Behavioral Issues with Thyroiditis

by W. Jean Dodds, DVM

Background

Behavioral and psychological changes have been associated with thyroid dysfunction in humans for several hundred years. About two-thirds of human patients with attention deficit-hyperactivity disorder were found to be hypothyroid in a recent study, and supplementing them with thyroxine was largely curative. In animals, hyperthyroid cats tend to be more irritable and show increased vocalization, whereas hypothyroid dogs -- especially those younger dogs with autoimmune thyroiditis -- can display a wide variety of aberrant behaviors.

Although genetic influences on behavioral disorders rarely account for more than half of the phenotypic expression of behavioral differences, inheritance clearly plays an important role. There are multiple genes involved and each can contribute to the overall expression of behavior. While application of newer molecular techniques offers the potential of identifying the DNA marker sequences responsible for behavioral variation, this is especially challenging because behavior is the most complex phenotype. It reflects not only whole body function, but also the body's dynamic changes in response to environmental influences.

For several thousand years now, animals have been bred and selected for their behavior as much as their conformation. This application of behavioural genetics is exemplified by the dramatic differences in behavior and physique among various dog breeds. Today, although dogs (and cats) have a great range of genetic and behavioral variability, a shocking 13 million of them -- 10% of the total pet population -- are being

destroyed annually because of behavioral problems.

Theory

How diminished thyroid function affects behavior is mechanistically unclear. It may relate to the adrenal axis, as some hypothyroid patients have reduced cortisol clearance with chronically elevated circulating cortisol levels. This would mimic a constant state of stress, which could suppress pituitary TSH output and reduce production of thyroid hormones. Chronic stress in humans has been implicated in the pathogenesis of affective disorders such as depression. Major depression has been shown in imaging studies to produce changes in neural activity or volume in areas of the brain which regulate aggressive and other behaviors. Dopamine and serotonin receptors have been clearly demonstrated to be involved in aggressive pathways in the CNS. Hypothyroid rats have increased turnover of serotonin and dopamine receptors, and an increased sensitivity to ambient neurotransmitter levels, as do mice, rats, and certain types of monkeys. In humans and dogs, mental function is impaired and the animal is likely to respond to stress in a stereotypical rather than a reasoned fashion.

Current Behavioral Issues

In recent years, clinicians have noted the sudden onset of behavioral changes in dogs around the time of puberty or as young adults. Most of the animals have been purebreds or crossbreeds with an apparent predilection for certain breeds. Neutering these animals usually does not alter the symptoms and the behaviors may even intensify. Many of these dogs belong to certain breeds or dog families susceptible to a variety of immune problems and allergies (e.g. Golden Retriever, Akita, Rottweiler, Doberman Pinscher, English Springer Spaniel, Shetland Sheepdog, and German Shepherd Dog). The clinical signs in these animals, before they show the sudden

onset of behavioral aggression, can include minor problems such as inattentiveness, fearfulness, seasonal allergies, skin and coat disorders (e.g. pyoderma, allergic inhalant or ectoparasite dermatitis, alopecia, and intense itching). These may be early subtle signs of thyroid dysfunction, with no other typical signs of thyroid disease being manifested.

The typical history starts out with a quite, well-mannered and sweet-natured puppy or young adult dog. The animal was outgoing, attended training classes for obedience, working, or dog show events, and came from a reputable breeder whose kennel has had no prior history of producing animals with behavioral problems. At the onset of puberty or thereafter, however, sudden changes in personality are observed. Typical signs can be incessant whining, nervousness, schizoid behavior, fear in the presence of strangers, hyperventilating and undue sweating, disorientation, and failure to be attentive (canine cognitive dysfunction). These changes can progress to sudden unprovoked aggressiveness in unfamiliar situations with other animals, people and especially with children.

In adult dogs, moodiness, erratic temperament, periods of hyperactivity, lack of concentration, depression, mental dullness, lethargy, malaise, fearfulness and phobias, anxiety, submissiveness, passivity, compulsiveness, and irritability may be observed. After the episodes, most of the animals behave as though they were coming out of a trance like state, and are unaware of their previous behavior.

Another group of dogs show seizure or seizure-like disorders of sudden onset that can occur at any time from puberty to mid-life. These dogs appear perfectly healthy outwardly, have normal hair coats and energy, but suddenly seizure for no apparent reason. The seizures are often spaced several weeks to months apart, may coincide with the full moon, and can appear in brief clusters. In some cases the animals become aggressive and attack those around them shortly before or

after having one of the seizures. The numbers of animals showing these various types of aberrant behavior appear to be increasing in frequency over the last decade.

In dogs with aberrant aggression, a large collaborative study between our group and Dr. Dodman and colleagues at Tufts University School of Veterinary Medicine has shown a favorable response to thyroid replacement therapy within the first week of treatment, whereas it took about three weeks to correct their metabolic deficit. Dramatic reversal of behavior with resumption of previous problems has occurred in some cases if only a single dose is missed. A similar pattern of aggression responsive to thyroid replacement has been reported in a horse.

