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THE EFFECT OF SALINE AND HYPERONCOTIC DEXTRAN INFUSION ON CANINE ILEAL SALT AND WATER ABSORPTION AND REGIONAL BLOOD FLOW

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SUMMARY

1. The unidirectional Na and H_2O fluxes, vascular pressures and total and absorptive site blood flows in the canine ileum were determined before and during I.V. saline infusion and subsequent I.V. infusion of hyperoncotic dextran. The intestinal perfusion solutions were isotonic saline or isotonic saline and mannitol, but the effects of I.V. saline or I.V. hyperoncotic dextran infusion were generally the same for both luminal solutions.

2. Continuous I.V. infusion of saline caused a continuous increase in the unidirectional flux of Na and H_2O into the ileal lumen, an increase in total blood flow, and an increase in venous pressure.

3. The net absorption of Na and H_2O was decreased by I.V. saline infusion.

4. The unidirectional fluxes of Na and H_2O out of the lumen, arterial pressure and absorptive site blood flow were not affected by I.V. saline infusion.

5. I.V. hyperoncotic dextran infusion reversed most of the effects of saline infusion.

6. The unidirectional fluxes of Na and H_2O into the lumen were significantly correlated with Starling forces during I.V. saline infusion.

7. It was concluded that intestinal transport of salt and water was subject to regulation by physical forces at the capillary level.

INTRODUCTION

There is considerable evidence that the transport of salt and water across certain epithelial tissues can be affected by physical or Starling forces such as colloid osomotic pressure and hydrostatic pressure. Effects

of hydrostatic pressure or colloid osmotic pressure on frog skin (Nutbourne, 1968), intestine (Humphreys & Earley, 1971) and kidney (Earley & Friedler, 1966; Daugherty, Belleau, Martino & Earley, 1968; Koch, Aynedjian & Bank, 1968; Imai & Kokko, 1972) have been demonstrated. For intestine, results show that increased serosal hydrostatic pressure or decreased serosal colloid osmotic pressure decrease the net transport of salt and water and also that these forces are more effective when exerted at the serosal surface than at the mucosal surface (Wilson, 1956; Hakim & Lifson, 1969).

Most of the work relating Starling forces to transport has been done on the kidney; little work has been carried out on other transporting organs, such as the small intestine, which may also be affected by Starling forces. Higgins & Blair (1971) studied canine intestinal salt absorption during volume expansion with saline and concluded that the observed decrease in net absorption was due to increased secretion into the gut lumen and could have been caused by altered Starling forces. Humphreys & Earley (1971) and Richet & Horynch (1969) reached similar conclusions in similar studies. San Martin & Mailman (1972) suggested that the effects of body tilting on gut transport were exerted through concomitant cardiovascular changes. However, there were no direct attempts in the above studies to determine the changes in Starling forces and to relate them to changes in salt and water transport by the intestine. If Starling forces have an effect on intestinal absorption, these forces must be exerted at the absorptive site. Blood flow within the gut is divided into four more-or-less independent parallel circuits, to the muscularis, submucosa, crypts and villi (Svanvik, 1973*a*). These separate, parallel vascular circuits could also have separate regulation by central or local mechanisms (Svanvik, 1973*b*; Lundgren & Svanvik, 1973). Therefore, attempts to relate large artery and vein pressures to total intestinal blood flow in order to calculate capillary forces may not yield results valid for the portion of the vasculature which is nearest the absorptive site. The present experiments were carried out in an attempt to relate the unidirectional Na and H_2O fluxes across canine ileum to blood flow and Starling forces at the absorptive site.

In these experiments, total and absorptive site intestinal blood flow were measured as clearances of ^3H_2O in the same manner that the clearances of creatinine can be used to measure, simultaneously, both renal plasma flow and glomerular filtration rate if the concentration of creatinine in the renal artery and vein and the amount excreted are known (Ganong, 1973). The permeability of the intestinal mucosa to ^3H_2O is enough to allow almost complete equilibrium between ^3H_2O in the lumen and the blood draining the portion of the intestine (unspecified as to its

exact anatomical nature) in contact with the luminal contents (Winne, 1972; Dobson, Sellers & Thorlacius, 1971). This portion of the intestine is presumably involved in the absorption of H_2O and Na and the venous blood draining this area will have the same ^3H_2O concentration as in the intestinal lumen. The luminal ^3H_2O concentration can then be used to calculate absorptive site blood flow. The concentration of ^3H_2O in the mesenteric vein blood draining the entire segment can be used to calculate total segmental blood flow.

METHODS

Animal preparation

Dogs, most of them female (mean weight = 19 kg), were maintained for at least one week on a standard animal hospital regimen. Food was withdrawn one day before the experiment. Water was allowed *ad libitum*. The dogs were anaesthetized with sodium pentobarbitone (30 mg/kg) and a tracheotomy performed. After a mid-line laparotomy, two ileal segments (25–40 cm long) were separated from the remainder of the intestine by transverse incisions. The most distal end of the segments was about 30 cm oral to the ileocaecal valve. Rubber plugs containing the inflow and outflow cannulae were tied into the ends of the two segments for perfusion of either isotonic saline (NaCl, 9 g/l.) or isotonic saline-mannitol (5 g %) (1/1; v/v). The saline-mannitol solution was employed in order to determine if the character of the solution in the lumen could influence the effects due to the experimental procedures. A branch of the mesenteric vein draining one of the segments was cannulated for blood sampling. The mesenteric vein cannula was connected to a saline manometer in order to measure mesenteric vein pressure. A femoral artery was catheterized and connected to a mercury manometer for measurement of arterial pressure and a femoral vein was catheterized for infusion of solution.

