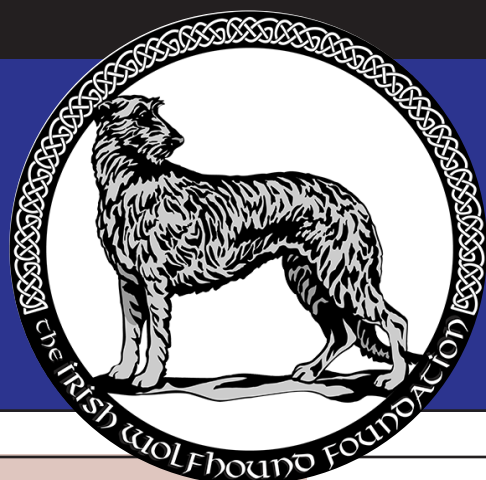


THE Irish Wolfhound Foundation



Focus

2024

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Focus

Audrey St Clair, Editor
537 Hackman Rd.
Lititz, PA 17543
thecoopersinn@aol.com
717-626-2658

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Why Does Research Take So Long?

Most of us have, at one time or another, responded to a request for help with Irish Wolfhound Foundation (IWF) research projects. We have donated money, brought our dogs in for testing, filled out questionnaires, let researchers have samples of blood and saliva, and, in some cases, made repeated visits to the vet for testing not directly related to the health of our dogs. Where has all this effort gone? How has it benefited the Irish Wolfhound breed? Whatever happened to all that work and money? Why does it take so long to see results?

First, to do a research effort one needs a question. Questions may seem simple but often they are not. The Life Cycle Study (LCSII), for instance, is an ongoing project with no definite end to find the diseases that are most common in our breed. Yes, we know from previous studies that most wolfhounds die of cancer or heart disease. These are complex diseases and it is probably more than the IWF can do to address them. The IWF has been working with other breeds and agencies (the AKC Canine Health Foundation and the Morris Animal Foundation) to address these more complex issues. The LCSII does provide annual feedback but it is on a limited number of dogs. We know from AKC statistics that around a thousand Irish Wolfhounds are individually registered annually and about twice that number are born to registered litters. We do not know what happens to most of these dogs. Thank you to everyone who continues to support the LCSII and provide data on your hounds. All

hounds are welcome in that study. Pet owners should be encouraged to enter and to continue to update. Reminders will be coming out soon. What do we get out of that study? We get ideas for future research and some idea of progress made.

There are also some studies that require testing dogs at a young age and then seeing what happens to them over time. The Lifetime Cardiac Study and the current Canine Osteosarcoma Early Detection (COED) study are two such studies. Dogs are enrolled young and followed through their lifetime so we don't see results for 4-10 years.

Even when results are back, the data needs to be analyzed and submitted for publication and review before it can get out to our veterinarians. Often reviewers even disagree with recommendations from the researchers and come up with additional questions.

As an example let's take two relatively recent and "simple" studies to determine whether it is wise to use certain drugs during and prior to surgery in order to prevent post operative bleeding. Post operative bleeding is fairly common in racing greyhounds and has been attributed to a disorder called fibrinolysis, a premature dissolution of blood clots. The use of epsilon aminocaproic acid (EACA) (brand name Amicar) is recommended for optional surgeries and trauma related injuries with hyperfibrinolysis. EACA is a relatively safe drug but does have some rare, but serious side effects. In humans it is recommended that some screening take place prior to using this drug and it is contra-

indicated in patients with known liver or kidney impairment.

Is there a problem?

The first step in any research is identifying a problem. The bleeding issue had been mentioned in numerous Facebook posts and even the IWCA website referred to the articles on greyhounds. In February of 2019 the IWF was approached by Dr. Daniel Fletcher, PhD, DVM, DACVECC, an expert in emergency veterinary medicine at Cornell University and a wolfhound owner. Dr. Fletcher wondered how serious the problem was in the breed and whether EACA was an appropriate treatment for it. He proposed a study to answer those questions.

