

THE METABOLIC EFFECTS OF INTESTINAL RESECTION IN MAN

C. C. BOOTH, M.D., M.R.C.P.

Physician and Lecturer in Medicine, Postgraduate Medical School of London, London, W.12

UNTIL recently, relatively little was known of the normal functions of different segments of the small bowel, and the metabolic effects of intestinal resection were therefore imperfectly understood. It is now recognized, however, that the small intestine, like the renal tubule, has specific functions in different parts of its length and it is possible, knowing the sites at which different substances are normally absorbed, to predict what pattern of malabsorption will follow a given resection. The deficiency states which are likely to occur may then also be predicted and appropriate treatment given.

For these reasons this paper first outlines some aspects of the physiology of the small intestine, emphasizing particularly the sites at which different food substances are absorbed. The effects of either proximal or distal resection on the anatomy and function of the remaining small intestine will then be described. An account is given of the deficiency states which may follow resection of different segments of the small intestine and treatment is also discussed.

Physiological Considerations

(1) *Rate of Intestinal Transit*

In mammals the rates of transit of the intestinal contents through the proximal and distal small intestine are different. The jejunum is an active organ showing vigorous peristalsis and substances therefore pass through it rapidly. The ileum, on the other hand, is sluggish and transit through the distal small intestine is slow. In the rat, for instance, substances pass through the proximal half of the small intestine in as short a time as 15 minutes, but may then take a further 90 minutes or more to pass on into the colon (Reynell and Spray, 1956; Booth, 1958). Studies of intestinal radiology and motility have shown that there is a similar although less marked difference in the transit of substances through jejunum and ileum in man.

(2) *Sites of Absorption in the Small Intestine*

Two factors decide the sites at which absorption of different substances occurs in the small intestine.

The first is the relationship between rate of absorption and upper intestinal motility. The second factor is the location of specific transport mechanisms in specific segments of the intestine.

The vigorous motility of the upper intestine plays a large part in determining where different substances are absorbed. If a substance is taken up rapidly by the intestinal mucosa, absorption is bound to occur from the proximal intestine after oral administration. On the other hand, if absorption occurs more slowly than transit through the jejunum, the substance will be propelled into the ileum by the active upper intestine before absorption is complete (Parkins, Dimitriadou and Booth, 1960). Studies in both experimental animals and in man have shown that glucose, iron and some water-soluble vitamins (such as folic acid, riboflavin, pyridoxine and ascorbic acid) fall into the first category. Although these substances can be absorbed from the distal as well as the proximal small intestine, absorption normally occurs relatively rapidly; this therefore happens in the duodenum or jejunum and absorption is usually complete before the ileum is reached (Fig. 1) (Verzar and McDougall, 1936; Hahn, Bale, Ross, Balfour and Whipple, 1934; Cox, Meynell, Cooke and Gaddie, 1958; Booth and Mollin, 1960a; Spencer and Zamchek, 1961; Booth and Brain, 1961; Stewart and Booth, 1961). Fat and protein, however, require digestion before absorption can occur, and these substances are absorbed more slowly. Although they are absorbed to a large extent in the jejunum (Frazer, 1943; Borgström, Dahlqvist, Lundh and Sjövall, 1957; Turner, 1958), their slower absorption allows the motility of the proximal intestine to propel them more distally before absorption is complete and some absorption therefore also occurs from the ileum (Fig. 1) (Parkins and others, 1960; Booth, Read and Jones, 1961; Booth, Alldis and Read, 1961).

The second factor of importance in determining the site of absorption is the distribution of transport mechanisms in different parts of the small intestine. Vitamin B₁₂ is unique in requiring an intrinsic factor secreted by the stomach to pro-

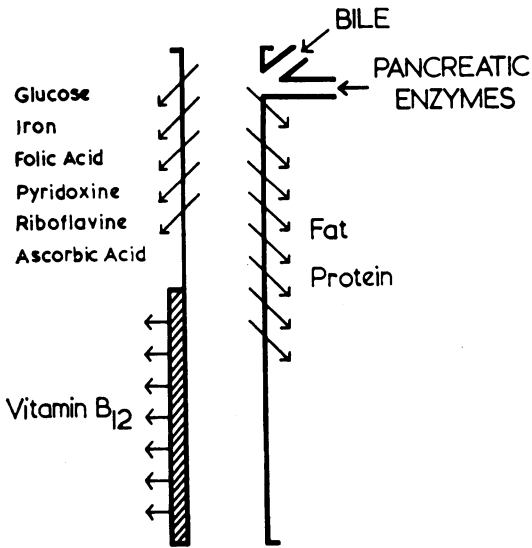


FIG. 1.—Diagrammatic representation of the sites of absorption in the small intestine.

mote its absorption (Berk, Castle, Welch, Heinle, Anker and Epstein, 1948), and it is also unique among the vitamins in that the transport mechanisms which ensure its absorption are localized to the ileum. Under physiological conditions vitamin B₁₂ is therefore specifically absorbed in the ileum in man (Fig. 1) (Booth and Mollin, 1959). The only other substances for which a specific site of absorption has hitherto been demonstrated are the bile salts. *In vitro* studies of rat and guinea pig intestine suggest that the transport of glycocholate and taurocholate may be localized to the distal ileum (Lack and Weiner, 1961). It is therefore possible that bile salts may prove to be reabsorbed in a comparable area in man.

(3) The Concept of Intestinal Reserve

Like other vital organs such as the liver and kidney, the small intestine has a remarkable functional reserve. The rat, for instance, is capable of absorbing more than 100 times its dietary requirement of pyridoxine (Booth and Brain, 1961) and there appears to be virtually no limit to the absorption of this water-soluble vitamin in man (Brain and Booth, 1961). This capacity of the small intestine to absorb increasing and unlimited amounts of such water-soluble vitamins is a function of the jejunum, for even when very large doses of either pyridoxine or ascorbic acid are fed, the ileum plays little part in absorption (Booth and Brain, 1961; Brain and Booth, 1961; Stewart and Booth, 1961).

The absorption of large amounts of fat, on

the other hand, cannot be achieved entirely by the jejunum. When increasing amounts of fat are given to normal individuals, there is a progressive increase in absorption and even when diets containing as much as 350 g. of fat are fed, more than 340 g. are absorbed (Wollaeger, Comfort and Osterberg, 1947; Annegers, Boutwell and Ivy, 1948). Although the jejunum plays an important part in absorbing such remarkable amounts of dietary fat, studies in both experimental animals and in man indicate that the ileum absorbs progressively more fat as the dietary fat is increased (Booth, Read and Jones, 1961; Booth, Alldis and Read, 1961). The jejunum is undoubtedly of major importance and as with pyridoxine and ascorbic acid, responds to an increased dietary load with an increased absorption, but as the dietary fat is increased more and more escapes the jejunum and passes on into the ileum to be absorbed there. The ileum is therefore an important part of the functional reserve of the small intestine for the absorption of fat.

