination to decrease the number of „go normal“ dogs.

## Statistics

Statistical analyses were performed using the program StatView 5.1 (SAS Inc.) and Microsoft Excel. Differences between incidences of CEA for different coat colors, sex distribution, several time periods and progression of CEA and age difference were evaluated by Chi-Square-test for groups with  $n > 5$ . For  $n < 5$ , Fisher exact test was used. Factorial Analysis of Variance (ANOVA) and Bonferroni-Dunn test were used for groups of continuous data, ANOVA for factor analysis and Bonferroni-Dunn for group analysis. A significance level of  $P \leq 0.05$  was selected. Normal distribution was tested before performing parametric tests.

## Results

The overall incidence of CEA for all breeds combined was found to be 12.4%. A total of 404 animals were affected with CRH; 35 with CRH/coloboma and 4 with a coloboma alone. The incidence of CEA in different breeds is summarized in Table 1.

### Rough Collie

Of 785 Rough Collies examined in Switzerland during the 8-year period 290 (36.9%) were affected with CRH alone; 22 (2.8%) dogs showed CRH in combination with a coloboma and 3 (0.38%) dogs had a coloboma alone. The over-all incidence of CEA was 40.1% in this breed. 380 animals were female, of which 136 (35.8%) had CRH and 9 (2.4%) had CRH and coloboma. Of the 363 male dogs, 134 (36.9%) were affected with CRH, 13 (3.6%) with the combination and 3 (0.8%) showed a coloboma alone. The differences between male and female dogs were not statistically significant. The incidence of CEA related to coat color was also investigated (Tab. 2). There was a slight difference in frequency between the coat colors but

Table 2: CEA in relation to coat color within Rough Collie/ Shetland Sheepdog.

| Color        | Total number of dogs examined | CEA            | % CEA              |
|--------------|-------------------------------|----------------|--------------------|
| Sable        | 417/314                       | 168/31         | 40.2%/9.8%         |
| Tricolor     | 222/207                       | 77/42          | 34.6%/20.2%        |
| Blue merle   | 122/102                       | 61/23          | 50%/22.5%          |
| Unknown      | 24/97                         | 9/13           | 37.5%/13.4%        |
| <b>Total</b> | <b>785/720</b>                | <b>315/109</b> | <b>40.1%/15.1%</b> |

the result was not significant ( $p = 0.0839$ ). Retinal detachment and retinal hemorrhage was found in a single case. The overall incidence of CEA varied from year to year, 2003 showing the highest and 2005 the lowest incidence (Tab. 3). The distribution into different age groups showed significantly more dogs with CEA diagnosed in the group A8 (dogs younger than 8 weeks) comparing with the older age group ( $p = 0.001$ ). Groups A7 and A6 showed a similar trend without being statistically significant (Tab. 4).

### Smooth Collie

Of the 101 Smooth Collies, 9 dogs (8.9%) showed signs of CEA and all of them had CRH. None of the dogs had a coloboma, intraocular hemorrhage or retinal detachment. 46 of the examined animals were females and of these 5 (11%) had CRH. Of the 50 males 4 (2%) were diagnosed with CRH. The difference was not significant ( $p = 0.2546$ ) and the incidence of CEA related to coat color was neither statistically significant ( $p = 0.4506$ ). For the group distribution no clear trend could be determined to diagnose more CEA when examining animals younger

Table 1: Incidence of CEA in six breeds (1999–2007).

| Breed               | CRH                | CRH/coloboma     | coloboma        |
|---------------------|--------------------|------------------|-----------------|
| Rough Collie        | 290 (36.9%)        | 22 (2.8%)        | 3 (0.38%)       |
| Smooth Collie       | 9 (8.9%)           | 0                | 0               |
| Shetland Sheepdog   | 95 (13.2%)         | 13 (1.8%)        | 1 (0.1%)        |
| Border Collie       | 9 (0.7%)           | 0                | 0               |
| Australian Shepherd | 1 (0.3%)           | 0                | 0               |
| NSDTR               | 0                  | 0                | 0               |
| <b>Total</b>        | <b>404 (11.4%)</b> | <b>35 (0.9%)</b> | <b>4 (0.1%)</b> |

