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# **Etiology of patellar luxation in small breed dogs**

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# Etiology of patellar luxation in small breed dogs

## Möjliga etiologier för patellaluxation hos små hundraser

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## SAMMANFATTNING

Patellaluxation (PL) är en vanlig ortopedisk sjukdom som karakteriseras av att patellan kan luxera från *trochlea ossis femoris*. Detta sker antingen manuellt, spontant när hunden är i rörelse eller så är patellan permanent fixerad utanför fåran. Sjukdomen är ofta asymtomatisk, men kan orsaka hälta, smärta och sekundära sjukdomar så som osteoartrit och ruptur av främre korsbandet.

Patogenesen är ännu inte klarlagd och olika teorier har föreslagits. Den mest erkända hypotesen hävdar att en abnormitet i höften och rotation av femur leder till en placering av quadricepsmuskulaturen och därmed orsakar PL. Detta reducerar trycket från patellan på trochlean, vilket gör trochlean hypoplastisk (Harasen, 2006b; Roush, 1993). Andra teorier är att PL orsakas av en muskelrelaterad defekt där quadricepsmuskulaturen är atrofisk, en felaktig bäckenkonformation (L'Eplattenier & Montavon, 2002) eller höga nivåer av östradiol (Gustafsson *et al.*, 1969). Vidare studier krävs för att säkerställa vilken teori som är korrekt.

Diagnosticering av PL görs genom observation i stående position och i rörelse, samt genom palpation av knäleden i både stående och sidoliggande position (Vidoni *et al.*, 2005). Ett standardiserat graderingssystem av PL har utvecklats och används både inom forskning och på kliniker.

Risikfaktorer för PL som har kunnat observeras är särskilda raser (såsom Chihuahua, Yorkshire terrier och Pomeranian), liten storlek och kön. Studier visar att små hundraser har upp till 12 gångers risk att utveckla PL, jämförelse med större hundraser (O'Neill, 2016). Dock har nyligen gjorda studier rapporterat att prevalensen även bland större hundraser ökar, och det kan misstänkas att stora hundar inte undersöks lika noggrant för PL som små hundar. Tikar anses generellt ha en högre risk för PL än hanar, vilket kan bero på hormonella skillnader mellan könen och/eller en högre muskelmassa hos hanhundar vilket kan stabilisera patellan. På senare tid har den genetiska forskningen intensifierats. Överrepresentationen av specifika raser som drabbas av PL samt den höga andelen av hundar med bilateral PL pekar på att sjukdomen är ärftlig. Troligen har PL ett polygenetiskt ursprung, då studier av stamtavlor visar på ett komplext nedärvningsmönster. Fragment på olika kromosomer har kopplats till PL. För att bedöma riskfaktorerna och genernas inverkan på uppkomsten av PL behövs mer studier inom området.

I Sverige ingår hundraser i hälsoprogrammet för PL, men Pomeranian är ej en av dem. Hittills har inga studier gjorts för att undersöka prevalensen av PL i den svenska Pomeranian-populationen.

## SUMMARY

Patella luxation (PL) is a common orthopaedic disease and is characterised by a patella that moves out of the trochlear groove, either manually, during locomotion or is permanently fixed out of the groove. The disease is often asymptomatic, but can lead to osteoarthritis, cranial cruciate rupture, lameness and pain.

The pathogenesis has not yet been established and different theories have been suggested. The most recognised theory holds that it is a deformity of the hip and rotation in the femur bone that leads to muscular displacement and further causes the patella to luxate. This reduces the pressure on the trochlear groove, and thus making the trochlear groove hypoplastic (Harasen, 2006b; Roush, 1993). Other theories suggest that PL comes from a muscle related defect where the quadriceps muscle is atrophic, a deficiency in the pelvis bone (L'Eplattenier & Montavon, 2002), or is due to high levels of estradiol (Gustafsson *et al.*, 1969). More research is needed to confirm which theory is correct.

Diagnosis of PL is done by inspection in standing position and during movement, and additionally by palpation of the stifle joint in both standing and lateral recumbency position (Vidoni *et al.*, 2005). A standardized classification system has been developed and is used widely.