On looking at the IWF data base of about 1500 IWs for which cause of death was known, 27 seemed to have died of excessive bleeding. This did not include dogs that had bleeding but did not die. It was also not very specific as to when the bleeding occurred, nor did it identify the cause. Nonetheless it indicated that additional study might be worthwhile. Certainly if even a few wolfhound lives could be saved, the proposed effort would be worthwhile.

The next step taken was to put a survey out to IW owners to see if the problem was more common than our data indicated and to get more information on incidents of bleeding. The results came back in March of 2019. One hundred responses were received, with some owners reporting on multiple dogs. In this type of survey, it is normal

Research (Continued on page 5)

Update for IWF Research



Your much appreciated donations and much appreciated participation supports research to improve the health of all Irish Wolfhounds.

Active research efforts continue and although progress often seems slow there is more information available to improve the health of the hounds. Thank You.

OSTEOSARCOMA- STILL LOOKING FOR THE GENE

In published data since 1966 osteosarcoma has been the number one killer of Irish Wolfhounds. 1 in 5 hounds dies from osteosarcoma.

Certainly part is IW rapid growth and giant size but consider the Great Dane growing just as fast and standing just as tall and the parent club reports only 12% of deaths are from osteosarcoma.

An IWF backed report from the University of Wisconsin showed the heritability index of osteosarcoma in the Irish Wolfhound was 67, remarkably high for a cancer. These observations and others keep the search for genetic markers of osteosarcoma alive despite a long and so far unsuccessful journey.

Dr Susannah Sample is concentrating on the subset of Irish Wolfhounds that have osteosarcoma at age 5 or younger. Using the new IW genome and investigating a narrowed population may lead to those elusive osteosarcoma genes.

Dr Samples reports the sequencing of all samples is completed. Data analysis is being done at Texas A & M Veterinary School and was delayed while funding transfers were corrected. The team is hopeful for preliminary results by spring. Any findings will need to be validated so if you have a control hound (over 10 without osteosarcoma) or a young hound with osteosarcoma please consider participating.

The IWF and IWCA also support other ways to decrease the osteosarcoma burden. Dr Jaime Modiano et al at the University of Minnesota are validating a blood test to detect osteosarcoma before it is clinically apparent. The goal is to treat these hounds so the osteosarcoma is never expressed. It sounds like magic but the science is sound and great strides have been made in hemangiosarcoma with this platform. The COED (Canine Osteosarcoma Early Detection) study closed enrollment a year ago. Participating hounds will be followed three years before a preliminary report is available. The research team notes 100% of IWs enrolled have responded to update requests.

Via directed donor funds from the AKC Canine Health Foundation, the IWF and IWCA support several studies utilizing histiotripsy or directed ultrasound as a treatment for osteosarcoma. Researchers have shown osteosarcoma can be eradicated leaving surrounding tissue intact. This is a very promising treatment and may cure some hounds but use will be limited by cost and the need for special equipment.

CARDIAC PROBLEMS BETTER UNDERSTOOD

Heart problems have long plagued the breed and even five years

ago were the second leading cause of death. Owner support and participation in studies has resulted in much improved understanding of IW heart disease. In the North American IW cardiomyopathy is preceded by atrial fibrillation in 99% of hounds so the less expensive EKG can be used as a screening test for cardiomyopathy. We now know most atrial fibrillation starts around age 5 years and that there are few abnormal hounds under age 3. Most atrial fibrillation is inherited in the IW and this inheritance is autosomal dominant with variable penetration. Thus some hounds carry the gene may present with afib at age 4 while others, even in the same litter, may carry the gene and not develop afib until age 10 or die of something else before developing afib. We know cardiomyopathy in the IW responds to medication. We know early treatment is associated with improved clinical outcomes.

At present the incidence of congenital valve disease is thankfully low in our breed. This was reinforced by a recent IWF puppy auscultation clinic where no puppy had a significant murmur needing a follow up echo.