Experimental

After completion of surgery, perfusion of the lumen of each segment was initiated at a rate of 2 ml./min using a dual channel roller pump (Cole-Parmer Model 7014-2). The solutions were at 38° C. Usually, the distal segment was perfused with saline and the proximal segment with saline-mannitol but there was no apparent difference in results when the solutions were switched. The solutions contained ^3H_2O, [^{14}C]-inulin (used as a volume marker) and ^{22}Na (New England Nuclear) sufficient to give counting rates of 20000, 4000 and 1000 cpm/2 ml., respectively. Perfusion was carried out for 60 min to allow equilibration of the intestinal contents and intestinal tissue before any samples were taken.

After the 60 min equilibration period four 15 min control periods were carried out, followed by ten 15 min experimental periods. During each period the gut effluents and a sample of mesenteric vein blood were collected and arterial and mesenteric vein blood pressure determined. Every 45 min a sample of femoral arterial blood was also collected.

Three different experimental procedures were carried out. One group of four animals was not infused in order to determine the effects of time on intestinal absorption and blood flow. A second group of seven animals was I.V. infused with isotonic saline (38° C) at a rate of 1 ml./min.kg beginning after the 60 min control period. A third group of seven animals was treated as in the second group but after 60–90 min of I.V. saline infusion, 25% hyperoncotic dextran (77000 mol. wt.:

Sigma Chemical Co.) in saline was I.V. infused for 20 min until 5 g dextran/kg had been infused. After completion of the intravenous dextran infusion, the intravenous saline infusion was reinstated.

Analyses

The radioisotope concentrations of ^3H_2O, [^{14}C]inulin and ^{22}Na in the gut effluent and in arterial and mesenteric vein plasma were counted to an accuracy of 2% in a three-channel liquid scintillation counter (Beckman Instruments, LS-150) in a cocktail of toluene/Triton X-100/Liquifluor (New England Nuclear) (2:1:0·13; v/v/v). Two ml. plasma or gut solution were counted in 10 ml. scintillation cocktail. Suitable corrections for quenching and spillover were carried out. Na and K concentrations in the gut solutions and plasma were determined by flame photometry (Eppendorf). Plasma colloids were determined as total solids by refractometry (National Instruments). Haematocrits were determined by centrifugation in capillary haematocrit tubes.

Calculations

Net and unidirectional Na and H_2O fluxes were calculated by the method of Berger & Steele (1958). Absorptive site and total blood flow were calculated as clearances of ^3H_2O based on the methods of Winne (1972) and Dobson *et al.* (1971). Total blood flow (BF_t) was calculated as $BF_t = {}^3H_{ab}/([{}^3H]_v-[{}^3H]_a)$, where $^3H_{ab}$ represents the amount of ^3H_2O absorbed and $[^3H]_a$ and $[^3H]_v$ represent the concentrations of ^3H_2O in the mesenteric artery and vein respectively. Absorptive site blood flow (BF_{as}) was calculated as $BF_{as} = {}^3H_{ab}/[{}^3H]_l-[{}^3H]_a$, where $[^3H]_l$ represents the concentration of ^3H_2O in the gut lumen. In practice, since $[^3H]_a$ was only about 4% of $[^3H]_l$ it was not used in the calculation of BF_{as}. It should be pointed out that although BF_{as} has been equated to a real mucosal blood flow (Winne, 1972; Dobson *et al.* 1971), this has not been rigorously proven. For this paper BF_{as} has been functionally defined as the virtual blood flow which completely equilibrates with the luminal ^3H_2O. The above clearances were corrected for the volume of distribution in the red blood cells which was found by direct measurement to be 0·77 of the red blood cell volume and this volume of distribution was reached essentially instantaneously (unpublished observations).

Statistical analysis was by paired *t* test on the differences between the average of the first four control periods in each animal and each of the ten subsequent periods of the control animals or the saline-infused animals. The average differences (± S.E. of mean) are given in the Figures. Control period values are given in the Figure legends. Statistical analysis of the results from animals infused with hyperoncotic dextran was by paired *t* test of the differences between the 15 min period just before hyperoncotic dextran infusion was begun and the average of the three 15 min periods during and following the dextran infusion. Single and multiple regression analysis was used to determine the relationship between the unidirectional Na and H_2O fluxes and the arterial pressure, mesenteric vein pressure and colloid osmotic pressure. Calculations were carried out using a UNIVAC 1108 computer with programs in FORTRAN and STIL languages.

RESULTS

Control animals

The results from the control animals can be summarized; there were no statistically significant changes in any parameter in any period for

either the saline- or the saline–mannitol-perfused gut segments. Hence, there was no effect of time, deterioration of the gut, etc., on intestinal absorption or blood flow.

Saline-infused animals

The net absorption of Na (Fig. 1) began to decrease shortly after the beginning of the intravenous saline infusion and became significantly lower than control period values after 60 and 30 min in the saline- and saline–mannitol-perfused gut segments, respectively. The net absorption from both the saline- and the saline–mannitol-perfused segments, observed during the control periods, was reversed to net secretion after 90 and 60 min of I.V. saline infusion, respectively. After 150 min of I.V. saline infusion the net control period Na absorption from saline of 0·82 μequiv/g.min was converted to a net secretion of 0·78 μequiv/g.min and net absorption of 0·41 μequiv/g.min from saline–mannitol was converted to net secretion of 0·69 μequiv/g.min. The changes in the net Na absorption from saline and saline–mannitol were similar although the amount of Na absorbed from saline was 100 % greater than the amount of Na absorbed from saline–mannitol during the control periods.

