IWHG Newsletter

December 2017

PATRON: TRUDIE SUMNER

Welcome

One of the things we love about the start of the new year is that it serves as a marker to reflect on where we have been, and where we are now.

As we say goodbye to 2017, we can look back on what we have achieved in the year, and look forward to new challenges in 2018.

We started the year by launching our Longevity Recognition Programme and starting our online library of research papers. We followed these up by launching our Puppy Buyer's Guide, updating our Liver Shunt Testing Guide, introducing quarterly reports from the Breed Health Coordinator and providing feedback on our dentition survey.

In May we had a change of officers, with Tim Finney standing down as Chairman and Rebecca Peek being elected. Jackie Watson also stepped down as Group treasurer and was replaced by Steven Ritchie.

The summer months were spent working on updating research and in the autumn, we worked to finalise our well-supported fundraising raffle and assemble a fantastic panel of experts for our biennial seminar.

This issue of our newsletter is our 'seminar special'. We have a tremendous, comprehensive write up of the event here . Thank you, Maura.

What else is new in this edition?

- We have the latest report from our Breed Health Co-ordinator, including details of the Breed's Annual Health Report, the Breed Health Co-ordinator's Symposium and the Large and Giant Breed's Working Group meeting here;
- we have managed to squeeze in a raffle update from Marion, here;
- a financial update here;
- a regional heart testing update, here;
- a summary end-of-year report from our secretary, here;
- and details of our new email addresses, here.

As we move into 2018, our immediate focus is to implement the action plan from the seminar. This means working to provide the data needed to underpin the Breed Health and Conservation Plan, liaising with the breed bodies and providing a forum in which everyone has the opportunity to contribute - and which can feed into a detailed BHCP that reflects a consensus within the breed.

We look forward to 2018 with continued optimism and with many new ideas and exciting developments planned for our Group.

Finally, can we thank you all for your continued support for the IWHG and wish you all a very Happy New Year for 2018 and the very best of health to you and your dogs.

IWHG

Regional Heart Testing Scheme Update

by Rebecca Peek (Chairman)

2017 has seen another full year of heart testing sessions throughout the UK and Ireland. In summary, total numbers of dogs seen remain at roughly the same level as last year and most sessions were full, though a few were short on numbers – these will be reviewed in the new year to ensure that these sessions continue to be viable. We were pleased to be able to continue to offer appointments at £45.00 per dog and to be able to continue to subsidise the Super Veterans sessions. The Irish Wolfhound Rescue Trust also continued to cover the cost of the Rescue hounds sessions.

We will be giving a full report on the year's activity in the Spring Newsletter, but in the meantime, we'd like to thank all our cardiologists again for making another year of the scheme possible. So, thank you to Sheena Milne, Serena Brownlie-Sykes and a huge thank you to Angela Bodey, who covers the majority of the sessions. A big thank you as well to all those that have hosted the sessions and provided venues and helped to manage and organise the days – it's a great team effort spread between many people.

As the Regional Heart Testing Scheme continues to grow and develop we regularly review the ways in which we can improve it. Organising and managing the scheme requires a great deal of time and effort and is a full-time job for those closely involved. Heart Testing Co-ordinator Wendy Heather spends most days, including weekends, dealing with the administration required, whether that's bookings, organising hosts and venues or liaising with the cardiologists. It really is like a full-time job, but, as with all IWHG roles, it is purely voluntary and has to be fitted in around real work!

So, we have decided that the Scheme could really do with two people and we're delighted to announce that

Anne Vaudin

will be taking on the role of

Heart Testing Administrator

from January 1st.

Most people already know Anne as our website manager and also as the Irish Wolfhound Club's Archivist, but she has agreed to take on the role of organising and managing the heart testing bookings. She will be the main point of contact for the day to day administration of the Scheme.

Wendy will remain as **Heart Testing Co-ordinator** and she will retain her top line responsibilities of organising the diary of sessions for the year, liaising with the cardiologists and the hosts, organising the venues and the overall reporting and management of the Scheme.

As part of streamlining our communications, we have introduced new email addresses for both of them and from the New Year,

Wendy will be contactable on: hearttestcoordinator@iwhealthgroup.co.uk

and Anne on: hearttestbooking@iwhealthgroup.co.uk

We have also introduced a new online form for heart test bookings. Most people will find booking this way to be quicker, more efficient and easier. Why not give it a try?

Dates and venues for 2018 will be published early in January and will be announced on Facebook and posted to our website.

Financial Update

by Steven Ritchie (Treasurer)

The main fundraising activity during the last quarter of 2017 was the raffle drawn at the 'Breeding For The Future' seminar in November, which raised the magnificent sum of £2,000.

£294 was received from easyfundraising in the quarter, and a great effort with loose change tins took in a further £177. Thank you everyone who continues to make donations by using easyfundraising when shopping online, and to those who fill their loose change tins.

Signing up for easyfundraising couldn't be easier and can be done at the following link

http://www.easyfundraising.org.uk/causes/iwhg.

If you don't have a loose change tin but would like one, please contact Wendy Heather who will be only too pleased to provide you with one. And thank you again to those of you who make monthly donations by standing order, it's very much appreciated.

Anyone who wants to make regular donations can do so by following this link and filling in a standing order form.

http://www.iwhealthgroup.co.uk/files/Standing-order.docx

A full update on fundraising in 2017 will be included in the accounts which will be published early 2018.

IWHG Raffle 2017

by Marion Finney

On behalf of the Irish Wolfhound Health Group, I would like to say a very big thank you to everyone who purchased tickets for our recent raffle drawn at the November seminar. Tickets were practically sold out by seminar day, so only very few lucky folk got some on the day.

We are very sorry some of our great supporters were therefore disappointed. The raffle raised £2000 for the IWHG, which is amazing, but again without you all this would not be possible.

We had a splendid line up of prizes, all donated very generously by our good friends and supporters. And I would like to thank these wonderful people - our Patron Trudie Sumner, Tim, Marion and Ian Finney, Linda Forret, Chris and Julie Amoo, Steven Ritchie, Dr Kurt Kramer, Rebecca Peek, Wendy Heather and Jackie Wilkinson.

I am sure all our winners are very happy with their prizes. Those lucky enough to win the holiday accommodation will be busy planning their weekends away, others enjoying their wine and other fantastic goodies.

A full list of winners can be found on our website,

http://www.iwhealthgroup.co.uk/files/raffle-results.pdf

I would also like to thank all those who sold tickets for the raffle, in particular Liz Thornton, who very kindly donated the raffle tickets, the group members who also put a lot of time and effort into promoting the raffle, and especially Gary for his excellent flyers and art work.

