THE NUTRITIONAL MANAGEMENT OF PATIENTS WITH A SHORT SMALL INTESTINE

PETER BRUCE McINTYRE MBChB MRCP

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ProQuest LLC.
789 East Eisenhower Parkway
P.O. Box 1346
Ann Arbor, MI 48106 – 1346

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SUMMARY

The work for this thesis has been inspired by the experience gained from managing patients with inflammatory bowel disease in a specialist centre. An increasing number of patients with Crohn's disease are now surviving repeated intestinal resections which result in a short residual intestine. These patients, and others who have undergone extensive bowel resection secondary to mesenteric vascular disease, neoplasia, or radiation damage may develop a variety of nutritional deficiencies.

Those least affected have a tendency to water and sodium depletion requiring oral or parenteral replacement while being able to nourish themselves satisfactorily in the normal way. In the most extreme cases, insufficient bowel remains for satisfactory nutritional function, and parenteral nutrition in the patient's home is necessary to sustain life.

This thesis describes the clinical and pathophysiological features of the short bowel syndrome, and reviews the current state of knowledge regarding the use of fluid and electrolyte replacement and dietary manipulation in the management of such patients. The use of supplementary liquid diets and the techniques and

problems of home enteral and parenteral nutrition are discussed.

Experimental work has been undertaken with a group of patients who suffered from varying disabilities due to a short small intestine. The problems of fluid and electrolyte balance have been studied by comparing the efficiency of different sugar-electrolyte mixtures in improving sodium and water balance. This work was performed in collaboration with Dr C R Newton at St Mark's Hospital.

In a series of dietary studies, a whole protein liquid diet has been compared with a chemically defined diet, and with solid food by measuring nitrogen, fat and calorie balances. The effects of varying the fat and fibre content of normal diets upon these parameters, and upon sodium, potassium, calcium and magnesium balance have been investigated.

During the investigation and treatment of these patients, techniques for enteral and parenteral nutrition in the home have been developed and refined. These techniques and their complications are described and the results of therapy on patients' medical and social state presented.

In the final discussion, the experimental results are drawn together and their relevance to clinical practice is discussed. Guidelines for the oral, enteral and parenteral electrolyte and nutritional support of patients with the short bowel syndrome are suggested.

The appendix to the thesis contains case histories of those patients who took part in the studies of electrolyte mixtures, solid diets, and liquid supplements given orally and by nasogastric tube.

INTRODUCTION

Definition of the Short Bowel Syndrome

The 'short bowel syndrome' is a relatively new term which has gained general acceptance in gastroenterological and surgical practice as a convenient label to describe the symptoms and pathophysiological disorders brought about by the surgical removal of a large proportion of the intestine without regard to the underlying disease.

Prior to the early 1960's the term does not seem to appear in the literature, and patients with what is now called the short bowel syndrome were described as having had 'massive' intestinal resections. The adjectives 'massive' and 'extensive' were used to indicate resection of more than 200cm of intestine. This length was decided upon early in the literature as it was thought to represent approximately one third of the total length of the small intestine, which Senn in 1888 had experimentally demonstrated to be the maximum which could safely be removed (230). The convention persisted for over seventy years (93,206). The question of how much intestine is required to sustain life received much attention, and two papers, by Flint in 1912 (71) and Haymond in 1935 (93) stand out as major contributions.

Flint (71) demonstrated experimentally that dogs could withstand removal of 50% of the intestine and regain normal health, but that when 75-80% was removed a normal state was never achieved although survival was possible. Using microscopic techniques he demonstrated hypertrophy of the intestinal villi and calculated a four-fold increase in the absorptive surface after resection. In theoretical terms, he suggested that 25% of the intestine might be able to adapt sufficiently to provide normal digestive function.

In 1935 Haymond (93) published an extensive review which included data on 1161 cases in whom the intestine had been measured at surgery or at necropsy. The mean length was found to be 657cm vindicating the concept that 'massive' resections removed one third of the intestine. The range of length however was vast, from 304cm to 1216cm. The analysis of 257 cases of massive resection prompted the conclusions that normal intestinal function can be expected after a 33% resection, that 50% is the upper limit of safety, and that resection of greater than 50% of the small bowel will generally result in poorer results although there will be exceptions. That these exceptions occurred is shown by the large number of anecdotal case reports which appear throughout the literature (9,25,27,46,71,91 93,113,137,152,165,170,225,237,255,270,273,277).

Causes

It is interesting to compare the common causes of the short bowel syndrome today with those which were responsible in the early decades of the twentieth century. Haymond (93) found the three most common causes of massive resection to be volvulus, strangulated hernia, and mesenteric thrombosis. Volvulus was subdivided into two very different groups, simple small intestinal volvulus and a condition known as Knotenbildung in which knot formation involved the sigmoid colon and ileum. In eleven cases massive resection followed intestinal damage at the time of criminal abortion, and tuberculosis was responsible in sixteen cases, with trauma and miscellaneous pathologies accounting for the remainder.

Although it is just over fifty years since regional enteritis gained the eponym 'Crohn's Disease', it has become one of the major causes of the short bowel syndrome. By its very nature as a chronic inflammation of the intestine characterised by intermittent exacerbations and the tendency to cause structural complications such as abcesses, fistulae and strictures, Crohn's disease often requires repeated surgery of the large and small bowel although a cure is never achieved. It would be unfair, and inaccurate, to hold the increase

in Crohn's disease wholly responsible for the increased incidence and interest in the short bowel syndrome. Acute vascular incidents both arterial and venous continue to necessitate the resection of the majority of the intestine as an emergency procedure. The increase in atherosclerosis generally has been accompanied by bowel infarction in some patients although this is usually part of a generalised arteriopathy and affects the older age groups. Of more concern has been the increase in venous catastrophies in young women associated with the increased use of oral contraceptive preparations. The advent of the regular use of radiotherapy in the treatment of pelvic and intra-abdominal neoplasia has brought with it a steady, if low, incidence of radiation enteropathy which may require intestinal resection (11,48,86,124,172,274).

Management

Since the mid 1960's more emphasis has been placed on the length of remaining bowel rather on that of the resected segment. Figure 1 demonstrates the intestinal brevity and rapid intestinal transit which are typical of patients with the short bowel syndrome. Increased understanding of the mechanisms of absorption (6,7,23,27,28,227) and the identification of specific sites for the absorption of individual nutrients

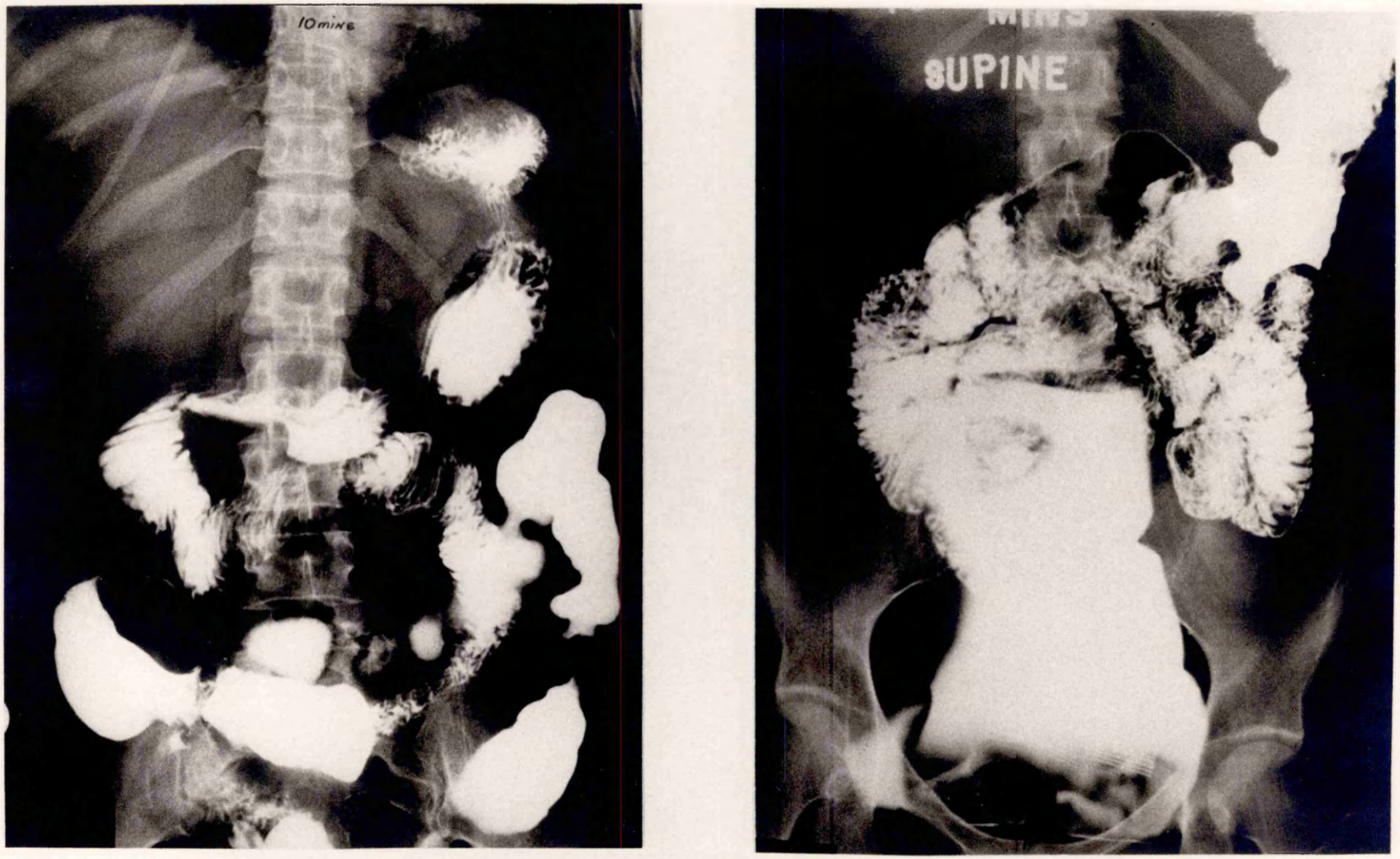


FIGURE 1 : Barium follow-through films taken at ten minutes after ingestion of barium in patients with a short bowel.

(22,24,25,29) led to more interest being taken in the type of bowel remaining. These experimental studies coupled with the anecdotal reports previously mentioned laid the foundations for the dietary manipulations which remain the mainstay of management (86,107,124,172). Increased understanding of nutritional requirements and the development of nutritional supplements and elemental diets has provided more alternatives in dietary practice. The development of safe and efficient techniques for the long term administration of intravenous fluids has established parenteral nutrition at home as a routine part of the medical repertoire which is now available at some centres.

This thesis has been planned and prepared to study and discuss some of the varied problems which face patients and their doctors dealing with the short bowel syndrome.

CLINICAL FEATURES OF THE SHORT BOWEL SYNDROME

The short bowel syndrome may be associated with any or many of a wide range of symptoms and pathophysiological features. The exact combination of fluid, electrolyte and nutritional problems experienced by any individual patient will depend not only upon the length of remaining intestine but also upon which type of intestine it is, jejunum, ileum or colon, and whether the remaining segment is proximal or distal. The underlying problems created by the short intestine may be further complicated by the superadded features of any continuing intestinal disorder, such as Crohn's disease or radiation enteritis.

The major features of the short bowel syndrome are diarrhoea, malnutrition and weight loss. There may be malabsorption of protein, carbohydrate and fat with consequent calorie depletion and steatorrhoea. There may also be debilitating fluid and electrolyte imbalances, and deficiencies of specific nutrients, minerals and vitamins.

Diarrhoea

The diarrhoea is often copious and, if steatorrhoea is a feature, malodourous. The rapid transit of food through

the shortened intestine allows the passage of unabsorbed sugars into the colon where the action of bacteria produces hydroxy-fatty acids. These exert a cathartic effect (18) as do bile acids which reach the colon in significant quantities if the terminal ileum has been resected (109,110,168). The result is the frequent and urgent passage of loose or frankly liquid stools often shortly after the ingestion of food, with painful skin excoriation particularly if the stool pH is acidic (206).

In some cases of Crohn's disease the colon may be severely affected and resection is necessary. The problems of diarrhoea in these patients are replaced by those of a high output small intestinal stoma, usually a jejunostomy. Without ileum or colon the capacity for water and sodium reabsorption is greatly diminished and there is a considerable risk of fluid and electrolyte depletion. Large quantities of sodium, calcium and magnesium may be lost from the intestine and the patient may suffer thirst, muscle cramps, hypotension and syncope from hyponatraemia, and tetany and carpopedal spasm from hypocalcaemia. Hypomagnesaemia may be manifest as muscle cramps, epileptiform seizures and calcium-resistant tetany. Potassium losses from the intestine are not a major problem but renal loss, in response to hyperaldosteronism secondary to

hyponatraemia, may be high leading to muscular weakness and irritability due to hypokalaemia.

The disability caused by diarrhoea or a high output stoma varies greatly among patients. At best, residual ileum and colon may keep diarrhoeal volume down to about 1 litre daily, and further improvement can be gained by the use of antidiarrhoeal drugs such as codeine phosphate and loperamide (181). The effects of these agents appear to diminish as the length of remaining intestine decreases however, and the most severely affected patients derive no benefit from drug therapy and continue to lose several litres of stoma fluid daily.

Malnutrition and Weight Loss

Patients with troublesome diarrhoea or a high output stoma quickly learn that a reduced intake of food and fluid will give some respite from the need for frequent visits to the lavatory. If they yield to this temptation however, the reduction in nutrient intake merely compounds the problems of malabsorption and is followed by more rapid weight loss and malnutrition. Like the problems caused by diarrhoea there is a wide spectrum of severity of weight loss. In the most extreme cases this may be profound and rapid following

copious fluid losses in the immediate postoperative period. If not adequately treated by parenteral replacement, these patients die of electrolyte imbalance. If this is avoided malabsorption of all major nutrients results in progressive malnutrition with loss of body fat and muscle mass. Although hypoproteinaemia may occur, it is seldom severe enough to cause oedema unless there is coexistent bowel disease. The outcome for these patients depends upon whether or not their remaining intestine can adapt sufficiently to improve absorption and allow them to regain their normal weight, or at least a stable state below their ideal weight. If insufficient bowel remains there will be progressive weight loss and eventual death from inanition, the fate of many of the survivors of 'successful' surgery in earlier times (71,91,93,165,237) unless measures are taken to increase nutritional intake either by the oral route, or by the use of parenteral feeding.

Specific Deficiencies

In general, the severity of diarrhoea, malabsorption and malnutrition is approximately proportional to the length of small intestine remaining. When the terminal ileum is resected however, there may be considerable problems despite a reasonable length of proximal small bowel

being present. This is because the terminal ileum is unique in having specialised sites for the absorption of vitamin B12 (22) and bile salts (29). A lack of vitamin B12 will result in pernicious anaemia and subacute combined degeneration of the spinal cord if allowed to persist. For this reason it has been recommended that intramuscular supplements should be given to all patients from whom 80-100cm of terminal ileum have been resected (86). The loss of the terminal ileum also interrupts the enterohepatic circulation of bile salts, leading to a reduction in the bile salt pool. Micelle formation is impaired with consequent reduction of fat absorption. When fat malabsorption is severe deficiencies of the fat soluble vitamins A, D and K may occur and supplements will be required. Deficiencies of the water soluble vitamins are rare until there is an extreme dearth of intestine.

Psychosocial

In common with many other chronic conditions the short bowel syndrome produces symptoms which reduce the wellbeing and physical activities of those afflicted. The depression of mood and deterioration of morale experienced by many patients is secondary not only to their physical problems, but is greatly increased by the social restrictions placed upon them. The persistent

need to open their bowel with the attendant threat of incontinence or leakage from a stoma appliance may be severe enough to restrict any activities outside the home. Family life is disrupted as eating becomes a chore rather than a social event, holidays are impossible, and financial problems arise if the patient is the principal breadwinner.

PATHOPHYSIOLOGY

As indicated in the section on clinical features, the short bowel syndrome has a wide variety of manifestations. To help describe the pathophysiology of the syndrome more clearly, it is advantageous to deal with the disturbances in gastric secretion and in the intestinal handling of water and electrolytes, minerals, and major nutrients separately, and to describe the changes which occur in the short bowel syndrome with reference to each nutrient.

GASTRIC ACID SECRETION

The majority of patients with the short bowel syndrome retain both the stomach, and all or part of the duodenum. This is due to the fact that in the diseases most commonly resulting in a short residual intestine, Crohn's disease and mesenteric vascular disease, the stomach and duodenum are infrequently affected. In Crohn's disease, gastroduodenal lesions are usually bypassed rather than being resected, and mesenteric vascular disease most commonly involves the superior mesenteric vessels which do not supply the stomach and duodenum.

Following bowel resection there is a period of gastric

hypersecretion which is well documented in the dog (189,278) but which is a less consistent finding in man (52,190,278). In the dog, this hypersecretion has been shown to be proportional to the length of small intestine resected (76,189) although there is disagreement as to whether it is greater following resection of proximal (49,222) or distal, (189,212) segments of intestine. Experimental work has demonstrated a similar magnitude of gastric hypersecretion in dogs after antrectomy and vagotomy (133), to animals with an intact antrum, suggesting that the antrum is not a prerequisite for hypersecretion. Gastric function studies have shown no increased response to histamine (212,278) indicating normal parietal cell numbers and function. Gastrin is inactivated by the small intestine (252), loss of which might prolong the action of this hormone. This is a simpler explanation than the loss of an unidentified inhibitory agent normally produced by the small intestine, suggested by Windsor et al after the demonstration of a prolonged post-cibal acid response (38,278).

Human studies have confirmed the presence of hypersecretion in some patients following intestinal resection. Raised basal acid outputs have been demonstrated (178,278), but the response to exogenous

stimuli such as pentagastrin is usually normal (178). Cimetidine has been used to reduce post-prandial hypersecretion (50,178) resulting in improved nutrient absorption by maintaining a more alkaline duodenal and jejunal pH (50). The role of gastrin remains under investigation; the majority of studies (50,178,276) have revealed normal levels in patients with a short intestine, but Straus et al (248) demonstrated elevated fasting and post-prandial gastrin levels and postulated the lack of a gastrin inhibitor, normally produced by the small bowel, to explain their findings in patients with massive resections.

In an extensive review of the problem of hypersecretion, Buxton (38) suggested that bacterial overgrowth might play a part by producing 'toxic' degradation products from dietary constituents and bile acids. These substances might then stimulate the production of a humoral agent in the intestinal mucosa resulting in acid hypersecretion and malabsorption. Although the exact mechanism of gastric hypersecretion remains unknown, it appears to be a transient phenomenon which may resolve in as little as two weeks after intestinal resection (278).

WATER AND ELECTROLYTES

Jejunum

Current understanding of the mechanisms which govern water and electrolyte absorption in the small intestine is based upon the results of many in vitro and in vivo studies performed during the last twenty years. It has become clear that the jejunum and ileum, while similar in some respects, handle the majority of solutes in different ways (55,262).

There is now much evidence to support the concept that the majority of water movement across the intestinal mucosa takes place by way of intercellular channels (260) rather than through the cells themselves as previously thought (72). The movement of water is an entirely passive process in response to osmotic pressures exerted by solutes. Rapid movement of water leads to a secondary shift of some solutes by a process known as solvent drag (74) which is quantitatively more important in the jejunum where mucosal permeability is high than in the less permeable ileum.

It is likely that sodium absorption in the jejunum is a mainly passive process in response to electrochemical and concentration gradients, with solvent drag playing

an important part secondary to water movement precipitated by the active absorption of glucose and amino acids. In addition there is probably an active transport mechanism for glucose and sodium absorption which depends on the presence of both substances for its satisfactory function (75,262). In contrast, potassium movement in the jejunum is entirely passive in response to concentration gradients and water flow (197,259,262).

Chloride absorption appears to be passive, but the handling of bicarbonate is rather different. It appears that bicarbonate can be absorbed against considerable concentration gradients down to a luminal concentration of 2-3 mmol/l (258). It is thought that this is mediated by the secretion of hydrogen ions which combine with bicarbonate to form water and carbon dioxide which then diffuse through the mucosa. The hydrogen ion secretion may be linked in a cation exchange with sodium thus explaining the observed phenomenon of bicarbonate-stimulated sodium absorption.

The details of the control mechanisims for jejunal absorption have yet to be elucidated. Although parasympathetic agonist and antagonist drugs (176), glucagon (101), secretin (100), cholecystokinin (64) and hydrocortisone (221) have been shown to affect the absorption of sodium, chloride and water, the doses used

were pharmacological and a true physiological role for these substances in the control of jejunal absorption has yet to be defined.

In the normal state the jejunum has a more rapid transit rate than the ileum which appears to be regulated in part by the presence of fat in the terminal ileum (246). The ileocaecal valve in particular was thought to be important from a purely mechanical point of view, but it now appears that it is the presence of undigested fat in the terminal ileum and possibly also the caecum which exerts a slowing effect on the transit of chyme through the proximal small intestine. With the loss of the terminal ileum, the jejunum is unable to retain fluids and nutrients as efficiently as necessary, and chyme passes through a shortened bowel with considerable rapidity, causing copious diarrhoea and steatorrhoea with the risk of electrolyte disturbances. These features are particularly severe in patients who have required colectomy. This is especially true of electrolyte disturbances of which hyponatraemia is the most common. This results from the obligatory loss of small bowel chyme containing high concentrations of sodium. The loss of sodium leads to secondary hyperaldosteronism with consequent renal sodium retention and increased potassium loss in the urine. It is probably the high urinary potassium losses which lead

to the hypokalaemia often seen in these patients, rather than excess loss from the small bowel.

Ileum

The ileal mucosa is less permeable to water and solutes than that of the jejunum leading to better retention of absorbed water than is possible in the proximal intestine. The reduced permeability also means that solvent drag is a less important mechanism for ion absorption than in the jejunum.

In vivo perfusion studies have demonstrated that there is active transport of sodium against considerable electrochemical gradients. It has been proposed that sodium absorption is linked with that of chloride which also demonstrates characteristics of an active transport system in contrast to its passive absorption in the jejunum. Turnberg et al (258) proposed a double ion exchange system to explain these active mechanisms which are associated with no electrical changes. Sodium is absorbed in exchange for hydrogen ions while chloride is exchanged for bicarbonate. The hydrogen and bicarbonate then form water and carbon dioxide which diffuse out of the intestine. Although there remains no direct proof of the existence of such a system, it accurately explains the experimental findings (262). The active

absorption of sodium and chloride in the ileum results in greater absorption of these ions per unit length of intestine than in the jejunum (119).

Potassium absorption in the ileum remains a passive process in response to concentration gradients. Absorption appears to be increased when the luminal concentration of sodium is low, possibly due to changes in potential difference across the mucosa (259).

The normal ileum is relatively inaccesible for study, and experimental data obtained from perfusion studies must be extrapolated from the results obtained from a small segment to the whole organ. Patients with ileostomies present an interesting group for study, anatomically and functionally between the normal state and that seen in the short bowel syndrome.

The normal ileostomy produces about 500g of effluent in 24 hours of which some 90% is water (102,139,241) Sodium concentration, normally 110-130 mmol/l (106,130,139,241) is lower than that found in the ileum of subjects with the colon in situ suggesting increased absorption by the ileum in these patients. The potassium concentration remains low, in the range of 5-11 mmol/l (106,130,139,241). The obligatory loss of sodium in quantities far higher than those found in normal stool

means that patients with an ileostomy have an inherent risk of developing salt depletion and dehydration. This has been reported on several occassions (80,103,104,131,182) associated with low urine volume and sodium concentration but only a minor reduction in the sodium loss from the ileostomy. This persistence of sodium loss even in the face of dietary sodium deprivation has been comfirmed experimentally (140,177) although Clarke et al (43) reported one patient whose sodium loss from the ileostomy dropped to 62 mmol/l when dehydrated. In general however, dietary sodium deprivation, although leading to secondary hyperaldosteronism is usually attended by only minor reductions in sodium loss from the ileostomy. Potassium losses may rise significantly to levels of 20-30 mmol/l (140,177) although the mechanism for this finding is unknown. Chronic depletion of total body water, exchangeable sodium and potassium has been reported in seemingly healthy ileostomists (44,103,261). In one series (261) the depletion appeared to be an intracellular phenomenon associated with normal plasma electrolytes and, in some cases, normal aldosterone levels. Newton et al (182) sampled the urine of patients with ileostomies and on the basis of low sodium concentrations of less than 10mmol/l defined a group requiring sodium repletion. These patients had raised aldosterone and renin levels which returned to normal

after oral rehydration and salt replacement. Kennedy et al (131) compared a group of ileostomists with matched controls. As a group, the ileostomists had raised aldosterone levels with low urinary sodium and raised urinary potassium losses. The findings from these different studies suggest that although there is a satisfactory aldosterone response to salt depletion in these patients the ileum appears to be unable to respond as effectively to this hormone as does the colon (148,149). This is confirmed by the demonstration that the administration of exogenous aldosterone and 9-alpha-fluorohydrocortisone does not alter the losses of sodium or water from ileostomies (84,141,149).

Colon

Under normal conditions the human colon functions as a salvage mechanism, principally to absorb water and electrolytes, thus converting liquid ileal chyme to solid stool. The colon receives 1000-1500ml of small intestinal content over a 24 hour period (198,211) containing electrolytes at concentrations similar to those found in plasma (59,198). The efficiency of the colon is such that it will absorb 95-99% of the sodium, chloride and water, and 50% of the potassium presented to it (198).

Sodium absorption is the most important colonic function because it affects the absorption of other electrolytes and water. There is an active transport mechanism which is not glucose-dependent (257) in contrast to that found in the small intestine (59). Sodium is 'pumped' out of mucosal cells across the basolateral membrane creating a concentration gradient down which sodium is absorbed. The pump creates a potential difference which facilitates the absorption of chloride against a concentration gradient (59,257), and the secretion of potassium (62). Water absorption is an entirely passive consequence of solute movement (62,257). Although bicarbonate can be absorbed by the colon (62), secretion is promoted by the presence of chloride in the lumen. It is likely that an anion exchange occurs (59,62,257) similar to the mechanism demonstrated in the ileum (258). The colon also differs from small intestine in its ability to increase the absorption of sodium, chloride and water in response to aldosterone (148).

Diarrhoea results from the colon being unable to cope with the demands of absorption placed upon it. This may occur in several ways relevant to patients with small bowel resection. Perfusion experiments have shown that the colon can absorb up to 5.7 litres of water in 24 hours (61), an estimate which correlated well with clinical studies of Asiatic cholera (16) and pancreatic

diarrhoea (208). This functional reserve is however, vulnerable to sudden fluctuations in the rate of delivery of fluid into the caecum. Diarrhoea results if 500ml of ileal-like fluid is instilled into the colon in one hour, a flow rate of 8.3ml/minute (61) and occurs with increasing frequency at higher flow rates (192). When a short intestine and rapid transit are present, a large bolus of fluid and food may enter the colon shortly after ingestion and precipitate diarrhoea.

Such a bolus may contain larger quantities of carbohydrate, fat and bile acids than normal ileal fluid. The excess carbohydrate exerts an osmotic effect in the colon with subsequent diarrhoea (54). Larger amounts of short chain fatty acids will be produced, but because they are very rapidly absorbed, it is unlikely that they contribute significantly to the osmotic disturbances (54).

Long chain fatty acids appear to have a greater part to play in the diarrhoea associated with steatorrhoea. Intestinal motility is increased (18) and they are metabolized to hydroxy-fatty acids by bacterial action. Hydroxy-fatty acids decrease sodium and water absorption by the colon and may thus contribute to diarrhoea (8). In some cases the substitution of medium chain triglycerides in the diet has been successful in

reducing the concentration of hydroxy-fatty acids and the volume of diarrhoea (244).

Bile acids are normally absorbed in the distal ileum (29) and enter the colon only in small quantities. After ileal resection faecal losses may be considerably increased (89,110) with important consequences. Bile acids reduce the absorption of, and in some cases promote secretion of sodium, chloride and water (168). In ileal resections of less than 100cm this is the most important cause of diarrhoea, as only minor steatorrhoea occurs (110). Longer ileal resections result in increased losses of bile acids which cannot be compensated for by increased synthesis (5,109). Jejunal bile acid concentration falls, and steatorrhoea becomes a major factor in the diarrhoea. It has been suggested that both hydroxy- and non-hydroxy-fatty acids contribute as the diarrhoea can be reduced by the use of medium chain triglycerides (110).

MINERALS

Calcium

Calcium is absorbed throughout the small intestine, the ileum being quantitatively more important although the

rate of absorption is faster in the jejunum (55). Absorption is regulated by the active metabolite of vitamin D, 1,25-dihydroxycholecalciferol. This is produced by two separate hydroxylations of cholecalciferol, vitamin D3, the first, at the 25 position, occurring in the liver, and the second at the 1 position being completed in the kidneys. A second metabolite, 24,25-dihydroxycholecalciferol is produced in the kidneys, but its exact metabolic role has yet to be fully defined (55,66).

Under the influence of 1,25-dihydroxycholecalciferol, calcium binding protein is secreted into the intestinal lumen where it takes up calcium. The complex is then absorbed. Calcium absorption is an active process at luminal concentrations of 1-5mmol/l and can occur against concentration and electrical gradients in the absence of water movement (117). At higher luminal concentrations, the active transport tends to become saturated and passive absorption occurs (55,117,194).

The complex nature of calcium absorption means that it can be disrupted in a number of ways. Reduction of the active absorption occurs when there are low levels of 1,25-dihydroxycholecalciferol as is found in patients with chronic renal failure, although the passive component of absorption remains normal (117). Low

levels of 1,25-dihydroxycholecalciferol may also result from malabsorption of vitamin D after small bowel resection (47,60), and in coeliac disease and pancreatic steatorrhoea (253).

When normal vitamin D levels are present calcium malabsorption may still occur because of inadequate dietary intake, or because of interference by other dietary constituents such as phytates, phosphates, oxalates and fatty acids (3,55). Much has been written about the effects of fat on calcium absorption, and the concensus has been that high quantities of dietary fat restrict calcium absorption. Agnew et al (3) studied patients after partial gastrectomy, normal subjects, and patients with malabsorption, and observed the effects of adding either long or medium chain triglycerides to a standard meal. The long chain triglycerides significantly depressed calcium absorption compared with medium chain triglycerides and compared with diets containing no added fat in the group as a whole, but these effects were not evident in the patients with malabsorption. Patients with steatorrhoea of greater than 10g faecal fat daily had significantly reduced calcium absorption compared with normals regardless of what type of fat was used as a supplement.

Calcium absorption is said to be reduced by fat because

of the production of calcium soaps by saponification with fatty acids. In experiments with rats, absorption of calcium from such soaps has been shown to be related to the fatty acid length, being least from long chain soaps, particularly when these contain saturated fatty acids (79). However, when fat was given as triglycerides along with calcium rather than as soaps produced in vitro, there was negligible formation of soaps in the intestine and no effect on calcium absorption.

Magnesium

Since the first reports of magnesium deficiency in man (15,26,70,88,155) there has been debate over the precise mechanism of its absorption, and extensive reviews of the literature pertaining to its absorption and roles in metabolism have been produced (10,251,267,268,269). Some of the apparent disagreement in experimental results may have arisen because of the study of several different species, a point raised by Brannan and her colleagues (33) who studied the jejunal and ileal absorption of magnesium from magnesium chloride using an in vivo perfusion method in human subjects. They demonstrated that magnesium absorption is active in both jejunum and ileum and that the mechanism tends to become saturated at a luminal magnesium concentration of

10mmol/l. Increasing luminal calcium concentration had no effect on magnesium absorption. In patients with chronic renal disease, magnesium absorption was significantly reduced possibly as a result of reduced levels of 1,25 dihydroxycholecalciferol. Hydroxylated metabolites of vitamin D have been used to increase the plasma magnesium levels of patients with a short intestine, but normal levels were achieved only with the use of magnesium supplements (229). Magnesium absorption therefore appears to be an active process independent of calcium but needing vitamin D for maximal activity. There may also be superimposed passive diffusion which becomes important only at higher luminal concentrations (55).

Magnesium depletion and deficiency is likely to develop in patients who lose large quantities of gastrointestinal content as a result of malabsorption, bowel resection, fistulous drainage, or prolonged nasogastric aspiration (268). Booth et al (26) reported hypomagnesaemia in 15 of 42 patients with malabsorption of various causes. In one patient with intestinal resection, magnesium loss was increased by a high fat diet of 138g/day but a positive balance was attained without magnesium supplements on a diet containing only 32g fat daily suggesting that magnesium is lost as insoluble soaps in steatorrhoea. However, a second

patient, also with small bowel resection, failed to maintain a positive magnesium balance on a low fat diet and required oral supplements.

Zinc

Zinc is one of the most important trace elements in the human diet. It is essential for the function of many enzyme systems (214) and deficiency has wide-ranging consequences. These include growth retardation, anorexia and disorders of taste, hypogonadism, impaired wound healing and cellular immunity, and a dermatitis which resembles acrodermatitis enteropathica, a genetically determined disorder of zinc absorption. (151,162,263)

Zinc is absorbed in the small intestine, although the exact site and mechanism is unclear (9). Normally, small quantities are excreted in the faeces, but in diarrhoeal diseases stool losses increase significantly (280). The losses are greatest when the entire intestine is present, and the zinc concentration is lower in fluid from high stomas or fistulae. Malabsorption of zinc exacerbates these excess losses, particularly if there is active inflammatory bowel disease (151,249). Oral supplements of zinc sulphate may be successful in mild cases, but patients needing intravenous feeding will

need parenteral zinc (280). The quantities required vary considerably depending on gastrointestinal losses but in general, a supplement of 3-12mg (50-200micromol) appears satisfactory in most cases needing parenteral nutrition (162,280).

VITAMINS

The majority of vitamins can be absorbed throughout the small intestine and depend upon the satisfactory transport of water or lipids for their own absorption. The exception is vitamin B12 which is selectively absorbed from the terminal ileum (22) in association with gastric intrinsic factor. Absorption is invariably abnormal if 6 feet or more of terminal ileum has been resected (22) and lifelong intramuscular supplements will be required.

Water soluble vitamins and folic acid are rapidly absorbed in the jejunum. Active transport systems have been identified for ascorbic and folic acid, and possibly exist for thiamine and riboflavine while pyridoxine is absorbed by diffusion. The method of absorption for nicotinamide, pantothenic acid and biotin remains unknown (112). The reserve capacity of the jejunum is so great that even when large doses of

pyridoxine were given to normal subjects, only small amounts reached the ileum, and absorption was essentially normal even in patients who retained between 4 and 8 feet of jejunum and no ileum. (32). Booth et al (23) found that absorption of folic acid was normal after resection of all but 3-4 feet of jejunum, and that it became abnormal only when as little as 8 inches of jejunum remained. It seems likely that patients able to maintain a satisfactory nutritional state without parenteral nutrients should be able to absorb sufficient quantities of water soluble vitamins from a normal diet.

The fat soluble vitamins A,D,E and K are absorbed after micelle formation in the small intestine. The proximal jejunum is the principal site of fat absorption (28) although theileum becomes more important at higher dietary intakes (25). Malabsorption of vitamins is likely when steatorrhoea is present regardless of the underlying disease and has been documented for vitamin D in coeliac disease and pancreatic disorders (254). Although jejunal resection can be compensated for by increased ileal absorption, terminal ileal resection interupts the enterohepatic circulation of bile salts, and possibly of 25 hydroxycholecalciferol itself. Thus malabsorption of vitamin D may be present when as much as 390cm of proximal small intestine remain (47). The absorption of vitamins A,E and K has received less study

although vitamin A absorption has been used as an indicator of fat absorption (6). It is likely that malabsorption similar to that of vitamin D will occur in steatorrhoea, and that a patient's vitamin K supply is further diminished by colectomy and the consequent removal of the bacterial source of this vitamin (17,175).

