antibody response to Rauscher virus in ET-treated mice is also described. The gamma-M antibodies, which appeared as early as the third day after a single antigenic stimulus, were readily detected by HA tests, but failed to precipitate with virus in immunodiffusion tests.

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Effect of pH on Active Transport of d-Glucose in the Small Intestine of Hamsters* (32786)

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Laszt(1) first noted that the absorption of glucose was dependent upon pH. While several studies on the effect of pH on glucose absorption have been reported over the years, the topic is still controversial. Groen(2) observed maximal glucose absorption in man at a pH of 7.0 while Goldenberg and Cummins (3) noted that glucose absorption was greater at alkaline pH than at acid pH. Ponz and Larralde (4), in the isolated jejunal loop of rats, found a plateau of optimal glucose absorption between pH 6.5 to 7.5. Broitman *et al.* (5) intubated intact rats and observed that glucose absorption increased as the pH was increased from 6.3 to 7.0.

A major difficulty in ascertaining an optimal pH for glucose absorption either in the intact animal or in isolated loops is the intraluminal pH adjustment by the small bowel. It is well recognized that in both man and animals, solutions introduced into the intestine undergo a change in pH towards neutrality, owing to the buffer capacity of intestinal secretions (3–7). The present study was therefore conducted using everted sacs in which the pH of the mucosal bathing solution could be maintained constant.

Material and Methods. Male golden hamsters weighing 84–120 gm were fasted for 24–48 hours, then killed by a blow on the head, decapitated and their blood drained. The sacs were immediately prepared as described by Wilson(8). Six to seven intestinal

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segments, each 4–5 cm in length, were obtained from the upper half of small intestine and placed in iced isotonic saline. Elapsed time prior to incubation was 15–19 min in all experiments. (Preliminary experiments showed that prolongation of this time led to decreased transport and considerable variation in duplicates). Following this temporary storage in iced saline, each sac was filled with isotonic saline and placed in the incubation medium.

All sacs were incubated in modified Krebs–Henseleit solutions containing 0.014 *M* phosphate buffer and 0.5 m*M*/liter *d*-glucose. Phosphate buffer was adjusted to give 6 different pH values: 4.80, 5.50, 5.90, 6.12, 7.26, and 7.82. Sodium concentration was adjusted to 154 meq/liter by addition of NaCl; osmolality varied from 260–270 milliosmols/liter. The relatively low glucose concentration (0.5 m*M*/liter) was used in order to produce adequate serosal-mucosal concentration gradients yet give measurable final mucosal concentrations. The pH of mucosal bathing fluid did not vary during the period of study.

Prior to incubation, all flasks were brought to 37°C, then incubated in a Dubnoff Incubator at 37°C for 15 min at 100 oscillations/min. Each everted sac, randomly selected by a table of random numbers, was placed in one of 6 different Erlenmeyer flasks containing 50 ml of each of the glucose–Ringer phosphate solutions and gased with 100% O_2. Evaporation within the 15-min incubation period was less than 2% (1.71 ± 0.098 SE).

At the end of the incubation period, the sacs were weighed, punctured, and the serosal fluids were drained into test tubes. After blotting on filter paper, the sacs were reweighed and the final serosal fluid volume was calculated. Glucose concentrations in mucosal and serosal fluids were determined by Dahlquist's (9) Tris (2-amino-2-hydroxymethyl propane-1, 3)-glucose-oxidase method.

Results. The water content of various parts of the small intestine, calculated by difference of wet and dry weight (15 hamsters) was 84.2 ± 0.05% SE. Dry weight was obtained by oven drying at 120°C for 24 hours. In order to see whether pH variation affected water content of the intestinal segment, numerous everted gut segments, 4–5 mm in length, obtained from the entire intestine, were randomized and 5 segments placed in 11 flasks containing glucose–Ringer phosphate solutions over the pH range 5.0–8.0. Final tissue water contents were similar at the various pH values and averaged 84.4 ± 3.0%.

