Thyroid Hormone Levels in Thoroughbred Mares and Their Foals at Parturition

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A high percentage of Thoroughbred mares and their foals on two large farms in central Kentucky were found to have low thyroid hormone levels (lower than established levels) at the time of parturition, even though management on the farms near the time of foaling varied. A number of factors were identified that could have contributed to the low levels of thyroid hormones in these mares and foals, which further substantiates how complex thyroid dysfunction is in horses and how difficult it is to diagnose. Attempts at treatment appeared to have little, if any, beneficial effect relative to thyroid function and may have contributed to the low thyroid hormone levels. Authors' addresses: Dept. of Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, 379 E. Campus Dr., Columbia, MO 65211 (Messer); Rood & Riddle Equine Hospital, 2150 Georgetown Rd., Lexington, KY 40580 (Riddle); Dept. of Clinical Sciences, College of Veterinary Medicine and Biomedical Sciences, Colorado State University, Ft. Collins, CO 80523 (Traub-Dargatz); USDA: APHIS, Centers for Epidemiology and Animal Health, Ft. Collins, CO 80521 (Dargatz); Animal Health Diagnostic Laboratory, College of Veterinary Medicine, Michigan State University, Lansing, MI 48909-7576 (Refsal); and Dept. of Animal Science, Louisiana State University, Baton Rouge, LA 70803 (Thompson). © 1998 AAEP.

1. Introduction
There is a wide spectrum of equine clinicians with varying beliefs about thyroid disease, ranging from those who believe thyroid disease is common and often diagnose it in horses who are infertile, have laminitis, or race poorly, to those who do not believe it even exists.¹ In adult horses, thyroid dysfunction is generally felt to be uncommon, and while it has been associated with a variety of clinical signs, a definitive diagnosis is often difficult.² One of the reasons for this is that many endogenous and exogenous factors can affect thyroid function and sometimes test results.³ Serum levels of thyroid hormones vary over a wide range, and low baseline levels may be misleading, which may result in many euthyroid horses being diagnosed as hypothyroid.⁴ Despite the difficulty in definitively diagnosing a thyroid dysfunction in adult horses, it is estimated that over $750,000 worth of thyroid hormone supplement is sold for use in horses annually.⁵ In a recent survey of horse owners, thyroid disease was ranked second as far as research priority.⁶

In neonatal foals, a distinct syndrome of congenital hypothyroidism and dysmaturity has been recognized, which is characterized by thyroid gland hyperplasia, musculoskeletal deformities, normal to low serum thyroid hormone levels, and decreased response to thyrotropin (thyroid-stimulating hor-
mone, or TSH). This syndrome has been recognized primarily in western Canada and in states bordering on western Canada. Mares giving birth to affected foals usually have normal thyroid hormone levels at the time of parturition. The purpose of the study reported here was to measure thyroid hormone levels in Thoroughbred mares and their foals at the time of parturition on two farms in central Kentucky, where management on the farms near the time of foaling varied. In addition, all foals were evaluated for conformational abnormalities or deformities that were present at the time of blood collection for thyroid hormone analysis.

2. Materials and Methods

A study was conducted in 1996 on two large Thoroughbred farms in central Kentucky to measure thyroid hormone levels in mares and their newborn foals at the time of parturition. The management of the two farms near the time of parturition varied in that one farm's (farm A) pastures contained endophyte-infected fescue grass, while the other farm's (farm B) pastures were nearly free of any endophyte-infected fescue grass. Before beginning this study, baseline serum levels of thyroxine (T\textsubscript{4}) were determined in mares on both farms at the time of breeding, and, based on those results, mares were supplemented daily with exogenous thyroid hormone throughout their pregnancy (a common practice followed on many breeding farms in central Kentucky). Mares on farm A with pastures containing endophyte-infected fescue grass were routinely removed from endophyte-infected pasture at approximately 30 days prior to foaling and treated with domperidone, a dopaminergic antagonist used to prevent or treat fescue-induced hypoprolactinemia. Mares on farm B were allowed daily access to pasture and were not treated with domperidone. Approximately 30% of the mares on farm A and 40% of the mares on farm B were estimated to be on some form of thyroid hormone supplementation throughout their pregnancy.

