

## WATER AND SALT ABSORPTION IN THE HUMAN COLON \* †

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Most knowledge about absorptive colonic function in man is derived from the study of patients with ileostomies (1, 2) and the comparison of results with the composition of stools of normal subjects. To obtain more direct and quantitative information concerning water and salt absorption from the intact and healthy human colon, the following studies were performed.

### METHODS

The subjects were healthy male volunteers aged 20 to 30 years. The cecum was intubated from above with a polyvinyl tube 1.8 mm in internal diameter, with a small rubber bag containing mercury affixed to its distal end. During the 3 to 4 days required for the tube to reach the colon the subject ingested clear liquids only. After the tip was located radiologically in the cecum, a radiopaque water-soluble solution was instilled to ascertain that no reflux into the ileum would take place. Thereafter, the colon was cleaned thoroughly by perfusing it with normal saline until the material expelled rectally was clear and relatively free of mucus. After this cleansing period, 2 hours were allowed for the subjects to expel or absorb the saline remaining in the colon.

All studies were performed after an 8 hour fast. The standard procedure consisted of infusing the test solution at a constant rate of 10 ml per minute into the cecum and collecting the perfusate through a rectal tube (size Fr. 24) placed into the rectum approximately 8 cm above the anus. The test solution contained 0.85 per cent sodium chloride, 1 per cent polyethylene glycol (PEG), a nonabsorbable reference substance with a molecular weight of about 4,000 (3-6), and tritiated water (0.5 to 1.0 mc per 1,000 ml). In three studies the design of the experiment was modified slightly by intubating the colon with a double polyvinyl tube and collecting samples from the mid-colon as well as from the rectal tube. Drainage from the collecting tubes was dis-

carded for the first 45 minutes or longer in order to establish a steady state. Thus, even if some fluid had remained in the colon from the wash period, it would have been flushed out during the equilibration period. Thereafter, specimens were collected at 20 minute intervals for 60 to 240 minutes.

The obtained material was analyzed for sodium and potassium by flame photometry (7), for chloride by potentiometric titration (8), and for bicarbonate by Auto-analyzer as described by Skeggs (9). Osmolality was determined by freezing point depression, and tritiated water by counting in a Packard Tri-Carb liquid scintillation spectrometer. PEG was analyzed turbidimetrically by the method of Hyden (10). Recovery of PEG added to clear, mucus-containing colonic washings *in vitro* averaged 95 per cent and demonstrated a variation of less than  $\pm 6$  per cent on repeated analysis.

Net water movement, unidirectional water fluxes, net sodium and chloride absorption, and potassium and bicarbonate secretion were calculated by methods previously used in the study of sodium and water absorption in the intact human small bowel (11). The equations used in the calculations of net water absorption and unidirectional water fluxes were:<sup>1</sup>

1) Net volume change in ml/min

$$= [V_{in}] - \left[ (V_{in}) \left( \frac{PEG_{in}}{PEG_{re}} \right) \right]$$

2) Flux out of the lumen in ml/min

$$= \frac{[(SA_{in})(V_{in})] - [(SA_{re}) \left( V_{in} \frac{PEG_{in}}{PEG_{re}} \right)]}{SA_{in}}$$

3) Flux into the lumen in ml/min

$$= \text{flux out of the lumen} - \text{net volume change}$$

4) Net electrolyte absorption or secretion was calculated as follows:

Net change in mEq/min

$$= [(E_{in})(V_{in})] - \left[ (E_{re}) \left( V_{in} \frac{PEG_{in}}{PEG_{re}} \right) \right]$$

<sup>1</sup> The symbols used in the equations are:  $V_{in}$  = volume infused, ml per minute;  $PEG_{in}$  = PEG concentration in mg per 100 ml in infused fluid;  $PEG_{re}$  = PEG concentration in mg per 100 ml in recovered sample;  $SA_{in}$  = specific activity of the radioactive tracer in the infused fluid, counts per minute per ml;  $SA_{re}$  = specific activity of the radioactive tracer in the recovered sample, counts per minute per ml;  $E_{in}$  = concentration of electrolyte in infused fluid, mEq per ml;  $E_{re}$  = concentration of electrolyte in recovered sample, mEq per ml.

