WHAT CAN POPULATION GENETICS DO FOR THE IRISH WOLFHOUND?

Ladies and Gentlemen, Dear Friends of the Irish Wolfhound!

It is a great pleasure for me indeed to be invited to speak at your conference on the pressing topic of genetic problems and new means and aspects to control them. In doing so allow me to begin by going far back into the history of life on this earth, as this appears necessary to better understand the genetic problems of today.

Life originated some three billion years ago and the next two billion years it consisted of unicellular microbes only. But then these creatures seem to have invented genetical exchange. Parts of their DNA, i.e. the compound that constitutes the genes, were transferred from one individual to another, thus conferring useful genetic qualities for survival or competition. We still suffer today from this faculty as bacteria that have become resistant to antibiotics can transfer this characteristic to others that lack them.

It appears that this has boosted evolution enormously as now we see the start of the creation of multicellular organisms. The prerequisite for it was systematic genetic exchange, i.e. sexual reproduction. This enabled the new complex forms of life to cope with environmental change and the menace of parasitic organisms and to evolve into more sophisticated forms. This required a double set of genetic materials: two strands of DNA both containing the same kind of codes for all functions of life, each stemming from one sexual partner which we call the call the father and mother of the individual in question. In order to achieve genetic complexity, nature has accepted heavy costs as two individuals are necessary for each act of reproduction. And it also accepted a serious drawback: Defective genes from one parents could hide behind the healthy one from the other if its gene was dominant that is alone capable to effect the normal function in the offspring individual. But this was acceptable as defect genes are normally infrequent and only the extremely rare coincidence of two identical defect genes lead to a defect individual, and this would be eliminated by selection.

Survival of the fittest requires genetic diversity, i.e. a high degree of heterozygosity. Heterozygosity means two different genes (alleles) occupy the same site on the DNA strand, homozygosity is the presence of two identical ones. A high degree of heterozygosity is mostly combined with vitality and genetic fitness.

From the early beginnings, higher developed animals hat to fend off infectious germs and other parasites. This lead to an everlasting arms race: parasites developed new forms their hosts were not able to fend off, then new variations of hosts appeared that were immune against the new parasites and saved the species, and so on. Higher vertebrates developed a genetic complex responsible for immunity, the Major Histocompatibility Complex (MHC). Unlike other genes, the genes of this complex consists of a very great number of alleles making this complex enormously polymorphic (multiform). The age-old arms race war produced the MHC genes very early, they are more ancient than today's animal species.

The infection risk by a host of parasites and dangerous germs tends to maintain a high level of MHC heterozygosity by selection but there are different ways to obviate risky homozygosity animals could use: inbreeding avoidance by MHC-dependent mate choice and abortion. It has been shown in some species that ova seem to be able to obviate fecundation by related sperm, by abortion or absorption of inbred fetuses, and perhaps by sperm competition favouring the more vital heterozygous spermatozoa. But the most interesting mode of maintaining heterozygosity is inbreeding avoidance. To achieve this, animals must have a mode of recognising kinship in potential sex partners. The natural „interest" of an animal is of course production of viable offspring that means among other precautions that the partner is unrelated. It has been shown that the way to find out the degree of kinship of another individual is its body odour. Interestingly, it has been detected that the MHC not only acts on immunity but also determines the body odour thus giving an "honest certificate" of genetic quality. As female animals have the by far greater burden of reproduction, it is foreseeable that females will have a major part in mate choice. These natural mechanisms ensure polymorphism in animal populations. Quite recently, it has been shown that alpha pairs in wolf packs, contrarily to common assumptions, prevailingly were unrelated.

After this excursions far back into early evolution we come to the beginnings of modern dog breeding. It was in the England of Queen Victoria that the basis of pedigree breeding and dog showing was laid. It as an English invention and became the most successful animal breeding system world wide, a refinement of the domestication process. A pedigree guarantees (more or less) an animals pure descent and allows to precisely plan matings and breeding development. It reflected the ideas of the Victorian era of pure nobility and aristocracy. Purebred animals were - and are - regarded as the aristocracy of a domesticated species.

At that time, aristocrats strictly observed purity too, it became the model for animal breeding. Necessarily, as aristocracy amounted to just a very small part of the population, marriage among related persons was common but with time it depleted genetic diversity and serious genetic diseases occurred, much alike the situation in modern dog breeds.

In animal breeding, the Victorian model has became obsolete and mostly replaced by cross breeding and hybrid production, as only genetically variable animals are able to bring the highest productions and support the enormous stress of intensive management systems.

Pet breeding is now the last field were the Victorian model still subsists. Undoubtedly, it has enormous merits and produced and improved the big number of wonderful dog breeds. Most unfortunately, a system of strict seclusion of genetically narrow populations cannot be maintained indefinitely, as we will see next. Never before dog breeds were so tightly genetically secluded and for such a long time in a kind of genetic „Golden Cage".