Vitamin B₁₂ behaves quite differently. In contrast to the substances already discussed, there is a striking limit to the amount of this essential nutrient which can be absorbed at any one time through the physiological intrinsic factor mechanism. Even when test doses of as much as 50 μ g. of vitamin B₁₂ are given, absorption is limited to between 1 and 2 μ g. (Glass, Boyd and Stephanson, 1954), and this limitation of absorption is not due to inadequate intrinsic factor secretion. Under physiological conditions the amount of B₁₂ which can be absorbed by the intestinal transport mechanisms in the ileum is therefore only just enough to satisfy the daily requirements and there is virtually no functional reserve. It is possible, however, to overcome this limit to absorption by giving very large and unphysiological doses of crystalline B₁₂ (Ross, Mollin, Cox and Ungley, 1954). Under these circumstances absorption probably occurs by diffusion and is not mediated by the physiological intrinsic factor mechanism. Such absorption occurs indiscriminately from the nasal mucosa (Monto, Rebuck and Brennan, 1953), from the rectum (Ross and others, 1954), or in the dog from the duodenum although not from the stomach (Rosenthal and Hampton, 1955). Absorption of such large and unphysiological amounts of crystalline B₁₂ can occur from the jejunum in man and does not require the specialized transport mechanism in the ileum.

Radiological Studies after Resection

(1) Intestinal Transit Time

Since there is a difference between the motility of the proximal and distal small intestine, the

TABLE I

NATURE OF INTESTINAL LESION AND INTESTINAL TRANSIT TIME IN PATIENTS WITH DISTAL (CASES 1 TO 9) OR PROXIMAL (CASES 10 AND 11) RESECTIONS

Case No.	Age	Nature of Intestinal Lesion*	Intestinal Transit Time†
1	36	Right hemicolectomy and resection of terminal 6 ft. of ileum (pathological specimens measured)	2 hours
2	30	Resection of terminal 6 ft. of ileum and cæcectomy (pathological specimens measured)	15 minutes
3	40	Right hemicolectomy and resection of 10 ft. of ileum (pathological specimens measured)	2 hours
4	48	Right hemicolectomy and resection of all but proximal 6 ft. of jejunum (surgical estimate)	30 minutes
5	30	Right hemicolectomy and resection of all but proximal 6 ft. of jejunum (surgical estimate)	20 minutes
6	25	Right hemicolectomy and resection of all but proximal 4 ft. of jejunum. <i>Side-to-side</i> jejunocolic anastomosis (surgical and radiological estimate)	30 minutes
7	25	Right hemicolectomy and resection of all but proximal 3 to 4 ft. of jejunum (surgical and radiological estimate)	30 minutes
8	1	Resection of approximately two-thirds of distal small intestine—30 in. of proximal jejunum remaining (measured at laparotomy)	30 minutes
9	80	Resection of ascending colon and all but proximal 8 in. of jejunum (measured at autopsy)	5 minutes
10	71	Resection of proximal 8 ft. of jejunum (pathological specimen measured)	4 hours
11	1	Resection of all small intestine but for distal 15 in. of ileum. <i>Gastro-ileal</i> anastomosis (surgical and radiological estimate)	1½ hours

* Method of estimating extent of intestinal resection is indicated in brackets.

† Intestinal transit time is the time after feeding at which barium reached the colon. Normal limits vary considerably, but are usually between 2 and 6 hours.

rates of transit after resection of proximal or distal bowel are different. There are limitations to barium follow-through studies in assessing intestinal transit time, and although they have proved valuable for this purpose after resection in experimental animals (Booth, Evans, Menzies and Street, 1959), the results given in Table I suggest that such studies, although useful, should be interpreted with caution in man. This Table records the times after feeding barium at which the radio-opaque material reached the colon in a group of patients who had undergone resection of either proximal or distal small intestine.

As might be expected, the transit of barium through the residual small intestine was more rapid in the patients with the distal resections (Cases 1 to 9, Table I), and the rate of transit was usually most rapid in those with the most extensive resections. After resection of only 6 or 8 ft. of the terminal ileum, for instance, barium took 2 hr. to reach the colon in one patient (Case 1, Table I), and when the resections were more extensive, leaving only 4 or 6 ft. of the proximal jejunum, the intestinal transit time was invariably more rapid, being 20 or 30 min. (Cases 4 to 7, Table I). In one patient in whom only 8 in. of the proximal jejunum remained, barium had appeared in the colon as early as 5 min. after feeding (Case 9, Table I). However, the relationship between intestinal transit and extent of resection was not

invariably so direct, for there was another patient with a resection of only 6 ft. of the terminal ileum whose intestinal transit time was as fast as 15 min. (Case 2, Table I).

After resection of 8 ft. of the proximal jejunum, on the other hand, barium took 4 hr. to reach the colon, a normal transit time (Case 10, Table I); and in a child with only 15 in. of the terminal ileum remaining, the transit time through the sluggish ileal segment was as long as 1½ hr. (Case 11, Table I).

(2) Radiological Appearances

It is usually claimed that there is 'compensatory hypertrophy' of the intestinal remnant after resection (Flint, 1912; Jackson, 1958). However, such hypertrophy has not always occurred and a number of cases have been recorded in which there was no enlargement of the remaining intestine (Shonyo and Jackson, 1950; Shelton and Blaine, 1954). In experimental animals it has been shown that hypertrophy may follow proximal resection (Booth and others, 1959) but does not follow distal resection (Jensenius, 1945; Booth and others, 1959), and is therefore unlikely to be 'compensatory' to loss of intestinal length. Fig. 2 illustrates that even as long as five years after resection of all but the proximal 4 ft. of the small intestine (Case 7) there may be no radiological enlargement of the intestine that remains.