REPORT ON ABNORMAL GENE TEST INVOLVING HEART MEDS

Three years ago a polymorphism in the ACE gene was described in dogs. In humans mutations in the ACE gene can decrease the effectiveness of ACE inhibitors, common medications used to treat heart failure. With support from the IWF, Dr Emily Seuss of CVCA investigated this in the Irish Wolfhound. 140 Irish Wolfhounds were genotyped and an astounding 83.3% were homozygous (had mutations from both sire and dam) for this mutation and 13.2% were heterozygous. Only 3.5% of the IWs genotyped did not carry this mutation. However after a two week challenge with benazepril (an ACE inhibitor commonly used to treat heart failure) ALL Irish Wolfhounds regardless of their genetic status responded appropriately to the medication. **THUS THIS MUTATION APPEARS NON FUNCTIONAL in the Irish Wolfhound. THERE IS NO PROBLEM WITH THE USE OF ACE INHIBITOR MEDICATIONS to treat heart failure in the Irish Wolfhound.**

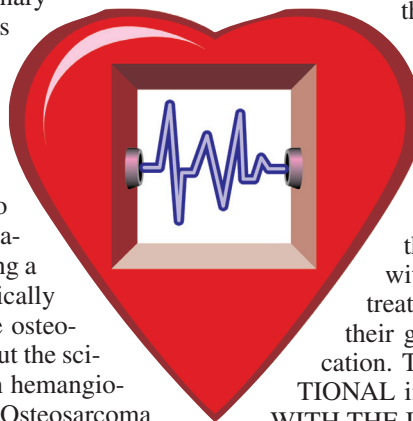
Dr Seuss sent a huge thank you to participating owners and hounds with this report.

CARDIAC CLINICS CONTINUE

The IWF continues to sponsor cardiac screening with EKG and Echo offered at the National and where possible, regional specialties. Support is given to EKG clinics at any IW gathering. There is less atrial fibrillation and cardiomyopathy than 10 years ago but not yet enough data to say with certainty awareness and more careful breeding has led to less cardiac disease in the IW.

THE OTHER CARDIAC ARRHYTHMIA

The number of hounds with VPCs or ventricular premature beats has increased over the last several years and the VPC study continues to enroll hounds. The original hypothesis that VPCs on screen-



ing EKGs in the Irish Wolfhound were benign does not apply to all hounds. After holter monitor recordings many of these hounds had arrhythmias needing medication and were at risk of fainting or sudden death.

In the Irish Wolfhound only atrial fibrillation is associated with developing cardiomyopathy. Unlike in the Boxer or Doberman, VPCs in the IW do NOT lead to cardiomyopathy. Dr Jackie Post recently presented a poster "Significance of Ventricular Premature Complexes in Irish Wolfhounds and the Development of Irish Wolfhound Cardiomyopathy" describing this. There was also a recent publication from Dr Lisa Freeman reporting the connection of pulsed diets and VPCs in the Irish Wolfhound. Continued publications from the data are expected as enough information is accumulated to support or disprove the original hypothesis. At present a holter monitor is recommended for any hound with VPCs found on a screening EKG.

SEIZURES

In her paper in 2006 Dr Magi Casal characterized seizures in the Irish Wolfhound. The inheritance was recessive with variable penetrance. Since that time work has continued to identify genes associated with seizure activity in the IW and also many other breeds. It has been a difficult journey. Seizures continue. The carrier population is exceedingly difficult to identify. Just remember if a seizure puppy is produced BOTH parents are carriers. They will never have seizures and if bred to others may not produce seizure progeny but they may be adding to the carrier population. The IWF continues to sponsor the effort for a genetic test for seizure carriers.

In a recent communication Dr. Casal reports in the last genome wide association data they found 3 regions of interest for epilepsy, not surprising as she feels there is a major gene with modifier genes associated with epilepsy in the IW. She states one of the regions of interest has been located before, but the dog genome wasn't as detailed at the time so we couldn't do much with that information other than sequence a potential gene. She continued, at the time we thought ANK3 had something to do with epilepsy, and we sequenced the entire gene, which was super long and cost a lot of money. But, alas, we did not find any mutations or variants that could be associated with causing epilepsy. In any case equipped with this new information, we have sent one affected dog for whole genome sequencing. We are waiting for the results and are very excited to analyze them. A project that has taken decades. It seems there is a light at the end of the tunnel.

