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WATER AND SODIUM ABSORPTION IN THE HUMAN INTESTINE

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SUMMARY

1. Studies are reported of total intestinal perfusion in man in which data relating to the absorptive capacity for water and sodium, flow rate transit time and intestinal volume have been obtained.

2. A 'bolus' of radiosodium added to the steady-state perfusion has allowed measurement of bidirectional fluxes of sodium ion across the mucosa to be determined.

3. The values obtained agree closely with those that can be predicted from small segmental studies reported in the literature.

4. Increasing absorption capacity with increasing flow rate does not seem to reflect a true increase in absorption per unit of intestine but rather a progression to more nearly continuous flow conditions.

INTRODUCTION

The total capacity for the human intestine to transport water and electrolytes has not been previously measured. Derived values can be arrived at by extrapolating the data of segmental studies (Borgstrom, Dahlqrist, Lundh & Sjovall, 1957; Fordtran, Levitan, Bikerman, Burrows & Ingelfinger, 1961; Levitan, Fordtran, Burrows & Ingelfinger, 1962). In considering the mechanisms of diarrhoeal states and potential oral fluid replacement in dehydration a more exact knowledge of these values becomes important. The present studies report the results obtained from total intestinal lavage in normal human subjects in which net water and sodium absorption has been measured. Bidirectional fluxes of sodium ion have also been measured using a bolus technique (Mitchell & Neptune, 1965).

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METHODS

A steady state of intestinal lavage was achieved by subjects drinking at a constant rate (2–6 l./hr) an electrolyte solution containing (m-equiv/l.): Na^+ 140, K^+ 10, Cl^- 105, HCO_3^- 35. Studies were carried out after a 12 hr fast and required approximately 1 hr to establish steady-state perfusion.

At steady state, an exactly known quantity of ^{24}Na (1 and 2·0 ml. of 0·05% T. 1824 dye in a total volume of less than 5 ml.) was given orally. Serial samples of the effluent stool were collected in 10 min periods and their volume determined. Sodium and potassium were assayed on all samples by Baird flame photometer and osmolarity was determined by Fisk osmometer. Radioactive sodium was measured by counting 3 ml. samples in plastic test tubes in a 2 × 2 in. (5 × 5 cm) sodium iodide well scintillation counter. Samples were counted for a minimum of 10,000 counts. T. 1824 concentrations in the samples were determined photocolorimetrically.

A plot was made of the quantity of radioactive material appearing in the effluent as a function of time after injection. A small correction was necessary for tracer returned to the lumen. Mean transit time (tt) for the bolus of tracer ^{24}Na to pass through the intestine was determined from:

$$\mathrm{tt} = \frac{\epsilon Q_r \bar{t}_1}{\epsilon Q_r},$$

where $\bar{t}_1$ is the time from ingestion of the tracer to the midpoint of collection of sample and Q_r is the quantity of tracer recovered. The average flow rate $\bar{F}$ of the solution through the intestine was the mean of the inflow and outflow volumes. Intestinal volume was obtained as the product of the mean transit time and average flow rate. Similar calculations were made using T. 1824 concentrations as the bolus marker.

The unidirectional sodium transfer rate from lumen to plasma, λ, is determined from the fraction of the dose recovered and the mean transit time,

$$Q_t = Q_a e^{-\lambda(\mathrm{tt})},$$

where Q_a = dose of radioactive sodium administered and Q_t = quantity of effluent radioactive sodium.

The flux of sodium from lumen to plasma was determined as:

$$\mathrm{Na}\ (L \rightarrow P) = \bar{F} \times \mathrm{tt} \times \mathrm{Na}^- \times \lambda \text{ m-equiv/min.}$$

Net transfer of water and sodium were determined from inflow–outflow balance in the steady state. In control studies the validity of this measurement was established by comparison with results calculated from changes in concentration of an unabsorbable marker PEG (Hyden, 1955). Unidirectional transfer of sodium from plasma to lumen ($P \rightarrow L$) was obtained by difference of net and ($L \rightarrow P$) flux values.