The secretory (unidirectional blood-to-lumen) flux of Na (Fig. 1) began to increase shortly after the beginning of the I.V. saline infusion and became significantly greater than control period values after 90 and 60 min of saline infusion in the saline- and saline–mannitol perfused-gut segments, respectively. The magnitude of the changes following I.V. saline infusion and the control levels of the secretory Na fluxes were about the same for both the saline- and the saline–mannitol-perfused gut segments. The secretory Na fluxes into the saline- and the saline–mannitol-perfused gut segments had increased by 270 and 230 % above control period levels, respectively, by the end of the experiment.

The absorptive (unidirectional lumen-to-blood) flux of Na (Fig. 1) from the gut segment perfused with saline–mannitol was not significantly changed from control periods during the 150 min of I.V. saline infusion. The absorptive Na flux from the saline-perfused segment remained constant during 90 min of I.V. saline infusion but after 90 min decreased significantly and remained decreased for the remainder of the 150 min infusion. Since, in the control animals, the absorptive flux of Na decreased after 60 min, although not significantly, the decreased Na absorptive flux during saline infusion may be due partly to an effect of time rather than due solely to the intravenous saline infusion. The control Na absorptive flux from the saline-perfused gut segment was about 100 % greater than the Na absorptive flux from saline–mannitol.

The net fluxes of H_2O (Fig. 2) from both saline and saline–mannitol

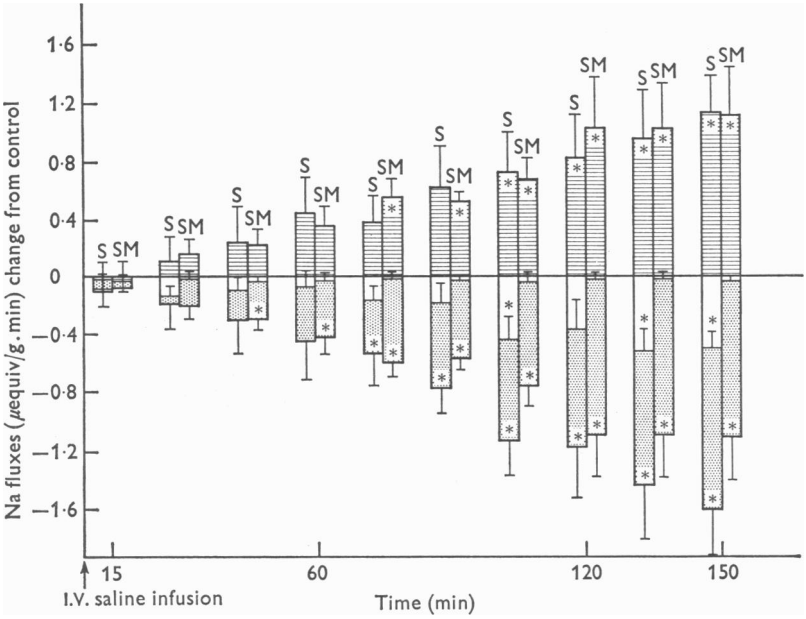

Fig. 1. Mean change (± S.E. of mean) from control period values of net, absorptive and secretory Na fluxes from saline- or saline–mannitol-perfused canine ileum during I.V. saline infusion (n = 7). Control period values (in μequiv/g. min) for saline-perfused gut were 0·82 ± 0·16, 0·61 ± 0·09, 1·43 ± 0·22 and for saline-mannitol-perfused gut values were 0·41 ± 0·11, 0·55 ± 0·07, 0·96 ± 0·14 for net (▦), secretory (▤) and absorptive (□) fluxes, respectively. * represents a value significantly different from control period values at least at the 5% level. The lack of any significant changes in dogs not I.V. infused with saline (n = 4) is not shown for ease of illustration. S, Saline-perfused gut; SM, saline–mannitol-perfused gut.

were significantly decreased after 60 min of I.V. saline infusion and the decreased absorption began shortly after the beginning of saline infusion. The net absorption observed in the control period was reversed to net secretion after about 90 min I.V. saline infusion. After 150 min of I.V. saline infusion the net H_2O absorption from saline of 4·9 μl./g.min was converted to net secretion of 4·6 μl._g.min and net H_2O absorption from saline–mannitol was converted from a net absorption of 5·1 μl./g.min to a net secretion of 2·3 μl./g.min. The secretory fluxes of H_2O (Fig. 2) into both saline and saline–mannitol were also increased shortly after the beginning of intravenous saline infusion and both became significantly greater than control period values after 45 min of saline infusion. At 105 and 120 min of saline infusion the secretory flux of H_2O into saline–mannitol became temporarily non-significant but was again significantly increased after these times. After 150 min of saline infusion the secretory

H_2O fluxes were 38 and 42% greater than control period values for the saline and saline–mannitol perfusion solutions, respectively. There were no significant changes in the unidirectional absorptive flux of H_2O during I.V. saline infusion (Fig. 2).

