



PURINA Pro Club

Boxer Update

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Hypothyroidism Testing Is Important in Making Breeding Decisions

Hypothyroidism, the end stage of autoimmune thyroid disease, is the most common endocrine disorder in dogs. Considered a hereditary condition, autoimmune thyroiditis is highly prevalent in Boxers. Since the pattern of inheritance is not known, breeders are encouraged to test Boxers for the disorder and to select against affected dogs when making breeding decisions.

Based on samples received at Michigan State University's Diagnostic Center for Population and Animal Health, Boxers rank sixth among all breeds for autoimmune thyroiditis. "We have evaluated 8,910 Boxers for our data bank," says Mary Dee Sist, D.V.M., an endocrine specialist. "Eighteen percent tested positive for autoimmune thyroiditis, and 4.5 percent were inconclusive or equivocal."

Though generally not life-threatening, hypothyroidism affects a dog's quality of life. Weight gain, lethargy, hair loss, skin problems, infertility, and behavioral abnormalities are some of the signs. The condition begins when a dog's own antibodies attack and destroy thyroid cells. When little thyroid tissue is left, a dog cannot make enough thyroid hormones and becomes hypothyroid.

The thyroid gland produces two hormones, triiodothyronine (T3) and

thyroxine (T4), which control the rate of metabolism. When the thyroid gland fails to function properly, it can lead to systemic signs associated with hypothyroidism.

"Thyroid hormones determine the body's metabolic rate, and the oxygen consumption of most every tissue in the body," says Duncan Ferguson, V.M.D., Ph.D., DACVIM, DACVCP, head of Veterinary Biosciences at the University of Illinois College of Veterinary Medicine. "In most cases, autoimmune thyroiditis is a hereditary condition that develops when a dog reaches midlife, usually between 2 and 6 years of age."

Managing hypothyroidism consists of administering a veterinarian-prescribed synthetic version of the T4 hormone and having blood tests taken periodically throughout a dog's life to monitor the supplemented levels. If left untreated, a dog rarely dies from hypothyroidism but is at greater risk for infection and obesity, which can strain the heart.

Testing for Hypothyroidism

According to experts, if a T4 is the only thyroid test performed, it should not be the basis for diagnosing hypothyroidism or making breeding decisions. Additionally, a normal T4 level does not ensure a dog is not hypothyroid.

"I would caution breeders not to

assume an animal is hypothyroid based solely on low serum T4 concentrations," Ferguson says. "In a subset of dogs with autoimmune thyroiditis and positive TgAA (thyroglobulin autoantibody), the presence of T4 autoantibodies (T4AA) can result in a normal-to-elevated total

MANAGING HYPOTHYROIDISM CONSISTS OF ADMINISTERING A VETERINARIAN-PRESCRIBED SYNTHETIC VERSION OF THE T4 HORMONE AND HAVING BLOOD TESTS TAKEN PERIODICALLY THROUGHOUT A DOG'S LIFE TO MONITOR THE SUPPLEMENTED LEVELS.

T4 when free T4 is low. T4 autoantibodies are seen in about 2 percent of hypothyroid dogs. The presence of antibodies invalidates the result of the T4 immunoassay and accounts for 10 percent of cases in which a normal T4 concentration incorrectly rules out hypothyroidism."

Sist recommends conducting a full panel of tests for a complete and accurate diagnosis. "Our laboratory measures several indicators for hypothyroidism," she says. "We conduct T4, free T4, T3, free T3, thyroid stimulating hormone (TSH), T3 autoantibody, T4 autoantibody, thyroglobulin autoantibody, and specific Tg binding testing. This helps to reduce equivocal results or determine when hormone values are low due to certain drugs — for example, steroids — or illness rather than thyroid disease."

The Orthopedic Foundation for Animals (OFA) requires free T4, TSH and TgAA testing before certifying a dog as having a normal thyroid. Breeders and owners must use an approved laboratory for thyroid certification. Thyroid testing should be performed at 2, 3, 4, 6 and 8 years

Signs of Hypothyroidism

Hypothyroidism can be difficult to detect in dogs, partly because dogs don't always show signs of the disorder. Here are common signs.

- Excessive weight gain with no corresponding increase in appetite;
- Lethargy, including sleeping more than usual, lack of interest in play and tiring on regular walks;
- Hair loss, particularly behind the ears and on the tail and flanks;
- Dry, flaky skin;
- Greasy, seborrheic skin;
- Intolerance of cold temperatures shown by excessive shivering and constant seeking of warm places to lie down;
- Slowed heart rate;
- Difficulty swallowing;
- Muscle weakness, stiffness and lameness;
- Chronic ear or skin infections; and
- Chronic gastrointestinal disorders, including constipation.