Each study lasted 2–4 hr and during this time records of heart rate, blood pressure and central venous pressure showed no evidence of fluid overloading. Weight and plasma specific gravity indicated retention of approximately 500 ml. of excess fluid during the experiment.

RESULTS

Figure 1 shows the relationship between net water absorption and perfusion rate of the intestine. Increasing rates of perfusion from 16–100 ml./min caused an increase in water absorption from 6·7 to 14·3 ml./min. The values are the mean and standard deviation of five studies on five subjects at each perfusion rate. The minute to minute variation in collection volumes of stool decreased as perfusion rates increased. In a typical study at 16 ml./min, the collection volume was 10·3 ± 6·9 ml./min, whereas at 100 ml./min the volume was 88·3 ± 19·3 ml./min.

The changes in net sodium absorption and unidirectional fluxes of the sodium ion with changing perfusion rates are seen in Fig. 2. It can be seen that, as with water transport, there is an increase in sodium transport with increasing perfusion rate. The net sodium absorption figures are the mean

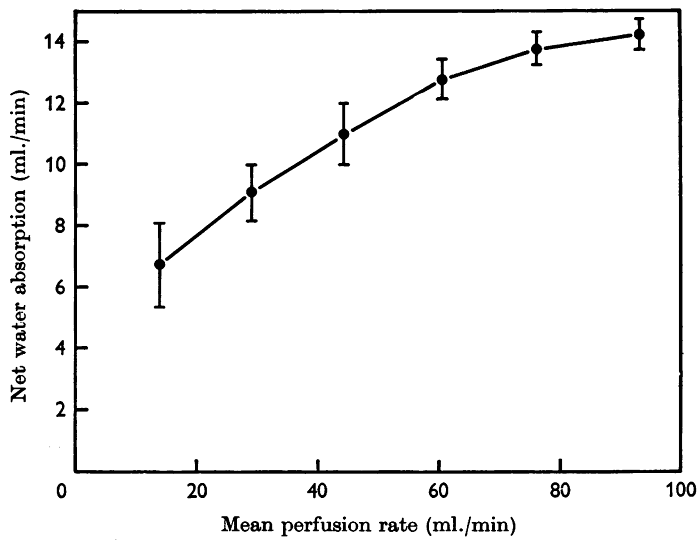

Fig. 1. The relation between net water absorption and rate of perfusion of the entire human intestine. Mean and standard deviation of five studies.

and standard deviation of five studies in five subjects at each perfusion rate. In the case of unidirectional fluxes these are values obtained from three studies at each perfusion rate. Relating the water absorption to sodium absorption figures indicates that the fluid absorbed had a mean concentration of 138·8 m-equiv/l. This was almost identical to the mean value for plasma in the individuals studied, 139·8 m-equiv/l.

In Fig. 3 transit time and intestinal volume are plotted against perfusion rate. The intestinal volume increases with increasing perfusion rates to reach a plateau at rates of 70–100 ml./min. Transit time diminishes with increasing perfusion rate and at the values where the volume of the intestine has reached a constant value it is a linear relation to perfusion rate.

The increase in volume and absorptive activity as perfusion rate increased has been integrated in Table 1, where the water absorption (ml./min) and sodium transport (m-equiv/min) have been expressed as a

