

Effect of inbreeding on the occurrence of genetic defects in Chinese Crested dogs*

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Summary

The aim of the study was to analyse the impact of inbreeding on the frequency of hereditary diseases and the number of genetically tested dogs. The pedigrees of 100 Chinese Crested dogs from Polish Kennel Club and information about genetic tests for hereditary eye diseases and other veterinary diagnoses were collected. Inbreeding coefficients and relatedness were estimated for all dogs examined. The relationship between the level of inbreeding and genetic testing was analysed with logistic regression. The relationship between the occurrence of eye disease carriers and sex or the level of inbreeding was also tested. A significant relationship ($P < 0.01$) was found between inbreeding and the number of animals genetically tested for PLL eye disease. The effect of sex or the level of inbreeding on the eye disease carrier status was non-significant ($P > 0.05$). However, in some inbred animals the status of the eye disease carrier could be connected with inbreeding, although this needs further research. We found that most of the dogs had related parents and genetic defects. We also found that the breeders often used related dogs, which reduced the genetic diversity of the group and caused hereditary diseases. We suggest that Chinese Crested dog breeders be more open about publishing DNA-test results, which is fundamental for the health of the breed.

Keywords: Chinese Crested dogs, genetic diseases, inbreeding, relatedness

The level of inbreeding and its impact on production and reproductive traits, health and, especially, on the occurrence of genetic defects, have been extensively studied in various species and breeds of domestic animals in recent decades. The stimulus for the development of pedigree and molecular methods describing the genetic structure of the population was the phenomenon of inbreeding depression occurring in many populations of domestic animals. It was particularly harmful in small populations of animal breeds that, due to low, often regional popularity, could not maintain a safe level of genetic variation. However, this problem also affected very popular breeds, such as Holstein-Friesian cattle, where the introduction of artificial insemination and the associated significant decrease in the number of sires drastically reduced the genetic diversity of the breed, causing increased homozygosity in populations with inbreeding depression and the occurrence of many hereditary diseases and defects (55). Howard et al. (29) claimed that, although the introduction of genomic selection made it possible

to select a more diverse group of bulls for mating, this did not translate into the wider range of sires presented to breeders, because again only the best evaluated few sires were offered. In addition to the analysis of genetic diversity for protection of genetic resources in small populations, researchers are also interested in the influence of excessive homozygosity on the fertility, conformation, longevity and production traits of various species of domestic animals. Research has been carried out on the level of inbreeding and its impact on various production traits, reproduction and health in large populations of farm animals, such as Holstein-Friesian cattle (17, 27, 28, 50) or the Charolaise cattle breed (49), as well as in small populations of local breeds, such as Ripollesa sheep (8), Markhoz goats (47) or Anglo-Arabian horses from Sardinia (23). Inbreeding depression affecting various production and reproductive traits, conformation and health was analysed in various livestock species. The influence of inbreeding depression on the survival of Brown Swiss calves and heifers was analysed (21). The impact of inbreeding on the fighting ability of Valdostana cattle was also investigated (52). Recently, the influence of

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inbreeding on the conformation traits of Anglo-Arabian horses (22) and Pura Raza Española horses (46) has also been studied.

Parallel to attempts at quantifying inbreeding depression caused by homozygosity, there has been a debate for many years about the essence of the phenomenon itself, which, despite molecular analysis methods being involved in its diagnosis, is still difficult for researchers to describe unambiguously (3, 10, 56). Homozygosity causes changes in the genetic variance of the population, reducing its additive part, which also hampers progress in both selected and other traits. In this case, the values of other non-additive components of genetic variation (dominant and epistatic variance) also decrease. Thus, an increase in homozygosity reduces the value of traits in animals, which is known as inbreeding depression. This depends on the frequency of genes and the intensity of selection. It can therefore be said that the phenomenon of inbreeding depression depends on factors operating in the population, such as genetic drift and selection pressure. It is different for different populations, with viability traits, i.e. survival, disease resistance and reproductive traits, due to the greater proportion of dominant patterns in the gene loci of these traits, usually being more susceptible to the impact of inbreeding than other additively conditioned traits. There are two theories explaining the phenomenon of inbreeding depression. One of them, the so-called “partial dominance hypothesis”, assumes that deleterious recessive alleles, which are fully expressed in homozygous individuals, are responsible for the development of inbreeding depression. These deleterious mutant recessive alleles initially occur only in heterozygotes, and kinship mating increases the likelihood of introducing both of them into the genotype of the offspring with a lethal or semilethal effect. The other theory, the so-called “theory of over-dominance”, refers to the dominant effect favouring heterozygotes as better in given traits than other genotypes. In such a situation, inbreeding, which results in a reduced number of heterozygotes, will also contribute to a reduction in the frequency of the dominant effect (7, 15, 29, 57). According to the over-dominance theory, selection that favours heterozygous systems at multiple loci reduces the importance of recessive mutations, whereas in the partial dominance theory, selection reduces the frequency of mutant recessive alleles in the population over time. In both cases, however, loci with moderate gene frequencies are likely to be more susceptible to inbreeding than loci with extremely high or extremely low frequency values. Reduction in the frequency of mutant recessive alleles is due to the fact that high-performance inbred animals are selected as parents of the next generation, and low-performance inbred animals are removed from the population by breeders or by the disclosure of a genetic defect that prevents their reaching the reproductive age. Therefore the magnitude of inbreeding depression can also be modified

by the environment (7, 11, 29). It has been shown that a slow accumulation of inbreeding works much better in the process of removing mutant recessive alleles than a steep increase in the value of inbreeding due to the mating of close relatives. Partial dominance is thought to be responsible for most of inbreeding depression in animal populations. However, inbreeding depression may also arise with the epistasis of dominant effects of various loci, which then causes a decrease in the frequency of heterozygotes in favour of the production of more homozygotes (7, 9, 29). The results of the analysis of weight at weaning obtained by Casellas (7) in a rabbit population indicated that the genetic background of inbreeding depression is distributed differently among individuals and is inherited from generation to generation.

