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The Small Intestine and the effect of Partial Resection

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INTRODUCTION

One of the pleasures most of us enjoy is to partake in a good meal. The food arrives in the stomach and after a short delay enters the duodenum and small intestine. We call the duodenum by a separate name, but its function and histological appearance are similar to those of the remaining small intestine.

ANATOMY:

Length:

The small intestine commences above at the level of the ligament of Treitz at the duodeno-jejunal junction and ends below at the ileocaecal valve.

The length of the small bowel can be measured by applying a black silk suture along its anti-mesenteric border. In 14 adults who did not have any known intestinal disease I found that the mean length was 13 feet with a range between 8 to 26 feet. The surface area of the small intestine is much greater than its length and diameter would suggest. The surface area is increased by the prominent circular folds (*volvulae conniventes*), the finger-like villi and their microscopical projections, the microvilli. It has been estimated that the small bowel mucosa of an adult exceeds 2 million square centimetres. If the mucosal lining of the small bowel of one adult were to be unfolded, it would be sufficient to cover the ceiling, walls and floor space of this lecture theatre.

Fig. 1.—Villous morphology.

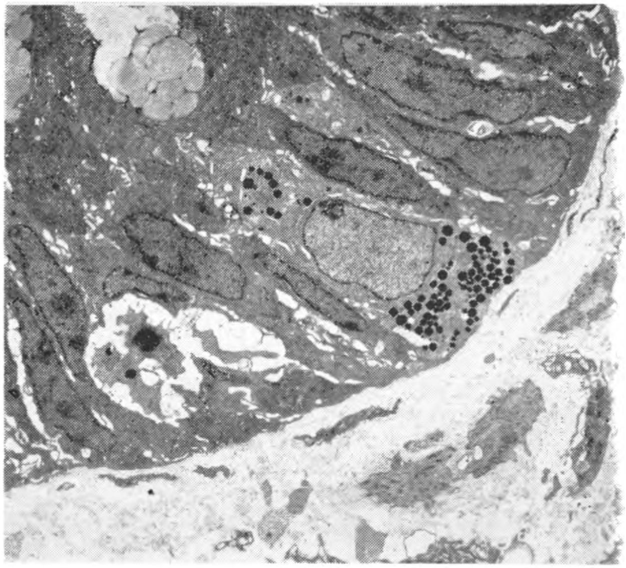

Fig. 2.—Electronmicroscopy of Argentaffin cell.

The intestine has three layers; a thin external serosal covering layer, a thick intermediate muscular layer and an inner mucosal layer. Looking at the inner surface of the small intestine we see that it has a fine, velvety appearance due to projection of its fine villi.

Histology:

Fig. 1 shows diagrammatically the villous morphology. The superficial part of the villus bathes in the intestinal juice, the succus entericus; the deep part is arranged into a crypt — the crypt of Lieberkuhn. The cells lining the villus are columnar and mucus-secreting goblet cells are interpersed between them. There are two other types of cells which are located in the base of the crypt — the Paneth cell and the Argentaffin cell.

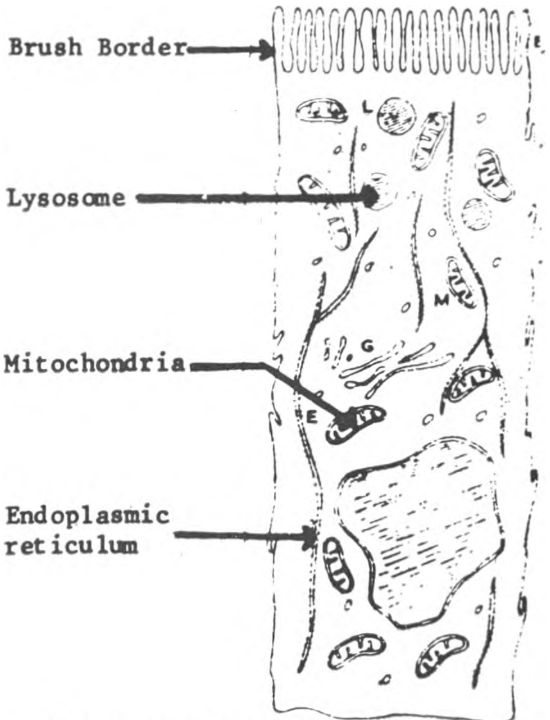

Fig. 3.—Electronmicroscopy of small bowel mucosa.

