# Disorders of the Equine Thyroid Gland

Babetta A. Breuhaus, DVM, PhD

**KEYWORDS**

• Horse • Hypothyroidism • Hyperthyroidism
• Nonthyroidal illness syndrome • Thyroid hormone
• Thyrotropin • Goiter

## THYROID GLAND ANATOMY AND FUNCTION

The thyroid gland, found dorsal to the trachea just distal to the larynx, is a smooth, firm, bilobed organ, approximately 2.5 cm × 2.5 cm × 5 cm,[1] weighing approximately 0.04 g/kg body weight.[2] This gland is not readily seen or palpated in normal horses, although it may become visible as horses age. Histologically, this gland is composed of cuboidal to low columnar epithelial cells arranged in follicles. The epithelial cells produce thyroglobulin, a glycoprotein containing multiple tyrosine residues. Iodine is concentrated in the gland, oxidized, and bound to tyrosine to form monoiodotyrosine (MIT) and diiodotyrosine (DIT). These iodotyrosine residues are then coupled to form thyroxine ($T_4$) and triiodothyronine ($T_3$), which remain bound to thyroglobulin and are stored within the follicles in an approximate ratio (in humans) of 23% MIT, 33% DIT, 35% $T_4$, and 7% $T_3$.[3] In humans, there is enough thyroid hormone stored within the thyroid gland to maintain euthyroidism for approximately 2 to 3 months if iodine ingestion were to cease completely.

Thyroid hormone secretion is stimulated by thyrotropin (thyroid-stimulating hormone [TSH]) from the anterior pituitary gland, which in turn is regulated by thyrotropin-releasing hormone (TRH) from the hypothalamus. TSH also has trophic effects on the thyroid gland, increasing epithelial (follicular) cell size and activity; increasing iodide uptake; increasing secretion of thyroglobulin into the colloid; increasing the synthesis of MIT, DIT, $T_4$, and $T_3$, and reuptake of colloid by follicular cells by endocytosis.[3] Once secreted, thyroid hormones travel in the blood, primarily bound to proteins, including thyroid hormone–binding globulin, transthyretin, and albumin. Although only the unbound free fractions are metabolically active, this protein binding helps maintain a pool of readily available hormone and prevents the circulating hormones from being rapidly excreted by the kidneys, which only excrete free $T_4$ and $T_3$. $T_4$ binds more tightly to binding proteins than does $T_3$, resulting in a lower metabolic clearance rate and a longer half-life (7 days for $T_4$ vs 1 day for $T_3$ in

Department of Clinical Sciences, North Carolina State University, 4700 Hillsborough Street, Raleigh, NC 27606, USA
*E-mail address:* Betta_breuhaus@ncsu.edu

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humans).[3] In addition to this tighter protein binding, $T_4$ does not bind with thyroid hormone receptors as avidly as does $T_3$. Together, these properties result in $T_3$ being more metabolically active than $T_4$. Because the thyroid gland releases a much larger amount of $T_4$ compared with $T_3$, the majority of $T_3$ is derived from deiodination of $T_4$ in the peripheral tissues by type 1 (D1) and type 2 (D2) deiodinases, which contain selenium as the iodine acceptor in the catalytic unit (selenocysteine). Type 3 (D3) deiodinase, which is also a selenoprotein, is the main $T_4$ and $T_3$ inactivating enzyme. The conversion of $T_4$ to reverse $T_3$ by D1 and D3 deiodinases is important to regulate thyroid hormone function.

The primary action of thyroid hormones is to stimulate oxygen consumption. Thyroid hormones stimulate protein synthesis and catabolism, help regulate lipid metabolism, and stimulate basal metabolic rate and body heat production. These hormones are not essential for life but play important roles in growth and organ maturation. The actions of thyroid hormones are divided into genomic and nongenomic actions. Genomic actions are mediated by thyroid hormone receptors that are nuclear transcription factors that increase or decrease the expression of genes that regulate cell function. Nongenomic actions can be initiated by receptors at the plasma membrane, within the cytoplasm, or at the mitochondrion. Nongenomic actions include roles in cell division, angiogenesis, protein trafficking, cell migration, platelet aggregation, nitric oxide synthase and $Na^+/K^+$-ATPase activation, modulation of $Ca^{2+}$-ATPase and $Na^+/H^+$ exchanger ($Na^+/H^+$ antiporter) activity, modulation of neurons and myocyte $Na^+$ currents, and epidermal growth factor receptor activity. For a detailed review on thyroid hormone actions, see elsewhere.[4]

The thyroid gland also contains parafollicular cells, commonly referred to as C cells. These cells secrete factors that help regulate follicular cell activity. They also secrete calcitonin, which is important in the regulation of extracellular calcium concentration. Calcitonin decreases osteoclastic bone activity and serum calcium concentration. Calcium regulation and calcitonin are discussed in more detail elsewhere in this issue by Ramiro Toribio.

