

GSD INHERITED AND ACQUIRED DISEASES

Dr Karen Hedberg BVSc 2013

GENETIC DISEASE

- ▶ The GSD has quite a large number in inherited diseases, many of which do not have specific DNA tests or even the mode of inheritance determined at this time.
- ▶ There are a large group of immune based conditions affecting the skin, gut and overall health in the GSD.
- ▶ Work is currently going on both here and overseas to see if genetic markers or specific genes can be isolated, tests developed for a range of diseases. Once tests are developed we can start reducing the incidence of these diseases occurring.

IMMUNE RELATED DISEASES IN THE GSD – INHERITANCE PATTERN CURRENTLY UNKNOWN

- ▶ **Aspergillosis** and other mycoses
- ▶ **Anal furunculosis** – almost exclusive to the GSD.
- ▶ **Exocrine pancreatic insufficiency (EPI)**- reasonable numbers seen in the GSD
- ▶ **Inflammatory bowel disease (IBD)**,
Small intestinal bacterial overgrowth (SIBO) and its related antibiotic responsive diarrhea (ARD),
- ▶ **Ocular** disease including **Pannus**, Plasmoma
- ▶ *Suppurative otitis externa (ear infections)*
- ▶ **Skin -Deep Staph pyoderma/folliculitis**,
SLE (Systemic lupus erythematosus and immune mediated skin disease, especially discoid lupus erythematosus (DLE).
- ▶ **Degenerative Myelopathy (DM)**- degeneration of the spinal cord.

OTHER DISEASES- INHERITED AND/OR BREED PREDISPOSITIONS

Bone – hip and elbow dysplasia

- spondylitis and discospondylitis

- cauda equina, panoestitis (more males)

Intestinal – **megaesophagus** (inherited and aquired)

Heart – persistent right aortic arch, cardiomyopathy

Skin - **acanthosis nigricans** (immune and hypothyroid)

Tumours – **haemangiosarcoma, lymphosarcoma**

Eyes – dermoids.

UNDERSTANDING THE MODE OF INHERITANCE RELATIVE TO A DISEASE

The major task facing controlling a breed inherited disorder, is establishing **the mode of inheritance**. If you are lucky, it may affect a single gene, with a recessive/normal pattern, and if you are really lucky, there may be a DNA marker or specific gene test found that can identify all three states of the gene ie. affected, carrier and normal. This still allows a breed club to keep its genetic pool and breed the problem out within two to three generations if they want to.

Of the recognised diseases, **more than half are believed to be single gene defects**, and around **70%** of those being inherited as in a simple autosomal recessive mode of inheritance.

Much work is being done to isolate genetic markers or the specific gene that causes these diseases. By studying dog breeding populations and related individuals carrying or being affected by the disorder, the abnormal gene or its marker may eventually be isolated (after a lot of hard work).

DNA AND DISEASE TESTING

- ▶ We should equally always look at any disease in regard to the numbers affected, the severity of the disease concerned and the impact on the animals health and well being and decide whether any animals **need** to be removed from the gene pool.
- ▶ Many breeders erroneously consider **affected dogs** cannot be used, but the beauty of having a DNA test is that, in the main, **no animal needs to be lost to the gene pool.**

GSD DNA TESTS

New DNA tests are appearing almost daily.

- ▶ **Dwarfism** –autosomal recessive condition. This test allows us for the first time to identify carriers. Carriers can still be bred with ideally only to normal partners. Puppies that are being retained can be tested and choices made (if needed) to select the normal or clear puppy to breed on with.
- ▶ **Degenerative myelopathy** –autosomal recessive. This test identifies a **major risk factor**. Quite a few breeds carry the mutation. Dogs carrying two copies of the abnormal gene have a high risk for developing DM. Older GSD – anywhere between 5-10% of dogs over 8 years of age can develop this condition. Care should be made to differentiate this condition and cauda equina.
- ▶ **Long coat** gene – autosomal recessive, certain degree of blending of alleles
- ▶ **Ivermectin sensitivity**