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The term "absorption" is used when the net result was a decrease in water and electrolyte content in the intestinal lumen. Secretion is used to denote a net increase in water and electrolyte content of the lumen. The formulas for calculating net change have been arbitrarily arranged so that absorption is indicated by a positive (+) and secretion by a negative (-) sign.

The calculation of net water and electrolyte absorption would be influenced if ileal material entered the large bowel during the experiments and thus diluted the non-absorbable reference substance. However, since a tube placed in the terminal ileum 30 cm proximally to the infusion tip did not drain any fluid during these experiments, contaminating fluid from above probably was very small in amount and not sufficient to influence the calculation. However, in studies done higher in the intestine (11), the amounts of gastric, biliary, and pancreatic fluids entering the segment from above must be taken into account.

The use of tritiated water for the measurement of unidirectional water fluxes in our experiments is based on the assumption that back flux of the radioisotope from the extracellular fluid to the colonic lumen will be relatively small because the tracer, once it leaves the intestinal lumen, is diluted in a large volume of body water.

In order to test the validity of this assumption, the colons of two subjects were intubated and perfused with 0.85 per cent sodium chloride solution containing PEG but no tritiated water. After this solution was infused for 45 minutes to achieve a steady state, 0.85 per cent sodium chloride solution, containing 0.5 mc tritiated water per 1,000 ml, was given intravenously at a rate of 10 ml per minute. This is the same rate of infusion and the same amount of tracer used in our colonic perfusion experiments. The number of counts of tritium recovered in 1 ml of colonic perfusate at no time exceeded 3 per cent of the concentration of the intravenously administered radioactive tracer. Since the concentration of tracer recovered in samples from the rectum after colonic perfusion with the test solution averaged 30 per cent of the original concentration, back flux would not appear to alter significantly our calculations for unidirectional water fluxes.

RESULTS

The results obtained in each subject are shown in Figure 1 and Table I. The mean water flux out of the lumen for the entire group was 7.8 ml per minute (range 7.2 to 8.7), flux into the lumen