Samples of blood were collected from 104 mare-foal pairs (52 mare-foal pairs on farm A and 52 mare-foal pairs on farm B) within 25 h postfoaling. The time after birth to when mares and foals were bled ranged from 0.8 h to 25 h, with a median time of 8 h. Samples were allowed to clot for at least 1 h and then were centrifuged; serum was harvested and frozen. Samples were analyzed for levels of thyroxine (T\textsubscript{4}), tri-iodothyronine (T\textsubscript{3}), reverse-tri-iodothyronine (rT\textsubscript{3}), and thyrotropin (e-TSH), in accordance with previously described methods. In addition, at the time of blood collection from the foals, each fetlock, carpus, and hock joint on each foal was scored for conformation abnormalities or deformities that were present. Fetlocks were scored for varus (range 0–2), valgus (range 0–2), contracture (range 0–3), and laxity (range 0–3) abnormalities. Each carpus was scored for varus (range 0–2) and valgus (range 0–2) deformities, as well as whether they were over (range 0–2) or back (range 0–2). Data were also collected on each mare-foal pair regarding breeding date, foaling date, date taken off pasture (farm A), date domperidone treatment initiated (farm A), time to first suckling, and occurrence of dystocia. Data were missing for a few samples as a result of damage during shipment to the laboratory for thyroid hormone analysis, so the number of observations used in the analyses may be smaller than 104.

Normal reference ranges used were those provided by the testing laboratories, or when not available from the laboratories, from published reports using comparable methodology; these ranges do not necessarily represent the normal reference range for the population of mares and foals studied (Table 1). The conformational scores for each foal were collapsed across joints to form two (varus deformities) or three (valgus, contracture, or miscellaneous deformities) categories. Thyroid hormone levels were evaluated for association with farm, conformational score, and time to first suckling by an analysis of variance. A value of p ≤ 0.05 was considered significant.

3. Results

The number of mares and foals on both farms with thyroid hormone levels above or below the normal reference range was remarkably high. Overall, 69.6% of the mares and 83.3% of the foals had T\textsubscript{4} values outside the normal range.

### Table 1. Reference Values for Thyroid Hormone Assays

<table>
<thead>
<tr>
<th>Value</th>
<th>Foal (nmol/L)</th>
<th>Mare (nmol/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T\textsubscript{3}</td>
<td>T\textsubscript{4}</td>
</tr>
<tr>
<td>Low</td>
<td>&lt;10</td>
<td>&lt;279</td>
</tr>
<tr>
<td>Normal</td>
<td>10–19\textsuperscript{e}</td>
<td>279–464\textsuperscript{e}</td>
</tr>
<tr>
<td>High</td>
<td>&gt;20</td>
<td>&gt;464</td>
</tr>
</tbody>
</table>

\textsuperscript{a}The reference range is not available for 1-day-old foals.
\textsuperscript{b}The reference range is not available for 1-day-old foals, using comparable methodology.
\textsuperscript{c}The reference range for normal, adult horses is from the Endocrine Laboratory, Animal Health Diagnostic Laboratory, Michigan State University.
\textsuperscript{d}The reference range for normal, adult horses is from the laboratory of D. L. Thompson, Dept. of Animal Sciences, Louisiana State University.
\textsuperscript{e}See Refs. 12, 13, 15, 16, and 27.
levels below normal reference ranges (normal adult $T_4 = 16.5-23.5$ nmol/L; normal $T_3$ for 1-day-old foals $= 279-464$ nmol/L). Though the mares were not considered to be low for $T_3$, 40% of the foals had $T_3$ levels below the normal reference range (normal $T_3$ for 1-day-old foals $= 10-19$ nmol/L). Sixty percent of the mares had $rT_3$ levels above the normal reference range (normal adult $rT_3 = 0.48-0.62$ nmol/L). Overall, there was no significant difference between mare e-TSH levels and foal e-TSH levels (adult mean e-TSH = 0.11 nmol/L vs. foal mean e-TSH = 0.1 nmol/L). The percentages of mares and foals with e-TSH levels above the normal adult reference range (normal adult reference range e-TSH = 0.01-0.09 nmol/L) on farm A were 22% and 23%, respectively, whereas the percentages of mares and foals with e-TSH levels above the normal adult reference range on farm B were 58% and 45%, respectively. With an evaluation of thyroid hormone levels on a continuous scale, mare e-TSH, mare $rT_3$, foal $T_3$, and foal $T_4$ were different by farm ($p < 0.05$). The percentage of foals with various types of conformational scores was similar between farms. The percentage of foals in the various gestational age categories was similar for the two farms. No foals were classified as premature (<300 day's gestational age). The mean time to first suckling for the foals was 2.1 h, with a range of 0.2-6.5 h.

4. Discussion

The investigation of thyroid dysfunction in horses, as in other species, is fraught with difficulties, because of the multisystemic and nonspecific effects of thyroid hormones and because of the currently available thyroid function tests; few are specific, and many are altered by extrathyroidal factors. The type of animals used to establish the normal range for a laboratory test is an often overlooked but critically important factor. For example, the use of a reference range derived from normal, adult horse test results for an interpretation of results from a neonatal animal is questionable. This is particularly true when thyroid hormone levels are interpreted in horses, since neonatal foals have much higher $T_3$ and $T_4$ levels than adult horses.

