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Intestinal Absorption of D-glucose (*in vitro*) in Hamster: Effects of a Large Dose of Reserpine.* (29621)

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The sympatho-adrenal system has been shown to be influential in intestinal absorption. Soulairac(1) reported that sympathectomy in the rat diminished intestinal absorption and reduces the "Coefficient of absorption" (*i.e.* mg sugar absorbed/100 g of rat/hour). Intestinal absorption of sugar is reduced, *in vivo*, after adrenalectomy(1,2) and thyroidectomy(1,3). The mechanism by which surgical removal of these endocrine organs results in a reduction of intestinal sugar absorption is not known. It therefore seemed pertinent to study sugar absorption and transport in the intestine of animals in which the humoral background was altered with a large dose of reserpine. An *in vitro* technique, utilizing isolated intestinal sacs, was selected for measurement of sugar absorption.

Materials and methods. A colony of hamsters, *Cricetus auratus*, each weighing from 100 to 125 g was maintained on an *ad libitum* diet of commercial Purina lab chow and intermittent feedings of fresh vegetable matter. Animals for reserpine treatment and controls were selected at random from the colony. Reserpine 2.5 mg/kg was administered intraperitoneally.

Animals were sacrificed at various periods, 6, 14, 20, and 24 hours after treatment with reserpine. Each animal was spinalectomized and the gut was removed. Two segments of intestine were used. Segment I, 1 to 7 cm from the pylorus, and Segment II, 8 to 14 cm from the pylorus, represented duodenal and jejunal tissue respectively. Histological examination confirmed morphological differences between the two areas.

Absorption and transport of D-glucose was measured *in vitro* by means of everted intestinal sac preparations; detailed descriptions have been published(4,5,6). Isolated segments were everted and suspended in Krebs-Ringer sodium bicarbonate buffered solution containing 100 mg % D-glucose. The everted intestinal sac was suspended in 8 ml of this solution and filled with 1 ml of the same solution. Thus the initial concentration in each side of the intestinal wall was identical. Uptake from the musocal side and concomitant increase on the serosal side was indicative of active transport. (The sugar moved against an apparent concentration gradient.) D-glucose concentrations in the mucosal and serosal compartments were analyzed colorimetrically using a glucose oxidase reaction (Glucostat from Worthington Biochemical Corp.). Dry weights of tissue were determined by analytical weighing and drying in an oven at 105°C for 24 hours. The results were calculated in terms of micromoles of sugar decreased in the mucosal compartment and the amount increased in the serosal compartment after 30 minutes of incubation.

The remaining pieces of gut, which had been flushed with cold Krebs-Ringer bicarbonate, were cut open, blotted, and quickly frozen at the temperature of dry ice. Using

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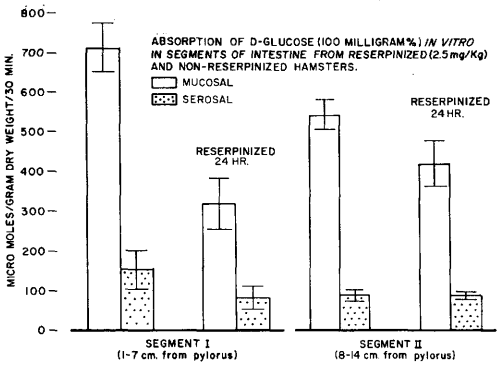

FIG. 1. Rates of mucosal uptake and serosal increase of glucose in intestinal segments, *in vitro*, from hamsters 24 hr after intraperitoneal administration of 2.5 mg/kg reserpine and from untreated hamsters.

pooled samples, catecholamine assays were done by a fluorometric method(7). In this technique oxidations were carried out at a pH 4.9, thus, equivalent readings for epinephrine and nor-epinephrine were obtained. Histamines were measured using the method of Shore *et al*(8).

Results. Several hours after administration of reserpine the animals showed a variety of outward manifestations of drug action. Some animals shivered or tremored, others rolled-up in a characteristic hibernal posture, almost all showed aggressive behavior when attempts were made to pick them up. In all animals there was a loss of appetite and in 75% of the animals there was a diarrhea and mucous-like stool. In 30% of the hamsters, observed for 14 hours or longer, body temperatures were notably lower. There was a reduction from usual ranges of 35°-37°C to 24°-32°C. In a few animals gross appearance of the gut, *i.e.*, the serosal surface and mesentery showed dilation and engorgement of blood vessels often giving a violaceous appearance.