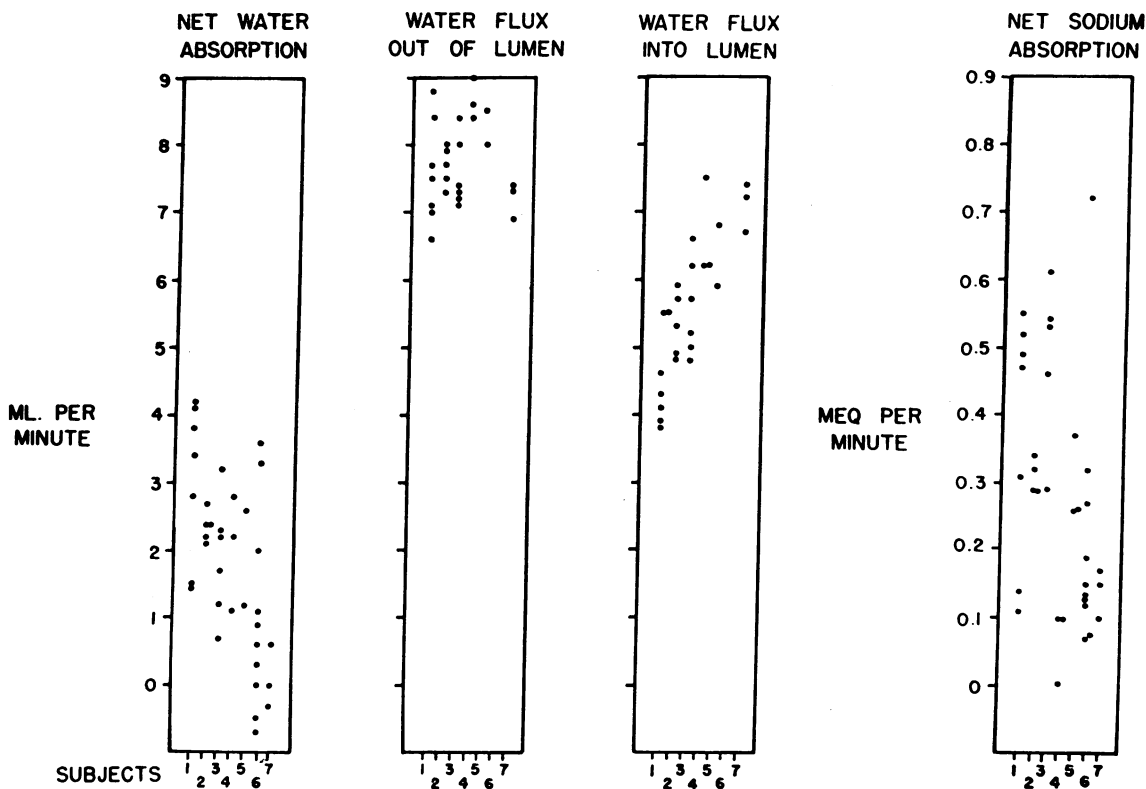


FIG. 1. RESULTS OF EACH 20 MINUTE COLLECTION PERIOD ARE REPRESENTED BY A DOT. The tests in the same subjects are arrayed in a vertical line.

TABLE I

*Net absorption of water, unidirectional water fluxes, net absorption of sodium and chloride, and net secretion of potassium and bicarbonate for each subject during colonic perfusion with 0.85% sodium chloride solution \**

Subject		Water flux			Net sodium absorption	Net chloride absorption	Net potassium secretion	Net bicarbonate secretion
		Net	Out of lumen	Into lumen				
			ml/min		mEq/min	mEq/min	mEq/min	mEq/min
1	Mean	3.0	7.6	4.6	0.37			
	SD	1.1	0.8	0.7	0.18			
	(n = 7)							
2	Mean	2.3	7.7	5.4	0.31	0.45	0.044	0.16
	SD	0.2	0.3	0.5	0.02	0.05		0.05
	(n = 5)				(n = 4)			
3	Mean	1.9	7.6	5.7	0.49	0.42	0.021	0.15
	SD	0.9	0.5	0.7	0.12			
	(n = 6)				(n = 5)			
4	Mean	2.1	8.7	6.6	0.10		0.027	
	SD	0.8	0.3	0.7	0.05		0.006	
	(n = 3)							
5	Mean	1.9	8.3	6.4	0.31		0.032	
	(n = 2)							
6	Mean	0.3			0.22	0.28	0.022	0.23
	SD	1.7			0.19	0.06	0.013	0.02
	(n = 10)							
7	Mean	0.1	7.2	7.1	0.14	0.41	0.041	0.17
	SD	0.4	0.3	0.3	0.04	0.14	0.045	0.06
	(n = 3)							
Mean for entire group:								
	Mean	1.7	7.8†	6.0†	0.28	0.39	0.031	0.18
	SD	1.0	0.5	0.9	0.14	0.08	0.010	0.04

\* Standard deviation is not given unless the results for at least three study periods are available. The number of test periods (n) in each subject is as indicated in the first column except where noted otherwise in a subsequent column.

† Excluding subject 6.

was 6.0 ml per minute (range 4.6 to 7.1), and net water absorption was 1.7 ml per minute (range 0.1 to 3.0). Mean sodium and chloride absorptions were 0.28 mEq per minute (range 0.10 to 0.49) and 0.39 mEq per minute (range 0.28 to 0.45), respectively. Mean secretions of potassium and bicarbonate were 0.031 mEq per minute (range 0.021 to 0.044) and 0.18 mEq per minute (range 0.15 to 0.23), respectively.

The three experiments in which the perfusate was sampled in the mid-colon permitted comparison of the right (ileocecal valve to splenic flexure) and the left (splenic flexure to rectum) colon with respect to water, sodium, and chloride absorption, and potassium and bicarbonate secretion. It ought to be stressed that the test solution entering the left colon was not 0.85 per cent sodium chlo-

ride any more. It contained 134 to 136 mEq per L of sodium, 121 to 126 mEq per L of chloride, 1.6 to 2.0 mEq per L of potassium and 13 to 16 mEq per L of bicarbonate. Despite these changes, the mid-colonic contents remained isosmolal in all three subjects. From the results shown in Table II, it appears that the right colon is more permeable to water than the left as judged from the larger unidirectional water fluxes that take place on the right side. Sodium and chloride absorption as well as potassium and bicarbonate secretion were also larger in the right than in the left colon.

