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Vol. 12 Summer 2013

### **High Rate of Hypothyroidism in Boxers Is Cause for Concern Among Breeders**

A study at Michigan State University (MSU) indicates that Boxers are rated fifth highest among all breeds for autoimmune thyroid disease, a disorder that often progresses to hypothyroidism.

Unfortunately for breeders who want to breed dogs of excellent conformation and temperament and who are striving to improve Boxer health, dogs may not show signs of the disease, if at all, until they are past breeding age. That's a problem, says Ray Nachreiner, D.V.M., Ph.D., professor at MSU, since the majority of primary hypothyroidism in dogs appears to be genetic. Studies of Boxers present a strong indication of genetic transmission.

While technically there are three classifications of hypothyroidism: juvenile onset, secondary hypothyroidism and primary hypothyroidism, the last type is the most common in dogs. It appears to have the same occurrence rate in males and females.

#### **Defining Hypothyroidism**

While hypothyroidism is not considered life threatening, the quality of life for a dog suffering from hypothyroidism is substandard. The word hypothyroidism combines hypo, which means lower than normal; thyroid, the endocrine gland that produces various hormones; and ism, which means behavior. Thus, hypothyroidism involves an inactive thyroid gland.

The thyroid gland produces two hormones called triiodothyronine (T3) and thyroxine (T4) that control the rate of metabolism. When the thyroid gland fails to function fully, if at all, it creates a systemic condition. The hormones, which are at a reduced level or nonexistent, fail to do their job of stimulating important physical and chemical processes at the cellular level.

Primary hypothyroidism has two main causes. One is autoimmune thyroiditis or inflammation of the thyroid gland. In this example, a dog's own antibodies attack and destroy thyroid cells in a typical autoimmune disease behavior. This condition of thyroiditis can exist for years without progressing. At other times, Nachreiner says, thyroiditis progresses and destroys the thyroid within just a few months. When there is little thyroid tissue left, a dog cannot make enough thyroid hormone and becomes hypothyroid.

If no cause is found for repeated seizures, it is known as primary or idiopathic epilepsy. Though the etiology is unknown, recent data by Nachreiner and his colleagues shows that even the idiopathic type may be the end result of autoimmune thyroiditis.

"We found that some dogs with autoimmune thyroid disease can become idiopathic if left untreated," Nachreiner says. "It appears that idiopathic hypothyroidism may be the end stage of autoimmune thyroid disease. This indicates that at least a portion of dogs with idiopathic thyroid disease has autoimmune thyroiditis as the origin of the hypothyroidism. Hypothetically, what if all idiopathic hypothyroid dogs were originally affected by autoimmune thyroiditis? Then 95 percent of hypothyroidism would be autoimmune in origin."

### **Difficulty Diagnosing Hypothyroidism**

Hypothyroidism can be difficult to diagnose. Many non-thyroid illnesses, such as fever, diabetes and almost any chronic debilitating condition, affect hormonal levels. These conditions are referred to as non-thyroidal illness (NTI) or euthyroid sick syndrome.

What may seem like signs of hypothyroidism may be caused by other conditions. Hair loss, for example, may be a sign of fleas, allergies or other problems. Hypothyroidism symptoms are usually gradual, and many dogs show no symptoms at all yet may be significantly affected. However, one MSU study conducted between Jan. 1, 2001, and April 1, 2002, found that many Boxers do show symptoms. Peter Graham, D.V.M., who leads the Canine Thyroid Health Study at MSU, notes that of 1,063 Boxers researched, signs of hypothyroidism were found as follows: 69 percent displayed alopecia or hair loss; 48 percent suffered from obesity or weight gain; 31 percent had hyperpigmentation; 18 percent had lethargy; 16 percent experienced pruritus or itchy skin; and 9 percent had flank alopecia.

### **Testing for Hypothyroidism**

While a blood test can detect the disease before the appearance of clinical signs, a single negative blood test will not guarantee that a dog will never develop thyroid disease. A dog that is negative at 2 years old can still become positive at 6 years old.

Since the majority of dogs tested have a positive blood test by 4 years old, annual testing for the disorder is recommended for the first four years, followed by testing every other year until the age of 8 years.

While a more extensive panel of tests might be needed in some cases, most dogs with thyroid disease can be detected through four tests:

- A TT4 assay determines total thyroxine and total indicates thyroid activity.
- A TSH assay detects thyroid stimulating hormone, a substance that stimulates the thyroid to produce more T3 and T4.
- A FT4 (Free T4) assay checks the amount of usable T4 in the dog's blood. Basically 99.9 percent of T4 is bound to blood protein, and only 0.1 percent is free. That small fraction is what the FT4 test

checks because that is the amount readily available to stimulate metabolism.

