THE ELECTRICAL POTENTIAL DIFFERENCE GENERATED BY THE LARGE INTESTINE: ITS RELATION TO ELECTROLYTE AND WATER TRANSFER *

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Studies of the physicochemical forces involved in the transfer of ions and water across biological membranes have received great impetus from the work on the isolated frog skin by Ussing, Zerahn and Koefoed-Johnson (1, 2). This type of approach would help to define the mechanisms involved in the transfer of fluid and electrolyte across the intestine *in vivo*. A previous study on the large intestine *in vivo* has stressed the striking concentration gradients developed between the lumen and the plasma (3). Evaluation of the driving forces for electrolyte and water transfer across the large intestine has not been possible, however, in the absence of measurements of transfer rates and electrical potential.

Recent studies on the isolated large intestine of the guinea pig and frog have indicated that the absorption of sodium is active, and that of chloride is passive (4, 5). The maintenance of an electrical potential gradient was found to be dependent upon active sodium transport. However, since the intestine can secrete (6) as well as absorb, even these studies provide limited information.

In the experiments reported here, the electrical potential difference across the large intestine of the anesthetized dog was measured. Simultaneously the net transfer of water, sodium, potassium, chloride and bicarbonate between the lumen and the blood were determined. The unidirectional movements of sodium and chloride were calculated from the rate of absorption of their radioisotopes. By correlating the electrical potential difference with observed chemical events, it was possible to obtain a more precise analysis of some of the forces influencing ionic and water transfer across the large intestine. Information was obtained which clearly demonstrates at least two active transport systems: sodium absorption and bicarbonate secretion.

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METHODS

Thirteen healthy mongrel dogs weighing from 9 to 17 Kg. were used. After anesthetization with 20 to 25 mg. per Kg. of pentobarbital sodium the abdomen was entered through a small midline incision. A segment of large intestine, 4 cm. distal to the caecum and 10 to 15 cm. in length, was divided and flared cannulae carefully tied into each end. Care was taken to keep the blood supply intact. The cannulae were exteriorized through two small stab wounds and the abdomen closed. The intestinal segment was rinsed clean with isotonic saline warmed to 37° C. An electrolyte solution from a reservoir was recirculated through the intestinal segment using plastic tubing and a Bowman infusion pump. The solution in the reservoir was maintained at 39° C. The initial total volume of perfusion solution varied from 100 to 200 ml. depending on the size of the intestinal segment, and the flow rate ranged from 5 to 10 ml. per minute. A modified Krebs-Henseleit solution was used with 100 mg. per cent of glucose and 1.25 mEq. of calcium per L. (7). The concentrations of Na^+, Cl^-, K^+ and HCO^-_3 in this solution were 138, 120, 5 and 22 mEq. per L., respectively. Penicillin (8 mg. per cent) and streptomycin (16 mg. per cent) were added to minimize bacterial contamination. Phenol red and radioactive isotopes were added to the perfusion fluid as described later.

The electrical potential difference across the wall of large intestine was detected with a pair of calomel electrodes and continuously recorded with a modified Brown-Minneapolis Honeywell recording potentiometer with an input impedence of one megohm. Two pieces of large bore polyethylene tubing (PE 320) filled with 1 M KCl and 3 per cent agar served as bridges from the calomel electrodes to the luminal solution and the peritoneal surface of the intestinal segment. The junction potential was less than 1 mV. in all instances. During the experiment an additional potential difference was measured between the luminal solution and circulating venous blood in the vena cava. In many instances the potential difference across the intestinal wall showed rhythmical phasic variations: The mean potential was then determined by planimetry. These variations in electrical potential will be the subject of a forthcoming report.

