

(5) Such a hormonal preparation from urine, when given in doses sufficiently large to cause regeneration of the atrophic secondary sex glands of castrated rats, will neither prevent nor correct the hypertrophy of the pituitary gland and adrenals after castration.

(6) Aqueous testicular extracts, which could have contained no more than an insignificant amount of the prostate-regenerating hormone, prevent the cellular changes from appearing in the pituitary gland after castration of rats and also completely inhibit the hyperfunction of the pituitary gland.

(7) Destruction of the germinal epithelium of the testes will cause pituitary hyperfunction without causing atrophy of the secondary sex glands.

The apparent and only obvious conclusion is that the testicle secretes a hitherto unrecognized water soluble hormone, one function of which is a control of the pituitary gland.

To facilitate discussion, it is essential that the two testicular hormones be differentiated. Using the Greek root "andros" the name "androtin" has been suggested for the benzene soluble substance which is responsible for the development and maintenance of the secondary sex glands and other secondary sex characteristics. This name corresponds in derivation to the name "theelin" suggested by Doisy for the ovarian hormone. The water soluble testicular factor, which is characterized by its action on the pituitary gland, has been called "inhibin" from the Latin verb "inhibere."

The arguments in favor of the presence of two testicular hormones are almost but not absolutely conclusive. It has been demonstrated that "inhibin" in doses which do not influence the secondary sex glands will prevent the hyperfunction of the pituitary gland of castrated animals. Also, as mentioned above, "androtin" in doses sufficient to cause regeneration of the atrophic prostate of castrated rats will not prevent the hypertrophy and hyperplasia of the pituitary gland. It remains to be shown whether or not hyperfunction accompanies hyperplasia and hypertrophy. Fortunately this point can readily be established by available experimental procedures.

There is but the remotest possibility that the established facts can be explained on a basis of hormonal dosage.

The hypothesis of the duality of testicular endocrine function has been developed to explain well-controlled animal experiments. In addition to this experimental evidence there are certain general considerations which lead to the belief that there might be two hormones secreted by the male gonads. The testicle is the male analogue of the ovary. "Androtin" is com-

parable physiologically and chemically to theelin. Until now there has been no suggestion of a testicular hormone comparable to ovarian progestin. The idea that the testicle produces two hormones is compatible with the histology of the gland.

Prostatic hypertrophy as observed clinically in many adults beyond middle age has had no satisfactory explanation. It is now a well-recognized fact that the pituitary gland can stimulate the testes to the production of sufficient "androtin" to cause prostatic hypertrophy in rats. If the testicular cells producing "inhibin" were to fail, previous to the failure of those structures which produce "androtin," the hypertrophic phenomenon could easily be explained. The absence of "inhibin" would result in hyperfunction of the pituitary gland which, as pointed out above, is a known cause of prostatic hypertrophy in rats. The brilliant researches of Martins and Rocha² indicate that there is every possibility that "inhibin" is not produced when the germinal epithelium is destroyed. The destruction of the germinal epithelium does not change the secondary sex characteristics which are maintained by "androtin."

In closing I should like to point out that although nearly all of the experimental facts presented have been established or confirmed in this laboratory, this hypothesis could not have been established had it not been for years of careful investigation in many other laboratories. In particular I wish to thank Professor E. C. Dodds for much assistance received from personal communications concerning the researches on "androtin."

A more intensive study of "inhibin" and "androtin" is now in progress in this laboratory.

D. ROY McCULLAGH

CLEVELAND CLINIC FOUNDATION

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² *Endocrinology*, 1931, Vol. 15, p. 421.