Risk factors that have been observed regarding PL include certain breeds (such as Chihuahua, Yorkshire terrier and Pomeranian), small size and gender. Reports have shown that small breed dogs have up to 12 times the risk to develop PL compared to larger breeds (O'Neill, 2016). However, recent studies argue that some larger breeds are increasingly affected and it can be hypothesised that large breed dogs are not as thoroughly examined for PL as small breed dogs. Female dogs have been reported to have a higher risk of PL than male dogs, which might be due to hormonal influences or that male dogs have more muscle mass and thus are able to stabilize the stifle joint better.

Recently the search for finding a gene that can be associated with PL has intensified. The overrepresentation in specific breeds and high proportion of dogs with bilateral PL points towards a disorder that is heritable (Wangdee *et al.*, 2014). Although, the complex inheritance pattern suggests that the disease is polygenic. Fragments on different chromosomes have been linked to PL, but further studies are needed to confirm the connection.

Four breed are involved in the Swedish screening program for PL, but Pomeranian is not one of them. So far, no studies have been done to examine the prevalence of PL in the Swedish Pomeranian population.



## **INTRODUCTION**

Patellar luxation (PL) is one of the most common congenital orthopaedic disorders of dogs and can be observed in a variety of breeds, including mixed-breeds (Bellumori *et al.*, 2013). The condition is characterised by a patella that moves out of the trochlear groove, either manually, during locomotion or is permanently fixed out of the groove. The disease is often asymptomatic, but can lead to osteoarthritis, cranial cruciate rupture, lameness and pain (O'Neill *et al.*, 2016). PL appears to be inherited (except for the acquired form, caused by an external trauma) and is common in small breed dogs (O'Neill *et al.*, 2016), which has led to the development of mandatory screening programmes for certain affected breeds in Sweden (Zanders, 2014).

The literature has described two types of patellar luxation: a medial and lateral type. The medial patellar luxation (MPL), where the patella slips out of the trochlear groove on the medial side, is the most commonly observed type. Lateral patellar luxation (LPL) is diagnosed when the patella slips out of the groove on the lateral side, and is only seen in up to 25% of all cases (Harasen, 2006a; Alam *et al.*, 2006; Vidoni *et al.*, 2005; L'Eplattenier *et al.*, 2002). However, small breed dogs are almost exclusively affected by MPL. Studies show that only 5 % of small breed dogs are diagnosed with LPL (Alam *et al.*, 2007; Soontornvipart *et al.*, 2012).

The aim of this literature review was to investigate what factors contribute to the overrepresentation of PL in small breed dogs, and if there is a strategy to lower the prevalence of PL in predisposed breeds in Sweden, with emphasis on Pomeranians.

## **MATERIALS AND METHOD**

The search for literature was mainly done in PubMed, Web of Science and Google Scholar. For general information regarding the disease, diagnostics and pathogenesis, a wide search using the few key words "patellar luxation and canine" was applied (patellar luxation AND canine). In order to obtain information about the genetic aspects and inheritance keywords such as "patellar luxation", "canine", "gene", "phenotype", "genotype", "inheritance" and "congenital" were used.

