ings do so signify. If iron is better utilized by the tissues in the presence of copper then we may ascribe to copper an additional function in iron metabolism other than its function in making iron available for hemoglobin synthesis. We offer no explanation for the decrease in the copper content of the spleens of animals receiving the high copper diet except that they seem unusual. Pending further experiments involving the use of higher levels of iron intake and more varied intakes of copper we reserve the privilege of making a more definite interpretation of the results here reported.

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Production of Exclusively Thecal Luteinization and Continuous Oestrus with Anterior-Pituitary-Like Hormone.

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The fact that rats do not respond to anterior-pituitary-like hormone (A.P.L.) in the first days of life has been observed repeatedly, and the conclusion has been drawn that they should not be used as test objects for this hormone earlier than the 18th to the 21st day of life. In an attempt to find an explanation for this fact we injected a series of 30 rats daily with A.P.L., starting on the 6th day of life. Although no mature follicles or corpora lutea had been formed after 10 injections and the ovary did not differ macroscopically from that of an untreated rat of the same age, histological examination of this organ reveals very pronounced changes. The thecal cells were very much enlarged and assumed the appearance of corpus luteum cells, whereas the granulosa cells were not luteinized and no signs of ripening of the follicles could be detected. These experiments show that at a very early age A.P.L. is unable to induce follicular maturation or the formation of normal or atretic corpora lutea; however, it does lead to luteinization of the thecal cells and thereby to the formation of thecal corpora lutea. These structures are not very prominent and therefore they can be readily overlooked upon macroscopical examination. (Fig. 1.) Histologically they are composed of a peripheral ring of corpus luteum cells and a central part of a few rows of normal granulosa cells in the center of which the ovum is included. (Fig. 2.)

It is difficult to find a satisfactory explanation for these observa-

FIG. 1.

To the left, thecal corpora lutea in the ovary of a rat treated with A.P.L. from the 6th to the 21st day of life. To the right, real corpora lutea and one blood point in the ovary of a rat treated with A.P.L. between the 21st and 26th day of life.

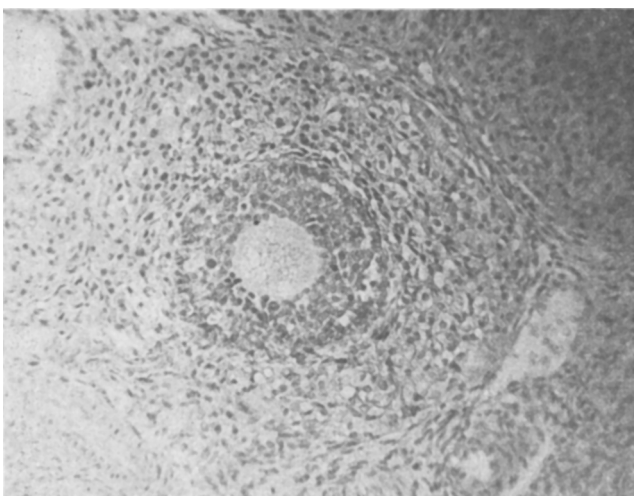

FIG. 2.

High magnification of thecal corpus luteum in the ovary of a rat treated with A.P.L. from the 6th to the 16th day of life. Luteinized thecal cells in the periphery. Normal granulosa cells and ovum in the center. No signs of follicular maturation.

tions. It is remarkable, however, that the hypophysectomized rat shows a very similar ovarian reaction when treated with A.P.L.[1] In

[1] Collip, J. B., Selye, H., and Thomson, D. L., *Nature*, 1933, **131**, 56.

the absence of the pituitary we could never induce maturation of the follicles or luteinization of the granulosa cells with A.P.L., but the luteinization of the theca cells is very conspicuous. This might suggest that the stimulation of granulosa elements is only possible in the presence of a pituitary factor which would obviously be lacking in the hypophysectomized animal and which, perhaps, cannot be supplied adequately by the immature pituitary during the first days of life.

If a thecal luteinization has been produced during the first days of life and the administration of A.P.L. is continued to the 26th day, the normal reaction of the ovary fails to develop. Whereas the control litter-mate receiving A.P.L. between the 21st and 26th day of life only shows maturation of follicles and corpus luteum formation, the ovary of the rat receiving the same amount of this hormone from the 6th until the 26th day shows nothing but thecal luteinization. Whether this phenomeon is due to an inhibition of follicular maturation by the corpus luteum hormone formed in the thecal cells is meanwhile open to discussion.

Following the formation of these thecal corpora lutea continuous oestrus has been observed both in hypophysectomized rats and in the animals of the present experimental series. As no signs of maturation could be detected in the granulosa, we have to assume that the luteinized thecal cells are responsible for the oestrus.

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Further Studies on the Exophthalmos in Rabbits Produced by Methyl Cyanide.*

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Chronic, progressive, bilateral exophthalmos has been produced in more than 150 prepubertal rabbits maintained on a diet of alfalfa hay and oats by the daily intramuscular injection of 0.05-0.1 cc. of methyl cyanide. [1, 2] Feeding fresh vegetables markedly inhibits its

* Aided by a grant from the Ella Sachs Plotz Foundation.

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[1] Marine, D., Spence, A. W., Cipra, A., PROC. SOC. EXP. BIOL. AND MED., 1932, **29**, 822.

[2] Marine, D., Baumann, E. J., *Trans. Assn. Am. Phys.*, 1932, **47**, 261.