# 2013 HEMOPET REPORT for the IWS THYROID STUDY PROJECT

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The following report summarizes our findings for the IWS Thyroid Study that began shortly after my presentation at the IWSCA 2006 National Specialty. Florence Blecher generously donated $500 to cover the initial set-up charges for the study. Our study has gathered data in 2 ways and is ongoing.

**Background**

Blood samples are submitted to us using the special Hemopet IWS Test Request Form and pricing [$55] plus the required IWS-Hemopet Thyroid Study Questionnaire. OFA Thyroid Registry testing is also offered [$85] and requires a completed and signed OFA Thyroid Registry Form and separate $15 check made out to OFA. At the 2007 IWSCA Specialty, the IWSCA Breeders' Committee authorized a $20 subsidy per dog, thereby reducing lab fees to owners. All submissions and results are kept strictly confidential; findings are only provided to the owner of record and their veterinarian. Only aggregate data summaries are released and made available to the IWSCA and its committees.

Thyroid study data from MSU thyroid profiles, IDEXX/ Vita-Tech in Canada, and Texas A & M University have also been entered into our data base when accompanied with a completed IWS-Hemopet Thyroid Study Questionnaire.

IWS are also enrolled in the collaborative genetic study with Hemopet and Dr. Lorna Kennedy, Centre for Integrated Genomic Medical Research, University of Manchester in the UK to identify the genetic DNA MHC/DLA markers associated with thyroiditis in the breed. There are two published papers to date on this research [Kennedy LJ, Quarmby S, Happ GM, Barnes A et al. Association of canine hypothyroid disease with a common major histocompatibility complex DLA class II allele. Tissue Antigens 68:82-86, 2006; Kennedy LJ, Hudson HJ, Leonard J, Angles JM, et al. Association of hypothyroid disease in Doberman pinscher dogs with a rare major histocompatibility complex DLA class II haplotype. Tissue Antigens 67:53-56, 2005.] We are an author on the 2006 paper.

To participate in the UK DNA study, we need 3-5 mL of whole blood in EDTA [LTT] sent along with a signed informed consent. All submissions to the UK for this study are anonymous. *However, please note that Dr. Kennedy currently has no research funding to analyze new DNA samples, so they are stored frozen at -30 $^{o}$C.*

All test submission forms and questionnaire are available from the www. iwsthyroidstudy.com.

**Current Findings**

When we began, we determined that the definitive data base needed to establish the norms and prevalence of hypothyroidism in IWS would ideally require 200-400 healthy dogs of varying ages and both sexes -- females not in estrus, coming into estrus, pregnant, or lactating. Since beginning the study in June 2006, we have enrolled 519 IWS.

Since mid-August 2006, 142 IWS whole blood samples have been submitted to Dr. Kennedy for the UK Thyroiditis Genome Project. Congratulations to those IWS supporters for this impressive effort !

We have entered results and questionnaire responses for 519 dogs. Samples were received from the US, Canada, England, Holland, Finland, Sweden, Australia, and New Zealand.

## SUMMARY OF RESULTS FOR HEMOPET IWS THYROID STUDY (through April 2014)

| # IWS | Testing Lab | THYROID STATUS * † | | | |
|---|---|---|---|---|---|
| | | Normal | Hypothyroid | Equivocal | Autoimmune Thyroiditis† |
| 231 | Hemopet/Antech | | | | |
| 267 | Hemopet | | | | |
| 17 | MSU | | | | |
| 2 | Antech Other | | | | |
| 1 | Vita -Tech | | | | |
| 1 | Texas A & M | | | | |
| **Total 519** | **6** | **429** | **85** | **10** | **14** |

* results status not categorized by testing laboratory to maintain anonymity. † 14 dogs had elevated thyroid autoantibodies and 10 of these were hypothyroid; 2 dogs also had Addison's disease; 34 hypothyroid dogs received thyroxine therapy.