## LITERATURE REVIEW

### Anatomy of the stifle joint

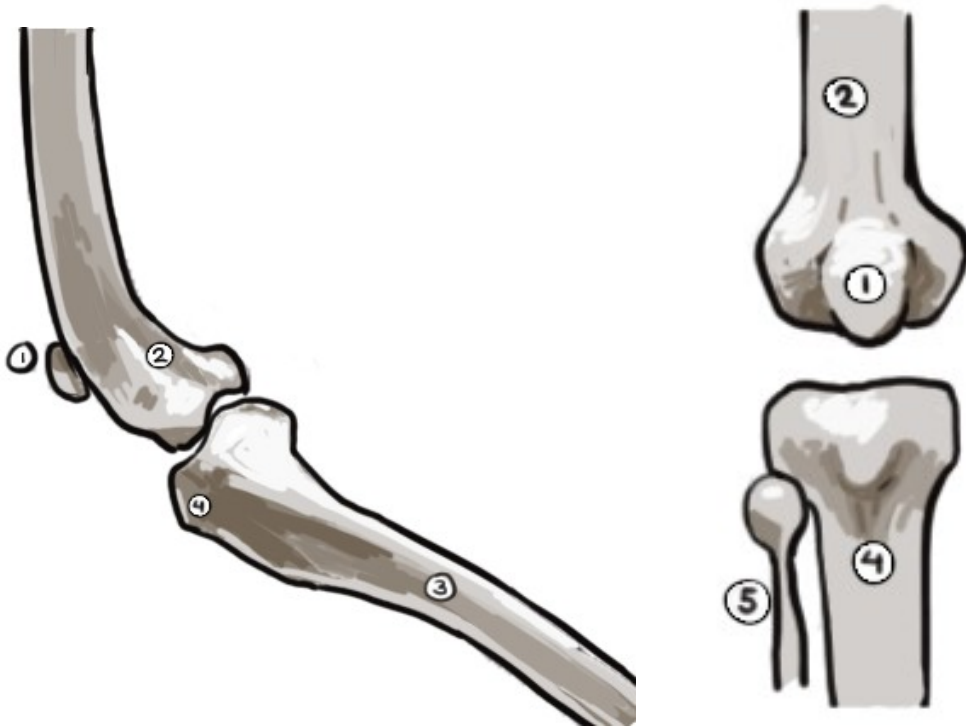


Figure 1. Anatomy of the stifle joint by Oliver Elm (2017)

The stifle (knee) joint comprise three bones, namely the femur (2), the tibia (3) and the patella (1). The patella is an ovate sesamoid bone located within the tendon of insertion of the quadriceps muscle group and lays in the *trochlea ossis femoris*. The distal tendon that attaches the patella to the tibial tuberosity (4) is the patella ligament. The patella is partly stabilized by the collateral ligaments and the cruciate ligaments. Normally the sideways-movement of the patella is limited, but can glide proximo-distally in the trochlear groove.

Under normal circumstances, the patella puts pressure on the articular cartilage of the femoral trochlea resulting in a groove, which helps stabilizing the patella.

### Pathogenesis

Patellar luxation is a developmental disease; meaning that skeletal changes may arise early in life and worsen as the dog matures. However, symptoms of PL are rarely seen until middle age, which makes PL difficult to diagnose in young dogs. The pathogenesis of PL has not been determined and different theories are trying to describe the course of events, which involves the entire hind limb (Harasen, 2006b; Pérez & Lafuente, 2014). When the quadriceps muscle contracts in a normal limb, the patella is drawn proximally on the femoral trochlea. However, if the femur is abnormal, the patella is instead pushed medially or laterally which leads to a luxating patella (Vidoni *et al.*, 2006)

The most acknowledged theory holds that a deformity of the hip, coxa vara, (by which the angle between *caput ossis femoris* and *collum ossis femoris* is declined) and the reduced

anteversion (inward twisting) of *collum ossis femoris* are the causes of the luxating patella (Harasen, 2006b; DeCamp *et al.*, 2015). The skeletal deformities displace the extensor muscles of the hind limb, primarily the quadriceps group, which results in decreased growth of the medial side and increased growth of the lateral side of the distal extremity of the femur. The effect of this is a medial curvature and rotation of the distal part of femur and proximal part of tibia. The patella is moved sideways due to these abnormalities, which reduces the pressure on the trochlear groove and thus making it hypoplastic (Harasen, 2006b; Roush, 1993).

An experimental study of fourteen Beagles showed that administration of estradiol benzoate resulted in hypoplastic trochlear groove. This indicates that hormones may play a role in the development of PL and that osteopathic deformities such as coxa vara and dorsal bowing of the femur follow as a result. Estradiol has previously been seen to inhibit the growth of cartilage, and counters growth hormones in the epiphyseal plate and joint cartilage. (Gustafsson *et al.*, 1969).

It has also been suggested that PL is caused by a muscle related defect. Atrophic and tense quadriceps muscles, especially the rectus femoris, create a “bowstring effect” that rotate the tibia internally, therefore causes the patella to move medially (L’Eplattenier & Montavon, 2002).

