ascorbic acid and Flavin phosphate (Vitamin B_2) and that cortin cannot maintain the life of adrenalectomized rats on a Flavin-free diet. Adrenalectomized rats can be maintained in good condition with Flavin phosphate. Young adrenalectomized rats furthermore have normal growth curves if given Flavin phosphate. Studies are being carried out in cats and dogs after adrenalectomy in the relation of Flavin phosphate to maintenance of life and general metabolism.

9164 P

Thyro-Parathyroidectomy and Pregnancy in the Rat.

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In studying the metabolism of thyro-parathyroid deficient rats it was found that a number of the animals which had become pregnant died at term, often during labor, death being preceded by convulsive seizures, occurring at intervals. This recalled the remarkable observation published by Halsted[1] in 1896, before the function of the parathyroids was known. Working with dogs, Halsted performed piecemeal extirpation of the thyroid and studied the changes produced in the remnants of the gland. He was particularly interested in determining the validity of Munk's contention that the thyroid was a superfluous organ. The dogs usually survived repeated operations and did not develop the fatal symptoms resulting from complete removal of the gland. However, 2 of the partly "thyroidectomized" dogs which had become pregnant developed tremors and convulsions at term, these symptoms subsiding after the pups were born.

Our observations seemed of sufficient importance to justify more detailed investigation and accordingly the study was extended to a group of 62 thyro-parathyroidectomized rats, this series being the basis of the present report. Total extirpation of the glands was performed at a relatively early age (less than 110 days, except in 6, operated at 135-140 days). The very young were allowed to ma-

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[1] Halsted, W. S., *Johns Hopkins Hosp. Reports*, 1896, **1**, 373.

ture and to attain a weight of 160-180 gm. before mating; the others were mated a few days after the operation. All the rats were maintained in an apparently good state of nutrition. As the subsequent course of events did not seem to be influenced by the administration of maintenance doses of thyroxine (Hoffmann-LaRoche), or desiccated thyroid (Eli Lilly), it seems unnecessary to dwell on the details in this communication.

Of the 62 operated rats, 42 did not survive one or more pregnancies, although they appeared in good health until nearly the end of gestation. Death occurred at term, either before or after the onset of labor. In many, tetany preceded the later semi-moribund condition. In others, tetany may have been overlooked, as the rats were not regularly inspected during the night. The results are briefly summarized in Table I.

TABLE I.

		Ratio of matings to pregnancies	Ratio of rats successfully reared to number born
Total number of thyro-parathyroidectomized rats	62		
Rats succumbing at end of first pregnancy	24	98/69	63/199†
" " " " " second "	12		
" " " " " third "	3		
" " " " " fourth "	3		
Number of surviving rats	20‡		
Surviving rats remaining sterile after repeated matings	3		
Surviving rats pregnant once	5	113/38	109/284
" " " twice	7		
" " " three times	3		
" " " five "	2		
Normal controls	16	57/44	159/387
Rats repeatedly and successfully pregnant	15§		

† In addition 411 mature fetuses were counted *in utero* and 33 more were born before the death of the mothers. In 2 rats several days past term, post-mortem examination disclosed partial fetal resorption.

‡ Of these, one was under observation 5½ months, 8 for 7½ months, and the remaining 11 for 10 to 11 months.

§ One of the normal controls died at the end of its second pregnancy. This was unusual, having occurred only 2 other times in approximately 1000 pregnancies in our colony.

From the data outlined above it will be noted that the proportion of successful matings was lower in the surviving than in the non-surviving group. It is obvious that this in itself assured a lower risk of mortality in the less fertile rats. Thyro-parathyroid deficiency was established in all the animals by the following criteria: (1)

failure to find remnants of thyroid or parathyroid tissue at autopsy; (2) failure in the normal metabolic response on exposure to cold, as described elsewhere;[2] (3) negligible excretion of guanidoacetic acid;[2] (4) low serum calcium (4-6.5 mg.) in every case where blood was available for analysis.

Summary and Conclusions. In pregnant rats deprived of their thyroid and parathyroids a very high rate of mortality occurred at term. While it seems logical to attribute these results to parathyroid deficiency, and indeed more recent experiments in this laboratory support this conclusion, nevertheless other factors may be of importance. Work is in progress in an attempt to elucidate the problem.

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Effect of Progesterone on Cell-Division in the Uterine Epithelium.

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It has been stated (see, for example, Sex and Internal Secretions, edited by E. Allen, 1932, p. 528) that the corpus luteum hormone, progestin, does not cause active proliferation with mitotic division in the endometrium, the proliferation observed after ovulation being ascribed to the action of oestrin and not progestin.

Examination of a cross section of the rabbit's uterus after injection of the castrated animal with progestin for five days, as in the usual method of assay, reveals very little evidence of mitotic division; it is, no doubt, this observation which has given rise to the conclusion that progestin does not induce cell division. The great increase, however, in extent of the surface epithelium and gland cells which is seen in the sections, obviously depending upon an increase in the total number of cells, suggests that cell-division has in some way been induced.

In the course of the experiments reported by Makepeace, Corner and Allen[1] it was noted that the uteri of animals examined after 3

[2] Bodansky, M., *et al., Endocrinology,* 1936, **20**, 822.

[1] Makepeace, A. W., Corner, G. W., and Allen, W. M., *Am. J. Physiol.,* 1936, **115**, 376.