## DIAGNOSTIC TESTS OF THYROID GLAND FUNCTION IN HORSES

### *Measurement of Thyroid Hormone Levels*

Single point-in-time measurements of thyroid hormone concentrations, although simple to perform, are not always considered to be the most reliable indicators of thyroid function. A variety of drugs, as well as physiologic or pathophysiologic states, can cause the measured values to be low, even when the thyroid gland itself is normal. In the horse, some of these causes include fasting; phenylbutazone or corticosteroid administration; strenuous exercise; diets high in energy, protein, zinc or copper; and nonthyroidal illnesses.[5–15] Thus, it is important that thyroid hormone measurements be performed in horses that have not received any medications for at least 2, and preferably, 4 weeks before testing. If a horse has been receiving thyroid hormone supplementation without prior documentation of hypothyroidism, it is best to wean the horse off the supplementation and then test thyroid function once the horse has not received any supplementation for at least 4 weeks.

If only single thyroid hormone measurements are available, it is also important to measure the free fractions of $T_4$ and $T_3$ because certain states (such as liver and other diseases), drugs (such as salicylates and phenylbutazone), or hormones (such as estrogen), can alter protein binding.[16] During illness in humans, measurement of serum-free $T_4$ concentration by direct methods often underestimates values when compared with measurements of free $T_4$ concentration after dialysis or ultrafiltration.[17–21]

This situation also seems to be the case in dogs[22] and horses.[15] Thus, serum concentrations of free $T_4$ measured by equilibrium dialysis are more likely to reflect the true thyroid status in ill horses compared with other methods of free $T_4$ concentration measurement. Measuring free $T_4$ concentrations by dialysis instead of directly may help prevent equine clinicians from misdiagnosing ill horses as being hypothyroid. Resting thyroid hormone and TSH concentrations from 71 healthy adult horses are given in **Table 1**.

### *Stimulation Tests*

Stimulation tests provide a better indication of thyroid status than single measurements of thyroid hormone concentrations. These tests involve measuring thyroid hormone concentrations before and after giving TRH or TSH to stimulate thyroid hormone release. Various techniques and results have been described.[7–9,23–27] These tests are usually not performed by ambulatory clinicians because multiple blood samples are required to be taken over several hours and sterile TRH and TSH are not readily available and can be expensive.

To perform a stimulation test, a control blood sample is obtained, TRH (1 mg to the average 450–500-kg horse) or TSH (5 IU) is given intravenously, and subsequent blood samples are obtained. According to most references, $T_3$ concentrations should double at 2 hours and $T_4$ concentrations should double at 4 hours. In 36 normal horses that participated in various studies conducted by the author, the mean (and range) increase in total $T_4$ concentration was 2.2 (1.3–3.8) times the control value at 4 hours. Increases in concentrations of free $T_4$ and free $T_4$ by dialysis (mean and range) were 1.7 (1.1–2.1) times and 1.8 (1.1–2.8) times the control values at 4 hours, respectively. Increases in concentrations of total and free $T_3$ (mean and range) were 3 (1.1–10.3) times and 4.2 (1–53) times the control values at 2 hours, respectively. The seemingly lower $T_4$ responses to TRH injection are in agreement with findings by others.[23,28–30] Closer examination of the data by the author revealed that, in general, the few horses with smaller increases in concentrations of $T_4$ or $T_3$ either started with higher resting values or their peaks occurred later ($T_4$) or earlier ($T_3$) than 4 or 2 hours. Horses with lower $T_4$ responses, in general, did not have lower $T_3$ responses. Horses with high responses tended to have very low resting thyroid hormone concentrations. Thus, one must be careful when interpreting the results of a TRH stimulation test.