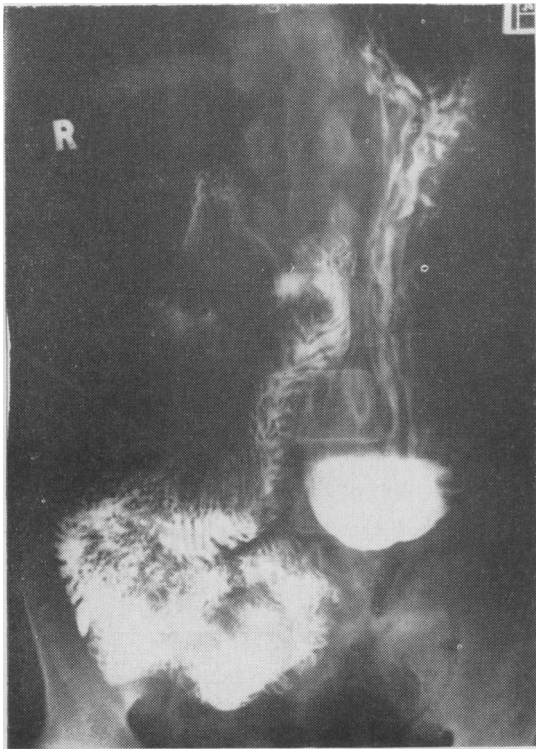


FIG. 2.—Barium follow through examination five years after resection of all but the proximal 4 ft. of jejunum showing no hypertrophy of residual small intestine (Case 7).

Laws and Pitman (1960) have pointed out that in all but the most massive resections radiological evidence of dilatation of the remaining small intestine is more likely to be due to obstruction than compensatory hypertrophy. However, the presence of fluid levels in both small and large bowel on films taken in the erect position does not necessarily indicate obstruction. After extensive distal resections, the intestinal contents are bulky, contain variable amounts of fat and are fluid, giving the characteristic appearance of fluid levels in erect films (Case 7, Fig. 3). These are merely a reflection of the fluid nature of the intestinal contents. Misinterpretation of the significance of fluid levels on plain abdominal X-ray films may lead to an unnecessary laparotomy.

An end-to-end anastomosis between small and large intestine usually proves entirely satisfactory, but stricture at the site of anastomosis is particularly liable to follow resection for Crohn's disease and sometimes occurs after resection for ileal tuberculosis. Although side-to-side anastomoses may sometimes be unavoidable at difficult emergency operations when extensive

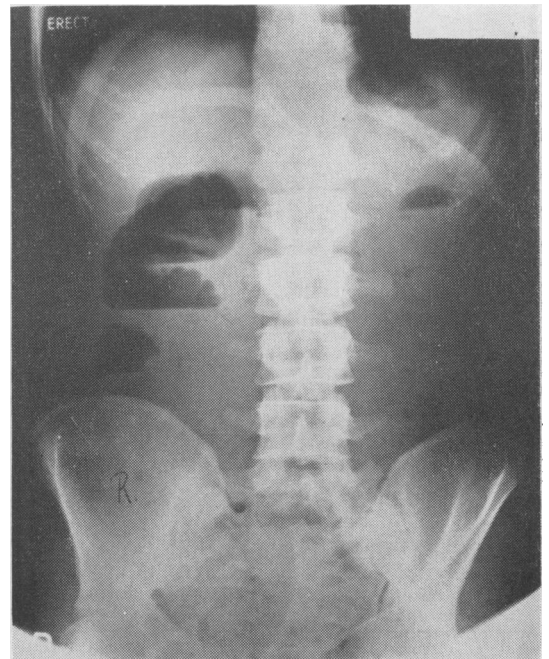


FIG. 3.—Fluid levels on erect films after resection of all but proximal 4 ft. of jejunum (Case 7). (From Laws and Pitman, 1960.)

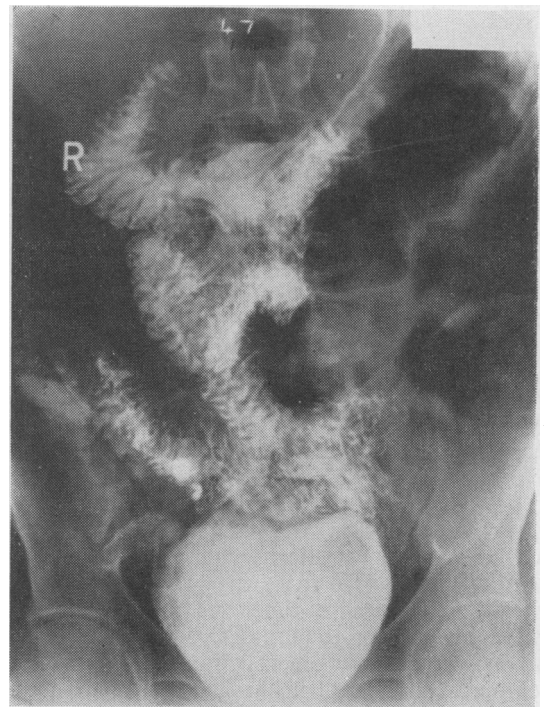


FIG. 4.—Large blind loop of terminal small intestine following side-to-side jejunocolic anastomosis (Case 6). (From Laws and Pitman, 1960.)

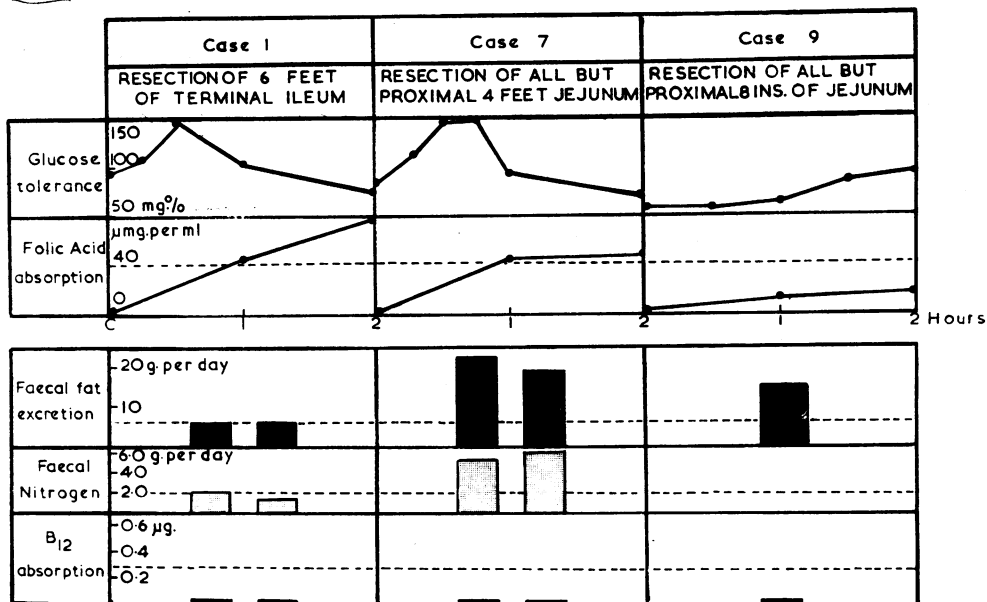


FIG. 5.—Intestinal function tests after resection of varying amounts of distal small intestine. Serum folic acid concentration should normally achieve a level of more than 40 µmg. per ml. after an oral test dose (Chanarin, Anderson and Mollin, 1958). Normal faecal fat excretion should be less than 6 g. per day and faecal nitrogen less than 2 g. daily. Control subjects absorb more than 0.28 µg. of radioactive vitamin B₁₂ from an oral dose of 1 µg. (Mollin, Booth and Baker, 1957). (Data from Booth and Mollin, 1960a.)

