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Glucose Absorption in Highly Inbred Strains of Mice.* (19532)

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Studies on glucose absorption in the rat, beginning with the work of Cori(1), have raised a number of questions chief among which is the relation of absorption rate to the concentration of the administered solution. Cori(1) and others have claimed that absorption is essentially independent of concentration, while MacKay and Bergman(2), Fenton (3), and others found absorption to increase with increasing concentration of the administered solution. Two different colonies of rats were used by Fenton(3) with differing results. While both colonies showed dependence of absorption rate on concentration, this was much less pronounced in one of the colonies studied. It seemed that this colony difference might account for the divergent results which have appeared in the literature and might best be investigated in mice of highly inbred strains and of known genetic background.

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The demonstration that glucose absorption is accomplished by phosphorylation has led to speculation on the role of the widely distributed alkaline phosphatase in the absorption process(4). It was decided to investigate changes during glucose absorption in the concentration of phosphatase (using chemical methods) and in distribution (using cytochemical technics).

Methods. Female mice of the C57 and A strains, approximately 6-8 months old were fasted for 24 hours. Both strains were derived from the colony of Dr. L. C. Strong, Yale University, and were maintained by brother-sister matings. Following the fasting period 0.25 ml of glucose solution (25, 50 or 75% concentration) was administered by stomach tube. Exactly one hour later the animals were sacrificed and the contents of the alimentary tract (stomach, small and large intestines) washed into a volumetric flask. The glucose content of these washings was determined by the method of Somogyi(5). A group of 23 mice was fasted and then sacrificed without

TABLE I. Milligrams Glucose Absorbed per Hour.

Strain	No. of animals	Glucose conc., %	Glucose administered, mg	Glucose absorbed, mg
C_{57}	19	25	62	57
A	6	25	62	56
C_{57}	25	50	121	79
A	9	50	121	80
C_{57}	19	75	184	109*
A	25	75	184	97*

* $p = .05$.

TABLE II. Phosphatase Activity of Intestinal Homogenates.

	Solution administered	No. of animals	Phosphatase activity*
A.	0	8	28.7
	.5 ml 25% glucose	5	27.6
B.	0	10	21.4
	.5 ml 25% glucose	10	18.3

* Expressed as mg phenolphthalein liberated by homogenate from one entire small intestine.

glucose injection. The reducing power of the gastrointestinal washings was determined and used to correct the values for unabsorbed glucose found for the injected animals. The exact glucose content of the administered solution was determined each time an experiment was carried out. Phosphatase activity of the small intestine was determined by the method of Huggins and Talalay(6) using a homogenate prepared with distilled water. Control mice were fasted 25 hours before being sacrificed. The experimental animals, fasted 24 hours, received 0.5 ml of 25% glucose solution by stomach tube and were sacrificed one hour later. In pilot experiments (Group A, Table II) the entire small intestine with its contents was homogenized. In later work (Group B, Table II) the small intestine was washed out before being homogenized. A cytochemical study of alkaline phosphatase activity in the duodenum was carried out by the method of Gomori(7).

Results. The absorption data are summarized in Table I. The only significant strain difference in absorption rate was noted with the 75% glucose solution. It should be noted that increasing the concentration of the administered solution increased the absorption rate. Animals which had been raised on synthetic diets showed absorption rates identical with those raised on stock diet and are therefore not included in the table. Data obtained with mice of the C_3H strain are similarly omitted because they were virtually identical with those from A strain mice. Residual reducing materials present in the alimentary tracts of fasting mice were equivalent to 3.9 mg of glucose.

Alkaline phosphatase activity of the small intestine determined chemically was only slightly less in animals fasted and then fed 0.5 ml of 25% glucose than in animals sacrificed after fasting (Table II). Histochemically some slight differences were detectable. Fasted animals showed intense phosphatase reactions at the cuticular borders of the mucosal lining cells with considerable reaction in the Golgi zone. The rest of the cytoplasm gave a faint reaction which was more intense in the apical than in the basal portion of the cells. Administration of 0.5 ml of 0.9% NaCl solution by stomach tube did not change this picture markedly. Similar feeding of 25% glucose usually led to a diminution of phosphatase reaction in the Golgi zone and slight intensification of the cytoplasmic reaction in the apical portion of the cell. Administration of 60% glucose produced the same shift of cytochemically determined phosphatase but in addition caused marked desquamation and shrinkage of the surface epithelium. Administration of solutions of arabinose, glycine or corn oil produced little change from the picture seen in fasted, untreated animals. Mice fed corn oil showed, however, clearly visible phosphatase reaction in the lacteals.

Discussion. Since it has been shown in an earlier publication(3) that the intestinal absorption of glucose depends very largely upon the rate of gastric emptying, the strain difference in absorption of 75% glucose solutions (Table I) might be ascribed to the slower gastric emptying of such solutions in the A strain mice. This in turn is likely to be a reflection of the degree of inhibition which concentrated glucose solutions are known to induce (enterogastrone, nerve reflexes). Mice of the A strain might then be thought of as being somewhat more sensitive to such inhibition than mice of the C57 strain. If such strain differences are at all common, it is

conceivable that the animals used by Cori might have been so sensitive to inhibition that the progressive reduction in rate of emptying of the stomach with increasing concentration of solution fed might abolish the usual concomitant increase in amount absorbed.

Chemical determinations of phosphatase activity of intestinal homogenates showed that a considerable amount of the enzyme is present in the fluid contents of the small intestine (compare groups A and B, Table II). Oral administration of 25% glucose probably decreases the amount of enzyme in the tissues and increases the amount in the intestinal fluid. The effect is small. The cytochemical study, in agreement with the chemical findings, showed some translocation of the enzyme but no dramatic changes in concentration.

Conclusions. 1. Glucose absorption in the mouse has been studied. Increasing the concentration of administered solution results in an increase in the amount of glucose absorbed. 2. Glucose solutions of 75% concentration were absorbed somewhat more readily by mice of the C57 strain than by those of the A strain ($p = 0.05$). 3. Administration of 25% glucose solutions leads to some diminution of the phosphatase activity of the small intestine determined both chemically and cytochemically.

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Prolongation of Effects of Adrenal Cortical Secretion by Ascorbic Acid: Proposed Mechanism of Action.* (19533)

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Systematic studies in this laboratory indicated an intimate relationship between ascorbic acid and the activity of the pituitary-adrenal axis. The alarm reaction (eosinopenia, lymphopenia, and adrenal cholesterol depletion) characteristic of acute exposure to stressors (*e.g.* epinephrin, trauma) was prevented by ascorbic acid treatment of rats, mice and guinea pigs(1-4). Although those data suggested that under such conditions the vitamin probably plays a compensatory role similar to cortical hormones, other observations indicated that the similarity is not complete. It was shown that the protective action of the vitamin against cold stress was not present in adrenalectomized rats(5) and that ascorbic acid *per se* failed to alter the adrenal cholesterol level, the blood leukocyte pattern, or the blood glucose levels(4). Further observations indicated that ascorbic acid is capable of enhancing the gluconeogenic activity of small or large doses of cortisone in adrenalectomized mice. These observations suggest a "synergism" between cortisone and ascorbic acid(6), since the vitamin *per se* does not alter the liver glycogen content(4).

The present communication presents data indicating that ascorbic acid treatment of rats prolongs the leukocytic effects of injected cortisone or of endogenously secreted cortical hormones (induced by ACTH).

Materials and methods. Female Wistar rats weighing about 205 g were used in 2

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