Possible Matings	Normal AA	Carrier Aa	Affected aa
Normal AA	All progeny normal	1/2 Normal, 1/2 carrier	All carriers
Carrier Aa	1/2 Normal, 1/2 carrier	1/4 normal 1/2 carrier 1/4 affected	1/2 carrier 1/2 affected
Affected aa	All carriers (B)	1/2 carrier 1/2 affected	All affected

DWARFISM

Diseases such as pituitary dwarfism are ***largely self limiting*** as it becomes very obvious very early that these animals are affected and thus never re-enter the breed.

Dwarfism DNA test has been available for quite a number of years. While we have few dwarves being produced – the problem is again, the lack of reporting. The only good part of this condition is that it is fairly easy to separate the dwarfs out by 6-8 weeks of age. Affected animals (dwarves) never enter the gene pool. Current statistics on carrier rates (France) is 11%, which means the odds of producing a dwarf is very low.

Where reasonable numbers are being produced by a sire, if this is reported, this can add to our knowledge and allow breeders to make more informed decisions prior to choosing breeding partners (be they male or female).

Do we need to instigate breed wide testing at this stage = NO.

DEGENERATIVE MYELOPATHY

- ▶ **DM** is a disease that occurs at the other end of the GSD life. Unfortunately it occurs usually after the prime breeding age (**usually 8-9 years and older, some as early as 5-6 years**) and the numbers that are seen would be in the order of between 2-5% of older GSD's.
- ▶ DM is a devastating progressive condition that gradually whittles away the mobility and effectiveness of the entire hindquarter. The disease affects **the myelin sheaths** of the spinal cord affecting from mid thoracic area back, with the messages getting slower and slower.
- ▶ The only good part of this disease is that it is not painful to the dog. The disease course runs some 12-18 months with severely affected dogs being euthanaised due to inability to stand etc.
- ▶ While this disease has a genetic basis, there appears to be some additional triggering factor that then manifests the disease as the dog's age. The disease is thought to have incomplete penetrance, ie. not all affected dogs end up exhibiting the disease.

DM CONT

- ▶ Current **Australian Statistics** from 1.1.12 are:-

	All breeds	GSD	OFA GSD
▶ Number tested		106	
▶ Normal	5192 (89.6%)	70 (66%)	51%
▶ Carrier	487 (8.4%)	25 (24%)	32%
▶ Affected	112 (1.93%)	11 (10%)	17%

- ▶ From these numbers one can see clearly that the **GSD is over represented in both the carrier and particularly affected animals**. This puts the number of affected animals in the current Australian population as around 10%. In reality, the real number of physically affected DM seen is probably closer to 5% (due to the variable expression within the affected population).
- ▶ Interestingly the OFA GSD stats are far higher, so it serves as a warning to take care.
- ▶ While I do not believe that we need to do extensive testing of breeding stock at this stage, it may be worth **testing heavily used stud dogs or bitches** that kennels are based on to give breeders more information when making breeding decisions. Where major animals within the kennel subsequently develop DM after their breeding career, ideally test retained progeny and take care with selecting clear breeding partners.

DM AND DWARFISM TESTING

- ▶ **The number of cases of DM are under reported (as are the dwarfs).** Again, use of the Health Report can assist us in ensuring we are improving the overall health of the breed as well as giving us better statistics.
- ▶ The problem arises more with **late onset diseases** such as DM, where often these animals have been bred from long before symptoms arise. These conditions are **thus more likely to increase silently** through the breed, where as dwarfism tends to stay at a very low level.
- ▶ Affected DM dogs, even if tested early on, can still be used at stud and for breeding purposes but ideally to clear partners.