So, to all concerned a very big thank you.

Marion

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Kennel Club Breed Health Co-ordinator (BHC) December 2017 Update

by Rebecca Peek (Breed Health Co-ordinator)

The last quarter of the year continued to be a very busy time with the Breed's Annual Health Reports being submitted, the Breed Health Co-ordinator's Symposium and the third Large and Giant Breed's Working Group meeting.

Annual Health Report (AHR)

As explained in an earlier report, historically Annual Health Reports have been submitted by breed clubs, now the information is to be collected by the breed health co-ordinator and submitted via an online survey. Previously our AHRs have been produced by the BHC/IWHG for the secretary of the clubs to submit with their annual KC returns, so there is little difference here for us, except that the BHC now returns the Report directly. The report is an annual overview of the key conditions of concern within the breed and a summary of what actions are being taken within the breed to overcome these and to educate owners, breeders and judges on breed health generally.

The most important part of the report is to list and rank the three health and welfare conditions that the breed considers to be the most important.

For some time now, this has been listed as

- Osteosarcoma,
- Heart Disease (AF & DCM) and
- Bloat (GDV).

This year, however, we felt that we also needed to add Pneumonia as a condition of importance and concern to the breed and so ranked it equally third with Bloat.

We have noted from increased correspondence with the Group and also commentary on social media, this currently seems to be a condition of increasing concern to owners and which seems to be experiencing a greater incidence. As a life threatening disease and as it currently appears to be as prevalent in the breed as bloat, if not more so, we believe it should be listed as a key concern within the breed.

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With the list we are also asked to describe the actions being taken to deal with these conditions and we are very lucky to be able to list a number of different research partners and projects as well as the Regional Heart Testing Scheme.

For Pneumonia we have an ongoing study with Dr Angela Bodey and the Nottingham Veterinary School, but we would like to stress that this can only produce meaningful data if the surveys are completed and returned by owners. As we know, Pneumonia is a condition that is apparently more prevalent in IWHs than other breeds and the breed has a unique presentation of it. However, it is often misdiagnosed and can be life threatening, but it can also respond well to treatment in many cases, if caught early. Because it is often not specifically diagnosed, we have opened the definition of the study to include Acute Respiratory Disease.

We know that experiencing any illness in your hound can be distressing, but we would urge everyone who has experienced this condition to support the study.

http://www.iwhealthgroup.co.uk/pneumonia.html

The full AHR will be posted to our website shortly, and will be found under KC Matters.

KC's Breed Health Symposium

This year the symposium was offered to non BHC guests and saw a marked increase in attendance. I was delighted to see the IW Club's Health Representative, Dr Das, there as well and also caught up with Dr Serena Brownlie-Sykes in her official capacity as BHC for her other love, Samoyeds.

It was a very full day and several of the speakers were also speaking at our own Seminar shortly afterwards so the content of their presentations is covered in more depth in our own Seminar Report, (Dr Katy Evans re the Breed Health and Conservation Plan, and Dr Cathryn Mellersh on the Give A Dog A Genome project).

One of the key presentations, and probably one of the key attractions for non-BHC audience members, was on **Epilepsy**. **Professor Holger Volk of the Royal Veterinary College (RVC)** is a leading authority on canine and feline epilepsy responsible for ground-breaking developments. He is also an excellent and engaging speaker, demystifying the subject in very user-friendly terms.

Epilepsy is the most common chronic neurological condition in dogs but it is not just a pure seizure disorder; it also causes comorbidities such as behaviour changes. The cause of epilepsy can vary, but more and more genetic factors have been identified in recent years. Recent research has also highlighted that drugs are not the only answer to getting back control when managing a patient with epilepsy. A holistic and comprehensive approach is essential to improve Quality of Life (QoL) and the management of epilepsy. Research is being done into the role of diet in relation to treatment, as this has been shown to have an effect in humans.

This link takes you to more information on how you could contribute to this study if you have a dog suffering from seizures.

https://www.thekennelclub.org.uk/media/460803/canine_idiopathic_epilepsy.pdf

Another of the areas of interest is the effect of the condition on the care-givers and what can be done to improve their QoL and also their influence on the diagnostic and treatment process. To that end Professor Volk with Dr Rowena Packer and the RVC, has developed an **Epilepsy App** to help owners manage the condition more effectively and which will also help inform their veterinary support on efficacy of treatment as it can send

Epilepsy is the most common chronic neurological condition in dogs

information directly to vets.
In addition, it has the potential to provide more meaningful data on a larger cohort of dogs to aid understanding and future research and drug development.

https://www.rvc.ac.uk/news-and-events/press-office/rvc-creates-a-dog-epilepsy-smart-phone-app-to-help-manage-mans-best-friend-s-fits

The presentation was full of new information and approaches and if you ever get the chance to attend a presentation by Professor Volk it is well worth it.

Brenda Bonnet gave an update on the work the **International Partnership for Dogs (IPFD)** is conducting and their earlier conference in the Spring.

This is a non-profit organization and its mission is to facilitate collaboration and sharing of resources to enhance the health, well-being and welfare of all dogs worldwide.

Several national Kennel Clubs (Sweden, Finland, Germany, France, Norway, the UK and the USA (AKC)) and other stakeholders in dog health [The Orthopedic Foundation for Animals (USA) and the Agria Pet Insurance-SKC Fund (Sweden)] have made formal, multi-year commitments to move this work forward. The FCI, which represents 91 national kennel clubs, is an Initiating Patron and Member; the Irish KC is a partner; VetCompass (UK) is a collaborating sponsor. It is an open, inclusive and transparent structure and is working to engage more partners globally. Most importantly, its open approach means that there are many projects and studies published on their website that anyone can access.

Please check it out, you'll find a wealth of information on its website https://dogwellnet.com/

Finally, a very helpful presentation from Zoe Belshaw of the Centre for Evidence Based Veterinary Medicine, on **Sniffing out the Science**. Zoe cautioned against taking anything we find on the internet at face value.

There's an increasing amount of information available about dog health, but knowing which sources of information can be trusted can be difficult. She suggested we use a website www.trustortrash.org as an excellent starting point for how to gauge the benefit of the article you're reading. I will see if we can use her slide presentation and add it to our website and FB Group as a guide for good research.

Zoe cautioned against taking anything we find on the internet at face value.