I would like to show you that all practices used in current pedigree dog breeding depletes genetic diversity and thus leads to growing risks of genetic disturbances. The most immediately harmful is close inbreeding, i.e. incestuous matings. It is not only an abomination in humans but also in dogs, not for reasons of moral but for safeguarding health of the progeny. One brother-sister mating alone decreases heterozygosity by 25%. But it is not the most deleterious practice on the breed level, this is champion breeding. As all the offspring of a sire are half sibs, over-use of a single stud may severely affect large parts of even the whole breed. As said before, in natural populations normally defect alleles are extremely rare, but there may be hundreds of them. For the reasons explained before, this does not affect the population. If, however, defect alleles of just one or a few studs are widely distributed in a breed, small wonder that defect offspring will multiply. We must be aware that every stud most probably bears a number of dangerous recessive alleles. Today, in most breeds the defect genes of famous former sires are highly concentrated and the probability of manifestation is correspondingly high. Thus a prepotent stud is often a prepotent source of future trouble, what ever his other merits may be.

Less serious but still harmful is excessive elite breeding, and in general, assortative mating. Using just the very best of the breeding stock may bring quick results but also depletes diversity, hits soon on the selection ceiling. So preferring to use also good but not only the extreme individuals may sometimes bring even better results and helps to maintain room for ulterior selection progress.

The most used inbreeding practice of the individual breeder is line breeding. Its injurious effects are slighter than those of incest breeding as the advance of the F. is less. Still, in a few generations we arrive at the F. values of a sib mating. In spite of this, the harmful effects of line breeding are astonishingly low, often permitting a breeder to linebreed all his life without apparent problems. But these presumably will hit the next generation of breeders, and in fact, the prevailing genetic diseases dilemma is the „heritage" of former successful line breeders.

Now a word on the frequently misunderstood and over-valued inbreeding coefficient (F). The actual loss of heterozygosity is never precisely reflected by this figures. As we will see, genetic loss is partly subject to incidence, so in reality it is frequently either higher or lower than the F. Besides, genetic loss occurs and accumulates since the beginnings of a breed and even earlier, not just in the few generations of a pedigree, so it is always much higher. Further, the impact of inbreeding seems to be less serious if the same value of F is due to a series of linebred generations instead by one or few generations of incestuous matings. This seems to be due to heterozygosity-preserving mechanisms as mentioned before, that could be more effective if applicable through more generations. At any rate, an inbreeding-free pedigree is liable to substantially reduce the defect risk in the progeny. in the long run An appropriate DNA-based homozygosity test should be a better indication of genetic variety tan F.

Current methods of defect control focus on marker detection, genetic screening and culling of carriers. While these are important measures they constitute both a purely symptomatic cure and a further risk. The latter can be serious if there is a great percentage of carriers. This would dangerously reduce the genetic pool. On the other hand, it could in some cases allow the use of carriers of otherwise good quality if they are only mated to non-carriers. At any rate, this approach alone would not answer the underlying problem if not combined with adequate breed-wide genetic management for enhancement of genetic variety.

This leads us to a tour d'horizon of population genetics. The genetic structure of a population changes trough the influnce of various factors. One of the most important is population size that determines the evil effect of hazard on the fate of alleles. What has pure chance got to do with the fate of dog breeds? Quite a lot, an everyday example may explain this.

If you toss a coin, you have two options for the outcome, but only one will turn up. One option necessarily fails. If you throw six times, chances are that you get both alternatives, but in different numbers for each. Hardly you will get just one face up six times, so one face will „win" over the other, or with other words, some options of one face will be „lost". Throw a hundred times, and there probably will be both options in about equal numbers. The higher the number of throws, the closer you get to a fifty-fifty ratio, provided the result is not biased by defective coin that makes it fall more frequently to one side. In a million casts, the deviation from a half-half distribution will be insignificant.

The same happens genetically to a breed. If the breed is very small, its gene pairs (alleles) are „cast" with every new generation, that means freshly distributed. Chances are, that comparable to the coin tossing example, some alleles of a gene pair in the populations get lost, others increase correspondingly in number, and finally one allele might totally disappear from the breed while the other holds the field, it is „fixed" in the population. The greater the breed population size, the smaller the number of alleles lost or fixed in that way, the less the risk of a substantial change of the genetic situation - provided it is the effective population size.

The effective population size is strongly dependent on the number of original founders of a breed and of genetic bottle necks, i.e. periods of reduced breeding e.g. in war times or when there is little demand for the breed. Effective population size means that part of the population that is responsible for the dimension of allele loss. It remains low if a breed is founded by few animals only even if it grows to big numbers quickly. Original homozygosity remains but further loss diminishes proportionally to population growth. If the population remains small, allele losses keep on high.