With increasing homozygosity, most dog breeds face similar problems due to the fact that they were created from a small number of founders, whose offspring were strictly selected and mated to maintain the unique characteristics of the breed. Hence, the gene pools of many, if not nearly all, dog breeds have been markedly reduced throughout their history. The founder effect at the beginning of the breed creation and then the bottleneck effect resulted in a high level of inbreeding due to a significant decrease in the number of dogs in the breed, which was related, among others, to the popularity of the breed and a change in the breeding policy by the breeders. A certain level of homozygosity is needed for the consolidation of the unique features of each breed, but the increase in homozygosity due to the frequent mating of kin (especially close ones) results in harmful recessive alleles causing numerous hereditary diseases in particular dog breeds (20). Farrell et al. (20) reported that over 80 hereditary diseases are directly or indirectly related to the breed standard and that they negatively affect the health and welfare of dogs, but are unavoidable without changing the breed standard. On the other hand, over 75% of inherited health problems in dogs are not related to the breed standard and can be minimized by appropriate actions of breeders, such as testing animals for genetic defects and eliminating confirmed carriers from breeding (20). Farrel et al. (20) noted that breeders in the UK were encouraged to test their dogs by incentive programmes, free diagnostics, and genetic testing days organized by breed clubs. What is most important, however, is the continuous increase in the public awareness of the importance of dog testing (20).

Breeding purebred dogs is not easy, because of fragmented populations (usually small breeding kennels) and the strong dependence of the breed size on its popularity among breeders, users and supporters, who buy puppies mostly as companion animals. Breeders of purebred dogs, who usually own several breeding animals, often mate related animals to obtain valuable offspring (33, 34, 54). The most popular stud dogs (show winners) usually have a greater number

of progeny than other dogs in the breed. This policy of the breeders increases the number of related progeny, which makes it difficult to find suitable (i.e. unrelated) pairs for mating and could also contribute to the dissemination of hereditary diseases (20, 33, 34, 44).

On the other hand, few dog breeds enjoy continued popularity. Such breeds include a large proportion of working dogs, such as German Shepherds, Golden Retrievers or Labrador Retrievers. The size of their population is large, and it is probably easier to find unrelated individuals for mating. On the other hand, maintaining a low level of inbreeding in small breeds can be difficult, if not impossible, due to their limited popularity. Hence, the Federation Cynologique Internationale (FCI) has developed a set of rules and recommendations for breeding purebred dogs in a way that makes it possible to obtain healthy offspring (25, 26).

To date, a lot of research has been done on inherited dog diseases. As many as 369 hereditary disorders have been identified in the 50 most popular dog breeds (13, 42). Many of these disorders are or may be due to inbreeding by breeders who often mate close relatives. One of the effects of inbreeding is the occurrence of genetic defects in the offspring. Some researchers have been developing genetic tests that can help exclude carriers of hereditary diseases from the breeding population (1, 40). It is also important to implement regular health tests (and obtain certificates). This allows the breeder to assess the current health status of potential parents and exclude them from reproduction if they are burdened with a disease for which there are currently no genetic tests (20, 37). However, Donner et al. (18), who studied over 100,000 purebred and crossbreed dogs, found that the same inherited diseases occurred in many breeds as well as in mixed breed dogs. For example, progressive retinal atrophy with progressive degeneration of rods and cones (prcd-PRA, PRA-rcd3) and progressive lens luxation (PLL) occurred in over 30 and 20 dog breeds, respectively. Therefore, Donner et al. (18) highly recommended genetic testing in dogs as an important veterinary diagnostic tool. Previously, Farrell et al. (20) also pointed out the need to make testing for genetic diseases mandatory and noted that the British Kennel Club still did not require many breeds to be tested for genetic diseases. Sargan et al. (51) reported that the recessive PLL gene is found mainly, though not exclusively, in bull terriers and other terrier breeds, causing the disease in all recessive homozygotes and some heterozygous carriers. However, the defect is difficult to remove from the population because it would require the elimination of all recessive homozygotes and all carriers, which would dramatically reduce the genetic pool of the population. This makes it necessary to test all animals for PLL prior to inclusion in breeding and to make an appropriate mating plan to avoid mating two heterozygous carriers (51).

One of the breeds with a usually small population are Chinese Crested dogs. As reported by Farrell et

