

leads to the conclusion that the sensitive proteins are probably histones, and suggests the possibility of identifying those of its amino acid constituents which take part in the reaction. Whether these X-ray-sensitive amino acids can be more specifically and perhaps quantitatively ascertained remains for future experimentation to determine.

Summary. Treatment with ammonia reduces the sensitivity of chromosomes to X-rays. Curves showing the decrease in sensitivity as a function of ammonia concentration are presented. The results are taken as evidence in support of the hypothesis, previously advanced, that the sensitivity of chromosomes to X-rays at the onset of prophase may be attributed to the presence of positive charges on the separating surfaces of the dividing chromonema. These separating surfaces are probably made up of proteins of the histone type.

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A Corpus Luteum-Stimulating Substance in the Rat Placenta.*

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In the majority of mammals the length of the pregnancy cycle exceeds that of the normal estrous or pseudopregnant cycles, and this prolongation is due in part, to a sustained function of the corpora lutea. The presence of foetal elements is in some way responsible for this continued activity of the maternal ovary.

The function of the corpora lutea of the rat during the first half of pregnancy is under the control of the hypophysis and the mechanism involved is apparently the same as that in pseudopregnancy. Luteal function is essential throughout pregnancy, however, as shown by the fact that bilateral oöphorectomy invariably terminates gestation.¹⁻⁴ Removal of the pituitary gland during the first half of pregnancy is likewise followed by death and resorption of the foe-

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¹ Harris, R. G., and Piffner, S. S., *Anat. Rec.*, 1929, **44**, 205.

² Johnson, G. E., and Challans, J. C., *Anat. Rec.*, 1930, **47**, 300.

³ Nelson, W. O., and Haterius, H. O., *Physiol. Zool.*, 1930, **3**, 231.

⁴ Hain, A. M., *Quart. J. Exp. Physiol.*, 1934, **24**, 101.

tuses, whereas pregnancy continues if hypophysectomy is performed after the tenth or eleventh day.^{5, 6} In the rat hypophysectomy results in a persistence of existing corpora lutea, but such persisting corpora are non-functional in the non-pregnant animal.⁷ From these considerations it is apparent that some extra-pituitary factor is responsible for the luteal function of late pregnancy.

That the uterus itself, the maternal placenta or the "metrial gland" are not concerned in this mechanism is indicated by the fact that the presence of numerous large deciduomata in the uterus fails to prolong the length of pseudopregnancy. Any influence in this regard of uterine distension or of uterine hormones is thus ruled out. Furthermore, the controlling factor is not resident in the foetuses themselves, for removal of all the foetuses by Caesarian section does not shorten the pregnancy cycle if the placentæ are left intact.⁸

Attempts to demonstrate a gonadotropic substance in the placentæ of animals other than those of certain primates and equidæ have thus far been unsuccessful, but the existence of some corpus luteum-stimulating substance of extra-pituitary source during pregnancy has been suspected by numerous investigators. These failures may be attributed to the type of tests used for the demonstration of a corpus luteum-stimulating principle.

In the present investigation the deciduoma reaction was employed as a test for corpus luteum function. Pseudopregnancy was induced by electrical stimulation of the cervix uteri during estrus and 4 days later the endometrium was mechanically traumatized. In 35 normal control animals deciduomata developed in every instance, while in 10 animals hypophysectomized on the day of endometrial trauma, the reaction did not occur. Of these latter animals, 2 were examined at 24 hours, 2 at 48 hours, 2 at 72 hours, and 4 at 96 hours; in no case was there any indication of decidual reaction, the uteri showing progressive atrophy. Being thus assured that the corpora lutea of pseudopregnancy are non-functional in the absence of the hypophysis, animals similarly prepared were used in attempts to maintain luteal function. Eleven animals hypophysectomized on the fourth day of pseudopregnancy just prior to endometrial trauma were injected twice daily with saline suspensions of fresh rat pla-

⁵ Pencharz, R. I., and Long, S. A., *Am. J. Anat.*, 1933, **53**, 117.

⁶ Selye, H., Collip, J. B., and Thomson, D. L., *Proc. Soc. Exp. Biol. and Med.*, 1933, **30**, 589.

⁷ Greep, R. O., *Anat. Rec.*, 1938, **70**, 32; *Endocrin.*, in press.

