# Thyroid Dysfunction as a Cause of Aggression in Dogs and Cats

**L.P. Aronson DVM & N.H. Dodman RVMS**
**Presented at the 43. Jahrestagung der Deutschen Veterinarmedizinischen Gesellschaft Fachgruppe Kleintierkrankheiten 29-31 August 1997 in HCC Hannover**

In human medicine, behavioral and psychological changes associated with thyroid dysfunction were noted in the nineteenth century. The behavioral abnormalities seen in the hyperthyroid cat have been well described in the literature, and mimic closely the restlessness, insomnia and irritability or aggression described in humans with thyrotoxicosis. Approximately 80% of hyperthyroid cats are hyperactive, while 10-25% are reported to be aggressive. Cats, as well as people, may experience the rarer manifestation of apathetic thyrotoxicosis, characterized by lethargy and depression. This is seen in approximately 10% of feline cases. Hyperthyroid cats are rarely presented to the veterinarian for behavioral signs, Perhaps because aggression is primarily wen when the cat is restrained, we as a profession are more likely to experience this aspect of the disease than the cats' owners, Treating the underlying thyroid problem generally resolves the behavioral problems however, and because onset is often insidious, it is only after the endocrine imbalance has been addressed that the owners appreciate the deterioration in their animal's behavior

While much has been written about the behavioral signs of hyperthyroidism in cats, the hypothyroid dog has been depicted, from a behavioral standpoint, as being lethargic and mentally dull. The hypothyroid human patient has been reported to show a wider range of behavioral symptoms. Particularly in the early stages of the disease reduced cognitive function and concentration together with impaired short-term memory may be confused with attention deficit-hyperactivity disorder, and in one study 66% of patients diagnosed with ADBD were found to be hypothyroid. Supplementing their thyroid levels was largely curative. Visual and auditory hallucinations may result from altered perception and have been misdiagnosed as schizophrenia or psychosis. Other behavioral symptoms have included fear - ranging from mild anxiety to frank paranoia, mood swings and aggression.

Scattered reports of aggression and hyperactivity in hypothyroid dogs suggested that dogs also might exhibit a wider repertoire of behaviors in

response to low thyroid levels. Hypothyroidism is the most prevalent endocrine disease in dogs. In a 1994 survey conducted by the American Kennel Club of its parent breed clubs, hypothyroidism was found to be the health issue of greatest concern overall, as well as for each of the seven groups except for the toy dog group, where it was rated fourth in importance. Despite the debate concerning diagnosis the condition is widespread throughout the canine, and probably the equine, population.

In dogs, as in humans, behavioral signs often precede the more traditional skin, coat and metabolic changes characteristic of the condition. To diagnose hypothyroidism we rely upon the six analyte panel offered by Antech Diagnostics, Irvine CA (as well as Michigan State University). These panels are interpreted for us by W. Jean Dodds DVM of Hemopet. Following her lead, we believe that truly euthyroid dogs in most breeds should have hormonal levels falling in the upper half of previously accepted normal ranges, This is particularly true of dogs under 18 months of age. We feel that the panel gives a clearer picture of overall thyroid function. Indeed of the cases treated so far only about 40% would have been considered hypothyroid on a standard T4 test, the rest would mostly fall in the borderline category. Some cases in which elevated autoantibody levels indicate autoimmune disease would otherwise have been considered thyroid normal at the time of presentation.

This table is presented in 2 parts because of size.

| Breed | Thyroid Dysfunction (208/319) | Aggression (177/319) | Seizures (43/319) |
|---|---|---|---|
| Golden Retriever | 27/38 | 9/10 | 5/5 |
| Akita | 21/28 | 19/23 | 0.1 |
| German Shepherd | 22/32 | 10/18 | 1/1 |
| Collie | 8/9 | 0 | 7/7 |
| Shetland Sheepdog | 7/11 | 2/3 | 0/1 |
| Labrador Retriever | 6/12 | 2/6 | 3/3 |
| Mixed breed | 14/31 | 5/15 | 2/4 |
| English Setter | 4/6 | 1/1 | 0 |
| TOTALS | 109/167 | 48/76 | 18/22 |

| Breed | Fearful (34/319) | Hyperactive (33/319) |
|---|---|---|
| Golden Retriever | 4/6 | 1/6 |
| Akita | 0 | 0/2 |
| German Shepherd | 2/3 | 2/2 |
| Collie | 0 | 0 |
| Shetland Sheepdog | 1/3 | 3/3 |
| Labrador Retriever | 0/1 | 0/2 |
| Mixed breed | 4/4 | 0/5 |
| English Setter | 1/3 | 1/2 |
| TOTALS | 12/20 | 7/22 |

