Evaluation of the thyroid status of Basenji dogs in Australia

A SEAVERS,[a] DH SNOW,[b] KV MASON[c] and R MALIK[d,e]

Objective To determine the thyroid status of Basenji dogs in Australia.

Methods Jugular or cephalic venipuncture blood samples were taken from 113 Basenji, comprising 47 males, 5 castrates, 48 entire and 13 spayed bitches, and sent on ice in plain and EDTA tubes to a single laboratory to determine haematocrit and serum concentrations of total thyroid hormone (thyroxine, TT4), thyroid-stimulating hormone (TSH) and cholesterol. In a subgroup of 8 dogs with abnormal elevated TSH concentrations and subnormal TT4 concentrations, 5 were further examined by dynamic endocrine testing using recombinant human (rh) TSH (54 μg).

Results Ages ranged from 1 to 14 years and weight range was 6.5 to 14.0 kg. TT4 concentrations (nmol/L) ranged from 2 to 27, with a median of 13 and a mean ± SD of 13.0 ± 5.7. Importantly, 85/113 (75%) of TT4 values were lower than the normal laboratory reference range (17–37). TSH concentrations (ng/mL) ranged from 0.05 to 5.37, with a median of 0.16 and a mean ± SD of 0.3 ± 0.6.

Conclusions Basenji have a similar reference range for serum TSH, but a considerably lower reference range for TT4 (2–27 nmol/L) than most breeds and crossbreds, resembling the sight hounds in this respect. Given the difficulty of accurately measuring TT4 concentrations that are so low, concomitant serial TSH determinations are essential to properly asses thyroid function. Taken alone, TT4 determinations are only of use when the value is within the reference range, in which case a diagnosis of hypothyroidism is likely excluded.

Key words: Basenji, greyhound, hounds, thyroid, thyroid-stimulating hormone, thyroxine

Abbreviations: fT4, free thyroid hormone; TGAA, thyroglobulin auto-antibodies; TSH, thyroid-stimulating hormone; TT4, total thyroid hormone (thyroxine); rh, recombinant human.

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Hypothyroidism is one of the most common canine endocrine diseases,[1,2] but perhaps also the most misdiagnosed. A definitive diagnosis is challenging because the clinician must first recognise clinical features that are not invariably characteristic and use confirmatory laboratory tests, which can be difficult to interpret, especially in the presence of non-thyroidal illness[3] or recent drug administration.[3,4] Importantly, it is recommended that thyroid function tests should only be performed in dogs with actual clinical signs consistent with hypothyroidism.[1] The situation is thus further complicated when a specific breed society decides to screen breeding stock for hypothyroidism on the basis of an alleged inherited basis for the condition. Driven by 'abnormal' results based on inappropriate laboratory reference intervals, which do not take breed differences into account, a situation may arise in which healthy individuals are unnecessarily removed from the gene pool on the basis of such testing.

An additional complication is that analytic techniques and reference intervals for different hormones vary from one laboratory to another. To complicate matters further, approximately 20% to 25% of hypothyroid dogs have a serum concentration of thyroid-stimulating hormone (TSH)[2] within the normal range, while 7% to 18% of normal dogs have an elevated serum TSH concentration.[2,5] This makes some investigators question whether it is indeed possible to diagnose canine hypothyroidism conclusively in some instances.[1]

Confirming a diagnosis of hypothyroidism thus requires evaluation of the thyroid status using a range of endocrine tests, of which the simultaneous determination of the total thyroid hormone (thyroxine) (TT4) and TSH concentrations in serum are probably the most useful, especially if the subsequent administration of thyroid replacement therapy produces unequivocal resolution of the abnormal clinical findings.[1] This is even more conclusive if clinical abnormalities are shown to recur upon withdrawal of thyroid supplementation.

Measurement of thyroglobulin auto-antibodies (TGAA) can provide useful additional information.[6,7] Dynamic endocrine testing using exogenous TSH (either bovine or recombinant human [rh]) is probably too expensive for routine use, although of great theoretical value.[8,9] Scintigraphy,[10] high-resolution ultrasonography[11,12] and thyroid biopsy[2] can provide additional useful information that may be helpful in certain situations.

