ABSORPTION AND SECRETION IN THE LARGE INTESTINE

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THE ABSORPTIVE function of the colon is confined to transforming the fluid chyme, received from the ileum, into a semi-solid mass. Our knowledge of this function has been largely inferred, by comparing the volume and content of the discharges from well-established ileostomies with the composition of the faeces of normal subjects (Table 1). From these data it is evident that the colon absorbs water, sodium and chloride and secretes potassium. In addition, bicarbonate ions are secreted into the colonic lumen (d'Agostino, Leadbetter and Schwartz, 1953).

The means by which the colon absorbs and secretes water and electrolytes have been elucidated in a series of animal experiments both *in vivo* and *in vitro*. Sodium has been shown to be actively absorbed by the colon of the rat (Curran and Schwartz, 1960), of the dog (Cooperstein and Brockman, 1959) and of the bull-frog (Chalfin, Cooperstein and Hogben, 1958; Cooperstein and Hogben, 1959). In these species, chloride absorption was shown to be entirely passive in nature. Potassium may be secreted passively into the colonic lumen to maintain the electrical neutrality, disturbed by the active movement of sodium ions in the opposite direction; or a coupled sodium-potassium pump may exist in the colon, actively transferring sodium ions from lumen to blood, and potassium ions in the opposite direction (Ussing, 1960). The type of transport system employed by the colon in water absorption remains obscure. One widely-held view is that water movement is passive and secondary to the transfer of solute—solute is absorbed, and water follows in response to the osmotic gradient set up (Curran and Schwartz, 1960). Many observations, however, particularly from *in vitro* experiments (for review, Shields, 1964), suggest that water may be actively transported by the intestine. Indeed, several mechanisms may be used in the absorption of water.

There have been few reported studies on the absorption and secretion of water and electrolytes in the *human* large intestine. Early

workers (Annis and Alexander, 1952; Parsons, Powell and Pyrah, 1952) showed that the colon absorbed sodium, chloride and water, and secreted potassium. In these experiments, however, only the *net* movements of water and electrolytes were measured. These substances are simultaneously exchanged in both directions across the intestinal mucosa (Visscher, Fetcher, Carr, Gregor, Bushey and Barker, 1944a; Visscher, Varco, Carr, Dean and Erickson, 1944b). When the amount of a substance moving from the bowel lumen into the body is greater than that moving in the opposite direction, the resultant or net movement is said to be 'absorption' whereas, when the amount moving from the body into the bowel lumen is greater than that moving in the opposite direction, the resultant, or net movement, is 'secretion'. The semantics of intestinal transport have been discussed elsewhere (Shields, 1964).

Within the last two years there have been several attempts to study this exchange of water and electrolytes across the colonic mucosa. Duthie and Atwell (1963) confirmed the bidirectional transport of water, sodium and potassium in segments of human colon, temporarily isolated during operation. However, some of our own experiments suggest that surgical trauma can alter the intestinal handling of sodium and potassium (Shields, 1965). Levitan, Fordtran, Burrows and Ingelfinger (1962) measured, in the intact colon of unanæsthetised subjects, the bidirectional movement of water, the *net* absorption of sodium and chloride, and the *net* secretion of potassium and bicarbonate. They introduced a tube, passed by mouth, into the cæcum. The entire length of colon was perfused with a test solution and the perfusate was collected by a tube inserted through the anus into the rectum. However, there have been no previous studies reported, in which the *bidirectional* movements of sodium, potassium and water have been *simultaneously* studied in the human colon of unanæsthetised subjects.

To this end we have developed further the

TABLE 1
THE COMPOSITION OF THE DEJECTA OF ESTABLISHED ILEOSTOMIES AND
OF THE FAECES OF NORMAL SUBJECTS⁺

	Composition of dejecta of established ileostomies	Composition of faeces of normal subjects
Weight (g.)	466	150
Volume (ml.)	400—500	100
Sodium—concentration ⁺⁺	115—145	25—50
—daily loss (mEq.)	53	2.5—5.0
Potassium—concentration ⁺⁺	6—30	80—132
—daily loss (mEq.)	5.5	8—13
Chloride—concentration ⁺⁺	75—100	10—50
—daily loss (mEq.)	35—50	1—5

+—Data from Davenport, (1961) Wells (1962), and Kanaghinis, Lubran and Coghill (1963)

++—Concentrations are in mEq. per litre ileostomy water.

TABLE 2
THE RATES OF MOVEMENT OF SODIUM, POTASSIUM AND WATER INTO AND
OUT OF THE LUMEN OF THE INTACT COLON OF FOUR NORMAL SUBJECTS

Substance	Direction	Mean rate $\pm$ standard deviation
Sodium (mEq. per minute)	out of colon	0.61 ± 0.09
	into colon	0.29 ± 0.08
	absorption	0.32 ± 0.09
Potassium (mEq. per minute)	out of colon	0.018 ± 0.005
	into colon	0.040 ± 0.01
	secretion	0.022 ± 0.01
Water (ml. per minute)	out of colon	7.5 ± 1.1
	into colon	5.4 ± 1.0
	absorption	2.1 ± 1.1

method of Levitan and others (1962). The test solution was Tyrode's solution containing radioactive sodium and potassium, and the stable isotope of water, deuterium oxide. Polyethylene glycol (molecular weight, 4,000) was added to the perfusing solution as a non-absorbable marker. This test solution was perfused through the colon by means of a peristaltic pump at a constant rate of 20 ml./minute. The details of the method and of the calculations are given elsewhere (Miles and Shields, 1965).