resections are carried out, they almost invariably result in the development of a large antiperistaltic intestinal loop caused by dilation of the blind end of small intestine immediately distal to the anastomosis (Case 6, Fig. 4). The dangers and disadvantages of such loops are well known.

Intestinal Function Tests after Resection
(1) *Distal Resections*

Since vitamin B₁₂ is absorbed in the ileum in man, resection of the ileum results in malabsorption of vitamin B₁₂. The precise amount of ileum which must be resected in order to cause B₁₂ malabsorption probably varies in different individuals. In general, however, B₁₂ absorption is invariably subnormal if 6 ft. or more have been removed (Booth and Mollin, 1959). The extent to which there is malabsorption of other substances depends on the extent of the intestinal resection. Details of the patients with distal resections described below have been given by Booth and Mollin (1960 a and b), who have classified these patients in three groups.

Group 1. In the first group are patients who have undergone resection of 6 or 8 ft. of the ileum. Such patients may fail to absorb B₁₂ but show no interference with the absorption of other

substances. An example of this type of malabsorption is illustrated in Fig. 5 (Case 1).

CASE 1

This patient was a young woman who had undergone a resection of approximately 6 ft. of the ileum, together with the ascending colon for Crohn's disease. A laparotomy performed for other reasons six years later revealed no active intestinal disease and a well-functioning end-to-end ileo-transverse anastomosis. Intestinal function tests (Fig. 5) showed that she absorbed glucose and folic acid normally. She had no steatorrhœa and the faecal nitrogen was normal. However, her absorption of vitamin B₁₂ was subnormal and this absorption defect was not corrected by preliminary treatment with chlortetracycline (Fig. 5). This is an example of an ileal resection causing an isolated absorption defect for vitamin B₁₂.

Group 2. The second group of patients have undergone more extensive resection of the distal small intestine. In these patients there is steatorrhœa in addition to malabsorption of vitamin B₁₂, but glucose and other water-soluble vitamins may be absorbed normally. The results of the intestinal function tests in such a patient are also illustrated in Fig. 5 (Case 7).

CASE 7

This patient, a young man aged 24, had undergone a

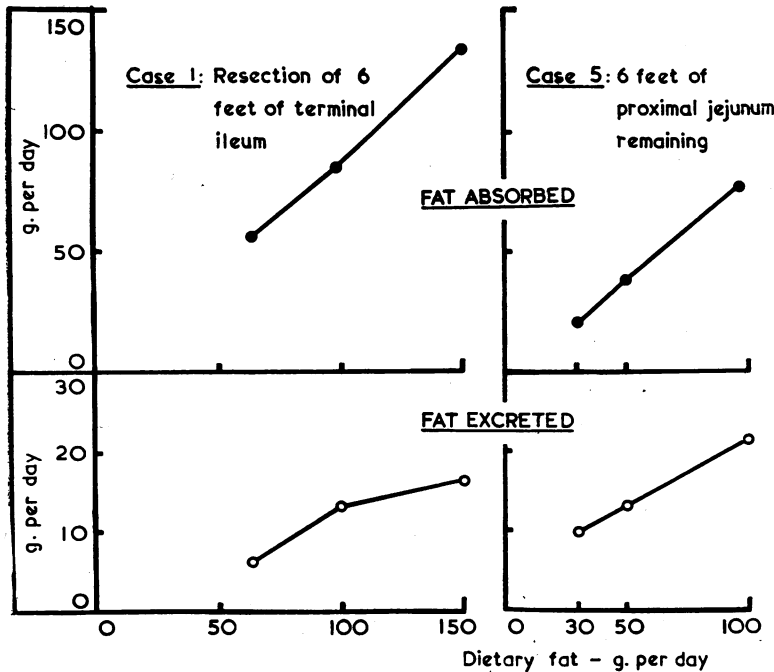


FIG. 6.—Effect of increasing dietary fat on faecal fat excretion after distal resection. Each point represents the mean daily fat absorption or excretion during successive six-day balance periods. (From Booth, Alldis and Read, 1961.)

resection of all the small intestine, but for the proximal 4 ft. of the jejunum an end-to-end jejuno-colic anastomosis had been performed. Since he had some residual proximal intestine he was able to absorb glucose and folic acid normally (Fig. 5). Other studies, not included in the figure, showed that he also absorbed normal amounts of ^3H -labelled pyridoxine and ascorbic acid. However, he had marked steatorrhœa, less than 70% of the dietary fat being absorbed. He also excreted between 5.4 and 6.6 g. of nitrogen in his stools, suggesting malabsorption of protein, and he was unable to absorb vitamin B_{12} (Case 7, Fig. 5). The absorption defect in this patient was therefore limited to vitamin B_{12} , fat and protein.

Group 3. The third type of malabsorption is illustrated by a patient who had undergone a massive intestinal resection (Fig. 5, Case 9).

CASE 9

This patient was an elderly lady who developed gangrene of the bowel as a result of mesenteric artery thrombosis. All the small intestine except the duodenum and proximal 8 in. of the jejunum was resected, end-to-end anastomosis being performed between the jejunum and the transverse colon. The results of the intestinal function tests, carried out six months post-operatively, are shown in Fig. 5 (Case 9). This patient's resection was so massive that there was not only steatorrhœa and failure to absorb vitamin B_{12} , but also interference with the absorption of glucose and folic acid (Fig. 5).

Effect of increasing dietary fat after distal resection. Since the ileum is an important part of the functional reserve of the small intestine for the absorption of fat, patients who have undergone distal resections are not able to tolerate large

amounts of dietary fat. When the fat intake is increased, increasing amounts of fat are excreted in the fœces and the resulting steatorrhœa may cause severe diarrhœa. This is illustrated by the results in two patients shown in Fig. 6.