ABSORPTION OF MAJOR NUTRIENTS

Protein

In man the assimilation of protein is normally an extremely efficient process, for of 70-100g exogenous and 30-200g endogenous protein presented to the intestine each day only 6-12g (1-2gN) appear in the faeces (78). Dietary protein is initially digested by gastric proteases producing mainly polypeptides, some oligopeptides (2-6 amino acid residues), and a few free amino acids. After the actions of the several pancreatic aminopeptidases, large quantities of oligopeptides and free amino acids are present in the intestinal lumen (78). It has been suggested that the final stage in peptide digestion occurs in the mucosal brush border where free amino acids are progressively cleaved from oligopeptides to produce tri- and

dipeptides (78,167).

The mechanisms whereby the products of digestion are absorbed into the bloodstream have been the subject of much investigation which has been extensively reviewed over the past ten years (77,78,167,235,240). It is now known that free amino acids and peptides are absorbed by different active transport systems (167) and that amino acids are more rapidly absorbed when present as di- and tripeptides than as the free form (2,167,231,233). Amino acids are absorbed from peptides in two main ways (2): first, the peptide may be transported intact into mucosal cells where it undergoes hydrolysis, which appears to be the predominant mechanism in the jejunum. Second, the peptide may undergo hydrolysis in the mucosal brush border with transport of the free amino acids (235). This is the predominant mechanism in the ileum (78,167). These two systems appear to be equally effective as peptide absorption rates in the jejunum and ileum are similar (2,235). Although free amino acids are more rapidly absorbed in the jejunum than in the ileum (1,234), the small bowel has a greater absorptive capacity for mixtures of oligopeptides and amino acids than for free amino acids alone (232,233).

Borgstrom et al (28) suggested that digestion and absorption is almost completed in the jejunum, a theory

supported by Nixon and Mawer (183) who claimed that maximal absorption took place in the duodenum and proximal jejunum. Using a multiple-lumen tube for small intestinal perfusion studies, Chung et al (42) have shown that while 60-65% of ingested protein in the form of bovine serum albumin is digested and absorbed in the proximal 150cm of the small intestine, the remainder is efficiently absorbed in the ileum, only 1-2% appearing at a collecting site 300cm distal to the duodenal-jejunal junction. This suggests that while 150cm of small bowel remains, about two thirds of ingested protein will be absorbed.

Patients with a short residual intestine lose greater quantities of nitrogen in their faeces or stoma effluent than normal. The losses have been reported to be in the order of 2.8 - 6.6gN/day (27) and 2.1-5.2gN/day (115). The higher losses suggested that a higher dietary input was necessary to maintain positive nitrogen balance. Althausen (6) however, had previously demonstrated that positive nitrogen balance could be maintained in a patient with resection of all but 45cm jejunum anastomosed to mid-transverse colon, on an intake of only 10.3gN daily (65g protein). The faecal nitrogen in this patient was never more than 3.9g/day.

More recently, Ladefoged and her colleagues (144) studied patients retaining between 30cm and 200cm small intestine and demonstrated a wide range for nitrogen absorption from 21% to 66% of dietary intake. In patients who had undergone a resection of greater than 150cm small bowel, Hylander et al (115) found absorption of 43% to 83% of ingested nitrogen compared with the normal range of 80-90% (28). These findings suggest that some patients with a short intestine will need a higher protein intake than normal, but that others may manage well with no increase.

Carbohydrate

In Western society, dietary carbohydrate is composed mainly of starch with smaller quantities of sucrose, lactose and fructose. Digestion takes place in a series of steps as food travels down the gastrointestinal tract. Initially, salivary amylase acts on the alpha 1,4 linkages of starch until inactivated by gastric acid. In the duodenum, pancreatic amylase continues the process producing oligosaccharides and branched dextrins. The final step takes place in the mucosal brush border where sucrase, maltase, isomaltase and lactase produce the monosaccharides glucose, galactose and fructose (56,209).

Glucose and galactose are absorbed by a carrier-mediated transport system distinct from that responsible for fructose absorption (111). It is responsible for 80% of glucose absorption and its efficiency is increased in the presence of sodium (209). Fructose absorption is slower, and occurs down its concentration gradient by facilitated diffusion. Glucose absorption proceeds rapidly in the small intestine and is completed in the proximal 100cm of jejunum (28). Such is the absorptive capacity of the jejunum that Booth (23) found no abnormality of glucose tolerance until only a few inches of jejunum remained. When the jejunum has been resected the ileum is capable of glucose absorption although oligosaccharide hydrolysis is slower (85). When unabsorbed carbohydrate reaches the colon, some attempt at 'colonic salvage' will occur as bacteria metabolise glucose to produce short chain fatty acids which are absorbed by the colon (20,215).

Fat

The absorption of dietary fat is perhaps the most complex of the processes responsible for the absorption of the three major nutrient groups, involving the secretions of several organ systems for its successful conclusion (82). The majority of dietary fat is in the form of long chain triglycerides which are subjected to

minor digestion by lingual and gastric lipases before reaching the duodenum. Pancreatic lipase is the most important enzyme involved in fat digestion and its action, in conjunction with pancreatic colipase, produces a mixture of free fatty acids and 2-monoglycerides. Fat absorption is a passive process which relies on the solubility of fatty acids and monoglycerides in the lipid cell membrane. To reach the membrane however, dietary fat must first traverse the unstirred water layer, estimated to be 600 microns in depth (210), coating the mucosa. This is achieved by the emulsification of fats by bile salts to form micelles, and will only occur when the bile salts are present in their critical micellar concentration. This has been estimated to be 0.25 mmol/l (58). Micelles disintegrate at the cell membrane, fatty acids and monoglycerides being absorbed, and bile salts proceeding down the intestine to the terminal ileum where they are reabsorbed. It has been estimated that the entire bile salt pool circulates through the intestine four or five times during the digestion and absorption of a fatty meal (30). As discussed in the section on the colon, resection of the terminal ileum leads to excessive faecal losses of bile salts, reduction of the bile salt pool, and in some cases to an inability to attain the critical micellar concentration resulting in steatorrhoea. In the mucosal cell triglycerides are

reformed from the absorbed fatty acids and monoglycerides, and leave the cell with phospholipids, cholesterol and proteins as chylomicrons. Medium chain triglygerides are subject to the above digestion and absorption processes but can also be absorbed without the need for predigestion. They differ from long chain triglycerides in that they are absorbed directly into the portal blood stream rather than being transported in the lymph. Although they form no part of the normal diet, they can be substituted for long chain triglycerides in conditions which reduce the ability to digest or absorb normal fats. Their use in the short bowel syndrome is however open to debate.

The whole small intestine is capable of fat absorption. When corn oil was used as the fat source, 90-95% was absorbed in the proximal 100cm of jejunum (28). Booth et al (24) subsequently demonstrated that the ileum plays an increasingly important part in fat absorption as dietary fat levels increase between 30g and 150g daily. The intact small intestine appears to be capable of absorbing almost unlimited quantities of fat. Masterton et al (166) studied two polar explorers who were able to absorb 263g and 276g respectively from diets containing 273g and 285g. Patients with bowel resection however, may have steatorrhoea at more modest intakes. Booth (24) found that resection of up to 8

feet of terminal ileum did not result in increased faecal fat levels when dietary fat intake was less than 64g daily but that increasing lengths of resection resulted in increased faecal fat losses at lower intakes.

In addition to electrolytes the colon has been shown to absorb short chain fatty acids (160,215). Carbohydrate in the colon undergoes anaerobic metabolism to acetic, propionic and butyric acids (20) which are then rapidly absorbed with secondary water absorption (54). It has been calculated that over 500kcal daily could be absorbed in this way (215).

MANAGEMENT OF THE SHORT BOWEL SYNDROME

The general aim of management for all patients with a short intestine must be not only to make maximum use of the residual intestine, but to do so using a combination of electrolyte replacement, dietary manipulation and supplementation, drug therapy and parenteral nutrients which is acceptable to the individual and reduces, rather than increases, the existing symptoms and restrictions.

FLUID AND ELECTROLYTE REPLACEMENT

The majority of our knowledge of the usefulness of oral electrolyte replacement mixtures has come from work done in developing countries. Large numbers of patients suffering from acute diarrhoeal conditions caused by Vibrio cholerae, enterotoxigenic Escherichia Coli and rotavirus have been treated with considerable success using sugar - electrolyte mixtures (199,200,220). These clinical reports have been complemented by the results of jejunal intubation experiments which have yielded much information about saccharide and electrolyte absorption.

In normal human volunteers, fluids entering the jejunum

acquire a similar sodium concentration and tonicity to plasma by equilibration with intestinal secretions (73,197). This suggests that an 'ideal solution' should have a sodium concentration close to that of plasma or greater, while remaining approximately isotonic when other ions and sugars are taken into account.

If solutions of sodium chloride are instilled into the jejunum, little absorption occurs (74,239). However, the absorption of sodium bicarbonate is better, suggesting that there is a transport mechanism for bicarbonate which stimulates sodium absorption (239,258). Bicarbonate absorption is best at luminal concentrations greater than that of plasma, and equilibration in the ileum is reached at a luminal concentration of about 40mmol/l (199). For these reasons, and also to combat the acidosis which may occur after colectomy, there is a theoretical need for bicarbonate in oral electrolyte replacement solutions. This has however been challenged by Fordtran (75) who has demonstrated that sodium absorption is best from glucose-electrolyte mixtures when chloride is the only anion present.

The solution recommended by the World Health Organisation for use in acute diarrhoeal diseases sought to combat the problems of dehydration, hyponatraemia, hypokalaemia and acidosis by incorporating sodium

90mmol, potassium 20mmol, chloride 80mmol, bicarbonate 30mmol and 20grams glucose in 1 litre of water (200) This solution has been instrumental in reducing the mortality incurred by patients with severe diarrhoea (12,207), and has been effective in avoiding the use of intravenous fluid replacement, with its attendant complications, in the majority of patients (40).

Since Schedl and Clifton (224) showed that glucose, sodium and water absorption are linked, the need for a sugar in electrolyte replacement mixtures has not been disputed. Solutions containing many different concentrations of glucose have been tested in an attempt to find the optimal concentration. In perfusion studies, maximal sodium and water absorption occurred when between 56 and 85mmol glucose per litre was used (239). In cholera patients 160mmol/l has been shown to be superior to 40mmol/l (199). This has been supported by Nalin et al who recommend a 2% glucose solution (110mmol/l) after extensive experience in the treatment of diarrhoeal diseases.

There has been debate as to which saccharide source is best to promote sodium and water absorption. Several studies have been undertaken using glucose as the standard against which all other carbohydrates must be judged. These have shown that sucrose (193,220,250) and

rice-powder (174) can be effective in promoting sodium and water absorption in patients with severe diarrhoea. Theoretically, the disaccharide maltose should be suitable for inclusion in oral electrolyte replacment mixtures as glucose is better absorbed from maltose than from solutions of free glucose itself (127,159). The use of a disaccharide also allows an increase in the sodium content without increasing the final osmolality of the mixture.

Experience with electrolyte replacement solutions in the short bowel syndrome is limited, glucose-containing mixtures being used with success in some cases (53), but not in others (81). In less extreme cases, glucose electrolyte mixtures have been given successfully to ileostomy patients who had a large stoma output to reverse dehydration and hyponatraemia (182,271). Griffin et al (87) used a mixture containing glucose polymer as a carbohydrate source to avoid parenteral fluid replacement in two patients with short residual intestine measuring 75cm and 25cm respectively. The latter patient retained most of the colon in addition to the short length of small bowel. The solution described by them has been successfully used in another patient who retained 125cm small intestine (147).

Although the majority of patients with an ileostomy have

a low output of less than 500g daily which correlates well with body weight (105), ileostomists with a high daily output (defined as more than 1000g) may benefit from treatment with codeine phosphate or loperamide to reduce the volume of effluent and the daily sodium losses (136). Newton (181) demonstrated that both codeine, and to a lesser extent Lomotil (diphenoxylate and atropine) reduced sodium and water loss from an ileostomy, but that Isogel (ispaghula husk), although improving effluent consistency, actually increased the losses of sodium.

DIETARY MANIPULATION

The theory behind current practices in dietary manipulation in the short bowel syndrome is based on the knowledge of the different absorptive functions of different parts of the small bowel. The work of Borgstrom et al (28) with normal subjects and Althausen et al (6,7), and subsequently Booth et al (23,25,27) with patients who had varying lengths of small bowel remaining, laid the foundations of present knowledge about nutrient digestion and absortion.

The common findings that fat, protein and calories were lost in greater quantities in the faeces than was normal

prompted the conclusion that in such patients, the diet should contain larger quantities of protein, more calories and smaller amounts of fat than usual (27). In short bowel cases, it has been common practice to restrict dietary fat intake for a number of reasons. A high fat intake was held to predispose to higher faecal output, with an increase in diarrhoea and higher losses of calcium and magnesium with the risk of bone decalcification, tetany and convulsions. Increased protein was advocated because of increased faecal losses, and also to provide a calorie source with extra carbohydrate in place of the restricted fat. This regimen has become the traditional staple of many who treat patients with a short intestine (86,107,142, 172).

Booth et al (23,25) subjected patients with bowel resections to variations in their dietary fat and studied the effects on calcium balance. In one case, diets containing 38g and 62g fat daily were compared. Although a positive calcium balance was attained on the lower fat diet on some occasions, this was not always accompanied by a low faecal fat loss. In another study in the same patient, the calcium balance was negative despite a low faecal fat loss. The most significant gain in calcium balance was seen following parenteral administration of vitamin D. In other patients, diarrhoea and tetany did follow a higher fat diet, but

the restriction required to regain control of bowel habit was never less that 40g fat daily. In one patient, magnesium losses were increased by a high fat diet of 138g/day and a positive balance was attained without magnesium supplements on a diet containing only 32g fat daily. However a second patient, also with small bowel resection, failed to maintain a positive magnesium balance on a low fat diet and required oral supplements. Support for the concept that a diet containing large amounts of fat is detrimental has been forthcoming from studies which showed reduction of steattorrhoea and diarrhoea when medium chain triglyceride were substituted in the diet (19,201,286). The effect on faecal nitrogen loss and weight gain was, however, more variable.

By contrast, patients have been shown to thrive without recourse to a low fat diet. Schwartz et al (227) commented on the constant percentage of dietary fat and nitrogen lost in the stool on diets of different composition, and found that merely increasing nitrogen and total calorie intake was sufficient to promote weight gain and good health. More recently the necessity of a low fat diet has been strongly challenged (236,281).

Simko et al (236) have stated that a high fat diet of 200g daily can be beneficial following studies in a single patient with only 137cm jejunum remaining and a terminal jejunostomy. He found that stoma effluent volume decreased as did the losses of bile acids on the high fat diet compared with one which contained 64g fat daily. Woolf et al (281) approached the problem by keeping dietary protein, fibre, fluid and mineral input constant and varying fat and carbohydrate only. They fed both diets, containing 40g and 120g fat respectively to 8 patients with short lengths of residual intestine. In a cross-over study they demonstrated no difference in the faecal dry weight or in the losses of water, calcium, magnesium or zinc between the two diets. This result was in accord with Bochenek et al (19) who had shown no benefit from the use of a diet containing 50g fat daily.

Most authors have stressed the fact that as dietary fat increases, the faecal fat increases in a linear manner (23,25,227). Few have emphasised the fact that the percentage of fat absorbed remains remarkably constant at about 60-65% of intake on diets containing varying quantities of fat (227). This means that patients may have a higher calorie intake on a higher fat diet and if there is no detrimental effect on stool volume and consistency, they may benefit from a more liberal

attitude to the quantity of fat that they are allowed in their diet.

Patients who develop low levels of vitamin D or hypocalcaemia may respond to oral supplements. Daily doses of 4000-12000iu have been recommended for patients with steatorrhoea (238) but excellent clinical results and reversal of abnormal levels of 25-hydroxycholecalciferol have been achieved using only 900iu calciferol daily in patients with intestinal resection and steatorrhoea (60). If oral treatment is ineffective, parenteral treatment with an hydroxylated metabolite of vitamin D is justified (66).

The treatment of magnesium depletion in the acute stage is straightforward, using intravenous or intramuscular magnesium sulphate in a dose of 1.5ml of 10% sol. (157). Oral supplementation of the diet of patients at risk is more difficult because of the cathartic action of some magnesium salts (269). Booth et al (26) recommended the use of magnesium chloride 0.25mmol/kg/day in patients with malabsorption, and Hessov et al (96) reported the use of 22mmol of the same salt daily for three months succesfully to reverse magnesium depletion in patients after small intestinal bypass procedures for obesity. Magnesium hydroxide 30mmol/day was used to improve the mental and physical state of one patient with massive

small intestinal resection (70), although 23mmol/day was unsuccessful and intramuscular magnesium sulphate was needed to reverse depletion in a similar patient (188). Magnesium oxide has recently been used in a dose of 15-20mmol daily to reverse symptomatic hypomagnesaemia in a group of seven patients with small intestinal resections (229).

LIQUID DIETARY SUPPLEMENTS

Liquid dietary supplements are used in many clinical situations other than the short bowel syndrome. They may be classified in two main categories, namely elemental, chemically - defined or defined - formula diets, and non-elemental, whole protein or polymeric diets. Chemically-defined diets were initially produced as a low-residue feed for space flight (279), and consisted of a mixture of protein as amino acids, and an energy source mainly as carbohydrate presented as mono- or oligosaccharides supplemented with minerals and vitamins. Little fat was included in the early formulations, of which Vivonex (Eaton Laboratories) is the best known example. The combination of free amino acids and oligo- and monosaccharides in large quantities resulted in a high osmolality which has been blamed for many of the side effects of these preparations.

To combat the problems of high osmolality, and in the light of reports (2,51,231,232,233) showing that short peptides were absorbed as well as, or better than free amino acids, newer chemically-defined diets contain nitrogen as mixtures of amino acids and short peptides (2-6 amino acids), carbohydrate as oligosaccharides and less free glucose, and more fat, often utilising medium-chain triglycerides (8 to 10 carbon atoms). These newer preparations, such as Nutranel (Roussel), which was used in the experimental work in this thesis, also have a higher nitrogen:calorie ratio, which may be important in maintaining positive nitrogen balance. All elemental diets have tended to have a low electrolyte content, with added minerals and vitamins.

Non-elemental, or polymeric diets have developed from whole food homogenates designed and formulated by hospital diet kitchens, often with additions of high protein and high calorie food supplements. In recent years the number of proprietary polymeric diets has increased enormously, reflecting the new emphasis being placed on enteral nutrition in patients suffering from a wide variety of conditions. Most proprietary feeds obtain their protein from hydrolysates of casein, soy protein isolate, or a combination of both. Both fat and carbohydrate are used as energy sources, the carbohydrate mainly as polysaccharides with some

oligosaccharides, and the fat from vegetable sources such as maize oil and mainly long-chain triglycerides. The osmolalities of such feeds are usually lower than those of chemically-defined diets and the electrolyte content is higher. Vitamin supplements are added as in the elemental diets. Commonly used polymeric diets include Clinifeed (Roussel), Nutrauxil (Kabivitrum), Isocal (Mead Johnston), and the preparation used in the experimental work in this thesis, Ensure (Ross Abbott). Many of the polymeric diets now contain no lactose to avoid the possible problem of diarrhoea in patients who are lactase deficient.

The rationale governing the use of chemically-defined diets is that they require little or no digestion and can be absorbed through the bowel wall in the form in which they are ingested. They are thus recommended "when digestion or absorption is impaired as in malabsorption states, the short bowel syndrome and as treatment following total gastrectomy" and "may be used in the preparation of the bowel prior to diagnostic procedures" (Vivonex data sheet). This latter recommendation is based upon the fact that the chemically-defined diets contain little residue and are said to promote small volume stools.

Polymeric diets are recommended for use as nutritional

supplements in any situation where the patients food intake is inadequate, and particularly when nasogastric tube feeding is required. Suggested indications include "semi-consciousness or coma, illness where anorexia limits food intake, conditions affecting the swallowing muscles, oral pathology and preoperative preparation and postoperative care" (Ensure data sheet).

Historically, much of the work done with patients requiring enteral supplementation of their diet has involved elemental diets. They have been used extensively in inflammatory bowel disease, both as a nutritional supplement (83,185) and as a primary treatment (13,184,186,187). Successful results have been claimed in complicated Crohn's disease (218) including the closure of enterocutaneous fistulae (37) and the healing of perianal fistulae and fissures (39) thus avoiding surgery. The wide range of conditions in which chemically-defined diets have been used has prompted extensive reviews (138,217) the more recent of which concluded that "the diet is of historic interest, but there is very little data available substantiating or refuting the claims made for it. Assumptions concerning its effect on the alimentary tract may be wrong. As such its widespread use is really unsupportable, especially in an era where cost containment of medical care is a daily issue" (138).

Perhaps the main criticism of the work done with elemental diets is the paucity of controlled studies comparing them with either whole food or polymeric diets in any clinical situation. In the postoperative period, elemental diets conferred no benefits on patients compared with polymeric feeds, (67,126) and their use in unconscious patients was associated with more gastrointestinal side effects and difficulty in maintaining nitrogen and other nutritional balances (126,128). As a means of reducing faecal weight they appear to be no more effective than a well designed low residue diet of normal foods (21), although stool frequency and consistency may change in healthy individuals (134). These results in subjects with normal gastrointestinal function are to be expected, as pancreaticobiliary enzyme activity was sufficient to efficiently digest the whole food diets, and the bowel's absorptive capacity was also normal. Despite their easy assimilation and absorption, elemental diets should not be expected to confer any advantages over polymeric diets or normal food under such conditions.

A stronger theoretical case for the use of elemental diets can be made in patients with a short length of small intestine. The absorptive surface may be markedly decreased, and in many cases, particularly where there is absence of the distal ileum or colon, the transit

time through the gut may be extremely short. Despite normal pancreaticobiliary secretion it can reasonably be postulated that elemental diets might well be beneficial to such patients.

The lack of studies of liquid diets in patients after extensive bowel resection is even more marked than in normal subjects. Kinney et al (137) maintained a young patient with an elemental diet after resection of the entire jejunum, ileum and ascending colon following volvulus of the bowel, thus managing to avoid the use of parenteral fluids on a regular basis. In 1969 Thompson et al (254) provided a further anecdotal report of a patient who retained only 4 inches of jejunum anastomosed to mid-transverse colon after a superior mesenteric artery thrombosis. Using a chemically-defined diet it was possible to provide 25-35% of daily calorie needs with a substantial contribution towards nitrogen requirements. Trials of medium-chain triglycerides and whole food resulted in profuse diarrhoea and large negative nutritional balances in this patient. Despite treatment with the elemental diet regular parenteral therapy was necessary and the patient finally succumbed to bacterial endocarditis.

In 1973 Voitk et al (266) reported a series of eight patients with extensive small bowel resection in whom an

elemental diet had been used in the immediate postoperative phase of treatment. It is unclear whether a trial of food alone in these patients would have been equally as successful as the elemental diet. As it was, food was tolerated by 4 of the 5 survivors after 19, 21, 22 and 52 days of elemental diet. It is interesting that these patients had a moderate amount of remaining intestine distal to the ligament of Treitz, measuring 130, 180, 200 and 200cm, thus constituting a relatively good prognosis group who might have tolerated food earlier if challenged.

There are indications that chemically-defined diets may not be any better than polymeric diets even in patients with the short bowel syndrome. Hecketsweiler et al (94), using a perfusion technique studied the absorption of nutrients from chemically-defined and polymeric diets in the proximal jejunum of 25 healthy volunteers. There was no significant difference in the total calorie, percentage nitrogen or percentage glucose absorption although the absolute values differed because of the different make-up of the feeds. In these subjects, the proximal 105cm of jejunum was capable of absorbing from elemental and polymeric diets respectively, 72% and 83% of glucose and 48% and 51% of nitrogen, (86% of fat was absorbed from the polymeric diet) presented to the intestine by perfusion at the ligament of Treitz. If

the known capacity for absorption in the duodenum is taken into consideration (28,216) it can be postulated that patients who retain 100cm jejunum should be able to cope with polymeric diets provided that other variables such as gastric emptying and bowel transit time remain equal.

Since these studies were published, an interesting report from Heymsfield et al (98) has suggested that chemically-defined diets may indeed be more efficiently absorbed than whole food. In one patient with a 250cm resection of small bowel and a retained colon, the percentage absorption of nitrogen increased from 55% to 88%, and energy absorption from 72% to 96% when an elemental diet was substituted for whole food. A second patient with an unknown length of bowel remaining, but with malabsorption responded to a similar regimen. Nitrogen and energy absorption increased from 41% and 72% respectively on whole food to 88% and 96% on an elemental diet. In both cases the elemental diet was given as a nasogastric tube feed over 20 hours, and whole food in six small meals. Balances of nitrogen, phophate, calcium and magnesium were positive in both patients on the elemental diet.

Nasogastric tubes have been used in some studies (98,137,266) to administer elemental diets, usually to

avoid their unpalatability. Although adequate preparation of the patient and the feed, combined with a positive attitude from medical and nursing attendants has been shown to improve patient compliance (187,242) some patients will continue to have problems. They may overcome difficulties with taste by drinking food supplements quickly, thus presenting a large bolus of food to their shortened intestine. It is logical to assume that the slower delivery of food via a nasogastric tube might be more successful in promoting efficient absorption of nutrients by reducing intestinal transit rates, increasing mixing of food with digestive enzymes and increasing mucosal contact time.

ENTERAL NUTRITION

The techniques of enteral nutrition and the equipment available have developed greatly in recent years. The large range of convenient, ready-to-use liquid feed preparations now available from pharmaceutical and food companies has led to increased enthusiasm for the treatment from medical and nursing staff. The use of fine-bore, silicone rubber feeding tubes has greatly improved the acceptability of the procedure to patients compared to the days when polyethylene tubes of much greater diameter were used, and the development of

simple peristaltic pumps has completed the hardware available for satisfactory nasogastric feeding. Nursing protocols have been developed which help to ensure the efficient and accurate delivery of a prescribed diet to a patient with the minimum of side effects.

The benefits of using liquid diets in the short-term support of hospital patients are well documented (97,129,282). The complications of enteral feeding are less serious and in some cases less frequent than those which are often associated with intravenous feeding, in addition to which the costs of both feeds and equipment are considerably less than the intravenous equivalent.

Although the use of nasogastric feeding tubes was described over thirty years ago (68), it is only in the past decade that significant progress has been made with regard to feeding tubes and liquid diets. In 1976 Woolfson et al (282) reported the use of a Ryle's tube of gauge 8F to maintained the nutritional status of 15 critically ill patients for up to 41 days using a mixture of glucose polymer, egg, and a hydrolysate of beef serum proteins. In the United States, central venous catheters were used successfully as nasogastric tubes to supply an elemental diet to patients (129,191). Over the next three years specially developed tubes became available, the work of Dobbie (63) and

Hoffmeister (108) resulting in the Dobhoff tube. This is a relatively stiff tube which contains a small mercury weight to facilitate passage into the duodenum. Another tube, manufactured as the Keofeed tube is made of silicone rubber and was used successfully by Heymsfield et al (97) when they made a strong case for the use of enteral nutrition as an alternative to parenteral support whenever this was possible. A wide range of silicone nasogastric tubes from many manufacturers is now available in an attempt to accomodate all personal likes and dislikes amongst clinicians and nutritional nursing staff.

When nasogastric feeding is deemed inadvisable because of oropharyngeal, oesophageal or gastric pathology or surgery, a feeding jejunostomy may be employed to make use of the remaining normal intestinal tract. The original technique of placing and retaining in position fine polyethylene catheters in the jejunum (150,153) was refined and adapted using central venous catheters inserted via a needle (191). A custom-designed catheter has since been designed with prolonged jejunal feeding in mind and its use reported by Chrysomilides and Kaminski (41).

The reported complications of nasogastric feeding include gastric retention with nausea, vomiting and the

risk of aspiration, abdominal cramps and diarrhoea, and a wide range of metabolic disturbances. Many of these can be pre-empted by simple precautions. The upper gastrointestinal symptoms tend to be worse when liquid feeds are given as a bolus, and for this reason a constant rate of administration is recommended by most authors (63,125,126,129,191,282). To facilitate the steady administration of feeds over 24 hours, peristaltic pumps are often advocated (63), although they may not be entirely necessary in a well-controlled hospital environment (125). Abdominal cramps and diarrhoea were for a long time considered to be due to the hyperosmolar nature of the elemental feeds commonly administered. However, it may not be the initial osmolality of the feed which is important, but the potential osmolality which results from the action of pancreatic amylase on glucose polymers in the proximal jejunum. Thus a seemingly innoccuous feed may result in osmotic diarrhoea in some patients (216). In general, there has been disagreement that osmolality is a major cause of diarrhoea, and in a number of publications the primary cause of diarrhoea whilst receiving nasogastric feeding was the concurrent administration of oral antibiotics (34,126,282).

The reported metabolic complications of parenteral feeding are legion and may occur rapidly because of the

direct administration of hyperosmolar fluids into the vascular system. Use of the enteral route should be associated with fewer problems, but, in a prospective study of 100 patients fed for a mean of 15.3 days a high incidence of metabolic disturbance occurred (265). Close reading of this publication reveals that, in most cases, the abnormality could be attributed to the underlying disease rather than to the nutritional support per se. Thus the majority of the cases of hyperglycaemia (29% of patients) were associated with either diabetes mellitus or systemic infection, and hypoglycaemia (2%) and hypokalaemia (8%) occurred in those receiving insulin therapy. In a similar way, hypernatraemia (10%) was observed in those patients with transient diabetes insipidus, and hyperkalaemia (40%) in those with renal insufficiency and metabolic acidosis. It is likely that the patients' disease and the fact that 46% required intensive care were of more significance in their metabolic disturbance than their tube feeding. Mild liver function abnormalities, with elevations of serum aminotransferase and alkaline phosphatase levels, were noted in almost 40% of patients receiving nasogastric feeding (126). These abnormalities were transient, and no patient developed serious hepatic dysfunction.

HOME ENTERAL NUTRITION

In common with patients requiring other forms of medical treatment the majority of those in need of nutritional support are treated for a relatively short period in hospital following which they remain healthy with no longterm therapy. A small number do however fail to thrive because of insufficient food intake, often due to the exacerbation of food-related symptoms such as nausea, vomiting, pain and diarrhoea. Others may have a malabsorptive state for which they are unable to compensate despite a good appetite. Patients with a short intestine often have a combination of both these problems.

In many patients borderline malnutrition has been satisfactorily treated by regular supplementation of the diet with a liquid polymeric feed (90). Patients in whom these measures have proved ineffective may be taught the techniques necessary to allow safe nasogastric or jejunal feeding to continue at home, and a small number of reports appear in the literature.

Main et al (161) reported the successful treatment of a young man with Crohn's disease who had spent long periods in hospital receiving repeated courses of parenteral nutrition for malnutrition secondary to his

Crohn's disease and repeated resections. Despite an oral diet of 3000kcal daily he was unable to maintain his weight or general health in a satisfactory state. The institution of an average daily supplement of 1700kcal and 55g protein given as a pump-regulated nasogastric feed overnight resulted in maintainance of weight at 90% of ideal, and haematological and biochemical parameters remained within the normal ranges. The supplementary feed used was an iso-osmolar, lactose-free polymeric preparation (Isocal,Mead Johnston).

Polymeric feeds were also used with success in the treatment of 23 patients suffering from a variety of conditions and all with protein/calorie malnutrition secondary to poor intake (180). A similar technique to that of Main et al (161) was employed although the delivery time in some cases was as long as 18 hours, giving the patient little independence. This appears illogical as one of the main aims of home treatment is to promote a more independent life-style. In this study the authors noted that fewer side effects and better weight gain were experienced by those patients whose feed delivery was controlled using a pump compared with those who were dependent on gravity.

In what was described as "a last resort" Heymsfield et al (98) used an elemental diet in two patients with

Crohn's disease and bowel resections resulting in malnutrition. Feeds containing approximately 1300kcal were given over 11 to 12 hours by night down a fine-bore tube. Feed delivery was again pump-controlled and resulted in weight gain and positive nutritional balances which were unattainable prior to supplementing the diet. The experience of these authors is encouraging because it shows that nasogastric nutrition at home is feasible and effective in a relatively small group of patients who would otherwise suffer malnutrition and possible death, or require parenteral nutrition with its potential complications.

HOME PARENTERAL FEEDING

The idea of feeding a person intravenously is not new. Glucose solutions were used in the early part of the twentieth century for both hydration and nutrition, casein hydrolysates were used in the 1930's and fat emulsions experimented with, especially in paediatric practice. Perhaps the first attempt to sustain a patient using all three simultaneously was reported by Clark and Brunschwig in 1942 (45). Their patient had required radical surgery to resect a neoplasm, resulting in the removal of larynx, upper trachea and upper oesophagus. For a period of 17 days, nutrients were

given entirely by the intravenous route. Varying quantities of a fat suspension containing olive oil and egg lecithin were combined with solutions of glucose, saline or a 10% casein digest. The patient remained in positive nitrogen balance and maintained his weight throughout the test period. During the parenteral feeding he remained well and ambulant, with no deleterious effects from his treatment other than the tendency for the peripheral veins to thrombose after infusion of nutrients. He subsequently remained well-nourished by infusing nutrient mixtures into a proximal oesophagostomy until recurrent tumour caused his death one year later.

Although the modern era of parenteral nutrition is often dated from 1968 when Dudrick et al (65) reported satisfactory growth in dogs fed exclusively with intravenous fluids, Wretlind (285) and Schuberth (226) had reported the results of their extensive studies on the effects of intravenous amino acid solutions and fat emulsions in both dogs and man in 1963. Both groups reported satisfactory clinical and biochemical results after prolonged treatment periods. While Wretlind (285) was able to use a soya bean oil emulsion as a calorie source, this preparation was not available in the United States, and cottonseed oil preparations proved toxic (285). Calories were therefore given as concentrated

glucose solutions, the infusion of which into peripheral veins is accompanied by rapid thrombophlebitis. To overcome this particular problem, techniques and specialised catheters were developed for use in the central veins. Broviac et al (35) initially described such a catheter made of silicone rubber which was placed in the subclavian vein and the tip positioned in the right atrium. The other end was then tunnelled subcutaneously and emerged on the anterior chest wall. This basic idea, with minor modifications (95,213), has become the most commonly used method for prolonged intravenous access and extensive experience with this catheter has now been reported (202). In 1979 Hickman et al (99) reported the use of a similar catheter and insertion technique in the treatment of leukaemic patients requiring bone marrow transplantation. This catheter had a wider internal diameter and thicker walls to facilitate the repeated administration of blood products, antibiotics and other drugs necessary in these particular patients.

These two catheter designs, the Broviac and the Hickman, have since become the most commonly used catheters for longterm parenteral nutrition. However, although the Broviac was initially designed to be introduced into the subclavian vein through a percutaneous introducer, most are now inserted by a direct 'cut down' onto the

cephalic vein (95,202) causing considerably more trauma to the patient (92), but fewer insertion-related complications. The percutaneous technique was pursued by Powell-Tuck (203) using a finer catheter which allowed easier access to the central veins and could be tunnelled with the minimum of trauma. A simple clip secured the catheter to the skin after insertion. This catheter is now available as the Vygon Nutricath. Figure 2 shows the three catheters described.