The Paneth cell is pyramidal in shape and contains a ribonucleoprotein and mucoprotein. The exact function of the Paneth cell is not known but in view of its chemical composition it is tempting to suggest that it may be related to protein metabolism. The second cell type, the Argentaffin cell, takes up silver stains (Figure 2). This cell may undergo malignant change to form the rare carcinoid tumour. Metatasis of a carcinoid tumour to the liver may produce a syndrome characterised by flushing, asthma-like attacks, diarrhoea and lesions involving the tricuspid and pulmonary valves of the heart.

Electronmicroscopy: (Figure 3).

The fine structures of the cell can be studied in detail under the electron microscope. The absorptive surface of the cell is increased by its numerous projections, the microvilli, which are most numerous in cells situated at the tips of the villi — in those sites where the greater part of absorption takes place. It has been estimated that there are about 1 000 microvilli per absorptive cell.

Immediately deep to the microvilli we see a band of filamentous material running in a perpendicular direction to the microvilli. These fibres constitute the terminal web. Within the cytoplasm, mitochondria, golgi apparatus, lysomes, endoplasmic reticulum and the nucleus are found.

The mitochondria are particularly numerous in cells that have an absorptive function. They contain the packets of energy required for the various metabolic processes in the cell (Figure 3).

The second inclusion organelle, the golgi apparatus, is situated supranuclearly and consists of non-granular, flattened channels and vacuoles. The golgi apparatus is thought to be associated with the synthesis of polysacharides, but may play a role in certain other absorptive processes in the cell.

The third organelle in the cyptoplasm is the lysosome which contains electrodense particles situated immediately below the brush border. Each lysosome is surrounded by a well-defined membrane.

Scattered throughout the cytoplasm is an open network of canals and cisterns known as the endoplasmic reticulum. The endoplasmic reticulum consists of two parts; the granular reticulum that contain ribosomes and the agranular reticulum that are without ribosomes. The ribosomes which are the main sites of protein synthesis are particularly prominent in Paneth cells.

The enzymes located in different organelles of the cytoplasm can be demonstrated by histochemical techniques (Figures 4 and 5).

Fig. 4.—Brush border enzyme leucine aminopeptidase stained histochemically with L-leucly-betanaphthylamine.

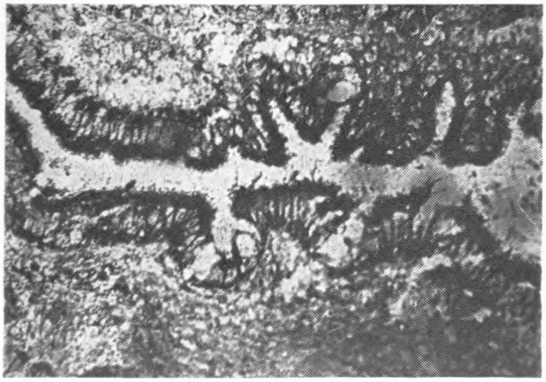

Fig. 5.—Mitochondrial enzyme succinate dehydrogenase stained histochemically by method described by Pearse (1967).

Autoradiography:

The study of division and movement of cells is known as cell kinetics. We can study the kinetics of cells lining the intestinal villi by autoradiographic techniques. In this method tritiated thymidine is injected into an animal. The thymidine component of tritiated thymidine is incorporated into the D.N.A. molecule of dividing cells. Tritium is a β emitter which shows up as a black granule on the autoradiograph.

Figure 6 shows an autoradiograph taken from the jejunum of a rat 2 hrs. after an injection of tritiated thymidine. The tritium has labelled the proliferative cells which are situated in the lower two-thirds of the crypt cells. The upper third of the crypt and the rest of the villus has failed to incorporate tritiated thymidine. These cells are mature adult cells which have lost their propensity to undergo cellular division.

