Progress report

Electrolyte absorption from the colon

Though man has always displayed a considerable if somewhat morbid interest in the workings of his bowel little scientific investigation of human large bowel function was carried out until the last decade. It has become clear that a prime function of the colon is the absorption of salt and water, and recently attention has been focused on the capacity of the colon to handle electrolytes and on the underlying mechanisms involved. This review summarizes recent advances in this field. Examples are given of disorders of electrolyte transport in the human colon to illustrate its clinical relevance.

Unfortunately none of the several approaches employed for investigation in vivo in man are entirely satisfactory. Both measurement of the appearance in the blood stream of test substances introduced into the lumen of the colon and the disappearance from the colon of substances instilled into isolated segments at laparotomy have limitations. The measurement of absorptive function by perfusion techniques with the aid of nonabsorbable markers, although tedious and uncomfortable for the subject, has yielded more direct and informative results. These techniques, together with the recent reports of measurement of electrical potential differences across colonic mucosa, are beginning to clarify the physiology and pathophysiology of colonic absorptive function in man.

Absorptive Capacity

An indirect assessment of the amounts of salt and water which the colon handles each day can be made by comparing the volume and composition of ileostomy discharge and of stool water. Daily absorption rates of 400 to 500 ml of water, 70 m-equiv sodium, and 35 m-equiv chloride, and a secretion rate of 4 m-equiv/day of potassium are the usual calculated values. The total daily loss in the stools is less than 5 m-equiv sodium, 9 m-equiv potassium, and 2 m-equiv chloride. This very low rate of excretion, which is unaffected by ingestion of ion exchange resins, explains the ability of man to survive on a very low salt intake for long periods, a facility which is severely impaired in patients with an ileostomy. These calculations for absorptive rates are based on the assumption that ileostomy discharge is representative of the fluid which enters the normal caecum from a normal ileum. Giller and Phillips have suggested recently that the volume of normal ileal contents in intact man is greater than ileostomy discharge measurements would suggest and have calculated that sodium and water absorption rates by the colon may be as much as three times greater than formerly proposed.

That the colon is capable of absorbing much more salt and water than these values for average daily loads is evidenced by the results of perfusion studies of the entire colon in vivo. Levitan and his coworkers calculated that the colon would absorb up to 2.5 l water and over 400 m-equiv sodium and 550 m-equiv chloride per day if it could be perfused with isotonic saline at a
constant rate of 10 ml/minute for 24 hours (ie, 14·4 l per day). These widely quoted figures cannot be used, however, out of the context of the conditions in which they were obtained. At slower perfusion rates, with solutions having an ionic composition nearer to that of colonic contents, absorptive capacity would be less since less solute would be presented to the mucosa for absorption. Diarrhoea may well occur at much slower rates of flow into the colon from the ileum than the figure of 2·5 l/day for colonic capacity for water absorption would suggest.

Transport Mechanisms

WATER
In common with other biological membranes the colonic mucosa transports water as an entirely passive consequence of the movement of solutes, and occurs mainly in response to osmotic pressure gradients set up by ion movement\textsuperscript{16, 17, 18}. Few workers now support an active process for water transport\textsuperscript{9}. Sodium absorption is the major determinant of water movement. Perfusion studies reveal isosmotic absorption of sodium and water in the colon as elsewhere in the alimentary tract\textsuperscript{17, 19}. Theoretically, colonic contents should thus be isosmotic with plasma but the osmolality of stool water is higher than plasma, being about 370 m osmole/kg\textsuperscript{20}. This is almost certainly due to rapid bacterial breakdown of substrates, mainly unabsorbed carbohydrate, into a number of smaller solutes in the lower bowel and voided stool, since stool water becomes isosmotic with plasma when bacterial growth is inhibited by intestinal antibiotics\textsuperscript{21}.

SODIUM AND POTASSIUM
The concentration of sodium in stool water is about one quarter of the concentration in plasma\textsuperscript{20} and perfusion studies reveal absorption continuing until the luminal concentration falls to below 24 m-equiv/l\textsuperscript{16}. The mucosal surface of the colon is electrically negative to the serosal surface\textsuperscript{8, 9}, and thus absorption of sodium occurs against an electrical as well as a chemical concentration gradient, strong evidence for an active process underlying sodium transport. Experiments in vitro in animals suggest that the electrical potential developed across colonic mucosa is produced predominantly by active sodium transport\textsuperscript{18, 22} and it seems likely that this is equally true of the electrical potential in the human colon\textsuperscript{9}.

The potassium concentration in stool water is much higher than in plasma and may exceed 100 m-equiv/l\textsuperscript{20}. Contraction of the volume of colonic contents may account for some of the rise in concentration from that in ileal effluent but secretion of potassium across the colonic mucosa also occurs. Perfusion studies demonstrated that potassium is secreted into isotonic saline\textsuperscript{3}, while the experiments of Devroede and Phillips\textsuperscript{17} showed that secretion occurred into solutions containing less than 15 m-equiv/l potassium and absorption when the concentration was greater than 15 m-equiv/l. This figure of 15 m-equiv/l may not represent the concentration above which potassium is normally absorbed, however, since these studies were performed with sodium omitted from the perfusate, a factor which may affect electrical potential differences across the mucosa\textsuperscript{23, 24} and thus modify potassium movement secondarily. The orientation of the electrical potential difference, lumen negative to serosa, will induce potassium to enter the lumen against a concentration gradient, but it is not clear whether the recorded potential difference of 30 to 40 mV is sufficiently large to account for the observed concentration...
HORMONAL INFLUENCES

