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Experimental Intersexuality: Modification of Sexual Development of the White Rat with a Synthetic Estrogen.*

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The authors have previously reported on the modifications of embryonic sexual development obtained by injecting large doses of estrogens into pregnant rats.¹⁻³ The naturally occurring alpha estradiol and its diesterified derivative, estradiol dipropionate, were used in this work.

Diethyl stilboestrol (4,4' dihydroxy-alpha-beta-diethylstilbene), which is chemically somewhat dissimilar to the naturally occurring estrogens, has been shown to possess many of their functions such as vaginal cornification, growth of the uterus and mammary glands,⁴ inhibition of lactation,⁵ restoration of pituitary castration changes,⁶ prevention of implantation of fertilized ova⁷ and inhibition of the effects of progesterone on the uterus.⁷

It seemed of interest to determine if this synthetic substance would have the ability of the natural estrogens to modify embryonic sexual development. Accordingly 40 pregnant rats were given large doses of diethyl stilboestrol† subcutaneously in oil solution. Administration was started in all cases on the 12th or 13th days of pregnancy and continued until the 20th or 21st day, or until resorption of the pregnancies was evident. Twelve of these treated animals carried their pregnancies to term (22nd day of pregnancy). The total dosage these animals received varied from 12 to 42 mg. Eighteen male and 28 female offspring were obtained.

The findings in these newborn are essentially identical with those obtained with the natural estrogens. The external genitalia of both males and females are of the female type and nipples are present in

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1 Greene, R. R., Burrill, M. W., and Ivy, A. C., *Science*, 1938, **88**, 310.

2 Greene, R. R., and Burrill, M. W., *Am. J. Physiol.*, Proceedings, 1939, p. 94.

3 Greene, R. R., Burrill, M. W., and Ivy, A. C., *Anat. Rec.*, 1939, **73**, in press.

4 Dodds, E. C., Lawson, W., and Noble, R. L., *Lancet*, 1938, **234**, 1398.

5 Folley, S. F., and Watson, H. M. S., *Lancet*, 1938, **235**, 423.

6 Jacobsen, E., *Endokrinologie*, 1938, **21**, 20.

7 Parkes, A. S., Dodds, E. C., and Noble, R. L., *Brit. Med. J.*, 1938, **1**, 535.

† Furnished by Dr. J. A. Morrell of E. R. Squibb and Sons and by Dr. C. O. Miller of Lakeside Laboratories.

all. Normally nipples are never found in the males of our colony and do not appear in the female until the 2nd to 4th day post partum.

In the female offspring the uteri are large and distended, the ovarian capsule does not develop and the gonads are bare.

Examination of 6 animals by serial sections has revealed changes similar to those obtained with the natural estrogens. In the males, prostates are absent, seminal vesicles, epididymides and vasa deferentia are inhibited and portions of the uteri are present. The upper (Müllerian) vagina is well developed; the lower vagina (that part which is derived from the urogenital sinus) is partially developed. In the females there is some persistence of the Wolffian ducts (cranial and caudal remnants) and some inhibition of the lower vagina.

From these results it is apparent that compounds other than the natural estrogens are capable of modifying embryonic sexual development in the rat.

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Growth-Stimulating Action of Ferric Chloride-Treated Wheat Germ Oil.*

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Several investigators have reported the existence of a growth-promoting factor, necessary for rats, that was either vitamin E or a substance closely related to it.¹⁻⁴ The pure substance, α -tocopherol, stimulates growth in rats which have plateaued in weight on a vitamin E-low diet.⁵ The possibility that more than one factor might possess this growth-stimulating action was shown by Martin,⁶ who

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¹ Evans, H. M., *J. Nutr.*, 1928, **1**, 23.

² Blumberg, H., *J. Biol. Chem.*, 1935, **108**, 227.

³ Olecott, H. S., and Mattill, H. A., *J. Biol. Chem.*, 1936, **114**, lxxvii.

⁴ Olecott, H. S., and Mattill, H. A., *J. Nutr.*, 1937, **14**, 305.

⁵ Emerson, G. A., and Evans, H. M., *J. Nutr.*, 1937, **14**, 169.

⁶ Martin, G., *J. Nutr.*, 1937, **13**, 679.