There are many potential complications of intravenous feeding. Those related to catheter insertion include haematoma formation, pneumo- and haemothorax, and trauma to other neck structures such as the subclavian or carotid artery, thoracic duct, or brachial plexus. Less immediate catheter-related complications such as thrombophlebitis, pulmonary embolism, and septicaemia may all be life-threatening. The incidence of thrombotic complications has been shown to be less when silicone catheters are used instead of those made of polyvinyl chloride, polyethylene, and Teflon (4,114,145,154,158,272). In a prospective radiological study, Laidlow et al (146) demonstrated a sleeve of fibrinous material encasing all but one of 38 silicone catheters placed in the superior vena cava. However, none of their patients had radiological or clinical evidence of central vein thrombosis or pulmonary

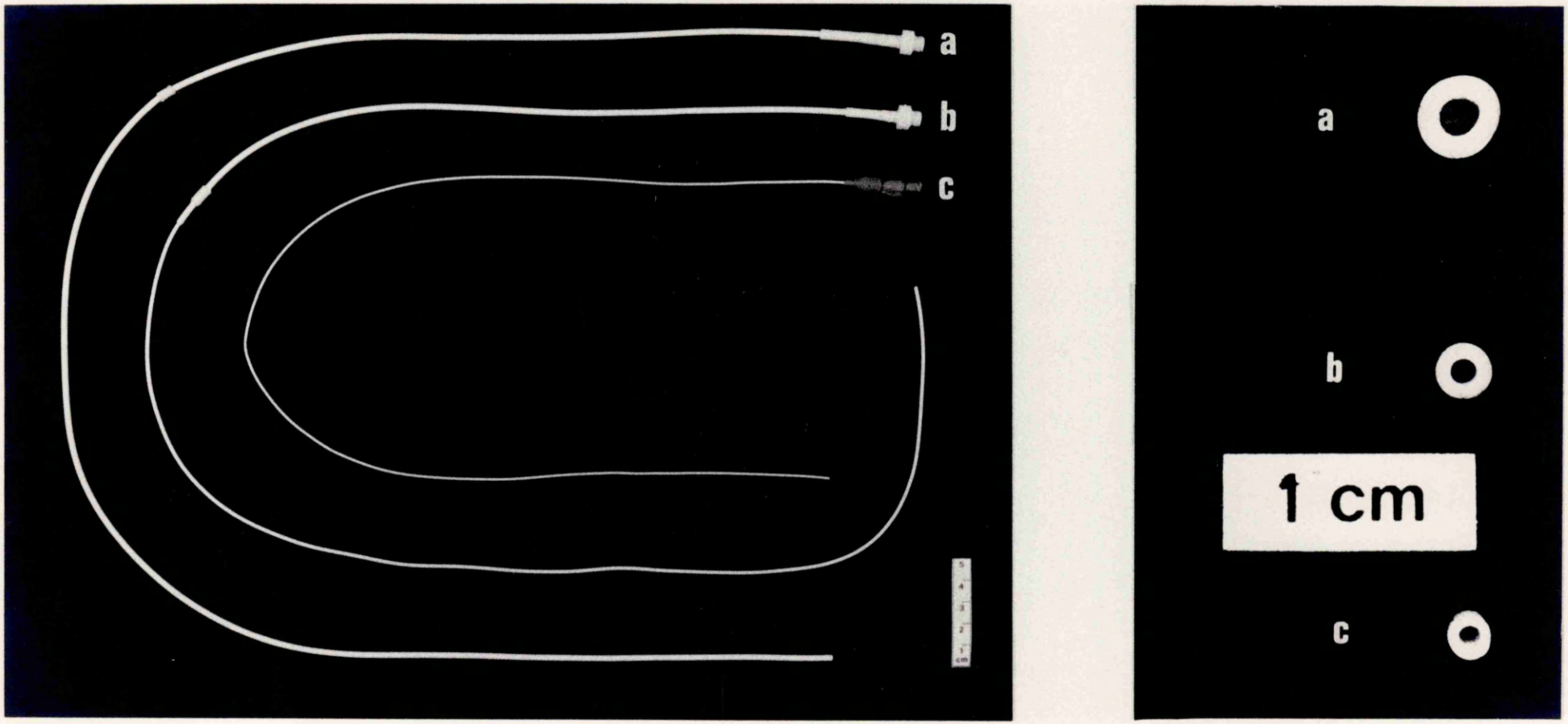


FIGURE 2 : Central venous catheters. a: Hickman b: Broviac c: Vygon.

embolism. It appears that while sleeves on catheters are to be expected, thrombosis and pulmonary embolism are not necessary accompaniments.

Catheter position appears to be a major determinant of thrombotic complications, probably because of inadequate dilution of hyperosmolar solutions in smaller veins with slower blood flow. Thrombosis is more likely to occur when the catheter tip is placed in the subclavian vein rather than in the right atrium (145,169) and cortical venous thrombosis and cerebral infarction has followed the incorrect placement of a catheter in the internal jugular vein (245).

Catheter-related sepsis remains potentially one of the most dangerous complications of parenteral nutrition and may be caused by either bacteria or fungi. The routine bacterial culture of the area round the catheter skin insertion site has been shown to correlate well with the organisms which most commonly cause septicaemia in these patients (204,243). To combat these problems and to help avoid metabolic upset by improving the efficiency of the delivery of the prescribed intravenous fluids many centres have formed multidisciplinary teams which have been successful in reducing complications and simplifying regimens (132,204).

As in the case of patients requiring supplementary enteral feeding, the numbers likely to need prolonged parenteral therapy are small. For them, the techniques of successful hospital treatment may be adapted for use in the home. The phrase "the artificial gut" was first coined by Scribner and the group from Seattle, USA in 1970 (228) who initially used arteriovenous shunts and fistulae for prolonged intravenous access at home. It was thromboembolic problems with these shunts which resulted in the development of the Broviac catheter and the subsequent refinements of catheterisation technique.

The first reports of significant numbers of patients treated at home appeared in the mid 1970's from centres in the United States of America, Canada and Denmark. Broviac and his colleagues in Seattle, reported their experience with 12 patients in 1974 (36) and extended this to 43 patients in 1976 (213), the treatment period ranging from 1 to 52 months. In 1973 and 1976, Jeejeebhoy and the group from Toronto published a comprehensive report giving clinical and biochemical details of 12 patients who had been treated at home for up to 5 years (121,122). The Toronto experience now includes over 70 patients the first of whom is still alive and well after 13 years treatment (Jeejeebhoy personal communication). In Denmark, home parenteral nutrition techniques developed over a similar timescale.

Ladefoged and Jarnum published their results of 19 patients surviving at home for 6 to 63 months in 1978 (143), and further reviewed their extensive experience of longterm intravenous nutrition, both in hospital and at home, in 1981 (120,145). A combined view of these major reports serves well to illustrate the variations in technique, and the similarity of application of home parenteral feeding at its inception.

In all series the majority of patients treated with home intravenous feeding had undergone repeated, or single, extensive resections of the small intestine as a result of Crohn's disease, or bowel infarction secondary to mesenteric vascular disease, both arterial and venous. There was therefore a high proportion of patients with features of the short bowel syndrome, either with or without a residual colon. In addition, a small number were treated for active Crohn's disease (36), sometimes complicated by enterocutaneous fistulae (36,143). Less common diagnoses included systemic sclerosis with total intestinal involvement, pseudo-obstruction (122), radiation enteritis, acrodermatitis enteropathica, systemic mast cell disease and severe postgastrectomy dumping and diarrhoea (36). There was no particular age group involved, although patients tended to be between 15 and 65 years of age.

Silicone catheters were the choice of all groups. The Seattle workers naturally favoured the Broviac which was also endorsed by the Danes after initial experience with non-silicone catheters. They noted an increased catheter survival time and a decrease in catheter-related complications when Broviac catheters were substituted. In Toronto, a silicone tube without an anchoring Dacron cuff was used, tethered to the skin by sutures. This was developed because of their experience with skin tunnel infection and the difficulty of removing some cuffed catheters. Intravenous solutions all contained amino acids and glucose, but Broviac used only glucose as an energy source in contradistinction to the other groups who included regular lipid emulsion in most patients' treatment regimen. Infusate was administered from different containers by different methods. While Ladefoged and Jarnum (143) were content to allow infusion under gravity alone, Broviac et al (36) administered fluids from 2 litre glass bottles by electric pump with an alarm system to avoid the problems of air embolism. The Canadian group approached this problem in a different way, employing three, 1 litre plastic bags to which was applied a constant pressure from pneumatic cuffs. The advantages claimed for this system were ease of use, independence from electrical power supply and therefore more social freedom for holidays and travel, and the increased safety against

infection and embolism inherent in a totally closed system (121).

Catheter sepsis and thrombosis were prominent complications in the Danish report (145). However, Jeejeebhoy et al (122) reported no catheter sepsis arising in patients who had no other site of sepsis, and in their 1976 paper (213), the Seattle group reported an incidence of only one episode of catheter sepsis per 5.5 patient years of treatment. When sepsis did occur it was potentially serious, both Ladefoged (143) and Broviac (36) reporting a single death attributed to septicaemia arising from the catheter. Central vein thrombosis was most frequent in the Danish series, particularly when non-silicone catheters were used. It is interesting to note that this occurred despite the prophylactic administration of heparin (145).

The success and merit of home parenteral feeding was not disputed by any group. Indeed both Broviac (36) and Jeejeebhoy (121,122) commented on the remarkable improvement in their patients' wellbeing and physical capabilities. Most patients in all studies coped well with the treatment, although Jeejeebhoy sounded a note of warning about the problems likely to be experienced by patients with a previous history of depressive disease. Two such patients failed to achieve as full

rehabilitation as the majority in Toronto. The psychological problems faced by patients on home parenteral nutrition have recently been reviewed and include significant depression secondary to the loss of the ability to eat (195). A further measure of the success of the treatment as a supportive therapy was that several patients, 4 in Seattle and 6 in Denmark managed to return to an exclusively oral diet after a period on parenteral feeding. In general, patients resuming oral food did so in less than twelve months, although two patients in Denmark restarted an oral diet after 13 and 24 months of home parenteral nutrition. These successes, and the wellbeing and rehabilitation of the majority were felt to more than offset the relatively low incidence of complications of a new technique.

The growing experience in the United Kingdom since 1978 has mirrored the early transatlantic experience. A register of all the patients who have received parenteral nutrition at home has been established (118), which reveals that most British patients are aged between 20 and 50 years and have a short bowel due to resections for Crohn's disease or mesenteric vascular disease. The majority are well rehabilitated, being able to return to work or look after their family, and cope with their treatment without major complications.

One patient has had successful pregnancies while on parenteral feeding (256). Few detailed reports appear in the literature as few centres have experience of more than a few patients (156,171,275).

The contribution of the Toronto group to the understanding of nutritional requirements and potential metabolic patients in patients receiving longterm parenteral nutrition cannot be overemphasised. In their initial reports of 1973 (121) and 1976 (122), Jeejeebhoy et al found protein requirements to be 1.1g/kg body weight, coupled with a total calorie provision of 27-40kcal/kg with a mean of 32kcal/kg. They also demonstrated that the nature of the non-protein calorie source is important: a patient receiving glucose alone had a tendency to develop fatty hepatic infiltration alone but this could be reversed by the regular use of 50-100g intravenous fat daily. Withdrawal of the lipid source resulted in the recurrence of fatty infiltration in this patient. Despite the daily use of fat providing seemingly adequate supplies, plasma levels of the essential fatty acid, linoleic acid and its metabolites tended to be reduced although there was no clinical evidence of deficiency.

Vitamin levels in the initial twelve patients from

Toronto were in general satisfactory with the exception of biotin, deficiency of which developed in a 12 month old patient receiving long-term parenteral feeding (173). Plasma levels of the trace elements copper, zinc and chromium were monitored and were found to be normal with the exception of chromium, the levels of which tended to be low. Frank chromium deficiency was later reported to be responsible for glucose intolerance and peripheral neuropathy which reversed after chromium supplements of 20micrograms daily (123). More detailed studies of zinc needs revealed the need for supplements of 3-12mg (50-200micromoles) zinc per day depending upon the volume of bowel content lost (280).

The longterm survival of patients on exclusively parenteral feeding has led to further deficiency syndromes being recognised. Abnormalities of some erythrocyte and leukocyte enzyme systems have been reported associated with low plasma selenium levels. Daily intravenous supplements of 100micrograms reversed both abnormalities (14). Although these findings were not clinically detectable, more serious effects of selenium deficiency have been reported, including generalised myopathy (135) and fatal cardiomyopathy (69).

AIMS OF CURRENT STUDY

This thesis aims to study and discuss certain aspects of the management of patients with a short intestine. The provision of an oral replacement solution to maintain fluid and electrolyte balance and avoid the need for intravenous therapy is clearly a desirable goal, for although the number of patients with a short small intestine is small, a larger number of patients with a high output ileostomy could also benefit from the use of such a mixture. An 'ideal' solution should effectively improve sodium and water balance while being palatable and acceptable to patients who will have to take it over a prolonged period. It should also be easy to prepare from readily available ingredients at low cost. The object of the experimental work in this thesis was to attempt to identify such a solution using the WHO cholera solution as a starting point.

The potential benefits of increasing dietary fat include improved palatability which could induce patients to increase their total calorie intake with a greater chance of compensating for their reduced absorptive capacity. The clinical studies using normal food aim to determine whether variation in the amounts of dietary fat and fibre affects the nutritional value of food for these patients, and whether restriction of fat is indeed

a useful way of reducing the amounts of nutrients, electrolytes and minerals lost by these patients in the stool.

Supplemental enteral nutrition is now an accepted form of treatment but the merits of elemental and polymeric preparations continue to be debated. A comparison of Nutranel with Ensure has been made to show if elemental diets are a more efficient way to provide nourishment to patients with a reduced absorptive area. In some cases, oral and nasogastric administration of the same feed has been compared to show if there is merit in the routine use of nasogastric tubes rather than simply allowing the patient to drink supplements.

Enteral supplements are at present usually given in liquid form but it is not known whether their use is in fact any more effective than giving normal food. The results obtained from the studies of solid and liquid foodstuffs have been compared to provide guidelines for dietary supplementation.

Techniques of nutritional support, both enteral and parenteral have been developed with reliable protocols for nursing care and patient instruction. These are described together with the medical and social results of the treatment given to a number of patients.

The overall aim of this thesis is to provide some logical guidelines for the management of patients with different disabilities and requirements and to indicate clearly the place of different forms of nutritional support in the treatment of the short bowel syndrome.

METHODS

CLINICAL

Electrolyte Mixtures

All the patients who participated in the tests of different carbohydrate-electrolyte mixtures had a proximal small bowel stoma, and had needed intravenous supplementation to maintain fluid and electrolyte balance. Intravenous supplements were continued throughout the test period in 6 of the 7 patients. Following an overnight fast the patient's jejunostomy appliance was emptied and he or she was asked to drink a 500ml bolus of a test solution over 5 to 10 minutes. Jejunostomy effluent was collected over the next three hours during which no further oral intake was allowed. The complete effluent collections were weighed and homogenised using a Silverson Laboratory Mixer Emulsifier. Aliquots were kept at -20^{o}C prior to analysis for sodium, potassium, chloride and polyethylene glycol.

Liquid Diets

A group of seven patients with proximal small bowel stomas participated in tests of two liquid feeds. Before

beginning the test period, each patient fasted overnight. The contents of the jejunostomy appliance and urinary bladder were discarded. Each liquid feed was freshly prepared in the ward kitchen by the same operator (PBM) each day. The patient received a diet sheet instructing him or her to take aliquots of feed, water or glucose-electrolyte mixture at regular intervals throughout the day. All liquids were taken as sip feeds by 5 patients and administered by nasogastric tube to the other 2 patients because of problems with palatability. Each diet was given over a period of 12-14 hours, kept constant for each patient. After an overnight fast the patients emptied their stoma appliance and urinary bladder to complete 24 hour collections, and began the next test day. Each patient received the diets in random order for 2 or 3 days depending on their tolerance, then crossed over to the other feed. Each patient's diets were based on their body weight and were constructed to contain equal amounts of nitrogen, sodium, and total fluid during each of the test diets. Total calorie input varied because of the difference in nitrogen:calorie ratio of the two test feeds. Patients JG,AP,BS and RT required intravenous saline and potassium throughout the test period to maintain fluid and electrolyte balance.

Solid Food Diets

Solid food diets were constructed to vary only in the quantity of fat and fibre that they contained. Three diets were prepared, designated high fat/high fibre, reduced fat/high fibre, and reduced fat/normal fibre. They were given for 2 or 3 days each in a randomised, cross-over manner to 4 patients and stoma and urine collections completed as described in the section on liquid feeds.

Preparation of Specimens

Stoma effluent specimens were collected into polythene buckets with a tight-fitting lid. The complete 24-hour specimens were weighed and homogenised. Aliquots were taken and kept at -20^{o}C before analysis to ascertain the concentrations of sodium, potassium, calcium, magnesium, fat and nitrogen. Larger aliquots were freeze-dried to determine the dry weight of the effluent and in preparation for bomb calorimetry. Twenty-four hour urine samples were collected into disposable plastic containers. The total volume was measured and an aliquot taken and frozen at -20^{o}C. Analysis was later undertaken for sodium, potassium, calcium, magnesium and urea concentrations. The quantity of nitrogen lost in

the urine was calculated from the urine urea.

Composition of Solid Food Diets

After discussion with an experienced Dietitian, solid food diets were designed to contain similar quantities of nitrogen, total calories, electrolytes and minerals, while varying the amounts of fat, fibre and carbohydrate. The nutritional value of each diet was calculated from standard food tables (196). Wherever possible, individual portions of foodstuffs, for example butter, preserves, cheese and soups were used to maintain consistent intakes. The amounts of electrolytes and minerals varies with the time of year: mean values given in the food tables were used, these being sodium 50mg/100g, potassium 150mg, calcium 120mg and magnesium 12mg/100g milk. The water used was obtained from the hospital supply and contained sodium 1.3mmol/l, potassium 0.2mmol/l, calcium 3.5mmol/l and magnesium 0.1mmol/l.

Measurement of Intestinal Length

The length of residual intestine was measured in one of two ways. When possible, direct measurement was undertaken during surgery by measuring along the mesenteric border of the intestine with a steel rule.

The intestine of patients BS and SG was measured in this way. In all other cases, measurements were made on a barium small bowel follow-through film by a consultant radiologist using an opsimeter.

Statistical Methods

For comparisons between diets and electrolyte mixtures, each patient acted as his or her own control. Differences were analysed using Student's 't' test for paired data.

LABORATORY

Flame Spectrophotometry

The concentrations of sodium, potassium, calcium and magnesium in urine and stoma effluent samples were measured using a Pye Unicam SP90A flame spectrophotometer. The light wavelengths used were; sodium 589nm, potassium 766.5nm, calcium 422.7nm and magnesium 285.2nm.

Preparation of Standard Solutions

Sodium

Using sodium chloride, solutions containing 0.1, 0.2, 0.3, 0.4, and 0.5 mmol sodium per litre were prepared, flamed, and a standard curve constructed.

Potassium

Solutions were prepared using potassium chloride and sodium chloride. The sodium was included to standardise the depressant effect of light emmitted by sodium on that emmitted by potassium. The standard solutions contained 0, 0.04, 0.08, 0.12, and 0.16 mmol potassium per litre, and 1.2 mmol sodium per litre. When test solutions were being processed, standard solutions were rechecked after every twenty test samples.

Calcium and Magnesium

Calcium chloride was used to prepare solutions containing 0.025, 0.05, 0.075, 0.1, 0.125, and 0.15 mmol calcium per litre. Standard solutions for magnesium were prepared using magnesium nitrate and contained 0.016, 0.025, 0.033, 0.041, 0.049 and 0.066 mmol magnesium per litre. The light wavelength used for magnesium

estimations was 285.2nm, and for calcium 422.7nm.

Measurement of Chloride in Stool

Chloride concentrations in jejunostomy fluid were determined using an EEL Chloride Meter (Evans Electroselenium Ltd). A solution of sodium chloride 100 mmol/l was used as a standard. Test blanks consisted of buffer, gelatin solution and distilled water.

Measurement of Polyethylene Glycol

The concentration of polyethylene glycol present in intestinal effluent was measured using the turbidimetric method of Hyden (116) as modified by Malawer and Powell (163) and Boulter and McMichael (31) to improve stability and reproducibility. The turbidity of samples was determined in a spectrophotometer (Unicam SP500 Series) against a water blank, using a blue photocell and a wavelength of 420 nm.

Measurement of Faecal Nitrogen

The nitrogen content of stoma effluent was determined using the Micro-Kjeldhal method as described by Wootton (283). Three measurements were made of each aliquot of intestinal content.

Measurement of Faecal Fat

Faecal fat was measured by the method of van de Kamer (264). This method is not entirely suitable for the complete extraction of medium chain fatty acids, (223) assuming as it does a mean molecular weight of 284 for fatty acids, equivalent to 16C:0 fatty acids. For this reason, gas liquid chromatography was utilised in the measurement of fatty acids in those patients who tested liquid feeds containing medium chain (8-10 C) triglycerides.

Gas Liquid Chromatography

Gas liquid chromatography was used in the determination of fatty acids in the jejunostomy effluent of those patients who took liquid diets, as 50% of the fat contained in Nutranel is in the form of medium chain triglycerides. Analysis was performed using a 3.0m x 2.0mm SP2100 DOH column through which samples were injected by an S8 autoinjector. Nitrogen was used as the carrier gas at a flow rate of 25ml/minute, and the analysis integrated using a Pye Unicam 4800 chromatography control centre. To improve resolution of isomers, further analysis was performed on a 25m bonded phase capillary column (SGE BPE). The identity of individual fatty acids was confirmed by mass

spectrometry on a Dupont 491 instrument. The chromatography and mass spectrometry were carried out at the Public Health Laboratory Service Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire.

Measurement of Urine Urea

Measurement of the urea concentration in urine samples was undertaken in the routine chemical pathology laboratory at St Bartholomews Hospital, London using a Technicon SMA 11, Computer-controlled, Multichannel Biochemical Analyser (Technicon Instrument Corporation).

Measurement of Urine Osmolality

Urine osmolality was measured in the same hospital chemical pathology laboratory as the urine urea concentrations, using an Advanced Digimatic Osmometer Model 3D11 (Advanced Instruments Inc).

Bomb Calorimetry

Aliquots of wet faecal homgenate were placed in pre-weighed conical flasks and the flasks re-weighed. The exact weight of the homogenate was determined by

subtraction of the weight of the empty flask from the total. Samples were then frozen at -20°C before being connected to a condenser and vacuum pump (Edwards High Vacuum pump Model ED 50) and freeze dried. This process was continued until a constant weight of flask and sample was obtained, usually in 36 to 48 hours. The flasks were then reweighed and the weight of dry stool determined by subtraction.

The theoretical basis of bomb calorimetry is the assumption that complete combustion of a substrate will occur in an atmosphere of excess oxygen. The apparatus used, a Gallenkamp Ballistic Bomb Calorimeter (Model CBB-330-010L) is illustrated in Figures 3 and 4. Samples are placed in a crucible inside the combustion chamber of the calorimeter. Oxygen is introduced to a pressure of 25 atmospheres. A thermocouple is attached to the outer casing of the combustion chamber, and the galvanometer scale set to zero. The sample is then ignited electrically, and the peak galvanometer reading noted. The galvanometer deflection is a measure of the change in temperature produced by the combustion of the sample in the calorimeter. An initial sample was combusted to ensure that the galvanometer deflection fell in the desired range. The procedure was then repeated with a total of six identical samples and the galvanometer deflections recorded. A correction factor

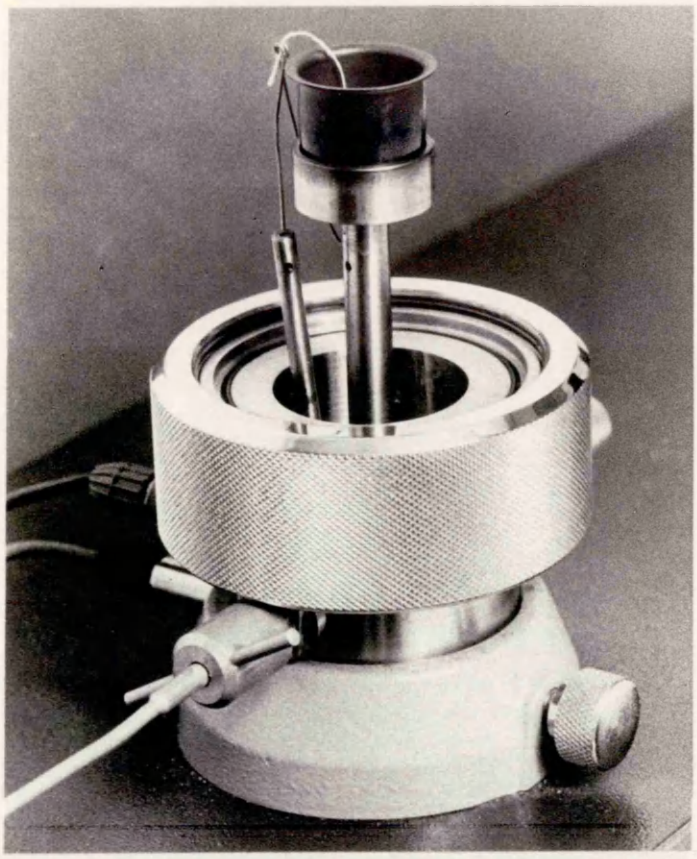


FIGURE 3 : Bomb calorimeter combustion chamber with crucible and cotton fuse in place.

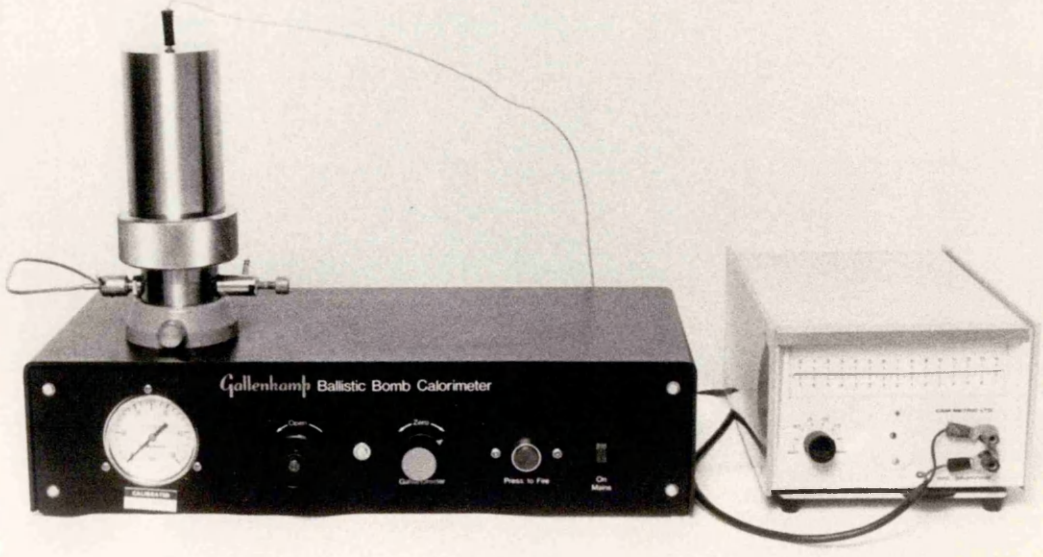


FIGURE 4 : Bomb calorimeter with combustion chamber closed and thermocouple attached ready for firing.

for the cotton fuse was subtracted in each case and the mean deflection calculated. The calorific value of the sample was obtained from the standard curve and a total calorific value for the 24 hour effluent collection calculated.

A standard curve showing galvanometer deflection plotted against kilocalories was produced by combusting multiple samples of Analar sucrose. This has a known calorific value of 3.96kcal per gram and the thermal emission is linear in the region around 4.00kcal. Six samples of each of the following weights were used; 0.5, 0.6, 0.7, 0.8, 0.9, 1.0, and 1.1 grams. The line produced is shown in Figure 5. Each point represents the mean value $\pm$ 1SD for a particular weight of sucrose.

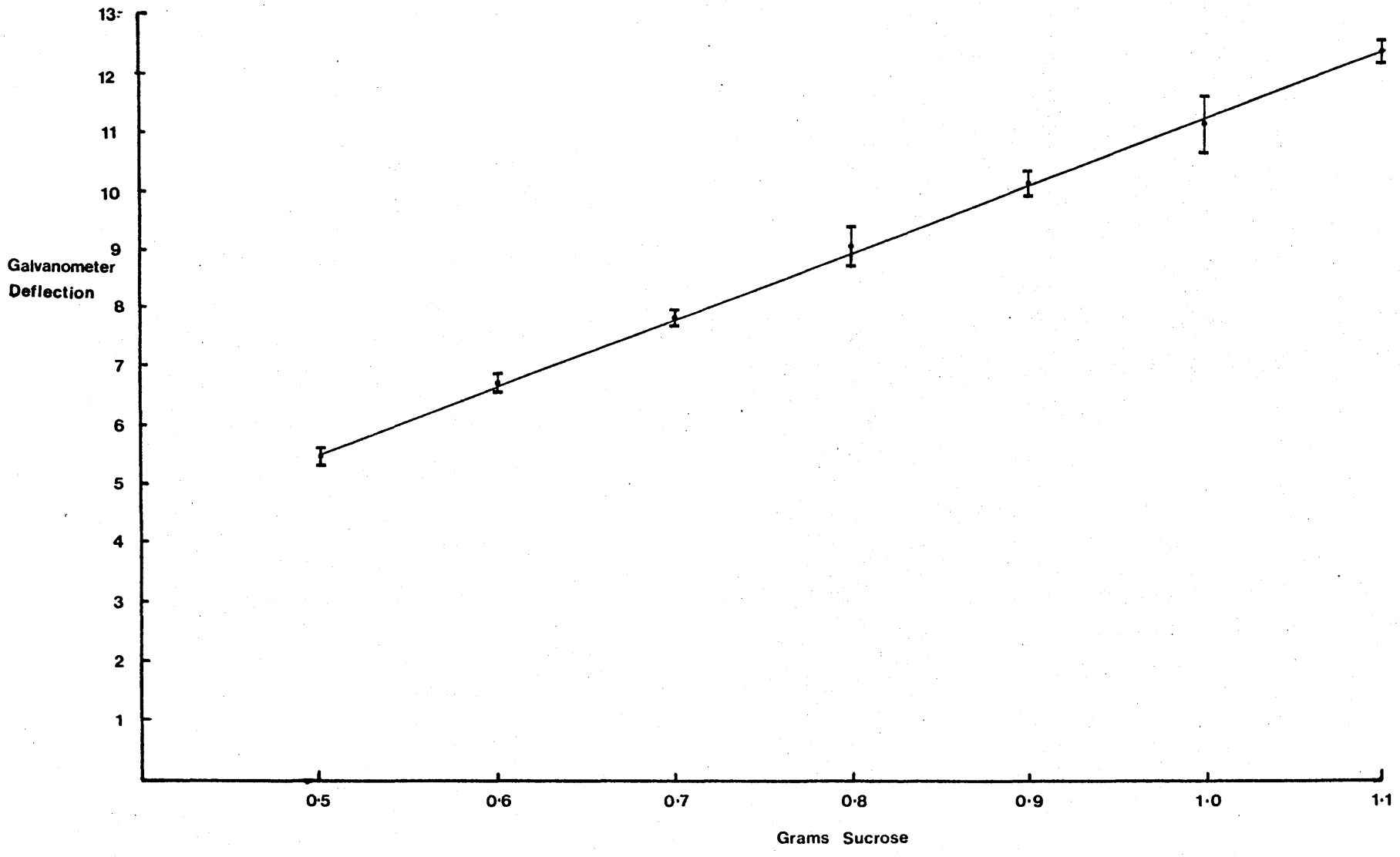


FIGURE 5 : Standard curve obtained from the combustion of different weights of sucrose.

RESULTS

ELECTROLYTE SOLUTIONS

Seven patients took part in tests of five different electrolyte replacement solutions. All had previously required regular intravenous therapy to maintain satisfactory fluid and electrolyte status. Figure 6 gives the patients' characteristics and an indication of their intestinal length measured from the duodeno-jejunal flexure to their jejunostomy. Six patients had required recurrent resections of small and large intestine for Crohn's disease. In addition, KB had required gastroduodenal surgery leaving a small gastric remnant anastomosed to duodenum. Patient JG had suffered from radiation enteritis following treatment for cervical carcinoma. Full case histories are given in the Appendix.

Each subject took each of the test solutions after an overnight fast and collected the effluent from their jejunostomy for the next three hours. The composition of the electrolyte mixtures is shown in Table 1.

The subjects have been arbitrarily divided into two groups depending on whether they could subsequently be maintained in fluid and electrolyte balance on oral

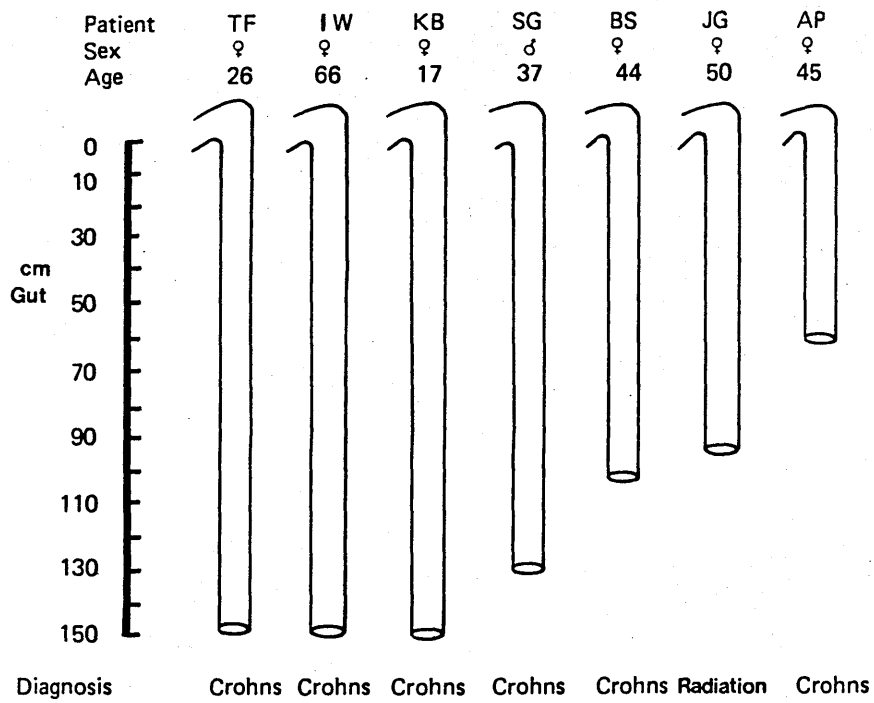


FIGURE 6 : Patients who took part in tests of different sugar/electrolyte replacement solutions.

	1	2	3	4	5
	Saline Glucose	Saline Bicarb. Glucose	Saline Bicarb. Maltose	Saline Bicarb. Sucrose	Electrolyte glucose 'Caloreen'
Concentration mmol/l					
NaCl	90	60	72.5	72.5	76
NaHCO3		30	42.5	42.5	9
KCl					12
Ca Gluconate					2.5
Glucose	110 (20g)	110 (20g)			110 (20g)
Maltose			55 (20g)		
Sucrose				55 (20g)	
Glucose Oligosaccharide (Caloreen)					17.5 (16g)
Osmolality mosm/l	279	284	269	275	294

In 10 other studies small changes were made as shown in the footnote and in Figures 7 and 8.

NaCl 76mmol/l in solution 1 for IW, 85 mmol/l for KB.
NaCl 42.5mmol/l and NaHCO3 42.5mmol/l in solution 2 for IW and KB and one study on TF.
NaCl 115mmol/l and NaHCO3 0mmol/l in solution 3 for one study on JG.

TABLE 1 : Composition of electrolyte solutions tested in 46 of 56 studies.

fluids (Group A, subjects TF,JG,IW,SG) or continued to require intravenous supplementation (Group B, subjects AP,BS,KB). Tables 2 & 3 show the net absorption or secretion of sodium, potassium, chloride and water from each test solution over the collection period in 56 studies where 80% or more of the marker polyethylene glycol was recovered (81% of the studies). With the exception of potassium, these are illustrated in Figures 7 and 8.