DETERMINING WHETHER A FAULT OR DEFECT IS INHERITED:

- ▶ 1. Does it affect more than one member of a litter? Obviously the larger the litter the more likely you are to get a significant result.
- ▶ 2. Has it recurred in a repeat mating, or in matings that are genetically similar?
- ▶ 3. Are there ancestors in common?
- ▶ 4. Test breeding can be carried out to see if the fault reappears (preferably not done where the problem is well recognised).

POLYGENETIC CONDITIONS

- ▶ Hip and Elbow dysplasia
- ▶ Current mode of inheritance unknown, minimum of 3-4 genes probable in each case.
- ▶ Work is being done in several countries trying to locate reliable markers for these diseases.
- ▶ **The more genes affecting a condition, the more environmental factors can influence the outcome and the slower the rate of improvement.**

BREED IMPROVEMENT SCHEMES

Breed improvement schemes, particularly with polygenetic conditions such as hip and elbow dysplasia, are reliant on producing *consistent repeatable results* such that breeders can assess the *relative value* of their breeding stock against a breed mean, and more importantly, continue to do so over generations of breeding.

In order to do this breeders need the following:-

- ▶ Consistent and reliable means of assessment.
- ▶ Ease of accessibility of the screening process (usually local veterinarians) at reasonable cost.
- ▶ A means of developing a breed average or median.
- ▶ Ideally a means of assessing the relative genetic merits of different sires based on progeny results (particularly in the numerically larger breeds).
- ▶ **A means of assessing improvements (or otherwise) of entire breeds over time.** That is, are we improving, has all this hard work by breeders (and money) achieved the desired result?

BREED IMPROVEMENT SCHEMES – A LONG TERM APPROACH NEEDED

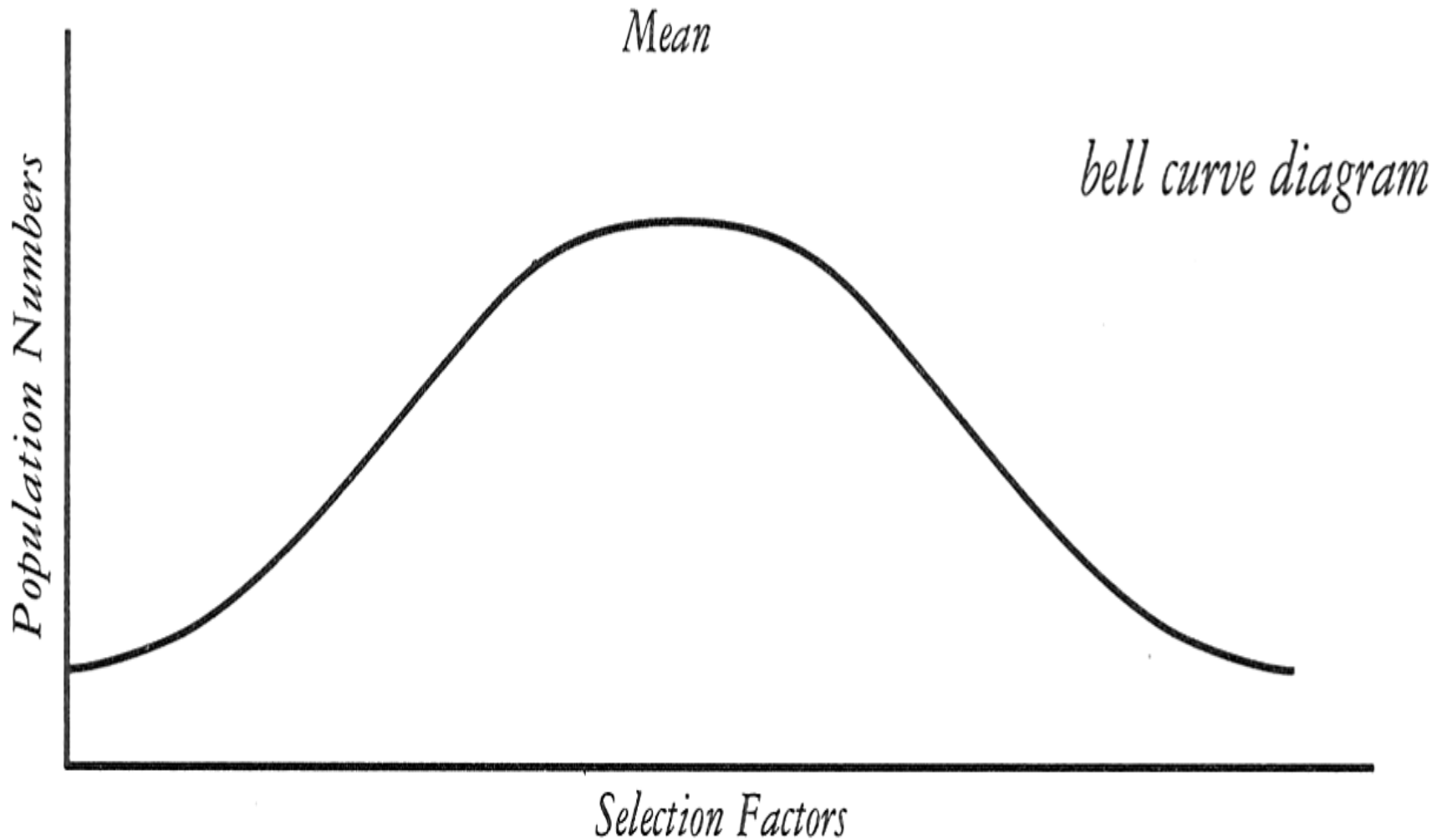
Most breeds have more than one condition that they are trying to control at any one time.