It is becoming clear that reference ranges for a wide range clinical and laboratory measurements in canine medicine are strongly influenced by breed, and this affects the interpretation of values for haematology and serum biochemistry (e.g. haematocrit, leucocyte counts, cholesterol concentrations) and the results of

[a]Oak Flats Veterinary Clinic, 58A Central Avenue, Oak Flats, New South Wales 2529, Australia; aines@bigpond.com
[b]Symbion, North Ryde NSW, Australia
[c]Dermcare, Springwood Queensland, Australia
[d]Post Graduate Foundation in Veterinary Science, Sydney, NSW, Australia
[e]Faculty of Veterinary Science, University of Sydney, NSW, Australia

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hormone assay determinations. For example, it has been shown that Greyhounds (and probably the other sight hounds) have higher haematocrits and higher blood viscosity[13] than other breeds; they also have a different ability to biotransform certain drugs in the liver, such as the thiobarbiturates, and have extreme echocardiographic parameters[14] and a propensity towards hypertension.[13] Likewise, concentrations of TT4 in the serum of Greyhounds,[15] Scottish Deerhounds,[16] Whippets,[17] Giant Schnauzers[18] and conditioned Alaskan sled dogs[19] are lower than in those in most other breeds and crossbred dogs, and higher values have been reported for the Polish Owczarek Nizinnys breed.[18] Recent recommendations on the use of TT4 concentrations as prognostic indicators in dogs with non-thyroidal illness[20] further emphasise the importance of establishing breed-specific reference ranges.

One of us (A.S.) has observed that clinically normal Basenji dogs in Australia appear, on average, to have lower serum concentrations of TT4 than the normal canine laboratory reference range. There is anecdotal evidence that this phenomenon may result in the erroneous diagnosis of hypothyroidism in asymptomatic patients, which are often young healthy animals, with the attendant institution of inappropriate life-long thyroid replacement therapy or withdrawal of valuable breeding stock, an action that might well prove catastrophic for a breed with a small gene pool. To shed more light on the possibility of breed-specific references intervals, we prospectively determined the thyroid status of a large and representative cohort of Basenji dogs in Australia to ascertain the reference range for TT4 and TSH in normal individuals of this breed. Although it was our intention to include only clinically healthy dogs, testing fortuitously included a small number of patients that may have had mild or 'subclinical' hypothyroidism. Further investigation of this subgroup of dogs provided vital additional data relating to the significance of TSH values, especially when considered in concert with serial TT4 determinations.

Materials and methods

Organisation and inclusion criteria

Basenji owners and breeders around Australia were contacted to seek their involvement, and 12 convenient veterinary clinics around the country were recruited as collection sites. Breeders and their veterinarians were invited to enrol known healthy animals in the survey. Any healthy Basenji over 1 year of age was eligible to be enrolled. The Basenji Club distributed a compulsory 41-item questionnaire, which inquired about the breeding status of the dog and its sire and dam, diet, supplements, recent medication, including heartworm preventatives, coat condition and temperament. Local veterinarians were used to reduce the risk that an unknown unhealthy dog would be included. Any food additives (e.g. Missing Link™, vitamin and mineral supplements, herbal and homeopathic treatments) had to be discontinued for at least 1 month preceding blood collection. Animals on medication in the preceding month were not eligible for inclusion.

Dogs and sample collection

Over a 3-day period in October 2006, 115 Basenji dogs attended their local veterinary clinic for blood collection. As Basenji ovulate only once a year, as a result of the shortening photoperiod associated with the autumn equinox, all animals were likely to be at least 100 days post-oestrus, parturition or vaccination and at least 50 days clear of lactation. Ambient temperature was between 10°C and 24°C at all collection sites. It was requested that dogs be given no food for 12 to 24 h prior to venipuncture. After examination, 114 Basenji were deemed healthy and blood was collected from the jugular or cephalic vein. This initial study cohort of 114 dogs consisted of 47 entire males, 5 castrated males, and 48 entire and 14 spayed bitches. The weight of the dogs ranged from 6.5 to 14.0 kg.

For the determination of haematocrit and measurement of serum TT4, TSH and cholesterol concentrations, 5 to 10 mL of blood was collected into EDTA and plain (clot) tubes. The decision to exclude fT4 from the current study was taken because commercial test kits were temporarily unavailable in Australia (and elsewhere) at the time of this study.

Laboratory investigations

All testing was done at a single laboratory (Symbion Vetnostics) in Sydney. Blood was transported on ice in a cooled foam container. Blood was allowed to clot in transit, and serum was subsequently harvested by centrifugation. Plain clot tubes were used to exclude possible interference by serum-separating gel in any of the hormone assays.

