The Effect of Hypothyroid Function on Canine Behavior

L. P. Aronson, W. J. Dodds*

Introduction

In human medicine, a wide range of behavioral symptoms have been reported in hypothyroid patients. In the early stages of the disease, reduced cognitive function and concentration, together with impaired short-term memory, may be easily confused with attention deficit-hyperactivity disorder (AD/HD) (Hauser et al. 1993). Visual and auditory hallucinations can be mistaken for schizophrenia or psychosis. Fear—ranging from mild anxiety to frank paranoia; mood swings; and aggression have also been reported in hypothyroid patients (Denicoff et al. 1990). We have seen a comparable range of behavioral manifestation in dogs (*Canis familiaris*), particularly in those whose hypothyroidism has not progressed to the more traditional skin, coat and metabolic changes characteristic of the condition.
Thyroid hormones modulate the activity of norepinephrine (Heal and Smith 1988), serotonin (Bauer et al. 2002) and their receptors (Sandrini et al. 1996). In hypothyroid animals, 5-HT turnover increases in the brainstem, while cortical 5-HT concentrations and 5-HT2A receptor density may decrease. Administration of thyroid hormone to hypothyroid animals increases cortical 5-HT concentration and desensitizes autoinhibitory 5-HT1A receptors in the raphe area, thereby disinhibiting cortical and hippocampal 5-HT release. There is also evidence that thyroid hormones increase the sensitivity of 5-HT2 receptors (Bauer et al. 2002).

In human medicine, thyroid hormones are frequently used to accelerate the anti-depressant effect of tricyclic antidepressants and selective serotonin reuptake inhibitors, which can often take 3 or 4 weeks to produce a noticeable psychiatric effect (Sandrini et al. 1996; Altshuler et al. 2003). Gur et al. (1999) demonstrated that in rats (*Rattus norvegicus*) administration of triiodothyronine (T3) for 7 days at a dose of 0.1 mg/kg SQ q 24h resulted in comparable elevation of basal 5-HT levels in the frontal cortex to those achieved after 4 weeks of clomipramine at a dose of 10mg/kg IP q 24h. Thyroid hormones may also be given to supplement the effect of antidepressants when they are not achieving the desired effect.
Deficiencies of thyroid, adrenal cortex and sex hormones impair learning and the ability to store memories and behave normally. The adrenal hormones are directly involved in learning and behavior, while thyroid and sex hormones appear to modulate learning, memory and behavior at a higher level (Fedotova 2000). Hypothyroidism often reduces cortisol clearance. Conversely, glucocorticoids inhibit TSH release in response to thyrotropin

releasing hormone (Otsuki et al. 1973), reduce conversion of T4 to T3 (Chopra et al. 1975) and have direct effects on the thyroid gland itself (Kemppainen et al. 1983), so that stress could further diminish the function of a suboptimal thyroid. The thyroid-adrenal axis could be expected to affect behavior at all levels.

Materials and Methods

Diagnosis

Simply relying upon the total thyroxine (T4) test alone has been shown to give misleading results in an estimated 40 percent of dogs (Dodds 1997), whereas 62 percent of dogs were misdiagnosed with an in-house ELISA test kit (Lurye et al. 2002). Likewise, the canine thyroid stimulating hormone (cTSH) test produces false positive and negative results between 20 and 40 percent of the time, and so is considered to be only 70 percent predictive of primary canine hypothyroidism (Iversen et al. 1999; Marca et al. 2001). Complete thyroid profiling (total and free T3 and total and free T4 levels, as well as circulating levels of thyroglobulin autoantibodies (TgAA), and T3 and T4 autoantibodies) should be performed. However, this information must be examined in conjunction with clinical evaluation of the animal. Reference ranges offered by most laboratories do not adequately address the disparate needs of different groups of dogs. Basal levels should be higher in toy and small breeds and somewhat lower in giant or very large breeds as well as sight-hounds (Dodds 1995; Gaughan et al. 2001; Hill et al. 2001). Basal levels should be higher in young dogs (up to about 18 months of age) and lower in geriatric animals (Wolford et al. 1987; Dodds 1995). A variety of circumstances can affect the optimal thyroid levels for an individual. These would include athletic/performance activities (Evason et al. 2004); altered levels of sex hormones—due to such causes as estrous, pregnancy or lactation; obesity; sickness or recent recovery from illness; vaccination; anesthesia or drugs that may influence thyroid function—corticosteroids, phenobarbital, potentiated sulfonamides, dietary soy or soy phytoestrogens, insulin, narcotic analgesics, salicylates, tricyclic antidepressants, furosemide, phenylbutazone and mitotane (Dodds 1995, 1997). Superimposed upon these effects are daily diurnal fluctuations in hormone levels. It is possible to accurately assess thyroid function in the face of these conditions, but they cannot be ignored.

