

Inherited Ocular Diseases in the Entlebucher Sennenhund

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Introduction

Inherited ocular diseases aren't uncommon with purebred dogs. As much as 147 different breeds with different defects are known. (Rubin 1989). Increased eye diseases with specific breeds lead to include an eye examination as part of the breed approval in addition to the x-ray and behavioral examination. These mass screening are today quite common, domestic (Switzerland) and abroad.

Already 1969 the first inherited ocular diseases with Entlebucher Sennenhunden have been discovered. 1974 seven cases have been published (Kraehenmann, 1974). In the middle of the 80, after a long period where no new cases have shown up, an increase of inherited ocular disease showed up in the Netherlands. The cases were offspring from Entlebucher Sennenhunden from Switzerland (Stades 1987). This started status examination including the ophthalmoscopic examinations with as many dogs as possible. Following are the results from this examination.

Animals, Material and Methods

Between 1987 and 1992 altogether 276 Entlebucher Sennenhunde from dog shows and clubs have been examined by the veterinary hospital of the University of Zurich. 49% were sirs and 51% dams with an average age of 4.4 years. The youngest examined dog was 6 month and the oldest was 15 years old.

The dogs have been examined 1.3 times in average. Some have been tested up to 10 times. Most of this dogs (72%) under went the test as a preventive exam and where not known to be sick. The remaining 28% had been examined because of their obvious eye problems. All of the dogs have been examined using a "Handspaltlampe" (1) and an indirect "Ophthalmoskop" (2). In indicated cases dogs have been "Kammerwinkel" gonioscopic examined (3) and topometric analyzed (4). Two dogs have been topographic examined (4) and it was possible to do an electroretinography with three dogs (5).

177 pedigrees out of the 276 dogs were available for a genealogical study. The gene frequency of each disease have been determined and calculated. It has been determined how fast the gene frequency could be reduced with breeding approaches.

Results

The research of the 276 dogs demonstrated three heaped eye diseases at Entlebucher Sennenhunde, which let us believe that there is an inherited component involved. These three diseases will be discussed in the order of their frequency.

Cataracts

42.4% of the examined dogs showed a bilateral symmetric cataract. Posterior polar cataract. This cataract develops earliest with 12 month latest with 26 month. Males and females are equally distributed. In 92% of these cases the disease were stationary and did not lead to objective poor eyesight. However 8% (9 of 117) of the cases developed a progressive cataract up to a mature cataract, with significant poor eyesight or blindness.

The analysis of the available pedigrees lead to assume a "autosomal recessive" heredity. The disease skips individual generations and shows healthy littermates next to the attacked. A typical zoom-in of a pedigree shows 3 dogs with cataract in one litter of 8 pups. Theoretically 25% of the F1 generation was expected to be attacked, in this case 2 dogs, since the parents were phenotypic normal.

Progressive Retina-Atrophy (PRA)

Bilateral symmetric retinal degeneration has been diagnosed in 24.9% of the examined dogs. First symptoms showed up at an age of 3 years. Significant symptoms were seen with 4 to 5 years and at this age first poor eyesight was manifested. First observations of the ophthalmoscopic examination were the hyperreflectivity of the tapetal fundus. This hyperreflectivity was particular strong in the periphery of the fundus, here often combined with noticeable radial stripes of the retina. The threat- and pupular reflexes were still normal at this early stage, and most of the dog owners didn't notice any poor eyesight. With further development of the disease attenuation of the retinal vasculature were visible.

Specifically the "arteriole" became very thin even a few "papille" diameters away from the "view nerve disc" and rarely were more than one branch noticeable. The "venolen" however were in contrast relatively long noticeable, even they were significantly attenuated. At the same time a partial spotted depigmentation of the non tapetal fundus has been realized. Fairly late in the development of the disease could a pallor of the optic disc been noticed. In the first place it became pale and than with increased "Demyelinisierung" of the "Axone" significantly smaller and rounder. The pupular reflexes were significantly reduced in this stage and the dogs showed a clear "Mydriasis" This "Mydriasis" in combination with the increased reflection of the tapetum fundus were often the first indication for the owner that the dogs eyes have changed. Night-blindness were the first objective sign of poor eyesight. The dogs are scared and insecure at dusk and refuse to walk and climb stairways when insufficient illuminated. Sometimes they will also hit objects in this condition.

At normal light conditions however these dogs behave absolute normal. This visual deficits will also be noticeable during daytime. Finally the effected dogs going blind between 6 and 8 years of age. Some dogs keep a rest view capability beyond this age.

The ophthalmoscopic picture and the visual deficits lead to the assumption of a rod/cone abiotrophy, as described for other dog breeds (Rubin, 1989).

The electroretinographic examination of a clinically and opthalmoscopically normal dog shows a normal adaptation to the darkness, "skotopische" red - and blue stimulation, as well as "Flicker" stimulation (Leber-Zuercher,1990). The elektoretiongram of the Entlebucher Sennenhunde sickened at PRA showed a total absence of the "biosignals" after stimulation of the brightly- and dark-adapted retina.

The occurrence of PRA with the Entlebucher Sennenhund lies with 24.9% over the one of the “hospital -population” of 3.7%. This indicates an inherited disease (Thrusfield,1988). The analysis of the existing family trees leaves also suspect an autosomal recessive heredity for the PRA (Abb.6). Again male dogs and bitches are affected in the same way, and the disease skips one or several generations.