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Table 3: Distribution of CEA per year in Rough Collie/Shetland Sheepdog.

| Year         | Total number of dogs examined | CEA            | % CEA              |
|--------------|-------------------------------|----------------|--------------------|
| 1999         | 63/70                         | 18/15          | 28.6%/21.4%        |
| 2000         | 39/50                         | 11/8           | 28.2%/16%          |
| 2001         | 67/92                         | 26/10          | 38.8%/10.8%        |
| 2002         | 64/77                         | 18/15          | 28.1%/19.4%        |
| 2003         | 134/129                       | 70/19          | 52.2%/14.7%        |
| 2004         | 124/105                       | 47/6           | 37.9%/44.7%        |
| 2005         | 51/70                         | 9/9            | 17.6%/12.8%        |
| 2006         | 147/82                        | 68/14          | 46.2%/17%          |
| 2007         | 96/40                         | 48/12          | 50%/30%            |
| <b>Total</b> | <b>785/720</b>                | <b>315/109</b> | <b>40.1%/15.1%</b> |

Table 4: Age at first examination to diagnose CEA in Rough Collie/Shetland Sheepdog.

| Groups              | Total number of dogs examined | CEA            | % CEA              |
|---------------------|-------------------------------|----------------|--------------------|
| Group A8 (< 8years) | 260/304                       | 140/57         | 53.8%/18.7%        |
| Group B8 (> 8years) | 504/393                       | 160/46         | 31.7%/11.7%        |
| unknown             | 21/23                         | 15/6           | 71.4%/26%          |
| <b>Total</b>        | <b>785/720</b>                | <b>315/109</b> | <b>40.1%/15.1%</b> |
| Group A7 (< 7years) | 67/73                         | 36/13          | 53.7%/17.8%        |
| Group A7 (> 7years) | 697/624                       | 264/84         | 37.8%/13.4%        |
| unknown             | 21/23                         | 15/6           | 71.4%/26%          |
| <b>Total</b>        | <b>785/720</b>                | <b>315/109</b> | <b>40.1%/15.1%</b> |
| Group A6 (< 6years) | 7/9                           | 4/1            | 57.1%/11.1%        |
| Group B6 (> 6years) | 757/688                       | 296/102        | 39.1%/14.8%        |
| unknown             | 21/23                         | 15/6           | 71.4%/26%          |
| <b>Total</b>        | <b>785/720</b>                | <b>315/109</b> | <b>40.1%/15.1%</b> |

than 8, respectively 7 or 6 weeks old. A variable distribution of CEA cases over the year was noticed.

### Shetland Sheepdog

Choroidal hypoplasia was present in 95 (13.2%) of total 720 examined dogs during the observation period.

13 (1.8%) of the dogs had a combination of CRH and coloboma and 1 (0.1%) dog was recorded with coloboma only. The overall incidence of CEA in this breed was 15.1%.

Of the 720 dogs, 358 were female and 336 males. 47 (13%) of the CRH affected animals and 6 (2%) of the CRH and coloboma patients were females. A similar

distribution could be shown in males. The only coloboma was in a male animal. The gender difference was not statistically significant ( $p = 0.7687$ ). All different coat colors are presented in Table 2. A statistically significant over-representation of sable, tricolor and blue merle color was remarkable compared with different other colors ( $p = 0.0035$ ). Intraocular hemorrhage was seen in one dog. The highest number of affected animals was diagnosed in 2004 (44.7%) compared to the year 2001 (10.8%). Statistical analysis performed between 1999–2007 was not significant (Tab. 3). A significant higher number of dogs with CEA in group A8 was found compared with group B8. A similar trend was noted in group A7 without being statistically significant (Tab. 4).