### *Suppression Test*

A $T_3$ suppression test has been described to confirm the diagnosis of hyperthyroidism.[31,32] A control blood sample is obtained before the intramuscular administration of 2.5 mg $T_3$ diluted in 5 mL of sterile saline, given twice daily for 7 doses (4 days). Additional blood samples are drawn 5 minutes before each dose of $T_3$,

**Table 1**
**Normal baseline concentrations of thyroid hormones in adult horses (n = 71)**

| | Total $T_4$ nmol/L | Free $T_4$ pmol/L | Free $T_4$ by Dialysis pmol/L | Total $T_3$ nmol/L | Free $T_3$ pmol/L | TSH ng/mL |
|---|---|---|---|---|---|---|
| Range | 6–46 | 6–21 | 7–47 | 0.3–2.9 | 0.1–5.9 | 0.02–0.97 |
| Median | 19 | 11 | 22 | 0.9 | 1.7 | 0.23 |
| 95% CI | 18–22 | 10–12 | 21–25 | 0.9–1.1 | 1.8–2.4 | 0.21–0.37 |
| Mean | 20 | 11 | 23 | 1.0 | 2.1 | 0.29 |
| SD | 9.4 | 2.8 | 8.9 | 0.5 | 1.3 | 0.23 |

*Abbreviation:* CI, confidence interval.

then twice daily on days 5 and 7, and in the morning of day 10. In normal horses, $T_4$ and $T_3$ measurements are within the reference range in the control blood sample. Administration of $T_3$ should result in a 10- to 20-fold increase in serum $T_3$ concentration, whereas serum $T_4$ concentration should gradually decrease, remaining suppressed for at least 5 days after the last dose of $T_3$. In hyperthyroid horses, control (pre-$T_3$) blood samples have increased concentrations of $T_4$ and $T_3$. The increase in serum $T_3$ concentration after $T_3$ administration is not as pronounced as in normal horses, but serum $T_3$ concentration does remain increased throughout the administration period. Serum concentration of $T_4$ is not suppressed.

### *Imaging*

Ultrasonographic examination of the thyroid gland reveals whether enlargement is because of solid tissue or is cystic. It also allows measurement of the gland, comparison to the contralateral gland, and provides guidance for biopsy. Nuclear scintigraphy is a well-established tool for the evaluation of thyroid function, detection of metastatic disease, and measurement of metabolic tumor volume in humans and small animals.[33,34] Nuclear scintigraphy of the thyroid gland has been described in the horse.[31,32,35,36] This technique is especially useful to determine thyroid gland function and whether there are differences in function between lobes. Such information is important if one is considering performing hemithyroidectomy to control hyperthyroidism.

## THYROID DISORDERS IN ADULT HORSES

### *Neoplasia*

Probably the oldest described and documented abnormalities of the thyroid gland in the horse are hyperplasia and neoplasia. It is not uncommon to find mildly enlarged or neoplastic thyroid glands at necropsy of older horses that showed no outward evidence while the horse was alive. Schlotthauer[2] examined the thyroid glands of 100 consecutive horses at necropsy. He divided the gross and histologic evaluation of the glands into 4 groups: normal (34%), hyperplastic (20%), colloid goiter (9%), and adenomatous (37%). Since then, multiple reports of thyroid tumors have been published, describing hyperplastic nodules, adenomas, adenocarcinomas, carcinomas, and C-cell tumors.[31,32,35–50] It has been suggested that thyroid tumors are more common in horses older than 17 years.[46] Although it has been suggested that thyroid tumors occur more often in domestic animals living in iodine-deficient areas,[51] there have been no studies to show this to be true in horses. Most thyroid tumors in horses are benign and do not seem to metastasize.

In most reports, serum concentrations of thyroid hormones remained normal in horses with thyroid tumors, although occasionally, thyroid tumors have been associated with hypothyroidism[36,52,53] or hyperthyroidism.[31,32,49] Reported clinical signs of hypothyroidism include lethargy, exercise intolerance, and poor hair coat. Clinical signs of hyperthyroidism include weight loss, tachycardia, tachypnea, hyperactive behavior, ravenous appetite, alopecia, and cachexia.

