

Summary. A condition simulating cretinism was produced in six young rabbits by injecting them intraperitoneally every second day with an antiserum (3 cc.) prepared by injecting hens with the proteins of the thyroid gland that are soluble in normal saline solution.

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Effect of Male Hormone Extracts, Theelin, and Theelol on the Chick Embryo.*

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This report presents the results of a preliminary investigation. Eggs from brown and from white leghorns were injected in the albumen before or on the third day of incubation with 0.1 cc. of an ethylene glycol solution of the substance to be studied. The animals surviving on the twentieth day of incubation were killed and the tissues fixed for histological study. Comparison was made with the tissues of animals injected with the solvent alone.

The results may be summarized as follows:

A. Ten standard bird units¹ of an extract from human male urine prepared by the procedure of Gallagher and Koch² were injected into each egg. This preparation was contaminated with 6.3 international rat units of the estrogenic substance always found in such extracts. The results on 56 animals were: Normal males 17; normal females 21; hermaphrodites 18. This diagnosis rests on the presence of a testis and either an ovary or an ovotestis. The Wolffian ducts varied greatly in size, ranging from normal (about 0.3 mm.) to 6 mm. in diameter. No relationship was apparent between the gonad and the size of the duct. The Müllerian ducts in the females likewise exhibited great variability both between individuals and between the 2 ducts of the same animal. Eight of the 17 males showed some abnormality of the Müllerian ducts.

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¹ Gallagher, T. F., and Koch, F. C., *Proc. Amer. Soc. Biol. Chem.*, 1933, VIII, lxxviii.

² Gallagher, T. F., and Koch, F. C., *Endocrinology*, 1934, **18**, 107.

B. Ten standard bird units of an extract of bulls' testicles prepared by the method of Gallagher and Koch³ were injected into each egg. The estrogenic contamination in this extract was 13.3 international rat units. Results based on 51 animals showed a normal sex ratio: Normal males 25; normal females 26, and no detectable changes in the gonads. Only a slight effect was manifest on the embryonic ducts. Twenty-five animals injected with 15 standard bird units of the same extract but freed from estrogenic activity likewise resulted in a normal sex ratio: Normal males 12; normal females 13, with no differences in the gonads or ducts.

C. 100 Y crystalline theelin administered to each egg. Results on 37 animals: Males 16‡ (2 appeared abnormal); females 21 (2 appeared abnormal).

D. 100 Y crystalline theelol injected into each egg. Results based on 31 animals: Males 14† (4 abnormal and 2 doubtful); normal females 17‡.

The histological changes produced by the extracts may be described as follows: The extract of bull testis produced no change. The urinary extract injections showed the cortical portion of the left gonad apparently normal ovarian tissue while the right gonad, and in many cases the medullary portion of the left, were distinctly testicular. Theelin and theelol caused a variable degree of replacement of testicular by ovarian tissue in the periphery of the left testis.

A comprehensive discussion of the results would be premature at this time. However, it is highly suggestive that the extract of bull testicles containing a higher concentration of the testicular hormone than the urinary extract gave no abnormal results. When we compare this to the relatively large number of sexually abnormal individuals obtained by treatment with urine extract, we are confronted with 2 possibilities. Either we have discovered a biological difference between the male hormone obtained from urine and that obtained from bull testicles comparable to the chemical difference discovered by Gallagher and Koch⁴ or we are dealing with a new biologically active substance found in urine and not in testicles.

Further work, now in progress, may clarify the complex situation with which we are dealing.

³ Gallagher, T. F., and Koch, F. C., *J. Biol. Chem.*, 1929, **84**, 495.

‡ Four animals were killed on the fourteenth day.

† Two males and one female were killed on the fourteenth day.

⁴ Gallagher, T. F., and Koch, F. C., *J. Biol. Chem.*, 1934, **104**, 611.