Water, Sodium, Chloride and Bicarbonate

Group A Subjects

a. With or without bicarbonate

Mean absorption of sodium was 24.8mmol (57.5%) from the 500ml of saline/glucose solution, and 27.8mmol (63.3%) from the solution where 30mmol chloride had been substituted by bicarbonate (difference not significant). Chloride absorption was less from the bicarbonate-containing solution but water absorption was similar (68.6% versus 63.2%).

b. Glucose versus maltose

Substitution of an equal weight of maltose for glucose in the solution, with appropriate increase in sodium concentration to preserve isotonicity, resulted in a

significant increase in sodium absorption to a mean of 39.2mmol (68.1%) over the saline/glucose solution ($p<0.02$). Chloride absorption was greater with the higher chloride concentration in solution 1, but water absorption was similar (69.6% and 63.2%).

c. Maltose versus sucrose

Substitution of sucrose for maltose in the two subjects tested resulted in less sodium absorption (sucrose 21.4mmol, maltose 34.0mmol). There was little chloride absorption and water absorption was also less (sucrose 34.6%, maltose 60.0%).

d. Addition of oligosaccharides

Addition of glucose oligosaccharide (Caloreen) resulted in absorption of only 15.8mmol of sodium (41.7%) from 500ml of solution, which was significantly less than from the saline glucose solution ($p<0.05$). Chloride absorption exceeded sodium absorption. Mean water absorption was 54.6%.

e. Water and tea

Ingestion of 500ml of water or tea resulted in absorption of 62.3% of the water and 44.7% of the water in the tea, but a marked net loss of sodium and chloride in all subjects.

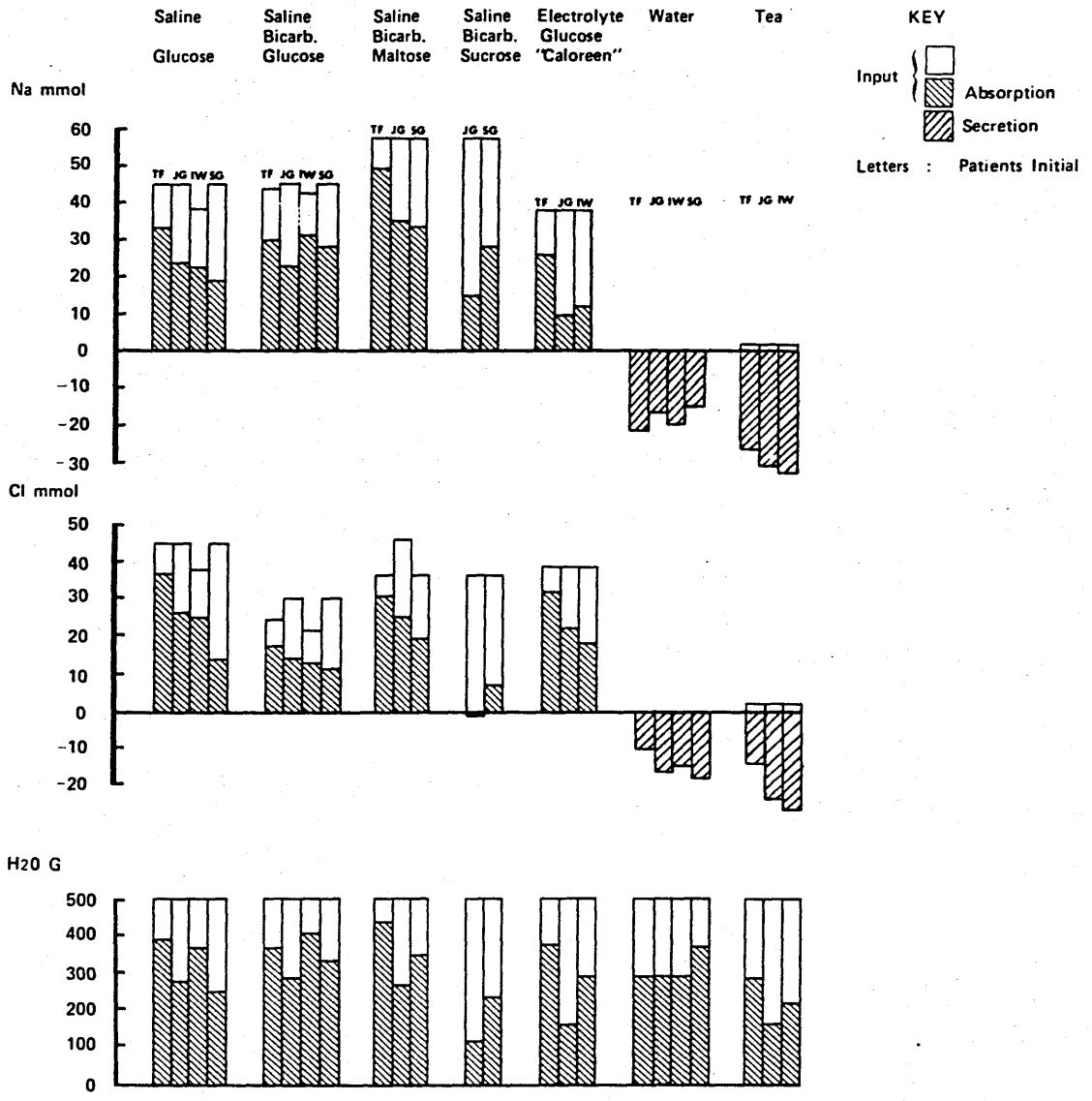


FIGURE 7 : Sodium, chloride and water absorption and secretion in patients who were able to stop intravenous therapy (Group A).

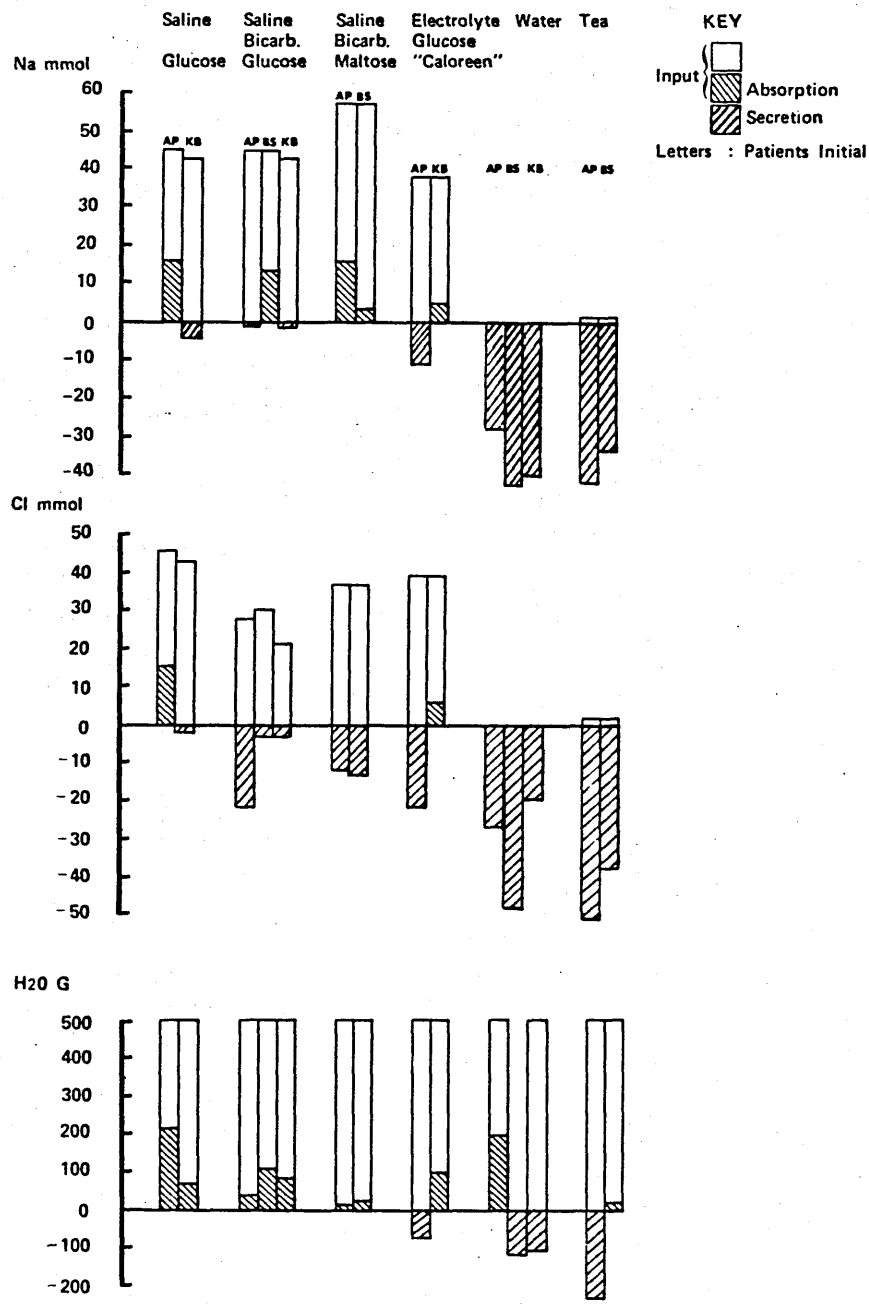


FIGURE 8 : Sodium, chloride and water absorption and secretion in patients who continued to require intravenous therapy (Group B).

	1 Saline glucose	2 Saline bicarb. glucose	3 Saline bicarb. maltose	4 Saline bicarb. sucrose	5 Electrolyte glucose 'Caloreen'	Water	Tea
Sodium mmol	24.8	27.8	39.2**	21.4	15.8*	-17.9*+	-29.5*+
(%)	(57.5)	(63.3)	(68.1)	(37.2)	(41.7)		
Potassium mmol	-1.5	-1.4	-0.8	-1.1	3.5	-1.3	1.3
(%)					(58.9)		(43.3)
Chloride mmol	25.2	13.7*	24.8	3.1	24.0	-14.5+	-20.8*+
(%)	(58.5)	(52.4)*	(63.2)	(8.5)	(61.5)		
Water ml	316	343	348	173	273	312	223
(%)	(63.2)	(68.6)	(69.6)	(34.6)	(54.6)	(62.3)	(44.7)

+ p<0.01 : Sodium mmol Water < 1,2,3 : Tea < 1,2,5
Chloride mmol Water < 1,2,3,5 : Tea < 1,2,5

* p<0.05 : Sodium mmol 5 < 1 : Water < 5 : Tea < 3
Chloride mmol 2 < 1,3 : Tea < 3
Chloride (%) 2 < 3

** p<0.02 : Sodium mmol 3 > 1

TABLE 2 : Water and electrolyte absorption and secretion in patients who were able to stop intravenous therapy (Group A).

	1	2	3	4	5		
	Saline glucose	Saline bicarb. glucose	Saline bicarb. maltose	Saline bicarb. sucrose	Electrolyte glucose 'Caloreen'	Water	Tea
Sodium mmol	5.8	4.2	9.7	-.-	-2.9	-36.1	-36.5
(%)	(13.2)	(9.5)	(16.8)				
Potassium mmol	-1.2	-1.6	-1.5	-.-	2.3	-1.4	0.3
(%)					(37.5)		(10.0)
Chloride mmol	6.6	-9.3	-12.1	-.-	-7.8	-31.0	-44.0
(%)	(15.1)						
Water ml	138.5	71.0	16.0	-.-	12.0	-7.0	-106.0
(%)	(27.7)	(14.2)	(3.1)		(2.4)		

-.- solution not tested

TABLE 3 : Water and electrolyte absorption and secretion in patients who continued to require intravenous therapy (Group B).

Group B Subjects

Group B subjects failed to absorb any of the solutions sufficiently well to be clinically useful, results ranging from a small net secretion to 16.8% absorption of sodium, and from 2.4-27.7% of water from the 500ml ingested. Water and tea tended to result in a small net loss of water, but a large loss of sodium and chloride was produced by ingestion of 500ml of both fluids in all subjects.

Potassium

In both groups of subjects, there was a small secretion of potassium with all the solutions except those containing the ion (solution 5, and tea, K=6mmol/l), where there was a small net potassium absorption.

Summary

Sodium absorption was greatest from the maltose-containing solution but sucrose and glucose oligosaccharides compared poorly with glucose as promoters of water and sodium absorption.

Ingestion of water and tea led to a negative sodium balance in all patients and to a negative water balance in the most severely affected.

Group A patients, who were subsequently able to stop intravenous fluids and to be maintained in satisfactory fluid and electrolyte balance using oral replacement could be identified by the fact that they excreted less than 250ml from their jejunostomy in the three hours after ingestion of a 500ml bolus of the glucose-bicarbonate-saline mixture.

Although absolute sodium absorption was greatest after the maltose solution, the difference between this and the glucose-bicarbonate-saline solution is not considered large enough to be clinically important or to justify the considerable cost of using maltose routinely in oral replacement solutions.

SOLID FOOD DIETS

Three solid food diets were constructed to contain different quantities of fat and fibre while keeping other constituents, including nitrogen, total calories and fluid input constant. Calcium intake was maintained at a similar level in all diets. Although there was a range of values for all dietary constituents for the group, each patient maintained a relatively constant input of each constituent on all diets. A daily supplement of 12mmol magnesium in the form of magnesium glycerophosphate was given throughout each test period. The diet constituents are shown in Table 4.

Four patients completed studies of the three solid food diets and provided 2-3 complete 24hr collections of stoma effluent and urine on each diet. All had a proximal small bowel stoma and retained less than 150cm small intestine between the duodeno-jejunal flexure and the stoma. Patient details are given in Figure 9. Two patients (AP and BS), who usually required supplementary parenteral nutrition at home received saline 0.9% with additions of potassium chloride to maintain fluid and electrolyte balance throughout the test period. The results of effluent and urine analysis are given in Tables 5 to 8.

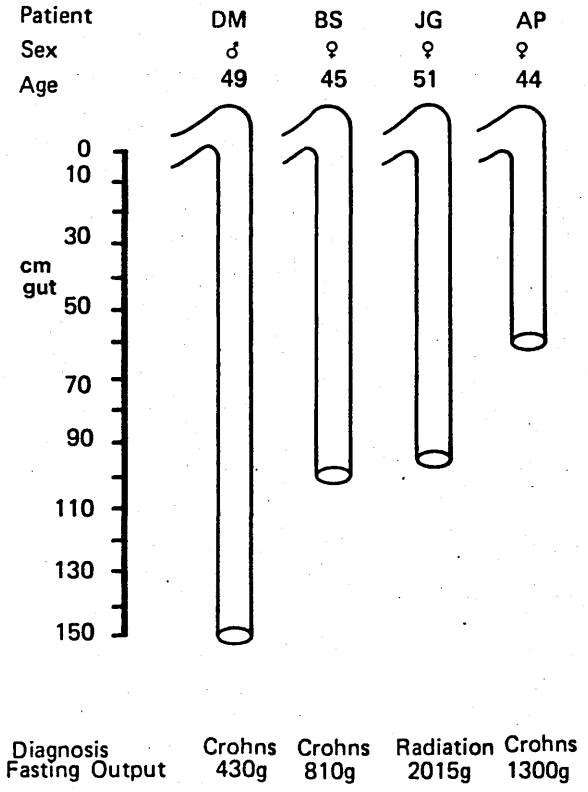


FIGURE 9 : Details of patients taking solid food diets.

Diet 1 (High Fat, High Fibre)

Patient	Nitrogen g	Fat g	Fibre g	Calories kcal	Calcium mmol	Magnesium mmol	Fluid ml
JG	11.0	68	29	1668	13.8	25.8	4240
DM	13.0	90	28	2022	23.8	28.7	2140
AP	11.7	102	27	2294	20.5	27.0	1960
BS	12.8	106	26	2168	23.6	27.8	1760

Diet 2 (Reduced Fat, High Fibre)

Patient	Nitrogen g	Fat g	Fibre g	Calories kcal	Calcium mmol	Magnesium mmol	Fluid ml
JG	11.0	44	24	1576	13.8	27.0	4190
DM	12.6	50	29	1694	20.6	28.3	1810
AP	13.0	42	27	1866	23.6	27.6	2160
BS	12.8	43	27	1640	23.6	27.6	1760

Diet 3 (Reduced Fat, Reduced Fibre)

Patient	Nitrogen g	Fat g	Fibre g	Calories kcal	Calcium mmol	Magnesium mmol *	Fluid ml
JG	11.2	46	15	1718	17.0	21.0	3820
DM	11.8	46	15	1718	27.5	21.8	2240
AP	12.0	41	14	1847	25.2	21.1	1960
BS	11.5	39	14	1539	22.9	20.8	1635

* Includes daily supplement of 12mmol

TABLE 4 : Constituents of solid food diets.

Diet 1

Patient	Weight(g) Wet	Dry	Calories Total	%absorb.	Nitrogen(g) Total	%absorb.	Fat(g) Total	%absorb.
JG	2040	164.3	808	51.6	3.07	72.1	28.8	57.7
DM	1790	150.1	793	60.8	4.50	65.4	33.9	62.3
AP	6507	469.5	2014	12.2	8.26	29.4	67.3	34.0
BS	3742	321.0	1458	32.8	7.44	41.9	41.2	61.2

Diet 2

	Weight(g) Wet	Dry	Calories Total	%absorb.	Nitrogen(g) Total	%absorb.	Fat(g) Total	%absorb.
JG	2295	183.9	821	47.9	5.45	50.5	27.1	38.4
DM	1687	121.7	536	68.4	4.55	63.9	14.9	71.2
AP	6183	387.9	1462	21.6	9.89	23.9	24.4	41.9
BS	3672	284.8	1158	29.4	7.76	39.4	28.1	35.6

Diet 3

	Weight(g) Wet	Dry	Calories Total	%absorb.	Nitrogen(g) Total	%absorb.	Fat(g) Total	%absorb.
JG	2313	168.8	795	56.9	3.56	68.2	21.6	51.9
DM	1762	128.2	546	68.2	5.81	50.8	11.3	75.4
AP	5786	354.6	1366	26.0	6.62	44.5	26.9	33.8
BS	3574	273.6	1192	30.4	5.74	50.1	23.9	38.7

TABLE 5 : Analysis of the jejunostomy effluent of patients taking solid food diets.

Diet 1

Patient	Sodium		Potassium		Calcium		Magnesium	
	mmol/kg	Total	mmol/kg	Total	mmol/kg	Total	mmol/kg	Total
JG	104.8	213.6	10.7	21.8	6.4	13.1	10.1	21.6
DM	118.8	212.6	10.3	18.5	12.7	22.7	10.8	22.4
AP	92.1	599.3	12.6	82.0	3.9	25.4	1.5	9.8
BS	93.3	349.8	14.1	52.7	5.1	19.1	5.7	21.2

Diet 2

Patient	Sodium		Potassium		Calcium		Magnesium	
	mmol/kg	Total	mmol/kg	Total	mmol/kg	Total	mmol/kg	Total
JG	89.8	206.2	10.1	23.2	5.3	12.2	7.3	16.7
DM	117.5	198.2	10.3	17.3	5.1	8.6	13.1	22.0
AP	94.2	582.4	12.2	75.4	3.6	22.2	2.2	13.6
BS	91.0	334.0	14.3	52.6	5.2	19.1	5.8	21.1

Diet 3

Patient	Sodium		Potassium		Calcium		Magnesium	
	mmol/kg	Total	mmol/kg	Total	mmol/kg	Total	mmol/kg	Total
JG	93.9	238.3	10.0	24.8	5.7	14.2	8.2	20.4
DM	112.4	198.0	11.2	19.7	14.4	25.3	4.3	7.6
AP	106.1	612.0	11.1	64.0	9.0	52.0	2.7	15.6
BS	95.8	344.3	13.0	46.5	5.1	19.2	4.6	16.4

TABLE 6 : Electrolyte and mineral analysis of the jejunostomy effluent of patients taking solid food diets.

Diet 1

Patient	Sodium		Potassium		Calcium		Magnesium	
	mmol/l	Total	mmol/l	Total	mmol/l	Total	mmol/l	Total
JG	104.2	146.2	28.2	39.1	0.6	0.8	0.3	0.4
DM	4.8	2.3	96.8	45.9	0.7	0.3	1.8	0.9
AP	144.0	102.2	100.0	71.0	0.4	0.3	0.2	0.14
BS	122.0	130.7	40.7	42.6	0.6	0.7	0.8	0.9

Diet 2

Patient	Sodium		Potassium		Calcium		Magnesium	
	mmol/l	Total	mmol/l	Total	mmol/l	Total	mmol/l	Total
JG	40.0	33.4	39.8	32.0	0.7	0.6	0.4	0.3
DM	4.3	2.0	120.1	49.7	0.8	0.4	1.5	0.6
AP	-.-	-.-	-.-	-.-	0.2	0.3	0.2	0.3
BS	74.0	94.5	36.0	45.9	0.4	0.5	0.4	0.5

Diet 3

Patient	Sodium		Potassium		Calcium		Magnesium	
	mmol/l	Total	mmol/l	Total	mmol/l	Total	mmol/l	Total
JG	170.0	111.3	41.6	27.3	1.8	1.2	0.4	0.3
DM	4.5	2.3	94.4	49.1	1.0	0.5	2.4	1.3
AP	184.0	278.8	65.0	87.8	0.4	0.6	0.2	0.3
BS	128.0	122.9	48.0	46.1	0.5	0.5	1.8	1.7

TABLE 7 : Electrolyte and mineral losses in the urine of patients taking solid food diets.

Diet 1

Patient	Volume ml	Urea mmol/l	Urea Total	Nitrogen g	Osmolality mosm/L
JG	1400	75	105	2.94	236
DM	475	585	281	7.86	905
AP	710	45	32	0.89	357
BS	1120	62	58	1.62	262

Diet 2

Patient	Volume ml	Urea mmol/l	Urea Total	Nitrogen g	Osmolality mosm/L
JG	840	95	81	2.26	202
DM	440	503	236	6.61	857
AP	1420	48	68.2	1.91	499
BS	1275	45	57.4	1.61	177

Diet 3

Patient	Volume ml	Urea mmol/l	Urea Total	Nitrogen g	Osmolality mosm/L
JG	655	102	67.1	1.88	350
DM	520	540	280.8	7.86	865
AP	1470	48	71.1	1.99	412
BS	960	90	86.4	2.42	358

TABLE 8 : Analysis of the urine of patients taking solid food diets.

Diets

As shown in Table 4 there was a significant difference in the amounts of fat and fibre in each diet. Despite encouragement, patients found it difficult to eat larger quantities of food while on the low fat diets. This resulted in a lower total calorie intake during these days. Intakes of fluids, calcium and magnesium were similar on all diets.

Stoma Effluent

Wet and Dry Weight

The mean wet and dry weights of stoma effluent for each patient during each diet are shown in Figure 10. Wet weight ranged from 1790-6570g on diet 1, 1687-6183g on diet 2 and 1762-5786g on diet 3. The dry weights folowed a similar pattern, from 150.1-469.5g on diet 1, 121.7-387.9g on diet 2 and 128.2-354.6g on diet 3. Only one patient (AP) experienced any appreciable change in wet weight between diets. Three patients had lower dry weights on the reduced fat diets (Diets 2 & 3), but the differences between diets were not significant.

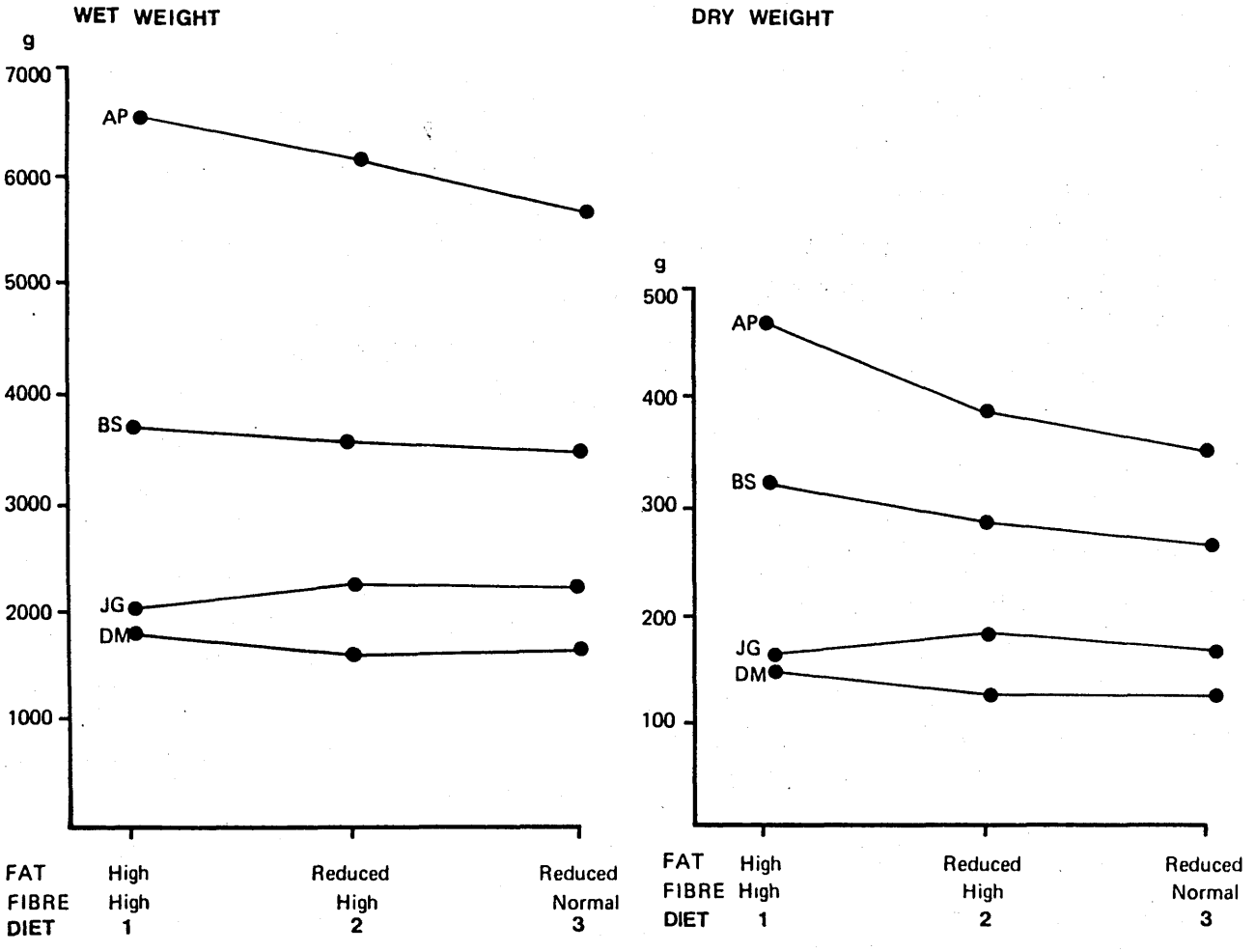


FIGURE 10 : Daily wet and dry weight of jejunostomy effluent on different solid food diets.

Calorie Absorption

Wide variation in the absorptive capacity of patients is demonstrated, the percentage of available calories absorbed ranging from 12.2-60.8% on Diet 1, 21.6-68.4% on Diet 2, and 26.0-68.2% on Diet 3, but no one diet appeared to provide calories more efficiently than the others. A graphic representation of percentage calorie absorption from the three diets is shown in Figure 11.

Fat Absorption

Fat excretion from the jejunostomy on different diets is demonstrated in Figure 12. There was a tendency to higher fat losses while on the high fat diet 1, range 28.8-67.3g/day compared with 14.9-28.1g/day (diet 2) and 11.3-26.9g/day (diet 3), which just fails to reach statistical significance at the 5% level. The percentage of fat absorbed from each diet did not show any trend between diets.

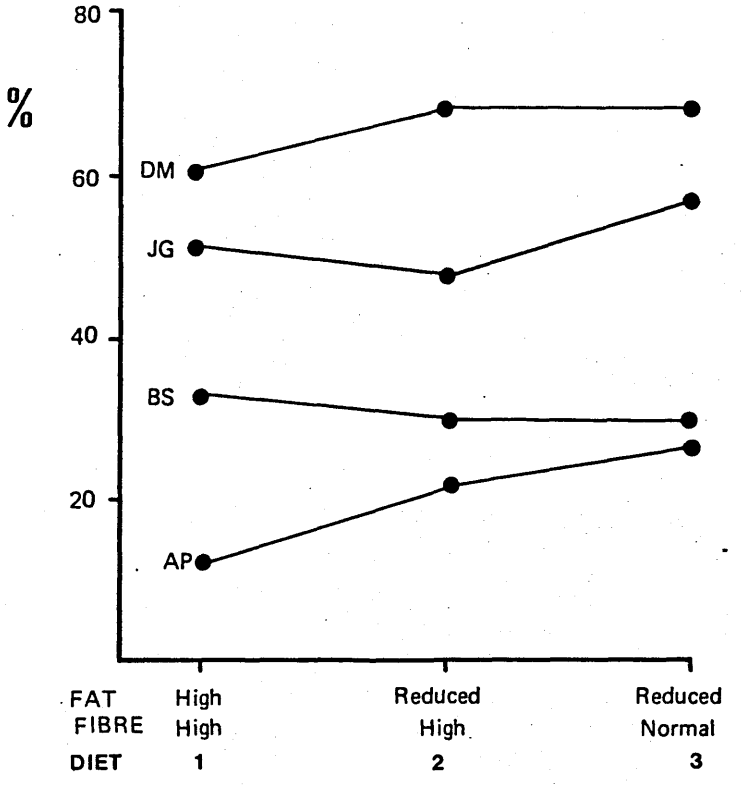


FIGURE 11 : Percentage calorie absorption achieved by patients taking solid food diets.

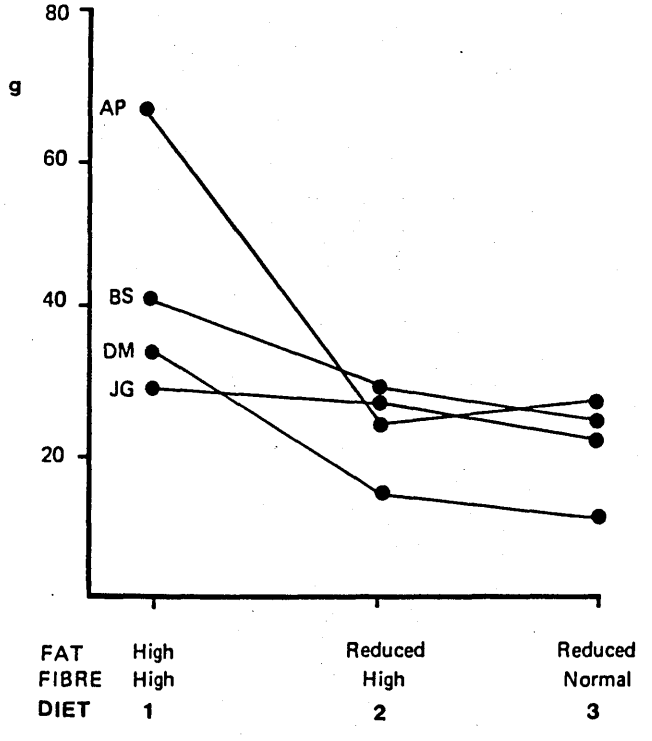


FIGURE 12 : Daily losses of fat in the jejunostomy effluent while taking solid food diets.

Nitrogen Balance

Losses of nitrogen in effluent and urine are shown in Figure 13 and balances of nitrogen input against total effluent and urine losses are graphed in Figure 14. With one exception (DM) these patients had a reversal of the normal pattern of nitrogen excretion, losing more in their stool than in the urine. Faecal nitrogen losses were high, but patients maintained a positive balance on all diets with the exception of DM who experienced minor negative balance on diet 3.

Sodium and Potassium

Individual patients experienced variation in the amount of sodium lost, but the range of sodium concentration remained similar on all diets, 92.1-118.8mmol/kg (diet 1), 91.0-117.5mmol/kg (diet 2) and 93.9-112.4mmol/kg (diet 3). Potassium concentration was more constant between patients and on different diets, 10.3-14.1mmol/kg (diet 1), 10.1-14.3mmol/kg (diet 2) and 10.0-13.0mmol/kg (diet 3). As shown in Figure 15 daily losses of sodium and potassium varied considerably from patient to patient, but remained similar for each individual while taking the different diets.

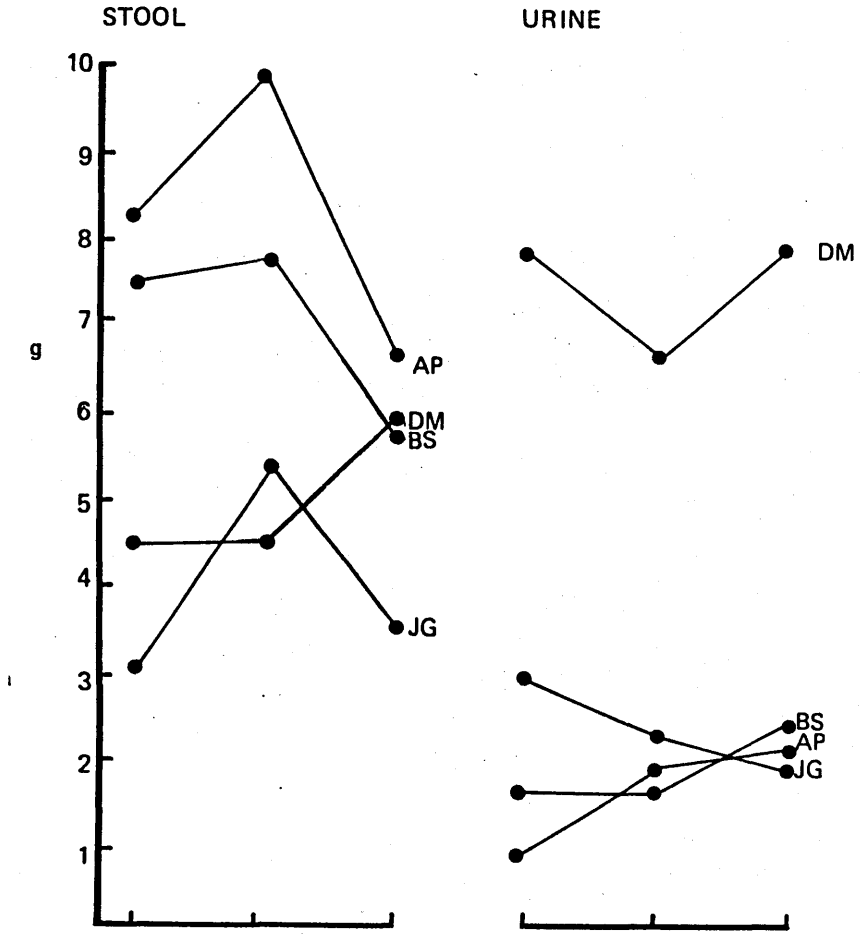


FIGURE 13 : Daily nitrogen losses in the jejunostomy effluent and urine while taking solid food diets.