A sudden onset of behavioral changes in an otherwise healthy young or older animal should alert the client and veterinarian to the possibility of an underlying thyroid imbalance. The age at onset can range widely from 6 months to 15 years; spayed females and neutered males are at increased risk in comparison to sexually intact animals; mid-sized to large breeds are more often involved; and purebreds are much more likely to be affected than mixed breeds. While abnormal behavior can reflect underlying problems of a psychological nature, it also can have a variety of medical causes. Therefore, the medical evaluation should include a complete history, clinical examination and neurological work up, routine laboratory testing of blood counts, blood chemistry and thyroid profiles, urinalysis, fecal exam and x-ray. Additional specific laboratory tests may be indicated based on the specifics involved. If all of these tests prove to be negative, evaluation by a qualified behavioral consultant should be undertaken.

Diagnostic and Treatment Misunderstandings about Thyroid Disease

Veterinarians commonly are confused about which tests are necessary to accurately diagnose thyroid dysfunction in the

dog and cat, as well as another animal species. During case review, many veterinarians contact us about the reference normal ranges provided by their commercial clinical laboratory. Many colleagues assume that these reference ranges are finite and apply to all breeds and breed types [toy and small breeds have higher basal levels, while large or giant breeds and sighthounds have lower basal levels], as well as all ages and physiological circumstances. For example, veterinarians are generally unaware that the printed reference ranges on laboratory reports typically pertain to adults, and not to very young, adolescent, [higher basal levels] or geriatric animals [lower basal levels].

Furthermore, these reference ranges are intended as general guidelines and may not apply to individuals that are athletic, performance animals; under general anesthesia; undergoing sex hormonal change; a pregnant or nursing mother; obese; a patient that is ill or recovering from illness, or taking specific drugs that might influence thyroid function (e.g. corticosteroids, phenobarbital, potentiated sulfonamides, dietary soy and soy phytoestrogens, insulin, narcotic analgesics, salicylates, tricyclic antidepressants, furosemide, phenylbutazone, and o, p1-DDD). Daily diurnal rhythm fluctuations and the presence of circulating thyroid autoantibodies also changes basal thyroid levels. However, knowledge of these variables that affect thyroid function and circulating levels of thyroid hormones does not preclude their measurement. It is especially frustrating when a veterinarian tells the client that thyroid profiles cannot be measured accurately because the patient is receiving drugs such as corticosteroids or anticonvulsants. As long as the effects of these drugs are taken into account, there is no reason to avoid measuring thyroid function, especially when thyroid dysfunction may be an important underlying component of the patient's clinical problem.

While diagnosing thyroid dysfunction in companion animals can be particularly frustrating, especially when used for

wellness screening of potential breeding stock, veterinarians may fail to appreciate that a simple total T4 test is usually nondiagnostic. In fact, the in-office testing of T4 has recently been shown to produce unreliable results in 52% of dogs and 62% of cats, and therefore should not be used even as a general diagnostic screening test. Complete thyroid profiling is the most accurate and correct way to diagnose thyroid dysfunction when coupled with clinical information about the animal. For genetic screening, thyroid testing requires not only thyroglobulin autoantibody (TgAA), but also circulating T3AA and T4AA, because not all dogs with autoimmune thyroiditis have positive TgAA, even though T3AA and/or T4AA are elevated [about 6% false negatives, presumably because the epitopes involved weren't recognized by the TgAA reagent.] Another significant problem is diagnostic over reliance on the canine endogenous TSH test. This test in the dog, unlike the equivalent one in humans, is only ~70% predictive, with a 20-40% discordancy rate (both false positives and false negatives occur).

In the cat, accurately diagnosing hyperthyroidism can be complicated when the animal has concurrent nonthyroidal illness or is very old. In geriatric cats with hyperthyroidism, the T4 can be suppressed to within the upper half of the normal adult reference range, not only because of the cat's age but also because of they commonly have other illnesses. Furthermore, the free T4 assay measured by equilibrium dialysis can provide misleading information, because the assay may be elevated in about a third of cats with pre-existing liver, kidney, and gastrointestinal disease. While some of these cats may also be hyperthyroid, others are clearly euthyroid.

Regarding treatment of thyroid disease, the most common confusion surrounds the expected thyroid values for patients receiving appropriate doses of thyroid supplement thyroid supplement, and whether the therapy should be given once or twice daily. In the dog, Larry supplement is best given twice

daily, even though the label directions which of which have been the same for many years indicate once daily dosing. The reason that twice daily dosing is preferred is to match the typical 12-16 hour physiological half-life of thyroxine in the dog. Monitoring of thyroid therapy should be performed at 4-6 hours post dose, and at that time the T4 and free T4 values should be in the upper third to 25% above the laboratory's normal reference range. Rechecking thyroid profiles on animals receiving thyroid supplement is best accomplished by performing the complete profile, and is essential for those animals with autoimmune thyroiditis to determine whether the autoantibodies present are waning. If the client has financial constraints and the case is not thyroiditis, a post-pill T4 and freeT4 will usually suffice. Finally, in the cat treatment with methimazole should be given twice daily or by topical application to the ear, as recently published data indicate that once a day treatment has an unreliable therapeutic effect. When monitoring cats on methimazole, it doesn't matter when the sample is drawn in relation to giving the medication, as the turn over time is long.

