

## Thyroid Hormones and Equine Metabolic Syndrome

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In the main article on equine metabolic syndrome (aka insulin resistance), I mentioned in passing that sometimes thyroid hormone supplementation is used to assist in weight reduction with these overweight, laminitis-prone horses. In this article I thought I'd discuss that in a bit more detail.

### The thyroid gland

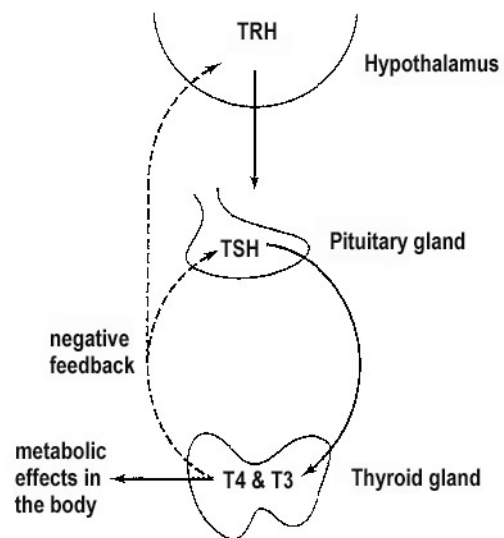
First, a brief description of the thyroid gland, the hormones it produces, and the regulation of its function. The thyroid gland consists of a pair of lobes (left and right), each about the size of a small hen's egg, that are located just behind the larynx in the horse's throatlatch area. The thyroid gland produces two principal hormones: thyroxine (T4) and tri-iodothyronine (T3). These hormones have wide-ranging effects on the body, but their most fundamental role in the adult body is to stimulate metabolism.

The secretion of these hormones by the thyroid gland is regulated by the pituitary gland (a small gland at the base of the brain). Among several other regulatory hormones, the pituitary gland secretes a hormone called thyrotropin or thyroid stimulating hormone (TSH). As its name indicates, TSH stimulates the thyroid gland to secrete T4 and T3.

But that's not all; secretion of TSH by the pituitary gland is regulated by the hypothalamus (a discrete area of the brain, located just above the pituitary gland). The hypothalamus secretes

thyrotropin releasing hormone (TRH) which directs the pituitary gland to secrete TSH.

Blood levels of T4 and T3 are kept within a fairly narrow range through a refined feedback loop involving all three of these tissues (thyroid gland, pituitary gland, and hypothalamus). A drop in T4/T3 stimulates TRH production, which stimulates TSH production, which then stimulates the thyroid gland to secrete more T4 and T3. Elevations in T4/T3 have the opposite effect: they suppress the release of TRH and TSH, and thus of T4 and T3.



## **Synthetic T4**

Levothyroxine or L-thyroxine is the active constituent in Thyro-L<sup>®</sup>, the most widely used brand of thyroid hormone supplement for horses. It is a synthetic form of the body's natural T4. L-thyroxine has been used by veterinarians for decades to help manage overweight horses who have or are prone to laminitis.

These horses are not hypothyroid in the usual sense of the word (defective thyroid gland), as recent studies have shown that their thyroid glands respond normally (by increasing the production of T4 and T3) when stimulated by an injection of TRH. However, they may have lower than normal levels of thyroid hormones in their bloodstream.

That's because the feedback loop involving the hypothalamus, pituitary gland, and thyroid gland may become disordered with any condition that affects the hypothalamus or the pituitary gland. Pain, stress, and systemic illness can each interfere with the central control of thyroid function and thus cause a drop in circulating thyroid hormones. Certain drugs, such as corticosteroids ("cortisone" of any variety) and anabolic steroids, can also interfere with this feedback loop at the level of the hypothalamus/pituitary gland. (And phenylbutazone ["bute"] can falsely lower T4 levels by competing with T4 for binding sites on plasma proteins.)

There is even a name for the situation in which thyroid responsiveness is normal, yet circulating levels of T4 and T3 are low: euthyroid sick syndrome. This reduction in circulating T4/T3 may well be a protective metabolic mechanism in the ill or injured body, so it may not be appropriate to "treat" it with supplemental thyroid hormones. Instead, manage the underlying problem, and the thyroid hormone levels return to the normal range on their own.

## **Synthetic T4 and equine metabolic syndrome**

That brings me once again back to equine metabolic syndrome. The biochemical and hormonal changes that occur with obesity (i.e. equine metabolic syndrome) can disrupt hypothalamic and pituitary function, and thus result in marginal or low levels of T4/T3. (Not in every case, but in many of these horses.) To put it simply, these horses are not overweight because they're hypothyroid; they're hypothyroid (at least, in terms of circulating T4/T3 levels) because they are overweight.

