THE KENNEL CLUB
DOG HEALTH

Breed Health and Conservation Plan

Shetland Sheepdog

Evidence Base

CONTENTS

INTRODUCTION

The Kennel Club launched a new resource for breed clubs and individual breeders – the Breed Health and Conservation Plans (BHCP) project – in September 2016. The purpose of the project is to ensure that all health concerns for a breed are identified through evidence-based criteria, and that breeders are provided with useful information and resources to raise awareness of current health and welfare concerns in their breed, and support them in making balanced breeding decisions.

The Breed Health and Conservation Plans take a complete view of breed health with consideration to the following issues: known inherited conditions, complex conditions (i.e. those involving many genes and environmental effects such as nutrition or exercise levels, for example hip dysplasia), conformational concerns and population genetics.

Sources of evidence and data have been collated into an evidence base which gives clear indications of the most significant health conditions in each breed, in terms of prevalence and impact. Once the evidence base document has been produced it is discussed with the relevant Breed Health Co-ordinator and breed health representatives where applicable. Priorities are agreed based on this data and incorporated into a list of actions between the Kennel Club and the breed to tackle these health concerns. These actions are then monitored and reviewed on a regular basis.

DEMOGRAPHICS

The number of Shetland Sheepdogs registered by year of birth between 1980 and 2019 are shown in Figure 1. The trend of registrations over year of birth (1980-2019) was -72.9 per year (with a 95% confidence interval of -92.0 to -53.8) reflecting the overall decrease in the breed's numbers over time. As shown in the graph below, the breed's numbers appeared to peak in 1989 with almost 5,000 registered, and have since gradually reduced to 701 in 2019.

[Put simply, 95% confidence intervals (C.I.s) indicate that we are 95% confident that the true estimate of a parameter lies between the lower and upper number stated.]

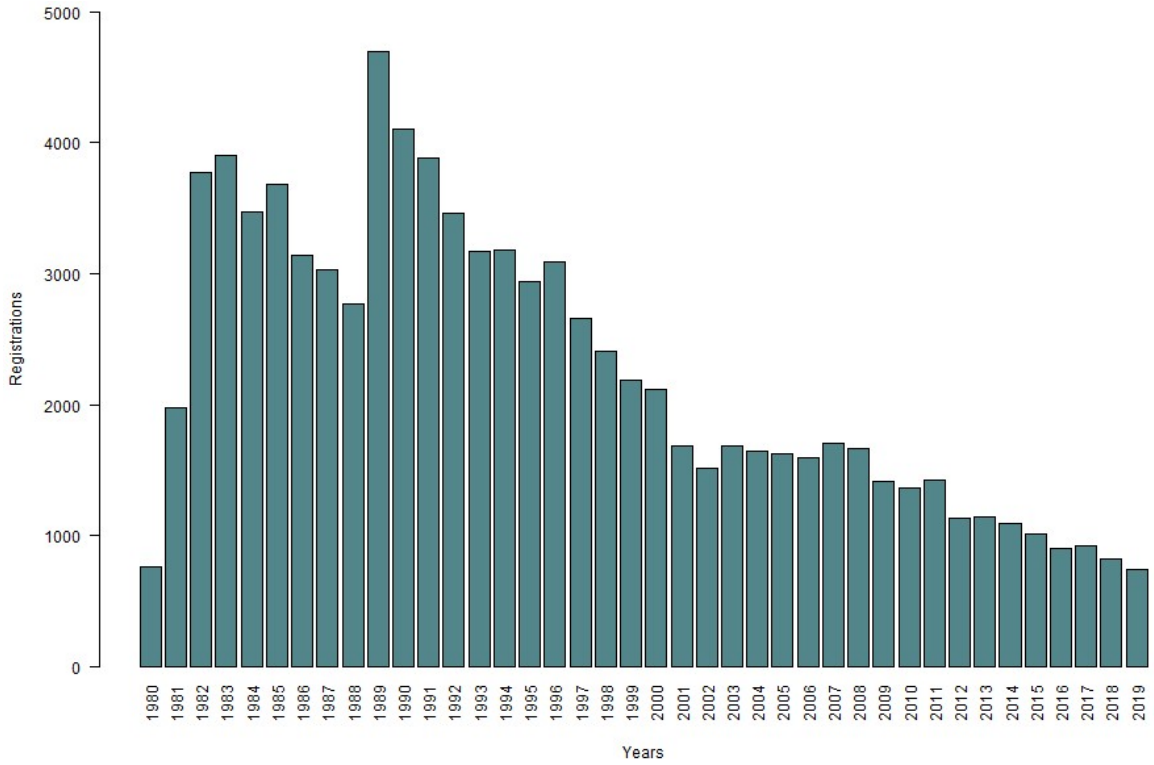


Figure 1: Number of registrations of Shetland Sheepdogs per year of birth, 1980 - 2019

BREED HEALTH CO-ORDINATOR ANNUAL HEALTH REPORT

Breed Health Co-ordinators (BHCs) are volunteers nominated by their breed to act as a vital conduit between the Kennel Club and the breed clubs with all matters relating to health.

The BHC's Annual Health Report 2019, yielded the following response to 'please list and rank the three health and welfare conditions that the breed considers to be currently the most important to deal with in your breed':

1. Generalised progressive retinal atrophy (GPRA)
2. Collie eye anomaly (CEA)

In terms of what the breed has done in the last year to help tackle these listed health and welfare concerns, the breed promoted the use of DNA tests for CEA and GPRA by obtaining discounts with laboratories, as well as this they continued to encourage owners to have regular clinical eye examinations by subsidising the costs. The breed supported research at the Animal Health Trust looking at one GPRA variant and continued to encourage hip scoring of all breeding stock.

BREED CLUB HEALTH ACTIVITES

The Shetland Sheepdog has an active Breed Health Coordinator (BHC) and a webpage on their club website dedicated to health which can be found under the Health heading at: https://www.essc.org.uk

BREED SPECIFIC HEALTH SURVEYS

Kennel Club Purebred and Pedigree Dog Health Surveys Results

The Kennel Club Purebred and Pedigree Dog Health Surveys were launched in 2004 and 2014 respectively for all of the recognised breeds at the time, to establish common breed-specific and breed-wide conditions.

2004 Morbidity results: Health information was collected for 694 live Shetland Sheepdogs of which 413 (60%) were healthy and 281 (40%) had at least one reported health condition. The most frequently reported specific conditions were retained puppy teeth (36 cases, 5.2% prevalence), cryptorchid/ undescended testicle/ missing testicle (20 cases, 2.9% prevalence), collie eye anomaly (17 cases, 2.4%), heart murmur - unspecified (16 cases, 2.3%) and colitis/ chronic colitis/ large bowel diarrhoea (15 cases, 2.2%).

2004 Mortality results: A total of 364 deaths were reported for the Shetland Sheepdog. The median age at death was 12 years and 6 months (min = 2 months, max = 19 years). The most frequently reported causes of death by organ system or category were kidney failure (47 deaths, 12.9%), old age (44 deaths, 12.1%), stroke/ cerebral vascular infarction (15 deaths, 4.1%), heart failure (13 deaths, 3.6%), cancer – unspecified (9 deaths, 2.5%) and acute kidney failure (9 deaths, 2.5%).

2014 Morbidity results: Health information was collected for 360 live Shetland Sheepdog of which 235 (65.3%) had no reported conditions and 125 (34.7%) were reported to be affected by at least one condition. The most frequently reported conditions were arthritis (16 cases, 4.4% prevalence), lipoma (16 cases, 4.4% prevalence), hip dysplasia (10 cases, 2.78%), skin (cutaneous) cyst (10 cases, 2.8%), and cryptorchidism (9 cases, 2.5%).

2014 Mortality results: A total of 56 deaths were reported for the breed. The median longevity for the Shetland Sheepdog was 11 years. The most frequently reported causes of death by organ system or category were cancer - unspecified (7 deaths, 12.5%), cardiomyopathy (7 deaths, 12.5%), old age (7 deaths, 12.5%), and kidney failure (6 deaths, 10.7%).

LITERATURE REVIEW

The literature review lays out the current scientific knowledge relating to the health of the breed. We have attempted to refer primarily to research which has been

published in peer-reviewed scientific journals. We have also incorporated literature that was released relatively recently to try to reflect current publications and research relating to the breed. Many of the papers below refer to populations residing overseas, and therefore may not be directly applicable to the UK population. However, given that breeders may make use of dogs abroad we have chosen to include them for reference.