al. (20), Chinese Crested dogs are ranked 64th in the British Kennel Club's registration ranking, with the number of dogs registered between 2004 and 2013 ranging from 390 to 638 per year compared to the top-ranked Labrador Retriever with around 40,000 animals registered per year. Chinese Crested dogs in Poland also belong to relatively small breeds, which may make them more homozygous, because, according to PKC breeding information (PKC Breeding Reports. Available online: <http://www.zkwp.pl>), only 100-250 Chinese Crested dogs per year were registered for breeding in Poland in the years 2009-2021. The modern Chinese Crested dogs probably descended from African or Mexican hairless dogs (48). They were bred in two varieties: the Hairless variety and the "Powder puff" variety, which were fully fur-coated. The hairless animals are covered by hair coat only on the head and neck, as well as on the tail and the lower parts of legs (the so-called "socks"). The hairlessness allele is the dominant mutation, lethal in the homozygous state. Therefore all dogs of the Hairless variety are heterozygous for those genes and can always produce "Powder puff" puppies, but two fully hair coated Chinese Crested dogs can never have hairless puppies. Chinese Crested dogs, as a breed bred from a small gene pool and – due to its limited popularity – relatively small in numbers, is susceptible to genetic diseases (14, 43). The most common problems in this breed are ophthalmologic, cardiologic and orthopaedic diseases, but neurological problems can occur as well. Typical hereditary eye diseases in dogs, including Chinese Crested dogs, include progressive retinal atrophy with progressive degeneration of rods and cones (prcd-PRA, PRA-rcd3) and progressive lens luxation (PLL) (19, 32, 40). According to Donner et al. (18), in 100,000 dogs examined, the frequency of the gene causing prcd-PRA was 0.034 in mixed breed dogs and 0.017 in purebred dogs, whereas the frequency of the PLL gene amounted to 0.006 in crossbreed dogs and 0.008 in purebred dogs. Sargan et al. (51) estimated the risk of PLL in Chinese Crested dogs from several US veterinary databases at 6.58% to 16.56% depending on the database. According to Gould et al. (24), the estimated frequency of the recessive gene causing PLL in Chinese Crested dogs in the UK was 0.15. The frequency of the PLL and prcd-PRA genes in the Polish population of Chinese Crested dogs has not yet been studied. The most frequently performed genetic tests in the Chinese Crested breed, also in Poland, are eye tests (PLL, prcd-PRA, PRArcd3), but they are not obligatory for Polish dog breeders. Chinese Crested dogs are also examined for cardiologic and musculoskeletal disorders. Dog breeders in Poland are aware of the possibility of performing genetic tests for eye diseases for this breed and know the recommendation of the Federation Cynologique Internationale (FCI) and the Polish Kennel Club (PKC) regarding the ban on mating two disease carriers (<https://www.zkwp.pl/regulaminy/>

FCI__Miedzynarodowy_Regulamin_Hodowlany_FCI.pdf). Nonetheless, as pointed out by Donner et al. (18) and Farrel et al. (20), the genetic testing of dogs to identify carriers of eye diseases is not as popular as one would expect. The question arises whether the low popularity of dog testing does not result in some way from their higher inbreeding. On the other hand, the occurrence of genetic defects in Chinese Crested dogs may also be related to the increased level of homozygosity of individual animals. The above problems have not been studied in this breed so far, so they need to be investigated. The aim of the present study was therefore to analyse the impact of inbreeding among Chinese Crested dogs on the occurrence of selected hereditary diseases and the frequency of animals being genetically tested for ophthalmologic diseases.

Material and methods

As the material, the study used pedigrees of 100 Chinese Crested dogs (39 males and 61 females) born in 1998-2015, registered at the Polish Kennel Club (PKC) and exhibited at international and national dog shows. The pedigrees of active breeding animals and young dogs, which can potentially become breeding animals, were selected from the author's own breeding kennel and from the online Chinese Crested pedigree database (The Chinese Crested Pedigree Database. Available online: <http://www.ccpedigrees.se/en/registry>). The pedigree analysis was performed for the group of 100 potentially "active" dogs, which are or could be used for mating, and for their ancestors from the pedigree file (animals born in the years 1979-2012, called "ancestors").

Individual inbreeding coefficients (F_x) for all dogs examined by the Meuwissen and Luo (41) method and coefficients of kinship (R_{xy}) for all animals, between males, between females, and for male-female pairs, were estimated according to Boichard's PEDIG package (4) up to 20 generations back. An animal is called "inbred" when its inbreeding coefficient is greater than 0 because its parents were related.

The pedigree completeness was estimated according to Boichard et al. (5) as the mean equivalent of complete generations (EqG) by applying the following formula:

$$EqG = \frac{1}{N} \sum_{j=1}^N \sum_{i=1}^{n_j} \frac{1}{2^{g_{ij}}}$$

where:

EqG – mean equivalent of complete generations,

N – number of animals examined,

n_j – total number of ancestors of the j-th animal in the population under study,

g_{ij} – number of generations between the j-th animal and its i-th ancestor.

Additionally, information about the health (genetic tests and veterinary diagnoses) of the 100 dogs published by their owners and breeders in the health database of the Polish Chinese Crested dogs were used (Polish Chinese Crested dogs health database. Available online: http://www.ravenq.damienet.pl/zdrowie/hod_a.htm). Information about Primary Lens Luxation (PLL) and Progressive Retinal Atrophy (prcd-PRA), as well as other ophthalmologic, cardiologic

and orthopaedic diagnoses, was collected for the dogs examined. This information on the health of the dogs obtained from the Internet database was, where possible, verified by contact with their breeders. For PLL and prcd-PRA, there were three groups of animals. The first group consisted of genetically tested dogs (denoted as "genetically tested"); the second group comprised dogs with genetically tested parents or other ancestors (denoted as "genealogically healthy"), whereas the third group was not known to have been tested for those diseases ("not tested"). Due to the difficulties in verifying information about genetic testing, especially of older animals, and the relatively small number of dogs examined, the last two groups were combined for the purpose of statistical analysis into one, as genetically untested animals.

The relationship between the level of inbreeding and the occurrence of carrierhood or the presence of genetic tests for PLL or prcd-PRA was analysed with logistic regression by the LOGISTIC procedure of SAS (53) according to the following formula:

$$\text{logistic} = \frac{e^x}{1 + e^x}$$

where x is the linear function $b_0 + b_1X$. The logistic function (logistic transformation of an argument) is typically used to convert log odds values into probability values (16).

In tables, to show the relationship between the level of testing for PLL/prcd-PRA genes and the level of inbreeding, and between the occurrence of PLL carriers and sex or the level of inbreeding, only two inbreeding classes were assumed: $F_x = 0$ and $F_x > 0$, because of the small number of animals tested for PLL and prcd-PRA. We could not investigate the relationship between the prcd-PRA carrier status and sex or the inbreeding level, because of the absence of test-confirmed prcd-PRA carriers among the 100 Chinese Crested dogs tested.