Numerator = Thyroid dysfunction; Denominator = Aberrant behavior Some dogs had more than one aberrant behavior. Data were taken from 319 cases representing 63 breeds (W.J. Dodds DVM unpublished data). As of January this year, 319 cases of dogs with a variety of behavior problems had been presented to Dr. Dodds for thyroid evaluation. Of these almost two thirds were diagnosed as being hypothyroid.

{The following data are provided by Dr. Jean Dodds (1/4/98) and were not included in the presentation by Dr. Aronson.}

{Out of 13 Bearded Collies (11 in Dr. Dodd's group, 2 in Dr. Aronson's), 10 were hypothyroid and exhibiting significant aggression. Two cases had hyperactivity with major attention deficit-type behavior and were hypothyroid. One case with bizarre erratic behavior had very normal levels of thyroid and I advised retesting in 6-12 months. The owners couldn't cope with the dog as an unruly pet, and I fear gave it away or put it to sleep.

Of my 10 cases with hypothyroidism there was considerable or nearly total improvement in their behavior once thyroid supplementation was given and dosage stabilized. This usually took about 6 weeks, but clear benefit was noted by the owners in 2-14 days. One case has since slipped back a little, but became better again once thyroid dosage was increased slightly. I am very encouraged by these cases. Its particularly remarkable in cases of working obedience dogs, as their owners are very aware of performance nuances - such as changes in power of concentration which wanes with

thyroid imbalance and is restored on supplement. This latter comment applies in general and not to the beardie cohort per se.}

Our figures have been similar, but we have only submitted blood on dogs which we suspect might be hypothyroid based on other signs of disease, breed or combination of behavioral signs. Interestingly, although hypothyroidism has classically been thought to primarily affect bitches, the breakdown by sex shows more male hypothyroid behavioral cases. However, more male dogs are presented for behavioral problems. Sixty three pure breeds as well as mixed breeds were represented in these cases, Table I represents data for the seven most commonly represented breeds as well as mixed breeds, and the four most commonly reported behavioral problems. The numerator represents the number of animals which were hypothyroid and the denominator the number showing aberrant behavior.

There were 177 cases reported to exhibit aggression (type unspecified), 43 with seizures; 34 fearful; and 33 hyperactive. While some breeds are clearly more prone to thyroid disease than others, our data include two Bichon Frises which both proved to be hypothyroid and responded behaviorally quite well to thyroid replacement therapy, although this is not a breed which has shown much evidence of hypothyroidism in the past. Breed alone should not rule out hypothyroidism as a possible cause of a behavioral problem, although clearly if a dog is of a breed with a higher incidence of the disease one's level of suspicion will be higher.

Initially at Tufts we were looking for a hypothyroid - aggression/hyperactivity connection. Aggression is the most common behavior problem among dogs presented to our clinic for treatment. While some of the cases showed more characteristic skin and coat problem or obesity in many cases the dog appeared healthy apart from its behavioral problems. Many of these cases fell into two categories.

1. Young dogs which were aggressive and whose owners often complained their dog could or would not listen/concentrate and/or repeatedly failed obedience classes.
2. Older dogs for whom aggression was a new and totally unexpected behavior.

Treating the latter category brought reports of a return to youthful energy levels which the owners thought had gradually diminished purely because of

the dog's age, while the former suddenly were able to concentrate and learn commands. Dogs were evaluated over at least eight weeks following diagnosis of a thyroid problem. Most of these dogs were placed on behavior modification programs, and it was recommended that exercise should be increased, and dietary protein reduced. Some were fitted with Promise collars. Two dogs had previously received psychopharmacological treatment. In one case, the dog's dominance was no longer controlled by 20mg q l2h fluoxetine and 40mg q 8h propranolol, thyroxine supplementation did not improve the dog's behavior and it was euthanatized. In the other case a dog with fear and intraspecies aggression had not been helped with amitryptiline, and the dog was completely weaned from the drug after complete remission of its aggression on thyroxine.