But the effective population is also heavily dependent on the number of sires used. It can never be higher than about four times the number of males. So if theoretically you use a single male on 1000 bitches, the offspring's effective population will be just about four and accordingly the inbreeding increase 25%. This is easy to understand because all the pups will be half sibs at least! This explains the imperative necessity to use as much studs as feasible.

You see that with all usual practices in dog breeding we deplete a breeds genetic heritage and increase the inherited disease risk accordingly. On a breeders' level, the normal step to enrich a line genetically is outbreeding. Crossing non-related dogs combines non-identical alleles according to the mating partners' genetic distance. His produces immediately improved vigour, health and decreases defect incidence, provided the partners are really non-related. This is called heterosis. In modern breeds it becomes difficult to find sufficiently non-related dogs to get enough genetic enrichment and accordingly substantial heterosis. Highly inbred dogs, lines, or breeds suffer from inbreeding depression. This is a loss of vigour, fertility, instincts (e.g. maternal care or libido) and many other physiological functions. It is due to a class of defective alleles called lethal, semilethal, sublethal or subvital. The degree of inbreeding depression depends on the severity of allelic loss and the presence or absence of such injurious alleles. If they are absent or eliminated during a long period of inbreeding, there may be no inbreeding depression for a long time, but most lines continuously inbred will succumb. However, even lines that survive are extremely homozygous, we could call them „genetically mutilated". They are genetically inflexible i.e. will not respond normally to selection and are in great jeopardy of dangerous infections. A way out from inbreeding depression in an entire breed is outcrossing with a closely related breed. After four generations of backbreeding there is hardly any difference from purebred individuals. A very small influx of genes from outside is sufficient to prevent any genetic loss in a population.

When we read about the great frequency of inbreeding and line breeding in former years we see that there were by far less problems incurred. This is in part due to the fact that genetic depletion was not as high yet as today. Another reasons is the greater effectiveness of natural selection. The advanced care, veterinarian techniques, and feeding allows for raising many pups that formerly would have died. So the anti-homozygosity effect of natural selection is substantially diminished. This fact again adds to the build-up of homozygosity. We cannot go on to use gene-depleting practices as recklessly as our ancestors could do. Optimal nutrition, inappropriate A.I., lack of exercise etc. all promote the survival and thus the breeding use of the unfit.

What are the ways out of the impasse? We have mentioned molecular markers for combating individual severe inherited defects. Slowly there will be more and more detected against many defects. But we also must care for the basic causes. We can elucidate the state of the genetic diversity of a breed by DNA breed studies in order to find out about the gravity of the depletion. We should ban incest matings and line breeding. No more depletion, but genetic enrichment should be the objective. The question arises if a show breed or any breed can do without strong pressure on type. Type is important indeed as dogs are being kept for their good looks also. But type should not be sought by methods too costly for the genetic heritage. So the only acceptable tool is selection, but since modern breeds are bred to conform to standard for such a long time, type is not likely to be lost by relinquishing the more harmful of the breeding methods. Of course selection is equally imperative to improve health and heterozygosity. DNA tests can also determine individuals according to their genetic distance (unrelatedness) and/or individual heterozygosity to arrange appropriate matings. Incest matings are an offence against the forthcoming progeny, over-use of sires an offence against the breed. Therefore, services per stud should be strictly limited. Of course valuable studs should be used more often but never should an individual be allowed to usurpate a breeds genetic heritage by his genes that unavoidably contain a number of dangerous alleles. The goal must be to prevent individual defect alleles to multiply in the stock.

When breeds increasingly engender sick offspring, breeders eventually will face the opposition of society and the authorities dealing with animal welfare. The present trend is towards increased sensitivity for animal suffering in areas that were so far unnoticed. Today society looks into the kennels, they are no more a secluded workshop of the breeder. Probably pet breeding laws will be enacted, and breeds that cannot be bred without an inacceptable percentage of sick or suffering progeny may be banned. So we should see to plan breeding such as to reconstitute health and hardiness as well as preserving standard traits. To combine both is not easy but it can and must be tackled. Breeding ethics oblige to change conventional ideas and actions.

Unfortunately this requires a fundamental change in todays' registration and show system away from the ancient Victorian model. It means that appropriately planned crossbreeding should be allowed again, as in the early days of the breeds, and shows should again become testing grounds for selecting breeders not just for conformation but also health, genetic variability and functionality. Registration should be dependent of an inbreeding limit. Brace and breeders' classes should be abolished or reformed, for at present they practically require uniform dogs as these are most easily obtained by in- or line breeding. The breeding system should change from being dominated by close breeding methods as listed above to a regime based on outbreeding. Breed uniformity maintenance must be warranted by appropriate selection only, a more tricky but obtainable objective and a great challenge to the breeders..