Biliary conditions

Gall bladder disease/ mucocele (GBM): An American study evaluated 38 dogs of the breed with gallbladder disease, of which 25 were diagnosed with gallbladder mucocele (Aguirre et al, 2007). This condition develops due to an abnormal accumulation of bile or mucus in the biliary system, which results in swelling of the gall bladder and biliary duct occlusion. Clinical signs include vomiting, abdominal pain or discomfort, anorexia, excessive respiratory and heart rate, fever, diarrhoea and excessive thirst/ urination. High levels of lipids and fats were also found in affected dogs, however the full paper could not be accessed so further findings cannot be reported here. There is also a strong association between the condition and hypercortisolism, hyperadrenocorticism and hypothyroidism (Cullen et al, 2014; Gookin et al, 2015).

A subsequent American study assessed the association of the *ABCB4* mutation with mucocele in the breed, using samples from 15 affected and 21 controls (Mealey et al, 2010). The median age of onset in the breed was nine years (range 5 – 12 years). The authors found the mutation to be significantly associated with disease in the affected individuals and suggested an autosomal dominant mode of inheritance, with possible incomplete penetrance, as none of the affected dogs were homozygous (carried two copies) for the mutation.

However, more recent research reassessed this mutation on a larger subset of dogs, including eight Shetland Sheepdogs with disease and 12 without (Cullen et al, 2014). Further to this, the presence of the mutation was assessed in a group of affected dogs of other breeds (n=28) and unaffected dogs (n=37). For the Shetland Sheepdog, just four of the eight affected carried this mutation, as well as nine out of the 12 unaffected, with no statistically significant difference between the two. This suggests the mutation is not significantly associated with disease in the breed, and whilst it cannot be ruled out that this mutation may form part of the basis for disease manifestation, it should not be relied upon as a definitive test.

An interesting study also looked to determine whether the onset of disease could be linked to the use of specific drugs, namely pathogen preventatives, steroid and non-steroidal pain relief, and osteoarthritis medication (Gookin et al, 2015). No association was found between the steroidal/ non-steroidal drugs and GBM, as well as with osteoarthritic treatment/ supplements, however there was an increased likelihood of GBM dogs having been treated with imidacloprid (a flea/tick preventative), with an odds ratio of 9.3; although it should be noted this was not strongly significant (p=0.04, 95% CI 1.1-78.2). This finding was not repeated in non-Shetland Sheepdog breeds. Concurrent diseases were also considered, with 17% of

dogs also affected by hypothyroidism, 14% by hyperadrenocorticism (Cushing's disease) and 7% diabetes mellitus. However, treatment for these diseases were not associated with GBM in the Shetland Sheepdog. The authors noted it is unlikely that imidacloprid is a primary cause for disease in the breed, but could contribute towards its manifestation. Further work is needed to determine whether the breed metabolises this drug differently to other breeds.

Cancer conditions

Gastric carcinoma (metaplasia): A Finnish study was undertaken to determine breed association with different types of gastric cancers, based on submissions made to a veterinary teaching hospital (Candido et al, 2018). A total of 734 Shetland Sheepdogs were included in the study, of which two were found to have metaplastic (malignant) form of cancer in gastric cells. The authors proposed the breed had a significantly raised relative risk of disease, with this being 5.83 (95% 1.75 – 19.45), but however that this form of gastric cancer remains rare.

Oral tumours: An older Japanese study investigated the incidence and type of oral tumours (epulides), finding that of 189 samples of acanthamotous epiludes (non-invasive but large growing tumours) the breed made up 38.2% (Yoshida et al, 1999). The breed also predominated in other tumour types: fibromatous (19.6%) and ossifying (11.4%). The authors did note the high population of the breed in the country at the time. The breed were also found to be over-represented in a paper looking at oral squamous cell carcinoma in dogs, although this was based on just four dogs out of a total of 84 samples submitted (Nemec et al, 2012).

Testicular tumours: A Norwegian study investigated tumours submitted to the Norwegian canine cancer register between 1990-98 to determine any breed-specific predispositions to testicular cancers (Nodtvedt et al, 2010). The Shetland Sheepdog was found to have a five times higher likelihood of developing testicular tumours than the all-breed average, with a proportional morbidity of 5.7 (95% CI 3.8 – 8.6). A total of 39.5% (out of a total of 38) tumours in the breed were testicular, with these mostly (80%, n=12) made up of Sertoli cell tumours (cells involved in the process of developing sperm).

Dental conditions

Maxillary canine-tooth mesioversion (MCM)/ misplaced/ lance canines: This condition is characterised by displacement of one or both upper canines, resulting in further dental disease. A recent study genome sequenced the breed to determine any genetic factors for disease (Abrams et al, 2020). One gene *FTSJ3* were found to be associated with this condition, as well as smaller body size. Thirty-nine cases and 39 controls were sequenced, with 69% of cases homozygous for the risk allele, and 31% heterozygous, indicating a complex mode of inheritance. Dogs with MCM were significantly smaller in weight. A DNA test is available for this condition.

It should however be noted that personal communications with the authors has raised doubt over the suitability of testing for this mutation in European/ British dogs, with the authors noting that whilst the variant is in higher frequencies within these populations (and these dogs often having a smaller conformation), it appears to have

poorer correlation with disease compared to American bred dogs. The authors recommendation for such dogs where the test may not be relevant is to consider the body size when mating individuals, as their observation has been that affected European dogs are significantly smaller than their unaffected counterparts.

Dermatological conditions

Dermatomyositis: This inflammatory condition affects the skin of an affected individual, with clinical signs such as lesions and scaly skin, leading to hairlessness/ alopecia, and in severe cases, infection, muscle lesions and subsequent problems moving, drinking, eating and development of megaesophagus. In severe cases where quality of life is poor, dogs may be euthanised. A case report described the disease in five individuals of the breed within the UK (of which four were sired by the same dog), and found elevated levels in serum creatine kinase (an enzyme associated with muscle degradation), as well several immunological markers (Ferguson et al, 2000).

An American study was subsequently undertaken to try to decipher the genetic basis of disease, with 61 dogs of the breed included for analysis (Clark et al, 2005). One microsatellite marker (FH3570) was found to be in linkage disequilibrium with the condition – meaning this area of the chromosome may be associated with onset of disease. However, the authors stressed further research is needed to identify any further markers on the chromosome and more in depth analysis needed to explore other possible markers.

Several years later a further American paper was undertaken on this condition, in which biopsies from four affected and four unaffected dogs were analysed for genetic and immunological markers (Wahl et al, 2008). A total of 285 genetic transcripts were found to be differentially regulated in affected dogs compared to controls, many of which were involved in the regulation of immune response, further suggesting an autoimmune component. The marker established in the previous paper was not found to be significantly associated with disease in this study. Interestingly, immunological tests found the samples from affected dogs did not differ notably from those of the controls, with the authors noting further work is needed here to identify specific changes between groups.

More recently, a major histocompatibility complex haplotype (MHC – a group of genes involved in the regulation of the immune system, otherwise known as dog leukocyte antigens, or DLAs in dogs) has been identified as associated with disease, and circulated at a high frequency within the breed (Evans et al, 2017). From this, the authors undertook whole genome sequencing and identified several variants in linkage disequilibrium from each other, within *PAN2* and *MAP3K7CL,* which were highly associated with disease. Three loci were found to have association with disease, with the authors noting the breed-specific frequencies of these different loci combinations in the breed. From this a risk-based DNA test has been produced.

Genetic diversity

A recent Finnish study looked at how breeding practices and geographical isolation can lead to differentiation in the diversity of different populations within a breed, and

how this impacts genetic diversity (Lampi et al, 2020). The Shetland Sheepdog was one of six breeds included in the study, with single nucleotide polymorphisms (SNPs – markers which can be used to look at the DNA code of an individual as a sign of genetic variation). The authors found that the European population differed remarkably from dogs found in the US, with the latter seeming to have two dominant ancestral populations, possibly as a result of the founder effect. Higher heterozygosity (the proportion of areas of the chromosome which when compared differ in their DNA sequence) was seen in the European population, indicating a more diverse gene pool.

Haematological conditions

von Willebrand's disease (vWD): An older American study investigated a severe bleeding reaction in 10 affected dogs of the breed, and concluded the dogs were affected by vWD type 3, an inherited disorder which results from an inability of the blood to clot properly, causing spontaneous haemorrhage and prolonged bleeding after injury or trauma (Raymond et al, 1990). A DNA test is available, with further information given on page 17.

