optic nerve, and the right optic tract and colliculus showed the typical Von Gudden picture of degeneration. The right unoperated optic nerve, and left tract and superior colliculus, which were anatomically intact but had never functioned, could not be differentiated from a normal control of the same age reared in the light. The occipital regions at this stage showed no alterations, nor could the 2 cortices be told from those of the control. This shows strikingly the difference between the 2 technics, and points toward the invalidity of removal of an end organ as a physiological method of inquiry into the effects of lack of function on the neurones of the second and third order.

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The Question of Sex Hormone Antagonism.*

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The preparation of active hormone substances in the Department of Physiological Chemistry and Pharmacology and the development of testis hormone detection methods for the laboratory mammal in the Department of Zoology has enabled the Chicago group[1] during the last 4 years to study more directly, by injections, the effects of separate or combined sex hormone action in the rat.†

The results here given have been the basis for a new conception regarding the interaction of hypophysial and gonadal secretions in the organism, which effectively removes the troublesome notion of sex hormone antagonism as an interpretation.

Injections into the castrated male gave results upon the male ac-

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[1] For a review of our publications on this work see papers by Gallagher and Koch, *J. Biol. Chem.*, 1929, **84**, 495; Moore and collaborators, *Am. J. Anat.*, 1930, **45**, Gallagher and Koch, Moore and Gallagher, *J. Phar. and Exp. Therap.*, in press.

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cessories (prostate gland and seminal vesicles) as follows: I. Oestrin—no effect; II, testis hormone—normal accessories; III, testis hormone + oestrin—normal accessories. No antagonism is evident with mixtures of gonad hormones. Injections into normal males gave IV, oestrin—testicular damage, castrate accessories; V, oestrin + testis hormone—testicular damage, normal accessories; VI, brain, heart or liver lipoids—normal or damaged testes and normal accessories. VII, Cryptorchidism caused marked testis damage but normal accessories.

We have advanced the working hypothesis that gonadal hormones suppress the hypophysis, making available to the organism a reduced amount of gonadal stimulating secretion; that hypophysis hormone is necessary for gametogenesis or hormone production by the gonads; that sex hormones act directly upon homologous accessories, with or without the presence of hypophysis secretion, and have no effect upon heterologous accessories; and that sex hormones have no direct action upon the gonads.

Applying this interpretation to the above mentioned results, (I) oestrin is without effect upon male accessories. (II) Testis hormone stimulates male accessories. (III) Oestrin is neither chemically nor biologically antagonistic to testis hormone in castrated males. (IV) Oestrin suppresses the hypophysis making unavailable the secretion necessary for gonadal function hence gametogenetic damage and lack of hormone production; without testis hormone accessories are castrate. The addition of testis hormone as in (V) rectifies the hormone loss but not gametogenetic damage. Gametogenetic damage as in (VI) or (VII) does not involve interference with hormone production hence accessories are normal.

The hypothesis also accounts logically for other observations made in this laboratory as follows: VIII 30-day-old males injected with oestrin experience testicular depression and castrate accessories. Here oestrin suppresses the hypophysis; hypophysial sex stimulating secretions are reduced; testis growth and endocrine function are inhibited and without the latter, accessories are castrate. IX 30-day-old males injected with testis hormone experience testicular depression but have normal accessories. Hypophysis secretion is again affected and testis growth suppressed but the injected testis hormone acts directly upon the accessories, consequently they are normal or precociously stimulated. X Fresh hypophysial implants or hypophysis hormone precociously matures young males since secretions introduced by either means act through the testis.

XI Hypophysectomy leads to testis degeneration and castrate accessories but addition of testis hormone rebuilds the castrate accessories without repairing testis damage. XII Testis hormone introduction into normal females suppresses oestrus cycles and addition of hypophysis extract returns the cycle. Here, testis hormone is believed to suppress hypophysis secretion necessary for ovarian control and cycles cease; replacement of the secretion by hypophysis hormone injection brings on a new cycle due to renewed ovarian activity. XIII Oestrin injected into normal males produces testis damage and loss of hormone production (IV) but additions of fresh hypophysial implants or hypophysis hormone repairs the damage and leaves normal accessories. Hypophysial suppression by oestrin is therefore counteracted by introduction of its secretion and normal conditions follow. XIV Injurious effects of testis hormone injection into young males (IX) are overcome by hypophysial secretion administration. XV Testes of animals maintained upon vitamin B deficient diets have normal seminiferous tubules but accessories castrate in type. Here, hypophysial secretions are believed to be low in response to a low nutritive state and not as a specific response to vitamin B absence. Introduction of male hormone or of hypophysis secretion replaces castrate accessories by normal ones. XVI Maintenance upon inanition diets containing excessive vitamin B requirements gives normal testes and castrate accessories. Absence of vitamin B is not specific but a lowered hypophysis secretion is believed to be the cause.

The working hypothesis outlined above has been productive in suggestions for further work and our own results as well as those of many others, find in it a ready explanation. With advances in our knowledge, modifications or additions will undoubtedly have to be made. The conflicting results when interpreted upon an antagonism basis, are here found to be entirely consistent.