CASE 1

The first patient was the lady who had an isolated absorption defect for vitamin B_{12} and no steatorrhœa when receiving a 60-g. fat diet. When the fat intake was increased the residual proximal intestine responded to the increased load with an increased absorption, but at the same time increasing amounts of fat escaped absorption and were excreted in the fœces, causing increasing degrees of steatorrhœa (Fig. 6).

CASE 5

The second patient had a more extensive distal resection and had steatorrhœa when on a diet containing as little as 30 g. of fat. As in the previous patient, more fat was absorbed when the dietary fat was increased, but the increased absorption was only achieved at the expense of an increased fœcal excretion of fat (Fig. 6).

Improvement in intestinal function. Althausen, Doig, Uyeyama and Weiden (1950) have demonstrated that there may be some improvement in intestinal function during the first few weeks after extensive distal resection of the small intestine. Glucose tolerance tests, flat one week post-operatively, may become normal at six weeks. In general, however, little or no improvement in intestinal function takes place after the first four to six weeks. In Case 7, for instance, there was a similar degree of steatorrhœa five years post-

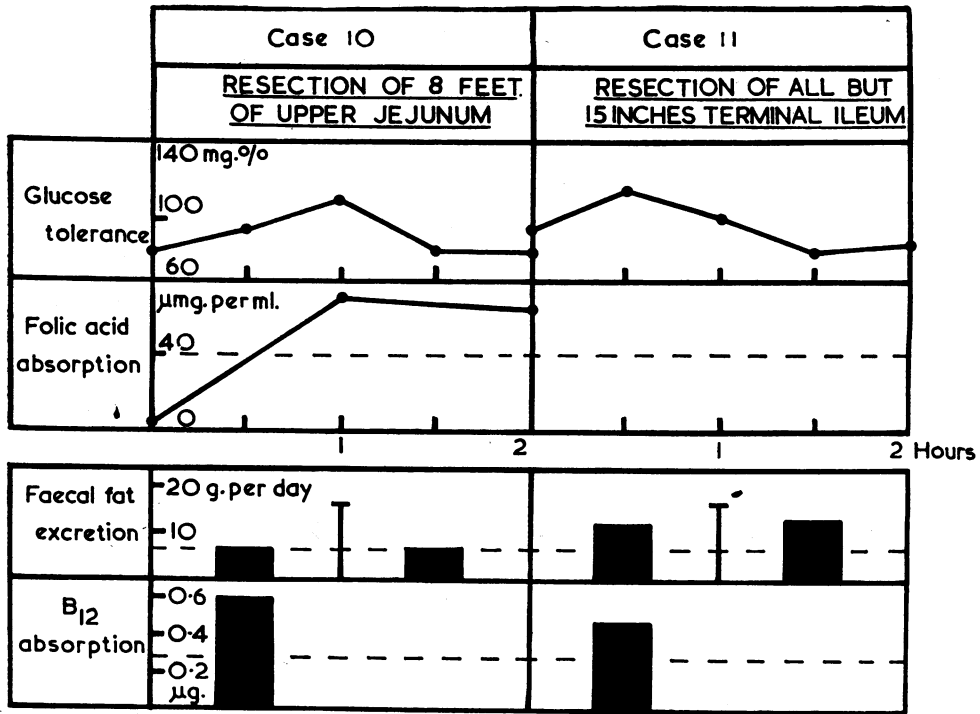


FIG. 7.—Intestinal function tests after resection of the proximal small intestine. (Data from Booth and Mollin, 1960a.)

operatively as had been demonstrated within two months of the resection. None of the patients with distal resections (Table 1), whose absorption of vitamin B₁₂ was subnormal, have hitherto recovered their ability to absorb this vitamin.

(2) *Proximal resections*

Although the transport mechanisms in the mucosa of the ileum are in general less active than those in the proximal intestine (Verzar and McDougall, 1936; Cummins and Jussila, 1955; Dawson and Isselbacher, 1960), the slower transit of the intestinal contents through the distal small bowel facilitates absorption in this area and the ileum is therefore capable of absorbing those substances which are normally absorbed in the jejunum. For these reasons, resection of the proximal small intestine does not usually cause any significant degree of malabsorption unless the resection is massive. This is illustrated by the two patients whose intestinal function tests are shown in Fig. 7. These results in these patients have also been described by Booth and Mollin (1960a).

CASE 10

The first patient had undergone resection of the proximal 8 ft. of the jejunum and an end-to-end anastomosis had been performed. His glucose tolerance was

repeatedly flatter than normal (Fig. 7), a finding which is in keeping with the observation that glucose is absorbed more slowly from the distal than from the proximal small intestine (Cummins and Jussila, 1955). Folic acid absorption, however, was normal. There was no steatorrhœa and, as might be expected, he absorbed vitamin B₁₂ normally. Apart from the rather flat glucose tolerance test, there was therefore no significant absorption defect in this patient, and the normal absorption of vitamin B₁₂ contrasts with the inability of the patients with a comparable distal resection to absorb this substance (Case 10, Fig. 7).

CASE 11

The second patient was a child who had had the misfortune to lose all the small intestine but for the distal 15 in. or so of terminal ileum, the stomach being anastomosed directly to the ileum and the closed duodenum forming a blind pouch. As in the previous patient, the glucose tolerance test was flatter than normal (Fig. 7). Folic acid absorption was not measured. This patient's resection had caused moderate steatorrhœa, 12 g. of fat being excreted in the stools daily on a dietary intake of 48 g., but this result indicates that the terminal ileum can absorb as much as 36 g. of fat from this diet. Even though so little of the ileum remained, the absorption of vitamin B₁₂ was normal (Fig. 7). Detailed studies in this patient have been reported by Clayton and Cotton (1961).