Serum thyroid hormone concentrations should be measured in horses with enlarged thyroid glands. Additional diagnostics should include ultrasonography and biopsy and, depending on those results, a $T_3$ suppression test and/or nuclear scintigraphy may be indicated. The diet should be examined to make certain that iodine intake is appropriate because too little can result in goiter. The recommended daily iodine ingestion in adult horses is 0.007 mg/kg or 0.35 mg/kg dry matter diet, assuming consumption of 2% of body weight. Iodine should be increased to 0.4 mg/kg dry matter diet for the last trimester of pregnancy.[54]

If thyroid neoplasia is diagnosed, it is not necessary to remove the thyroid glands immediately if serum thyroid hormone concentrations are normal and the glands are not enlarged enough to compromise breathing or eating. If serum thyroid hormone concentrations are low, the horse can be supplemented with one of several products, described in more detail in the following sections. If the horse is hyperthyroid or if the glands begin enlarging rapidly, they should be surgically removed[55] and the horse placed on replacement therapy. If surgery is contemplated, it should be performed before the glands get large enough to complicate their removal. If the size of the gland is not a problem but the horse is hyperthyroid, propylthiouracil (PTU) can be administered orally to decrease concentrations of circulating thyroid hormones. PTU inhibits thyroid hormone synthesis by antagonizing thyroid peroxidase (catalyzes oxidation of iodide to iodine), inhibiting thyroglobulin synthesis, inhibiting thyroid follicular cell growth, and inhibiting the conversion of $T_4$ to $T_3$ (inhibits D1 deiodinase).[56] Use of PTU in horses was first described in an equine experimental model of hypothyroidism.[57–59] With a daily oral dose of 4 mg/kg it took approximately 4 weeks for horses to become hypothyroid. More recently, PTU (8 mg/kg/d) was administered orally to treat a hyperthyroid horse.[32] Once the serum concentrations of thyroid hormones decreased, this dose was given every other day. The dose of PTU should be titrated to keep thyroid hormones concentrations in the normal range. When administering PTU, gloves and mask should be worn.

### *Hypothyroidism*

Disorders of thyroid function can result from alterations in TRH, TSH, or thyroid hormone synthesis or release, alterations in conversion to $T_3$ in peripheral tissues, and alterations in thyroid hormone receptor sensitivity. The prevalence of primary hypothyroidism in adult horses is very low. Autoimmune thyroid disease is common in humans and dogs, but, with the exception of one report, has not been described in horses. In the one study that is available,[60] 156 of 622 slaughtered horses from Eastern Europe were found to have grossly abnormal thyroid glands. In 80% of these 156 horses, histologic appearance was consistent with a Hashimoto thyroiditis–like disease, including variation in follicle size and shape, rarefaction of colloid, and lymphocytic infiltration and fibrosis. Serum obtained from 9 of these horses revealed higher thyroglobulin, antithyroglobulin, and antithyroid peroxidase autoantibody titers than in 9 healthy horses. Neither did the report indicate how the serum was obtained from the affected horses nor did it indicate what the time frame was in relation to the time of death. Thyroid hormone concentrations were not measured. There was no information on whether the horses exhibited any signs of hypothyroidism.

Extrapolating from humans and dogs, one might expect hypothyroidism in horses to be manifested as lethargy, cold intolerance, and weight gain or obesity. Traditionally, horses that were thought of as easy keepers, those that gained weight on little feed and tended to accumulate fat in the crest of the neck and over the rump, were considered to be hypothyroid. These horses were also thought to be prone to developing laminitis as well as various other problems, including infertility in mares, anhidrosis, and exertional rhabdomyolysis. Horses with these problems often were administered long-term supplemental thyroid hormones, either without actual thyroid hormone measurement or despite measurement of normal circulating concentrations. Evidence that has accumulated over the past 10 years suggests that many of the clinical signs traditionally associated with hypothyroidism in horses are more appropriately signs of equine metabolic syndrome or insulin resistance. Studies have also been unable to substantiate hypothyroidism as a cause for infertility in mares[61,62] or anhidrosis.[63] In reports of horses made hypothyroid by surgical thyroidectomy[64–71] or by PTU administration,[56–59] neither obesity nor laminitis occurred. In studies of young growing

