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INTESTINAL GROWTH AND IN VITRO TRANSPORT OF GLUCOSE IN THE RAPIDLY GROWING RAT[1]

M. A. TORAASON, National Institute for Occupational Safety and Health, Cincinnati OH 45226

G. L. WRIGHT, Department of Physiology, Marshall University School of Medicine, Huntington WV 25701

ABSTRACT. We examined the *in vitro* transport and utilization of glucose by the intestinal epithelium in rats during the period of rapid growth between 8 and 12 weeks of age. The dry weight per centimeter in length of jejunum increased in direct proportion to body weight during this interval. The absorption of glucose at the mucosal surface (per unit length of gut) did not change with growth. In contrast, the serosal secretion of glucose decreased indicating the utilization of glucose was elevated. It was further shown that the increase in glucose usage was highly correlated with the increase in intestinal dry weight that occurred during the four week interval. The data indicate the increase in intestinal tissue with growth did not result in a corresponding increase in the capacity of the intestinal epithelium to absorb glucose. We attributed the discrepancy in the transport of glucose at the mucosal and serosal surfaces to increased diversion of absorbed glucose for metabolism by intestinal tissue.

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INTRODUCTION

In normal circumstances, the metabolism of glucose provides the chief source of energy required for bodily functions. In comparison with the information available on the metabolism of the intact animal, relatively little is known concerning the metabolism and functional aspects of glucose metabolism in specific organ systems.

The small intestine actively absorbs and utilizes the basic metabolite D-glucose. Heat exposure (Toraason *et al* 1980), semi-starvation (Esposito 1967), fasting (Sanford and Smyth 1974), and diabetes (Anderson 1974, Schedl and Wilson 1971) produce alterations in intestinal hexose transport that could affect the well-being of the organism. Despite concern for the effects of experimental manipulation and diseased states on intestinal transport, little attention has been given to alterations of epithelial sugar absorption and metabolism that occur during normal growth.

In order to gain information concerning the changes in transport occurring during intestinal growth in the rat, we made *in vitro* measurements of mucosal absorption, serosal secretion, and intestinal utilization of the metabolite D-glucose during the period of rapid growth between 8 and 12 weeks of age.

METHODS AND MATERIALS

Male Sprague-Dawley rats were purchased from Charles Rivers Breeders at 6 weeks of age and housed within our facility until utilized in experiments. The animals were maintained at 23 ± 2 °C at a 14 hr light/10 hr dark photo-period. Tap water and Purina rodent chow were freely available.The animals were randomly divided into 3 groups for glucose transport measurements at 8, 10, and 12 weeks of age. The mucosal absorption of glucose, serosal secretion of glucose, intestinal utilization of glucose, and water transport by the jejunum were determined by the segmented flow perfusion technique of Fisher and Gardner (1974). Rats were anesthetized (stage III) with ether, and a midline incision was made in the abdomen. An inflow cannula was inserted approximately 1.0 cm posterior to the Ligament of Treitz. The intestine was then severed at the ileocecal valve and perfused with warm Krebs bicarbonate solution (Umbreit *et al* 1964) throughout its length. After flow established, the intestine was removed from its blood supply, allowed to hang free, and immediately severed 40 cm below the inflow cannula. An outflow

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cannula was inserted and the preparation washed in warm saline. The sample segment was then suspended in nylon netting within a water jacketed organ chamber that was gassed with moist 5% CO_2 in O_2 and maintained at 37±1 °C. The jejunum was perfused with slugs of oxygenated Krebs bicarbonate solution containing 5.0 mg/ml D-glucose separated by bubbles of 5% CO_2 in O_2. All solutions were preheated to 37 °C and perfusate flow rate was maintained at 4 ml/min by a variable speed peristaltic pump. Fifty min after commencing perfusion, three 10 min samples of luminel effluent and serosal secretion were collected. At the end of the experiments, jejunal segments were blown free of moisture, blotted with absorbent paper, weighed, and dried to constant weight at 110 °C. Transport rates were calculated as described by Fisher and Gardner (1964), and D-glucose concentrations were determined with a glucose auto analyzer. Body growth and transport data are shown as regression lines describing their relationship to intenstinal mass.

RESULTS

The body weights of the Sprague-Dawley rats increased by approximately 100% between 8 and 12 weeks of age (fig. 1). The increase in jejunal dry weight per centimeter of length was of the same magnitude and showed a high level of correlation ($r=0.98$, $P<0.001$) with body weight gains. Despite the doubling of jejunal mass, glucose absorption was unaltered (fig. 2a). By comparison, glucose utilization showed a linear increase with increasing jejunal mass ($r=0.72$, $P<0.01$) (fig. 2b), whereas serosal secretion of glucose exhibited an inverse relationship to intestinal dry weight ($r=0.56$, $P<0.05$) (fig. 2c). The net movement of water across the intestine showed no significant relationship to changes in jejunal mass (fig. 2d).

