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Inactivation of Estrone in Normal Adult Male Rats.

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Previous observations have shown that estrogens and androgens are inactivated by the liver in castrate rats of the appropriate sex,^{1, 2} and that normal female rats inactivate testosterone propionate.³ Estrogens and androgens have been demonstrated to be present in both sexes.⁴ It has recently been found that of all tissues hitherto examined the greatest concentration of estradiol is in the testes of horses.⁵ These facts indicate that a system must be present to inactivate the estrogens occurring in males. The following experiment was designed to investigate this problem.

The technic employed in this experiment was similar to that previously described.³ The pellets of estrone (keto-hydroxy-estratriene*) were prepared in a mold and uniformly compressed. Normal adult male rats of the hooded type were employed. In one group the pellet was implanted in the subcutaneous tissues; in another group in the spleen. In a third group it was implanted in the spleen, and this organ was subsequently transplanted between the skin and subcutaneous tissues, and after an interval of 16 days its vessels were ligated. The right testis was removed in half the number of animals of each group at the time the pellet was implanted to provide an additional control. The animals were sacrificed 42 days after insertion of the pellets, and the organs were quickly dissected and immediately weighed on a damped balance. A group of 8 normal adult male rats served as controls.

The results are shown in Table I, which indicates the site of the pellet, the number of animals in each group, the average weight of the animals and the average weights of the right testis, left testis, bulbo-urethral muscles, seminal vesicles and prostate, respectively for each group. The average amount of estrone absorption in each group is also shown, determined by weighing the pellet at the beginning and at the termination of the experiment.

¹ Biskind, G. R., and Mark, J., *Bull. Johns Hopkins Hosp.*, 1939, **65**, 212.

² Biskind, G. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1940, **43**, 259.

³ Biskind, G. R., *PROC. SOC. EXP. BIOL. AND MED.*, 1941, **46**, 452.

⁴ Gustavson, R. G., In *Sex and Internal Secretions*, Chap. xiv, 1939.

⁵ Beall, D., *Biochem. J.*, 1940, **34**, 1293.

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TABLE I.

Location of pellet	No. of animals	Avg body wt, g	Right testis, mg	Left testis, mg	Bulbo-urethral muscles, mg	Prostate, mg	Seminal vesicles, mg	Avg daily absorption 42 days, mg
None	8	460	1721	1696	507	1024	506	—
Spleen	4	434	1485	1566	512	1205	439	.016
"	4	475	1687*	1921	539	1276	539	.016
Transplanted spleen	3	335	362	367	191	468	190	.012
"	3	313	1563*	370	169	358	163	.016
Subcutaneous tissues	4	285	273	283	139	276	139	.023
"	4	279	1600*	358	147	332	146	.012

*Right testis removed at time of implantation of pellet.

A pellet of estrone implanted in the subcutaneous tissues of a normal adult male rat produced marked atrophy of the testes. This effect was mediated by the inhibition of the hypophyses with suppression of the gonadotropic hormone.⁶ When the pellet was implanted in the spleen, permitting the absorbed material to be transported to the liver by way of the portal system, the specific effect was not evident. Transplantation of the spleen and ligation of its vessels diverted the absorbed hormone into the systemic circulation and produced results similar to those produced by the pellet in the subcutaneous tissues. This excluded the spleen as the site of inactivation.

Removal of one testis caused slight hypertrophy of the remaining testis. In the groups in which one testis had been removed at the time of implantation of the pellets and the remaining testis had undergone atrophy, the latter was of slightly greater average weight than in the groups in which both testes atrophied simultaneously. Thus, where there was but one testis there was no greater degree of atrophy; therefore confirming the observation of Hertz and Meyer.⁷

The prostates, bulbo-urethral muscles and seminal vesicles showed diminution in weight in the groups that suffered testicular atrophy. These changes were probably due both to loss of specific testicular stimulation, and to the direct effect of estrone.⁸ The histologic changes in all the organs will be described in a subsequent publication.

Summary and Conclusions. Pellets of estrone were implanted in the subcutaneous tissues, the spleen, and the transplanted ligated spleen, respectively, of groups of normal adult male rats. At the

⁶ Meyer, R. K., Leonard, S. L., Hisaw, F. L., and Martin, S. J., *Proc. Soc. Exp. Biol. and Med.*, 1930, **27**, 702.

⁷ Hertz, R., and Meyer, R. K., *Am. J. Physiol.*, 1938, **124**, 259.

⁸ Freud, J., *Biochem. J.*, 1933, **27**, 1438.

time of implantation of the pellet the right testis was removed in half the number of animals of each group. Marked atrophy occurred in the testes and related genital organs when the pellet was present in the subcutaneous tissues or in the transplanted ligated spleen. No changes occurred in these organs when the pellet was present in the normally situated spleen, indicating that when the absorbed estrone passes through the liver of normal adult male rats before reaching the organs it specifically affects, it is inactivated.

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Death of Embryos in Guinea Pigs on Diets Low in Vitamin E.

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The need of vitamin E for the successful completion of pregnancy in rats is well known.¹ More recently it has been shown to be essential in mice also.^{2, 3} We have found no reference in the literature describing resorption of the embryo due to vitamin E deficiency in guinea pigs. The failure to demonstrate this heretofore has been due undoubtedly to the fact that guinea pigs on vitamin E-low diets usually die of muscular dystrophy before the onset of sexual maturity.

It seems worthwhile, therefore, to place on record certain observations which indicate that the guinea pig, like the rat and mouse, requires an abundant supply of vitamin E, and that an inadequate intake results in death of the embryo *in utero*.

Experimental. The basal diet V consisted of:

Casein (commercial)	200
Sucrose	150
Cornstarch	360
Yeast	50

¹ Evans, H. M., and Burr, G. O., *Memoirs of the Univ. of Cal.*, 1927, No. 8.

² Bryan, W. L., and Mason, K. S., *Am. J. Physiol.*, 1940, **131**, 263.

³ Goettsch, M., and Pappenheimer, A. M., *Proc. Am. Inst. Nutrition*, 1941, Chicago.