# Thyroid Disease in Horses: Fact or Fiction?

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Spontaneous occurrence of equine thyroid disease, most notably hypothyroidism, has been propagated in veterinary texts despite the fact that there is limited evidence that hypothyroidism is a significant problem in this species. In contrast, feeding diets either deficient or excessive in iodine may cause goiter and other problems consistent with either hypo- or hyperthyroidism. Further, enlargement of the thyroid gland, due to a thyroid adenoma, is a relatively common problem in older horses. These benign tumors are clinically insignificant although they can be surgically removed for cosmetic reasons. However, an occasional older horse may develop a thyroid adenocarcinoma that produces excessive thyroid hormone and clinical hyperthyroidism manifested by increased activity and weight loss (Figure 1). Surgical removal of the abnormal gland is necessary to resolve this problem.

**Figure 1. 26-year-old Arabian mare with thyroid adenocarcinoma resulting in excess thyroid hormone production and syndrome of equine hyperthyroidism (hyperactivity and weight loss).**

### HYPOTHYROIDISM IN FOALS

Goiter in foals has long been recognized when mares have consumed excess iodine (> 40 mg iodine daily) during gestation. Next, decreased triiodothyronine ($T_3$) concentrations have also been described as a component of the fetal and neonatal problems observed in mares grazing *Acremonium coenophialum*-infected fescue. More recently, a syndrome of congenital hypothyroidism and dysmaturity (CHD) has been described in foals born in the Western United States and Canada. In the latter syndrome, foals are typically post-mature (350–370 day gestation length) and are born with mandibular prognathism (monkey jaw), forelimb contracture (Figure 2), rupture of the common digital extensor tendons and incomplete ossification of carpal and tarsal bones (Figure 3). Goiter is notably absent in affected foals (and their dams) but thyroid gland stimulation testing produces blunted responses and histological examination reveals hyperplastic thyroid tissue.

**Figure 2. A 4-day-old foal with congenital hypothyroidism and dysmaturity: flexural deformities often result in inability to fully extend the forelimbs (left) and mandibular prognathism or monkey jaw (right).**

The syndrome appears to be related to pasture access in late gestation. Prolonged gestation may occur towards the middle of the foaling season while foals delivered toward the end of the foaling season are often the most severely affected because mares have been at pasture for a longer period. Although the cause has not yet been clearly identified, it is likely multifactorial. High levels of nitrates in irrigated pastures and water sources have been found on some affected farms. Similarly, lack of mineral supplementation and low glutathione peroxidase activity in plasma collected from mares and affected foals have implicated marginal selenium status as a risk factor. Next, on several farms in the Pacific Northwest on which affected foals have been observed, heavy contamination of pasture with weeds (especially mustard) has been noted. Exposure to plants containing glucosinolate compounds (including mustard and others) may be an important cause as feeding glucosinolates to pregnant rats produces similar fetal lesions. Finally, the syndrome can vary greatly from year to year as several normal foal crops can be followed by a devastating year when more than 75% of foals may be affected to varying degrees. Treatment is largely supportive (assisted feeding, splinting, etc.) and less severely affected foals may grow to pursue a normal athletic career.