LYMPHOMA

In addition Dr Casal reported they found a region of interest for lymphoma and have sent an affected hound for whole genome sequencing to confirm. In this region of interest there is a gene that codes for a protein with known interactions with lymphomas in people.

PNEUMONIA

The Irish Wolfhound has a higher incidence of pneumonia than many other breeds. It is unknown if IWs have an inherited vulnerability. Many hounds have recurrent episodes leading to longer and longer courses of antibiotics. Because of the rapidity of clinical deterioration initiation of broad spectrum antibiotics are recommended early and the length of treatment needed is not clear.

NEW APPROACH

The IWF has sent a letter of support for Dr. Corey Fisher from the University of FLA for his project "The Use of Stem Cells to treat Canine Pneumonia." Currently pneumonia treatment involves antibiotics and supportive care but targeted treatment to repair lung damage is lacking and mortality for severe pneumonia in dogs remains high at 20-30%. Stem cells have been previously shown to greatly improve the healing process in lung tissue in mice and rats. The hypothesis is dogs requiring supplemental oxygen because of pneumonia will have faster recovery with a single infusion of mesenchymal stem cells than dogs receiving standard therapy. This study is already recruiting from

the FLA Emergency clinic and awaiting further funding approval from AKC CHF. Both IWCA and IWF will offer further support via the directed donor funds when the project is approved.

There is another pneumonia proposal from Dr. Mark Dunning UK to characterize the pulmonary microbiome. Are IWs different than breeds not prone to pneumonia? If hounds are different are they more prone to pneumonia? They also plan to evaluate the subclinical carriage of respiratory pathogens in the IW to see if that might contribute to the frequency and severity of pneumonia. Innovative ways to approach pneumonia are of great interest and hopefully this project will be ready for review soon.

BLEEDING

Although bleeding is reported as a cause of death in only 1-2% of hounds in data collections, everyone seems to know of a hound bleeding or possibly dying after bleeding. There are many reasons to bleed. Because IWs are sight hounds and delayed post operative bleeding is so well described in Grey hounds this seemed a good place to start. Dr Dan Fletcher began investigations at IWANE and was able to test hounds for hyperfibrinolysis. (Fibrinolysis is the breakdown of clots.) In delayed bleeding the hound is able to form a clot but the clot breaks down too soon leading to renewed bleeding. There is a treatment for this (Amicar) He found compared to normal controls (dogs of comparable size but not IWs.) IWs did form weaker clots. This was published and set the stage for future research but did not answer the question, should IWs have Amicar available for surgeries? Should it be considered after trauma? It has certainly helped Greyhounds.

And then came word of a mutation linked to hyperfibrinolysis in the Scottish Deerhound. The genetic test is called Depohgen and is commercially available. In the deerhound this mutation is associated with early clot breakdown. Amicar is recommended for dogs with positive tests. About 24% of Deerhounds carry this mutation.

Preliminary tests showed a high incidence of this mutation in the Irish Wolfhound with about 75% of hounds positive. A study was quickly submitted by Dr Fletcher and, with heroic participation by hounds and owners, blood samples for 20 normal, 20 heterozygous (carrying one copy of the mutation), 20 homozygous (carrying two copies of the mutation) were collected and processed at Delaware Valley 2023. It is not clear in the IW that this mutation is functional. There is some evidence that homozygous variant dogs do appear to have enhanced fibrinolysis compared to heterozygous and normal dogs. Dr Fletcher offered his personal opinion as a wolfhound owner that if he had a homozygous hound undergoing significant surgery he would treat with aminocaproic acid. The evidence is not clear enough to recommend this test in the Irish Wolfhound. But if there is any history of delayed bleeding in your hound's relatives checking and treating may be prudent.

