

9614

Gonadokinetic Effects in Parabiotic Rats.

EUGENE CUTULY AND ELIZABETH C. CUTULY. (Introduced by
D. Roy McCullagh.)

From the Department of Biochemical Research, Cleveland Clinic, Cleveland, Ohio.

It has been shown¹ that in parabiotic rats the testes of a hypophysectomized partner could be completely maintained in or restored to a normal condition by gonad-stimulating hormone emanating from the pituitary of a castrated twin. It was also reported that the pituitaries of cryptorchid and of normal partners were in this respect much less potent than those of castrates. The data which will be presented in this report for the most part confirm and extend the previous work.

As regards the response of the testes of a hypophysectomized parabiotic twin it has been our experience that the following factors are of greatest importance in the final analysis: (1) The type of partner; whether castrated (regardless of sex), cryptorchid, or normal. (2) The time necessary for adequate vascular anastomosis between the partners. (3) The time necessary for a physiological process to become manifest or to run to completion.

Experience has shown that the scrotum in the rat reacts to testicular hormone much as do the accessory sexual organs.^{2, 3} From the results of our former and present studies in parabiotic rats we have found it possible to conclude that the scrotum in a hypophysectomized parabiotic rat is qualitatively more sensitive to testicular hormone than are the prostate and seminal vesicles. This has proved to be an important criterion in our work on parabiotic rats, as a pair does not have to be sacrificed in order to discover from the condition of the accessory sexual glands and the interstitial cells of the testes whether or not testicular hormone is being produced. Further, our previous observations, confirmed by later results, have shown that within certain limits the size of the testes in a hypophysectomized parabiotic rat is an index to the degree of their gametogenic activity. This is especially true when the testes are large, since the interstitial tissue at best forms but a small fraction of the whole testis. For these reasons, the hypophysectomized

¹ Cutuly, E., McCullagh, D. R., and Cutuly, E. C., *Endocrinology*, 1937, **21**, 241.

² Cutuly, E., McCullagh, D. R., and Cutuly, E. C., *Am. J. Physiol.*, 1937, **119**, 121.

³ Hamilton, J. B., *Proc. Soc. Exp. Biol. and Med.*, 1936, **35**, 386.

parabiotic rat can, without being sacrificed, serve as a test object for the so-called gametokinetic and luteinizing or interstitial cell-stimulating hormones.

Our observations are based on 10 pairs of animals of which 9, at the time this article was written were still alive and healthy after 2-13 months of parabiotic life. In most instances the pairs consisted of littermates joined at 50-70 days of age. Most of these pairs went through a preliminary stage during which one partner was a normal rat and the other was hypophysectomized. Finally, however, 8 of the normal partners were castrated, one was made cryptorchid, and one was permitted to remain normal. In 2 cases the castrate was a female.

Normal + Hypophysectomized. In no instance did the normal twin provide enough hypophyseal hormone to prevent eventual atrophy of the testes in the hypophysectomized partner. Sometimes such atrophy was retarded, taking 1-2 weeks longer to occur than that in a non-parabiotic hypophysectomized control where testicular atrophy is markedly evident grossly 15 days after pituitary ablation. During this time, and subsequently, the genital organs of the normal twin remained apparently normal. These findings are similar to those we obtained previously.

Cryptorchid + Hypophysectomized. That a cryptorchid's hypophysis may in some way provide more gonadokinetic hormone than the pituitary of a normal animal was demonstrated in the one pair of this type. At first this pair consisted of a normal male with a hypophysectomized male. Under these conditions the testes of the hypophysectomized test partner underwent rapid atrophy. The normal twin was then made cryptorchid. No evidence of gonadal stimulation was observed in the hypophysectomized partner at first, but 40 days after the normal animal had been rendered cryptorchid, the scrotum of the hypophysectomized twin began to become flushed and edematous, indicating the presence of male hormone. Development of the scrotum and testes continued, but at a very slow rate. Seven weeks after the initial stimulation was noticed, the testes and scrotum of the hypophysectomized twin appeared to be only about $\frac{1}{3}$ normal. Throughout this time, the scrotum of the cryptorchid partner remained turgid and flushed, showing that the abdominal testes were still producing male hormone.

This experiment left no doubt that an animal with abdominally located testes was able to supply a hypophysectomized partner with more gonad-stimulating hormone than the same animal with normal testes. This result lends support to the idea that the pituitary of a

cryptorchid animal lies somewhere between those of the normal and the castrate in gonad-stimulating potency,^{4, 5, 6} and also indicates the necessity for long-continued observations in parabiotic experiments of this type. In some short-time experiments¹ it was found that cryptorchid and normal partners had about equal effects on the testes of hypophysectomized test animals.