**Figure 3. Dorsopalmar carpal and lateral tarsal radiographs of a 4-day-old foal with congenital hypothyroidism and dysmaturity demonstration incomplete ossification of cuboidal bones.**
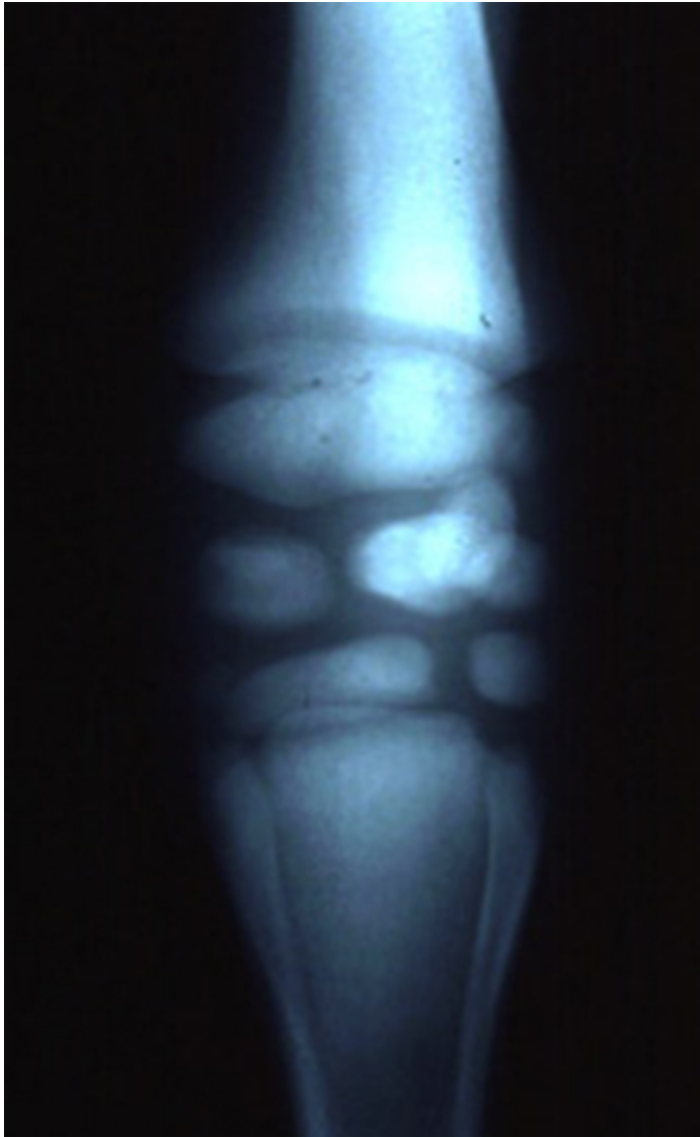
### HYPOTHYROIDISM IN ADULT HORSES

Despite the fact that the hypothalamic-pituitary-thyroid axis is one of the best-studied endocrine systems in the horse, whether or not clinical hypothyroidism occurs in adult horses remains unclear. Thyroidectomy produces hypothermia, bradycardia, lethargy, coarse haircoat, decreased appetite, decreased exercise tolerance and mild anemia. Decreased libido and sperm counts have been described in thyroidectomized stallions and some thyroidectomized mares had irregular estrus cycles. Nevertheless, horses remained fertile and thyroidectomized mares could carry a fetus to term.

In non-thyroidectomized adult horses, low circulating $T_4$ and $T_3$ concentrations have been detected during evaluation for a variety of complaints. Thus, "hypothyroidism" has been implicated as a cause of poor performance, myopathy, infertility, agalactia and alopecia. In addition, hypothyroidism has been suggested to play a role in development of anhidrosis and laminitis. However, there are few cases of "hypothyroidism" in which dysfunction of the gland has been established by documenting blunted responses to administration of thyrotropin (TSH) or thyrotropin-releasing hormone (TRH). Further, medication use, notably phenylbutazone, can artifactually reduce serum $T_4$ concentration and lead to suspicion of hypothyroidism. Thus, knowledge of medication use is essential when interpreting thyroid hormone concentrations in horses.

There are several explanations for our lack of understanding of the role of hypothalamic-pituitary-thyroid axis in clinical disease and the tendency to attribute a number of vague disorders in adult horses to "hypothyroidism". First, the axis is a dynamic system. Assessment of $T_4$ and $T_3$ concentrations in a single blood sample provides only a "picture in time" and does not reflect whether the rate of thyroid hormone synthesis is normal, increased or decreased. Despite the fact that Irvine and coworkers in New Zealand performed elegant studies several decades ago to illustrate this point, their results have remained somewhat "undiscovered" by many authors of equine texts. As would be expected, these investigators were the first to document that synthesis of thyroid hormones by the gland increases during exposure to a cold environment or with the onset of training. However, circulating hormone concentrations, measured as protein-bound iodine in plasma, were actually low in the face of a higher

secretion rate because $T_4$ and $T_3$ were also being utilized (and cleared from plasma) at greater rates by the tissues. Measurement of low $T_4$ concentrations in such instances could inadvertently lead to suspicion of "hypothyroidism".

