used. In all instances, rabbits receiving subarachnoid injections were paralleled by rabbits injected with identical amounts of the same serum intravenously, and the bleedings and precipitin tests of each were done at the same time.

Summary: (1) Rabbits receiving a single dose (0.5 c.c.) of normal horse serum into the subarachnoid space, produce precipitins in the blood in greater abundance, of higher titer, and which persist longer than those in control rabbits receiving a similar injection intravenously.

(2) Repeated subarachnoid injections (0.5 c.c.) of normal horse serum in rabbits, induce precipitins in the blood early. These may appear in high titer as soon as one week after the initial injection, whereas in rabbits similarly treated intravenously, no precipitins were found at this time. They may appear a few days thereafter and reach a high titer.

(3) No anaphylactic manifestations occurred in rabbits treated repeatedly with subarachnoid injections of normal horse serum when the precipitin content of the blood was high.

(4) Anaphylactins, as determined by passive transfer of anaphylaxis, were demonstrated in sera with high precipitin content.

(5) These experiments may explain clinical manifestations of intolerance to horse serum, observed when an initial intravenous injection of antimeningococcic serum followed a series of intraspinous injections of such serum.

5 (1587)

Experimental gigantism produced by feeding pituitary gland.

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Growth of the individual stops, when the size is reached which is specific for the species to which the individual belongs. The causes which lead to the cessation of growth are not fully known. In man it happens sometimes, that growth continues beyond the normal maximum size of the species; this condition is known as gigantism. Clinical evidence points to the conclusion

that at least one form of gigantism is due to an overfunction of the hypophysis gland. Attempts, however, to produce gigantism by feeding hypophysis to animals have been unsuccessful.

The experiments to be discussed presently will show that in salamanders hypophysis feeding produces gigantism and that it is the anterior lobe alone which possesses the ability of maintaining growth after the normal size of the species is reached.

The effect of the hypophysis diet depends, however, on the developmental stage of the salamanders. Larvæ do not respond to the anterior lobe diet; the growth-promoting effect of the gland commences after metamorphosis has taken place.

Of the species *Ambystoma opacum*, quite a number of specimens have been kept and measured for several years in my laboratory. In a chart the growth during three years is shown for four specimens; after the first year the animals grow very little and, at certain periods, may show even a decrease in size. The largest animal of this species raised in my laboratory was 115 mm. long, the largest normal animal in my possession at present is 111.5 mm. long. I went through the collections of several museums; the largest specimen I found measured 117.7 mm.; of two breeding females caught recently, one measured 112 mm., the other one 106 mm.

Of four animals raised in the laboratory from eggs of the same female and kept on a normal diet two were started on the anterior lobe at an age of 62 weeks, about 12 months after metamorphosis and about 4 months after sex maturity had been reached, and two animals were kept as controls. The result is shown in the growth curves. In spite of the advanced age both hypophysis-fed animals started to grow at a rate that, under normal conditions, would be characteristic of an early period after metamorphosis, while the controls continued to grow at a low rate, although they were fed so excessively large quantities of normal food that both of them succumbed finally. The largest control animal measured 115 mm., when it died; would it have survived and increased steadily at the same rate—which, however, would not be expected from the curves of other normal animals—it would measure 118 mm. today, whereas the largest hypophysis-fed animal, which died a few days ago, measured 138 mm. The

surviving anterior lobe-fed animal is passed around together with the largest normal animal kept at present in the laboratory. The hypophysis-fed animal is about 131 mm. long and two years old, the normal animal measures 111.5 mm. and is three years old. In the species *A. opacum* feeding of the anterior lobe resulted in gigantism.

Similar experiments were made in the species *A. tigrinum*. The normal growth curve of this species seems to resemble the growth curve of *A. opacum*. After the first year the rate of growth becomes very low as shown in the slides; the records of this species do not go, however, beyond 80 weeks and it is uncertain, when growth in *A. tigrinum* stops. The largest animal that I could find in the museum collections measured 208.7 mm. Larger specimens are found in the western states, but these are most likely derived from larvæ in which by abnormal processes of the inner secretory system growth was greatly stimulated already during the larvæ period, and which on account of this abnormal condition studied as yet very little, cannot be used for comparison with our eastern race. The largest normal animal raised in my laboratory measures 195 mm.

Every single individual of this species fed on the anterior lobe of the hypophysis not only outgrew all the controls and other normal animals raised in my laboratory, but also the largest animals which I found so far in museum collections. In one series of five specimens the two smaller individuals were selected for the purpose of the experiment and started on anterior lobe at an age of 37 weeks, about 27 weeks after metamorphosis; the three larger specimens were kept as controls. The controls grew only little after this time and were soon outgrown by the experimental animals in which the high rate of growth that prevailed during the early period was not only maintained but even surpassed by the rate of growth produced by the hypophysis diet. The largest hypophysis-fed animal of this series measures now 264 mm. and still is growing most vigorously, while the largest control animal measures only 192 mm. Both animals are passed around. Similar results were obtained in the other series and at present I possess five hypophyseal giants of this species, coming from two different broods.

If the animals are fed on the posterior lobe of hypophysis growth is not only not stimulated, but even greatly retarded as may be seen from two live animals, a control and a posterior lobe fed animal, both descendants of the same female and of the same age.

Feeding of anterior lobe causes (1) a very marked acceleration of growth and (2) a continuation of growth beyond the specific size of the species resulting thus in hypophyseal gigantism. Feeding of posterior lobe has neither of these two effects, but even retards growth.

Since in these experiments the hypophysis was fed without the addition of normal food and in large doses, one may think that the results were caused not by the action of a specific substance contained in the hypophysis but merely by the greater food value of the gland. Part of the acceleration of growth may have been actually due to merely quantitative differences in the food substances; but it should be pointed out that it is impossible to renew growth by feeding even large quantities of normal food after growth has come practically to a standstill. As regards the continuation of growth beyond the normal size of the species, it is obvious that the alteration of this specific character of growth cannot be due to an increased amount of food and it seems, therefore, that at a stage where growth ceases or is greatly diminished under normal conditions, cell proliferation can be actually enforced by the specific growth-promoting substances contained in the anterior lobe of the hypophysis.

6 (1588)

Observations on bacterial metabolism.

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In the course of an investigation of the cultural requirements of certain of the pathogenic bacteria, a substance which occurs in meat infusion, and also in some of the proteins has been found to be essential for the growth of the streptococcus, and for certain