10888 P

Intersexuality in Adult Brown Leghorn Male as a Result of Estrogenic Treatment During Early Embryonic Life.*

L. V. DOMM.

From the Whitman Laboratory of Experimental Zoology, University of Chicago.

Since the publication of Lillie's[1] work on the free-martin many investigators have attempted to duplicate this condition in birds by transplanting gonads of either sex onto the chorio-allantoic membrane. While these early attempts were probably invariably negative it is now known that early application of the chemically prepared sex hormones will cause varying modifications in development of the embryonic reproductive system of birds as well as other forms.[2-8]

The present study records post-embryonic transformations in embryos that had been treated with estrogens prior to the period of sexual differentiation. Brown Leghorn eggs received single injections between the 3rd and 5th days of incubation and the treated embryos were allowed to hatch and mature. The estrogens used were progynon-B (1500 to 3000 R.U.) and theelin (0.5 to 1 mg). The quantity administered per injection was .05 or 0.5 cc. A total of 410 eggs were treated in this set of experiments of which 69 hatched. Of this number 51 (24♂ and 27♀) developed beyond the period of sexual differentiation and form the basis of this study.

The males of this experiment reveal an interesting sexual transformation. The sexes could invariably be distinguished at the period

* This investigation has been aided by a grant from the Rockefeller Foundation to the University of Chicago. Grateful acknowledgments are made to Dr. Erwin Schwenk, Schering Corporation, for progynon-B; to Dr. Oliver Kamm, Parke Davis & Co., and Prof. F. C. Koch, the University of Chicago, for theelin; to Mrs. Sally Johnson, A. M. Guhl and M. Posner for excellent assistance.

1 Lillie, Frank R., *J. Exp. Zool.*, 1917, **23**, 371.

2 Kozelka, A. W., and Gallagher, T. F., PROC. SOC. EXP. BIOL. AND MED., 1934, **31**, 1143.

3 Willier, B. H., Gallagher, T. F., and Koch, F. C., *Proc. Nat. Acad. Sci.*, 1935, **21**, 625; *Physiol. Zool.*, 1937, **10**, 101.

4 Wolff, E., and Ginglinger, A., *Arch. d'Anat., d'Hist., et d'Emb.*, 1935, **20**, 219.

5 Dantchakoff, V., *Bull. Biol.*, 1936, **70**, 241; 1937, **71**, 269; 1938, **72**, 187.

6 Domm, L. V., and Dennis, E. A., PROC. SOC. EXP. BIOL. AND MED., 1937, **36**, 766.

7 Greene, R. R., Burrill, M. W., and Ivy, A. C., *Sci.*, 1937, **86**, 200; 1938, **87**, 396; 1938, **88**, 130.

8 Moore, C. R., PROC. SOC. EXP. BIOL. AND MED., 1939, **40**, 544.

of sexual differentiation. Some males appeared quite normal at this time while in others feminizing effects were evident in the plumage, but in none of these cases did a complete henny plumage appear before the end of the first year though this has occurred in recent experiments. However, following the first molt many of them developed a henny plumage while others developed the plumage prevalent preceding the molt.† Head furnishings were invariably masculine though in some they became strikingly feminine during the molting period and remained so for a time, then again became masculine. Most of them are known to crow and tread though sexual libido does not appear to be as intense as in normals.

Post-mortem revealed striking modifications of the reproductive system. The left testis invariably showed a remarkable change in size and form, being smaller than the normal and instead of having the characteristic ellipsoid shape it is invariably flattened and ovary-like. The smooth even surface characteristic of the normal testis is replaced by an irregular uneven surface similar to that of the ovary. The right testis is rarely so strikingly modified, being larger, and its modifications are of the same character though less extreme.

Variously developed oviducts occur, though in some they are entirely absent. The left oviduct is generally better developed than the right and in certain cases appears entirely female. In a few instances only anterior parts of the oviduct persisted. The right, where present, is always better developed than that found in normal hens. In a few cases the right appears to be essentially a normal oviduct. Vasa deferentia are found though they are not always as prominently convoluted nor as large in diameter as those of cocks.

Fourteen cases have been studied histologically. In these the left gonad is an ovotestis with irregular surface cortex underlying which are testis tubules showing varying degrees of spermatogenesis. The cortical layer, composed of a stroma containing cortical cords, varies in depth, and occasionally one finds distended medullary tubules between it and the underlying testis tubules. In one case scattered follicles of varying size, with normally developed ova containing yolk granules and nucleus, have been found in the cortex. Modifications of the right gonad are similar but less extreme, and the gonad, though noticeably modified macroscopically, may not reveal a signifi-

† Seven individuals remain under observation and have now about completed the second yearly molt. Four of these have again developed the plumages present during the preceding year, 2 of which were female and 2 male. That of the remaining 3 was principally intermediate in character and fluctuated somewhat during the year. Two of these are developing intermediate plumage while in the other the new plumage is male.

cant cortical component. None of our cases have revealed follicles in the right gonad.

The degree of sex-reversal attained is probably proportional to the quantity of estrone introduced though considerable variation occurs with any given dosage. The basis for the changes observed is the intersexual composition of the zygotically male gonads brought about by administration of estrone. Differences in response of gonads is attributable to differences occurring in normal development of testis rudiments on opposite sides. The left testis passes through a stage from approximately 7 to 11 days during which a definite germinal epithelium containing germ cells is present over the entire free surface, whereas the right only occasionally shows scattered traces of this structure. It is this germinal epithelium of the testis, particularly the left, which becomes activated by the introduced estrones and develops into ovarian cortex. The differences in response between testes clearly indicates that they basically possess the same fundamental asymmetrical condition long known to be characteristic of right and left ovaries in birds.

The phenomenon of sex-inversion in the fowl has come to be associated entirely with a masculinization of the female while the opposite condition, a spontaneous development of female characters by genetically determined males has not been generally admitted. These experiments show that such transformations are possible and it is therefore altogether probable that some of the hermaphroditic fowl reported in the literature may actually have been feminized males, owing to development of ovarian cortex on testes, rather than masculinized females as interpreted.

10889

Electrocardiographic Changes in Ethylene Glycol Poisoning.

O. LEONARD HUDDLESTON.

From the Department of Physiology and Pharmacology, University of Colorado School of Medicine, Denver, Colorado.

During the course of some experiments on the pathology of ethylene glycol poisoning of pups some striking alterations in cardiac rhythm were noted. These observations prompted the formulation of a series of experiments designed to determine the cause of the cardiac arrhythmia. Repeated electrocardiograms were made on 4 littermate puppies 6 weeks of age and on 4 adult dogs. The ethylene glycol was administered orally as a 4% solution which the animals