horses, thyroidectomy resulted in decreased growth rate, delayed physeal closure and tooth eruption, cold insensitivity, lethargy, a coarse hair coat, a coarse and thickened face, decreased rectal temperature, decreased serum phosphorus concentration, and increased serum cholesterol concentration.[64] However, in subsequent studies in adult horses, there were very few, if any, clinical signs associated with experimentally produced hypothyroidism. In addition, semen from thyroidectomized stallions is fertile,[66] and thyroidectomized mares are capable of conceiving and carrying foals to term.[64,66] Thyroidectomy also did not alter the response of blood lipids to feed deprivation.[68] Thyroidectomy has been shown to result in decreased resting heart rate, cardiac output, respiratory rate, and rectal temperature[71] and increased serum concentrations of triglycerides, cholesterol, and very-low-density lipoproteins.[67] However, despite statistical differences, all these measurements in adult horses remained within normal range, making it impossible to use them to help identify a hypothyroid horse clinically. To date, in a few published case reports of horses that were actually documented to be hypothyroid, clinical signs were primarily lethargy, exercise intolerance, and poor hair coat.[37,53,54] There is one report of keratoconjunctivitis sicca in a hypothyroid horse.[72] Overall, the number of horses documented to have naturally occurring primary hypothyroidism remains low.

### *Nonthyroidal Illness Syndrome (Euthyroid Sick Syndrome)*

Nonthyroidal illness results in central hypothyroidism. Release of hypothalamic TRH is decreased by several mechanisms. Decreased leptin concentration (eg, from fasting or poor appetite) reduces the set point for thyroid hormone feedback inhibition of TRH release. At the same time, local concentrations of $T_3$ are increased, both by increased iodothyronine deiodinase D2 (eg, from sepsis or trauma), leading to increased conversion of $T_4$ to $T_3$ in the hypothalamus, and by decreased iodothyronine deiodinase D3 leading to decreased conversion of $T_3$ to diiodothyronine ($T_2$) (deactivation).[73] TSH release is also inhibited, partly because of the decreased TRH and secondarily to negative feedback from stress, glucocorticoids, and locally produced cytokines, including interleukin 6, tumor necrosis factor $\alpha$, and interferon $\gamma$.[73] In addition, nonthyroidal illness can result in decreased thyroid hormone–binding proteins and decreased binding protein affinity and capacity.[73] This effect of illness decreases the serum concentrations of total $T_4$ or $T_3$, but has less of an effect on serum concentrations of the free fractions. In fact, if free fractions are measured by equilibrium dialysis or ultrafiltration, the free $T_4$ concentration is often normal or increased and there is only a modest decrease in concentration of free $T_3$.[73]

Nonthyroidal illness syndrome has been well described in humans and dogs. Most assume that the syndrome exists in horses, but few studies have documented it, much less characterized it in horses. Preliminary evidence suggests that nonthyroidal illness in horses and foals is similar to that in other species.[15,74] This is important because horses with nonthyroidal illness syndrome will have low thyroid hormone concentrations, especially total $T_3$ and $T_4$, which may lead to the misdiagnosis of primary hypothyroidism. In such cases, treatment of the underlying disease rather than thyroid hormone supplementation is indicated.

## THYROID HORMONE SUPPLEMENTATION

Horses that have undergone thyroidectomy or that have been properly diagnosed as hypothyroid can be supplemented with $T_4$ or a combination of $T_4$ and $T_3$. $T_4$ is available in several forms. Iodinated casein contains approximately 1% $T_4$ and is given at 5 to 15 g/horse/d orally.[64] The recommended starting dosage of levothyroxine has been

20 μg/kg/d orally,[75,76] but more recent studies suggest that doses as high as 50 to 100 μg/kg/d may be well tolerated, at least for a short period.[29,30,77,78] It should be noted that horses in those studies were administered $T_4$ in a small meal of grain, which may have affected absorption, because fiber or bran cereal can decrease the oral absorption of thyroid hormones in humans.[79] Thus, the required dose of $T_4$ may vary, depending on whether it is given to fasted horses or if it is fed with a meal. Serum thyroid hormone concentrations should be monitored during supplementation so that dosages can be adjusted to maintain thyroid hormone levels in the normal range. If a sensitive TSH assay becomes commercially available, dosages should be adjusted to normalize TSH. In people receiving levothyroxine, it takes 4 weeks for thyroid hormone and TSH concentrations to stabilize.[79]