Each experiment lasted four to seven hours and hourly samples of 5.0 ml. were removed from the lumen. In

order to maintain volume, each sample was replaced with five ml. of the original solution and the resultant change in solute concentrations calculated. Chemical determinations of Na^+, K^+, Cl^- and HCO_3^- were done on each hourly sample. During each experiment, two samples of plasma were analyzed similarily. Na^+ and K^+ were determined by flame photometry using lithium as an internal standard, Cl^- by the method of Cotlove, Trantham and Bowman (8), and HCO_3^- by the method of Van Slyke and Neill. Osmolality of the plasma and luminal content were determined by the freezing point depression method (9).

Phenol red (0.004 per cent) was added to the original solution, and the optical density of each hourly sample was determined at 550 mμ after a 15-fold dilution with 0.1 N NaOH (10). At the end of each experiment, the amount of phenol red left in the perfusate and saline washings was determined spectrophotometrically. Recovery of the dye was 97 ± 2 per cent, and this slight loss justifies its use as an indicator of volume change. The net water flux was calculated with the equation:

$$\text{Net water flux} = \frac{V_0 - \frac{D_0}{D_1} \cdot V_0}{t} \qquad 1)$$

where t is the time in hours, D_0 is the initial optical density, D_1 the optical density at the end of the hourly period, and V_0 the volume of the initial solution.

The net flux (M_{net}) of each ion was calculated by using the equation:

$$M_{net} = \frac{V_0C_0 - V_1C_1}{t} \qquad 2)$$

where V_0 and C_0 are the total volume and concentration at the beginning of any hourly period, and V_1 and C_1 the volume and concentration at the end of that period. A positive net flux denotes movement from the lumen to the blood.

Trace amounts of Na^{24} and Cl^{36} were added to the original perfusion solution and the influx of these ions from lumen to blood determined by the rate of disappearance of their radioisotopes. The initial sample was taken one-half to one hour after perfusion was begun. The Na^{24} disintegration rate was determined on each sample in a well-type scintillation counter without interference from the beta particles of Cl^{36} which were absorbed by the glass wall of the vial containing the sample. The Na^{24} was then allowed to decay and the Cl^{36} distintegration rate counted with a Geiger-Muller tube after duplicate 1 ml. samples were dried on filter paper bonded to copper discs. A minimum of 10,000 disintegrations were counted and the activities were at least two to three times background.

The influx (M_i) of Na^+ and Cl^- from lumen to blood was calculated with the equation:

$$M_i = \frac{r_0V_0 - r_1V_1}{\bar{r}} \cdot \bar{C} \qquad 3)$$

where r_0 is the absolute cpm per ml., V_0 the volume at the beginning of any hourly period, r_1 and V_1 are these values at the end of that period, $\bar{r}$ the mean cpm per ml., and $\bar{C}$ the mean concentration of the ion in the perfusate.

In order to justify the use of Equation *3*, the following assumptions were made: First, the isotopic movement from lumen to blood is unidirectional, since the activity of Na^{24} and Cl^{36} in the blood was found to be indistinguishable from background. Second, that the rate of change in concentration and isotopic activity of Na^+ and Cl^- in the luminal fluid was linear with time. Their arithmetic mean was used since calculations made on the basis of an exponential decline gave similar results, and the change in concentrations was less than 2 per cent and the change in isotopic activity less than 10 per cent during each sampling period. Third, the kinetics of Na^+ and Cl^- transfer across the intestinal epithelium can be described in terms of two compartments: lumen and plasma.

The outflux (M_0) of Na^+ and Cl^- from blood to lumen was obtained with the equation:

$$M_0 = M_i - M_{net}. \qquad 4)$$

The intestinal segment was weighed and measured at the end of the experiment and the flux arbitrarily expressed as microequivalents (μEq.) per Gm. of wet tissue per hour. Water movement was expressed as ml. per Gm. of tissue per hour.