The Large and Giant Breeds Working Group

The large and Giant Breeds Working Group held its third meeting in November at the Kennel Club Building in London. Following on shortly after our own Seminar where Dr Tom Lewis spoke, (see Seminar Report), Tom was the invited guest at

this session as well and we had a very stimulating and thought-provoking discussion on the topics of Estimated Breeding Values(EBVs), Population Genetics and the role of test results in the MateSelect database.

One of the key concerns was the meaningfulness of test results, such as for hips and elbows, when there can be such a difference in the measurement and standards of the tests globally. This is particularly important as test results can sometimes be obtained more cheaply in other countries and so some people are sending off results and there is a concern that the findings may not be consistent with UK results. So far there is no universal standard for tests and even within the UK the interpretation and understanding of test results can be misunderstood or misinterpreted.

This, of course might have an impact on how effective EBVs might be in this area. So far IWHs do not have compulsory testing for Hips and Elbows, but nevertheless the discussion is still important as the principle applies to many official tests.

Communications via KC emails

We have started using the KC database to distribute emails to registered owners who have expressed an interest in being kept informed. This is particularly helpful if we want to publicise a research project. We have sent out two emails recently, so if you are not receiving them but would like to, please contact the team at MateSelect and ask to be added

mateselect@thekennelclub.org.uk

Breed Health and Conservation Plan

As we know, Irish Wolfhounds are in the second phase of breeds being processed and this is now about to happen. This means that all data available on the breed will be gathered by the KC over the next six months or so and we will be providing the data and references we have as well – this includes all studies that are ongoing. This will include the KC's own Breed Health Surveys from 2004 and 2014, neither of which generated sufficient numbers to provide significant data.

So, we will be launching our own Breed Health Survey early in the New Year with the aim of generating more meaningful and up to date data for the BHCP. So, my key responsibility for the New Year will be to get our own Breed Health Survey off the ground and I will be contacting everyone to respond within a short time frame, so keep an eye out for messages on Facebook and on websites and through KC emails.

That's it for this edition, except to wish you all a very Happy New Year and a healthy and successful 2018.

IWHG Seminar 11th November 2017

by Maura Lyons

This year saw the most successful IWHG seminar yet. It was very well attended by wolfhound owners and breeders, with also several representatives from other breeds. We were very lucky to have some excellent speakers and would like to thank them for their support and collaboration and the time they gave us. The following is just a taster of some very dense and sometimes complex presentations to bring those not there up to speed!

Dr Katy Evans

KC Health Research Manager

KC Breed Health and Conservation Plan (BHCP)

Katy Evans explained the Breed Health Conservation Plan and the process involved in creating it. The Kennel Club will be creating a BHCP for every breed and it is a KC requirement. It will take a holistic view of a breed's specific health status with consideration to known hereditary conditions, conformational concerns and population genetics (inbreeding, effective population size etc.).

More details about the project can be found here... https://www.thekennelclub.org.uk/health/breed-health-and-conservation-plans/

The first phase involved 17 priority breeds and is nearly completed. Irish Wolfhounds will be getting processed in the second phase likely to start in the middle of next year.

The BHCP will ensure that existing and newly emerging diseases and health issues are identified using evidence-based criteria. This will mean that breeders are provided with up-to-date and accurate breed specific data with which to make decisions prioritising health within breeding strategies.

There are four stages to creating a complete BHCP for a breed.

Firstly, the key health issues which affect a breed must be identified –

this will be achieved by collating data from a range of sources, namely: breed related scientific literature;

- the Kennel Club's breed health surveys conducted in 2004 and 2014;
- VetCompass;
- insurance data from Agria UK for the preceding twelve-month period;
- breed specific health surveys if these have been conducted;
- judges' monitoring reports;
- the breed's annual health report;
- results from official DNA schemes, and KC BVA schemes;
- the British Veterinary Association 'Sightings reports' for the last 6 years will also be requested.

Once all of the evidence is gathered and studied then **stage two** will be created, in which the most significant health problems are identified based on prevalence and impact. A draft document will be produced and meetings will take place between all the stake holders (this includes the IWHG, breed bodies and the veterinary and research communities) to agree priorities and actions.

The **third stage** will develop and provide clear advice and guidance for breeders and breed bodies as to how to move forward and ensure the breed is a healthy and sustainable population into the future.

During **stage four** it may be decided that more information is needed and plans will be drawn up to collect the required information. The whole process is designed to be dynamic and proactive, monitoring the health of the population over many years and responding to any changes in the prevalence or type of conditions being reported. Importantly, it is being produced in collaboration with the breed and with its close involvement.

Dr Tom Lewis

KC Geneticist

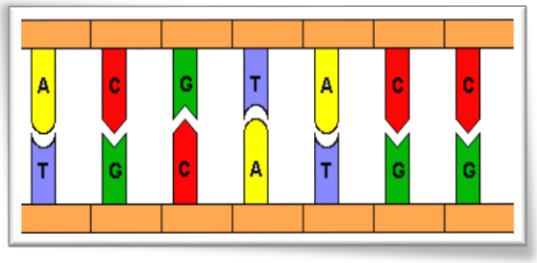
Population Genetics and How to Breed Within a Small Gene Pool

Tom is the KC's quantitative genetics expert and spoke to us about *Population Genetics and How to Breed Within a Small Gene Pool.* Whatever the size of the population there are several genetic forces acting on a breed's gene pool.

- Mutations – these are the only method by which novel genes can enter a closed gene pool.
- Selection – natural versus artificial
- Loss of genetic diversity – due to inbreeding and/or drift
- Migration – can increase or decrease diversity depending on the viewpoint
- Outcrossing – new genetic material can be brought into a breed by introducing a new breed or breeds

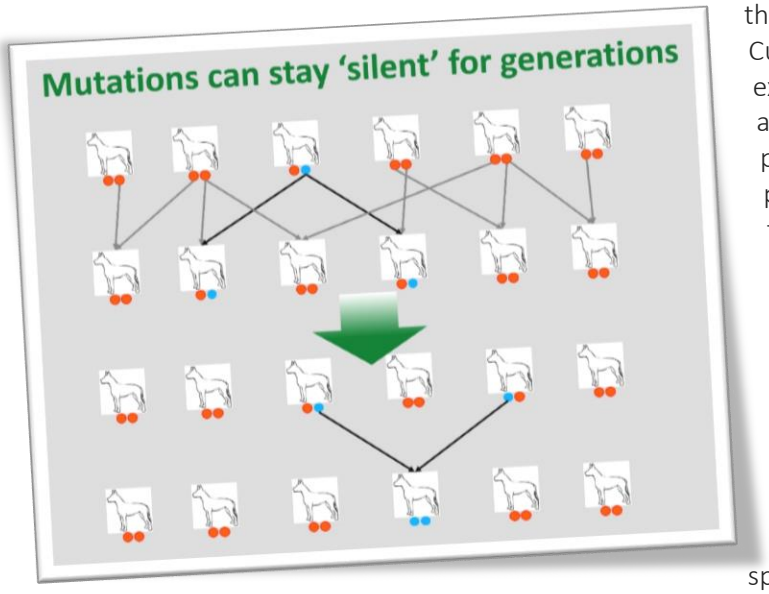
Tom went on to explain the basic structure of DNA and how changes in that basic structure at the DNA level can affect the efficiency of the resultant protein, which leads to changes in the expression of traits.