Concentrations of TT4 and TSH in serum were measured using commercial test kits (Biomediq DPC kits) according to the manufacturer's recommendations, using an Immulite 2000 for specimen analysis. Serum cholesterol concentrations were measured by Roche Modular Analyser using appropriate reagents. The haematocrit values for the EDTA anti-coagulated blood specimens were determined using a Becton Dickinson QBC microhaematocrit centrifuge. Repeat samples were run to validate unusually high or low results, especially for TSH. One dog's sample with a high TT4 was re-assayed but rejected because of haemolysis of the sample in transit from a geographically remote collection site. Pertinent details for the remaining 113 dogs and the results for the various laboratory tests were entered into a commercial spreadsheet program (Excel®; Microsoft), which was used to inspect, sort, order and analyse the data. The data were entered also into a statistical software program (Minitab®) for further analyses and the creation of scatter plots.

Dynamic thyroid testing

To characterise the subgroup of dogs that were outwardly normal, but had increased TSH concentrations accompanied by TT4 values lower than the canine reference range, thyroid function was examined further by dynamic endocrine testing in April 2007. Specifically, the extent to which the serum TT4 would increase following administration of rhTSH was studied.[8] Food, but not water, was withheld as before. A 1.1 mg vial of

Table 1. Results from 113 Basenji dogs screened for thyroid status

Analyte	Range	Median	Mean ± SD	Reference range for normal dogs
TT4	2–27	13.0	13.0 ± 5.7	17–37 nmol/L
TSH	0.05–5.37	0.15	0.3 ± 0.6	0–0.6 ng/mL
Cholesterol	2.9–8.9	5.5	5.5 ± 1.3	3.6–8.8 mmol/L
Haematocrit	0.38–0.60	0.48	0.47 ± 0.05	0.39–0.55 L/L

rhTSH (Thyrogen®; Genzyme, Sydney) was freshly dissolved in 1.2 mL of sterile water for injection to produce a 0.9 mg/mL solution, following the manufacturer's directions. Seven aliquots (0.06 mL) of this solution were drawn up into human insulin syringes (100 U/mL; i.e. 6U = 54 µg rhTSH), which were used because of their minimal dead space.

The remaining aliquots of diluted rhTSH were stored at −20°C, as has been recently recommended,[9] and subsequently used in May 2007 to test a further five 'control' Basenji dogs, each with a TSH value of less than 0.6 ng/mL, to further establish the normal response of this breed to dynamic endocrine testing. Following collection of a baseline blood specimen from the cephalic vein, 54 µg of rhTSH was injected intravenously. Animals were observed for 30 min to monitor any adverse events, and then allowed to go home, although food was still withheld. Dogs were returned 6 h later for collection of a second blood specimen. Samples were transported to the laboratory and processed as described previously.

Results of dynamic rhTSH testing were interpreted according to the criteria of (i) De Roover et al,[9] whereby thyroid function was considered acceptable if the TT4 value 6 h after rhTSH was > 31 nmol/L, or if the post-stimulation TT4 was > 1.5-fold of the baseline value and (ii) Larsson[21] whereby if 0.5 × baseline TT4 plus the difference/increase in TT4 after stimulation was >30, the dog was considered to be euthyroid and if <15 was considered hypothyroid, with in-between values being equivocal.

Results

TT4, TSH, cholesterol and haematocrit measurements

The mean, median, standard deviation (SD) and range for all measurements obtained are shown in Table 1 with the relevant laboratory reference ranges.

The distributions of the T4 and TSH concentrations for the 113 Basenji dogs are shown in Figures 1 and 2, respectively.

Of the 113 Basenji dogs, 85 (75%) had TT4 values less than 17 nmol/L, which is lower than the laboratory normal reference range (Figure 3), and only 8 had TSH concentrations higher than 0.60 ng/mL, the upper limit of the reference range. Thus, 77 Basenjis had 'low' TT4 values with corresponding 'normal' TSH values.

Cholesterol and haematocrit values were within reference ranges, except for 1 dog with an elevated serum cholesterol concentration, 1 dog with a slightly low haematocrit (0.38 L/L), and 4 dogs with slightly elevated values.