Immunological conditions

Vesicular cutaneous lupus erythematosus (VCLE): This condition, which appears to have a seasonal component, affects adult dogs of the breed, resulting in lesions that form on more sparsely haired parts of the body, such as the lower abdomen, groin and within the ear. A French study investigated the disease in 11 Shetland Sheepdogs (including one crossbreed) with a median age of onset of six years (range 3 – 11 years) (Jackson et al, 2004). It was noted that similar dermatological conditions have been reported in the breed in the past, including idiopathic ulcerative dermatosis and bullous pemphigoid, and likely sit under the umbrella of the VCLE term (Jackson and Olivry, 2001). The authors suggested an autoimmune cause for disease based on the type and number of immune cells found in samples from the affected dogs. It was similarly proposed that exposure to UV light aggravated or induced disease in these individuals.

Metabolic conditions

Hypercholesterolemia/ hyperlipidemia: Excessively high levels of lipoproteins consisting of cholesterol can result in the development of secondary disease, such as deterioration of artery walls (atherosclerosis) and heart disease. In dogs this condition usually occurs as a result of another condition, such as disorders of the thyroid, liver and kidney (Sato et al, 2000). A Japanese study measured cholesterol levels in 64 dogs of the breed, following reports of hypercholesterolemia in the breed, but without showing any clinical signs. A total of 43.8% of the dogs were found to have levels within the upper limits of reference ranges, with only two of the dogs having another concurrent condition which could be causative of disease (hypothyroidism). Just one dog showed clinical signs attributed to high levels of cholesterol.

A later study (again within Japan) looked at possible predispositions for hyperlipidemia (resulting from excessive cholesterol or triglyceride levels), using 900

samples from a number of breeds, and found the Shetland Sheepdog to have higher levels of plasma cholesterol (Mori et al, 2010). The authors noted no sex predisposition in the breed, but that in general Shetland Sheepdogs had higher levels of cholesterol, free fatty acids, and reduce adiponectin (a hormone involved in the regulation of glucose levels and fatty acid breakdown). The levels of cholesterol remained stable over time (and age) but remained highly elevated compared to control breeds/ crossbreeds.

More recently, a study was undertaken to identify genetic markers for disease and assessed the suitability of uncoupling proteins (UCPs), which are involved in the metabolic regulation and associated with similar conditions such as insulin resistance and diabetes in humans (Udagawa et al, 2014). Several SNPs of the *UCP3* gene were found to be associated with dogs of the breed exhibiting high levels of blood cholesterol and could be a candidate for future research, however further work is needed to confirm this association.

Obesity: An older American study of prevalence and risk factors for obesity across dogs in veterinary centres across the US established the Shetland Sheepdog as predisposed to obesity, with an odds ratio of 1.9 (95% CI 1.2 – 2.8) (Lund et al, 2006). Other risk factors included older age, being neutered, and having a primarily semi-moist food source.

Multi-drug resistance (MDR): This condition results in an inappropriate reaction in an affected individual to particular drugs and toxins, due to an inability of the body to correctly remove particular products out of the bloodstream. Affected dogs may show an altered response to drugs such as sedatives, prophylactic treatments (e.g. parasitic) and chemotherapy drugs, with onset of neurological clinical signs such tremors, loss of appetite, salivating, and in severe cases, comas, blindness and death.

A German study was undertaken to determine the mutation frequency for the *MDR1* gene across a number of breeds, including the Shetland Sheepdog (Gramer et al, 2011). In total an allele frequency of 30% was estimated for German dogs, based on 960 dogs of the breed, of which 49 were affected, 43 carriers, and 8 clear. It was apparent however that this frequency varied widely across countries, with the highest being in the UK (36%) and lowest in Japan (1%). This was similar to an earlier German study which also found a mutation frequency of 30% in 140 tested Shetland Sheepdogs, with the breed having the third highest frequency for homozygous (affected) tested dogs (Geyer et al, 2005).

A more recent Australian study also looked at breed associated with the mutation, and found of 773 submissions a 23.8% proportion were heterozygous (carriers) for the mutation, and 3.9% homozygous (affected), again highlighting the difference in mutation frequency across countries (Soussa et al, 2020). Further information on DNA test results for UK dogs received to date are given on page 17.

Musculoskeletal conditions

Displacement of the superficial digital flexor tendon: Reports indicate the breed may be predisposed to this disease, causing lameness and pain in the limbs of affected

dogs (Mauterer et al, 1993; Solanti et al, 2002), however no full papers were available and no evidence could be found for this condition affecting dogs within the UK.

Neurological conditions

Epilepsy: A further Japanese study was undertaken to assess suspected familial idiopathic epilepsy in 11 dogs of the breed (Morita et al, 2002). The authors noted the possible multifactorial nature of the disease in the breed, and complex heritability. Age of onset appeared between one to one and a half years of age, with variation in frequency of episodes, ranging from once a week to once every six months. Affected dogs showed signs such as excessive salivation, tensed muscles, repetitive jaw movements, and staring, prior to onset of an episode, with fatigue, disorientation, hunger and thirst exhibited following a seizure. Following neurological assessment, the dogs were suggested to be affected by frontal lobe epilepsy.

Leukodystrophy: This condition is a result of a disorder in the material that encapsulates nerves (myelin), or white matter, in the nervous system (Wood and Patterson, 2001). A case report of three litters of Shetland Sheepdogs, born to one bitch and two different sires, were studied due to the onset of progressive neurological disease. The 19 puppies were affected between the age of one and three weeks of age and showed intermittent clinical signs such as problems eating and defecating, lethargy and seizures. Affected pups were either subsequently euthanised or died at home. A later study investigated a report of a similar clinical signs, which affected a family of American Shetland Sheepdogs (Li et al, 2006). Analysis of affected samples indicated a possible association with a mutation that affects proteins involved with energy production within cells (mitochondria), however further work is needed to confirm association and identify the specific mutation.

Neural tube defects: An Australian case report of four related puppies of the breed was published recently, describing a number of brain and spine abnormalities, including spina bifida, malformed vertebrae, anencephaly (missing parts of the brain and/ or skull), encephalocele (protrusion of the brain through openings in the skull) and other musculoskeletal abnormalities (Thomas et al, 2020). Given the familial component it was suggested there may be a genetic basis to disease, however further research is needed to identify whether other environmental factors have an impact on disease. No other papers could be found that mention this condition in the breed.

Paroxysmal exercise-induced dyskinesia (PED): This movement disorder occurs in episodes with dogs showing clinical signs such as imbalance (ataxia), involuntarily movements, tremor, reduced mental ability and uncontrolled tension of muscles. Four affected dogs, one from Germany and three related dogs from the Netherlands were included for genome sequencing (Nessler et al, 2020). Certain factors appeared to exacerbate onset of episodes, including hot weather and excitement or stress. Genomic analysis identified a mutation in the *PCK2* gene, with affected dogs heterozygous (carriers) for the mutated form, implying an autosomal dominant mode of inheritance, however further work is needed to confirm this association with

disease. A change in diet appeared to partially resolve clinical signs in the dogs studied, with this being changed to a low glycemic, high protein diet.

Ocular conditions

Collie eye anomaly/ Choroidal hypoplasia (CEA/CH): This inherited condition is congenital (present from birth), and found in a number of herding breeds. The disease is characterised by the formation of lesions, choroidal hypoplasia (vascular abnormalities seen on the optic disc) and coloboma (holes near to or within the optic disc), and can result in vision impairment or, when in association with other conditions such as retinal detachment or haemorrhage, complete blindness. Older papers have found the prevalence of the condition to be between 72% in the UK population (Bedford, 1982).

A more recent Danish study looked at the concordance of the *NHEJ1* DNA test and clinical diagnosis of disease in the breed, finding that out of 56 dogs, all but four were assigned an incorrect diagnosis, with this being on a clinical basis, that were later confirmed as unaffected through genotyping (Fredholm et al, 2015). Interestingly, all of these dogs were merle, with the authors noting that dogs of this colouration are more difficult to assess by ophthalmological examination, as the ocular tapetum (a layer of tissue that sits behind the retina) is less well developed or absent. Therefore, it was proposed that the test had a good reliability for identifying heredity status in the breed. Further information regarding the test is given on page 17.

Progressive retinal atrophy (PRA): PRA is classified by a deterioration of the retina, which over time can lead to visual abnormalities and, in some cases, blindness. There are several different mutations that have been found as responsible for onset of disease. The condition has been recognised in the breed for some time, and determined as not due to the *prcd* mutation that affects a number of other breeds (Karlstam et al, 2011). A Norwegian study undertook a genome-wide association study on 15 affected dogs of the breed and 14 controls and identified a mutation within the *CNGA1* gene associated with disease (Wiik et al, 2015). The authors noted that whilst this mutation contributes to some cases of disease, at least one other mutation is responsible for disease in the breed. A yet unpublished mutation has also been discovered by the Animal Health Trust (AHT) research group, with DNA tests available for both this and the *CNGA1* mutation. Further analysis is given on page 19.