DNA is made up of long strings of nucleotides. These are arranged in a double-stranded fashion, where each strand is complimentary to the other; if we know the sequence of one strand then we can accurately predict the sequence of the other strand.



DNA strands are packaged into chromosomes within the nucleus of the cell. Genes are arranged on these chromosomes, and chromosomes are inherited by an individual, one from the father and one from the mother. Genes are used as templates for the cell to create proteins and these proteins are what makes an organism live, grow and function.

Mutations in the DNA strand can be caused by mistakes in the DNA replication machinery causing the predicted nucleotides to be substituted or replicated, or sometimes extra nucleotides are inserted or deleted. These changes will affect how a DNA molecule creates its protein, and therefore will affect the structure of the protein, which in turn affects the efficiency of that protein.



Because each dog inherits an allele (one version of a gene) from each of its parents, one of the alleles may still work well enough and produce enough functional protein so that the effects of a mutated allele may be hidden for several generations.

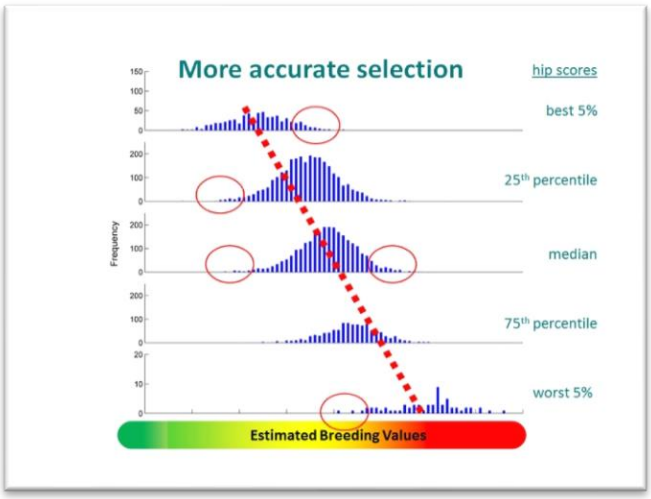
Selection changes the allele frequency within a population. As breeders select for a specific trait, then the allele frequencies associated with that trait will change within a population. Simple traits, those controlled by one gene, can be expressed in either a dominant or recessive mode. Complex traits are influenced by several genes, for example a 3-gene trait can have seven possible genotypes leading to a continuous variation of that trait within the population.

When plotted on a graph, these give a normal Bell Curve distribution where extremes of the trait appear in only a small proportion of the population, and most of the population exhibits the middling values of the trait. Think of height, weight, body size, etc.

For any complex trait, by breeding we are using artificial selection to select for specific narrow areas of the *bell curve* in order to achieve the desired phenotypic change, thereby altering the allele frequency within the population. So, basing selection on phenotype alone may not give us the best outcome *genetically* for an individual or for a population. Phenotypic change will only be achieved if the trait is at least in part influenced by genetics, and we should remember that genetic risk can be modified by environmental factors.

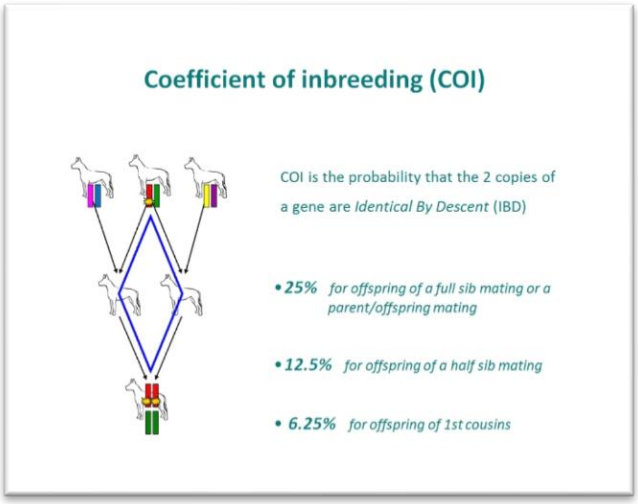
This all leads to the conclusion that using Estimated Breeding Values (EBVs) is a more accurate measure of probable expression of a complex trait in offspring. EBVs are effectively

a risk analysis and can be easily compared for different dogs as part of trial matings on paper to determine which combination of dogs has a higher or lower genetic risk for a particular health concern.



Since selection occurs against the background DNA, then it will alter the allele frequencies in lots of genes, as it results in the 'hitch-hiking' of other alleles to a high frequency. However, mutations are usually detrimental and can cause disease and all organisms carry several damaging mutations.

The Coefficient of Inbreeding (COI) is the probability that both alleles an individual inherits will be identical by descent, that is, originate in the same ancestor. For a brother-sister mating the probability would be 25%, for offspring of first cousins the probability would be 6.25%.



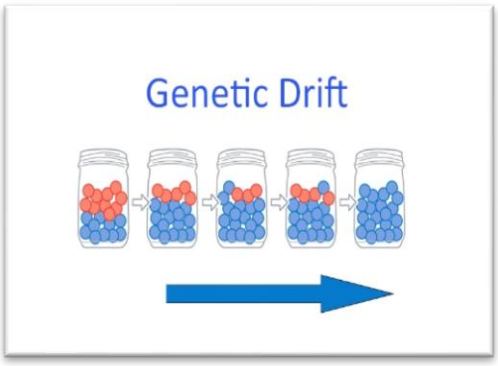
Remember that most mutations will not be expressed if they only occur in a single allele and the individual still has a functioning allele from the other parent. This is what we know as recessive inheritance. This mode of inheritance can result in a detrimental mutation invisibly spreading down through the generations, until it might be several generations removed from the originator – but that originator may now appear on both sides of an individual pedigree.

Over time, natural selection can act against the detrimental effects of inbreeding if the population is large enough as individuals with detrimental mutations would normally be 'culled' out of the population.

