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Effect of Replacement Therapy on Eruption of the Incisor of the Hypophysectomized Rat.*

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A series of 7 hypophysectomized rats and their litter mate controls was treated for various periods with daily injections (usually 20) of the growth-promoting hormone of the pituitary body. The experimental animals were operated upon at the age of 45 to 64 days. The rate of eruption of the incisors of these animals was measured for varying lengths of time preceding, during, and after replacement therapy (Table I).

A horizontal marking with a fine file (Swiss jeweler's screw head file) was made near the gingival line along the disto-labial margin of the upper incisor. With an adjustable caliper provided with fine points the distance was measured between the point where the marking crossed the disto-labial margin and the point where the surface of the gingivae crossed the same margin. This distance was read in twentieths of a millimeter with the aid of a stage micrometer and a dissecting microscope. The distance between the same points mentioned above was read 7 days later. The difference between the 2 readings represented the rate of eruption for that period. New marks had to be made each week in the normally erupting teeth. Operated and control animals received the same preparation† subcutaneously once daily in a dose proportional to the body-weight.

To obtain some idea of the accuracy of the individual measure-

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† Made by the method of van Dyke and Wallen-Lawrence and kindly furnished by the Wilson Laboratories.

ments, 8 experiments on teeth of different lengths were performed. Each experiment was made up of 4 measurements on the same tooth. The standard deviations calculated for these experiments were found

TABLE I.

Effect of Growth-Promoting Hormone on Rate of Eruption of Upper Incisors of Hypophysectomized Rats.

No.	Period of Injection		Maximum Wt. Gain		Approximate Average Weekly Rate of Eruption in mm.					% of Increase
	No. of Successive Days	Days Following Hypophysectomy	gm.	%	3 weeks preceding therapy	During therapy Mean	During therapy Max. per wk.	1st week after therapy	1st 3 wks after therapy	
314	20	54-73	68	60.7	0.18	0.95	1.3	0.75	0.38	427
324	20	77-96	46	40.4	0.36	0.8	1.2			122
319	20	89-108	0	0	0	0	0			0
268	21	125-145	28	21.7	0.33	0.66	0.9	0.95	0.5	100
317	12	139-150	32	22.4	0.10	0.26	0.45	0.24	0.14*	160
268	20	167-186	15	10.5	0.27†	0.63	0.75	0.25	0.25	137
268	20	224-243	0	0	0.20	0.1	0.2			0
258	21	294-314	43	27.4	0.29	0.51	0.75	0.2	0.25	75
258	20	336-355	39	22.3	0.27†	0.45	0.75	0.85	0.61	66
258	20	393-412	0	0	0.56	0.38	0.55			0
186	17	412-428	0	0	0	0				0

*First 17 days after replacement therapy.
†This average is based on the records of only 2 weeks preceding the treatment because the rate of eruption of the third week was still increased by a previous period of replacement therapy which was administered 4 weeks before.

to have the following values expressed as percentages of the mean values: 1.80, 5.26, 8.44, 7.94, 5.65, 6.44, 11.20, and 4.48. These deviations are probably greater than the actual ones because these experiments were performed at the beginning of this study and the technique has improved since then.

The degree of retardation in the eruption-rate of the rat incisor

TABLE II.
Comparison of Mean Rates of Eruption of Upper Incisors of Normal and Hypophysectomized Rats.

Group	Number of Individuals	Number of Measurements	Mean weekly Eruption rate mm.	Standard Deviation mm.
I Control	14	190	1.980	±0.377
II Treated Control	10*	49	2.028	±0.838
III Hypophysectomized	5†	20	0.210	±0.163
IV Treated Hypophysectomized	5†	26	0.610	±0.324

*From Group I.
†Same individuals.

after hypophysectomy is summarized by the data of Table II. In the computation of the data, those obtained from 2 of the hypophysectomized rats are not included since the incisors of these animals were no longer erupting. There was unquestionably a significant difference between the eruption rates of the teeth of Groups I and III. The mean rate of incisor-eruption was not significantly altered in the normal animal by the administration of growth-promoting hormone although the body-weight was definitely increased (Groups I and II).

The rate of eruption of the rat incisors which is retarded following hypophysectomy[1] can be accelerated by replacement therapy. The increase in the rate of eruption can be observed within a week following the beginning of replacement therapy and continues for about a week after treatment is stopped. Except for some individual variations, the acceleration is greatest in the animals operated upon most recently and appears to become smaller as the interval between the time of the operation and the time of replacement therapy increases (Table I, Fig. 1). Two animals that were given replacement therapy during the fourteenth month following hypophysectomy (Rats 186, 258) showed no change in the rate of eruption of their incisors. Another animal (Rat 268) responded to replacement therapy when administered during the fifth and sixth month following the operation but showed no response to treatment during the eighth month following hypophysectomy (Fig. 1). The fact that neither control nor hypophysectomized animal responded to the third series of injections was not due to an inactive hormone-preparation; other animals, normal and operated, responded in a typical fashion from the same preparation administered

[1] Schour, I., and van Dyke, H. B., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 934.

