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Glucose depolarizes villous but not crypt cell apical membrane potential difference: a micropuncture study of crypt–villus heterogeneity in the rat

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Brush-border membrane potentials and fractional resistances have been recorded from enterocytes at different points along the crypt-villus axis of rat ileum in vitro. Microelectrode impalements were obtained under visual control and brush-border membrane potentials were higher in crypt than in villous cells (-57 ± 1.6 against -50 ± 1.6 mV referred to the mucosal side). Replacing mannitol with D-glucose in the mucosal perfusate resulted in a rise in transmural potential difference (0.5 ± 0.17 to 1.0 ± 0.21 mV ($n = 37$)) and apical membrane potential was depolarized. This occurred consistently only in the upper two-thirds of the villus (-54 ± 1.7 to -47 ± 2.3 mV ($n = 17$)) and not in crypt cells (-56 ± 2.6 to -57 ± 2.4 mV ($n = 10$)) or at the crypt-villus junction. The glucose-induced apical membrane depolarization in villous enterocytes was blocked by phlorizin, a competitive inhibitor of sodium-dependent glucose uptake (-50 ± 2.1 to -53 ± 2.8 mV ($n = 9$) in the presence of phlorizin and glucose). Transmural resistance, R_t, and fractional resistance, F_R, were unaltered by glucose (61 ± 3.4 to 61 ± 3.5 $\Omega \cdot cm^2$ ($n = 50$)) and (0.60 ± 0.06 to 0.57 ± 0.06 ($n = 17$)). This micro-puncture technique provides direct evidence for functional differentiation along the crypt-villus axis and indicates that active electrogenic accumulation of glucose is confined to villous epithelium.

Introduction

It is generally assumed that absorption from the small intestine largely occurs on the villi while secretion is derived from the crypts but the evidence upon which this is based is largely circumstantial [1] Recent studies have improved our understanding of the differentiation of transport function of migrating enterocytes in small intestine [2,3] In neonatal and adult intestinal epithelium micropuncture measurements of membrane potentials were correlated with enterocyte differentiation and the results have had implications for the site of absorption and secretion along the crypt-villus axis [4,5]

The uptake of glucose across the brush-border membrane is linked to Na^+ entry by an electrogenic active transport process [6,7] and this is associated with a decline in brush-border membrane potential in some epithelia [8–10] We have, therefore, examined the electrical behaviour of individual enterocytes in crypt and villus in response to glucose, in order to gain further insight into the relationship between Na^+-dependent glucose uptake and enterocyte position on the crypt-villus axis The experiments described below were carried out preliminary to a study on mechanisms of secretion in the small intestine, and for this reason the ileum was chosen as the most appropriate segment

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Materials and Methods

Adult male Sprague-Dawley rats, weighing 150–200 g and maintained on standard diet with free access to drinking water, were killed by cervical dislocation A 15 cm length of ileum was removed, drawn over a glass rod moistened with buffered saline solution, and stripped of its external muscle A small piece of stripped intestine was then mounted on a perspex half-chamber The tissue was fixed horizontally, with slight stretching, mucosal side up, by means of a ring of UHU Supalok-3 quick curing adhesive piped onto a sheet of parafilm covering the area surrounding the central hole in the chamber This central hole was covered with a piece of stiff nylon mesh to provide additional support for the tissue The chamber was fixed to the stage of a conventional Zeiss-Jena microscope (Microinstruments, Oxford) The use of a powerful quick-setting adhesive obviated the need for clamping the tissue The preparation was bathed on both sides by buffered saline solutions of identical composition at 30 °C, pre-warmed and gassed with 95% O_2/5% CO_2 to pH 7 4, and continuously perfused by gravity and negative hydrostatic pressure The choice of temperature was dictated by the tendency of the preparation to increase mucus production at higher temperatures, the mucus being a hindrance to visualization of the microelectrode tip The tissue was also apt to deteriorate more rapidly The presence of stopcocks anterior to the chamber allowed manual solution changes to be carried out on either side of the preparation during individual cell impalements The surface area of the tissue exposed to the perfusate solutions was 0 5 cm^2