The cells in the base of the crypt divide and march up along the villus length. If we take specimens of the bowel at longer intervals after thymidine injection we see that the advancing column of labelled cells progresses along the villus. Figure 7 shows an autoradiograph taken 48 hours after an injection of thymidine. The whole length of the villus, including its tip, has been labelled with tritium.

There are two measurements we can carry out with the aid of autoradiography:

1. Cell cycle time. (Fig. 8).
2. Cell turnover time.

Cell cycle time is the time taken for one cell to divide into two. In a study using 13 rats cell cycle time was found to be 14 hours. The second measurement cell turnover time is the time taken for a labelled cell to migrate up along the villus to reach the tip of the villus. The cell turnover time in the same group of animals was 43,5 hours.

PHYSIOLOGY

Knowledge of the morphology of the cell corresponds with studies of its physiological role. The main function of the small intestine is to regulate digestion and absorption of nutrients.

Borgström and his colleagues (1956) have shown that the absorption of a moderate amount of carbohydrate, fat and protein given orally takes place in the proximal 100 cms. of jejunum. Many authors have inferred from these findings that the jejunum is the more efficient site of nutrient absorption than the ileum. Dowling and Booth (1967) have shown that the absorption of glucose from the intact ileum was no less than that from the jejunum. The same authors interposed a segment of ileum between the duodenum and jejunum and demonstrated that the villi of the interposed ileum were significantly lengthened.

Comparison of proximal vs. distal resection.

The ileum can probably carry out all the functions normally attributed to the jejunum. Indeed, removal of the ileum produced more severe changes in nutrition than removal of an

Fig. 6.—Autoradiograph of section through mucosa of rat 2 hours after injection of tritiated thymidine.

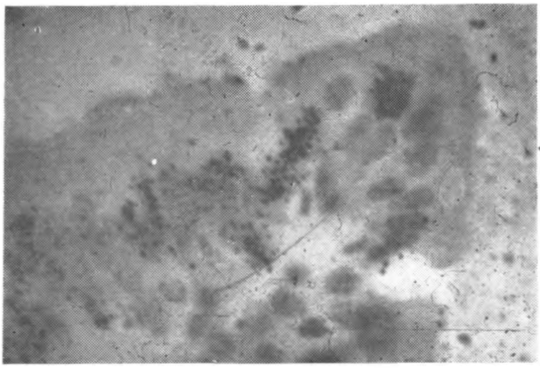

Fig. 7.—Autoradiograph of rat's small intestine taken 48 hours after injection of tritiated thymidine.

equal length of jejunum (Jensenius, 1945; Kremen *et al.*, 1954; Kalser, *et al.*, 1960; Nygard, 1966). We determined weight changes and fat balance studies in 14 dogs. (Wapnick, *et al.*, 1969a). Half the animals had a distal 75% resection and half had a proximal 75% small bowel resection (Figure 9). The dogs were weighed and fat balance studies carried out before and four weeks after small bowel resection. The fat results are shown in Figure 10. All dogs developed increased steatorrhoea and lost weight after small bowel resection. These changes were significantly ($p<0{,}01$) more severe after ileal resection than after jejunal resection.

The reasons put forward in explanation of why resection of the ileum produces greater weight loss and steatorrhoea than removal of an equal length of jejunum are as follows:

Firstly, these differences may be related to intestinal transit time. Transit time is more rapid in the jejunum than in the ileum (Ingelfinger and Abbot, 1940). Removal of the ileum would remove a portion of the alimentary tract in which food normally takes a longer period of time to pass through. Food would now remain in contact with the jejunal mucosa for a shorter period of time and digestion would be less complete than after ileal resection.