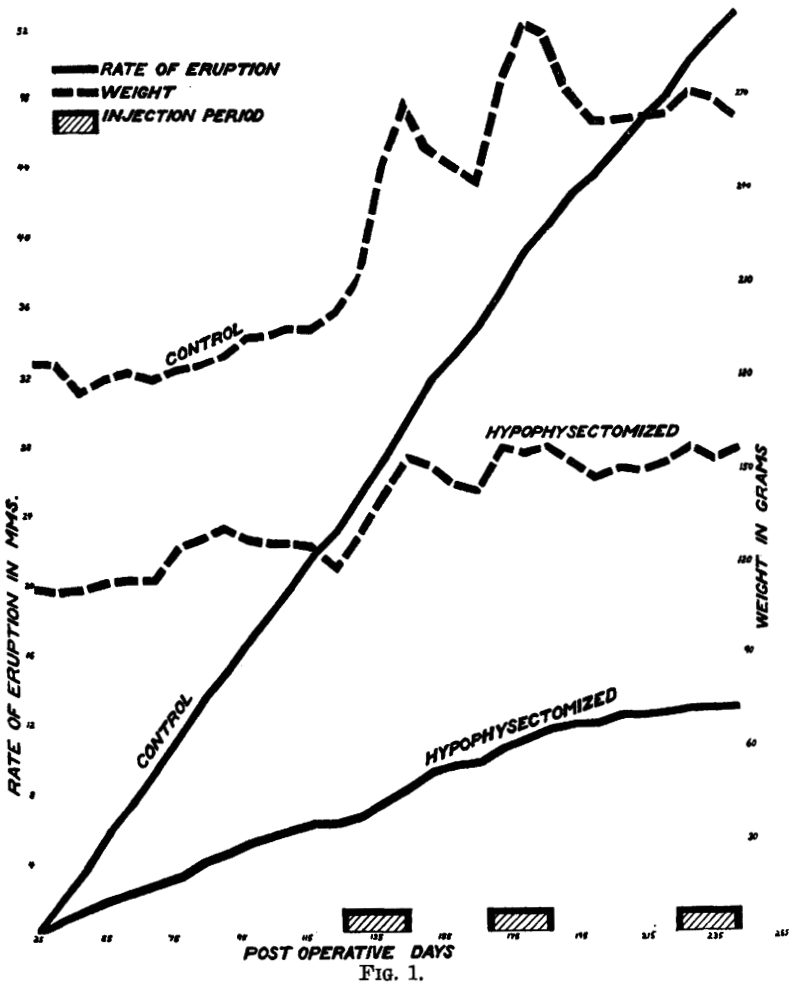

FIG. 1.

Effect of treatment on weight and incisor-eruption rate of hypophysectomized rat (268) and litter-mate control (266).

at the same time. One animal (Rat 319) did not respond during the fourth month following hypophysectomy. The atypical reaction of this animal may be associated with the fact that it was ovariectomized previous to the time of replacement therapy. However, in all the hypophysectomized animals, increase in weight and acceleration in eruption-rate were always associated.

The data in Table II on 5 of the hypophysectomized rats were selected as follows: the last 2 weekly measurements before treatment are the source of the data for Group III; the measurements during treatment as well as in the first week after treatment are the source of the data for Group IV. If the mean eruption-rates of

these 2 groups are compared by Fisher's method,[2] they are found to be significantly different ($t = 4.94$).

Summary. 1. Following hypophysectomy the eruption of the incisor of the rat becomes progressively slower and finally ceases.

2. If not administered too late after operation, growth-promoting hormone increases the eruption-rate of the incisor. An increase in body-weight, following the administration of hormone to the hypophysectomized animal, is always associated with an increase in the rate of the eruption of the incisor.

3. In the normal animal, the administration of growth-promoting hormone under the experimental conditions described, although definitely increasing body-weight, does not appreciably alter the eruption-rate of the incisor.

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Production of Ulcers in the Prostomach of Rats by Protein Restriction.

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Büchner, Siebert and Molloy[1] found that marked ulceration could be produced in the prostomach of rats by stimulating the gastric secretion with histamine on starvation days. Some ulceration also occurred in rats starved every other day during a period of 17 days, without histamine. Bürkle-de la Camp[2] confirmed these results with histamine but did not observe ulcers in the prostomach of rats after short periods of simple starvation. The question of ulceration following starvation was of particular interest because irritation of the parapyloric region by the gastric secretion was believed to explain a peculiar and intense hunger sensation that repeatedly developed with starvation or protein restriction in the senior author of the present report (Hoelzel and Kleitman[3]). Moreover, the observation that protein restriction led to an increase

[2] Fisher, R. A., *Statistical Methods for Research Workers*, 1930, 107.

[1] Büchner, Siebert and Molloy, *Beiträge z. path. Anat. u. allg. Path.*, 1928, **81**, 391.

[2] Bürkle-de la Camp, *Deut. Z. f. Chir.*, 1929, **220**, 31.

[3] Hoelzel and Kleitman, *Arch. Int. Med.*, 1927, **39**, 710.