Dogs were evaluated on a 6 point subjective scale by their owners (Table 2. Only the scoring system is shown below). Aggression was classified as dominance, fear, territorial, intraspecies, or predatory. Of the 57 cases of aggression treated with thyroxine replacement (levothyroxine sodium (Soloxine) at a dose of 0.1 mg/12-15# body weight q 12h, only one showed a worsening of aggression, 6 failed to respond and one showed less than 25% improvement. The remainder showed more than 25% improvement to complete resolution.

Data collected over the same period for 20 dogs with dominance aggression treated with behavior modification, exercise, diet and Promise Collars alone, showed that one dog was euthanatized for worsening behavior, two were placed after failure to improve or worsening of behavior, 3 failed to improve and 3 showed less than 25% improvement. Although the sample size is not large, the successful outcome of cases treated with thyroid replacement was significantly better than that of those treated with behavioral modification alone. We have also successfully treated one case where a hypothyroid horse exhibited intraspecies aggression with thyroid replacement. This horse had failed to respond to behavior modification or cyproheptidine.

Table 2. Scoring Behavior Problems Medicated with Thyroid

-1 Problem became worse
0 No appreciable change
1 <25% improvement
2 >25, but <50% improvement

3 >50 but <75% improvement
4 >75% improved to completely resolved

After our initial success with aggressive dogs, we have looked at the role of hypothyroidism in other behavioral conditions. Although the sample size is too small to be conclusive, it would certainly seem worthwhile to look for an underlying thyroid deficiency in these cases. Similarly, other behavioral conditions have shown variable response to thyroid supplementation. We have not seen much improvement in those dogs we have treated with seizure-related disorders, although Dodds has found seizure activity to be responsive to thyroid replacement, however, our sample size is extremely small.

The mechanism whereby diminished thyroid function affects behavior is unclear. Hypothyroid patients have reduced cortisol clearance, and the constantly elevated levels of circulating cortisol mimic the condition of an animal in a constant state of stress, as well as suppressing TSH production and thereby further reducing T4 and T3 levels. In humans, and seemingly in dogs, mental function is impaired and the animal is likely to respond to stress in a stereotypical rather than a reasoned fashion. We have noted that the type of aberrant behavior exhibited by hypothyroid dogs tends to be typical of the behavioral problems seen for its breed, or predominant breed, rather than hypothyroidism producing a specific behavioral problem. Chronic stress in humans has been implicated in the pathogenesis of affective disorders such as depression. Major depression has, in turn, been shown in imaging studies to cause changes in neural activity or volume in the amygdala, prefrontal cortex and hippocampus - areas of the brain which regulate aggressive and other behaviors. The role of the neurotransmitters dopamine and serotonin has been clearly demonstrated in aggressive pathways in the CNS. Hypothyroid rats have been shown to have both an increased turnover of serotonin; and dopamine receptors with an increased sensitivity to ambient neurotransmitter levels. Interestingly, several of the dogs which failed to respond to thyroid replacement or in which response was suboptimal have subsequently been treated with selective serotonin reuptake inhibitors or tricyclic antidepressants either without or with limited success. Given the far reaching effects of thyroid hormones throughout the body it is likely that these as well as other mechanisms are involved in its behavioral role.

Psychiatrists at Harvard Medical School have recently used low level thyroxine replacement for euthyroid and suboptimal thyroid normal patients with some success. They feel that the thyroid damps down the background noise in the brain, thereby enabling the patients to function better. In a limited number of cases where we have tried to boost dogs with suboptimal but normal thyroid levels into the optimal range, we have failed to achieve behavioral improvement. However, we have tried this in only a half dozen or so cases to date. Dodds reports some success using this strategy in a larger number of cases.

Case Study I.