An alternative explanation for the observation that ileal resection produces a more severe form of malabsorption than proximal resection is that the ileum is the main site of bile salt absorption (Baker and Searle, 1960). Bile salts are required for the breakdown and absorption of fats. Removal of the ileum will reduce the reabsorption of bile salts and fats, whereas these changes are unlikely to occur after jejunal resection (Hofmann and Grundy, 1965). The third explanation offered is related to alterations in intestinal flora. After ileal resection the colon bacteria is brought into close proximity with the jejunum. Fourthly, ileal resection is frequently associated with the removal of the ileocaecal valve. Retention of the ileocaecal junction in man has been shown to minimise the degree of steatorrhoea which occurs following ileal resection (Kalser, 1960).

Endocrine aspects of the small intestine:

In addition to its role in nutrition, the small intestine functions as an endocrine organ. One of its hormones, secretin, the first to be isolated, is released from the duodenum and jejunum after the intake of a meal. This hormone stimulates the exocrine part of the pancreas to release a copious alkaline secretion.

The gut also releases a hormone which stimulates the beta cells of the pancreas to release insulin. Macintyre *et al.*, (1964) showed that the administration of glucose by the intrajejunal route produced a significantly higher blood insulin level and a significantly lower blood glucose value than when glucose was given at the same rate and concentration intravenously. Removal of part of the alimentary tract containing this insulinotrophic hormone should lower the insulin response to an oral glucose load.

Blood glucose and insulin levels were determined in 22 control and 10 patients who had undergone a partial resection of the small intestine. Insulin levels were determined one and two hours after an oral (50g) glucose load. On a separate day these measurements were repeated before and 5 minutes after an intravenous (25g) glucose load. The glucose and insulin measurements were determined by Professor J. Jones of the Department of Physiology. There was a significantly greater ($p<0{,}05$) rise in blood sugar but no significant rise in blood insulin levels in the patients who had undergone resection of the small intestine as

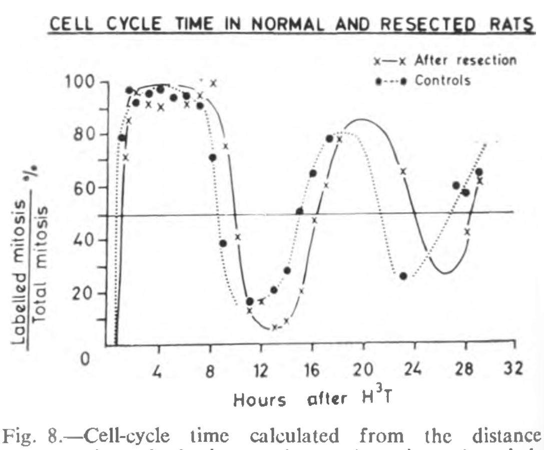

Fig. 8.—Cell-cycle time calculated from the distance along the horizontal line at the points where it is intersected by the ascending limb of the first and descending limb of the second curve.

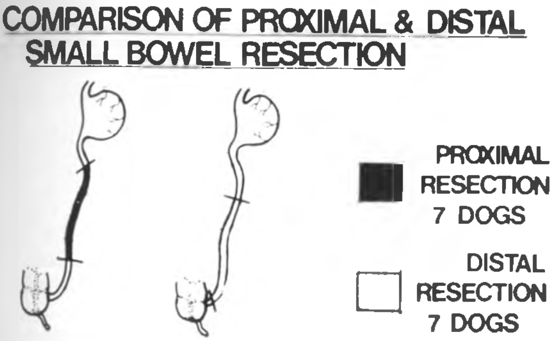

Fig. 9.—Small bowel resection in dogs.

compared with the controls. Patients who had had a major resection showed a significantly lower ($p<0,05$) rise in blood insulin after intravenous glucose as compared with the controls. The lowering of the oral response to glucose may be attributed to part removal of gut insulinotrophic hormone, but alternatively, it could be due to the diminished sensitivity of the pancreas to release insulin following the absorption of glucose by the gut.

Insulin increase following the introduction of intraluminal glucose administration was studied in 10 rabbits. The animals were anaesthetised with saggital (Nembutal). In half a jejunal, and in the remainder an ileal recirculating loop (measuring 15 cms.) was constructed (Figure 11).