Equine metabolic syndrome is not a condition of primary thyroid hormone deficiency, so treating these horses with supplemental thyroid hormone is not the answer. L-thyroxine can help

these horses, but not without consequences. A recent study<sup>1,2</sup> revealed the likely mechanism by which L-thyroxine can help with weight loss and perhaps even laminitis management in these overweight, insulin-resistant, laminitis-prone horses. But it also revealed some potential risks of going that route.

Researchers took 12 healthy adult horses and fed them an increasing dose of L-thyroxine over an 8-week period. Not only did the horses lose weight (an average of about 40 lbs each over the course of the study), but their *insulin sensitivity improved*. As I discuss in the main article on equine metabolic syndrome, insulin resistance is one of the hallmarks of equine metabolic syndrome, and it's thought to be one of the key factors involved in the increased risk for laminitis in these horses.

*However*, in that study L-thyroxine also suppressed the horses' thyroid function. The higher the dose of L-thyroxine given, the more weight was lost, but also the more the horses' thyroid function was suppressed. That makes sense, because the body tries to keep its T4 and T3 levels in a fairly narrow range. If we're supplying the body with T4, then it will produce less of its own to compensate (through that feedback loop I mentioned). In that study, serum thyroid hormone concentrations increased to over 4 times the baseline level at the highest L-thyroxine dose, and the thyroid response to TRH stimulation was suppressed.

So, there are at least three risks to using L-thyroxine for weight loss or laminitis management in overweight horses. The first is hyperthyroidism (excessive thyroid hormone levels) if too high a dose of L-thyroxine is used. The second is hypothyroidism (inadequate thyroid hormone production) if the L-thyroxine is abruptly stopped. L-thyroxine supplementation should be phased out gradually, to give the horse's body time to reset its thyroid feedback loop and resume normal production of its own T4.

The third risk is perhaps less obvious: reliance on L-thyroxine in place of appropriate dietary management and exercise yields a poor response, in terms of weight loss, laminitis management, and overall health. L-thyroxine alone is not a suitable substitute for modifications in diet and exercise. As I said in the main article, *there are no safe shortcuts to healthy weight reduction in overweight horses*. If it is used for this purpose, L-thyroxine must be used *in conjunction with* appropriate dietary changes and daily exercise.

**Pergolide and equine metabolic syndrome**

Before finishing, I also want to comment on the use of pergolide in horses with equine metabolic syndrome. Pergolide is a drug that is used in the treatment of equine Cushing's disease, a condition in which the regulation of certain pituitary hormones is diminished because of oxidative damage to some of the regulatory cells in the hypothalamus. As a result, the pituitary gland sort of runs amok; without the tight regulation of the hypothalamus, it becomes hyperactive and produces an excessive amount of adrenocorticotrophic hormone (ACTH, and a couple of other hormones), which causes excessive production of cortisol by the adrenal glands.

Excessive and poorly regulated production of ACTH is not a feature of equine metabolic syndrome. Furthermore, pergolide has been shown to be *ineffective* in correcting insulin resistance or managing laminitis in horses with equine metabolic syndrome. It is, however, a useful drug in the management of confirmed equine Cushing's disease. As it is an expensive drug, it should be reserved for horses who are strongly suspected of having, or are confirmed to have, equine Cushing's disease.

I hope that clears up some questions you may have had about equine metabolic syndrome. It all sounds rather complicated; and biochemically it is. But its treatment is quite simple: good horsekeeping, especially calorie control and regular exercise. One of my favorite quotes is by Dr. Ric Redden, a world-renowned equine veterinarian and farrier who specializes in treating laminitis and other conditions of the equine foot: "Laminitis that is directly associated with obesity is quite easy to prevent. It's a simple formula, one I have heard many times from old horsemen. It's a great line for maintaining a healthy horse: *The fat ones get less and the thin ones get more.*"

**References**

1. Sommardahl CS, Frank N, Elliott SB, et al. Effects of oral administration of levothyroxine sodium on serum concentrations of thyroid gland hormones and responses to injections of thyrotropin-releasing hormone in healthy adult mares. *American Journal of Veterinary Research*, 2005 Jun; 66(6): 1025-1031.

2. Frank N, Somvardahl CS, Eiler H, et al. Effects of oral administration of levothyroxine sodium on concentrations of plasma lipids, concentration and composition of very-low-density lipoproteins and glucose dynamics in healthy adult mares. *American Journal of Veterinary Research*, 2005 Jun; 66(6): 1032-1038.
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