- ▶ ***The more conditions one is looking at to control, the slower the overall rate of improvement.***
- ▶ Thus the aim should be to take out the worst affected animals (of any one condition) but try and retain **at least 75% of the population** for breeding purposes.
- ▶ The more conditions one is aiming at, ***the higher this retention figure*** may need to be. Trying to clear every animal with the slightest abnormality will result in a drastically reduced population base and ironically, a higher chance of seeing new conditions as a result of this narrowing to the genetic base of the breed.

BREED IMPROVEMENT SCHEMES ARE LONG TERM

- ▶ Any breed improvement scheme must to be looked at in ***the long term***. To alter or improve a breed average (ie. shift the entire population mean) takes consistent effort and numerous generations to see what has been achieved.
- ▶ Improving breeding stock within a kennel can be relatively easy, however a single breeder alone cannot improve an entire breed on their own.
- ▶ **The greater the level of participation, the more likely the scheme is to work across a breed.**

BELL CURVE POPULATION SPREAD



POPULATION SPREAD

- ▶ Populations can be described by a bell curve which can apply to any feature you wish to look at, be it height through a breed, litter size, hip dysplasia (HD) scores and so on. With this curve, the top of the curve is the mean of the population factor being assessed eg. height with the extremes at either end of the scale ie. the shortest and tallest.
- ▶ If your breed has a height limit such as German Shepherds, while we wish to breed strong, well boned dogs (who generally are on the large end of the scale), we have to fit (or attempt to fit) the vast majority of dogs under the limit, so the breeders will usually discard the tallest and the smallest, and generally work with the medium to large range of the population.
- ▶ This same principle can be applied to any genetic problem within a breed. **If the incidence of a problem is small across the whole breed, eg. affecting 5-10%**, it can be fairly easy for breeders or clubs to say not to breed with affected animals.
- ▶ If however, the problem has a **variable expression and/or a complex means (polygenetic) of inheritance, this can affect virtually every member of the breed** eg. hip dysplasia, to some degree.