Blood was taken for fasting glucose and insulin estimation and glucose (2g/Kg weight) was introduced into the recirculating loop of the anaesthetised animal. Further samples of blood were taken one hour afterwards. Four of the rabbits with jejunal loops and one with an ileal loop showed a rise in blood insulin. The mean change in insulin of the rabbits who had a jejunal loop was not significantly different from that of the controls.

Although the ileum can carry out all the known functions of the jejunum, it has certain unique characteristics and is the main site of vitamin B12 and bile salt absorption.

SMALL BOWEL RESECTION

The small intestine has a complex morphology and physiology. This organ is essential for the maintenance of life. We can successfully remove the oral cavity, oesophagus, stomach, colon and rectum, and yet keep our patient in good nutritional state. However, removal of the greater part of the small intestine leads to malabsorption and, if severe, death may ensue.

I have prospectively studied 24 patients who have had a limited or a major resection of the small intestine at Harari Hospital between June, 1969 and April, 1971. In all cases at least 10 inches of bowel was resected. Two patients with volvulus had a jejunal resection and 22 had an ileal resection. Six patients were females and 18 were males. The majority of patients were between 20-40 years of age.

The greater number of cases required a resection of the small bowel for gangrene due to ileosigmoid volvulus (compound volvulus). In this condition the ileum and sigmoid colon are knotted around each other. The operative findings in a patient with this condition are shown in Figure 12. In this patient 16 feet of gangrenous bowel was removed.

Table 1

Reasons for carrying out small bowel resection

	No. of cases
Volvulus	18
Tumour	2
Hernia	2
Adhesions	1
Trauma	1
	24

Indications for small bowel resection:

The various conditions for which a resection of the small intestine was performed are shown in Table 1. There were two patients in this series who had developed an intussusception associated with a small bowel tumour, two had a strangulated

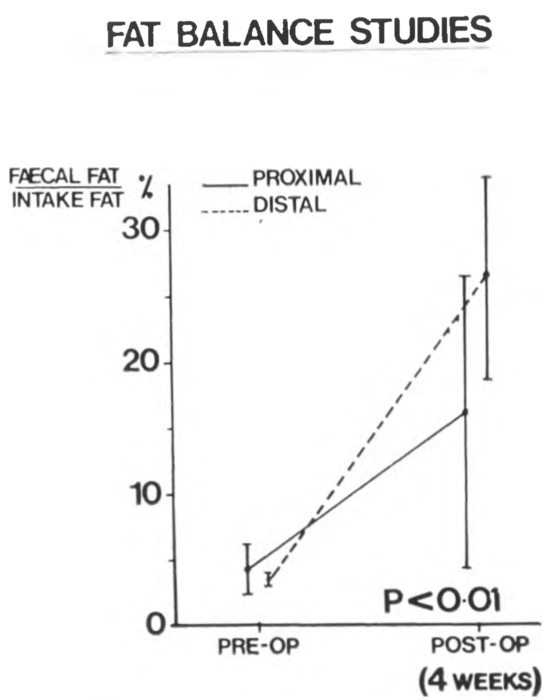

Fig. 10.—Fat balance studies after proximal and distal small bowel resection.

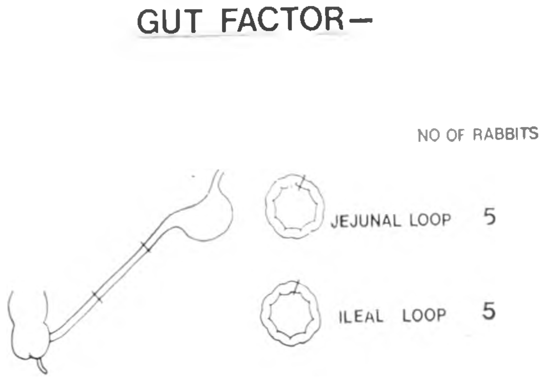

Fig. 11.—Recirculating loops in rabbits constructed for glucose studies.

hernia, one who had adhesions and one who had sustained a blunt injury to the abdomen. This series differs from similar reviews in Britain where Crohn's disease and mesenteric infraction constitute the common conditions requiring small bowel resection.