Effect of increasing dietary fat after proximal resections. In contrast to the results in the patients with distal resection (Fig. 6), increasing amounts

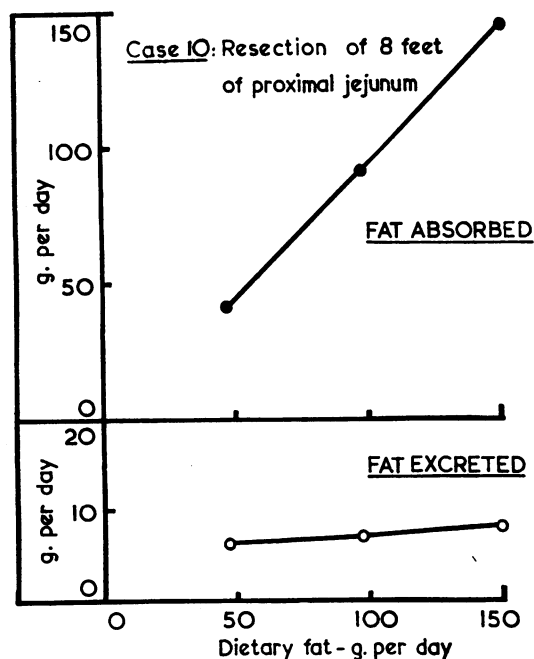


FIG. 8.—Effect of increasing dietary fat on faecal fat excretion after proximal resection. (From Booth, Alldis and Read, 1961.)

of dietary fat may be well tolerated after resection of the proximal intestine. This is illustrated by the results of successive fat balances in the patient who had undergone resection of the jejunum (Fig. 8).

CASE 10

This patient (Case 10, Fig. 8) excreted a mean of only 6.5 g. of fat daily during a six-day balance, when he received a diet containing just less than 50 g. of fat. When the dietary fat was increased there was a slight increase in faecal fat excretion (Fig. 8), but the mean daily excretion when the diet contained as much as 150 g. of fat was only 8.2 g. and the amount of fat absorbed increased progressively as the fat intake was increased. The results in this patient emphasize again the remarkable functional reserve of the ileum for the absorption of fat.

Treatment and Prognosis

(1) Distal resections

Since patients with resection of the distal small intestine fail to absorb vitamin B₁₂, it is not surprising that they may develop B₁₂ deficiency and megaloblastic anaemia. As after total gastrectomy, the onset of this deficiency in the adult is delayed for several years after the resection, for it only occurs when the body stores of vitamin B₁₂ in the liver have been exhausted. Patients with resection of the ileum, like patients with Addisonian pernicious anaemia, therefore require treatment with

vitamin B₁₂ indefinitely. As in Addisonian pernicious anaemia (Ross and others, 1954), it is possible to treat such patients with oral B₁₂, providing that sufficiently large and unphysiological doses are given. For regular treatment, however, this method is not to be recommended, monthly injections being a surer and safer route of administration. Whether patients require other treatment depends on the extent of the distal resections.

Group 1. The patients in this group have an isolated absorption defect for vitamin B₁₂ and no other treatment than monthly B₁₂ injections is usually required (Booth and Mollin, 1959, 1960a). This is illustrated by the patient whose intestinal function tests were shown in Fig. 5 (Case 1).

TABLE 2

SERUM B₁₂ CONCENTRATION AFTER ORAL ADMINISTRATION OF 3,000 µg. VITAMIN B₁₂ TO A PATIENT WITH RESECTION OF THE ILEUM (CASE 1)

Time after Oral Dose (hours)	Serum B ₁₂ Concentration (µg. per ml.)
0	50
½	380
1	510
2	500
3	510
4	560

CASE 1

This lady has previously been reported by Booth and Mollin (1959, 1960a). She developed a mild macrocytic anaemia (Hb. 11.9 g./100 ml., R.B.C. 4.1 M. per c.mm.) six years after her intestinal resection. Her serum B₁₂ concentration was subnormal, being 50 µg. per ml.,* and examination of her sternal marrow revealed megaloblastic change. In order to determine her response to oral treatment she was first given a single oral dose of 3,000 µg. crystalline vitamin B₁₂ and the serum B₁₂ concentration was measured at intervals during the next four hours. As the results given in Table 2 show, the serum B₁₂ level rose to normal after this very large dose of B₁₂ was given. These observations illustrate that the jejunum is capable of absorbing B₁₂ from such large and unphysiological doses, although unable to assimilate sufficient of the dietary B₁₂ which is absorbed through the agency of intrinsic factor. Although daily oral doses of crystalline B₁₂ could have been continued, she has not been given further oral therapy, but has received regular monthly injections of 200 µg. of vitamin B₁₂ for the past four years. She has remained well without other treatment.

Group 2. Since the patients in this group fail to absorb B₁₂, they too develop B₁₂ deficiency. However, their proximal intestine remains and they are able to absorb other water-soluble vitamins normally. They also appear to be able to absorb sufficient of the fat-soluble vitamins to maintain

* Normal range: 140 to 900 µg. per ml. (Ross and Mollin, 1956).

their requirements. They therefore do not usually develop other vitamin deficiencies. Iron deficiency usually indicates bleeding from an anatomical lesion of the bowel and is not due to malabsorption. Provided they are treated with a high-protein, low-fat diet, these patients appear to require no vitamin supplements other than monthly injections of vitamin B₁₂. These aspects of their treatment are shown by the following case reports.

Megaloblastic anemia due to B₁₂ deficiency. The development of B₁₂ deficiency in this group of patients is illustrated first by the young man whose intestinal function tests were shown in Fig. 5 (Case 7).

CASE 7

This patient had undergone resection of all but the proximal 4 ft. of the jejunum and he had marked steatorrhœa and creatorrhœa and failed to absorb vitamin B₁₂ (Case 7, Fig. 5). Characteristically, he absorbed glucose, folic acid, ascorbic acid and pyridoxine normally. He was treated with a high-protein, low-fat diet and, apart from oral iron and ascorbic acid, no vitamins were given. Despite the extent of his resection, he was able to absorb his food sufficiently well to maintain his body weight. As expected, however, his serum B₁₂ concentration fell steadily and four years post-operatively he had developed a megaloblastic anemia (Hb. 9.5 g./100 ml., R.B.C. 2.4 M. per c.mm.) associated with B₁₂ deficiency (serum B₁₂ concentration 60 µg. per ml.). He is now being treated with injections of vitamin B₁₂ (200 µg. once monthly) and remains well. Since he absorbs ascorbic acid normally, he clearly does not require this vitamin and since iron may also be absorbed in the proximal intestine, the oral iron has also been stopped. His steatorrhœa is controlled by a low-fat diet and he usually has one stool daily. He has no evidence of any other deficiency state. Serum proteins are normal, prothrombin time remains normal, there are no electrolyte deficiencies and there is no evidence of demineralization of bone.

In infants B₁₂ deficiency may develop more rapidly after a distal resection than in adults. This may be due in part to the smaller store of vitamin B₁₂ in the infant liver (Mollin and Ross, 1956) and probably also to the greater B₁₂ requirement of the growth period. This may be illustrated by the case of a child who developed a large volvulus of the small intestine soon after birth. A detailed report of this patient has been given by Clark and Booth (1960).