Subjects

Thyroid function data were obtained for more than 1500 dogs presented to veterinarians for a range of behavioral problems. Some dogs were referred to the authors for treatment; others we consulted on but did not see personally. Thyroid function was determined based on laboratory results, clinical presentation, and other factors as described above. While some dogs would be deemed hypothyroid by any laboratory, others would be described as borderline or having suboptimal thyroid function.

The reference ranges used for adult dogs are as follows: TT4 optimal range 2–4 ug/dL; free T4 optimal range 1–3ug/dL; TT3 optimal range 50–150 ng/dL; free T3
optimal range 3–8 pg/dL; T4 AA <2.0; T3 AA <2.0; TgAA <20. However, depending upon the specific case demographics, these may vary. There are different optimal ranges for puppies, geriatrics, large/giant breeds and sight-hounds. These optimal ranges have been developed over 20+ years of data collection and analysis by the second author. Cases were considered 'borderline' when some of the analytes of the profile were below the optimal ranges, but other analytes were within the lowest end of the optimal reference ranges. Follow up was obtained on one or more occasions with post-treatment complete thyroid profiles and interviews with the referring clinic and/or client. This is an on-going study and earlier reports have been made on some of these data (Dodman et al. 1995; Aronson and Dodman 1997; Dodds 1997, 2004; Aronson 1998; Dodds and Aronson 1999).

Results

Of the 1500 cases presented for behavioral problems, 921 (61%) were determined to be hypothyroid or have suboptimal thyroid function using the determined criteria. Statistical analysis of the first 499 cases using neural network correlative analysis has been undertaken and showed a highly statistically significant relationship between thyroid dysfunction and dog-to-human aggression ($p = <0.001$, with a suggestion of a trend also towards dog-to-dog aggression (p slightly > 0.05). Other behavioral associations remain to be analyzed. Spayed and castrated animals are at greater risk than intact ones; mid sized and larger breeds are also more likely to be affected; the incidence is far greater in purebred dogs.

Treatment was recommended with levothyroxine sodium at a dose of 0.1mg/ 5.5 – 7.0 kg body weight, *per os*, q12h. (Doses were adjusted to allow for age, breed and other factors affecting the individual dog.) Follow up was not available for all cases referred. In those for which it was available, approximately 62 percent showed greater than 50 percent behavioral improvement (36 percent showed more than 75 percent improvement to complete resolution of the problem), 25 percent showed between 25 and 50 percent improvement, 10 percent failed to improve and 2 percent got worse.

A favorable behavioral response to thyroid replacement therapy was usually apparent within the first week of treatment, although metabolic deficits were not corrected for three weeks, and skin and coat issues could take months to resolve.

Discussion

Behavioral presentations

In dogs, as in humans, hypothyroidism appears to present as impaired mental function; reasoned behavior is lost in favor of a panicked response. In general, behavioral problems are most noticeable when the animal is psychologically or physiologically stressed.The behaviors displayed by hypothyroid dogs fall into several distinct patterns.

In some animals problems appear at a very early age (6 months or less). They generally show poor or variable attachment to their owners, and they are difficult to train. Behaviors are lost from one training session to the next. Owners often describe these dogs as appearing to have AD/HD. These dogs may become fixated on one activity—such as playing Frisbee—and only value their owners' presence for providing this.

Perhaps more common is the dog that exhibits a sudden change of personality and behavior at puberty or as a young adult. It may be that this is the age at which owners become more aware of the behaviors as the animal is larger and more difficult to live with, and odd behaviors that may be tolerated in a puppy become less endearing. Neutering usually has little or no effect on the behaviors, which may intensify as the dog ages. While certain breeds are over-represented, and distinct familial patterns may be observed, breed or lack thereof, cannot rule the condition out.

Those breeds most represented include those in which allergies and other immune problems are also most common. These would include: English Setter, Golden Retriever, Akita, Rottweiler, Doberman Pinscher, English Springer Spaniel, Shetland Sheepdog, and German Shepherd Dog. Like their younger cohorts, these dogs may show few, if any, signs of being hypothyroid other than behavioral ones. As opposed to being lethargic and obese, these dogs are often underweight and hyperactive.

Many have a worried or tragic appearance. They may have seasonal allergies; recurrent skin, ear and foot infections; shed excessively; and/or chronic gastrointestinal problems. Some of these dogs present with a sudden onset of aggression—usually owner directed or intraspecific. Others will become fearful, whining incessantly, and showing nervousness in new situations or around strangers; they may hyperventilate and sweat excessively. Their fear may also lead to aggression. Some dogs develop apparently obsessive behaviors such as tail chasing and pacing.