The controversial practice of administering thyroid hormones to obese euthyroid horses in an attempt to promote weight loss and decrease episodes of laminitis has received attention in the past 5 to 10 years. Anecdotally, many practitioners report that horses remain overweight despite thyroid hormone supplementation and that there is no evidence that the incidence of laminitis is altered. In fact, it would be difficult to design a study to test whether or not thyroid hormone supplementation alters the onset or severity of laminitis. However, the common practice has been to adjust the thyroid hormone dose to maintain serum thyroid hormone concentrations within the normal range. If this procedure is followed in a euthyroid horse, one is simply exchanging the horse's own thyroid hormones for a supplement. In addition, in many cases there has been no attempt to control or alter the diet. In order to lose weight, it is recommended that the feed intake be controlled at 1.5% to 2% of the desired body weight per day, preferably as grass hay or other feed that is low in soluble carbohydrates. If this diet is achieved, a horse is likely to lose weight, with or without thyroid hormone supplementation.

There is some evidence that thyroid hormone supplementation might be useful in accelerating weight loss and improving insulin sensitivity, which might decrease bouts of laminitis. Administration of increasing doses of levothyroxine at 2-week intervals (50–200 μg/kg/d) to 8 euthyroid horses increased serum total and free $T_4$ concentrations and blunted thyroid hormone and TSH responses to TRH. Serum concentrations of free $T_3$ were increased and TSH concentrations were decreased only at the highest dose. The horses showed no adverse clinical signs except agitation (also only at the highest dose) and lost weight.[29] Plasma concentrations of triglycerides, cholesterol, and very-low-density lipoproteins decreased, and insulin sensitivity increased.[77] It would be difficult to design a study to test whether or not thyroid hormone supplementation alters the onset or severity of laminitis.

Untreated hyperthyroidism or long-term $T_4$ administration in people can have undesirable effects, including loss of bone density,[80] tachycardia, increased heart rate variability, atrial premature contractions or atrial fibrillation,[81–83] left ventricular hypertrophy,[84] and increased risk of myocardial infarction and congestive heart failure.[80] To explore the potential effects of long-term thyroid hormone administration to euthyroid horses, Frank and colleagues[30,78] administered 48 mg (100 μg/kg/d) levothyroxine per day to 6 euthyroid mares for 48 weeks. Every 4 weeks they performed physical examinations, complete blood cell counts, and serum chemistry panels and measured serum concentrations of cardiac isoenzymes. They performed cardiac ultrasonographic examinations, TRH stimulation tests, and intravenous glucose tolerance tests at weeks 16, 32, and 48. This dose of levothyroxine increased the serum total $T_4$ concentrations 4 to 5 times the presupplementation concentrations. Serum total $T_3$ concentrations were decreased at week 32 but returned to the presupplementation concentrations by week 48. However, free fractions were not measured. At this

level of supplementation, total $T_4$ and $T_3$ concentrations no longer responded to TRH. The horses lost weight, even though intake was not controlled or measured (horses spent time at pasture). Heart rate was variable, with no consistent pattern. Results of evaluation of blood remained within the reference range. Echocardiographic measurements remained fairly stable, except that the left ventricular free wall thickness appeared to be steadily increasing, ultimately becoming statistically significantly increased at 48 weeks. Fractional shortening was decreased at 16 and 32 weeks but remained within normal range; the clinical significance of this data is unclear. Resting serum insulin concentration and acute insulin response to glucose decreased, whereas insulin sensitivity increased. These changes were correlated to body weight, and it is impossible to determine whether they were caused directly by the thyroid hormone administration or indirectly by the weight loss. The investigators concluded that thyroid hormone supplementation may be useful in the treatment of obesity and insulin resistance.

## THYROID HORMONES IN FOALS

When considering thyroid function in foals, it is important to know that serum thyroid hormone concentrations are much higher in neonates, slowly decreasing to adult concentrations over the first weeks of life.[74,85,86] For this reason, it is important to use age-matched reference ranges. Thyroid hormone and TSH concentrations from 18 normal foals aged less than 12 hours are given in **Table 2**.