Transmural potential difference (V_t) was measured by means of Agar/0 5 mol l^{-1} KCl bridges in series with paired calomel half cells, and recorded on a high impedance electrometer with an output to a chart recorder Transmural resistance (R_t) was determined from the voltage drop across the tissue in response to a bipolar rectangular d c (direct current) pulse of 50 μA and 1 s duration, supplied by a constant current pulse generator, and was corrected for the resistance of the solution between the Agar bridges All electrical potential measurements were made under open-circuit conditions, and were referred to the mucosal side of the preparation The fractional resistance, F_R, defined as the ratio of the change in brush-border (apical) membrane potential (V_a) to the change in V_t, i e $\Delta V_a/\Delta V_t$, in response to a single current pulse, was determined during cell impalements This allowed the relative resistance of the apical membrane to be determined, while also giving a good indication of the validity of an impalement

Microelectrodes were manufactured from 'kwik-fil' borosilicate glass capillaries of 1 mm outer diameter (Clark Electromedical Supplies, Reading) pulled on a Campden Instruments horizontal micropipette puller The pipettes were back-filled with 0 5 mol/l KCl, and the resulting microelectrodes had a tip resistance of 100–200 $M\Omega$ Impalement of selected morphological regions of the ileum was achieved as follows the mucosal surface of the tissue was viewed under the microscope fitted with a 40 × water-immersion objective to give a total magnification of 500 × As the tissue was moderately stretched when mounted on the chamber, the crypt openings were often clearly visible, Nomarski optics were available to highlight these and other features The microelectrode tip was guided by means of a motorized micromanipulator (Geb Marzhauser, Wetzlar) into the field of view Enterocytes at specific regions on the villus, which had a leaf-like appearance when viewed from above, could be impaled by focussing down onto or beyond the tip of the villus, and then bringing the electrode tip into focus before advancing the electrode into a cell The distance travelled by the electrode tip in the vertical plane could be assessed from the micrometer readings on the micromanipulator The microelectrode was angled at about 30° to the plane of the tissue To impale crypt cells, the shank of the microelectrode was guided carefully between adjacent villi, keeping the tip in focus, until it lay directly above and close to the opening of a crypt The microelectrode was then lowered vertically so that the tip entered the crypt opening The cells surrounding the crypt opening were easily distinguishable, and could be impaled without much difficulty, those within the crypt, lining its lumen, could not be seen From this region it was possible, nevertheless, to obtain stable impalements of relatively long duration

Microelectrode recordings were judged acceptable if they fulfilled the following criteria (1) abrupt negative deflection of the potential on entering a cell, (2) establishment of a stable potential difference equal or more negative than the value of the initial potential deflection This took from 30 seconds to more than 3 minutes, and may reflect the time taken for the membrane to seal around the electrode tip It was, therefore, particularly important to reject impalements where the measured potential difference declined to a value lower than the initial deflection, as such impalement profiles could result from inadequate sealing, (3) the potential difference remaining stable for at least 30 seconds, or subsequently until altered by an experimental manoeuvre, (4) the transmembranal potential deflection due to transmural current pulses did not diminish appreciably with time, which might indicate impalement damage, (5) abrupt return of the potential difference to the initial baseline value ± 1 mV when the microelectrode tip was withdrawn from the cell

For the acquisition of impalements in the presence of mannitol, the crypt-villus axis was arbitrarily subdivided into six regions comprising three villus, two crypt and one intermediate region These were the tip, middle and basal third of the villus (TV, MV and BV, respectively), the crypt (C) and the single layer of cells surrounding the crypt opening (CS), and finally the crypt-villus junctional region (CVJ) For experiments in which mannitol was replaced with D-glucose, results from the upper villus regions (TV and MV) were amalgamated, as were those from the two crypt regions (CS and C)

Buffered saline solutions contained, in mmol/l NaCl, 120, $NaHCO_3$, 20, K_2HPO_4, 2 4, KH_2PO_4, 0 4, $CaCl_2$ $2H_2O$, 1 2, $MgCl_2$ $6H_2O$, 1 2, and mannitol, 10 In glucose-containing solutions, the mannitol was replaced by 10 mmol/l D-glucose All chemicals listed above were of reagent grade Phlorizin dihydrate was obtained from Sigma (Poole, Dorset)

The means of experimental groups are given with their S E and statistical analysis is by paired or unpaired Student's 't' test, as appropriate

