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Improving the enforcement of Finnish animal welfare legislation related to animal breeding

Part III: Problems and control criteria in dog breeding

Katariina Mäki and Riitta Kempe

Luke

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Natural Resources Institute Finland, Helsinki 2025

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Abstract

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This report defines control criteria and thresholds (breeding restrictions) under Finnish animal welfare legislation for genetic diseases in dogs that negatively affect their well-being. It addresses diseases and issues that were not included in the initial 2020 report, or for which further clarification was deemed necessary for the development of control criteria.

According to the proposed control criteria and thresholds, **breeding dogs must not have serious genetic diseases or traits that could lead to significant welfare issues.**

The prevalence of hereditary diseases increases in consanguineous animal populations as genetic variation decreases. This results in increased morbidity throughout a dog's life and a significantly reduced lifespan. It also causes reproductive problems, puppy mortality, malformations in puppies, reduced immunity, and increased susceptibility to inflammation. The report therefore calls for genetic variation to be maintained and increased in breeding populations and suggests that puppies should not be bred from close relatives.

Intense fear can severely restrict dogs' and their owners' lives, causing significant welfare issues. Severe fear is a stressful condition that puts the whole body on alert. Long-term exposure to this state increases the risk of illness and obsessive-compulsive behaviour. Fear is also a common cause of bite incidents. Since genes largely regulate fearfulness and aggression, dogs that can cope with an active daily life without displaying excessive fear or aggression should be used for breeding.

Atopic dermatitis is a highly hereditary inflammatory skin disease that causes significant itchiness. If left untreated, it can lead to serious welfare issues for dogs. In humans, prolonged itching is considered a serious symptom, and the perceived discomfort is comparable to prolonged pain. Unfortunately, however, dog owners often fail to recognise the serious welfare issues that atopy causes their dogs. Atopy also places a burden on owners, as it requires lifelong treatment that is time-consuming and can place psychological and financial strain on them. This can negatively affect owners' commitment to managing the condition. However, effective treatment can eliminate symptoms, though it does not eliminate the risk of passing the disease on to offspring. Overall, the risk of offspring developing atopy can be reduced by ensuring that breeding dogs have healthy skin.

Atopy is the main cause of **pododermatitis** in dogs. This multifactorial disease is also influenced by the dog's conformation. Chronic and progressive skin inflammation resulting from an abnormal position or shape of the paws can significantly reduce quality of life and is a debilitating condition.

Heart disease is a significant cause of morbidity and mortality in dogs worldwide. Welfare damage is usually due to congestive heart failure. In this condition, the heart is unable to maintain normal blood flow, resulting in a reduced oxygen supply to the body and fluid build-up in the tissues. Heart failure progresses gradually and can eventually lead to death. Some heart diseases can also cause sudden death in young dogs. The most common heart conditions in dogs are chronic and incurable. To reduce the incidence of heart disease, breeding programmes for many breeds require heart examinations to identify suitable breeding stock.

Many **dental problems** are related to the structure of the skull and jaw. Despite being painful, dental defects and diseases can often go unnoticed by dog owners. For example, they can destroy the jawbone and even cause it to fracture. Dog breeding programmes should prioritise conformation and structure that reduce the risk of serious oral and dental problems, ensuring that dogs have healthy teeth and a functioning bite.

With regard to musculoskeletal disorders, this report builds on the previous one by considering the following conditions: chondrodystrophy, intervertebral disc disease, chondrodysplasia (short limbs), patellar luxation, cranial cruciate ligament disease, and osteochondrosis.

Chondrodystrophic dogs are those whose **intervertebral discs degenerate prematurely**. This degeneration is caused by a retrogene located on chromosome 12 (CDDY). Degeneration of the discs makes them prone to protruding into the spinal canal or even rupturing. This can result in damage to the spinal cord and nerves, causing pain and paralysis. In the most severe cases, euthanasia is necessary. Dogs susceptible to herniated discs may experience multiple herniations in different vertebral canals throughout their lifetime.

The primary objective of breeding should be to prevent the premature degeneration of intervertebral discs, as this is the primary risk factor for disc herniation and spinal cord injury. This can be achieved by reducing the frequency of the predisposing retrogene in breed populations. Another possibility is X-ray screening of breeding dogs to reduce the risk of disc herniation. A long-term breeding strategy may require a combination of genetic testing and cross-breeding.

A retrogene on chromosome 18 (CDPA) causes short stature in dogs by prompting the growth plates in their limbs to close prematurely. This can result in varying degrees of **rotation and bending of the limbs, as well as incongruity of the elbow joint**. In cases where the limbs are very short and twisted, the misalignment can cause them to rub against the chest. The misalignment predisposes dogs to osteoarthritis, chronic pain, and pododermatitis. These joint problems and the resulting pain often become more apparent as the dog ages, and the condition worsens. When breeding, preference should be given to dogs with normal limb structure and posture.

Patellar luxation, cranial cruciate ligament disease, osteochondrosis, and osteoarthritis are among the most common musculoskeletal disorders in dogs. These conditions are usually painful and often become chronic, causing welfare problems for affected dogs over a considerable period of time.

Structural weaknesses in the stifle joint can lead to **patellar luxation**. In turn, luxation increases the risk of cranial cruciate ligament disease. Patellar luxation is relatively common in small dogs, as well as in larger breeds with straight hind legs. According to Finnish screening statistics, patellar luxation occurs in almost every second dog of certain breeds. Only dogs without patellar luxation should be used for breeding.

Cranial cruciate ligament disease (rupture) is highly hereditary, although it often occurs alongside trauma. Many of the predisposing factors are also hereditary. If a dog is diagnosed with and treated for this disease, there is about a 50% chance that they will develop the same lesion in the other knee within the next year. The incidence of cranial cruciate ligament disease could be reduced through selective breeding. This could be achieved by collecting data on affected dogs and excluding them from breeding programmes while promoting healthy, functional conformation. Progress could be enhanced by risk prediction based on pedigree and/or genome data (e.g. estimated breeding values, genetic testing).

With regard to **eye diseases**, the report supplements the breeding restrictions listed in the previous report for conditions that cause pain or discomfort, pose a threat to vision and require surgical treatment or ongoing medication.

Some characteristics that define a dog's breed are caused by **gene variants** that also cause or predispose dogs to welfare issues. These variants are selected and maintained to preserve breed characteristics. This report addresses such gene variants, including those responsible for certain coat colours, excessive skin folds, shortened tails, and hairlessness.

It shows that most genetic diseases and health problems in dogs become apparent by the age of three. Therefore, it is important to refrain from large-scale breeding of dogs under the age of three, to allow any potential genetic issues to manifest.

Many diseases and defects that cause welfare problems in dogs are related to their conformation. Heritabilities for conformation traits are usually high, making it relatively easy to reduce unhealthy conformations through breeding, particularly if a large gene pool is maintained by making use of all available tools.

This report proposes regular reviews and updates to the breeding restrictions. After the transition period, measures to reduce retrogenes causing chondrodystrophy and short stature in breeds should be examined. Similarly, the relationship between extremes of dog size, coat type and welfare issues should be investigated.

Keywords: dog, genetics, animal breeding, animal protection, animal welfare, legislation, hereditary diseases, health

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1. Background and objective of the report

This report aims to alleviate welfare problems in dogs caused by harmful animal breeding. It defines control criteria and thresholds (i.e. breeding restrictions) for genetic diseases in dogs that cause significant welfare issues, as set out in Finnish animal welfare legislation. These criteria and thresholds are intended to serve as a tool to assist the relevant authority in assessing whether animal welfare legislation has been breached during the breeding process and informing the subsequent course of action. The tool will be made available to the Ministry of Agriculture and Forestry (MoAF), the Food Authority and veterinary inspectors. It will also inform the preparation of the new animal welfare legislation, which is being led by the MoAF.

This report supplements the 2020 report, '*Improving the enforcement of animal welfare legislation in animal breeding: Problems and interventions in dog breeding*'. The previous report focused on the genetic traits of brachycephalic dogs that cause significant welfare issues and require the urgent enforcement of animal welfare legislation. This report addresses diseases and issues not covered by the first report, or for which further clarification was needed to establish control criteria:

- inbreeding,
- behaviour problems,
- gene variants predisposing to severe welfare issues,
- skin diseases,
- heart disease,
- eye diseases,
- oral and dental diseases,
- chondrodystrophy,
- exaggerated short limbs,
- cranial cruciate ligament disease,
- patellar luxation, and
- osteochondrosis.

This report does not cover some topics that may be relevant to the welfare of dogs, and these should therefore be explored in future reports. These topics include extremes in dog size and coat volume, and permanent fontanelles. Additionally, the proposed control criteria should be updated regularly, for instance every five years.

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2. Which diseases and defects in dogs are genetic?

The guidelines of the European College of Veterinary Ophthalmologists (ECVO), for example, can be used to assess the hereditary nature of diseases and defects in dogs. Although the guidelines are designed for eye diseases, they can also be applied to other diseases and defects. According to the ECVO Vet advice document, an ocular disorder is defined as **known to be hereditary** when:

- there are published reports in peer reviewed scientific literature regarding a condition in a particular breed with evidence of inheritance
- there are DNA-based tests available for the eye disease

An ocular disorder is defined as **presumed to be hereditary** when:

- the frequency is greater than in other breeds
- the frequency increases in a given breed as a whole
- the frequency is greater in related dogs within a breed
- the lesion has a characteristic appearance and location
- the lesion has a characteristic age of onset and course of progression (predictable stages of development and time for each stage to develop)
- the lesion looks identical to an entity which has been proven to be inherited in another breed

And more specifically, also when

- the incidence of affected animals (from a National ECVO Panel database, ECVO database and ACVO database which is the base of the OFA Eye Certification Registry in the USA) is greater or equal to 1% of the examined population with a minimum of five affected animals per five-year period. Regardless of the population of dogs examined, if 50 or more affected individuals are identified in a five-year period, the entity will be listed for that breed
- there is an overwhelming opinion by a majority of the Hereditary Eye Diseases committee members that clinical experience could indicate that a particular condition should be listed for a breed in spite of the absence of direct evidence of affected animals on the ECVO database, ECVO Panel database or the OFA Eye Certification Registry reports.
- there is a specific request from a breed club, that a condition be included for their breed. Such requests are reviewed critically and must have received agreement by a majority of the Hereditary Eye Diseases committee.

3. Defining breeds and types of dogs at risk

Should the risk of transmitting the disease be assessed before mating takes place? When answering this question, it is important to identify which breeds or types of dogs are at significant risk of contracting the disease. Like the previous report (Kempe and Mäki, 2020), this report lists the breeds mentioned in the literature as being at risk, but these lists should not be considered fully comprehensive. The lists vary from country to country and from dataset to dataset, depending on the prevalence of each breed within a given country or study population. Rare breeds are missing from the research data, even if they are at a high risk. Conversely, if the same breeds appear in several studies in different countries, the risk can be considered genuine.

Epidemiologic information on diseases in the Finnish dog population that would exclude a dog from breeding will start to be accumulated in the near future from the reporting obligations of veterinarians.

Breed predisposition to hereditary diseases is also discussed in the book Breed Predispositions to Disease in Dogs and Cats by Gough, Thomas and O'Neill.

4. The impact of inbreeding on the prevalence of inherited diseases

The draft Animal Welfare Act states that *the prevalence of hereditary diseases often increases, particularly in inbred animal populations.* The draft states: "*It is also important to ensure that the gene pool of the animal population is adequate to prevent an increase in disease and a loss of vitality.*"

Inbreeding occurs when related animals reproduce with each other. Inbreeding is generally considered to be the mating of cousins or closer relatives. The degree of inbreeding is measured by the inbreeding coefficient.

An individual's inbreeding coefficient

An individual's inbreeding coefficient is the probability that a randomly selected pair of genes contains two identical copies, one of which was passed to the individual by their father and the other by their mother. This means that the individual carries two copies of the same allele (variant) of a gene from a given ancestor. Such a gene pair is always homozygous.

The inbreeding coefficient can be calculated using either a pedigree or a DNA sample. When calculated from a pedigree, the coefficient is usually an underestimate by a factor of 5–10 (e.g. Dreger et al. 2016, Mäki 2010), unless the data extend to the breed's founder individuals.

An individual's inbreeding coefficient is calculated by dividing the genetic relationship between their parents by two (see Table 1). The genetic relationship between individuals describes the proportion of alleles they are likely to share. The closer and more numerous the shared ancestors of a male and a female in the pedigree, the closer their relatedness, and hence the higher the inbreeding coefficient of their offspring.

Table 1. Inbreeding coefficients of close relative matings (so called 'fast inbreeding').

Mating	Genetic relationship (%)	Inbreeding coefficient (%)
Parent x offspring	50	25
Full siblings	50	25
Grandparent x offspring	25	12.5
Half siblings	25	12.5
Cousins	12.5	6.25

Inbreeding coefficient of an animal population

The inbreeding coefficient of an animal population is the average of the inbreeding coefficients of individuals born within a specific timeframe. If the population is closed, i.e. if no new reproducing individuals enter from outside, genetic relatedness between animals increases with each generation. This increases the probability that reproducing individuals are related to each other. Consequently, inbreeding also increases.

The faster inbreeding accumulates, the more harmful it is (e.g. Hedrick 1994, Wang et al. 1999, Doekes et al. 2019, Yordy et al. 2020). The rate of inbreeding is described by the population's effective size (Wright 1931, 1933). The smaller the effective population size, the faster

the rate of inbreeding and the greater the loss of genetic diversity across generations. Effective population size is related to the number of individuals in a population that produce offspring. It is the number of reproducing individuals needed to explain the genetic diversity of a given generation. Put simply, the effective size is the number of individual genomes that make up a population's gene pool.

The effective population size can be calculated from the rate of inbreeding. The most accurate method is DNA analysis, although pedigrees of breeds going back to founder dogs can also be used. Otherwise, the result will be an underestimate by a factor of 5–10, as in the calculation of the inbreeding coefficients.

The "50/500" rule (Franklin, 1980) has become a general guideline in conservation genetics. The effective population size should be at least 50–100 individuals to avoid the immediate adverse effects of interbreeding. An effective population size of 50 corresponds to an increase in the average inbreeding rate of a population by 1% per generation. An effective size of 100 results in a 0.5% increase in the reproductive rate per generation. Although animal populations may sometimes fall to this magnitude without adverse effects, long-term adaptation to environmental conditions requires a high degree of genetic variation, averaging over 500 effective sizes. These figures are used as general criteria for determining the conservation needs of species.

Adverse effects of inbreeding

As can be seen from the Online Mendelian Inheritance in Animals database (omia.org), which is maintained by the University of Sydney, most deleterious mutations are recessive. This means that they do not cause harm when they occur in a heterozygous form, because one of the gene variants in the pair is a wild-type gene that functions normally and prevents the mutation from being expressed. Inbreeding reduces the proportion of heterozygous gene pairs in each generation by a proportion indicated by the inbreeding coefficient. For instance, when half-siblings produce a litter together, the homozygosity of the offspring's genomes increases (and the heterozygosity decreases) by 12.5%, compared to their parents.

Inbreeding causes a loss of fitness traits (e.g. Falconer and Mackay, 1996; Kristensen et al., 2015). Reproductive problems, increased pup mortality, pup deformities, reduced immunity, and susceptibility to inflammation are among the consequences. This phenomenon is known as inbreeding depression. Signs of inbreeding depression are generally considered to appear when the coefficient of inbreeding reaches 5–10%. Inbreeding depression is caused by an overall increase in homozygosity, as well as a reduction in the heterozygosity of genes that regulate the immune system, known as DLA (dog leukocyte antigen) genes.

A great deal of research has been conducted about inbreeding depression. A few examples are given below:

- In humans, even relatively low inbreeding coefficients (3–6%) have been shown to be associated with increased morbidity and other signs of inbreeding depression (Rudan et al. 2003).
- In mice with an inbreeding coefficient of 25%, survival characteristics were 57% worse than in mice with an inbreeding coefficient of 0% (Meagher et al. 2000).
- In dairy cows, a 1% increase in the inbreeding coefficient was associated with a 36 kg decrease in milk production over 305 days (Doekes et al. 2019).

- In dogs, inbreeding reduces litter size and impairs the fertility of bitches, as well as the survival rate of pups born (Leroy et al. 2015, Chu et al. 2019, Schrack et al. 2017, Windig et al. 2022).
- A large study of dogs by Bannasch et al. (2021) found that inbreeding increases morbidity throughout a dog's life.
- Donner et al. (2023) found that the disease burden from monogenic diseases in dogs increased as genome-wide heterozygosity decreased.
- Inbreeding significantly shortens the lifespan of dogs (extensive Finnish data: Kraus et al. 2022, Irish Wolfhound: van Gemert et al. 2022).

Increased homozygosity has also been found to be associated with osteochondrosis, laryngeal paralysis and a narrower-than-normal trachea in the Bouvier (Ubbink et al. 2011).

The prevalence of immune system disorders and diseases is high in many dog breeds (Pedersen 1999, Tournebize et al. 2022). According to Pedersen (1999), inbreeding is the single most important risk factor for these diseases. Studies have shown an association between increased homozygosity and autoimmune diseases (Pedersen et al. 2015a and 2015b; see Section 4.2), as well as inflammatory susceptibility (Ricketts 2022). A similar association appears to apply to allergies and cancers (Ujvari et al. 2018).

A study by Kraus et al. (2022) found that cancer was a more common cause of death in breeds with lower-than-average genetic diversity. It also resulted in earlier deaths. The protective effect of genetic diversity was demonstrated already by Dorn et al. (1968), who found that purebred dogs had a higher risk of cancer than mixed-breed dogs. An Italian study by Vascellari et al. (2009) found that purebred cats and dogs were almost twice as likely to develop cancer as mixed breeds.

Reduced genetic diversity and inbreeding have increased the incidence of certain types of cancer in some dog breeds, with varying ages of onset (see Section 4.1). The loss of genetic diversity can affect cancer risk directly, through the accumulation of cancer-causing gene mutations, or indirectly, by impairing immune function (Ujvari et al. 2018).

Inbreeding can also lead to favourable allele combinations and protect against some diseases (Mooney et al. 2021). However, the overall effect is generally negative due to the reduction in overall fitness it causes.

The amount of inbreeding in dog breeds

Inbreeding coefficients (COIs) estimated in dog breeds by modern genomic methods are typically high, averaging at 25% (e.g. Bannasch et al. 2021, Dreger et al. 2016). A high inbreeding coefficient can also be observed in any other closed breeding line. By contrast, landrace breeds and recently crossbred breeds have lower inbreeding coefficients (e.g. Barbet, American Eskimo Dog, and Australian Labradoodle; Mellanby et al. 2013; Bannasch et al. 2021). This is because new breeding individuals have been introduced from outside, which lowers the genetic relatedness within the population.

Inbreeding accumulated in dogs during domestication due to a genetic bottleneck. Another important genetic bottleneck occurred during the formation and development of breeds (Ostrander & Kruglyak 2000, Ostrander & Wayne 2005, Calboli et al. 2008, Mellanby et al. 2013, Marsden et al. 2015, Mooney et al. 2021). Gray et al. (2009) estimated that domestication and the formation of breeds destroyed 5% and 35% of the original diversity, respectively.

Many breeds have originated from a small number of founder individuals that were inbred to fix desirable traits in the breed. Furthermore, strict selection has been based on conformation, appearance, size, and colouring.

Tournebize et al. (2022) studied the genome sequences of 40 dog breeds in order to establish when modern breeds began to diverge from African village dogs, which exhibit the lowest level of inbreeding. They confirmed that most breeds exhibited extremely strong founder effects within the last 25 generations, or between 75 and 125 years ago. This finding aligns with the historical development of breeds, as many were created during the Victorian era.

Genetic bottlenecks have also occurred in the history of breeds because of wars, when the number of breeding individuals in a breed collapsed and the gene pool was reduced (e.g. Larson et al. 2012). The high use of popular sires in breeding is also a genetic bottleneck that reduces variation and increases inbreeding, even in breeds with large numbers of individuals. Furthermore, the genomes of popular sires become over-represented within a breed, causing deleterious genetic variants to spread across it (Calboli et al. 2008, Leroy 2011, Pedersen et al. 2015a).

Breeding

Inbreeding coefficients for individual litters

When planning a litter, the inbreeding coefficient should be calculated based on at least five generations. The appearance of common ancestors in the closest generations causes the most harmful form of inbreeding, known as 'fast inbreeding'. The best rule of thumb is to avoid cousin combinations with fast inbreeding and a COI of 6.25%. The kinship between direct cousins is already evident in a three-generation litter pedigree, but it would be preferable not to exceed a COI of 6.25% in a five-generation pedigree.

The Finnish Kennel Club operates as follows for closely related combinations:

- *Close relative combinations (sire/dam x offspring with a COI of 25%; full siblings with a COI of 25%) are prohibited. Puppies born from such combinations can only be registered under a breeding ban.*
- *Other close relative combinations (grandfather/grandsire x offspring with a COI of 12.5%, half-siblings with a COI of 12.5%, and aunt/uncle x offspring with a COI of 12.5%) are not recommended* (Suomen Kennelliitto 2018).

In these combinations, the COI is always at least 12.5% or 25%.

The inbreeding coefficient of a whole breed

The most effective methods for maintaining genetic diversity in animal populations and reducing the rate of inbreeding are:

- using as many unrelated individuals as possible for breeding, and
- keeping the number of offspring of breeding individuals as equal as possible.

The General Breeding Strategy of the Finnish Kennel Club (Suomen Kennelliitto, 2018) outlines the following:

- *The general recommendation is that the lifetime number of offspring of any dog should not exceed 5% of the puppies registered in the breed population in one generation (four years). The number of offspring should be distributed as evenly as possible over the years.*
- *If the average effective population size of the breed, taking foreign populations into account, is 50 or less over the last 3–4 generations, as calculated by the inbreeding rate, or 200 or less as calculated by the number of breeding dogs, then further genetic variation should be introduced to the breed through crossbreeding and/or the introduction of landrace dogs.*

The maximum recommended number of offspring per individual is stated in the breed-specific breeding strategies of each breed under the Finnish Kennel Club.

4.1. Cancer

Cancer accounts for 15–27% of all deaths in pedigree dogs (Adams et al. 2010, Bronson 1982, Proschowsky et al. 2003, Michell 1999). Schifman and Breen (2015) estimate that the incidence of cancer in dogs is ten times higher than in humans.

Cancer is typically an age-related disease (Bonnett & Egenvall 2010) and age-related cancers are usually caused by mutations that are not passed on to offspring. Early-onset cancers, however, are more likely to be influenced by inherited mutations (Nunney 2013).

Cancers occur in both pedigree and mixed-breed dogs. Some breeds have a higher-than-average risk of certain types of cancer, which suggests heredity.

Early-onset and life-shortening histiocytic sarcoma, for example, occurs in Flat Coated Retrievers and Bernese Mountain Dogs (Dobson 2013, Ostrander et al. 2019, Rowell et al. 2011). Histiocytes are a type of white blood cell. When a dog develops histiocytosis, these cells proliferate abnormally and invade different tissues. Histiocytic sarcoma also occurs in Rottweilers and Golden Retrievers (Affolter & Moore 2002, Shaiken et al. 1991, Hayden et al. 1993, Hédan et al. 2021). Abdominal cancer has been reported in Belgian Shepherds (Scanziani et al. 1991). Irish Wolfhounds, Scottish Deerhounds, Great Danes and other large breeds are at hereditary risk of aggressive bone cancer (osteosarcoma; Letko et al. 2021, Momen et al. 2021, Phillips et al. 2007). According to a study by Song et al. (2013), brain and central nervous system cancers are particularly common in Boxers, Golden Retrievers, French Bulldogs, Boston Terriers and Rat Terriers. Schifman and Breen (2015) provide a comprehensive table of cancer types associated with different dog breeds.

A Swedish study by Bonnett et al. (1997) found that the Bernese Mountain Dog, Irish Wolfhound, Flat Coated Retriever, Boxer and St. Bernard had the highest number of cancer-related deaths. A later study using the same database identified the top breeds as the Bernese Mountain Dog, Irish Wolfhound and Leonberger (Bonnett et al. 2005). In Denmark, the five breeds with a cancer death rate of more than 20% were the Bernese Mountain Dog, Flat Coated Retriever, Golden Retriever and Rottweiler (Proschowsky et al. 2003). A British study by Adams et al. (2010) found that the top five breeds were the Irish Water Spaniel, Flat Coated Retriever, Hungarian Vizsla, Bernese Mountain Dog and Rottweiler (see Table 1). The

Adams study also examined the average age at which dogs died of cancer, finding that it was lowest in English Bulldogs and Leonbergers (Table 2).

Mode of inheritance

Different mechanisms may underlie hereditary cancer susceptibility. In some breeds, a particular type of cancer may be caused by a single mutation. For instance, renal cystadenocarcinoma and nodular dermatofibrosis (RCND) in German Shepherds is an uncommon condition that is passed on through a dominant mutation (Lingaas et al. 2003). A similar disease occurs in humans under the name Birt-Hogg-Dube syndrome.

Cancer susceptibility may also be linked to an inherited dysfunction in growth restriction genes, which inhibit the formation of cancer cells. This kind of dysfunction can strongly predispose individuals to a wide variety of cancers that occur at a young age. Examples of concurrent tumours in different parts of the body are also known in dogs (Nakagawa et al. 2009, Rebhun & Thamm 2010). In humans, such a dysfunction is, for example, the rare dominant Li-Fraumeni syndrome.

The genetics of hereditary cancers may resemble human BRCA1 mutations, which cause disease susceptibility. Relatives of those affected have a higher risk of developing cancers such as breast and ovarian cancer, rather than inheriting a particular cancer directly. Rivera et al. (2009) demonstrated a significant correlation between mutations in the BRCA1/2 genes and mammary tumours in English Springer Spaniels.

Heritabilities for osteosarcoma have been estimated as follows:

- 0.65 in Irish Wolfhounds (Momen et al. 2021)
- 0.69 in Scottish Deerhounds (Phillips et al. 2007)
    - The mode of inheritance was suggested to be a dominant major gene.
- 0.21 in Leonbergers (Letko et al. 2021)
    - The prevalence of osteosarcoma in this study was 20%.

The mode of inheritance of histiocytoma has been suggested to be polygenic (Padgett et al. 1995a, Abadie et al. 2009), with an estimated heritability of 0.30 in Bernese Mountain Dogs (Padgett et al. 1995a). Many other types of cancer are also likely to be polygenic.

Table 2. Breeds of dogs with the highest cancer mortality in the British study by Adams et al. (2010). The study included data from 15,881 dogs of 165 breeds. The average cancer mortality rate for the entire dataset was 27%.

Cancer as the cause of death in ≥ 50% of dogs:
Irish Water Spaniel
Flat Coated Retriever
Approximately 45% of dogs:
Wirehaired Vizsla
Bernese Mountain Dog
Rottweiler
Spinone
Leonberger
Staffordshire Bull Terrier
Welsh Terrier
Approximately 40% of dogs:
Giant Schnauzer
Airedale Terrier
Golden Retriever
Boxer
Briard
French Bulldog
Bullmastiff
Approximately 35% of dogs:
Alaskan Malamute
Saluki
Nova Scotia Duck Tolling Retriever
Basset Griffon Vendéen
Beagle
English Setter
Norwegian Elkhound
Siberian Husky
Keeshond
Tibetan Terrier
Basset Hound
Labrador Retriever
Approximately 30% of dogs:
Afghan Hound
Rhodesian Ridgeback
Red and White Irish Setter
Standard Poodle
German Shorthaired Pointer
Cocker Spaniel
Field Spaniel
Welsh Corgi Pembroke and Cardigan
Gordon Setter

Table 3. Average life expectancy of dogs that died from cancer (Adams et al. 2012).

Below 7 years: English Bulldog Leonberger
7–8 years: Bullmastiff Nova Scotia Duck Tolling Retriever Bernese Mountain Dog
8–9 years: Scottish Deerhound Rottweiler French Bulldog Spinone Irish Water Spaniel
9–10 years: Newfoundland Flat Coated Retriever Giant Schnauzer German Wirehaired Pointer Bull Terrier Boxer

4.2. Autoimmune diseases

In an autoimmune disease, the body produces antibodies that attack its own cells and tissues. The body's defence mechanism (the immune system) recognises these structures as foreign tissue and gradually begins to destroy them. Autoimmune diseases can affect the skin, eyes, brain, kidneys, joints, bone marrow or blood.

In some cases, autoimmunity can target a specific organ, such as the pancreas in type 1 diabetes or the thyroid gland in hypothyroidism. Alternatively, autoimmunity can affect the whole body, as in systemic lupus erythematosus (SLE), where almost all organs can be affected.

Autoimmune diseases in dogs can be particularly challenging to diagnose and treat. Some require lifelong treatment.

Prevalence

It is estimated that around five in every 100 people have an autoimmune disease (Duodecim Health Library 2022). Information on the prevalence of autoimmune diseases in different dog breeds is scarce.

Addison's disease, also known as adrenal insufficiency, is one of the most extensively researched autoimmune diseases in dogs. Symptoms of the disease are caused by a lack of metabolic hormones, which cannot be produced by a damaged or destroyed adrenal cortex.

Addison’s disease occurs in several purebred and mixed-breed dogs (e.g. Boag & Catchpole 2014, Oberbauer et al. 2006, see also omia.org). In the general dog population, prevalence

rates range from 0.06% to 0.4% (Decôme & Blais 2017, Bellumori et al. 2013, Hanson et al. 2016, Wiles et al. 2017). In some breeds, however, a prevalence of up to 9% has been reported (Oberbauer et al. 2002 and 2006, Famula et al. 2003, Hughes et al. 2007). An increased risk of Addison's disease has been identified in breeds such as the Bearded Collie, Portuguese Water Dog, Standard Poodle, White West Highland Terrier, Leonberger, Wheaten Terrier and Nova Scotia Duck Tolling Retriever (Oberbauer et al. 2002 and 2006, Famula et al. 2003, Hughes et al. 2007, Klein & Peterson 2010, Boag & Catchpole 2014, Van Lanen & Sande 2014, Hanson et al. 2016).

A particularly high prevalence of autoimmune diseases has been reported in Bearded Collies. According to the Bearded Collie Foundation for Health (2018), 11.2% of dogs in the US have one or more of these diseases. Of these, more than half have Addison's disease or SLO (symmetrical lupoid onychodystrophy). SLO is a painful nail disease that occurs in several breeds. The literature reports autoimmune diseases in breeds such as the Bearded Collie, Gordon Setter, English Setter, Giant Schnauzer, Labrador Retriever, Welsh Corgi, Boxer and German Shorthaired Pointer (Auxilia et al. 2001, Mueller et al. 2003, Scott et al. 1995, Wilbe et al. 2010a and 2010b, Ziener & Nødtvedt 2014, see also omia.org).

There is also a significantly higher prevalence of autoimmune diseases in Nova Scotia Duck Tolling Retrievers than in other dogs (Bremer et al. 2015).

Mode of inheritance

Both genetic and environmental factors regulate susceptibility to autoimmune diseases (Friedenberg et al. 2017, Pedersen et al. 2012a, 2012b, Wilbe et al. 2010a, 2010b). According to Pedersen (1999), hereditary susceptibility is the main factor in the development of immune-related diseases in dogs. Many autoimmune diseases are prevalent in specific breeds. Environmental factors often trigger disease onset in genetically susceptible individuals. Other causes of autoimmune diseases include cancers, tick-borne diseases, and drug side effects.

In humans, heritability estimates for autoimmune diseases have ranged from 0 to 1, averaging 0.60 (Selmi et al. 2012). Studies in dogs are relatively scarce. However, in the few existing studies, heritability estimates have been very high, ranging from 0.50 to 0.75 (Greer et al. 2009, Famula et al. 2003, Oberbauer et al. 2002, 2006).

DLA genes

The DLA (Dog Leukocyte Antigen) region is one of the genetic factors associated with autoimmune diseases. It contains genes that play a role in the immune system.

The DLA region encodes proteins that recognise various harmful pathogens and cell types (e.g. cancer cells) and distinguish them from the body's own cells. This ability to distinguish between one's own structures and foreign ones is vital for the immune response to target foreign cells outside the body. However, sometimes the body's normal functioning is disturbed, and the rejection reaction is mistakenly directed at its own cells. The result is an autoimmune disease, whereby the body attacks its own cells. Overall, the DLA region plays a key role in canine immunity: the greater the diversity of the region's genotype, the greater its capacity for protein production and the wider the range of diseases against which the body can defend itself (Mäki & Mujunen 2018).