#### DISCUSSION

It is apparent that during perfusion of the entire colon net water absorption occurred in 31 out

of 36 test periods and that net sodium and chloride absorption as well as net secretion of potassium and bicarbonate were observed in all experiments. More chloride than sodium absorption occurred in our studies. However, since the infused solution contained 0.85 per cent sodium chloride, the chloride concentration was higher in the infusate than in the extracellular fluid. The resulting chemical gradient for chloride (but not for sodium) between colonic contents and body fluids probably explains the greater chloride than sodium absorption observed in our experiments (12). In addition, the greater chloride than sodium absorption in these experiments may be partially explained by exchange of chloride with bicarbonate, for according to D'Agostino, Leadbetter and Schwartz (13), sodium and chloride are exchanged with plasma potassium and bicarbonate, respectively, in the dog's large intestine.

The osmolality of ileal effluent, colonic contents, and feces is probably always very close to that of plasma (2, 14). Similarly, in our experiments the osmolality of the test solution remained essentially unchanged during its passage through the colon, and hence the osmolality of the solution absorbed must have been isotonic with plasma.

During our experiments, which extended from 40 minutes to 4 hours, no diminution of colonic absorptive powers became apparent. Were the colon able to maintain this rate of absorption for 24 hours, it could absorb during this time about 2.45 L of water, 403 mEq of sodium, and 562 mEq of chloride from a 0.85 per cent sodium chloride solution infused at a rate of 10 ml per minute, and during the same time it could secrete about 45 mEq of potassium and 259 mEq of bicarbonate.

The results of the studies of Curran and Schwartz (15) on water and sodium absorption in the rat colon suggest that our values for net water absorption may not be directly applicable to water absorption from ileal effluent. These investigators (15) used different concentrations of sodium chloride made isotonic by the addition of mannitol and found that water absorption decreased in a linear fashion with decreasing sodium concentration. Water absorption ceased when mannitol accounted for about one-half of the osmolality, and the sodium chloride concentration was less than 75 mEq per L. If the mechanisms

TABLE II  
Comparison of mean values of water fluxes and net absorption of water, sodium, and chloride, and net secretion of potassium and bicarbonate in the right (cecum to splenic flexure) and left (splenic flexure to rectum) colon \*

Subject	Net water absorption		Water flux out of the lumen		Water flux into the lumen		Net sodium absorption		Net chloride absorption		Net potassium secretion		Net bicarbonate secretion	
	right colon	left colon	right colon	left colon	right colon	left colon	right colon	left colon	right colon	left colon	right colon	left colon	right colon	left colon
	ml/min		ml/min		ml/min		mEq/min		mEq/min		mEq/min		mEq/min	
5 (n=4)	1.0	0.9	7.3	1.0	6.3	0.1	0.26	0.05	0.21	0.07	0.020	0.012	0.16	0.07
6 (n=10)	0.2	0.1			0.17	0.05	0.10	0.04	0.30	0.11	0.032	0.009	0.13	0.04
7 (n=3)	0.2	-0.1	6.2	1.0	6.0	1.1								

\* The number of experiments (n) in each subject is as indicated in the first column.

of water absorption in the rat colon apply to man, water absorption from ileal effluent will be less than from 0.85 per cent sodium chloride solution, since human ileal fluid contains only 95 to 117 mEq per L sodium (2), and other solutes, which are not actively absorbed (probably like mannitol), are present in sufficient concentration to make the solution isotonic with plasma.

Our findings of larger net water and electrolyte movement in the right than the left colon have to be evaluated in the light of the differences in the electrolyte content of the test solutions perfusing these segments (see results). Thus, on the basis of the experiments of Curran and Schwartz (15) one would expect less water absorption in the left than in the right colon because of the fall in sodium concentration of the test solution entering the left side. Furthermore, the fall in chloride concentration and the rise in potassium and bicarbonate concentrations in the fluid bathing the left colon would tend to decrease chloride absorption and potassium and bicarbonate secretion because of a decrease in the chemical gradient of these electrolytes between the lumen of the colon and plasma. On the other hand, the larger unidirectional water fluxes in the right than in the left colon cannot be readily attributed to difference in composition of the fluids entering the different colonic segments. It is possible that the greater permeability of the right colon to water may be explained in part by the presence of larger mucosal area in the right as compared to the left colon, or to more rapid transit through the left than the right. Cellular differences cannot, however, be excluded.