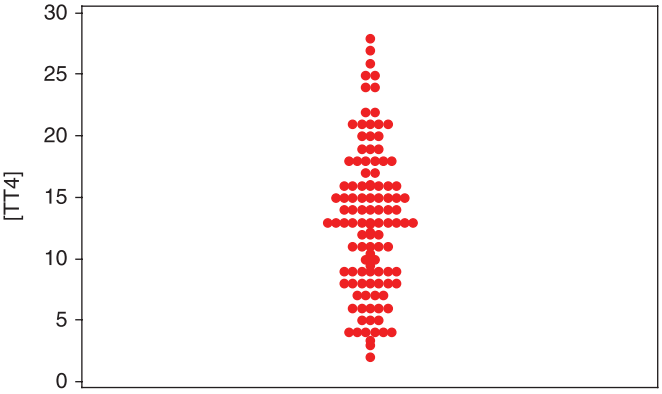

Figure 1. Scatter plot of serum total thyroid hormone (TT4) concentrations for 113 Basenji dogs. The Y-axis represents the serum TT4 concentration in nmol/L, and each dot represents the value for an individual dog. By inspection, 85/113 (75%) TT4 values in this cohort of Basenji dogs were < 17 nmol/L (i.e. lower than the laboratory normal reference range).

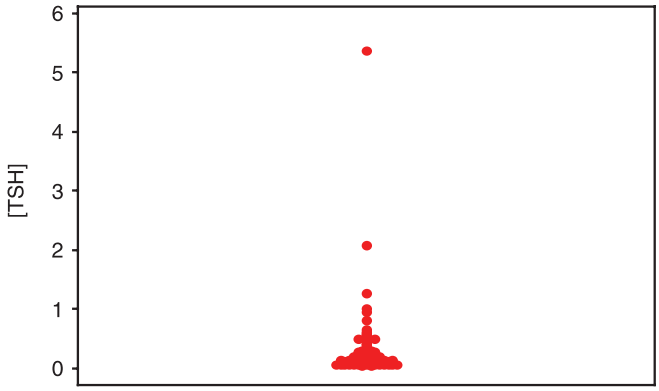

Figure 2. Scatter plot of serum thyroid-stimulating hormone (TSH) concentrations for 113 Basenji dogs. The Y-axis represents the serum TSH concentration in ng/mL, and each dot represents the value for an individual dog. By inspection, eight dogs had TSH concentrations > 0.6 ng/mL (i.e. greater than the upper limit of the laboratory reference range).

rhTSH testing of dogs with TSH concentrations above the reference range

Considering the normal reference range for serum TSH to be ≤ 0.6 ng/mL, 8 dogs had elevated TSH concentrations (0.63, 0.67, 0.82, 0.95, 1.02, 1.28, 2.09 and 5.37 ng/mL, respectively) (Figure 2), which with their corresponding TT4 (11, 4, 7, 9, 5, 9, 9 and 4 nmol/L) (Figure 3) and cholesterol concentrations (5.2, 7.4, 5.8, 7.9, 5.1, 7.2, 7.1 and 7.9 mmol/L) (Table 2), suggests that some or all of these dogs may have had clinical or subclinical hypothyroidism. To test this proposition, this subgroup underwent further examination and testing.

Of this original subgroup of eight dogs, five were essentially normal on repeat physical examination, including assessment of heart rate and rhythm, arterial and jugular pulses, mucous

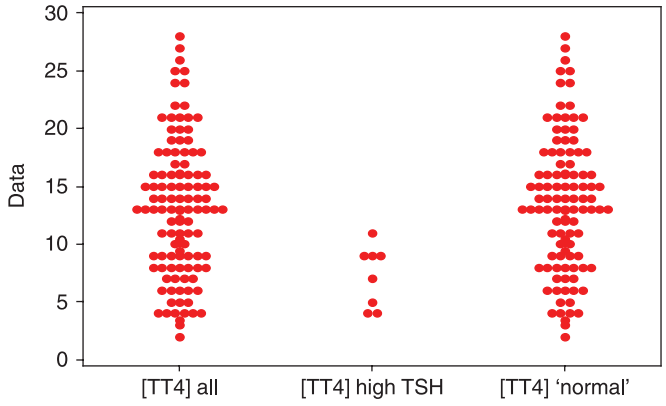

Figure 3. Scatter plot of serum total thyroid hormone (TT4) concentrations for 113 Basenji dogs, subdivided further on the basis of their serum thyroid-stimulating hormone (TSH) concentration. The Y-axis represents the serum TT4 concentration, and each dot represents the value for an individual dog. The three sets of data represent the entire study cohort (Left), dogs with TSH concentrations above the reference range (n = 8; Middle) and dogs with TSH concentrations within the reference range (Right). Without exception, dogs with high serum TSH concentrations had TT4 concentrations below the laboratory's normal reference range.