When artificial selection is employed, particularly if the detrimental effect doesn't manifest until after breeding age then the situation can arise where the mutation spreads throughout the population. A smaller population is at greater risk from this effect than a larger one as there is a certain amount of buffering capacity against the effects of genetic drift within a larger population.

Both these effects are why we should monitor the COI of potential litters and where possible work to decrease the average COI of a litter within a population. When considering COI, it is important to take into account the number of generations being considered and only compare like for like, as the COI of any given dog or litter will increase the higher the number of generations being considered. This is easily achieved using the ancestors tab within www.iwdb.org.

Inbreeding and genetic drift both act by changing allele frequencies. Within a closed gene pool, like a dog breed, inbreeding is unavoidable over the long term, which is why it is extremely important to measure and monitor the COI of litters being produced.



To monitor the genetic health of the population as a whole it is more effective to measure the *rate of inbreeding*, which is the change that occurs in the average COI over time.

Tom and others at the Kennel Club analysed the data they had for all pedigree dog breeds during 2015 and published the following paper looking at population trends from 1980 to 2014. This paper can be found here

https://cgejournal.biomedcentral.com/articles/10.1186/s40575-015-0027-4

By looking at statistics such as registration figures; distribution of

progeny over sires and dams; average COI and effective population size, they were able to conclude that the single most detrimental breeding strategy for the genetic health of a population is the overuse of popular sires. The analysis for Irish Wolfhounds can be found here… https://www.thekennelclub.org.uk/for-vets-and-researchers/kc-research-publications-and-health-data/breed-population-analyses/

Tom ended his talk with a note of cautious optimism. The rate of inbreeding is improving but popular sires are still making a significant genetic contribution.

The effective population size is a measure of the number of breeding individuals within a population which would be required to achieve the rate of inbreeding seen by random selection. An effective population size of 50 or under means the future of the population can be considered to be at risk. An effective population size of 50-100 means that the rate of inbreeding will increase sharply with each future generation. The higher this figure is, the better a population is able to withstand the negative effects of inbreeding.

Currently, the Irish Wolfhound population is experiencing a negative rate of inbreeding but when we consider the rate over the whole period 1980 to 2014 the effective population size is 222.2, which is actually the 12th highest effective population size of 121 different breeds which the figure was calculated for.

This could be due to the diligence of breeders heeding warnings about trying to reduce the average COI of litters and avoiding the popular sire syndrome, or it could be due to an increase in importation of puppies, and use of sires from outside the UK. These dogs only come with a 3-generation pedigree, so will have lower COIs than is actually the case,

> *"the single most detrimental breeding strategy for the genetic health of a population is the overuse of popular sires."*

thereby skewing the overall statistics. Or it could be due to a little bit of both.

There is no room for complacency with a specialised breed like the Irish Wolfhound. Breeders should continue to ensure that they reduce the overuse of popular sires, and strive to reduce the level of contemporary inbreeding by monitoring the COI of potential litters.

Dr Cathryn Mellersh

Head of Canine Genetics, AHT

Give A Dog A Genome

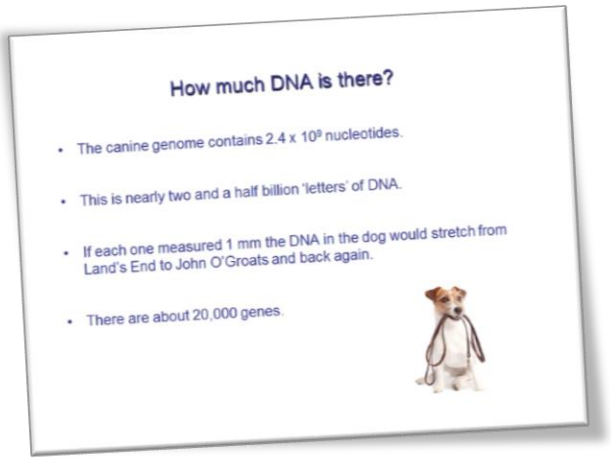
An overview of the GADAG project can be found at http://www.aht.org.uk/cms-display/genetics_gdg.html

Cathryn explained why the GADAG project was necessary by outlining the challenges faced by researchers trying to identify genetic causes of diseases, particularly those with complex inheritance patterns.

The dog genome has about 20,000 genes and these are contained within approximately 2.4 billion nucleotides, so comparing one genome to another to identify the small areas of mutation which may cause disease is an immense computational undertaking.

By comparing an affected genome to the reference dog genome (a boxer named Tasha), it is possible to identify differences in the genome, but if you compare the genomes of any two dogs there would be differences in around 2-4 million places! These differences may indicate candidate variants for the disease-causing process, but they may simply indicate the natural variation that occurs between dogs and between breeds.

The GADAG project, by having reference genomes for many different breeds will allow more comparison of whole genomes thereby reducing the level of candidate variation to a more manageable level. Currently the project is sequencing 77 breeds of dog with some breeds contributing more than one individual dog, so there is a total of 85 dogs over 77 breeds. For some breeds healthy older dogs were sequenced and for some breeds the dogs that are sequenced are those affected by a disease of interest to that breed.



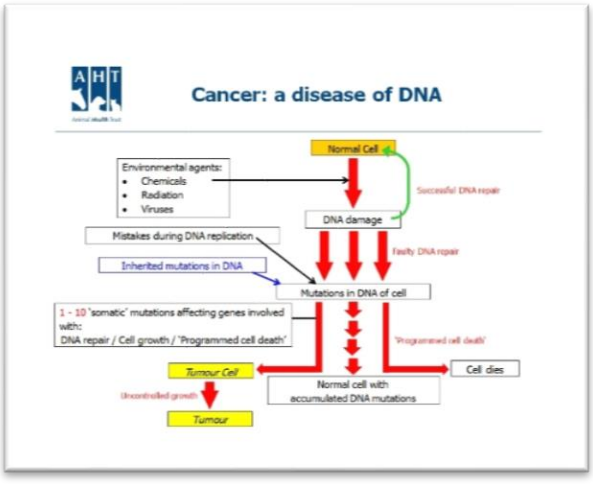
Progress has been good and continues to be, but an unforeseen challenge is the limitation of information technology, which is now creating a bottleneck in processing the information provided by the sequencing laboratory; the sheer volume of memory required for the data is beyond anyone's expectation!

Importantly, the AHT is very keen to ensure that these genomes are available to other researchers and institutions by uploading them to a public resource so that they can also be used by other groups working on identifying disease causing mutations.