These same changes can occur in adult dogs. Separation anxiety may appear suddenly. Noise phobias—particularly thunderstorm phobia—most commonly arise in this group. This is also the stage at which some dogs start to show other signs of hypothyroidism—lethargy, weight gain, reduced energy, change in the character of the bark. Superstitious behaviors—watching the

ceiling or wall for no apparent reason, refusing to walk on particular surfaces—may appear. Episodic dyscontrol and other behaviors related to partial seizures are also seen. Although not a behavioral phenomenon per se, tonic clonic seizure activity is also commonly related to hypothyroidism. Particularly noticeable in performance and service dogs, some will lose concentration and no longer be able to perform at their previous skill level. Older dogs may suddenly become irritable and show aggression, food guarding and other behaviors at complete odds to their younger selves. They sleep more, seek out heat sources, and show reduced scenting, hearing and visual acuity. While these signs might be attributed to advancing age or even cognitive dysfunction, they will resolve with treatment of the hypothyroidism along with the behavioral problems.

The prevalence of hypothyroidism within the canine population is unknown, but is estimated in some breeds to be as high as 40 percent, and there is evidence that it is increasing (Dodds 1995). A recent study (Hamilton et al. 1998) compared total T4 and cTSH levels between a group of 21 bearded collies with no overt signs of hypothyroidism or aberrant behaviors (control group) with an experimental group of 22 bearded collies of similar age and sex distribution that exhibited problem behaviors but also showed no signs of hypothyroidism. Fifty-two dogs were excluded from the study because they exhibited signs of hypothyroidism, of these 34 had behavioral signs as well. Total T4 levels were significantly lower ($p = 0.01$) in the experimental group when compared to the control group. The behaviors exhibited by the experimental group included noise and thunderstorm fears; fearful/anxious/shy behavior; separation anxiety; hyperactivity; poor concentration/learning; compulsive behaviors; mood swings, irritability and aggression—primarily territorial. We have seen more owner directed and dog-to-dog aggression, but otherwise behaviors seem similar to those we have found. Beaver and Haug (2003) also report owner directed aggression as a result of hypothyroidism.

We have seen a wide range of problem behaviors in dogs that are clinically hypothyroid or have suboptimal thyroid function. Some in this latter group appear completely healthy and others show minor problems such as seasonal allergy, ear infections, skin and coat disorders, etc. Many of these dogs responded to thyroid replacement on a twice-daily dosing regimen. In some cases, the dogs have been treated with a variety of other psychoactive drugs prior to presentation, as well as a number of other medical regimens. In general, such treatment was unsuccessful.

While we know that thyroid can exert an effect on behavior by affecting levels of serotonin and norepinephrine, it would seem there are other mechanisms involved in producing some of its behavioral effect. Given that levels of endogenous glucocorticoids inhibit thyroid hormone production and release, as well as the conversion to the active form, it is not surprising that in dogs with borderline and suboptimal thyroid function, stress will induce a truly hypothyroid state that manifests initially in behavioral problems.

Our results suggest that thyroid replacement has an important role in the

treatment of canine behavior, just as it does in human psychiatry. Therapeutic doses of levothyroxine are not harmful, provided any withdrawal of treatment is made gradually; wider use of such therapy could be beneficial to many dogs. In our opinion, it would be prudent to include a full thyroid panel in the work-up of most, if not all, behavioral cases.

Acknowledgement

The authors wish to thank Dr. Robert Keller, Chairman, Computer Sciences, Harvey Mudd College, Pomona, CA for his statistical analysis of the data.

References

Altshuler L L, Frye M A and Giflin M J 2003 Acceleration and augmentation strategies for treating bipolar depression. *Biological Psychiatry* 53: 691–700

Aronson L P 1998 Systemic causes of aggression and their treatment. In: Dodman NH and Shuster L (eds.) *Psychopharmacology of Animal Behavior Disorders* pp. 64–102. Blackwell Sciences: Malden, USA

Aronson L P and Dodman N H 1997 Thyroid function as a cause of aggression in dogs and cats. *Proceedings Deutschen Veterinaermedzinischen Gesellshaft* p 228

Bauer M, Heinz A and Whybrow P C 2002 Thyroid hormones, serotonin and mood: Of synergy and significance in the adult brain. *Molecular Psychiatry* 7: 140–156

Beaver B V and Haug L I 2003 Canine behaviors associated with hypothyroidism. *Journal of the American Animal Hospital Association* 39: 431–434

Chopra I J, Williams D E, Orgiazzi J and Solomon D H 1975 Opposite effects of dexamethasone on serum concentrations of 3,3',5 triiodothyronine (T3). *Journal of Clinical Endocrinology and Metabolism* 41: 911–920