Results and discussion

The pedigrees of the dogs analysed had an equivalent of complete generations (EqG) ranging from 2.5 to almost 7 generations – on average, over 5.5 generations (Fig. 1). For 581 ancestors, the mean EqG was equal to 1.86 generations, and the maximum amounted to slightly over 7 generations. Among the

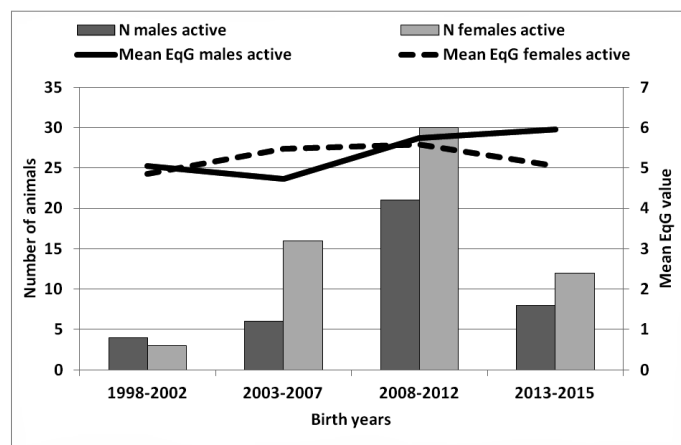


Fig. 1. Distribution of animals from the examined population by birth years and mean EqG values

“active” Chinese Crested dogs, about 84% were inbred, including approximately 90% of males and over 80% of females. The mean inbreeding coefficient in this group of dogs was 5.5% for all animals and 6.6% for inbred animals. In contrast, only about 20% of the 581 ancestors of the dogs were inbred, with average inbreeding values of 1.8% for all ancestors and 8.8% for inbred ones. These results were similar to or lower than those for other dog breeds obtained by different authors (2, 12, 36-38, 58).

The average kinship values for the “active” Chinese Crested dogs were 11.1% for all pairs and 11.4% for related pairs. About 97% of the pairs were related. All “active” Chinese Crested males were related to each other (100% of males), and about 90% of them were inbred, whereas among females, over 95% were related to each other, and over 80% were inbred. In the group of ancestors, there were 15.5% of inbred female ancestors and more than 23% of inbred male ancestors. The percentage of related male × female pairs was very high (over 97%), which may lead to difficulties in choosing animals for mating and the occurrence of inbred offspring potentially burdened with genetic defects. On the other hand, the high proportion of inbred animals and related pairs of Chinese Crested dogs means that in their pedigrees there are a large number of common ancestors up to 5 generations back, which contributes to the accumulation of inbreeding and may be responsible for genetic defects in these animals.

Only 16 out of the 100 Chinese Crested dogs (16%) were non-inbred (Tab. 1). In over one half of the dogs, inbreeding values were low. F_x values higher than 6.3% were found in 33 dogs (33%), whereas among the 581 ancestors only 70 animals (about 12%) were inbred more than 6.3%, and about 80% of the animals were non-inbred. This was caused, on the one hand, by the better quality of the pedigrees of younger animals, and on the other hand, by the more frequent occurrence of common ancestors in their pedigrees.

Another problem we investigated was the appearance of the popular stud dog effect in that group of animals. Table 2 shows the number of occurrences of top 10 stud dogs in the pedigrees of “active” Chinese Crested dogs, i.e. the number of males and females in progeny. It should be noted that those 10 males appeared as many as 78 times in the pedigrees of the 100 dogs analysed. They sired 40 (40%) of the 100 dogs. Four of these males (S5, S8, S9 and S10) occurred in the pedigrees only as fathers and sired a total of 16 of the 100 animals analysed. The remaining six males appeared in the pedigrees also 2-4 generations back (as grandfathers and earlier) and sired another 38 descendants. Additionally, four of those stud dogs (S2, S3, S4 and S7) were related. Male S4 (a confirmed PLL

Tab. 1. Distribution of the Chinese Crested dogs by birth years and inbreeding classes

Birth years	N	Inbreeding class				
		$F = 0$	$F \leq 0.0625$	$0.0625 < F \leq 0.125$	$0.125 < F \leq 0.25$	$F > 0.25$
1998-2002	7	1	5	1		
2003-2007	22	4	9	5	4	
2008-2012	51	7	26	10	8	
2013-2015	20	4	11	3	1	1
Total	100	16	51	19	13	1

Tab. 2. Number of progeny of the top 10 sires in the pedigrees of the Chinese Crested dogs

Sire ID	Inbreeding coefficient value	Number of progeny		
		Males	Females	Total
S1	0	8	17	25
S2*	0.07764	5	7	12
S3*	0.03125	6	3	9
S4*	0.01270	4	2	6
S5	0	4	1	5
S6	0	3	2	5
S7*	0.03040	0	5	5
S8	0.01563	1	3	4
S9	0	2	2	4
S10	0	2	1	3

Explanation: * – Closely related dogs (see: Figure 2) are shown in italic

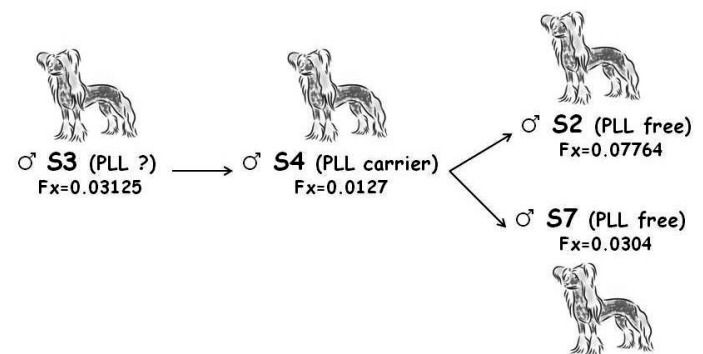


Fig. 2. Kinship of 4 stud dogs from the top 10 list in Table 2

gene carrier) was a son of S3 and the father of males S2 and S7, which were both confirmed to be PLL free (Fig. 2). They all sired a total of 32 descendants (including 18 of the 100 dogs analysed). It can therefore be concluded that the popular sire effect was clearly visible in that group of dogs, which is also confirmed by the high kinship values of individuals from the “active” group, and that is not beneficial for a breed such as the Chinese Crested dog.