I have divided the patients into three main groups according to the extent of the resection (Table 2):

Six patients had undergone a minor resection involving less than 3 feet of small bowel; 5 had had a moderate resection whereby 3-10 feet of bowel was removed, and 13 had undergone a major resection requiring the removal of more than 10 feet of small intestine.

Table 2

Extent of small bowel resection

	No. of cases
Minor (<3 feet)	6
Moderate (3-10 feet)	5
Major (>10 feet)	13
	24

Clinical Features:

The main clinical features which occur following small bowel resection are shown in Table 3. The majority of patients lose weight and complain of diarrhoea. Many patients show a disturbance of carbohydrate, fat and protein metabolism. Dehydration may occur and some patients develop electrolyte and mineral disturbances.

Carbohydrate Metabolism:

Carbohydrate metabolism is usually studied by means of a glucose tolerance study. In a review of 93 cases of small bowel resection in the literature,

Table 3

Clinical features following small bowel resection
- Diarrhoea
- Loss of weight
- Interference in metabolism
  - Carbohydrate
  - Protein
  - Fat
  - Water, Electrolytes, Minerals
- Anaemia

a glucose tolerance study had been carried out in 13. Glucose tolerance was impaired in six patients and normal in seven. All the patients with a flat curve had less than 30 cms of residual bowel. In the present series glucose tolerance studies were performed in 15 patients. It was normal in 13 patients. Impaired glucose tolerance was seen in two patients, both of whom had undergone a major resection and suffered from severe malabsorption. Xylose absorption studies carried out in 8 patients was impaired in 5

Protein Metabolism:

Protein absorption may be studied indirectly by estimation of the serum albumin. The normal serum albumin value varies between 3,4-4,7 g. per 100 cc. of plasma. In 7 patients who had undergone a more limited resection it was 3,3 mg. In the patients who had undergone a major resection, the mean serum albumin value was 2,7.

One patient admitted under Mr. Fleming is of particular interest. This patient had undergone a major resection of the small intestine 9 months prior to admission to Harari Hospital. He complained of severe weight loss and his serum albumin was only 0,8g. He demonstrated some of the typical features seen in adults with kwashiorkor; skin pigmentation, cheilosis with reddening and softening of the hair.

Fig. 12.—Gangrene of 16 feet of ileum in a patient operated upon for ileosigmoid volvulus.

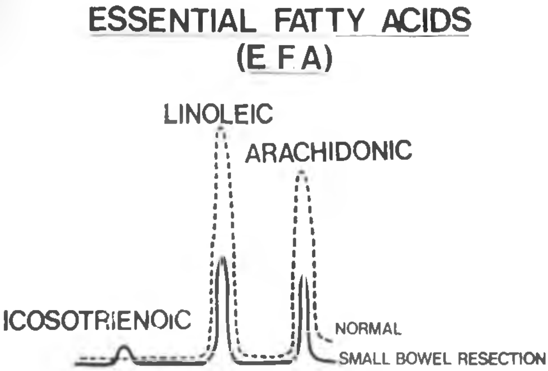

Fig. 13.—Electrophoretic pattern of essential fatty acids (diagrammatic).

Fat Metabolism:

The third main constituent in the diet is fat. A defect in fat absorption is usually shown by fat balance studies, or if these cannot be carried out, then by measurements of faecal fats over a 3-day period. In 5 patients who had undergone a major resection, faecal fat measurements were carried out. The normal range is lower than 6g. per 24 hours. The mean faecal fat estimation in these patients was 22,8g/24 hours.

The essential fatty acids, arachidonic, linoleinic and icosotrienoic can be measured in the blood by gas chromatography. An increased ratio of icosotrienoic/archidonic above 4 is suggestive of essential fatty acid deficiency. Figure 13 shows a diagrammatic representation of a typical electrophoretic pattern of a control patient and a patient who had previously undergone a major resection of the small intestine. The fatty acid measurements were performed by Dr. Norden and Miss Patterson of the Department of Biochemistry, (U.R.). The medium value of the ratio referred to above was significantly higher ($p<0,05$) in patients submitted to a previous resection of the small intestine as compared with the controls.