Denicoff K D, Joffe R T, Lakschmanan MC, Robbins J and Rubinow DR 1990 Neuropsychiatric manifestations of altered thyroid state. *American Journal of Psychiatry* 147: 94–99

Dodds W J 1995 Estimating disease prevalence with health surveys and genetic screening. *Advances in Veterinary Science and Comparative Medicine* 39: 29–96

Dodds W J 1997 What's new in thyroid disease? *Proceedings American Holistic Veterinary Medical Association* pp. 82–95

Dodds W J 2004 Behavioral issues and thyroiditis: theory and case review. *Proceedings American Holistic Veterinary Medical Association* pp. 55–59

Dodds W J and Aronson L P 1999 Behavioral changes associated with thyroid dysfunction in dogs. *Proceedings American Holistic Veterinary Medical Association* pp. 80–82

Dodman N H, Mertens PA and Aronson LP 1995 Aggression in two hypothyroid dogs. *Journal of the American Veterinary Medical Association* 207: 1168–1171

Evason M D, Carr A P, Taylor S M and Waldner, C L 2004 Alterations in thyroid hormone concentrations before and after athletic conditioning. *American Journal of Veterinary Research* 65: 333–337

Fedotova Y O 2000 The effects of peripheral endocrine hormone deficiencies on the

processes of behavior, learning and memory. *Neuroscience and Behavioral Physiology* 30: 373–378

Gaughan K R, Bruyette D S and Jordan F R 2001 Thyroid function testing in greyhounds. *American Journal of Veterinary Research* 62: 1130–1133

Gur E, Lerer B and Newman M E 1999 Chronic clomipramine and triiodothyronine increase serotonin levels in rat frontal cortex in vivo: Relationship to serotonin autoreceptor activity. *Journal of Pharmacology and Experimental Therapeutics* 288: 81–87

Hamilton Andrews S, McBride E A and Brown I 1998 Canine hypothyroidism and aberrant behavior. MSc dissertation Hamilton Andrews S, University of Southampton New College, UK

Hauser P, Zametkin A J, Martinez P, Vitiello B, Matochik J A , Mixson A J and Weintraub B D 1993 Attention deficit-hyperactivity disorder in people with generalized resistance to thyroid hormone. *New England Journal of Medicine* 328: 997–1001

Heal D J and Smith S L 1988 The effects of acute and repeated administration of T3 to mice on 5-HT1 and 5-HT2 function in the brain and its influence on the actions of repeated electroconvulsive shock. *Neuropharmacology* 27: 1239–1248

Hill R C, Fox L E, Lewis D D, Beale K M, Nachreiner R F, Scott K C, Sundstrom D A, Jones G L and Butterwick R F 2001 Effects of racing and training on serum thyroid hormone concentrations in racing greyhounds. *American Journal of Veterinary Research* 62: 1969–1972

Iversen L, Jensen A L, Hoier R and Aaes H 1999 Biological variation of canine serum thyrotropin (TSH) concentration. *Veterinary Clinical Pathology* 28: 16–19

Kemppainen R J, Thompson F N, Lorenz M D, Munnell J F and Chakraborty P K 1983 Effects of prednisone on thyroidal and gonadal endocrine function in dogs. *Journal of Endocrinology* 96: 293–302

Lurye J C, Behrend E N, Kemppainen R J 2002 Evaluation of an in-house enzymelinked immunosorbent assay for quantitative measurement of serum total thyroxine concentration in dogs and cats. *Journal of the American Veterinary Medical Association* 221: 243–249

Marca M C, Loste A, Orden I, Gonzalez J M and Marsella J A 2001 Evaluation of canine serum thyrotropin (TSH) concentration: comparison of three analytical procedures. *Journal of Veterinary Diagnostic Investigation* 13: 106–110

Otsuki M, Dakoda M and Baba S 1973 Influence of glucocorticoids on TRF induced TSH response in man. *Journal of Clinical Endocrinology and Metabolism* 36: 95–102

Sandrini R M, Vitale G, Vergoni A V, Ottani A and Bertolini A 1996 Effect of acute and chronic treatment with triiodothyronine on serotonin levels and serotonergic receptor subtypes in the rat brain. *Life Sciences* 58: 1551–1559

Wolford S T, Schroer R A, Gohs F X, Gallo P P, Falk H B, and Dente A R 1987 Effect of age on serum chemistry profile, electrophoresis and thyroid hormones in beagle dogs two weeks to one year of age. *Veterinary Clinical Pathology* 17: 35–42

Keywords
aggression, behavior, dog, fear, hypothyroidism, learning

**PetShrink, 117 Lyman Rd, Berlin, MA 01503, USA*
Hemopet, 11330 Markon Dr, Garden Grove, CA 92841, USA
*Corresponding author: dvm@petshrink.com