THYROID HORMONES AND THEIR EFFECT ON REPRODUCTIVE FUNCTION

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Thyroid hormones are described as unique because they exert effects within almost every tissue of the body throughout the life of an individual. In humans, thyroid hormone deficiencies have resulted in a number of abnormalities with respect to growth, development, behavior, metabolism and reproduction. This discussion will focus solely on thyroid hormones and their influence on reproduction.

The thyroid gland is an organ located just over the trachea. Although it is often thought that only one "thyroid hormone" exists, there are two principal hormones produced from this gland, thyroxine (T_4) and triiodothyronine (T_3). In general, T_3 is considered to be more physiologically significant at the cellular level even though both hormones act on tissues. Thyroxine (T_4) is considered the precursor because it is processed in greater quantity and readily converted to T_3. Production and secretion of these hormones are heavily dependent on the presence of iodine, an element necessary for proper function of the thyroid gland.

Often heard are claims made by veterinarians and horse owners relating thyroid hormone levels to reproductive problems of a mare. Clinical cases have been reported identifying thyroid hormone treatment as responsible for improving the fertility of certain mares. Although it is hard to dispute clinical success, little research has been done to adequately test the ramifications of thyroid disease on infertility in the horse. Work in several other species including humans, dogs, sheep and camels does appear to show abnormal levels of thyroid hormone as having adverse effects on reproduction.

Hypothyroidism, or abnormally low levels of thyroid hormones, seems to be less common in horses than in other species. In order to understand the effects of low thyroid levels on the body, scientists routinely use thyroidectomized (thyroid gland removed) animals for study. Lowe and associates (1974) removed the thyroid gland from mares in an attempt to find resulting effects on reproductive function. No abnormalities were found. A later study by Lowe and coworkers (1987) confirmed that LH and progesterone concentrations, length of the estrous cycle and pregnancy rates were similar for thyroidectomized mares when compared to untreated control mares. Removing thyroid hormone levels from the circulation did however create signs of lethargy, edema to the rear limbs and coarse hair coats. These mares displayed tranquil estrous behavior when presented to a stallion and only mildly antagonistic behavior when not in estrus. Apparently, researchers at the University of Florida at Gainesville are just completing an extensive study that contradicts findings from earlier work. Reportedly in this study, inadequate levels of thyroid hormone were responsible for lower conception rates, increased incidence of early embryo death, poor estrous behavior and irregular follicle growth and ovulation.

Thyroid hormones have a significant mode of action on seasonal reproduction. In 1994, work by researchers in Michigan implicated thyroid hormones as having a role in decreasing LH secretion at the end of the breeding season, resulting in the normal cessation of follicular activity and ovulation. Along with follicle stimulating hormone (FSH), luteinizing hormone (LH) and indirectly, gonadotropin – releasing hormone (GnRH) are hormones responsible for follicle growth and ovulation. In 1995, Swinker and associates evaluated the correlation of thyroid hormone levels to ovulation in non-cycling mares

treated with varying doses of a hormone structurally similar to GnRH. There was a negative correlation found between circulating T_3 and T_4 levels and ovulation. Lower levels of thyroid hormones were evident near ovulation in GnRH-treated mares while elevated levels were found in nonovulating controls. In an attempt to study seasonal changes in plasma T_3 and T_4 concentrations in the horse, researchers from Clemson University monitored 30, nonlactating, clinically-healthy mares from October through March. Although T_4 levels tended to decrease during late December and January, no significant seasonal variation was found for either thyroid hormone. A wide range of hormonal values were observed due to individual variation among mares. This possibly explains why no seasonal changes were found.

Most of the thyroid research in horses seems to focus on the effects of the disease on foals. Mares exposed to iodine-deficient diets tend to give birth to stillborn or weak foals that die soon thereafter. McLaughlin and coworkers (1986) implicated low total serum concentrations of T_3 and/or T_4 as a cause of musculoskeletal abnormalities in newborn foals. It has been shown that overfeeding of iodine (83 mg/day) to pregnant mares also leads to the development of weak foals at the time of birth. Low-iodine as well as excessively high-iodine diets fed to mares can create a goiter, an enlargement of the thyroid gland, on the developing foal.

Regardless of species, very little has been published with respect to the influences of thyroid hormones on male reproductive characteristics. Researchers discovered that high circulating thyroid hormones were capable of suppressing LH secretion in prepubertal ram lambs. One study was found reporting a positive correlation between T_3/T_4 concentrations and the number of spermatozoa in an ejaculate of male llamas under European conditions. Serum T_3 levels were negatively correlated with ejaculate volume. It was not clear whether T_3 and T_4 levels were implicated as having a direct effect on sperm production or whether both thyroid hormone concentrations and sperm production were similarly affected by other factors such as daylength and temperature patterns. Apparently, no harmful effects of thyroid hormone imbalances have been reported in stallions, with the possible exception of libido. Stallions showing general symptoms of thyroid deficiency such as obesity and lethargy tend to have low sex drive. This symptom seems to coincide with mares having placid estrous behavior when thyroid deficient.

Although a further understanding is still needed, some evidence has been presented supporting the theory of thyroid hormones being an influential factor on reproduction. A true assessment of thyroid hormone influence on a horse's well-being can only occur once all other factors have been adequately resolved. Along with nonthyroid-related illnesses, certain drugs such as phenylbutazone and glucocorticoids may secondarily depress thyroid hormone concentrations and give a false reading. It is important to remember that true hypothyroidism (abnormally low thyroid levels) is relatively rare in the horse.

Normal values for thyroid function vary greatly depending on the laboratory that evaluates the samples. It's even harder to assess what's normal when different laboratories use different units of measure (ng/dl, ng/ml, nmol/L, etc.). According to Dr. Bob Douglas of BET Reproductive Laboratories, T_4 values greater than 10 ng/ml are normal for stallions and values greater than 12 ng/ml are normal for mares. If thyroid replacement therapy is desired, 5 to 10 mg of L-thyroxine per 500 kg body weight per day is commonly used as a starting dose. Keep in mind that thyroid deficient horses may have several visible symptoms that need to be remedied before or in conjunction with thyroid therapy. Consult your veterinarian to see if evaluating thyroid hormone levels is appropriate for your horse.