Examples from Case Studies

Aggression

Chip W. - Parsons Jack Russell terrier, 7 year-old neutered male. Mood swings, aggression towards the owners, dry flaky, greasy skin and itching. Seven days after the diagnosis of hypothyroidism the dog's behavior totally changed; he no longer attacks household members and the scratching has significantly diminished.

Tater N. - Bull Terrier, 3 year-old neutered male. Originally diagnosed with rage syndrome, thyroid tests confirmed autoimmune thyroiditis. He is also deaf, and had been in several homes after developing behavioral problems. His current home is with an animal health technician, where

everything was fine for a few months. Then he would suddenly jump up during sleep and roar like a lion. He attacked any person or animal or thing nearby, and then would become fully awake but unaware that anything had happened. After a diagnosis of autoimmune thyroiditis, twice daily thyroid supplement was initiated. Within 6 weeks his abnormal behavior had disappeared to the extent that he is now 90% rage-free.

Bailey A. - Dalmatian, 6 year-old intact female. Unpredictable, aggressive behavior began at age 2 and has continually worsened. She sheds excessively and is extremely lethargic, sleeping most of the day and night. Thyroid testing confirmed end-stage hypothyroidism, and thyroxine supplement for just 10 days resulted in restoration of normal energy pattern, and a calming of her overall demeanor.

Passivity

Daphne O. - Golden retriever, 8 year-old spayed female. Began with anxiety and panic attacks; diagnosed with autoimmune thyroiditis. Before treatment was given, she became very lethargic, nonresponsive, and seemed unaware of her surroundings. Treatment with thyroxine twice daily restored her to normal activity level and behavior almost immediately.

Briar G. - Clumber spaniel, 5 year-old intact female. Acting very fatigued with signs of muscular weakness and massive coat shedding for two months. Not interested in any activity, refused to be touched or interact with other animals, children, or adults in the household. Testing revealed significant hypothyroidism, and treatment with twice daily thyroxine restored her attentiveness, energy level, as sociable behavior.

Phobias

Sherman C. - Cocker spaniel, 6 year-old intact male. This dog

becomes easily excited and agitated during thunderstorms and other periods of noise, such as fire crackers. During these episodes he vocalizes, paces constantly, and cannot be touched. Diagnosed with autoimmune thyroiditis, he is now on twice daily thyroxine and once daily melatonin. His temperament is normal and his noise phobia appears to be under control. [This case illustrates the benefit of melatonin either alone or with thyroxine therapy, as needed, in managing phobias.]

Cognitive Disorder

Sally F. - English setter, 4 year-old spayed female. A top-winning obedience and agility dog, she suddenly began to lose concentration and misunderstand routine performance commands, especially during competition events. As the breed at highest risk for autoimmune thyroiditis, the owner requested testing, which confirmed the presence of thyroid autoantibodies and clinical hypothyroidism. Treatment with thyroid supplement twice daily restored her cognitive function within 30 days.

Hazel S. - Bloodhound, 6 year-old spayed female. This experienced search and rescue dog suddenly appeared to lose her concentration and scenting ability. With the exception of minor skin infections, she had produced a healthy litter and had never been ill. Testing revealed significant hypothyroidism, which responded to twice daily replacement with thyroxine and a restoration of her scenting and tracking ability.

Seizure Disorder

Rocky McC. - Golden retriever, 2 year-old intact male. Presented with cluster seizures. Thyroid testing revealed elevated TgAA, although basal thyroid levels were normal. A rabies vaccine had been given one month before the onset of seizures, and the area had been treated with pesticides. He

was fed a raw food diet, but the allopathic veterinarian declined to accept him as a patient unless his diet was changed to commercial pet food. A holistic veterinarian was contacted, and he is now taking thyroxine and Pb. He has been seizure-free for 6 months.

Daisy M. - Labrador retriever mix, 5 year-old spayed female. This dog has idiopathic epilepsy under relatively poor control (seizures every 3 weeks). When routine booster vaccinations would normally be given, vaccine antibody titers were measured for parvovirus, distemper virus, and coronavirus. Titer results for parvovirus and distemper were extremely high indicating a very good level of immune memory, but coronavirus titer was poor. Her neurologist insisted on a polyvalent booster vaccination because of the low coronavirus titer and risk of contracting parvovirus disease. Needless to say the client was amazed, because the vaccine titer for parvovirus was very high, and gastrointestinal immunity affords coronavirus protection rather than serum antibody levels. Booster vaccination was not given and another specialist agreed to prescribe thyroxine twice daily, as very low thyroid function was also discovered.

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