DISCUSSION

Through use of the segmented flow perfusion technique, a steady-state of glucose absorption was reached in 5 to 10 min, and 45 to 50 min of perfusion were required to achieve a steady-state of water and glucose secretion at the serosal surface. After about an hour of perfusion of the intestinal segment, a steady-state condition was attained with regard to glucose transport across the wall. At this point, the utilization of glucose by the tissue comprising the gut wall was calculated as the difference between mucosal absorption and serosal secretion of glucose. The value obtained reflected the active metabolism of glucose by the tissue rather than glucose accummulation since tissue concentrations of glucose did not increase during this interval (Fisher and

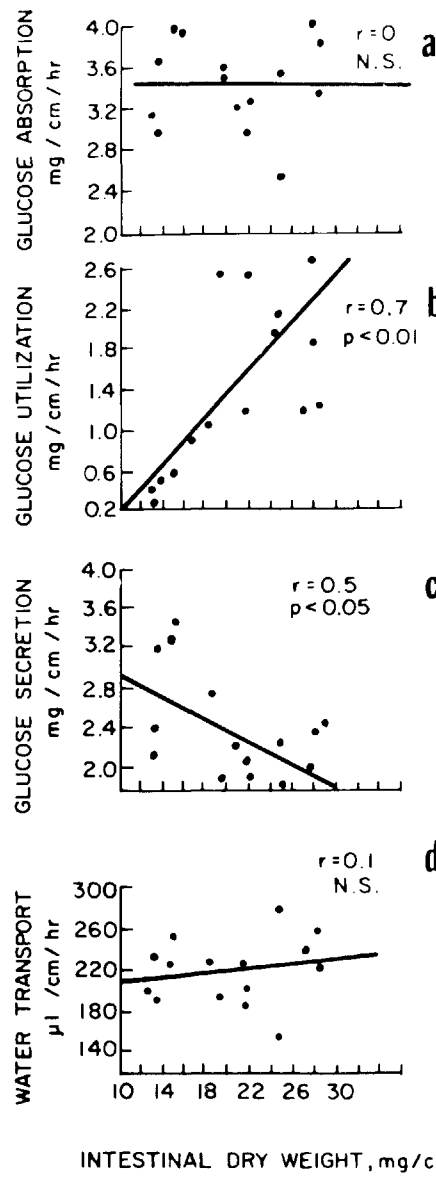

FIGURE 1. The relationship between the dry weight of intestine and body weight in rapidly growing Sprague-Dawley rats.

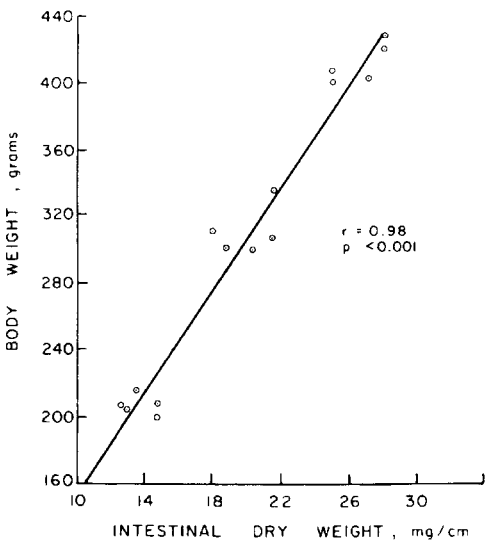

FIGURE 2. The glucose absorption, utilization, and secretion, and the net water movement across the wall of jejunal segments perfused *in vitro* shown in relation to the dry weight of intestine.

Gardner 1974). Our use of this method in examining glucose transport and metabolism in growing rats led to a number of interesting observations. It appeared that, despite a doubling of body and intestinal weight, *in vitro* glucose absorption at the mucosa and water transport across the wall were unchanged per unit length of jejunum. Furthermore, serosal secretion of glucose decreased during the period of rapid growth, which most probably reflected the increased diversion of absorbed glucose for metabolism by tissue in the gut wall of larger rats.

Fisher and Parsons (1953) examined intestinal sugar uptake in rats and deduced that relatively few epithelial cells were responsible for active transport of glucose, while all cells utilized glucose as a basic source of energy. The present findings suggest that glucose absorption is independent of intestinal growth and reflects the establishment of a fixed capacity for the absorption of glucose at an early age, agreeing with Calingaert and Zorzoli's finding (1965) that intestinal accumulation of 6-deoxy-D-glucose is maximum in 21 to 28 day-old mice. Crane (1977) conservatively estimated that the absorptive capacity of the small intestine is 5 to 10 times greater than necessary to maintain adequate caloric intake. The capacity of the jejunum of the rat to transport glucose relative to the basal metabolic requirement appears to be markedly reduced in 12 week old rats compared to younger and considerably smaller 8 week old rats, although this may not be expected to affect seriously the nutrition of the larger animal.

It is not clear whether the increase in jejunal dry weight during the growth of the animal represents an increase in villous or crypt cell mass or an increase of muscle mass. The clarification of this question in future work will provide considerable insight into the cellular component responsible for increased glucose utilization and may explain the lack of change in glucose absorption during intestinal growth. In addition, it is not certain what the effects of different glucose concentrations in the luminal contents might have on intestinal transport activity in the growing animal. The perfusate concentration of glucose used in the present study was relatively high, and it will be interesting in future work to determine if a similar pattern of absorption and secretion with growth can be obtained with low levels of glucose in the luminal perfusate.

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