Signalment: Seven-year old, 28kg, spayed female German Shepherd Dog

Problem: Fear aggression and intraspecies aggression. Previous treatment had included clorniprantine 25mg q 12h. (Note: this dose is too low to produce significant behavioral effect). No change was reported in problem behaviors, although the dog had behaved more affectionately with its owners. Owner is an obedience trainer, and extensive obedience training and following a behavior modification (desensitization and counterconditioning) program had not helped, The dog had to be muzzled when strangers came to the house or for walks off the owners' property.

Physical Examination: Evidence of arthritis and hip dysplasia, otherwise the dog appeared healthy

Thyroid panel abnormalities: Total T3 86 ng/dl (normal 100-250, optimal 125-225); Total T4 1.39 pg/dl (normal1.5-4.5; optimal 3-5); Free T4 0.92ng/dl (normal1.0-4.0; optimal2-4).

Treatment: Soloxine (levothyroxine sodium) 0.4mg q 12h. Clomiprarnine dose dropped to 25mg q 24h before dog started thyroid replacement

Follow-up: Five days after dog started on thyroid replacement therapy the owner took it to a neighborhood park and let it play off leash with a number of dogs. She reported that the dog showed no aggression and it played like a puppy, including a game of tug-of-war over a stick played with a puppy. The dog showed no aggression. The dog also accepted and greeted appropriately strangers coming onto its property or encountered on walks. Several weeks later, the dog was no longer behaving like a puppy, but like a mature German Shepherd with arthritis. It showed appropriate aggression when

other dogs acted aggressively towards it, or if they were too exuberant in their greeting. Inappropriate aggression has not returned over the succeeding twelve months. The dog has remained fit and active. Clomipramine has been completely withdrawn,

Case Study 2.

Signalment: 5yr old, 33kg, spayed female, Coonhound.

Problem: Aggression directed at owner, her husband and his teenage daughters from a previous marriage. The dog would growl and threaten if confronted over food, stolen objects, when woken, asked to move, or otherwise disturbed, particularly while it was sleeping in the owner's bed. This behavior had been increasing over the previous year since the owner's marriage, and at the time of presentation was occurring on at least a daily basis. Prior to that time there had been three isolated incidents of aggression when the dog was confronted over food or stolen objects either by the owner or children the dog knew well. The dog had never bitten. It was friendly with strangers, but did growl and threaten strange dogs occasionally.

Physical examination: The owner reported a 4kg weight gain in the dog over the previous 2 months. The dog also had a history of urinary incontinence, for which it had been receiving diethylstilbestrol (DES), and vaginitis. The dog was lethargic, with a poor, dull hair coat. Multiple open sores were apparent on the forepaws resulting from the dog licking and chewing - this was later attributed to atopy. Otherwise the dog appeared normal on physical examination.

CBC and Biochemical Profile: The only abnormality was severe hypercholesterolemia: 601 mg/dl; reference range. 110-314mg/dl.

Thyroid panel: Total T4, 14 nmol/L (reference range 5-50; optimal range 30-50); Total T3 0.0 nmol/L (normal 1.0 2.5; optimal 1.25-2.25); Free T4 15 pmol/L (normal 12-33; optimal 20-40); Free T3 5.1 pmol/L (normal 2.8-6.5; optimal 3.5-6.5); T4 Autoantibody10 (<20); T3 autoantibody 84 (< 10).

Follow-up.- The dog was placed on 0. 7mg levothyroxine sodium PO q 12h, and within a week aggressive behavior had decreased by 60-70%, Its aggression continued to decrease over subsequent weeks. Lethargy disappeared after about 6 weeks of thyroid replacement therapy. The dog

had also lost all the weight it had gained, and skin and coat condition improved. There was a single incident in which the dog growled during these 5 weeks. The dog continued to receive DES. There were no further incidents of vaginitis. On two subsequent occasions the efficacy of the thyroxine in controlling the dog's aggression was demonstrated. One time the dog did not swallow its morning pill. it spent the day sleeping, but growled when a family member approached its food bowl to feed it. On the second occasion the owner ran out of medication and the dog was not medicated for 48h, Within 24h aggression had returned to the same level it had been at prior to medication, After thyroxine supplementation was resumed aggression was extinguished over the subsequent 2-5days. Although the dog slept more during this period, it was not lethargic as it had been prior to treatment.