RESULTS

Electrical

The electrical potential difference across the epithelium of the large intestine ranged in different experiments from 10 to 40 mV. In all instances the lumen was negative with respect to the peritoneal surface. The potential difference between the luminal solution and circulating blood was the same when the KCl agar bridge on the peritoneal surface of the intestine was placed in the vena cava. In some instances, rhythmical phasic variations in the potential were noted to occur with a periodicity of 3 to 5 minutes, duration of 15 seconds to 2 minutes, and amplitude of + 1 to + 20 mV. In one dog with a Thiry-Vella loop of colon, the potential between the lumen and the venous blood was noted to vary from 20 to 50 mV. over a six month period. The potential difference across the wall of the small intestine and gall bladder was measured by the technique described, using the modified Krebs-Henseleit solution. The absence of an appreciable potential difference across these organs emphasizes the significance of the observed potential in the colon.

TABLE I

Net rates of H_2O and electrolyte transfer during absorption *

H_2O	HCO_3^-†	K^+†	Na^+†	Cl^-†	P.D.
ml./Gm./hr.					
+0.42‡	+6.0	−2.5‡	+61.0	+53	19 mV.
(±0.11)§	(±3.6)	(±1.2)	(±14.5)	(±12.7)	

* Eleven dogs, 55 one hour sampling periods.
† Values for HCO_3^-, K^+, Na^+ and Cl^- expressed as μEq. per Gm. of intestinal segment per hour.
‡ (+) denotes movement from lumen to blood; (−) denotes movement from blood to lumen.
§ ± = standard deviation.

Chemical

Two patterns of electrolyte and water transfer were observed. The first pattern (Tables I and II) was observed in 11 dogs and was characterized by the net absorption of water, sodium and chloride into the blood. The concentration of sodium in the luminal fluid was always less than that observed in the plasma. Thus sodium was absorbed against both a concentration and an electrical gradient. The absorption of chloride into the blood was in the direction of its electrical gradient but against its concentration gradient. The net transfer of potassium was from blood to lumen. Like chloride it moved with the electrical but against its chemical gradient. In the original perfusion solution the ratio of Cl^- to HCO_3^- was 6:1, but these ions were absorbed in the ratio of 9:1 (range, 6:1 to 20:1). The net effect of the ionic movements was an alteration of the electrolyte pattern of the luminal fluid, with sodium and chloride concentrations decreasing, and potassium and bicarbonate increasing. This concentration pattern has been observed previously (3).

The second pattern was observed in the two remaining dogs (Table III), and was characterized by a profuse bicarbonate secretion into the lumen with an accompanying net secretion of water, sodium and potassium. In this instance, bicarbonate was the predominant ion being transported against a chemical and electrical potential

TABLE II

A representative experiment showing net rates of H_2O and electrolyte transfer during absorption

Time	H_2O	HCO_3^-*		K^+*		Na^+*		Cl^-*		P.D.
hr.	*ml./Gm./hr.*†	*μEq./Gm./hr.*	*mEq./L.*	*μEq./Gm./hr.*	*mEq./L.*	*μEq./Gm./hr.*	*mEq./L.*	*μEq./Gm./hr.*	*mEq./L.*	*mV.*
0			22.1		6.0		138		120	16
0–1	+0.85‡	+ 7.1	23.9	− 3.3‡	7.4	+ 99.5	139	+109	119	16
1–2	+0.43	+ 3.8	24.9	− 0.9	8.1	+ 97.0	133	+ 57.0	118	17
2–3	+0.64	0	25.4	− 2.8	9.5	+ 86.0	132	+ 82.0	117	20
3–4	+0.57	+ 9.5	27.8	− 6.6	11.7	+ 81.0	131.5	+ 73.0	116	22
4–5	+0.58	+ 4.2	30.6	− 4.7	13.6	+ 64.0	131	+ 62.0	115	24
5–6	+0.53	+ 9.0	31.3	− 4.3	15.8	+ 80.0	129	+ 69.0	113	26
	+3.40	+33.6		−22.6		+507.5		+452.0		

* Plasma values of HCO_3^-, K^+, Na^+ and Cl^- were 22.0, 4.1, 149 and 118 mEq. per L., respectively.
† Net weight of tissue, 21.2 Gm.; length, 12.2 cm.
‡ (+) denotes movement from lumen to blood; (−) denotes movement into lumen.

