Influence of Hypophysectomy on Oxidative Enzymes and Size of Parietal Cells in Gastric Mucosa.* (26240)

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Although hypophysectomy of the rat results in a profound involution of the gastric chief cells and a fall in their capacity to secrete pepsinogen(1), the changes which occur in parietal cells is less clear. Crafts and Walker(2) reported a moderate elevation in pH of the gastric juice and reduction in total acidity; similar changes were observed in the dog(3). Structurally, Friedman(4) described a 50% reduction in number of parietal cells without presenting supporting evidence and Baker and Abrams(1) observed an irregular reduction in cell size with some loss of fuchsinophilic granules and mitochondria.

The objectives of this study were to observe after hypophysectomy (a) if a reduction in size of parietal cells is demonstrable by quantitative means, and (b) if alteration occurs in oxidative enzymes in the mucosal cells. The latter point is important because of the irregular mitochondrial depletion previously observed(1) in parietal cells and the depressed functional state of the chief cells.

Procedure. Young adult female Sprague-Dawley rats were fed Purina Laboratory Chow and starved 18 hours prior to being killed. At termination of the study, completeness of hypophysectomy was proven by microscopic examination of sections of the pituitary area.

For the study of parietal cell area, the rats were divided into 3 groups: (a) hypophysectomized, vehicle-treated; (b) hypophysectomized and treated twice daily with 125 μg somatotropin,‡ 15 μg of corticosterone and 2 μg of l-thyroxine (STC), and (c) nonhypophysectomized, vehicle-treated. The somatotropin was dissolved in distilled water at a concentration of 2 mg/ml, the l-thyroxine in water (40 μg/ml), the hormone first being dissolved in one drop of 0.1 N NaOH, and the corticosterone was suspended in 0.9% NaCl (150 μg/ml) with Tween 80 as the suspending agent. The 3 hormones were drawn into the syringe and injected together at one site. The nonhormonal ingredients of the injection media were administered to groups a and c in similar manner and volume. Fifteen or 16 days elapsed between hypophysectomy and initiation of hormone treatment; treatment was continued for 15-16 days. Groups b and c received daily the amount of food consumed by Group a on the previous day. When killed, the stomach was expanded before removal by injection of 2.5 ml of formol-alcohol-acetic acid fixative. After fixation for 48 hours, strips of glandular mucosa which extended along the greater curvature from the horizontal ridge to the pylorus were embedded, sectioned, and stained with periodic acid-leucofuchsin and methylene blue.

Outlines of parietal cells were drawn with a camera lucida at a magnification of 1900×. The areas studied were in the region of the neck and isthmus of the gastric glands, these areas being selected at regular intervals throughout the section. All parietal cells in each area which were cut through the nucleus were drawn. The area of each cell outline was determined with a planimeter. An average of 52 to 54 cells in each of the 3 groups was measured.

Oxidative enzymes were studied in the mucosa of 8 pairs of hypophysectomized and nonhypophysectomized rats, the latter being pair-fed against the operated animal. Mean initial body weight for the nonhypophysecto-

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TABLE I. Effect of Hypophysectomy and Replacement Therapy on Area of Parietal Cells.

Group	No. of rats	Mean body wt (g) Initial	Final	Mean area of parietal cells (μ^2)	Probability of error*
1. Hypophysectomized, vehicle	9	154 ± 2†	148 ± 3	122 ± 5	1 *vs* 2 <.02
2. Hypophysectomized, STC‡	9	158 ± 2	172 ± 5	141 ± 5	2 " 3 <.05
3. Nonhypophysectomized, vehicle	10	159 ± 1	182 ± 3	163 ± 8	1 " 3 <.001

* Student-Fisher t. † Stand. error of mean. ‡ STC = somatotropin, thyroxine and corticosterone.

mized rats was 173 ± standard error 2 g and for the hypophysectomized rats 172 ± 4 g; final weights were 202 ± 2 and 148 ± 3 g, respectively. Twenty-nine to 80 days elapsed after the operation before killing. Pieces of mucosa were frozen over liquid nitrogen and sectioned at 6 μ in a cryostat. The following histochemical reactions were carried out on these sections: succinic dehydrogenase (SD)(5), lactic, malic, isocitric and α-glycerophosphate dehydrogenases (LD, MD, ID, GD)(6), diphosphopyridine nucleotide diaphorase (DPND)(7), and cytochrome c oxidase(CO)(8).

Observations and discussion. Hypophysectomy reduced the mean area of parietal cells from a mean of 163 ± 8 μ^2 to 122 ± 5 μ^2, this difference being significant at the 0.1% level (Table I). Treatment of hypophysectomized rats with STC caused a significant increase in area but did not restore it to the level seen in nonhypophysectomized controls.

