

experiments reduced the coronary output by from 27% to 86% (average 45%) in the presence of normal sinus rhythm. Four injections in one preparation were without result. The effect was maximal within 30 to 75 seconds after the beginning of the injection and lasted for one to 6 minutes. It showed no tendency to diminish with successive injections, though not more than 4 were administered to any one preparation. Four injections in 3 preparations, in which ventricular fibrillation was maintained by faradic stimulation of the ventricle, brought about a decrease in coronary flow by from 16% to 48% (average 28%). A late rise in coronary flow (averaging 16% for all injections) was frequently recorded. This late increase in flow was measurably reduced with successive injections.

Amplitude of beat. The amplitude of ventricular contraction was increased following every injection by from 18% to 300% (average 92%). This commenced later than the slowing of coronary flow, reached its maximum in 1 to 3 minutes, and persisted for 3 to 15 minutes. The effect of angiotonin upon amplitude of beat showed no consistent tendency to diminish with successive injections.

Heart Rate. Significant effects upon the heart rate were not recorded. In some experiments the rate of beat diminished slightly during the period of reduced coronary flow.

Summary. Upon the isolated hearts of cats perfused with Ringer-Locke solution renin produced no significant effect. Angiotonin on the other hand brought about decrease in coronary flow and increase in amplitude of beat, but no consistent effect upon heart rate.

11405 P

Pituitary Function in Parabiotic Triplet Rats.

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Rat ovaries that have been made to function under the stimulus of the male pituitary as in the experiments of Goodman¹ (ovarian grafts), Witschi and Levine² (parabiosis) and Pfeiffer³ (mascu-

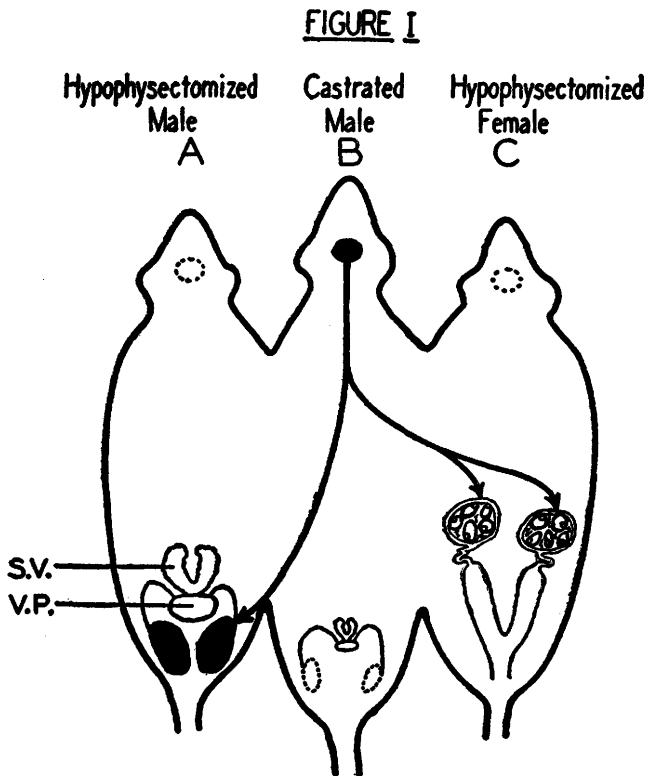
¹ Goodman, L., *Anat. Rec.*, 1934, **59**, 223.

² Witschi, E., and Levine, W. T., *Proc. Soc. Exp. Biol. and Med.*, 1934, **32**, 101.

³ Pfeiffer, C. A., *Am. J. Anat.*, 1936, **58**, 195.

linized female pituitaries) have uniformly failed to become luteinized. The luteinizing hormone, however, has been shown to be present in small amounts in the pituitaries of normal male rats and abundant in those of castrated animals (Hellbaum and Greep⁴). Cutuly, *et al.*,⁵ have shown that the pituitary of a castrated male stimulates the interstitial cells as well as the seminiferous tubules of a parabiotic hypophysectomized male partner. Furthermore, there is considerable experimental evidence for assuming that the luteinizing hormone is identical with the substance responsible for the internal secretory function of the male gonad. The available evidence then is contradictory in that the male pituitary appears to secrete luteinizing hormone if the end organ is a male gonad, and *only* follicle-stimulating hormone if the end organ is a female gonad.