Water absorption following small bowel resection:

Water absorption may be severely impaired after small bowel resection and marked dehydration may ensue. Water absorption following small bowel resection does not appear to have been studied in detail previously. Failure to absorb adequate amounts of water can be studied by the Kepler Power test. The amount of urine collected over a four-hour period following the intake of a litre of water is determined.

Urinary excretion was significantly lowered ($p<0,002$) in 13 patients who had undergone a major resection of the small intestine as compared with 11 healthy controls.

Water absorption was studied further in seven goats who underwent a distal small bowel resection and five control animals who underwent laparotomy, but in whom a resection was not performed. Body weight, serum renin and plasma volume were measured before and again six weeks after operation. Renin was measured in the Department of Physiology (U.R.) using a bioassay and blood volume was determined by injection of iodinated albumin. Renin, a hormone released from the juxtaglomerular apparatus of the kidney is increased in the blood when blood volume in decreased, serum sodium is raised, and in conditions which lead to secondary alsosteronism. Goats who had undergone a resection of the small intestine lost weight, showed a fall in blood volume and a rise in serum renin.

Changes in electrolytes, calcium and magnesium:

In addition to showing clinical and biochemical evidence of dehydration, patients who had undergone major resection of the small intestine often had deranged serum electrolytes with hypoalbuminaemia and hypomagnesaemia. Hypocalcaemia is not infrequently encountered in the early stages after major small bowel resection (Pietz, 1956) and may lead to tetany and later cause oesteoma-

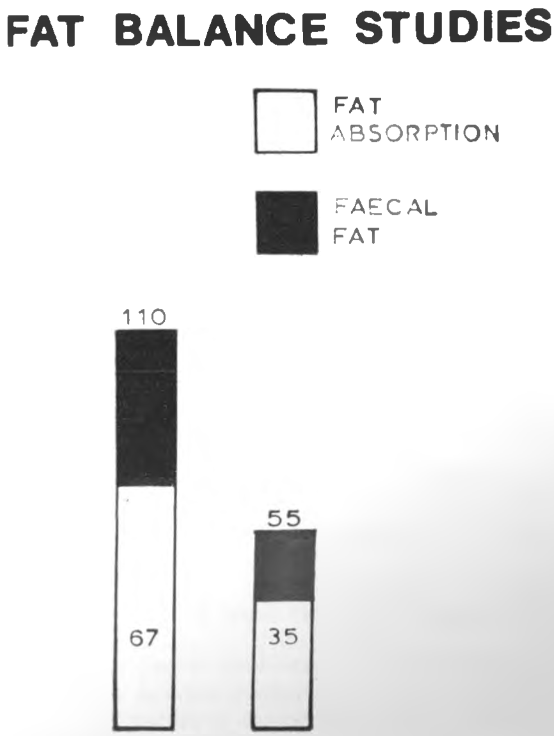

Fig. 14.—Fat balance studies reported in the literature. The left taller block represents fat absorption after a high fat diet and the shorter right block after a low fat diet.

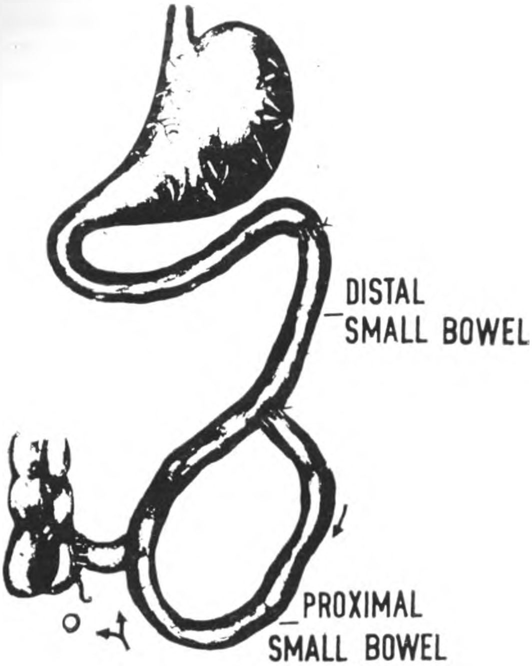

Fig. 15.—Recirculating loop.

lacia. In those patients who are likely to develop calcium deficiency magnesium deficiency should also be excluded (Fletcher *et al.*, 1960).