In humans, almost all autoimmune diseases are linked to genes in the HLA region, which corresponds to the DLA region in dogs. Similarly, DLA genes in dogs have been associated with

various immunological issues, particularly autoimmune diseases (e.g. Tsai et al. 2013, Barrientos et al. 2013, Short et al. 2014, Jokinen 2011, Massey et al. 2014). Some DLA alleles are risk factors for autoimmune diseases; others have been shown to offer protection against disease. The same allele can protect against one disease and predispose to another.

Based on their own study and other published literature, Gershony et al. (2019) concluded that two specific sets of DLA alleles (haplotypes) are associated with different autoimmune diseases in several dog breeds. Although other genes are required for disease onset, this pattern of two haplotypes may be an important indicator of disease susceptibility. Therefore, inherited susceptibility would apply to autoimmunity in general, with other genes determining in which organ the disease develops.

In some cases, an individual's risk of disease is greatest when they have two different haplotypes. For example, in dogs, those with both the Addison's disease risk haplotype 1 and the SLO risk haplotype 5 appear to be at the greatest risk of developing Addison's disease (Gershony et al. 2019). A similar phenomenon has been observed in human cases of Addison's disease and type 1 diabetes. Heterozygous individuals are at a higher risk of developing the disease than individuals who are homozygous for either haplotype (Myhre et al. 2002, Noble & Valdes 2011, Skanes et al. 1986).

Breeding

The relationship between DLA genes and autoimmune diseases is complicated, so DLA gene testing alone cannot be used for breeding purposes.

Dogs with confirmed autoimmune diseases should not be used for breeding.

Increasing genetic diversity should reduce the incidence of autoimmune and other genetic diseases.

5. Genetic diseases and defects that cause significant welfare problems

5.1. Behavioural disorders

The government's proposal to parliament for an act on animal welfare and related legislation states the following:

'*Mental functioning can be impaired by various behavioural disorders, some of which have been found to be hereditary*.'

It also states:

'*Inheritance of animal temperament should also be taken into account when selecting breeding animals.*' *Animals that are particularly timid or aggressive should not be used for breeding. Excessive fear and aggression cause the animal stress, often making it difficult for it to adapt to its environment or live with people or other animals. The behaviour of fearful and aggressive animals can also pose a safety risk to other animals, as well as to their carers and other people who encounter them*.'

Behavioural disorders that impair mental functioning include excessive fearfulness, aggression, separation anxiety, and obsessive-compulsive symptoms.

Sanna Immonen's 2013 thesis provides a thorough overview of the causes of separation anxiety, fear of noises, and obsessive-compulsive disorder in dogs. Katriina Tiira's 2019 book on canine behaviour and personality is also comprehensive and covers canine behavioural disorders and their genetic background. These works serve as the primary sources for this section of the report, featuring longer quotations in italics.

Behavioural disorders are often associated with fearfulness, anxiety, and chronic stress, all of which are major impairments to well-being. Furthermore, undesirable behaviour can affect the owner's attachment to their dog, increasing the likelihood of abandonment or euthanasia.

Large differences in the prevalence of anxiety-related traits have been observed between breeds, suggesting a strong hereditary component (Salonen et al., 2020). Most behavioural disorders manifest during the first three years of a dog's life.

Stress and other welfare issues

Generalised and intense fear can severely limit the lives of dogs and their owners, causing significant welfare problems.

Severe fear is a highly stressful state for the body, characterised by increased cortisol levels and heart rate, and a heightened state of alertness (Tiira 2019a). Persistent stress increases the risk of illness and the likelihood of obsessive-compulsive behaviour (Sulkama et al. 2022). Severe obsessive-compulsive behaviour can significantly impair a dog's well-being and may also cause physical injury. Dogs with severe fears and separation anxiety experience more frequent and severe skin diseases (Dreschel 2010). In humans, and presumably in dogs too, prolonged stress can lead to depression.

Normal stress is defined as a situation in which an animal is required to adapt to the demands of its environment within normal limits. By contrast, excessive stress requires such high levels of energy and adaptive effort that it disrupts other biological functions, such as growth and reproduction, and often causes suffering in the animal (Mariti et al. 2012). The stress response becomes problematic when the animal is unable to control the situation or lacks a decisive behavioural model (Weiss 1972). Having a sense of control has therefore been found to reduce the stress response (Weiss 1968). When the stress response becomes chronic, it has detrimental physiological and emotional effects (Casey 2002). (Immonen 2013)

Behaviours indicative of acute stress include lip licking, yawning, panting, vocalising, crouching, and shaking (Beerda et al. 1997, Stephen & Ledger 2005). Symptoms of chronic stress include repetitive behaviours (stereotypies), increased activity, nose poking, self-cleaning, paw lifting, faecal eating and vocalising (Hetts et al. 1992, Hubrecht et al. 1992, Beerda et al. 1999). (Immonen 2013)

Many of the behaviours associated with acute stress are normal for dogs, but when excessive, they are indicative of stress. It can be difficult to determine whether an observed behaviour is normal, or stress related.

5.1.1. Fearfulness

Fear is a natural and necessary reaction for survival. However, when it becomes a temperament trait, it can limit a dog's and owner's ability to live a normal life. A fear of unfamiliar things, people or situations can make everyday life difficult. For instance, a dog may be afraid of people outside or household appliances. A dog is said to be fearful if its owner frequently observes gestures or emotions indicating fear. The more a dog experiences fear in its daily life, the more its welfare is compromised.

Fear can be divided into social and non-social fear, depending on the situation and the object of the fear. A dog may, for instance, be afraid of strangers, other dogs, being alone (separation anxiety), new situations, loud noises, high places, or slippery floors (Tiira 2019a).

Finnish studies have estimated that 26–28% of dogs are fearful (Tiira et al. 2016, Salonen et al. 2020).

Separation anxiety

Separation anxiety occurs when a dog is left alone or separated from someone it cares about (Tiira 2019a). However, not all problems with being alone are separation anxiety; the dog may simply be afraid of being left on its own. Sometimes, a dog's issues with being alone stem from frustration.

The development of separation anxiety is closely related to a dog's temperament, physiology, and genes. Controlling environmental factors does not usually prevent separation anxiety (Immonen 2013).

Separation anxiety can be classified according to the severity of the symptoms, the underlying condition (e.g. discomfort, anxiety or fear; Palestrini et al. 2010 and Table 3), and the type of behaviour observed in the dog (Table 4).

Table 4. The classification of behaviours indicative of separation anxiety, according to the underlying condition and symptom severity (Immonen, 2013).

Signs of discomfort		*Licking lips, yawning, lifting paws*
Anxiety reactions		*Orientation to the environment, vocalisation (Palestrini et al. 2010)*
Fear reactions	**Hyperactive**	*Stereotypic behaviour, such as jumping at the door or excessive drinking (Lund & Jorgensen 1999); licking, which can result in self-injury (Simpson 2000)*
	Freezing	
Other signs		*Withdrawal, loss of appetite, drooling, hyperventilation, and gastrointestinal symptoms such as vomiting and diarrhea (Takeuchi et al. 2000).*

Table 5. Classification of separation anxiety behaviours by type.

Exploratory behaviour	*Walking around the house and sniffing at or near the door (Lund & Jorgensen 1999)*
Playing with things, including showing hunting behaviour	
Destructive behaviour	*For example, tearing, scratching and chewing furniture, carpets, clothes, doorknobs, and windows (Lund & Jorgensen 1999)*
Vocalisation	*Barking, whining and howling, like the vocalisations of a puppy (Overall et al. 1999, Lund & Jorgensen 1999, Ibanez & Anzola 2009)*
Defecating indoors, and vomiting	*(Lund & Jorgensen 1999, Ibanez & Anzola 2009, Simpson 2000)*

These symptoms can also occur for other reasons. Not all problems with being alone are caused by separation anxiety; they can also be caused by boredom or illness.

The acute stress response associated with separation anxiety causes the animal to try to escape, defend itself, or avoid the situation through passivity (Ogata & Dodman 2011). Dogs with separation anxiety appear very distressed (Horwitz 2002) and may injure themselves trying to escape from the dwelling (Simpson 2000). The mere anticipation of separation can lead to anxiety (Gray 1987). (Immonen 2013)

In a Danish study, separation anxiety was the second most common behavioural problem in dogs (Lund et al. 1996). A survey found that 34% of dogs showed signs of separation anxiety when left alone (Blackwell et al. 2008), while a Spanish study found that around 20% of dogs suffered from separation anxiety (Martinez et al. 2011). (Immonen 2013)

A Finnish study found that approximately 17% of dogs had separation problems (Tiira et al. 2016). Salonen's (2020) study observed severe separation anxiety behaviour in 5% of dogs.

There are clear differences in the prevalence of separation anxiety among different breeds of dog. Onset typically occurs at around 1.5 years of age.

Fear of noises

In this condition, the fear response is triggered by loud and unexpected sounds, such as thunder, fireworks and gunshots. This fear can also generalise to include a variety of everyday sounds (Tiira 2019a). *68% of dogs that were afraid of fireworks were also afraid of other loud sounds, such as thunder, gunshots, and the banging of car exhaust pipes (Dale et al. 2010). The frequent co-occurrence of fears of thunder, fireworks, and gunfire suggests that fear of noises can easily be generalised to similar sounds (Blackwell et al. 2013).*

Fear is not always focused on sound alone: dogs may also fear the flashes of fireworks or thunder and the smell of fireworks, and fears may also generalise to the darkening sky. In the context of thunder, dogs may also become sensitive to changes in barometric pressure and other storm-related factors (Mills 2005).

A fear of noises can manifest as mild anxiety or fear, or as a severe phobia, like other fears (Overall 2002). (Immonen 2013)

Typically, the fear worsens with age and may not manifest until the age of two or older (Tiira 2019a).

According to Immonen (2013), the most common symptoms of a fear of noises are trembling, groaning, vocalising, pacing, hiding and seeking attention. A dog experiencing this fear may also destroy property or defecate indoors. The fear reaction can last for months at worst (Riemer, 2019). Such fear reactions are a serious welfare problem and need to be treated to improve the dog's quality of life.

Acute stress reactions associated with noise phobia lead to defensive behaviour, whereby the animal tries to escape, defend itself, or freeze to avoid the stimulus that is causing the fear (Ogata & Dodman 2011). Thus, dogs can respond either actively or passively in a fearful situation (Mills 2005). A dog's passive response to fear can easily go unnoticed by the owner and does not usually cause them harm, so the problem is not addressed (Mills 2005). However, even minor symptoms such as licking, shaking, and paw lifting can indicate increased stress in a dog (Hetts et al. 1992, Beerda et al. 1999, 2000). (Immonen 2013)

A study by Salonen et al. (2020) investigated anxiety-related characteristics, the most common of which was fear of noise. According to various studies, noise fear affects approximately 20–50% of dogs, including 32–39% in Finland (Salonen et al. 2020, Tiira, 2019a, Tiira et al. 2016). *However, noise fear is often overlooked and under-treated, so its true prevalence is unclear (Mills 2005).*

Several studies have found differences in the prevalence of noise fear between breeds (McCobb et al. 2001, Mills 2005, Blackwell et al. 2013). (Immonen 2013)

5.1.2. Aggressiveness

Dog aggression is most commonly directed at the owner, family members, strangers or other dogs. Behaviours include staring, growling, barking, nipping and biting (Mikkola et al. 2021).

Aggressive gestures are part of a dog's normal communication and can occur outside of aggressive situations, such as during play. However, aggressive behaviour can become excessive, posing a health threat to humans and other animals (Mikkola et al. 2021).

Tiira (2019) categorises aggressive dog attacks according to their target and severity:

1. Dog attacks on other dogs resulting in serious injury or death.
2. Dog bites on humans resulting in non-serious injuries.
3. Deaths or serious injuries requiring medical attention caused by dogs to humans.

The classification should be based on the bite itself rather than its secondary consequences. Even a small bite can sometimes become infected to the point of being life-threatening, in which case death or serious injury requiring medical attention would be a secondary consequence of the bite rather than an indication of the dog's level of aggression. Additionally, when discussing aggressive behaviour, it is important to consider the target, as aggression towards other dogs, strangers, and owners/family members is often motivated by slightly different things. Furthermore, aggression towards the owner may be determined by different genes than other types of aggression (K. Tiira, email communication).

The prevalence and forms of aggression differ between breeds. Some breeds show more aggression than others. For example, aggression is increased in breeds bred for guarding duties.

Aggressive behaviour, particularly towards people, is often motivated by fear (Tiira et al. 2016, Mikkola et al. 2021). This is known as fear aggression. A fearful dog may learn to use aggression to avoid a fearful stimulus, such as a person. However, aggression towards strangers, other dogs and the owner can also occur without fear, for instance when defending resources such as food, toys or sleeping places, or when defending territory. Aggressive behaviour may also be triggered by pain.

5.1.3. Obsessive-compulsive symptoms and stereotypic behaviour

Stereotypies involve the repetition of certain motor patterns that serve no purpose. Obsessive-compulsive symptoms involve the repetition of a specific, inappropriate action (Salonen, 2020). While obsessive-compulsive symptoms and stereotypic behaviour are not the same, they are difficult to distinguish and will therefore be discussed together in this report.

Obsessive-compulsive or stereotypic behaviours are repetitive behaviours that resemble normal behaviours but occur in excessive or inappropriate contexts (Dodman et al. 2010). Stereotypic behaviour is thought to be a substitute behaviour in situations of conflict, frustration, or stress (Luescher 2003).

The occurrence of stereotypic behaviour in distressing situations suggests that it is a coping strategy (Moon-Fanelli et al. 2007) (Immonen 2013). The classification of stereotypic behaviour is presented in Table 6 (Luescher 2003, Immonen 2013).

Tiira (2019) describes stereotypic behaviour and obsessive-compulsive symptoms as the repetition of behaviour that has no clear function or purpose and is likely influenced by environmental and genetic factors. While some animals may have a slightly higher genetic susceptibility, stereotypic behaviour is usually caused by an environment that lacks opportunities to fulfil behavioural needs, or early weaning, or some other factor that causes the animal to seek relief or an outlet for its need to act (H. Rautiainen, personal communication).

Table 6. Classification of stereotypic behaviour (Luescher 2003, Immonen 2013)

Motor	*Spinning around, tail chasing, tap-dancing, jumping in place, light chasing, freezing*
Oral	*Licking oneself, the air or one's nose, chewing foot, sucking flank, scratching with teeth,* *licking or chewing objects, overeating or drinking, eating foreign objects, nibbling the air ('catching flies')*
Aggression	*Aggression towards oneself (e.g. growling or biting own hindquarters, hind legs or tail), attacking inanimate objects (e.g. a food bowl), unpredictable aggression towards people*.*
Vocal	*Rhythmic barking or whining*
Hallusinations	*Staring at shadows or chasing patterns of light. Sudden startling or awakening for no apparent external reason*

Many of the above behaviours may also be caused by pain, for example.

The prevalence of obsessive-compulsive and stereotypic behaviour in dogs is not well understood. Some dog breeds exhibit obsessive-compulsive behaviour much more frequently than others. The typical obsessive-compulsive behaviours exhibited by different breeds can vary significantly. For instance, Border Collies and other shepherd dogs have a high propensity for compulsive staring and catching 'invisible' flies, whereas the most common compulsive behaviour in Staffordshire Bull Terriers is tail chasing (Sulkama et al. 2022).

Obsessive-compulsive and stereotypic behaviour may only occur occasionally, but in some dogs the symptoms are so severe that contact with the dog is impossible when it is stuck in the behaviour. The most severe cases result in a diagnosis of obsessive-compulsive disorder (Tiira 2019a).

Stereotypic behaviour can act as a substitute for relieving stress when a specific need is not met. For instance, an animal may seek a sense of reward through sucking (H. Rautiainen, personal communication). This has been studied in minks and horses, for example, where inhibiting stereotypic behaviour using mechanical aids may cause stress and other welfare issues (Hemmann 2014). Stereotypic behaviour is an animal's way of coping with a challenging situation. Therefore, an animal that has found a way to cope may be better off than one that has not (T. Koistinen, email communication).

5.1.4. Inheritance of behavioural disorders

The brain structure of different dog breeds has evolved through breeding and is associated with their behaviour (Hecht et al. 2019). These differences indicate the potential for selective breeding of these traits.

Behavioural and personality traits arise from the interaction between genes and environmental factors. Genes regulate neurotransmitters in the brain; for example, a lack of serotonin is known to predispose an individual to anxiety, fearfulness and depression. A particular combination of genes can increase susceptibility, whereas certain combinations can protect against behavioural disorders.

Separation anxiety, obsessive-compulsive symptoms, fear-induced aggression, noise sensitivity, and other anxiety symptoms often co-occur (Salonen et al. 2020, Tiira 2019a, Immonen 2013), suggesting that they are influenced by same genes. Dogs that are afraid of strangers and new situations tend to be more fearful of loud noises and more anxious about being left alone than confident dogs (Salonen et al. 2020, Tiira 2019a). Studies by Sulkama et al. (2021, 2022) have associated obsessive-compulsive disorder, fearfulness and aggression with hyperactivity, impulsivity and an inability to concentrate (ADHD). Similar associations have also been found in human studies. These traits may have common underlying neurobiological pathways and brain structures.

Fearfulness

Estimated heritabilities for fearfulness and noise fear have ranged from 0.16 to 0.80 (e.g. Friedrich et al. 2019, Ilska et al. 2017, Arvelius et al. 2014, van der Waaij et al. 2008, Lindberg et al. 2004, Ruefenacht et al. 2002, Goddard & Beilharz 1982, 1983, 1985).

Genomic regions have also been identified for fearfulness and separation anxiety (Zapata et al. 2016, Friedrich et al., 2019). Sarviaho et al. (2019) identified regions in German Shepherd Dogs associated with noise fear, fear of strangers, and fear of new situations. These were located on different chromosomes. In humans, the genomic region associated with fear has been linked to neuropsychiatric disorders such as schizophrenia and bipolar disorder; the region associated with noise fear contains candidate genes related to hearing, as well as the OXTR gene, which is associated with anxiety, stress, and social behaviour (Kis et al. 2014).

In Great Danes, a genomic region associated with fearfulness has been identified on chromosome 11. The corresponding region in humans has been associated with a rare syndrome that includes neurological symptoms as well as accelerated growth in childhood (Sarviaho et al. 2020).

Aggressiveness

Aggression and fearfulness appear to be influenced by the same genomic regions, and genetic correlations have also been found between the two traits. A study of aggression towards other dogs and strangers found that an increase in aggression was accompanied by an increase in fearfulness (Duffy et al. 2008; statistically significant genetic correlations of 0.36–0.41 and 0.31–0.32, respectively). Additionally, a separate genomic region has been identified as being associated with aggression towards the owner and other dogs within the same family (Zapata et al. 2016).

Aggression towards strangers, other dogs, the owner, and family members may be genetically distinct traits (Liinamo et al. 2007, Zapata et al. 2016).

Obsessive-compulsive disorder and stereotypic behaviour

Studies have identified a clear genetic predisposition to obsessive-compulsive disorder, with relatives of affected dogs often exhibiting similar symptoms (Overall & Dunham 2002, Tiira et al. 2012). (Immonen 2013)

The CDH2 gene has been linked to obsessive-compulsive disorder, such as flank or blanket sucking, in Dobermans (Dodman et al. 2010). This gene has also been associated with obsessive-compulsive symptoms in humans. In Belgian Shepherd Malinois, obsessive-compulsive symptoms (such as spinning in circles) were particularly prevalent in good working dogs that

were homozygous for a variant of the CDH2 gene (Cao et al. 2014). Compulsive staring, snapping at invisible flies and chasing light in Border Collies are also likely to be the result of selective breeding for efficient working traits (Salonen 2020).

The heritability of stereotypic behaviour has been estimated in at least one other animal species: minks, where it is moderate (about 30%; Hansen et al. 2010). Minks exhibiting stereotypic behaviour are not recommended for breeding (Hernesniemi 2016).

5.1.5. Other factors that predispose individuals to behavioural disorders

Fears may be caused by early fearful experiences, poor socialisation, a lack of maternal affection (Tiira et al. 2016), a single traumatic event, or repeated exposure to a mild stimulus (sensitisation). A stressed animal may also develop a fear of a previously accepted voice (Mills 2005).

Other factors that commonly contribute to behavioural disorders include temperament, gender, age, breed, whether the animal has been spayed or neutered, the owner's experience of owning dogs, lack of interaction with other animals, stressful environmental factors and low levels of exercise and activity. Behavioural problems may also be caused by a medical condition, particularly if the problematic behaviour emerges in relation to something with which the dog is already familiar. Chronic pain and itching can affect behaviour. Obsessive-compulsive behaviour may also be associated with epileptic seizures. Furthermore, epileptic dogs have been found to exhibit greater anxiety and fear than other dogs (Levitin et al. 2019). In older dogs, obsessive-compulsive symptoms may be a consequence of dementia (Mills 2005, Tiira 2019a, Puurunen et al. 2020, Sulkama 2022).

A study by Mikkola et al. (2021) found that older dogs were more likely than younger dogs to behave aggressively. This may be due to factors such as pain caused by illness. Sensory impairment may make it difficult for the dog to detect approaching humans and cause it to react aggressively to sudden situations. Male dogs behaved more aggressively than females, though sterilisation had no effect on aggression. Dogs that were new to their owners were more likely to behave aggressively than dogs whose owners had previous experience of owning a dog. Small dogs were more likely to behave aggressively than medium or large dogs. Zapata et al. (2016) suggest that the small size gene is associated with all behavioural problems in small dogs.

5.1.6. Determining the severity of behavioural disorders

In humans, excessive fear and anxiety are defined as conditions in which symptoms are severe enough to cause significant impairment of functioning (World Health Organization 2018). The same definition could be used for dogs.

Various behaviour tests and breeding inspections are used to determine the characteristics of potential breeding dogs. All of these include observations for fearfulness and aggression.

The purpose of the **Character Test** is to assess and record how the dog behaves in situations that put its nervous system under stress (Finnish Working Dog Association 2019). The test measures the dog's capability to function (equivalent to courage in humans), as well as its nerve stability. According to the test guidelines, nerve stability refers to a dog's *innate strength or weakness of nerves when subjected to intense and variable internal stress.* Good nerve stability is defined as the *ability to manage states of tension without experiencing unnatural exhaustion, hysteria, or other signs of internal imbalance*.

The guidelines for the Character Test mention symptoms of nervousness in dogs, including severe restlessness, body tremors, an increased pulse rate not due to physical exertion, increased swallowing, inappropriate movements, seeking refuge by reaching for the handler, and diarrhoea or vomiting. To define a dog's reaction, action or state of mind as nervous, its **behaviour must be abnormal in relation to the stimuli and/or arousal**. A dog is classified as restless or nervous according to the following criteria:

- **Slightly restless** (score +1). The dog passes all subtests. He shows slight signs of restlessness and becomes mentally stressed as the test progresses. The length of the recovery period between sub-tests varies.
- **Slightly nervous** (-1): The dog shows clear signs of restlessness and seeks support from its handler during the subtests. He requires longer recovery times between subtests and exhibits inconsistent behaviour due to nervousness. He moves and vocalises unnecessarily.
- **Nervous** (-2): During the test, the dog shows severe restlessness, tremors, increased swallowing and inappropriate movements. It may vomit and have diarrhoea. He seeks shelter. He has great difficulty in coping with all the subtests and is unable to concentrate.
- **Very nervous** (-3): All the above behaviours are very intense. The dog's internal stress levels are extremely high, and he is unable to cope with all the subtests.

Similar things are observed in the **Mental Description** (Mentalbeskrivning Hund) as in the Character Test, although the performance of the test itself differs (Finnish Working Dog Association 2020).

The Finnish Kennel Club has drawn up guidelines for a special breeding inspection which assesses the dog's behaviour. This test focuses particularly on everyday situations and issues such as handling, surface phobia, and sensitivity to sounds. Issues that may cause a dog to fail the breeding inspection include strong fears and aggression (Suomen Kennelliitto 2021a).

During the breeding inspection, the dog's attitude towards the test assistant, handling, a strange dog walking at a distance, unusual surfaces, crowds, and sounds is observed. Additionally, any severe stress-related or stereotyped behaviour is noted. The dog's courage is assessed according to the following classification:

- relaxed, no signs of insecurity
- P0: occasionally slightly insecure
- P1: mildly insecure; may show signs of restlessness or withdrawal.
- P2: insecure
- P3: fearful
- P4: highly anxious.

The breeding inspection form describes what constitutes mildly insecure, insecure, fearful and highly anxious behaviour (see Table 6).

Table 7. Descriptions of insecure and fearful behaviour in the breeding inspection form (Suomen Kennelliitto 2021a).

Class	Behaviour
Mildly insecure (P1)	• Mild signs of uneasiness or restlessness: may make noises, move back and forth, move slowly and tensely, lick lips, whimper, tail may drop or become tense. • The dog may dodge slightly but allows itself to be touched. • May also become more vacant or start to make eye contact with the handler in a more pronounced way. • Dip the backquarters and/or flinch, stiffen for a moment, lick lips, yawn. Changes speed of movement and/or posture, may momentarily move closer to or behind the handler, stop for a moment, slow down, tense up or curve. May glance at assistants, lower posture, lower tail. May vocalise and/or jump towards the handler. • When spotting a strange dog or group of people, may also sniff the ground, look away, yawn, repeatedly lift a leg, sit down, turn around, put the leash in his mouth, etc. • On unusual surfaces: very slight signs of concern or avoidance (posture slightly low, stiff or backward, moves slowly, may stop for a moment, may lick lips, slight lip commissure retraction, etc.)
Insecure (P2)	• Doesn't allow touching • Quails • Retreats, evades, flees • Stops and refuses to move forward • Avoids action (e.g. when encountering an unusual surface, stops, tries to jump or turn over the platform, lies on its back or performs other actions to avoid entering the platform, such as sitting down, rolling over or giving paw) • Tries to move away from the assistant or into the lap of the handler • Obvious changes in movement speed or posture (e.g. swerving, moving or trying to get behind the handler, 'stress pulling' away from the sound, pressing against or jumping on the handler) • Tail presses down • The posture lowers sharply • Glances around nervously, barks or pants • Becomes passive or withdrawn
Fearful (P3)	• Retreats or runs away, or refuses to move forward • Doesn’t allow itself to be touched • Tries hard to climb onto the lap of the handler • Crouches • Tail firmly between legs • Tremors • Pants
Highly anxious (P4)	• Trying to escape in a panic • Intense fear can also manifest as a collapse to the ground.

Aggressive behaviour is categorised into five main types on the breeding inspection form (see Table 7).

Table 8. Descriptions of aggressive behaviour in the breeding inspection form (Suomen Kennelliitto 2021a).

Class	Behaviour
A1	stiff posture, weight on front, stares, hairs may rise
A2	stares, hairs may rise, growls and/or barks, grabs air with teeth and/or shows teeth, does not attack
A3	growls and/or barks, grabs air and/or shows teeth, rushes towards people, attacks
A4	attacks strongly towards people, the strange dog or a voice; agitated, does not calm down; may bark; hair up; attacks and bites without leaving a mark
A5	angry (disproportionate to the situation or uncontrolled rage); attacks and bites without leaving a mark; attacks and bites the handler

In addition to longer behavioural and temperament tests, fearfulness can be detected quickly and easily by observing how the dog behaves when meeting a stranger and when exploring an unfamiliar space. **A fearful dog will avoid strangers and keep its tail between its hind legs rather than leaving its owner's side to explore** (K. Tiira, personal communication).

Salonen's (2020) study used an owner survey focusing on seven anxiety-like traits: noise sensitivity, fearfulness, fear of surfaces and heights, inattention/impulsivity, compulsion, separation related behaviour and aggression. The fear section of the questionnaire had previously been validated by behavioural tests and tests of noise sensitivity, fear and anxiety. Dogs were classified into high, moderate or low groups for each trait according to how frequently they exhibited the behaviour in question:

- Always (100 % of the time)
- Almost always (60–100 %)
- Often (40–60 %)
- Sometimes (20–40 %)
- Rarely (0–20 %).

For example, dogs that displayed a fear response to sounds on at least 40% of occasions were categorised as belonging to the high sound fear group.

5.1.7. Breeding

Since the behavioural disorders presented here, including fear aggression, are genetically correlated, breeding choices can affect their prevalence simultaneously. Breeding should also consider the behavioural tendencies of the dog's close relatives.

According to the Finnish Kennel Club's breeding strategy (Suomen Kennelliitto 2018), a dog used for breeding must have good nervous stability and breed-specific functional ability. This reduces the probability of it passing on character traits, such as shyness, to its offspring that make everyday life difficult and reduce well-being. Excessive fear or aggressive reactions are not desirable in any breed. While a dog may become frightened in unusual or unexpected situations, if everyday situations consistently cause the dog to become fearful or angry, or if the dog lacks the ability to handle and recover from agitation, this should be interpreted as an overreaction.

Breeding should avoid combinations which, according to existing knowledge, have a higher-than-average risk of producing offspring with an unbalanced temperament. The risk of such

inheritance is higher than average if the dog itself is timid, mentally weak, or aggressive (Suomen Kennelliitto 2014).

Therefore, breeding should be done with dogs that are brave enough to cope with an active daily life without displaying excessive fear or aggression. This ability to cope and adapt is known as resilience. Resilience in a puppy can be strengthened during the early stages of life through socialisation and exposure to a variety of positive experiences and environmental factors (Tiira 2019b). There is also some evidence that the owner's personality, the strength of the attachment between dog and owner, and positive owner-dog interactions (play, exercise, training and diet) are important factors in supporting resilience. Good maternal care also contributes to resilience, so these traits should be taken into account when breeding.

5.2. Skin conditions

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5.2.1. Atopic dermatitis

Atopy can cause skin symptoms in dogs, and less commonly, eye or respiratory symptoms. This article deals with atopic dermatitis. It is thought that around 10-15% of dogs have canine atopic dermatitis, but the exact prevalence is not known (Mazrier 2016).

Canine atopic dermatitis is defined as *a genetically predisposed, inflammatory, and pruritic (itchy) allergic skin disease with characteristic clinical features, commonly associated with IgE antibodies to environmental allergens* (Halliwell 2006). However, the current understanding is that this definition oversimplifies the complex and individualised clinical presentation and causative agents of atopic dermatitis. Some dogs with atopic dermatitis (14–25%) do not have an atopic allergic predisposition, i.e. they do not have IgE-mediated allergies or sensitisation to common allergens. This form of atopic dermatitis has been referred to as atopic-like dermatitis (Botoni 2019, Prelaud, 2007).

Canine atopic dermatitis is an immune-mediated disease. Initially, the immune system activates the T-helper 2 (Th2) response, which contributes to inflammation. Inflammation is a condition that does not necessarily involve pathogens, such as viruses or bacteria, entering the body.

The weakened skin barrier associated with atopic dermatitis allows fluid to escape from the body and allergens to enter it, where they encounter immune cells. Additionally, the skin's normally diverse microbiome becomes depleted.

Atopic dermatitis can be triggered by environmental allergens such as pollen or dust mites, or by food or microbes (Nuttall 2019, Marsella 2021). Environmental factors that predispose to and protect dogs against atopic dermatitis have been studied in several countries. Predisposing factors include growing up in an urban environment, high levels of hygiene in the home, and regularly washing the dog. Protective factors include living in a household with multiple dogs, the mother's diet during lactation (including non-commercial food) and walking the dog in the forest (Nødtvedt 2006, 2007, Harvey 2019, Meury 2011, Rostaher 2020).

Symptoms and impacts on well-being

The symptoms of atopic dermatitis can be categorised as primary or secondary. The primary symptoms are itching and redness. In the Favrot study, itching was the primary symptom in 61% of dogs (Favrot 2010a).

Secondary symptoms result from itching (skin damage caused by the dog itself), chronic inflammation, and a weakened skin barrier. These include self-induced hair loss, skin breakouts, skin thickening and darkening, and microbial skin and ear infections (Favrot 2010a, Bizikova 2015a, Hensel et al. 2015). Conjunctivitis has been observed in 21–30% of atopic dogs (Bizikova 2015a).

Symptoms have typical sites of occurrence. In dogs, these are most found on ears and lips, around the eyes, on the tips of the limbs, in the armpits, under the stomach and around the anus (Figure 1) (Favrot 2010a, Jaeger et al. 2010, Bizikova 2015a, Hensel et al. 2015). The Jaeger et al. (2010) study found that 62% of dogs had symptoms in their paws and 50% had an ear infection. Some differences in the typical locations of symptoms have been reported between breeds (Wilhelm et al. 2011, Jaeger et al. 2010).

