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Acute effects of dexamethasone on cation transport in colonic epithelium

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SUMMARY Single pharmacological doses of glucocorticoid hormones stimulate net Na^+ and water absorption, K^+ secretion and electrical potential difference in rat distal colon and human rectum after five hours. To determine the cellular basis of these effects, the Na^+ and K^+ transport properties of epithelial cell membranes in rat distal colon were studied *in vitro* five hours after *in vivo* treatment with dexamethasone 600 μg/100 g body weight. Compared with control tissues, dexamethasone increased transepithelial voltage 3·5-fold ($p<0·001$) and short circuit current 4·5-fold ($p<0·001$), and decreased total resistance by 20% ($p<0·005$). Measurements of cell membrane voltages obtained with intracellular microelectrodes indicated that the dexamethasone-induced rise in transepithelial voltage reflected a significant decrease ($p<0·05$) in apical membrane voltage, consistent with the induction of apical Na^+ channels and the stimulation of electrogenic Na^+ absorption. Apical addition of 10^{-4} mol/l amiloride (a Na^+ channel blocker) and then 30 mmol/l tetraethylammonium chloride (TEA; a K^+ channel blocker) to control tissues had little or no effect on transepithelial electrical parameters, indicating the absence of significant apical Na^+ and K^+ conductances. In contrast, in dexamethasone treated tissues, amiloride and TEA produced electrical changes that were consistent with the inhibition of glucocorticoid-induced apical Na^+ and K^+ conductances. Kinetic studies of the basolateral membrane Na^+–K^+ pump revealed that five hours after administration, dexamethasone had no effect on the maximum capacity of the pump for Na^+ transport, but significantly increased the affinity of the pump for Na^+, and the number of Na^+ ions binding to each pump site. Thus, the acute stimulatory effects of dexamethasone on distal colonic Na^+ absorption and K^+ secretion reflect increased apical membrane conductance to Na^+ and K^+, and an increase in the 'efficiency' of the basolateral membrane Na^+–K^+ pump.

Previous studies have shown that ion transport processes in mammalian colon are readily influenced by changes in circulating levels of corticosteroid hormones.[1–6] Chronic administration of mineralocorticoid or glucocorticoid hormones generally produces similar effects *in vivo*, which include stimulation of Na^+ absorption, K^+ secretion, and mucosal Na^+–K^+–ATPase activity.[1–6] The initial effects are rapid, and perfusion studies in rat colon have shown that a single pharmacological dose of the glucocorticoid dexamethasone (600 μg/100 g body weight) increases Na^+ and water absorption, K^+ secretion, and transmural electrical potential difference (pd) after only five hours, while mucosal Na^+–K^+ATPase activity (which constitutes the basolateral membrane Na^+–K^+ pump) is unchanged.[7] Rectal dialysis studies indicate that single pharmacological doses of the glucocorticoids hydrocortisone (100 mg) and methylprednisolone (40 mg) also enhance Na^+ and water absorption, K^+ secretion, and pd after five hours in both normal subjects and patients with active ulcerative colitis.[8] These findings are of particular interest as they suggest that systemically administered glucocorticoids decrease diarrhoea in ulcerative colitis by stimulating colonic Na^+ and water absorption, as well as by their better known anti-inflammatory action.

The present study was done in rat distal colon to

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determine the cellular basis for the acute effects of glucocorticoid hormones on colonic cation transport. Although *in vivo* studies indicate that glucocorticoids induce an early increase in electrogenic Na^+ absorption,[7] it is unclear whether this reflects enhanced Na^+ entry at the apical membrane, increased activity of the basolateral membrane Na^+–K^+ pump, or a combination of these possibilities. It is also unclear whether the accompanying increase in K^+ secretion is passive – that is, paracellular and pd-dependent, or active – that is, transcellular and pd-independent, or a combination of active and passive transport. In order to determine the acute effects of glucocorticoid hormones on colonic epithelial cell membranes, the conductive properties of the apical membrane to Na^+ and K^+, and the kinetics of the basolateral membrane Na^+–K^+ pump, have been compared in normal rat distal colon and distal colon from animals treated with a single dose of dexamethasone.

