

Hepatic Inactivation of Testicular Androgen in the White Leghorn Cockerel.*†

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Both the ovary and testis show a marked hypertrophy when grafted into the spleen of a castrate rat of the same sex.¹⁻³ This hypertrophy apparently occurs because the liver removes from the blood stream the sex hormone produced by the graft and in so doing frees the pituitary from the usual inhibition which the gonads exert upon its secretion of gonadotropin. Heller and Jungck⁴ found hypertrophy of the spleen-grafted ovary to be prevented by subcutaneous administration of estradiol-benzoate.

The fact that the chick is used in a successful method of androgen assay⁵ suggests this animal's use for hepatic inactivation studies.

Experimental. All chicks used in these experiments were single-comb white leghorn cockerels which were allowed to eat standard feed *ad libitum*. Castration, carried out under ether anesthesia, was performed by means of an incision made in the posterior left intercostal space. When a testis graft was made into the spleen, castration was done as described and jeweler's forceps were used to make the autotransplantation. Chicks for these transplants were selected at random and

operated on at the age of 5 and 7 days (series I) and others at the age of 20 or 21 days (series II). At the time of the first operation other chicks were designated as controls.

Each chick was weighed and the comb height and length measured on every fifth day. A comb factor reading was obtained by multiplying the height and length in millimeters and dividing by two ($\frac{H \times L}{2}$). This

factor has been found to give a reliable indication of the comb growth changes and thereby an estimation of the amount of sex hormone to which the comb has been exposed. To adjust for differences in body weight the total number of comb factor units (c.f.u.) of each was divided by the average body weight of that group, thus obtaining the average number of c.f.u. per gram body weight for each series.

Results and discussion. Histological study of the spleens showed that the grafts, although not greatly enlarged, had "taken." As mentioned earlier the liver destroys the estrogen or androgen produced by a gonad placed in the spleen of the rat.¹⁻⁴ Data presented in Table I indicates that hormone produced by the spleen-grafted testis of the chick is also partially inactivated by the liver. The comb at all times indicates the amount of hormone which is allowed to pass into the general circulation and shows whether or not the inactivation is complete. Our work suggests use of the chick comb to have a marked advantage over use of the rat for this type of androgen assay; not only can as many measurements be taken as desired, but a sensitive quantitative response is given even to very small amounts of hormone.

The relative amount and effectiveness of the androgen secreted by the controls, as shown

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¹ Biskind, M. S., and Biskind, G. R., *Proc. Soc. Exp. Biol. and Med.*, 1944, **55**, 176.

² Biskind, M. S., and Biskind, G. R., *Proc. Soc. Exp. Biol. and Med.*, 1945, **59**, 4.

³ Biskind, M. S., and Schelsnyak, M. C., *Endocrinology*, 1942, **30**, 819.

⁴ Heller, C. G., and Jungck, E. C., *Proc. Soc. Exp. Biol. and Med.*, 1947, **65**, 152.

⁵ Breneman, W. R., *Endocrinology*, 1941, **28**, 222.

TABLE I.
Effect of Intrasplenic Testis Transplants Upon Comb Growth.

	Age 36 days				Age 46 days		
	Control	S I	S II	S 89	Control	S I	S II
Avg body wt	369.0	354.0	345.2	275.9	513.2	503.4	486.0
Avg comb factor units	371.6	251.9	232.2	111.4	839.4	506.3	435.1
Avg comb factor units per g wt	0.995	0.697*	0.671*	0.396*	1.587	0.983*	0.908*
No. in group	16	15	14	12	16	15	14

* T value is significant at 1%. (Snedecor, George W., *Statistical Methods*, The Iowa State Press, Ames, Iowa, 4th ed., 1946.)

S I: chicks caponized at 5 or 7 days of age.

S II: chicks caponized at 20 or 21 days of age.

S 89: chicks caponized at 5 days of age.

by the number of comb factor units, and of that which passed through the liver of the spleen-graft chicks may be seen from Table I. Complete inactivation did not occur, as shown by comparison of series I and II with the chicks of series 89 (caponized controls), which were operated on at 5 days of age and otherwise given similar treatment. It is also seen that the number of c.f.u./g body weight in series I is larger than that in series II. This is explained by the fact that the transplants in series I had a longer time to grow and secrete than did those of series II grafted 2 weeks later. This explanation is supported by the fact that the difference in number of c.f.u./g body weight for series I and II at 46 days (7.6%) is greater than that at 36 days (3.7%). The comparison at 36 days shows that enough hormone had passed the liver to augment comb growth by at least 40.9%.

The fact that in other animals incomplete

inactivation of endogenous hormone has not been reported under these conditions suggests either that inactivation is different in the chick or that the chick permits the detection of this minute quantity of hormone. The comb shows a progressive cumulative change which makes possible the measurement of a slight failure of inactivation occurring over an extended period of time. Although at sacrifice some testicular material was found in the normal testis location in a few birds, the data indicate that its effect was insignificant.

Summary. These data show that: (1) the testis hormone is partially removed from the circulation by the liver of the chick, and that (2) the comb gives a sensitive indication of the extent of hepatic inactivation of androgens. This may justify speculation that some androgenic activity may be retained by the products of hepatic metabolism.

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Excretion of Adrenal Corticoids in the Sweat.

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In experiments on the urinary excretion of adrenal corticoids in strenuous exercise it was noted that, with the onset of hot weather, the excess steroid excretion in the urine was strikingly reduced. It occurred to us that this might be due to the excretion of steroids in

the sweat and the following study was carried out.

Two healthy adult subjects ran on a motor-driven treadmill at speeds of 8 to 12 miles per hour and a grade of 10% for periods of 30 to 45 minutes. The running was interrup-