NORMAL BLOOD VALUES for IWs

Sighthounds often have "normal" common blood test results out of the "normal" canine ranges. This has been characterized in the Greyhound. Working with the Greyhound Health Initiative and supported by the IWF Dr Dan Fletcher collected blood from 150 hounds. All the blood is processed and in the hands of statistics people. A draft of the reference intervals is promised to the IWF by the end of the year and will be distributed as quickly as possible.

Without you and the participating hounds none of this would be possible

Thank You



Life Cycle Study

Heart Testing 2024



This year the IWF sponsored testing at the IWCA National Specialty, the Irish Wolfhound Association of the West Coast, the Irish Wolfhound Association of Delaware Valley and at Northern California Irish Wolfhound Association. Still being added to the total are EKGs from the Great Lakes Irish Wolfhound Association match. Special thanks to Carole Silverthorne and Anne Livingston for running the IWCA and IWADV clinics when the usual crew was unable to make it. The team of cardiologists included Dr. William Tyrrell (IWCA), Dr. Steve Rosenthal (IWCA & IWADV), Dr. Brett Boorstin (IWAWC), and Dr. Justin Williams (NCIWC).

A total of 115 dogs were tested so far and we have results on 107 of those. 68 of these were bitches and 39 were males. Since testing was done at shows, most of the dogs were between 2 and 4 years of age but we also tested 36 veterans and 22 of those were over 7 years old. Only 15 dogs had abnormal EKGs and only 5 had abnormal echoes. There were a few dogs that had minor valve leakage and “innocent” murmurs.

The IWF has purchased a new EKG machine with better capability to store, analyze and distribute EKGs electronically. Our cardiologists have been using this. This makes it possible to send owners the results of the testing, including the EKG strip, as attachments to an email. It also makes it

possible for technicians to take an EKG and send it to doctors to review the results from a distance.

This was the first year that the IWF sponsored testing at IWAWC. Dr. Boorstin, who helped with heart testing at the IWCA National in 2022 and with IWADV and trained under Dr. Tyrrell had moved to California. He brought two of his technicians, Kate Watkins and Christine Komada with him to Santa Maria and they tested 26 wolfhounds, almost half the entry. We are hoping to see Brett, Kate and Christine at the National Specialty in Utah next year.



Dr Boorstin doing heart testing in California



Two technicians Kate Watkins and Christine Komada helping Dr Boorstin at Santa Monica

Research (Continued from page 1)

to get more responses from people who have seen the problem, yet there were responses from 51 affected dogs and 53 not affected. Of the affected dogs, only 23 died and only 29 were within one week of surgery. There is no way of knowing how many people read the survey and didn't respond. We don't even have a good estimate for the number of wolfhounds, or wolfhound owners in the country. The survey did tell us that the problem was real. Thanks to all who responded and especially to those who had not seen the problem. Your response was every bit as important.

While this number of dogs is nowhere near the number of IWs affected with heart disease or cancer, it was possible that a fairly simple and inexpensive treatment could save IW lives. It was worth doing the study. That left the question: is what we were seeing in Irish Wolfhounds the same as what had been seen in greyhounds?

Dr Fletcher proposed a study comparing a number of Irish Wolfhounds with a control group of unrelated dogs matched in size and age. This would use a specialized test TEG, that has to be done within 30 minutes of collecting blood and also processing that blood for additional testing while it was fresh. The intent was to determine if the kind of issues seen in greyhounds were also seen in IWs.

Generally the next step in any study is getting researchers under a contract or grant. This is no easy process. The IWF and Cornell University had to agree on a contract and get the necessary signatures before anything was official. This is a process that may take six months to a year and we could not get a contract started before the end of the summer at best. Meanwhile, the best chance we had of getting enough dogs, researchers and equipment together in one spot was the IWANE Specialty in late June. The IWF Board agreed to pay some of the expenses that could be billed directly up front and Dr. Fletcher took on some expenses in his research budget. In fact, the company making the machines for TEG testing contributed some materials as well. We agreed in principle on the work to be done and at IWANE 27 Irish Wolfhounds had blood drawn and tested with the TEG machines. Again, thanks to those owners who participated in June of 2019.