Furthermore, research has shown that the conformation of the pelvis bone have an impact on the development of PL, and that small sized individuals (compared to normal sized individuals of the same breed) were more prone to develop PL. Evaluation of the pelvis showed that the origin of the sartorius muscle were positioned significantly more medial in dogs with PL than in dogs without PL. This could exert a medial pull on the patella and thus cause a medial displacement (L’Eplattenier & Montavon, 2002).

## **Diagnostics and secondary diseases**

Diagnosis of PL is done by inspection in standing position and during movement, and additionally by palpation of the stifle joint in both standing and lateral recumbency position (Vidoni *et al.*, 2005). A classification system has been developed to grade the variable clinical and pathologic changes seen in PL. Singleton (1969) adapted the classification system first described by Putnam (1968) and described four grades based on the palpation of the patella along with the degree of rotation of the tibial tuberosity (Pérez & Lafuente, 2014; DeCamp *et al.*, 2015)

### ***Classification system***

- Grade 0: Normal patella with no luxation, regardless of the limb’s position. Dogs with loose patella, i.e. a patella that can be manipulated to the ridges of the trochlea, but not out of the groove, are in general considered as normal.
- Grade I: The patella can be completely luxated manually, but will return to its normal position within the trochlear groove when released. No crepitation is apparent.

- Grade II: The patella can be completely luxated manually, with flexion and internal rotation of the tibia or with flexion but without internal rotation of the tibia. The patella is luxated until it is replaced manually and crepitation may occur. The proximal tibial tuberosity may be rotated up to 30 degrees with medial luxations.
- Grade III: The patella remains luxated most of the time (ectopic), but can be manipulated to the trochlear groove, however when the pressure is released, the patella will relaxate. The trochlear groove is hypoplastic.
- Grade IV: The patella will be luxated at all times (ectopic) and cannot be manually replaced into the trochlear groove. The patella is situated just above the medial/lateral condyle and a gap occurs between the patellar ligament and the distal end of the femur.

### **Lameness**

The degree of lameness in PL varies between individuals and may be intermittent or continuous. In some cases, no lameness can be detected. In a study consisting of 432 dogs, 61.6% were PL positive but only 19% showed signs of lameness (Vidoni et al., 2006).

When showing signs of lameness, puppies and young adult dogs are often seen with an intermittent “skipping” gait, where one leg is carried for several steps before returning to normal (Harasen, 2006a; DeCamp *et al.*, 2015). Harasen (2006a) stated that “*The nonweight-bearing phase corresponds with luxation or subluxation of the patella and the gait returns to normal when the luxation spontaneously reduces*”. Older dogs with lower grade of PL (1 or 2) are often presented with more continuous hind limb lameness, and as time progresses, may exhibit acute signs of lameness if secondary diseases, such as osteoarthritis or cranial cruciate rupture develop (DeCamp *et al.*, 2015). Dogs with PL of grade 3 show a more abnormal and “crouched” gait and are using their legs in a semiflexed, internally rotated way, while dogs with grade 4 are usually carried by their owners and have a crab-like posture (Pérez & Lafuente, 2014).

Signs of lameness can worsen if the dog gains weight, osteoarthritis occurs, the patella luxation becomes permanent or if the cruciate ligament ruptures.

### **Osteoarthritis**

Secondary osteoarthritis (OA) may be seen in PL and is the result of a low grade inflammation the affected stifle. When the patella becomes luxated, it prevents the dogs from bending its knee properly, which can lead to friction and rubbing of the surface of the joint (O’Neill *et al.*, 2016). Crepitation can be observed in dogs with PL and is a sign of chronic OA (Vidoni *et al.*, 2006). The complex condition has a multitude of interacting biochemical and biomechanical factors and changes typically involve all joint tissues. OA is a syndrome characterised by low grade inflammation with pro-inflammatory cytokines such as interleukin (IL)-1 $\beta$  and tumour necrosis factor (TNF)- $\alpha$  involved. A deterioration of the articular cartilage leads to cartilage softening. Chondrocytes attempt to repair cartilage degradation by increasing the production of extracellular matrix (ECM) macromolecules, but fail in attempt to maintain the homeostasis between synthesis and degradation of ECM components. Fibrillation of the superficial layers of the cartilage occurs followed by cartilage loss, which can lead to erosions and exposure of the underlying subchondral bone plate (cartilage ulcers). The subchondral bone responds with formation of a thicker bone (bone sclerosis) as well as

micro fractures of the trabecular bone (Man, 2014). New bone at the joint margins, called osteophytes, is also seen and the synovial membrane and joint capsule always show some degree of synovitis and capsulitis in OA joints.