Methods

ANIMALS

Non-fasting male Sprague-Dawley rats weighing 250-300 g were used in all experiments. The glucocorticoid treated animals were injected intraperitoneally with a single 600 μg/100 g body weight dose of dexamethasone phosphate five hours before removing the colon. Control and dexamethasone treated animals had received 20 g/day of regular Purina chow and tap water *ad libitum*. After removal, the colon was rinsed with NaCl-Ringer solution at 37°C containing (in mmol/l): Na^+ 136·2; K^+ 7·0; Cl 121; Ca^{++} 2·0; Mg^{++} 1·2; HCO_3^- 25; H_2PO_4 1·2; SO_4 1·2; glucose 11·1 and gassed with 95% O_2/5% CO_2 (pH 7·4). A 2-3 cm segment of distal colon was obtained 3 cm proximal to the anus, stripped of serosa and muscle layers, and mounted vertically between modified open topped Ussing chambers as previously described.[9] Both sides of the tissue were bathed with 12 ml of stirred, gassed NaCl-Ringer solution at 37°C and pH 7·4. Tissue area was 1 cm^2.

Transepithelial voltage (V_t) was measured with 1 mol/l KCl–4% agar bridges placed on either side of the tissue and attached to calomel half-cells. Two second transepithelial current pulses (120 $\mu A/cm^2$; Anapulse stimulator Model 302-T, and stimulus isolation unit Model 305, WP Instruments, New Haven, CT, USA) were passed via Ag/AgCl electrodes placed at the back of each chamber. Glass fibre-filled microelectrodes (tip diameter <0·5 μm) were prepared with a horizontal pipette puller (Campden Instruments, London, Model 753), filled with 0·5 mol/l KCl, and had tip resistances of 40-100 MΩ in NaCl-Ringer solution. Cells were impaled from the apical (mucosal) side of the tissue, and microelectrodes were positioned with an accuracy of 1μm using a remotely controlled three dimensional hydraulic micromanipulator (Narishige Scientific Instruments, Tokyo, Japan, Model MO-103). Membrane voltages were measured within ±0·1 mV with a high impedance electrometer (WP Instruments, Model 750), and microelectrodes were referenced to the serosal solution such that basolateral membrane voltage (V_b) was monitored directly. The entire apparatus was mounted on an anti-vibration table. V_t and V_b were monitored on digital voltmeters interfaced with a microcomputer (BBC Model B) and a dual beam oscilloscope, and recorded on a chart recorder and microcomputer driven printer.

Apical membrane voltage (V_a) was calculated as $V_a = V_t - V_b$, and the ratio of the changes in apical and basolateral membrane voltages in response to the transepithelial current pulse was assumed to equal the membrane resistance ratio, α (α=ratio of the apical to basolateral membrane resistance). Total tissue resistance, R_t (calculated as $R_t = \triangle V_t/I$, where $\triangle V_t$ is the change in transepithelial voltage in response to the transepithelial current pulse, I), and α, were corrected for series resistance of the bathing solution as previously described.[10]

Initial studies were done with microelectrodes to determine the effects of dexamethasone on the basal electrical properties of the epithelium when bathed in NaCl-Ringer solution. After 25–35 minutes, when transepithelial electrical parameters were constant, three to five cell impalements lasting 45–90 seconds were performed applying the transepithelial current pulse at five second intervals. The Na^+ channel blocker amiloride (a gift of Merck, Sharp and Dohme) was then added to the mucosal solution to a final concentration of 10^{-4}mol/l and three to five impalements obtained five minutes later. Impalements were judged to be successful if (i) V_b reached a steady value after 10 seconds, (ii) V_b and α remained stable during the impalement, (iii) the microelectrode tip resistance was unchanged by the impalement, and (iv) the microelectrode recorded the baseline voltage (V_t) upon withdrawal. Average values of microelectrode measurements were calculated for each tissue under pre- and postamiloride conditions before obtaining a mean value for the group.

In further studies in which only transepithelial measurements were obtained, the effects of the mucosal addition of the K^+ channel blocker tetraethylammonium chloride (TEA: final concentration 30 mmol/l) were determined in distal colon from control and dexamethasone treated animals, having first added 10^{-4}mol/l amiloride to block apical membrane Na^+ channels.