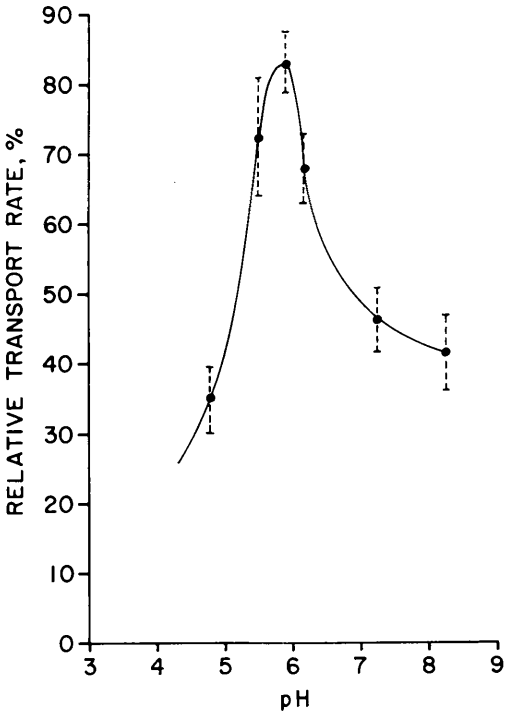

FIG. 1. Relationship between relative glucose transport rate and pH in 131 gut sacs from 25 animals. Vertically dashed lines represent ± 1 SE of the mean. At pH 4.80 relative transport rate was 35.0 ± 4.7% SE (25 animals); at 5.50, 72.9 ± 8.3% (10 animals); at 5.90, 83.7 ± 4.7% (25 animals); at 6.12, 68.1 ± 5.1% (24 animals); at 7.26, 46.2 ± 4.6% (23 animals); and at 7.82, 41.7 ± 5.9% (24 animals).

A total of 131 sacs (25 animals) were studied. In order to minimize variability between animals, results were expressed in each animal as a percentage of the highest value obtained among the 6 sacs. The value thus obtained for each sac is referred to as "relative transport rate." Mean values at 6 different pH levels are shown in Fig. 1.

The pH had a pronounced effect on glucose transport rate. Maximum transport occurred at about pH 5.9 with a sharp decrease at either more acid or more alkaline pH. In over

60% of animals, maximum transport occurred in the pH range 5.90–6.12. Over 90% of animals showed maximum transport between pH 5.50–6.50. Mean transport rates at pH 4.80 and pH 7.26–7.82 were significantly lower than at pH 5.50–6.12.

Comment. Although several studies, in both man and animals, have been concerned with the effect of pH on glucose absorption, the pH optimum has remained controversial. A major difficulty in such *in vivo* studies is the maintenance of constant intraluminal pH during the study period. It is now well recognized that intraluminal pH tends toward neutrality during perfusion, owing to the buffer capacity of enteric secretions. The present study was therefore performed in everted gut sacs in which pH could be precisely maintained.

In the present studies, pH was maintained by means of phosphate buffers. Although it is possible that phosphate per se may have specific effects on glucose transport, this seems unlikely since Laszt (1), Ponz and Larralde (4) and Darlington *et al.* (10) have shown that phosphate does not have measurable effects.

The data indicate that pH has a pronounced effect on glucose transport, with a pH optimum of about 5.9. It is concluded that intraluminal pH may be of considerable importance in the intestinal absorption of glucose.

Summary. The effect of pH on glucose transport was studied in 131 everted gut sacs of upper small bowel from 25 hamsters, using phosphate buffered solutions over the pH range 4.80–7.82. The relationship between pH and glucose transport rate revealed a bell-shaped curve with a pH optimum of 5.9. Under these conditions, in which intraluminal pH adjustment by the small bowel was eliminated, a pronounced effect of pH on glucose absorption was demonstrated.

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The Protective Effect of Guanylic Acid against Isoproterenol Toxicity* (32787)

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Kokas and co-workers (1) found that pretreatment of intact rats with a guanylic acid derivative decreased the cardiac hypertrophy produced during a chronic forced swimming experiment. More recently, work from this laboratory (2) showed that adrenalectomized rats given injections of guanylic acid (GA) had a significantly extended survival time after tourniquet shock. Our data also indicated (3) that this guanine nucleotide could suppress the cardiac hypertrophy, the elevation in plasma FFA and the decrease in liver glycogen which results from adrenalin injection. Similarly, guanylic acid has been shown by Sydow (4) to have significant cardiovascular effects. The mechanism of these effects of guanylic acid remains unknown.

To further elucidate the cardiovascular effects of these nucleotides, we investigated and compared the effect of chronic and acute administration of guanylic and adenylic acid

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