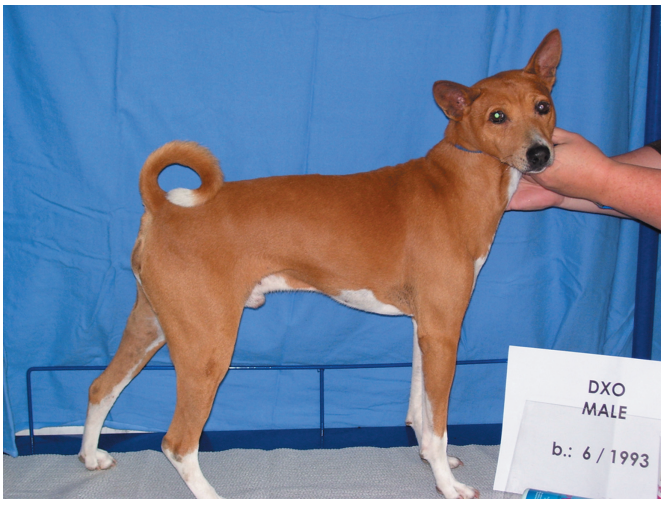

Figure 4. Photograph of a dog with 'sub clinical hypothyroidism' based on elevated TSH concentration and suboptimal response to rhTSH. Note that outwardly the dog looks completely normal, with no abnormal physical findings or clinical signs.

membrane colour and refill, evaluation of the coat and rectal temperature determination. Of the remaining three dogs, one had been euthanased 3 months after the initial survey as a result of an acute neurological condition diagnosed presumptively as a cerebrovascular accident by the attending veterinarian (regrettably, the brain and thyroids were not examined grossly or histologically postmortem). One was unavailable because of geographical remoteness from the rhTSH test site. The last (which had had the highest TSH value of 5.37 nmol/L) was originally noted by the senior author (A.S.) to be lethargic and have hypertrichosis over shoulders and neck, and hypotrichosis elsewhere, and on the basis of the physical and laboratory findings it was considered to have hypothyroidism and given replacement therapy prior to the donation of rhTSH as part of this project. After several months of thyroid supplementation (100 µg thyroxine twice daily), the serum TT4 had increased to 30 nmol/L and the TSH had decreased to 0.06 ng/mL, with a corresponding cholesterol value of 6.5 mmol/L and resolution of all abnormal physical findings. This bitch remains well almost 2 years later.

The five dogs were then subjected to dynamic thyroid testing using rhTSH based on a recently published protocol.[8] Because of the scarcity of information on rhTSH testing in sight hounds, seven additional Basenjis with serum TSH values less than 0.60 were included as breed-specific 'controls'. All five dogs from the subgroup and a further two control dogs all weighed less than 12 kg. One dog was found to have an elevated TSH concentration at the time of testing and was therefore included together with the subgroup dogs. Based on reported data for other breeds and data from the six Basenji controls, it would seem that at least two of the dogs tested could be considered to be clinically or 'subclinically' hypothyroid on the basis of a low TT4, an increased serum TSH and a subnormal response to exogenous rhTSH (Table 2, Figure 4). Two dogs were accordingly given a trial of thyroid supplementation. After 3 months of thyroxine (100 µg twice daily), the male dog had a 4-h 'post-pill' TT4 of 29 nmol/L and the TSH decreased from 4.53 to 0.04 ng/mL, with a corresponding cholesterol value of 5.9 mmol/L. There was no change in the animal's clinical status as assessed by its owner. After 4 months, the owner reported the dog to be voraciously hungry, losing weight and restless. The dose was reduced by half and the dog remained well and stable for a further 10 months. After a total of 14 months of thyroid supplementation, this dog then experienced a sudden decline in general health and was euthanased. Histology sections taken peri-mortem showed bilateral shrunken glands with severe chronic lymphocytic thyroiditis along with a dermatopathy due to follicular inactivity and atrophy consistent with the cutaneous effects of hypothyroidism. This histology supports the significance given to the cTSH level both alone and serially and additionally supports the results and interpretation of the rhTSH testing. The second dog's owner declined further testing, but reported the dog to be clinically well and healthy while receiving 70 µg thyroxine twice daily.

Overall results for 'normal' Basenji dogs, excluding results for the subgroup of eight dogs with elevated TSH concentrations, are shown in Table 3. Considering this data set, the reference range of TT4 concentrations for normal Basenji dogs was 2 to 27 nmol/L compared with a reference interval of 17 to 37 nmol/L for all dogs.

TT4/TSH ratio determinations

In the present cohort, 14 dogs (12%) had a TT4/TSH ratio of less than 17.3,[2] a value that is strongly suggestive of hypothyroidism. Calculation of this ratio would appear to provide little extra benefit over TSH determinations in the Basenji breed, perhaps because of errors inherent in measuring low TT4 concentrations.