TABLE III

An experiment showing net rates of H_2O and electrolyte transfer during secretion

Time	H_2O	HCO_3^-*		K^+*		Na^+*		Cl^-*		P.D.
hr.	*ml./Gm./hr.*†	*μEq./Gm./hr.*	*mEq./L.*	*μEq./Gm./hr.*	*mEq./L.*	*μEq./Gm./hr.*	*mEq./L.*	*μEq./Gm./hr.*	*mEq./L.*	*mV.*
0			25.8		5.9		149		129	25
0–1	−0.42‡	− 62.0	32.9	− 7.0	6.6	− 32	146	+ 7‡	122	25
1–2	−0.57	− 49.0	36.2	− 7.2	7.0	− 43	145	− 3	117	23
2–3	−0.13	− 23.0	39.1	− 7.2	7.9	− 23	145	+ 7	115	20
3–4	−0.05	− 20.0	42.9	− 5.5	8.9	− 20	142	− 1	114	22
	−1.17	−154.0		−26.9		−118		+10		

* Plasma levels of HCO_3^-, K^+, Na^+ and Cl^- were 24.1, 3.8, 150 and 116 mEq. per L., respectively.
† (+) denotes movement from lumen to blood; (−) denotes movement from blood to lumen.
‡ Net weight of tissue, 23.5 Gm.; length, 12.0 cm.

TABLE IV

Chloride flux ratios

Expt.	No. of one hour flux periods	$\frac{[Cl^-_{plasma}]}{[Cl^-_{lumen}]}$	$\frac{M_1}{M_0}$*	Observed† ratio	Calculated† ratio	$\frac{\text{Observed}}{\text{Calculated}} \times 100$
						%
1	7	$\frac{113}{118}$	$\frac{103}{30}$	3.3	2.7	123
2	6	$\frac{120}{113}$	$\frac{44}{9}$	5.0	2.4	200
3	5	$\frac{114}{127}$	$\frac{63}{18}$	3.1	2.2	140
4‡	6	$\frac{116}{129}$	$\frac{52}{46}$	1.2	2.4	50
5‡	4	$\frac{115}{117}$	$\frac{28}{22}$	1.3	2.5	50

* M_1 is influx (lumen to blood); M_0 is outflux (blood to lumen). Flux expressed as μEq. per Gm. per hour.

† Observed ratio calculated from $\frac{M_1}{M_0} \cdot \frac{[Cl^-_{plasma}]}{[Cl^-_{lumen}]}$; calculated ratio from antilog $\frac{E(mV.)}{60}$.

‡ Experiments 4 and 5 characterized by net secretion of water into the lumen, Experiments 1, 2 and 3 by net absorption.

gradient. Again chloride was absorbed in the direction of its electrical gradient. Both sodium and potassium entered the lumen along their electrical gradient, but the ratio of sodium to potassium secreted into the lumen was 5:1 as compared to a much higher ratio in the plasma. This demonstrates that even with secretion of bicarbonate into the lumen, the concentration pattern in the luminal fluid is still that of a decrease in sodium and chloride and an increase in potassium and bicarbonate.

In the five experiments presented in Table IV the fluxes of chloride into the blood (M_1) and into the lumen (M_0) are given. Since net chloride movement was from the lumen to the blood, the ratio $M_1:M_0$ is greater than 1.0.