### Border Collie

A total of 1'248 Border Collies were examined. 9 (0.7%) animals showed a CRH. 4 were female, 4 males and one animal was of unknown sex. All coat colors were present. 5 (0.7%) of total 709 black/white dogs were affected with CRH. 3 (0.9%) of 320 tricolors dogs and 1 (1.4%) of 68 blue merle dogs were affected. 4 (44%) of the 9 animals affected with CRH were younger than 8 weeks and 5 (55%) animals older than 8 weeks. All dogs were older than 7 weeks at the time of the first examination.

### Australian Shepherd

571 Australian Shepherds were examined. The group consisted of 305 females, 255 males and 11 of unknown sex. All of the Australian Shepherd coat colors were present; the majority with 33.4% was blue merle. Only one female blue merle Australian Shepherd dog was affected with CRH. No cases of coloboma, intraocular bleeding or retinal detachment were found. The age of the dog with CRH was under 8 weeks.

### Nova Scotia Duck Tolling Retriever

Although CEA has been described in this breed, none of the 102 dogs examined in Switzerland showed signs of the anomaly.

## Discussion

CEA has been often described in the Collies and, less frequently in the Shetland Sheepdog, Border Collie, Australian Shepherd, and Nova Scotia Duck Tolling Retriever. The incidence of CEA varies from country to country. The current incidence in Switzerland with 40.1% affected Rough Collie is comparable to that in Norway with 40.8% (Bierkas, 1991). In contrast, only 15.1% of Shetland Sheepdogs are affected with CEA in Switzerland. However, reports from England and Scotland showed a significantly higher frequency. Bedford (1982b) noticed

between 1980–1982 a percentage of 64% affected Collies and 72% Shetland Sheepdogs in England. An even higher number of CEA cases (80%) has been recorded 40 years ago in the Shetland Sheepdog in Scotland (Lawson, 1969). The Netherlands had 40.6% affected Collies (Stades and Barnett, 1981) and 48% affected Shetland Sheepdogs (Barnett and Stades, 1979). In Germany an incidence of 61.1% for the Rough Collie and 39.7% for the Shetland Sheepdog was reported (Hennecken, 1993). A retrospective evaluation of congenital ocular defects in Australia indicated that CEA is the second most common congenital defect after persistent hyaloids remnants in Australian Shepherd dogs (Munyard et al., 2007). In the United States 79.9% (Donovan and Wyman, 1965) and even 97% (Yakely, 1972) affected Collies had been reported years ago. The distribution of CEA within the Rough Collie in Austria was 12.6% in 1988 (Holzhacker, 1988), a study in Switzerland by Kellner and Leon 14 years ago showed a frequency of 31.6% (Kellner, 1985). It is difficult to compare these results because the dogs in different studies have been examined at various ages and many adults may have been "go normal" dogs.

In our study a significant higher number of Rough Collies and Shetland Sheepdogs less than 8 weeks old could be diagnosed with CEA. These results confirm that with increasing age the choroidal defects may become masked and these "go normal" animals are then reported as "clear" at later examinations. Our additional groups A7/6 and B7/6 failed to reveal clear information probably because of the small number of animals in these groups. In the author's opinion the best age to examine the puppies is  $\leq 8$  weeks. Neither gender nor coat color appeared to play a significant role in Collie Eye Anomaly. Studies from Norway (Bierkas, 1991) and the Netherlands (Stades and Barnett, 1981) came to the same conclusion. A Finnish study compared affected dogs pooled into two groups (dogs born in 1988–1991 and dogs born in 1994–1997). The authors (Leppanen and Saloniemmi, 1998) detected a significant increase in CEA prevalence. During our study period, no significant changes in the incidence of CEA were observed but it seems to have increased from 31.58% in Rough Collie (Kellner, 1985) to 40.1% in the current study, although strict breeding regulations were always in effect. Reasons for this increase could be that in the past few years an age of not more than 8 weeks at first examination has been enforced to the breeders. Furthermore, imported breeding dogs of uncertain ophthalmic status and genetic background could also influence the results. Choroidal hypoplasia without coloboma was the most common finding regarding the main ophthalmoscopic features. Severe lesions such as coloboma, retinal detachment and intraocular hemorrhage were rarely seen. Similar results could be demonstrated earlier (Blogg, 1970; Bedford, 1982b). In 1982 Bedford (1982a) diagnosed in Hertfordshire 6% with CEA affected Border Collies. In comparison with 0.7% affected Border Collies in Switzerland these results were remarkably high.