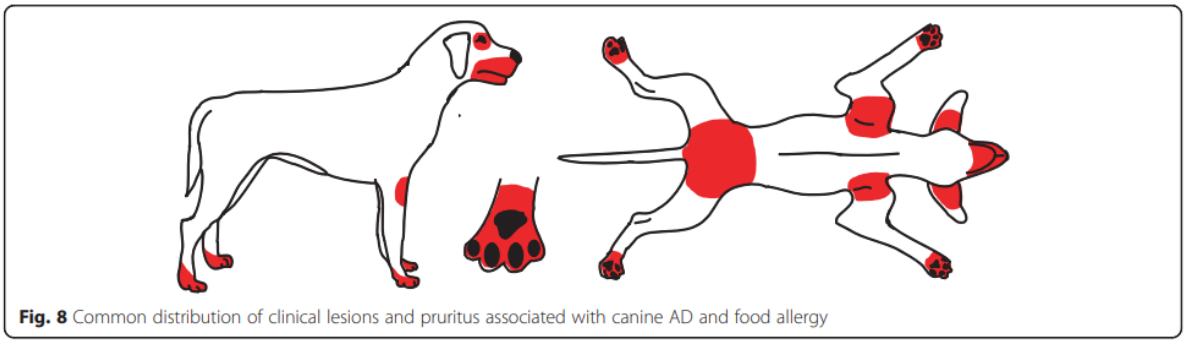


Figure 1. Typical sites of atopic dermatitis symptoms in dogs (Hensel et al. 2015).

Evaluation methods have been developed to assess the adverse effects of atopic dermatitis and other skin diseases in dogs (Noli, 2011a and b; Favrot, 2010b; Linek and Favrot, 2010). These methods are based on owners' assessments of the welfare issues experienced by themselves and their dogs.

These publications found that owners of more severely ill dogs felt that they needed to spend more time caring for them, and that the psychological and financial burden was greater. In particular, the impact of symptoms on sleep was perceived as a significant burden (Favrot 2010b, Noli 2011b). In addition to severe symptoms, owners may also perceive complex treatment as a burden (Spitznagel 2021).

However, a Finnish study found that the severity of symptoms does not necessarily correlate with the perceived impact of the disease on the well-being of the dog or owner (Seppänen et al. 2019). Owners may not be able to recognise that their dog's symptoms are causing harm. Some owners do not accept that atopic dermatitis is a lifelong condition, or do not understand that treatment must be continued for the dog's lifetime (Linek & Favrot 2010).

In humans, prolonged itching is considered a serious symptom, and the perceived harm can be equated with prolonged pain (Kini 2011).

Diagnosis and typical patient

Atopic dermatitis is a clinical diagnosis, meaning there is no specific test for it (Hensel et al. 2015). It is diagnosed based on typical symptoms and by ruling out other diseases that cause similar symptoms, such as parasitic infections. Variations in the typical clinical presentation can complicate the diagnosis.

Atopic dermatitis presents similarly regardless of whether there is an underlying allergic sensitisation or whether the triggering factor is an environmental allergen or a food. Symptoms triggered by environmental allergens typically appear in dogs aged between six months and three years (75% of cases) and may vary between seasons (Favrot 2010, Bizikova 2015a). Dogs with food sensitivities may be affected at a younger or older age than others. Some also exhibit gastrointestinal symptoms. Discriminatory diagnostics require an elimination diet with provocation stages (Favrot 2010a, Bizikova 2015a, Hensel et al. 2015).

Generally, no differences in morbidity have been observed between females and males (Favrot 2010b). However, individual studies have found a higher risk of disease in either sex of some breeds (Rostaher 2020, Bizikova 2015b).

Any dog can get atopic dermatitis, but certain breeds are particularly susceptible. The breeds identified as susceptible vary between studies from different countries and continents. The most common breeds identified in most studies are Golden Retrievers, Labrador Retrievers, White West Highland Terriers, German Shepherds, Boxers, Cocker Spaniels and French Bulldogs (Bizikova 2015b).

In Sweden, data from insured dogs were analysed, revealing that the breed most susceptible to atopic dermatitis was the Bull Terrier (Nødtvedt 2006). A study by Jäger et al. (2010) investigated breed susceptibility on three continents. Of the breeds found to be more susceptible, Golden Retrievers and German Shepherds were found to be susceptible in almost all study sites. An Australian study identified three breed groups at a higher risk of atopy: mastiffs, terriers, and retrievers (Mazrier 2016).

Favrot (2010b) developed eight criteria to aid diagnosis, which are listed below. Meeting five of these criteria results in a diagnostic sensitivity of 0.85 and a specificity of 0.79 (Favrot 2010b). Sensitivity refers to the proportion of patients with a positive diagnosis who actually have atopy (the so-called 'true positive'). Specificity refers to the proportion of patients with a negative diagnosis who do not have atopy (true negatives). The closer these numbers are to one, the better the diagnostic method. Hensel et al. (2015) provide practical guidelines for diagnosing atopic dermatitis.

Favrot's criteria for diagnosing atopic dermatitis (Set 1) (Favrot 2010b):

4. affected ear pinnae (but not pinnal margins)
5. affected front paws
6. age of onset < 3years
7. chronic or recurrent yeast infections
8. corticosteroid-responsive pruritus
9. mostly indoor lifestyle
10. nonaffected dorsolumbar area
11. pruritus without skin lesions at onset

Treatment and prognosis

Once a dog has developed atopic dermatitis, it usually experiences symptoms for the rest of its life. While atopic dermatitis is incurable, an effective treatment is available for most affected dogs (Nuttall 2019).

Treatment of atopic dermatitis is complex. It aims to avoid exacerbation triggers, prevent inflammation, and treat itching and inflammation. Most dogs require continuous medication to prevent itching and inflammation. Sedation therapy is effective for some dogs. It is also the only treatment that can prevent disease progression (Nuttall 2019).

Mode of inheritance

Atopic dermatitis is caused by a combination of environmental and genetic factors. The underlying genes of the disease may differ between breeds or geographical areas (Bizikova 2015b, Wood 2010, Tengvall et al. 2020). Genetic studies have identified several candidate genes that influence the immune system and skin barrier function, among other things (Bizikova 2015b, Nuttall 2019).

Strong breed predispositions are a sign of a genetic contribution to the disease. In British guide dogs, for example, the heritability estimate was high (47%), and the risk of developing the disease was highest (65%) if both parents had atopic dermatitis. The risk was lower if only one parent was affected, and lowest if neither parent had the disease (Shaw et al. 2004).

In a Swiss study, White West Highland Terriers were observed from birth until they were three years old. Of these, 52% developed atopic dermatitis. The heritability estimate was 31%. The risk was significantly higher if the mother had atopic dermatitis (Rostaher 2020).

In German Shepherds, a link was demonstrated between atopic dermatitis and the gene that controls the protein Plakophilin 2 (PKP2). Plakophilin 2 is crucial for the formation and proper functioning of the skin structure, suggesting an aberrant skin barrier as a potential risk factor for atopic dermatitis. (Tengvall et al. 2016).

Breeding

For most dogs, symptoms of atopic dermatitis appear by the age of three years. For risk breeds, it is best to select healthy dogs over this age for breeding.

Atopic dermatitis is highly heritable and causes significant welfare problems. It is also worth noting that a dog made symptom-free by medication can still pass atopic dermatitis on to its offspring.

5.2.2. Conformational pododermatitis

Pododermatitis is inflammation of the paws, affecting the footpads, nails, nail folds, and interdigital spaces (the skin between the toes). It is a complex problem that can be caused by a number of skin or general health conditions (Duclos 2013). The most common causes are atopic dermatitis and conformation problems (Nuttall 2019), which are both hereditary. In this article, we will focus on conformational pododermatitis.

Predisposing factors and underlying causes

Pododermatitis is a multifactorial disease. The contributing factors can be categorised as *primary, predisposing, secondary,* or *perpetuating* (Gow 2015a, Nuttall 2019).

The most common *primary cause* of pododermatitis is atopic dermatitis.

Predisposing factors rarely cause the disease alone but contribute to its development. These include short hair, which damages hair follicles more easily than long, soft hair, obesity, and joint disease (Nuttall 2019, Kovacs 2005, Paterson 2012).

The distinction between predisposing and primary causes is not always clear. Improper paw shape and/or conformation can be considered either a predisposing or a primary factor (Gow 2015a, Nuttall 2019).

Secondary causes are infections. On the other hand, altered paw anatomy predisposes the skin to bacterial and yeast infections.

Factors that perpetuate pododermatitis arise from ongoing inflammation and skin damage and prevent healing. These include skin thickening and scarring, nodules and "cysts", deep tissue pockets, ulceration, ingrown hairs, and fistulas. These changes lead to the accumulation of dirt and secretions, as well as infections (Duclos 2008, Nuttall 2019).

Pseudo paw pad formation and furunculosis

Especially in heavy and overweight dogs, and dogs with wide paws, partial weight transfer occurs from the paw pads to the hairy skin. This hairy skin is not designed to withstand such stress, however, and begins to thicken and resemble a paw pad. This thickened skin contains hair follicles and is known as a pseudo paw pad (Duclos 2008, Nuttall 2019).

The hair follicles of the pseudo paw pad continue to function, producing hair, skin cells, sebum and sweat. However, these contents cannot escape as the opening is constricted by the thickened surface. The hair follicle bulges and may break inside the skin. Once inside the dermis, the contents of the hair follicle cause strong foreign body and inflammatory reactions in the skin. Initially, this appears as a lump or blister, and when it bursts it becomes a fistula. An inflamed, broken hair follicle is called a furuncle. Furuncles can occur anywhere on hairy skin.

Furunculosis is a colloquial term for inflammation that typically affects the interdigital spaces. The intense inflammation that develops cannot be discharged through the thickened false paw pad and therefore travels in the other direction, i.e. between the toes. Therefore, furunculosis of the interdigital spaces is the result of a skin condition affecting the paw pads (Duclos 2008, Bajwa 2016, Nuttall 2019).

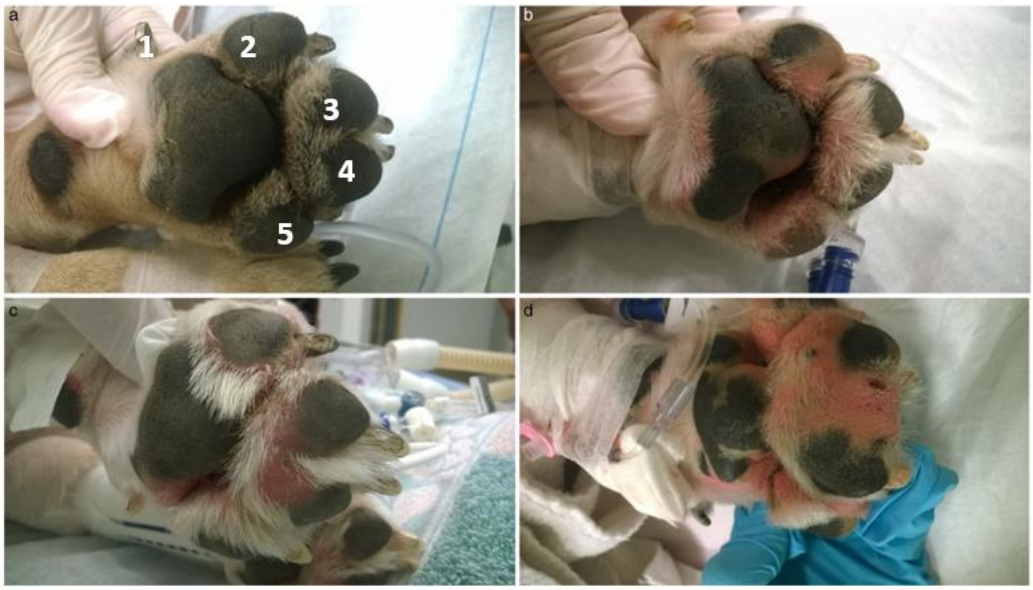


Figure 2. The different degrees of pseudo paw pads in English Bulldogs.: a) normal paw pads b) mild, c) moderate, d) severe (Seppänen et al. 2019).

Prevalence

The exact prevalence of inflammation due to conformation problems of the paws and furunculosis is unknown, but these are common issues encountered by veterinarians specialising in skin diseases.

A Finnish study found that 93% of 27 English bulldogs aged 2–5 years had varying degrees of pseudo paw pads and that nine of them had furunculosis at the time of the study (Seppänen et al., 2019). As pseudo paw pads worsen with age, they are expected to be less severe and less frequent in younger dogs than in older dogs. In a study by Kovács et al. (2005), approximately 15% of beagles bred for use in experiments had furunculosis. This figure increased to 55% when dogs over four years of age were evaluated.

Breeds at risk

Large breeds are particularly susceptible to structural and positional defects of the paws. In the Duclos study (2008), 28 dogs were treated for furunculosis using laser surgery. Labrador Retrievers were by far the most common breed (46%), but other large breeds were also treated (e.g. Irish Setters, St. Bernards, Alaskan Malamutes, Bullmastiffs, Pyrenean Mountain Dogs, Rottweilers, Dobermanns, and English Bulldogs).

The distribution of weight across the paws has been studied in Labrador Retrievers, which have wider paws and a greater distance between the toe pads than sighthounds. This can cause the weight-bearing surface to partially shift from the paw pads to the hairy skin (Besançon 2004). Since dogs carry more weight on their front paws, pseudo paw pads are more prevalent on the front paws than the hind paws (Besançon 2004, Kovács 2005, Duclos 2008, Schwarz et al. 2017, Seppänen et al. 2019). Labrador Retrievers have been found to carry more weight on the outer edges of their paws. This results in pseudo paw pads and consequent furunculosis on the outer edges of their paws (between toes 4 and 5) (Duclos 2008, Schwarz et al. 2017). In many heavy-built dogs, false toes occur on toes 3 and 4, which are

the main weight-bearing toes. This leads to furunculosis between the middle toes (Seppänen et al. 2019, Besançon 2004).

Pseudo paw pads and furunculosis are also found in small dogs. Small breeds such as Pekingese and White West Highland Terriers may have splayed feet, which can cause weight bearing on the hairy skin (Whitney 1970).

Symptoms and impacts on well-being

Symptoms of conformational pododermatitis include itchiness or pain in the paw area, redness, swelling, hair loss, ulcers and lumps that may rupture and secrete blood or pus (furuncles). The paws may become very swollen. Pain may manifest as lameness or tenderness to touch. Furuncles may leave scars, in which case they may not be painful, but they are less responsive to treatment. Symptoms may be present in one or more paws (Bajwa 2016, Gow 2015a, Nuttall 2019).

In addition to the furunculosis they cause, pseudo paw pads constrict the pads and cause abrasion damage. The skin between the toes is prone to inflammation and soreness.

Conformational pododermatitis can cause significant pain, making it difficult or impossible for an otherwise lively dog to move around. In the worst cases, paw inflammation can completely cripple the dog, rendering it immobile (Gow 2015b, Bajwa 2016, Nuttall 2019).

Treatment and prognosis

It is important to treat skin inflammation and pain to improve the dog's quality of life. The aim of treatment is to identify and address the underlying causes of pododermatitis where possible. If the cause is a chronic inflammatory disease, such as atopic dermatitis, managing the disease early on can prevent irreversible, unresponsive changes to the skin on the paws resulting from chronic inflammation.

If a dog has both atopic dermatitis and paw malposition, the inflammation can be severe. In some cases, the underlying conformational causes can be addressed; for instance, there are treatments for joint problems that can alleviate the symptoms. However, it is not always possible to correct structural problems to the extent that the symptoms cease (Paterson 2012, Bajwa 2016, Nuttall 2019, Gow 2015b).

Surgical treatment of pseudo paw pads is possible in severe cases. They can be removed using a surgical laser (Duclos 2008). However, the underlying cause of the problem must be considered, as if left uncorrected it can easily lead to recurrence (Nuttall 2019, Gow 2015b). In fusion podoplasty, the hairy skin between the toes is completely removed to prevent the formation of pseudo pads or furunculosis (Swaim 1991, Papazoglou 2011, Lilja 2016).

Mode of inheritance

The structural and positional defects of the paws have a complex origin. They can be caused by joint and back problems, many of which are hereditary. However, not all joint and back problems lead to skin problems on the paws. Structural predisposing factors, such as a heavy build and splayed feet, are desirable traits in many breeds and are encouraged through breeding.

Breeding

Conformational pododermatitis in the paws are challenging because it cannot always be cured through treatment. At their worst, they can cripple otherwise healthy, young dogs full of life. Therefore, it is important to only breed dogs with healthy paws.

Further research is required into breed-specific conformational factors and defects that lead to pseudo paw pads. Breed-specific risk factors can be identified by collecting data on individual dogs. Data from both affected dogs and healthy individuals is needed to achieve this. This information can be collected through veterinary visits and by examining paws and conformation at shows and breeding inspections. The risk of joint and back problems should also be reduced through breeding.

Since skin conditions on the paws tend to appear with age and are rare in young dogs except in cases of allergy, breeding should be postponed until later in life, particularly for high-risk breeds.

5.3. Heart disease

Heart disease is a major cause of morbidity and mortality in dogs worldwide. According to a study by Bonnett et al. (2005), it is the fourth most common cause of death in insured Swedish dogs.

Welfare issues

The welfare issues caused by heart disease are usually due to congestive heart failure. In heart failure, the heart is unable to maintain normal blood flow, resulting in a reduced oxygen supply to the body and a build-up of fluid in the tissues. The condition progresses gradually and eventually leads to death. Symptoms include coughing, shortness of breath, reduced exercise tolerance, weakness, fainting and restlessness at night.

Some heart conditions can lead to sudden death in young dogs.

Treatment options

Most common heart conditions in dogs are chronic, and there is no cure. Exceptions to this include angioplasty for pulmonary arterial stenosis and surgical repair of an open arterial duct. There is an antiarrhythmic drug for arrhythmias, but its effectiveness varies. Medications can alleviate the symptoms of heart failure, improving the dog's quality and duration of life.

Dog breeds/types at risk

Several studies have examined the prevalence of heart disease in dogs. The breeds most at risk vary between studies because heart disease is common in dogs and the breeds studied differ from one study to another.

One study (Egenvall et al. 2006) investigated the prevalence of heart disease as a cause of death in dogs under 10 years of age of different breeds, using data from a Swedish insurance company. The risk was highest in Irish Wolfhounds, Cavalier King Charles Spaniels, Great Danes, St. Bernards, Newfoundlands, Leonbergers, Dobermanns, Finnish Hounds, Boxers, Giant Schnauzers, Cocker Spaniels, and Flat Coated Retrievers (see Table 9).

Table 9. The dog breeds at the highest risk of dying from heart disease by the age of 10 (Egenvall et al. 2006).

Table 2. The number of dog-years at risk (DYAR) represented by each of 12 higher-risk breeds.[a]

Breed (Rank-Model Rank)	DYAR	Number of Deaths					Age, Median (Range)	Mortality (95% CI)		
		Total	Male	Female	With MMVD[b] (% of all)	With DCM[c] (% of all)		Total	Male	Female
Irish Wolfhound (1; 1)	2,390	85	53	32	3 (4)	38 (45)	7.5 (1.0–10)	356 (280–431)	459 (336–583)	259 (169–349)
Cavalier King Charles Spaniel (2; 2)	33,977	840	525	315	309 (37)	32 (4)	8.3 (0.6–10)	247 (231–264)	309 (283–336)	185 (165–206)
Great Dane (3; 3)	4,357	78	55	23	1 (1)	43 (55)	6.4 (0.3–9.5)	179 (139–219)	279 (206–353)	96 (57–136)
St Bernard (4; 4)	2,518	38	29	9	0 (0)	23 (61)	7.6 (2.3–10)	151 (103–199)	251 (160–342)	66 (23–109)
Newfoundland (5; 5)	8,086	117	76	41	0 (0)	73 (62)	7.5 (1.2–10)	145 (118–171)	202 (157–248)	95 (66–124)
Leonberger (6; 6)	6,993	74	43	31	1 (1)	29 (39)	7.4 (0.3–9.9)	106 (82–130)	124 (87–162)	88 (57–119)
Dobermann (7; 7)	7,714	61	39	22	1 (2)	36 (59)	7.8 (4.3–9.9)	79 (59–99)	108 (74–142)	54 (31–76)
Finnish Hound (8; 8)	12,534	66	44	22	2 (3)	20 (30)	6.3 (0.5–10)	53 (40–65)	74 (52–96)	33 (19–47)
Boxer (9; 9)	13,269	61	39	22	0 (0)	27 (44)	8.1 (0.2–10)	46 (34–58)	59 (41–78)	33 (19–47)
Giant Schnauzer (10; 11)	6,984	28	19	9	0 (0)	10 (36)	7.4 (0.6–9.6)	40 (25–55)	58 (32–83)	24 (8–40)
English Cocker Spaniel (11; 10)	24,596	98	51	47	4 (4)	42 (43)	7.6 (0.9–9.9)	40 (32–48)	44 (32–56)	36 (26–47)
Flat-Coated Retriever (12; 12)	21,818	57	40	17	2 (4)	21 (37)	7.8 (0.4–10)	26 (19–33)	38 (26–50)	15 (8–22)
Total	145,236	1,603	1,013	590	323 (20)	394 (25)	8.0 (0.2–10)	110 (105–116)	145 (136–153)	78 (72–85)

[a] The total number of cardiac deaths, the cardiac deaths by sex, myxomatous valve disease (MMVD), and cardiomyopathy (DCM) are shown. Also shown is the age distribution at cardiac death, and breed-specific, and sex and breed–specific cardiac mortality (cardiac deaths per 10,000 DYAR), with 95% confidence intervals (CIs). Breeds were eligible if either ≥25 dogs had life claims of cardiac diagnosis or there were >8,000 DYAR. The study population was life-insured dogs during 1995 to 2002 in Sweden. Breeds are ranked by decreasing order of cardiac mortality. Included is the rank from the Cox proportional frailty model. Data are based on a total of 43,335 dogs.
[b] Included in the MMVD classification.
[c] Included in the DCM classification.

Other breeds with an above-average risk of heart disease include American Staffordshire Terriers, Chihuahuas, German Shepherds, French Bulldogs, English Bulldogs, Weimaraners, Malteses, Rottweilers, Labrador Retrievers, Golden Retrievers, Poodles, Miniature German Pinschers, Schnauzers, Yorkshire Terriers, Australian Shepherds, Border Collies, Dachshunds, Dogue de Bordeauxs, and Bull Terriers (see Table 9). (Hunt et al. 1990, Tidholm 1997, Baumgartner & Glaus 2003, Egenvall et al. 2006, MacDonald 2006, Oliveira et al. 2011, Brambilla et al. 2020, Lucina et al. 2021).

5.3.1. The most common hereditary heart diseases in dogs

The most common hereditary heart diseases in dogs include valvular and myocardial degeneration, as well as various congenital defects. Congenital defects are present at birth, whereas degenerative diseases develop over time, sometimes at an early age.

Degenerative cardiac diseases

Myxomatous mitral valve degeneration (MMVD) (https://omia.org/OMIA000654/9615/)

- Several names: mitral valve disease, valve degeneration, endocardiosis.
- Usually affects the left atrioventricular valve but can also affect the right atrioventricular valve.
- Usually develops slowly with no clinical signs in the early stages. Gradually leads to heart failure.

- The degenerated valve leaks, resulting in a murmur. The intensity of the murmur indicates the degree of valve degeneration and predicts the progression of heart failure (e.g. Häggström et al. 1995).
- The disease typically occurs in small and medium-sized dogs. In most breeds, it occurs at an older age and progresses slowly. An exception is the Cavalier King Charles Spaniel, in which the disease is particularly common and occurs at an unusually early age.
    - In the VetCompass veterinary database, cardiac murmur was the most common disease/symptom treated in Cavaliers (affecting 30.9% of the study population of 1749 dogs; Summers et al. 2015).
    - According to Swedish insurance data, the disease is 20 times more prevalent in Cavaliers than in other breeds (Bonnett et al. 2005, Egenvall et al. 2005).
    - Cavaliers are also at a higher risk of dying from this disease than other breeds (Egenvall et al. 2006, Mattin et al. 2019). It caused around 50% of deaths in dogs under 10 years old and 23% of deaths in dogs under 8 years old (Bonnett et al. 2005, Egenvall et al. 2005). In the UK, heart disease accounted for 43% of deaths in the breed (The Kennel Club 2013).
- Mode of inheritance: polygenic. The heritability estimates were 0.33 for the presence of a murmur and 0.67 for its intensity (Lewis et al. 2011, British Cavalier King Charles Spaniel data).

<u>Myocardial degeneration</u>

Dilated cardiomyopathy (DCM) (https://omia.org/OMIA000162/9615/)

- Progressive myocardial degeneration
- Occurs in dogs of all ages but is most common in middle-aged and older dogs.
- Causes enlargement of the heart (especially the left ventricle), poor myocardial contractility, and heart failure. Symptoms may appear suddenly.
- Typically occurs in large dogs. Susceptible breeds include Boxers, Dobermanns, Irish Wolfhounds, Great Danes, Newfoundlands, Cocker Spaniels, American Cocker Spaniels, Portuguese Water Dogs, and Weimaraners (omia.org). For example:
    - Particularly common and severe in Dobermanns, affecting 20–50% of dogs (Wess et al. 2010, Heikkinen 2013).
    - In Great Britain, the prevalence in Great Danes is 36% (Stephenson et al. 2012).
    - In Irish Wolfhounds, the prevalence is around 20–26% (Distl et al. 2007, Vollmar 2000). The breed was 29 times more likely to die of cardiac causes than average (Egenvall et al. 2005, Swedish insurance data). Compared to all other breeds in the dataset, this breed had the highest probability of dying by 5, 8, and 10 years of age (91% of insured dogs of this breed died by 10 years of age).
- The disease is associated with ventricular arrhythmias and atrial fibrillation. These arrhythmias worsen the prognosis and can lead to sudden death without prior symptoms (Vollmar 2000, Brownlie 1991, Vollmar et al. 2019, Simpson et al. 2016).
    - Brownlie and Cobb (1999): 12% of asymptomatic Irish Wolfhounds had atrial fibrillation. 46% of dogs diagnosed with DCM were found to have atrial fibrillation on initial examination. All individuals who had developed heart failure had atrial fibrillation. Vollmar (2000) and Martin et al. (2009): 88–94% of dogs with DCM had atrial fibrillation.

    - The heritability estimate of atrial fibrillation in Irish Wolfhounds in North America was found to be 0.69 (Fousse et al. 2019).
- Research carried out in the 1990s investigated how long dogs lived after diagnosis. Several breeds were involved. The one-year survival probability was 38% at two years of age and 28% at one year of age. Following a heart failure diagnosis, these probabilities were 18% and 8%, respectively (Monnet et al. 1995, Tidholm et al. 1997). Today, survival can be prolonged with the help of drugs.
- Various proposals have been made regarding the mode of inheritance. Polygenic inheritance is considered the most likely (Distl et al. 2007, Philipp et al. 2012, Simpson et al. 2016). Several major genes (quantitative trait loci, or QTLs) may be present in a single breed.
    - In the Portuguese Water Dog, for example, a recessive variant causing the juvenile form has been identified. A genetic test for this variant is available (Dambach et al. 1999, Alroy et al. 2000, Sleeper et al. 2002).
    - In Welsh Springer Spaniels, a dominant variant has been identified in a particular lineage. This mutation occurred in the sire of the litter (Yost et al. 2019).
    - In Schnauzers, a recessive variant has been identified (Leach et al. 2014). 1.5% of dogs tested were homozygous (affected). One in five dogs tested carried at least one copy of the variant. Homozygotes had a high risk of disease and an 80% shorter average lifespan. The variant was also found in Giant Schnauzers, where it was associated with the same disease and premature death (Leach et al. 2022).
    - Two variants associated with this disease have been identified in Dobermanns (Mausberg et al. 2011, Meurs et al. 2012). However, these do not explain all cases, suggesting that there are likely multiple underlying variants.

Right ventricular cardiomyopathy or arrhythmogenic right ventricular cardiomyopathy (ARVC)(https://omia.org/OMIA000878/9615/)

- Occurs in Boxers and English Bulldogs (Meurs et al. 2010, Holdt et al. 2022).
- Occurs in dogs of all ages but is most common in middle-aged and older dogs.
- The arrhythmia can develop into ventricular fibrillation, which is fatal. Symptoms can include sudden death, meaning that many dogs die without being diagnosed.
- Mode of inheritance: polygenic. A variant strongly associated with the disease has been identified but does not explain all cases (Meurs et al. 2010, Cattanach et al. 2015). This variant is also strongly associated with dilated cardiomyopathy in Boxers (Meurs et al. 2013).

Ventricular arrhythmias and sudden death (https://omia.org/OMIA001040/9615/)

- Has been described in young German Shepherds, Leonbergers, Rhodesian Ridgebacks and Boxers, with no other clinical signs of cardiac abnormality (Moise et al. 1994, Jesty et al. 2013, Meurs et al. 1999, 2019, Wiberg et al. 2019). The heart also appears normal upon pathological examination (Moïse et al. 1994).
- Studies by Moïse et al. (1994, 1997a–c, 1999) describe this phenomenon in German Shepherd dogs. Arrhythmias occur between three and 24 months of age with varying degrees of severity. At one extreme, arrhythmias occur infrequently and are not life-threatening. At the other extreme, the dog dies suddenly, usually around 5–9 months of age. The arrhythmias disappear after 24 months of age, after which the

dog is healthy. However, it can still pass arrhythmias on to its offspring (Cruickshank et al. 2009).
- An autosomal dominant mode of inheritance has been proposed in Boxers (Meurs et al. 1999), while a polygenic mode has been suggested in German Shepherds (Cruickshank et al. 2009).
    - In US German Shepherds, the heritability estimate was 0.46–0.52 for each of the three severity levels (Cruickshank et al. 2009).
    - A recessively inherited variant associated with arrhythmias has been identified in a particular lineage of Rhodesian Ridgebacks (Meurs et al. 2019).

Congenital heart diseases

Subaortic stenosis (SAS) (https://omia.org/OMIA000952/9615/)

- Can manifest in varying degrees of severity, ranging from mild to severe. In mild cases, there are no symptoms. The more severe the stenosis, the more severe the symptoms and the shorter the life expectancy. Symptoms range from fainting and weakness to breathing difficulties (heart failure symptoms) and sudden death in a seemingly healthy dog.
- Susceptible breeds include the Boxer, Bouvier, Bull Terrier, Pitbull Terrier, Bullmastiff, German Shepherd, Dogue de Bordeaux, Golden Retriever, Newfoundland, and Rottweiler (Ontiveros & Stern 2021, Ontiveros et al. 2019, Oliveira et al. 2011, Ohad et al. 2013, Bussadori et al. 2009, Chetboul et al. 2006).
- There are several proposals regarding the mode of inheritance:
    - Polygenic or autosomal recessive, proposed in the Golden Retriever (Stern et al. 2012, Ontiveros et al. 2019).
    - Autosomal recessive – proposed in the Dogue de Bordeaux, Bullmastiff, Golden Retriever and Rottweiler (Ontiveros et al. 2019, Ohad et al. 2013).
    - Autosomal dominant with incomplete penetrance, which actually refers to polygenic, has been proposed in humans and Newfoundland dogs (Pyle et al. 1976, Stern et al. 2014, Petsas et al. 1998).
    - In Newfoundland dogs, a variant of the PICALM gene has been associated with the disease (Stern et al. 2014), but this association is weak, and the variant is not useful for genetic testing (Drögemüller et al. 2015).
    - In a study of Newfoundland dogs, the severity of the disease in the parents did not predict the severity in the offspring; for example, mild stenosis in the parent may be inherited as severe stenosis in the offspring (Pyle et al. 1976).

Pulmonary stenosis (PS) (https://omia.org/OMIA000842/9615/)

- The symptoms and manifestations are like those of aortic stenosis.
- Often occurs concurrently with aortic stenosis (26.4% of cases in the Oliveira et al. (2011) study).
- Susceptible breeds include the Boxer, Bouvier, Bull Terrier, Bullmastiff, English bulldog, German Pinscher, Pitbull Terrier, French Bulldog, German Shepherd, Schnauzer, Dogue de Bordeaux, Golden Retriever, Newfoundland, Rottweiler, American Staffordshire Terrier), White West Highland Terrier, and Chihuahua (e.g. Oliveira et al. 2011, Ontiveros et al. 2019, Bussadori et al. 2001, 2009).