In Table V the unidirectional sodium fluxes are

TABLE V

Sodium flux ratios

Expt.	No. of one hour flux periods	$\frac{[Na^+_{plasma}]}{[Na^+_{lumen}]}$	$\frac{M_i}{M_0}$*	Observed† ratio	Calculated† ratio	$\frac{\text{Observed}}{\text{Calculated}} \times 100$
						%
1	5	$\frac{143}{135}$	$\frac{81}{24}$	3.3	0.55	600
2	6	$\frac{150}{135}$	$\frac{93}{34}$	2.7	0.40	670
3	6	$\frac{145}{141}$	$\frac{55}{26}$	2.1	0.50	420
4‡	6	$\frac{146}{138}$	$\frac{30.7}{38.7}$	0.80	0.40	200
5‡	4	$\frac{150}{142}$	$\frac{40}{63.8}$	0.64	0.42	147

* M_i is influx (lumen to blood); M_0 is outflux (blood to lumen). Flux expressed as μEq. per Gm. per hour.

† Observed ratio for sodium calculated from $\frac{M_i}{M_0} \cdot \frac{[Na^+_{plasma}]}{[Na^+_{lumen}]}$; calculated ratio from 1/antilog $\frac{E(mV.)}{60}$.

‡ Experiments 4 and 5 characterized by net secretion of water into the lumen, Experiments 1, 2 and 3 by net absorption.

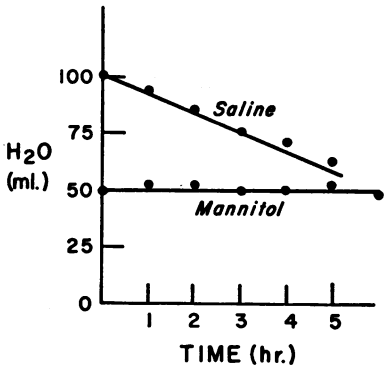

FIG. 1. VOLUME OF PERFUSATE AT EACH SAMPLING HOUR IS PLOTTED AGAINST TIME

See text.

presented. In the first three experiments there was a net transfer of sodium from lumen to blood and the ratio of sodium influx (M_i) to the sodium outflux (M_0) is greater than 1.0. The ratio of sodium fluxes was less than 1.0 in the remaining two experiments since there was net sodium movement into the lumen.

For electroneutrality the sum of the charges of the ions being transferred must equal zero. This was not observed in each sampling period due to slight errors in the chemical results used in calculating net transfer, but the average of the net transfer of ions in each experiment, as well as the mean for all experiments, was found to approach zero.

Water

The data from two experiments presented in Figure 1 show that there was no significant absorption of water without net absorption of solute. In one a saline solution was recirculated through the lumen and in the other isotonic mannitol was used. Changes in water content were quite small in the latter experiment because of the slight absorption of mannitol. However, in the two experiments in which there was extensive bicarbonate secretion, net water transfer was quite variable as indicated by the experiment represented in Table III. The osmolality of the luminal contents remained essentially constant, indicating that absorption or secretion was isotonic.

DISCUSSION

The preceding results confirm the previous observations on the isolated large intestine which showed that sodium was absorbed against its electrical and chemical gradient (4, 5). This net transfer requires energy and can be defined as active. In two experiments the secretion of bicarbonate was observed to be against its electrical and chemical gradient; this secretion also must be active. Since chloride absorption and potassium secretion were observed to be in the direction of their electrical gradients and opposite to their chemical gradients additional information is necessary to describe their means of transfer more fully.

Ussing (11) has developed the following equation to describe the passive movement of an ion across a semi-permeable membrane:

$$\frac{M_i}{M_0} = \frac{a_0}{a_i} \cdot e^{(zF/RT) \cdot E} \qquad 5)$$

or

$$\log \frac{M_i \cdot a_i}{M_0 \cdot a_0} = \frac{zF}{RT} \cdot E = \frac{E(mV.)}{60} \cdot \text{at } 37^\circ \text{ C.}$$

where M_i and M_0 are the influx and outflux of the ion; a_i and a_0, respectively, the chemical activity of the ion in plasma and lumen; z, F, R, T., respectively, the charge of the ion, the Faraday, the gas constant and absolute temperature; and E(mV.), the electrical potential difference across the membrane in question.

