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THE THYROID DILEMMA

Hypothyroidism is the most common endocrine disorder of canines, and up to 80% of cases are believed to result from autoimmune (lymphocytic) thyroiditis. It takes destruction of at least 75% of the thyroid gland by targeted T-lymphocytes, before classical clinical signs of hypothyroidism are manifested. Thus, accurate diagnosis of the early compensatory stages of canine autoimmune thyroiditis that lead up to hypothyroidism affords important genetic and clinical options for prompt intervention and case management. The heritable nature of this disorder poses significant genetic implications for breeding stock.

Despite the fact that thyroid dysfunction is the most frequently recognized endocrine disorder of pet animals, it is often difficult to make a definitive diagnosis. As the thyroid gland regulates metabolism of all body cellular functions, reduced thyroid function can produce a wide range of clinical manifestations, sometimes vague, other times classical, and occasionally very unusual. Many of these clinical signs mimic those resulting from other causes and so recognition of the condition and interpretation of thyroid function tests can be problematic. Further, development of thyroid dysfunction is a continuum that begins with normalcy and progresses gradually over months to several years to end-stage disease.

Baseline Thyroid Profiles

A complete baseline thyroid profile should be measured and typically includes total T4, free T4, thyroid autoantibodies, and may also include total T3, free T3 and cTSH. If included in thyroid profiles, the T3 and freeT3 assays usually reflect thyroiditis when both are spuriously elevated due to presence of T3 autoantibody. The autoantibody (AA) assays (T3AA, T4AA, TgAA) are especially important in screening breeding stock for heritable autoimmune thyroid disease.

The normal reference ranges for thyroid analytes of healthy adult animals tend to be similar for most

breeds of companion animals. Exceptions are the sighthound and giant breeds of dogs which have lower basal levels. Typical thyroid levels for healthy sighthounds, such as retired racing greyhounds, are at or just below the established laboratory reference ranges, whereas healthy giant breeds have optimal levels between the lower end and midpoint of these ranges.

Further, because young animals are still growing and adolescents are maturing, optimal thyroid levels are expected to be in the upper half of the references ranges. For geriatric animals, basal metabolism is usually slowing down, and so optimal thyroid levels are likely to be closer to midrange or even slightly lower.

All animals are not the same

- Puppies have higher basal thyroid levels than adults
- Geriatrics have lower basal thyroid levels than adults
- Large/giant breeds have lower basal thyroid levels
- Sighthounds have much lower basal thyroid levels

Genetic Screening for Thyroid Disease

Most cases of thyroiditis have elevated serum TgAA levels, whereas only about 20-40% of cases have elevated circulating T3 and/or T4 AA. The presence of elevated T3 and/or T4 AA supports a diagnosis of autoimmune thyroiditis but underestimates its prevalence, as the diagnosis in some cases is revealed only by finding an elevated TgAA or lymphocytic infiltrates within thyroid biopsies. Measuring AA levels also permits early recognition of the disorder, and facilitates genetic counseling. It is recommended that affected dogs not be used as breeding stock.

The commercial TgAA test can give false negative results if the dog has received thyroid supplement within the previous 90 days. False negative

THE THYROID DILEMMA (CONT'D)

TgAA results also can occur in about 8% of dogs verified to have high T3AA and/or T4AA. Low-grade false positive TgAA results may be obtained if the dog has been vaccinated within the previous 40-90 days, or occasionally in cases of non-thyroidal illness (NTI). Published studies indicate that prevalence of thyroiditis is directly associated with body weight, is highest in dogs 2-4 years old, and like other autoimmune disorders, more likely to occur in females than males.

Screening for Canine Thyroid Dysfunction

- Complete thyroid antibody profile preferred
- cTSH poorly predictive, unlike humans, as some dogs have a slightly different bioform of TSH not recognized by the assay
- Basal levels affected by certain drugs (steroids, phenobarbital, sulfonamides)
- Basal levels lowered by estrogen; raised by progesterone [sex hormonal cycle effects]

Thyroxine treatment is best given twice daily

- Dividing the daily dose q 12 hrs avoids "peak and valley" effect
- Achieves better steady state over 24 hrs; half life 12-16 hrs
- Dosing once daily results in undesirable peaks and valleys
- Dosing should be given directly by mouth rather than in food bowl, as calcium binds thyroxine and can retard absorption

