

physectomized rats. The actual amounts of carbohydrate deposited were increased only in proportion to the change in absorption rate; the amount of carbohydrate apparently oxidized was increased approximately in proportion to the increase in oxygen consumption. The maintenance of carbohydrate levels in the fasted hypophysectomized rats was not improved in any case by the thyroxin treatment. It was concluded, therefore, that thyroxin substitution therapy in hypophysectomized rats can completely restore the rate of absorption of glucose from the intestine, as it does the basal metabolic rate; but that it does not otherwise improve the carbohydrate metabolism of these animals.

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Effects in Female Young Born of Pregnant Rats Injected with Androgens.

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Hormonal factors are known to influence parturition and the condition of the young. Interference with parturition in the rat has been reported with pituitary and placental extracts and pregnancy urine,¹ pituitary implants,² luteal extracts,³ hypophysectomy,⁴ estrogens,⁵ and androgens.⁶ The present report deals with some of the permanent effects on female rats whose mothers received androgenic substances during pregnancy.

Study has been made of 10 female young which have grown to

¹ a. Teel, H. M., *Am. J. Physiol.*, 1926, **79**, 170; b. Evans, H. M., and Simpson, M. E., *PROC. SOC. EXP. BIOL. AND MED.*, 1929, **26**, 595; c. Levin, L., Katzman, P. A., and Doisy, E. A., *Endocrinology*, 1931, **15**, 207; d. Hoopes, E. C., *PROC. SOC. EXP. BIOL. AND MED.*, 1934, **31**, 1115; e. Hain, A. M., *Quart. J. Exp. Physiol.*, 1932, **22**, 249.

² Engle, E. T., and Mermod, C., *Anat. Rec.*, 1928, **38**, 11.

³ Nelson, W. O., Piffner, J. J., and Haterius, H. O., *Am. J. Physiol.*, 1930, **91**, 690.

⁴ Pencharz, R. I., and Long, J. A., *Am. J. Anat.*, 1933, **53**, 117.

⁵ a. Parkes, A. S., *J. Physiol.*, 1930, **69**, 463; b. Hain, A. M., *Quart. J. Exp. Physiol.*, 1935, **25**, 131.

⁶ a. Dantchadoff, V., *Compt. rend. Soc. de biol.*, 1937, **124**, 516; b. Greene, R. R., and Ivy, A. C., *Science*, 1937, **86**, 200; c. Hamilton, J. B., and Wolfe, J. M., *Anat. Rec.*, in press; d. Scipiades, E., *PROC. SOC. EXP. BIOL. AND MED.*, 1937, **37**, 242.

maturity and have either been sacrificed or have died from abnormalities resulting from effects of androgen injections in their mothers. Female young, born after adequate androgenic treatment of the pregnant mother (500 gamma of testosterone propionate* in 0.1 cc. of peanut oil injected subcutaneously daily during the last third of pregnancy), superficially resemble males in that the clitoris is large and penis-like, the perineum extensive and scrotum-like, and the pin-point vaginal opening absent.

Outstanding phenomena observed in these animals at maturity were as follows:

(1) Upon gross inspection no vaginal aperture was seen (Fig. 1) and the peripheral portion of the vagina was absent beyond a small tubercle about 1 cm. from the perineum. The fluid-containing cavity within the uterus and cervical portion of the vagina was abruptly terminated at the tubercle.

(2) The nipples were either absent or were markedly underde-



FIG. 1.

Expansion of the cervix and the cervical portion of the vagina by fluid. With successive estrous cycles the swelling may reach dimensions of 35x30x32 mm., and apparently cause death of the animal. Note opposite the pointer the absence of a vaginal introitus.

* Furnished by the Ciba Company.

veloped. Absence and underdevelopment were seen in the same animal. Mammary glands were nearly normal in appearance.

(3) The internal reproductive system with the above exceptions was intact and some degree of ovarian function was evidenced by uterine, vaginal, and mammary histology, by the presence of follicles and corpora lutea, and by fluid in the uterus and vagina.

(4) The uterus and existent portion of the vagina were greatly bloated with retained fluid in 6 of the animals (Fig. 1). The dimensions of the expanded uterine cervix and vagina were as great as 35x30x32 mm. Apparently this large distension by fluid, which followed the assumption of functional activity of the reproductive system, proved fatal in the majority of these animals, seemingly partly by compression of the colon. The urinary system was also affected, the bladder and urethra being held taut by the subjacent expansion of the reproductive system.

The preliminary study of permanent abnormalities in rats resulting from injections of hormones to the mother during pregnancy, suggest the following inferences:

(a) Pseudohermaphroditism may be produced by androgen injection, the females presenting a masculine appearance with a penis-like clitoris, scrotum-like perineum and an absence of proper development of the nipples and the outer portion of the vagina.

(b) The absence of nipples in the normal male rat may be correlated with the presence of male hormone.

(c) Possible harmful effects on the foetus must be guarded against in clinical use of hormonal substances in large amounts or at critical times during pregnancy.

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Myenteric Activity Modifications Induced by Caffeine.

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Enteric motility is dependent largely upon mechanical distension and upon the *chemical* nature of the contents. To study the effect of the purine complex, caffeine, upon the intrinsic myogenic responses¹ of the mammalian small intestine, excised segments of the

¹ Gasser, H. S., *J. Pharm. and Exp. Therap.*, 1926, **27**, 395.