in the alcohol insoluble iodine per total gland was somewhat less, namely 23% and 69% respectively; nevertheless there was here a distinct loss as a result of the anterior pituitary administration. In the blood on the contrary, the alcohol insoluble iodine showed a rise of 82% in the first experiment and of 179% in the second experiment. In this case a few individual determinations which for technical reasons were unreliable were omitted. If they are included the increase in the first experiment was 34%. The determinations of the alcohol soluble iodine did not indicate a noticeable change either in the thyroid gland or in the blood.

These findings of a decrease in the alcohol insoluble fraction of iodine in the thyroid glands harmonize well with the histological changes which result from the injections of acid extracts. As Loeb and Bassett[1] have shown, the hypertrophy of the thyroid gland produced under these conditions is associated with a marked decrease in the amount of colloid in the acini and, what is left of it stains very poorly with eosin, a condition pointing to a marked liquefaction and absorption of the colloid. Inasmuch as the iodine in the thyroid is mainly contained in the colloid, the fact that by far the greater part of the colloid in the individual acini has been liquefied and absorbed justifies the assumption that a diminution in the amount of iodine has taken place in the thyroid, notwithstanding the marked proliferation of the acinar epithelium and the resulting increase in the amount of gland tissue which has taken place as a result of the administration of anterior pituitary extract.

These experiments which we are extending at the present time, strongly suggest the conclusion that extracts of cattle anterior pituitary produce in the organism of the guinea pig changes in the iodine distribution which correspond to those noted in man in cases of Graves disease.

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Long Continued Injections of Acid Extract of Anterior Pituitary on Thyroid Gland and Sex Organs.*

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In former experiments on the effects of the injection of acid extract of cattle anterior pituitary on the thyroid gland of guinea

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pigs, we had found indications that these effects did not increase with continued injections. To determine the effects of long continued administration, a considerable number of young guinea pigs were given daily injections of anterior pituitary extract over a long period of time. Excluding those animals which were examined within the first 6 weeks after the beginning of the experiment, 10 guinea pigs received injections during a period of time varying between 47 and 74 days. The individual amounts injected daily varied between 1 cc. and 3 cc. of the extract. In some cases a few initial doses of ½ cc. were given. The total amounts injected ranged between 47 and 135 cc. The initial weights of the individual guinea pigs were between 185 and 205 gm. except one animal weighing 230 gm. There was a great difference between the weights reached at the end of the experiment. Some animals had gained considerably, while others remained unchanged.

The microscopic examination of the organs showed that the severity of the effects of extract did not correspond to the amount injected. The animals evidently varied greatly in resistance. The resistant animals showed the least changes in their organs and these gained most rapidly in weight, while the most susceptible ones showed the greatest changes in their thyroid and sex organs, and did not gain as much or as rapidly in weight as the others. The former group became most readily adapted even to increasing doses of the extract. Thus those animals receiving the largest daily doses gained most in weight and their thyroid and sex organs showed the least change from normal or no change at all.

Effect on the Thyroid Gland. The relation between gain in weight and lack of hypertrophy in the thyroid can readily be seen. The thyroids of those animals which tolerated the largest doses of extract and gained most in weight showed least hypertrophy or none at all. The colloid was normal in quantity and of normal consistency. On the other hand, with one apparent exception, the glands of those that gained least in weight showed the greatest hypertrophy and their acini contained much less colloid. But even in those cases in which the thyroid showed definite hypertrophy and in which as a result of thyroid hypertrophy there was least gain in weight, there is apparent a relative increase in colloid due to new formation of this substance and some reduction in hypertrophy as compared to the changes in the thyroid gland of control guinea pigs which received only 6 to 8 injections of acid extract.

Effect on Sex Organs. We may distinguish 3 types of effects. (a) The sex organs were found normal. In the ovary the follicles

matured and ovulation took place, vagina, cervix and uterus behaving in accordance with the stage of the sexual cycle. These were the effects in guinea pigs in which there was considerable gain in weight, and in which the thyroid showed no hypertrophy. (b) In the animals which did not gain in weight or gained little, the thyroid gland (with one possible exception) showed hypertrophy. The ovaries were hypotypical, contained much interstitial gland and, in one case also a pseudolutein body. Vagina, uterus, and mammary gland were in a resting condition. (c) There was an intermediate group in which the guinea pigs gained much in weight, but less than in Group A. The thyroid showed no or only a trace of hypertrophy. The follicles developed well in the ovaries and proestrus as well as ovulation could occur, but at the same time interstitial gland and pseudolutein bodies or the latter alone formed. The other sex organs behaved normally, except that we found a quiescent vagina in a case in which both interstitial gland and pseudolutein tissue were present. Hypertrophy of the thyroid and the resulting deficiency in weight caused a hypotypical condition of the ovaries; in addition the acid extract was responsible more directly for the formation of interstitial gland and pseudolutein bodies.

We may conclude that after a long continued series of injections of acid extract of cattle anterior pituitary a gradual adaptation, partial or even complete, to the effects of the injections may take place in young guinea pigs and that there seems to exist a considerable difference in the ability of individual animals to acquire this increased tolerance. We may attribute the hypotypical condition of the ovaries largely to the relative undernourishment caused by the induced hypertrophy of the thyroid gland.

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Production of Experimental Polycythemia with Cobalt.

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During a continuation of our studies on nutritional anemia, a polycythemia was observed in rats receiving a certain mixture of metals with Cu as a supplement to a milk-Fe diet, whereas the same