SUCCESS OF THE GSDCA HIP SCHEME

- ▶ The GSDCA HD and ED scheme has been, when viewed from the long term, spectacularly successful.
- ▶ The breed hip average some 35 years ago was around **18**. This has gradually decreased over the years to the current rolling breed mean 2004-2009 of **6.73**
- ▶ The non GSDCA GSD population's average is starting (slowly) to drop. The 2004-2009 average is **10.74**
- ▶ There are 4 main reasons for the success of the GSDCA Hip Scheme
 1. Having a cut off point ('A' stamp – max 8/hip)
 2. Regular publishing of sire averages
 3. Breed survey, excellent show awards tied to A and Z stamp passes.
 4. Introducing compulsory HD/ED Xrays – LRL in 2000

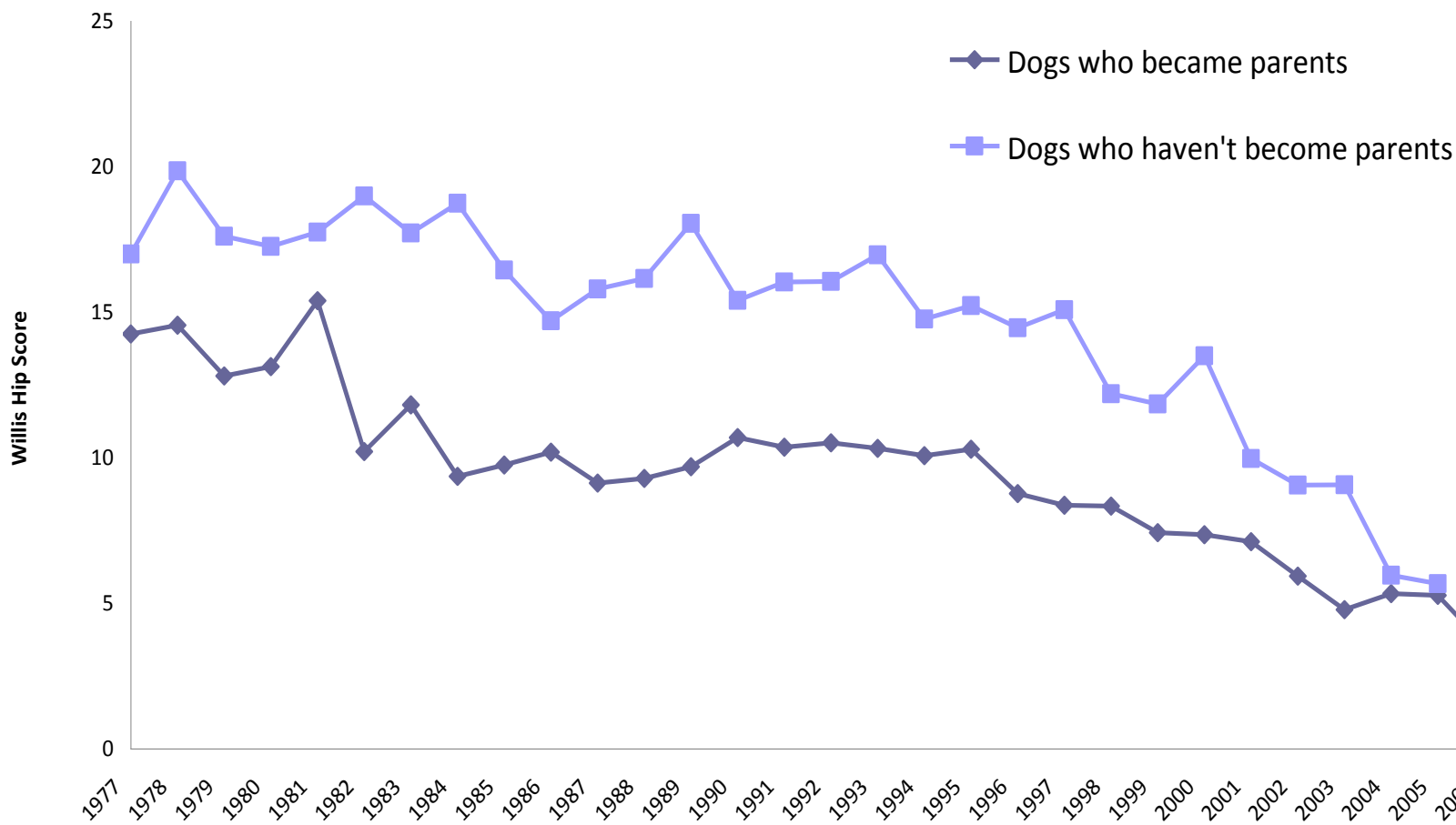
DECREASING BREED MEAN

GSDCA Annual Count & Mean	Count	Mean
1/7/97 to 30/6/98	301	11.49
1/7/98 to 30/6/99	750	10.64
1/7/99 to 30/6/2000	647	11.35
1/7/2000 to 30/6/2001	566	9.98
1/7/2001 to 30/6/2002	529	9.64
1/7/2002 to 30/6/2003	511	9.88
1/7/2003 to 30/6/2004	514	8.22
1/7/2004 to 30/6/2005	487	7.02
1/7/2005 to 30/6/2006	443	6.66
1/7/2006 to 30/6/2007	399	6.26
1/7/2007 to 30/6/2008	456	6.28
1/7/2008 to 30/6/2009	415	5.95
1/7/2009 to 30/6/2010	410	5.65
1/7/1996 to 30/6/2010	6,585	8.62

Non GSDCA Dogs	Averages	
2004	(37)	13.05
2005	(56)	11.63
2006	(98)	10.44
2007	(149)	10.67
2008	(167)	10.31
2009	(158)	8.33
2010		
total 2004-2009		10.74
Total 1998-2010 835		10.81

AVERAGE HIP SCORE RELATIVE TO BREEDING

Average Willis Hip Scores of German Shepherds by Year of Birth



GSDCA ELBOW SCHEME

The elbow scheme is similarly improving, initially some **33%** of all dogs were affected (early 1990's) with quite a high percentage of these being grade 2 animals. Some states has even higher percentages.

We are now at the point that the **Grade 2** elbows are eliminated from our breeding population. The overall percentage of heavily affected dogs has significantly dropped. We still need to watch this area and avoid doubling up on the problem.

