

Mammary Growth in Male Mice Receiving Androgens, Estrogens and Desoxycorticosterone Acetate.*

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The mammary ducts of male guinea pigs grew following the injection of $\Delta 5$ -transandrostenediol, testosterone propionate and 17-methyltestosterone.¹ The mammary tissue of immature male and female rats developed following injections of testosterone² and so did that of spayed virgin rats given androstenediol and androstenedione.³ A secretory response in the mammary gland of spayed pre-adolescent female Rhesus monkeys was produced by testosterone propionate, dehydro-androsterone, $\Delta 5$ -transandrostenediol and androsterone.⁴ (See Turner⁷ for review.) The injection of various estrogens and progesterone was followed by the growth of the mammary glands in male mice.^{5, 6}

The present experiment demonstrated the influence of various estrogenic and androgenic substances and desoxycorticosterone acetate§ on the mammary gland of young unoperated or castrated male mice weighing 16 to 25 g (Table I).

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The dibenzanthracene compound was supplied by Prof. J. W. Cook of the Royal Cancer Research Institute, London, the estradiol benzoate by the Schering Corporation through the courtesy of Dr. E. Schwenk, and the stilbestrol and triphenylethylene by Drs. G. A. Harrop and J. A. Morrel of the Squibb Institute of Medical Research and E. R. Squibb and Sons Biological Laboratories.

TABLE I.

| | Size of glands | Total dose per mouse mg | Volume of oil per injection cc | Avg wt of mouse in every group g | No. of mice |
|---|----------------|-------------------------|--------------------------------|----------------------------------|-------------|
| Androstenedione | ++++ or +++++ | 8 | .1 | 23 | 5 |
| Testosterone | ++ to +++++ | 8 | .1 | 17 | 10 |
| | +++ to +++++ | 4 | .025 | 19 | 5 |
| Dehydro-androsterone | ++ to +++++ | 4 | .05 | 22 | 10 |
| Cis-androsterone | + | 8 | .1 | 24 | 5 |
| Δ^5 -transandrostenediol | + to 0 | 4 | .1 | 26 | 10 |
| Desoxy-corticosterone acetate | +++++ | 4 | .1 | 22 | 5 |
| | + | 2 | .05 | 21 | 5 |
| 9:10 dihydroxy 9:10 di-n-propyl 9:10 dihydro-1:2:5:6 dibenzanthracene | +++++ | 1 | .05 | 22 | 16 |
| Idem, castrated mice | ++++ | -0.5 | .025 | 17.5 | 5 |
| Triphenylethylene | ++++ or +++++ | 40 | .05 | 15 | 7 |
| | ++++ | 10 | .06 | 19 | 10 |
| | ++++ | -5 | .03 | 23 | 10 |
| Estradiol benzoate | + | 0.666 | .05 | 19 | 5 |
| | + | 0.066 | .05 | 20 | 5 |
| | ++ | -0.016 | .05 | 25 | 5 |
| Stilbestrol | +++ | 2 | .05 | 21 | 5 |
| | ++++ | 0.2 | .05 | 20 | 5 |
| | ++++ | -0.05 | .05 | 23 | 5 |
| Oil of sesame | 0 | — | .05 | 18 | 4 |
| Not treated | 0 | — | — | 21 | 5 |

The synthetic crystalline chemicals were dissolved in sesame oil and administered subcutaneously in 8 equal injections, one injection every other day. The mice were killed on the 16th day and all the mammary glands were studied (method described elsewhere⁵) for quantitative or qualitative differences of response. Usually 5 mice were used in each series.

Mammary glands of the untreated or oil-injected control mice consisted of one main duct with one or several branches. The total duct system extended for a length of one to 3 mm. The glands showing the least response are designated +. These glands equalled or slightly exceeded in size those of the oil-injected controls but showed an increased number of small, broader branching ducts usually terminating peripherally in nodular enlargements. These glands responded definitely but to a limited extent. Glands designated ++ were considerably increased in size and the duct system was increasingly complex. Growing buds were usually found at the distal ends of the peripheral ducts. The stages designated +++ and ++++ were developed more extensively. The spread glands in the latter stage exceeded 12 sq mm in area and showed a dense system of branching ducts. The presence of many terminal buds demonstrated that the growth was still in progress.

Administration of androsterone⁷ resulted in the least mammary growth, 8 mg giving a response of +. Similar mammary responses were obtained in mice which received 4 mg. Δ^5 -transandrostenediol or large amounts of estradiol benzoate (0.666 mg to 0.066 mg) or stilbestrol (2 mg). Testosterone (4 and 8 mg), dehydroandrosterone (8 mg), large amounts of triphenylethylene (40 mg) and smaller amounts of estradiol benzoate (0.016 mg) or stilbestrol (0.2 to 0.05 mg) showed a ++ to +++ response. The greatest responses occurred in mice which had received androstenedione (8 mg), desoxy-corticosterone acetate (4.0 mg), 9:10 dihydroxy 9:10 di-n-propyl 9:10-dihydro-1:2:5:6 dibenzanthracene (1.0 or 0.5 mg) or triphenylethylene (10 or 5.0 mg).

The response of the glands of different mice in the same series was quite uniform. The individual mammary rudiments in some mice showed some variations in response, the larger ones being considered in the above experiments.

It is particularly interesting that the injections of 3 synthetic estrogenic chemicals differing rather strikingly from the naturally occurring estrogens; namely, triphenylethylene, stilbestrol and the dibenzanthracene compound are followed by mammary growth. The mammary growth in mice receiving desoxycorticosterone acetate

indicates again an overlap in physiological activity as well as the stimulating effect on the glands of animals receiving the various androgens.

The slighter mammary response in animals receiving the larger amounts of estradiol benzoate and also triphenylethylene and stilbestrol reaffirms the "stunting effect" on mammary tissues of large amounts of estrogens.⁶

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Effect of Sodium Dehydrocholate (Decholin) on Bile Salt, Chloride and Cholesterol of Bile in Dogs.

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Bile salts have been used for a number of years as cholericics. While it is generally accepted that the volume of bile after the administration of bile acids is increased,^{1, 2} few reports are available on the effect of these substances on the various constituents of the bile.^{7, 9} It is important to know whether or not following administration of certain bile salts, the patient excretes an increased amount of bile salt in the hepatic bile or whether the cholericic action is merely expressed by an increased water content. One of the most widely used cholericics is sodium dehydrocholate (Decholin). The following experiments were undertaken to determine what effect sodium dehydrocholate (Decholin) has on the 24-hour excretion of certain constituents of the bile.

Method. Two to 3 g sodium dehydrocholate (Decholin) were given daily for a period of 3 to 4 days to each of 5 dogs whose common duct had been doubly intubated by the method of Rous and McMaster,³ and whose cystic duct had been doubly ligated. Twenty-four-hour specimens of hepatic bile were collected before, during, and after the Decholin feeding. Bile was analyzed for chloride by the Wilson-Ball⁴ method, for cholate by the Gregory-Pascoe method

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