Results

Enterocytes in the six designated regions of the crypt-villus axis were impaled under visual control and the results of apical membrane potentials and fractional resistances for tissues perfused with buffered saline are shown in Table I Apical membrane potentials (V_a) in crypt epithelial cells exceeded those in all other regions by up to 7 mV, but the difference was statistically significant only between crypt and mid villus The fractional resistance (F_R) values exceeded 0 50 for all regions under investigation indicating that the greater proportion of the transcellular resistance resides in the brush-border membrane

We attempted to assess the effects of D-glucose on V_a and F_R during single impalements and the results are illustrated in two figures of which the first shows the responses of the apical and transmural potential difference in villus and crypt epithelium, respectively, to the addition of glucose during single impalements (Fig 1)

Glucose (10 mmol) was introduced in place of mannitol first to the mucosal side of the preparation A rapid and well-marked depolarization of V_a occurred which was apparent occasionally in cells at the base of the villus ($-58 \pm 2\,6$ to $-54 \pm 3\,4$ mV, P = n s), but developed into a consistent

TABLE I

DISTRIBUTION OF BRUSH-BORDER MEMBRANE POTENTIALS AND FRACTIONAL RESISTANCES ALONG THE CRYPT-VILLUS AXIS IN THE PRESENCE OF 10 mmol/l MANNITOL

Brush-border membrane potentials (V_a) and fractional resistances (F_R) were recorded from six arbitrarily divided crypt-villus regions as shown The values of V_a and F_R represent steady-state determinations in the presence of 10 mmol/l mannitol Statistical comparison was by unpaired Student's 't'-test mid villus differs from crypt (V_a) at $P < 0\,005$ P = n s for all other paired groupings Number of observations in parentheses

	V_a (mV)	F_R
Villus tip	−50 ± 3 1 (14)	0 57 ± 0 04 (14)
Mid villus	−50 ± 1 6 (42)	0 55 ± 0 03 (42)
Base villus	−52 ± 2 1 (20)	0 54 ± 0 04 (19)
Crypt-villus junction	−54 ± 2 3 (15)	0 58 ± 0 04 (14)
Crypt opening	−52 ± 2 8 (18)	0 60 ± 0 04 (17)
Crypt	−57 ± 1 6 (17)	0 62 ± 0 03 (17)

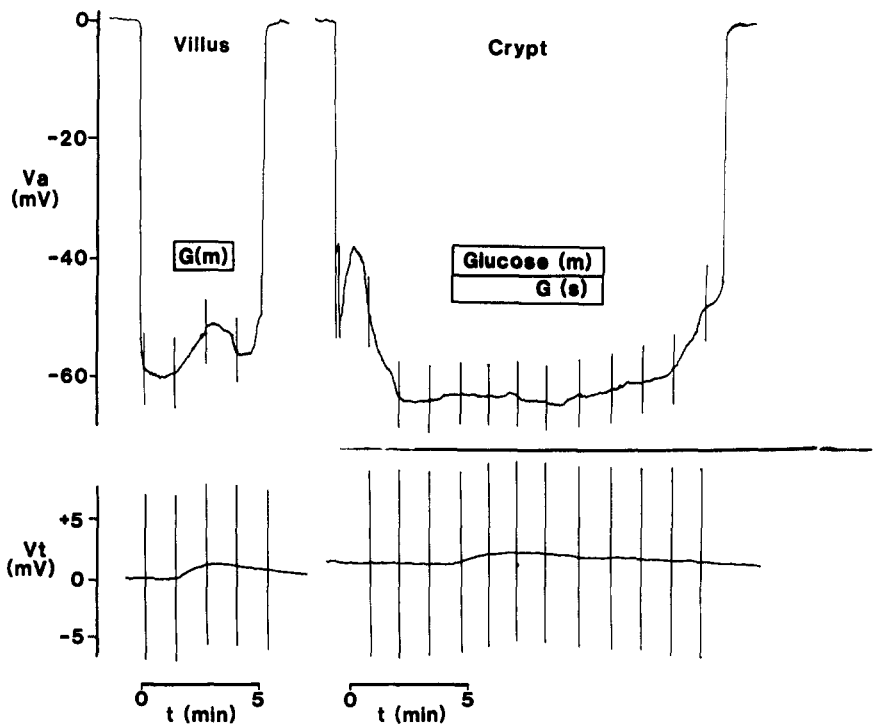

Fig 1 Effect of 10 mmol/l D-glucose on apical membrane potential (V_a) and transmural potential difference (V_t) in villus and crypt epithelia during single impalements Glucose was added isosmotically in exchange for mannitol initially to the mucosal perfusate (m), during the impalement of a crypt cell glucose was added subsequently to the serosal perfusate (s) The bipolar deflections in V_a and V_t represent the voltage changes elicited by bipolar DC current pulses used in the determinations of tissue resistance (R_t) and fractional resistance (F_R) Potential differences are given in mV, with the polarity referred to the mucosal side