Finally, the activity of the basolateral membrane Na^+–K^+ pump in the two experimental groups

was determined using a technique similar to that previously reported.[10] Tissues were bathed on the mucosal side with K^+ gluconate Ringer solution containing (in mmol/l): K^+ 140; HCO_3^- 25; Ca^{++} 10 (methane sulphonate); Mg^{++} 1·2; SO_4^{--} 1·2; $H_2PO_4^-$ 2·3; $MeSO_3^-$ 20; gluconate 113·8, and glucose 11·1; and on the serosal side with Na^+ gluconate Ringer solution (similar to NaCl Ringer solution, but Cl^- replaced with equimolar gluconate). The polyene antibiotic nystatin (Sigma Chemical Co., St. Louis, MO, USA) was then added to the mucosal solution to a final concentration of 480 U/ml. This drug combined rapidly with lipid in the apical membrane, forming water filled pores which rendered the membrane freely permeable to monovalent ions,[11] resulting in a decrease in R_t while V_t increased to about 40 mV (mucosal side negative). When the effects of nystatin were complete (generally within 5 minutes), the serosal solution was replaced with K^+ gluconate Ringer solution, leading to a rapid fall in V_b and thus V_t and the equivalent short circuit current, Isc ($Isc=V_t/R_t$) to zero. Equal aliquots of Na^+ gluconate were then added first to the serosal solution (where they had no effect) and then to the mucosal solution to final concentrations of 10, 20, 30, 40, and 50 mmol/l. Increases in mucosal (and thus intracellular) Na^+ rapidly hyperpolarised the basolateral membrane, as reflected by the increases in V_t and Isc, with steady values occurring after 2–3 minutes. The kinetics of the basolateral Na^+–K^+ pump were assessed by plotting $\triangle$Isc against the mucosal Na^+ concentration ($[Na^+]$) using an iterative least-squares curve-fitting routine to fit the data to a model of highly cooperative binding[12]:

$$\triangle \text{ Isc} = \frac{Isc_{max}}{1 + \left(\frac{K_m}{[Na^+]}\right)^n}$$

where Isc_{max}=the apparent maximum short-circuit current, K_m=the mucosal Na^+ concentration required to achieve 50% Isc_{max}, and n=the number of Na^+ ions binding to each Na^+–K^+ pump site.

Results are expressed as mean±SEM for each group of tissues. Statistical comparisons were made using the two tailed Student's *t* test for paired or unpaired data as appropriate.[13]

Results

The effects of dexamethasone on the basal transepithelial electrical properties of rat distal colon, and their sensitivity to amiloride, are shown in Table 1. Compared with control tissues, dexamethasone increased basal transepithelial voltage 3·5-fold ($p<0·001$) and basal short circuit current 4·5-fold ($p<0·001$), and decreased total resistance by 20% ($p<0·005$). Table 2 shows that the dexamethasone induced rise in transepithelial voltage reflected significant depolarisation of the apical membrane ($p<0·05$), a change which is consistent with the induction of Na^+ channels in the apical membrane.

Tables 1 and 2 also show that the apical (mucosal) addition of amiloride had no effect on transepithelial or microelectrode measurements in distal colon from control animals, indicating that amiloride sensitive apical Na^+ channels are normally absent from this epithelium under *in vitro* conditions. In contrast, in dexamethasone treated tissues, amiloride significantly decreased the transepithelial voltage

Table 1 *Effect of dexamethasone on basal electrical properties of rat distal colon*

	V_t (mV)	R_t (Ωcm^2)	Isc ($\mu A/cm^2$)
Control (n=23)			
Basal	−5±1	185±6	26±4
+amiloride	−5±1	182±6	25±4
p*	NS	NS	NS
Dexamethasone treated (n=20)			
Basal	−17±2†	148±9‡	115±26†
+amiloride	−5±1	165±11	33±7
p*	<0·001	<0·001	<0·001

Results are expressed as mean±SEM. V_t=transepithelial voltage (mucosal surface negative); R_t=total resistance; Isc=short-circuit current; n is the number of tissues studied.
*difference between basal and postamiloride value; †=$p<0·001$; ‡=$p<0·005$ compared with basal value in control tissues.

