Desoxycorticosterone Acetate, Mammary Gland Growth, and Carcinogenesis in Mice*

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Whether the carcinogenic action of estrogen is an expression solely of its ability to establish and sustain a mammary gland or whether this hormone has in addition to mammary stimulation an independent carcinogenic property per se has been questioned (5). Desoxycorticosterone acetate has been reported to be as effective as estrogen in stimulating the development of mammary glands in young male mice of cancer-susceptible strains (6). If desoxycorticosterone acetate were to sustain mammary stimulation as effectively as estrogen and yet lack carcinogenic potency, it would support the thesis that estrogens are mammary-stimulating and in addition are in a direct sense carcinogenic. It has been reported that sustained treatment of mice with desoxycorticosterone acetate did not lead to mammary tumors (3, 4).

Because in the latter reports (3, 4) no evidence was presented concerning the extent of mammary stimulation, the experiments described here were undertaken to check whether sustained and adequately frequent treatment with desoxycorticosterone acetate would produce verifiable, sustained stimulation of the mammary gland and still not produce tumors.

Male C3H mice from the same stock (colony K. B. DeOme) which developed a high incidence of mammary tumors after treatment with the estrogen triphenylethylene (2) were injected subcutaneously 4 times weekly with 0.05 cc. or 0.1 cc. of 0.5 per cent desoxycorticosterone acetate in sesame oil. Thirty-three animals were injected. Four to six glands were removed from each animal and were prepared as total mounts for microscopic examination to determine the extent of mammary stimulation.

As a control, 10 mice were treated with the estrogen, triphenylethylene. Four times weekly a dose of 0.06 cc. of 2 per cent triphenylethylene (1.2 mgm.) in olive oil was administered. Thus a total of 4.8 mgm. per week in 4 equal doses was given in these experiments. This dosage and frequency of dosage compare favorably with that of 5 mgm. once a week, which in earlier experiments (2) induced tumors after sustained treatment. The minimum dosage and frequency of administration of both desoxycorticosterone acetate and triphenylethylene used in these experiments were those reported (6) to have produced equally marked mammary stimulation.

Table I summarizes the experiments. It may be seen that animals ranging in age from 4 to 34 weeks, intact and castrate, were treated for periods of time ranging from 2 to 23 weeks. In no case did the gland mounts show more than normal mammary development after treatment with desoxycorticosterone acetate. Figs. 1 and 2 are typical of the animals treated with desoxycorticosterone acetate regardless of the length or duration of the treatment. Marked stimulation and growth of the mammary gland resulted from treatment with triphenylethylene after only 8 doses (Figs. 3 and 4).

Treatment was not carried beyond 23 weeks (92 doses) because independent confirmation of negative results came to our attention (1). Mice of strains RIII and 46 were treated twice and thrice weekly respectively with a total of 2 mgm. and 1.5 mgm. per week of desoxycorticosterone in olive oil. A few mice were treated for more than 50 weeks with negative results.

It may be concluded that desoxycorticosterone

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1 We wish to express our thanks to Dr. Evelyn Anderson of the University of California Medical School for the crystalline desoxycorticosterone acetate.
TABLE 1: THE COMPARATIVE EFFECT ON THE MAMMARY GLANDS OF MALE C3H MICE TREATED 4 TIMES WEEKLY WITH DESOXYCORTICOSTEROE AND TRIPHENYLETHYLENE

<table>
<thead>
<tr>
<th>Initial age, weeks</th>
<th>Hormone</th>
<th>No. of animals</th>
<th>No. of doses</th>
<th>Total administered hormone in mgm.</th>
<th>Mammary gland development</th>
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<td>T†</td>
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<td>27</td>
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</table>

$ For the first 36 doses 0.05 cc of 0.2% desoxycorticosterone in sesame oil was given per dose; the remaining doses were 0.1 cc. All others receiving desoxycorticosterone were given 0.1 cc per dose.
† Mice receiving triphenylethylene (T) were given 0.06 cc of 0.2% triphenylethylene in olive oil.
* The significance of minus and plus used here is demonstrated in Figs. 1 to 4.
† D refers to desoxycorticosterone acetate.

Desoxycorticosterone acetate has slight, if any, stimulating action on the mammary glands of intact or castrate male mice. Its lack of carcinogenic action is therefore irrelevant.

REFERENCES


Fig. 1.—Mammary gland from a C3H mouse showing the small amount of stimulation produced by 36 injections of desoxycorticosterone acetate over a period of 9 weeks beginning when the animal was 4 weeks old. Mag. × 25.

Fig. 2.—Same as Fig 1 except that this animal had received 52 injections of desoxycorticosterone acetate over a period of 15 weeks. Mag. × 7.

Fig. 3.—A mammary gland from a C3H male mouse showing the extensive proliferation produced by 8 injections of triphenylethylene. The animal was 4 weeks of age at the beginning of the experiment. Mag. × 7.

Fig. 4.—Same as in Fig. 3 except that 27 injections of triphenylethylene were given. Mag. × 7.
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