Relevant statistics are harder to obtain with Elbow statistics as a reasonable percentage of affected animals are not recorded as they are removed from the breeding pool very early on (between 4-9 months of age). We still have a slight problem collecting statistics from these dogs today.

Across the board, the numbers of puppies that have severe hip or elbow conditions has dropped dramatically, to the extent that rarely are any puppies euthanaised for either condition in the current era (in my state at least!).

OVERALL PICTURE

The overall picture covers many aspects within each area and may have different slants within various breeds. Compromises often have to be made when balancing out the relative importance of different problems both within that animal and the breed as a whole.

- ▶ **The overall picture should be remembered.** Trying to eliminate all dogs with hip dysplasia (HD) did not work (attempted in both German Shepherds and Labradors) and the end result was a greatly reduced genetic pool. Cases of HD were still occurring and breeds no longer resembled the standard.
- ▶ The main aim today of most hip schemes is **a gradual reduction in the breed average while at the same time allowing breeders to preserve valuable bloodlines** and decrease the incidence of really severe HD. The inheritance of HD varies in different breeds.
- ▶ The higher the degree of inheritance, the more rapidly changes can occur within a breed when selecting for the characteristic. Also, a dog that has a good hip score, may not necessarily throw low scores in his progeny, while a litter brother with a slightly higher score may have a far lower progeny average.

HIPS - EARLY INTERVENTION – IS IT REALLY NECESSARY??

JPS – juvenile pelvic symphiotomy – can only be done between 12-20 weeks of age, jury is still out on the effectiveness of this technique, particularly if done over 16 weeks.