After the IW It still took awhile to get the project under contract but finally in late February of 2019, a contract was signed. Time to completion (Final report and submission of a journal article was estimated at 12 months.) Three weeks later,

almost everything went on hold for COVID. At Cornell there were staff shortages and new procedures. Clinical needs took precedence over research.

Many IW activities were also delayed or canceled, including the 2000 National Specialty. Everyone working on the research had other priorities. In March of 2021, some of the testing still had not been completed but, by May of 2021, enough had been done to give some preliminary conclusions. Dr. Fletcher was still not allowed to travel but he gave a presentation by Zoom and sent it to the IWF for our website.

Later that year an article was submitted to the Journal of Veterinary Emergency and Critical Care. This, was not the end of the story. Quality journals like the JVECC are peer reviewed. That is the article had to be submitted to a group of experts in the area. These reviewers may ask questions, suggest changes and additional work and even disagree with conclusions. When their input is received by the authors, the authors must respond to the critiques and questions. They may have to do additional work or make substantial changes to the article. This process can go back and forth more than once. Reviewers are usually volunteers with other jobs. Authors may move on to other projects or finish a degree and leave the school. Everyone involved has other work to do.

Once an article has been agreed upon and is ready for publication the exact date of publication depends on the other articles the journal has to publish. If an article is of general interest to all dogs it may take precedence over an article about a single, relatively rare problem in an uncommon breed. In the case of this study, the final publication date was May of 2024, more than five years after the study was initiated and the first people volunteered to help by filling out the questionnaire.

Meanwhile, at Washington State's University, a genetic test (DEPOHGEN) had been developed that seemed to be linked to post operative bleeding in Scottish Deerhounds. The proof was largely based on anecdotal data and was not conclusive but the gene coded for a protein involved in clot maintenance so the mechanism made sense. It was decided to test some other breeds to determine the incidence of the gene. At the 2023 National Specialty the IWF gathered cheek swabs on almost 100 Irish Wolfhounds and those were tested for DEPOHGEN at WSU. The results were surprising. Out of 94 wolfhounds from around the country, 24% had two copies of the gene and 52% had one copy of the gene. Why surprising? Many IW

surgeries do not result in serious post operative bleeding. We don't know the exact percentage because we don't really know how many IWs have surgery or how many have bleeding issues but certainly it isn't 75%.

Like most studies this gave rise to more questions. Was the DEPOHGEN predictive of post operative bleeding? If so, should wolfhound breeders use the test in making breeding decisions? A proposal from Cornell addressed the first of these questions.

Fortunately, given our prior experience they turned out to be very flexible and responsive. For instance, the plan had to be approved by an organization that supervises animal experiments even though all we were planning to do was draw some blood from each dog. Travel plans had to be made and some supplies procured even before the contract was signed. Fortunately both parties were able to move forward in good faith.

In order to show that the DEPOHGEN was predictive, the Cornell researchers could not start out knowing the genetic makeup of the dogs. The IWF then had to arrange for genetic testing and pick the dogs to participate in the study and schedule the blood testing. Naturally, at the last minute some changes occurred when dogs or owners weren't available on the day. Again we have to thank those people who did the genetic testing, in a rush, and showed up for the testing that day.

So when will the results be out? Dr. Fletcher spoke briefly on his findings at the IWCA specialty in May of 2024 and that is on the IWCA website. We have some preliminary results and the paper should be ready for submission by the end of the year. Nice it is submitted the review process will begin. Publication will depend, again, on the reviewers and the number of suggestions they have. This article has more interest than the first study simply because there are more breeds that have been shown to have the DEPOHGEN mutation and those dogs will also be interested in the results.

A third study also will be submitted at the end of the year. For this study a group of IWs had blood collected and tested to determine if the norms for blood testing in Irish Wolfhounds are different from the norms that labs use for all breeds.

