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Precocious Development of Sexual Characters in the Fowl by Homeoplastic Hypophyseal Implants. II. The Female.*

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In a series of experiments daily subcutaneous homeoplastic hypophyseal implants were made on juvenile light brown Leghorn females.¹ These ranged in age from 28 to 59 days respectively when experiments began. In only one experiment was the entire hypophysis employed, while in all others only the anterior lobe was utilized. The number of implants received in any one experiment varied from 19 to 28. Weights were taken and measurements of head furnishings made at regular intervals as in experiments on cockerels. Treated females remained in excellent condition and were not adversely affected throughout any of the experiments. In none of the experiments was there a significant difference in weight between treated and control. In some the treated individuals were a trifle heavier than their respective controls, in others the reverse was true. This was not the case with treated males which were usually significantly heavier than their controls.

The first and most obvious effect to be noted was the phenomenal growth of head furnishings. These, pale and small when experiments began, became reddish and turgid after 5 to 6 days' treatment and revealed steady growth. Bird No. 178 was 22 days old when experiment started. It received 28 daily implants and was killed on the day following the last treatment. Its comb measured 1.3 cm. in length and 0.4 cm. in height when the experiment began, while on the day following the final implant it measured 4.0 cm. in length and 2.1 cm. in height, a creditable size for a pullet 4 months of age. The comb was quite stout, firm, and erect, resembling much more a male comb of similar size than the flabby, lumpy comb of similar dimensions on an older female. The comb of the control was of the same size as that of the treated individual when the experiment commenced but measured only 1.8 cm. in length and 0.6 cm. in height at the conclusion of the experiment, a rather significant difference. Normally the comb of the female reveals no appreciable

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¹ For similar experiments with males see Domm, *PROC. SOC. EXP. BIOL. AND MED.*, 1931, **29**, 308.

growth until it is several months older. No changes were noticed in either plumage, spurs, or behavior.

Necropsy revealed no signs of ovulation. The general appearance of treated ovaries was similar to that of controls though they were somewhat larger. The oviducts, however, showed a remarkable hypertrophy, having become large and convoluted, a phenomenon which normally precedes ovulation. Even the cloacal stumps of the rudimentary right oviduct were considerably larger in treated than controls. Right rudimentary gonads appeared somewhat larger, while rudimentary Wolffian ducts were notably larger in treated individuals. As in the male, thyroids were apparently not affected. Liver and spleen, as in the male, showed little if any apparent effect.

Histologically ovaries from treated individuals appeared unmodified. Follicles in such ovaries were evidently no more numerous than in controls and showed approximately the same degree of development. Sections of the oviduct in treated individuals, however, revealed a striking difference indicating a favorable action on the ovary. In experiment H 5, to which female No. 178 (see above) belonged, control oviducts had a diameter of less than 1 mm. and revealed low mucous folds without tubular glands or evident muscle layer, while experimental oviducts had a diameter of 4 mm. and revealed high mucous folds extending into lumen, many well-developed tubular glands and conspicuous peripheral muscle layer. It was difficult to detect any histological change in sections of rudimentary right gonads though experimental gonads appeared somewhat larger than controls. Sections of rudimentary Wolffian ducts examined revealed a distinctly larger lumen, a somewhat deeper columnar epithelium, and a much more conspicuous muscle layer in treated individuals. A preliminary study of thyroid sections revealed no modifications.

The experiments were conducted precisely as those on cockerels, utilizing hypophyses from similar sexual types. Some of them were conducted simultaneously on males and females of the same age. Results appeared to be similar whether we employed the entire hypophysis or merely the anterior lobe. The hypophysis of the capon appeared to be most effective, that of the hen least.

It is assumed that the gonad-stimulating hormone, liberated by the hypophyseal implants, acted directly on the gonad tissues of the host producing a precocious endocrine, rather than gametogenetic, functioning, which in turn is responsible for the precocious development of other sexual characters. It is further assumed that the male hormone liberated by the stimulated medullary tissue is respon-

sible for the growth of head furnishings and rudimentary Wolffian ducts while the female hormone liberated by the stimulated cortical tissue is responsible for development of the oviduct.

Preliminary experiments in collaboration with Dr. H. B. Van Dyke using a purified gonad-stimulating hormone prepared from sheep pituitary glands yield even more pronounced effects in some respects.

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Influence of (H⁺) Concentration on the Anesthetic Value of a Series of General and Local Anesthetics and Hypnotics.

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The purpose of this investigation was to determine whether any differences were to be observed in the relative anesthetic effects over widely different pH ranges, comparing a series of general anesthetics with a series of local anesthetics and a series of hypnotics. Alcohols such as allyl and isoamyl, and also general anesthetics such as chloroform, ether, chloretone, etc., do not form salts and consequently their distribution between oil and water is not markedly changed by a change in the (H⁺) concentration of the water phase.

Local anesthetics like neothessin, cocaine and butyn are lipo-soluble organic bases with relatively low solubility as free bases in water, but in the presence of acids they form water-soluble salts. Consequently the oil-water distribution coefficient shifts from a high oil-solubility and low water solubility on the basic side, to a low oil-solubility and high water solubility on the acid side.

In the case of the barbituric acid hypnotics exactly the reverse relation is found. The barbituric acids are lipo-soluble organic acids possessing very low water-solubility but on addition of alkali to the water phase water-soluble salts of the barbituric acids are formed. Consequently the distribution coefficient shifts from a high oil-low water solubility on the acid side, to a low oil-high water solubility on the basic side.

It follows from the above that if the induction of anesthesia is in any measure dependent upon the lipoid-water distribution coefficient of the anesthetic a shift from the acid or neutral to the basic side should exert little or no effect on the alcohols and general anesthetics, should increase the effect of bases like cocaine and decrease the effect of pseudo acids of the barbituric acid type.