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DRAMATIC RESPONSE OF PROSTATIC WEIGHT AND ORNITHINE DECARBOXYLASE TO LOW LEVELS OF TESTOSTERONE IN CASTRATED RATS. B. Marchetti, M. Plante, R. Poulin and F. Labrie, MRC Group in Molecular Endocrinology, CHUL, Quebec G1V 4G2, Canada.

Low levels of circulating androgens have been shown to be important in human prostatic cancer. After surgical or medical castration by treatment with estrogens or LHRH agonists, the adrenals continue to secrete precursor steroids which may be converted into active androgens in prostatic and peripheral tissues. In the present study, we have examined the effect of low concentrations of plasma testosterone continuously released in castrated adult rats by silastic implants on ventral prostate and seminal vesicle weight as well as on the activity of prostatic ornithine decarboxylase (ODC). The results show that prostatic tissue is dramatically sensitive to very low doses of circulating T as demonstrated by the two-fold increase in prostate weight from castrated values of 51 ± 4 to 110 ± 8 mg at serum T values of 0.34 ng/ml. Low concentrations of T also elicited a marked stimulation of ventral prostate ODC activity, a 30-fold stimulation of enzymatic activity being observed in the range 0.05-0.5 ng T/ml. ODC activity was maximally stimulated at concentrations of T of 1.3 ng/ml, thus giving an overall stimulation of > 80-fold above castrated levels. These stimulatory effects of T were completely neutralized by the concomitant administration of the pure antiandrogen Flutamide. The extremely high androgen sensitivity of prostatic tissue has major therapeutical implications and strongly supports the choice of complete neutralization of androgens for optimal therapy of prostatic carcinoma. In fact, castration levels of serum T stimulate ventral prostate growth at 25-40% of the maximal growth obtained with serum T values found in intact adult men.

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TESTICULAR FUNCTIONS AFTER ORAL ADMINISTRATION OF CYPROTERONE ACETATE

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Antiandrogens interfere with the action of androgens on target organs mainly by competitive antagonism. Cyproterone acetate (CA) exhibit an antiandrogenic and progestational activity. Thus CA is expected to have a potent antifertility effect and a gonadotrophin-suppressing action. CA was administered at a dose of 12 mg orally twice a day to adult male Wistar rats for 1, 2 or 6 weeks. The testis weight was reduced significantly at 6 weeks. There was a marked decrease in the number of step 19 spermatids per 100 Sertoli cells whereas spermatids at step 7, pachytene spermatocytes and type A spermatogonia were also decreased but to a smaller extent. About a quarter of spermatids at step 7 matured to step 19. The nuclear diameter of Leyding cells was found to be reduced. The amount of protein per testis decreased presumably due to increased breakdown of protein resulting from antiandrogenic effect. Total RNA increased whereas total DNA and DNA synthesis remained unchanged. At 2 weeks the concentration of testosterone (T) and DHT in serum increased indicating a competitive binding to androgen receptors thus displacing T and DHT. The amount of T per testis decreased suggesting a gonadotrophin suppression, hence reduced stimulation of Leydig cells.