observation only in the middle third and tip villus areas ($-54 \pm 1\,7$ to $-48 \pm 2\,1$ mV, $P < 0\,001$) Glucose was then substituted for mannitol on the serosal side but produced no further change (Fig 2) We have as yet no explanation for the comparatively wide scatter of unstimulated apical membrane potentials from villus epithelial cells as against potentials recorded from crypt epithelium

TABLE II

EFFECT OF D-GLUCOSE ON BRUSH-BORDER MEMBRANE POTENTIALS IN FOUR CRYPT-VILLUS REGIONS

The results show the mean values ± S E of the observations shown individually in Fig 2, including additional observations on the effects of mucosal glucose on upper villus membrane potentials, and bilateral glucose on potentials from all four regions of the crypt-villus axis The three ranks of data represent statistical comparison by paired Student's 't' test, in which the sequential effects of mucosal glucose, bilateral glucose and a final post-glucose period are compared to the initial glucose-free control values

	Upper villus	Base villus	Crypt-villus junction	Crypt
Control	$-54 \pm 1\,7$ (17)	$-58 \pm 2\,6$ (7)	$-63 \pm 1\,8$ (5)	$-56 \pm 2\,6$ (10)
10 mM glucose (m)	$-48 \pm 2\,1$ (17)	$-54 \pm 3\,4$ (7)	$-63 \pm 1\,3$ (5)	$-57 \pm 2\,4$ (10)
	$P < 0\,001$	n s	n s	n s
Control	$-52 \pm 2\,5$ (7)	$-57 \pm 2\,4$ (8)	$-55 \pm 3\,8$ (7)	$-58 \pm 2\,7$ (9)
10 mM glucose (m + s)	$-46 \pm 3\,3$ (7)	$-51 \pm 3\,4$ (8)	$-56 \pm 3\,3$ (7)	$-59 \pm 2\,7$ (9)
	$P < 0\,02$	n s	n s	n s
Control	$-55 \pm 3\,0$ (8)	$-55 \pm 2\,6$ (6)	$-53 \pm 4\,7$ (5)	$-58 \pm 3\,8$ (7)
Post-glucose (mannitol)	$-52 \pm 2\,5$ (8)	$-53 \pm 2\,2$ (6)	$-56 \pm 4\,4$ (5)	$-58 \pm 3\,5$ (7)
	n s	n s	n s	n s