Table 2 *Effect of dexamethasone on transepithelial and cell membrane voltages in rat distal colon*

	V_t (mV)	V_a (mV)	V_b (mV)	α(% of basal value)
Control (n=9)				
Basal	−4±1	+48±3	−52±3	100
+amiloride	−3±1	+47±2	−50±2	96±17
p*	NS	NS	NS	NS
Dexamethasone treated (n=5)				
Basal	−12±3†	+37±3‡	−49±2§	100
+amiloride	−3±1	+49±3	−52±4	147±16
p*	<0·05	<0·05	NS	<0·05

Results expressed as mean±SEM. V_t=transepithelial voltage (mucosal surface negative); V_a=apical membrane voltage (positive with respect to cell interior); V_b=basolateral membrane voltage (negative with respect to serosal solution); α=membrane resistance ratio (ratio of apical membrane and basolateral membrane resistance); n is the number of tissues studied.
*difference between basal and postamiloride values; †=$p<0·005$; ‡$p<0·05$; §=NS compared with basal value in control tissues.

Table 3 *Effect of dexamethasone on the sensitivity of rat distal colon to amiloride and tetraethylammonium chloride (TEA)*

	V_t (mV)	R_t (Ωcm^2)	Isc ($\mu A/cm^2$)
Control (n=14)			
Basal	−6±1	188±7	31±6
+amiloride	−6±1	186±7	29±6
p*	NS	NS	NS
+amiloride +TEA	−9±1	186±8	50±5
p†	<0·001	NS	<0·001
Dexamethasone treated (n=10)			
Basal	−18±4‡	128±9‡	137±25‡
+amiloride	−5±1	143±12	35±8
p*	<0·01	<0·02	<0·005
+amiloride +TEA	−7±1	150±14	47±8
p†	<0·005	<0·01	<0·001

Results are expressed as mean±SEM. V_t=transepithelial voltage (mucosal surface negative); R_t=total resistance; Isc=short-circuit current; n=number of tissues studied.
*difference between basal and postamiloride value;
†difference between postamiloride and postamiloride+TEA value;
‡=p<0·001 compared with basal value in control tissues.

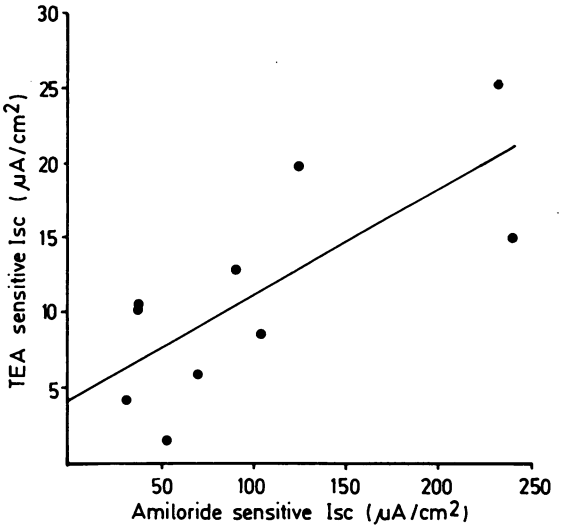

Fig. 1 *Relationship between tetraethylammonium chloride (TEA)-sensitive and amiloride sensitive short circuit current (Isc) in rat distal colon (n=10) five hours after treatment with dexamethasone (600 μg/100 g body weight). Line (y=0·071x + 4·219; r=0·758; p<0·02) is the least squares fit to the data, where the standard error for regression of y on x = 4·7 $\mu A/cm^2$.*

(p<0·001) and short circuit current (p<0·001), and significantly increased total resistance (p<0·001) (Table 1). As shown in Table 2, these changes reflected hyperpolarisation of the apical membrane (p<0·05) and a rise in apical membrane resistance, as judged by the 47% increase (p<0·05) in the membrane resistances ratio, α, and are consistent with amiloride inhibition of apical membrane Na^+ channels. Thus, dexamethasone stimulates the early appearance of amiloride sensitive Na^+ conductive channels in the apical membrane which enhance apical Na^+ entry, resulting in a rise in electrogenic Na^+ absorption.

