magnesium for optimal growth in a synthetic medium. The addition of this substance to an otherwise synthetic medium supports growth approximately equivalent to that obtained in Difco Micro Inoculum Broth or trypticase soy broth. The unidentified factor(s) can be found in Wilson's liver L, asparagus juice, yeast extract, soybean meal, and Alpha protein. It is not replaceable by any known growth factors tested. It is stable to HCl hydrolysis, treatment with HNO_2 and H_2O_2 and is separated from aqueous solution with acetone.

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Intestinal Absorption of Glucose in Hypothalamic Obesity. (19893)

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The demonstration that the obesity which often appears in rats as a result of damage to the hypothalamus is primarily due to hyperphagia(1) has not entirely dispelled the traditional concept that this disorder may be a manifestation of some disturbance of metabolism. Among the more commonly indicted metabolic processes are those involved in intestinal absorption. Soulairac(2) has reported that hypothalamic lesions in rats may elevate the rate of glucose absorption from the intestine. Unfortunately, his data are too few for statistical analysis, and although he claimed that changes in the rate of glucose absorption run parallel with changes in the appetite for food (and specifically for glucose) he failed to show that the animals in which he found an increased rate of glucose absorption (10 days after placing the lesions) were either hyperphagic or obese. The relationship of Soulairac's finding to hypothalamic obesity, therefore, appears doubtful. On the other hand, Brooks(3) concluded, on the basis of indirect evidence (food-feces ratios), that the rate of intestinal absorption of food in rats with hypothalamic obesity was not elevated above that in controls.

The present investigation was undertaken since direct observations of the rate of glucose absorption in rats with clearly established hypothalamic obesity have not heretofore been reported.

Experimental. Large bilateral electrolytic hypothalamic lesions were placed in a series of male rats (of both Sprague-Dawley and Long-Evans strains, weighing between 220 g and 300 g) using the Krieg-Johnson* stereotaxic apparatus. The rats were operated upon in several groups, a few non-operated rats from each group being reserved as controls. The animals were then kept in individual cages for periods ranging from 29 to 47 days and fed Rockland chow pellets *ad libitum*. Twenty-one rats were used for glucose absorption determinations: 10 unoperated controls, 9 with hypothalamic obesity (HO), and 2 HO thyroxinized.† In addition, 3 unlesioned rats were thyroidectomized (3-4 weeks prior to use) and five were rendered hyperthyroid† to serve as method controls. The determination of glucose absorption was carried out on anesthetized rats exactly as described by Bogdanove and Barker(4). Following a 48-hour fast the rats were given nembutal (45 mg/kg)

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† Thyroxine was injected subcutaneously in 200 μg doses thrice daily for 7 to 11 days.

TABLE I. Glucose Absorption by Control, HO, Thyroxinized HO, Thyroidectomized and Thyroxinized Unlesioned Rats.

	No. of rats	GCA*	Range	S.E.
Controls	10	114.0	74-162	±9.60
HO	9	107.4	93-132	±3.82
HO thyroxinized	2	173.5	163-184	—†
Thyroxinized	5	191.6	170-204	—†
Thyroidectomized	3	75.2	63-86	—†

* Glucose coefficient of absorption = glucose absorbed/100 g/hr.

† Sample too small for statistical analysis.

TABLE II. Mean Rates of Weight Gain for Control and HO Rats.

	Rate of gain, g/day	Range, g/day	S.E.
Control	2.87	1.9-3.8	±.215
HO	3.77*	1.9-5.5	±.383

* 36% increase over controls, significant at 5% level.

intraperitoneally, the abdomen opened, and ligatures placed around the ascending part of the third portion of the duodenum and the lowest ileum. A measured volume (3 cc/100 g) of isotonic glucose was introduced into the ligated intestinal loop by multiple injections. After a 25-minute absorption period the rats were sacrificed. Residual glucose was estimated by the Somogyi-Nelson colorimetric method(5). The absorbed glucose was expressed as the glucose coefficient of absorption (GCA) = mg glucose absorbed/100 g/hr. Statistical analysis utilized the method of Student's t.

Results. The absorption data are presented in Table I. The GCA of 114.0 for the controls is close to the value of 116.6 obtained in earlier work with this technic(4). The GCA of 107.4 for the HO rats does not differ significantly from that obtained for the controls ($p = .5$-$.6$).