CASE 8

In this patient at least two-thirds of the distal small intestine was resected within a week of birth and the jejunum was anastomosed to the transverse colon. She recovered from this procedure and for the first 10 months of life her growth and development were normal for her age (Fig. 9). During this period she must therefore have been able to absorb or derive from tissue stores sufficient nutrients to maintain normal development. She then began to lose weight, had attacks of vomiting and developed severe diarrhœa. For the next three months her weight declined steadily. At 13 months, however, a mild macrocytic anemia was recognized

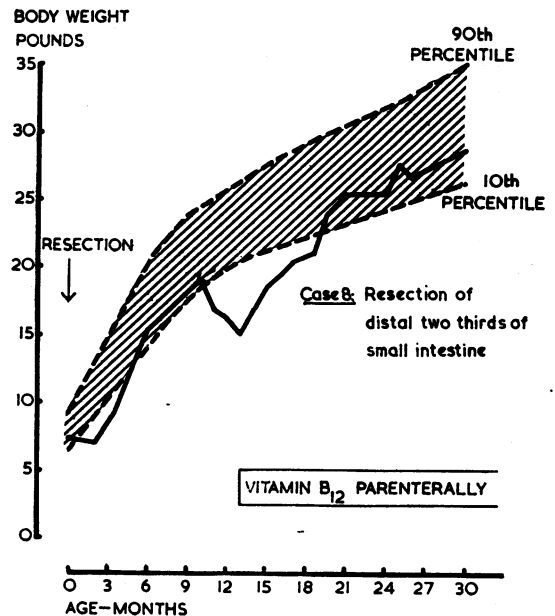


FIG. 9.—Body weight and response to treatment with vitamin B₁₂ after resection of approximately distal two-thirds of small intestine in an infant (Case 8). (From Clarke and Booth, 1960.)

(Hb. 11.0 g./100 ml., R.B.C. 3.7 M. per c.mm.) and her bone marrow was now found to be megaloblastic. Her serum B₁₂ was measured and was found to be extremely low, being 25 µg. per ml. Intestinal function tests were similar to those in the young man with a similar resection (Case 7, Fig. 5); she absorbed glucose normally, but had steatorrhœa, absorbing no more than 73% and 81% of a 30-g. fat diet during successive balance periods, and she was unable to absorb any of a test dose of radioactive B₁₂.

Her response to treatment with vitamin B₁₂ (100 µg. daily by intramuscular injection for nine days) was remarkable (Fig. 9). Within 24 hours her diarrhœa and vomiting had ceased and she had started to put on weight. There was a reticulocyte response of 9% on the seventh day after the first injection and her sternal marrow became normoblastic. For 18 months she received no parenteral treatment other than vitamin B₁₂ (100 µg. every two weeks), and yet she continued to put on weight and grow at the rate expected for her age. This is a further example of a distal intestinal resection causing a pure B₁₂ deficiency state.

The results in these patients indicate the dangers of B₁₂ deficiency after resection of the distal small intestine. It is clear that patients with such resections, like patients who have undergone total gastrectomy, should be given prophylactic injections of vitamin B₁₂.

Iron-deficiency anemia. A transient iron-deficiency anemia is not unusual in the immediate post-operative phase and may be related to blood loss at the time of resection. If iron deficiency is persistent, or occurs later, it is usually due to

bleeding from an associated anatomical lesion of the bowel, such as a blind loop, and is not due to malabsorption. The side-to-side anastomosis in Case 6, for instance, was followed by the development of a large blind loop of the terminal small intestine (Fig. 4) and this patient suffered from recurrent iron-deficiency anaemia due to blood loss from the blind loop. His anaemia was only cured when the blind loop was corrected by further surgery.

Dietary management. Although no treatment other than vitamin B₁₂ may be necessary in some patients with lesions of the distal small intestine, dietary management may also be important in others, particularly if the lesion is extensive (Booth and Mollin, 1960b). Since these patients have lost their ileum, there is little functional reserve for fat absorption and on high fat intakes steatorrhoea may be severe, causing incapacitating and troublesome diarrhoea. If marked steatorrhoea continues for any appreciable length of time, the persistent loss of electrolytes in the faeces may lead to hyponatraemia, hypokalaemia and hypocalcaemic tetany. In some cases magnesium deficiency may also occur (Fletcher, Henly, Sammons and Squire, 1960). These deficiencies are usually the result of taking a high-fat diet and the diarrhoea and electrolyte deficiencies may often be corrected simply by restriction of the dietary fat. This is illustrated by the following case report:

CASE 4

The patient was a 48-year-old housewife who had a 19-year history of regional enteritis involving the ileum. She had undergone repeated intestinal operations, resection or short circuits of the distal small intestine being performed on five occasions. For 10 years she had suffered from diarrhoea, passing six or eight bulky fatty stools daily. At the end of this time a further laparotomy revealed two blind loops of the terminal small intestine. These were resected and an end-to-end anastomosis was performed between the end of the remaining small intestine and the transverse colon. There was no evidence of regional enteritis at this operation. The amount of small bowel remaining was uncertain, but seemed unlikely to exceed 6 ft. Post-operatively she was treated first with a low- and then with a high-fat diet and on the latter regime she had marked diarrhoea, passing eight or 10 stools daily. Her weight fell and two months after the operation she was very ill. She was thin and wasted and had spontaneous tetany. Investigations now revealed multiple electrolyte deficiencies (serum sodium 143, potassium 2.7 and calcium 3.6 mEq./l.). There was also evidence of severe magnesium deficiency, for the serum magnesium was only 0.3 mEq./l. (normal range 1.5 to 1.8 mEq./l.) (Alcock, McIntyre and Radde, 1960). She had low-serum proteins (albumin 2.7, globulin 2.4 g. %) and a megaloblastic anaemia due to B₁₂ deficiency (Hb. 7.2 g./100 ml., R.B.C. 1.8 M. per c.mm. and serum B₁₂ concentration 15 µg. per ml.). Bone X-rays, however, showed no evidence of osteomalacia and a bone biopsy was normal. Intestinal function tests were characteristic of a patient with an extensive resection of the distal small intestine—

she absorbed glucose and folic acid normally but had steatorrhoea and failed to absorb vitamin B₁₂.