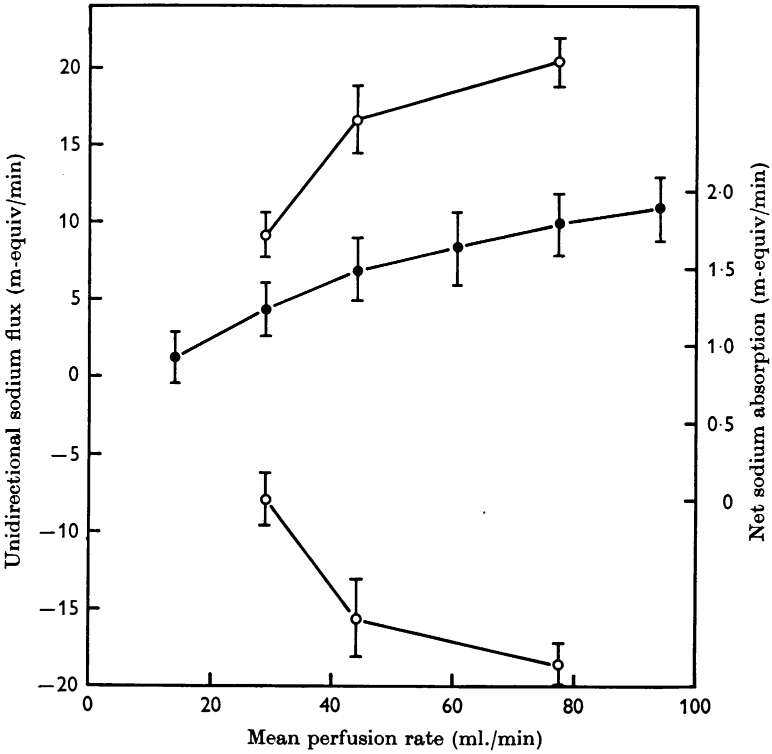

Fig. 2. The relation between sodium transport and perfusion rate in the entire human intestine. Net absorption and unidirectional ion flux valves expressed as mean and standard deviation of five studies.

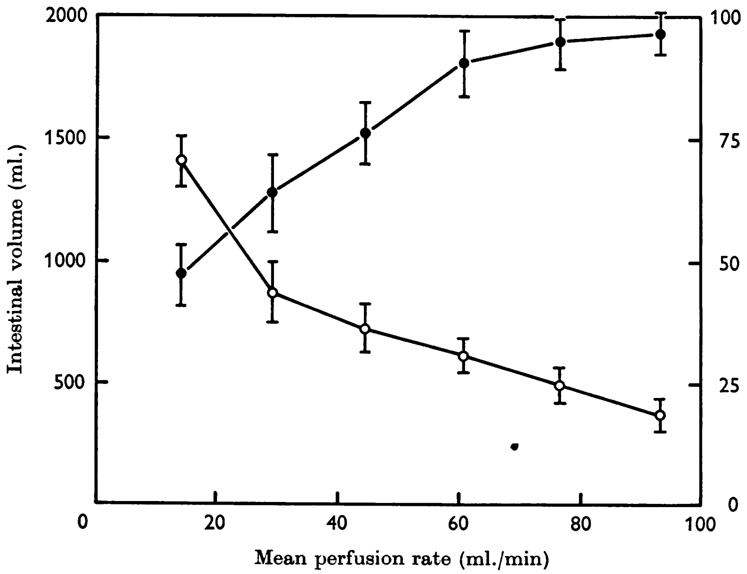

Fig. 3. The relation of transit time and intestinal volume to perfusion rate in the human intestine.

TABLE 1. Values for water and sodium absorption in perfusion studies of the entire human intestinal tract. Corrected values are made to a standard intestinal volume of 1 l.

Perfusion rate (ml./min)	Gut volume (ml.)	Water absorption (ml./min)		Sodium transport (m-equiv./min)					
				m-equiv/min			Gut volume (m-equiv. min^{-1}. l.$^{-1}$)		
		ml./min	ml./ min^{-1}. l.$^{-1}$	$L \to P$	Net	$P \to L$	$L \to P$	Net	$P \to L$
16·7	947 ± 95	6·7 ± 1·4	7·3 ± 1·7	—	0·92 ± 0·14	—	—	1·19 ± 0·15	—
33·4	1260 ± 156	9·1 ± 0·9	7·3 ± 0·6	9·11 ± 1·41	1·13 ± 0·51	7·98 ± 1·43	—	0·90 ± 0·33	—
50·0	1516 ± 129	11·0 ± 1·0	7·3 ± 0·7	16·96 ± 2·55	1·42 ± 0·70	15·54 ± 3·01	—	0·94 ± 0·34	—
66·7	1827 ± 124	12·8 ± 0·6	7·1 ± 0·8	—	1·62 ± 0·19	—	—	0·89 ± 0·19	—
83·4	1931 ± 109	13·8 ± 0·5	7·2 ± 0·7	20·29 ± 1·24	1·88 ± 0·13	18·87 ± 1·22	—	0·97 ± 0·13	—
100·0	1958 ± 94	14·3 ± 0·3	7·3 ± 0·5	—	1·93 ± 0·20	—	—	0·99 ± 0·11	—

Mean ± S.D.

function of a standard intestinal volume (1 l.). It appears that the absorptive capacity of the intestine when so expressed does not change with changing perfusion rates. None of the differences in ml./min^{-1}.l.$^{-1}$ or m-equiv.min^{-1}.l.$^{-1}$ is significant between any of the values at any flow rate.