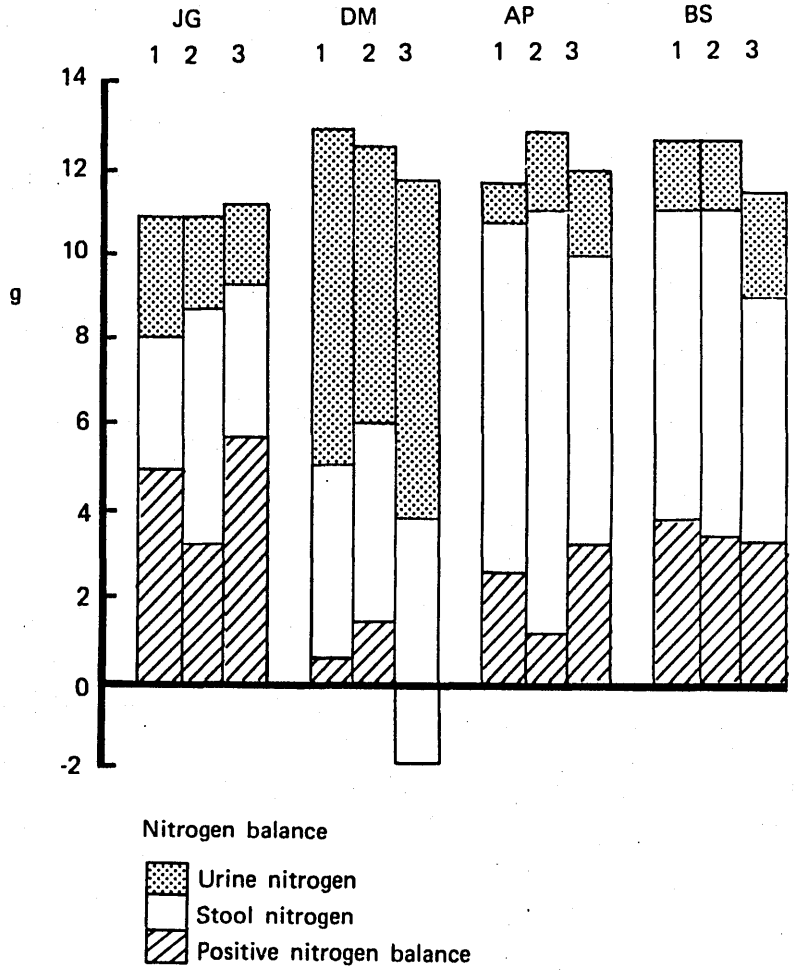


FIGURE 14 : Nitrogen balances achieved by patients taking solid food diets.

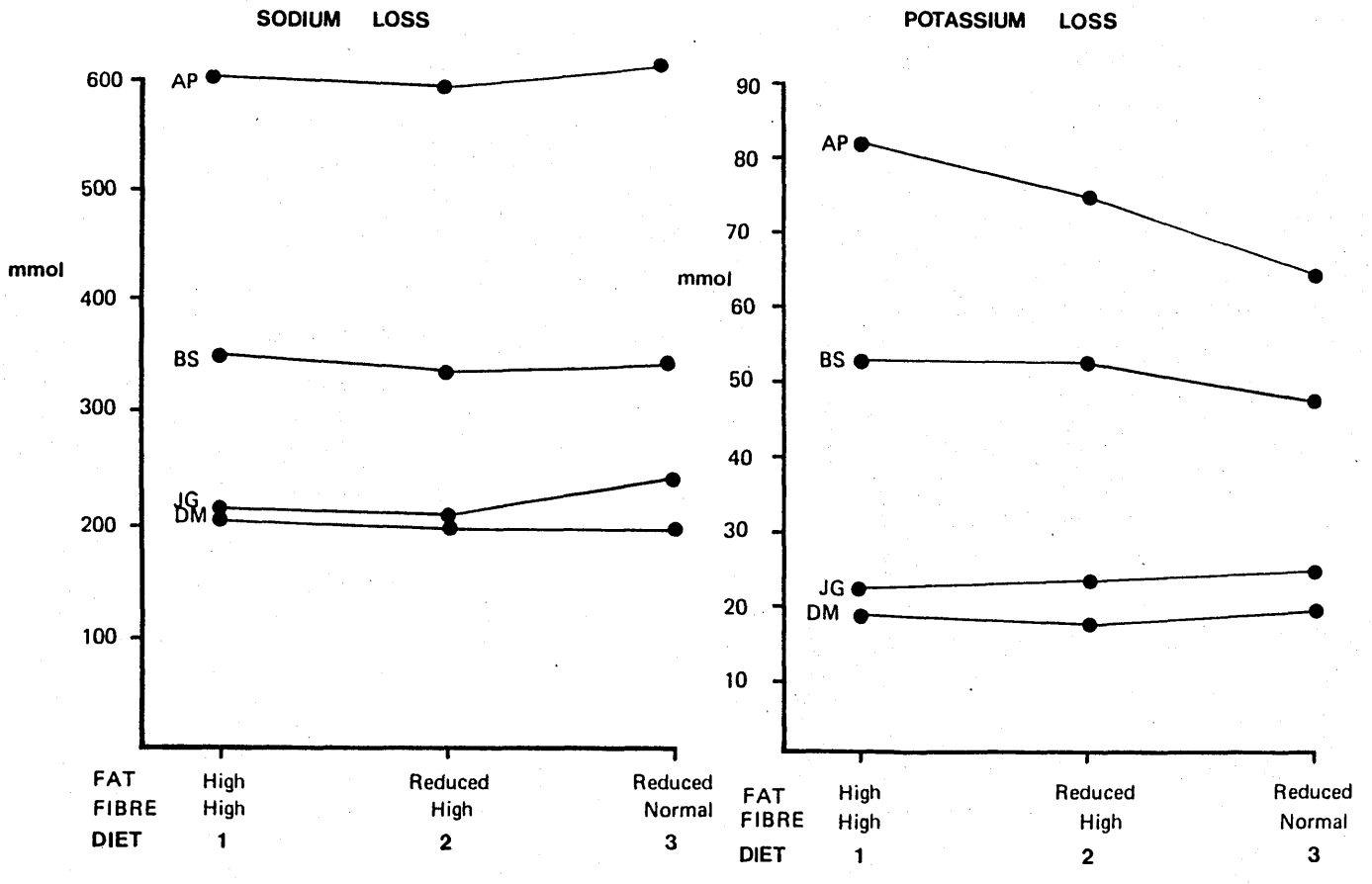
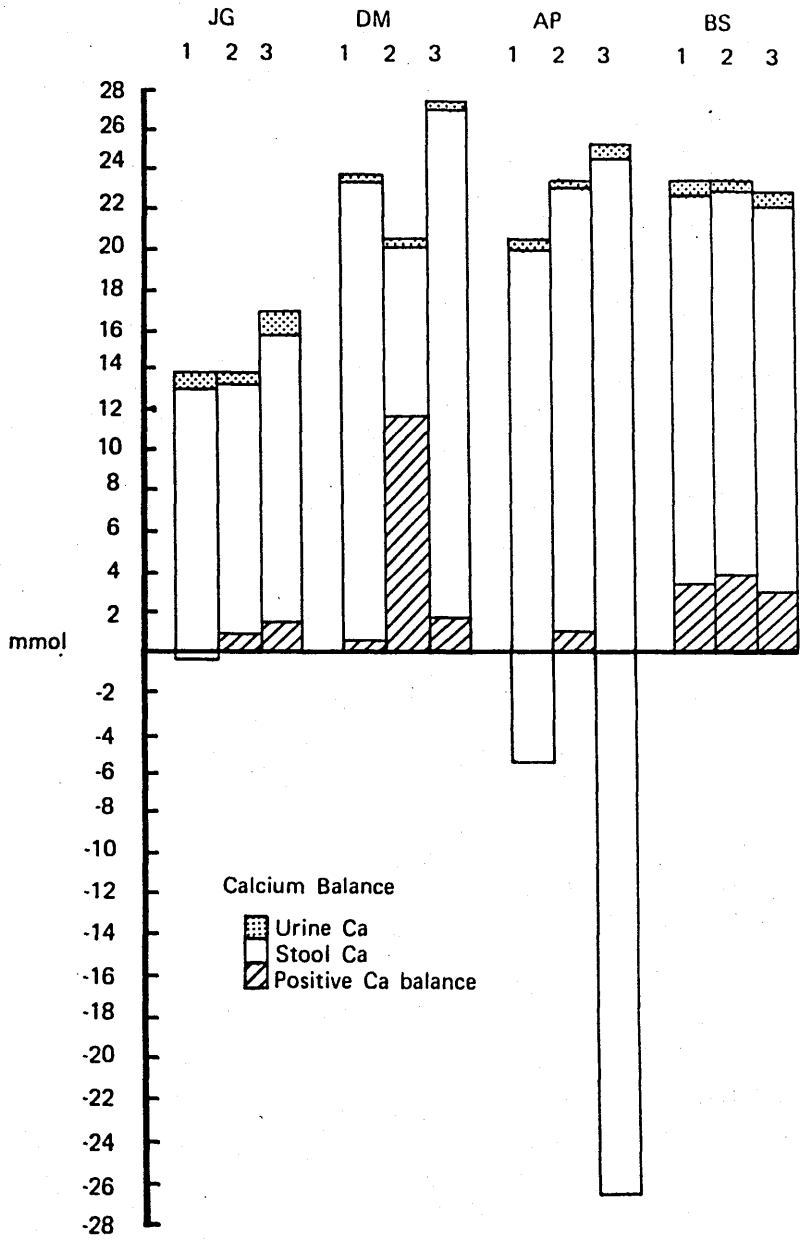


FIGURE 15 : Daily losses of sodium and potassium in jejunostomy effluent while taking solid food diets.

Calcium and Magnesium

Calcium loss in the group as a whole was lowest on diet 2, range 3.6-5.3mmol/kg, compared with 3.9-12.7mmol/kg (diet 1) and 5.1-14.4mmol/kg (diet 3). By contrast, magnesium concentration tended to be lower on diet 3, 2.7-8.2mmol/kg compared with 1.5-10.8mmol/kg (diet 1) and 2.2-13.1mmol/kg (diet 2). No significant differences in calcium or magnesium excretion occurred between diets.

Urine calcium and magnesium losses were universally low. Balances of input against combined stool and urine losses are shown in Figure 16. Most patients maintained a positive balance for both minerals on all diets.



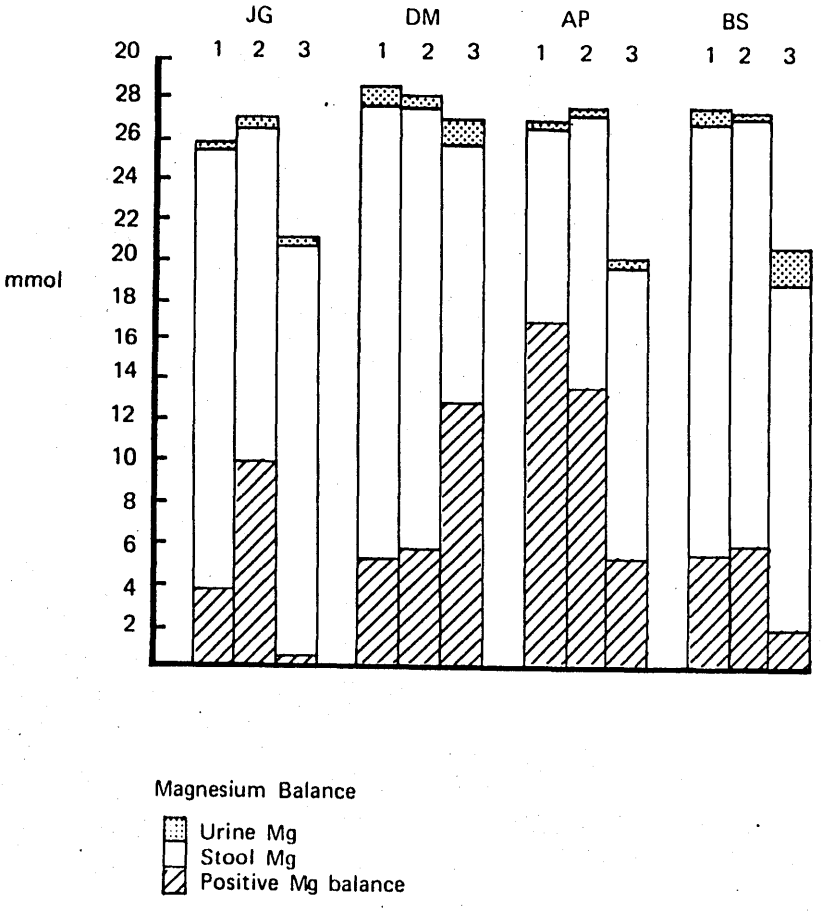


FIGURE 16 : Calcium and magnesium balances achieved on solid food diets.

Summary

Four patients compared the effects of three diets which contained significantly different quantities of fat and fibre, but maintained other constituents constant. Despite their efforts, fewer calories were consumed when the diets contained smaller amounts of fat.

Diets with lower fat and fibre content were no more benefial than those with higher fat and fibre, stoma output, electrolyte and mineral losses being similar for each patient on all diets.

Patients maintained a positive nitrogen balance on all diets, and absorbed a similar percentage of calories from each. When taking a higher fat diet, more fat was excreted in the stoma effluent, but the percentage absorbed remained relatively constant indicating that more fat had been absorbed.

These findings, that low fat diets tend to provide fewer calories, that a constant percentage of fat and calories is absorbed from diets of different composition, and that higher dietary fat had no detrimental effect on fluid, electrolyte and mineral losses, suggests that low fat diets are not mandatory for all patients with a short bowel.

LIQUID DIETS

Seven patients with a proximal small bowel stoma took each of two liquid feeds as their only nourishment and provided 1-3 complete 24 hour collections of urine and stoma effluent on each feed. The polymeric feed Ensure (Abbott Laboratories) was compared with the chemically defined feed Nutranel (Roussel). Table 9 gives the constituents of each feed and Table 10 the fatty acid profile as states by the manufacturers. Table 11 shows the amounts given to each patient. The patient group consisted of 3 males and 4 females, whose ages ranged from 23-51 years. Five patients had had Crohn's disease and recurrent intestinal resections, one had had radiation enteritis after radiotherapy for carcinoma of the cervix, resulting in small intestinal fistulae and small bowel resections, and the seventh had suffered recurrent enterocutaneous fistulae after a complicated colectomy for ulcerative colitis. Figure 17 gives a schematic representation of the patients studied. No patient retained more than 150cm small bowel, and all had an intact oesophagus, stomach, duodenum and pancreatico-biliary duct system. The weight of a 24hr collection of jejunostomy effluent during fasting varied between 430 and 2680g. Two patients, BS and AP were unable to tolerate full quantities of either feed. Their tests were conducted using half the ideal

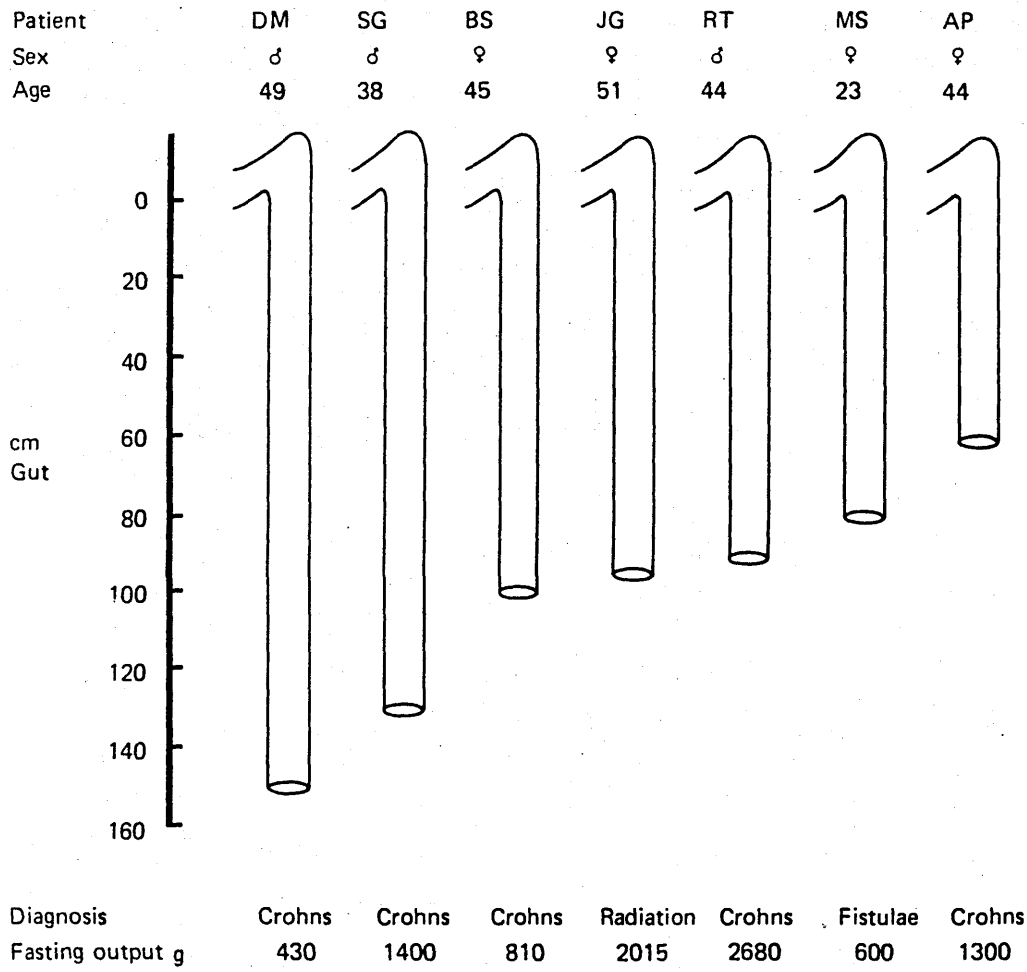


FIGURE 17 : Patients who participated in studies of liquid diets.

	ENSURE	NUTRANEL
Protein Source	Sodium & calcium caseinate 87% Soy protein isolate 13%	Whey protein isolate
Carbohydrate	Hydrolysed corn starch 70% Sucrose 30%	Maltodextrin 98.7% Lactose 1.3%
Fat	Corn oil	Corn oil 50% Coconut oil 50%
Nitrogen (g)	0.6	0.64
Fat (g)	3.7	1.0
Carbohydrate (g)	14.6	18.8
Total calories	106	100
Sodium (mmol)	3.7	2.0
Potassium (mmol)	4.0	3.6
Calcium (mmol)	1.4	1.2
Magnesium (mmol)	0.89	0.42
Chloride (mmol)	4.1	2.5
Phosphorus (mmol)	1.8	1.2
Copper (micromol)	2.0	2.0
Manganese (micromol)	4.0	7.0
Iron (micromol)	17.0	18.0
Zinc (micromol)	25.0	11.0
Iodine (micromol)	0.064	0.047

TABLE 9 : Consituents of liquid diets per 100ml.

Chain length	Name	ENSURE %	NUTRANEL %
6:0	Caproic	-.-	0.5
8:0	Caprilic	-.-	30.5
10:0	Decanoic	-.-	18.5
12:0	Lauric	0.13	0.5
14:0	Myristic	0.2	-.-
16:0	Palmitic	11.7	5.3
16:1	Palmitoleic	-.-	0.2
18:0	Stearic	2.3	1.2
18:1	Oleic	25.2	16.3
18:2	Linoleic	59.23	26.0
18:3	Linolenic	0.93	0.5
20:0	Arachidic	0.3	-.-
	Others	-.-	0.5

TABLE 10 : Fatty acid profiles of liquid feeds : percent of fat.

DAILY INPUT : ENSURE

Patient	kcal	Nitrogen g	Fat g	Na mmol	K mmol	Ca mmol	Mg mmol	Fluid ml
JG	1875	10.5	64.8	64.8	70.0	24.5	15.6	2500
SG***	1867	10.4	63.9	63.9	69.0	24.2	15.4	2900
MS	2050	11.6	71.4	71.4	77.2	27.0	17.2	3000
DM	2000	11.3	69.6	69.6	75.2	26.3	16.7	3000
AP*	1000	5.7	34.8	34.8	37.6	13.2	8.4	1500
BS*	1000	5.7	34.8	34.8	37.6	13.2	8.4	1500
RT	2000	11.3	69.6	69.6	75.2	26.3	40.7**	2500

DAILY INPUT : NUTRANEL

Patient	kcal	Nitrogen g	Fat g	MCT g	Na mmol	K mmol	Ca mmol	Mg mmol	Fluid ml
JG	1680	10.5	16.8	8.2	33.5	59.2	19.3	6.7	2500
SG	1950	11.5	18.4	9.0	36.8	64.9	21.2	7.4	3050
MS	1856	11.6	18.6	9.1	37.1	65.4	21.3	7.4	2900
DM	1804	11.3	18.0	8.8	36.1	63.6	20.8	7.2	3000
AP*	904	5.7	9.0	4.4	18.1	31.9	9.3	3.6	1500
BS*	904	5.7	9.0	4.4	18.1	31.9	9.3	3.6	1500
RT	1804	11.3	18.0	8.8	36.1	63.6	20.8	31.2**	2500

* Able to tolerate half quantities only.
** Includes daily supplement 24 mmol magnesium glycerophosphate.
*** Incomplete diet on one test day.

TABLE 11 : Constituents of liquid diets given to each patient.

quantities. In presenting the results the mean values for each parameter on each diet is used for comparisons and are shown in Tables 12 and 13.

Wet and Dry Weight

The mean wet and dry weights of stoma effluent for each patient on each diet are shown in Figure 18. There is wide patient-to-patient variation in wet weight on both diets, from 1316-2917g on Ensure, and from 1557-3802g on Nutranel. A similar pattern is present for dry weight, being in the range 82.5-191.8g on Ensure, and 66.0-254.5g on Nutranel.

Calorie Absorption

The percentage of available calories absorbed from each feed is shown in Figure 19. There is again a wide variation from patient to patient, absorption ranging from 35.6-79.9% on Ensure, and from 28.7-78.9% on Nutranel. With the exception of patient RT there was little difference between feeds for each patient.

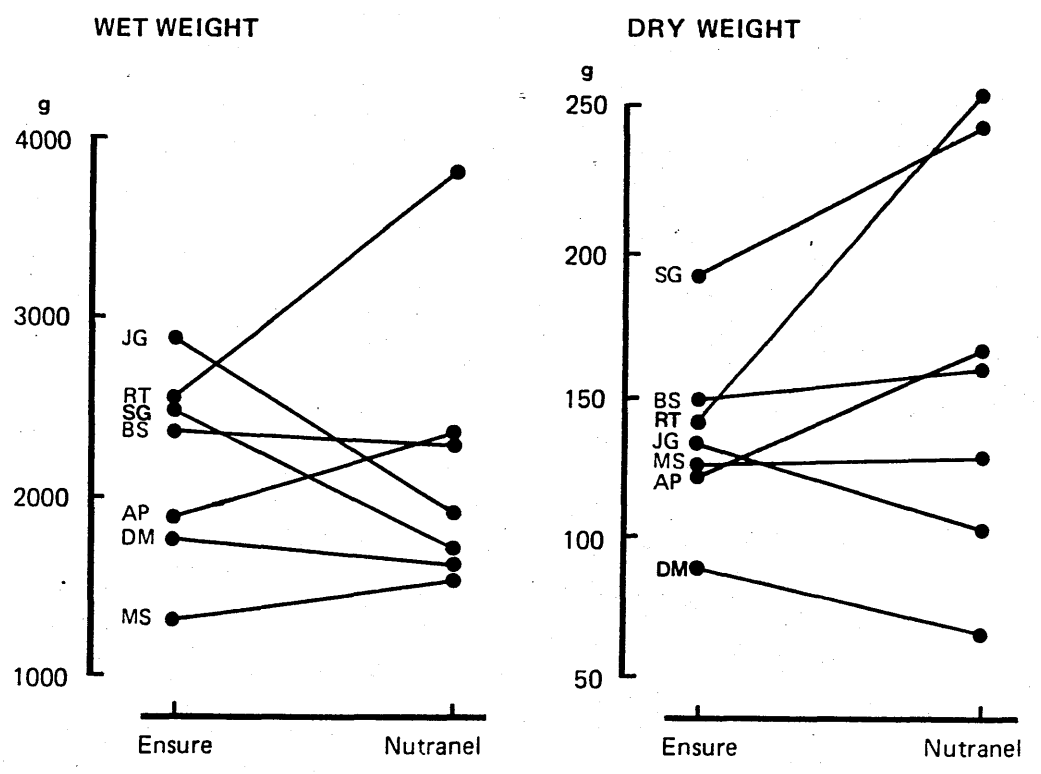


FIGURE 18 : Wet and dry weights of jejunostomy effluent from patients taking liquid diets.

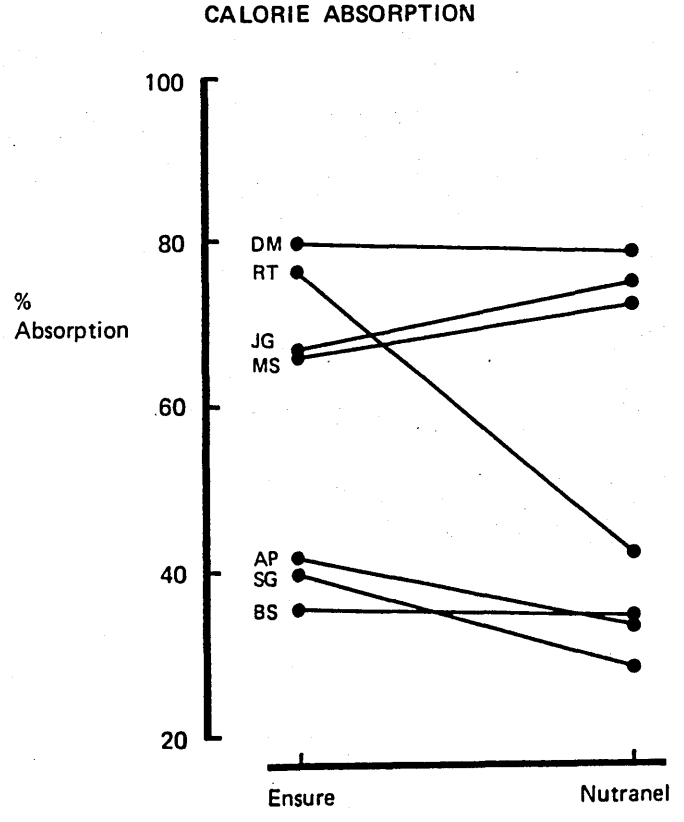


FIGURE 19 : Percentage of calories absorbed by patients while taking liquid diets.

Patient	Weight(g) Wet	Dry	Calories Total	%absorb.	Nitrogen(g) Total	%absorb.	Fat(g) * Total	%absorb.
JG	2917	131.5	616	66.9	2.82	73.1	27.8	57.1
SG	2010	191.8	1149	39.5	4.23	59.3	-.-	-.-
MS	1316	124.0	695	66.2	2.57	77.8	29.8	58.3
DM	1783	82.5	402	79.9	2.99	73.5	18.8	73.0
AP	1905	121.3	593	41.7	1.71	70.0	23.9	31.3
BS	2414	149.8	644	35.6	3.61	36.7	14.0	59.8
RT	2562	139.5	476	76.2	2.15	81.0	20.2	71.0

	Sodium mmol/kg	Total	Potassium mmol/kg	Total	Calcium mmol/kg	Total	Magnesium mmol/kg	Total
JG	97.0	283.4	11.9	34.4	3.5	10.2	9.3	24.7
SG	74.5	148.1	11.5	23.3	5.7	11.6	8.9	16.9
MS	92.0	121.1	11.5	15.2	18.8	24.7	17.5	23.1
DM	108.0	192.6	8.7	15.4	7.0	12.8	7.2	12.8
AP	100.1	190.1	9.7	18.5	21.2	40.9	4.2	8.0
BS	96.4	232.9	11.7	27.8	3.8	9.1	3.0	7.2
RT	66.2	169.6	8.8	22.5	6.5	16.7	5.5	14.1

-.- = samples lost during analysis.

* Measured by the method of van de Kamer

TABLE 12 : Analysis of the jejunostomy effluent of patients taking Ensure.

Patient	Weight(g) Wet	Dry	Calories Total	%absorb.	Nitrogen(g) Total	%absorb.	Fat(g) * Total	%absorb.
JG	1924	104.7	416	75.0	2.44	77.5	15.1	10.1
SG	1794	243.0	1376	28.7	3.31	71.2	-.-	-.-
MS	1557	128.0	508	72.4	2.65	77.2	7.48	60.2
DM	1641	66.0	377	78.9	2.77	75.5	4.0	77.8
AP	2366	163.7	596	33.4	2.96	48.1	5.4	40.0
BS	2303	158.6	587	34.5	3.49	38.8	4.9	45.6
RT	3802	254.5	1019	43.0	4.51	61.9	16.6	7.8

	Sodium mmol/kg	Total	Potassium mmol/kg	Total	Calcium mmol/kg	Total	Magnesium mmol/kg	Total
JG	97.2	186.4	10.5	20.1	6.7	13.0	1.3	2.5
SG	70.1	125.4	12.2	21.8	16.7	29.3	7.5	13.1
MS	81.5	126.9	13.8	21.3	13.0	19.6	5.5	7.4
DM	98.9	162.3	10.4	17.1	6.3	10.3	4.1	6.7
AP	86.4	201.1	11.2	26.1	7.0	16.9	2.2	5.1
BS	88.9	205.9	10.5	24.8	4.9	11.2	1.6	3.6
RT	67.0	254.2	10.7	39.9	3.5	13.1	3.4	14.3

-.- Samples lost during analysis

* Measured by the method of van de Kamer.

TABLE 13 : Analysis of the jejunostomy effluent of patients taking Nutranel.

Fat Absorption

Results for six patients are shown in Figure 20. Samples from patient SG were lost prior to fat analysis. Measured by the method of van de Kamer (264), the percentage of available fat absorbed was 31.3-73.0% on Ensure, and 7.8-77.8% on Nutranel. Daily fat losses were significantly less ($p<0.01$) for all patients when taking Nutranel, a result which is not surprising as the intake of fat from Nutranel was approximately 25% of that from Ensure. Although RT and JG experienced a striking reduction in percentage fat absorption when taking Nutranel, differences for the other patients were less marked, and no significant trend was seen in the group as a whole.

Gas liquid chromatography of effluent samples allowed identification and measurement of individual fatty acids excreted by each patient on each feed. Medium chain triglycerides (8-10 carbon atoms) were excreted in very small quantities by all patients. There was higher excretion when patients took Nutranel, which contained half its fat as MCT, than when they took Ensure, which contained no MCT. The percentage fat absorption was little different on Ensure than on Nutranel. Tables 14 and 15 give the results of chromatographic analysis of effluent samples obtained for each feed.

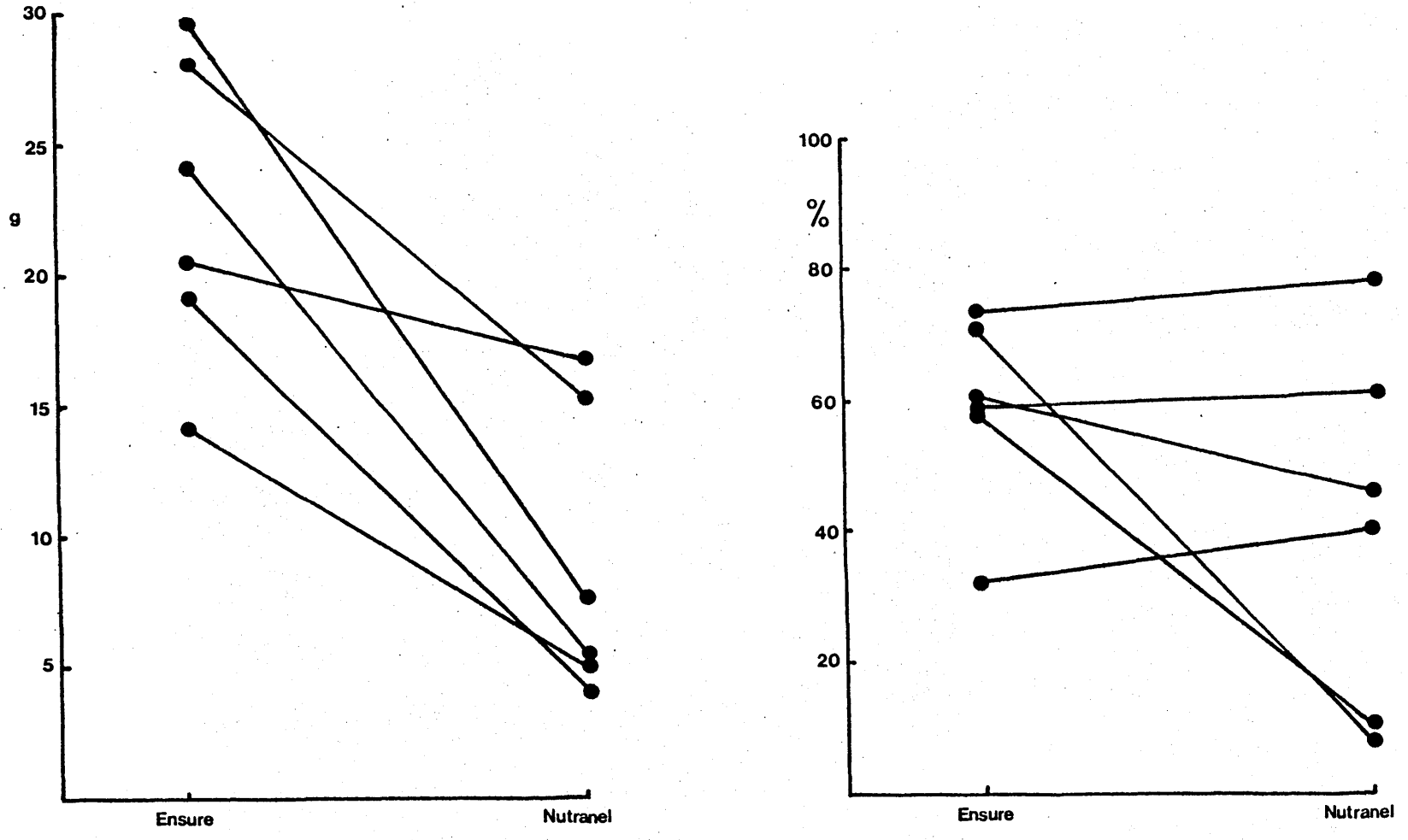


FIGURE 20 : Fat losses in jejunostomy effluent of patients taking liquid diets expressed as grams/24hr and as percentage absorption.

Grams per kilogram dry stool

Patient	8:0	10:0	12:0	14:0	15:0	16:1	16:0	17:0	18:2	18:1	18:0	19:0	20:0	24:0	Total
JG	-.-	T	0.11	0.33	0.06	0.4	12.25	0.11	17.58	27.39	25.52	0.09	0.5	0.12	84.46
MS	-.-	1.13	2.59	2.16	0.18	4.18	25.83	0.2	62.12	55.61	20.43	-.-	1.84	0.36	176.63
DM	-.-	0.02	0.11	0.3	0.06	1.73	16.67	0.18	35.2	31.31	8.68	0.37	0.75	0.73	96.11
AP	-.-	-.-	0.09	0.24	0.01	1.56	15.44	0.13	25.9	32.53	6.77	0.02	0.64	0.09	83.42
BS	-.-	-.-	0.04	0.15	0.01	0.63	12.2	-.-	23.19	19.5	4.9	-.-	0.83	0.27	61.72
RT	-.-	-.-	0.52	0.93	-.-	2.44	12.82	0.1	26.69	24.88	8.61	-.-	0.32	-.-	77.31

T = less than 0.05 g/kg

-.- = not detectable

TABLE 14 : Fatty acid excretion in the jejunostomy fluid of patients taking Ensure.

Grams per kilogram dry stool

Patient	8:0	10:0	12:0	14:0	15:0	16:1	16:0	17:0	18:2	18:1	18:0	19:0	20:0	24:0	Total
JG	-.-	0.26	6.78	5.53	0.12	0.32	11.98	0.15	6.97	10.9	10.14	0.33	0.66	0.11	54.25
MS	-.-	0.72	2.2	1.6	0.95	1.14	7.02	0.29	16.17	17.11	4.88	0.02	2.23	0.64	54.97
DM	-.-	0.06	0.03	0.08	-.-	0.15	1.70	0.08	4.02	3.81	1.50	0.03	0.27	0.11	11.64
AP	-.-	0.43	0.07	0.24	0.18	0.56	5.49	0.14	12.53	11.1	3.12	0.17	0.43	0.09	34.55
BS	-.-	0.34	0.03	0.04	-.-	0.15	1.54	0.03	3.55	3.6	0.48	-.-	0.15	0.02	9.93
RT	-.-	0.43	0.4	1.16	0.13	2.86	14.58	0.1	21.97	20.44	7.15	0.21	0.99	0.2	70.62

-.- = not detectable

TABLE 15 : Fatty acid excretion in the jejunostomy effluent of patients taking Nutranel.

