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Effect of Testosterone Propionate on Development and Growth of Mammary Carcinoma in Female Mice.*

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Estrogen, when administered to male mice of certain strains, will result in the appearance of spontaneous mammary carcinoma.[1, 2, 3] The females of these strains ordinarily have a high incidence of spontaneous mammary carcinomas, which do not normally occur in the males. It has further been demonstrated that the incidence can be increased and the time of appearance of the mammary carcinoma hastened by the administration of estrogen to the females of these same strains.[4] Recently, Lacassagne[5] tested the effect of testosterone upon development of mammary carcinoma in females of a high incidence strain and noted no alteration from the controls. The dosages used, however, were small.

It is the purpose of this communication to report the results of long term injections of testosterone propionate* upon subsequent development and growth of spontaneous mammary tumors in female mice with an extremely high incidence (95%).[6]

Forty female mice of the C_3H strain, born at approximately the same time, were kept under similar experimental conditions. They were then bred at maturity and all except 2 animals had their litters within several weeks of each other. The remaining 2 animals had litters one month after the first of the entire group. The litters were killed within 24 hours after birth and the animals were then divided into 2 groups of 20. For every animal in one group, there was a sister litter mate in the other. At the age of 4½ months, injections

1 Lacassagne, A., *Am. J. Cancer*, 1936, **27**, 217.

2 Gardner, W. U., Smith, S. M., Strong, L. C., and Allen, E., *J. A. M. A.*, 1936, **107**, 656.

3 Burrows, H., *Brit. J. Surg.*, 1935, **23**, 191.

4 Suntzeff, V., Burns, E. L., Moskop, M., and Loeb, L., *Am. J. Cancer*, 1936, **27**, 229.

5 Lacassagne, A., *Compt. rend. Soc. de Biol.*, 1937, **126**, 385.

* We are indebted to Doctors Gregory Stragnell and Max Gilbert of the Schering Corporation for the generous supply of testosterone propionate (Oreton) which was used in this experiment.

6 Andervont, H. B., and McEleney, W. J., *Public Health Reports*, 1937, **52**, 772.

of testosterone propionate in sesame oil were given to one group of 20, dosage 0.5 mg in 0.05 cc of oil 3 times weekly for a period of 4 months. The second group served as controls, and were given 0.05 cc of sesame oil, without the hormone, 3 times a week.

Only the final results will be given as this experiment and others will be reported in detail at a later date. Of the 20 treated animals, six (30%) only developed spontaneous mammary carcinoma. All of these arose within 4 months after injections were commenced. These were single tumors and all animals died by the 11th month of life without the development of a second tumor. Four mice of the group died in the 12th month of life without any evidence of tumor at autopsy. Ten are still living and healthy without tumors at 16 months of age. The testosterone had no effect upon the growth rate of the six tumors which arose during the period of injections, when compared with the control tumors.

In the control group, all of the animals (100%) developed one or more tumors by the 11th month of life. The distribution of tumors was as follows: 8 mice had one tumor; 7 had 2 tumors; 4 had 3 tumors; and 1 had 5 tumors. All animals died from tumors by the 14th month of life.

The effect of large doses of testosterone propionate on the tumor *per se* was then tried on a series of 40 female mice in which tumors had already developed. These tumors ranged in size from 3 mm to 18 mm and were divided into 2 groups as nearly identical as possible. Group No. 1 was given 1.0 to 2.5 mg of testosterone propionate in 0.05 to 0.1 cc of sesame oil daily for 4 weeks. Group No. 2 (Control Group) was treated with 0.05 to 0.1 cc of sesame oil daily. Measurements were made in 3 diameters every third day until death. No difference in growth rate could be detected between the treated and untreated animals.

Testosterone *per se* has no effect on the growth of spontaneous mammary carcinoma in the female of the C_3H strain mice. Testosterone, when administered at an early age (4½ months or younger) to animals that have had one litter, will prevent the development of tumor provided there were none present when the treatment became effective. It is assumed that those tumors which developed were microscopic when treatment was commenced and were not influenced in their growth rate.[7, 8]

[7] Shaw, D. T., and Nathanson, I. T., unpublished data.

[8] Nathanson, I. T., and Shaw, D. T., unpublished data.