

of this series likewise were fixed prior to the time of metamorphosis, no information upon the functional differentiation of the anterior lobe is available.

Although the number of "albinos" in each series is very low, the evidence is so unmistakable that one may safely conclude that the developmental relationship between the epithelial hypophysis and infundibulum in urodeles is essentially as Burch has shown for *Hyla*, namely, that the functional differentiation of the former is dependent upon contact with the latter.

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Studies on the Cause of Increased Growth During Pregnancy.

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Slonaker,¹ Hain,² and Stein³ have shown that pregnancy favorably affected the growth curve in rats over littermate virgin controls. Cole⁴ observed that even in pregnant rats precociously matured with mare gonadotropic hormone there was an increased growth rate and this was confirmed by Cole and Hart.⁵ The increased rate of growth was accompanied by increased food consumption starting as early as 48 hours after copulation. Lactation neither enhanced nor reduced this favorable effect. The data in this paper relate to the factors involved in this phenomenon.

Pseudopregnancy. Goss⁶ and Slonaker⁷ showed that a single pseudopregnancy increased growth in the rat though the effect of repeated pseudopregnancies was not determined. In our previous paper⁵ one animal was cited having only 2 pregnancies followed by 13 periods of pseudopregnancy over a 9-month period. This animal continued to gain over her littermate control throughout this period and at autopsy this increase amounted to 119 g. We were, therefore, interested to ascertain if repeated pseudopregnancies would have as marked an effect as normal pregnancies had shown. This is im-

¹ Slonaker, J. R., *Am. J. Physiol.*, 1927, **82**, 318.

² Hain, A. M., *Quart. J. Exp. Physiol.*, 1932, **22**, 71.

³ Stein, S., *Endocrinology*, 1934, **18**, 721.

⁴ Cole, H. H., *Am. J. Physiol.*, 1937, **119**, 704.

⁵ Cole, H. H., and Hart, G. H., *Am. J. Physiol.*, 1938, **123**, 589.

⁶ Goss, H., *Anat. Rec.*, 1926, **32**, 232.

⁷ Slonaker, J. R., *Am. J. Physiol.*, 1929, **89**, 406.

portant if true because it rules out the fetus and fetal placenta as a factor in its causation.

In Fig. 1 are shown relative average growth rates of 5 rats carried through an average of 20 pseudopregnancies as compared to littermate virgin controls. Also included are the average growth curves of 5 rats carried through 9 normal pregnancies.

This figure shows that the increased growth response from repeated pseudopregnancies is nearly as great as that obtained from a series of true pregnancies. The average nose-anus length of the pseudopregnant rats was 23.0 as compared to 22.2 cm for the controls.

Inasmuch as only 5 pseudopregnant animals were used it seemed desirable to run another larger group. Ten others were carried through 6 pseudopregnancies and compared to littermate virgin controls. These rats were carefully selected for size in order that there would be a minimum of variation between and within the groups. At 140 days this group averaged 307 g in weight and 22.0 cm in

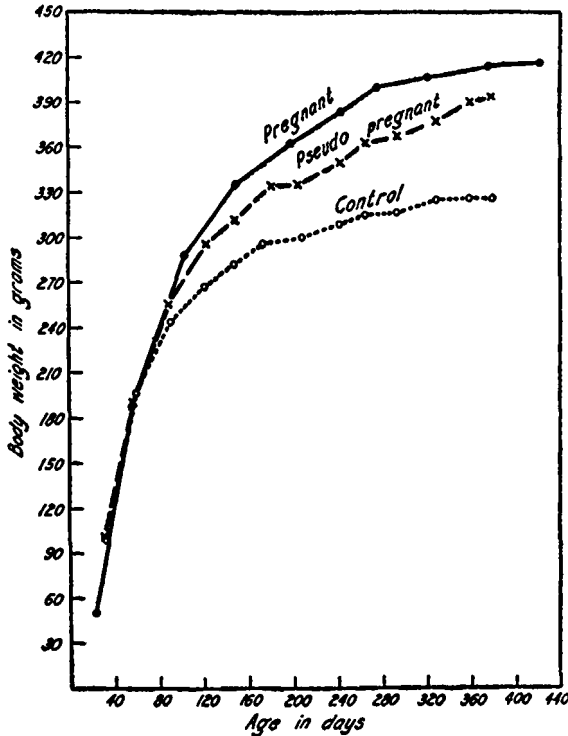


FIG. 1.