- Mode of inheritance: monogenic (e.g. Beagle, Patterson et al. 1981). An autosomal recessive mode of inheritance has also been proposed in English Bulldogs (Ontiveros et al. 2019).
- Can occur to varying degrees within the same litter (Ontiveros et al. 2019, Patterson et al. 1981).

Patent ductus arteriosus (PDA) (https://omia.org/OMIA000779/9615/)

- A foetal vascular connection between the aorta and the pulmonary artery; a short-circuit. This connection normally closes immediately after birth.
- Can be surgically repaired. If left untreated, leads to heart failure in most dogs within the first year of life (Eyster et al. 1976, Stanley et al. 2003).
- Susceptible breeds include the Stabyhoun, Dobermann, German Shepherd, New-foundland, Maltese, Poodle, Cavalier King Charles Spaniel, Border Collie, Chihuahua, and Australian Shepherd (Oliveira et al. 2011, den Toom et al. 2016, Brambilla et al. 2020).
    - In the Dutch Stabyhound population, the prevalence was 1.05% between 2009 and 2012. Therefore, the disease is 7–13 times more prevalent in this breed than in the rest of the dog population (den Toom et al. 2016).
- Mode of inheritance: polygenic threshold trait, with heritability demonstrated in Miniature Poodles in the 1970s (Patterson et al. 1971).
    - Heritability estimate in the Stabyhoun is 0.41–0.51 (den Toom et al. 2016).

Septal defects

- The larger the opening, the more likely it is to cause symptoms. A small opening is often asymptomatic.
- Ventricular septal defect (VSD); https://omia.org/OMIA001041/9615/):
    - Allows blood to flow directly between the ventricles, bypassing the pulmonary circulation. This results in oxygen deprivation, shortness of breath, and poor exercise tolerance.
    - In nearly half of cases (48%), occurs alongside another developmental disor-der, most commonly pulmonary stenosis or patent ductus arteriosus (Oliveira et al. 2011).
    - Susceptible breeds: German Pinscher, French Bulldog, German Shepherd, and Maltese (e.g. Oliveira et al. 2011, Lucina et al, 2021).
    - Mode of inheritance: polygenic.
- Atrial septal defect (ASD) https://omia.org/OMIA000089/9615/
    - Rare
    - Mode of inheritance not known

Valve dysplasias

- Mitral valve dysplasia (MD or MVD) and tricuspid valve dysplasia (TD or TVD; https://omia.org/OMIA001345/9615/)
- Both dysplasias cause valve leakage and therefore increase the risk of heart failure.
- Susceptible breeds for TVD: Labrador Retriever, English Bulldog, Golden Retriever and Dogue de Bordeaux (Famula et al. 2002, Ohad et al. 2013, Oliveira et al. 2011).

- An autosomal recessive (Ohad et al., 2013; Dogue de Bordeaux) and a recessive major gene (Famula et al. 2002) have been proposed as the modes of inheritance of TVD. Autosomal dominant inheritance with incomplete penetrance, usually meaning polygenic, has also been proposed (Andelfinger et al. 2003).
    - The high heritability estimate of TVD in US Labrador Retrievers (0.71; Famula et al. 2002) suggests the presence of a major gene.

Diagnosing inherited heart disease in dogs

Heart auscultation

Heart auscultations are performed to identify murmurs. Murmurs are associated with various cardiac conditions, such as degenerative valve disease and congenital heart disease. It is not possible to determine which cardiac condition is present based on a murmur alone. However, it is not possible to determine which cardiac condition is present based on a murmur alone. A cardiac ultrasound is usually recommended as a follow-up test instead. Murmurs cannot always be detected in association with dilated cardiomyopathy. A murmur may also be the result of another illness or may be benign, i.e. not associated with a cardiac condition.

Murmur findings are assessed as follows:

- The timing of the murmur: systolic, diastolic or continuous.
- Location of maximal intensity murmur: mitral valve region, pulmonary artery region, aortic region, tricuspid valve region or non-localised.

The intensity of a heart murmur is classified according to the following scale:

- Grade 1 – Very faint murmur with low intensity that can only be heard in a peaceful setting
- Grade 2 – Localised faint murmur, which can nevertheless be heard immediately
- Grade 3 – Medium-level murmur, can also be heard from a broader area, own heart sounds audible
- Grade 4 – Strong murmur, which can be heard from a broad area, own heart sounds become inaudible, no palpable thrill
- Grade 5 – Strong murmur with a palpable thrill. Readily audible when the stethoscope comes close to the dog's chest
- Grade 6 – Strong murmur with a palpable thrill. Audible even when the stethoscope is lifted off the dog's chest

The intensity of a murmur is not static or easily categorised; it can vary over time. For instance, the intensity of a murmur caused by aortic stenosis or a ventricular septal defect can change significantly over time, becoming stronger or weaker (Finnish Kennel Club – Suomen Kennelliitto, Heart Working Group 2014).

Ultrasound examination

An ultrasound examination shows the structure of the heart and can be used to assess its function. It can also be used for diagnosis and determining the severity of disease. This examination is always performed alongside an electrocardiogram (Wiberg 2016a).

An ultrasound scan can detect all possible heart diseases simultaneously (Wiberg 2016a). For instance, ventricular septal defect often occurs alongside other cardiac developmental

disorders, such as pulmonary stenosis and patent ductus arteriosus. For this reason, Oliveira et al. (2011) consider ultrasound imaging to be important for breeds with cardiac developmental abnormalities, even when the abnormality that potentially explains the clinical findings has already been identified.

Electrocardiogram (ECG)

An electrocardiogram is performed to check the heart's electrical activity and detect possible arrhythmias. Most commonly, a five-minute ECG recording is taken. Some transient arrhythmias may not be detected in such a short recording. In this case, a 24-hour long-term recording (Holter monitoring) is used.

Heart Disease in Breeding

A few studies have examined the impact of breeding programmes on heart disease in dogs.

- A compulsory breeding programme based on auscultation and ultrasound examination significantly reduced the incidence of myxomatous mitral valve degeneration in Danish Cavalier King Charles spaniels over eight to ten years (Birkegård et al. 2016).
- Following a breeding programme based on auscultation appeared to delay the onset of a murmur associated with myxomatous mitral valve degeneration until later in life (Swift et al. UK, 2017). However, adherence to this voluntary programme was poor.
- A compulsory breeding programme based on ultrasound examinations reduced the prevalence of severe pulmonary and subaortic stenosis in Italian Boxers between 1999 and 2004. (Bussador et al. 2009)

Although risk genes for heart disease have been identified in certain dog breeds, they do not account for all cases. Therefore, clinical heart examinations of breeding dogs are necessary for breeding programmes.

Age at examination and breeding

Congenital heart diseases can usually be detected by the age of one year. They are often associated with a murmur, which is frequently audible in puppies but not always in cases of stenosis (Wiberg 2016b). Conversely, a murmur in a puppy does not necessarily indicate heart disease; it may be harmless and disappear with age.

In most cases of degenerative cardiac diseases, dogs are over two years old at diagnosis (Oliveira et al. 2011). In breeds and lines where degenerative diseases and juvenile arrhythmias are common, dogs should not be used for breeding before reaching this age. Additionally, the number of litters per dog should be minimised to prevent the spread of harmful genetic variants that cause heart disease.

When it comes to heart diseases that occur in middle age, breeding decisions should also consider the health of the breeding dog's parents. Only dogs whose parents were examined when they were at least five years old and found to be healthy should be used for breeding.

Suitable testing methods for different diseases

Auscultation can be used as a basic screening test for myxomatous valve disease (MMVD) and congenital heart disease (Wiberg 2016b). If a murmur is detected, ultrasound imaging of the heart should be performed and, if necessary, an ECG should be recorded.

Ultrasound is the most reliable test for determining the cardiac status of a breeding dog. It is the only suitable test for screening for cardiomyopathies, such as DCM and ARVC. If arrhythmias associated with the disease are present, an additional ECG (either a five-minute ECG or a Holter monitor) is required. ARVC usually requires Holter monitoring. Sudden death caused by juvenile ventricular arrhythmias also usually requires Holter monitoring.

The Finnish Kennel Club's Heart Working Group comprises expert veterinarians specialising in heart disease. The working group has defined the examinations that should be carried out on breeding dogs regarding heart disease. The diagnostic criteria for these diseases are based on scientific, peer-reviewed publications. To ensure consistency, the WG recommends that ultrasound examinations of breeding dogs are performed by a WG-approved veterinarian. Currently, there are 16 such veterinarians in Finland (as of 26/10/2022).

The Heart Working Group has compiled information on heart screening at https://www.kennelliitto.fi/kasvatus-ja-terveys/koiran-terveys/koiran-terveystutkimukset/sydansairauksia-kartoitetaan-sydankuuntelun-ja-ultraaanitutkimuksen-avulla and https://www.kennelliitto.fi/-kasvatus-ja-terveys/koiran-terveys/koiran-terveystutkimukset/sydanlausunto/mita-sydan-tutkimus-tutkii. It has also made recommendations for the screening of breeding dogs in breeds with heart disease, upon request: https://www.kennelliitto.fi/kasvatus-ja-terveys/koiran-terveys/koiran-terveystutkimukset/sydanlausunto/kennelliiton-sydantyoryhman-ohjeistuksia-eri-roduille.

Validity of the test result

For degenerative diseases, breeding dogs that are found to be healthy should undergo annual testing, as the disease can progress significantly within a year. Changes can usually be detected before symptoms appear, which is important for breeding purposes. For example, changes in dilated cardiomyopathy can be detected two to three years before symptoms appear (Wiberg, 2016a).

For congenital disorders, one ultrasound examination is sufficient if the dog is at least 12 months old. If auscultation is the only examination method used, this should be repeated at least every 24 months.

5.4. Dental and oral disorders

Dogs can suffer from oral and dental diseases, some of which are related to small size and brachycephaly.

A previous study by Kempe and Mäki (2020) discussed typical dental problems in brachycephalic dogs. The positioning of the teeth in these dogs is affected due to the shortened jaw. The number of teeth remains the same as in mesocephalic and dolichocephalic dogs. Additionally, small dogs have larger teeth in relation to the size of their jaw. These factors lead to malformations of the head and mouth structures, various dental diseases and malocclusion especially in small brachycephalic dogs. If the teeth do not fit properly within the confines of a short jaw, crowding can occur, causing the teeth to rotate and/or move out of place.

Other dental problems in brachycephalic dogs include unerupted deciduous teeth (see Figure 3), partially or fully unerupted teeth, dental cysts and progressive periodontitis.

In addition to the typical dental issues associated with brachycephalic dogs, there are many other oral and dental problems related to the conformation of the dog. Such diseases and

defects are inherited in a polygenic manner. Since conformation traits typically have high heritabilities, reducing these defects through breeding is relatively easy.

Figure 3. Unerupted deciduous teeth (Gawor 2013).

A dog's normal dentition consists of 42 teeth, arranged as follows:

- 12 incisors,
- 4 canines,
- 16 premolars, and
- 10 molars.

Dental problems to consider in breeding

(Sources, unless otherwise noted: Kuntsi 2021; Kuntsi, personal communication).

For non-conformational problems, the mode of inheritance is mentioned if there are published studies on it.

In particular, in brachycephalic dogs:

- twisted teeth (especially the maxillary second, third and fourth premolars; Döring et al., 2018; Selba et al., 2020);
- crowding of the teeth, and
- displacement of teeth. The tooth may be in the palate, for example.

Severe periodontitis

- Potential problem in all dogs weighing less than 5 kg and brachycephalic dogs, where tooth crowding causes plaque to accumulate.
- Tight spaces between teeth and a diet of soft foods increase the risk.
- The bacterial mass (plaque) that accumulates on the tooth surface first causes gingivitis, which progresses to periodontitis. Removing plaque cures gingivitis; must be done regularly to prevent the infection from recurring.
- Periodontitis destroys the jawbone around the tooth, resulting in increased tooth mobility and pain.
    - Can also cause tooth loss and tooth root abscesses, and, in the worst cases, fractures of the jawbone.
    - An untreated root abscess can erupt through the skin into the mouth or renal cavity.
    - Predisposes to disease elsewhere, e.g. the heart, liver and kidneys.

- An incurable condition.
- Progression can be halted by careful dental care and, in some cases, surgery. For example, a deepened gum pocket can be lowered. In advanced periodontitis, the only treatment is tooth extraction. (Chrons & Kuntsi-Vaattovaara 2006; also, with illustrative photos)

Tooth roots close to critical structures

- Tooth roots can be located close to critical structures, making dental procedures like extractions risky.
- Critical structures close to the teeth that the tooth roots can reach include the nasal cavity, the infraorbital canal, and the eye socket.
    - An inflammatory abscess around the root can perforate the bone under the eye.
    - The nerve canal can pass through the roots of the tooth, making extraction difficult.
- In dogs weighing less than 5 kg, the first mandibular tooth (M1) is disproportionately large compared to the jawbone, and the roots of the large teeth in the lower jaw form a large part of its supporting structure. These dogs are prone to periodontal disease, which poses a risk: if periodontal disease destroys the jawbone, there may be so little bone around the tooth's root that it fractures. The jaw may also fracture during tooth extraction or later, for example due to trauma or even normal chewing (Chrons & Kuntsi-Vaattovaara 2006).

Unerupted or partially erupted teeth

- Late tooth eruption is common in breeds such as the Lhasa Apso and Shih Tzu. Puppies may still be missing teeth when they leave for their new homes.
- Poorly erupted teeth accompanied by deep gum pocket are typical of breeds such as the Chihuahua.
- Unerupted teeth are typical of Boxers and other brachycephalic dogs.
    - The most common unerupted tooth is the mandibular first premolar (P1).
    - In brachycephalic dogs, dental radiography is recommended at one to two years of age (e.g. when having a hip X-ray), as unerupted teeth are associated with a high risk of surrounding follicular cysts (dentigerous cysts). A follicular cyst is a fluid-filled sac surrounded by a thin capsule of connective tissue (Figure 4). This destroys the jawbone and surrounding teeth, sometimes causing a jaw fracture. The roots of adjacent teeth are often eroded by pressure damage. Cysts can grow to a large size in less than a year. Treatment is easier if only the unerupted tooth can be removed rather than having to treat the potentially developing cyst. Treatment of a cyst involves removing the cyst, the unerupted tooth and any adjacent teeth that are severely decayed. In older dogs (10 years old), cysts are unlikely to develop.

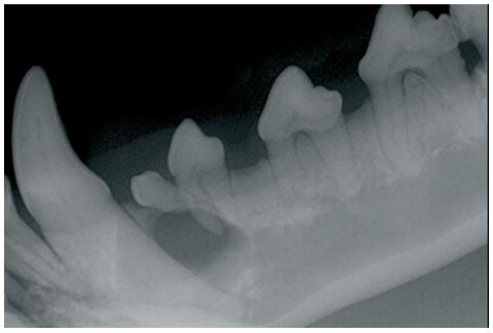


Figure 4. Follicular cyst (Gawor 2013).

Disproportionately large teeth for the size of the jaws

- Small dogs and dolichocephalic dogs, which have long, slender muzzles.
- The small jawbone compared to the mandibular canine tooth makes it easily fractured at the root when the tooth is removed.

Misaligned teeth

- For example, mesial version of the canines (lanced canines). A protruding upper canine tooth.
    - Typical of Shetland Sheepdogs, Miniature German Pinschers, Miniature Schnauzers, and small terriers.
    - Removal is recommended but can be difficult as the tooth's root is usually connected to the nasal cavity.
    - Orthodontic treatment is not recommended as the upper canine rarely bypasses the lower canine.

Congenital enamel defects (amelogenesis imperfecta)

- Localised enamel damage or deficiency in one tooth is usually caused by an external factor, whereas in hereditary enamel hypoplasia, enamel is missing in almost all teeth.
    - Examples of breeds affected include the Akita, American Akita, Lancashire Heeler, Parson Russell Terrier, Standard Poodle (see Figure 5), Border Collie, Alaskan Malamute, Greyhound, and Samoyed.
    - In the absence of enamel, the teeth of a young dog are susceptible to pulpitis. Another risk of lacking enamel is periodontitis: a rough tooth is more likely to accumulate plaque.
    - The mode of inheritance in the Akita, American Akita, Greyhound, Parson Russell Terrier, Standard Poodle and Samoyed is autosomal recessive (Gandolfi et al. 2013, Hytönen et al. 2019, Mannerfelt & Lindgren 2019, Pedersen et al. 2017).
        - Akita and American Akita: a causal variant in the ACP4 gene. The proportion of carriers is 22% in both breeds (Hytönen et al. 2019). Genetic test available.
        - Greyhound and Parson Russell Terrier: a variant in the ENAM gene (Gandolfi et al. 2013, Hytönen et al. 2019). The proportion of carriers in Parson Russell Terriers is 9%, and a genetic test is available (Hytönen et al. 2019).

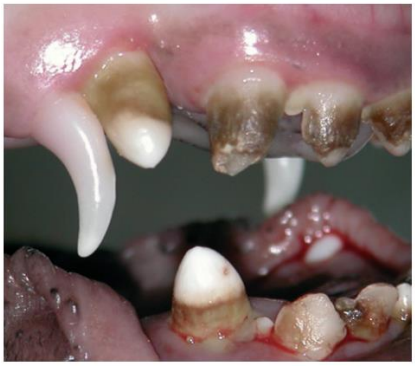


Figure 5. Enamel hypoplasia (Gawor 2013).

Short and/or narrow lower jaw

- Long, narrow muzzle: sighthounds, dachshunds, poodles.
- The canine tooth of the lower jaw can hit the soft tissue and cause pain. Treatment is required (orthodontic treatment, tooth shortening and pulp amputation, or tooth extraction).
- If the problem is detected in the deciduous teeth, the deciduous canine teeth can be removed as a preventive measure (Chrons & Kuntsi-Vaattovaara 2006).

Extremely crooked head/muzzle

- E.g. Bull Terrier: normal bite is rare.
- The lower canine does not fit into the space provided for it in the upper jaw.
- The teeth wear each other down and become worn to the point that they require removal or root canal treatment.

Massive gingival hyperplasia

- Examples include Boxers, Bernese Mountain Dogs, Collies, and White West Highland Terriers.

Eosinophilic granuloma complex

- Inflammation of the mucous membranes of the mouth and tonsils caused by eosinophilic cells.
- Mucosal ulceration and scarring.
- Particularly prevalent in Siberian Huskies and Cavalier King Charles Spaniels.

Craniomandibular osteopathy

- Overgrowth of the bones of the skull and mandible.
- 4–8 months of age
- Symptoms range from mild to severe and usually disappear once growth has finished.
- Pain, swelling of the jaw, difficulty opening the mouth and eating, and sometimes intermittent fever.
- Described in many breeds and studied in particular in White West Highland Terriers, Cairn Terriers, Scottish Terriers, Australian Terriers, Weimaraners, German Wirehaired Pointers, and Basset Hounds.
- Hytönen et al. (2016) proposed an autosomal dominant mode of inheritance with incomplete penetrance in White West Highland Terriers, Cairn Terriers and Scottish

Terriers, but did not exclude other modes of inheritance. Letko et al. (2020) reported a related variant, possibly causal, in the Basset Hound.

Extremely large mouth and teeth

- Related to structure: large teeth and jaw structure, giving the appearance of a big dog's head on a small dog.
- Leads to an incomplete opening of the mouth.
- e.g. Scottish Terrier

Dental and oral examinations and treatments

While the dog is awake, it is possible to assess the bite and calculus and detect visible tooth damage. However, a thorough examination can only be performed under anaesthesia. X-rays can reveal the spread of inflammation around the tooth root or bone loss in the jawbone, for example. Fractures of the tooth root and unerupted teeth, for example, can only be detected by dental radiography (Chrons & Kuntsi-Vaattovaara 2006).

While most dental and oral problems can be successfully treated, in some cases, treatment can be time-consuming and expensive (Gawor 2013).

Breeding

The Nordic Kennel Union (NKU) has drawn up Breed Specific Instructions (BSI) regarding exaggerations in pedigree dogs. The BSI implies recommendations to the show judge to observe the breed specific areas of risk and encourages judges to note issues as well as soundness in these areas and compile the report after judging (NKU 2023).

About bite and teeth, it is generally stated that *All dogs should have healthy clean teeth and a well functioning bite corresponding to what the breed standard requires. Incorrectly placed teeth may cause damage to the gums. Jaws should close normally. The gums should not display any signs of excessive growth, injury, irritation or damage. Such deviations could be clinical signs of impaired health and should be handled accordingly.*

For individual breeds, the BSI specifically mentions the following oral and dental risks that should be monitored:

- Bull Terrier and Miniature Bull Terrier: Mouth: Narrow lower jaw with canine teeth going up into the upper palate. The unique type of head explains the tendency for faulty bite. Look for a correct head and a strong lower jaw.
- Chihuahua: Muzzle and mouth: Overly short muzzle, faulty bites, dentition, and jaws.
- Collies: Mouth: Narrow lower jaw resulting in inverted canine teeth going up into the upper palate. Required in the breed standard: ”The lower jaw shall be strong and well marked”.
- Shar pei: Mouth: The padding of the lower lip can fold over the teeth. When the lower lip is constantly rolled in and ”interfering with the bite”, it is a disqualifying fault according to the standard. (Constant tight lip interferes with the development of the lower jaw).
- Shih tzu: Mouth: Narrow lower jaw.
- Staffordshire Bull Terrier: Mouth: Lower canine teeth going up into the upper palate.
- Yorkshire Terrier: Mouth: Poor jaws and dentition.

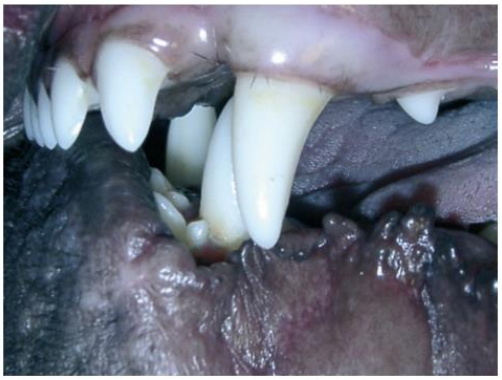


Figure 6. The padding of the lower lip folding over the teeth (Gawor 2013).

In 'Hereditary Oral Disorders in Pedigree Dogs - Proposals for their evidence and assessment', Gawor (2013) discusses hereditary oral and dental disorders in pedigree dogs, their identification, investigation, and impact on quality of life. The article includes numerous photographs illustrating the various diseases. It also lists the 49 breeds in which these diseases are most prevalent. It presents a screening test protocol for breeding purposes and ready-to-use forms for assessing and recording diseases in Poland. Commissioned by FECAVA (the Federation of European Companion Animal Veterinary Associations), the article can be found at https://www.fecava.org/wp-content/uploads/2019/09/Autumn-2013.pdf.

Gawor (2013) describes the proposed examination protocol:

- The examination must be carried out by an authorised veterinary surgeon, licensed for that purpose. It must follow the agreed protocol which will be specific to the breed and condition as will the certificate issued if the animal is approved. In Poland competent Veterinary surgeons are authorized by a Committee of the PSAVA. Authorization has to be verified regularly, and attention is paid to the Veterinary surgeon's CPD and CE record. More information is available on http://www.pslwmz.org.pl/index.php/stomatologia (also in English).
- The diagnosis of a particular disease is based on precise criteria such as clinical assessment, imaging and laboratory tests (histopathology and/or genetic).
- An animal which receives a certificate confirming the absence of diseases that can be inherited can be declared to have: No evidence of oral and maxillofacial genetic, hereditary or breed predisposition diseases.

For all conditions examined a score of 1-3 points is given:

- One point indicates a low impact on the quality of life. Treatment is not always necessary.
- Two points are assigned to animals with more serious problems whilst
- 3 points would result in the animal being disqualified from breeding because of the severe effect of the condition on the health, functionality and quality of life of the dog.

Points can be given for more than one condition in an animal. When the total number of points collected during evaluation of the animal exceeds 3, this fact should also be treated as the presence of eliminating fault. The list of conditions, standards of assessment and other methodology will be reviewed every year by the Project Management Board of PSAVA.

5.5. Chondrodysplasia and chondrodystrophy

Dwarfism (chondrodysplasia) has been reported in several dog breeds. When only the limbs are shorter than normal, this is known as dwarfism. While short stature is not normal for a dog, in some breeds it is a desirable trait that has been maintained through selective breeding. Parker et al. (2009) found that short limbs are a defining feature of at least 19 breeds of dog, including Basset Hounds, Dachshunds and Corgis. They defined short-limbed dogs as meeting the following criteria:

- Withers height of less than 15 inches (38.1 cm) and a withers height to body length ratio of less than one.
- The skeletal structure of the limbs is heavy and large in relation to the size of the dog.
- Forelimbs that are bent, curved and/or paws that are turned outwards.

Mode of inheritance

Short-limbed dogs have an extra copy of a growth factor gene called functional fibroblast growth factor 4 (FGF4). This gene acts as a promoter of tissue growth during development. The excess copy of the gene causes over-expression, resulting in the growth process of the long bones in the limbs being timed incorrectly during the foetal period. This causes the growth plates of the limb bones to close prematurely, preventing the bones from reaching their normal size and resulting in short, curved limbs (Parker et al. 2009).

Two FGF4 retrogenes that cause limb shortening have been identified:

1. The FGF4 retrogene located on chromosome 18 (CFA18) causes severe limb shortening. The short-limbedness (chondrodysplasia, CDPA) caused by this retrogene is an incompletely dominant trait; dogs with two copies of the retrogene are shorter than those with one copy (Parker et al. 2009).
2. The FGF4 retrogene on chromosome 12 (CFA12) has a weaker effect on limb length than the retrogene on chromosome 18 (Brown et al. 2017). Dogs with one or two copies of this retrogene are also known as chondrodystrophic (CDDY).

Dogs with one copy of the FGF4 retrogene (CFA12 or CFA18) have limbs that are slightly shorter than normal. Two copies of both CDPA and CDDY result in significantly shorter limbs than either retrogene alone (Brown et al. 2017; see Figure 7).

Figure 7. Normal limbs (Siberian Husky), CDDY (Beagle), CDPA (White West Highland Terrier), CDDY and CDPA (Dachshund). Photos: Sanni Hänninen (Siberian Husky); Pixabay: José Somovilla (Beagle), Morten Hjerpsted (Westie), Congerdesign (Dachshund).

Table 10. The frequencies of CDDY (CFA12 FGF4 Retrogene) and CDPA (CFA18 FGF4 Retrogene) in the breeds studied by Batcher et al. (2019). Due to the large size of the table, only part of it is presented here; the full table can be found in the online publication: https://www.frontiersin.org/files/Articles/562649/fvets-07-00431-HTML/image_m/fvets-07-00431-t001.jpg.

		CFA12 *FGF4* Retrogene				CFA18 *FGF4* Retrogene			
Breed	Total	0	1	2	Frequency	0	1	2	Frequency
Beagle	29	0	0	29	1.00	19	0	0	0
Cavalier King Charles Spaniel	25	0	0	25	1.00	6	0	0	0
Clumber Spaniel	6	0	0	6	1.00	6	0	0	0
Dachshund	509	0	30	479	0.97	3	9	482	0.98
Cocker Spaniel, American	13	0	1	12	0.96	6	0	0	0
Cocker Spaniel, English	14	0	1	13	0.96	14	0	0	0
Bulldog, French	113	0	14	99	0.94	71	2	0	0.01
Dandie Dinmont Terrier	28	1	5	22	0.88	0	1	27	0.98
Welsh Corgi, Pembroke	63	3	15	45	0.83	0	2	61	0.98
Welsh Corgi, Cardigan	7	1	1	5	0.79	0	2	4	0.83
Skye Terrier	13	2	2	9	0.77	0	0	9	1.00
Basset Hound	38	3	20	15	0.66	1	4	27	0.92
Pekingese	32	5	15	12	0.61	1	1	22	0.94
Coton de Tulear	14	3	6	5	0.57	0	1	12	0.89
Poodle, Miniature and Toy	119	28	46	45	0.57	38	10	5	0.19

FGF4-retrogenes in different dog breeds

Interpretation of the Table 10: For example, five of the Pekingese dogs had no CDDY retrogene, 15 were heterozygotes (one normal allele and one copy of the retrogene), and 12 were homozygotes (two copies of the retrogene). Of all the genotypes studied in the breed, 61% were retrogenic in this gene. For the CDPA retrogene, one dog had no retrogene, one was heterozygous, and 22 were homozygous. Of all the genotypes studied in the breed, 94% were retrogenic in this gene.

Parker et al. (2009) reported that CDPA is fixed in the following 15 short-legged breeds: Basset Hound, Cairn Terrier, Dandie Dinmont Terrier, Pekingese, Lancashire Heeler, Swedish Vallhund, Dachshund, Norwich Terrier, Petit Basset Griffon Vendéen, Shih Tzu, Skye Terrier, Tibetan Spaniel and West Highland White Terrier, as well as the Cardigan and Pembroke Welsh Corgis.

Batcher et al. (2019) identified CDPA in 32 breeds and CDDY in 40. Both retrogenes were present in 23 breeds (see Table 10). CDPA was fixed in 15 breeds, meaning that no or very few normal chromosomes exist in them. CDDY was fixed in the Beagle, Cavalier King Charles Spaniel, and Clumber Spaniel, and nearly fixed in the Dachshund, Cocker Spaniel, American Cocker Spaniel, and French Bulldog.

A large study by Donner et al. (2023) found that the frequency of CDDY was 11.4% in mixed-breed dogs and 13.9% in pedigree dogs. CDDY was detected in 89 breeds or breed varieties at a frequency of over 1%.

Welfare issues

In most chondrodystrophic dogs, the intervertebral discs in the spine degenerate prematurely (Hansen 1952). These degenerated discs are prone to herniating into the spinal canal or even rupturing (see Table 11).

Table 11. The welfare issues to which CDDY and CDPA expose their carriers.

FGF4-retrogene	Phenotype/term	Causes	Possible welfare issues
CFA12 (CDDY), dominant	Chondrodystrophy: premature disc degeneration	Disc herniation and rupture	Pain and paralysis Spinal cord and nerve damage Permanent spinal cord damage
CFA18 (CDPA), incompletely dominant	Chondrodysplasia: short limbs	Elbow incongruity	Abnormal movements Osteoarthritis and pain Abrasions associated with incorrect positioning and abnormal flexion of the limbs Callus formation and inflammation of the paws Strain on the shoulder joint
		Curved limb conformation, abnormal flexion and position of limbs	

CDDY therefore sets a high level of susceptibility to disc herniation. It also lowers the age at which morbidity occurs: chondrodystrophic dogs were significantly smaller (median weight 8.1 kg vs. 25.0 kg) and younger than other dogs at the time of surgical treatment (5.5 years vs. 9.0 years; Batcher et al. 2019).

The premature closure of the growth plates of the limb bones in short-legged dogs makes these dogs prone to varying degrees of angular front limb deformity (ALD). ALD refers to excessively curved limb conformation and elbow incongruity. Typical welfare risks are included in Table 11.

5.5.1. Premature disc degeneration and herniation

A dog usually has seven cervical vertebrae, 13 thoracic vertebrae, seven lumbar vertebrae, and three fused sacral vertebrae. There is a disc between each vertebra except for the sacral vertebrae and the first and second cervical vertebrae. The discs are composed of a tough outer ring (*annulus fibrosus*) and a gel-like center (*nucleus pulposus*).

In chondrodystrophic dogs, premature degeneration of the intervertebral discs begins in the first year of life (Hansen type I disc disease; Hansen, 1952). As the dog grows older, the degeneration continues. The gelatinous core of the disc hardens and calcifies over time, reducing its ability to absorb shock and protect the spine from external forces (Braund 1993, Cappello et al. 2006). In non-chondrodystrophic dogs, degeneration of the intervertebral discs occurs later in life (Hansen type II intervertebral disc disease; Hansen 1952 and 1959, Ghosh et al. 1976).

Calcifications may disappear with age, for example because of asymptomatic herniation (Lappalainen 2021). A histopathological study by Stigen et al. (2019) revealed that all herniated discs were calcified.

In addition to degeneration related to chondrodystrophy, disc herniation is influenced by factors relating to the dog's structure and habitat, as well as by genes with minor effects (e.g. Bergknut et al. 2012, Dorn & Seath 2018, Jensen & Ersboll 2000, Packer et al. 2013 & 2016).

