DISCUSSION

THE HISTOLOGICAL CHANGES IN THE PITUITARY CAUSED BY ESTROGEN

LONG-CONTINUED estrogen injections into animals are known to result in enlargement of the pituitary, vascularity, loss of chromophil granules and increased numbers of chromophobe cells showing mitoses, hypertrophy of the Golgi apparatus and mitochondria. It has been stressed repeatedly by Severinghaus[1] that these changes are all cytological manifestations of excessive discharge by the pituitary of secretory products. However, estrogen inhibits pituitary secretion of FSH and growth hormone.

Severinghaus has regarded the cytological changes that are indicative of hyperfunction of the pituitary resulting from estrogen as an unsolved contradiction to the physiological evidence of hypofunction. He writes: "How may these apparent contradictions of cytology and physiology be reconciled? No complete and convincing answer is available, but certain suggestions may be relevant." His suggestions are based on the assumption that the cytological and the physiological evidence are concerned with the same pituitary factor, namely, the gonadotropic.

It seems to me the difficulty in this apparent paradox is that the cytologist is assuming that the hyperfunction, of which he sees microscopic evidence, is of the gonadotropic hormone. It seems that all can be reconciled if one thinks of the possibility that the cytological appearance of hypersecretion may be a matter of secretion of the pituitary factor stimulating the mammary gland, which is produced with such intensity that the pituitary is diverted from producing adequate amounts of gonadotropin and growth hormone, and is stimulated to compensate by excess production of precursor cells.

Those studying pituitary histology have largely overlooked the mammary gland hyperplasia and secretion of milk induced by estrogen. Meites and Turner[2] review their own experiments and others, proving that estrogen induces lactation in virgin animals and increases the lactogen content of the pituitary. Those who have studied induction of lactation by estrogen have usually not studied pituitary histology. In parabiotic rats, the writer[3,4] found excess endogenous estrogen caused enlargement and degranulation of the pituitary, secretion by the mammary gland, regression of corpora lutea and stunting of body growth. It seems reasonable to suppose that when the pituitary is stimulated by estrogen to lactogen production in excess, a demand is made upon all available precursor cells so that there is inability of the pituitary to form FSH, LH and growth hormone. Furthermore, this may explain the histological appearance of the pituitary in pregnancy. The so-called pregnancy cells are no longer regarded as a specific type of cell, but as degranulated chromophils. Because these cells show hypertrophy of Golgi apparatus and mitochondria and loss of cell granules, Severinghaus[1] interprets these changes as indicative of secretion by the pituitary, and again implies that he means secretion of gonadotropins, as he states that "Physiological experiments have led to a rather general conception that pregnancy inhibits the secretory activity of the anterior lobe. . . . Cytological findings point strongly in an exactly opposite direction." In the light of what has been said, is it not reasonable to regard the cytological changes in the pituitary in pregnancy as due to the high estrogen production by the placenta? Bachner[5] and Severinghaus[1] pointed out similarity between the effects of estrogen on pituitary cytology and the appearance of the pituitary in pregnancy. It seems reasonable to ascribe the histological changes to hypersecretion of the pituitary factor stimulating the mammary gland during the period when the breast is undergoing hyperplasia preliminary to lactation and to secretion of lactogen when the final period of pregnancy is reached.

ISOLDE T. ZECKWER
DEPARTMENT OF PATHOLOGY,
UNIVERSITY OF PENNSYLVANIA
MEDICAL SCHOOL

[1] A. E. Severinghaus, in "Sex and Internal Secretions" by E. Allen. Second edition, 1939. Williams and Wilkins Company, Baltimore.
[2] J. Meites and C. W. Turner, *Endocrinology*, 30: 711, 719, 726, 1942.
[3] I. T. Zeckwer, *Arch. Path.*, 30: 461, 1940.
[4] I. T. Zeckwer, *Federation Proceedings*, 1: 186, 1942.

G. J. ROMANES ON THE EXCITABILITY OF MUSCLE

ALL students of evolutionary theory are familiar with the fundamental contributions of George John Romanes in that field, but it is to be regretted that his physiological studies are not nearly so well known. Inasmuch as the elucidation of the electrical and chemical factors underlying muscular fatigue is a most important objective of research in neuromuscular physiology, Romanes' work along this line should be recalled.

In a letter[1] to Charles Darwin, dated August 13, 1877, Romanes says:

[5] F. Bachner, *Ztschr. f. Geburt. u. Gynäk.*, 106: 87, 1933.
[1] Ethel Romanes, "Life and Letters of George John Romanes," second edition, Longmans, Green, London, 1896, page 64.