Mineralocorticoids have been shown to influence salt and water absorption.
from the large bowel. Aldosterone increased sodium and water 
absorption from the whole colon34, increased the potential 
difference across the recto-sigmoid mucosa2, and increased 
potassium secretion in isolated segments of human colon35. Stool 
sodium concentrations were reduced and potassium 
concentrations increased in normal subjects given mineralocorticoids, 
an effect inhibited by spironolactone36. The stools of patients with endogenous 
hyperaldosteronism showed similar changes in the concentration of sodium 
and potassium36, 37. Though such evidence suggests that mineralocorticoids 
play a role in regulating salt and water absorption in the colon their 
physiological importance is uncertain. It might be that in chronic diarrhoea the 
resulting loss of salt and water would stimulate the production of endogenous 
aldosterone, which would alter the ionic composition of the stools secondarily 
as diarrhoea continued. This phenomenon of secondary hyperaldosteronism 
has been described in patients with chronic purgative addiction38, 39, and may 
well be responsible for an excessive faecal and urinary loss of potassium 
leading on to the hypokalaemia so striking in these patients.

AMMONIA
The colon is a quantitatively important site for the production and absorption 
of ammonia40. It is produced predominantly in the lumen by the action of 
bacterial ureases on urea40 and is probably absorbed by a process of passive 
non-ionic diffusion41. Neomycin inhibits the production of ammonia by its 
effect on bacteria but does not influence ammonia absorption40. Although 
ammonia is produced from urea in the stomach and small bowel by mucosal 
ureases, which are present in higher concentrations than is colonic mucosal 
urease, the colon is quantitatively more important in the production of high 
plasma ammonia levels in cirrhosis40. The rationale for colonic irrigation 
and neomycin therapy in the management of hepatic encephalopathy is 
emphasized by these observations.

Disturbances in Electrolyte Absorption from the Colon
Although simple determinations of stool electrolyte concentrations can reveal 
much about disordered colonic function in diarrhoea, these measurements 
are rarely made, and reports in the literature are often sketchy. From a survey 
of the literature Fordtran and Dietschy16 pointed out that in a variety of 
different forms of diarrhoea there was a linear relationship between sodium 
and water losses in the stools. As diarrhoea increases in severity sodium 
concentrations tend to rise and potassium concentrations fall, so that in very 
severe diarrhoeic stool ion concentrations approach those in plasma. This 
relationship is present in diarrhoea of both small and large bowel origin. 
Presumably rapid transit through the colon limits the contact time between 
luminal contents and mucosa and thereby reduces the extent of the changes 
normally produced by colonic mucosa. It has been held that the diarrhoea 
of patients with a villous adenoma of the rectum is especially rich in potas-
sium48 but stool potassium concentrations in these patients are no higher than 
in normal subjects. The relationship found between severity of diarrhoea and 
electrolyte losses in other forms of diarrhoea is also valid for villous adenoma-
tata, and there is no convincing evidence of a specific potassium secretory 
process in this disease. It is possible that a secondary hyperaldosteronism 
could increase potassium losses and cause hypokalaemia in these patients 
as in purgative addiction38. The excessive fluid production is attributed to 
secretion predominantly of sodium and chloride by the tumour itself5. 
The cellular origin of the villous adenoma is uncertain but if it arises from
a secretory crypt cell this might explain some of its clinical characteristics.

Patients with ulcerative colitis and Crohn’s disease of the colon absorb less sodium and water and secrete more potassium than normals, and the permeability of the rectosigmoid area is reduced in distal colitis. These observations provide an insight into the mechanism of the diarrhoea of these patients.

A rare but fascinating disorder of intestinal electrolyte transport has been termed ‘congenital chloridorrhoea’. It is characterized by severe watery diarrhoea from birth, metabolic alkalosis, and an excessive loss of chloride in the stools, the concentration of chloride being higher than the sum of the sodium and potassium concentrations. The basis of the defect is thought to lie in the malabsorption of chloride in the ileum and colon, probably due to absence or reversal of the normal chloride/bicarbonate exchange process, for which good evidence in the ileum and suggestive evidence in the colon has been cited. A similar but acquired chloridorrhoea has been reported rarely in patients with hypokalaemia, itself usually the result of prolonged diarrhoea. The high stool chloride concentration returns to normal when the hypokalaemia is corrected and it is possible that the chloride/bicarbonate exchange is depressed by hypokalaemia in these cases. Hypokalaemia itself may thus perpetuate diarrhoea by this mechanism. Although the incidence of this phenomenon is unknown it is clearly important to consider this possibility in patients with prolonged diarrhoea.

The cathartic action of bile salts is well recognized. Recently it has been suggested that bile salts may be responsible for the watery diarrhoea encountered in some patients after removal of the terminal ileum, the site at which bile salts are normally re-absorbed. Hofmann suggested that sodium and water absorption in the colon is impaired by bile salts, a view supported by perfusion studies, and some of these patients obtain relief from diarrhoea by the oral ingestion of cholestyramine, which binds bile salts.

The importance of the study of colonic absorptive function is emphasized by these examples of disorders of electrolyte transport. A greater understanding of the pathophysiology of all forms of diarrhoea may well emerge as the normal mechanisms for ion transport in the colon become more clearly defined. Much could be learnt from even simple determinations of stool electrolyte concentrations, but this investigation, which could be a valuable aid in the diagnosis of difficult cases of persistent diarrhoea, is as yet infrequently applied.

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References


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