Table 2. Signalment and laboratory data for 7 control Basenji dogs and 8 Basenji dogs with serum TSH concentrations initially above the reference range

Age (years)	Gender	Oct 06 TSH (ng/mL)	April 07 TSH (ng/mL)	Oct 06 TT4 (nmol/L)	Cholesterol	Hct	April 07 TT4 before and after rhTSH (mmol/L)
Normal Basenji dogs with TSH concentrations initially within the reference range							
8	FN	0.27	0.19	15	6.1	0.51	12 → 36[a]
7	M	0.25	N/A	9	3.4	0.52	12 → 25[b]
2	M	0.24	N/A	19	4.4	0.46	12 → 31[b]
9	M	N/A	0.15	N/A	5.5	N/A	9 → 42[a]
4	MN	N/A	0.53	N/A	5.4	N/A	11 → 25[b]
3	F	0.19	0.13	11	3.3	0.46	10 → 38[a,c]
Basenji dogs with TSH concentrations that were initially or subsequently above the reference range							
6	F	0.63	1.01	11	5.2	0.46	11 → 21[b]
4	MN	0.58	0.95	13	4.0	0.50	18 → 28[b]
14	M	0.67	0.29	4	7.4	0.41	6 → 20[b]
10	FN	0.82	1.6	7	5.8	0.48	3 → 7[d]
8	MN	0.95	0.42	9	7.9	N/A	8 → 18[e]
10	M	1.02	N/A	5	5.1	0.43	N/A[f]
10	MN	1.28	N/A	9	7.2	0.53	N/A
13	M	2.09	4.53	9	7.1	0.4	10 → 8[d]
12	FN	5.37	N/A	4	7.9	0.49	N/A[g]

M, entire male; MN, castrated male; N/A, not applicable; F, entire female; FN, spayed female; Hct, haematocrit; rh, recombinant human; TSH, thyroid-stimulating hormone; TT4, total thyroid hormone (thyroxine).
[a]Normal thyroid function based on normal baseline TT4 on at least one occasion, normal (initial) TSH concentration and normal TT4 response to rhTSH.
[b]Dogs considered to be euthyroid,[9] equivocal,[21] or hypothyroid[8,22] depending on the criteria used.
[c]rhTSH tested in October 2007 using rhTSH frozen for 7 months.
[d]Dogs fulfilling all described criteria for hypothyroidism based on rhTSH testing.
[e]Borderline hypothyroid, but TSH normal and dog still healthy 18 months later.
[f]Acute cerebral syndrome attributed to a cerebrovascular accident 3 months after initial testing and before an rhTSH stimulation test could be arranged.
[g]Repeatedly high TSH (5.37 ng/mL) on re-testing and responded clinically to thyroid supplementation, with a concurrent reduction in the serum TSH concentration (to 0.06 ng/mL), so was considered to be clinically hypothyroid.

Table 3. Laboratory measurements in 105 Basenji dogs thought to be euthyroid on the basis of normal haematocrit, cholesterol and serum TSH concentration less than 0.60 ng/mL

Analyte	Range	Median	Mean ± SD	Reference range for normal dogs
TT4	2–27	13.0	13.4 ± 5.7	17–37 nmol/L
TSH	0.05–0.6	0.15	0.19 ± 0.1	0–0.6 ng/mL
Cholesterol	2.9–8.9	5.5	5.5 ± 1.3	3.6–8.8 mmol/L
Hct	0.38–0.60	0.48	0.47 ± 0.05	0.39–0.55 L/L

Hct, haematocrit; TSH, thyroid-stimulating hormone; TT4, total thyroid hormone.

Discussion

The data from the present study suggest that the majority of Basenji dogs have TT4 concentrations lower than normal range for the majority of pedigree and crossbred dogs. In this respect, they resemble certain other breeds, including racing Greyhounds, Whippets and Deerhounds (the so-called 'sight hounds'). Thus, taken alone, TT4 concentrations are of limited utility in determining thyroid function in such breeds. It is therefore essential to consider a simultaneous panel of tests to determine thyroid status, including the serum concentrations of TT4 and TSH. Sequential determinations may be of additional benefit in equivocal cases. The decision to exclude fT4 from the current study was taken because commercial test kits became temporarily unavailable in Australia (and elsewhere) at the time of this study. It would be of particular interest to also measure fT4 (by equilibrium dialysis) and TGAA in a representative cohort of Basenji.