Anaemia is a fairly common finding following small bowel resection. The fall in haemoglobin may be attributed to iron, folic acid or vitamin B12 deficiency. The majority of patients in this series had normal serum Fe measurements. Vitamin B12 is absorbed exclusively in the terminal ileum. Vitamin B12 absorption was studied in patients following the oral administration of radioactive cyanocolamin. Serum was collected eight hours afterwards, and the measurements, using a scintillation counter, were carried out by Mr. J. Stiema in the Department of Medicine of the University of Rhodesia.

All the patients who had undergone a previous major or moderate resection of the ileum showed marked impairment of vitamin B12 absorption.

Management following small bowel resection:

Patients who had previously undergone a major resection of the small intestine required careful and constant medical supervision. Treatment was directed at early detection and correction of the various metabolic changes discussed above. Diarrhoea is often troublesome after operation, but it can usually be controlled by the use of drugs such as kaolin, Lomotal, isogel or codeine. Patients in Africa who have undergone a resection of the small intestine are particularly sensitive to milk as many show alactasia (Wapnick, 1972). These patients can often tolerate larger amounts of sour rather than fresh milk (Wapnick, 1972).

The diet should be high in carbohydrate, protein, minerals and calories. It has been taught that fats should be given in minimal amounts to patients suffering from steatorrhoea following small bowel resection. From an extensive review of the literature (Wapnick, 1971b) as well as experimental evidence (Wapnick *et al.*, 1969a) (Figure 14) it is felt that the traditional concept of insisting that these patients take a diet of very low fat content requires further evaluation. Pinter *et al.*, (1969) concluded that diets of a low fat content are frequently unacceptable to patients. These authors found that their patients gained weight, showed less diarrhoea and less severe creatorrhoea and steatorrhoea when medium chain fatty acids were substituted for dietary fat.

In some patients conservative methods proved to be inadequate in maintaining satisfactory nutrition following small bowel resection, and revisional surgical procedures may have to be considered. In 1868, Nicoldani suggested that a loop of bowel should be interposed in an antiperistaltic direction between the distal small intestine and the colon. Hammer *et al.*, (1959) carried out this procedure in dogs and found that it was of some value. I have reviewed 18 cases where this procedure had been followed up and reported in the literature. The authors claimed that some benefit was noted in the majority of them. The function of the reversed segment of bowel is that it acts as a partial brake on the rapid intestinal passage of food. The second method which has been tried is to construct the residual bowel into a recirculating loop (Altman and Ellison, 1965) (Figure 15). The food recirculates several cycles in the loop before passing on into the colon. This operation has been carried out on two occasions in man with apparent success. Frederick *et al.*, (1965) found that vagotomy and drainage reduced weight loss and malnutrition in these patients.

The exact value of these operations is limited, and some have stated that they are of no proven value. May (1966) points out that many patients show clinical improvement following small bowel resection. Functional improvement following small bowel resection has been shown to occur in animals (Stassof, 1914; Dowling and Booth, 1967; Wapnick *et al.*, 1969b).

The author is engaged at present in an experiment to try and lengthen the available surface area of the small intestine. In a previous study Wapnick (1971) showed that it was possible to graft mucosa to ectopic sites and suggested (Wapnick, 1972) that this procedure could possibly be combined with the mucosal eversion operation suggested by Cywes (1972). The author is at present investigating the possibility of constructing a colon tube lined by small bowel mucosa. It is hoped that such a procedure may be of possible value to those patients who cannot maintain satisfactory nutrition following small bowel resection.

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