One of these genes may be the CDPA retrogene (Batcher et al., 2019). For instance, Packer et al. (2016) discovered an association between obesity and relative back length and hernia risk (the longer the back, the higher the risk).

Symptoms

The symptoms of a herniated disc result from spinal cord and nerve damage. X-rays, CT scans or MRIs show narrowing of the intervertebral space and the presence of calcified material between the vertebrae. The herniated disc material puts pressure on the spinal cord, resulting in pain and paralysis. Symptoms can range from back pain that lasts a few days to complete paralysis of the hind legs. If the herniated disc is in the cervical spine, symptoms can include severe neck pain and, in some cases, paralysis of the front and back legs. Some dogs experience symptoms only once, while others experience recurrent symptoms. In the most severe cases, a herniated disc can lead to permanent spinal cord damage and euthanasia (Lappalainen, 2021).

Treatment

Herniated discs can be treated either conservatively or surgically. Conservative treatment includes complete rest, non-steroidal anti-inflammatory drugs (NSAIDs) and physiotherapy. This approach usually yields good results in less severe cases.

The recommended treatment for recurrent or persistent pain and paralysis is surgery to remove the material from the herniated disc that is pressing on the spinal cord. While the prognosis is usually good, recovery from severe paralysis can take a long time. Even in dogs that have undergone surgery, the disease can recur (Lappalainen, 2021).

Prevalence of disc herniation in chondrodystrophic dogs

Disc herniation is the most common spinal disease in dogs. A study by Bergknut et al. (2012), which used data from a Swedish insurance company, included 665,249 dogs insured for veterinary expenses and 552,120 dogs insured for life. Intervertebral disc disease claims occurred in 0.3% of all dogs in the dataset (including non-chondrodystrophic dogs). The disease was more prevalent in males and older dogs.

Dachshunds have the highest incidence of the disease (e.g. Bergknut et al. 2012) and have also been the most studied breed.

Pain and paralysis due to a hernia can result in the dog being euthanised. In a study by Bonnett et al. (2005) of insurance company data in Sweden between 1995 and 2000, intervertebral disc herniation was the fifth most common cause of death in all dogs. Among dachshunds, it was the leading cause of death. More recent data from 2011–2016 show that disc herniation remains the leading cause of death in standard Dachshunds (DogWellNet.com, Agria Breed Profiles). However, the overall mortality rate for dachshunds during this period was below average compared to other breeds.

A Danish Master's thesis (Mørck Andersen & Marx 2014) estimated the prevalence of intervertebral disc disease to be 16.0% in Wire-haired Dachshunds, 17.4% in Long-haired

Dachshunds, and 21.6% in Smooth-haired Dachshunds. The risk of intervertebral disc herniation was significantly higher in 'domestic' dogs than in working dogs. Of the dogs with a history of herniation, 44% had been euthanised as a result. Some of the Wire-haired Dachshunds are also heterozygous for the CDDY retrogene, which may account for their slightly lower morbidity rate compared to other variants.

However, in a study by Bruun et al. (2020), no significant difference in the risk of intervertebral disc disease was found between the different dachshund variants. Around one in five (18%) of the dogs became ill, and of these, one in three had to be euthanised. When all symptomatic dogs were included in the analysis, intervertebral disc disease was found to affect one in four (26%) dachshunds (Bruun et al. 2020).

Studies of animal hospital data have found that Beagles, Cocker Spaniels, Pekingese, Lhasa Apsos, Dachshunds, Pembroke Welsh Corgis, French Bulldogs and Shih Tzus are significantly more susceptible to intervertebral disc disease (Brown et al. 2017). Mayousse et al. (2017) found that French Bulldogs were, on average, younger (4.1 years) than other breeds. Batcher et al. (2019) suggested that this may be due to a combination of the CDDY retrogene and the DVL2 variant in French Bulldogs.

The importance of disc herniation

Dogs susceptible to disc herniation may develop multiple herniations between different intervertebral spaces during their lifetime (Mayhew et al. 2004). It is a painful and highly heritable condition. It is associated with a high mortality rate and high surgical costs. Long-term aftercare can contribute to the dog's poor quality of life. Conservative treatment involving several weeks of restricted exercise and crate rest can be very challenging for the dog, impacting its psychological and physical well-being.

Several breeds of dog with the CDDY retrogene and susceptible to disc disease are very popular. Consequently, there are millions of dogs with the disease worldwide. The health and economic consequences of the disease are enormous.

Breeding programmes should be implemented to prevent intervertebral disc disease in breeds at risk (Bruun et al. 2020). These programmes offer more long-term benefits than advanced surgical or medical treatment (Brown et al., 2017).

Breeding

The main risk factor for disc herniation and spinal cord injury is early disc degeneration, so breeding should primarily prevent this. The primary means of achieving this is to reduce the prevalence of CDDY in breeds and eventually eliminate it altogether.

Genetic testing

The CDDY retrogene and its copy number (0, 1 or 2) can be detected in a dog's genome by a commercial genetic test. By favouring dogs and combinations without CDDY in breeding programmes, the production of individuals susceptible to the disease can be avoided (Dickinson & Bannasch 2020).

The effect of the CDDY dose is not yet fully understood. If there were a difference in disease risk between heterozygous dogs (with one copy of the retrogene) and homozygous dogs

(with two copies of the retrogene), using heterozygous dogs in breeding might slightly improve the situation in breeds with a high prevalence of CDDY.

Almost all the breeds studied exhibit allelic variation that can be utilised for breeding purposes, albeit with some breeds displaying minimal variation. In breeds with a relatively low prevalence of the CDDY retrogene, it should be possible to significantly reduce or even eliminate its prevalence. This would almost entirely eradicate type I disc disease (Brown et al. 2017, Dickinson & Bannasch 2020). Eradicating the CDDY retrogene from breeds and breeding lines would not significantly alter the appearance of dogs, as short stature is primarily caused by the CDPA retrogene. This gene could be retained if its associated health risks could be reduced through breeding programmes.

Due to its dominant mode of inheritance and high frequency in certain breeds, Bannasch and Bellone (2021) recommend a cautious reduction of CDDY. A rapid reduction would lead to an excessive narrowing of the breed's genetic variation. Bannasch and Bellone (2021) make the following recommendations:

- In breeds with low CDDY frequencies (less than 0.25), CDDY can be eliminated in a single generation through genetic testing.
- In breeds with frequencies between 0.25 and 0.5, the frequency should be reduced gradually over several generations by using dogs with two copies of the normal chromosome as the other parent in litters.
- Breeds with a higher frequency (above 0.5) should reduce the frequency much more slowly over several generations.
- In breeds where CDDY is fixed and the normal chromosome is absent, it is impossible to remove CDDY or reduce its presence without crossbreeding. However, current knowledge suggests that reducing the prevalence of CDDY should be a priority in breeding programmes (Dickinson & Bannasch 2020; Batcher et al. 2019).

The UC Davis Veterinary Genetics Laboratory has been studying the frequency of CDDY in various dog breeds. This data will be updated as more dogs are tested. The data can be accessed via this link.

A long-term breeding strategy may require a combination of genetic testing, breeding heterozygous dogs, and crossbreeding, which could entail amending breed standards for certain breeds (Dickinson & Bannasch 2020).

In breeds where CDDY is fixed, it takes two generations before the risk of CDDY-associated intervertebral disc disease is reduced, even with crossbreeding. Mating a homozygous dog with a dog that does not have CDDY results in all offspring being chondrodystrophic CDDY carriers. If several of these first-generation (F1) crosses have occurred, the resulting dogs can be bred together in the next generation (F2), resulting in a quarter of the offspring having no CDDY and no risk of developing the disease. These F2 generation dogs comprise 50% of the original breed.

If an F1 generation heterozygous dog is mated with a dog that does not have CDDY, on average half of the offspring will be CDDY-free.

Backcrossing to the original breed immediately after the F1 generation will not produce CDDY-free offspring.

X-ray screening

A spinal X-ray cannot determine the extent of disc degeneration. However, several studies have shown that the number of calcified intervertebral discs detected on X-ray at 24–48 months of age is associated with the risk of intervertebral disc disease and the dog's symptomatology (Stigen et al. 2019, Lappalainen et al. 2014, Mørck Andersen & Marx 2014, Jensen et al. 2008, Mayhew et al. 2004). However, some studies have only investigated symptoms via owner surveys and have not made a specific hernia diagnosis. If owners were aware of the number of calcified intervertebral discs in their dogs, this may have influenced their assessment of their dogs' symptomatology (Cizinauskas, email communication, 2021).

X-rays can detect 50–70% of calcifications, whereas histopathology can detect 100% (Rohdin et al. 2010, Stigen et al. 2019). Dogs with five or more calcified intervertebral discs detected on X-ray were found to have a 14–18-fold increased risk of developing symptoms compared to dogs with fewer than five or no calcifications (Lappalainen et al. 2014, Bruun et al. 2020). The former group also exhibited more severe symptoms. Dogs with fewer calcifications showed symptoms at a later age than those with more calcifications (Lappalainen et al. 2014).

The CDDY retrogene has been linked to X-ray-detectable calcifications; dogs with two copies of the retrogene had 2.5 times more disc calcifications than those with one copy (Batcher et al. 2019).

Therefore, the genetic cause of the disease is degeneration, and calcification is a sign of degeneration. Assessing and measuring these calcifications may therefore indirectly provide insight into the problems caused by the CDDY retrogene. X-ray screening of breeding dogs is the only feasible option for breeding within a breed if the CDDY retrogene is highly prevalent or fixed within the breed, leaving no dogs free of it (Bruun et al. 2020). However, it is unclear how effective this approach will be in reducing the risk of disease in dogs carrying the CDDY retrogene that causes degeneration of the intervertebral discs. X-ray screening can only reduce the prevalence of genes with a minor effect.

The high heritability of the observed number of calcifications suggests that reducing calcifications through breeding could be achieved relatively quickly. Heritability estimates in Dachshunds have ranged from 0.15 to 0.87 (Stigen & Christensen 1993, Jensen & Christensen 2000, Lappalainen et al. 2015). A value of 0.87 is unusually high, typically indicating the presence of a gene with a large effect; in this instance, the gene appears to be the CDDY retrogene.

A Finnish study based on X-ray data from over 1,500 Dachshunds examined the genetic progress made in reducing calcifications between 1997 and 2013 (Lappalainen et al. 2015). Progress was only slight. The researchers attributed this to the small number of dogs screened (less than 10% of registered dogs) and the low selection intensity, since dogs with high levels of calcified intervertebral discs were also used for breeding.

Standardised X-ray screening

To reduce welfare issues, the effectiveness of X-ray screening in reducing the incidence of intervertebral disc herniation during the transition period should be investigated. This would require compulsory screening of breeding dogs and effective breeding restrictions. Data on morbidity in different breeds/breeding lines will also need to be collected. Changes in morbidity are an indicator of the breeding programme's effectiveness.

An expert veterinarian specialising in X-ray diagnostics can assess the X-rays and provide a grading based on the number of calcifications detected. Currently (as of 1 July 2022), the

Finnish Kennel Club issues gradings for the following breeds: Coton de Tuléar, Bichon Havanais, Pekingese, Swedish Vallhund, Dachshunds, French Bulldog, Skye Terrier, Tibetan Spaniel, Welsh Corgi Pembroke and Cardigan.

The recommended age for radiographs is 24–42 months (Lappalainen, 2021). The following scale is used in Finland (Suomen Kennelliitto 2020a):

- IDD0, Free – No abnormal findings
- IDD1, Mild – 1–2 partially or completely calcified intervertebral discs
- IDD2, Moderate – 3–4 partially or completely calcified intervertebral discs
- IDD3, Severe – 5 or more partially or completely calcified intervertebral discs.

When breeding, preference should be given to dogs with the fewest possible calcifications (Lappalainen et al. 2014, Rohdin et al. 2010, Chai et al. 2018, Jensen et al. 2008). Dogs with more than five calcifications (an IDD3 result) should particularly be excluded from breeding.

5.5.2. Premature closure of the growth plates

Dogs with short legs are prone to varying degrees of angular limb deformity (ALD). This condition is characterised by excessively curved limb conformation and can affect both the forelimbs and the hind limbs. These deformities are caused by premature closure of the growth plates.

Premature closure of the growth plate in the tibia causes the hind leg to bend inwards at the hock (**pes varus**; bowed legs). When the outer edge of the tibia (shin bone) grows longer than the inner edge, the distal limb bends inwards towards the midline. This condition typically develops around the age of six months (Ramadan & Vaughan 1979). Pes varus may also be associated with patellar luxation. A 2015 health survey in England diagnosed pes varus in 0.9% of dachshunds. However, mild cases are likely to go undiagnosed (Dachshund Health UK).

Premature closure of the distal ulnar physis (PCDUP, or short ulna syndrome) results in premature growth arrest of the ulna. This results in the ulna and radius growing at different rates. As the radius continues to grow, the proportions of the bones become abnormal. If the radius is too long in relation to the ulna, it forms a step in the joint, or it becomes excessively curved (see Figure 8). Sometimes, the radial head subluxates laterally. The radius twists around the ulna, causing the limb to twist outwards from the central axis. This creates the valgus position typical of short-legged dogs, whereby the paws rotate outwards, and the wrists bend inwards (see the Dachshund in Figure 7 on page 54).

Premature closure of the growth plates in the **elbow joint** causes the parts of the joint to become **incongruent**. This is a form of elbow dysplasia, which is a developmental disorder of the elbow joint. In an incongruent elbow joint, the joint space between the humerus and the ulna is widened, and the trochlear notch of the ulna does not align as closely with the trochlea of the humerus as it should. There may also be a step between the ulna and the radius.

The aetiology, welfare implications and treatment options for elbow incongruity are discussed in depth in Ollila's literature review (2015) and Koskinen's licentiate thesis (2016), the main sources used here.

In a study by Lappalainen et al. (2023) involving three short-legged breeds, incongruity was present in most dogs: 92% of Dachshunds, 96% of Skye Terriers and 73% of Glen of Imaal Terriers. The prevalence of the two most severe degrees was 13% in Dachshunds, 39% in Skye

Terriers and 5% in Glen of Imaal Terriers. However, as the sample was not randomised, the figures cannot be generalised to these breeds.

As early as the 1970s, it was demonstrated that incongruity was associated with short stature and was also heritable (Rasmussen & Reimann 1977). In Skye Terriers, a recessive mode of inheritance with incomplete penetrance has been proposed (Lau 1977); this description also fits the polygenic mode of inheritance associated with forelimb structure.

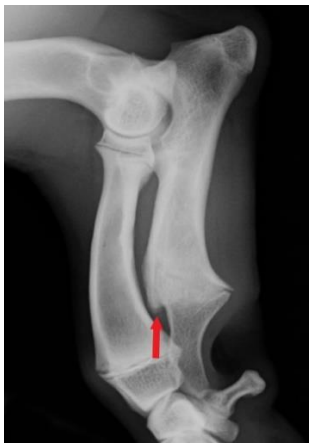


Figure 8. Elbow incongruity. The red arrow shows remodelling of the cranial metaphysis. Figure by Anu Lappalainen.

Welfare issues

The first clinical signs of elbow joint incongruity are typically pain and lameness. In a study by Lappalainen (2016), approximately one third of Skye Terrier puppies had a limp during growth, and some continued to limp into adulthood. Those with moderate to severe incongruity on X-rays were the ones that limped as puppies or adults. The study included 50 dogs. All dogs that limped as adults had also limped during puppyhood.

Due to incongruity, the elbow joint does not extend properly, causing pain when the elbow is bent. The flexion and extension of the limb is produced solely by the shoulder joint (Lau 1977, Ramadan & Vaughan 1978), which becomes stressed. In a study by Lappalainen et al. (2023), pain in the shoulder joint was observed in just over a quarter (27%) of Dachshunds. This proportion was 10% in Skye Terriers and 5% in Glen of Imaal Terriers.

In contrast to normal gaits, when a dog does not bend its elbow joints much at all, the movement remains shallow and paddling. This can particularly affect older dogs, causing the upper surfaces of the middle toes' claws to wear down when the forepaws drag on the ground as the foot is brought forward (Kallio, email communication 2022).

Elbow incongruity, limb rotation and bending cause osteoarthritis, chronic pain and lameness, limiting limb movement (Lappalainen et al. 2023). Incongruity limits the extension of the shoulder joint. A study by Lappalainen et al. (2023) found that dogs with more severe incongruity had shorter forelimbs than those with milder incongruity.

According to a study by Knapp et al. (2016), short-legged dogs are 3.5 times more likely to develop elbow joint disease caused by incongruity than other dogs.

Changes in how a dog uses its limbs due to their length can cause mechanical stress to bones, joints, ligaments, tendons, and muscles. Increased valgus is associated with shoulder joint pain and owner-perceived lameness and reduces wrist flexion and elbow and shoulder

extension (Lappalainen et al., 2023). Forelimb rotation affects the wrist in particular, causing pain and lameness, as well as limiting wrist flexion and extension.

If misalignment of the limbs also changes the position of the paws, the skin and soft tissues may wear away. Misalignment and improper weight bearing can cause calluses to form on the paws, resulting in thickened, cracked skin. The paws may also become inflamed (see section 5.2.2). If the limbs are very short and twisted, they may also rub against the chest (Kirsti Schildt, personal communication).

The pes varus of the hind limbs causes a dog to have bowed legs. At its most severe, the dog experiences mobility issues. If left untreated, this severe condition can lead to painful and disabling osteoarthritis (Dachshund Health UK).

Joint problems and pain due to angular limb deformity often only become more apparent as the dog ages and the condition worsens.

Treatment options

Elbow incongruity often requires surgery in symptomatic dogs. The most common surgical procedure is ulnar osteotomy (cutting the distal part of the ulna). Surgery should be performed early enough to realign the joint surfaces and improve the fit between the radius, ulna, and humerus.

Several surgical techniques have yielded moderate to good results, although the number of chondrodysplastic dogs involved has been limited. Of the aspects that can be observed clinically prior to surgery, the prognosis for the development and progression of osteoarthritis is mainly influenced by elbow incongruity and the strength of the valgus position.

Pododermatitis caused by conformational deformities is often challenging to treat, with no curative treatment available. However, if the deformity can be corrected surgically, the cause of the inflammation will also be eliminated (see also 5.2.2 Conformational pododermatitis).

X-ray is used to diagnose pes varus in the hind limbs. Severe pes varus is treated surgically. The prognosis for timely surgery is good (Johnson et al. 1989, Dachshund Health UK).

Breeding: front and hind limb structure

Favouring dogs with normal front and hind limb structure and position (see Mujunen 2015, for examples) in breeding can reduce limb flexion and rotation in chondrodysplastic breeds. In breeds with an abundant coat, it can be challenging to judge structure because the structure and angulation of the forelegs are not visible under the coat. Trimming can also hide positional errors and leg curvature. Lappalainen et al. (2023) have developed a method of measuring carpal valgus and front limb rotation in standing dogs.

No heritabilities have yet been estimated for canine pes varus and pes valgus. However, in blue foxes, the estimated heritability for pes valgus is 0.11 (Kempe et al. 2021).

For the CDPA retrogene, heterozygous dogs have longer limbs than homozygous dogs and are therefore less likely to have structural defects. Conversely, dogs that are homozygous for both retrogenes are likely to be at the highest risk. Retrogenes with copy numbers (0, 1 or 2) can be detected in a dog's genome using a commercial genetic test.

Ollila's (2015) literature review drew attention to the breed standards of certain short-legged dog breeds. These traits are characterised as desirable, despite having been identified as being due to elbow dysplasia and/or causing pain.

Ollila (2015) states that: '*For example, forelimb movements that are "low" or "not exaggeratedly high" (Suomen Kennelliitt, 2014) are consistent with the symptoms described by Lau (1977): forelimb movements in Skye Terriers with premature closure of the growth plate were low because limb flexion and extension were produced solely from the shoulder. Breed standards also describe the ideal individual in some short-legged breeds as follows:*

- *forelimbs "curved" or "slightly curved", or "short, bowed, front feet to turn out slightly from pasterns"*
- *forearms "slightly curved at the top when viewed from the front" or "slightly curved". (Suomen Kennelliitto 2014).'*

Ollila states that these breed standard requirements are characteristics related to premature closure of the growth plates. Elbow incongruity is reflected in the dog's forelimb movement, which is described as 'paddling' because of the lateral swinging motion of the elbow while walking.

Lappalainen et al. (2023) argue that the breed standards for short-legged dogs should be reviewed, with changes made to the aspects of the standard that damage the dogs' welfare.

Breeding – X-ray screening

Elbow incongruity is diagnosed using X-rays. This condition is most clearly visible on a mediolateral radiograph of a 90°-flexed elbow joint with the entire forearm visible (Lappalainen 2020).

A screening method using X-rays has been developed to prevent incongruity (Lappalainen et al., 2016) and is used by the Finnish Kennel Club (Suomen Kennelliitto 2021b). Currently, incongruity grades are issued for the following breeds: Alpine Dachsbracke, all Bassets except Basset Hound and Grand Basset, Bichon Frisé, Griffon Vendéen, Cairn Terrier, Česky Terrier, Coton de Tuléar, Dandie Dinmont Terrier, Drever, Glen of Imaal Terrier, Bichon Havanese, Pekingese, Lhasa Apso, Swedish Vallhund, Lancashire Heeler, Maltese, Pug, Dachshunds, Norfolk Terrier, Norwich Terrier, Small Portuguese Podengo Pequeno (small), French Bulldog, Sealyham Terrier, Shih Tzu, Skye Terrier, Scottish Terrier, Tibetan Spaniel, White West Highland Terrier, Russian Bolonka and Welsh Corgis.

For breeding purposes, a dog must be at least 12 months old because this is the earliest age at which the normal structure of a dog's elbow joints can be established.

The scale is based on measuring the width of the humeroulnar joint space and the presence of osteophytes. Joint incongruity is assessed using the INC0–INC3 scale (Lappalainen et al. 2016):

- INC0 (congruent)
- INC1 (mildly incongruent)
- INC2 (moderately incongruent)
- INC3 (severely inconruent)

The INC2 and INC3 elbow joints are clearly abnormal and increase the risk of developing elbow osteoarthritis.

5.6. Stifle joint

Diseases of the canine stifle joint include cranial cruciate ligament disease, patellar luxation, osteochondrosis and osteoarthritis. These are among the most common musculoskeletal disorders in dogs (Johnson et al. 1994). These diseases are usually painful and often progress to chronicity, causing welfare problems for affected individuals over a considerable period of their lives (e.g. Guthrie et al. 2012, Taylor-Brown et al. 2015, O'Neill et al. 2016).

The estimated prevalence rates are 0.56–2.55% for cranial cruciate ligament disease (Taylor-Brown et al. 2015, Witsberger et al. 2018, Adams et al. 2011, Nečas et al. 2000), 0.02–0.06% for osteochondrosis (Johnson et al., 1994; LaFond et al., 2002), and 1.3–52% for patellar luxation. These estimates are based on veterinary data and screening for breeding purposes (O'Neill et al. 2016, LaFond et al. 2002, Lavrijsen et al. 2013, Wangdee et al. 2014, Nilsson et al. 2018, Finnish Kennel Club Breeding Database).

Engdahl et al. (2021) studied a Swedish pet insurance dataset comprising nearly 600,000 insured dogs and over 1.7 million dog-years at risk. Dog-years at risk take into account the amount of time that each dog in the dataset was insured (a dog insured for one year equals one dog-years at risk; a dog insured for six months equals 0.5 dog-years at risk). The dataset included 93 different stifle joint diagnoses in 9,624 dogs between 2011 and 2016. The prevalence of stifle diseases was 55.4 cases per 10,000 dog-years at risk. The median age at the first diagnosis of a stifle disease was 5.6 years.

The most common stifle diagnoses associated with veterinary care claims in the Engdahl et al. (2021) data were:

- cruciate ligament rupture (43.5% of stifle events);
- patellar luxation (29.8%);
- pain or unspecified stifle symptoms (21.2%);
- degenerative changes (11.6%), and
- arthritis (6.8%).

Each of the following diagnostic categories separately occurred in less than 5% of all dogs with stifle joint claims:

- traumatic injuries,
- meniscal injuries,
- osteochondrosis,
- fracture,
- pain or unspecific signs (patella/fabella),
- tumour,
- other malformations and growth disorders, and
- immune-mediated and inflammation (patella/fabella).

The incidence of cruciate ligament disease and patellar luxation is probably higher than reported, as some cases may have been categorised as 'pain or unspecified signs'. For example, in the case of a ruptured cruciate ligament, symptoms are usually present before the ligament breaks permanently, as it gradually degenerates. The actual diagnosis may only become clear at this point.

Cruciate ligament rupture was among the top three diagnostic categories in all 12 breeds accounting for the highest proportion of dogs with stifle joint disease claims, and the condition affected dogs of all sizes.

Patellar luxation on the other hand was among the top two diagnoses for all small breeds among these 12 breeds (Yorkshire terrier, Bichon frisé, Miniature and Toy Poodles, Jack Russel Terrier and Chihuahua), but not even on the top five list for the large breed dogs.

Three of the breed groups had significantly increased relative risk of stifle joint disease:

- Pinscher and schnauzer, molossoid and Swiss mountain and cattledogs,
- Terriers, and
- Companion and toy dogs.

The other breed groups had significantly decreased relative risk. The breeds with the highest relative risk of stifle joint disease were the Bulldog, Boerboel, Presa Canario, Dogue de Bordeaux and American Bulldog (Table 12). The relative risk was significantly higher for 25 breeds and lower for 24.

Some breeds, such as the Rottweiler and Labrador retriever, were primarily affected by cranial cruciate ligament rupture, while others, such as the Chihuahua, were primarily affected by patellar luxation. Others, for example the miniature and toy poodles, Bichon frise and Yorkshire terrier, were affected by both conditions.

5.6.1. Patellar luxation

Patellar luxation is one of the most common orthopaedic conditions in dogs (Engdahl et al. 2021, O'Neill et al. 2016, Ness et al. 1996). During luxation, the patella (kneecap) slips out of its normal position in the trochlear groove of the femur. It can move medially (inward), laterally (outward), or in both directions. In small dogs, the patella usually moves inwards (Lappalainen 2016), whereas in large dogs, it moves outwards.

While the stifle joint is typically normal at birth (e.g. LaFond et al. 2002), problems can develop as the dog grows. Initially, the condition may be asymptomatic; however, the dog may later develop osteoarthritis, chronic pain, and lameness. When the patella slides out of and back into its groove, it can prevent the dog from bending its knee, causing severe friction of the joint surfaces and leading to osteoarthritis. In some dogs, the patella remains permanently luxated, resulting in permanent disability (O'Neill et al. 2016).

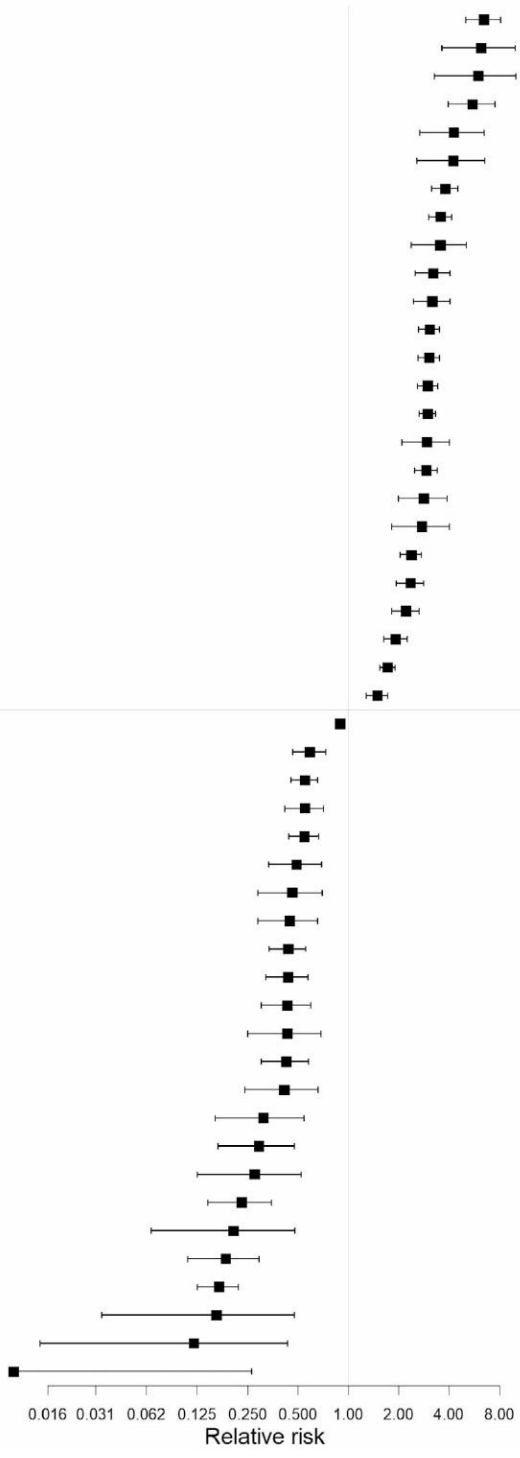
If the patella is dislocated, the dog may experience pain due to stretched ligaments and the bone being in an abnormal position. The intensity of the pain depends on the nature, severity and duration of the luxation, as well as the nature of the underlying structural defects. Most dogs with patellar luxation experience mild to severe pain and mobility issues over extended periods (UFAW 2011). The functional deformity of the stifle joint associated with patellar luxation also increases the risk of cranial cruciate ligament disease.

In terms of canine welfare, chronic diseases that occur at a young age and do not clearly reduce lifespan can pose a significant welfare harm, particularly if they are highly prevalent and severe (Collins et al. 2010). Patellar luxation typically occurs from a young age (O'Neill et al. 2016, Bound et al. 2009, Hayes et al. 1994). Although the condition may initially be asymptomatic, dogs may subsequently develop osteoarthritis, chronic pain and lameness (Gibbons et al. 2006, Hulse 1981, Vidoni et al. 2006).

In terms of welfare problems, patellar luxation has been identified as one of the five most significant hereditary diseases in dogs (Priester 1972, Hodgman 1963). Although these studies are old, their lists of the most common hereditary diseases in dogs remain relevant today.

Table 12. The breeds with highest and lowest relative risk (RR) of stifle joint disease (Engdahl et al. 2021). RR = 0.5 means two times decreased risk, RR 0.125 means eight times decreased risk etc. (CI, confidence interval; DYAR, dog-years at risk). Four breeds, German Shepherd Dog, Jack Russell Terrier, Golden Retriever and Labrador Retriever had RRs that were not different from 1 and are therefore not included in the figure.