Renal (kidney) conditions

Kidney disease: A Swedish study investigated the incidence and mortality of kidney disease across a number of insured dogs (Pelander et al, 2015). The Shetland Sheepdog had the second highest mortality for kidney disease out of all breeds investigated, with a mortality of 49 (95% CI 39 – 60), based on 73 deaths out of a total of 27,840 dog years at risk (DYAR – the number of full years a dog was insured for). The mean age at death was 7.3 years. A total of 119 cases of disease were reported in the breed, out a total of 38,330 DYAR, leading to an incidence of 31 (95% CI 25 – 37). The mean age at diagnosis was 8.0 years. The majority of cases

(n=133) had an undetermined cause (65%), followed by infection/ inflammation (20%), metabolic/ nutritional/ dystrophical (degeneration) (10%), cancer/ neoplasm (3%) and congenital/ development (2%).

INSURANCE DATA

There are some important limitations to consider for insurance data:

- Accuracy of diagnosis varies between disorders depending on the ease of clinical diagnosis, clinical acumen of the veterinarian and facilities available at the veterinary practice
- Younger animals tend to be overrepresented in the insured population
- Only clinical events that are not excluded and where the cost exceeds the deductible excess are included

However, insurance databases are too useful a resource to ignore as they fill certain gaps left by other types of research; in particular they can highlight common, expensive and severe conditions, especially in breeds of small population sizes, that may not be evident from teaching hospital caseloads.

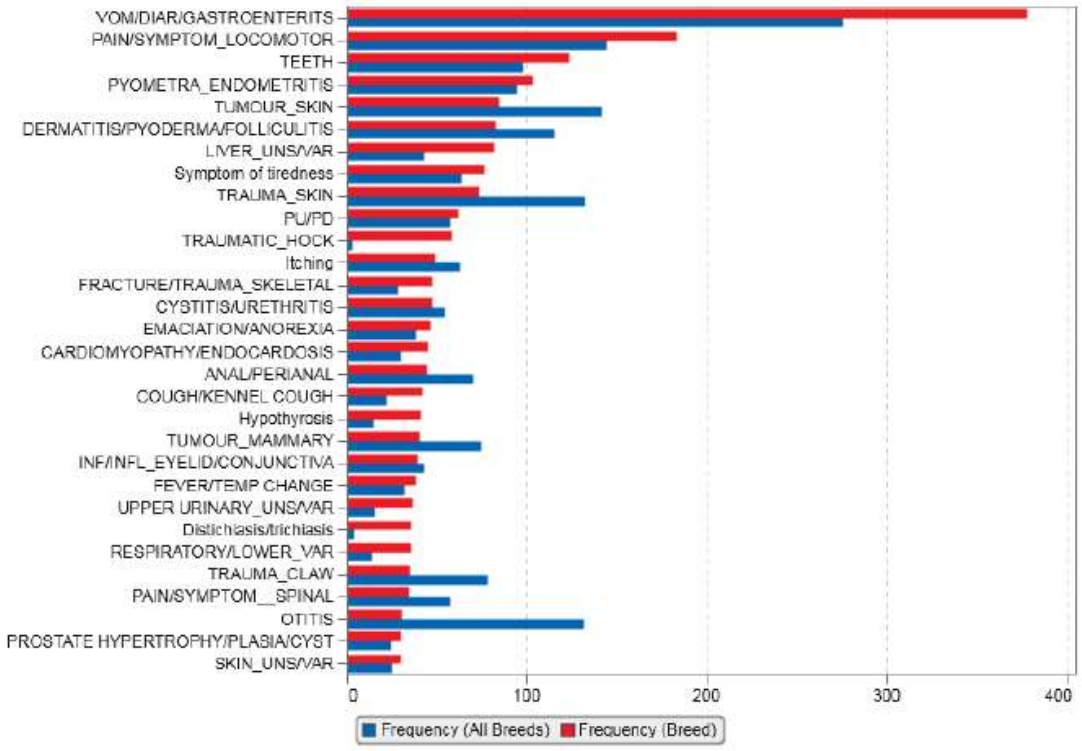
Swedish Agria Data

Swedish morbidity and mortality insurance data were available from Agria for the Shetland Sheepdog. Reported rates are based on dog-years-at-risk (DYAR) which take into account the actual time each dog was insured during the period (2011-2016), e.g. one whole year of insurance is equivalent to one DYAR. The number of DYAR for Shetland Sheepdog in Sweden during this period was 15,000 < 25,000.

A summary is given below, with the full report available at: https://dogwellnet.com/

Swedish Agria insurance morbidity data

The most common specific causes of veterinary care episodes (VCEs) for Agria-insured Shetland Sheepdog in Sweden between 2011 and 2016 are shown in Figure 2. The top five specific causes of VCEs were: vomiting/ diarrhoea/ gastroenteritis, pain during locomotion, teeth disorder, pyometra/ endometritis, and skin tumour.



Reminder: Categories are shown only if at least 8 animals had the diagnosis.

Figure 2: The most common specific causes of VCEs for the Shetland Sheepdog compared to all breeds in Sweden between 2011 and 2016, from Swedish Agria insurance data.

The specific causes of VCEs ordered by relative risk are shown in Figure 3 for the Shetland Sheepdog. In this analysis, the top five specific causes of VCEs ordered by relative risk were: trauma to the hock, distichiasis/ trichiasis, eye disorder, infection/ inflammation of the liver, and trauma to the hip. Rare conditions that occur sporadically may appear as a high relative risk; which may apply to some of these conditions.

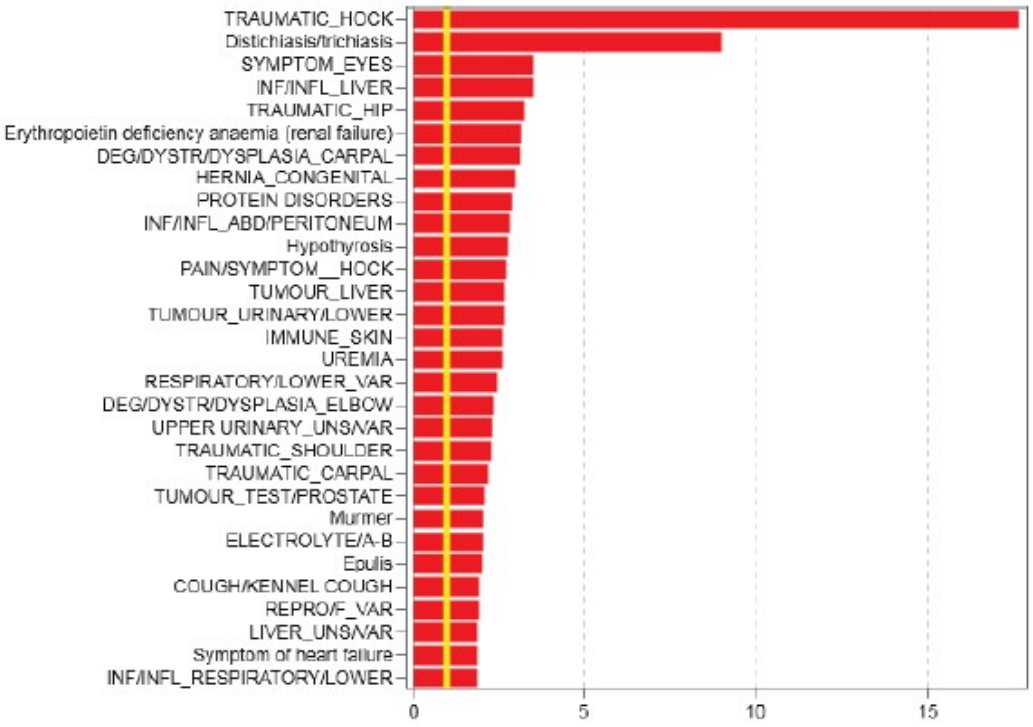


Figure 3: The specific causes of VCEs for the Shetland Sheepdog ordered by relative risk compared to all breeds in Sweden between 2011 and 2016, from Swedish Agria insurance data. The yellow line indicates the baseline risk for all breeds.

Swedish Agria insurance mortality data

The most common specific causes of death or euthanasia for Agria-insured Shetland Sheepdog in Sweden between 2011 and 2016 are shown in Figure 4. The five most commonly reported reasons for death were: dead/ euthanised, vomiting/ diarrhoea/ gastroenteritis, upper urinary – unspecified/ various, erythropoietin deficiency anaemia (renal failure) and epilepsy.