Dr Mike Starkey Head of Molecular Oncology, AHT

Identification of Genetic Risk of Osteosarcoma in Irish Wolfhounds

Mike started by speaking about cancer; cancer is a disease of DNA, a tumour arises due to an accumulation of damaging mutations within the cell's DNA. This damage can be caused by environmental factors, but if the cell's repair machinery is faulty then this damage can become fixed as a mutation in the DNA. It should be noted that most mutations don't actually affect genes.



Mutations may be detrimental only to the cell they occur in, resulting in programmed cell death. A kind of cell suicide designed to prevent acquired mutations causing further damage to the tissue. Sometimes, these mutations occur within the critical genes regulating essential processes like DNA repair, DNA replication and programmed cell death.

The accumulation of mutations is what can lead to uncontrolled cell growth, which becomes a tumour, this occurs in 95% of all cancers.

As few as between 2 and 11 mutations in specific genes in somatic DNA are needed to create a cancerous tumour. For example, only 2 mutations cause stomach cancer and 11 are required to create colon cancer.

Inherited mutations are genetic risk factors which are present in all cells of the body and causes an increased risk of developing disease. Mike explained that human studies have shown that disease risk usually comes from an accumulation of many mutations each of which causes a small increase in risk of disease development. Occasionally, it has been shown that one mutation can cause a large increase in disease risk.

There are different modes of expression for these additive risk factors, most are autosomal dominant but some are recessive and some are known to be linked to the X chromosome ('X-linked').

Without using whole genome sequencing it can be extremely difficult to recognise or identify genetic risk factors that are not located within the boundary of a gene.

More recently it has been accepted that epigenetics may also play a role, these are genetic modifications which are caused by environmental factors but are shown to be inheritable. These modifications may also influence disease susceptibility. Currently, there aren't many DNA tests for cancers.

It opens up the possibility of creating a DNA test which may be able to identify individual dogs with an increased risk of developing osteosarcoma later in life.

With specific reference to our Irish Wolfhound project, bone cancer in Irish Wolfhounds has been shown to have a heritability of 0.76 (where a heritability of '0' would mean the variability in expression of the trait is not influenced by genetic variability, at the other end of the scale, '1' would mean the trait is wholly influenced by variations in genotype among the population).

This represents the proportion of the variation in the risk of developing osteosarcoma that is due to genetic differences between individuals.

The relative risk of an Irish Wolfhound developing osteosarcoma is 27.5 times higher than 77 other breeds studied in a 2002 AKC survey.

So why are we interested in identifying these DNA mutations which can confer an increased risk of disease development? It opens up

the possibility of creating a DNA test which may be able to identify individual dogs with an increased risk of developing osteosarcoma later in life. This allows us to monitor them more closely and perhaps affect changes in environment which may inhibit or discourage tumour development.

We can promote the development of drugs targeting DNA mutations inferring increased risk and encourage the development of drugs which prevent tumour creation.

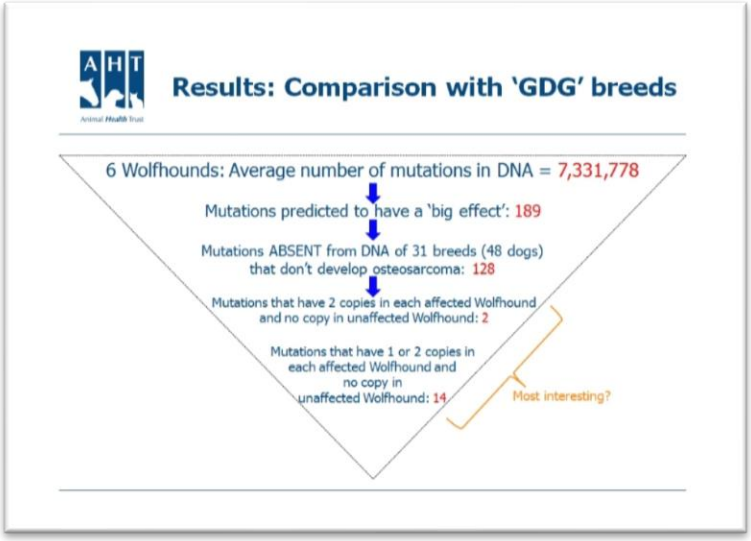
Previously, during this study the researchers have used genome-wide association studies (GWAS) using a library of 173,000 SNPs (single nucleotide polymorphisms) to compare DNA from 151 affected dogs with that of 136 unaffected dogs which were over 6 years old. This method was used to search for SNPs which showed an increased or decreased association with affected dogs. Using this method, no associations were found.

This could be because the risk factors are very rare or conversely, that they are very commonly carried; by only comparing wolfhound to wolfhound it's difficult to be certain of a cause. However, when comparing chromosome 11 of the Greyhound, a region found to have 3 markers associated with osteosarcoma in that breed, 95% of 287 wolfhounds carry the 2 most common SNPs, and 95% of 52 wolfhounds carry all the same SNPs in this 60,000-base region.

Additionally, 8% of the DNA comprising chromosomes 1-38 contain the same SNPs in all 287 wolfhounds, meaning that this DNA is *fixed* in the population. These fixed areas are known to contain genes involved in bone development.

So, it may not be useful to compare affected wolfhound to unaffected wolfhound if all are carrying many of the same risk factors.

A new approach was needed and this is where the GADAG project can be helpful. They have fully sequenced the genomes of 5 affected wolfhounds and 1 unaffected wolfhound – this unaffected dog used was not blindly chosen. They have used a dog who died at age twelve, and had shown no evidence of any cancer. Additionally, this dog only had one copy of the chromosome 11 SNP most strongly associated with osteosarcoma in Greyhounds. These genomes can then be compared to the CanFam reference genome and also compared to other breeds known to have a decreased risk of developing osteosarcoma.



From the variations that were found this way a process was followed to determine which variations would be of most interest to the researchers. This technique is needed to bring the number down to a manageable level in order that each one can be individually investigated. In the 6 wolfhound genomes there were an average of 7.3 million variants so we can see it is essential to identify the most interesting candidates.

The most interesting mutations are those that...

- Are not found in the DNA of dogs from breeds that do not develop osteosarcoma – but need to be distinguished from wolfhound-specific variants that are not associated with osteosarcoma
- Found less often (1 copy instead of 2, or 0 copies instead of 1) in the DNA of unaffected wolfhounds
- Are predicted by computer programs to be deleterious

When using the GADAG sequences to compare the genomes, the results so far indicate;

- Mutations predicted to have a harmful affect = 189
- Mutations absent from the DNA of 31 breeds that don't develop osteosarcoma = 128
- Mutations that have 2 copies in each affected wolfhound and no

copy in the unaffected wolfhound = 2

- Mutations that have 1 or 2 copies in each affected wolfhound and no copy in the unaffected wolfhound = 14

The bottom two categories are of most interest.