Table 3 shows coefficients of kinship between all top 10 stud dogs. It should be noted that only for one of the 45 possible pairs of stud dogs the relatedness coefficient is equal to zero (S2-S6) and in only two cases it is below 0.01 (S3-S5 and S5-S9). For the rest of the stud dogs, the kinship values exceed 0.01. However, in four closely related dogs, kinship values exceed

Tab. 3. Values of the coefficient of kinship between the top 10 sires in the pedigrees of Chinese Crested dogs

Sire ID	S2 ¹	S3 ¹	S4 ¹	S5	S6	S7 ¹	S8	S9	S10
S1	0.3829	0.0500	0.2737	0.0710	0.2343	0.1746	0.1338	0.0887	0.3025
S2 ¹		<i>0.2747</i>	<i>0.5590</i>	0.0305	0.0	<i>0.3103</i>	0.0558	0.0578	0.1360
S3 ¹			<i>0.5170</i>	0.0089	0.0897	<i>0.2961</i>	0.0162	0.0178	0.0481
S4 ¹				0.0221	0.1879	<i>0.5254</i>	0.0414	0.0310	0.0994
S5					0.0506	0.0182	0.0106	0.0084	0.0268
S6						0.1161	0.0348	0.0291	0.0856
S7 ¹							0.0426	0.0307	0.0896
S8								0.0149	0.0477
S9									0.0592

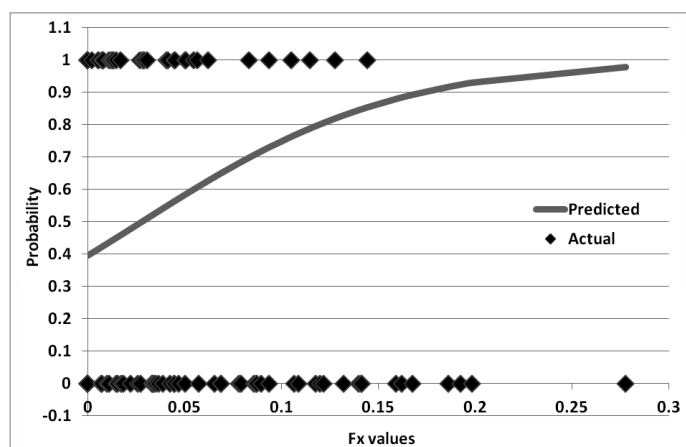
Explanation: ¹ – For closely related dogs (see: Figure 2) the R_{xy} values are marked in italic

those resulting from a father-son (0.5) or grandfather-grandson (0.25) kinship. This probably results from the presence of the same common ancestor on both sides of the pedigree.

Many authors (6, 20, 33, 34, 39, 45) indicated the existence of the popular sire effect in dog breeding, emphasizing its clearly negative impact on the genetic condition and health of many dog breeds. They also noted a narrowing of the genetic pool of breeds due to the overuse of some reproducers (dog show winners), which may have up to 2,500 offspring,

Tab. 4. Distribution of animals (N = 100) by the level of inbreeding and classes of testing for PLL or prcd-PRA

Hereditary ophthalmologic disease test group	Level of inbreeding		
	$F_x = 0$	$F_x > 0$	Total
Genetically tested for PLL	9	32	41
Genealogically healthy for PLL	5	24	29
Not tested for PLL	2	28	30
Genetically tested for prcd-PRA	3	10	13
Genealogically healthy for prcd-PRA	11	39	50
Not tested for prcd-PRA	2	35	37

**Fig. 3.** Plot of the fact of being (“Actual” = 1) or not being (“Actual” = 0) tested for PLL depending on the inbreeding level in comparison with its calculated probability (“Predicted”)

thus increasing the level of homozygosity. In addition, the popular sire effect creates large groups of related animals, which could lead to future difficulties in selecting pairs for mating. Moreover, these authors emphasized that, especially in breeds with multiple genetic defects, such as the Chinese Crested dog, the popular sire effect may contribute to the spreading of these defects. Therefore, they recommended a more even use of stud dogs and the introduction of restrictions on the number of offspring per sire per year. According to restrictions introduced recently by the FCI, stud dogs can sire no more

than 5% of all puppies born in a given year (25, 33).

We also investigated the frequency of DNA tests performed and published by the breeders of the population analysed here. The distribution of animals in groups by the level of inbreeding and classes of testing for PLL or prcd-PRA is presented in Table 4. For purposes of statistical analysis, we combined the group of animals whose ancestors were probably genetically tested and the group of untested animals into one group (Tab. 4).

