UPDATE – UC DAVIS ADDISON'S STUDY IN TOLLERS

Written by Jane Folkman and reviewed by Angela Hughes from UC Davis.

The University of California, Davis Addison's disease study officially began in December, 2003 after the US Annual meeting and show held in Maryland earlier that September. It was begun as a result of club members noticing an unusually large number of affected Tollers. This observation was supported by the Toller Health Coalition Survey which found that approximately 1% of the Tollers included in the survey had been diagnosed with Addison's disease. This represents a 10-fold increased risk over the general dog population. As a result, Addison's disease is the number one health issue identified by the Health and Genetics Committee of the NSDTC (USA). Thanks in large part to club members, 554 Toller DNA samples have been submitted to date specifically for the Addison's study at UC Davis and an additional 130 Toller DNA samples have been submitted for other studies. Combined, these databases likely represent the largest bank of Toller DNA in the US and continued contributions will only make them a better resource for current and future research in the breed.

The primary goal for the Addison's research is to locate the gene(s) responsible for Addison's disease so that a genetic test can be developed and used by breeders in the future to greatly reduce the incidence of Addison's disease in our breed. Additionally, the researchers would like to better understand the unusual features of Addison's disease in Tollers including the age at diagnosis (early vs. late) and the type of Addison's (typical primary vs. atypical).

A previous study by Peterson and colleagues (1996) involving a large number of dogs with Addison's disease found the average age of onset of Addison's disease was 4 years old with 25% and 75% of the dogs diagnosed under 2 ½ and 6 ½ years of age, respectively. However in Tollers, researchers and breeders are seeing a broader range with an onset at a few months of age up to 10+ years old with a large portion diagnosed under 2 years of age. Addison's disease is due to destruction of the adrenal glands which can be caused by cancer, injury, or other diseases. It is thought that most cases of random Addison's disease in dogs are due to immune-mediated destruction of the adrenal gland. It is also possible that environmental cues could be involved. Research in Tollers at UC Davis has shown that there is a strong genetic factor involved with this disease, but any correlation with the immune system or the environment has yet to be determined. When the gene(s) responsible are uncovered, it will shed more light on the causes of Addison's disease.

The adrenal glands produce mineralocorticoids and glucocorticoids that are responsible for proper regulation of various pathways in the body including metabolism, blood pressure, electrolyte balance, and stress response. Addison's disease occurs when these hormones are not being produced resulting in clinical signs including but not limited to any of the following: lethargy, decreased appetite, vomiting, weakness, diarrhea, increased drinking and urinations, and shivering. Treatment will depend on the type of Addison's that the dog has (some do not need mineralocoticoid supplementation

which regulates the electrolyte balance). All Addison's patients will need some form of corticosteroids. For a typical primary Addisonian who needs both mineralocorticoids and corticosteroids they are usually treated with an injection of desoxycorticosterone pivalate (DOCP; trade name: Percoten-V) to replace the mineralocorticoids every 21 to 28 days depending on the dog's serum electrolyte concentrations and with oral prednisone daily to replace the glucocorticoids. Alternately they can be treated daily with oral fludrocortisone acetate (trade name: Florinef) which has mineralocorticoid and some minimal glucocorticoid activity and prednisone. Costs for either treatment option will depend on a number of factors including where you live, how much your dog weighs and the doses and frequencies of the drugs each dog needs to control their clinical signs. From what Dr. Hughes has heard from Toller owners, it costs them in the realm of about $100 per month for medications. They will also need to do follow-up monitoring of serum electrolyte concentrations and any other abnormalities noted in each patient. For atypical Addisonian (those maintaining their serum electrolyte concentrations in the normal range and thus do not need mineralocorticoid supplementation), only oral prednisone is required and this is fairly inexpensive. These atypical Addisonians should have their serum electrolytes monitored at least a few times a year so they can be diagnosed early if a mineralocorticoid deficiency develops.

Dr. Anita Oberbauer at UC Davis is also investigating the genetics of Addison's disease in other breeds including the Portuguese Water Dog (PWD), Standard Poodle, Bearded Collies, Leonbergers, Great Dane and West Highland Terrier. Addison's has been found to be inherited in the PWD, Standard Poodle and Bearded Collie and is likely influence by a major autosomal recessive gene in the PWD and Standard Poodle but the mode of inheritance is less definitive in the Bearded Collie.

Addison's disease appears to be an autosomal recessive disease in the Toller like in the Standard Poodles and PWD according to Dr. Angela Hughes. However, final confirmation of the mode of inheritance cannot be done until the exact genetic mechanism is understood. Until then, the researchers feel that Toller breeders should treat Addison's disease like an autosomal recessive disease and employ breeding strategies to breed away from it.

When asked to give specific breeding advice, this is what Dr. Hughes said, "I look at the family history and the pedigrees and then calculate what each dog's potential risk is based on known affected individuals. Based on the 1% incidence, approximately 18% of Tollers would be carriers assuming an autosomal recessive mode of inheritance." One can assume that dogs with a know history of Addison's would have an increased risk of being a carrier.

This research has been funded by the Center for Companion Animal Health at the University of California, Davis and by the AKC Canine Health Foundation with support from the Toller Donor Advised Fund. The Toller Donor Advised fund receives donations from the NSDTRC (USA) and members.

The best way for Toller owners to support this research is to submit DNA cheek swabs to the study and complete the required research questionnaire. People can also contribute financially to the Toller Donor Advised fund that has supported this research.

For more information and instructions on participating, please contact Many Eakins Email: Sartoller@aol.com or Dr. Angela Hughes Email: ahughes@ucdavis.edu

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