The IWH's case: this is a very large breed, competing with the Great Dane for the size record of dog breeds. Big dogs have a deplorably short life span, the reason for it is unknown. Strangely, the biggest wolves from Siberia or the Polar regions reach 15 years in captivity, an age that we find frequently in small and toy breeds only. Probably the dog originated from a small southern wolf variant, but there is also another possible factor. Often we hear that in former days even large dogs seemed to live far longer. In fact, today's conditions restrict a dogs' exercise the more the larger its size. Feral and roaming dogs cross big distances by trotting. Toy Dogs must trot even when on leash and can get much exercise even in a small apartment. The amount of exercise on the average decreases geometrically with size. In order to get as much exercise as the average toy dog, an IWH would probably have to trot by a bicycle an hour everyday. It would be interesting to know the life expectancy of IWH or other large dogs practising that.

In recent studies on dog morbidity it was shown that IWH and Great Danes were the breeds with the highest mortality. It was also shown that canine mortality generally increased with body size. But regardless of size, mixedbreeds of the equivalent weight class always lived notably longer than pedigree dogs. This reveals the degree of inbreeding depression in pedigree dogs, but it also shows the possibility that improving genetic variability could probably lead to a substantial increase of life expectancy in large breeds. Besides, relieving the selective pressure on over-size by introducing an upper size limit into the standard would substantially reduce problems related to excessive giant size. Generally speaking it is no more ethical to apply standards with no upper size limit in giant breeds and lower limits in toys. Even so, the IWH would remain the impressive large size breed it is renowned for.

Other important health risks of the IWH do not appear to be related to size, neither tumour incidence nor heart problems. They must be approached by two ways, genetic screening with the help of molecular genetics, and boosting of genetic variety. The latter measure helps greatly to prevent the uprise of new inherited problems.

Large breeds are also greatly affected by genetic bottle necks as their keeping is costly and in times of need very few survive. So the homozygosity level of the breed is probably very high, so DNA breed study would be desirable. On this basis, world -wide genetic management should be brought into play. This could reveal reserves of non-relatedness in the breed and answer the question of the urgency of crossbreeding. It might turn out the best would be to reconstitute the breed again just as Capt. Graham did 120 years ago. He used Deerhounds, a Borzoi, and Great Danes and the few remaining real wolfhounds he found . We really should reconsider the idea of breed purity along the lines I have drawn. The IWH is a breed composed of several breeds, and even one great Pyrenees (or Tibet mastiff?) was used by Graham to boost size, i.e. a non-gazehound breed, and he succeeded to retain the original type! The present state of genetic knowledge and the world-wide new breed-organisation should allow for an effective and lasting sanitation of this wonderful breed.

As it is a most important concern to disseminate the „Canine Diversity Message", I have have long been advancing the following ethical theses, and I would like to put them to the distinguished list's members' kind but severe critiques, judgments, and comments:

1. Inbreeding including incest, line and back breeding, popular sire breeding and exaggerated elite breeding are depleting the breeds genetic heritage, I call them „close breeding methods " though habitually this term is used for incest matings (a euphemism).

2. As these methods increase the genetic defect risk they can be seen as a kind of animal experiment that should be reserved to scientific institutions and are only acceptable for an important purpose; the slightly better chance to get a champion does not justify it, as dog breeding should not be gambling with canine health, the more so since

3. all breed clubs use to solemnly state that their breed's health is their first and foremost concern. This is of doubtful credibility as long as the above cited methods are not strictly banned in their code of ethics. Even their breed's absolute purity, while rightly being a sacred principle, must be secondary in a genetic emergency situation.

4. Inbreeding was once a valuable tool in shaping today's breeds. As these have now reached a high degree of homogeneity it has lost its importance and turned into a fatal and disastrous habit

5. In order to enjoy a life worth of living, dogs have the right to be provided with an adequate genetic diversity outfit, just as much as to good care, feeding, and freedom from abusive treatment

6. The forthcoming research findings of genetic markers are not a warrant to continue in the old way as these are helpful symptom cures without effect on the underlying evil

7. Incest matings are an abomination in dog breeding too, not for any moral reasons but for the disastrous consequences. Highly inbred progeny is „genetically mutilated".

8. And finally, on the grounds of the above said and the overwhelming practical and scientific evidence, close breeding is abusive breeding, for all breeding aims could be obtained, if less easily and quickly, by appropriate selection methods.

I tentatively would think if all close breeding stopped today the hereditary defect rate would immediately shrink by 10 - 20%, what an enormous relieve of suffering, vet expenditures, and emotional distress... But every mating of relatives that could be dissuaded from may prevent one or more sick dogs and thus is worth while the convincing effort.

A prominent professor of canine genetics once called my ideas „too evangelistic". He thinks that pedigree dogs are now being in a genetic bottleneck they just have to go through (like inbred lab mice strains - my comment).

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