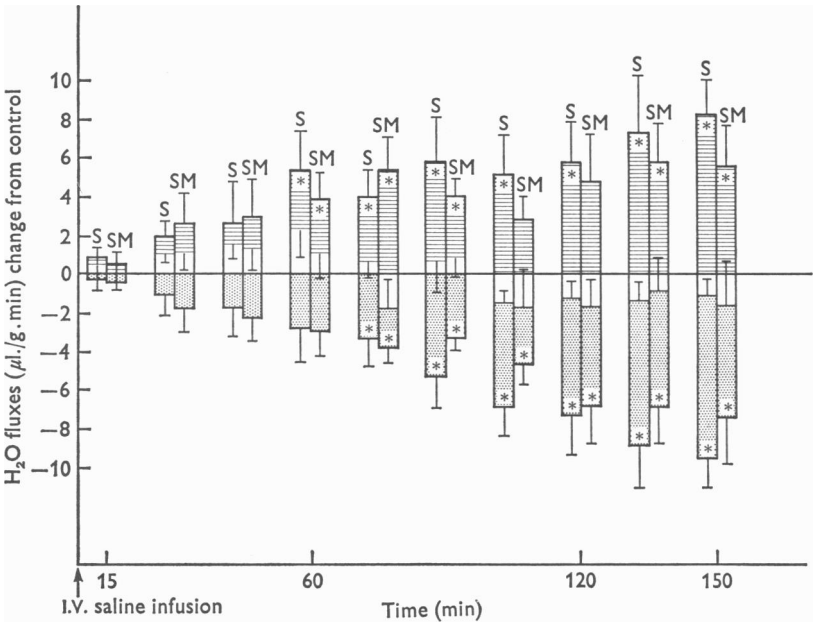

Fig. 2. Mean change (± S.E. of mean) from control period values of net, absorptive and secretory H_2O fluxes from saline- (S) or saline–mannitol-perfused (SM) canine ileum during I.V. saline infusion (n = 7). Control period values (in μl./g.min) for saline-perfused gut were 4·94 ± 1·11, 12·8 ± 1·4, 17·8 ± 2·2 and for saline–mannitol-perfused gut values were 5·10 ± 1·24, 15·8 ± 1·6, 20·9 ± 2·5 for net (▦), secretory (▤) and absorptive (□) H_2O fluxes, respectively. * represents a value significantly different from control period values at least at the 5% level. The lack of any significant changes in dogs not I.V. infused with saline (n = 4) is not shown for ease of illustration.

Total intestinal blood flow increased rapidly during I.V. saline infusion and became significantly greater than control period values after 15 min of saline infusion (Fig. 3). After 150 min of saline infusion total intestinal blood flow was 246% above control period levels. In contrast to total blood flow, absorptive site blood flow was not significantly changed from control during any period during 150 min of I.V. saline infusion (Fig. 4) for either the saline- or the saline–mannitol perfused gut segments.

Mesenteric vein pressure remained relatively constant during 30 min of saline infusion but then rapidly increased and became significantly different from control after 30 min of saline infusion (Fig. 5). Mesenteric

vein pressure had increased 67% above its control period value after 150 min of I.V. saline infusion. Arterial pressure was not significantly changed during saline infusion; its control value was 121 (±5) mmHg and its final value, after 150 min of saline infusion, was 119 (±6) mmHg. Total solids had decreased significantly (3·21 ± 0·24 g%; $P < 0·001$) below the control period level of 5·6 ± 0·3 g% after 150 min of saline infusion. The haematocrit had decreased significantly (by 0·17 ± 0·01; $P < 0·001$) below its control period value of 0·43 ± 0·02 after 150 min of

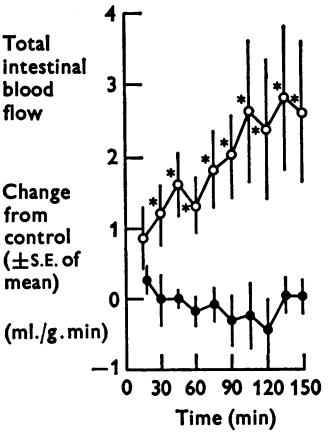

Fig. 3. Mean change (± S.E. of mean) from control period values of total ileal blood flow in control dogs (●, $n = 4$) and dogs during I.V. saline infusion (○, $n = 7$). Control period value was 1·08 (± 0·18) ml./g.min. * represents a value significantly different from control period value at least at the 5% level.

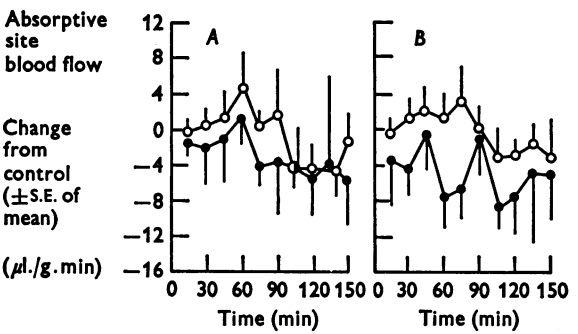

Fig. 4. Mean change (± S.E. of mean) from control period value of absorptive site blood flow through saline- (*A*) or saline–mannitol-perfused (*B*) ileum in control dogs (●, $n = 4$) and dogs during I.V. saline infusion (○, $n = 7$). Control period values were 28·7 (± 3·3) and 32·1 (± 5·0) μl./g.min for saline- and saline–mannitol-perfused segments, respectively. There were no significant differences from control periods.

saline infusion. The decreases in haematocrit and total solids were approximately linear with respect to time of I.V. saline infusion although the rate of fall tended to decrease after 60 min of saline infusion. The mesenteric vein plasma Na concentration increased by 6·3 ± 1·4 m-equiv/l. significantly ($P < 1\%$) above its control value of 151 ± 5 m-equiv/l., an increase of about 4%, after 150 min of I.V. saline infusion.

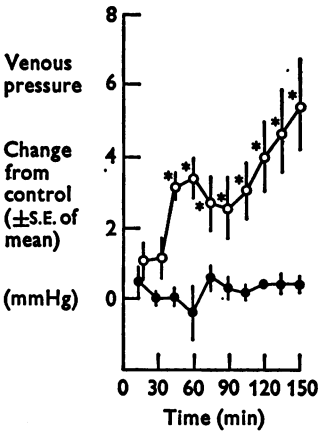

Fig. 5. Mean change (S.E. of mean) from control period value of mesenteric venous pressure in control dogs (●, $n = 4$) and dogs during I.V. saline infusion (○, $n = 7$). Control period was 7·63 (± 0·52) mmHg. * represents a value significantly different from control period at least at the 5% level.