**Summary of Findings for Thyroid Function Testing**

**These results indicate that 16.4 % (85 of 519) of the IWS tested were hypothyroid**. Some of these hypothyroid dogs were subsequently retested after being placed on thyroxine therapy, but they were only counted once in the data base. Ten dogs tested in the equivocal category and needed to be retested in another 4-6 months. [Note: in 2007, 8% of the IWS tested were hypothyroid. In 2008 that number was 13.5%. In 2009 that number increased to 16.8%; although it decreased slightly in 2010 to 15.4%, and increased slightly in 2011 to 15.8%, and returned to 15.1% in 2012. For this 2013 report, 16.4.1% of the total number of IWS tested were hypothyroid.]

**Fourteen dogs were diagnosed with autoimmune thyroiditis** based upon finding elevated levels of either T3AA, T4AA or TgAA [i.e. T3 or T4 autoantibody, or thyroglobulin autoantibody]. [Note: in 2007, 3 dogs were diagnosed with autoimmune thyroiditis. In 2008 and 2009, that number increased to 5 and 7dogs, respectively. For 2010, the total increased by one dog to 8, and increased again to 9 in 2011, and 12 in 2012. In the current report, the number had increased to 14. The latest cases had extremely high thyroglobulin autoantibodies, which reflected the early acute inflammatory phase of this thyroid destructive process.

**Two dogs had Addison's disease** (autoimmune hypoadrenocorticism).

As autoimmune endocrine disorders have a heritable basis, the above thyroid testing data support the need to actively screen all IWS breeding stock, in contrast to earlier assumptions that IWS are at relatively low risk for developing hypothyroidism.

Review of the data collected so far indicates that the normal reference ranges for IWS typically fall within those limits established by us for other medium-sized breeds.

**Summary of Findings for UK Thyroiditis Genome Project**

Of the 142 IWS samples submitted to Dr. Kennedy to date, 101 have been genotyped (82 healthy control IWS and 19 thyroiditis/ hypothyroid cases). This includes one pair of siblings where one is affected and the other healthy. These DNA Study blood samples were collected throughout North America and sent frozen in dry ice from Hemopet to Dr. Kennedy's lab in the UK. This is part of Hemopet's contribution to her collaborative research study.

Dr. Kennedy's findings to date showed that like some breeds studied, but in contrast to some other breeds, the IWS does not appear to have a strong association between their MHC/major histocompatibility complex genes and hypothyroidism. Nonetheless, the results show an interesting increase between the IWS case vs control groups at DLA (Dog Leukocyte Antigen) Haplotype 8 (23.5% of cases vs 5.3% of controls).
Additional characterization of the IWS population found no increase in the number of hypothyroid IWS that carried the haplotypes 3, 5 and 10, which were previously found linked to hypothyroidism in several other breeds with the gene DLA-DQA1.

While the IWS as a breed does have several DLA class II haplotypes that carry the rare DQA1*00101 genetic marker allele associated with affected dogs of other breeds, none of the affected IWS cases had this haplotype. In contrast, a different haplotype was raised in the 19 IWS cases. The frequency of the hypothyroidism risk allele in the IWS breed as a whole group has been estimated by Dr. Kennedy to be at 25%.

Further definitive conclusions about these IWS hypothyroidism gene associations will require more samples of healthy and hypothyroid IWS. Dr. Kennedy estimates needing another 35 healthy control and 43 hypothyroid IWS to screen their DNA with the new higher density more powerful genomic array. With the cooperation of the IWSCA and IWS owners, we can and need to make this happen ! Currently, the continuation of this study is being financed through the generous donations of three individual IWS fanciers. At this writing, the IWSCA Breeder Committee has yet to endorse further participation by the parent club.

To confirm this finding, we need to send more blood samples to the UK from **affected** thyroiditis/ hypothyroid IWS to determine if this is the significant associated haplotype, If this finding is confirmed, then the thyroiditis marker in IWS has been identified.

This important research should benefit the health and longevity of all future IWS.

[ Definitions: A haplotype is a combination of alleles for different genes that are located closely together on the same chromosome and that tend to be inherited together. An allele is a pair or series of different forms of a gene that can occupy the same place (locus) on a particular chromosome and that control the same characteristic.]