Discussion: While these are two of the more dramatic cases of hypothyroid aggression we have treated, they are illustrative of the response we have experienced. Metabolically, thyroid replacement takes about three weeks to be effective. Frequently, behavioral response is reported within the first week of treatment. Several owners also report dramatic resumption of previous aberrant behaviors if even a single pill is missed or not swallowed by the dog. Similarly, the horse mentioned earlier showed a rapid resumption of aggression when its dose was halved while its owner awaited the arrival of more medication. Hypothyroidism may be linked to a number of different behavioral conditions. Aberrant behavior may be one of the earliest signs of thyroid deficiency. The condition is clearly more prevalent in some breeds than in others, and a genetic predisposition is probably involved in the expression of the disease. However, environmental factors are probably also involved, and there have been numerous reports of owners and animals in the same household having thyroid dysfunction and/or other autoimmune diseases.

At Tufts we have seriously considered obtaining a thyroid panel on all dogs presented for evaluation, and we feel that it is a very good screen for a condition which may underlie a wide variety of behavioral problems, and one which is relatively easily and cheaply treated. It is our recommendation that hypothyroidism be considered as a rule out for dogs and horses showing inappropriate aggression. It should also be a rule out for dogs which show an inability to learn or concentrate on the owner, or for older dogs which have developed a personality change either rapidly or more gradually. It is probably a good rule out for dogs which exhibit fears or anxieties and possibly for some dogs with compulsive disorders

Bibliography:

1. Cameron DL, Crocker AD. The hypothyroid rat as a model of increased sensitivity to dopamine receptor agonists. Pharm Biachem & Behav,1990, 37:627-632.

2. Denicoff KD, Joffe RT, Lakschmanan MC, Robbins J, Rubinow DR. Neuropsychiatric manifestations of altered thyroid state. Am J Psychiatry, 1990, 147:94-99.

3. Dluhy RJ. The adrenal cortex in hypothyroidism. In Braverman LE, Utiger RD (eds) Werner and Ingbar's The thyroid, a fundamental and clinical text (7th edition). Philadelphia. Lippincott-Raven, 1996:841-844.

4. Dodman NH, Mertens PA, Aronson LP. Aggression in two hypothyroid dogs, behavior case of the month. J Am Vet Med Assoc,1995, 207:1168-1171

5. Gibbs M. Correlations between hypothyroidism and cortisol in mental disorders. 1997 in prep

6. Hauser P, Zametkin AJ, Martinez P,et al. Attention deficit-hyperactivity disorder in people with generalized resistance to thyroid hormone. NE JMed, 1993, 328:997-1001.

7. Herman JP, Cullinan WE. Neurocircuitry of stress: central control of the hypothalamo- pituitary-adrenocortical axis. TINS 1997, 20:78-84.

8. Henley WN, Chen X, Klettner C, Bellush LL, Notestine MA. Hypothyroidism increases serotonin turnover and sympathetic activity in the adult rat. Can J Fhysiol Pharmacol 1991;69-.205-210.

9. Joseph RJ, Peterson ME. Review and comparison of neuromuscular and central nervous system marifestations of hyperthyroidism in cats and humans. Prog Vet Neurol 1992, 3:114-119.

10. Uchida Y, Dodman N, DeNapoli J, Aronson L. Characterization and treatment of 20 canine dominance aggression cases. J Vet Med Sci 1997, 59:397-399.

11. Whybrow PC. Behavioral and psychiatric aspects of thyroto-xicosis. In Braverman LE, Utiger RD (eds) Werner and Ingbar's The thyroid: a fundamental and clinical text (7th edition). Philadelphia. Lippincott-Ravm 1996:696-700.

12. Whybrow PC. Behavioral and psychiatric manifestations of hypothyroidism. In Braverman LE, Utiger RD (eds) Werner and Ingbar's The thyroid- a fundamental and clinical text (7th edition). Philadelphia. Lippincott-Raven, 1996:866-870.