

In another series of dogs 1 cc. of irradiated ergosterol (Viosterol) was injected daily into the tissues around experimental fractures in the same manner as were the bladder extracts. The results of these experiments were also negative. That is, there was no definite difference in the healing on the control and injected sides.

*Conclusions.* Neither extracts of bladder prepared as described above nor irradiated ergosterol influenced osteogenesis when injected at the site of experimental fractures and bone defects. It is possible that the stimulation of osteogenesis noted when bladder epithelium is transplanted into bone defects is due to a local excess of calcium which is produced by the living bladder epithelial cells. It is also possible that phosphatase is a factor in the production of bone around the bladder transplants.

## 6017

**Exophthalmos Produced by Injections of Acid Extract of Anterior Pituitary Gland of Cattle.**

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In former investigations<sup>1</sup> we observed that by injections of acid and alkali extracts of anterior pituitary of cattle, it was possible to produce in the guinea pig changes in the thyroid gland identical with those in very pronounced cases of Graves' disease in man, namely, a marked hypertrophy and hyperplasia of the acinus cells, softening and absorption of colloid and irregular shape of the acini, associated often with an almost complete disappearance of the lumen of the acinus. There was also a loss of weight induced by these changes which indicated an hyperactivity of the gland. Silberberg found that administration of KI to a certain extent inhibited these changes. This corresponds to the action of this substance in Graves' disease. Siebert noted a marked rise of the basal metabolism in guinea pigs under the influence of acid or alkali extracts and more recently found that simultaneous administration of KI tends to counteract the effect on basal metabolism. Closs, Loeb and MacKay<sup>1</sup> found the changes in the distribution of organic and inorganic

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<sup>1</sup> Closs, Carl, Loeb, Leo, and MacKay, Eaton, *PROC. SOC. EXP. BIOL. AND MED.*, 1931, **29**, 170.

iodine in the thyroid gland and blood of guinea pigs injected with acid extract similar to those which occur in Graves' disease.

During the winter, 1930-31, we observed that guinea pigs injected with acid extract frequently showed a greater bulging of the eyes than normal guinea pigs. In view of the correspondence of this change to the exophthalmos which is so characteristic of Graves' disease, we followed the alterations in the eyes on a large number of guinea pigs. Our inability to measure these changes accurately or representing them objectively, caused us to hesitate to publish these observations. The method we have adopted recently makes it possible to demonstrate the bulging of the eye in a relatively objective manner.

We selected in each case 2 guinea pigs with similar eye color, similar prominence of eyes, and of similar weight, varying in different pairs approximately between 180 and 210 gm. The similarity of eye color is a necessary precaution, because there exists certain variations in the character of the eyes of individual guinea pigs. Then one of the 2 animals of each pair received daily intraperitoneal injections of  $2\frac{1}{2}$  to 3 cc. acid extract of anterior pituitary. After a series of from 4 to 6 injections, the eyes of the injected animals were distinctly more prominent than those of their partners. Thus it was possible by merely comparing the eyes of the 2 partners, to determine correctly in about 70% to 100% of the pairs which one of the 2 animals had been injected. As a matter of routine, a number of observers were shown these pairs and they made a diagnosis independently of each other. As a rule their judgment coincided. In a certain percentage of animals, no distinct difference developed between the 2 partners, or it developed somewhat later. When such a bulging of the eyes had been established it could remain noticeable for a long period of time, if the injections of extract were continued. However, it seems that if the guinea pigs lose a great deal of weight and become weak, this symptom may disappear; it also disappears in complete narcosis and after death. The exophthalmos depends therefore on a functional condition and not on an organic change. Whether it is due directly to hyperthyroidism needs further investigation.

In their first observations, Loeb and Bassett noted that the changes produced by injections of extracts in the thyroid gland of rats are missing or much less pronounced than in the thyroid of guinea pigs. Correspondingly, we found that a bulging eye cannot be definitely obtained in rats.

We may thus consider that in addition to the other similarities between the symptoms of Graves' disease in men and those pro-

duced by administration of preparations of anterior pituitary in guinea pigs we now have established the occurrence of exophthalmos.

## 6018

**Effect of Amytal upon Basal Metabolism in Guinea Pigs.\***

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Deuel, Chambers and Milhorat<sup>1</sup> have shown that there was only a very slight lowering of basal metabolism in dogs which had been injected with sodium amytal. A series of experiments was carried out to determine what effect doses of amytal sufficient to cause the animals to remain quiet would have upon the basal metabolism of normal guinea pigs, and upon guinea pigs which had been given various substances which would cause a rise in the basal metabolic rate. We used the isoamylethylbarbituric acid (Amytal—Lilly) which was prepared according to the directions given on the label of the bottle. 0.10 cc. of a saturated solution of the potassium salt of the amytal was injected subcutaneously into guinea pigs which had an average weight of about 400 gm., 5 or 10 minutes before placing the animals on the metabolism apparatus. The guinea pigs remained perfectly quiet throughout the 2-hour period in which they were on the apparatus. No shivering occurred. No ill effects from the use of the amytal and no increased tolerance for the drug were noted. The average basal metabolism of 76 normal guinea pigs without amytal was 3.59 calories per kilo per hour, while in 72 other guinea pigs which had been injected with amytal, the average basal metabolism was 3.52 calories per kilo per hour. Thus the average metabolism of this latter series was approximately 2% below the average of the series which had not received amytal. The maximum and minimum variations are approximately the same in both sets, being plus or minus 10%. Twenty-four guinea pigs were used to determine what effect amytal has upon basal

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<sup>1</sup> Deuel, Harry J., Jr., Chambers, William H., and Milhorat, Adolph T., *J. Biol. Chem.*, 1926, **69**, 249.