When gas liquid chromatography was used to measure individual fatty acids, the values obtained for total fat losses were lower for all patients on both feeds, as shown in Table 16. The reasons for this discrepancy are not clear, but there were several differences in the methods used. The van de Kamer method is a titrimetric method, and as such may measure acids other than fatty acids whereas the chromatography was specific for fatty acids. Wet stool was used for the van de Kamer in contrast to the chromatography when the stool was dried prior to analysis. It is possible that some volatile fatty acids were lost during this preparation.

Nitrogen Balance

Figure 21 demonstrates the nitrogen balance for each patient on each feed. The balances are derived from the values of calculated nitrogen input, and the measured losses as faecal nitrogen and urine urea converted to nitrogen. A positive balance was maintained on both feeds by all patients. With the exception of DM there was a strong tendency for the group to lose more nitrogen from their stoma than in the urine.

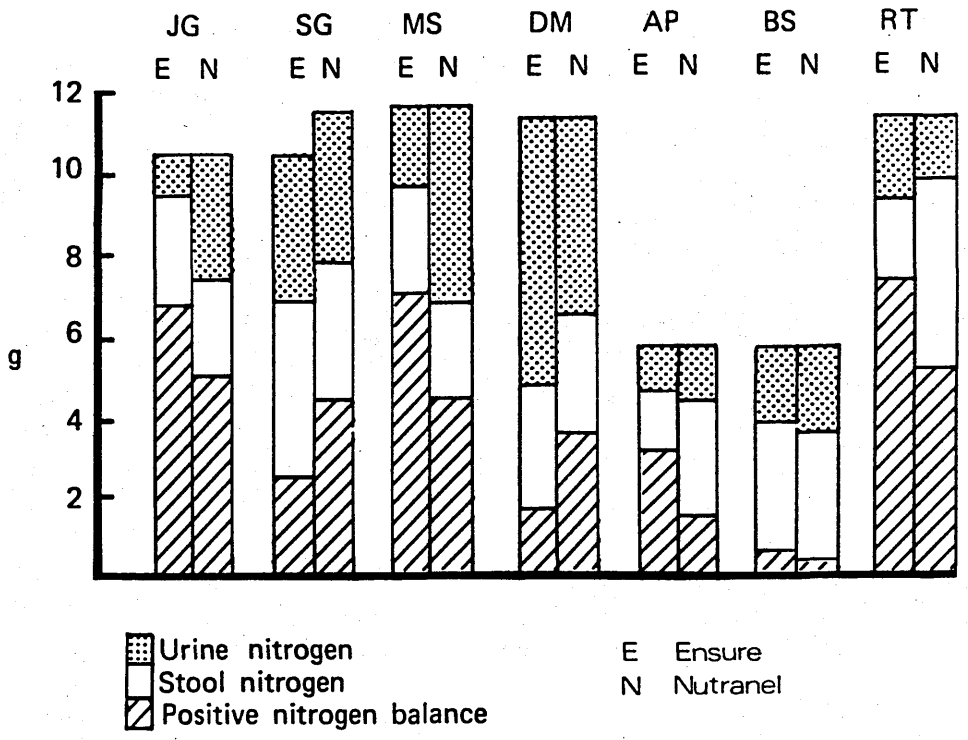


FIGURE 21 : Nitrogen balances of patients while taking liquid diets.

Patient	Ensure		Nutranel	
	van de Kamer g/24hr	GLC g/24hr	van de Kamer g/24hr	GLC g/24hr
JG	27.8	11.1	15.1	5.5
MS	29.8	22.3	7.4	7.0
DM	18.8	7.9	4.0	1.1
AP	23.9	10.1	5.4	5.6
BS	14.0	9.2	4.9	1.6
RT	20.2	10.8	16.6	17.1

Patient	Ensure		Nutranel	
	van de Kamer % absorbed	GLC % absorbed	van de Kamer % absorbed	GLC % absorbed
JG	57.1	82.9	10.1	62.3
MS	58.3	68.8	60.2	62.4
DM	73.0	88.6	77.8	93.9
AP	31.3	71.0	40.0	37.8
BS	59.8	73.6	45.6	82.2
RT	71.0	84.5	7.8	5.0

TABLE 16 : Fat loss in jejunostomy effluent measured by the van de Kamer method and gas liquid chromatography.

Sodium and Potassium

Figure 22 shows the mean concentration of sodium and potassium present in the stoma effluent of each patient whilst taking each liquid diet. There was a wide range of sodium concentration while taking each feed, 66.2-108.0mmol/kg on Ensure and 67.0-98.9mmol/kg on Nutranel, and a tendency for patients to lose less sodium while taking Nutranel than while taking Ensure which was not statistically significant. The concentration of potassium in stoma effluent was much less variable in each group, 8.7-11.8mmol/kg on Ensure and 10.4-13.8mmol/kg on Nutranel, with minimal variation for individual patients. There was no statistically significant difference in sodium or potassium concentration in stoma effluent between the two feeds. Mean daily balances of oral intake versus stool losses for sodium and potassium are shown in Figures 23 and 24. Each patient lost more than 100mmol sodium daily on each feed, and the balances were strongly negative in four patients, and precarious in the remaining three, demonstrating the need for supplementation in these patients by either the intravenous or oral route. Intravenous saline with potassium supplements was given to JG, AP, BS and RT throughout the test periods. There was no consistent difference between diets. Patients AP and BS had notably high losses even on half quantities

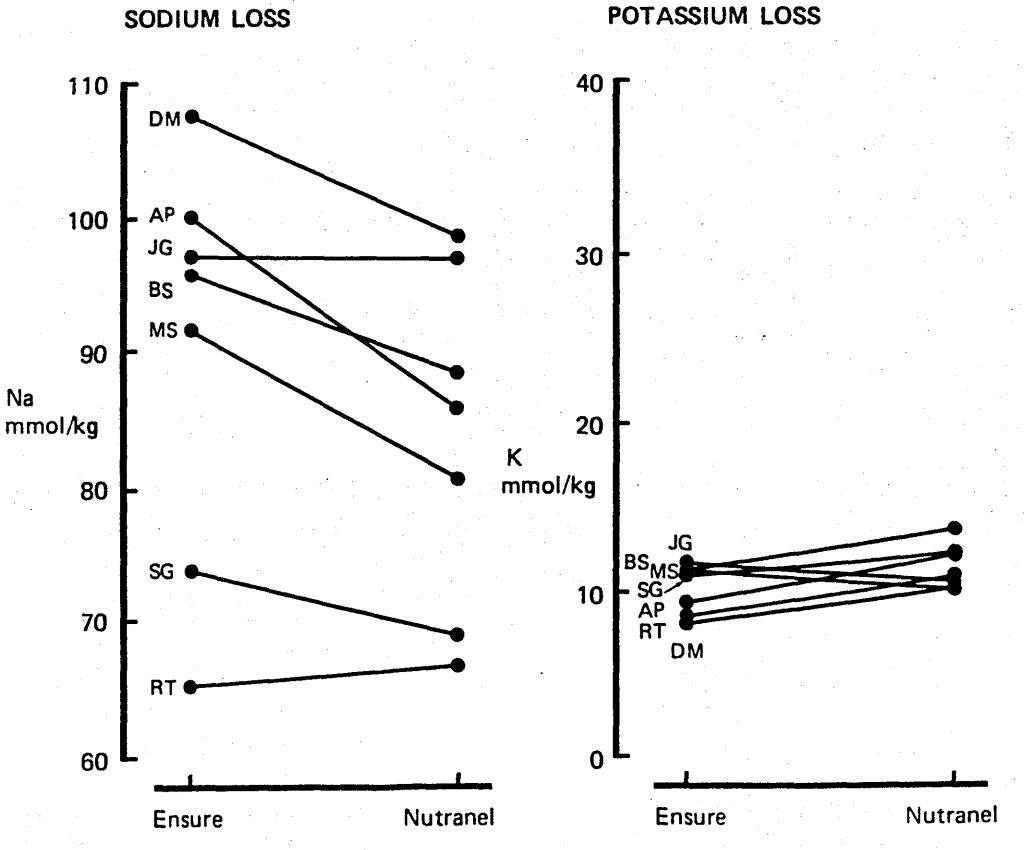


FIGURE 22 : Sodium and potassium concentration in the jejunostomy effluent of patients taking liquid diets.

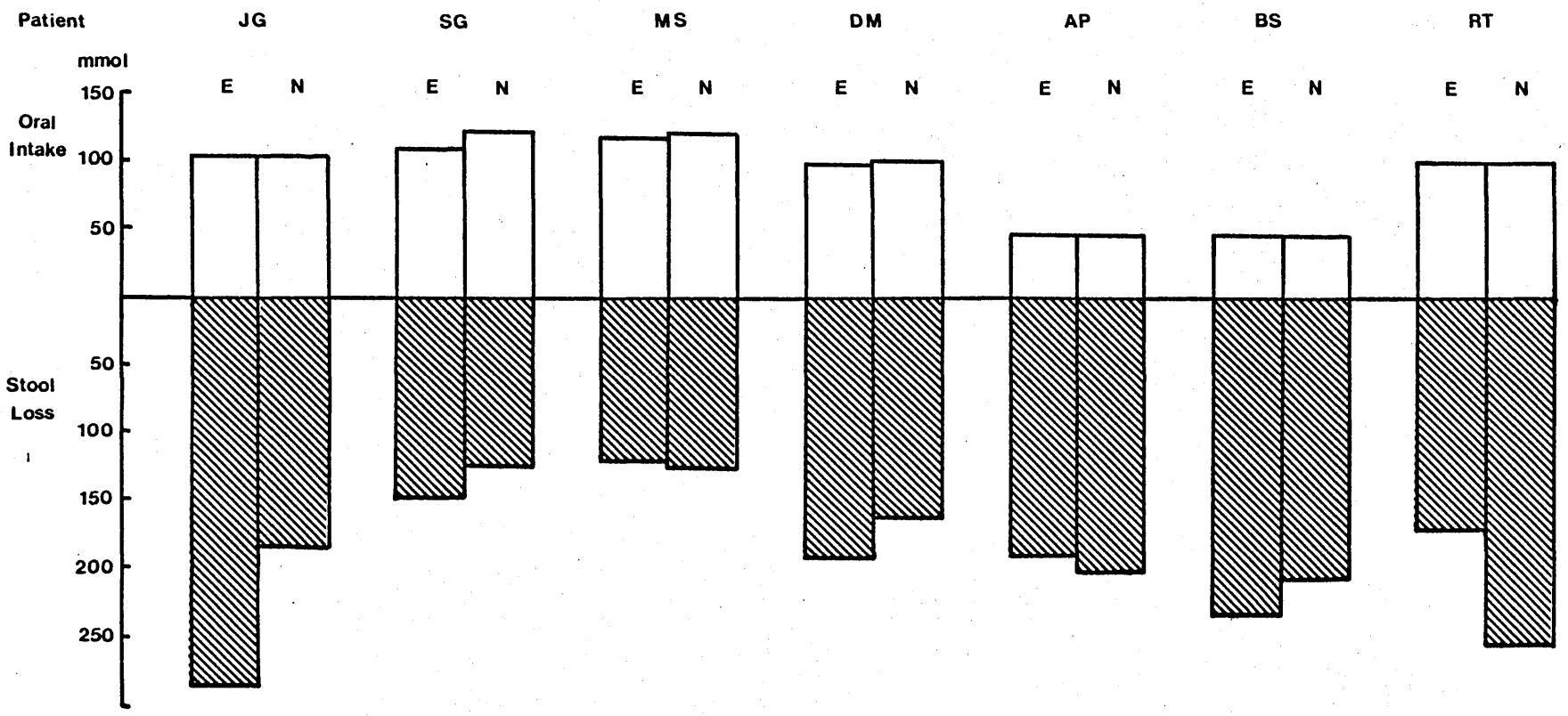


FIGURE 23 : Sodium balances while taking liquid diets.

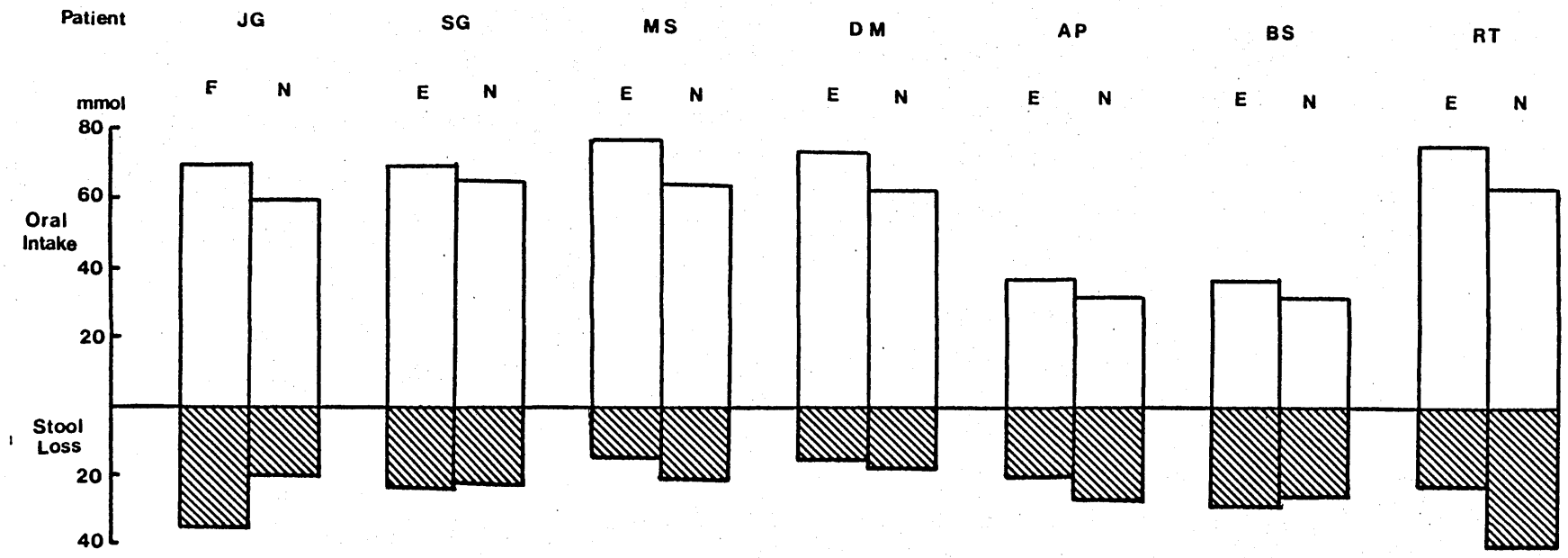


FIGURE 24 : Potassium balances while taking liquid diets.

of feed. Daily potassium losses were similar on both feeds in all but two cases, and all patients remained well without recourse to intravenous supplements.

Calcium and Magnesium

Calcium concentration ranged from 3.5-21.2mmol/kg on Ensure, and from 3.5-16.7mmol/kg on Nutranel. Although three patients experienced marked differences in calcium concentration on the two feeds, the other four lost calcium in similar concentrations on both feeds. Figure 25 shows the mean daily calcium balances of oral input versus stool losses for each patient. Only AP and SG experienced any difference in total calcium excretion between feeds.

The range of magnesium concentration in stoma effluent was higher on Ensure, 3.0-17.5mmol/kg, than on Nutranel, 1.3-7.5mmol/kg. The effluent of all patients had a lower magnesium concentration when they were taking Nutranel, the difference being significant at the 5% level. Figure 26 shows the mean daily balance of stool losses versus oral intake of magnesium for each patient. Six patients lost less magnesium while taking Nutranel than while taking Ensure. This difference was significant at the 5% level.

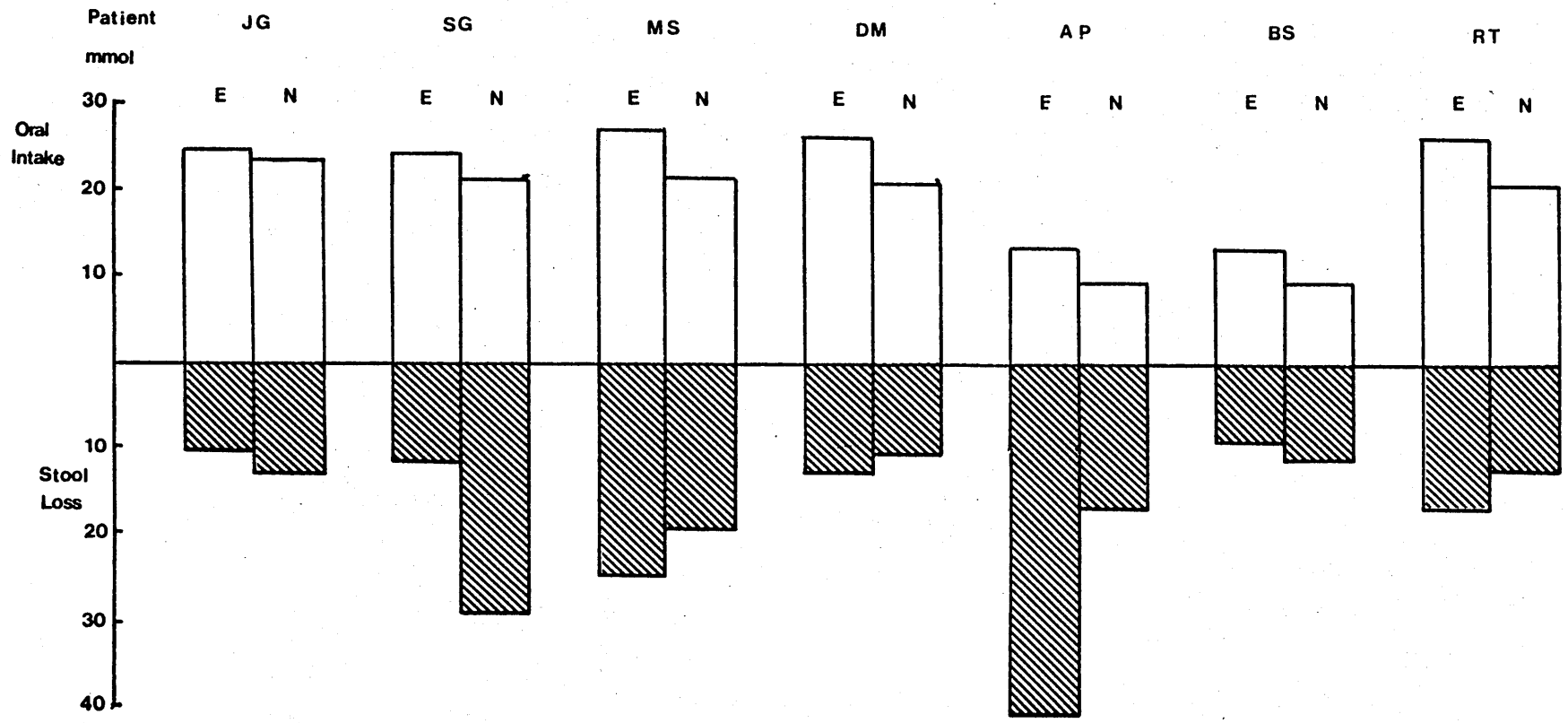


FIGURE 25 : Calcium balances while taking liquid diets.

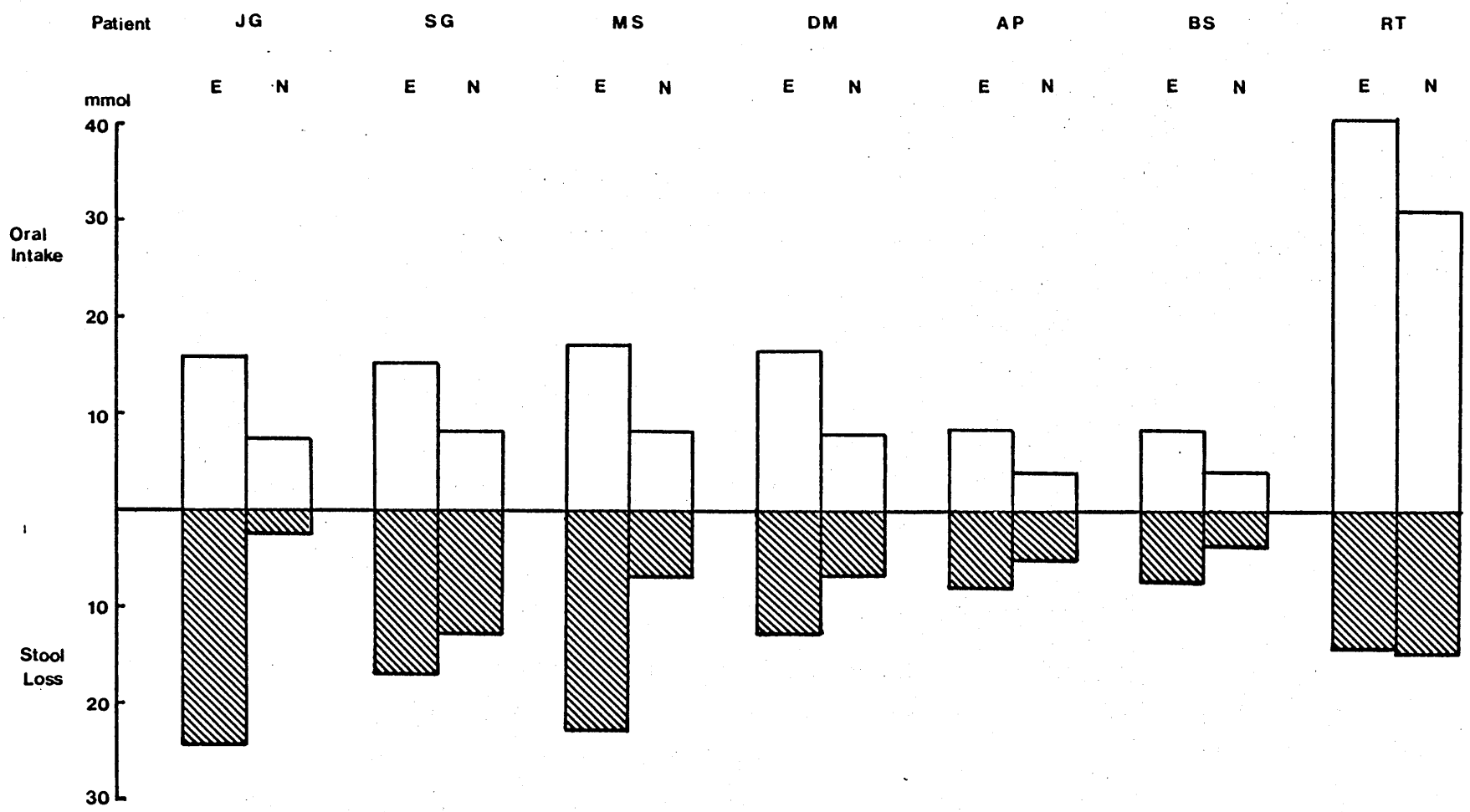


FIGURE 26 : Magnesium balances while taking liquid diets.

Summary

A comparison of an elemental feed and a polymeric feed was completed by seven patients with a short intestine. Although their stoma losses were considerable, the quantities lost by each patient were remarkably consistent from day to day. All patients had a strong tendency to sodium depletion as demonstrated by the sodium balance data.

Even in the most severely affected patients, the elemental diet failed to confer any benefit, either by promoting better nitrogen balance and calorie absorption, or by reducing intestinal losses, when compared with the polymeric feed.

Although patients lost less magnesium in their stoma effluent when taking the elemental diet, this is likely to be due to the lower intake on that diet, and balances were little different on the two feeds.

NASOGASTRIC VERSUS ORAL FEEDING

To ascertain whether there was any benefit to be gained from giving a liquid feed by nasogastric tube at a constant slow rate, rather than as an oral supplement taken as frequent small drinks, three patients took equal quantities of the same feed by each method over 12-14 hours per day, for 2-3 days. Patients MS and RT received Ensure, WD took Nutranel. The study protocol was identical to that used for the tests of liquid diets. The periods of nasogastric or sip feeding were conducted in random order. Throughout both test periods RT took an oral supplement of 24mmol magnesium as the glycerophosphate. The constituents of the feeds given to each patient are shown in Table 17 and patient details in Figure 27. Table 18 summarises the effluent analyses.

Wet and Dry Weight

There was a tendency for all patients to lose less stoma effluent on the nasogastric feeds than when taking sip feeds as shown in Figure 28. Wet weights for nasogastric feeds ranged from 749-2562g compared with 895-3556g on sip feeds. The corresponding ranges for dry weights were 58-139.5g and 73-240.4g respectively.

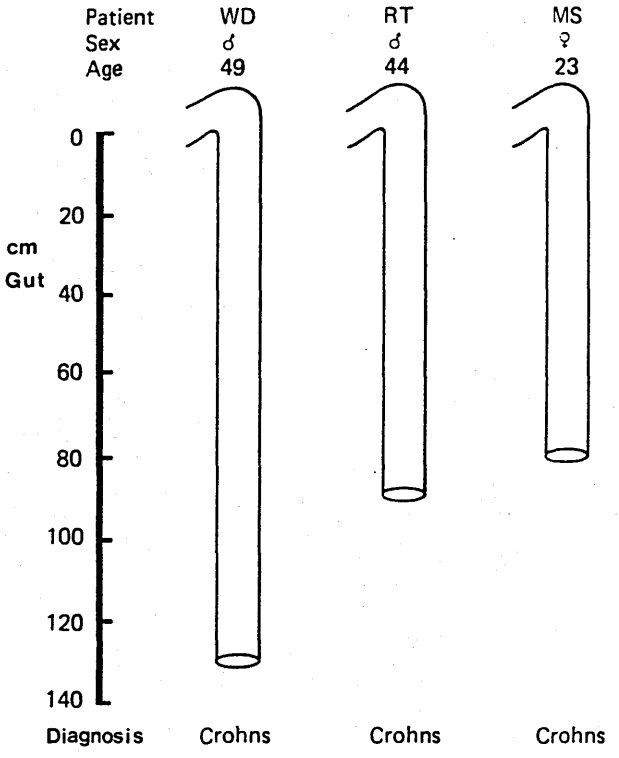


FIGURE 27 : Patients who took liquid diets by both oral and nasogastric routes.

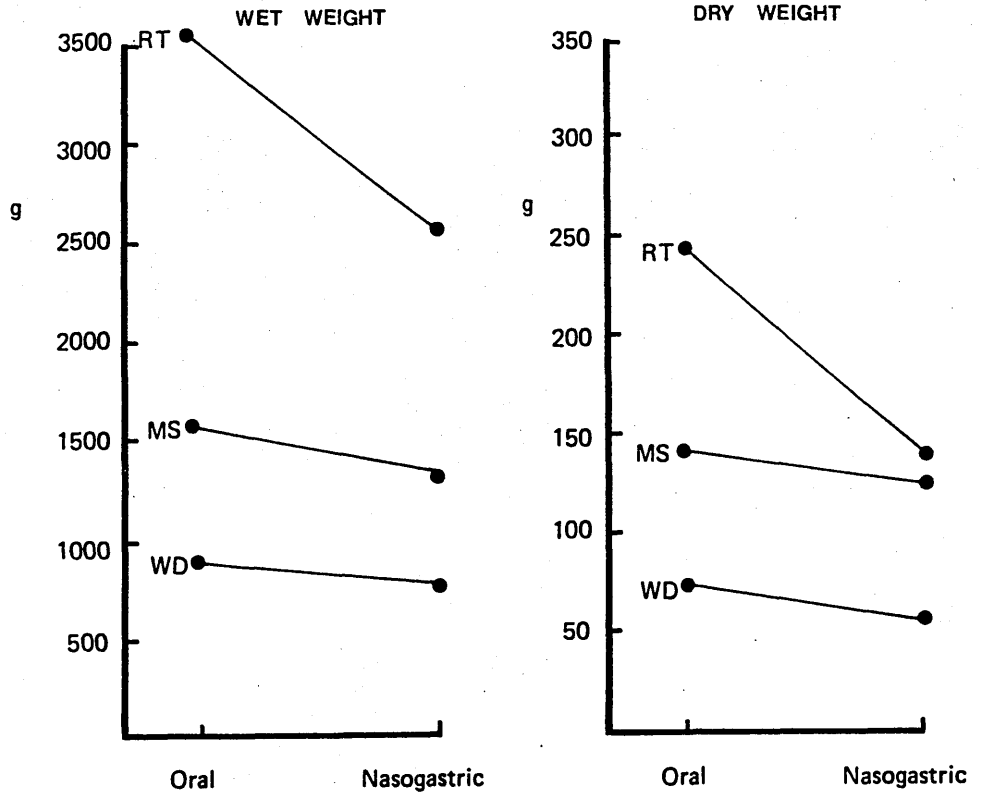


FIGURE 28 : Wet and dry weights of jejunostomy effluent of patients taking oral and nasogastric diets.

Patient	Calories	Nitrogen g	Fat g	Na mmol	K mmol	Ca mmol	Mg mmol	Fluid ml
MS	2050	11.6	71.4	71.4	77.2	27.0	17.2	3000
RT	2000	11.3	69.6	69.6	75.2	26.3	40.7*	2500
WD	2090	13.2	21.1	42.2	74.4	24.3	8.5	2850

Fluid indicates total intake and includes feed, water and electrolyte mixture used to maintain sodium and water input constant.

* Taking 24mmol magnesium glycerophosphate supplement daily.

TABLE 17 : Constituents of liquid feeds used in the comparison of oral and nasogastric feeding.

Oral

Patient	Weight(g) Wet	Weight(g) Dry	Calories Total	Calories %absorb.	Nitrogen(g) Total	Nitrogen(g) %absorb.	Fat(g) Total	Fat(g) %absorb.	Sodium mmol/kg	Sodium Total	Potassium mmol/kg	Potassium Total	Calcium mmol/kg	Calcium Total	Magnesium mmol/kg	Magnesium Total
MS	1553	141.3	726	64.6	3.55	69.4	16.2	77.4	94.0	142.4	13.5	21.2	15.8	23.9	15.1	22.4
RT	3556	240.4	1041	47.9	4.29	62.0	23.3	66.5	72.4	336.2	11.7	54.2	3.0	13.9	4.7	22.3
WD	895	73.0	325	84.5	3.86	70.8	3.3	84.6	35.7	31.3	34.4	30.0	40.3	35.2	7.2	6.4

Nasogastric

MS	1315	126.1	695	66.1	2.57	77.9	22.3	69.7	92.0	121.1	11.5	15.2	18.8	24.7	17.5	23.1
RT	2562	139.5	666	66.7	2.15	81.0	11.7	83.2	66.2	169.6	8.8	22.5	6.5	16.7	5.5	14.1
WD	749	58.0	275	86.8	4.46	66.2	4.9	76.8	53.6	39.6	24.2	18.9	39.9	28.7	9.2	6.7

TABLE 18 : Analysis of jejunostomy effluent of patients taking oral and nasogastric diets.

Nitrogen Absorption

The percentage of ingested nitrogen absorbed by each patient from each feed is shown in Fig 29. Two patients absorbed more from the nasogastric feed than from the oral diet. The percentage of nitrogen absorbed was similar to that of fat, 62.0-70.8% from the oral feed, and 66.2-81.0% when given by nasogastric tube.

Calorie Absorption

Figure 30 demonstrates that there was little difference in the percentage calorie absorption between the two methods of feed administration. On sip feeds the subjects absorbed from 47.9-84.5% and on nasogastric feeds from 66.1-86.8% of available calories.

Fat Excretion and Absorption

There was no discernable pattern in the losses of fat. The subject taking the low fat preparation Nutranel (WD), consistently lost less fat than those taking Ensure, but the percentage of fat absorbed was similar. The absorption was not affected by the method of feed administration, being 66.5-84.6% from sip feeds and

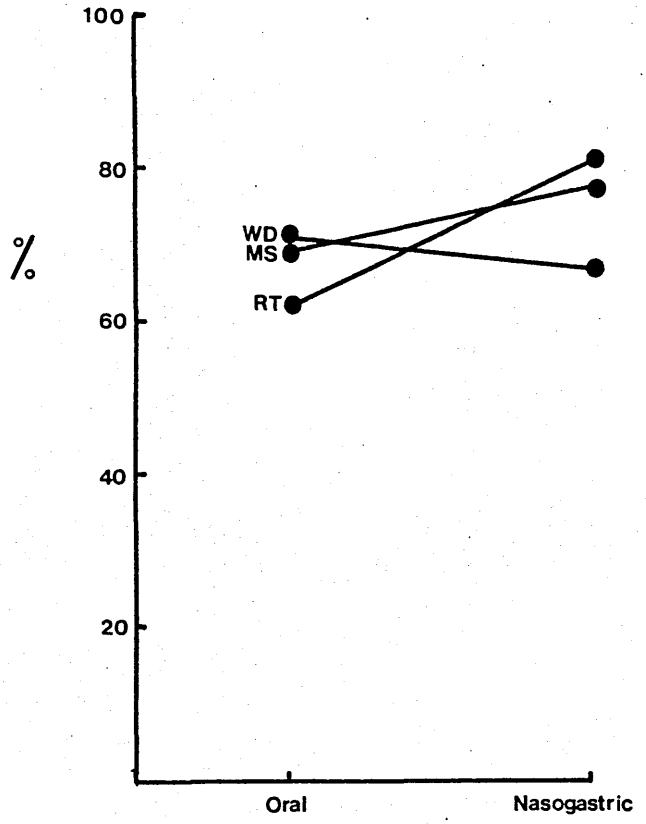


FIGURE 29 : Percentage of nitrogen absorbed from liquid diets given orally or by nasogastric tube.

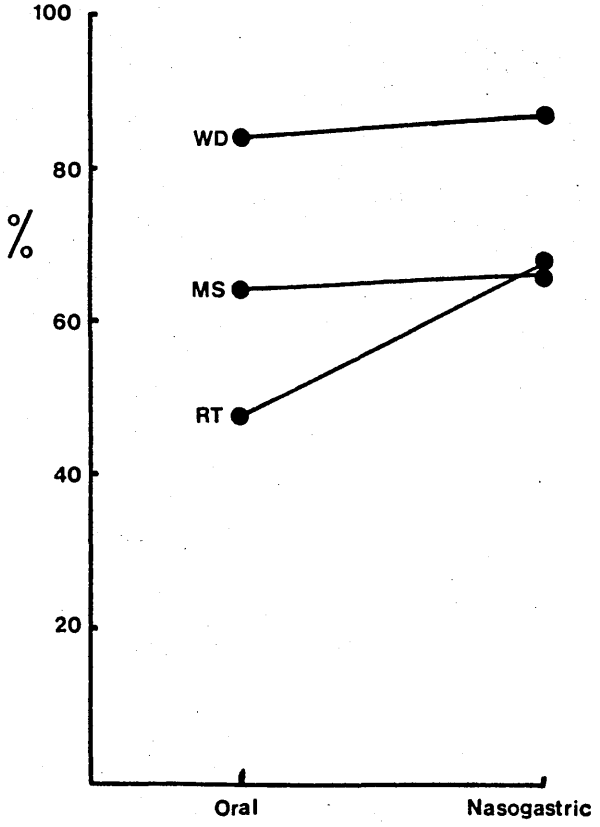


FIGURE 30 : Percentage of calories absorbed from liquid diets given orally or by nasogastric tube.

69.7-83.2% from nasogastric feeds. Daily fat losses measured by gas liquid chromatography are shown graphically in Figure 31.

Sodium and Potassium

The concentrations of sodium and potassium in the stoma efluent varied little. As a consequence, the total daily losses shown in Figure 32 depended upon the total volume of effluent losses and varied accordingly.