Thanks to everyone who submitted samples for all of these projects. It may be awhile yet before all the questions we asked are answered. One thing is certain, there will be additional questions. Most of the dogs in these studies are also in the Life Cycle Study so we will be watching their health through their lifetime. Please stay in touch.

What Health Tests Should Irish Wolfhounds Have?

Breeding Irish Wolfhounds should be tested for hip dysplasia, elbow dysplasia, congenital heart problems and congenital eye problems. These tests can be performed after the age of two.

ALL adult Irish Wolfhounds should be screened for congenital heart problems, preferably annually. Heart disease is often treatable if caught early.

Puppies should be tested for liver shunt before going to their new homes.

2025 Irishwolfhound Breeder's Symposium

The Irish Wolfhound Breeders' Symposium 2025 will be held on Feb 1, 2025 at the Doubletree Hotel Westport- St Louis, MO, hosted by Gretchen Bernardi and Melanie Mercer DVM with support from the IW Foundation. Topics will include genetic testing and diversity, breeding plans with a goal of improving the health of our hounds and an afternoon session featuring a panel of experienced IW breeders.

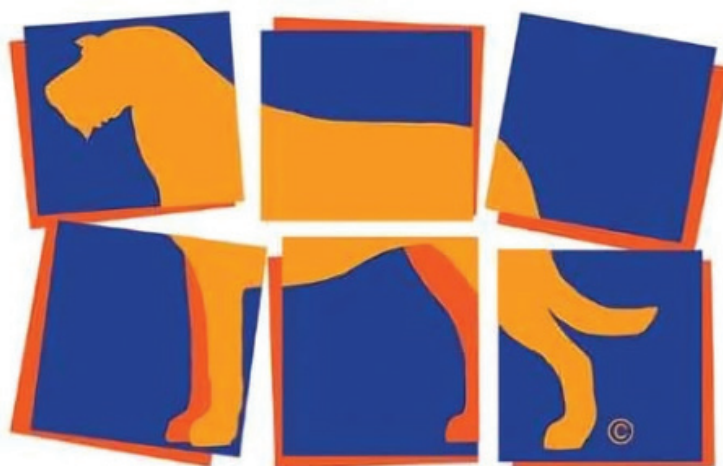
We hope you'll join us for this educational event. It is open to EVERYONE - If you're a breeder: we hope to provide practical information to help you develop your breeding program. If you're NOT a breeder: you can better understand what a good breeder considers in their program as well as personally get to know other supporters of our breed.

Contact Melanie at iwbreederssymposium@aol.com or 214-641-6578 for more information or to register.

Registration for the event including buffet lunch and dinner on site Saturday is \$155.

Registration without meals- \$50.

Hotel bookings for the group rate can be made directly at <https://group.doubletree.com/qelfs>



IRISH WOLFHOUND BREEDERS' SYMPOSIUM

The Irish Wolfhound Foundation, Inc. **Treasurer's Report**

\$495,698.62 Total Cash Assets @11/30/24

Category Funds:

\$234,309.26 General Endowment

\$31,857.28 Rescue Fund

\$229,532.08 General Fund

Disbursements – 10/1/2024–11/30/2024

\$8,086.38 Health Research

\$8,086.38 Total Disbursements

Donations - 10/1/2024–11/30/2024

\$15,951.91 General Fund

\$125.00 Rescue Fund

\$16,076.91 Total Donations

Help the Hounds

Check out the IWF website www.iwfoundation.org

*There are a number of ways you
can help us help Irish Wolfhounds:*

- ❖ **Donate** - We are grateful for donations of any size.
- ❖ **Join** - Membership in the IWF is a great way to support everything we do.
- ❖ **Gift a Membership** - How about giving your vet the gift of membership?
- ❖ **Include the IWF in Your Estate Planning** - consult your tax advisor for guidance.
- ❖ **Enter Studies** - Larger studies give us better data which leads to more reliable conclusions.
- ❖ **Bring Your Hound to Screening Clinics** - This not only supplies us with more data, it helps your hound!
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