- ▶ **TPLO – triple pelvic osteotomy** - this is recommended for cases of *mild* HD, should be done before final fusion of the pelvis – therefore before 9 months.
- ▶ **FEMORAL HEAD REPLACEMENT** – this is usually only done after final fusion of the growth plates, was originally >12 months but is now being done on dogs 9 months. Usually only recommended for cases of severe HD, where there is significant arthritic remodelling of both the femoral head and the acetabulum.

OVERSERVICING OF VETS??

This problem has been with us for some time and tends to raise its ugly head on regular occasions.

The various components to this are (and not necessarily in order of importance) as follows:-

- ▶ **Weight** - Breeders need to include the weight for age chart in their puppy packs and impress upon new owners the need to stay within normal limits for rates of weight gain and weight for age.
- ▶ **Conformation** – **deep hindquarter angulation coupled with excessive looseness of hocks** and hey presto, your puppy has hip dysplasia! (regardless that it is primarily the hocks and ligaments that are the issue).
- ▶ Couple that occasionally with too much weight, too rapid a weight gain and growth, these puppies are often **sore along the back** as well, so they arch over the back, further accentuating the already extreme hindquarter problem.

OVERSERVICING CONT.

- ▶ Puppies that have this excessive conformation are the most likely candidates **for early X raying by inexperienced vets and the subsequent “corrective” or “preventative” operations.** When I see these “extreme” puppies, my primary concern is assessing the puppy, correcting any dietary issues and slowing the rate of growth (if excessive) and covering the soreness many of these puppies have. I generally add zinc to the diet as zinc is often relatively unavailable, and zinc helps strengthen ligaments.
- ▶ **Desexing** – quite a few of these puppies are **“picked up”** at the time of desexing (around 5-6 months). Owners often get – “Oh, we will just check the hips at the same time while the puppy is anaesthised”. Owners are rung immediately (usually while the puppy is still on the table) saying the puppy will need an operation to improve long term quality of life etc.

OVERSERVICING CONT

- ▶ Owners are quite often made to feel that they would be **failing to adequately care** for their pet if they don't go ahead and have corrective surgery – often committing to further surgery **fairly immediately**.
- ▶ **Ignorance (both owner and veterinarian)** – just because a breed has had a poor history in the past doesn't automatically mean a puppy will have bad hips.
- ▶ We, the GSDCA should be pushing far and wide that the national rolling breed average is around 8 total, far below the vast majority of breeds commonly held to have HD problems. **The odds of getting good hips is today actually fairly high.**
- ▶ **Costs (who pays???)** – unfortunately the majority of breeders find out after the fact, after surgery, desexing etc. Some owner are quite belligerent, and if the problem was severe, one can understand the angst, and this is a problem to be sorted between breeder and owner. However, being asked to pay large sums **after the fact** has its own issues as well.

TYPE OF CORRECTIVE OPERATION - ?EFFECTIVENESS

- ▶ Further complicating the issues involved is the type of operation and the effectiveness of the various operations at different ages. Some of these operations only work at certain ages.
- ▶ **JPS** (juvenile pubic symphysiodesis) generally, the earlier the better, which can be as early as 12 weeks, ideally at 16 weeks but not after 20 weeks of age.
- ▶ **TPLO**, triple pelvic osteotomy is best done before nine months and is **only really suitable for mild cases**.
- ▶ Severe cases really require total hip replacements, which the surgeons usually do not like doing much under 12 months and then one at a time, usually 6-12 weeks apart.
- ▶ As a further note, there are still ongoing discussions between vets and specialists as to the **relative merits and worth** of some of these operations, particularly the JPS.