When comparing the six wolfhound genomes to those stored in the WGS Consortium breeds, the results so far indicate;

- Mutations absent from the DNA of 93 breeds that don't develop osteosarcoma = 19
- Mutations that have 1 or 2 copies in each affected wolfhound and no copy in the unaffected wolfhound = 4
- Mutations that have 2 copies in the unaffected wolfhound = 7
- Mutations that have 0 copies in one affected wolfhound = 3

The bottom two categories are probably of least interest.

Studying these 19 mutations in greater detail the researchers found that

- 18 are SNPs and 1 is a deletion
- In total these affect 17 genes – 1 gene is actually affected by 3 variants

The researchers have also looked at the consequences of these mutations in order to predict the severity of the changes in the finished protein.

- 15 cause a change in an amino acid – 4 of these are predicted to be harmful
- 1 creates a stop codon, leading to a shortened protein – this is predicted to be harmful
- 2 create new splice regions which may alter the RNA – difficult to predict whether these are likely to be harmful
- The deletion causes a loss of nine amino acids from the protein chain – this is predicted to be harmful

"The aim of this new study would be to identify mutations which could be specific targets for new drugs to prevent osteosarcoma development and/or spread."

The researchers then looked to see if any inherited mutations in the 17 affected genes have been implicated as genetic risk factors in human cancers, and the answer is yes.

Inherited mutations in two of the 17 genes have been shown to cause an increase in genetic risk factor in some human cancers.

Further work now continues to establish how likely it is that any of the 19 mutations actually are genetic risk factors for osteosarcoma. They do this by going back to the original population of 287 UK dogs used in the original GWAS project. They can also try to demonstrate the effect of some of the mutations experimentally.

Further research will include identifying those mutations prevalent in the affected wolfhounds which are not predicted to have a 'big effect' but which are not present in the WGS consortium breeds that don't develop osteosarcoma.

Mike also proposed a new study; 'Identification of recurrent mutations in DNA in osteosarcomas'. This study would look for those somatic mutations responsible for switching on the disease process, turning a genetic predisposition into cancer. To achieve this, the team need to genome sequence the actual tumour cells from a biopsy of an osteosarcoma and compare that with the normal genome of the same dog from cheek swab or blood sample. To achieve this the team still need to collect more samples from bone cancer tumours.

Details about the project and how you can help can be found here...

http://www.iwhealthgroup.co.uk/animal-health-trust.html

The aim of this new study would be to identify mutations which could be specific targets for new drugs to prevent osteosarcoma development and/or spread.

This was certainly a very interesting talk with many exciting developments in such a short time since the funding was provided and the larger GADAG project announced. The IWHG are excited to support this project and are looking forward to the next update.

Dr Regine Vandamme

Of First Avenue kennel and Veterinary Reproduction Specialist

Getting Older – How to Manage Possibilities and Short Cuts.

Regine explained that her first experience of Irish Wolfhounds was with a dog that was taken to her for surgery and the owner did not want him back, so Regine adopted him aged 4 and he died 9 months later of DCM. This interested her in learning about the reasons for a short lifespan in the breed and working towards improving longevity.

A study in Holland and Belgium into lifespan of Irish Wolfhounds conducted in 1998 concluded that the average age at death was 5.5 years in males and only slightly older in females. Regine started to look at possible reasons for this, and decided within her own small breeding program her goal would be to have wolfhounds that had an average lifespan of 8, 9 or 10 years.

So, what is needed to start a breeding program with a goal like this?

- breed with dogs with good health
- ensure their ancestors have good longevity
- use dogs with good temperament
- the dogs must conform to the Breed Standard
- Also, sometimes you have to get some good luck

Regine believes longevity runs in families, so in1994 Regine started breeding older wolfhound bitches (6 years and over) with young males (whose parents and ancestors have lived to a good age). From 1998 she has used even older bitches and paired them with older males, this can involve using frozen semen as males' semen quality can drop as he gets older.

There can be problems using this strategy: older dogs and bitches have more somatic genetic mutations, there is more risk during whelping and an increased likelihood of a long whelping time. So, the bitches must be in good health and Regine supplements them with vitamin B and folic acid starting three months before the mating. Regine is a vet specialising in reproduction and so is well placed to counteract any increased risk. Anyone else employing these strategies should have a good relationship with their vet and ensure that the vet is aware of and in agreement with any breeding proposals.

Three of Regine's wolfhounds at seven years old.
The two males lived till 10 years and 3 months.
The female lived till 9 years and 6 months.

Frozen semen can be a useful tool in taking a short cut to longevity as the health and lifespan of the sire can be assessed retrospectively. The best quality semen is collected when the dog is between 1 and 6 years old. The majority of health problems are likely to appear between the ages of 2 – 4.5 years, so it is possible to store him when he is young and full of vitality, wait until he reaches seniority and is still exhibiting good health and then use him. In this way breeders can tap into a valuable resource many years after a desirable dog has passed away. However, as in normal circumstances the health status of the dog's ancestors must be known.

If you are considering using stored semen, ensure that the quality has been tested by the collecting clinic and that there are enough sperm cells within the sample.

An ideal scenario would be if the male had already produced puppies naturally to assess them, and even better if he also has produced puppies from his stored semen. Regine's preference for frozen semen is that it should be implanted transcervically, but for fresh semen it can be either inserted into the vagina or transcervically, both procedures can be carried out without anaesthesia.

The timing of the procedure is critical and ovulation must be determined by monitoring the progesterone levels in the blood.

No plan is ever perfect and we should remember to be realistic in our expectations, if we aim to have a breed with an average longevity of 9 or 10 years, it unfortunately means that some dogs will still die young, but as breeders we should think about the best plan for the breed and work with that in mind.

Regine truly believes that an average of 9-10 years is achievable within the medium term if we all work towards the same goal.

Action Plan from Seminar

A lively discussion followed all the talks and at the end of the day the audience were asked to help draft an action plan for the IWHG to move forward with some of the ideas and concepts that had been mentioned throughout the day.

In order to facilitate an accurate BHCP being formulated **it was decided to create a breed specific online health survey** which could be taken into consideration when developing the Irish Wolfhound plan. The BHC/IWHG would contact Katy for help to create a useful survey.

The Breed Club representatives were in agreement and would help to raise awareness of the Health Survey once it is available and encourage all their members to complete the survey for their own dogs.