DISCUSSION

A balanced electrolyte solution resembling the composition of plasma has been used to produce 'steady-state' perfusion of the entire human intestine. Under these conditions measurements have been made of absorption capacity and volume changes. Similar principles have been used to study flow and volume interrelationships in small bowel segments by Dillard, Eastman & Fordtran (1965).

The values for net water and sodium absorption were obtained from input–output balance over a period of at least 2 hr and their reliability depends on the constancy of perfusion. This increases with increasing rates of perfusion. At a perfusion rate of 16 ml./min the value of outflow was $10{\cdot}3 \pm 6{\cdot}9$ ml., while at 100 ml./min it was $88{\cdot}3 \pm 19{\cdot}3$ ml. It appears therefore that at high rates of flow there is a greater approximation to the steady state perfusion required for reliable application of the method. The amount of water and sodium absorbed at these high rates of flow is of the same order of magnitude as might be deduced from segmental studies. Water and sodium exchange from an isotonic solution before reaching the pylorus is so small as to be neglected (Lee, Code & Scholer, 1955). In the small intestine the studies of Fordtran *et al.* (1961) would suggest that the entire small bowel might absorb 15 ml./min whilst from the work of Levitan *et al.* (1962) the colon would absorb another 1·7 ml. giving a total capacity of approximately 16·7 ml./min. The deductions of Wilson (1962) from the work of Borgstrom *et al.* (1957) give a value of 12·5 ml./min. The present method indicates that the measured value for total bowel water absorption is 14·3 ml./min. The agreement is similar in the measurement of net sodium absorption. The results obtained by the present method are therefore very close to those predicted.

The net exchange of sodium is the resultant of unidirectional fluxes of the ion between the lumen and plasma in both directions across the mucosa. Previous attempts to determine these transfer rates have used lavage solutions of constant specific activity radiosodium according to the technique used by Vaughan (1960) in dogs. It was observed that in such a situation the specific activity of sodium in the effluent was essentially the same as that of plasma. If, however, a steady state perfusion is established the sudden introduction of a bolus of radiosodium will allow calculations of the unidirectional flux from lumen to plasma since the bolus can be identified and quantitated in the effluent stool without any significant contamination with backflux from the plasma. This method has been described as applied to monkeys (Mitchell & Neptune, 1965) and man (Love & Phillips, 1965). The values measured again are of the same order of magnitude as those predicted from segmental studies.

The relationships described between flow rate volume changes and absorptive capacity are worthy of comment. It appears that as flow rates increase both volume and absorptive capacity increase to reach a plateau at high flow rates. This type of relationship has been noted in the work of Dillard *et al.* (1965). In the small intestinal segments, however, the plateau was reached at much lower flow rates than those reported here for the whole bowel. It is interesting that the absorptive capacity increased with volume but that if calculated to a fixed arbitrary volume (1 l.) the capacity was constant. There are various possible explanations. Firstly, it may be that the absorptive area is increased by stretching of the bowel. Secondly, there may be some contribution of a rising hydrostatic pressure in the lumen. That this increases absorption has not been demonstrated (Fisher, 1955; Smyth & Taylor, 1957). Thirdly, it may be that the area is increased by a more near approximation to continuous flow. It can be imagined that at low flow rates the perfusion is accomplished as a series of isolated boluses but as rates increase the bolus chain becomes more nearly continuous, so exposing the entire bowel mucosa at one time. This explanation gains some weight as the volume collections become more constant at higher rates of perfusion. It seems therefore that the increase in absorption rate with flow increases can be taken to represent absorption capacity of the intestine only at perfusion rates of 5 l./hr and lower values are an artifact of the method.

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