The observation that a majority of Basenji have low TT4 concentrations in association with normal TSH values does not exclude the possibility that there is a finite prevalence of subclinical and/or clinical hypothyroidism in this breed. Establishing whether or not this is indeed the case, requires much greater emphasis on TSH determinations, because of the very limited usefulness of TT4 values in this breed. It is expected that a Basenji with hypothyroidism would have an elevated serum TSH concentration (because of the absence of negative feedback by normal fT4 concentrations in the circulation), and in long-standing cases this would be accompanied by abnormal physical findings, hypercholesterolaemia and non-regenerative anaemia.

The study also included a larger proportion of entire animals than is customary in most other surveys from the UK or North America. As the main impetus for the testing was from the Basenji Club, more breeders than pet owners participated, especially as the initial drive was to create an easy and readily applicable one-off screening protocol for prospective breeding stock. As the mating season is almost always close to the autumn equinox, October was chosen to remove any effects of oestrus or dioestrus on endocrine testing.

Because dogs were recruited for this study on the basis of being 'healthy', we likely selected against the detection of symptomatic hypothyroid patients. Yet despite this study design, one dog with mild signs of hypothyroidism was included. Seven additional dogs that may have had 'subclinical hypothyroidism', presumably referable to progressive lymphocytic thyroiditis, were detected on the basis of a TSH concentration above 0.6 ng/mL and, in at least two cases; hypothyroidism was confirmed by a reduced response to exogenous rhTSH. The absence of anaemia or overt hypercholesterolaemia in these cases suggests that enough functional thyroid tissue remained at the time of testing to prevent biochemical changes or florid clinical signs developing. Following such animals over time would be of great interest, as it is anticipated that the TSH concentration would continue

to rise, and eventually for characteristic clinical and biochemical aberrations to develop when more than 75% of thyroid tissue was destroyed.[3] Procuring thyroid biopsies from these cases antemortem or at necropsy would also be of great interest, to provide histological support for this speculation. The three dogs in this study with the most compelling evidence for reduced thyroid function were older than 10 years of age, suggesting that the development of hypothyroidism is a protracted process, and that hypothyroidism may well be a late-onset disease state in Basenji dogs.

Basenji dogs in Australia may have a higher incidence of hypothyroidism than other dogs, with a prevalence of at least 3%, depending on the stringency of the definition, compared with a stated prevalence of hypothyroidism in all dogs of 0.2%.[16] It is problematic that the determination of thyroid status is more challenging in this breed because of the lower range of expected TT4 values. The requirement for a panel of endocrine tests, including TT4 and TSH, is emphasised by the present investigation, as is the need to correlate the laboratory findings with the clinical status of the patient. Dynamic endocrine testing using rhTSH was shown to be helpful, especially when the TSH was only marginally elevated and the patient was essentially asymptomatic, presumably because there was sufficient remaining functional thyroid tissue to maintain euthyroidism in response to increased circulating TSH concentrations.

There remains a need in Australia for a central laboratory facility or compounding pharmacist to prepare smaller individual doses of rhTSH (50 or 100 µg for small and large dogs, respectively) for veterinarians in a cost-effective manner, thereby permitting more widespread use of dynamic thyroid testing. The stability of rhTSH after freezing makes this an achievable objective. The apparent safety and ease of administration make it an excellent option if the cost was not so prohibitive (currently A$3000 per kit). Determination of serum TGAA and thyroid gland biopsy would provide further useful information in relation to the pathogenesis of hypothyroidism in Basenji dogs. Indeed, we plan to undertake further studies along these lines and using a Basenji thyroid gland bank that has been established to receive and process biopsy and necropsy specimens.

The determination of serial 'post-pill' TSH and TT4 concentrations was shown to be useful for confirming the efficacy of therapy in two cases in the present study. Sequential measurement of TSH, in addition to TT4, is therefore likely to be helpful in monitoring the efficacy of therapy in hypothyroid dogs, especially in breeds such as the Basenji in which the normal range of TT4 values is so low.

Conclusion

Taken alone, TT4 concentrations are of limited utility in determining thyroid function in sight hounds and highlights the need for further work to be done on compiling breed-specific ranges. In breeds such as the Basenji, it is therefore essential to consider a panel of tests conducted simultaneously to determine thyroid status; namely, serum concentrations of TT4 and TSH, and possibly fT4 and cholesterol, and in some cases utilising sequential determinations. Furthermore, rhTSH testing remains a valuable additional tool to aid definitive diagnosis, provided the breed-specific lower starting concentration of TT4 is factored into the formula used to define normality. Larsson's criteria applied to rhTSH testing currently appear most applicable to dynamic thyroid testing in the Basenji.