The relationship between passive ionic transfer and electrical and chemical potential gradients is evident from Equation *5*. Any significant deviation from this equation must be explained in terms of an energy expenditure or other factors not considered. One of these factors, "solvent drag," will be discussed with relation to the transfer of chloride.

Since sodium is actively transported, the ratio of its unidirectional fluxes does not follow the above equation. However, as noted in two experiments (Table V, Experiments 4 and 5), net sodium movement was from a higher to a lower electrochemical potential and accompanied bicarbonate and water into the lumen. At the observed potential the observed flux ratio for sodium is larger than the calculated value. One possible explanation for this finding is that sodium is still being actively transported even though this "active transport" is being overwhelmed by the other forces acting on the sodium ion.

Flux rates of sodium across the isolated large intestine of the frog have been expressed as μEq. per unit area (12), but recalculation of values on

a weight basis gave net sodium fluxes of 30 to 60 μEq. per Gm. of tissue per hour. Thus the rate of sodium absorption across the isolated frog colon at 25° C. is of the same order of magnitude as the rate of sodium absorption in the dog.

Chloride is transferred from a higher to a lower electrochemical potential. The electrical potential difference between lumen and blood is the major driving force. With net water secretion into the lumen there is still net chloride transfer from lumen to blood (Table III). In comparing the dog and frog colon with respect to the transepithelial fluxes of chloride the following differences occur: One, the net chloride flux during absorption in the dog (Table I) is greater than the net flux of 10 to 20 μEq. per Gm. of tissue per hour in the frog. Two, unlike the observations on the frog *in vitro,* the data presented here do not suggest appreciable exchange diffusion of chloride.

In Table IV the calculated and observed ratios of chloride are compared in five experiments, and they do deviate from the values calculated for passive diffusion. These deviations could be explained by the following factors: *1*) Although chloride is transferred predominately by passive diffusion there may be a component of active chloride transport or exchange diffusion.[1] *2*) In the presence of rhythmical potential variations the potential difference as determined by planimetry may not be the true mean potential. *3*) It is likely that the last factor, "solvent drag," is the most important for the following reasons:

"Solvent drag" is the physical effect of net water flow exerted upon solute and is a function of membrane structure as defined by Ussing and Andersen (4). This flow reduces solute movement in the opposite direction, while enhancing it in the same direction. Net water flow into the blood (Table IV, Experiments 1 through 3) would increase chloride influx and/or decrease outflux. Net water flow into the lumen would have the opposite effect (Table IV, Experiments 4 and 5). Such an effect was observed on the chloride flux ratios: The chloride ratio is lower than predicted by Equation *5* when net water secretion occurs and higher than predicted when net water absorption takes place. On the other hand, the observed sodium flux ratio (Table V, Experiments 4 and 5) is larger than the calculated value for passive diffusion despite net water transfer into the lumen. This indicates that active sodium absorption was still operative during net sodium transfer into the intestine.

The limitations of Equation *5* as presented here for the *in vivo* intestine have been predicted by Ussing and he has developed an equation which takes "solvent drag" into account (13). A rough estimate of the "solvent drag" force can be obtained from the flux ratio of water which was not measured. However, Berger has recently measured D_2O fluxes across the colonic mucosa of the unanesthetized dog (14). In experiments characterized by net water absorption, the water flux ratios were 1.23 to 1.32. If one uses this figure to recalculate the chloride ratios (Table IV, Experiments 1 through 3) there is a closer agreement between the observed and calculated results. This suggests that chloride transfer is influenced by "solvent drag" as well as by the electrochemical gradient.

The net flux of potassium from blood to lumen was in the proper direction for passive transfer (Tables I through III). This does not rule out an active secretion of potassium, or a sodium-potassium exchange at one surface of the epethelial cell, a mechanism postulated for the kidney and frog skin (15, 16). The unidirectional transfers of potassium were not measured and the nature of the experiment did not permit the attainment of the steady state where $M_i = M_o$ in order to test the relationship:

$$E = 60 \log \frac{K^+_{lumen}}{K^+_{plasma}}.$$

Subsequent studies have revealed that, in some instances, potassium secretion may be active, and this will be the subject of a forthcoming report.