The effects of the sequential addition of amiloride and the K^+ channel blocker TEA to the mucosal solution bathing control and dexamethasone treated distal colon are shown in Table 3. Dexamethasone produced changes in the basal electrical properties and the amiloride sensitivity of the distal colon which were similar to those presented in Table 1. Amiloride again had no effect in control tissues, but produced changes in the dexamethasone treated tissues consistent with inhibition of electrogenic Na^+ absorption. The subsequent addition of TEA to control tissues significantly increased transepithelial voltage (p<0·001) and short circuit current (p<0·001) without changing total resistance. These changes are consistent with the inhibition of serosal to mucosal K^+ movement, although the lack of effect on total resistance suggests that there are normally relatively few TEA sensitive K^+ conductive channels in the apical membrane of rat distal colon. In contrast, addition of TEA to dexamethasone treated tissues produced a significant increase in total resistance (p<0·01), as well as increases in transepithelial voltage and short circuit current, consistent with TEA inhibition of a relatively large, dexamethasone-induced K^+ conductance in the apical membrane.

Figure 1 illustrates the relationship between the TEA sensitive and amiloride sensitive currents in the dexamethasone treated tissues. Individual tissues showed a wide variability in their response to dexamethasone, but overall, there was a significant positive correlation (r=0·758, p<0·02) between the dexamethasone induced TEA sensitive K^+ current and the dexamethasone induced amiloride sensitive Na^+ current.

The ability of the basolateral membrane Na^+–K^+ pump to extrude Na^+ across the membrane in control and dexamethasone treated tissues is shown in Figure 2. The calculated maximum short circuit current – that is, the apparent Isc_{max}, in the control and dexamethasone treated tissues was similar (73±1·0 $\mu A/cm^2$ and 74±1·0 $\mu A/cm^2$, respectively). In the dexamethasone treated tissues, however, the apparent K_m was lower (11·5±0·2 mmol/l) and the Hill coefficient was higher (2·2±0·1) than the corresponding values in the control tissues (14·0±0·4 mmol/l, p<0·01 and 1·4±0·1, p<0·001, respectively).

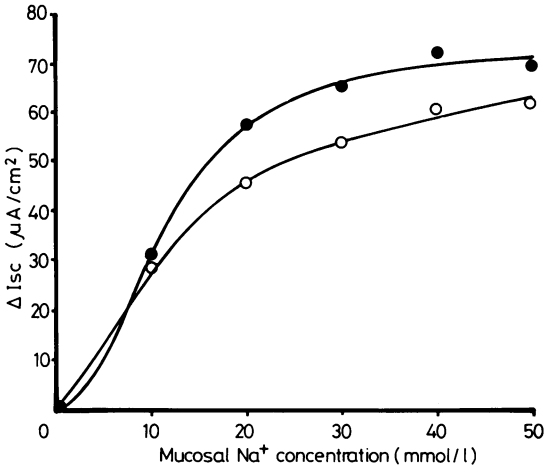

Fig. 2 *Change in short circuit current from zero (△Isc) at increasing mucosal concentrations of Na^+ in tissues from 13 control (○) and 14 dexamethasone treated (●) animals. Each point represents that mean of the data at each concentration of Na^+, and the curves through the points are the best fits to the equation describing the model of highly cooperative binding (see Methods). The best fit values for the lines are $Isc_{max}=73\pm1$ μA/cm², $K_m=14{\cdot}0\pm0{\cdot}4$ mmol/l, $n=1{\cdot}4\pm0{\cdot}1$ in control tissues, and $Isc_{max}=74\pm1$ μA/cm², $K_m=11{\cdot}5\pm0{\cdot}2$ mmol/l, $n=2{\cdot}2\pm0{\cdot}1$ in dexamethasone treated tissues.*

Discussion

As previously reported,[9 14] the present study has shown that amiloride sensitive apical Na^+ channels are normally absent from rat distal colon, an epithelium in which Na^+ is absorbed predominantly by an electroneutral Cl^--dependent process.[3] TEA sensitive apical K^+ channels are also virtually absent from rat distal colon, which is normally characterised *in vitro* by net K^+ absorption.[15] As the electrochemical driving forces for K^+ across the apical and basolateral membranes are almost equal in control tissues,[16] net K^+ absorption *in vitro* reflects the combined effects of (i) an apical K^+ absorptive process, which has the features of a K^+–H^+ exchange,[15] (ii) the absence of a significant apical K^+ conductance, which limits passive K^+ movement along its electrochemical gradient from cell to mucosal solution,[16] and (iii) a relatively high basolateral membrane K^+ conductance, which favours passive K^+ movement from cell to serosal solution.[16]

