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Variation in tissue resistance in rat small intestine: Its relationship to observed potential changes

In a previous paper[1] it was shown that the increase in the potential difference between the mucosal and serosal surfaces of rat small intestine, in the presence of actively transported amino acids in the mucosal bathing fluid, was greatest in the ileum and smallest in the proximal jejunum. Similar observations were made both *in vivo* and *in vitro*. The same study, as well as many others[2], suggests that the change in potential difference (PD) is proportional to the rate of amino acid transfer. Varying patterns of amino acid absorption along the length of the intestine have been reported[3] but the differences do not appear to account for the pattern of PD changes observed. It was suggested[1] that either the stoichiometry between amino acid and ion transport varied along the intestine or the results could be due to differences in tissue resistance.

The present study was designed to choose between these alternatives. We have examined the effects of L-histidine on electrical parameters of the small intestine and also compared histidine transfer in the mid-intestine and ileum. Histidine was chosen because it is very little metabolised during transfer[4] and gives a comparatively large maximum PD[1].

Abbreviation: PD, potential difference.

The techniques used to measure PD, both *in vivo* and *in vitro*, and short-circuit current were those previously described[5,6]. Transfer of histidine was assessed as "mucosal transfer" (the total amount appearing in the gut wall and serosal fluid) using a ^{14}C-labeled tracer in the everted sac preparation[7]. A preliminary measurement showed that the serosa to mucosa flux was less than 5 % of the mucosa to serosa flux under the conditions of the experiment and the latter thus constitutes a good estimate of the net flux. The concentration of L-histidine chosen (40 mM) was the highest used in the PD measurements and was expected to bring the transfer system close to saturation.

In one set of experiments with 30-min incubation periods, using intestines from 9 animals, 44 ± 3 μmoles of histidine were transferred by the mid-intestine and 27 ± 1 μmoles by the ileum. The sacs represented the middle and terminal fifth of the combined jejunum and ileum[8]. Thus, although it is always difficult to choose an appropriate parameter of transfer, there is no evidence of a larger transfer in the ileum.

Changes in the PD across the wall of the intestine were determined for each of a range of concentrations between 2.5 and 40 mM mucosal L-histidine, using 6 sacs for each concentration, and allowance was made for osmotically induced potentials as previously described[1]. In agreement with this earlier study, L-histidine gave a maximum PD change of around 5 mV in mid-intestine, using the *in vitro* preparation. In the ileum, the initial PD changes were much larger but were rather poorly maintained. In a previous study of hexose-induced potentials[5] similar difficulties were experienced with preparations of ileum. For this reason, comparisons between mid-intestine and ileum were made using the *in vivo* technique. These studies gave PD maxima of 5 mV in mid-intestine (the same as *in vitro*) and 9.5 mV in the ileum. In both regions, the apparent K_m for the PD change was 20 mM, double the value in the *in vitro* preparation. Both the maximum PD change and the apparent K_m were estimated from a plot of 1/PD change against 1/concentration as previously described[1]. A similar difference was previously observed for L-alanine. These experiments confirm that amino acids produce much larger PD changes in the ileum.

The values obtained from measurements of tissue resistance are given in Table I. The presence of maximal amounts of histidine or mannitol in the mucosal bathing medium had no detectable effect on the tissue resistance, but the resistance of the ileum was about double that for the mid-intestine. The lack of effect of transferred substrate on tissue resistance is in agreement with earlier findings for glucose[6].

TABLE I

TISSUE RESISTANCE FOR EVERTED MID-INTESTINE AND ILEUM OF THE RAT

Results as mean ± S.E. (number of experiments in parentheses).

Mucosal medium	*Resistance (Ω/cm length of gut)*	
	Mid-intestine	*Ileum*
Krebs bicarbonate buffer	14.4 ± 2.0 (6)	27.5 ± 2.9 (6)
+ 40 mM mannitol	14.7 ± 1.6 (4)	30.1 ± 1.2 (4)
+ 40 mM L-histidine	15.2 ± 2.1 (3)	27.0 ± 4.4 (3)

Several authors have noted the inherent dangers of measuring changes in PD rather than short-circuit current, and changes in the ionic composition of the bathing media have been shown to alter the tissue resistance of rat intestine[9]. This study shows that similar problems arise when comparing electrical changes in different regions of the small intestine. Nevertheless, it is difficult to interpret short-circuit current measurements in situations in which ion fluxes are far from the steady state[10], and it is impossible to make valid measurements *in vivo*[11]. Under these conditions PD measurements can still provide useful information.

The present work confirms the previous observation of larger amino acid evoked PD changes in the ileum than jejunum which cannot be explained by differences in rates of amino acid transfer. However, it seems likely that the differences can be attributed to differences in tissue resistance without the need to invoke a difference in the stoichiometry between amino acid and ion transport.

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