The present experiments were devised to bring the entire repro-



⁴ Hellbaum, A. A., and Greep, R. O., *Am. J. Anat.*, 1940, in press.

⁵ Cutuly, E., McCullagh, D. R., and Cutuly, E. C., *Endocrinology*, 1937, **21**, 241.

ductive systems of each sex under the simultaneous influence of a single male pituitary.

Male rats, aged 21 days, were gonadectomized and joined in parabiosis with 2 littermates—a male on one side and a female on the other. (See also Fig. 1 drawn like that of DuShane and others.⁶) Four to 6 days later the 2 outside triplets were hypophysectomized. Autopsies were performed 7 to 16 days after hypophysectomy. The gonads, sexual accessories, thyroids and adrenal glands were weighed and examined grossly. Vaginal smears were followed in some instances. The observations reported are based on 8 sets of triplet parabionts in which all except the central animal had been completely hypophysectomized.

On the 7th day following the joining of these animals the vaginas of the hypophysectomized females opened and rapid testicular growth in the hypophysectomized male became apparent. The autopsy findings, illustrated by the data from a typical experiment (Table I), show that the principal physiological action of the castrated male pituitary on the ovary of a hypophysectomized female triplet parabiont is to promote the growth of follicles and cause the continuous secretion of estrogen as attested by persistent vaginal cornification and a distended uterus. The ovaries have not yet been examined microscopically for the presence of interstitial-cell or luteal stimulation but there was no evidence of luteinization by gross inspection. The hypophysectomized male parabiont, which had derived its gonadotropic stimulus from the same pituitary gland that produced only follicle growth in the female, showed a marked stimulation of the testes, and the secondary sexual structures, such as the prostate and seminal vesicles, were greatly enlarged.

The secondary sexual structures of the central castrate remained entirely atrophic in all cases.

The peculiar ability of the castrated male rat pituitary to evoke

TABLE I.
Organ Weights of 3 Animals Which Had Been Joined Together for 19 days. Rats "A" and "C" Had Been Hypophysectomized for 13 Days and the Central Animal "B" Had Been Castrated Since the Start of the Experiment.

Rat	Body wt at death, gm	Testes, mg	Seminal vesicles, mg	Ventral prostate, mg	Ovaries, mg	Empty uterus, mg	Adrenals, mg	Thyroid, mg
A	52	1036	54	106			6.6	4.45
B	67		8	7			20.5	7.60
C	52				44.4	286	9.6	6.34

⁶ DuShane, G. P., Levine, W. T., Pfeiffer, C. A., and Witschi, E., *Proc. Soc. Exp. Biol. and Med.*, 1935, **33**, 339.

a follicular response in a female and at the same time stimulate the testes of a male to secretory function is difficult to interpret considering the results which have been obtained with purified follicle-stimulating extracts of the pituitary.^{7, 8, 9} Several explanations suggest themselves but all are purely conjectural: (a) the threshold for luteinization of the ovary may be far above that necessary to produce stimulation of testicular interstitial cells; (b) possibly the interstitial cell stimulating and luteinizing hormones are not identical; (c) it may be extremely difficult to cause luteinization of follicles which grow rapidly and become cystic.

11406 P

Efficacy of Pellets of Posterior Hypophysis and of Pitressin in Oil in Diabetes Insipidus.

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The efficacy of the subcutaneous administration of dried posterior pituitary gland in diabetes insipidus has not been reported previously. Pellets of this material have been prepared and implanted subcutaneously into 4 cats with experimentally produced diabetes insipidus* and into 2 patients with diabetes insipidus. The results are shown in Table I. It is to be noted that mixing the material with tyrosine or impregnating the pellet with beeswax did not prolong the effect in the cats. An inflammatory reaction which occurred at the site of implantation of sterile pellets in the patients later required drainage. An attempt was made to prolong the action in man by impregnation of the pellets with lanolin or beeswax. The reaction which developed at the site of implantation was so severe that the pellets had to be removed before complete absorption occurred.

⁷ Greep, R. O., and Fevold, H. L., *Endocrinology*, 1937, **21**, 611.

⁸ Greep, R. O., *PROC. SOC. EXP. BIOL. AND MED.*, 1939, **42**, 454.

⁹ Chow, B. F., Greep, R. O., and van Dyke, H. B., *J. Endocrinology*, 1940, **1**, 439.

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