⁸ Selye, H., and McKeown, T., *Proc. Roy. Soc. London*, SB, 1935, **119**, 1.

cental tissue. In all 11 cases deciduomata were found in various stages of development when the animals were examined 24 to 96 hours after hypophysectomy. To avoid the toxicity of the fresh material various rat placental extracts were prepared and tested in the same manner. A crude alkaline aqueous extract was found to be active (2 animals). Combined isoelectric precipitates (pH 5.2 to 6.7) from aqueous alkaline extracts produced deciduomata in each of 6 animals while the concentrated supernatant fluid was inactive. Approximately one gram equivalent of fresh tissue was given daily in 2 doses. Pseudopregnant rats oophorectomized at the time of endometrial trauma did not develop deciduomata and the injection of fresh placental extracts in such animals failed to induce deciduoma formation.

Fresh placenta or the active extracts when injected into 13 normal adult females beginning on the day of estrus inhibited the ensuing cycles; deciduomata developed in all animals following uterine trauma 4 days after the beginning of injections. In these 13 animals, one gram equivalent of fresh tissue or more was given daily; smaller amounts in 17 similar animals failed to inhibit the estrous cycle and consequently no deciduomata formed. It should be noted that toxic materials are likewise capable of inhibiting the estrous cycle and permitting the development of deciduomata, rendering the non-hypophysectomized rat unreliable as a test for corpus luteum stimulation.

The length of pseudopregnancy in the rat is subject to considerable variation but in the majority of animals its duration is 12 to 14 days. If deciduomata are present in such animals their breakdown is heralded by external hemorrhage 2 to 4 days prior to the appearance of the next estrous cycle. To determine the influence of placental extracts on the prolongation of the function of the corpora lutea of pseudopregnancy, 4 animals were treated from the 8th to the 16th day of pseudopregnancy with one gram equivalent of placental extracts daily. In all 4 cases deciduomata were found at autopsy on the 17th day.

Attempts to maintain the corpora lutea of normal pregnancy beyond term have thus far been unsuccessful. The injection of large amounts of fresh placental suspension into 4 rats at frequent intervals from the 19th day of pregnancy onward did not delay parturition. Live foetuses of normal birth weight were delivered on the 21st to 22nd day. This may indicate that the termination of pregnancy is determined by a primary failure of the corpus luteum.

The active material in the rat placenta apparently is unlike any

known gonadotropic substance. One gram equivalent or more injected into 21-day-old male and female rats daily for 5 days caused no increase in the weights of the ovaries, uteri, testes or seminal vesicles. As much as 5 g of fresh placenta injected intravenously into an estrous rabbit failed to induce ovulation or the formation of hemorrhagic follicles or corpora lutea. These tests establish its dissimilarity to any known gonadotropic substance of pituitary origin and differentiate it from the pregnancy hormones of the human being and the mare. Active extracts tested on 6-week-old pigeons gave negative results. Five grams equivalent in 5 daily subcutaneous injections or one-tenth gram intracutaneously over the crop gland resulted in no proliferation of the crop epithelium.

These experiments indicate that in normal pregnancy in the rat the foetal placenta secretes a substance which is responsible for the maintenance and function of the corpora lutea during the latter half of pregnancy. The functional corpora lutea induced by the act of copulation carry pregnancy to the 10th or 11th day at which time the hormone secreted by the developing chorion acts to maintain and enlarge these corpora whose continued secretion prolongs gestation to term.

In view of these and other considerations together with the available information on the chorionic hormones of the human being and the mare, it is probable that a similar mechanism is active to a greater or lesser extent in maintaining the luteal function of pregnancy in many mammals.

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Influence of Diet on Gonad Activity of English Sparrow, *Passer domesticus* (Linnaeus).

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Since the work of Rowan,¹ Bissonnette,² and more recently of Kirschbaum and Ringoen,³ and others, exposure to increased light during the spring months has been considered the predominant factor in inciting the development of the gonads of birds that com-

¹ Rowan, W., *The Riddle of Migration*, The Williams and Wilkins Co., 1931.

² Bissonnette, T. H., *J. Exp. Zool.*, 1931, **58**, 281.

³ Kirschbaum, A., and Ringoen, A. R., *Anat. Rec.*, 1936, **64**, 453.