Recent studies indicate that the effects of glucocorticoid hormones on colonic ion transport are time dependent: a single dose of dexamethasone (600 μg/100 g body weight) stimulates Na^+ absorption and K^+ secretion, and increases pd *in vivo* after five hours,[7] while Na^+–K^+–ATPase activity does not increase until a further seven to 19 hours have elapsed.[7 17] We have shown that a single dose of dexamethasone produces changes at the apical membrane five hours later which have implications for the active (transcellular) movement of both Na^+ and K^+. Dexamethasone induces amiloride sensitive Na^+ channels which increase passive Na^+ movement into the cell down its electrochemical gradient, leading to an increase in electrogenic Na^+ absorption. The transepithelial responses to TEA (Table 3) and the positive correlation between the TEA sensitive and amiloride sensitive short circuit currents in the dexamethasone treated tissues (Fig. 1) indicate that the glucocorticoid also induces apical K^+ channels in parallel with the apical Na^+ channels. Although the effects of TEA on the apical membrane voltage and membrane resistance ratio were not determined in the present study, TEA has been shown to produce similar transepithelial changes, depolarise the apical membrane, and increase the membrane resistance ratio in distal colon from animals treated chronically with dexamethasone,[18] indicating that TEA does in fact inhibit a dexamethasone induced apical K^+ conductance. The presence of apical K^+ channels in dexamethasone treated tissues alters the electrical driving force for K^+ across the apical membrane in such a way as to enhance K^+ movement from the cell (and ultimately from the serosal solution) to the mucosal solution.

The experiments in the nystatin treated tissues provided a means of expressing basolateral membrane Na^+–K^+–ATPase activity in terms of transport function–that is, a change in current generated by the Na^+–K^+ pump in response to a change in intracellular Na^+ concentration, rather than the ability to release phosphate from ATP. As shown in Figure 2, Isc_{max} was similar in the control and dexamethasone treated tissues, indicating that dexamethasone had no effect on the Na^+ transport capacity of the basolateral membrane Na^+–K^+ pump after five hours. This is in agreement with a previous study in which mucosal Na^+–K^+ activity in rat distal colon was unchanged five hours after a similar single dose of dexamethasone.[7] The other kinetic parameters derived from the data in Figure 2 show that the increase in electrogenic Na^+ transport seen in the dexamethasone treated tissues reflects a small but significant increase in the affinity of the Na^+–K^+ pump for Na^+ (as judged by the decrease in K_m), and a 57% increase in the number of Na^+ ions binding to each pump site. It should be noted that total Na^+–K^+–ATPase activity (and presumably Isc_{max}) eventually increases 12–24 hours after dexamethasone administration,[7 17] but it is unclear whether this change is induced by a sustained increase in

apical Na^+ entry, or whether it reflects a direct stimulatory effect of the glucocorticoid on maximal Na^+–K^+–ATPase activity in the basolateral membrane, as seen in the kidney.[19,20]

The time course of the transport effects of dexamethasone are consistent with the activation of corticosteroid receptors present in the colonic mucosa.[21] Dexamethasone administered at high doses occupies mineralocorticoid as well as glucocorticoid receptors in the colonic cytosol.[22] Recent studies, however, indicate that mineralocorticoids and glucocorticoids (including dexamethasone) induce changes in distal colonic Na^+ absorptive and K^+ secretory processes which are both qualitatively and quantitatively different,[2,3] suggesting that they act through different types of corticosteroid receptor. The synthetic glucocorticoid RU 26988, which activates specific glucocorticoid receptors without binding to specific mineralocorticoid receptors, has also been shown to stimulate Na^+ absorption, K^+ secretion, and transmural pd in distal colon in adrenalectomised rats.[23] The present study has shown that after activation of glucocorticoid receptors by dexamethasone, there is an early increase in the conductance of the apical membrane of the distal colon to Na^+ and K^+ ions, and an increase in the 'efficiency' of the basolateral Na^+–K^+ pump.