Breed	Incidence per 10,000 DYAR (95%CI)	RR (95%CI)
Bulldog	355 (278 - 448)	6.45 (5.04 - 8.15)
Boerboel	344 (200 - 551)	6.22 (3.62 - 9.96)
Presa Canario	331 (181 - 556)	5.98 (3.27 - 10.0)
Dogue de Bordeaux	305 (218 - 415)	5.52 (3.94 - 7.52)
American bulldog	236 (148 - 358)	4.27 (2.68 - 6.47)
Chow chow	234 (143 - 361)	4.22 (2.58 - 6.53)
Pomeranian	208 (173 - 248)	3.79 (3.15 - 4.53)
Boxer	195 (166 - 227)	3.56 (3.04 - 4.15)
Bullmastiff	196 (131 - 281)	3.54 (2.37 - 5.09)
Dobermann	177 (139 - 222)	3.21 (2.52 - 4.04)
Cane corso	175 (135 - 223)	3.18 (2.45 - 4.05)
Staffordshire bull terrier	167 (145 - 192)	3.06 (2.64 - 3.52)
Bichon frise	167 (143 - 192)	3.04 (2.61 - 3.52)
Yorkshire terrier	163 (142 - 187)	2.99 (2.59 - 3.42)
Rottweiler	162 (145 - 180)	2.98 (2.66 - 3.33)
Bolognese	163 (116 - 222)	2.94 (2.09 - 4.03)
Cairn terrier	160 (137 - 186)	2.93 (2.50 - 3.41)
Boston terrier	156 (111 - 215)	2.83 (2.00 - 3.88)
Prazsky krysarik	152 (100 - 222)	2.76 (1.81 - 4.01)
French bulldog	130 (113 - 150)	2.38 (2.05 - 2.74)
Bernese mountain dog	129 (107 - 155)	2.35 (1.94 - 2.82)
American staffordshire terrier	122 (100 - 146)	2.21 (1.82 - 2.66)
Bichon havanais	106 (89.9 - 123)	1.92 (1.63 - 2.25)
Chihuahua	93.8 (84.5 - 104)	1.72 (1.55 - 1.91)
Poodle, miniature & toy	82.0 (70.5 - 94.9)	1.49 (1.28 - 1.73)
Mixed breed	50.7 (48.6 - 53.0)	0.89 (0.85 - 0.94)
English cocker spaniel	32.9 (26.0 - 41.0)	0.59 (0.47 - 0.74)
Jämthund	30.8 (25.5 - 36.8)	0.55 (0.46 - 0.66)
Danish-Swedish farmdog	30.6 (23.3 - 39.6)	0.55 (0.42 - 0.71)
Border collie	30.5 (24.7 - 37.3)	0.55 (0.44 - 0.67)
Collie, rough	27.3 (18.7 - 38.6)	0.49 (0.34 - 0.69)
Welsh springer spaniel	25.7 (16.1 - 38.9)	0.46 (0.29 - 0.70)
Shih tzu	24.7 (16.0 - 36.5)	0.45 (0.29 - 0.66)
Schnauzer, miniature	24.4 (18.9 - 31.1)	0.44 (0.34 - 0.56)
English springer spaniel	24.3 (18.1 - 32.1)	0.44 (0.32 - 0.58)
Poodle, standard	24.1 (16.9 - 33.4)	0.43 (0.30 - 0.60)
Parson Russell terrier	24.0 (14.0 - 38.4)	0.43 (0.25 - 0.69)
Chinese crested dog	23.7 (16.8 - 32.3)	0.42 (0.30 - 0.58)
Dalmatian	23.0 (13.4 - 36.9)	0.41 (0.24 - 0.66)
Siberian husky	17.3 (8.95 - 30.3)	0.31 (0.16 - 0.54)
Rhodesian ridgeback	16.3 (9.31 - 26.5)	0.29 (0.17 - 0.48)
Bearded collie	15.3 (6.99 - 29.0)	0.28 (0.13 - 0.52)
Drever	12.9 (8.07 - 19.5)	0.23 (0.14 - 0.35)
German hunting terrier	11.4 (3.71 - 26.7)	0.21 (0.07 - 0.48)
Norwegian elkhound, grey	10.4 (6.14 - 16.4)	0.19 (0.11 - 0.29)
Dachshund, standard	9.59 (7.17 - 12.6)	0.17 (0.13 - 0.22)
Norrbottenspitz	9.05 (1.87 - 26.5)	0.16 (0.03 - 0.48)
Icelandic sheepdog	6.65 (0.81 - 24.0)	0.12 (0.01 - 0.43)
Basenji	0 (0 - 14.7)	0 (0 - 0.27)



Prevalence

Patellar luxation is common in certain breeds of dog, with symptoms appearing at a young age. It is relatively common in toy dogs, as well as in larger breeds with straight hind legs (e.g. LaFond et al. 2002, Vidoni et al. 2006, Lappalainen 2016).

High prevalence has been reported in breeds such as:

- Pomeranians (O'Neill et al. 2016, Hodgman 1963, Priester 1972, LaFond et al. 2002, OFA 2021: 30% of those examined were affected);
- Chihuahua (Engdahl et al. 2021a, O'Neill et al. 2016, Hodgman 1963, Priester 1972);
- Australian Terrier (OFA 2021: 18% of those examined affected);
- Cairn terrier (Hodgman 1963);
- Silky Terrier (LaFond et al. 2002);
- Yorkshire Terrier (Engdahl et al. 2021a, O'Neill et al. 2016, Hodgman 1963, Priester 1972, OFA 2021: 18% of those examined affected);
- Miniature Pinscher (LaFond et al. 2002);
- Poodles (Engdahl et al. 2021a, Hodgman 1963, Priester 1972);
- Boston Terrier (Priester 1972);
- French Bulldog (Engdahl et al. 2021a, O'Neill et al. 2016);
- Bichon Frisé (Engdahl et al. 2021a);
- Jack Russell Terrier (Engdahl et al. 2021a); and
- Labrador Retriever (Gibbons et al. 2006, Bound et al. 2009).

When comparing the prevalence of disease between different breeds and types of dog, relative risk should be used instead of absolute prevalence rates. The relative risk takes into account the number of individuals of the breed/type in the data, so that the high number of individuals of the popular breeds does not erroneously increase the importance of the rare diseases in the dog population.

O'Neill et al. (2016) reported that 12 breeds were more susceptible than mixed-breed dogs to patellar luxation requiring treatment (see Table 13).

Table 13. Prevalence of patellar luxation in English veterinary data (O'Neill et al., 2016). Mixed breed used as a reference. Source: The epidemiology of patellar luxation in dogs attending primary-care veterinary practices in England

Breed	N of dogs in the data	Prevalence (%)
Pomeranian	1 040	6.5
Yorkshire Terrier	6 980	5.4
Chihuahua	4 619	4.9
French Bulldog	1 280	4.0
Lhasa Apso	1 686	3.8
Cavalier King Charles Spaniel	4 461	3.8
Bichon Frisé	2 839	3.8
Pug	1 998	3.5
English Bulldog	1 786	2.9
White West Highland Terrier	5 275	2.5
Jack Russell Terrier	13 520	1.7
Shih Tzu	4 151	1.4
Mixed breed	47 300	1.2
Staffordshire Bullterrier	16 746	0.5

According to Finnish screening statistics, patellar luxation occurs in almost every second dog of certain breeds. For instance, 44% of examined Pomeranians, 52% of Yorkshire Terriers, and 31% of Chihuahuas born between 2014 and 2018 were found to have patellar luxation (Finnish Kennel Club Breeding Database). Prevalence rates in screening data are usually higher than in veterinary and insurance data because the latter only include treated dogs and cases for which insurance reimbursement for veterinary expenses has been paid.

The prevalence of patellar luxation is remarkably high in many breeds, especially when the screening data are considered. The most severe cases are not always included in these statistics: the disease typically presents symptoms before the screening age, at which point it is treated surgically, and the dog does not receive an official grade. Additionally, there are cases where a dog is taken for screening after recovering from patellar repair surgery, resulting in a grade that no longer reflects the original condition.

Mode of inheritance

Patellar luxation is a polygenic disease affected by genes and the environment. Some gene loci and candidate genes have been identified in the hope of genomic breeding (Lavrijsen et al. 2014, Soontornvipart et al. 2013, Srinarang et al. 2018). However, no genetic tests are currently available. The medial and lateral forms may be genetically distinct diseases, in which case they would be affected by different genes (Ruotanen 2016).

Estimated heritabilities have ranged from very low to moderate to high, depending on the breed and the statistical estimation model used:

- Flat Coated Retriever: 0.17 (Lavrijsen et al. 2013)
- Chihuahua: 0.18–0.25 (Nilsson et al. 2018, Ruotanen 2020, Zanders 2014)
- Bichon Frise: 0.18–0.21 (Nilsson et al. 2018, Zanders 2014)
- Kooikerhondje: 0.27 (Wangdee et al. 2014)
- Pomeranian: 0.03–0.44 (Ruotanen 2020, Zanders 2014, Wangdee et al. 2017)
- French Bulldog: 0.03 (Zanders 2014)
- Finnish Spitz: 0.17 (Ruotanen 2020)
- Japanese Spitz: 0.06 (Ruotanen 2020).

Low heritability may indicate a limited number of allelic options within the breed for modifying the trait through selective breeding. It may also indicate that the system used to measure or classify the trait is not effective in detecting differences between dogs.

In their master's thesis, Ruotanen (2020) also investigated the genetic correlation between left and right patellar luxation, which was found to be 1 in all four breeds. This suggests that, genetically, it is the same trait.

Predisposing factors

Patellar luxation is associated with small size, particularly small limbs. A 12-fold increase in risk has been reported for small breeds compared to larger breeds (Priester 1972, Hayes et al. 1994, Hulse 1981, Asher et al. 2009). This association has also been reported by Priester (1972) and Vidoni et al. (2006). Chase et al. (2009) found a link between the insulin-like growth factor 1 (IGF1) gene and patellar luxation. IGF1 encodes a protein that promotes growth. Thus, breeding for small size may also increase the risk of patellar luxation.

Also, structural weaknesses of the stifle joint, where limb positioning is incorrect and the trochlear groove is shallow, predispose dogs to patellar luxation (Lappalainen 2016). Breeding dogs to have a specific body shape may have inadvertently caused positional defects in the femur and tibia, the main cause of patellar luxation (O'Neill et al. 2016).

In bowed hind legs, the quadriceps muscle exerts a force that pulls the patella out of position in an inward direction, in addition to extending the knee. In contrast, knock-knees predispose the patella to dislocating outwards. The most common type of tibial misalignment is torsion, where the lower part of the tibia rotates outwards.

Despite the abnormal force pulling the patella to the side, the patellar collateral ligaments can hold it in place. However, over time, the ligaments stretch, and the patella starts to move out of its groove (Eskelinen 2018, Soparat et al. 2012, Fitzpatrick et al. 2012).

In Pomeranians with the most severe degrees of patellar luxation, increasingly complex limb deformities, such as increased femoral rotation, have been reported (Soparat et al. 2012).

Other identified risk factors include sex (females more than males; O'Neill et al. 2016, Bound et al. 2009, Daems et al. 2009, Priester 1972), spaying/neutering (Vidoni et al. 2006, O'Neill et al. 2006) and body weight below the breed average (O'Neill et al. 2016).

Assessment of patellar luxation

Patellar luxation is assessed through palpation and manipulation of the stifle joint. The Finnish Kennel Club's current assessment guidelines are based on the Putnam (1968) grading scale, but have five grades instead of four:

- Grade 0: The patella does not luxate.
- Grade 1: The knee joint is almost normal. The patella can be moved more easily than normal, and it can luxate if the knee is extended. The patella may luxate from time to time but will return to its original position. The attachment point of the patellar ligament may be slightly twisted.
- Grade 2: The patella is usually in place when the limb is extended. However, it luxates when the knee is flexed or rotated and remains out of the trochlear groove until manually repositioned. Twisting of the top of the tibia up to 30 degrees inwards (in small dogs).
- Grade 3: The patella is usually luxated. It can be temporarily put back into place. Twisting of the top of the tibia up to 30–60 degrees.
- Grade 4: The patella is permanently dislocated and will not remain in the groove without surgery. Twisting of the top of the tibia up to 90 degrees.

The risk of clinical symptoms increases significantly as patellar luxation becomes more severe. In grades 2 and 3, dogs will exhibit significant mobility issues. When walking, the dog will briefly hold their hind limb off the ground (the patella is dislocated) before walking normally again (the patella has returned to its position; Lappalainen 2016). In the most severe form of patellar luxation, the patella is permanently dislocated.

Patellar luxation can progress to a more severe form over time, so findings at a young age are not necessarily indicative of the final outcome. According to Finnish Kennel Club guidelines, a definitive result can only be obtained once the dog is three years old. A grade obtained before this age is valid for two years (Suomen Kennelliitto 2020b). If a dog is found to have the worst grade, it cannot be used for breeding, and the Finnish Kennel Club will

register any offspring born under a breeding ban (Suomen Kennelliitto, Dog Registration Guidelines 2023).

X-rays have shown promising results in a few studies as a screening method (Mortar et al. 2009, Marttinen 2016). In practice, X-rays can reliably measure the depth of the trochlear groove in relation to the patella. However, the relative depth of the trochlear groove as a predisposing factor is secondary to other structural defects and measuring it does not rule out other functional defects that can lead to patellar luxation.

The Putnam scale is well suited to evaluating the degree of structural defect and selecting the surgical method, but not to evaluating welfare damage to the dog or the need for surgery.

In severe patellar luxation that starts at a very young age, the knee angulation is almost straight, and the trochlear groove is very shallow because the knee has already adapted structurally to the dislocation during growth. The groove's shallowness is a typical consequence of a lack of contact during growth (straight knee): in this case, the patella moves back and forth without causing major damage, or a connective tissue trough forms on the side of the groove. Even if no major damage is caused, the angulation error will still result in a functional impairment for the dog (Kallio, email communication, 2021).

Mild lesions, as assessed by the Putnam scale, often present with the most severe symptoms and are also the most prone to cartilage damage and associated osteoarthritis. In these knees, the angle of the knee is closer to normal, resulting in greater pressure between the patella and the trochlear groove. Also, the groove is usually deeper, and the groove ridges are higher. This means that even the occasional dislocation of the patella can cause severe cartilage damage. If left untreated, mild dislocations often progress to grade III over time, as the dog would rather accept a permanently dislocated patella than constantly experience it snapping over the broken cartilage edge of the trochlear ridge (Kallio, email communication, 2021).

Treatment options

In the epidemiological review by O'Neill et al. (2016), 39% of cases were treated with medication, 13% underwent surgery, and 4% were referred to a specialist. However, in the specialist data, 83% of cases were reported to have undergone surgery (Alam et al. 2007). Such data is likely to be particularly selective for more severe cases.

Treatment may require multiple operations, and the prognosis may be poor. Surgery is neither simple nor risk-free, with complications reported in 18–29% of cases (Gibbons et al. 2006, Arthurs & Langley-Hobbs 2006). Recovery takes a few months and requires systematic rehabilitation of the knee.

In a study by Wangdee et al. (2013), patellar luxation occurred in one in ten dogs even after surgery. The surgical outcome was successful in all cases of grade II patellar luxation. The disease recurred in approximately one in ten dogs with grade III luxation and in over one in three dogs with grade IV luxation (grading was from I to IV). Conversely, the surgical prognosis for patellar luxation assessed as mild on the Putnam scale is favourable: pain is alleviated, osteoarthritis is prevented, and normal mechanics are restored (Kallio, email communication 2021).

Breeding

According to Ruotanen (2020), selective breeding based on an individual's phenotype has not been effective. Zanders (2014) suggested that variation between veterinarians can lead to significant variation in patellar luxation grading. However, a dog's grade may change within a few days as it may use its musculature to compensate for pain (Kallio, personal communication, 2021).

- When ligaments first fail, there is swelling in the knee as well as pain and ligament damage. If the dog tenses its thigh muscles because of the pain, it may be able to balance the patella better in the trochlear groove, making the patella feel more stable. However, as the pain eases over time, the patella can easily dislocate again, even if the dog is no longer symptomatic.
- Indeed, if a dog's hind leg is very straight – that is, if the dog has a clearly deformed structure – muscle tension can exacerbate the tendency of the patella to dislocate. Even in cases of mild patellar luxation, the knee can get stuck into a tightly dislocated position due to pain.

Therefore, it is typical of patellar luxation that a dog's condition can vary. In addition to skeletal structure, the patellofemoral mechanism is affected by many factors. These include pain, joint swelling, angulation, range of motion in the leg and hip function. As mentioned previously, the degree of luxation increases over time as the ligaments stretch and the ridge lowers. The nature of the disorder makes screening difficult, which is probably the main cause of low heritabilities and inefficient breeding. Progress in breeding would require the systematic exclusion of all affected dogs from breeding programmes.

Currently, mild patellar luxation is accepted for breeding in all pedigree dog breeds (Finnish Kennel Club, PEVISA programmes). However, a healthy joint is only grade 0, where the patella remains in place. Since the degree of luxation tends to worsen over time, breeding young dogs with only mild luxation at the time of mating is likely to perpetuate the condition in the dog population.

In female dogs, the increase in weight-bearing and stomach growth during pregnancy, along with the resulting change in knee posture, brings additional risks. In this case, even a grade II medial dislocation can cause problems with patellar luxation.

Based on the above, the following measures could be taken to reduce the prevalence of patellar luxation:

- Creating a database of dogs with symptomatic patellar luxation that have undergone or require surgical treatment and exclude these dogs from breeding programmes.
- Using only dogs with a grade of 0 on the Putnam scale for breeding (no abnormalities).
- Refraining from breeding dogs before the age of three.
- Breeding for healthier and more functional conformation. Conformational traits are usually highly heritable, meaning they can be relatively easily modified through selective breeding.
- Using risk predictions based on pedigree and/or genomic information (e.g. estimated breeding values or possible future genetic testing) when selecting breeding dogs.
    - Estimated breeding values (BLUP) or simpler risk predictions (e.g. the Epi Index used for Finnish Spitzes).

- Breeding values and risk predictions could combine different data sources, such as data on symptomatic and/or surgically treated dogs, measurements of correlated conformational traits, screening results, and possible genomic risk values.

5.6.2. Cranial cruciate ligament disease

The cruciate ligaments are strong, short structures located in the middle of the stifle (knee) joint, connecting the femur to the tibia. The cranial cruciate ligament is more important functionally than the caudal ligament because it supports the femoral head on the tibial articular surface during flexion of the hind leg. It also limits the knee joint's rotational movement.

If the cranial cruciate ligament fails, the knee joint becomes loose, and the femur can slide backwards on the tibial articular surface. This movement damages the joint capsules and cartilage surfaces. As a result of cruciate ligament damage, degenerative osteoarthritis quickly develops in the knee joint due to an inflammatory reaction (Kallio 2018).

Cranial cruciate ligament disease (CCLD) was previously considered to be a sudden, traumatic injury. However, it is now known that around 80% of these injuries are initially partial (Griffon 2010, Kallio 2018). The knee may initially be robust or exhibit mild looseness. The injury gradually progresses as the cruciate ligament degenerates. Rather than healing, the ligament breaks down. Osteoarthritic changes often develop in the knee as the ligament damage and joint laxity progress (Kallio 2018).

Treatment options

A ruptured cruciate ligament causes pain and lameness in dogs. When the ligament is broken, the dog is usually unable to bear any weight on the affected leg.

For small dogs, conservative treatment involving pain medication, physical rehabilitation and weight management can be attempted, although surgery is preferable. In a study by Bogen et al. (2020), dogs that underwent surgery were less likely to be euthanised than those that received conservative treatment. With conservative treatment, osteoarthritic changes usually develop in the knee. There is also a risk of meniscus tear and associated pain. Often, meniscal damage requires surgical treatment.

In larger dogs, cranial cruciate ligament damage is always treated surgically. Early treatment is necessary to prevent the progression of osteoarthritis. Several dozen surgical techniques are available (Bergh et al. 2014). While the outcome of treatment is usually good, even surgery does not completely prevent the development of osteoarthritis in the knee joint (Kallio 2018). Recovery from surgery takes weeks or months and requires dedicated rehabilitation. Regular physical therapy is usually necessary to aid recovery.

Progressive osteoarthritis causes chronic pain. According to an owner survey, long-term chronic pain was observed in around 30% of dogs after surgery (Mölsä et al. 2013).

While long-term treatment outcomes for CCLD are generally positive, the condition often leads to osteoarthritis and chronic pain. In severe cases, this can result in euthanasia. Of the 333 Swedish and Norwegian dogs treated for CCLD in the Bogen et al. (2020) veterinary hospital data, 18.3% had been euthanised due to causes related to the CCLD. This proportion was higher in dogs treated conservatively (29%). The most common reason for euthanasia due to CCLD was persistent lameness of the affected limb.

In the Swedish insurance data of Engdahl et al. (2021b), which covered over 600,000 dogs, 17% of those with claims for CCLD treatment were euthanised. In almost all these cases, the reason for euthanasia was specifically related to the CCLD. The euthanised dogs were between 0 and 4.25 years old. By contrast, Mölsä et al. (2013) reported that only 2% of dogs were euthanised. These differences are probably due to different kind of data: Mölsä et al.'s data were from an owner survey of 253 Finnish cases, conducted on average 2.7 years after diagnosis.

Prevalence

CCLD is one of the most common orthopaedic diseases in dogs (Johnson et al. 1994), as well as being the most common stifle joint disease requiring surgical treatment (Griffon 2010, Guthrie et al. 2012, Kallio 2018). Rupture of the caudal cruciate ligament in the absence of CCLD is much less common, often being caused by trauma (Johnson et al. 1994, Johnson & Olmstead 1987).

A study by Taylor-Brown et al. (2015) examined 171,522 English dogs from veterinary clinical data and found that CCLD occurred in slightly more than one in 200 dogs (0.56%). In Swedish insurance data (Engdahl et al. 2021b), the incidence was 23.8 cases per 10,000 dog-years at risk. A total of 181 breeds had at least one insurance claim for cruciate ligament treatment in at least one dog. Of these breeds, 26 had a significantly higher relative risk, while 18 had a lower one.

The prevalence of the disease varies greatly between breeds and even between litters, indicating a hereditary component. CCLD tends to occur at a younger age in large and giant breeds, and these dogs are euthanised at a younger age than those of smaller breeds (Engdahl et al. 2021b).

CCLD has been reported particularly in the following dog breeds:

- Rottweiler (Guthrie et al. 2012, Nečas et al. 2000, Whitehair et al. 1993, Witsberger et al. 2008, Taylor-Brown et al. 2015, and Adams et al. 2011, who reported a risk five times higher than that of other breeds),
- Labrador Retriever (Guthrie et al. 2012, Witsberger et al. 2008, Nečas et al. 2000),
- Newfoundland (Whitehair et al. 1993, Witsberger et al. 2008),
- Golden Retriever (Guthrie et al. 2012, Taylor-Brown et al. 2015),
- Boxer (Guthrie et al. 2012, Nečas et al. 2000),
- White West Highland Terrier (Adams et al. 2011, Taylor-Brown et al. 2015),
- Yorkshire Terrier (Adams et al. 2011, Taylor-Brown et al. 2015),
- Staffordshire Bull Terrier (Whitehair et al. 1993, Taylor-Brown et al. 2015),
- Bichon Frise (Engdahl et al. 2021b), and
- Jack Russell Terrier (Engdahl et al. 2021b).

Nečas et al. (2000) also added the American Staffordshire Terrier, Fila Brasileiro, American Cocker Spaniel, Chow Chow, German Shorthaired Pointer, Saint Bernard and Bullmastiff to the list. The disease is also highly prevalent in mixed-breed dogs (Bellumori et al. 2013).

Predisposing factors

Most predisposing factors for CCLD are related to a dog's conformation, other diseases, and resulting stifle joint dysfunction (Griffon 2010, Comerford et al. 2011, Kallio 2018).

Conformation

In terms of conformation, a significant factor in the development of CCLD is straight hind leg angulation, i.e. a knee that is too straight when viewed from the side. Knee angulation is the angle between the femur and the tibia behind the knee. In a dog of normal conformation, this angle is about 135 degrees. If the knee is too straight, the angle increases, and in the worst case, the tibia and femur can become almost parallel. This puts additional stress on the cranial cruciate ligament.

Other stifle joint conditions

Conditions such as patellar luxation in small dogs and osteochondrosis in larger ones often lead to CCLD (Gibbons et al. 2006, Campbell et al. 2010, Nganvongpanit et al. 2011, Boge et al. 2020). In addition to the inflammatory response and osteoarthritic changes, patellar luxation is associated with a change in the position of the knee. Untreated medial dislocation, in particular, which involves the tibia rotating inwards, damages the cruciate ligament (Kallio 2018, Comerford et al. 2011).

In a study by Campbell et al. (2010), it was found that 41% of dogs with medial patellar luxation also had concomitant CCLD. The worst grade of patellar luxation has particularly been associated with cranial cruciate ligament rupture (Campbell et al. 2010, Nganvongpanit et al. 2011).

The Engdahl study (2021a) found that patellar luxation was the most common stifle diagnosis in Chihuahuas, Yorkshire Terriers, Miniature and Toy Poodles, and French Bulldogs. It was also the second most common diagnosis after cruciate ligament rupture in Bichon Frisé and Jack Russell Terrier. All these breeds are at an increased risk of medial patellar luxation. CCLD was among the three most common stifle diagnoses in all these breeds.

Osteochondrosis can interfere with the normal development of the cranial cruciate ligament during growth. Later, osteochondrosis-related cartilage damage, joint inflammation and osteoarthritic changes can lead to cruciate ligament failure (Kallio 2018).

Hip pain can also increase the load on the knee, which may lead to CCLD (Kallio 2018).

Other predisposing conditions

In the Engdahl study (2021b), certain diagnoses, including musculoskeletal, skin, gastrointestinal, urinary, eye and liver conditions, as well as general whole-body conditions such as fatigue, were more prevalent in dogs with CCLD. It is possible that some of these conditions, or the treatments associated with them, acted as predisposing factors for the disease. For instance, atopic skin disease is typically treated with long-term cortisone therapy, and ligament rupture is a symptom of cortisone-induced Cushing's disease.

In a study by Bogen et al. (2020), 40.2% of dogs treated for a cruciate ligament injury had a concomitant disease. The most common of these were patellar luxation for orthopaedic diseases and skin diseases for other diseases.

CCLD can affect dogs of all ages, but the typical age at which symptoms first appear may provide a clue as to the underlying cause of the disease in a particular breed. In osteochondrosis, CCLD may be symptomatic even before growth is complete. In some small breeds, most cases of occur in old age; in these cases, degenerative general diseases may be a significant underlying cause (Kallio 2018). In older dogs, diseases affecting general health, such as hypothyroidism and cortisol overproduction (Cushing's disease), are predisposing factors.

A dog diagnosed with and treated for CCLD has approximately a 50% chance of developing the condition in the other knee within a year (Buote et al. 2009, Muir et al. 2011). This finding again highlights the importance of conformation, individual susceptibility, and hereditary predisposition in the development of the disease, rather than individual trauma.

Excess weight is also a significant predisposing factor for cruciate ligament injury. A review of insurance data by Taylor-Brown et al. (2015) found that risk was related to dog breed, being overweight, and age (dogs over three years old were at a higher risk than younger dogs). Spayed bitches were 2.1 times more likely to be diagnosed than intact bitches. Similar results were reported by Whitehair et al. (1993).

Mode of inheritance and breeding

Cranial cruciate ligament damage is a polygenic disease caused by a combination of genes and other factors, as listed above. Many of these factors are also hereditary. In terms of breeding, the main known predisposing factors are conformation, patellar luxation and osteochondrosis. Therefore, reducing the prevalence of these diseases would also reduce CCLD.

Nearly 100 risk variants have been identified for CCLD (Baker et al. 2017, study in Labrador Retrievers). Genomic loci associated with the disease have also been identified in Newfoundland dogs (Wilke et al. 2006).

Moderate to high heritabilities have been estimated for the disease depending on the breed, statistical model, and method used (genomic analysis or regression analysis):

- Boxer: 0.28 (Nielen et al. 2003)
- Labrador Retriever: 0.48–0.89 (Baker et al. 2017, Cook et al. 2020)
- Newfoundland: 0.27 (Wilke et al. 2006).

Based on the above, the following measures could be taken to reduce the prevalence of CCLD:

- Creating a database of affected dogs and exclude these dogs from breeding programmes.
    - This would not apply in cases where the ligament has been broken because of a very strong external force. This can occur in situations involving a violent collision, such as a car accident. In such cases, other structures in the knee are usually broken too. Inherently strong cruciate ligaments do not break during play or even during heavy exercise typical for canines.
    - Information on individuals requiring surgical treatment is particularly important because there is no screening method for the disease, and the dog is usually already used for breeding by the time the disease occurs.
- Breeding for healthier and more functional conformation (Anderson et al. 2020, Griffon 2010, Wilke 2010).
    - Measuring conformation traits associated with the disease and genomic risk areas.
    - Conformation traits are typically highly heritable, meaning they can be relatively easily modified through selective breeding.
- Reducing other hereditary risk factors.
    - Especially patellar luxation, osteochondrosis and hip dysplasia; also obesity.

- Using risk predictions based on pedigree and/or the genomic information when selecting breeding dogs.
    - Estimated breeding values (BLUP) can be used for this purpose, as can simpler risk predictions (e.g. the Epi index used for Finnish Spitzes).
    - In a study by Baker et al. (2017), genomic loci associated with the disease were used to estimate individual risk. Genomic risk scores differed markedly between diseased and control dogs. A genomic test is available for US-based Labrador retrievers and is under development for a wider population and other at-risk breeds.
    - Breeding values and risk predictions could combine different data sources, such as data on affected dogs, conformational measurements, and screening results for patellar luxation and hip dysplasia.

5.7. Osteochondrosis

Osteochondrosis (OC) is the abnormal ossification of epiphyseal cartilage during endochondral ossification, resulting in cartilage damage at the affected site. OC occurs in both humans and many other species, most commonly pigs, horses and dogs.

In dogs, OC is particularly prevalent in the shoulder, elbow, stifle and hock (Olsson 1987). This part of the report mainly deals with shoulder osteochondrosis, the most common location for the condition in dogs, for which a screening method is available for use in breeding programmes.

A large proportion of stifle osteochondrosis cases are likely to be diagnosed as secondary disorders, such as CCLD and osteoarthritis (see Cranial Cruciate Ligament Disease). Diagnosing stifle osteochondrosis in growing dogs by radiography is challenging and often requires CT scanning. Elbow osteochondrosis is often the result of incongruence or fractured coronoid process. In the elbow joint, osteochondrosis may be difficult or impossible to demonstrate as a separate disease on imaging. Hock osteochondrosis is relatively rare in dogs (J. Kallio, personal communication, 2022).

OC is the same disease, regardless of where it occurs. Therefore, knowledge of all symptomatic and euthanised dogs is valuable for breeding purposes, as it adds to the information gathered from relatives. This increases the likelihood of selecting the right dogs for breeding, thereby reducing the disease.

5.7.1. Shoulder osteochondrosis

Shoulder osteochondrosis is usually diagnosed using X-rays. On X-rays, osteochondrosis appears as a radiolucent lesion or flattening, beneath which there is typically an increase in bone density (Reunanen 2021).

There are three different forms/stages of osteochondrosis (Ytrehus 2007).

- *latens*: lesion confined to epiphyseal cartilage,
- *manifesta*: lesion accompanied by delay in endochondral ossification, and
- *dissecans* (OCD): cleft formation through articular cartilage.

Prevalence

Lavikka's (2016) data on 129 treated Border Collies revealed that osteochondrosis was most prevalent in the shoulder joints (affecting 93.9% of patients). In Nečas et al.'s (1999) veterinary database of 112 dogs, 76% of treated cases were in the shoulder joint; the rest were in the stifle (16%), hock (4.4%), and elbow (3.6%) joints.

Changes were bilateral in 25% of cases in the Nečas et al. (1999) data. Rochat (2012, cited in Lavikka, 2016) reports bilateral changes in 27–68% of dogs.

Osteochondrosis is particularly prevalent in large and giant breeds. The following breeds have been cited as being at risk in the literature (Ohlert et al. 2016, Maddox et al. 2013, McKee & Macias 2004, La Fond et al. 2002, Morgan et al. 1999, Nečas et al. 1999, Padgett et al. 1995b, Knecht et al. 1977):

- Bernese Mountain Dog,
- Boxer,
- Border Collie,
- Bouvier,
- Bull Terrier,
- Dalmatian,
- English Setter,
- Fila Brasileiro,
- Irish Wolfhound,
- Great Swiss Mountain Dog,
- Newfoundland,
- Labrador Retriever,
- Rottweiler, and
- Great Dane.

According to data from Lavikka's (2016) study, the prevalence of osteochondrosis requiring treatment in Border Collies in Finland was between 2.5% and 3.8% during 2011–2015. Between 2018 and the beginning of November 2022, 1,006 Border Collies were recorded as having an osteochondrosis grade in the Kennel Club's breeding database, of which 98 (9.7%) were diagnosed with osteochondrosis. A large number of screenings have also been performed, e.g. on Rhodesian Ridgebacks (7.6% (9/119)) and German Pointers (11.1% (7/63) and 19.0% (29/153) for the wirehaired and shorthaired variants, respectively). Screening for osteochondrosis has only been available in Finland for a few years.

In Switzerland, screening has revealed a prevalence of 14% in the Great Swiss Mountain Dog and 8% in the Border Collie out of 351 and 511 dogs examined respectively (Ohlert et al. 2016). In Belgium, the prevalence varied between 0% and 10% in Great Swiss Mountain Dogs, Bernese Mountain Dogs, Labrador Retrievers, and Golden Retrievers (Coopman et al. 2008).

As most screenings are of potential breeding dogs, which are assumed to be healthy, the prevalence is not representative of the population as a whole. X-rays of symptomatic dogs with osteochondrosis are rarely sent for centralised grading and recording in the screening programme (Ohlert et al. 2016). However, this would be important for breeding purposes.

Mode of inheritance

Osteochondrosis is a polygenic inherited disease. Although risk loci and candidate genes have been identified in pigs and horses, there is no single genetic factor that can fully explain the condition. Heritability estimates in pigs and horses range from 0.14 to 0.52 (Grondahl & Dolvik 1993, Reiland et al. 1978, van Grevenhof et al. 2009).