Figure 3 shows a logistic curve fitted to the data from Table 4 for PLL. The equation of this curve is $\text{logit}[P(\text{PLL} = 0)] = -0.4179 + 15.112 * F_x$. Wald chi-square test values for the regression coefficient indicate a highly significant relationship ($P < 0.01$) between inbreeding and genetic testing for PLL, which means that the breeders tested animals with low or zero values of F_x much more than the other animals. The same analysis of testing for prcd-PRA gave negative results (the regression coefficient was not significant $P > 0.05$) – probably because in that group of dogs few genetic tests for prcd-PRA had been performed (Tab. 4) and no carriers of the recessive mutation of this gene had been identified (Tab. 5). A low proportion of genetically tested animals can be very harmful for the breed as a whole, as the use of untested animals for mating (especially if they are carriers of PLL) can spread a defect and even produce whole litters with the defect. Although the frequency of the PLL mutation is usually lower than that of prcd-PRA, testing for PLL is very important because some PLL carriers may also show signs of this disease (24, 51). If the breeder decides to use a potential disease carrier for breeding, mating such an animal with a healthy individual is not burdened with the risk of disease in the litter, but half of the offspring will continue to be carriers of the mutant allele. Thus, the knowledge of the genotypes of breeding animals is necessary for considered and safe mating, which prevents the occurrence of disease among the offspring. Moreover, every buyer of a dog would like to have a healthy animal. The occurrence of defects in the offspring of untested animals may

Tab. 5. Distribution of genetically tested animals by classes of heterozygous carrier or homozygous animals free from PLL or prcd-PRA and by sex or the inbreeding level

	Sex		Level of inbreeding	
	Males	Females	$F_x = 0$	$F_x > 0$
No. of animals genetically tested for PLL	15	26	9	32
including: PLL carriers	5	12	3	14
PLL free	10	14	6	18
No. of animals genetically tested for prcd-PRA	5	8	3	10
including: prcd-PRA carriers	0	0	0	0
prcd-PRA free	5	8	3	10

reduce the price obtained by the breeder and even make him liable for compensation for having sold an animal carrying a disease.

Table 5 shows the distribution of genetically tested animals in the PLL and prcd-PRA classes by sex and the level of inbreeding.

The table shows the number of detected male and female (or inbred vs. non-inbred) carriers of PLL and prcd-PRA. The relationship between the sex of the dog and the incidence of being a PLL carrier was analysed with logistic regression as well, and it was found in both cases non-significant ($P > 0.05$). However, there were almost twice as many female PLL carriers as male ones. This result proves that Chinese Crested bitches are probably tested genetically more often than males because their owners wish to obtain healthy progeny. Therefore, there is probably no relationship between the PLL carrier status and the inbreeding level of animals, which is also confirmed by similar proportions of animals with $F_x = 0$ and $F_x > 0$ in the “PLL carriers” and “PLL free” groups. On the other hand, no heterozygous carriers were detected among dogs that were genetically tested for prcd-PRA, and maybe that was the reason for the low number of animals tested (Tab. 4 and 5), although, as reported by Donner et al. (18), the frequency of the prcd-PRA gene in purebred dogs is higher than that of the PLL gene. Furthermore, the absence of PLL-affected animals among the Chinese Crested dogs analysed in this study leads us to suppose that the breeders had avoided mating two PLL carriers although it is not obligatory for breeders of Chinese Crested dogs in Poland, unlike in some other countries.

Because of the small number of veterinary diagnoses of other hereditary diseases in the animals studied here, it was not possible to statistically investigate the relationship between the occurrence of the diseases and the level of inbreeding in individuals. Therefore we limited ourselves to presenting data on the number and nature of veterinary examinations, their results and the inbreeding of the dogs. We also tried to find out which and how many animals that had undergone a veterinary examination had also been genetically tested for PLL and/or prcd-PRA. Out of the 100 dogs, 19 did not have any test results (although there may have been unpublished diagnostic test results for some of these dogs),

and 13 (68%) of these were inbred, with F_x values ranging from over 5% to almost 20%. Within this group, there may be other carriers of genetic diseases, and, with the wrong selection of pairs for mating, they may produce offspring with genetic defects. Given the widespread occurrence of various hereditary diseases in Chinese Crested dogs, it would be appropriate to introduce the obligation to perform genetic tests or examinations and to disclose their results, especially when choosing candidates for stud dogs and breeding bitches. Many other

authors have recently made similar recommendations (6, 18, 45, 51), but so far they have met with little positive response from the breeders (20).

There were 41 animals genetically tested for Primary Lens Luxation (PLL) (Tab. 4), including 17 dogs that were carriers of this disease (39.5% of all tested). There were 3 carriers of PLL among the 16 non-inbred individuals, and the remaining carriers of this disease (14 animals) were inbred, with the highest F_x value recorded in this group reaching 5.7% in a dog born in 2001. It can therefore be concluded that the carrier status was not associated with the level of inbreeding of individuals, which was confirmed by statistically insignificant logistic regression analysis (Tab. 5).

For 37 out of the 100 Chinese Crested dogs, prcd-PRA results were unavailable. On the other hand, only 13 dogs had a genetic test result for prcd-PRA (Tab. 4), and all were classified as healthy. Among those animals, 3 were not inbred, and the inbreeding coefficient values of the remaining 10 dogs ranged from 0.02% to 14.4%. Because of the absence of prcd-PRA carriers, we were not able to statistically verify the relationship between the level of inbreeding of the animals and their carrier status for this disease (Tab. 5).

In addition to PLL, the dogs were also tested for other hereditary ophthalmological, cardiologic and orthopaedic diseases, as shown in Table 6.