In nonhypophysectomized rats the parietal cells stained intensely with all of the enzyme procedures (Figs. 1A and C) except that for ID. With ID the cytoplasm was a faint pink and sparse, formazan granules appeared in at least the larger parietal cells. GD was weaker than the other enzymes. The stain for CO appeared as densely packed fine granules; the other procedures which utilized nitro blue tetrazolium revealed large globular and finer formazan bodies, at least the latter appearing to be mitochondria.

Chief cells of control rats stained much less intensely (Fig. 1A and D), for the most part only fine mitochondria being revealed. Again only ID failed to be revealed clearly.

The mucous epithelial cells of the mucosal surface and foveolae stained strongly with all procedures except that for ID. These cells were unique in showing a prominent concentration of activity in the cytoplasm immediately above the nucleus.

Finally the technics for dehydrogenases and DPND revealed large globular bodies in the superficial epithelium and underlying connective tissue located between foveolae. The significance of these bodies is not understood.

Hypophysectomy did not selectively suppress any of the enzymes studied in any of the 3 cell types observed. The overall quantity of activity for all enzymes was reduced somewhat in the parietal cells in association with reduction in cell size. However, parietal cells continued to stain intensely as illustrated by the preparations for CO (Fig. 1D and DPND (Fig. 1B). Since chief cells involute markedly after hypophysectomy, their total activity for each enzyme was reduced (Fig. 1B and D). However, they still contained all of the enzyme activities and in some cases the staining intensity was even greater than that in the controls.

These observations suggest the presence of a general depression in oxidative activity of parietal and chief cells in the hypophysectomized rat which could be associated with the reduced production of HCl and pepsinogen. However, none of the enzymes studied was affected to a greater degree than the others.

Summary. Gastric parietal cells were reduced in size after hypophysectomy of the rat. Treatment with STC enlarged the cells but did not restore their normal size. Histochemical demonstration of cytochrome c oxi-

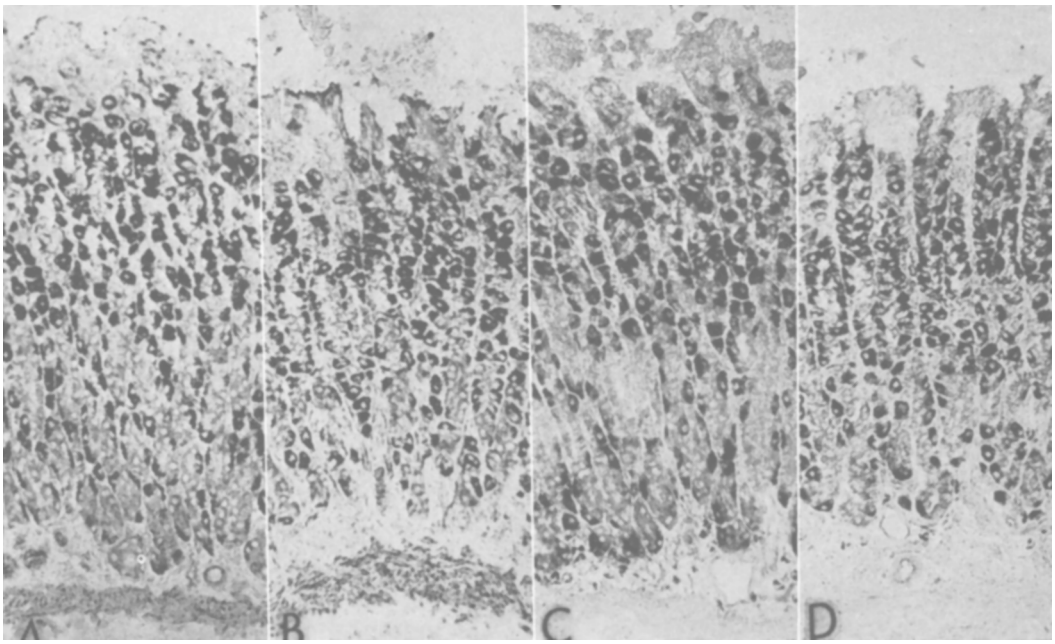

FIG. 1. In all cases the black cells are parietal cells and the gray ones deep in the glands are chief cells. A and B, DPN diaphorase; C and D, cytochrome c oxidase. A and C were prepared from a nonhypophysectomized control; B and D from a rat which had been hypophysectomized 29 days. In B and D the parietal and chief cells are smaller and their total activity somewhat less, these changes being more marked in the chief cells.

dase, DPN diaphorase and 5 dehydrogenases did not reveal any one which was affected more than the others in either parietal or chief cells. In both cell types some overall reduction in activity occurred coincident with a reduction in cell size.

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