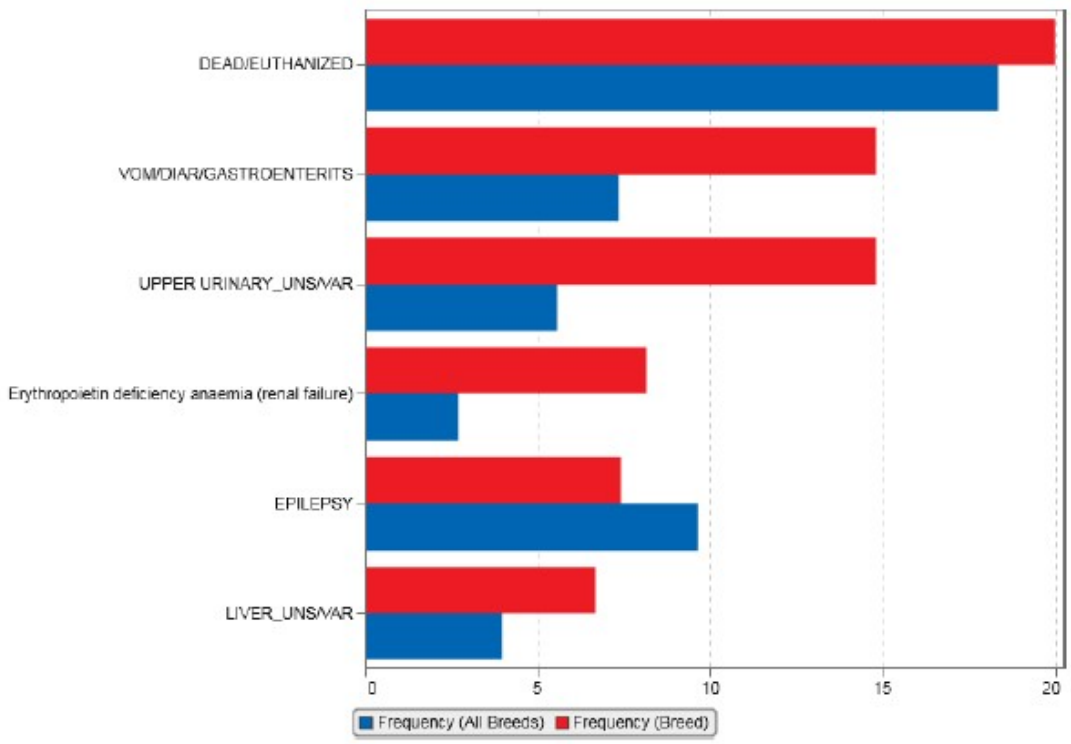


Figure 4: The most common specific causes of death or euthanasia for the Shetland Sheepdog compared to all breeds in Sweden between 2011 and 2016, from Swedish Agria insurance data.

BREED WATCH

The Shetland Sheepdog is listed as a category 2 breed on Breed Watch, meaning judges are required to complete a mandatory monitoring form following a judging appointment at Championship Certificate level. The point of concern judges are currently required to monitor is:

- Misplaced upper canine teeth

In Sept 2021, 'excessively small eyes' was removed as a point of concern for the Shetland Sheepdog. A report on the percentage of dogs shown that are affected by these visible points of concern are in Table 2, an asterisk represents a newly reported concern.

Table 2: Percentage of dogs affected by visible points of concern between 2017 and 2019.

Point of Concern	2017	2018	2019
Excessively small eyes	0.25%	0.09%	0.45%
Misplaced upper canine teeth	0.12%	0.26%	0.22%
* Incorrect dentition	0.03%	0.20%	0.00%
* Lack of front angulation	0.00%	0.06%	0.00%
* Other	0.09%	0.00%	0.40%
* Significantly overweight	0.00%	0.09%	0.13%
* Significantly underweight	0.19%	0.00%	0.00%
* Unsound movement	0.09%	0.03%	0.00%
* Weak hind movement	0.00%	0.03%	0.00%
* Wet eyes	0.06%	0.00%	0.00%
Total dogs reported for	**3,212**	**3,512**	**2,240**

NB: As of quarter 4 in 2019 the methods through which judges reported monitoring forms has changed, in that judges no longer receive reminders. Consequentially, a reduction in the number of full reports received has been seen across all breeds, which will reflect the total numbers for 2019.

PERMISSION TO SHOW

As of the 1st January 2020 exhibits for which permission to show (PTS) following surgical intervention has been requested will no longer be published in the Breed Record Supplement and instead will be detailed in BHCPs, and a yearly report will be collated for the BHC. In the past five years, six PTS have been granted for the Shetland Sheepdog (not including neutering or caesarean sections), with five being for the removal of a tooth/teeth and one being for the removal of the femoral head after hip dislocation.

ASSURED BREEDERS SCHEME

Currently within the Kennel Club (KC)'s Assured Breeder Scheme there are the following requirements for the Shetland Sheepdog:

- Eye testing under the British Veterinary Association (BVA)/KC/ International Sheepdog Society (ISDS) eye scheme

It is also recommended that all breeding stock are tested for the following prior to breeding:

- Hip scoring under the BVA/KC Hip Dysplasia Scheme
- DNA test for Collie eye anomaly / Choroidal hypoplasia (CEA/CH)

BREED CLUB BREEDING RECOMMENDATIONS

There are no breed club breeding recommendations currently included under the Assured Breeder Scheme.

DNA TEST RESULTS

There are currently five recognised DNA tests for this breed, which are:

- CEA/CH
- Multiple drug sensitivity (MDR1)
- von Willebrand disease (vWD)
- Progressive retinal atrophy (BBS2-PRA)*
- Progressive retinal atrophy (CNGA1-PRA)

*The AHT was the only laboratory able to provide testing for this mutation, and unfortunately in July 2020 was forced to close.

Whilst other DNA tests may be available for the breed, results from these will not be accepted by the Kennel Club until the test has been formally recognised, the process of which involves collaboration between the breed clubs and the Kennel Club in order to validate the test's accuracy.

Laboratories that test for these DNA tests and the methods through which the Kennel Club accept results can be found through:

https://www.thekennelclub.org.uk/search/breeds-a-to-z/breeds/pastoral/shetland-sheepdog/

Please note that caution should be taken when drawing conclusions from DNA data, given that not all laboratories send results directly to the Kennel Club to be recorded on the database and that these data pertain to Kennel Club registered dogs only.

To date (Oct 2020), a total of 1,121 DNA test results have been received for the breed, with information for the relevant tests given below.

CEA/CH

Test results for this allele associated with disease were formally published by the Kennel Club from Jan 2010, with the total results received shown in Table 3. Results from the linkage test were more recently published, however due to the nature of the test hereditary status cannot be applied.

Table 3: DNA test results for CEA/CH received for the Shetland Sheepdog to date.

DNA tests	Clear	Carrier	Affected	Hereditarily Clear	Total tested
CEA/CH	138 (36.0%)	77 (20.1%)	0 (0.0%)	166 (43.9%)	381
CEA/CH (linkage)	42 (48.8%)	42 (48.8%)	2 (2.3%)	N/A	86

Similarly, the three-year average mutation frequency of the allele tested for by the DNA test (not linkage) is shown in Figure 5. Over 2017-19 the average mutation frequency for CEA/CH in the breed was 3.5%, compared to 14.2% in 2009-11, indicating a notable decrease in frequency over time (Figure 5).

However, there is a caveat to consider, in that the presence of dogs with hereditary status, which make up the majority of results particularly in later years (71.7% during 2017-19), will cause a downward bias in mutation frequency. Therefore, whilst the initial findings can be acknowledged, it is important to consider this may change over time and is not an absolute reflection, and breeders should continue to test prior to breeding.