In this study, we identified a large percent of Thoroughbred broodmares and their foals that had low $T_4$ levels (lower than established levels) at the time of parturition on two farms where the management varied. On one farm (farm A), mares were allowed access to endophyte-infected fescue pasture daily up until 30 days before expected parturition, at which time the mares were removed from pasture and treated with domperidone, a dopaminergic antagonist, until they foaled. The endophyte fungus, Acremonium coenophialum, produces certain ergopeptide alkaloids that have dopaminergic agonist activity that inhibits prolactin secretion from the anterior pituitary gland of horses. In foals exposed in utero to endophyte toxin, total progestagens, cortisol, and $T_3$ levels were significantly lower than corresponding levels in foals not exposed to endophyte toxin. The same investigators found that, compared with control foals not exposed to endophyte toxin, foals born to mares exposed to endophyte toxin late in gestation had large, distended thyroid follicles lined by flat cuboidal epithelial cells. We did not perform any histopathologic examinations in this study, but we did find that 40% of the foals had low $T_3$ levels.

In addition to inhibiting prolactin, dopamine and dopaminergic agonists have been shown to decrease basal and thyrotropin-releasing hormone-stimulated TSH secretion in humans. Dopamine may exert a tonic control on TSH secretion, since dopamine antagonists have been shown in humans to increase serum TSH levels in hypothyroid patients. In this study, mares on farm A (endophyte infected) had lower e-TSH levels than mares on farm B (endophyte free). Although it is not significant, foals on farm A had lower e-TSH levels than foals on farm B. In consideration of the high percentage of mares and foals having low $T_4$, the levels of e-TSH in mares and foals were lower than would be expected and the number of mares and foals with high TSH levels was smaller than would be expected. This could be due, in part, to the endophyte-infected fescue pasture on farm A, but it also could be due to thyroid hormone supplementation on both farms.

Besides endophyte-infected fescue and thyroid hormone supplementation, there may be several other factors that should be considered. The effect of late-term pregnancy on thyroid hormone levels in mares appears to be variable, with studies showing either no change or a decrease in thyroid hormones in late pregnancy. This is in contrast to what happens in humans, in which thyroid hormone levels increase in late pregnancy as a result of estrogen-induced increases in thyroid-binding globulin and of stimulation of the thyroid gland by TSH-like activity of human chorionic gonadotropin, but it could be an explanation of the high number of mares with low $T_4$ in this study. Two studies involving Thoroughbreds have shown that resting $T_4$ levels were well below the normal range of values used by the respective laboratories of the investigators, leading to the conclusion by both investigators that measurement of $T_4$, as an indication of thyroid function in the Thoroughbred, is unreliable. It could be that Thoroughbred broodmares normally have thyroid hormone levels that are lower than the published reference ranges.

Another factor, which is not addressed in this study but which affects thyroid hormone levels, is nutrition. It has been shown that short periods of food deprivation result in low thyroid hormone levels. Diet composition has been shown to affect the level of $T_4$ in the serum of Thoroughbred horses. During pregnancy, a deficiency in energy intake can contribute to lower concentrations of thyroid hormones in maternal plasma during late gestation, which can result in a reduction in the fetal nutrient supply and in low thyroid hormone levels in the newborn.
Yet another finding in this study was that 60% of the mares had high rT₃ levels, with mares on farm B having significantly higher levels than mares on farm A. Increases in rT₃ in adult horses have been recognized in association with dexamethasone administration and food deprivation, and in stressed neonatal foals. Extrathyroid illness, also called euthyroid sick syndrome, is characterized by low T₃ and high rT₃ and is caused by inhibition of the enzyme 5′deiodinase, which is responsible for the conversion of T₂ to T₃ and for the conversion of rT₃ to T₂. This syndrome represents an adaptive mechanism to decrease the metabolic rate during periods of illness and stress and the thyroid gland is considered to be normal. The mares in our study had low T₄, normal T₃, and high rT₃. The cause of this finding requires further study.

Even though there were several foals in our study with a variety of conformational abnormalities or deformities, we did not identify any foals with typical signs of congenital hypothyroidism-dysmaturity syndrome, despite having 83.3% of the foals with low T₄ levels and 40% of the foals with low T₃ levels.

5. Summary
A high percentage of Thoroughbred mares and their foals on two large farms in central Kentucky were found to have low thyroid hormone levels (lower than established levels) at the time of parturition, even though management on the farms near the time of foaling varied. A number of factors were identified that could have contributed to the low levels of thyroid hormones in these mares and foals, which further substantiates how complex thyroid dysfunction is in horses and how difficult it is to diagnose. None of the mares or foals was known to be clinically ill or showing any signs associated with thyroid dysfunction. Attempts at treatment appeared to have little, if any, beneficial effect relative to thyroid function and may have contributed to the low thyroid hormone levels.

References and Footnotes