In all but two experiments there was net absorption of bicarbonate along its electrical gradient. Although the original perfusate contained 6 times as much chloride as bicarbonate, up to 20 times as much chloride was reabsorbed in 11 experiments. Thus despite net absorption of bicarbonate, the concentration of bicarbonate in the

[1] Chloride transfer across the isolated large intestine of the frog during absorption involves a component of exchange diffusion. If exchange diffusion were operative in the dog the chloride flux ratios would be significantly less than and not greater than the values calculated for passive diffusion (12).

lumen increased. This suggests that the epithelium of the large intestine is less permeable to bicarbonate than chloride, or there is active secretion of bicarbonate into the lumen. The latter mechanism can occur, as shown in Table III, where bicarbonate secretion into the lumen was opposite to its electrochemical gradient and was accompanied by water, sodium and potassium. The ratio of bicarbonate to water in the net secretion was 130 mEq. per L. in these latter instances. This is not unreasonable when compared to pancreatic secretions containing 110 mEq. per L. of bicarbonate or more, and gastric secretions as high as 150 mEq. per L. of hydrogen ions. The variations in active bicarbonate secretion may be due to changes in neurohumoral influences, since stimulation of the pelvic nerves and administration of cholinergic drugs induced alkaline secretion by the colon (6).

In this discussion the term bicarbonate secretion has been used for brevity. However, these experiments do not distinguish among bicarbonate secretion, hydroxyl ion secretion or hydrogen ion absorption. Previous studies on the isolated frog large intestine suggested that in addition to sodium there was another ion being actively transported, although this ion was not identified (12). If active bicarbonate secretion is under the influence of a neurohumoral mechanism it is not surprising that it could not be demonstrated in the *in vitro* system, but was clearly demonstrated and found to have considerable variability *in vivo*.

Driving forces for net water flow are the gradients of hydrostatic and osmotic pressure. The latter is created by the two ion transport mechanisms: sodium absorption and bicarbonate secretion. It was noted that there was no significant net transfer of water without solute. In addition to electrical and chemical forces, this net water movement can be a third driving force for other diffusing solutes (11). The effect of this "solvent drag" has been discussed previously with regard to the transfer of chloride.

In the preceding discussion the assumption has been made that the measured potential difference represents the transmucosal potential. This assumption seems justified in view of the following observations: First, the isolated large intestine when stripped of its outer muscular coat can generate a potential difference and actively transport sodium (4). Second, Rehm has presented evidence that no significant potential difference can be measured across the muscularis and peritoneal surface of the stomach in the presence of a significant electromotive force across the stomach wall (17). Third, the peritoneal cavity and circulating venous blood were found to be equipotential in the present study.

Transepithelial potential differences have been considered to be due directly to the unidirectional active transport of an ion (1), *e.g.,* sodium absorption and/or bicarbonate secretion. However, recent studies indicate that such bioelectrical potentials may be diffusion potentials resulting from active ion-exchange mechanisms involved in active transport (16). It is interesting that strophanthidin, a known inhibitor of cation transport (18), causes a drop of at least 50 per cent in the observed potential and partial inhibition of the sodium and bicarbonate active transport mechanisms across the large intestinal epithelium (19).

SUMMARY

An electrical potential difference of 10 to 40 mV. (the lumen being negative with respect to the blood) was measured across the large intestine of 13 anesthetized dogs. Correlation of this potential difference with chemical events demonstrated two active transport mechanisms: sodium absorption and bicarbonate secretion. Net water flow occurred, and its direction and magnitude were dependent on the degree of active transport of sodium and/or bicarbonate. The absorption of chloride was in the direction of its electrochemical potential gradient, probably modified by net water movement. Potassium was transferred from the blood to the lumen, in the direction of its electrical gradient but opposite to its chemical gradient.

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