An OA joint will result in decreased ability to use the joint and/or through the sensation of pain. Nociceptors respond to neuropeptides such as substance P, calcitonin gene related peptide (CGRP), neuropeptide Y and vasoactive intestinal peptide and can be found in the joint capsule, tendons, ligaments, periostium and subchondral bone (Goldring & Goldring, 2007). Stimulation of the nociceptor leads to pain perception in the central nervous system. In addition, a reflex can be activated that result in a state of muscle hypertonia or spasm in the surrounding muscles of the joint, which further contributes to the pain. The joint pain makes the patient unwilling to move and muscle atrophy can occur, leading to a decreased support of the stifle joint (Johnston, 1997).

### ***Cranial cruciate ligament***

MPL has reported to increase the risk of degeneration and rupture of the cranial cruciate ligament (CrCL) and seems to occur mostly in middle aged to older dogs. The rupture is a result of long-term degeneration of the ligament's extra-cellular matrix (ECM). After rupture, the CrCL loses the normal function of preventing the tibia from moving cranially and stabilizing the stifle (Comerford *et al.*, 2011). At least 15% to 20% of dogs with MPL are estimated to rupture their CrCL (DeCamp *et al.*, 2015). It has been hypothesized that this association is caused by the displacement of the extensor mechanisms of the stifle joint, an internal rotation of the proximal tibia and a less stabilizing effect of the quadriceps cranially (Alam *et al.*, 2006). In addition, OA and erosion of the cartilage may further encourage degeneration of the CrCL (DeCamp *et al.*, 2015).

### ***Treatment***

Not all affected dogs show symptoms of PL and clinical relevance must be considered before determining if the patient should be treated surgically or if conservative treatment is sufficient. Conservative treatment includes rehabilitation to enhance the mechanism of the quadriceps. Different surgical techniques have been developed and are chosen depending on radiographic findings and intraoperative evaluation (Pérez & Lafuente, 2014).

### ***Risk factors in PL***

PL is observed in a variety of dog breeds but the majority are small breed dogs including Miniature and Toy Poodles, Yorkshire terriers, Pomeranians, Chihuahuas, Boston terriers, Pekingese, Bichon Frisé, French Bulldog and Cavalier King Charles spaniels (Harasen, 2006; Zanders, 2014; O'Neill *et al.*, 2016; Alam *et al.*, 2006; L'Eplattenier & Montavon, 2002). Reports have shown that small breed dogs have up to 12 times the risk to develop PL compared with larger breeds (O'Neill *et al.*, 2016). However, recent studies argue that some larger breeds, such as Labrador Retrievers, Flat coated retrievers and Kooiker dogs, are increasingly affected (Lavrijsen *et al.*, 2014; O'Neill *et al.*, 2016; Wangdee *et al.*, 2014; DeCamp *et al.*, 2015; Alam *et al.*, 2006). MPL is the most common form of PL in general, and small dogs are almost exclusively affected with MPL. LPL is more common in large

breed dogs, and a study done by Lavrijsen *et al.* (2013) even showed that LPL is the most common type of PL for the Netherlands population of Flat Coated Retrievers (61% of cases).

Even though several studies have pointed out specific breeds as risk factors for PL, Bellumori *et al.* (2013) found no difference in expression of PL between purebred dogs and mixed-breed dogs. Presence of PL was examined in 2176 dogs; out of these 1710 were purebred and 466 were mixed-breed, which show that breed itself is non-significant with a mean P-value of 0.49. The authors further discussed that PL is an example of size-oriented predisposition, since it emerges among smaller dogs. The prevalence of PL seems to decrease with increasing bodyweight (Asher *et al.*, 2009; Lavrijsen *et al.*, 2014; Vidoni *et al.*, 2006). This theory is supported by L'Eplattenier & Montavon (2002), who described that dogs with PL were significantly smaller and lighter.