Calcium and Magnesium

Figure 33 demonstrates that there were no significant differences in calcium and magnesium losses between sip and nasogastric feeds. Patients MS and RT, with a higher intake of magnesium, tended to lose more than WD.

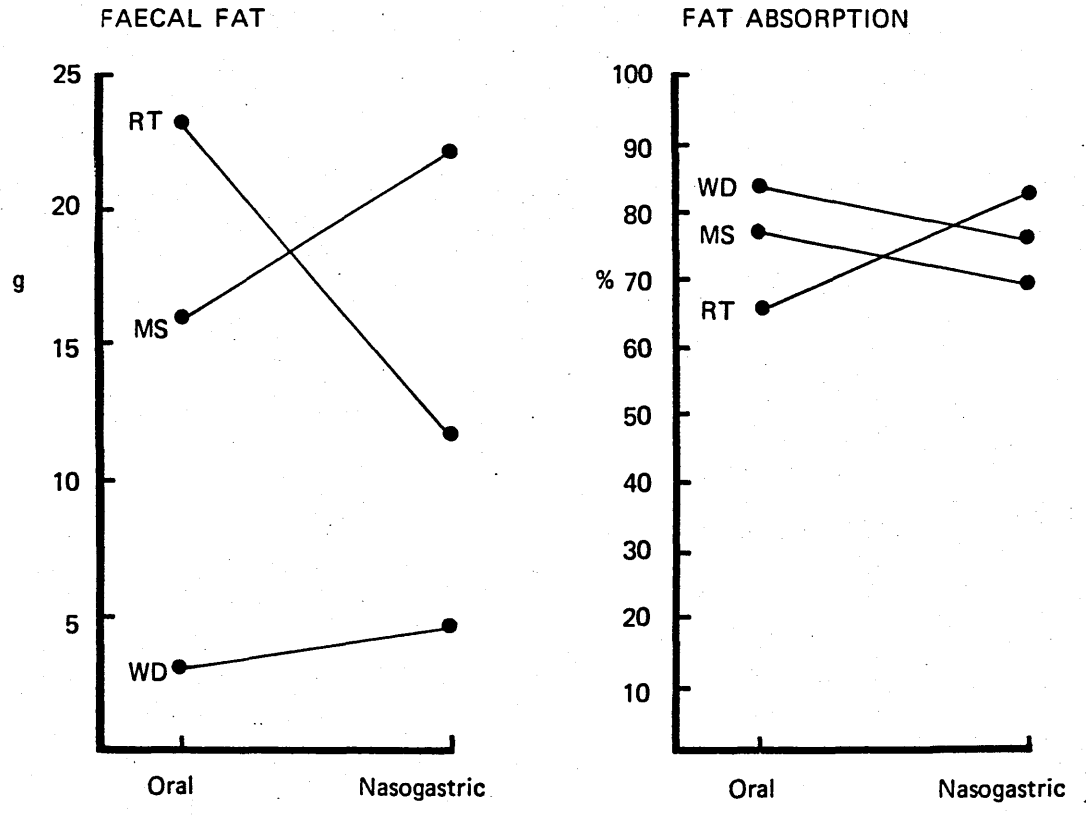


FIGURE 31 : Daily losses of fat in jejunostomy effluent expressed as grams/24hr and as a percentage absorbed.

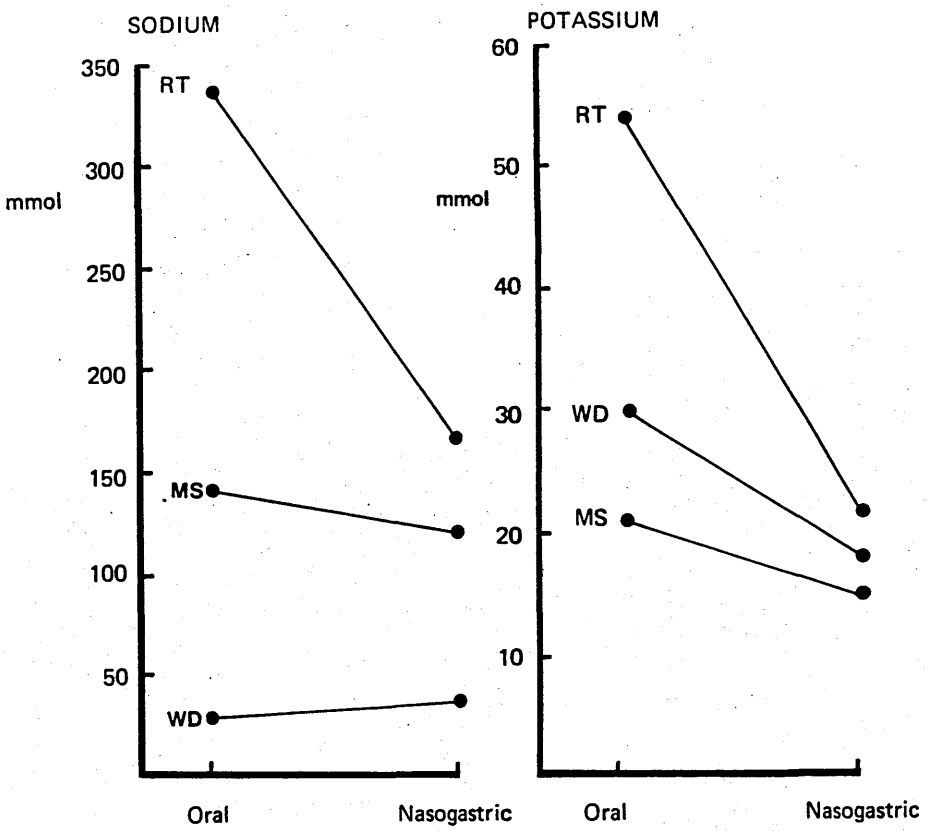


FIGURE 32 : Daily losses of sodium and potassium in the jejunostomy effluent while taking oral and nasogastric diets.

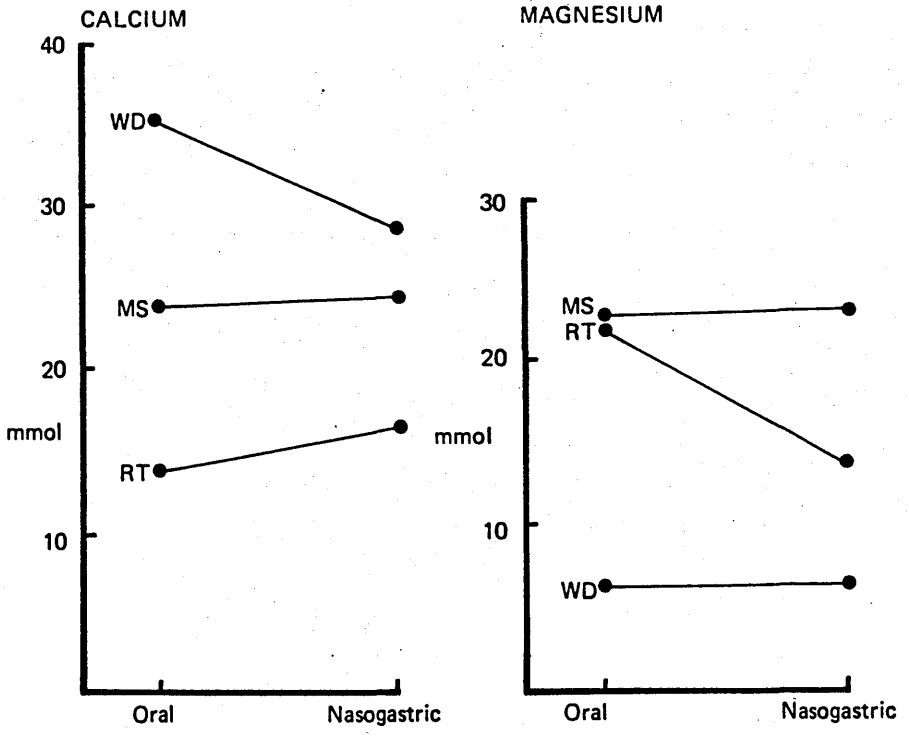


FIGURE 33 : Daily losses of calcium and magnesium in the jejunostomy effluent while taking oral and nasogastric diets.

Summary

A small study of oral and nasogastric administration of liquid diets was completed. Although the numbers were too small for statistical analysis, there are some interesting trends in the results.

When taking feeds by nasogastric tube, there was a tendency for effluent volume and electrolyte losses to be lower.

Higher percentages of available calories and nitrogen were absorbed from the nasogastric feeds and two of the three patients absorbed more fat than from the oral diet.

These preliminary results suggest that nasogastric administration of liquid feeds may be more effective than oral administration. The benefits may be increased as the rate of administration is decreased.

HOME ENTERAL NUTRITION

A method of self-intubation was devised, and patients were taught to pass a soft fine-bore silicone-rubber tube on themselves. The tube used (Vygon 2395.06) has no stilette, thus avoiding the risk of traumatising the oropharynx and oesophagus, and is passed slowly with frequent sips of water as it is pliable and cannot be advanced only by pushing. The use of a fine silicone tube removes much of the discomfort usually associated with nasogastric intubation and encouraged good patient compliance as confirmed by their clinical progress.

All patients learned the technique quickly and were able to pass the tube after a few minutes practice. When the tube has been advanced to a mark 60cm from its tip, juice is aspirated using a small (2ml) syringe and gentle suction, and tested for acid with litmus paper. The position is regarded as satisfactory only when acid has been obtained, and the tube is retained in place by taping it to the patient's cheek and nose. The feed is placed in a reusable enteral feeding bag with integral giving set (Viomedex VX516) and the rate of infusion controlled using a simple peristaltic pump (Viomedex enteral nutrition pump). Figures 34 and 35 show the pump and feeding bag used, and Figure 36 shows a patient passing her tube and setting up her infusion.

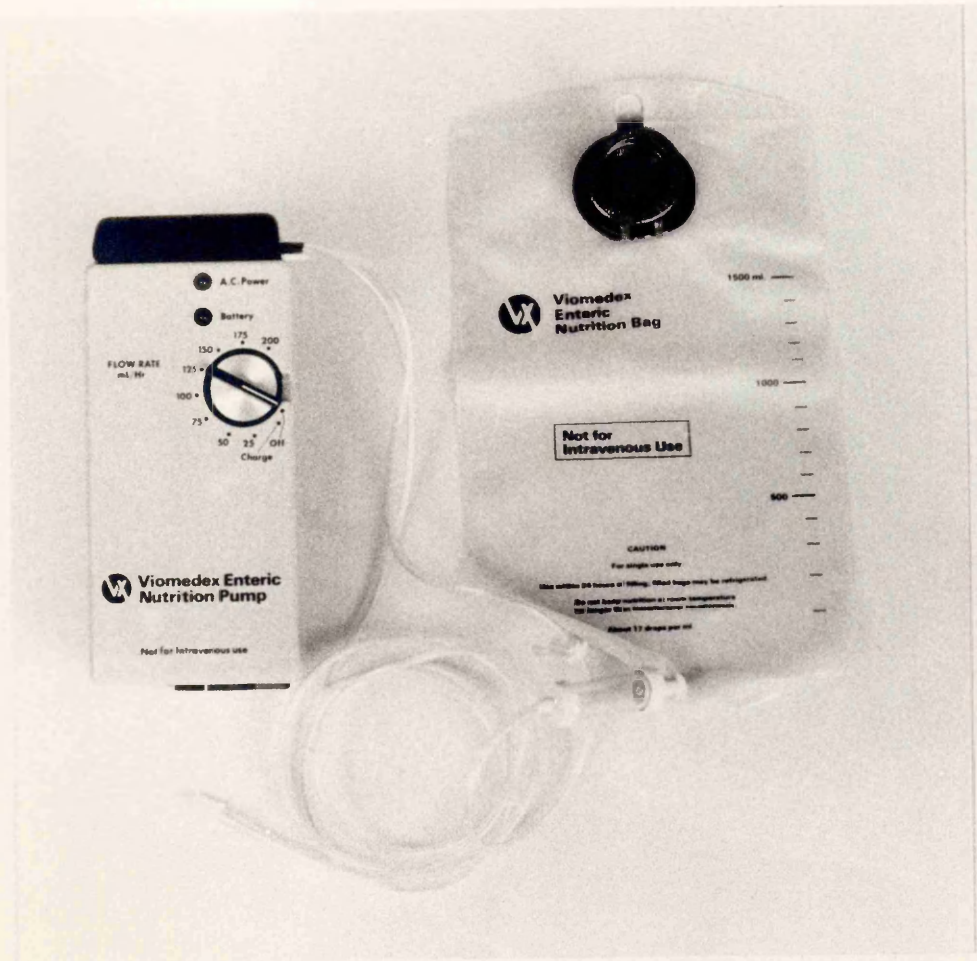


FIGURE 34 : The peristaltic pump and enteral feeding bag used for nasogastric feeding.

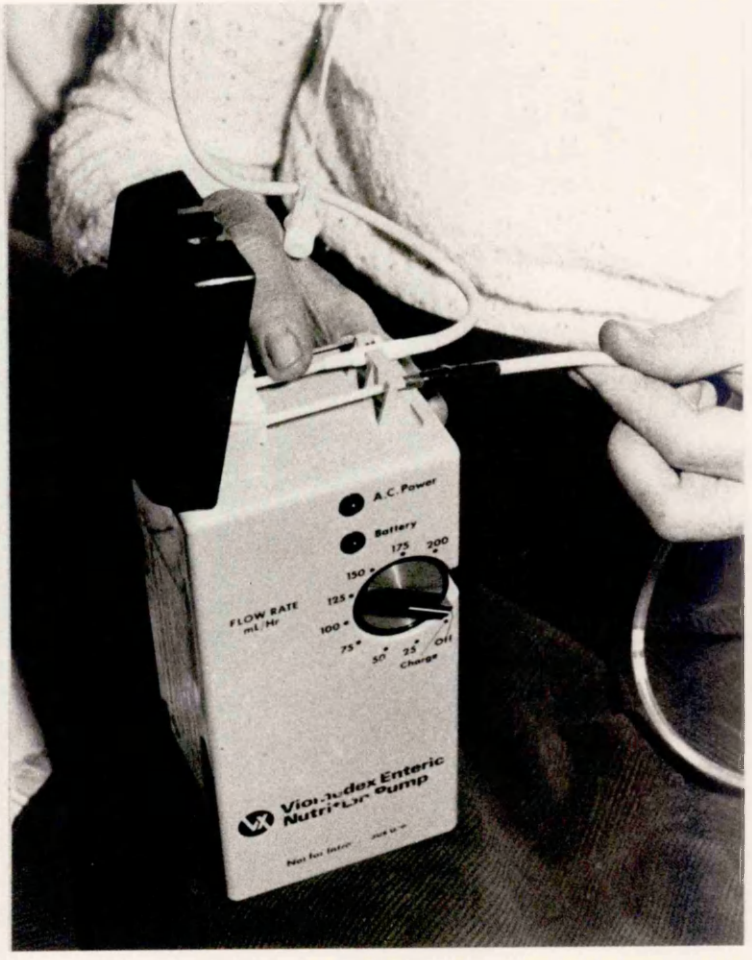


FIGURE 35 : Correct placement of the silicone insert of the enteral giving set in the feeding pump.

Six patients have used this system with considerable success. Five have administered a liquid feed , and one (JG) has used the technique to give 2 litres of glucose/electrolyte mixture overnight to maintain water and sodium balance. Of the five patients who required nutritional supplements three, DM, MS and WD had a short small intestine and weight loss despite a good appetite and dietary intake. The other two, CW and MW, had active inflammatory bowel disease with anorexia, abdominal pain and diarrhoea resulting in an inadequate intake. Details of these five patients are given in Table 19 and case histories of all patients appear in the Appendix.

Patients gained weight at a mean rate of 0.54kg/week (range 0.42-0.61kg/week) over the first 12 to 16 weeks of treatment, following which it was possible for some patients to decrease the frequency and quantity of their nocturnal supplements. One patient (CW) who had profound hypoalbuminaemia of 15g/l at the start of treatment regained normal levels of 35g/l during therapy. No patient suffered regurgitation or aspiration of the feed, and there were no metabolic complications. The two patients with stomas noticed an increase in the amount of effluent produced overnight, but did not have to empty their appliance more frequently than usual. Patients CW and MW underwent

further surgery, proctocolectomy and proctectomy with ileostomy respectively, following which their symptoms abated, allowing satisfactory nutrition without nocturnal supplements. Patient DM has been able to discontinue nasogastric feeds since attaining his ideal weight but continues to require liquid supplements by day to maintain his weight. The other two patients, MS and WD, continue to administer nocturnal feeds intermittently to maintain their body weight. MS also administers glucose/electrolyte mixture overnight when needed. Figure 37 demonstrates the weight gained by these patients while taking nocturnal nasogastric supplements.

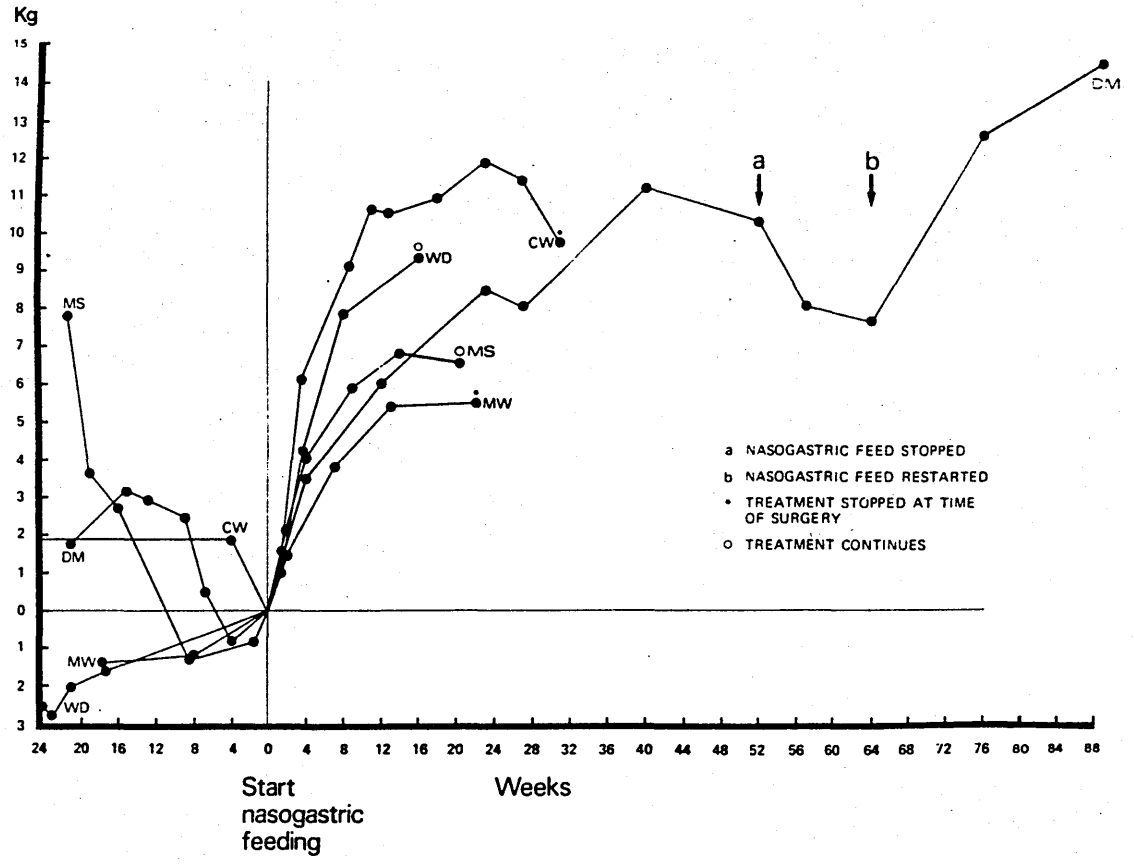


FIGURE 37 : Changes in body weight before and during supplemental nocturnal nasogastric feeding.

Patient	DM	MS	WD	CW	MW
Age	48	22	49	15	49
Sex	M	F	M	M	F
Diagnosis	Crohn's	Fistulae	Crohn's	Crohn's	Ulcerative colitis
Remaining small gut(cm)	150	80	130	All	All
Remaining colon	None	None	Left	All	Caeco-rectum
Stoma	Yes	Yes	No	No	No
Wt Loss (% IBW)	15.6	32.8	22.3	46.3	31.5
Feed Used	Isocal	Ensure	Nutranel	Isocal	Isocal
Calories	1500	1000	2000	1500	1125-750
Nights/week	5	7	7	7	7
Wt gain (kg/week)*	0.50	0.48	0.58	0.61	0.42
Wt gain (Total kg)	14.4	6.5	9.3	9.7	5.5
Weight before treatment (kg)	65.0	39.0	51.3	26.3	39.4
Weight after treatment (kg)	79.4	45.5	60.6	36.0	44.9
Ideal weight (kg)	77.0	58.0	66.0	49.0	57.5

* Weight gain over first 12-16 weeks.

TABLE 19 : Details of patients receiving nocturnal nasogastric feeding.

HOME PARENTERAL NUTRITION

Catheter Insertion and Care

The technique used for the insertion of central venous catheters for home parenteral feeding is essentially the same as the that developed by Powell-Tuck for use in inpatients (203). The method is illustrated in Figure 38. The subclavian vein is entered by the infraclavicular route through a small skin incision. The catheter is fed into the vein through the introducer and its position in the superior vena cava checked radiologically before proceeding further. Chest X-ray films showing the correct positioning of catheters inserted from right and left side are shown in Figure 39. The skin tunnel is made by passing a second, longer introducer subcutaneously from a point medial to the nipple to the primary insertion site . The catheter is then passed down this introducer, a small portion of which is retained at the skin entry site. This ensures secure fixing of the catheter in the clip which is then sutured to the skin and covered with an occlusive dressing. The procedure is carried out in a specially designed unit with laminar air flow under totally aseptic conditions. Recently, cuffed catheters have been inserted using a modification of this technique.

Patients are trained to care for their catheter, and learn the aseptic procedures necessary for setting up and changing infusions, heparinising the catheter, and changing the dressing. They must also learn and understand the alarm systems of the infusion pump, and receive some education about relevant basic anatomy and physiology. The training is undertaken by a Nursing Sister with a special interest in nutritional care with the aid of a patient manual which explains the treatment and its rationale. Each procedure and the equipment necessary is described in a detailed step by step manner. Figure 40 shows representative pages from the manual.

Fluid Administration

Solutions of amino acids, glucose, electrolytes, minerals and trace elements are administered from a single 3-litre bag (Travenol Laboratories Ltd.). When stored in a domestic refrigerator they have a shelf life of four weeks. Additions of vitamins are made by the patient immediately prior to infusion, because of their tendency to degradation with time and when exposed to light. To allow maximum patient freedom by day, the 3-litre bag is usually given during the night over 10-14 hours. If additional electrolyte solutions are needed,

Questions you may ask

Will I be able to cope?

There are many people throughout the world receiving intravenous nutrition in their own home. Those people felt the same apprehension that you may be feeling, but they have been able to overcome this and carry out their own care very safely. In fact, intravenous nutrition may be safer at home than in hospital because the same expert person is looking after the treatment all the time.

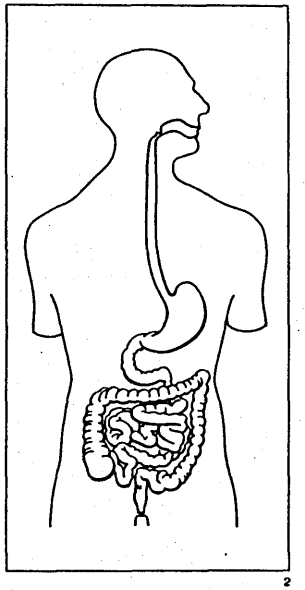
The procedures are not difficult, once you have learned how to handle the equipment, and you will be helped to do this by the Sisters at the hospital.

Is intravenous nutrition as good as eating?

Intravenous nutrition does not give the same pleasure as eating but provides all the same nutrients.

To remain healthy the body requires a regular supply of calories for heat and energy, protein for growth and the creation of new tissue, vitamins, minerals, salts (electrolytes) and water. These are all found mostly as large particles, in the food we eat. These particles are broken down to much smaller ones by the action of substances called enzymes, which are produced by the wall of the stomach, the small bowel and by the pancreas. When small enough they are absorbed through the wall of the small bowel into the many blood vessels which surround it and are then able to travel in the blood to provide nourishment for all the cells of the body.

The non-absorbable parts of the food, fibre from fruit skins, some vegetables and cereal, pass through the small bowel into the large bowel (colon) where much of the remaining water is removed and the residue expelled as faeces. If the small bowel, which is actually about 22 feet long, is diseased or removed, food will not be broken down and absorbed in large enough quantities to maintain health. In these circumstances it is possible to bypass this action and introduce a mixture containing particles similar to those absorbed through the small bowel, directly into the blood. This is intravenous feeding.



Methods

Looking after the catheter and giving the feed.

1. Changing the dressing
2. Setting up the infusion
   a. Intralipid
   b. 3-litre bag
   c. Changing from Intralipid to 3-litre bag
3. Injecting vitamins
4. Changing extension tube
5. Injecting Hepsal
6. Clearing blocked catheter
7. Changing hub and repairing catheter.

Changing the dressing:

To be performed every week or if wet or loose.

Equipment

- Dressing pack
- Mepore dressing
- Sterile gloves
- Chlorhexidine in spirit spray
- Povidone iodine powder
- Op-site spray
- Masks

1. Wipe working surface with tissue or piece of kitchen roll to remove any dust. Spray with spirit.
2. Put on mask.
3. Wash hands.
4. Loosen clothing to expose dressing. Remove tape from catheter.
5. Open dressing pack.
6. Pour Chlorhexidine in spirit into container.
7. Open Mepore dressing, and gloves.
8. Remove old dressing.
9. Observe the skin around the catheter for redness or discharge.
10. Using forceps pick up all the cotton wool balls in turn, soak in spirit and clean the skin around the catheter, using strokes from the catheter outwards.
    DO NOT TOUCH THE SKIN OR COTTON WOOL BALL WITH THE FINGERS
11. When the skin is clean, hold the Povidone iodine spray six inches from the skin and spray the area.
12. Do the same with the Op-site spray.
13. Put on gloves.
14. Peel the plastic from the back of the Mepore dressing. Try to avoid touching the pad.
15. Stick on the dressing.

FIGURE 40 : Pages from the manual given to patients receiving home parenteral nutrition.

these are given separately from 1 or 2-litre containers. When intravenous fat is needed it is usually given before the 3-litre bag.

All home parenteral feeding patients control the rate of their infusion overnight using a sophisticated volumetric pump with multiple alarm systems. The pump chosen was the Valleylab IV5000 and latterly the IV6000B (Kontron Instruments Ltd). The main benefit of these pumps is that when setting up an infusion, the giving set can be primed by gravity flow without touching the pump. This greatly simplifies this aseptic procedure for the patient. The fact that the infusion can be run by gravity allows patients to move round their home without the encumbrance of the pump, for example when cooking or visiting the toilet. A number of coathooks strategically placed round the house from which to hang the infusion bag allows maximum mobility.

Patients Treated

From January 1980 to July 1984, sixteen patients received intravenous fluids at home. One patient (PS) had two courses of home parenteral nutrition having failed to consistently thrive because of recurrent Crohn's disease. Eight patients had Crohn's disease,

seven with a short intestine after recurrent resections, and three with extensive active disease in their remaining gut. Four others had a short bowel, following intestinal resection for mesenteric vein thrombosis in two, after resection of mesenteric desmoid tumours in a third, and after radiation enteritis and resections in the fourth. Chronic bowel obstruction prevented oral nutrition in three patients, one with a large desmoid tumour, one with systemic sclerosis, and one with a hollow visceral myopathy and "pseudo-obstruction". One patient had severe malabsorption and brittle diabetes after pancreatectomy for chronic pancreatitis, and one had radiation enteritits. Patient details are given in Table 20.

Fluid Regimens

With one exception (PS), patients administered fluids every night, and all but three (KB,TF,AP) received three litres each infusion. AP required five litres daily to replace large jejunostomy losses while TF and KB were able to remain well on two litres daily. Three patients, KB, GF and RT used electrolyte solutions only to maintain fluid and electrolyte balance. Seven patients, CD, ED, KD, SG, AL, JS and PS were prescribed fat emulsion (Intralipid 10%) two or three times weekly.

Patient	Age	Sex	Diagnosis	Indication for HPN	Stoma
SG	33	F	Crohn's	Active disease	No
CD	43	F	Crohn's	Active disease Short bowel	Yes
PS	29	F	Crohn's	Active disease Short bowel	No
PS	31	F	Crohn's	Active disease Short bowel	No
KB	18	F	Crohn's	Short bowel	Yes
TF	29	F	Crohn's	Short bowel	Yes
RT	45	M	Crohn's	Short bowel	Yes
BS	47	F	Crohn's	Short bowel	Yes
AP	46	F	Crohn's	Short bowel	Yes
ED	51	F	Mesenteric Infarct, UC, Ca colon	Short bowel	Yes
PW	40	F	Mesenteric Infarct	Short bowel	No
JS	44	F	Desmoid Resection	Short bowel	Yes
GF	44	F	Radiation Enteritis	Short bowel	Yes
AL	44	M	Systemic Sclerosis	Obstruction	No
AS	19	F	Desmoid	Obstruction	No
KD	21	F	Visceral Myopathy	Obstruction	Yes
DP	25	F	Pancreatitis Diabetes	Malabsorption	No

TABLE 20 : Details of patients who received home parenteral nutrition.

Patient	Fluids l/day	Lipid ?	Duration (months)	Catheter (no:)	Complication	Rehab. Grade
SG	3	Yes	5	1		1
CD	3	Yes	3 *	2		3
PS	3	Yes	21 *	2	Septicaemia	3
PS	3	Yes	26	2		3
KB	2 E	No	2	1		2
TF	2	No	12 *	2		3
RT	3 E	No	12 *	2		1
BS	3	No	30 *	5	Pneumothorax Migration	1
AP	5 E	No	33 *	5	Septicaemia Migration	1
ED	3	Yes	7	2		1
PW	3	No	18 *	2	Haematoma	1
JS	3	Yes	1 *	1		1
GF	3 E	No	2 *	1		1
AL	3	Yes	33 *	6	Septicaemia Migration Thrombosis	2
AS	3	No	1	1	Pneumothorax	3
KD	3	Yes	1 *	1		3
DP	3	No	6 *	1		3

'E' indicates that electrolyte solutions were given in isolation, or in addition to a 3litre feeding bag (AP).

* Patients who were continuing treatment at 1.7.84

TABLE 21 : Treatment details for patients who received home parenteral nutrition.

Table 21 gives details of each patient's treatment.

Complications

Early

Early complications were related to catheter insertion. Two patients suffered small pneumothoraces, neither of which required intercostal drainage. One patient had a haematoma after puncture of the subclavian artery, but suffered no serious sequelae.

Delayed

Catheter sepsis was an infrequent problem. Three patients developed septicaemia, one caused by candida, one by pseudomonas species, and one by staphylococcus epidermidis which was introduced during a period of inpatient psychiatric treatment in another hospital.

Catheter migration occurred on six occasions and was felt to contribute to the one episode of subclavian vein thrombosis which developed in these patients while receiving home parenteral feeding.

A total of 37 catheters were inserted which at first sight appears a large number. However, only 11 were replaced because of catheter problems, 3 after sepsis, 6

after migration, and 2 after trauma and leakage. Nine catheters were changes electively when a new cuffed version of the fine-bore Vygon catheter became available, 5 were removed at termination of treatment or on the death of the patient, and 12 remained in place and were functioning well.

No patient suffered metabolic complications from the parenteral feeding. Several exhibited minor elevations of serum transaminases and alkaline phosphatase but these were of no clinical significance.

Clinical Outcome and Rehabilitation

The duration of individual courses of treatment ranged from 1-33 months, a total of 213 patient-months (16.5 patient-years). On 1.7.84 twelve patients were continuing treatment, three had stopped as parenteral feeding was no longer needed, and two had died of their primary disease and its complications. The parenteral feeding did not contribute to either death. Of the 12 continuing treatment, 6 were well with no evidence of active disease. Two, CD and PS continued to require treatment for active Crohn's disease. Abdominal pain was a major problem for TF and DP and the patients with systemic sclerosis and pseudo-obstruction continued to

have bouts of vomiting and abdominal distension.

Rehabilitation can be graded on four levels. At best, grade 1, patients are leading a near normal life, working full time or running the home and able to socialise fully. In grade 2, patients work part-time or run the home with help. Social activities are somewhat restricted. In grade 3, although independent as regards their treatment, patients are unable to work and only able to get out occasionally. At worst, patients in grade 4 are unable to cope with their parenteral feeding unaided and are virtually housebound. Of the twelve patients still receiving home parenteral feeding, six can be classed as grade 1, one as grade 2, and five as grade 3. Of the five who stopped treatment, two attained grade 1, one grade 2, and two grade 3. It is important that no patient was in grade 4 except in the terminal stages of illness when inpatient treatment was needed.

DISCUSSION

In this chapter the results of the experimental work of the thesis are discussed, and their implications for clinical management assessed. Guidelines for the treatment of patients are proposed.

Electrolyte Mixtures

The studies of water and sodium absorption from different sugar-electrolyte solutions have identified a useful oral replacement solution which is now being used routinely in patients with a short small intestine, and have suggested directions in which further investigation may proceed.

Glucose and maltose have been shown to promote more sodium and water absorption in these patients, than sucrose. This may be because only the glucose portion of the sucrose the fructose promotes sodium absorption only secondary to solvent drag. Although glucose is well absorbed from solutions of glucose oligosaccharrides (127), the solution containing Caloreen was disappointing. It is possible that the osmotic load produced by the rapid hydrolysis of the polymer by pancreatic amylase reduces absorption in these patients.

In their demonstrations of the efficacy of glucose polymer in promoting sodium and water absorption, the effect of amylase was eliminated by Jones et al (127) in their jejunal intubation study with a proximal occlusive balloon and minimised by Griffin et al (87) by their administration of the 750ml of test solution to their patients by slow intestinal infusion over 90 minutes.

Sodium concentration appears to be important in determining the efficacy of oral replacement solutions. In this thesis, sodium concentration was varied to maintain the overall osmolality of the solutions close to that of plasma. This resulted in a range of sodium concentration from 83mmol/l in the Caloreen mixture to 115mmol/l in the maltose and sucrose mixtures. The low sodium concentration may partly explain the poor performance of the Caloreen mixture, but does not explain the low absorption from the sucrose solution. Conversely, the higher sodium concentration of the maltose solution may be partly contributing to the increased absorption achieved compared with the glucose containing solutions in which the sodium concentration was 90mmol/l.

The mixture containing glucose, saline and bicarbonate was the best compromise among those tested and has been successfully used in many patients with the short bowel

syndrome and ileostomy diarrhoea. It is however, not ideal, as some patients find it unpalatable. Based on the results presented, further studies could be aimed at ascertaining whether increased sodium concentration is indeed associated with improved sodium and water balance, and experiments with different flavourings may improve palatability.

The inability of patients in Group B to absorb sufficient quantities of sodium and water to remain well despite having a theoretically sufficient length of intestine raises the possibility that they had residual inflammatory bowel disease which, although not detectable radiologically, was disrupting intestinal function at a cellular level, producing a secretory state. Perfusion studies would be necessary to determine whether this is indeed the case.

Solid Food Diets

The solid food diets used contained different quantities of fat and fibre while maintaining other constituents constant in an attempt to ascertain which, if any, was most beneficial for patients with a short bowel. There has been recent debate concerning the need for the traditional low fat diet (23,86,124,172) after the

results obtained by Woolf et al (281) and Simko et al (236) which showed that an increased fat intake is not uniformly detrimental (281), and may be beneficial in some (236).