- A TgAA assay determines the amount of antibodies produced by abnormal cells in thyroid tissue. These autoantibodies, the first indicator of autoimmune thyroid disease, react to a dog's thyroglobulin (Tg), a protein that stores a large amount of thyroid hormone. Nachreiner and his colleagues have been looking for indications of thyroid disease in all breeds using retrospective analyses from 189,808 samples received at the MSU Animal Health Diagnostic laboratory. They found that 22.5 percent of samples received from Boxers was positive for TgAA. "These studies will continue as we update retrospective analyses with additional data from samples received," Nachreiner says.

### **A New Diagnostic Tool**

Recent research by Richard W. Nelson, D.V.M., DACVIM, professor and chairman of the Department of Medicine and Epidemiology at the University of California-Davis, has identified another way to detect hypothyroidism in dogs. Nelson and his team have found that ultrasound examination of the thyroid gland provides a way to differentiate hypothyroidism from disorders causing euthyroid sick syndrome or non-thyroid illnesses.

The study, supported by an American Kennel Club Canine Health Foundation grant, involved using the ultrasound technique in Golden Retrievers and later in Beagles, Toy and Miniature Poodles. The first phase involved evaluation of the size of thyroid glands in three groups of Golden Retrievers: those that were healthy, hypothyroid and euthyroid sick. The second phase measured the thyroid glands in normal Beagles, Toy and Miniature Poodles and compared findings in the normal Golden Retrievers.

"What we found is that there is a direct correlation between the size of the thyroid gland and the size of the dog and that dogs with hypothyroidism have a smaller gland measurement for their breed," Nelson says. The finding allowed Nelson and his team to determine the standard gland size for Golden Retrievers, Beagles and Poodles. Additional research will need to be done to determine the standard measurements for other breeds.

### **Disease Progression**

The veterinary profession is trying to understand why some dogs show clinical signs and low thyroid test results as early as 1 year old, while a littermate may take six or seven years or may never develop the disease, Nachreiner says. "What sets off the disease in those dogs that have the genetic makeup for promotion of the disease? Some speculate that vaccine protocols play a role, since it is an autoimmune disease.

"Diet may play a role as well. In the model of obese chickens with autoimmune disease (Brown et al., Wayne State University), increased iodine in the diet resulted in earlier thyroid disease compared to chickens fed a control diet. It seems that the excess iodine changed the Tg molecule making it more immunogenic and bringing the thyroiditis on more quickly. Important in this study is that the chickens had to have the genes for thyroid disease first. The high iodine diet in most chickens won't have an affect on thyroid function.

"These factors appear to be worth studying, though other factors may be better understood as studies progress."

### **Important Steps for Breeders**

"While hypothyroidism takes a back seat to more life-threatening conditions such as cardiomyopathy, subaortic stenosis and cancer, it ranks high as a health concern on surveys that we have conducted over the years," said Wendy Wallner, D.V.M., chairman of the Health and Research Committee of the American Boxer Club (ABC). "We recommend breeders test for hypothyroidism."

One research proposal for a thyroid study is being considered by the American Boxer Club for funding this year, and at the 2002 ABC National Specialty in May, a health seminar featuring Peter Graham, D.V.M., director of the MSU Canine Thyroid Health Study, was presented on hypothyroidism.

Wallner encourages breeders to remember:

- Testing is the only way to determine if a dog is affected;
- Dogs that test normal as young dogs may be affected as they age; and;
- Hypothyroidism can affect every organ of the dog

-- it is a systemic condition and needs to be treated. Treatment for hypothyroidism usually involves the use of a hormone supplement prescribed by a veterinarian. L-thyroxine is most commonly used, and most dogs respond well to hormone supplementation.

"I think at this point, the best a breeder can do is test all breeding stock and remove from their breeding program any dogs that are affected," Wallner says. "While this won't solve the problem of hypothyroidism in the breed due to the fact that many dogs will not show signs of disease until they are past breeding age, it can help to reduce the incidence by removing from breeding programs those dogs who are affected at a young age."

### **Clinical Signs of Hypothyroidism in Boxers\***

<b>Clinical Sign</b>	<b>Number of Cases</b>	<b>Percent of Total</b>
Alopecia (Hair Loss)		
Obesity/Weight Gain	736	69
Hyperpigmentation	512	48
Lethargy	328	31
Pruritus (Itchy Skin)	191	18
Flank Alopecia	165	16
Pyoderma (Inflammation 83 8 Percent with Pus-Filled Lesions)	91	9
Otitis (Ear Inflammation)	83	8
Crusts	80	8
Scales	62	6
Cool Skin	54	5
	50	5

\*Clinical signs of hypothyroidism seen in 1,063 Boxers with thyroid submissions to Michigan State University between Jan. 1, 2001, and April 1, 2002. Information provided by Peter Graham, D.V.M., Animal Health Diagnostic Laboratory, Michigan State University, May 2002.