There was also discussion about setting up a Facebook group for interested owners and breeders to discuss the concerns they wanted to be considered within the BHCP.

There was also discussion about the possible development of EBVs based on Serena Brownlie's heart testing data collected over the past 30 years and this is a project that Tom has been considering already.

This of course would be an exciting development and the IWHG is hopeful that they can look forward to discussing this further with Serena and Tom in the future.

We also discussed whether the IWDB could be utilised and this heart research data saved onto a private research area of the IWDB to be available for genuine researchers. Per Arne said it was likely to be possible, if the researchers wanted the facility to be available.

All in all, it was a very educational day stimulating much discussion, with plans for the future being formulated and hopefully leaving all attendees with many ideas to implement in their own breeding programs in order to keep our breed healthy for many generations into the future.

New IWHG email addresses

by Gary Bogart

The IWHG is introducing standardised email addresses for our officers and key post holders. These new email addresses will make it easier for people to contact us, as well as reducing the chance of data breaches and other disruptions.

The new addresses will provide email continuity with breed bodies, The Kennel Club and research institutions.

Organisations will not have to update their contact details when IWHG personnel change positions.

It will also make it much smoother when someone new joins the IWHG, as they will inherit the email address and have access to all the correspondence of the previous post-holder, thus being more prepared and able to deal with ongoing matters.

Just add the following email addresses to your contact list and you will never have to update them again.

Simple!

chairman@iwhealthgroup.co.uk
Rebecca Peek

secretary@iwhealthgroup.co.uk
Linda Forret

treasurer@iwhealthgroup.co.uk
Steven Ritchie

hearttestcoordinator@iwhealthgroup.co.uk
Wendy Heather

hearttestbooking@iwhealthgroup.co.uk
Anne Vaudin

researchcoordinator@iwhealthgroup.co.uk
Maura Lyons

End of Year Review

by Linda Forret (Secretary)

The Irish Wolfhound Health Group continues to monitor and promote the health and welfare of Irish Wolfhounds. Liaising with breed bodies and the Kennel Club, we endeavour to ensure that any concerns are highlighted and reviewed in the most appropriate ways. Research is continuing, and with the most up-to-date and evidence backed research, we have updated guides for both the owner and the veterinary surgeon. These guides are freely available to download from our website:

http://www.iwhealthgroup.co.uk/guidelines.html

Education continues to be a big part of our remit, and to that end we held our most recent seminar in November. More details of that can be found here in this newsletter, but suffice to say that this hugely popular event was very well received.

Funds Our new Treasurer, Steven Ritchie, revised the way of presenting our accounts, and we have moved from a cash basis to an accruals basis. All our income comes from donations that we receive. These donations come in many forms, from regular donations from supporters, to the profits made and donated from particular events, and our Loose Change Tins. Our thanks to all of you who contribute to the group in any way. Every penny counts, and we sincerely appreciate all of you.

Heart Testing

The heart testing scheme continues to offer sessions throughout the whole of the UK as well as having a session in Dublin. The dedication of our cardiologists in providing these sessions must be commended and appreciated. There are still variations in the sessions, with some being very popular while at other sessions we would like to see a few more attendees. Publishing of the results, on a purely voluntary basis is now available, and it would be wonderful to see many more of you taking up that option.

http://www.iwhealthgroup.co.uk/publication-of-results.html

Health

During 2017, we have updated information for major health conditions. We have a number of surveys on our website and always need more people to provide information that can be used by our researchers to improve the health of the breed. Understandably, it will not be your first thought to complete a survey when your hound develops an illness, but without information through these surveys, research is affected and progress falters.

All information gathered is treated in strict confidence, so if any of your hounds have ever been affected by liver shunt, epilepsy or PRA it would be extremely helpful to take a little time to complete this survey.

http://www.iwhealthgroup.co.uk/health-survey.html

Osteosarcoma

We continue to support the Animal Health Trust research and are looking for information from owners.

If your dog is suspected to have OA, or is at least 6 years old and shows NO sign of the disease and blood is being taken for any clinical reason, ask your vet for a little extra, collected in an EDTA tube (1-2ml). If a suspected case is having a biopsy a small piece would be appreciated by AHT (see website for full details)

See our website for full details.

http://www.iwhealthgroup.co.uk/animal-health-trust.html

Nottingham University Vet School student Emily Holdsworth, has been assigned to the Irish Wolfhound osteosarcoma project to conduct research into **attitudes to amputation amongst wolfhound owners**.

We are asking you to support this research by completing one (or both) of the following surveys:

Survey one

http://www.surveymonkey.co.uk/r/IW-amputation

Please complete this survey if you have experience of amputation in your wolfhound but it was for a reason other than bone cancer.

Survey two

http://www.surveymonkey.co.uk/r/canine_amputation1

Please complete this survey if you have never experienced Osteosarcoma (bone cancer) or amputation in your wolfhound.

This is a short-term, time limited project and any help would be really appreciated.

Pneumonia

Pneumonia is a condition that presents itself in a unique way in Irish Wolfhounds. It can be a life-threatening condition, but can also respond well to treatment, particularly if caught early. It is a condition of great concern to owners and there is much informal evidence to suggest that it is occurring more frequently.

We have been gathering evidence on pneumonia for some years now and have developed treatment guidelines that have helped owners and been successful in the treatment of wolfhounds.

We need to gather more data to better understand this condition, and this is dependent on surveys being completed and information collected. The links to the pneumonia survey is here:
http://www.iwhealthgroup.co.uk/files/pneumonia-survey.pdf

http://www.iwhealthgroup.co.uk/files/pneumonia-survey.docx

If any of your wolfhounds have ever experienced pneumonia, please click on one of the survey links. The information you provide may make a difference.

GADAG

Dr Cathryn Mellersh AHT and Tom Lewis KC are very enthusiastic about the huge progress that has been made this year. Irish Wolfhounds were one of the first breeds to participate. Six genomes are involved, including the match funded one, and the genome is already sequenced, the data downloaded and the next step of pre-analysis processing underway.

Atrial Fibrillation

Nottingham Vet School has begun a new research project studying AF in giant breed dogs. There is already a proven link between atrial fibrillation and blood clots in humans, but not yet proven in dogs. If you have a dog with a confirmed diagnosis of AF there is an online questionnaire a link to this is on our website.

http://www.iwhealthgroup.co.uk/nottingham-university-1.html

This is an abridged version of the IWHG end-of-year review that has been sent to breed bodies for inclusion in their magazines.

https://www.facebook.com/groups/IWhealthgroup/