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JOURNAL ARTICLE

Testosterone autoregulation of its biosynthesis in the rat testis: inhibition of 17 alpha-hydroxylase activity

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Using the in vitro perfused rat testis, the effects of testosterone (T) on its own biosynthesis, and in particular on the inhibition of specific steroidogenic step(s) in the biosynthetic pathway from cholesterol to T, were examined. Rat testes perfused in vitro for 1 hour with medium containing 1.5 microM T secreted significantly less T than control testes in response to physiologic or maximal luteinizing hormone (LH) stimulation. To locate the site(s) of this rapid inhibition, the effects of arterial T infusion on steroidogenesis by testes also infused with pregnenolone (PREG), progesterone (PROG), 17 alpha-hydroxyprogesterone (17-PROG), or androstenedione (ADIONE) were measured by summing all the possible reaction products from each substrate. This approach allowed us to examine the effect of T in situ on the reactions: LH-stimulated PREG secretion; PREG to PROG; PROG to 17-PROG; 17-PROG to ADIONE; and ADIONE to T. Only PROG to 17-PROG (17 alpha-hydroxylase activity) was inhibited by arterial T infusion. A kinetic examination of the PROG to 17-PROG reaction demonstrated that the specific inhibition by T was competitive. The apparent km for PROG in this system was 16.0 microM, whereas the apparent ki of T was 1.6 microM, indicating a relatively high degree of sensitivity of the reaction to T. Taken together, these data confirm that T is able to regulate its own synthesis and indicate that this autoregulation is the result of rapid, specific inhibition by T of 17 alpha-hydroxylase activity.

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