Female dogs have been reported to have a higher risk of PL than male dogs, with a male:female ratio of 1:1.86 in large breed dogs according to Alam *et al.* (2007) and Gibbons *et al.* (2006). In small breed dogs, the male:female ratio of 1:1.5 has been observed in several studies (Gibbons *et al.*, 2006; Zanders, 2014, Kalff *et al.*, 2014). It has been hypothesised that this unbalance is due to hormonal influences. On the contrary, other studies could not observe any difference between the genders (Vidoni *et al.*, 2005; Wangdee *et al.*, 2014) and the relevance of oestrus cycle is discussed. In the actual study, all females were in anoestrus, which arguably could affect the results (Vidoni *et al.*, 2005). It has been noted that female dogs are showing an increasing tendency for PL at times of heat and with increasing number of litters. The effects may be due to the influence of oestrogens and requires further clarification (Koch, 1998; Zanders, 2014). A more severe degree of patellar luxation has also been noted in females. “*The proportion of female dogs with grading 2 or higher was 6.23 %, compared with 4.18 % for males*” as quoted by Zanders (2014). Male dogs might also have more muscle mass and thus be able to stabilize the stifle joint better (Zanders, 2014).

## **Genetic research**

Recently the search for finding a gene that can be associated with PL has intensified. The overrepresentation in specific breeds and high proportion of dogs with bilateral PL points towards a disorder that is heritable (Wangdee *et al.*, 2014).

A trait can be inherited in different patterns. A Mendelian trait is controlled by a single locus and shows a simple Mendelian inheritance pattern. Hermans *et al.* (1987) concluded that the transmission of LPL in Shetland ponies most probably is monogenic recessive (i.e. a Mendelian trait) due to the fact that unaffected horses could produce affected offspring, and affected horses would always produce affected offspring. Non-Mendelian traits are more complex and unpredictable. Polygenic inheritance is an example of this, and is defined by multiple genes determining a character. It has been suggested that, because of the sex predisposition and lack of Mendelian segregation pattern, PL is a polygenic disorder (Priester, 1972; Hayes, 1994, Zanders, 2014). Pedigrees of Pomeranian dogs show a convoluted pattern regarding the occurrence of PL, disabling the attempt to draw any conclusions. Affected animals can produce unaffected offspring, as well as affected. Likewise, parental animals without PL can produce both unaffected and affected descendants (Soontornvipart *et al.*, 2012).

Estimation of the heritability ( $h^2$ ) is used to determine the proportion of variance in a particular trait that can be explained by genetic factors, as opposed to environmental factors. The heritability varies from 0.0 to 1.0, where 1.0 indicates that the variation between individuals depends solely on genes. The additive genetic variation can be defined as the total variation that is passed on to offspring and the genetic effects can be added, i.e. each allele is expressed in the offspring.

Heritability can be calculated by using the formula:

$$h = \frac{\textit{additive genetic variation}}{\textit{phenotypic variation}}$$

Zanders (2014) showed high levels of heritability in Bichon Frisé and Chihuahua (0.18-0.25), but concluded that environmental factors, such as sex, neuter status, time of birth and exercise, are important in the development of PL (Zanders, 2014). A study done on 339 Pomeranians in Thailand showed heritability as high as 0.44 (Wangdee *et al.*, 2017).

Fragments located on chromosome 10, 36 and X has been linked to PL in a study of 39 small breed dogs (23 dogs where affected with PL). The fragments alone did not appear to be responsible for the disorders, but may play an important role in the pathogenesis. The authors found a fragment on the X chromosome to be close to a gene, which translates into the protein kinase catalytic subunit PRKX. The PRKX is involved in tissue formation, cellular differentiation and epithelial morphogenesis and might cause a malformation of the sartorius muscle, leading to PL. The fragment on chromosome 36 is located closely to the ATP synthase gene and an error in this gene might lead to over-contraction of the quadriceps leading to PL (Chomdej *et al.*, 2014).