Castrated + Hypophysectomized. In our experience the testes of hypophysectomized rats joined with castrated male or spayed female rats have invariably been maintained normal or, if atrophic at the start, have been returned to a normal condition within a period of 5 weeks. We have been able to confirm our previous findings that the gonadotropic hormone complex passing from a castrated partner will cause in the testes of a hypophysectomized twin parallel stimulation of the interstitial cells and spermatogenic elements. In addition, it has been found that hypophysectomized rats with testes maintained by pituitary gonadotropic secretion from a castrated male or female twin are capable of siring normal litters for at least 6 months following their hypophysectomy. The external genitalia of 2 such hypophysectomized rats are shown in Figs. 1 and 2.

The anterior hypophyses of castrated rats whose hypophysectomized partners receive complete gonadal activation are entirely similar to those of non-parabiotic castrated animals. They show characteristic castration cells, a marked increase in granulated basophils, a decrease in chromophobes and an apparent diminution in the number of eosinophils (Fig. 3).

The gonad stimulation occurring in hypophysectomized rats paired with castrated partners is so clear cut and invariable that it has been possible to employ this reaction as an indicator of hypophyseal gonadokinetic activity in the castrate. Studies in which the inhibiting effect of male and female hormones on the gonad-stimulating potency of the hypophysis has been so demonstrated will be reported elsewhere.

Conclusions. Autopsy data correlated with observations on living animals have established the following points: (1) The testes of hypophysectomized parabiotic rats may be stimulated by hypophyseal secretion from normal, cryptorchid, or castrated partners. (2) Gonadal stimulation in hypophysectomized test animals is greatest when they are joined with castrated partners and least when

⁴ Evans, H. M., and Simpson, M. E., *Am. J. Physiol.*, 1929, **89**, 371.

⁵ Martins, T., *Compt. rend. Soc. de biol.*, 1930, **105**, 789.

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

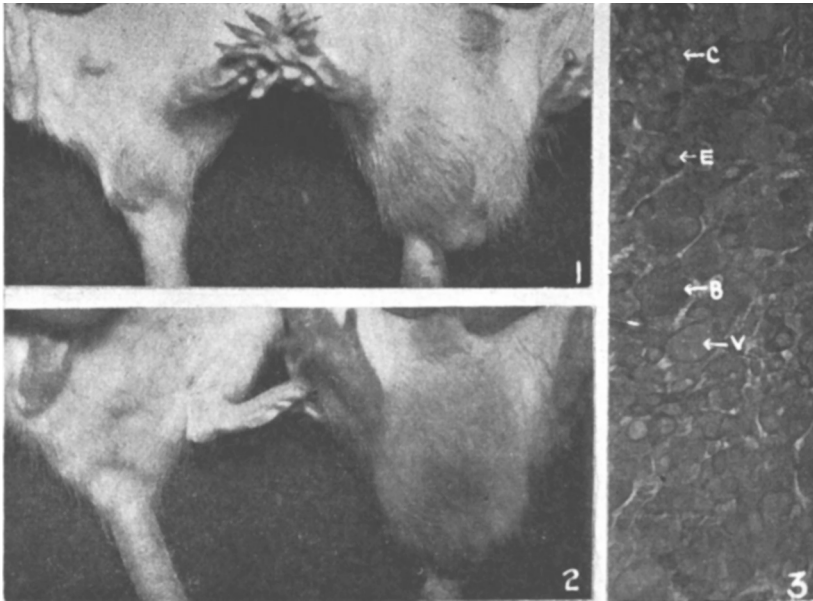


FIG. 1.

Turgescent scrotum containing large testes maintained for a year in a hypophysectomized male rat (right) joined with a castrated male.

FIG. 2.

Same as Fig. 1, except that castrated partner (left) is a female.

FIG. 3.

Portion of anterior pituitary of a male parabiont castrated for 100 days during which time the entire genital tract of a hypophysectomized male twin which had undergone atrophy was completely repaired. Vacuolated basophilic castration cell (V), Granulated basophil (B), Eosinophil (E), Chromophobe (C). Zenker-formol fixation, Mallory trichrome. ($\times 300$.)

they are joined with normal partners. (3) Growth of the scrotum in hypophysectomized parabionts indicates interstitial cell activity, and increase in testicular size reflects predominantly spermatogenic activity. (4) Both these types of activity progress simultaneously under the influence of hypophyseal hormone from a partner, or regress simultaneously in the absence of adequate hormonal stimulation. (5) These results do not support the idea that the castrate hypophysis produces only, or chiefly, gametokinetic hormone, but are in agreement with our previous findings which indicated that the hypophyseal gonadokinetic hormone complex in castrate, cryptorchid and normal parabiotic rats differed only in degree but not in type.