Dextran-infused animals

The changes in intestinal transport and the cardiovascular effects during and following intravenous hyperoncotic dextran infusion after I.V. saline infusion are illustrated in Fig. 6. The effects of saline infusion were similar to those presented above (allowing for the differences in the times of infusion). Fig. 6 represents the average changes (± S.E. of mean) between the period just before I.V. dextran was infused and the average of the three periods during and following dextran infusion. The effects of hyperoncotic dextran infusion were transient and were largely over 30 min after the completion of dextran infusion. The effects largely paralleled the changes in plasma total solids which also returned to their pre-dextran level 30 min after the dextran infusion was completed. There were no significant effects of hyperoncotic dextran infusion on the net flux of Na or H_2O, nor on the absorptive flux of Na nor on total intestinal blood flow. The secretory fluxes of H_2O and absorptive site blood flow for the saline- and saline–mannitol-perfused segments were significantly

decreased by intravenous hyperoncotic dextran while both arterial and mesenteric vein pressures were significantly increased. Hyperoncotic dextran infusion also significantly decreased the secretory flux of Na and the absorptive flux of H_2O from saline–mannitol-perfused gut segments but did not significantly change these fluxes from saline-perfused gut

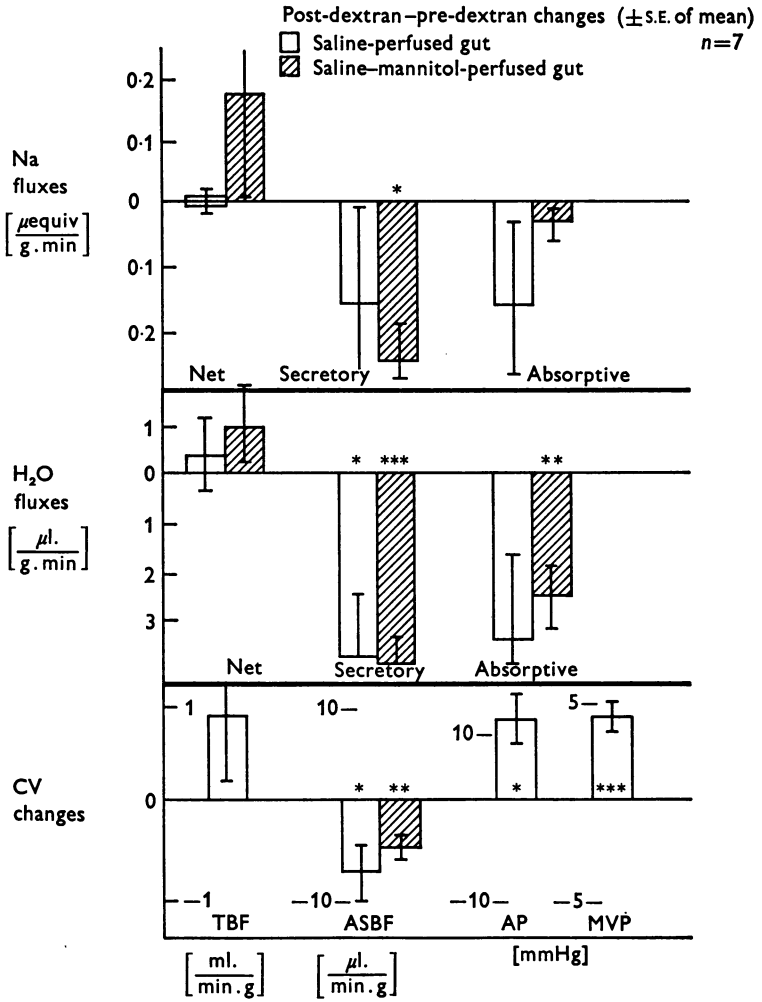

Fig. 6. Mean changes (S.E. of mean) in Na and H_2O fluxes and cardiovascular effects (CV) in canine intestine due to I.V. hyperoncotic dextran infusion after prior intravenous saline infusion (n = 7). TBF, ASBF, AP and VP represent total intestinal blood flow, absorptive site blood flow, arterial pressure and venous pressure, respectively. *, **, *** represent a value significantly different from the pre-dextran period value at the 5, 1 and 0·1 % level, respectively.

segments. Total solids were significantly increased ($P < 5\%$) by 0·78 ($\pm 0{\cdot}26$) g% from their pre-dextran value of 3·00 ($\pm 0{\cdot}14$) g%. The haematocrit was significantly decreased ($P < 0{\cdot}1\%$) by 0·11 ($\pm$ 0·004) from its pre-dextran value of 0·27 ($\pm 0{\cdot}02$).

Relationship between Starling forces and secretory fluxes

Figs. 7 and 8 represent empirical relationships between observed and calculated unidirectional Na and H_2O secretory fluxes, respectively. The graphs represent the data (saline- and saline–mannitol-perfused gut segments) from all periods for control experiments and those during which I.V. saline was infused but do not include data from periods during or after which hyperoncotic dextran was infused I.V. (see Discussion). The graphs were obtained in the following manner: linear regression analysis was carried out with the observed unidirectional Na or H_2O secretion into the lumen *versus* the arterial blood pressure, mesenteric vein pressure and plasma colloid osmotic pressure (the physical factors contributing to the Starling forces). The linear regression equations were calculated and the correlation coefficients and their significance levels determined both singly for each parameter and for the combined parameters (Table 1).