Glaucoma

From the examined dogs, 3.3% had glaucoma (9/276). Eight of these dogs were examined because of clear eye-problems. One dog was diagnosed on the occasion of a check-up. Effected dogs first showed a jam unilaterally of the “episkleralen” vessels, a “Mydriasis” and a more or less clear cornea-edema. The eye-pressure was clearly increased in all cases. With an exception the effected eyes showed a clear scope (Umfang) -increase (Buphthalmus) and an atrophy of the “Sehnervenscheibe” and the retina. In chronic cases, the lens was secondarily “luxiert”.

The examination of the “Kammerwinkel, chamber-angles” (goniodysgenesis) with a gonioscopic lens showed a “dysplastisches” Ligamentum pectinatum on effected dogs in the glaucoma changed eye as well as in the healthy eye. In contrast to the normal Lig.pect. with its slim “Trabekeln” were the “Kammerwinkel, chamber-angles” in these cases generally narrowly and closed from a dense pigmented tissue. In single squares were base-wisely a normal Lig.pect. observable. In one case a tonographic examination could be done in the glaucoma changed eye as well as in the healthy eye. This was an experiment in order to measure objectively the drainage capability (Gelatt, 1991). In both eyes was these drainage capability (Abflussmoeglichkeit) smaller than 0.1 ul/mmHg/min. Normal is 0.24ul/mmHg/min with the dog (Gelatt, 1991).

The occurrence of the Glaucoma of 33% is only slightly above of the hospital-population of 1.0%. On the basis of the observations in Holland (Stades, 1987) nevertheless must be dealt with a considerable inherited component. The evaluation of the existing pedigrees revealed again an autosomal recessive mode of inheritance, however the data on hand are insufficient for a more exact statement.

Calculation of the Gene Frequency (Genfrequenzen)

Under the assumption of an autosomal recessive inheritance of all three eye-diseases after the law of Hardy and Weinberg (Black, 1972), the gene frequencies and the frequency of the three possible gene combinations can be calculated. p is the frequency of the normal gene and q the one of the mutated gene. The formula $p+q = 1$ is valid. In the breeding-population means p^2 , $2pq$ and q^2 the frequencies of the genotypic normal, homozygotic individuals, the heterozygotic, phaenotypic normal and the homozygotic animals with changed Phacnotypus (Pirchner, 1969). The frequency of this Gene combinations of the three eye-diseases in the Entlebucher Sennenhund is presented in table 1. In all cases, the majority of the mutated genes is in the phaenotypic normal carriers.

The decrease of the gene frequency with a breed with phaenotypic normal animals calculates itself after the formula $1/q_n - 1/q_0 = n$ (Pirchner, 1969). With q_n as the desired frequency, q_0 the starting frequency and n the number of generations, which are required to achieve the expected goal. If the frequency of the three diseases are assumed 1%, then several generations are required to achieve it. The results, under assumption of a generation-time of 2 years, are presented in table 2.

Multiple characteristic-carrier

11.9% of the examined dogs showed more than one inherited eye-disease. Most frequent, the combination was Cataract/PRA with 7.9%, followed from Cataract/Glaucoma with 2.2% and PRA/Glaucoma and Cataract/PRA/Glaucoma with 1% each. 18.6% of the dogs with polar cataracts also had a PRA, 5.3% had a glaucoma and in one case were all three illnesses in the same individual manifesto. From the dogs with PRA, 34% showed a polar cataract, 2.4% a glaucoma and once again one case all three illnesses. 44% of the dogs with glaucoma had a polar cataract simultaneously, in one case each was the glaucoma with PRA, resp. with PRA and polar cataracts combined.

Discussion

The examination of 276 Entlebucher Sennenhunde showed that specifically cataracts and PRA have an extremely often occurrence. The observed cataracts frequently are the same described with other races, as for example with the Labrador and the Golden Retriever (Rubin,1989). The same is valid for the retinal degeneration (rod/cone-abiotrophy), with respect to the time of its occurrence, their clinical symptoms and the ophtalmoscopic results. They are similar to that with the poodle and Cocker spaniel (Rubin,1989). While the majority of the dogs with polar cataracts don't suffer relevant losses of their eyesight, all Entlebucher Sennenhunde sickened with PRA become blind.

The frequency of the glaucoma with the Entlebucher Sennenhund is currently only slightly higher as with the other spital population, so that no urgent action must be taken in contrast to the cataract and PRA.

Since already the polar cataract can be manifested with 1 to 2 years of age, it should be no difficulty to improve the situation in a few years with breeding-exclusion of effected animals. A reduction of the frequency on less than 1% will however take at least 17 years. A must is that all dogs are undergoing a selection-procedure.

More difficult will be the obliteration of the PRA. Since the disease can be first diagnosed ophtalmoscopic in the 3 year of life, the possibility exists, that the effected animal has reproduced itself one or several times to this time. With it, the disease is widened in the population further.

If assumed that all three diseases are recessive inherited, the majority of mutated genes lie in the phenotypic normal, heterozygotic carriers. After the law of Hardy and Weinberg (Black, 1972) cataract with 45.6% can be expected, PRA and the glaucoma with 66.7%, resp. 35%. That leaves only little genotypic normal animals, namely 12% for cataracts, 26% for PRA and 59.9% for the glaucoma. That is a big disadvantage with a breed with a comparatively narrow breeding-basis, above all else if other undesirable characteristics, like for example the hip dysplasia, must also be wiped out still.

The start position for breeding is complicated through the occurrence of individuals with multiple eye diseases. In order to reduce the occurrence of the PRA and the polar cataracts significantly, it needs big breeding-efforts over a long time period therefore.