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Observations on the production of experimental scurvy in the guinea pig.

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The customary method of producing experimental scurvy in the guinea pig with a monotonous cereal diet is open to several points of criticism. The protein may be inadequate, inorganic salts deficient and the physical texture unsatisfactory. Our work led to a search for some good food material capable of dietary analysis; and through the results obtained by Osborne and Mendel[1] and others the soy bean seemed most suitable. Its protein is adequate for maintenance and growth (of the rat) and the only inorganic constituents deficient are Na, Ca and Cl. We used soy bean flour autoclaved at 15 pounds for 30 minutes. To it was added Ca lactate and NaCl. Dried brewer's yeast and fresh raw Jersey milk supplied the two recognized dietary accessories (vitamines). Young guinea pigs on this diet gain in weight faster than on the usual cabbage-carrots and oats ration. After 10 days, while still gaining in weight they develop swelling of the joints and general tenderness—symptoms considered indicative of experimental scurvy. Later occurs loss in weight followed by death. Stools were frequent and pasty; toward the end diarrheal. A marked polyuria was present from the beginning of the diet. Addition of over 7 per cent. cellulose as roughage did not change the result. Orange juice, 5 c.c. daily, or fresh cabbage prevented and cured these symptoms promptly with increase in weight.

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Further experiments with thyroidectomy in Amphibia.

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The thyroid gland anlage was removed from a large number of *Rana sylvatica* larvæ 6 to 8 mm. in length. From the time

[1] Osborne, T. B., and Mendel, L. B., 1917, *Jour. Biol. Chem.*, *32*, 369.

the larvæ averaged 18 mm. in length (225 experimental and 182 control animals) the experimental larvæ grew more rapidly than the controls, and most of them became ultimately much larger than the controls, the largest being 72 mm. in length as against 50 mm. for the controls. Thirty thyroidless animals failed to metamorphose and in twelve others the thyroid regenerated, permitting metamorphosis at the normal time. The rest of the experimental larvæ were killed or died before this time. Six of the thyroidless larvæ are still alive, nine months after the normal time of metamorphosis. They practically ceased growing six months ago.

In the absence of the thyroid the secretory (anterior) portion of the hypophysis underwent physiological hypertrophy to compensate for the loss of the thyroid, as both normally are concerned with metabolism, although not in an exactly similar way. This hypertrophy probably accounts for the gigantism and infantilism (retention of the larval form) of the thyroidless larvæ. Normally, synapsis begins in the testis after metamorphosis, and in the ovary a short time before metamorphosis. In our experimental animals so far examined, synapsis in the testis was practically completed at the time of metamorphosis of the controls and differentiation of the ovary also was hastened greatly. The hypertrophy of the hypophysis probably accounts for this sexual precocity. The growth in size of the gonads continues with that of the other parts of the body and is independent of the changes normally occurring in metamorphosis. Both processes, however, depend upon the general metabolism. Failure of metamorphosis is due to abnormal metabolism, brought about, either by loss of normal thyroid secreton or by abnormal secretion of the hypophysis which is affected by removal of the thyroid. Both causes may be involved, and also, the secretion of still other glands may be changed after loss of thyroid function. Failure of metamorphosis may depend directly upon an abnormal calcium metabolism with which the thyroid is believed to be concerned, since the initiation of metamorphosis is probably brought about by growth of the skeleton. The condition in thyroidless larvæ may be neotony, as Allen has called it. The hypophysis of axolotls should be investigated to see if it is the cause of failure of metamorphosis in these animals. In the obser-

vations so far made, the hypophysis of the female is much larger than that of the male, both in our thyroidless and control animals. If this point is established by further study, it may account for the fact that the ovary differentiates earlier than the testis.

In one of our experimental animals, the thyroid regenerated, and then hypertrophied. The animal underwent metamorphosis a month before the normal time, and at a size about one third normal. Its ovaries were in a stage of differentiation, much further advanced than normal. Its hypophysis could not be studied on account of poor fixation.

The various other organs and ductless glands of the thyroidless animals are being studied at this time. In general they are all larger than normal, but we have not yet determined whether there is present true hypertrophy or whether the size is merely proportional to the size of the larvæ which are larger than normal.

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Generalized analgesia in cats after exposure to a war gas $(CH_3)_2SO_4$.

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Procedure.—Cats were subjected to the action of dimethyl sulphate fumes in a concentration of 4.5 to 10,000 of air for one hour. The dimethyl sulphate, which is a liquid at ordinary temperatures with a specific gravity of 1.32 and a boiling point of 188° C., was vaporized by an electric hot plate in the gas chamber. An electric fan in the gas chamber kept the available fumes mixed with the air. The temperature of the gas chamber was maintained between 25–30° C.

With this strength of gas the cats usually succumbed in 30–60 hours.

In cats which are gassed as described above a strong generalized analgesia is observed within a few hours after exposure to the dimethyl sulphate fumes, and reaches a high degree within twenty-four hours. If the animal survives, the analgesia may still be well marked six months afterwards.