

THE UNIVERSITY OF MANITOBA

THE INTERRELATIONSHIP BETWEEN THYROID HORMONES AND OVARIAN SEX  
STEROIDS IN RAINBOW TROUT, SALMO GAIRDNERI.

BY

© DANIEL GABRIEL CYR

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DOCTOR OF PHILOSOPHY

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THE INTERRELATIONSHIP BETWEEN THYROID HORMONES AND  
OVARIAN SEX STEROIDS IN RAINBOW TROUT, Salmo gairdneri

BY

DANIEL GABRIEL CYR

A thesis submitted to the Faculty of Graduate Studies of  
the University of Manitoba in partial fulfillment of the requirements  
of the degree of

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## ABSTRACT

The interrelationship between thyroid hormones ( $T_4$ = L-thyroxine;  $T_3$ = 3,5,3'-triiodo-L-thyronine) and ovarian sex steroid hormones was assessed in rainbow trout. Both the effects of thyroid hormones on circulating levels of 17 $\beta$ -estradiol ( $E_2$ ) and sex steroid secretion by ovarian follicles and the effects of  $E_2$  on thyroid function were studied.

Seasonal variations in circulating levels of  $T_3$  and  $T_4$  were inversely correlated with levels of  $E_2$  and testosterone (T) under controlled laboratory conditions. While the spawning time could be altered by manipulating the photoperiod, the relationship between serum thyroid hormones,  $E_2$  and T remained unchanged. In immature trout of the same age, serum  $E_2$  levels were low and serum  $T_4$  and  $T_3$  levels were higher than in mature trout.

An experimentally-induced long-term (22 days) physiologic elevation in plasma  $T_3$  significantly increased the gonadosomatic index (GSI) of female trout. Combined treatment of  $T_3$  and salmon gonadotropin (GtH) caused the greatest increase in GSI and significantly increased plasma  $E_2$ . Short-term (7 days) treatment with pharmacological doses of  $T_3$  did not alter the GSI and decreased the sensitivity of the ovary to GtH. Physiologic elevations of plasma  $T_3$  for 7 days significantly increased the sensitivity of the ovary to GtH suggesting that  $T_3$  exerts a biphasic dose-dependant effect on the ovary.

In vitro incubations of ovarian follicles (theca and granulosa) with GtH and  $T_3$  show that  $T_3$  acts upon the follicles to

amplify GtH-induced  $E_2$  secretion.  $T_3$  is more potent than  $T_4$  and the stimulation is independent of de novo protein synthesis. Incubation of either thecal cells or granulosa cells alone demonstrated that  $T_3$  amplified GtH-induced T secretion by the theca and stimulated T to  $E_2$  conversion by the granulosa.  $T_3$  stimulation of GtH-induced  $E_2$  secretion by the follicles was blocked by theophylline, suggesting that  $T_3$  may inhibit phosphodiesterase activity.

The administration of  $E_2$  to immature trout significantly decreased plasma  $T_3$  with no effects on total plasma  $T_4$  levels. This effect was largely the result of a 10-fold decrease in the  $V_{max}$  of the hepatic 5'-monodeiodinase (5'D).

Compartmental analysis of plasma  $T_4$  kinetics showed a decrease in metabolic clearance rate (MCR) and  $T_4$  degradation rate (DR) for  $E_2$ -treated trout. Since plasma  $T_4$  levels were unaltered by  $E_2$ , the decreased  $T_4$  DR indicates depressed  $T_4$  secretion by the  $E_2$ -treated thyroid. This decrease in  $T_4$  DR is most reasonably explained by the decreased conversion of  $T_4$  to  $T_3$  which was supported by the depressed in vivo conversion of [ $^{125}I$ ] $T_4$  to [ $^{125}I$ ] $T_3$  and  $^{125}I^-$ .  $E_2$  had little influence on the  $T_3$  MCR but decreased the  $T_3$  DR and lowered both tissue and plasma  $T_3$  pools.

To determine the effects of  $E_2$  on the properties of the plasma proteins that bind  $T_4$  and  $T_3$ , immature trout were injected with  $E_2$ .  $E_2$  decreased the proportion of [ $^{125}I$ ] $T_3$  bound to plasma sites without significant effect on [ $^{125}I$ ] $T_4$  binding. Separation of plasma binding proteins of control trout by agrose filtration on Bio-Gel A-1.5m revealed that both  $T_3$  and  $T_4$  bound to two main

sites corresponding to presumed prealbumin and  $\beta$ -globulin fractions and that a small portion of  $T_4$  also bound to lipoprotein. Addition of a calculated amount of unlabelled  $T_3$  displaced [ $^{125}I$ ] $T_3$  from the 55 KDA (prealbumin) site indicating its role as the  $T_3$  high-affinity site.  $E_2$  treatment initiated production of vitellogenin (VTG) which bound a very small proportion of  $T_4$  but did not bind  $T_3$ . Kinetic analysis of [ $^{125}I$ ] $T_3$  or [ $^{125}I$ ] $T_4$  binding conducted on miniature G-25 Sephadex columns in the presence of varying concentrations of the homologous ligand indicated that  $E_2$  increased the capacity of the low-affinity, high-capacity  $T_3$  binding site without effect on the high-affinity  $T_3$ -binding site and without major effect on  $T_4$  binding to either its high-affinity or low-affinity sites.

In conclusion, a strong interrelationship exists between thyroid hormones and ovarian sex steroids in rainbow trout. The interactions between these two endocrine systems appears to regulate the partitioning of energy between somatic growth and ovarian development.  $T_3$  appears to stimulate growth and enhance early ovarian function. Once committed to vitellogenesis  $E_2$  depresses the thyroid system at several levels with presumed reduction in somatic growth processes.

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