Estimates of heritability for canine osteochondrosis have been obtained for Bernese Mountain Dogs and Labrador Retrievers, with highly variable results ranging from 0 to 0.77 (Hartmann et al. 2010, Guthrie & Pidduck 199, Morgan et al. 1999).

Symptoms, treatment and prognosis

Osteochondrosis (latens and manifesta) may heal with growth, remain unchanged, or lead to detached fragment of cartilage (dissecans; Reunanen & Grøndalen 1974).

The mild forms of osteochondrosis (latens and manifesta) are often asymptomatic. A detached fragment inside the joint (the dissecans form) and/or contact between synovial fluid and the bone surface usually causes a sterile inflammatory reaction, resulting in a warm, swollen and painful joint (Johnston 1998, Reunanen 2021).

The most common symptom of osteochondrosis is an obscure limp that appears at around 3–9 months of age. This increases with exertion and decreases at rest. Sometimes the lameness can be difficult to notice, especially if it is mild or bilateral. Shortened stride length and pain on flexion or extension of the limb may be noted. Sometimes, symptoms do not manifest until adulthood.

Osteochondrosis manifesta were found in 70% of young pigs studied, but clinical disease was found in only 7% (Ytrehus et al. 2004a). In humans, approximately half of the juvenile osteochondrosis lesions observed on X-rays were treated conservatively (Cahill 1995). The situation appears to be similar in dogs, according to patient data (Kallio, email communication, 2022).

Osteochondrosis (dissecans) that has progressed to a detached flap of cartilage often leads to obvious osteoarthritic changes (Grøndalen 1974, Ohlert et al. 2016, Reunanen 2021). In the worst case, severe osteoarthritis and/or an inflammation of the bicep tendon develops in the shoulder joint, which is associated with an inflammatory reaction or osteoarthritis of the shoulder joint (Reunanen 2021, Kallio, personal communication, 2022). Osteoarthritis causes chronic pain

Early detection and treatment of osteochondrosis usually results in a better prognosis and slows down the development of osteoarthritis. The prognosis is influenced by the location of the lesion, the chosen treatment and the dog's age (Bieżyński et al. 2012, Johnston 1998, Olivieri et al. 2007, ELL; Kallio, email communication, 2022).

Shoulder osteochondrosis has the best prognosis of all the joints. The prognosis is worse if:

- severe changes are detected at the onset of symptoms
- the dog is large
- the lesion has progressed to a severe stage and operative treatment is delayed or not carried out
- there is pre-existing osteoarthritis of the joint
- osteochondrosis is in the hock, elbow or stifle.

For asymptomatic or mildly symptomatic dogs, conservative treatment (i.e. weight management, rest and pain medication) may be appropriate. Otherwise, the joint is treated surgically.

Surgical treatment of shoulder osteochondrosis has a good prognosis.

Lavikka's (2016) PhD thesis data on 129 Finnish Border Collies showed that osteochondrosis (predominantly in the shoulder joint) was most often treated surgically (73.6% of patients). Mild to moderate osteochondrosis developed in 40.5% of patients; however, 80% of dogs were evaluated by their owners as having recovered sufficiently to tolerate physically or moderately demanding work or leisure activities. Those operated on shortly after the onset of symptoms were better able to withstand physical exertion than those operated on later.

Predisposing factors

Osteochondrosis is more prevalent in male dogs than in females. The same applies to humans and pigs, but not to horses.

Apart from sex, researchers agree on only two risk factors for osteochondrosis: hereditary predisposition and an abnormal joint structure, which is also hereditary. An abnormal structure places greater than normal stress on a particular area of the articular surface and may therefore predispose to osteochondrosis (Grøndalen 1974). Knock-knees predispose the knee to osteochondrosis because they cause greater pressure load on the lateral femoral condyle (Olsson 1987). Uneven growth of the elbow and radius predisposes to elbow osteochondrosis (Olsson 1987).

Other suggested risk factors include rapid growth due to excessive energy intake, being overweight, external trauma, circulatory disturbances, and hormonal factors. However, trauma alone is not sufficient to explain osteochondrosis, as the changes that occur are specific to certain sites and are often bilaterally symmetrical (De Lahunta et al. 1974, Grøndalen 1974, Woodard et al. 1987, Ytrehus et al. 2004b and 2007).

Practical patient data indicates that the main risk factors for shoulder osteochondrosis are heredity, hip dysplasia and strenuous physical activity during the growth period (around 4–8 months), which is exacerbated by being lively, being overweight as well as destructive training and rewarding practices (Kallio, email communication, 2022).

Osteochondrosis in breeding

Due to the hereditary nature of osteochondrosis, the condition can be reduced through systematic, selective breeding. When selecting breeding dogs, one can consider the dog's own screening results, the results of its relatives, and information on affected dogs in the population.

The Finnish Kennel Club developed instructions for shoulder osteochondrosis examinations in 2016. The grading scale has three categories (Suomen Kennelliitto, 2022):

- OC Unaffected: The humeral head is round and even.
- OC Open to Interpretation: Very mild or atypical changes.
- OC Affected: There is a flattened or radiolucent area on the posterior surface of the humeral head.

A certificate can be issued for a dog under 12 months old if signs of osteochondrosis are found in the joint (OC Affected). The OC Unaffected or Open to Interpretation grades cannot be obtained before the age of 12 months.

5.8. Eye diseases

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Since the 1950s, dogs have been examined for hereditary eye diseases and their elimination through breeding, following the discovery of a progressive, blinding retinal disease in Irish Setters. For decades, the focus was mainly on blinding progressive retinal atrophy (PRA), hereditary cataracts that can lead to blindness (HC) and retinal dysplasia (RD). Today, numerous other known or presumed hereditary changes in different parts of the eye are also recognised. Some of these changes are of minor importance for the animal's welfare. Known and presumed hereditary diseases are listed and described in Chapter 6 of the ECVO Manual, which is published by the European College of Veterinary Ophthalmologists (ECVO).

The ECVO Hereditary Eye Disease (HED) Committee provides dog owners and breeders with advice on the significance of eye disease in relation to individual well-being and breeding (see the ECVO Manual, Chapter 8: Veterinary Advice). Breeding choices should aim to prevent or reduce the occurrence of serious diseases or conditions that threaten vision, cause pain, or require surgery or continuous medication. ECVO breeding recommendations are directly related to ocular health, and when making breeding choices, other diseases occurring in the breed must always be taken into account, especially in the case of milder eye diseases

Some eye diseases only manifest themselves in young adulthood or middle age. To obtain comprehensive information on the occurrence of hereditary eye diseases and their modes of inheritance, ECVO recommends that animals used for breeding undergo an official eye examination annually, and others undergo the examination 3–4 times in their lifetime, e.g. at 1, 3, 6 and 9 years of age. Gonioscopy, i.e. an examination of the iridocorneal angle of the eye for changes that predispose to angle-closure glaucoma, is recommended every three years for breeds/types of dogs in which the disease occurs (ECVO Manual, Chapter 8, 'Age and frequency recommendations').

Registered pedigree dogs are examined for eye diseases to various degrees in different countries and continents. Veterinarians who are specifically approved for this purpose may provide certificates regarding hereditary eye diseases. These certificates are collected and stored in registers in different ways, depending on the country or continent. In some countries, such as Finland, they are public.

In Finland, the certificates only affect the registration of puppies in the Finnish Kennel Club in breeds that have a programme for combating hereditary diseases and defects (PEVISA, abbreviation for the Finnish term), and even the only for the diseases mentioned in the program. In other breeds, breeding choices are guided by breed-specific breeding strategies, but the final decision is always made by the breeder. Since dogs are currently considered property under the law, owners can prevent the publication of the certificate in the Finnish Kennel Club's breeding database if the result is undesirable and the breed is not included in the PEVISA programme. Such dogs can therefore also be used for breeding, and their puppies are registered with the Finnish Kennel Club as normal. On the other hand, dogs may be excluded from breeding due to minor eye changes, despite them being otherwise healthy.

The ECVO also maintains a list of existing genetic tests for eye diseases on its website (ECVO Manual, Chapter 10: DNA Tests for Hereditary Eye Disease, and Chapter 10.1: Known Genes, Mutations and Genetic Testing). Information on known gene mutations and available genetic tests can also be found on the omia.org website, and breed-specific information on the dog-wellnet.com website (genetic testing). Genetic testing is recommended for animals used for breeding in the high-risk breeds and/or breed combinations. However genetic testing does not replace clinical eye examinations because they do not provide information about the overall condition of the eyes. Additionally, the same hereditary eye disease may be caused by more than one gene mutation within a breed.

The ECVO recommends excluding from breeding individuals with eye diseases that cause pain/discomfort and/or threaten vision, or that require surgery and/or continuous medication. This recommendation applies to both known and presumed hereditary diseases.

Kempe and Mäki (2020) compiled a list of breeding restrictions relating to diseases and defects of the eyes and surrounding tissues, particularly those associated with brachycephaly. The following list complements these restrictions and is in accordance with the ECVO recommendations:

<u>Known or presumed hereditary eye diseases that may cause pain or discomfort:</u>

- hard, misplaced eyelashes that rub against the surface of the eye (distichiasis and ectopic cilia, severe),
- inward-turning eyelids (entropion),
- insufficient tear production due to immunological inflammation of the lacrimal gland (or other causes), resulting in inflammation of the conjunctiva and cornea, known as dry eye disease, or keratoconjunctivitis sicca,
- punctate keratitis causing corneal ulcers,
- severe changes in the iridocorneal angle of the eye, which predispose to glaucoma,
- angle-closure or open angle glaucoma,
- lens luxation,
- advanced cataracts causing secondary uveitis (if left untreated), and
- ocular melanosis, in which abnormal proliferation of melanocytes in the uvea can lead to obstruction of aqueous humor outflow structures and secondary glaucoma.

<u>Known or presumed hereditary eye diseases that can threaten vision:</u>

- exophthalmos due to shallow orbit (brachycephalic dogs)
    - corneal pigmentation,
    - corneal ulcers that can lead to perforation,
    - bulging of the eyeball out of the orbit,
- chronic superficial keratitis,
- pigmentary keratitis,
- macular corneal dystrophy (Labrador Retriever),
- insufficient tear production due to immunological inflammation of the lacrimal gland (or other causes), resulting in inflammation of the conjunctiva and cornea, known as dry eye disease, or keratoconjunctivitis sicca,
- severe corneal dystrophy (stromal or endothelial),
- cataract,
- lens luxation,

- severe remnants of foetal tissue – persistent pupillary membrane (PPM), iris-cornea and iris-lens, or lamina) - persistent hyperplastic tunica vasculosa lentis / persistent hyperplastic primary vitreouss (PHTVL-PHPV), grades 2–6,
- severe changes in the iridocorneal angle predisposing to glaucoma,
- glaucoma (angle-closure or open angle),
- ocular melanosis, in which abnormal proliferation of melanocytes in the uvea can lead to obstruction of aqueous humor outflow structures and secondary glaucoma.
- (congenital) retinal detachment,
- severe optic nerve hypoplasia (coloboma),
- diseases causing progressive retinal degeneration
    - PRA and other hereditary retinal diseases,
- excessive skin folds covering the eye, (e.g. Chow Chow and Shar Pei), and
- drooping eyelids obscuring vision, due to abundant skin in the head, heavy ears and excessive eyelid opening, i.e. macroblepharon(many spaniels, hounds and bassets).

<u>Known or presumed hereditary eye diseases that may require surgical treatment:</u>

- eyelid malpositions:
    - entropion
        - spaniels, retrievers, molossians and other similar breeds lateral lower eyelid +/- lateral canthus,
        - brachycephalic and round-headed dogs with a small muzzle and a steep stop: medial eyelid margins and medial canthus,
    - ectropion and excessive eyelid opening, (macroblepharon), e.g. spaniels, bloodhounds, St. Bernards, Great Danes and similar breeds,
    - shallow orbit and protruding eyes: brachycephalic dogs,
- skin folds covering and/ or rubbing the eyes,
- eyelid drooping due to loose forehead skin and large, heavy ears,
- congenital tissue defects of the eyelids (coloboma),
- imperforate lacrimal punctum (puncta aplasia), i.e. unopened tear canal openings,
- abnormally located extra eyelashes (distichiasis, ectopic cilia)
    - quality often proportional to hair quality: stiff ones cause more harm than soft ones,
- prolapse of the third eyelid gland (known as 'cherry eye'),
- third eyelid cartilage eversion,
- malpositioned tissue in the eye and/or surrounding tissue (known as dermoids),
- punctate keratitis (in the case of deep corneal wounds/corneal perforation),
- dry eye disease
    - parotid duct transposition if the condition is unresponsive to medical treatment,
- iris melanoma,
- lens luxation,
- cataracts, and
- glaucoma.

Surgical procedures that do not necessarily lead to a breeding ban: tear canal puncta opening, prolapsed third eyelid gland (cherry eye), cartilage eversion and dermoid. They typically cause minor harm to the wellbeing, can be corrected at once and mode of inheritance is unclear.

Known or presumed hereditary eye diseases requiring continuous medication:

- chronic superficial keratitis, i.e. pannus,
- pigmentary keratitis,
- punctate keratitis,
- lymphocytic-plasmacytic inflammation of the third eyelid (plasmoma), often in conjunction with pannus,
- macular corneal dystrophy in Labrador Retrievers,
- immunological lacrimal gland inflammation (or other causes) leading to low tear production and resulting conjunctival and corneal inflammation, known as dry eye (keratoconjunctivitis sicca),
- lens induced uveitis i.e. inflammation of the uvea secondary to advancing,
- ocular melanosis and associated secondary glaucoma, and
- glaucoma.

Bedford (2013) wrote an article titled 'Hereditary Ocular Disease in the dog' which contains pictures illustrating eye diseases in dogs. The article was commissioned by FECAVA (the Federation of European Companion Animal Veterinary Associations).

5.9. Welfare problems caused by individual gene variants

Hundreds of gene variants (mutations) that are associated with hereditary diseases have been identified in dogs. Commercial genetic tests are available for most of these variants. Information on known gene variants, related studies, the effect of the variants on the phenotype and possible genetic tests is available in the OMIA database, which is maintained by the University of Sydney (omia.org).

Donner et al. (2023) analysed samples from over one million dogs in more than 150 countries and discovered that 57% of the dogs were carriers of at least one of the 242 gene variants examined, either as heterozygotes or homozygotes. The significance of these gene variants can vary greatly between breeds.

Some variants cause a specific disease whenever they occur in a certain genotype, while others act as risk factors, forming part of a broader system that leads to disease.

Causal gene variants cause a trait or disease

A gene variant that causes a trait when present in one or two copies is called causal. If a gene variant associated with a hereditary disease is dominant, only one copy is needed to cause the disease. If the variant is recessive, two copies must be present for the disease to occur.

A gene variant is called lethal if it causes death when present in double (homozygous) form. A variant is semilethal if it results in more than 50%, but less than 100%, of individuals dying when homozygous. For example, the hairless characteristic of the Chinese Crested Dog is dominantly inherited, and the dominant *FOXI3* gene variant is lethal when present in homozygous form. This variant causes carriers to develop ectodermal dysplasia, a skin disease manifested by hairlessness or sparse hair, as well as abnormal tooth morphology. A dog only has a normal coat and teeth if it has two recessive, or wild-type, gene variants.

The lethal variant's effect is seen in smaller than normal litter sizes. When two hairless Chinese Crested Dogs are bred together, on average, every fourth (25%) offspring is

homozygous for the lethal *FOXI3* variant and dies. The remaining offspring are either hairless heterozygotes or have normal coats. On average, two out of three, or 67%, are hairless (carriers of the lethal variant) and one out of three, or 33%, have normal coats. This is the typical genotype ratio of offspring from a cross between heterozygotes for the lethal variant.

Genetic variants that act as risk factors

Some of the known genetic variants in dogs are predisposing factors to specific diseases. For instance, a recessively inherited variant in the *SLC2A9* gene causes homozygous dogs to exhibit increased levels of uric acid in their urine and blood (hyperuricosuria, or HUU), which predisposes them to urolithiasis.

The magnitude of the risk of disease caused by risk variants can vary and may differ between breeds/types of dogs.

Genetic variants related to breed characteristics

Some of the characteristics that are desired in certain breeds of dog are caused by genetic variants that also cause or predispose to a welfare problem. Some of these variants are lethal, such as the dominant hairlessness variant described above. Unlike other harmful genetic mutations, however, those responsible for or linked to breed characteristics are not eliminated from breeds because they are selected to preserve those characteristics, despite the accompanying diseases and defects.

Welfare problems related to gene variants that control coat colour

Some dog coat colours are associated with welfare issues or make dogs more susceptible to them. These include merle coat patterns, blue dilution and deafness associated with white colouring.

The reliability of genetic tests

Some genes/diseases have proven difficult to test. For instance, when testing for the degenerative myelopathy risk gene (https://omia.org/OMIA000263/9615/), the results received by some dogs and their parents could not be true based on the laws of inheritance. Turba et al. (2017) and Santos et al. (2020) investigated this phenomenon and concluded that the current test for the *SOD1* gene is unreliable.

When testing risk variants, it is also important to establish whether the variant poses a significant risk to the dog's welfare or whether the link to a welfare problem is weak. Risk variants should not be tested in breeds or types of dogs where they have not been found to be associated with a significant disease risk.

Gershony and Oberbauer (2020) have produced an informative and comprehensive package on canine genetic testing.

The 'Harmonization of Genetic Testing for Dogs' database on dogwellnet.com (International Partnership for Dogs, 2021) evaluates testing laboratories and the suitability of various tests for different breeds. The website also provides advice if needed.

5.9.1. Adverse gene variants associated with breed-typical appearance

*Asterisk meaning: The Council of Europe's 1995 Resolution on the Breeding of Pet Animals recommends avoiding or stopping breeding altogether unless serious defects can be eliminated.

Chondrodysplasia and chondrodystrophy

See section 5.5.

Merle variants*

Variants of the merle gene cause marbling colouration in a dog's coat, whereby patches of a lighter colour appear in different areas (Figure 9).

Figure 9. A dog with merle colouring. Photo: Pixabay.

Merle is an incompletely dominant trait (Clark et al. 2006, Langevin et al. 2018, Murphy et al. 2018). Some merle genotypes can cause a range of developmental disorders affecting the eyes and ears. One or both of a dog's ears may be deaf. In extreme cases, the eyes may be abnormally small and underdeveloped (microphthalmia). The eye may also be completely absent. Microphthalmia may also be associated with developmental disorders of other parts of the eye, which can result in blindness or impaired vision.

Variants of the *PMEL* gene

Merle colouration is caused by the attachment of a so-called SINE (Short Interspersed Element) to the *PMEL* gene, which regulates pigmentation (Clark et al. 2006). This affects the ability of cells to produce normal pigment. The SINE element has a poly-A tail consisting of a long string of repeating base pairs. The length of this tail varies and causes variations in the merle pattern and severity of health problems. The variants can be divided into four main categories (Langevin et al. 2018, Murphy et al. 2018):

- *Cryptic merle (Mc)*: not usually visible in the dog's phenotype and usually associated with no health problems.
- *Atypical merle (Ma)*: a solid steel-grey coat. In some sources, this is called dilution merle (Md).
- *Classic merle (M)*: marbling; paler patches compared to the rest of the coat.
- *Harlequin merle (Mh)*: black patches on a white background (white areas lack pigment). Note: this variant should not be confused with a variant of the *PSMB7* gene (harlequin locus, H).

The longer the variant, the more strongly it is reflected in the dog's phenotype, and the more severe the associated health problems. The highest risks are associated with so-called double merle genotypes (Mh/Mh, M/M, Mh/M, Mh/Ma and M/Ma) and harlequin merle heterozygotes. Therefore, even one harlequin merle variant can cause problems. Dogs with severe symptoms are usually almost completely white and deaf and blind. Research publications by Clark et al. (2006) and Langevin et al. (2018), among others, provide illustrative examples of how different merle genotypes affect a dog's phenotype

Merle colouring occurs in Shetland Sheepdogs, Australian Shepherds, Border Collies, Chihuahuas, Dachshunds, and Beaucerons, among others (see https://omia.org/OMIA000211/9615/). The harlequin pattern in Great Danes is also caused by the merle variant together with a variant of the *PSMB7* gene (the harlequin locus, H). This *PSMB7* gene variant is lethal when homozygous (Clark et al. 2011, https://omia.org/OMIA001454/9615/). Harlequin Great Danes are heterozygous for both merle and the harlequin variant of the *PSMB7* gene.

In horses, a variant of the *PMEL17* gene causes silver colouring and a syndrome involving multiple congenital ocular anomalies (MCOA syndrome; Andersson et al. 2013). Homozygous individuals have a variety of eye defects, while heterozygotes exhibit milder symptoms.

A dog's genotype does not always reflect its phenotype

Certain coat colours can mask the merle variant in a dog's phenotype. Examples include yellow (ee) and sable (Ay-; the dog is mostly yellow or reddish-brown in colour). If a dog lacks brown or black pigment (eumelanin), the merle variant will not be visible in its phenotype. This genotype combination is called a hidden merle. In a study by Ballif et al. (2021), a dog without a visible merle pattern was found to be a carrier of the harlequin merle variant (Mh) through genetic testing. This variant was passed on to its offspring, who received the merle variant from their other parent as well. This resulted in a puppy being born without eyes.

Merle variants also exhibit an unusually high level of mosaicism. This means that different cells in an individual may contain different variants, with some cells having one type of merle genotype and others having a different one. This means that an individual can have more than two types of merle gene. Mosaicism is caused by spontaneous mutations that shorten the poly-A tail, and these mutations occur frequently. Almost one in five merle dogs studied (181 in total) exhibited mosaicism (Langevin et al. 2018).

Due to mosaicism, a cheek cell sample does not necessarily reflect the variants that an individual will pass on to their offspring. These variants are only visible in germline cells (the progenitor cells from which all tissues originate). In males, the genotype of germline cells can be determined from sperm.

Breeding

According to the Finnish Kennel Club's Dog Registration Guidelines (2023), the club does not register puppies born from a combination of two merle dogs. The dog is assessed based on its appearance. The following colour combinations are prohibited in all breeds unless breed-specific guidelines specify otherwise:

- merle – merle
- harlequin – harlequin (harlequins have an additional *PSMB7* gene variant in addition to the merle gene), and
- harlequin – merle.

A study by Langevin et al. (2018) recommends testing all breeding dogs of merle breeds, particularly males that are frequently used for breeding. Males should be tested using semen. In females, the germline genotype cannot be easily tested. Langevin et al. (2018) therefore recommend taking a hair sample from the merle area in addition to a cheek cell sample.

Pelles et al. (2019) recommend genetic testing of breeding dogs to reveal hidden merle genotypes and avoid creating double merles. Ballif et al. (2021) emphasise the critical need for testing, highlighting not only hidden merles, but also cryptic and mosaic merles whose complete is not visible in the coat.

Tail – short or bobtail*

Gene: *T (T-Box)* (https://omia.org/OMIA000975/9615/)

Mode of inheritance: dominant (Haworth et al. 2001, Indrebø et al. 2007, Hytönen et al. 2009).

Heterozygotes have a short or bobtail, ranging from three-quarters of the normal length to very short.

Breeds: several, see OMIA for details.

Lethal when homozygous; serious developmental disorders leading to severe caudal dysplasia and death in the early fetal period or after birth.

Extreme skin wrinkling in the Shar Pei

Gene: *HAS2* (https://omia.org/OMIA001561/9615/)

Mode of inheritance: additive (Olsson et al. 2011, 2013, 2016). This is a copy number variant (CNV), whereby the dog has extra copies of the same DNA region. The larger the CNV, the more wrinkled the skin becomes.

This variant affects the production of hyaluronic acid, which leads to skin wrinkling (Figure 10). The composition of the Shar Pei's wrinkly skin predisposes individuals to inflammation, eye damage, brachycephalic obstructive airway syndrome (BOAS), and autoinflammatory syndrome (Shar Pei Autoinflammatory Disease, SPAID), among other things. The greater the degree of skin wrinkling, the greater the risk of disease. *HAS2* heterozygotes have a risk of SPAID that is more than four times higher than average, and homozygotes have an eight times higher risk (Olsson et al., 2016). SPAID includes intermittent symptoms such as:

- Familial Shar pei Fever (FSF),
- arthritis,
- bullous dermatitis (cutaneous mucinosis),
- ear infections, and
- amyloidosis.

Chronic or recurrent inflammation can lead to the accumulation of inflammatory proteins in the body, increasing the risk of damage to internal organs, often the kidneys (amyloidosis).

It has also been suggested that an incompletely dominant variant of the *MTBP* gene is involved in SPAID (https://omia.org/OMIA001561/9615/). The variant affects inflammatory and apoptotic processes. Apoptosis is a form of programmed cell death that is regulated by genes controlling cell division. In incompletely dominant inheritance, heterozygotes express

the trait, but to a lesser extent than homozygotes. In this case, heterozygotes are 2.13 times more likely to develop SPAID than individuals with two copies of the normal gene variant (Metzger et al. 2017).

Figure 10. Shar pei. Photo: Pixabay.

Dominant hairlessness*

A desired characteristic in hairless breeds, excluding the American Hairless Terrier (in which hairlessness is recessive and caused by a different gene).

Gene: *FOXI3* https://omia.org/OMIA000323/9615/

Mode of inheritance: dominant (Drögemüller et al. 2008, Shirokova et al. 2013).

Lethal when homozygous.

The *FOXI3* gene plays a role in the development of various organs, including hair follicles, teeth, mammary and salivary glands, nails, and eyes. In its heterozygous form, this mutation variant causes a disease called ectodermal dysplasia. In humans, this rare hereditary disease causes underdevelopment of the teeth and hair, as well as the skin glands. In heterozygous dogs, the variant causes the following:

- Missing teeth,
- Malformed teeth,
- Missing sweat glands,
- Hairlessness or very sparse hair – the amount of hair is regulated by genes with smaller effects,
- Underdeveloped hair follicles,
- Blockage of hair follicles, which causes itching and inflammation requiring antibiotic treatment. The underlying cause is anatomical, so the problem cannot be prevented with medication.

If hairless show dogs have excessive hair, it may be removed prior to shows using methods that cause skin damage, such as epilation or chemical hair removal (NKU, 2018).

Hairlessness itself is an extreme trait that requires special measures, such as protecting the dog from the sun and cold. If the dog is not cared for properly, the trait causes welfare problems.

Ridge on a ridgeback dog

A ridge pattern on the back consisting of hairs growing in the opposite direction to the rest of the coat. This pattern is a breed standard requirement for the Rhodesian Ridgeback and the Thai Ridgeback.

Gene: large duplication covering three *FGF* genes (*FGF3, FGF4, FGF19*) and the *ORAOV1* gene (https://omia.org/OMIA000272/9615/)

Predisposes the dog to a tubular skin defect that causes neurological symptoms (dermoid sinus; see Figure 11).

Mode of inheritance of the ridge: dominant (Hillbertz & Andersson 2006, Salmon-Hillbertz et al. 2007).

Mode of inheritance of the dermoid sinus predisposition: incompletely dominant. The incidence is low in heterozygotes and higher in homozygotes.

Dermoid sinus can lead to chronic abscesses and infections. Sinuses that extend to the spinal cord can cause fatal inflammation. Dermoid sinuses are corrected surgically in Rhodesian Ridgebacks before they are released to new owners. However, not all puppies can be successfully operated on, and those that cannot, are euthanised.

The prevalence of dermoid sinus has been reported to be 2.5–7.9% in the United States, Sweden and Germany (Miller & Tobias 2003, Salmon Hillbertz 2005, Distl 2022). In Finland, dermoid sinuses occurred in around 4% of Rhodesian Ridgebacks between 2006 and 2015 (Breed-specific Breeding Strategy 2018–2022).

The heritability of dermoid sinus in German data on Rhodesian Ridgebacks was 0.78 (Distl 2022).

In many countries, puppies of this breed with no ridge or with an inadequate ridge are euthanised. In Finland, they are registered with a breeding ban and sold as pets. Twenty per cent of the population is removed from breeding programmes due to inadequate ridges.

A dog's genotype is not always reflected in its appearance: a dog may carry the gene for a ridge, even if its appearance suggests otherwise.

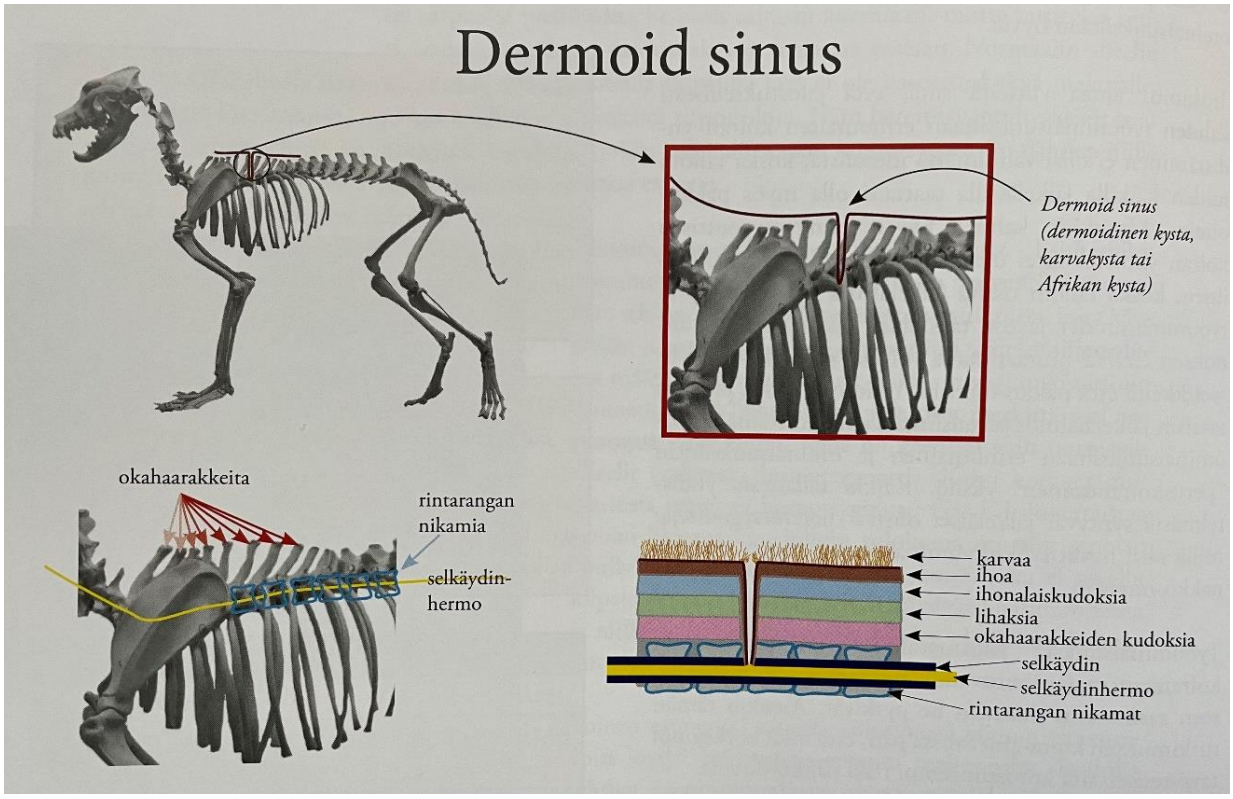

Figure 11. Dermoid sinus (Mäki & Mujunen 2018).

Hyperuricosuria (high uric acid levels in urine and blood)

Gene: *SLC2A9* (https://omia.org/OMIA001033/9615/)

Mode of inheritance: recessive (Bannasch et al. 2008)

Breeds: the Dalmatian, the Black Russian Terrier, and the English Bulldog, among others. The gene variant is fixed in Dalmatians (all individuals are homozygous) and the heritability of the clinical disease is 0.87 (Bannasch et al. 2004). The gene variant has been found at a lower frequency in many other breeds (Karmi et al. 2010a, Donner et al. 2023; see OMIA).

Susceptibility to urate stones and urolithiasis. Urinary stones were present in 34% of male Dalmatians (Bannasch et al. 2004). Dalmatians have a 5–9 times higher risk of urinary stones than other dogs (Agria insurance statistics). In the Finnish population, 21.6% of Dalmatians have had urate crystals or stones. These have caused welfare problems for 4.3% of dogs, according to an owner survey, or the dog has undergone surgical treatment or been euthanised due to the problem (Breed-specific Breeding Strategy 2018–2022).

Dilute blue coat colour

Gene: *MLPH* (dilution colour; dilution or D locus; https://omia.org/OMIA000031/9615/).