The increasing incidence of CEA reported in this study

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**Anomalie de l'œil du Colley en Suisse**

Dans cette étude rétrospective, on décrit les résultats de 3'527 examens ophtalmiques effectués durant une période de 8 ans (1999–2007) chez 6 races quant à l'anomalie de l'œil du Colley (AOC). On fait la différence entre les 3 formes principales, à savoir, a) l'hypoplasie choroïdale (CRH) b) CRH associée à un colobome et c) colobome seul. Parmi 101 Colleys à poil court (smooth), 8,9 % présentaient une CRH. Par contre, chez les Colleys à poil longs, les taux d'atteinte, avec 36,9 % de CRH, 2,8 % de CRH associée à un colobome et 0,38 % de colobome seul, étaient nettement plus élevés. Chez les Bergers des Shetlands (Shetland sheepdog) 13,2 % des chiens présentaient une CRH associée à un colobome et 0,2 % un colobome seul. Une chienne Berger australien présentait une CRH alors que 0,7 % des Borders colleys en étaient affectés. On n'a pas diagnostiqué d'AOC chez les Nova Scotia Duck Tolling Retriever. L'exploitation statistique des résultats n'a démontré chez aucune des races examinées de différences significatives pour ce qui est du sexe ou de la couleur du poil. Par contre, des différences significatives ont été constatées entre les chiens qui étaient plus jeunes ou plus âgés que 8 semaines lors du 1<sup>er</sup> examen. Des AOC ont été diagnostiqués plus fréquemment chez les jeunes Colleys à poil long et chez les Bergers des shetlands.

**Anomalia dell'occhio del Collie in Svizzera**

In questo studio retrospettivo relativo alla Collie Eye Anomaly (CEA) vengono descritti i risultati ottenuti su 6 razze di 3'527 esami oculari effettuati su un periodo di 8 anni (1999–2007). Questi sono stati suddivisi secondo le tre forme di sintomi a) ipoplasia coroidea, b) ipoplasia coroidea e coloboma e c) solo coloboma. Dei 101 Collie a pelo corto (Smooth), 8,9 % erano affetti da ipoplasia coroidea. Per contro, per quel che riguarda i Collie a pelo lungo, la percentuale dei cani infettati era così elevata che i risultati davano il 36,9 % affetti da ipoplasia coroidea, 2,8 % da ipoplasia coroidea e coloboma e lo 0,38 % da solo coloboma. Tra gli Shetland Sheepdog il 13,2 % dei cani presentavano una ipoplasia coroidea, l'1,8 % la combinazione tra ipoplasia coroidea e coloboma e lo 0,2 % solo un coloboma. Una femmina di Australian Shepherd era affetta da ipoplasia coroidea mentre lo 0,7 % dei Border Collie presentava una ipoplasia coroidea. Nessun caso è stato diagnosticato nella razza Nova Scotia Duck Tolling Retriever di CEA. L'interpretazione statistica dei risultati ha dimostrato che nessuna delle razze esaminate mostrava differenze rilevanti in relazione al sesso o al colore del pelo. Per contro differenze significative sono state rilevate tra cani che al primo esame erano di età inferiore o maggiore di 8 settimane. Le razze con un incremento diagnosticato di CEA sono i giovani dei Rough Collie e degli Shetland Sheepdog.

requires a carefully directed program to control CEA in Switzerland. Although the incidence of blindness is low today a routine eye examination in the breeds affected with CEA is strongly recommended.

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