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Hypothyroidism Testing

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of age for continued certification. For information, visit the OFA Web site at www.offa.org.

Signs of hypothyroidism are usually gradual, and many dogs show no signs yet may be significantly affected. Thyroidglobulin antibodies, T3AA and T4AA, the markers of autoimmune thyroiditis, can begin forming long before a dog shows clinical signs of hypothyroidism. This is compounded by the fact that the onset of hypothyroidism usually isn't until a dog is 2 years of age or older, and a dog that tests negative for the condition at 2 years of age could still become positive later in life.

Thus, breeders may not realize a Boxer is hypothyroid until the dog has already been bred. Young adult dogs may be affected but test negative because the thyroid gland has not been sufficiently destroyed to reduce hormone levels or it is too early in the disease process to increase TgAA.

Dogs suffering from some non-thyroidal illnesses may have low thyroid hormones when tested, as their illnesses can affect normal levels of T3 and T4. Euthyroid sick syndrome results from chronic, debilitating conditions such as diabetes, congestive heart failure, hepatic disease or even acute conditions like renal failure. When the underlying disorder is treated, the thyroid condition returns to normal.

Ferguson recommends testing young Boxers to determine whether thyroid gland antibodies are present in their blood. "The definitive test for the presence of autoimmune thyroiditis is the thyroglobulin autoantibody (TgAA) assay," he says. "This test evaluates whether a dog has developed antibodies against the major protein of the thyroid gland called thyroglobulin. This initial indicator of the disease can help pinpoint an affected dog long before signs manifest."

By the time T4 concentration falls, the thyroid gland may be about 75 percent destroyed by autoimmune thyroiditis. The TgAA level would be the first to appear abnormal. "The peak distribution for the onset of hypothyroidism is 2 to 6 years," says Ferguson. "This age coincides with the peak incidence of TgAA positive titers. Animals with abnormal TgAA titers have been followed, and they generally progress to full-blown hypothyroidism within two years."

Research by Raymond Nachreiner, Ph.D., D.V.M., professor of veterinary endocrinology at Michigan State Uni-

versity, and his colleagues supports the hypothyroidism cycle. Thyroid autoantibodies were detectable in less than 5 percent of dogs younger than 2 years, but were positive in 9 to 11.5 percent of dogs between 2 and 6 years, peaking around age 4. The study included over 367,000 samples. Tests for low thyroid hormone, by contrast, peaked around age 8.

Thus, experts recommend that owners and breeders run thyroid panels annually from 2 to 4 years of age.

At the University of Illinois, Ferguson is using molecular genetic technology to improve the sensitivity of the canine

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TSH assay that is used to detect thyroid stimulating hormone, a substance that stimulates the thyroid to produce T3 and T4.

"Our hope is to improve the test to be sensitive and specific enough to use alone as a screening test for primary hypothyroidism," he says. "So far, we've had only modest success in developing additional and better antibodies that would serve as an improved assay. We have developed a highly purified standard for this assay that might allow greater consistency in assay standards used by the various assays available."

Breeding Considerations

Hypothyroidism probably developed in Boxers because it was linked genetically with a desirable trait, Ferguson says. "The ability to eliminate the condition from a breed will become possible only when a true genetic test is developed," he says. "Hypothyroidism is a multifactorial, perhaps multigenic, disease. The fact that its prevalence varies among breeds suggests it can be managed by careful selection against breeding animals with the disease."

Since hypothyroidism, caused by autoimmune thyroiditis, is prevalent in Boxers, "correctly diagnosing the disease provides breeders with more information so they can make better breeding choices," Sist says.

Jerold Bell, D.V.M., clinical associate professor of genetics at Tufts University Cummings School of Veterinary Medi-

cine, says, "Hypothyroidism is a disease process that causes morbidity to a dog and financial expense to the owner. Fortunately, it usually is not fatal, and it is easy to control with medication. Hypothyroid dogs should be selected against for breeding, as should dogs with several affected first-degree family members."

"We are on the verge of gaining considerable knowledge about the canine genome," Ferguson says. "Hopefully, we'll soon know more information about the mutation that causes hypothyroidism in Boxers and other breeds as well. In the meantime, breeders should not ignore test results in which dogs test positive for hypothyroidism. Doing so would be irresponsible."

Another step breeders can take to help reduce the prevalence of hypothyroidism in the breed is "to submit both normal and abnormal thyroid panel results to the Orthopedic Foundation for Animals for publication on its open health reporting Web site," Bell says. "This way, pedigrees of individual dogs and prospective males can be viewed for the prevalence of hypothyroidism in making informed breeding decisions. Autoimmune thyroiditis should not be ignored, and breeders should openly report testing results to OFA and select against it." ■

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