Mode of inheritance: recessive (Drögemüller et al. 2007, Bauer et al. 2018, Van Buren et al. 2020).

Breeds: see OMIA.

When an individual is homozygous for the recessive d1 variant (and possibly other recessive variants, such as d2 and d3), they are predisposed to an inflammatory skin disease known as blue dog syndrome (CDA), also referred to as colour dilution alopecia, colour mutant alopecia or black hair follicular dysplasia. The syndrome includes

- progressive hair loss,
- recurrent bacterial infections of the hair follicles (folliculitis),
- dry and flaky skin, and
- sensitivity to sunlight and cold air.

Symptoms range from mild (a weaker-than-normal coat) to severe (hairlessness; severe skin problems).

Having two different recessive variants (d1/d2; Bauer et al., 2018) may also predispose an individual to the disease.

Deafness related to white spotting

Gene: *MITF* (white spotting, https://omia.org/OMIA000214/9615/)

Mode of inheritance: recessive (Karlsson et al. 2007, Bannasch et al. 2010, Strain 2012).

Breeds: Dalmatian, Bull Terrier and Beagle, among others – see OMIA for more information.

The piebald (sp) and extreme white (sw) variants are associated with an increased risk of deafness. The effect of these variants varies by breed. The extent of the whiteness can range from small white spots to an entirely white coat. These white spots lack pigment cells, which are important for the function of the inner ear. The greater the amount of white on the head, the greater the likelihood of deafness.

Screw (kinked) tail (Robinow-like syndrome)

Gene: *DVL2* (https://omia.org/OMIA002186/9615/)

Shortening of the muzzle (with a shorter hard palate and skull base, a smaller hard palate-to-skull-base ratio, and a higher facial index), which increases the risk of BOAS.

Shortening of the tail, vertebral malformations and fusions, which cause screw tail. In addition to the DVL2 mutation, other genes are likely to contribute to the formation of screw tails. Screw tails (including those caused by mutations in genes other than the DVL2 gene) are associated with vertebral malformations that can cause neurological symptoms:

> Vertebral malformations in screw-tailed dogs are associated with hunchback (kyphosis), spinal curvature (lordosis), and a sideways curved spine (scoliosis), and are most prevalent in the thoracic spine (Moissonnier et al. 2011, Gutiérrez-Quintana et al. 2014).
>
> Neurological symptoms in Pugs, French Bulldogs and English Bulldogs have been found to be caused by spinal cord compression resulting from vertebral deformities (Moissonnier et al. 2011, Schlensker & Distl 2013, Gutiérrez-Quintana et al. 2014).

Mode of inheritance: recessive (Mansour et al. 2018), but there is an additive effect on skull proportions (Niskanen et al. 2021).

Breeds: fixed and causes a typical appearance in English Bulldogs, French Bulldogs and Boston Terriers. Occurs mainly as heterozygous in several other breeds (see OMIA).

Was discussed in the previous report (see sections 7.3.8 and 9.2.9; Kempe & Mäki 2020), and new information has since become available (see Niskanen et al. 2021).

6. Breeding restrictions

Breeding organisations should map and monitor hereditary diseases, defects, and structural traits that impair the welfare of dogs within breeds/breeding lines, taking steps to reduce them if necessary.

Studbook registers should be opened for the planned breeding of animals outside the studbook, if necessary, to prevent and reduce the accumulation of hereditary diseases and the effects of inbreeding depression.

6.1. Screening requirement for breeding dogs

The Kempe and Mäki (2020) report, section 9.1, is proposed for application:

'*The breeder must be able to demonstrate that the animals they use for breeding meet the requirements of animal welfare legislation (see Chapter 4.1). This means that the animals must be suitable for breeding, as determined by appropriate screening carried out prior to mating, if they belong to a breed or breeding line, or if their characteristics correspond to a breed or breeding line in which a trait or disease that causes moderate or significant impairment to welfare is commonly found*.

Appropriate screening tests use methods that have been found to be scientifically appropriate for the respective diseases or defects, and the statement given in the case of progressive diseases and defects is also sufficiently recent.

The statement must indicate that the animal was identified at the time of examination, that the veterinarian checked the identification mark, and that the statement was given to the correct individual. If there are no uniform assessment criteria for the defect or disease, the risk contained in the breeding combination must be assessed based on the phenotypes of the animals and their close relatives.'

Veterinarians performing screening examinations for breeding dogs must be familiar with the relevant examination methods, diagnostics and existing uniform assessment criteria.

6.2. Proposals for breeding restrictions

This section supplements the corresponding section of the Kempe and Mäki (2020) report (9.2). These breeding restrictions were also drawn up in cooperation with experts and authorities. The restrictions do not apply to diseases, symptoms, or traits caused by trauma.

Breeding restrictions should be reviewed at regular intervals (e.g. every five years) and updated, if necessary, when new information on the inheritance of diseases and defects becomes available.

The proposed breeding restrictions clarify the limits of the legislative requirements. In practice, when breeding with the aim of improving the quality of the animal population, the criteria should be stricter.

6.2.1. General

The general breeding restrictions (Kempe and Mäki, 2020, Section 9.2.1) are proposed to be supplemented with the following (in bold):

The following are not to be used for breeding:

- a dog that has undergone surgery to correct or prevent a structural defect or weakness, or to alleviate symptoms; or that has been found to clearly need such an intervention, or
- a dog that requires continuous or repeated medication, or a special diet due to a hereditary disease, defect, or behavioural disorder.

6.2.2. Inbreeding

The following combinations are not to be used for breeding:

- a dog is bred with its father, mother, grandfather, grandmother, uncle or aunt, or
- siblings or half-siblings are combined with each other, are not permitted for breeding purposes.

6.2.3. Behavioural disorders

The following are not to be used for breeding:

- dogs whose behavioural disorder is due to a hereditary disease (e.g. diseases causing chronic pain, itching or epilepsy),
- dogs that (often/almost always) show excessive insecurity or fear in everyday situations that significantly impairs their ability to function (e.g. towards sounds, strange people, situations, or other animals).
    - For example, retreat, try to escape, try hard to get onto the lap of the handler, crouch, hold the tail tightly between the legs, tremble, or pant (see section 5.1.6 for example descriptions of classifications P3 and P4 in Table 4, and descriptions of the Character test for nervous and very nervous dogs). This also applies to a strong fear of thunder, for example.
    - Insecure dogs are not recommended for breeding (see section 5.1.6 for example descriptions of classification P2 in Table 4, and a description of a Character test for a slightly nervous dog).
- dogs that show excessive aggression in unprovoked situations often or always.
    - Section 5.1.6: Example descriptions of classifications A3–A5 in Table 5.
- dogs whose abnormal repetitive behaviour (compulsive symptoms and/or stereotyped behaviour) is severe.
    - The dog gets stuck in the behaviour and cannot be contacted.

6.2.4. Atopic dermatitis and conformational pododermatitis

It is recommended that dogs from risk breeds, breeding lines or types only be used for breeding from the age of three years.

See Kempe and Mäki (2020), section 9.2.6, for breeding restrictions related to skin conditions. In addition, the following are not to be used for breeding:

- dogs diagnosed with atopic dermatitis
    - Note that a single ear infection or self-limiting dermatitis does not necessarily lead to a diagnosis of atopic dermatitis. In atopic dermatitis, the symptoms are either recurrent or long-lasting.
- dogs with recurrent or chronic paw infections that impair well-being
    - If necessary, the dog should be examined by a veterinarian before mating.

6.2.5. Heart disease

Congenital heart diseases:

- The minimum age for cardiac examination in breeds/breeding lines/types of dogs with a high incidence of congenital heart diseases is 12 months.
- If auscultation alone is performed, the examination is valid for 24 months. An ultra-sound examination is valid for the dog's lifetime.

Degenerative heart diseases:

- The minimum age for cardiac examination in breeds/breeding lines/types of dogs with a high incidence of degenerative heart diseases is 24 months.
- The examination is valid for 12 months.

The following are not to be used for breeding:

- Dogs diagnosed with hereditary heart disease.

6.2.6. Dental and oral disorders

The proposed breeding criteria are those presented in Section 9.2.4 of the Kempe and Mäki (2020) report, updated with added points in bold.

The following are not to be used for breeding

- a dog that has experienced or is currently experiencing significant symptoms due to the structure of the skull/jaw and/or dentition, e.g.,
    - jaw fracture
    - clearly noticeable pain or difficulties in eating
    - dental malposition, where the teeth have abnormal contact with soft tissues or other teeth, e.g. teeth that damage the gums or canines that are recessed into the palate,
- a dog with a clearly noticeable problem with the fit of the teeth related to a short jaw, such as twisted and/or displaced teeth,
- a dog whose jaws do not close normally,
- a dog whose tongue is paralysed,
- a dog whose lower lip twists between the teeth and interferes with the bite, and
- a dog with other significant oral and dental symptoms or diseases that are considered hereditary.

6.2.7. Musculoskeletal disorders

Restrictions on breeding related to musculoskeletal disorders and diseases can be found in section 9.2.6 of Kempe and Mäki (2020). In addition to, or instead of, the above restrictions, the following is proposed:

Disc degeneration caused by chondrodystrophy

Dogs with the FGF4 retrogene on chromosome 12 should be avoided in breeding programmes. The prevalence of the retrogene and/or calcifications in breeds/breeding lines should be actively reduced.

In breeds/breeding lines where the retrogene is prevalent, a breeding programme based on X-ray screening should be implemented. However, it is likely that screening for calcifications alone will not effectively prevent degeneration and reduce disc herniations, and eliminating the retrogene is ultimately the only way to achieve effective change. If the breeding programme does not clearly reduce morbidity over a couple of generations, controlled cross-breeding programmes are the only way to eliminate the disadvantages associated with the retrogene, and are the only acceptable alternative for continuing breeding.

If a dog is to be used for breeding that belongs to a breed, breeding line or type that is commonly affected by the FGF4 retrogene on chromosome 12 and disc herniation, or has a background with such breeds, the dog must be genetically tested or screened by X-ray before breeding. If, based on the genetic test result, the dog has one or two copies of the retrogene in question, an X-ray is also required before breeding. If the genetic test result shows that the dog does not have any copies of the retrogene, an X-ray is not required.

The dog must be aged 24–48 months at the time of the X-ray.

<u>The following are not to be used for breeding:</u>

- a dog with a history of paralysis or disc herniation (Kempe and Mäki, 2020), or
- a dog with an X-ray result showing a severe degree of intervertebral disc disease (IDD3).
    - It is not recommended to breed two dogs with a moderate degree of disease (IDD2).
    - The criteria may be tightened after a transition period if necessary.

Premature closure of the growth plates

For breeding purposes, the dog must be at least 12 months old at the time of the X-ray.

<u>The following are not to be used for breeding</u>

    - dogs with severe and/or symptomatic curvature of the forearms, outward rotation of the paws, inward bending of the wrists (pes valgus), or bending or twisting of the hind legs (pes varus). Additional information on these structural defects is expected in the coming years thanks to a new measurement method (Lappalainen et al. 2023), which will also enable us to determine the severity of the condition in individual dogs.
- a dog with a screening result indicating a severe degree of the disease or defect (INC3; Lappalainen et al. 2016).

    - It is not recommended to breed two dogs with a moderate degree of disease (INC2).
    - The criteria may be tightened after a transition period if necessary.

After the transition period, it must be determined whether measures are needed to reduce FGF4 retrogenes on chromosomes 12 and 18.

Patellar luxation

The screening result for a 3-year-old dog is final. Results obtained before this age are valid for two years. It is recommended that dogs from high-risk breeds, breeding lines or types only be used for breeding from the age of three years.

The following are not to be used for breeding:

- a dog whose patella is permanently or usually dislocated (grades III and IV).
    - A dog with a grade II patellar luxation is not recommended for breeding, nor it is recommended that two dogs with patellar luxation be mated. Ideally, only dogs with a non-luxating patella (Grade 0) should be used for breeding.
- a dog with nearly straight knee angulation (180 degrees).

Cranial cruciate ligament disease

The following is not to be used for breeding:

- a dog that has undergone surgery for a cranial cruciate ligament injury or is in need of such treatment.
    - The exception is cases where the cruciate ligament has been torn because of a very strong external force, in which case other structures in the knee are almost always broken too.

Osteochondrosis

The dog must be at least 12 months old at the time of the X-ray screening.

The following are not to be used for breeding:

- a dog diagnosed with osteochondrosis

6.2.8. Eye diseases

See Kempe and Mäki (2020), section 9.2.5, for breeding restrictions related to eyes and periocular tissues.

6.2.9. Genetic variants

According to Evira (now the Finnish Food Authority), *breeding between carriers of lethal variants can result in offspring with permanent deformities. Such animals' phenotype or genotype can be considered to cause them suffering or significant harm. Evira's view is that the deliberate use of this mating method contravenes Section 8 of the Animal Welfare Act and Section 24 of the Animal Welfare Decree* (Evira 2008).

If a genetic test is available for a common breed/lineage/type-specific disease or defect that causes significant welfare harm, it should be used to ensure that the genotypes of the offspring do not cause them significant welfare harm (Table 14). The test used must reliably predict the risk of the offspring developing the disease. This requires the test to be based on a peer-reviewed study demonstrating causality or a significant risk. A genetic test can be performed on a dog of any age. The test is not required if the dog's genotype can be reliably determined from its phenotype or inferred based on confirmed lineage.

For example, considering eye diseases, a genetic test should be performed on breeds that commonly have for example open-angle glaucoma and/or other eye diseases that are blinding and/or cause significant welfare impairment (e.g. primary lens luxation PLL, PRAs, macular corneal dystrophy) and for which the gene mutation(s) causing the condition are known in the breed.

A dog with clinical problems that cause significant welfare impairment should not be used for breeding, regardless of genotype.

- *T/T-Box* (short tail or bobtail):
    - Carriers must not be combined with each other (Evira, now the Finnish Food Authority, 2008).
    - Genetic testing should be used if necessary.
- *FOXI3* (dominant hairlessness, ectodermal dysplasia):
    - Carriers must not be combined with each other (Evira, now the Finnish Food Authority, 2008).
    - Only dogs with healthy skin may be used for breeding.
    - Dogs used for breeding must have a veterinary report stating that the criteria in section 6.2.6 (Teeth and Mouth) are met.
    - The dominant variant of the *FOXI3* gene causes a disease associated with hairlessness and welfare problems. The prevalence and significance of these issues should be discussed in more detail after the transition period.
- *DVL2* (screw tail, Robinow-like syndrome)
    - Breeding restrictions related to the brachycephalic phenotype of dogs apply (Kempe and Mäki, 2020, sections 9.2.3–9.2.8).
- *HAS2* (extreme skin folds and Shar Pei autoinflammatory syndrome, SPAID):
    - Homozygous dogs must not be produced.
    - The significance of the mutation should be discussed in more detail after the transition period.
- *MTBP* (Shar Pei autoinflammatory syndrome, SPAID):
    - Homozygous dogs must not be produced.
- Duplication of the *FGF3, FGF4, FGF19, and ORAOV1* genes (hair ridge pattern):
    - Dogs with a confirmed dermoid sinus should not be used for breeding.
    - Two dogs that are homozygous for the duplication should not be mated together.
    - The wild-type gene variant should be favoured, and ridgeless dogs should be accepted for breeding.
- *SLC2A9* (hyperuricosuria):
    - The frequency of the gene variant should be decreased in breeds/breeding lines where it is prevalent and clinical disease occurs.
    - Production of homozygous dogs should be avoided.

        - After the transition period, breeding restrictions can be imposed if necessary.
- SINE-insertion in the *PMEL17* gene (merle coat pattern):
    - The following risk genotypes must be prevented in puppies: Mh/Mh, M/M, Mh/M, Mh/Ma and M/Ma, as well as the Mh variant in a single copy (i.e. heterozygous form).
        - Genetic testing should be used if necessary.
- *PSMB7* (harlequin coat pattern):
    - Carriers must not be bred with each other (Evira, now the Finnish Food Authority, 2008).
- *MLPH* (blue dilution coat colour):
    - If blue dog syndrome is common in the breed or in dogs related to the breeding dog, homozygous offspring should be avoided for recessive gene forms (especially d1).
- *MITF* (deafness associated with white colouring):
    - Extensive whiteness of the head should be avoided in breeding.
    - A dog that is congenitally deaf on both sides should not be used for breeding (Kempe and Mäki, 2020).
        - BAER hearing testing should be performed, if necessary, before mating.

Table 14. Table 1. Use of genetic test results.

Mode of inheritance	Safe mating combinations
Autosomal recessive	Sire/dam/both are genotypically healthy*.
X-linked recessive	The dam is genotypically healthy*.
Dominant (autosomal or X-linked)	The sire and dam are both genotypically healthy*.

*healthy = two normal gene variants

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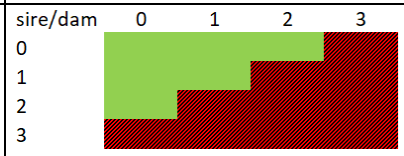
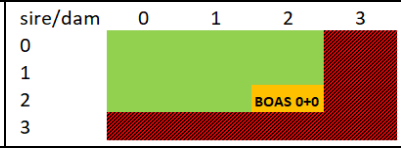
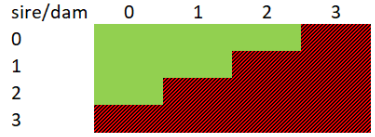
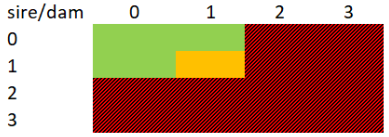
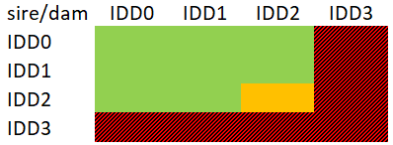
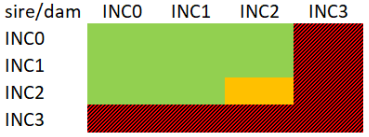
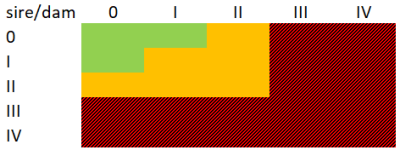
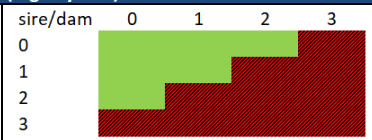
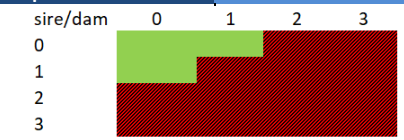
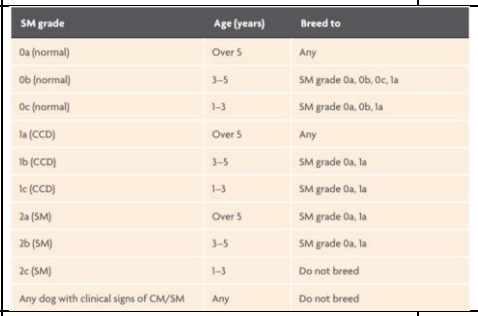
Annex: Animal protection control criteria – Dog breeding

The criteria presented can also be applied to other similar diseases, symptoms or features. The criteria do not apply to diseases, symptoms and features caused by trauma.

Disease, defect, characteristic or veterinary procedure	For more information, see the section/chapter of the reports II and III.	Breeding ban during the transitional period (e.g. 5 years)	Breeding ban after the transitional period	Other things to consider
GENERAL				
Surgical intervention to correct a structural defect or weakness or an identified, clear need for such a procedure (more detailed definition will follow)	II. Chapter 6, Table 2, and Chapter 8.1	x	x	
Need for continuous or repeated medication, or a special diet comparable to this, due to a hereditary disease, defect, or behavioural disorder	III. 6.2.1	x	x	
*Relative muzzle length (Craniofacial Ratio, CFR)	II. Chapter 7.3.1	No ban, but if below 0.33, a veterinary examination must be performed before mating on the points marked with an asterisk (*).	<0.33 (one third)	
***BREATHING AND THERMOREGULATION**	II. Chapters 7.2.1 and 7.3.1			
Clearly noticeable signs of BOAS, e.g. clearly increased, abnormal upper respiratory sounds when awake at rest		x	x	
Other clear signs of respiratory distress (e.g., cyanosis, fainting, chronic gastrointestinal symptoms)		x	x	
*Dogs at risk: A BOAS test or equivalent stress test should be performed on the litter's sire and dam before mating		Failed	Failed	The minimum age for testing is 18 months. Testing performed at an age under three is valid for 24 months.
*Dog's own BOAS grade		3	2-3	
*BOAS grades of a mating combination		See Figure 1	Will be tightened if necessary	
Figure 1. Allowed combinations in green and prohibited combinations in red stripes.				
*Dog's own nostril stenosis grade		3	2-3	
*Nostril stenosis grades of a mating combination		See Figure 2	Will be tightened if necessary	
Figure 2. Allowed combinations in green and prohibited combinations in red stripes. Orange (2+2) allowed, if the BOAS grades of the dam and the sire are 0.				
MUSCULOSKELETAL DISORDERS	II. Chapters 7.2.3 and 7.3.2			

Disease, defect, characteristic or veterinary procedure	For more information, see the section/chapter of the reports II and III.	Breeding ban during the transitional period (e.g. 5 years)	Breeding ban after the transitional period	Other things to consider
Clear conformational pain and/or mobility difficulties		x	x	
Other significant skeletar or joint symptoms considered hereditary	II. Chapter 6, Table 2, and Chapter 8.1	x	x	
A tail that is tightly wrapped around the anus or curls inwards, making defecation difficult		x	x	
Dogs at risk: veterinary examination/measurement of the litter's sire and dam before mating		See Figure 3 (left)	See Figure 3 (right)	
Figure 3. Allowed combinations in green, prohibited combinations in red stripes. Orange (mild+mild) not recommended. On the left are the criteria during the transitional period, and on the right the criteria after that. 0 = Healthy/Borderline; 1=Mild; 2=Moderate; 3=Severe.				
Chondrodystrophy (CDDY, 12-FGF4RG) X-ray grades, column C: allowed combinations in green, prohibited combinations in red stripes. Orange not recommended. Nervous system symptoms, see column A, row 63.	III. Chapters 5.5 and 6.2.7		Will be tightened, if necessary	For breeds and types of dogs at risk, a genetic CDDY test result or an IDD X-ray is required. For carriers of CDDY (1 or 2 copies), an X-ray is required. The dog must be 24-48 months old at the time of the X-ray.
Severe and/or symptomatic bending and/or rotation of the limbs caused by premature closure of the growth plates (short limbs). Column C: Elbow incongruence X-ray grades - allowed combinations in green, prohibited combinations in red stripes. Orange not recommended.	III. Chapters 5.5 and 6.2.7		Will be tightened, if necessary	The minimum age for X-ray is 12 months.
Patellar luxation: predisposing, nearly straight (180 degrees) knee angulation. Column C: Allowed Putnam grades of mating combinations in green, prohibited combinations in red stripes. Orange not recommended.	III. Chapters 5.6 and 6.2.7		Will be tightened, if necessary	The screening result for a 3-year-old dog is final. Results obtained before this age are valid for 24 months. It is recommended that dogs from high-risk breeds, breeding lines or types only be used for breeding from the age of three years.
Surgery for a cranial cruciate ligament disease or a need of such treatment	III. Chapters 5.6 and 6.2.7	x	x	
Osteochondrosis	III. Chapters 5.7 and 6.2.7	x	x	The minimum age for X-ray is 12 months.
***DENTAL AND ORAL DISORDERS**	II. Chapters 7.2.4 and 7.3.3			

Disease, defect, characteristic or veterinary procedure	For more information, see the section/chapter of the reports II and III.	Breeding ban during the transitional period (e.g. 5 years)	Breeding ban after the transitional period	Other things to consider
Significant symptoms due to the structure of the skull/jaw and/or dentition, e.g., jaw fracture or clearly noticeable pain or difficulties in eating		x	x	
*Dental malposition, where the teeth have abnormal contact with soft tissues or other teeth, e.g. teeth that damage the gums or canines that are recessed into the palate		x	x	
*Clearly noticeable problem with the fit of the teeth related to a short jaw, such as twisted and/or displaced teeth		x	x	
*Jaws do not close normally, severe jaw disproportion		x	x	
Paralysed tongue		x	x	
Lower lip twists between the teeth and interferes with the bite		x	x	
Other significant oral and dental symptoms or diseases that are considered hereditary	II. Chapter 6, Table 2, and Chapter 8.1	x	x	
***EYE DISEASES**	II. Chapters 7.2.5 and 7.3.4			
*Significant symptoms of irritation, dry eye and/or pain, e.g. misplaced eyelashes or eyelid rotation, causing corneal ulcers		x	x	
*Skin folds covering and/or rubbing the eyes		x	x	
*Nasal fold that covers the nose		x	x	
*Incomplete closing of the eyes		x	x	
*Eyelid reflexes		Decreased/absent	Decreased/absent	
*Visible sclera of the eye when looking straight ahead		In two or more quarters	Other than outer side of the eye and more than minimally	
Eyeball previously bulged out of its socket		x	x	
Blindness in female dogs		x	x	
Hereditary blindness in male dogs		x	x	If blindness is caused by something other than heredity, a veterinary certificate or treatment report must be provided.
A diagnosed hereditary eye disease causing significant welfare impairment, e.g. PRA or lens luxation	II. Chapter 6, Table 2, and Chapter 8.1	x	x	
Dogs at risk: veterinary examination/measurement of the litter's sire and dam before mating, e.g. eyelid rotation		See Figure 4 (left)	See Figure 4 (right)	

Disease, defect, characteristic or veterinary procedure	For more information, see the section/chapter of the reports II and III.	Breeding ban during the transitional period (e.g. 5 years)	Breeding ban after the transitional period	Other things to consider
Figure 4. Allowed combinations in green, and prohibited combinations in red stripes. 0 = Healthy/Borderline; 1=Mild; 2=Moderate; 3=Severe.				
***SKIN**	II. Chapters 7.2.6 and 7.3.5			
Atopic dermatitis	III. Chapters 5.2 and 6.2.4	x	x	
*Recurrent or chronic skin infections, e.g. ear infections, furunculosis, pododermatitis		x	x	If necessary, the dog should be examined by a veterinarian before mating.
*Visible inflammation/intertrigo requiring treatment in skin folds (e.g. tail, nose, lips, anus, vulva)		x	x	
*Excessive skin or skin folds that can cause eye, ear, or skin problems; e.g. deep skin folds that do not ventilate or skin that covers the eyes		x	x	
*Tail pressing on the base of the tail, causing a difficult-to-treat stricture and/or problems with defecation		x	x	
NEUROLOGICAL DISEASES/DEFECTS	II. Chapters 7.2.7 and 7.3.6			
History of paralysis or disc herniation		x	x	
Congenital, bilateral deafness		x	x	
Clearly noticeable symptoms of syringomyelia	II. Chapter 9.2.7	x	x	
Dogs at risk: veterinary examination/measurement of the litter's sire and dam before mating, syringomyelia		See Figure 5	See Figure 5	Minimum age at screening is 18 months. The result obtained under the age of 3 is valid for 24 months.
Figure 5. Breeding guidelines and restrictions to avoid syringomyelia (British Veterinary Association, Syringomyelia Information Leaflet: https://www.bva.co.uk/canine-health-schemes/cmsm-scheme/).				
Other significant neurological symptoms considered hereditary	II. Chapter 6, Table 2, and Chapter 8.1	x	x	
REPRODUCTION	II. Chapters 7.2.8 and 7.3.7			

SM grade	Age (years)	Breed to
0a (normal)	Over 5	Any
0b (normal)	3–5	SM grade 0a, 0b, 0c, 1a
0c (normal)	1–3	SM grade 0a, 0b, 1a
1a (CCD)	Over 5	Any
1b (CCD)	3–5	SM grade 0a, 1a
1c (CCD)	1–3	SM grade 0a, 1a
2a (SM)	Over 5	SM grade 0a, 1a
2b (SM)	3–5	SM grade 0a, 1a
2c (SM)	1–3	Do not breed
Any dog with clinical signs of CM/SM	Any	Do not breed

Disease, defect, characteristic or veterinary procedure	For more information, see the section/chapter of the reports II and III.	Breeding ban during the transitional period (e.g. 5 years)	Breeding ban after the transitional period	Other things to consider
A defect, disease, or characteristic that prevents natural reproduction; e.g., one's own/offspring's body structure; or a vaginal septum, the removal of which would require surgical intervention		x (also artificial insemination prohibited)	x (also artificial insemination prohibited)	
A defect, disease or characteristic that worsens with reproduction, or for which reproduction may trigger the onset		x (also artificial insemination prohibited)	x (also artificial insemination prohibited)	
A female dog is not fit enough to reproduce		x	x	
Forced mating		x	x	
Number of caesarean sections		Performed two	Performed two	

GENE VARIANTS (breeding restrictions in columns C and D)	II. Chapter 6, Table 2, and Chapters 8 and 8.1			
T/T-Box (short tail or bobtail)	III. Chapters 5.9 and 6.2.9	Carrier x carrier matings	Carrier x carrier matings	Genetic testing should be used if necessary.
FOXI3 (dominant hairlessness, ectodermal dysplasia)	III. Chapters 5.9 and 6.2.9	Carrier x carrier matings	Carrier x carrier matings	1) Mouth and teeth: a veterinary statement confirming that the breeding criteria (lines 32–39) are met. 2) Only dogs with healthy skin are allowed in breeding.
HAS2 (extreme skin folds and Shar Pei autoinflammatory syndrome SPAID)	III. Chapters 5.9 and 6.2.9	Homozygous dogs must not be produced	Homozygous dogs must not be produced	
MTBP (Shar Pei autoinflammatory syndrome SPAID)	III. Chapters 5.9 and 6.2.9	Homozygous dogs must not be produced	Homozygous dogs must not be produced	
Duplication of the FGF3, FGF4, FGF19, and ORAOV1 genes (hair ridge pattern)	III. Chapters 5.9 and 6.2.9	Dogs with a diagnosed dermoid sinus should not be used for breeding. Two homozygous dogs should not be mated together.	Dogs with a diagnosed dermoid sinus should not be used for breeding. Two homozygous dogs should not be mated together.	
SINE-insertion in the PMEL17 gene (merle coat pattern)	III. Chapters 5.9 and 6.2.9	Risk genotypes must be prevented in puppies	Risk genotypes must be prevented in puppies	Genetic testing should be used if necessary.
PSMB7 (harlequin coat pattern)	III. Chapters 5.9 and 6.2.9	Carrier x carrier matings	Carrier x carrier matings	
MITF (deafness associated with white colouring)	III. Chapters 5.9 and 6.2.9	A dog that is congenitally deaf on both sides may not be used for breeding.	A dog that is congenitally deaf on both sides may not be used for breeding.	BAER hearing testing should be performed, if necessary, before mating. Extensive whiteness of the head should be avoided in breeding.
INBREEDING				

Disease, defect, characteristic or veterinary procedure	For more information, see the section/chapter of the reports II and III.	Breeding ban during the transitional period (e.g. 5 years)	Breeding ban after the transitional period	Other things to consider
Mating a dog with its father, mother, grandfather, grandmother, uncle, or aunt	III. Chapter 4. and 6.2.2	x	x	
Mating a dog with its sibling or half-sibling	III. Chapter 4. and 6.2.2	x	x	
BEHAVIOURAL DISORDERS				
Behavioural disorder due to a hereditary disease (e.g. epilepsy or a disease causing chronic pain or itching)	III. Chapter 5.1.5 and 6.2.3	x	x	
Excessive insecurity or fear in everyday situations (often or always), which significantly impairs the ability to function	III. Chapter 5.1.1 and 6.2.3	x	x	
Excessive aggression in unprovoked situations (often or always)	III. Chapter 5.1.2 and 6.2.3	x	x	
Severe abnormal repetitive behaviour (compulsive symptoms and/or stereotyped behaviour)	III. Chapter 5.1.3 and 6.2.3	x	x	
HEART DISEASE				
Congenital heart disease	III. 5.3 and 6.2.5	x	x	The minimum age at examination in risk breeds/breeding lines/types of dogs is 12 months. If auscultation alone is performed, the examination is valid for 24 months. An ultrasound examination is valid for the dog's lifetime.
Degenerative heart disease	III. 5.3 and 6.2.5	x	x	The minimum age at examination in risk breeds/breeding lines/types of dogs is 24 months. The examination is valid for 12 months.
AUTOIMMUNE DISORDERS	III. 4.2	x	x	

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