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## JOURNAL ARTICLE

# Effects of long-term administration of androgens and estrogen on rhesus monkey prostate: possible induction of benign prostatic hyperplasia

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Rhesus monkeys were used to investigate the role of androgenic steroids and estradiol in the induction of hyperplastic changes in stromal and glandular prostate tissues. Adult male rhesus monkeys were procured from the wild and, after routine quarantine procedures, were randomly divided into 5 groups of 5 animals each. Gluteus maximus muscles were injected with 2.5 mg of androstenedione (Group II), 2.5 mg of dihydrotestosterone (DHT) or 0.25 mg of estradiol (Group III), 2.5 mg androstanediol (Diol; Group IV), or Diol in combination with 0.25 mg of estradiol (Group V). Group I consisted of untreated controls. Animals were injected with steroids 3 times a week for 2 years. Treatment with androstenedione (Group II) resulted in stromal hyperplasia in the caudal lobe and an increase in epithelial cell height in all zones except in the central zone of the caudal lobe. In monkeys treated with DHT and estradiol (Group III), stromal hyperplasia in both lobes, a decrease in tubular size, and degranulation and vacuolation of epithelial cells were noticed. Injection of Diol alone (Group IV) or in combination with estradiol (Group V) resulted in a widening of stroma in the central and peripheral zones of cranial and caudal lobes, whereas the tubular size decreased. Diol also induced epithelial cell hypercellularity in the central and peripheral zones of the caudal lobe and in the peripheral zone of the cranial lobe. Prostate-specific antigen levels in Group IV animals gradually increased from 6 months of treatment and were maximal after 18 months of injections. Serum estradiol levels increased to detectable levels in all groups except Group IV. Serum testosterone levels decreased to very low or undetectable levels in all groups, whereas prostate-specific acid phosphatase increased in all treated groups. Prolactin levels were elevated in all treated groups except in animals injected with androstenedione. These results indicate that repeated long-term injections of androstenedione or DHT and estradiol induced stromal hyperplasia, which may be an estrogen-related effect. Androstanediol-induced hypercellularity and stratification of glandular epithelium is comparable to human prostatic intraepithelial neoplasia. These results also suggest that the rhesus monkey is a suitable animal model for experimental induction of prostate diseases.

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