

2. MECHANISM OF STEROID ACTION

10. EVIDENCES THAT PROGESTINS EXERTS ITS RELAXANT EFFECT IN THE UTERUS BY BLOCKING Ca^{2+} CHANNELS

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It has been demonstrated that progesterone and some 5 α and 5 β progestins inhibit the spontaneous myometrium contractility. Although it has been proposed that progesterone (P) interferes with the membranal Ca^{2+} transport, the mechanism of action of these compounds is still unclear.

With the aim to elucidate the role of Ca^{2+} in the effect of P, epipregnanolone and pregnanedione, we studied the relaxant-time₅₀ (t_{1/2}) of the effective doses 84 of these steroids on tonic contractions induced by a depolarizant high-K⁺ solution and by low-Na⁺ media in the isolated uterus. A significant difference (p < 0.05) was observed in the relaxant effect of the progestins tested in both ionic solutions. Two main considerations are derived from these results: a) The K⁺ depolarizant solution induces the opening of voltage-sensitive Ca^{2+} channels increasing the intracellular Ca^{2+} concentration leading to a contraction. The steroids probably relax the uterus blocking this Ca^{2+} influx. b) The low-Na⁺ solution increases the intracellular Ca^{2+} concentration by a transmembranal Na/Ca exchange mechanism. This system is not blocked by the steroids, explaining the difference in the t_{1/2} observed. These results suggest a possible blocking effect of steroids on the voltage-sensitive Ca^{2+} channels.

11. STEROID INDUCED SODIUM DEPENDENT AMMONIA RELEASE FROM ISOLATED SECTIONS OF

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Sodium dependent ammonia release from isolated sections of rat intestine was measured as a means of following steroid induced transport changes. Dose response curves for testosterone, dexamethasone, and aldosterone stimulated ammonia release from distal sections of the rat (3 week old) small intestine demonstrate both activation and inhibitory effects. Typical dose response curves, having different thresholds (TEST < DEXA < ALDO) but similar maxima are subject, at higher concentrations, to an inhibitory effect common to all three steroids. The inhibition caused the ammonia release to fall to about half maximum. Aldosterone is peculiar in that this inhibition is overcome at higher concentrations. Testosterone is peculiar in that the inhibition is complete at high concentrations—due possibly to competition with its active metabolite. The results may be understood in terms of a two stage mechanism of steroid action.

12. STIMULATORY EFFECT OF THYROID RELEASING HORMONE (TRH) AND CHLORPROMAZINE (CPZ) ON PROLACTIN (PRL) SECRETION IN ESTROGEN PRIMED WOMEN WITH KALLMANN'S SYNDROME

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OBJECTIVE: Mode of action of CPZ on PRL secretion.

METHOD: TRH (500 μ g I.V.) and CPZ (25mg I.M.) tests were performed in 2 women with Kallmann's Syndrome before and during the 4 weeks of Ethinyl estradiol 0.5mg/daily administration.

RESULTS: Significantly low serum PRL levels and flat response of PRL to CPZ before estrogen therapy were obtained compared to the PRL response during estrogen kx. PRL response to TSH were normal.

CONCLUSION: 1) Estrogens are involved in regulation of PRL secretion from lactotrophs.
2) CPZ can act directly at the level of Anterior Pituitary not via Hypothalamus since the primary defect in Kallmann's Syndrome is believed to be in the hypothalamus.