Thyroidectomy depressed the GCA of unlesioned rats to 75.2, while thyroxine treatment elevated it to 191.6. These changes are of about the order reported by Althausen and Stockholm(6), indicating the method to be as sensitive as the Cori technic (used by these workers) in demonstrating alterations of the GCA in either direction.

The GCA of 173.5 for the thyroxinized HO rats indicates that the glucose absorptive capacity of these animals responds to changes in thyroid status.

In Table II are the mean rates of weight gain for rats from the control and HO groups. The obese rats had thick deposits of subcutaneous fat (particularly prominent in the thoracic region, where little or no fat is deposited in the normal rat) and massive retroperitoneal deposits of adipose tissue. Heavy deposits of fat were found in all obese animals at these sites, as well as in the mesentery, omentum, and pericardial region. (HO thyroxinized rats lost much of this excessive adiposity during the brief period of hyperthyroidism). Even though some obese animals gained less weight than some controls, there could be no doubt of their excessive corpulence.

Discussion. Our failure to find a difference between the GCA for unoperated rats and that for animals with distinct hypothalamic obesity might be interpreted in 2 ways: either that the use of anesthesia in these experiments obscured the existence of an altered rate of intestinal absorption of glucose in HO rats, or that HO may exist without alterations in the rate of glucose absorption by the intestine.

Anesthesia appears to lower the rate of intestinal absorption of all substances thus far examined in a uniform, nonspecific manner (7,8). Experimental alterations of glucose absorption under anesthesia correlate well with those reported in the unanesthetized animal(6,9). In the present experiment we have shown that nembutal does not prevent the rise in GCA resulting from thyroxinization of both unlesioned and HO rats. We therefore believe that the first interpretation of our findings would have little validity, and that HO can develop without an increase of GCA above that found in controls.

This finding is compatible with the concept that HO primarily owes its origin to hyperphagia(1). Although many other metabolic processes remain to be examined in HO animals, we are thus far unaware of any findings which refute the opinion advanced by Brobeck (10) that those metabolic derangements which have been found in such animals are readily

explained as secondary phenomena resulting from the hyperphagia.

On the other hand, the development of unquestionable obesity in some of our lesioned rats which did not gain weight more rapidly than the controls suggests that they deposited fat at the expense of other body constituents. Apparently a slowing or cessation of growth can obscure the significance of weight gain as a criterion of obesity. Cessation or diminution of growth together with obesity was observed by Hetherington and Ranson in hypophysectomized HO rats(11) and by Scow(12) in force-fed thyroidectomized rats. In both of these cases a combination of growth hormone deficiency (resulting in negative N balance) and excessive food intake could explain the phenomenon(12). The same explanation might well hold for our HO rats which did not exhibit an excessive weight gain. Support for this concept comes from the observation(13) that the anterior pituitaries of many of the lesioned rats show a striking degranulation of the acidophiles, similar to that found after thyroidectomy. This suggests that the secretion of growth hormone by these cells might be severely disturbed by hypothalamic lesions which also produce obesity.

Summary. 1. Hypothalamic obesity (HO) was produced in rats by means of electrolytic lesions. Glucose intestinal absorption determinations yielded the following glucose coefficients of absorption (GCA): Control, 114.0; HO, 107.4; HO thyroxinized, 173.5; thyroxinized, 191.6; thyroidectomized, 75.2. These results indicate that the intestinal absorption of glucose need not differ from control values in order for obesity to occur. 2. Thyroxine elevated the GCA of HO rats as well as that of unlesioned rats. Unlesioned thyroidectomized and thyroxinized rats served as method controls. 3. Observations on HO rats which did not exhibit excessive weight gain suggest that hypothalamic lesions may interfere with the secretion of growth hormone by the pituitary.

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Comparison of Effects of Various Brands of ACTH on Normal Subjects.* (19894)

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The purpose of this study was to compare the effects of several types of commercial brands of ACTH in their ability to produce a reduction in circulating eosinophils and to increase the urinary excretion of 17 ketosteroids in human subjects. Additional studies were aimed at depleting the ascorbic acid contents in the adrenal glands of hypophysectomized rats by means of injections of the same lots of ACTH as were used in the human subjects. Commercial preparations of ACTH have their dosages based on the rela-

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