change, becoming narrower at the base and more pointed. Within a shorter or longer period the crenated corpuscle becomes rounded and smaller, the crenations become thin and slender and the hemoglobin tint is definitely deeper than in the coarsely crenated stage. At this stage the refractile nodule has disappeared and the vibrating, twisting flagellum may or may not be present. Finally, the needle-like spicules disappear from the cell and a perfectly round, smooth microcyte 5μ in diameter without della and with dense hemoglobin has been formed.

(b) The other method observed is as follows: A spindle red corpuscle is observed slowly growing smaller, remaining apparently motionless during the process, while the anchoring fibrin-threads become more prominent and definitely thicker at their point of attachment to the corpuscle. The hemoglobin tint deepens, the cell becomes rounder and finally a typical microcyte with dense hemoglobin content, and without della appears. In this method the non-hemoglobin constituents have been wrung out of the corpuscle by the twisting of the anchoring fibrin threads which tear, contract and disappear at a certain time. See Fig. 1.

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Effect of Various Anterior Pituitary Preparations on Basal Metabolism in Guinea Pigs.

WALTER J. SIEBERT AND ROBERT S. SMITH. (Introduced by Leo Loeb.)

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Loeb,[1] and later Loeb and Bassett,[2] and Silberberg[3] studied the effects of various anterior pituitary preparations upon the thyroid gland; the former investigators also correlated the changes in the thyroid thus produced with those that take place in the sex organs under the influence of anterior pituitary preparations.[4] It was found that various preparations have different effects. Intraperitoneal injections of acid and alkaline extracts of fresh cattle glands cause a

[1] Loeb, Leo, *J. Med. Res.*, 1920, xli, 481.

[2] Loeb, Leo, and Bassett, R. B., PROC. SOC. EXP. BIOL. AND MED., 1929, xxvi, 860.

[3] Silberberg, Martin, PROC. SOC. EXP. BIOL. AND MED., 1929, xxvi, 166.

[4] Loeb, Leo, and Bassett, R. B., PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 490.

very marked hypertrophy of the thyroid gland in a very short time; while on the contrary the feeding of Armour's anterior pituitary tablets produced structural changes indicating a decreased activity of the gland. Loeb and Siebert[5] found that the oral administration of anterior pituitary substance prepared in our laboratory does not produce the same effects as the Armour preparation. According to Loeb and Bassett[2] repeated subcutaneous inoculations of anterior pituitary gland tissue obtained from freshly killed guinea pigs caused only very slight hypertrophic changes, if any, in the thyroid gland, while inoculations with somewhat larger quantities of fresh cattle gland produced definite hypertrophic changes.

In view of the effect of these preparations on the thyroid gland in guinea pigs and considering the significance of the thyroid gland in basal metabolism, we thought it of importance to study the action of these various anterior pituitary preparations on the basal metabolism in guinea pigs.

Our principal findings are as follows:

1. Daily subcutaneous injections of either acid or alkaline extracts of anterior pituitary glands of cattle cause a very marked and rapid rise in basal metabolism, which reaches a maximum of approximately +60% within the first 10 days. Then the basal metabolism gradually returns to a level approximately 15% higher than the average found in normal guinea pigs.

2. Feeding daily one 5 grain Armour anterior pituitary tablet to a guinea pig causes a gradual steady rise in basal metabolism which reaches a maximum of approximately +60% in about 30 days. There seems to be a cumulative effect in this case, and there is no tendency on the part of the metabolism to return to a lower level subsequently throughout the period of our investigation.

3. Feeding daily 5 grain pills of dried anterior pituitary substance prepared in our laboratory from fresh cattle glands causes a slight gradual rise in basal metabolism which reaches its maximum of approximately +25% in about 20 days, after which there is a gradual return to almost the normal level.

4. Daily subcutaneous inoculations of fresh guinea pig anterior pituitary gland tissue cause a very slight gradual rise in basal metabolism which reaches a maximum of approximately +15% in about 5 days, after which there is a decline. These latter experiments extended only over a period of 10 days, whereas in the former ones

[5] Loeb, Leo, and Siebert, W. J., PROC. SOC. EXP. BIOL. AND MED., 1930, xxvii, 495.

the effects of the above mentioned preparations were studied over periods of 30 days.

We may therefore conclude that all the various preparations of anterior pituitary substance which we used cause a rise in basal metabolism; however, the subcutaneous injection of acid or alkaline extracts produces the most rapid and greatest rise. Also the other preparations differ in the degree and the sharpness of the rise, and in the character of the curve following the period when they have reached the maximum point. The basal metabolism of all the animals, except those fed with Armour's anterior pituitary tablets, returns approximately to the normal level after some time, notwithstanding the continued administration of the various preparations during this period. These experiments furthermore suggest that some of these preparations may affect the basal metabolism, at least partly, through changes which they produce in the thyroid gland, while others affect it independently of such changes. We intend to study this question more directly in subsequent experiments.

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Induced Oxidations in Blood. Hemoglobin Destruction by Methylene Blue in Lactic Acid Peroxidation.

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We have previously reported experiments[1] which showed that the observations of Barron and Harrop[2, 3] that methylene blue added to blood increases the rate of oxygen consumption and decreases lactic acid production, may, in part, be accounted for by the oxidation of formed lactic acid. The incubation of washed dog erythrocytes in a solution containing added dl-lactate, in the presence but not in the absence of methylene blue, results in a disappearance of lactate.

Further study indicates that the lactic acid is oxidized to pyruvic acid, apparently quantitatively. That this oxidation is not mediated by the lactic "dehydrogenase" of the Wieland school is evi-

[1] Wendel, PROC. SOC. EXP. BIOL. AND MED., 1929, xxvi, 865.

[2] Harrop and Barron, *J. Exp. Med.*, 1928, xlviii, 207.

[3] Barron and Harrop, *J. Biol. Chem.*, 1928, lxxix, 65.