The amount of sugar absorbed and transported was notably altered in intestine from treated hamsters. In intestinal segments, 24 hours after treatment, the rate of absorption was significantly reduced ($P<.005$) particularly in the duodenal portion. Comparisons between segments from treated and untreated animals, after 24 hours, are presented in Fig. 1.

Little influence on intestinal absorption and transport of glucose was observed within the first 6 hours after treatment. However, at 14 hours a trend toward a reduction in absorption and transport of the sugar was evident. In some segments taken from the animals 14 and 20 hours after treatment, the uni-directional movement of sugar was greatly disrupted. This was evident in 3 segments where there was uptake of D-glucose from both sides (Table I). Rates of absorption and transport of D-glucose at various periods

TABLE I. Amounts of D-Glucose Absorbed and Transported in Intestinal Sac Preparations, from Reserpinized and Non-reserpinized Hamsters. Starting concentration of D-glucose 100 mg %.

		Values* expressed in μMoles/g dry wt/30 min				
		Segment I (duodenum)			Segment II (jejunum)	
Exp conditions		Mucosal uptake	Serosal increase		Mucosal uptake	Serosal increase
Controls	(11)†	713 ± 59	152 ± 31	(12)	543 ± 44	87 ± 16
Reserpinized 6 hr	(2)	751 1029	164 177	(2)	749 347	139 47
14 "	(3)	105 184 210	16 (—)‡ 39 52	(3)	394 124 (leaked)	45 22 (—) (leaked)
20 "	(3)	51 190 288	35 123 (—) 435	(3)	261 562 417	56 300 129
24 "	(7)	320 ± 67	81 ± 31	(9)	417 ± 58	84 ± 9

* Means and S.E.M., and individual values where applicable.
† No. of segments given in parentheses.
‡ (—) in this case D-glucose absorbed also from the serosal side.

after treatment with reserpine are presented in Table I.

The catecholamine content of gut tissue decreased from 0.14 μg/g wet weight to zero level within 24 hours after reserpine treatment. In untreated animals the histamine content of the gut was 1.0 μg/g wet weight. There was an initial decrease in the reserpine treated animals to 0.8 and 0.85 μg/g wet weight at 6 and 14 hours respectively and a notable rise to 1.5 and 1.2 μg/g wet weight at 20 and 24 hours respectively.

Discussion. These data demonstrate altered intestinal absorption of glucose, *in vitro,* in hamsters treated with reserpine in doses known to deplete body stores of catecholamines.

Whether the reduction in absorptive capacity involves a neuro-humoral regulatory influence is not clear, since a large dose of reserpine may induce other cellular effects. Removal of sympatho-adrenal influences may well be expected to alter cellular mechanisms of sugar absorption. In this respect Soulairac (1) has observed that sympathectomy in rats reduces intestinal absorption of sugar.

It is apparent also that in terms of the concentration of sugar used (100 mg %) the first segment has greater capacity of moving glucose from the mucosal to the serosal compartment. The fact that various areas of the intestine differ in functional capacity to absorb and move sugar *in vitro* has been reported in rats(9,10) and in hamsters(11). It is noteworthy that reserpine treatment produced greater sustained effects in the duodenal segments. Even after 24 hours these segments continued to show significantly lowered levels of absorption. That 2.5 mg/kg was sufficient to affect the catecholamine background of the gut was evidenced by the fall to zero level in segments taken from the treated animals.

Although the pharmacologic effect in the animals was great, the dose was within the range tolerated by the hamster. Folk *et al* (12) showed that reserpine 5 mg/kg administered intraperitoneally was frequently followed by a loss of body weight, reduction in heart rate, and a marked hypothermic response. A large number of our animals (30%) also showed a drop in body temperature.

Reserpine is also known to effect histamine storage. Whether the measured histamine changes have any connection with the observed alterations in glucose absorption cannot be ascertained from these studies.

Summary. Intestinal absorption of D-glucose, *in vitro,* was measured in hamsters which had been given a single large dose of reserpine (2.5 mg/kg) intraperitoneally. Rates of sugar absorption in reserpinized hamsters were altered and 24 hours after treatment the duodenal area continued to show significant reduction. In the same animals intestinal catecholamine analyses were made in order to provide a meaningful guide to reserpine activity. The gut showed characteristic depletion in reserpine treated animals. Histamine levels of the same tissue showed considerable variation.

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