Next, commercial TSH is no longer available and the cost of a dose of compounded TRH is around $100. When combined with further costs of laboratory analysis of several samples and the inconvenience of performing the test in the field, it is not surprising that stimulation tests are rarely pursued in practice. Rather, many veterinarians simply elect to treat "hypothyroidism" by administering supplemental thyroxine for a few weeks and using owner assessment for confirmation of the suspected diagnosis. It is likely that there is a placebo effect (on the owner) with this approach, as they all want to see an improvement in their horse's condition when they are paying for medication. Another problem is that some commercial laboratories include measurement of $T_4$ in the serum biochemical profile. When a horse is examined for a vague clinical disorder and a low $T_4$ is the only abnormal laboratory result reported, it is only natural to include "hypothyroidism" as a differential diagnosis for the client complaints. To add to the confusion, veterinarians have also anecdotally described an apparent "thyroid responsive syndrome" in which weight loss and improvement in the degree of laminitis are produced with supplementation of exogenous thyroid hormone as the exclusive treatment of obesity. The interpretation is that these horses must have been clinically hypothyroid. Recently, researchers at the University of Tennessee studied whether supplementation with exogenous thyroid hormone affected body weight, thyroid hormone concentrations, and glucose tolerance. During an 8-week period of supplementation with progressively increasing doses (24 mg levothyroxine daily for weeks 1–2, 48 mg levothyroxine daily for weeks 3–4, 72 mg levothyroxine daily for weeks 5–6, and 96 mg levothyroxine daily for weeks 7–8), horses lost approximately 20 kg body weight and thyroid hormone concentrations progressively increased with increasing levels of supplementation. At the highest dose (4 times the recommended dose), horses appeared to be more excitable (consistent with hyperthyroidism) and it was not clear what dose was needed to induce weight loss. In addition, sensitivity to insulin was also improved at the end of the 8-week supplementation period. Although these findings suggest that supplementation with exogenous thyroid hormone may be of benefit to obese horses, it is unclear whether similar results can be achieved with a lower level of supplementation.

In people that are on exogenous thyroid replacement therapy, endogenous TSH is monitored regularly in order to adjust the dose of replacement hormone to minimize suppression of endogenous TSH. Unfortunately, measurement of TSH requires species-specific reagents and validated assays are not commercially available for use on horse plasma or serum. Once TSH assays become available, we may actually find that supplementation with exogenous thyroid hormone could be detrimental to some horses by excessively suppressing the hypothalamic-pituitary-thyroid axis. Finally, it is also important to remember that systemic use and topical application of iodinated medications or shampoos can actually accelerate thyroid hormone production and induce signs of apparent hyperthyroidism (tachycardia, sweating, excitability, tremors and weight loss) in some horses.

Recently, the author reviewed the results of approximately 7300 equine thyroid hormone profiles submitted to the Endocrinology Laboratory at Michigan State University's Diagnostic Center for Population and Animal Health from 2002–2008. Information obtained from submission forms included age and sex but reason for testing and concurrent medication administration could not be assessed due to lack of completion of a large percentage of submission forms. TT4 (reference range [RR] 7–27 nmol/L), free thyroxine (FT4, RR 6–24 pmol/L), total triiodothyronine (TT3, RR 0.7–2.5 nmol/L) and free triiodothyronine (FT3, RR 1.7–5.2 pmol/L) were measured by specific radioimmunoassays validated for equine serum samples. TT4 was within RR values in 62%, low in 18%, and elevated in 20% of samples. FT4 was within RR values in 83%, low in 16%, and elevated in 1% of samples. TT3 was within RR values in 58%, low in 41%, and elevated in 1% of samples. FT3 was within RR values in 62%, low in 29%, and elevated in 9% of samples. There were no significant correlations between any of the thyroid hormone concentrations. Further, there were no effects of age or sex on the percentage of either increased or decreased thyroid hormone concentrations. Despite TT4 being elevated in one-fifth of all samples submitted, hyperthyroidism due to adenocarcinoma would be a rare diagnosis but other causes of an elevated TT4 have not been described in horses. Values below the lower limit of the RR were reported for

one or more thyroid hormones in 16–41% of samples and, thereby, could have provided support for a diagnosis of hypothyroidism. However, many of these patients may also have low thyroid hormone concentrations due to concurrent disease (euthyroid sick syndrome) or there may have been other factors that artifactually lowered circulating thyroid hormone concentrations. In conclusion, accurate interpretation of circulating thyroid hormone concentrations in horses requires complete knowledge of the patient's condition.

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