EFFECT OF INSULIN DEFICIENCY ON THE TRANSPORT OF GLUCOSE BY RAT SMALL INTESTINE

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There have been a number of reports on the effect of diabetes induced by alloxan on the transport of sugars by rat small intestine [1–6]. The interpretation of these reports has been complicated by the toxic side effects and metabolic disturbances associated with the use of alloxan [7]. In the present studies, insulin deficiency was induced by the injection (65 mg/kg body weight, i.v.), one week before the experiment, of the diabetogenic antibiotic streptozotocin [8], or by the injection (i.v.) of 1 ml anti-insulin-serum [9], one hour before the experiment. Everted sacs were prepared from the upper and terminal ileum of normal and insulin deficient rats (280–320 g) by the method of Wilson and Wiseman [10]. The sacs (6 from each region) were filled to a standard distension with Krebs Henseleit [11] bicarbonate buffer (pH 7.4) containing glucose (approx. 1 mg/ml) and each was incubated in 10 ml of the same medium in a 50 ml conical flask. The medium, cooled in ice, was kept gassed with 95% O_2 and 5% CO_2 prior to the experiment. The flasks were stoppered and shaken for 30 min at 37°C. The sacs were then removed, blotted, and opened, and their contents (serosal fluid) and the incubating media (mucosal fluid) analysed for glucose by a modified glucose oxidase method [12].

Blood glucose levels in insulin deficient animals used for experiment were all above 250 mg/100 ml. In some of the experiments with these animals, insulin (100 mU/ml) was added to both the mucosal and serosal fluid of alternate sacs in each region prior to incubation.

In the following discussion, it is assumed that the development of a final concentration ratio of greater than unity is evidence for the presence of an active process of sugar absorption [13]. Insulin deficiency increased the final concentration ratio of glucose developed by sacs in both regions. In the case of the upper ileum, these results agree with those reported for alloxan induced diabetes [1–6]. The effect was particularly apparent in the terminal ileum, where ratios significantly greater than one were obtained, whereas normally sacs from this region are incapable of accumulating glucose against its concentration gradient [14].

Jervis and Levin [15] found that the hyperphagia of chronic alloxan diabetes in rats, induced an increase in the size and weight of the intestine at 6–12 months. Increased sugar transport might arise under these conditions as a result of intestinal hypertrophy but this possibility is precluded in the present experiments with anti-insulin-serum, since rats were used only one hour after injection. Insulin at high concentration (100 mU/ml) in the incubating media failed to restore the transport of glucose to normal, so confirming the findings of Aulsebrook [6] with intestine of alloxan diabetic rats. This failure was particularly striking in the terminal ileum rendered insulin deficient with anti-insulin-serum, where the induced final concentration ratios of greater than unity, were unaffected by the presence of insulin. It is possible that the insulin molecule is unable to penetrate the epithelial cell or that in doing so, it is hydrolysed by the endogenous proteolytic enzymes. Alternatively the observed effects of insulin deficiency on active transport may arise from secondary metabolic disturbances involving the energy supply for transport processes in the small intestine. It is concluded that the absorption of glucose by rat small intestine, *in*

Table 1
Effect of insulin deficiency on the transport of glucose by sacs of everted rat small intestine.

	Initial concn. of glucose in both serosal and mucosal fluids (mM)	Final concn. of glucose in serosal fluid (mM)	Final concn. of glucose in mucosal fluid (mM)	Glucose final concentration ratio (serosal/mucosal)
Terminal ileum				
Normal	5.89	4.34 ± 0.26	5.38 ± 0.10	0.80 ± 0.04 (24)
Streptozotocin diabetes	5.89	8.01 ± 0.27	5.57 ± 0.07	* 1.45 ± 0.06 (35)
Streptozotocin control minus insulin	6.22	7.34 ± 0.18	5.97 ± 0.16	* 1.24 ± 0.06 (6)
Streptozotocin plus insulin (*in vitro*)	6.22	7.84 ± 0.30	5.87 ± 0.18	* 1.34 ± 0.04 (6)
Anti-insulin-serum control minus insulin	5.71	6.29 ± 0.43	5.33 ± 0.09	* 1.18 ± 0.08 (12)
Anti-insulin-serum plus insulin (*in vitro*)	5.71	6.50 ± 0.51	5.13 ± 0.08	* 1.27 ± 0.10 (12)
Upper ileum				
Normal	6.07	7.75 ± 0.21	4.43 ± 0.10	1.71 ± 0.04 (24)
Streptozotocin diabetes	6.92	11.20 ± 0.41	4.39 ± 0.13	* 2.55 ± 0.08 (18)
Streptozotocin control minus insulin	6.22	10.71 ± 0.67	5.16 ± 0.20	* 2.08 ± 0.01 (6)
Streptozotocin plus insulin (*in vitro*)	6.22	11.38 ± 0.38	5.41 ± 0.18	* 2.10 ± 0.03 (6)
Anti-insulin-serum	6.28	9.60 ± 0.29	4.34 ± 0.12	* 2.22 ± 0.07 (11)

Values are ± S.E.M. with the number of sacs in parentheses. * denotes P values $\leqslant 0.05$ compared with normal intestine. Sac length about 3 cm. Initial serosal volume 0.5–1.0 ml. Initial mucosal volume 10 ml. Gas phase 95% O_2 and 5% CO_2. Incubation period 30 min, temperature 37°C. 70 oscillations/min, amplitude 5 cm. Initial glucose serosal/mucosal concentration ratio was 1.00.

vitro, is stimulated in experimental insulin deficiency. Studies are in progress to elucidate the mechanism of this stimulatory response.

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