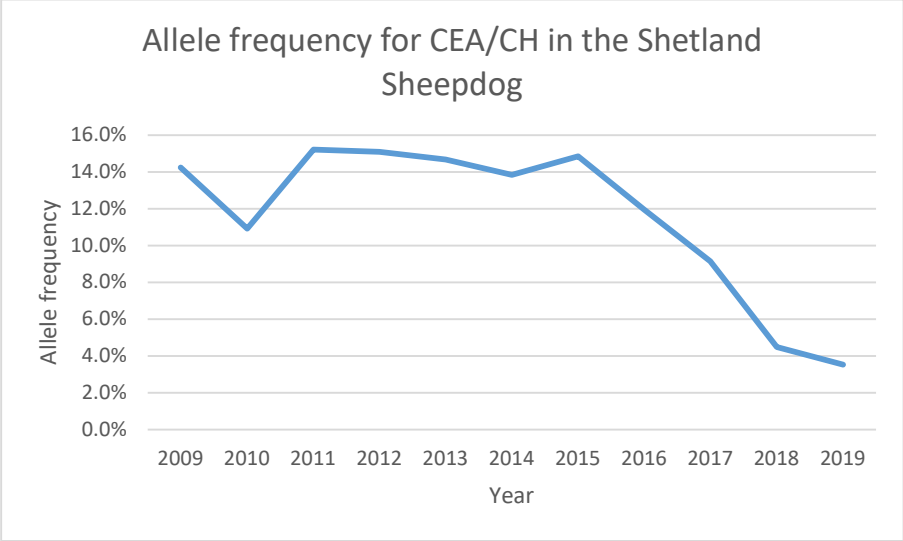


Figure 5: Allele frequency for CEA/CH in the breed between 2009 and 2019.

Please note that it has been anecdotally reported that not all breeders DNA test their dogs for this condition if they have previously been diagnosed as clinically affected through the BVA/KC/ISDS Eye Scheme. Therefore this mutation frequency data should be interpreted with caution. Further, results from the linkage test are not included in this analysis.

vWD3

Test results for this allele associated with disease were also formally published by the Kennel Club from Jan 2010, with the total results received shown in Table 4. As the first result recorded for the breed was in 2018, mutation frequency analysis will be provided at a later date once a sufficient number of years have passed to give meaningful results.

Table 4: DNA test results for vWD received for the Shetland Sheepdog to date

Clear	Carrier	Affected	Hereditarily Clear	Total tested
48 (72.8%)	0 (0.0%)	0 (0.0%)	18 (27.2%)	66

MDR1

Test results for this allele associated with disease were also formally published by the Kennel Club from Jan 2010, with the total results received shown in Table 5.

Table 5: DNA test results for MDR1 received for the Shetland Sheepdog to date.

Clear	Carrier	Affected	Hereditarily Clear	Hereditarily Carrier	Hereditarily Affected	Total tested
152 (34.5%)	163 (37.0%)	55 (12.5%)	30 (6.8%)	37 (8.4%)	4 (0.9%)	441

The three-year average mutation frequency of the allele tested for by the DNA test is shown in Figure 5. Over 2017-19 the average mutation frequency for MDR1 in the breed was 31.8%, compared to 41.1% in 2007-9, with a degree of fluctuation evident over time (Figure 6). Overall it appears the allele frequency has gradually decreased over time, but is still high within the tested population. Again, hereditary status will result in a downward bias in frequency.

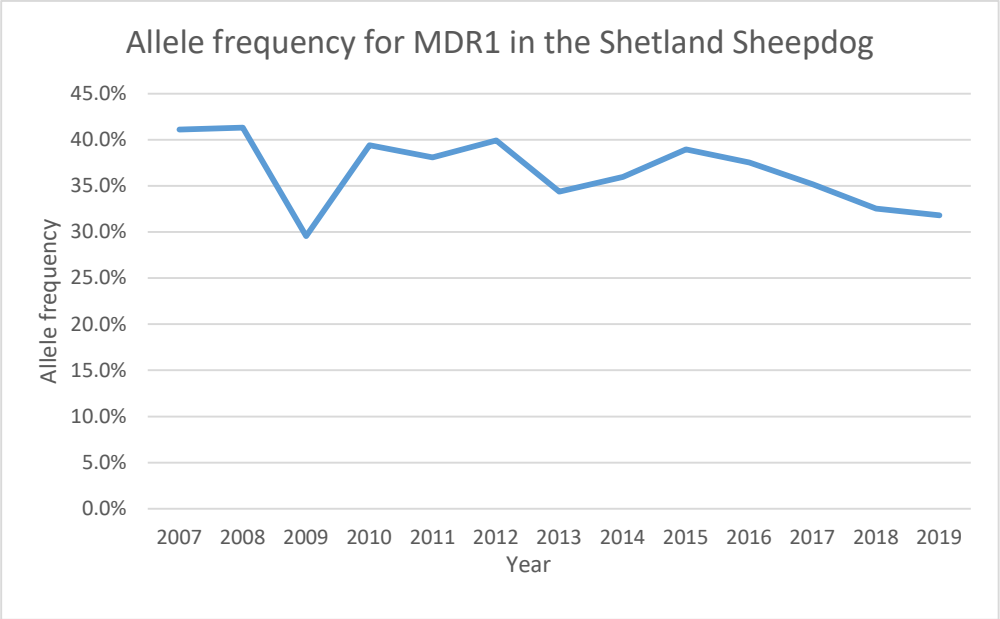


Figure 6: Allele frequency for MDR1 in the breed between 2007 and 2019.

PRA (CNGA1)

Test results for this allele associated with disease were formally published by the Kennel Club from June 2020, with the total results received shown in Table 6. Mutation frequency analysis will be provided at a later date, once a sufficient number of years have passed that will give a meaningful trend.

Table 6: DNA test results for PRA (CNGA1) received for the Shetland Sheepdog to date.

Clear	Carrier	Affected	Hereditarily Clear	Total tested
37 (47.4%)	0 (0.0%)	0 (0.0%)	41 (52.6%)	78

PRA (BBS2)

Test results for this allele associated with disease were also formally published by the Kennel Club from June 2020, with the total results received to date (Oct 2021) shown in Table 7. As with the above, mutation frequency analysis will be provided at a later date, once a sufficient number of years have passed that will give a meaningful trend.

Table 7: DNA test results for PRA (BBS2) received for the Shetland Sheepdog to date.

Clear	Carrier	Affected	Hereditarily Clear	Total tested
37 (30.6%)	9 (7.4%)	1 (0.8%)	74 (61.2%)	121

As a note, as of January 2022 hereditarily clear status will no longer apply after two generations and dogs will need to be retested to confirm the status of that individual. This is to prevent the possibility of misclassification of status and therefore unintentional breeding of affected puppies. Where parentage is confirmed by DNA profile, the major contributor to erroneous status will be removed. Therefore, a less stringent restriction for HC status is applied where parentage is confirmed by DNA test.

CANINE HEALTH SCHEMES

All of the BVA/KC Canine Health Schemes are open to dogs of any breed with a summary given of dogs tested to date below.

HIPS

To date (Oct 2020), 822 Shetland Sheepdogs have been hip scored under the BVA/KC Hip Dysplasia Scheme, with a 15-year median hip score of 10 (range 0-89) and 5-year of 11 (range 0-76).

Figure 7 shows the mean hip score per year of birth between 2003 and 2019 for the Shetland Sheepdog. The trend shows a large amount of fluctuation, with an overall slight degree of improvement over this time period.

It is worth noting that scores for later years will reflect younger dogs (e.g. dogs born in 2018 will be no more than 2 years of age) and therefore these will have had fewer years for disease to manifest and a generally lower mean score.

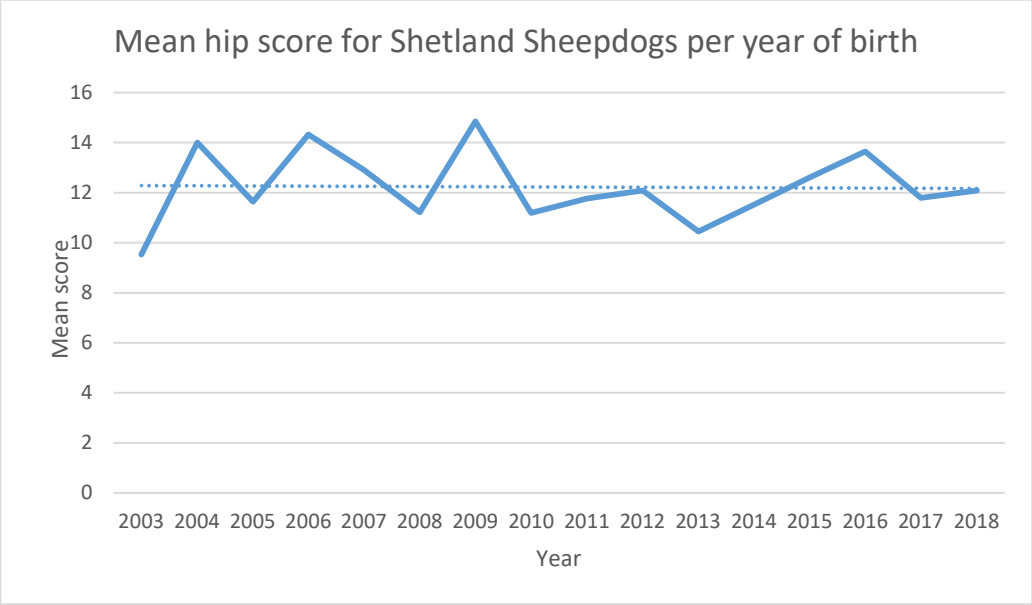


Figure 7: Mean hip score per year of birth for the past 15-year period.