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References

1 Bastl CP, Binder HJ, Hayslett JP. Role of glucocorticoids and aldosterone in maintenance of colonic cation transport. *Am J Physiol* 1980; **238:** F181–F6.
2 Charney AN, Wallach J, Ceccarelli S, Donowitz M, Costenbader CL. Effects of spironolactone and amiloride on corticosteroid-induced changes in colonic function. *Am J Physiol* 1981; **241:** G300–G5.
3 Foster ES, Zimmerman TW, Hayslett JP, Binder HJ. Corticosteroid alteration of active electrolyte transport in rat distal colon. *Am J Physiol* 1983; **245:** G668–G75.
4 Jorkasky D, Cox M, Feldman GM. Differential effects of corticosteroids on Na^+ transport in rat distal colon in vitro. *Am J Physiol* 1985; **248:** G424–G31.
5 Will PC, Cortright RN, DeLisle RC, Douglas JG, Hopfer U. Regulation of amiloride-sensitive electrogenic sodium transport in the rat colon by steroid hormones. *Am J Physiol* 1985; **248:** G124–G32.
6 Clauss W, Durr J, Skadhauge E, Hornicke H. Effects of aldosterone and dexamethasone on apical membrane properties and Na-transport of rabbit distal colon in vitro. *Pflugers Arch* 1985; **403:** 186–92.
7 Binder HJ. Effect of dexamethasone on electrolyte transport in the large intestinal of the rat. *Gastroenterology* 1978; **75:** 212–7.
8 Sandle GI, Hayslett JP, Binder HJ. The effect of glucocorticoids on rectal transport in normal subjects and patients with ulcerative colitis. *Gut* 1986; **27:** 309–16.
9 Sandle GI, Hayslett JP, Binder HJ. Effect of chronic hyperaldosteronism on the electrophysiology of rat distal colon. *Pflugers Arch* 1984; **401:** 22–6.
10 Wills NK, Lewis SA, Eaton DC. Active and passive properties of rabbit descending colon. A microelectrode and nystatin study. *J Membr Biol* 1979; **45:** 81–108.
11 Cass A, Finkelstein A, Krespi V. The ion permeability induced in thin lipid membranes by polyene antibiotics nystatin and amphotericin B. *J Gen Physiol* 1970; **50:** 100–24.
12 Lewis SA, Wills NK. Interaction between apical and basolateral membranes during sodium transport across tight epithelia. In: Schultz SG, ed. *Ion transport by epithelia*, New York: Raven Press: 1981: 93–107.
13 Snedecor GW, Cochran WG. *Statistical methods*. Ames, Iowa: Iowa State University Press, 1967: 549.
14 Will PC, Lebowitz JL, Hopfer U. Induction of amiloride sensitive sodium transport in the rat colon by mineralocorticoids. *Am J Physiol* 1980; **238:** F261–8.
15 Foster ES, Hayslett JP, Binder HJ. Mechanism of active potassium absorption and secretion in the rat colon. *Am J Physiol* 1984; **246:** G611–G7.
16 Sandle GI, Foster ES, Lewis SA, Binder HJ, Hayslett JP. The electrical basis for enhanced potassium secretion in rat distal colon during dietary potassium loading. *Pflugers Arch* 1985; **403:** 433–9.
17 Will PC, DeLisle RC, Cortright RN, Hopfer U. Induction of amiloride-sensitive sodium transport in the intestines by adrenal steroids. *Ann N Y Acad Sci* 1981; **372:** 64–78.
18 Sandle GI. Glucocorticoid-induced Na and K channels in the apical membrane of rat distal colon. [Abstract]. *Gut* 1985; **26:** A1146.
19 Finkelstein FO, Hayslett JP. Role of medullary Na-K-ATPase in renal potassium adaptation. *Am J Physiol* 1975; **229:** 524–8.
20 Rodriquez HJ, Sihka SK, Starling J, Klahr S. Regulation of renal Na^+–K^+–ATPase in the rat byadrenal steroids. *Am J Physiol* 1981; **241:** F186–F95.
21 Pressley L, Funder JW. Glucocorticoid and mineralocorticoid receptors in gut mucosa. *Endocrinology* 1975; **97:** 588–96.
22 Marusic ET, Hayslett JP, Binder HJ. Corticosteroid-binding studies in cytosol of colonic mucosa of the rat. *Am J Physiol* 1981; **240:** G417–G23.
23 Bastl CP, Barnett CA, Schmidt TJ, Litwack G. Glucocorticoid stimulation of sodium absorption in colon epithelia is mediated by corticosteroid IB receptor. *J Biol Chem* 1984; **259:** 1186–95.