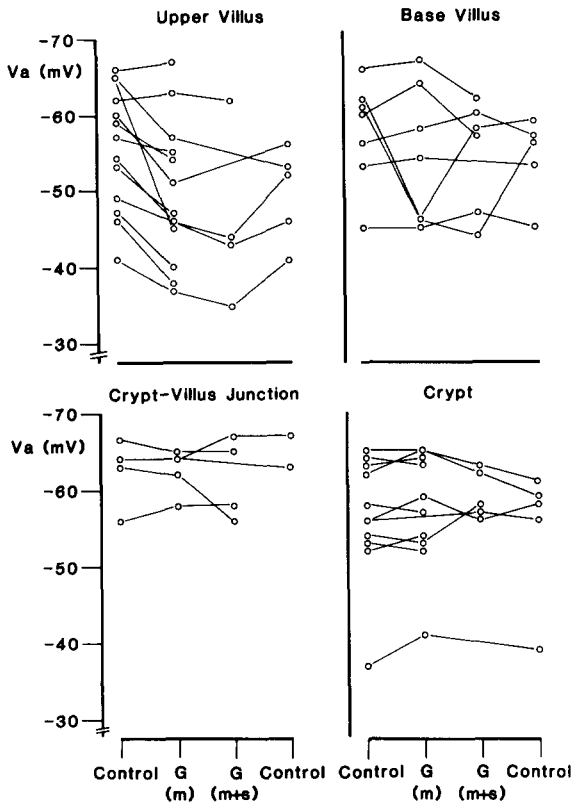

Fig 2 Effect of uni- and bilateral glucose on brush-border membrane potentials along the crypt-villus axis Each group of observations represents individual impalements from four designated regions upper and base villus, crypt-villus junction, and crypt The values recorded during a single impalement in a maximum four-stage sequence are joined by unbroken lines The first and last stages represent control periods during which the preparation was bathed on both sides by buffered HCO_3 saline containing 10 mmol/l mannitol During the second stage mannitol was replaced with 10 mmol/l D-glucose on the mucosal side, and during the third stage glucose was present on both sides V_a, apical membrane potential, G, glucose addition, m, mucosal side application, m+s, mucosal plus serosal side application

It is for this reason that Fig 2 shows the results of individual impalements with serve as their own controls

In contrast to the effects in villus epithelial cells, glucose applied either to the mucosal or subsequently the serosal aspect of the tissue had no significant effect on V_a in the crypt regions where V_a in the absence and presence of glucose was $-56 \pm 2\,6$ mV and $-57 \pm 2\,0$ mV ($P =$ n s) respectively, or at the crypt-villus junction ($-63 \pm 1\,8$ to $-63 \pm 1\,3$ mV, $P =$ n s) (Fig 2, Table II)

Luminal glucose caused a rise in transepithelial potential difference from $0\,5 \pm 0\,17$ to $1\,0 \pm 0\,21$ mV, $P < 0\,001$, becoming more positive with respect to the mucosal reference (Table III) The rise in V_t, however, was always much smaller than the depolarization of V_a (ΔV_t 0 5 mV against ΔV_a 6 mV, Tables II and III), suggesting a parallel depolarization of the basolateral membrane potential (V_b) most likely brought about by the effects of electrical coupling via the very low resistance extracellular shunt pathway With glucose subsequently present in both mucosal and serosal perfusate solutions, no further modification in the rise in V_t was observed When glucose was finally washed out by mannitol-containing perfusate on both sides of the tissue, V_t slowly returned towards prestimulated values, but remained slightly elevated, at the point at which V_a had returned to its prestimulated level (Table III)

The effects of glucose on transmural resistance (R_t) were negligible ($63 \pm 5\,0\ \Omega$ cm^2 before, and $65 \pm 5\,5\ \Omega$ cm^2 after glucose, $P =$ n s , Table III), making a change in the extracellular shunt conductance an unlikely possibility, since in a leaky epithelium the transepithelial conductance will be determined chiefly by the extracellular conductance

TABLE III

EFFECT OF 10 mmol/l D-GLUCOSE ON TRANSMURAL POTENTIAL DIFFERENCE (V_t) AND TRANSMURAL RESISTANCE (R_t)

V_t and R_t (means ± S E) in the presence of glucose on the mucosal side and thereafter on both sides of the tissue are compared to values in control medium containing mannitol Pre- and post-glucose control values are likewise compared as in Table II Statistical comparison is by paired Student's 't' test Number of observations in parentheses

	V_t (mV)	R_t (Ω cm^2)
Control (mannitol)	0 5 ± 0 17 (37)	61 ± 3 4 (50)
+ 10 mM glucose (m)	1 0 ± 0 21 (37)	61 ± 3 5 (50)
	$P < 0\,001$	n s
Control	0 4 ± 0 27 (17)	63 ± 5 0 (26)
+ 10 mM glucose (m + s)	0 9 ± 0 30 (17)	65 ± 5 5 (26)
	$P < 0\,005$	n s
Control	0 7 ± 0 30 (12)	65 ± 5 6 (22)
Post-glucose (mannitol)	1 1 ± 0 32 (12)	66 ± 6 2 (22)
	$P < 0\,005$	n s

To demonstrate that the effect of V_a and V_t attributed to glucose was not an artifact of the mechanical changing of solutions, the mucosal or serosal perfusate was occasionally switched to a solution identical in composition Apart from an occasional small transient fluctuation in V_a there was no significant effect on V_a or V_t The changes in V_a were readily reversible on return to nominally glucose-free conditions (Fig 2 and Table II)

