4592

Effect of Thyroxin Upon Normal, Hypophysectomized, and Thyroidectomized Tadpoles.*

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The removal of the thyroid gland anlage and the buccal anlage of the hypophysis from amphibian larvae affords animals in which these glands have never functioned. In the first series *Rana aurora* tadpoles kept for over 4 months after the operation were placed in thyroxin solutions of 1-500,000; 1-1,000,000; and 1-2,000,000 concentration in tap water. In all cases there was a very rapid tendency to metamorphosis that proceeded with equal speed and to an equal degree in each of the groups, resulting in the appearance of all 4 limbs except in a few cases in which the right fore-limb failed to pierce the skin. The tail rapidly shrivelled and typical changes took place in the position of the eyes, the character of the mouth, the retrogression of the gills, and, all of the other features characteristic of thyroid induced metamorphosis. The rapidity of the changes of metamorphosis was to a slight degree inversely proportional to the concentration of the thyroxin solution, as we should expect; but some diversity in size of specimens precludes our attaching too great importance to this point.

Controls maintained during this time under identical conditions failed to show any tendency to metamorphosis. The largest had only the hind-limbs developed to the point of showing the knee-joints, and the fore-limbs had not appeared in any, nor was there any shortening of the tail or other evidence of metamorphosis. Because of these facts we may conclude that the thyroid gland and anterior lobe of the hypophysis in the normal specimens placed in thyroxin were not factors to be considered; probably because they had not yet become active to any significant degree.

This view is strengthened by the fact that the thyroidectomized and hypophysectomized tadpoles responded to the thyroxin to the same degree as the unoperated specimens.

From the earlier work upon thyroidectomized and hypophysectomized tadpoles it has been clear that these glands are not essen-

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tial to development, until the appearance of the hind-limb buds. But beginning with the stage to which our specimens belong, they play an increasingly important rôle.

Table to Show the Influence of Thyroxin Solutions upon *Rana aurora* Tadpoles. Figures Refer to Averages Made up from Groups of 5

	Length at start	Length	Change in length
Thyroxin solution 1–500,000. 11 days in solution			
Thyroid	33 mm.	18 mm.	—15.0 mm.
Hypophysis	34 mm.	20 mm.	—13.5 mm.
Normal	32 mm.	18 mm.	—13.6 mm.
14 days in solution—1–1,000,000			
Thyroid	45 mm.	26 mm.	—19.2 mm.
Hypophysis	41 mm.	23 mm.	—18.0 mm.
Normal	33 mm.	17 mm.	—15.6 mm.
15 days in solution—1–2,000,000			
Thyroid	44 mm.	32 mm.	—12.2 mm.
Hypophysis	46 mm.	33 mm.	—13.0 mm.
Normal	39 mm.	27 mm.	—11.8 mm.
Control tadpoles not kept in thyroxin solution			
4 Normal	42 mm.	41 mm.	—1.0 mm.
2 Thyroidectomized	57 mm.	57 mm.	0.0 mm.
2 Hypophysectomized	37 mm.	38 mm.	+1.0 mm.

Large numbers of tadpoles of all these types were kept in the laboratory and none showed the characteristic thyroid changes. All of the specimens in thyroxin solutions showed them markedly and none of the 8 controls showed them in the slightest degree.

It may be contended that the concentration of thyroxin in the above experiment was not weak enough to demonstrate small differences in the response of these 3 classes of tadpoles, so an experiment was undertaken in which dilutions of 1:20,000,000 and 1:40,000,000 were employed. The number of thyroidectomized specimens was limited so that groups of 5 each were chosen, and the following averages represent surviving lots of from 3 to 5. Each lot of tadpoles was kept in 200 cc. of solution for 42 days. In no case was complete metamorphosis induced, although there was an approach to it in a few cases. Because of the slow development it is fair to say that the more extreme dilution is not far from the threshold of stimulation, but the effect is very marked as shown by a comparison with the controls.

An examination of the above table will show that hypophysectomized and thyroidectomized tadpoles respond to this very dilute thyroxin solution with a readiness fully comparable to that shown by the controls. In this case, hind leg length is taken as a criterion of the degree of metamorphosis rather than total length, because it is in many ways a more satisfactory one. The results are similar. Still greater dilutions and larger numbers of specimens might show

Table to Show the Influence of Very Dilute Thyroxin Solutions upon *Bufo halophilus* larvae. Measurements taken after 42 days.

	Total length	Trunk length	Hind leg length
Control in tap water			
	mm.	mm.	mm.
Normal	23.63	10.23	.77
Thyroidectomized	22.96	9.37	.85
Hypophysectomized	27.17	11.43	1.31
Thyroxin solution 1:40,000,000			
Normal	18.30	8.76	3.81
Thyroidectomized	30.47	12.77	5.63
Hypophysectomized	24.32	10.12	4.68
Thyroxin solution 1:20,000,000			
Normal	19.05	8.77	4.04
Thyroidectomized	26.15	10.60	4.65
Hypophysectomized	19.67	8.00	3.63

quantitative difference in response but the writer feels justified in concluding that (1) metamorphosis of thyroidectomized and hypophysectomized tadpoles is readily induced by extremely dilute solutions of thyroxin. (2) The early secretion of these glands does not render the tadpoles either more or less sensitive to thyroxin than the normal ones. (3) The presence of neither the hypophysis nor the thyroid gland is essential or even apparently conducive to the reaction of the tadpole to the thyroxin. Work done several years ago in feeding iodine to thyroidectomized and to hypophysectomized tadpoles demonstrated the fact that elemental iodine would produce metamorphosis when fed to thyroidectomized and hypophysectomized tadpoles. The present work tends to show that there is no difference in the speed of their response to thyroxin.

4593

Effect of Fatigue on Protein Consumption.

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Some recent papers on protein consumption and basal metabolism set forth the fact of regular weekly variations in urinary nitrogen excretion. Borgstrom and Bost[1] and Borgstrom, Hafkesbring and Bost[2] showed that in a series of analyses of urine collected over a period of months there was evidence of a weekly cycle of values.

[1] Borgstrom, P., and Bost, R. W., *Am. J. Physiol.*, 1926, lxxix, 229.

[2] Borgstrom, P., Hafkesbring, R., and Bost, R. W., *Am. J. Physiol.*, 1926, lxxix, 237, 245.