Tab. 6. Number of animals tested and untested for PLL and having results of other veterinary examinations

Veterinary examination	Total	Genetic test for PLL	
		Animals tested ¹	Animals untested
Ophthalmological	37	16 (10)	21
including status: “healthy”	35	15 (9)	20
“dry eye syndrome (KCS)”	2	1 (1)	1
Cardiologic	13	8 (4)	5
including status: “healthy”	12	8 (4)	4
“valvular regurgitation”	1	0	1
Orthopaedic (kneecaps)	15	8 (3)	7
including status: “healthy”	15	8 (3)	7

Explanation: ¹ The number of confirmed PLL carriers is given in brackets

The PRA-rcd3 genetic test was performed for only five animals, and all five were classified as “healthy”. Besides, there was one inbred animal for which PRA-rcd3 test result was mentioned as genealogically healthy. One of these five animals, a male, was non-inbred, whereas the remaining four were inbred, including two males with $F_x = 2.9\%$ and 5.5% and two females with $F_x = 4.1\%$ and 14.4% . As shown in Table 5, ophthalmological examination certificates were available for 37 Chinese Crested dogs, 35 of which were healthy, and 2 had dry eye syndrome (KCS). Both dogs affected by KCS were inbred: a female with an F_x value of 1.2% and a male with $F_x = 4.5\%$. Similarly, 70% of all ophthalmologically healthy animals were inbred. Cardiologic examination certificates were available for 13 dogs, all of which were healthy except one male with valvular regurgitation (Tab. 6). This animal had not been genetically tested for the PLL gene or the prcd-PRA gene, but the result of his ophthalmological examination was “clear”. The dog was inbred, and his F_x value exceeded 8.5% . Kneecaps had been examined for patella dislocation in 15 animals, all of which were healthy. Most of them, about 73%, were inbred (F_x from 1.1% to 27.8%) and three (two females and one male) were also confirmed PLL carriers (Tab. 6). One non-inbred dog that had been examined for hip dysplasia, with a result of A (healthy hips), had also been genetically tested for PLL and prcd-PRA and found “clear” for both. Two inbred females ($F_x = 4.1\%$ and 14.4%) had been genetically tested for canine multiple system degeneration (CMSD) and canine dilated cardiomyopathy (DCM) and were both found healthy. In addition, one of them had been examined for degenerative myelopathy (DM) and found healthy, but that female was a confirmed carrier of PLL. One inbred female ($F_x = 1.8\%$) had been examined for the Legg-Clave-Perthes Disease (LCP) and was classified as healthy, but had not been genetically tested for either PLL or prcd-PRA. It can therefore be concluded that most of the dogs tested for various hereditary diseases turned out to be healthy, even if they were inbred, and the proportion of dogs that had been examined or had undergone molecular tests was relatively high. However, there were also cases of animals that were carriers of both PLL and other hereditary diseases, so it is advisable to make genetic tests for ophthalmic diseases obligatory.

Jansson and Laikre (30) have recently investigated how the exclusion of disease carriers and, in some cases, also genetically burdened animals from breeding affects the inbreeding level. They found that the elimination of carriers of prcd-PRA and hip dysplasia as well as dogs affected by these diseases had no influence on the inbreeding level of the Swedish Lapphund breed. That breed, however, is more numerous (over 7000 animals) than Chinese Crested dogs. Previously, Jansson and Laikre (31) studied the 26 dog breeds registered in Sweden and found that their health status

did not depend on the level of inbreeding. Machová et al. (38) found that the Czech Spotted dog breed is now relatively healthy despite the high level of inbreeding in most of the active population. It is, however, a unique dog breed, used primarily as laboratory animals, and it was created assuming that the homozygosity level must be as high as possible because all animals had to be genetically almost identical for laboratory purposes. Machová et al. (38) pointed out that Czech Spotted Dog breeders must avoid the popular sire effect, i.e. the use of only a small number of best sires, if they want to keep future generations of those dogs in relatively good health.

Previously, Leroy and Rognon (35) simulated two breeding scenarios for four French dog breeds to prevent a decrease in their genetic diversity. One scenario assumed the elimination of homozygous animals affected by inherited diseases and heterozygous carriers from breeding. The other scenario concerned the popular sire effect and assumed a limited number of progeny per sire. Leroy and Rognon (35) found that the exclusion of carriers of genetic diseases from breeding could have a positive effect on genetic diversity, but only if the number of animals in the active breeding population was at least medium in size. They also concluded that restrictions on the number of progeny per stud dog could partially prevent the decrease in genetic diversity of a dog breed.

Windig and Oldenbroek (61) simulated genetic management of Dutch Golden Retriever dogs to maintain their genetic diversity and found that the most effective method was to restrict the average relatedness of mated animals as much as possible. Those authors concluded that managing the mean relatedness of all breeding animals in this way would be most effective in reducing the inbreeding rate in the population. It must be pointed out, however, that Golden Retrievers are one of the most popular dog breeds in the world, with very large populations everywhere. In this dog breed, it is quite easy to find animals with low kinship values (for example, cousins sharing one common ancestor) or even unrelated. The Chinese Crested dog is not an equally popular breed (20), and therefore it is less numerous, which makes it difficult to find unrelated animals within the population. This was partially confirmed by our research, in which over 90% of animals were related, including 97% of male $\times$ female pairs, and the vast majority of the 10 most popular stud dogs were more or less related to each other. Nevertheless, minimizing the relatedness of mated animals as much as possible should be an important guideline for all breeders of Chinese Crested dogs.

Wang et al. (59), who analysed data for pedigree Bullmastiffs, Bernese mountain dogs, English setters and Labrador retrievers bred in France, Sweden, and the UK, found that exchanging breeding animals between countries is the best method for maintaining and preserving genetic diversity on the optimal level,

which could counteract the dissemination of genetic diseases. This solution could also prove beneficial for Chinese Crested dogs, provided that the breeders will import only healthy animals.