The results confirm that the human colon absorbs water and sodium and secretes potassium, and that these *net* movements are incorporated in a much more rapid two-way traffic across the intestinal mucosa (Table 2). Thus, the large intestine handles a greater quantity of water and electrolytes than is

immediately apparent from comparing the amount of fluid that enters the colon at one end with that which is expelled at the other. Of particular interest is the fact that the movement of sodium into the body from the bowel lumen is more than twice that moving in the opposite direction. Such a finding is in general agreement with animal studies (Visscher and others, 1944b) that the colon is an extremely efficient absorber of sodium ions. Nevertheless more sodium and, of course, water are absorbed, albeit less efficiently, in the small intestine since the latter presents a larger total surface area.

Such direct measurement of the exchange of fluid and electrolytes across the colonic mucosa permits a more accurate and meaningful assessment of colonic function. Although these studies were confined to three or four hours,

FIG. 1.—Water absorption in the colon. The values for the daily work performed by the colon are obtained from the data in Table 1. The values for the total functional capacity of the colon are derived from the data in Table 2.

FIG. 2.—Sodium absorption in the colon. The values for the daily work performed by the colon are obtained from the data in Table 1. The values for the total functional capacity of the colon are derived from the data in Table 2.

the colon did not show any change in its behaviour during this time. If the colon maintained these rates of movement for 24 hours—and there would seem little objection to this assumption—then it would absorb 3 litres of water and 460 mEq. of sodium, and secrete 32 mEq. of potassium (Figs. 1, 2 and 3). Thus, although the colon is called upon to absorb

FIG. 3.—Potassium secretion in the colon. The values for the daily work performed by the colon are obtained from the data in Table 1. The values for the total functional capacity of the colon are derived from the data in Table 2.

only 400 ml. water each day, it has a capacity to absorb seven times this amount, and, in doing so, will handle over 18 litres of fluid—10.8 litres leaving, and 7.8 litres entering, its lumen. Similarly, the reserve capacity of the colon for sodium absorption is almost seven times the work that it is called upon to perform. Finally the daily loss of potassium from the body by colonic secretion is low, but, if the colonic lumen were perfused continuously, then the rate of potassium secretion would be greatly accelerated.

Several important conclusions can be drawn from these observations. First, despite the reserve capacity of the colon, there is a definite limit to the extent to which the colon can compensate for a loss in absorptive function of the small intestine. Secondly, if the ability of the colon to handle water and electrolytes is impaired then mainly small bowel content will be lost from the body. Third, even although the colon has preserved its normal absorptive ability, and only the small intestine is diseased, then the passage of increased quantities of fluid over the colonic mucosa will bring about increased secretion of potassium ions by the colon. Abnormal losses of potassium have been demonstrated with the over-use of laxatives (Coghill, McAllen and Edwards, 1959).

There is some evidence that the absorptive function of the colon may be modified in response to the body's needs. It has been known for some time that, with salt deprivation, sodium almost entirely disappears from the faeces (Field, Swell, Dailey, Trout and Boyd, 1955). We have recently re-investigated this problem in dogs, and have shown that the colon increased the rate of sodium absorption by reducing the amount of sodium it allows to 'leak' back into its own lumen. (Clarke and Shields, 1963). Such intestinal conservation of sodium is brought about at the expense of increased potassium secretion. Since sodium depletion is a powerful stimulus to the secretion of aldosterone, we investigated the effects of aldosterone infusions upon isolated segments of colon in both man and the dog (Shields and Elmslie, 1962). The intestinal handling of potassium ions was influenced by aldosterone—potassium secretion was increased significantly because more potassium ions entered the intestinal lumen. This action of aldosterone upon the intestine was blocked by spironolactone (Elmslie, Mulholland and Shields, 1965). In addition, using the technique of colonic perfusion, we have shown that, in primary hyperaldosteronism, there is an increased loss of potassium from the colon, because the bowel allows more potassium ions to enter than under normal conditions (Miles and Shields, 1965). The altered handling of potassium by the colon is reversible, returning to normal with the removal of the tumour.

With these refined techniques it is now possible to characterise fully the disturbances in colonic function when the colon itself is diseased. In their pioneer investigations, Duthie and his colleagues (Duthie and Atwell, 1963; Duthie, Watts, de Dombal and Goligher, 1964) have shown that the colon's ability to handle water and electrolytes is disturbed in villous papillomatosis and ulcerative colitis. Unfortunately these studies, using isolated segments of bowel investigated at operation, permit only one measurement in each patient. Nevertheless, much interesting information has been obtained—for example, that the excessive losses of fluid from a segment of bowel containing a villous papilloma is caused by the cells composing the tumour being intrinsically different from normal colonic mucosal cells. We are engaged in similar studies of the diseased colon, employing, however, the technique of colonic perfusion so that several estimations may be made upon the same patient and so, in this way, the effect of drugs and various forms of treatment, surgical and medical, may be assessed.

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