The growth rate of 5 rats carried through an average of 20 pseudopregnancies as compared to that of 5 littermate virgin controls and to that of 5 rats carried through 9 normal pregnancies.

nose-anus length as compared to 257 g and 20.8 cm for their controls—a difference of 50 g and 1.2 cm. As may be seen from Fig. 1 the original pseudopregnant group weighed 305 g and their controls 275 g at this age—a difference of 30 g. As the increase of the second pseudopregnant group over their controls exceeded that of the first at this age we felt it was unnecessary to carry them further.

The fact that repeated pseudopregnancies have nearly as marked an effect on growth as true pregnancies makes it appear that the fetuses and their attending membranes are not responsible for stimulating the increased growth during pregnancy. We, therefore, looked for other causes.

Effect of the gonads. Two approaches were made in the study of the question. First we compared the rate of growth of 9 rats, castrated 24 hours after mating with normal males, to the rate of growth of 9 littermate controls castrated on the same day without previous mating. This experiment was staged to ascertain if increased food intake of the bred animals would occur as rapidly in the absence of the ovaries.

The very definite anticipated increase in appetite within 48 hours after mating did not occur. This delay might possibly be laid to the operation. The surgery did reduce appetite during the first 24 hours but by the second day it had returned to the preoperation level. As an increased appetite occurred in both groups on the 6th day it is unlikely that mating had any effect in the absence of the ovary. This inference that the ovary might be involved in stimulating appetite caused us to study the effect of progesterone on this phenomenon. Gaunt and Hays⁸ have shown that progesterone has an influence on appetite in the adrenalectomized animal.

First, attempts were made to maintain pregnancy in rats castrated 24 hours after mating by use of progesterone,* but the doses used were insufficient. The 7 animals receiving progesterone for 20 days after castration had an average daily food consumption of 15.3 g while their littermate controls castrated but receiving no progesterone had an average daily food consumption over the same period of 17.6 g.

A second experiment using progesterone was then carried out. In this case groups of 4 normal virgin females were used with littermates distributed between the groups. For 12 days one group received 1.5 mg daily of progesterone dissolved in sesame oil, followed by

⁸ Gaunt, R., and Hays, H. W., *Am. J. Physiol.*, 1938, **124**, 767.

* Progesterone (Proluton) was supplied through the courtesy of Dr. Erwin Schwenk, Schering Corporation, Bloomfield, N. J.

3 mg doses daily for 8 additional days. Another group received sesame oil alone. The dose was increased because 1.5 mg proved to be insufficient to stop the cycle while 3 mg did this successfully. The average weight of the progesterone group at the beginning and end of the injections was 179 g and 223 g respectively, and for the controls 180 g and 213 g respectively. The average daily food consumption for the 2 groups was 12.7 g for the progesterone group and 13.0 g for the sesame controls. These experiments give no evidence that progesterone stimulates appetite.

Conclusions. 1. Inasmuch as pseudopregnant rats gain at nearly the same rate as those going through normal pregnancy it would appear that the fetus and its membranes are responsible only in part, if at all, for the increased growth rate of pregnant rats. 2. Progesterone apparently does not stimulate appetite. If the ovary is indirectly involved it may be by depressed estrogen secretion following mating inasmuch as appetite is increased following castration. This increase, however, is not observed until the sixth day as compared to the second day in pregnancy.

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Gonadotropic Hormones. VII. Influence of length of period of administration of equine hormone.*

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In a previous study¹ it was shown that the administration of a *known total dose* of chorionic gonadotropic hormone prepared from blood of pregnant women over periods of 10, 15, or 20 days, produced a much greater increase in ovarian and uterine weights of immature rats than when the same total dose was given in 5 days (Fig. 1). The opposite result was obtained with an acid extract of sheep anterior pituitary glands, as the injection of a known dose in 5 days produced a greater increase in ovarian weight than when the administration of the same total dose was spread out over periods of 10, 15,

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¹Fluhmann, C. F., *PROC. SOC. EXP. BIOL. AND MED.*, 1933, **30**, 1014.