On the other hand, Windig and Doekes (60) performed a simulation study and analysed different scenarios of outcrossing in dog breeding. They found that the effectiveness of this method of reducing the inbreeding level and the frequency of detrimental alleles was limited. Even though the use of outcrossing could increase the effective population size, it must be followed by good management of the dog breed.

Recently, Broeckx (6) described and summarized all possible strategies of dog breeding that could reduce the frequency of genetic disorders and increase the number of animals in the population. He pointed out that DNA tests for autosomal recessive genetic diseases, if they are available and sufficiently good, could facilitate the use of animals for breeding. This also applies to carriers, as the results of such tests could be used in mating them with genotypically healthy individuals. For hereditary diseases whose mode of inheritance is yet unknown, that author proposed test mating, but, as he himself admitted, this particular method of intentionally producing hereditarily affected progeny is ethically disputable. Another approach could be to use pedigree information to calculate the probability of a specific genotype in the future parent (dominant homozygous for genetic disease). Commercial software for such calculations is already available. Broeckx (6) drew attention to genetic defects that are a part of breed standards and suggested the possibility of changing regulations, which could be difficult for some breeds and could trigger debate concerning their very existence, as well as their health and welfare status. However, maintaining or increasing genetic diversity is also very important in dog breeding. Broeckx (6) mentioned three rules that dog breeders should follow in their breeding programmes. The first one is to increase the number of breeding animals eligible for reproduction. The second: if a genetic test for a hereditary disease is available, the breeders, particularly those of less numerous breeds, should mate carriers to healthy animals rather than exclude them from breeding. The third rule is to avoid the popular sire effect, that is, the use of only the best and most popular sires, which may have much more progeny than other sires, in order to prevent the loss of genetic diversity (6).

The Polish Chinese Crested dog population can generally be classified as a small one, and hence one with a high level of inbreeding and relatedness. In such populations, genetic defects tend to occur more often, which may be related to the increased level of inbreeding and the high number of inbred animals. Our study was conducted on 100 Chinese Crested dogs which were, or were intended to be, breeding animals. They turned out to be mostly inbred (about

84% of the animals) and to a large extent related (about 97% of the animals). We selected 10 stud dogs with the highest number of offspring. Half of them were inbred, and almost all of them were more or less related, including 4 stud dogs that were directly related and formed a male line with a direct kinship: father-son-grandson. All this indicates that the genetic diversity of breeding Chinese Crested dogs in Poland may be poor. Therefore, when choosing animals for mating, breeders should take into account the level of their relatedness, that is, select those with no or the least common ancestors up to the 5th generation back. It might also be advisable to look for foreign stud dogs not related to Polish female dogs and, of course, tested and reasonably healthy. In our study of Chinese Crested dogs, we used a limited number of animals and we found no relationship between the occurrence of hereditary diseases and the individual inbreeding level of animals. For most ophthalmological, cardiology and orthopaedic diseases, genetic tests have not yet been developed, and we found only a few affected dogs, in most cases inbred. This problem requires further research involving more affected animals. We found heterozygous carriers only for PLL, one of the two DNA-tested ophthalmological diseases that we analysed, the other being prcd-PRA. We found that the PLL carrier status probably did not depend on the sex or level of inbreeding of the animals. We were unable to analyse the relationship between the occurrence of prcd-PRA carriers and their sex or inbreeding level, because there were no heterozygous carriers detected. The last question this paper aimed to answer was whether the breeder's willingness to DNA-test his animal (or to publish the results of such tests) depends on the individual inbreeding coefficient value for that animal or not. We found that such a relationship may exist and is statistically significant for the number of animals tested for PLL, with a lower number of published test results for highly inbred animals. However, confirmation of this relationship requires further studies on a larger number of dogs.

In summary, most of the Chinese Crested dogs in this study were inbred and related to each other. This fact can be partially attributed to the popular stud dog effect that we found in this group dogs, in which 10 stud dogs appeared in pedigrees 78 times, and one of them appeared as many as 25 times. Almost all of the 10 most popular stud dogs were related to each other. And four of those 10 stud dogs were very closely related to each other, which additionally reduced the genetic pool. As mentioned in the literature, the popular stud dog effect is very harmful for the breed, as it contributes to its increased homozygosity and accelerates the spread of hereditary diseases. We therefore suggest that Chinese Crested dog breeders use stud dogs more evenly, as recommended by the FCI, and choose unrelated or distantly related animals for mating, which means that they should have no or as

few as possible common ancestors in their pedigrees up to the 5th generation back.

A serious problem for individual animals was the carrier status of the Primary Lens Luxation (PLL) with a concomitant presence of ophthalmologic and cardiac diseases. Ten dogs had been diagnosed as PLL carriers and had undergone an ophthalmological or cardiologic examination, and one of them had been diagnosed with dry-eye syndrome (KCS). On the other hand, two animals diagnosed with heart or eye diseases had not been genetically tested for either PLL or prcd-PRA, so it is not known whether they were carriers of these genes. Therefore, it is very important to introduce obligatory testing of dogs intended for breeding, as carriers of genetic defects are common in this breed.

The PLL carrier status has probably a only minor relationship with the sex or inbreeding level of animals. No carriers were detected among dogs that were genetically tested for prcd-PRA, and that may have been the reason for the low number of dogs tested. However, dogs affected by cardiac or ophthalmologic diseases were all more or less inbred. This suggests that some relationship may exist between inbreeding and the occurrence of those diseases, and it needs further research involving a larger number of animals.

We found a significant relationship between the number of animals DNA-tested for PLL (or with results of such tests published) and their inbreeding coefficients. That leads us to suggest that breeders should be more open about publishing DNA test results of their Chinese Crested dogs. This information is important for the other breeders and fundamental for the breed as a whole because two PLL carriers are not allowed to mate and because some carriers of this mutation may also show signs of disease.

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