Testing animals on thyroxine therapy

- Monitoring for resolution of clinical signs
- Blood samples should be drawn 4-6 hrs post-pill for BID therapy
- Thyroid antibody profile preferred; a must for thyroiditis cases
- Minimum testing needed is T4
- FreeT4 is also helpful, as T4 can be suppressed with concurrent NTI
- FT4(ED) should be used in presence of T4AA, to avoid autoantibody interference
- Post-pill therapeutic ranges should be at upper 1/3 to 1/3 **above** the reference ranges

Testing older cats

- Basal thyroid levels in older cats should be lower than adults
- Other illnesses often lower T4, masking hyperthyroidism
- FT4(ED) more sensitive, but less specific than T4 for diagnosing hyperthyroidism
- FT4(ED) should always be evaluated together with T4
- FT4 (ED) can be high in cases of GI, renal, or liver disease

Thyroid testing for genetic screening purposes is less likely to be meaningful before puberty. Screening is initiated, therefore, once healthy dogs and bitches have reached sexual maturity (between 10-14 months in males and during the first anestrus period for females following their maiden heat). As the female sexual cycle is quiescent during anestrus, any influence of sex hormones on baseline thyroid function will

be minimized. This period generally begins 12 weeks from the onset of the previous heat and lasts one month or longer. The interpretation of results from baseline thyroid profiles in intact females will be more reliable when they are tested in anestrus. Once the initial thyroid profile is obtained, dogs and bitches should be rechecked on an annual basis to assess their thyroid function and overall health. Obtaining annual test results provides comparisons that permit early recognition of developing thyroid dysfunction. This allows for prompt treatment, where indicated, to avoid the appearance or advancement of clinical signs associated with hypothyroidism.

Screening for Canine Autoimmune Thyroiditis

- Complete thyroid antibody profile required
- Test intact bitches during anestrus
- Need T3AA, T4AA, TgAA; not just freeT4, TSH, TgAA
- OFA Thyroid Registry is a limited panel
- Some cases (~8%) are T3AA and/or T4AA +, but TgAA -

Treating Canine Autoimmune Thyroiditis

- Treat cases + for T3AA and/or T4AA, or TgAA with thyroxine
- While controversial, clinical evidence supports this approach rather than waiting until dog gets ill or has aberrant behavior[†]
- If only low-grade TgAA +, retest profile in 2-4 mos
- Treat with thyroxine BID; retest profile in 2-4 mos
- Always monitor with thyroid antibody profile
- For recently vaccinates, wait 90 days before retesting

Do not breed dogs with autoimmune thyroiditis

- Heritable trait, regardless of clinical status
- Screen relatives annually from puberty
- Consider for breeding, if negative, after age three

[†] Data from humans and dogs with thyroiditis show that AA levels gradually become reduced over a period of 5-10 months. This is believed to result from negative feedback inhibition of pituitary TSH production, which in turn, reduces stimulation of receptors mediating the targeted lymphocytic destruction of thyroid acinar cells.

[To be continued next month, with discussion of diagnostic profile recommendations and interpretations]

References: Nachreiner RE, Refsal KR, JAVMA 201: 623-629, 1992; Thacker EL et al, AJVR 53: 449-453, 1992; Nachreiner RE et al, AJVR 54: 2091-2098, 1993; Dewey CW et al, Prog Vet Neurol 6: 117-123, 1995; Dodds WJ, Adv Vet Sci Comp Med, 39: 29-96, 1995; Thacker EL et al, AJVR 56: 34-38, 1995; Peterson ME et al, JAVMA 211:1396-1402, 1997; Dodds WJ, Can Pract 22 (1): 18-19, 1997; Nachreiner RE et al, AJVR 59:951-955, 1998; Scott-Moncrieff JCR et al, JAVMA 212:387-391, 1998; Scott-Moncrieff JCR, Nelson RW, JAVMA 213:1435-1438, 1998; Iverson L et al, Vet Clin Pathol 28:16-19, 1999; Jensen AL et al, J Comp Pathol 114: 339-346, 1999; Dodds WJ, Aronson LP, Proc AHVMA, 80-82, 1999; Scott-Moncrieff JC et al, JAVMA 221: 515-521, 2002; Beaver BV, Haug LI, JAAHA 39: 43 1-434, 2003.

Information for the topic, 'Syngomyelia in Cavalier King Charles Spaniels', in the August 2005 issue of Antech News was excerpted from www.CavalierHealth.org and the referenced scientific literature.