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References

1. Panciera DL. Is it possible to diagnose canine hypothyroidism? *J Small Anim Pract* 1999;40:152–157.
2. Dixon RM, Mooney CT. Evaluation of serum free thyroxine and thyrotropin concentrations in the diagnosis of canine hypothyroidism. *J Small Anim Pract* 1999;40:72–78.
3. Thoday K. The thyroid gland. In: Hutchison M, editor. *Manual of small animal endocrinology*. 1st edn. BSAVA, Cheltenham, 1990;2:25–57.
4. Daminet S, Ferguson DC. Influence of drugs on thyroid function in dogs. *J Vet Intern Med* 2003;17:463–472.
5. Petersen ME, Melian C, Nichols R. Measurement of serum total thyroxine, triiodothyronine, free thyroxine, and thyrotropin concentrations for diagnosis of hypothyroidism in dogs. *J Am Vet Med Assoc* 1997;211:1396–1402.
6. Dixon RM, Mooney CT. Canine serum thyroglobulin autoantibodies in health, hypothyroidism and non-thyroidal illness. *Res Vet Sci* 1999;66:243–246.
7. Nachreiner RMF, Refsal KR, Graham PA, Bowman MM. Prevalence of serum thyroid hormone autoantibodies in dogs with clinical signs of hypothyroidism. *J Am Vet Med Assoc* 2002;220:466–471.
8. Sauvé F, Paradis M. Use of recombinant human thyroid-stimulating hormone for thyrotropin stimulation tests in euthyroid dogs. *Can Vet J* 2000;41:215–219.
9. De Roover K, Duchateau L, Carmichael N, van Geffen C, Daminet S. Effect of storage of reconstituted recombinant human thyroid-stimulating hormone (rhTSH) on thyroid stimulating hormone (TSH) response testing in euthyroid dogs. *J Vet Intern Med* 2006;20:812–817.
10. Espineira MMD, Mol JA, Peeters ME et al. Assessment of thyroid function in dogs with low plasma thyroxine concentration. *J Vet Intern Med* 2007;21:25–32.
11. Bromel C, Pollard RE, Kass PH et al. Ultrasonographic evaluation of the thyroid gland in healthy, hypothyroid, and euthyroid golden retrievers with nonthyroidal illness. *J Vet Intern Med* 2005;19:499–506.
12. Reese S, Breyer U, Deeg C et al. Thyroid sonography as an effective tool to discriminate between euthyroid sick and hypothyroid dogs. *J Vet Intern Med* 2005;19:491–498.
13. Bodey AR, Rampling MW. Comparison of haemorrheological parameters and blood pressure in various breeds of dog. *J Small Anim Pract* 1999;40:3–6.
14. Snyder PS, Sato T, Atkins CE. A comparison of echocardiographic indices of the non racing, healthy greyhound to reference values from other breeds. *Vet Radiol Ultrasound* 1995; 36:387–392.
15. Gaughan KR, Bruyette DS. Thyroid function testing in Greyhounds. *Am J Vet Res* 2001;62:1130–1133.

16. Ferguson DC. Update on diagnosis of canine hypothyroidism. *Vet Clin North Am Small Anim Clin* 1994;24:515–537.
17. Van Geffen C, Bavegems V, Duchateau L et al. Serum thyroid hormone concentrations and thyroglobulin auto antibodies in trained and non-trained healthy whippets. *Vet J* 2006;172:135–140.
18. Palolahti TI, Jarvinen A-K. Serum total thyroxine and thyrotropin concentrations in clinically normal dogs representing two breeds. *J Vet Intern Med* 2000;14:233–233.
19. Panciera DL, Hinchcliff KW, Olson J, Constable PD. Plasma thyroid concentrations in dogs competing in a long distance sled dog race. *J Vet Intern Med* 2003;17:593–596.
20. Mooney CT, Shield RE. Dixon RM. Thyroid hormone abnormalities and outcome in dogs with non thyroidal illness. *J Small Anim Pract* 2008;49:11–16.
21. Larsson M. Determination of free thyroxine and cholesterol as a new screening test for canine hypothyroidism. *J Am Anim Hosp Assoc* 1988;24:209–217.
22. Daminet S, Fifle L, Paradis M, Duchateau L, Moreau M. Use of recombinant human thyroid-stimulating hormone for thyrotropin stimulation test in healthy, hypothyroid and euthyroid sick dogs. *Can Vet J* 2007;48:1273–1279.

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