Fractional resistances were similar to those determined in the initial presence of 10 mmol/l mannitol (Table I), and were not significantly modified by D-glucose suggesting that Na^+-coupled glucose uptake across the apical membrane is not mediated through electrodiffusive ion movement The biggest change occurred in enterocytes from the villous tip region, where F_R fell from $0\,71 \pm 0\,08$ to $0\,65 \pm 0\,07$ after the addition of glucose ($n = 7$), but the change was not statistically significant

Experiments were then performed to demonstrate that the effects of glucose on V_a and V_t are related to the stimulation of an electrogenic transport process involving Na^+-dependent glucose uptake across the brush-border membrane as the initial step In these experiments enterocytes from the middle region of the villus were impaled and the tissues subsequently exposed to glucose (10 mmol/l) on the mucosal side V_a was reduced from $-54 \pm 1\,7$ mV to $-47 \pm 2\,3$ mV ($n = 17$) and V_t became more positive by 0 5 mV in the presence of glucose After the changes in V_a and V_t had peaked, the inhibitor of active glucose uptake, phlorizin dihydrate (10^{-4} mol/l), was added to the mucosal perfusate Phlorizin had no significant effect on V_a or V_t in the absence of glucose V_a was $-43 \pm 0\,9$ mV in mannitol Ringers, and $-42 \pm 4\,2$ mV after addition of 10^{-4}mol/l phlorizin ($n = 4$), $P =$ n s , while V_t was, respectively, $-2\,5 \pm 0\,43$ mV and $-2\,8 \pm 0\,42$ mV ($n = 4$), $P =$ n s There was no change in R_t ($46 \pm 4\,9$ Ω cm^2 before and $45 \pm 6\,2$ Ω cm^2 after phlorizin, $n = 4$) Phlorizin, however, inhibited the electrical changes induced by glucose The depolarization of V_a was reversed, occasionally to more negative values than under control conditions ($-50 \pm 2\,1$ mV in mannitol Ringers, and $-53 \pm 2\,8$ mV in the presence of glucose and phlorizin, $P =$ n s) The rise in V_t induced by glucose was also abolished Neither glucose nor phlorizin had any significant effect on F_R ($0\,64 \pm 0\,08$ to $0\,63 \pm 0\,08$ ($n = 9$)) or R_t ($40 \pm 3\,5$ to $41 \pm 3\,5$ Ω cm^2 ($n = 9$)) The results of these experiments are summarised in Table IV, and are consistent with the

TABLE IV

ACTION OF GLUCOSE ON TRANSMURAL POTENTIAL DIFFERENCE (V_t), BRUSH-BORDER MEMBRANE POTENTIAL (V_a), FRACTIONAL RESISTANCE (F_R) AND TRANSMURAL RESISTANCE (R_t) IN MID VILLUS ENTEROCYTES IN THE PRESENCE AND ABSENCE OF PHLORIZIN

Mannitol was replaced with 10 mmol/l glucose in the mucosal perfusate, and subsequently 0 1 mmol/l phlorizin was added, also to the mucosal perfusate, before returning to control mannitol solutions The experimental manouevres were carried out sequentially during single impalements, and the results in the form of means ± S E represent steady-state values in the case of V_a and V_t Statistical comparisons, by paired Student's 't' test, were made between stages 1 and 2, 1 and 3, and 1 and 4 of the four-stage sequence mannitol, glucose, glucose + phlorizin, mannitol Number of observations in parentheses

	V_t (mV)	V_a (mV)	F_R	R_t (Ω cm^2)
Control (mannitol)	0 3 ± 0 21 (15)	−54 ± 1 7 (17)	0 60 ± 0 06 (17)	44 ± 3 6 (16)
+ 10 mM glucose (m)	0 8 ± 0 29 (15)	−47 ± 2 3 (17)	0 57 ± 0 06 (17)	43 ± 3 2 (16)
	$P < 0\,005$	$P < 0\,001$	n s	n s
Control	−0 3 ± 0 19 (9)	−50 ± 2 1 (9)	0 64 ± 0 08 (9)	40 ± 3 5 (9)
+ 10 mM glucose (m)				
+ 0 1 mM phlorizin (m)	−0 4 ± 0 22 (9)	−53 ± 2 8 (9)	0 63 ± 0 08 (9)	41 ± 3 5 (9)
	n s	n s	n s	n s
Control	−0 5 ± 0 30 (5)	−47 ± 2 5 (5)	0 60 ± 0 13 (5)	44 ± 5 4 (5)
Post-glucose/phlorizin (mannitol)	−0 7 ± 0 29 (5)	−54 ± 4 2 (5)	0 55 ± 0 11 (5)	45 ± 5 5 (5)
	n s	n s	n s	n s

inhibition of a Na^+-dependent glucose uptake across the brush-border membrane of villus enterocytes which is rheogenic but does not involve primary or secondary changes in the conductance of the brush-border membrane