#### SUMMARY

A method using constant perfusion of the colon via an orally introduced tube was used to study unidirectional water fluxes as well as absorption of water and electrolytes in the colon of healthy intact men.

The perfusion fluid was 0.85 per cent sodium chloride solution containing tritiated water and a nonabsorbable reference substance, polyethylene glycol. The test solution was sampled via a rectal tube in all cases and in three cases in the mid-

colonic area as well. A total of 36 test periods of 20 minutes each was carried out in seven subjects.

Under the conditions of our experiments, the entire colon absorbed on the average 1.7 ml of water, 0.28 mEq of sodium, and 0.39 mEq of chloride per minute, and at the same time secreted 0.031 mEq of potassium and 0.18 mEq of bicarbonate per minute. The mean water flux out of the lumen was 7.8 ml per minute and flux into the lumen was 6.0 ml per minute. Larger unidirectional water fluxes were observed in the right than in the left colon.

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#### REFERENCES

1. Welch, C. S., Wakfield, E. G., and Adams, M. Function of the large intestine of man in absorption and excretion. Study of a subject with an ileostomy stoma and an isolated colon. *Arch. intern. Med.* 1936, **58**, 1095.
2. Kramer, P., Kearney, M. M., and Ingelfinger, F. J. The effect of specific foods and water loading on the ileal excreta of ileostomized human subjects. *Gastroenterology* 1962, **42**, 535.
3. Shaffer, C. B., and Critchfield, F. H. The absorption and excretion of the solid polyethylene glycols ("carbrowax" compounds). *J. Amer. pharm. Ass., sci. ed.* 1947, **36**, 152.
4. Sperber, I., Hyden, S., and Edman, N. J. The use of polyethylene glycol as a reference substance in the study of ruminant digestion. *Ann. agr. Coll. (Sweden)* 1953, **20**, 337.
5. Borgström, B., Dahlqvist, A., Lundh, G., and Sjövall, J. Studies of intestinal digestion and absorption in the human. *J. clin. Invest.* 1957, **36**, 1521.
6. Aberdeen, V., Shepherd, P. A., and Simmonds, W. J. Concurrent measurement, in unaesthetized rats, of intestinal transport and fat absorption from the lumen. *Quart J. exp. Physiol.* 1960, **45**, 256.
7. Annino, J. S. *Clinical Chemistry, Principles and Procedures*, 2nd ed. Boston, Little, Brown, 1960, p. 99.
8. Sanderson, P. H. Potentiometric determination of chloride in biological fluids. *Biochem. J.* 1952, **52**, 502.

9. Skeggs, L. T., Jr. An automatic method for determination of carbon dioxide in blood plasma. *Amer. J. clin. Path.* 1960, **33**, 181.
10. Hyden, S. A turbidometric method for determination of higher polyethelene glycols in biological materials. *Ann. agr. Coll. (Sweden)* 1955, **22**, 139.
11. Fordtran, J. S., Levitan, R., Bikerman, V., Burrows, B. A., and Ingelfinger, F. J. The kinetics of water absorption in the human intestine. *Trans. Ass. Amer. Phycns* 1961, **74**, 195.
12. Ussing, H. H. *The Alkali Metal Ions in Biology*. Berlin, Springer-Verlag, 1960, p. 132.
13. D'Agostino, A., Leadbetter, W. F., and Schwartz, W. B. Alterations in the ionic composition of isotonic saline solution instilled into the colon. *J. clin. Invest.* 1953, **32**, 444.
14. Dempsey, E. F., Carroll, E. L., Albright, F., and Henneman, P. H. A study of factors determining fecal electrolyte excretion. *Metabolism* 1958, **7**, 108.
15. Curran, P. F., and Schwartz, G. F. Na, Cl, and water transport by rat colon. *J. gen. Physiol.* 1960, **43**, 555.