ELBOWS

To date (Sept 2020), 31 Shetland Sheepdogs have been elbow graded under the BVA/KC Elbow Dysplasia Scheme, with one dog graded as a 1 in 2014 and the rest grade 0.

EYES

The Shetland Sheepdog is currently on the BVA/KC/ISDS Known Inherited Ocular Disease (KIOD) list (formally Schedule A) for the following conditions:

- CEA
- Retinal Pigment Epithelial Dystrophy (RPED) - formerly known as Central Progressive Retinal Atrophy (CPRA)

KIOD lists the known inherited eye conditions in the breeds where there is enough scientific information to show that the condition is inherited in the breed, often including the actual mode of inheritance and in some cases even a DNA test.

A total of 2,070 Shetland Sheepdogs have been tested in the past 20 years, of which 204 were affected by CEA and one was affected by CPRA (2010). The number of dogs tested per year and their respective results are given in Figure 8 below. Whilst the number of dogs tested affected for both CEA and CPRA/ RPED have notably decreased over time, it is worth noting that the number of dogs tested overall per year has also dropped.

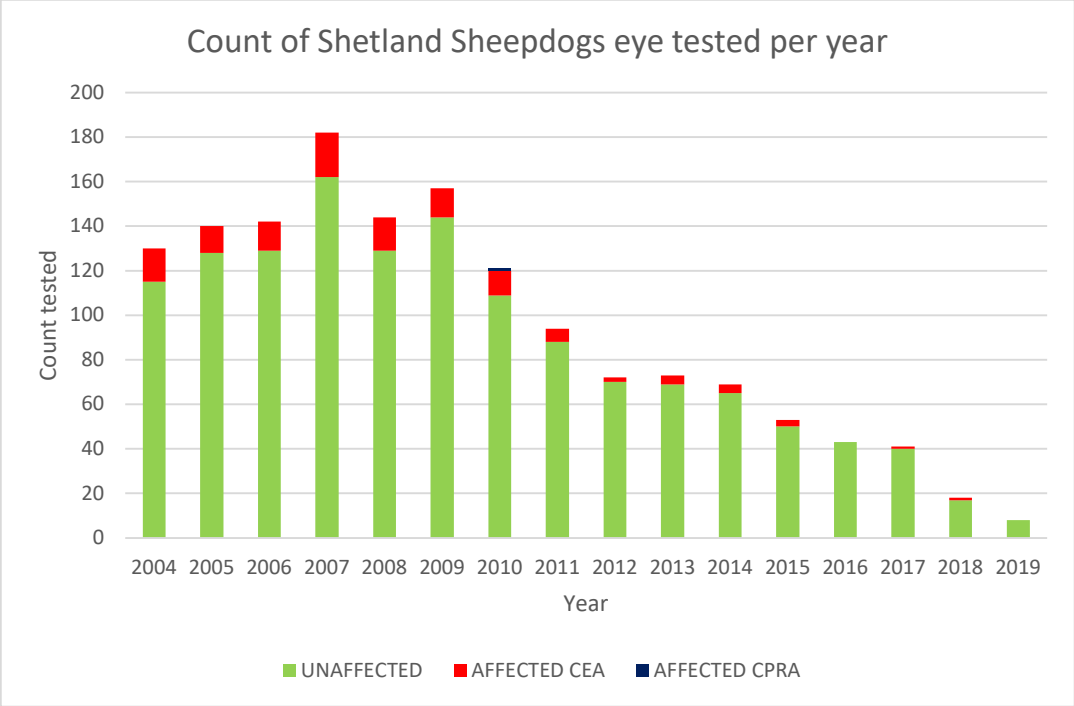


Figure 8: Number of Shetland Sheepdogs eye tested per year and those that tested affected for CEA and/ or CPRA.

In terms of litter screening, the below table gives a breakdown of dogs screened under 12 weeks of age per year between 2005-20, and the number of those determined to be clinically affected with CEA.

Table 8: Count of puppies examined as part of litter screening and number reported affected for CEA.

Year	Count affected	Total tested
2005	0	6
2006	1	5
2007	1	9
2008	2	11
2009	0	6
2010	0	1
2011	0	0
2012	0	0
2013	0	1
2014	1	2
2015	0	0
2016	0	1
2017	0	2
2018	0	3
2019	0	10
2020	0	5

Schedule B has been incorporated into an annual sightings reports, which records the results of conditions not listed on KIOD for dogs which have participated in the scheme. Results of Shetland Sheepdogs tested to date are shown in Table 9 below.

Table 9: Reports on Shetland Sheepdogs that have participated in the BVA/KC/ISDS Eye Scheme since 2012.

Year	Number Tested	Comments
2012	146 Adults 200 Litters	40 – distichiasis 1 – persistent pupillary membranes (PPM) 4 – other cataract 1 – GPRA-like appearance
2013	97 Adults 209 Litters	24 – distichiasis 1 – persistent hyperplastic primary vitreous (PHPV) 3 – other cataract 1 – multi-ocular defects 1 – corneal lipid deposition 46 – choroidal hypoplasia
2014	93 Adults 200 Litters	16 – distichiasis 1 – corneal lipid deposition 2 – PPM 2 – multifocal retinal dysplasia 1 – GPRA-like appearance 1 – asteroid hyalosis 45 – choroidal hypoplasia
2015	102 Adults 198 Litters	10 – distichiasis 1 – chorioretinopathy 2 – corneal lipid deposition 3 – PHPV
2016	129 Adults 187 Litters	18 – distichiasis 1 – PPM 2 – other cataract
2017	45 Adults 160 Litters	10 – distichiasis 21 – choroidal hypoplasia
2018	58 Adults 137 Litters	15 – choroidal hypoplasia
2019	*Awaiting report*	

REPORTED CAESAREAN SECTIONS

When breeders register a litter of puppies, they are asked to indicate whether the litter was delivered (in whole or in part) by caesarean section. In addition, veterinary surgeons are asked to report caesarean sections they perform on Kennel Club registered bitches. The consent of the Kennel Club registered dog owner releases the veterinary surgeon from the professional obligation to maintain confidentiality (vide the Kennel Club General Code of Ethics (2)).

There are some caveats to the associated data;

- It is doubtful that all caesarean sections are reported, so the number reported each year may not represent the true proportion of caesarean sections undertaken in each breed.
- These data do not indicate whether the caesarean sections were emergency or elective.
- In all breeds, there was an increase in the number of caesarean sections reported from 2012 onwards, as the Kennel Club publicised the procedure to vets.

The number of litters registered per year for the breed and the number and percentage of reported caesarean sections in the breed for the past 10 years are shown in Table 10.

Table 10: Number of Shetland Sheepdog litters registered per year, and number and percentage of caesarean sections reported per year, 2009 to 2019.

Year	Number of Litters Registered	Number of C-sections	Percentage of C-sections	*Percentage of C-sections out of all KC registered litters (all breeds)*
2009	450	2	0.44%	0.15%
2010	404	2	0.50%	0.35%
2011	392	6	1.53%	1.64%
2012	339	15	4.42%	8.69%
2013	341	19	5.57%	9.96%
2014	313	29	9.27%	10.63%
2015	284	23	8.10%	11.68%
2016	268	18	6.72%	13.89%
2017	252	20	7.94%	15.00%
2018	232	18	7.76%	17.21%
2019	199	19	9.55%	15.70%
2020	177	11	6.21%	14.41%

GENETIC DIVERSITY MEASURES

The effective population size is the number of breeding animals in an idealised, hypothetical population that would be expected to show the same rate of loss of genetic diversity (rate of inbreeding) as the population in question; it can be thought of as the size of the ‘gene pool’ of the breed. In the population analysis undertaken

by the Kennel Club in 2020, an estimated effective population size of **125.1** was reported (estimated using the rate of inbreeding over the period 1990-2019).

An effective population size of 100 or below (inbreeding rate of 0.50% per generation) results in the rate of loss of genetic diversity in a breed/population increasing dramatically (Food & Agriculture Organisation of the United Nations, "Monitoring animal genetic resources and criteria for prioritization of breeds", 1992).