Another study of 339 Pomeranians showed regions on chromosome 5 (gene SC5D) and chromosome 32 (gene BMPR1B) to be associated with PL. Gene SC5D has been linked to lathosterolosis in humans, “*a disorder associated with multiple congenital anomalies including abnormal bone calcification, limb malformation and liver disease*” as quoted by Wangdee *et al* (2017). Gene BMPR1B translates to a protein receptor involved in formation of endochondral bone and embryogenesis (Wangdee *et al.* 2017).

Involvement of chromosome 7 has been suggested in yet another genetic study, made on 59 dogs where 75 % were diagnosed with PL (Soontornvipart *et al.*, 2013). Lavrijsen *et al.*, (2014) also concluded that chromosome 7 is participating in the development of PL in a study made on Flat Coated Retrievers (45 cases and 40 controls), as well as chromosome 31. The gene (TNR) on chromosome 7 derives from the same ancestral gene as the one that cause Ehlers-Danlos syndrome type III in humans. Ehlers-Danlos syndrome is a connective tissue disorder and type III (also known as hypermobility type) is associated with subluxations, dislocation and OA. The authors suggest that this gene, in combination with other genetic factors, might affect Flat-Coated Retrievers to develop PL (Lavrijsen *et al.*, 2014).

### **Kennel clubs regulations and breeding policies**

The Swedish Kennel club (SKK) has decided that the result of a patellar luxation examination ought to be centrally registered for all breeds. Only examinations made on dogs over 12 months and by approved veterinarians, specializing in dog and cat veterinary medicine, are submitted to the SKK registry (SKKa, 2017). The classification system used in the SKK

differs slightly from the one developed by Putnam, in the regard of having grades ranging from 0 to 3 (see below).

- Grade 0 = Normal
- Grade 1 = The patella can be luxated manually, but will spontaneously return to its normal position when the pressure is released
- Grade 2 = The patella can easily be luxated, either manually or spontaneously, and remains luxated
- Grade 3 = The patella is permanently luxated

In addition, a few breeds (Chihuahuas, Kooiker dogs, Bichon Frisés and Russkiy Toys) have mandatory examination for breeding animals prior to mating in order to be able to register the puppies within SKK (SKK, 2017b). In the United States Pomeranian is the highest ranked breed for PL with 36.2 % of affected individuals; Yorkshire terrier is second with 23.4 % and Australian terrier is third with 19.0 % (OFA, 2017). In Thailand, a study consisting of 238 Pomeranians showed that 75 % (177) had PL (Soontornvipart *et al.*, 2013)

The effective population size is defined as the number of individuals in a population who contribute to the next generation, while the census population size is the actual number of individuals within a population. Each breed has in general a rather closed genetic pool and an effective population size far smaller than the census population size. This results in loss of heterogeneity (the probability that two randomly sampled alleles in the population are identical), accumulation of detrimental genes and (an often desired by the breed standard) an exaggeration of anatomical features (Hedhammar *et al.*, 2011). The challenge is, as Hedhammar *et al.* (2011) stated, “*Achieving a balance between preserving a homogenous and specific breed type and the need for strong selection for health, longevity and performance...*” Today, dogs are registered in national kennel club databases and a linkage between these is non-existing (Hedhammar *et al.*, 2011). It has been suggested that national populations differs between countries to the extent that national databases are irrelevant outside the country’s borders, due to the genetic diversity between the populations (Bateson, 2010). However, similarities such as diseases and genetic material do not support that hypothesis (Hedhammar *et al.*, 2011).

The Swedish Pomeranian Breed club has a developed a breed strategy where PL is included. Approximately 40 dogs are examined each year and 60 % of those are considered free of PL. The majority of dogs with observed PL are diagnosed as grade 1 or grade 2 (SKK, 2017c). In 2016, 560 Pomeranians where registered in the Swedish Kennel Club (SKK, 2017d), and the proportion of examined dogs are not enough to draw any conclusions about the Pomeranian population as a whole (SKK, 2017c).