TABLE 1. Correlation coefficients (significance of linear correlation) of least-squares regression line, calculated by single or multiple regression analysis, of the observed Na and H_2O secretory fluxes into the canine ileum *vs* arterial pressure, mesenteric vein pressure and total plasma solids

	Correlation coefficients of regression line	
Forces	Secretory Na flux	Secretory H_2O flux
Arterial pressure	$-0{\cdot}28$ ($P < 1\%$)	$-0{\cdot}17$ ($P < 5\%$)
Mesenteric vein pressure	$0{\cdot}53$ ($P < 0{\cdot}1\%$)	$0{\cdot}24$ ($P < 1\%$)
Total plasma solids	$-0{\cdot}44$ ($P < 0{\cdot}1\%$)	$-0{\cdot}40$ ($P < 0{\cdot}1\%$)
Total forces	$0{\cdot}67$ ($P < 0{\cdot}1\%$)	$0{\cdot}45$ ($P < 0{\cdot}1\%$)

Singly, the observed unidirectional secretory fluxes of Na and H_2O were each significantly correlated with arterial pressure, mesenteric vein pressure and plasma colloid osmotic pressure, although not to the same extent. There was also a significant linear correlation when these latter three parameters were considered together. Considered singly, the secretory Na flux was best correlated with mesenteric vein pressure ($r = 0{\cdot}53$) although colloid osmotic pressure was correlated almost as closely ($r = 0{\cdot}44$). The correlation of the secretory Na flux with all three Starling forces, considered together, was greater than the correlation with any one of the driving forces considered separately. In contrast to the correlation of the Na flux with the combined Starling forces, the secretory flux of H_2O was correlated well only with the colloid osmotic pressure.

The correlation of the secretory H_2O flux with all three Starling forces, considered together, was not improved as compared with the correlation with the colloid osmotic pressure alone. For purposes of clear graphical representation, the calculated Na and H_2O fluxes were divided into nine equal intervals and the average ($\pm$ S.E. of mean) of the observed values corresponding to each calculated value in the interval was determined.

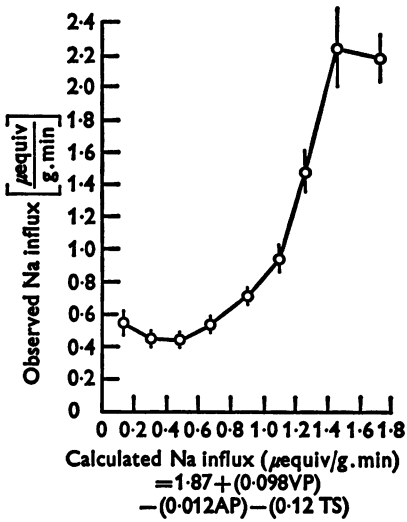

Fig. 7. Observed blood-to-lumen (secretory) Na flux (S.E. of mean) in relation to a calculated Na flux determined by multiple regression analysis. AP, VP and TS represent arterial pressure, mesenteric venous pressure and total plasma solids, respectively. The calculated Na fluxes were divided into nine intervals and averaged for purposes of graphing and the corresponding observed Na fluxes were then averaged. The correlation coefficient of observed *vs.* calculated Na flux was 0·67 ($P < 0{\cdot}1\%, n = 225$).

This method of visual representation was utilized for clarity since the relatively large number of control values grouped in the first two intervals distorted the graph visually. It can be seen that, although the unidirectional Na and H_2O secretory fluxes were linearly correlated with the Starling forces, there was also a curvilinear relationship superimposed over the linear relationship such that at low levels of these driving forces the observed fluxes remained relatively constant as the driving forces increased.

DISCUSSION

Intravenous saline infusion reduces the net absorption of both Na and H_2O by the canine ileum and can convert net absorption from the lumen to net secretion into the lumen when the volume of saline infused is

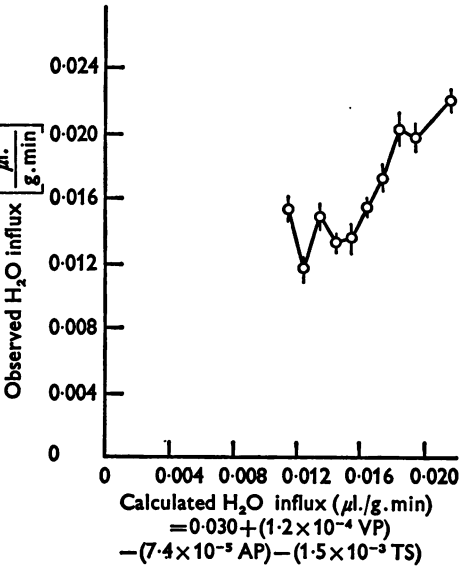

Fig. 8. Observed blood-to-lumen (secretory) H_2O flux (S.E. of mean) in relation to a calculated H_2O flux determined by multiple regression analysis. AP, VP and TS represent arterial pressure, mesenteric venous pressure and total plasma solids, respectively. The calculated H_2O fluxes were divided into nine intervals and averaged for purposes of graphing and the corresponding observed H_2O fluxes were then averaged. The correlation coefficient of observed *vs.* calculated H_2O flux was 0·45 ($P < 0·1\%$, $n = 225$).

sufficiently great. The reduced absorption of Na and H_2O is due primarily, if not completely, to an increase in the blood-to-lumen flux of both Na and H_2O. Concomitant with these changes in absorption, I.V. saline infusion results in increased venous pressure and total intestinal blood flow and decreased plasma colloid concentration. However, blood flow at the intestinal absorptive site is unaffected despite a 250% increase in total intestinal blood flow. Intravenous hyperoncotic dextran infusion significantly reduces the secretory flux of H_2O and reduces absorptive site blood flow but has no effect on total blood flow when compared with levels following I.V. saline infusion. Concomitant with these changes in intestinal absorption following I.V. hyperoncotic dextran infusion, arterial and venous pressure and plasma colloid concentration are all increased while the haematocrit is decreased. The results of these experiments are consistent with the hypothesis that Starling forces can alter the net transport of Na and H_2O across the small intestine by altering the unidirectional flow of salt and H_2O from the blood into the lumen.