Annual mean observed inbreeding coefficient (showing loss of genetic diversity) and mean expected inbreeding coefficient (from simulated 'random mating') over the period 1990-2019 are shown in Figure 9. Both the observed and the expected have steadily increased over this period studied, implying a continued loss of genetic diversity over time. This may be explained by the breed's prolonged fall in population, which results in breeders having fewer options to select when breeding from their dogs.

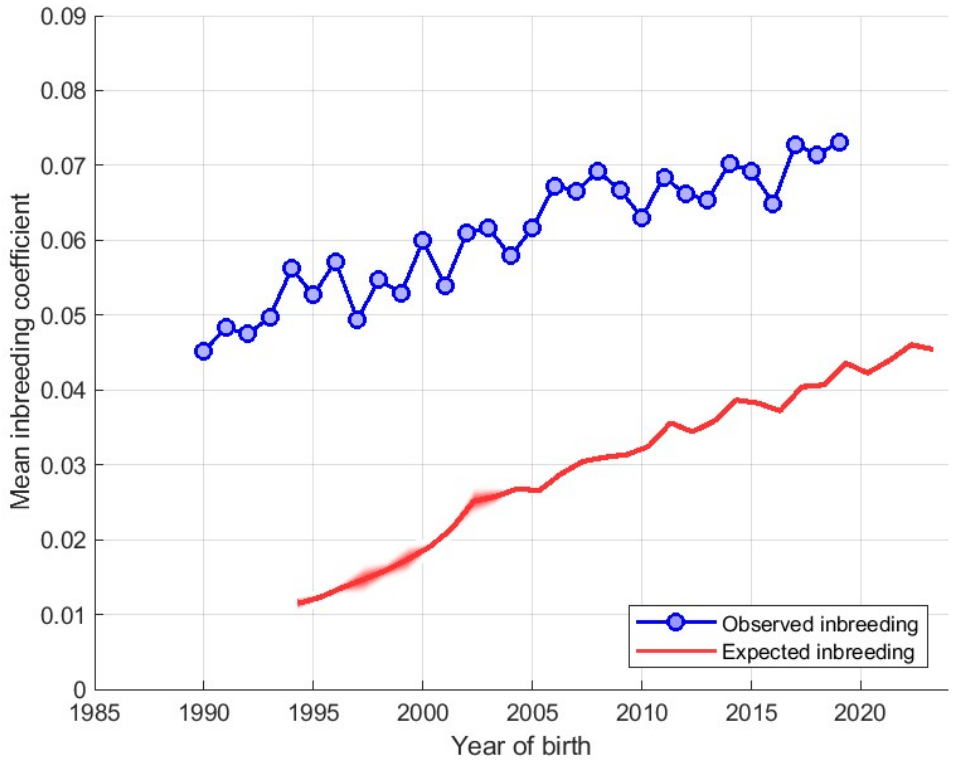


Figure 9: Observed and expected inbreeding coefficients between 1990 and 2020.

Below is a histogram ('tally' distribution) of number of progeny per sire and dam over each of six 5-year blocks (Figure 10). A longer 'tail' on the distribution of progeny per sire is indicative of 'popular sires' (few sires with a very large number of offspring, known to be a major contributor to a high rate of inbreeding). Several popular sires have been evident in the breed throughout the period analysed, with one individual responsible for almost 3% of progeny registered in the past five years. However, this is increasingly difficult to avoid given the drop in the breed's registrations over time.

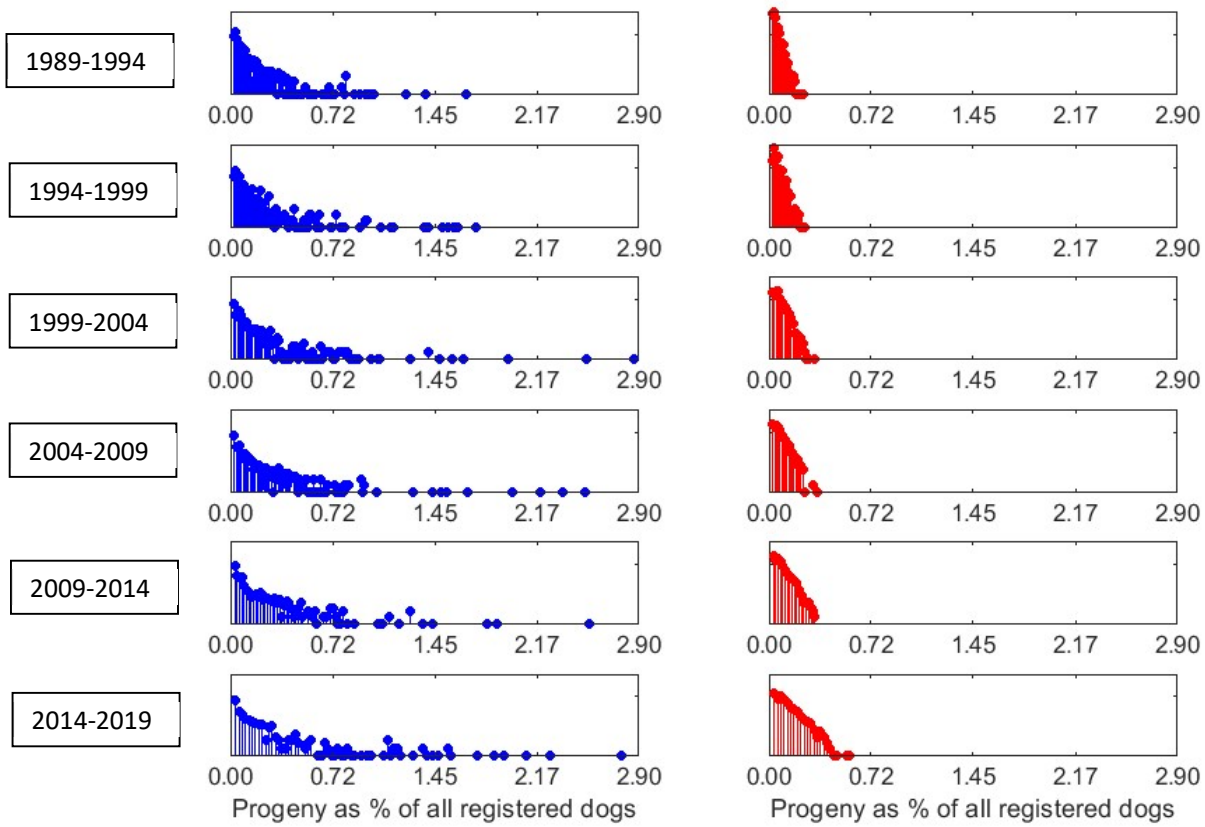


Figure 10: Distribution of proportion of progeny per sire (blue) and per dam (red) over 5-year blocks (1989-94 top, 2014-19 bottom). Vertical axis is a logarithmic scale.

CURRENT RESEARCH

The Breed Health Co-ordinator has been working with a research group in the USA to collate samples of dogs affected by idiopathic epilepsy, as well as controls.

The breed are also continuing to monitor research at the North Carolina State University and the Virginia Maryland College of Veterinary Medicine, which aim to pinpoint the underlying cause of GBM in dogs and investigate possible treatments and preventative strategies. Further information regarding this research can be found here: https://www.americanshetlandsheepdogassociation.org/gallbladder-mucoceles/

The Kennel Club Genetics Centre is also working with the breed to collect PRA samples, with the aim to produce more DNA tests to test for the different causative mutations in the breed.

PRIORITIES

In the breed's experience and given the data portrayed in the evidence base above, the priorities for the breeds at this time are:

- Generalised progressive retinal atrophy (GPRA)
- Collie eye anomaly (CEA)

ACTION PLAN

Following the correspondence between the Kennel Club and the breed regarding the evidence base of the Breed Health & Conservation Plans, the following actions were agreed to improve the health of the Shetland Sheepdog. Both partners are expected to begin to action these points prior to the next review.

Breed Club actions include:

- The Breed Clubs to consider making a proposal for the inclusion of MDR1 DNA testing as a recommendation under the Assured Breeder Scheme
- The Breed Clubs to continue to monitor the use of popular sires and encourage breeders to consider genetic diversity when breeding
- The Breed Clubs to undertake a breed health survey, with the Kennel Club to assist in development and dissemination

Kennel Club actions include:

- The Kennel Club to put forward a proposal to the Eye Panel Working Party that RPED be removed from Schedule A for the breed, and request that GPRA be added to encourage testing for this condition
- The Kennel Club to provide analysis for UK insurance data for the breed
- The Kennel Club to investigate the possibility of providing the BBS2-PRA DNA test under CombiBreed

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