Screening programs have been able to reduce the frequency of inherited diseases, but not been able to fully eliminate the problem of PL (Hedhammar *et al.*, 2011, Lavrijsen *et al.*, 2013). Selection on phenotypic observation is adequate when the incidence is high and the average



of PL in a breed is severe (van Grevenhof *et al.*, 2016). Vidoni *et al.* (2006) concluded that to achieve good results, the diagnostic screening should be as standardized as possible.

## DISCUSSION

PL is a welfare problem and can lead to severe pain and disability in affected individuals, thus minimizing the total numbers of affected individual is crucial. As the literature suggests, PL seems to be a complex disorder with an even more complex pathogenesis and further studies need to be done to establish the true regulating mechanism behind PL. Genetic studies have so far not been able to demolish nor confirm any of the suggested theories.

Risk factors for PL that have been identified include certain breeds, small size of these breeds and gender. It can be hypothesised that since PL is a disorder typically associated with small breeds, larger breeds are not evaluated as thoroughly. However, this tendency seem to be shifting as some larger breeds, for example Flat Coated Retriever, are being considered predisposed to PL and it is generally acknowledged that the diagnose of PL in large breed dogs is increasing.

Bellumori *et al.* (2013) concluded that there was not any difference between purebred dogs and mixed-breed dogs, but found that the size was of relevance. The term mixed-breed is somewhat vague, and the familiar bond between the two categories where not established in the study. This means that a mixed-breed dog with PL might be significantly related to a dog of a predisposed breed, thus making the conclusion that breed does not play an important role in the development of PL inconsequential.

Results (Gustafsson *et al.*, 1969) showing that the administration of estradiol lead to the development of PL supports the findings of a higher proportion of affected females than males, since estradiol levels are naturally lower in the latter. Vidoni *et al.* (2005) presented results showing no difference in frequency of PL between the genders but pointed out that all females were in anoestrus, also a state with lower concentration of estradiol. Further studies to determinate the correlation between estradiol and PL are needed. Chomdej, *et al.* (2014) linked fragments on chromosome X to PL and concluded that the protein PRKX is a possible factor in the development of PL. However, X-linked disorders generally show a higher frequency in males than females even if inactivation of genes may occur. The study in question was made on 39 small breed dogs, which is a low number to draw clear conclusions from since genetic variation may occur between individuals. Only one study (Wangdee *et al.*, 2017) involved a larger number of dogs, making the conclusion that gene SC5D and gene BMPR1B are affecting the development of PL more reliable, although more studies need to be done to confirm the results.

The heritability of PL has been reported to be significant and ranges from 0.18 to 0.44. By implementing a screening programme for affected breeds, the incidence has been reduced (Lavrijsen *et al.*, 2013) and is therefore a suitable first step to control the frequency of PL. The high level of heritability that has been shown in PL supports this action. In Sweden only four breeds are included in the screening programme, and it is noticeable that breeds such as

Pomeranian and Yorkshire terrier are not included. Pomeranian tops the list of affected individuals in the United States (36.2 %), tailed by Yorkshire terrier (23.4 %) (OFA, 2017), and the patella status amongst Pomeranians in Thailand seem to be even worse, according to Soontornvipart *et al* (2012). The familiar bond between the Swedish and the American populations has not been established, and therefore no conclusions can be drawn based on this observation. The same goes for the Pomeranian population in Thailand. However, out of the few Pomeranians evaluated in Sweden, 40 % were diagnosed with PL (SKK, 2017c). Zanders (2014) evaluated the frequency of PL in the Swedish and Finnish Pomeranian population and found that 23.3 % of males and 36.9 % of females were affected. She found that the Finnish and Swedish populations share ancestry and consequently the two populations could be added to obtain enough data. Since examination of PL is not mandatory for Pomeranians, one can argue that the acquired data of Zanders (2014) and SKK is biased. PL can be asymptomatic and therefore it is possible that an even larger percentage of Pomeranians are affected. Studies to evaluate the patella status in Swedish Pomeranians need to be done, in order to determine if a screening programme is needed for the breed in question.

## CONCLUSION

PL is a common orthopaedic disease and can cause great suffering for affected dogs. The etiology is not clear and more research is needed. In Sweden, a few breeds are included in the screening programme and evaluating other high-risk breed's patella status in the Swedish population might be a subject for future studies.

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