SOLUTIONS

Maintain good ongoing relations with puppy buyers, if not, often the first you know of a problem is a distressed (and aggressive) puppy owner on the phone. Avoid this by:-

- ▶ Hand out **weight for age charts**, show people how to use them, highlight that there should not be excessive rates of weight gain and the importance of staying between the suggested limits.
- ▶ Try and **avoid using high performance growth diets**, especially on backyard pets – they far are more likely to be over fed (and be hyperactive!).
- ▶ **Emphasise** that you, the breeder, **want** to hear of any problem that your vet is worried about, **particularly** if it concerns hips or elbows as you do not anticipate any significant problems in this area.
- ▶ Ring puppy buyers when their puppies are around 3-4 months of age, check the weights and diets. Check again close to desexing time.
- ▶ Be particularly vigilant in certain areas where the vets appear to be pushing early intervention, ask puppy buyers to get **second opinions** before any major surgery, and above all
- ▶ To let you, the breeder, know **before any major operations** are carried out.

LONG COATS - STATISTICS

- ▶ It should be remembered that the coat type a German Shepherd **exhibits** is a **blend** of its genetics, there is not always a hard and fast cut off point.
- ▶ Current statistics on long coats are almost exactly on the estimated levels of simple recessive conditions which go as follows:-
- ▶ $\frac{1}{4}$ **normal short** (not carrying any long coat gene, minimal ruff, shorter coat)
- ▶ $\frac{1}{2}$ **carrier – normal coat** (carrying the long coat gene, carries a reasonable amount of ruff and feathering but coat still tight, weatherproof)
- ▶ $\frac{1}{4}$ **long coat** (heavy feathering, heavy ruff, pants etc)

Possible Matings	Normal Short AA	Normal Aa	Long Coat aa
Normal Short AA	All progeny normal short	1/2 Normal short 1/2 Normal	All normal
Normal Aa	1/2 Normal short 1/2 Normal	1/4 normal short 1/2 normal 1/4 long coat	1/2 normal 1/2 long coat
Long aa	All carriers – normal	1/2 normal 1/2 long coat	All long coat

LONG COATS

The Australian situation is very different to the German one. We have a small gene pool (for both varieties) and that becomes **vanishingly small** with the long coat population. This in reality is **too small to give enough genetic viability and variability** at this stage to produce enough healthy and sound dogs to breed on with.

With restricting the gene pool to long coats only, there are very real concerns that **this variety will go backwards in health areas** in particular. We have no health data of any depth available to us at this point, nor to be fair, does any country at this stage.

The GSDCA has in its charter the requirement to improve the health and welfare of the breed. By restricting intervarietal inbreeding at this early stage of Long coat development, we are **directly failing to assist** this section of the breed.

Owners of long coat bitches are being forced to look overseas to get the quality needed to continue breeding, with all the inherent risks currently here as well. It is currently not financially viable to import long coated stud dogs due to the limited market.

LONG COATS CONT.

- ▶ I would suggest that we ask the ANKC to allow interbreeding of the 2 varieties where the proposed dog to be used is a proven long coat carrier either by progeny or by DNA testing. **Resultant litters will be at least 50% long coat without losing type, reducing genetic variability or diminishing health requirements.**
- ▶ There should be open interbreeding of the two varieties for a minimum of 7-10 years, even if done along the lines suggested above. This can be revisited at the end of this time.
- ▶ The impact on the coat quality and length should be assessed in the normal short coated variety as well, at the end of this time.
- ▶ Of interest, in Saint Bernards – allowed to interbreed coats, swing lately to predominantly short coats.
- ▶ Collies (Rough and Smooth) judged as varieties, allowed to interbreed) – few smooth being bred and/or retained.

KEEP PROBLEMS WITHIN PERSPECTIVE

- ▶ ***The most important point is to keep the problems a breed has within perspective.*** This means that if there is a minor problem that does not affect the animal's soundness, either as a working animal or its quality and length of life, it should be kept in proportion relative to other problems within the breed.
- ▶ ****Genetic problems that result in a high incidence of blindness, crippling arthritis, a vastly shortened life span (eg. the storage diseases), or there is pain and suffering for both the dog and the owner (be it monetary or emotional stress), then efforts should be made by breeders and breed clubs to decrease the incidence of these problems.***

CANE PASTORE TEDESCO

DISEGNO DEL DOTT. WALTER GORRIERI