Discussion

The response of rat ileum to D-glucose reported here provides direct evidence of functional heterogeneity of transport activity along the crypt-villus axis and confirms the conclusions reached by Kinter and Wilson [11] and Stirling and Kinter [12], who localized the accumulation of ^{14}C-labelled monosaccharides primarily to the microvillus membrane of small intestinal villus epithelial cells, and showed a gradient of radioactivity uptake along the villus, this being greatest at the villus tip

Earlier workers had described a depolarization of apical membrane potentials but in those studies impalements had not been made under direct vision and the site of the cells involved was uncertain It is likely however that the majority were villous cells [5–10,13,14]

The fall in apical membrane PD always exceeded the rise in transmural values as expected for a leaky epithelium such as rat ileum where the resistance of the extracellular shunt pathway is so low that it will be the main determinant of the resistance of the whole epithelium [14] Thus, a change in apical membrane potential V_a would result in a change of similar orientation at the basolateral membrane and vice versa By contrast, Okada et al [10] observed that the depolarization of V_a after 20 mmol/l D-glucose was similar in magnitude to the rise in V_t in rat ileum This surprising result was interpreted in terms of a reduced intracellular K^+ activity due to an increase in basolateral membrane K^+ conductance coupled with enhanced (Na^+ K^+)-ATPase activity [15] We could not confirm such a phenomenon in our studies The depolarization in the present study generally remained constant so long as glucose was present in the mucosal perfusate which accords with the findings of White and Armstrong [9] with D-galactose in bullfrog intestine In Necturus small intestine the peak depolarization due to galactose was followed by a steady repolarization resulting from a secondary increase in basolateral K^+ conductance [16]

Glucose was most consistently effective in eliciting changes in V_a in enterocytes from the upper villus region, but a small number of impaled cells did not respond to glucose despite a rise in V_t In view of the heterogeneous nature of the small intestinal epithelial cell population it is possible that recordings were sometimes made from cells which take no part in active solute transport

The effectiveness of phlorizin in opposing the changes in PD elicited by glucose demonstrates effectively that the glucose-induced changes are due to stimulation of electrogenic coupled Na^+-glucose uptake across the brush-border membrane From the experiments reported here the frequency of apical membrane depolarization in response to glucose in enterocytes at the base of the villus was less than 50% of the total number of observations, increasing at the upper villus to greater than 90%

The distribution of apical membrane potentials along the crypt-villus axis of rat ileum in the absence of glucose differs from that recorded by Cremaschi et al [3,5] in rabbit and hamster ileum These authors were able to demonstrate a gradual rise with increasing distance from the base of the villus We, on the other hand, have consistently observed higher membrane potentials in the crypt than on the villus in the nominal absence of glucose This discrepancy may be due to differences in the balance between absorption and secretion in the different species studied, but it was not feasible in the present study to shed further light on this possibility Interesting in this respect is the observation that rat jejunum, which is known to secrete Cl^- in vitro [17], appears to display in the absence of actively transportable solute a crypt-villus distribution of apical membrane PD similar in orientation to that found in the rabbit and hamster ileum by Cremaschi and co-workers (Stewart and Turnberg, unpublished observations)

The most straightforward interpretation of the results presented here is that Na^+-dependent glucose uptake is restricted to the villus epithelium The manifestation of this process is a fall in the brush-border membrane potential difference and a concomitant rise in transmural PD and these

changes are indicative of an electrogenic transport step at one or both limiting cell membranes Since neither transmural nor fractional resistance were affected by the presence of glucose it is unlikely that the uptake of glucose is mediated by a change in the permeability of the brush-border membrane to electro-diffusive ion movement This micropuncture technique, under direct vision, provides clear cut evidence for differentiation of absorptive function along the crypt-villus axis

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