INTERACTIONS BETWEEN THYROID HORMONES AND REPRODUCTIVE FUNCTION IN PREPUBERTAL AND SEXUALLY MATURE MERINO RAMS.

by

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SUMMARY

A number of hormones secreted by various endocrine glands are directly or indirectly involved in normal functioning of the reproductive processes in various species and the thyroid hormones appear to be one of those that are intricately linked with reproduction. Thyroid hormones may influence reproductive activity either by direct action on the gonads or by effects mediated at the level of the hypothalamo-pituitary axis. Investigations carried out were designed to examine the interactions between thyroid hormones and male reproductive function in mature, prepubertal and postpubertal Merino rams. Hypothyroidism or hyperthyroidism was induced in these rams for 8-10 weeks and their reproductive endocrine axis and testis functions were assessed.

In a preliminary experiment, mature Merino rams (5 years old) were made hypothyroid or hyperthyroid for 8 weeks. Neither hypothyroidism nor hyperthyroidism had any apparent effect either on spermatogenesis or on daily sperm production, but motility of ejaculated spermatozoa and circulating testosterone levels were reduced in both conditions. The decreased spermatozoal motility suggest that reduced testosterone levels had altered the androgen-dependent maturation of spermatozoa in the epididymis. The ratio of testosterone concentration in the plasma from internal spermatic vein to that in peripheral blood plasma was higher in hyperthyroid than in control and hypothyroid rams suggesting elevation of testosterone clearance rate in hyperthyroid rams. Testosterone production and particularly the response to human chorionic gonadotrophin (hCG) was very much reduced in hypothyroid rams, suggesting a requirement of thyroid hormones for normal
functioning of Leydig cells. Reduced basal LH and response to LH releasing hormone (LHRH) indicates the influence of thyroid hormones on the pituitary gland. Serum prolactin levels were higher than controls in both hypothyroid and hyperthyroid rams, whereas there were no differences in FSH levels. These results suggest that thyroid hormones can influence the reproductive function in mature rams through their actions at both the pituitary gland and testis.

In a second experiment, hypothyroidism or hyperthyroidism was induced in postpubertal rams (12-16 months old) for 8 weeks to compare with the results obtained in the mature animals. Postpubertal rams were similar to the mature rams since spermatogenesis or daily sperm production were not altered, but sperm maturation and circulating testosterone levels were reduced in both hypo- and hyperthyroid rams. Secretion of LH and testosterone were again reduced in hypothyroid animals. Elevated testosterone clearance rates (TCR) without changes in sex hormone binding globulin (SHBG) in hyperthyroid and lower SHBG levels without changes in TCR in hypothyroid rams indicated that an apparent disassociation between SHBG and TCR can occur in rams.

In a third experiment effects of hypothyroidism and hyperthyroidism on the development of reproductive endocrine function in ram lambs (16 weeks old) were studied. Hyperthyroidism was associated with decreases in LH pulse frequency, basal LH and mean LH concentrations, together with arrested testicular growth and aspermatogenesis. Hypothyroid lambs showed normal pubertal development. After intravenous injection of exogenous LHRH hyperthyroid lambs showed similar LH responses to control and hypothyroid rams but reduced testosterone response. Basal secretion of testosterone and the
response to hCG were reduced in hyperthyroid rams. These results indicate that retarded testicular development in hyperthyroid ram lambs results from changes in hypothalamo-pituitary activity manifested in a decreased LH pulse frequency. However in this study the hyperthyroid lambs did not grow; therefore I examined further the basis for the retarded testicular development in these animals by comparing sexual maturation of hyperthyroid rams, with that of ram lambs maintained at a constant body weight by restricting dietary intake. Hyperthyroid and restricted-intake lambs remained at a constant body weight during the period of treatment whilst control lambs gained body weight. The testis of the restricted-intake lambs underwent normal growth; however testis growth was suppressed in hyperthyroid animals. Hyperthyroidism but not food restriction was also associated with decrease in LH pulse frequency compared with controls. Even after cessation of treatment in hyperthyroid animals testicular growth was reduced for up to 30 weeks. It was concluded that hyperthyroidism directly influences sexual maturation in ram lambs through an action at hypothalamic and/or higher brain centres which control the LHRH pulse generator. Transient hyperthyroidism during an important phase of sexual maturation may cause permanent impairment of sexual development.

To obtain a better understanding of the finer influence of thyroid hormones on the reproductive endocrine axis and testis function mature rams (5 years old) were thyroidectomized and supplemented with daily subcutaneous injections of $T_4$ at subnormal, normal, and supranormal dose levels and the reproductive functions were assessed. This approach, it was anticipated would give the indication of the threshold level of thyroid hormones required for normal reproductive function.
Spermatogenic function was not affected but sperm maturation and circulating testosterone levels were lower in thyroidectomized rams. Steroidogenic capacity of the Leydig cells was also reduced in these rams. Serum LH pulse frequency and LH secretion in response to LHRH were very much reduced in thyroidectomized rams. Supplementation with only 30% of normal thyroxine restored the above mentioned effects to normal. Rams supplemented with supranormal T4 levels showed a similar effect on the various reproductive functions as hyperthyroid rams in the first experiment. These results, therefore, indicate that thyroxine at low levels (30%) can maintain normal function of the reproductive system in the rams suggesting a passive role for thyroid hormones in male reproductive function in sheep.