The magnitudes of the total and absorptive site blood flow observed

in these experiments require comment. Total blood flow was about 1 ml./min.g which is at the higher side of published values (Grim, 1963). We attribute this to the small amount of trauma required for cannulation of the mesenteric vessel using our technique. In other types of experiments, requiring more dissection of the blood vessels, total blood flow was decreased in rough proportion to the degree of trauma involved (unpublished observations). Absorptive site blood flow, in the present experiments, was about 3% of the total blood flow, both flows being expressed per gram of total gut weight. Svanvik (1973*a*) has found that, in the cat, villous blood flow was about 15% of total blood flow under conditions where total blood flow was about 0·25 ml./min.g. Considering the differences in total blood flow between these two experiments, for the same total blood flow the villous flow determined by Svanvik and our absorptive site blood flow would be comparable on a basis of the fraction of total blood flow. If the absorptive site blood flow, as measured in these experiments, is the blood flow through the villi, which constitute about 10% of total ileal weight, then absorptive site blood flow would be about 0·3 ml./min.g villi (corresponding to 0·03 ml./min.g total thickness weight). This figure can be compared to blood flows of about 0·15–0·30 ml./min.g villi, determined by others (Svanvik, 1973*a*).

Neither the absorptive site blood flow nor the arterial-venous hydrostatic pressure gradient is greatly changed during the course of I.V. saline infusion. Arterial pressure decreased only 2 mmHg over the entire experiment while venous pressure increased by 5 mmHg resulting in a decrease of only 7–8% in the pressure gradient for blood flow. Since neither absorptive site blood flow nor the blood pressure gradient changed significantly the absorptive site resistance to blood flow must also have remained constant. The constancy of absorptive site blood flow can be contrasted with the 250% increase in total intestinal blood flow which would require a decrease in the resistance to blood flow in the remainder of the intestine. Changes in mesenteric resistance are primarily due to changes in pre-capillary resistance. (Wallentin, 1966) and therefore will result in more or less arterial pressure being transmitted to the capillaries.

Although I.V. saline infusion did not significantly affect absorptive site blood flow, I.V. hyperoncotic dextran infusion significantly decreased absorptive site blood flow about 25% while significantly increasing arterial and venous pressure 13 and 4 mmHg, respectively, as compared with the period just before dextran infusion. The relative increases in arterial and venous pressure represent an increase in the arterial–venous pressure gradient of about 8%. The absorptive site resistance and, therefore, the precapillary resistance must have increased. The effect of

hyperoncotic dextran in reducing absorptive site blood flow may reflect a myogenic type of reflex (Johnson, 1967).

Capillary pressure is determined by arterial and venous pressure and the relative magnitudes of the precapillary and post-capillary resistances. Since pre- and post-capillary absorptive site resistances remained relatively constant during saline infusion, arterial and venous pressures could be employed directly as a relative measure of capillary pressure in determining their relationship to the unidirectional secretory fluxes (Figs. 7 and 8). This direct use of arterial and venous pressure could not be employed during I.V. hyperoncotic dextran infusion since there were changes in the absorptive site resistance and therefore also changes in the relative magnitude of the pre- and post-capillary resistances. Also, it is very likely that the effective colloid osmotic pressure of dextran in the body is different from the effective colloid osmotic pressure of the plasma proteins. Therefore, plasma colloid osmotic pressure, measured as total plasma solids, could not be equated between the experiments employing I.V. saline infusion and those employing I.V. hyperoncotic dextran infusion. Qualitatively, the decreased secretory H_2O fluxes which were observed would be the expected change due to an increase in colloid osmotic pressure.

Although there was a significant linear correlation between the observed fluxes of Na and H_2O into the lumen of the gut and the arterial and venous pressure and plasma colloid concentration these secretory fluxes were relatively constant as the driving forces increased in their lower range. The relatively low and constant influxes when net driving forces are low may represent only the diffusive component of movement into the gut lumen. The magnitude of the diffusive component would depend on the concentration of Na and H_2O in the blood and the area and thickness of the surface available for diffusion. The relatively high influx of H_2O as compared with Na when the driving forces are low is consistent with this possibility since the diffusion of H_2O is more rapid than that of Na. As the net driving forces on capillary Na and H_2O increase, convection or bulk flow is added on to the diffusive component and the influx increases.

A comparison of the correlation coefficients for single regression analysis (Table 1) suggests that the secretory flux of Na and H_2O are, at least partly, independent. The secretory flux of H_2O is correlated primarily with the colloid osmotic pressure whereas the secretory flux of Na is correlated with both colloid osmotic pressure and venous pressure. These findings are consistent with the results of Shields & Code (1961), who found that increased venous pressure increased the secretion of Na into the intestinal lumen but had little effect on the secretory flux of H_2O.

Also consistent is the finding that hyperoncotic dextran infusion had a greater effect in decreasing the secretory H_2O fluxes than the secretory Na fluxes despite an increase in both arterial and venous pressure which would tend to oppose the effect of increased plasma colloids. Possibly, there are two channels for the movement of Na and H_2O. One channel may be permeable to both Na and H_2O and would be subject primarily to colloid osmotic pressure as a driving force. The other channel may be relatively more permeable to Na and would be subject primarily to capillary hydrostatic pressure as a driving force. For example, the model of standing gradient osmotic flow proposed by Diamond & Bossert (1967) postulates fluid flow in the lateral spaces of the cell in which the fluid nearer the tight junction is hypertonic while the fluid nearer the blood is isotonic. If increased hydrostatic pressure forced fluid through the tight junctions, relatively more Na than H_2O could be secreted into the lumen. If increased colloid osmotic pressure pulled fluid from the basilar end of the lateral spaces then both Na and H_2O secretion could be changed equally.