Reduction of dietary fat and fibre made no appreciable difference to effluent weight, calorie absorption, and nitrogen balance. Higher dietary fat intake did produce higher faecal fat levels, in agreement with previous reports (23,25,227). However, the increased faecal fat losses were not associated with increased electrolyte and mineral losses for the group as a whole, confirming the results of Woolf et al (281).

The traditional guidelines for a low fat diet emanate from studies performed on a small group of patients who retained different lengths of bowel, some with a colon in situ, and some without (23,25). The same is true of the more recent studies, where the results obtained from a heterogeneous group of patients have been analysed together and expressed as a mean for the group with wide standard deviations (281), or where a single patient has been studied (236).

The patients presented here are also a heterogeneous group, with different lengths of intestine, different pathologies, and different degrees of disability. The

results for each individual reveal that in some cases a particular diet conferred some benefit although this was not significant in the group as a whole. The same phenomenon was noted by Booth et al (23,25), some patients responding well to fat restriction, and others not. Thus it may be suggested that because no two short bowel patients are identical, a single dogmatic approach to dietary treatment is inappropriate.

All the patients in this study had a stoma. It is possible that patients with a colon will respond badly to increased dietary fat, and experience worse diarrhoea because of the cathartic effect of unabsorbed fatty acids (54) and bile salts (110). Thus, these findings can not be extrapolated to all patients with a short intestine but do support the development of a more liberal attitude to the amount of dietary fat which these patients are allowed.

Liquid Diets

Although in the normal state digestion and absorption of food is well-nigh completed in the proximal 100cm of jejunum, (28) and elemental diets have been shown to be no better a means of providing nutrition than polymeric diets in patients with a normal small intestine

(67,126), intestinal transit is much more rapid in the short bowel syndrome, and foodstuffs may thus traverse the bowel before digestion is complete. In such cases predigested food might be expected to be more completely absorbed notwithstanding the presence of an intact pancreaticobiliary system. To test this hypothesis, a polymeric diet and a chemically defined diet were compared in a group of patients who might reasonably be expected to benefit from predigestion of foodstuffs.

There were however, no significant differences between the two diets. Each patient absorbed similar percentages of nitrogen, fat and calories from each diet, neither of which significantly reduced the weight of stoma effluent when compared with the other. Although both feeds produced positive balances of potassium, calcium and magnesium, all patients had a strong tendency to sodium depletion. This agrees with previous findings that patients with an ileostomy are unable to retain sodium (102,106) and this tendency is exaggerated in patients with a short bowel because of the larger volumes of their stoma losses. It is therefore extremely important that such patients receive sufficient sodium in their diet, and use an oral electrolyte replacement solution when necessary.

These studies of liquid diets have shown that the presentation of protein as peptides, carbohydrate as oligosaccharrides, and fat as medium chain instead of long chain triglycerides is not beneficial even to those patients with an extremely short small intestine.

The results of the liquid diet studies have, however, shown that these preparations should be useful in patients with a short intestine. Although earlier work (7) demonstrated no benefit from "synthetic" diets, the results in these patients show that in some cases, absorption of nitrogen and calories was greater from the liquid diets than from the solid food diets. These results are shown in Table 22 which is compiled from Tables 5,12 and 13. Although these differences are not large enough to justify the substitution of a normal diet with a liquid preparation, satisfactory results could be achieved by using liquid food supplements for patients who are unable to eat enough normal food to maintain a good nutritional state.

Some patients are unable to tolerate large quantities of liquid supplement orally, and in such cases nasogastric administration of feeds may be useful. The study comparing oral with nasogastric administration of the same feed is too small to allow firm conclusions, but there is a suggestion that slow nasogastric feeding may

Calories

	Solid Diet			Liquid Diet	
	1	2	3	Ensure	Nutranel
JG	72.1	50.5	68.2	73.1	77.5
DM	65.4	63.9	50.8	73.5	75.5
AP	29.4	23.9	44.5	70.0	48.1
BS	41.9	39.4	50.1	36.7	38.8

Fat

	Solid Diet			Liquid Diet	
	1	2	3	Ensure	Nutranel
JG	57.7	38.4	51.9	57.1	10.1
DM	62.3	71.2	75.4	73.0	77.8
AP	34.0	41.9	33.8	31.3	40.0
SB	61.2	35.6	38.7	59.8	45.6

TABLE 22 : Percentage absorption of calories and fat from solid and liquid diets.

be more efficient than simply drinking a liquid supplement. Even if this is not the case, the use of the nasogastric technique to allow 24 hour feeding and thus increase the total calorie intake may produce satisfactory enteral nutrition and avoid the need for parenteral therapy. In inpatients, the nasogastric tube can remain in place continually, with food taken in addition to the nasogastric feed. For patients needing treatment at home, self-intubation at night allows a normal daytime life style, with nocturnal nasogastric supplements.

Home Enteral Nutrition

The theoretical reasoning behind the use of liquid dietary supplements has been confirmed by the clinical studies with patients who had failed to thrive on a normal diet, but who all achieved satisfactory weight gain while receiving nocturnal nasogastric feeding at home. It is particularly encouraging that these results were achieved with no mechanical or metabolic complications, and that a technique which on initial description appears somewhat offputting, should be aesthetically acceptable to, and well tolerated by patients. Nocturnal tube feeding does therefore have an important part to play in breaking the 'nutritional

deadlock' which develops in patients with a short bowel, or as a result of chronic intestinal disease as was the case in two patients and in previous reports (98,161).

Home Parenteral Nutrition

Although the judicious and energetic use of electrolyte replacement solutions and dietary supplements, either orally or by nasogastric tube, will produce a rapid and sustainable improvement in the health of many patients with a short intestine, there remain those for whom there is no alternative, other than inanition and death, to longterm parenteral nutrition. The development of suitable catheters and solutions, reliable equipment, and aseptic nursing techniques combinmed with enthusiastic patient teaching and support has made treatment at home rather than in hospital a feasible proposition.

At the time of writing, the patients reported represented one of the largest groups undergoing home parenteral nutrition in the United Kingdom. Comparison with earlier reports (36,120,121,122,145) is encouraging in that metabolic complications have been avoided, and the level of rehabilitation has been generally aceptable

to both patients and their medical and nursing attendants.

While it is possible that some patients will experience sufficient intestinal adaptation to be able to stop parenteral supplements (120,122), it is likely that treatment for the majority will be lifelong. In such cases, an exclusively parenteral diet may be lacking in certain trace elements and/or vitamins, deficiencies of which may take many months or years to develop. The identification of deficiency syndromes (69,123,135,173, 280) and the ability to measure trace elements in blood and tissue specimens should help to ensure that longterm parenteral nutrition does not merely lead from one state of malnutrition to another. The encouragement of oral diet whenever possible may help to provide trace elements, the exact requirements of which remain as yet unknown.

Of the patients presented here, it is possible that PS and TF may adapt sufficiently to thrive on oral diet again, and that GF and RT may have periods when oral electrolyte replacement is sufficient for there needs. The outlook for the remainder is lifelong treatment but from the experience gained to date, this should be compatible with a good quality of life.

The overall outlook for patients with a short intestine is thus less dismal than before. The availability of an effective electrolyte mixture and liquid feeds for dietary supplementation mean that chronic dehydration and malnutrition can be dealt with by the enteral route in many cases. The findings that increased amounts of dietary fat can be tolerated by such patients without producing detrimental biochemical upset encourage the use of more palatable diets, which should also lead to better nutritional status. Finally, for those in whom more conservative measures are unsuccessful, parenteral nutrition at home has been shown to be an effective, low risk treatment which is acceptable to patients in the longterm and which can result in a return to a normal role as spouse, parent, and breadwinner often after many years of poor health and limited social function.

APPENDIX

K B dob 1.8.63

This girl had a life-long history of ill health beginning at the age of eighteen months with attacks of pain and altered bowel habit. She failed to thrive until 1969 when she developed an anal fissure. Crohn's disease was diagnosed. In 1973, after treatment with prednisolone had failed to control her symptoms, a left hemicolectomy and colostomy was performed. The remaining colon and rectum was resected in 1974 and an ileostomy raised. Epigastric pain and high volume stoma losses became a problem in 1978 and proved resistant to medical treatment. Forty-five centimetres of diseased ileum were resected, but she developed a postoperative enterocutaneous fistula which failed to heal spontaneously and recurred after surgery. Investigation of abdominal pain in 1979 revealed a stricture in the duodenum which was bypassed surgically. Her fistula persisted and she was referred to St Mark's Hospital in February 1980.

At that time her stoma output was 4-6 litres daily, she had a suprapubic abcess and fistula, a gastroduodenal stricture and was malnourished. She weighed only 29.5kg and was 145.5cm tall. At laparotomy in April 1980 she

was found to have severe duodenal deformity and a gastrojejunal fistula. A partial gastrectomy and gastroduodenal anastomosis was performed with resection of the old small bowel fistula, following which 105cm of jejunum remained in situ. Histological examination of the resected bowel demonstrated Crohn's disease in all specimens. Postoperative abdominal pain and vomiting persisted, and in May 1980 gastroscopy demonstrated a stricture of the gastroduodenal anastomosis which was dilated. Despite these measures, chronic abdominal pain and opiate dependence together with a large volume stoma effluent continued to dominate her clinical course. She was taught to administer her intravenous fluids herself, and after the jejunostomy had been reconstructed in August, she was discharged home in September 1980 on home parenteral nutrition. She had a further minor procedure performed on the stoma in October but was well enough to stay at home until late December thereafter, maintaining fluid and electrolyte balance with intravenous saline each night. Throughout 1981 she continued to suffer chronic, severe pain, partly due to gastric ulceration which responded slowly to prolonged treatment with intravenous cimetidine. A high stoma output, post-transfusion hepatitis, and latterly urinary frequency and incontinence further complicated her management. She remained on parenteral nutrition continually, but finally died in June 1981.

W D dob 23.8.32

This man was well until 1956 when he developed abdominal pain for which appendicectomy was performed. Ileal Crohn's disease was suspected. He remained well until 1973 when he developed an intra-abdominal abcess which was treated by right hemicolectomy and ileocolic anastomosis. Recurrent disease necessitated resection of the anastomosis and 35cm ileum in 1975. He then suffered intermittent diarrhoea and weight loss until 1980. Despite dietary supplements of Casilan, Caloreen and Vivonex he lost 6kg in nine months with persistent hypoalbuminaemia treated by repeated albumin transfusions in addition to prolonged treatment with prednisolone and sulphasalazine. He was referred to St Mark's Hospital in June 1980.

Investigations confirmed steatorrhoea and a protein-losing enteropathy. A barium follow-through demonstrated recurrent anastomotic Crohn's disease which was resected with 63cm ileum leaving approximately 150cm proximal small bowel. Cholecystectomy was performed for chronic cholecystitis and gallstones. Throughout 1981 he was well, but subsequently began to lose weight in January 1982 with recurrent hypoalbuminaemia. Barium follow-through revealed further anastomotic recurrence and a short residual small intestine which measured

130cm. In an effort to preserve as much bowel as possible resection was avoided. Treatment with prednisolone was started and he began to supplement his diet with Nutranel in February 1982. Although he was initially successful in taking a supplement of 1600-2000kcal daily, palatability became a problem after discharge. In June 1982 he began nasogastric supplements using a similar quantity of Nutranel with good weight gain in the next few months.

T F dob 22.6.55

This lady first developed mouth ulceration in 1970 which recurred in 1971 in association with perianal abcesses, generalised malaise and lassitude and a refractory microcytic anaemia. She developed diarrhoea and weight loss shortly afterwards and was investigated at her local hospital. Faecal fat excretion, xylose absorption and jejunal biopsy were normal. Radiology revealed duodenal dilatation only. She was placed on a gluten-free diet which continued until 1975 with little change in her symptoms.

She was referred to St Mark's Hospital in 1975 with diarrhoea, abdominal and anal pain and weight loss to less than the third percentile. Her height was between

third and tenth percentiles, bone age 19-21 years. Radiology showed Crohn's disease affecting terminal ileum, colon, and rectum with multiple perianal fistulae. Despite treatment with prednisolone and azathioprine she developed a rectal stricture. Proctocolectomy and ileostomy were performed in July 1976. The ileostomy output remained greater than 1 litre daily despite codeine phosphate and loperamide.

In 1977 postprandial abdominal pain and vomiting secondary to recurrent jejuno-ileal disease was treated with metronidazole, cotrimoxazole and prednisolone. She failed to gain weight and parenteral nutrition was given from September to December 1977. Over the next year her stoma was revised surgically because of leakage of effluent and she continued to take inadequate amounts of food because of pain and high volume stoma losses. Parenteral nutrition was re-introduced in May 1978 and she continued this treatment at home from July 1978 to April 1979 in addition to prednisolone and azathioprine.

After discontinuing parenteral nutrition, salt and water depletion became a major problem in 1980. She developed subacute small intestinal obstruction secondary to adhesions which were lysed at operation, when no active Crohn's disease was seen. Continued low weight and low sodium status prompted admission for nasogastric feeding

which was successful in achieving her optimum weight. She was not prepared to administer this treatment at home however, and her weight decreased after discharge. Abdominal pain, resistant to antispasmodics, mild analgesics and occasionally to pethidine became an increasing problem in 1982. An exploratory laparotomy revealed no recurrent disease, and no obstructing adhesions. Azathioprine and prednisolone were stopped.

Since 1982 she has been unable to take sufficient calories, fluid and electrolytes orally to allow her to thrive. The ileostomy continued to produce greater than 1 litre of effluent daily, and she has suffered recurrent oral ulceration and arthralgia of the right knee. A further trial of nasogastric electrolyte replacement was unsuccessful and home parenteral nutrition was restarted in May 1983. This has maintained her weight and a satisfactory nutritional status but has not improved her symptoms. She is unable to work, but looks after the home with help from her husband.

J G dob 28.6.31

This lady had never been seriously unwell until March 1978 when cervical carcinoma was diagnosed. A vaginal hysterectomy was followed by a six week course of radiotherapy and a radium implant for local spread. She was vaguely unwell during treatment.

In January 1980 an attack of 'gastroenteritis' with abdominal pain was followed in February by emergency admission and laparotomy. A small bowel perforation was treated by resection and end-to-end anastomosis from which she made an uneventful recovery. Her bowel habit remained variable in frequency and consistency however, requiring regular treatment with codeine phosphate.

Readmission was precipitated by an episode of subacute small bowel obstruction in August 1981. At laparotomy the terminal ileum was found to be gangrenous and a modified right hemicolectomy was performed. Breakdown of the anastomosis necessitated further laparotomy, colectomy and mucous fistula with a terminal ileostomy being performed. The total length of small intestine resected was said to be 100cm. Her postoperative course in an Intensive Therapy Unit was complicated by two pneumotharaces and left subclavian vein thrombosis secondary to attempts at central venous catheterisation

and parenteral nutrition. She developed a stoma output of between 2 and 7 litres daily with rapid weight loss and was referred to St Mark's Hospital in November 1981.

She had lost 12.5kg, was lethargic and complained of muscle cramps. There was hypomagnesaemia which required parenteral replacement. Her stoma output settled from a maximum of 13 litres to 1.5-2 litres daily at the time of discharge in February 1982. Oral replacement of sodium and water losses was possible using a glucose/electrolyte solution in addition to codeine phosphate, loperamide and magnesium hydroxide supplements.

Throughout 1982 she required repeated admissions for intravenous saline infusions. It proved impossible to train her to safely administer parenteral fluids or to look after a central venous catheter with satisfactory aseptic technique. She therefore started nasogastric administration of a glucose/electrolyte mixture overnight, giving 2 litres each night and drinking a further 1-2 litres by day. Supplements of zinc sulphate and essential fatty acids as topical sunflower seed oil were added in June 1982.

In January 1983 she developed hypocalcaemia, hypomagnesaemia and dehydration secondary to an increase

in her stoma output to 5 litres daily. Despite a good appetite, weight loss was a problem. The addition of fludrocortisone resulted in reduction of her daily output to 1.2 litres. Supplements of magnesium, zinc, electrolytes and fatty acids continued from discharge in March 1983.

Continuing weight loss remained a problem and in May 1983 she began to administer a calorie supplement by nasogastric tube at night using Ensure with good results. She stopped fludrocortisone and other supplements of her own accord in November 1983 and gradually deteriorated until their reintroduction in March 1984 since when she has remained well.

S G dob 2.11.44

This gentleman first had problems with Crohn's disease in 1961. Diarrhoea, pain and weight loss were successfully treated with medical therapy until 1972 when an exacerbation required right hemicolectomy and ileal resection. He remained reasonably well until 1976 when colonic involvement was diagnosed, and anorectal disease became his major problem in 1977. Pelvic sepsis complicating the colitis was treated by sigmoid colectomy and colostomy that year. He suffered

recurrent episodes of subacute small bowel obstruction over the next five years, and on one occassion was admitted to St Mark's Hospital. Abcess formation, active colonic disease and small bowel obstruction required surgical treatment, with resection of the remaining colon and rectum, and diseased small intestine, leaving 130cm proximal gut in situ. He lost large volumes from his jejunostomy, usually of the order of 3 litres daily, which responded poorly to codeine and loperamide. Sodium and water losses were replaced using an oral glucose/electrolyte mixture and he has been able to maintain a satisfactory weight by eating a large diet, and tolerating the consequent large volume of stoma effluent.

D M dob 19.7.34

This man presented with symptoms of acute appendicitis in 1966. At appendicectomy, ileal Crohn's disease was diagnosed and treated expectantly. Following three years of variable health with diarrhoea, abdominal pain and weight loss, an ileo-transverse colostomy was performed, bypassing the diseased ileum. He remained well for 18 months but then developed a low output enterocutaneous fistula in the right iliac fossa which persisted until 1972 when he was referred to St Mark's Hospital.

Examination revealed anal Crohn's disease, and radiology demonstrated terminal ileal disease with normal proximal small bowel and colon. An extended right hemicolectomy was performed with resection of 90cm ileum and side-to-end ileocolic anastomosis in December 1972. Crohn's disease was confirmed on histological examination of the specimen. He suffered recurrent wound abcesses throughout 1973 and in December 1974 he developed obstructive symptoms. Colonoscopy revealed recurrent disease at the anastomosis which proved resistant to treatment with oral prednisolone. At laparotomy in March 1975 a duodeno-ileal fistula was demonstrated at the anastomosis which was the site of his recurrent abcesses. Anastomotic resection and reanastomosis was perfomed, removing 23cm ileum. A further anastomotic recurrence, resistant to medical therapy required resection in 1977 when the remaining small intestine measured 225cm.

Over the next year he gradually lost weight and suffered intermittent diarrhoea and abdominal pain. Investigation in 1978 revealed anastomotic recurrence with new rectal involvement and deterioration of the anal lesion. Proctocolectomy and ileal resection was performed leaving 150cm proximal small bowel in situ. The postoperative course was complicated by abdominal abcesses, empyema of the gallbladder which required

cholecystotomy and removal of gallstones, and a chronic perineal sinus. His jejunostomy output was consistently greater than 2 litres daily and his weight remained low at 68kg.

In September 1979 he weighed 59.4kg and full reassessment was undertaken. There was steatorrhoea and lactose intolerance with a normal pentagastrin stimulation test. Treatment with a low fat diet, cimetidine and antidiarrhoeal medications failed to consistently decrease the stoma output. His diet was supplemented with medium chain triglycerides to 3500kcal per day. On this diet and supplements of ox bile and cimetidine his weight gradually increased but he became intolerant of MCT and stopped the supplements.

In May 1980 he was taught to pass a nasogastric feeding tube himself and thereafter took 4 cans Isocal at night, decreasing to 3 cans after three months. He continued treatment for one year and then attempted to withdraw the supplements. Rapid weight loss followed which was reversed by restarting the nocturnal feeds. In September 1981 he did manage to revert to oral supplements by day and to dispense with nasogastric feeds and has remained well since.

A P dob 27.12.37

In 1962 this lady developed diarrhoea and abdominal pain for the first time. A radiological diagnosis of Crohn's disease was made. She received medical treatment until 1965 when, following several attacks of subacute small bowel obstruction, a right hemicolectomy with ileocolic anastomosis was performed. Crohn's disease was confirmed histologically. In 1966 a second laparotomy was performed for small bowel obstruction. Adhesions responsible for the obstruction were lysed and the intestines reported as being normal throughout. She remained well until 1968 when recurrent abdominal pain prompted radiological investigation. Recurrent Crohn's disease at the ileocolic anastomosis was diagnosed and subsequently resected with reanastomosis of the bowel.

In 1970 she developed perianal Crohn's lesions which were treated with prednisolone and azathioprine. For the next eight years she was troubled by recurrent fistulae-in-ano which required local surgical procedures resulting in variable continence exacerbated by loose stools and general malaise. Radiological reassessment in 1978 revealed recurrent small bowel disease which failed to respond completely to medical treatment including prednisolone and azathioprine. By 1981 jejuno-ileal, colonic and anal diease with a recto-

vaginal fistula were causing severe diarrhoea, abdominal pain, incontinence and social embarrassment. Further treatment with systemic prednisolone, azathioprine, an elemental diet and antibiotics was unsuccessful. A proctocolectomy with jejuno-ileal resection was performed and a terminal jejunostomy raised in May 1981. Approximately 120cm of healthy jejunum remained.

She subsequently developed problems with high volumes of stoma effluent, from 3-5 litres daily with associated thirst, syncope, nausea and a noticably rapid intestinal transit of approximately 10 minutes. Treatment with codeine phosphate, lomotil, low residue diets and oral electrolyte replacement solutions was unsuccessfull and she required intermittent infusions of intravenous saline to maintain fluid and electrolyte balance. She was transferred to St Mark's Hospital in August 1981.

At that time she weighed 45.5kg, with a smooth beefy tongue with angular cheilosis and a fasting stoma output of 2.51/24hours. It was not possible to reduce her output using cimetidine, loperamide, codeine phosphate, fludrocortisone or propantheline in maximal dosage. A subclavian catheter was inserted for the purposes of electrolyte repletion and she was discharged in September 1981 administering 3 litres of saline intravenously each night. She was well enough to take a

holiday in Malta in December 1981 taking her intravenous solutions with her.

In January 1982 it was noted that she was continuing to lose weight. Her jejunostomy had retracted causing effluent leakage. The stoma was refashioned and the remaining intestine measured 60cm. A further attempt was made to control her high volume output with medical therapy, but all measures including oral prednisolone proved unsuccessful. She commenced supplementary home parenteral nutrition in March 1982 and has continued to require 5 litres of intravenous fluids daily to maintain a satisfactory nutritional state. Despite these problems she has returned to work as a part-time school secretary, and is fully able to look after her home and family and to enjoy a satisfactory social life.

B S dob 11.5.1937

This lady developed inflammatory bowel disease in 1974 and required emergency admission with toxic dilatation of the colon in 1979. A panproctocolectomy was performed, complicated postoperatively by persistent sinuses in the left iliac fossa and perineum. Over the next 3 months her general condition deteriorated and further investigation revealed an enterocutaneous

fistula communicating via an abcess cavity in the left side of the abdomen with the jejunum. Attempts at percutaneous drainage with a 'skinny' needle were unsuccessful. She underwent laparotomy with drainage of the abcess and resection of 12cm jejunum in December 1979 with a stormy postoperative course and parenteral feeding.

From April until August 1980 she remained reasonably well despite a persistent discharge from the abdominal and perineal wounds. Barium meal and follow through showed no abnormality but a sinogram demonstrated a recurrent fistula communicating with the small bowel.

She was transferred to St Mark's Hospital in September 1980. There was weight loss of 19kg, persistent pyrexia and intermittent abdominal pain and diarrhoea. Laparotomy was performed in October 1980 when a jejunal fistula communicating with a left subphrenic abcess, an enterocutaneous fistula communicating with two loops of small intestine, and a perineo-vaginal fistula were identified. Four limited small intestinal resections were performed, leaving a total of 285cm from duodeno-jejunal flexure to ileostomy. The perineo-vaginal fistula was laid open. Parenteral nutrition was needed for support in the postoperative period. Histology of all resected specimens was diagnostic of Crohn's

disease. She was finally discharged in November 1980.

After only two weeks at home, she was readmitted with a left-sided abdominal abcess which required surgical drainage following which nasogastric feeding produced weight gain of 8kg. Azathioprine was introduced but she developed side effects necessitating cessation of treatment before discharge in March 1981.

Emergency readmission was necessary in May 1981. At laparotomy, multiple small perforations of the small intestine were found. Four short segments of bowel were resected. Multiple enterocutaneous fistulae developed postoperatively and parenteral nutrition was again needed, but her fistulae persisted. A further laparotomy was performed in August 1981. A large pelvic abcess was drained and small intestine containing a fistula was resected. The remaining small bowel measured 100cm. A recurrent low output enterocutaneous fistula was treated with metronidazole and erythromycin and healed spontaneously. The jejunostomy output was between 3 and 6 litres daily despite loperamide, codeine phosphate, lomotil, fludrocortisone and cimetidine. It was initially possible for her to replace these losses with intravenous saline, but gradual weight loss despite a good food intake necessitated the reintroduction of supplementary parenteral nutrition. She was discharged

in January 1982 and has continued home parenteral feeding.

Since 1982 this lady has managed to cope with a difficult home environment and looks after her family and home independently. She took a part-time job in a dry-cleaning firm in August 1983, and now works full-time.

M S dob 22.2.59

This young lady had her first attack of ulcerative colitis in 1979. Although there was dilatation of the colon she responded to treatment with oral and rectal prednisolone and sulphasalazine. All treatment was stopped by May 1980. She required oral prednisolone for a relapse in July 1980 and suffered a further attack in November despite prophylactic oral prednisolone and sulphasalazine. Barium enema showed severe pseudopolyp formation and a total colitis. Her attack settled and she was referred to St Mark's Hospital for consideration of elective surgery in March 1981.

An acute relapse with colonic dilatation needed urgent surgery in April 1981 at which time the colon was found to have perforated and the peritoneal cavity was

contaminated with faeces. Colectomy with mucous fistula and ileostomy was performed. During the next nine months she required parenteral nutrition to support her through recurrent abdominal abcesses with small bowel fistulae. She required five further major surgical procedures resulting in multiple resections of small intestine and the rectal stump. She retained 110cm jejunum with a loop stoma at 80cm. She was discharged in March 1982 taking a normal diet and oral electrolyte supplements despite which she lost weight rapidly and was readmitted for reassessment in August 1982. She was taught to pass a nasogastric feeding tube herself and was discharged in September 1982 administering 4 cans Ensure each night and drinking a further 4 cans each day in addition to a normal diet. She continued this regime until January 1983 and since then has used the nasogastric tube mainly for electrolyte replacement and occassional nutrient supplements. She continues to take 2 cans Ensure orally each day, and now works full time as a secretary. Further surgery to close her loop stoma is planned.

R T dob 2.6.1939

This gentleman initially became unwell in 1965 when an appendicectomy was performed. At that time suspicions of Crohn's disease were raised and later that year a terminal ileal resection was carried out. Histological examination of the resection specimen confirmed the diagnosis. He remained well on minimal treatment until 1972 when loss of weight was associated with abdominal pain and a right iliac fossa mass. He was treated with oral prednisolone for 4 months with moderate success.

In 1979 he required three hospital admissions for subacute small bowel obstruction. All episodes responded to conservative management, including intramuscular and oral steroids, sulphasalazine and a low residue diet. Investigation of low back pain revealed minor degenerative changes in the lumbar spine. Following a further admission for small bowel obstruction in early 1980 he underwent resection of the ileocolic anastomosis including 15cm ileum and 10cm colon. Histology confirmed recurrent Crohn's disease.

He remained asymptomatic until 1982 when abdominal pain and diarrhoea was accompanied by weight loss from 60kg to 54.6kg (ideal 62kg). Full reassessment was undertaken, including colonoscopy which showed the

colon to be grossly abnormal from sigmoid to splenic flexure. Medical treatment with prednisolone and azathioprine was unsuccessful, and proctocolectomy with a further small bowel resection was undertaken. It transpired that his previous resection had been more extensive than reported, and following this resection of 35cm, only 100cm of small bowel remained, terminating in an end jejunostomy. Histology of the specimen again showed Crohn's disease. Despite antidiarrhoeal therapy the output from his jejunostomy remained in the range of 3-5 litres/24hours. He required repeated readmissions for intravenous electrolyte replacement and was subsequently referred to St.Mark's hospital for consideration of home parenteral nutrition in May 1983.

He weighed 40kg and laboratory investigations revealed anaemia, hypoalbuminaemia and hypomagnesaemia. After studies of food absorption it became clear that he was able to maintain a good nutritional state on a large diet, provided that the high stoma losses were replaced parenterally. He was discharged on codeine phosphate, loperamide and oral zinc supplements, and administers 3 litres of saline with potassium and magnesium supplements intravenously each night.

C W dob 21.10.65

This young man first became unwell in 1973 with diarrhoea and an anal fissure. Biopsy of this lesion revealed a granulomatous process which was treated with anti-tuberculous therapy. In August 1974 he required surgery for pyloric stenosis secondary to a chronic duodenal ulcer. A truncal vagotomy and gastro-jejunostomy was performed together with appendicectomy and biopsy of a mesenteric lymph node. Histology of this node suggested 'early Crohn's disease'. He remained well until June 1978 when diarrhoea recurred with abdominal and anal pain, rectal bleeding, weight loss and erythema nodosum. A barium enema revealed severe terminal ileal and colonic Crohn's disease. Despite prolonged treatment with oral prednisolone he failed to thrive and between February 1979 and June 1980 he lost weight and failed to grow. He was referred to St Mark's Hospital in June 1980.

His height and weight were both below the third percentile. He was generally unwell, with pallor and oedema of both legs. Multiple perianal fistulae complicated severe anal Crohn's disease. He started treatment with azathioprine in addition to oral prednisolone, codeine phosphate and loperamide. Nasogastric feeding commenced with 8 cans Isocal and

additional supplements of iron, zinc and folic acid. He was discharged in September 1980 and continued to take 4 cans Isocal each night by nasogastric tube with resultant gain in weight and height. A recurrence of his Crohn's colitis and the development of a colo-vesical fistula was accompanied by a cessation of growth and weight gain and necessitated proctocolectomy in February 1981. Following a recovery complicated by pelvic abcess and vesico-cutaneous fistula formation, he has required no further nasogastric supplements and has exhibited excellent catch-up growth and weight gain which is shown in Figure 41.

I W dob 12.7.13

This lady developed severe diarrhoea and weight loss in 1976. Radiological investigation demonstrated ileocolonic Crohn's disease which proved resistant to medical therapy. In 1977 she underwent panproctocolectomy, and an ileostomy was fashioned. Although the entire small intestine remained, she had high volume losses which were resistant to anti-diarrhoeal treatment. She was referred to St Mark's Hospital in 1978.

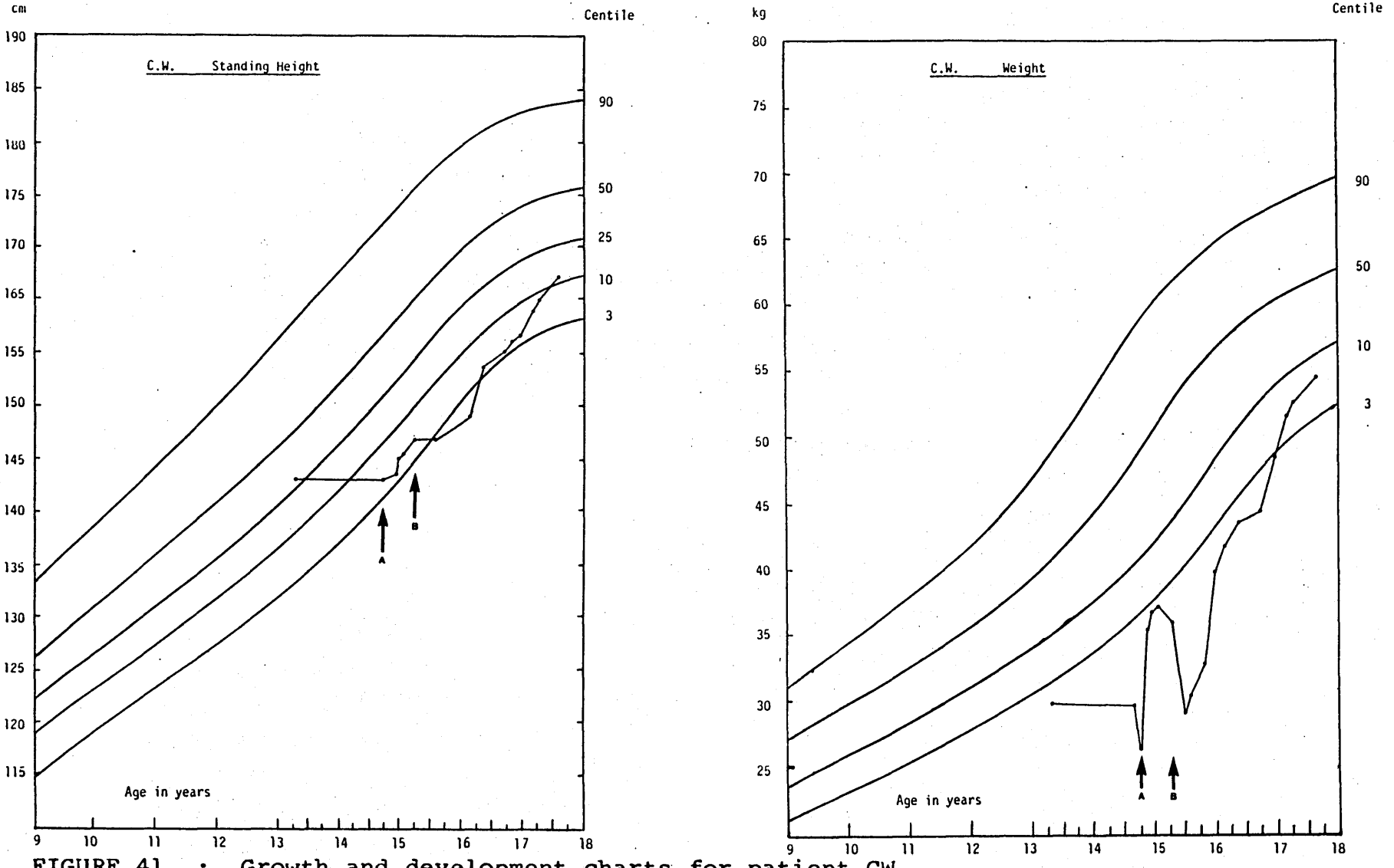


FIGURE 41 : Growth and development charts for patient CW.
Nasogastric supplements started at A, and continued to surgery at B.

Despite dietary manipulation and further medical treatment she continued to have troublesome ileostomy diarrhoea and leakage, which necessitated refashioning of the stoma in 1979. There was no evidence of recurrent small bowel Crohn's disease at operation. During 1980 she required periods of inpatient parenteral fluid replacement, but was finally stabilised using an oral glucose/electrolyte mixture and returned to the supervision of her local hospital.

M W dob 27.9.31

This lady first developed ulcerative colitis in 1961. Her disease ran a relapsing course over the next ten years during which she required intermittent, and latterly continuous treatment with sulphasalazine, and topical and oral prednisolone. She was referred to St Mark's Hospital for assessment in May 1971.

She was malnourished, with weight loss, hypocalcaemia and adrenal suppression. Her treatment was changed to intramuscular ACTH with good effect. Relapse of her colitis in November 1971 prompted elective colectomy and caecorectal anastomosis complicated by a postoperative pelvic haematoma and abcess formation. Following discharge she was troubled by frequent, loose stools

exacerbated by continuing inflammation in the rectum.

By April 1980 she had lost more weight secondary to poor dietary intake. Small bowel radiology, lactose tolerance and faecal fat excretion were all normal. Nasogastric feeding was commenced in June 1980 using 3 cans of Isocal each night. Abdominal discomfort and bloating were treated by reducing her nocturnal supplement to 2 cans Isocal until proctocolectomy and ileostomy was performed in October 1980. She has required no dietary supplements since operation.

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