Thyroid hormones are essential for normal organ development and growth, and, as might be expected, deficiencies result in more significant clinical problems in foals than adults. Thyroid disorders known to occur in foals include nonthyroidal illness syndrome,[74] congenital goiter, and a syndrome of musculoskeletal abnormalities associated with thyroid gland hyperplasia. Little more is known about these disorders since they were reviewed in a previous volume in the Veterinary Clinics of North America.[76]

### *Congenital Goiter*

Enlarged thyroid glands at birth are associated with low serum thyroid hormone concentrations and can be caused by either too little[87,88] or too much[89–91] iodine in the mare's diet during gestation or by ingestion of goitrogenic plants. Clinical signs in these foals can be mild, with the foal exhibiting little more than the goiter, to a more severe presentation, with the foal born weak, with poor sucking and righting reflexes, hypothermia, and developmental abnormalities of the musculoskeletal system, including tendon contracture or rupture and delayed bone development,

**Table 2**
**Normal baseline concentrations of thyroid hormones in equine neonates aged less than 12 hours (n = 18)**

| | Total $T_4$ nmol/L | Free $T_4$ pmol/L | Free $T_4$ by Dialysis pmol/L | Total $T_3$ nmol/L | Free $T_3$ pmol/L | TSH ng/mL |
|---|---|---|---|---|---|---|
| Range | 238–337 | 46–118 | 78–184 | 3.4–10.8 | 2.4–20.3 | 0.12–0.72 |
| Median | 277 | 78 | 106 | 8.2 | 7.8 | 0.22 |
| 95% CI | 268–296 | 70–90 | 96–125 | 6.3–8.5 | 6.6–11.6 | 0.21–0.41 |
| Mean | 282 | 80 | 110 | 7.4 | 9.1 | 0.31 |
| SD | 28.2 | 20.3 | 29.5 | 2.3 | 5.0 | 0.20 |

*Abbreviation:* CI, confidence interval.

particularly of the small cuboidal bones of the carpus and tarsus. The hair coat may also be sparse. Mustard has been suggested as a potential dietary goitrogen in the horse, and selenium deficiency may contribute. One of the most commonly identified causes of excessive iodine ingestion is kelp, a seaweed product. Mares supplemented with kelp remain euthyroid because the adult thyroid gland can increase iodine excretion to balance absorption. However, the fetal thyroid gland cannot autoregulate until very close to term. Excessive iodine ingestion by the mare crosses the placenta and inhibits the fetal thyroid gland, resulting in congenital goiter and hypothyroidism.

Treatment of these foals includes supportive care, correcting the mare's diet if necessary, and, if the foal is actually hypothyroid at the time of birth, thyroid hormone supplementation. Because $T_3$ has higher and more rapid biologic activity than $T_4$, a combination of $T_3$ and $T_4$ administration may be indicated in an extremely weak foal. However, dosage recommendations for foals are not well established. An attempt should be made to increase thyroid hormone concentrations to an appropriate level for the age of the foal. The current dosage recommendation for levothyroxine ($T_4$) for foals is 20 to 50 μg/kg/d orally, and for $T_3$ is 1 μg/kg/d orally.[92] Irvine[93] suggested that $T_4$ be given at 0.176 × body weight in kg × desired $T_4$ in μg/L/d and that the dose of $T_3$ would be one-third of the $T_4$ dose. Exercise should be restricted in foals born with incompletely ossified cuboidal bones and/or ruptured extensor tendons. Lightweight splints may be necessary to prevent foals from knuckling or to prevent collapse of the cuboidal bones. If used, splints must be applied carefully and monitored closely.

### *Thyroid Gland Hyperplasia and Musculoskeletal Deformity*

A syndrome characterized by thyroid gland hyperplasia, increased gestational length, and musculoskeletal abnormalities (including mandibular prognathia, flexural limb deformities of the front legs, ruptured digital extensor tendons, and incomplete ossification of the carpal and tarsal bones) has been described, primarily in the Pacific Northwest region of the United States and Canada, but it has sporadically been reported elsewhere as well.[94–101] Despite prolonged gestation, foals are born dysmature and often have a silky hair coat. The cause is unknown, but nitrate, low iodine, low selenium, or goitrogenic plant ingestion by the mare during gestation has been proposed.[99,100] At the time of birth, baseline serum concentrations of $T_4$ and $T_3$ are usually within the normal neonatal ranges, but the response to TSH administration is decreased.[100] Because thyroid hormone concentrations are normal at the time of birth and because thyroid hormone supplementation often does not reverse the musculoskeletal changes in these foals, they are usually not administered.

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