The changes in the fluxes of Na and H_2O were, in general, not significantly different from control within the first 60 min of saline infusion. However, the slope of the curves suggests that the effect of saline infusion, although initially small, occurred within 15 min. The effects of saline infusion on total intestinal blood flow and venous pressure were also rapid. The lack of change in mesenteric vein pressure during the first 30 min of saline infusion and the sudden rise therefore probably reflects filling of the normally partially collapsed veins. Further filling caused stretching and a rise in pressure.

In summary, saline and hyperoncotic dextran infusion can influence the movement of Na and H_2O from the blood into the lumen of the gut. This response is homoeostatic in that it tends to correct an imbalance of body fluid volume or oncotic pressure. The effects are exerted through changes in plasma colloid oncotic pressure and venous pressure without large changes in absorptive site capillary resistance or blood flow. The mechanism is related to changes in physical forces which can be affected differently at the intestinal absorptive site as compared with the remainder of the intestine.

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REFERENCES

BERGER, E. & STEELE, J. (1958). The calculation of transfer rates in two compartment systems not in dynamic equilibrium. *J. gen. Physiol.* **41**, 1135–1151.

DAUGHERTY, T. M., BELLEAU, L. J., MARTINO, J. A. & EARLEY, L. E. (1968). Interrelationship of physical factors affecting sodium reabsorption in the dog. *Am. J. Physiol.* **215**, 1442–1447.

DIAMOND, J. & BOSSERT, W. (1967). Standing gradient osmotic flow. A mechanism for coupling of water and solute transport in epithelia. *J. gen. Physiol.* **50**, 2061–2083.

DOBSON, A., SELLERS, A. F. & THORLACIUS, S. O. (1971). Limitation of diffusion by blood flow through bovine ruminal epithelium. *Am. J. Physiol.* **220**, 1337–1343.

EARLEY, L. E. & FRIEDLER, R. M. (1966). The effects of combined renal vasodilation and pressure agents on renal hemodynamics and the tubular reabsorption of sodium. *J. clin. Invest.* **45**, 542–551.

GANONG, W. F. (1973). *Review of Medical Physiology*, 6th edn, p. 518. Los Altos, California: Lange Medical Publications.

GRIM, E. (1963). The flow of blood in the mesenteric vessels. In *Handbook of Physiology*, Section 2: Circulation, vol. II. Washington, D.C.: American Physiological Society.

HAKIM, A. A. & LIFSON, N. (1969). Effects of pressure on water and solute transport by dog intestinal mucosa *in vitro*. *Am. J. Physiol.* **216**, 276–284.

HIGGINS, J. T. & BLAIR, N. P. (1971). Intestinal transport of water and electrolytes during extracellular volume expansion in dogs. *J. clin. Invest.* **50**, 2569–2579.

HUMPHREYS, M. H. & EARLEY, L. E. (1971). The mechanism of decreased intestinal sodium and water absorption after acute volume expansion the rat. *J. clin. Invest.* **50**, 2355–2367.

IMAI, M. & KOKKO, J. P. (1972). Effect of peritubular protein concentration on reabsorption of sodium and water in isolated perfused proximal tubules. *J. clin. Invest.* **51**, 314–325.

JOHNSON, P. C. (1967). Autoregulation of blood flow in the intestine. *Gastroenterology* **52**, 435–441.

KOCH, K. M., AYNEDJIAN, H. S. & BANK, N. (1968). Effect of acute hypertension on sodium reabsorption by the proximal tubule. *J. clin. Invest.* **47**, 1696–1709.

LUNDGREN, O. & SVANVIK, J. (1973). Mucosal hemodynamics in the small intestine of the cat during reduced perfusion pressure. *Acta physiol. scand.* **88**, 551–563.

NUTBOURNE, D. (1968). The effect of small hydrostatic pressure gradients on the rate of active sodium transport across isolated living frog skin membranes. *J. Physiol.* **195**, 1–18.

RICHET, G. & HORYNCH, A. (1969). The effect of an expansion of extracellular fluids on net Na flux in the jejunum of rats. *Nephron* **6**, 365–378.

SAN MARTIN, R. & MAILMAN, D. (1972). Effect of head upward tilting on unidirectional Na and H_2O fluxes across the canine ileum. *Proc. Soc. exp. Biol. Med.* **140**, 694–699.

SHIELDS, R. & CODE, C. F. (1961). Effect of increased portal pressure on sorption of water and sodium from the ileum of dogs. *Am. J. Physiol.* **200**, 775–780.

SVANVIK, J. (1973*a*). Mucosal blood circulation and its influence on passive absorption in the small intestine. *Acta physiol. scand.* suppl. 385, 1–44.

SVANVIK, J. (1973*b*). Mucosal hemodynamics in the small intestine of the cat during regional sympathetic vasoconstrictor activation. *Acta physiol. scand.* **89**, 19–29.

WALLENTIN, I. (1966). Studies on intestinal circulation. *Acta physiol. scand.* **69**, suppl. 279, 1–38.

WILSON, T. H. (1956). A modified method for study of intestinal absorption *in vitro*. *J. appl. Physiol.* **9**, 137–140.

WINNE, D. (1972). The influence of blood flow and water net flux on the absorption of tritiated water from jejunum of the rat. *Naunyn-Schmiedebergs Arch. exp. Path. Pharmak.* **272**, 417–436.