She was first treated with oral potassium supplements and subsequently with injections of calciferol. This treatment restored her serum potassium and calcium to normal levels, but, although her tetany now disappeared, her serum magnesium remained as low as before. At the same time she was treated with a low-fat diet (32 g. daily). Her body weight and serum magnesium level during the next three months, together with the amount of fat and protein in the diet, are shown in Fig. 10. As this figure shows, her serum magnesium rose to normal levels on the low-fat regime without any supplements of magnesium being given. She was subsequently given a high-fat diet (138 g. daily) and the serum magnesium level once again fell, only rising to normal again when the low-fat diet was resumed. Magnesium balances* (Table 3) revealed the reason for this response. On the low-fat diet the patient was in positive magnesium balance and excreted between 8.4 and 13 g. of fat daily in the stools. The high-fat diet caused an increase in the faecal fat and a negative magnesium balance was induced (Table 3), the increased faecal fat excretion presumably washing magnesium out of the body, possibly in the form of insoluble soaps. This patient's diarrhoea was very much improved when the low-fat diet was given and no further electrolyte supplements have been necessary.

These results illustrate the importance of a low-fat diet in this patient. However, in such patients it is equally important that sufficient dietary protein should be given. If there is an extensive lesion of the distal small intestine, there may be interference with protein absorption and so the faecal nitrogen may be high (Case 7, Fig. 5). A high-protein diet is therefore required to compensate for the faecal loss of protein. This is also illustrated by the results in Fig. 10.

CASE 4

Initially the patient was given a diet containing approximately 60 g. of protein and on this regime she lost weight (Fig. 10). Although her diarrhoea had been much improved by the low-fat diet, her faecal nitrogen was high (between 3.7 and 6.6 g. per day), indicating malabsorption of protein. It was not until the dietary protein was increased to 120 g. that she began to put on weight and her serum albumin rose to normal levels. This response indicates that increasing amounts of protein can be absorbed from the limited small intestine available when the dietary protein is increased, as may also occur with fat (Fig. 6). She had continued to receive a high-protein, low-fat diet and the only vitamin supplement she has received is vitamin B₁₂. She has remained well.

Group 3. The treatment of patients who have undergone massive resection of the small intestine may be less rewarding and prognosis should therefore be guarded. The minimum amount of the small intestine required to support life has not yet been firmly established, but it appears to be surprisingly little, survival being comfortably possible

* Magnesium studies in this patient were carried out in collaboration with Dr. I. McIntyre.

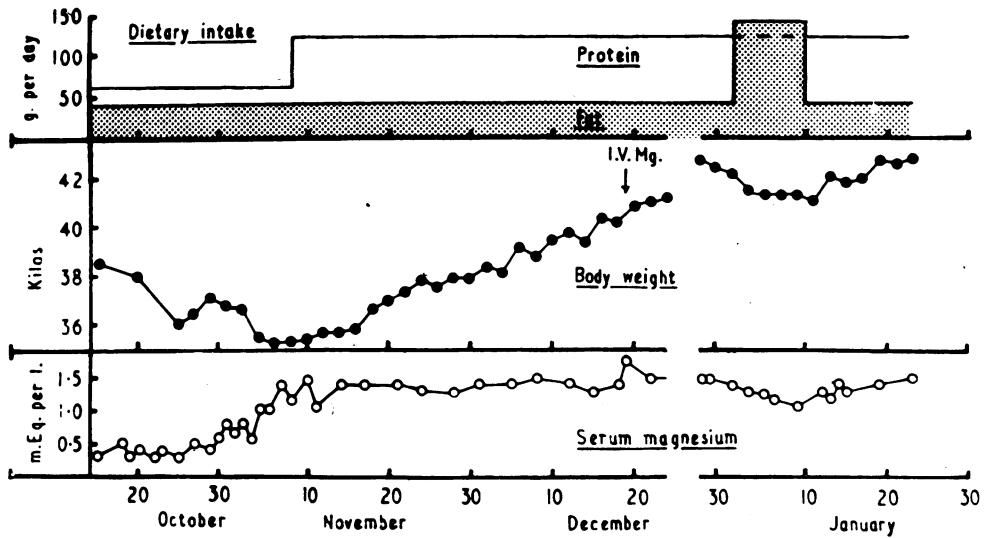


FIG. 10.—Response of body weight and serum magnesium to treatment with diets of varying protein and fat content (Case 4).

TABLE 3
EFFECT OF VARYING DIETARY FAT ON MAGNESIUM AND FAT BALANCES* AFTER EXTENSIVE RESECTION OF THE DISTAL SMALL INTESTINE (Case 4)

Regime	Balance No.	Dietary Fat (g./day)	Fæcal Fat (g./day)	Dietary Mg. ++ (mEq./day)	Fæcal Mg. ++ (mEq./day)	Urinary Mg. ++ (mEq./day)	Mg. ++ Balance (mEq./day)
Low fat diet	1	32	8.4	14.0	7.2	0.2	+ 6.6
	2	32	13.0	12.0	9.1	0.0	+ 2.9
High fat diet	1	138	19.0	14.0	24.0	1.9	-11.9
	2	138	21.0	14.0	20.0	0.8	- 6.8

*All balances were carried out over three day periods.

with only 14 to 18 in. of residual small intestine (Meyer, 1946 and 1954; Cogswell, 1948; Althausen, Uyeyama and Simpson, 1949; Schwartz, Medwid, Roberts, Sleisinger and Randall, 1956; Kogan, Shapira, Janowitz and Adlersberg, 1957). But life is possible with very much less small intestine than this. One patient has been described who survived for three years after resection of all but the proximal 7 in. of the jejunum (Jackson, Linder and Berman, 1951), and another, whose intestinal function tests were shown in Fig. 5 (Case 9), and in whom only 8 in. of jejunum remained, survived for as long as nine months even though over 80 years of age (Harrison and Booth, 1960). The most extensive resection yet recorded is that of Kinney, Goldwyn, Barr and Moore (1961), whose patient has survived for one year after resection of the entire jejunum, ileum

and right colon. This unfortunate person has been taught to pass a naso-gastric tube through which he feeds himself with small amounts of a fat-free synthetic diet at frequent intervals. He also receives supplemental vitamin therapy. Although only his duodenum remains, he is able to live comfortably at home, a tribute to his courage and to the skill of his medical advisers.

An example of the treatment and progress of a patient with a massive resection is provided by the elderly lady, previously referred to, who had undergone resection of all but the proximal 8 in. of the jejunum. In view of her age, it is perhaps not surprising that, despite vigorous supportive treatment, she suffered from progressive malnutrition which led ultimately to her death. This patient has been reported in detail by Harrison and Booth (1960).

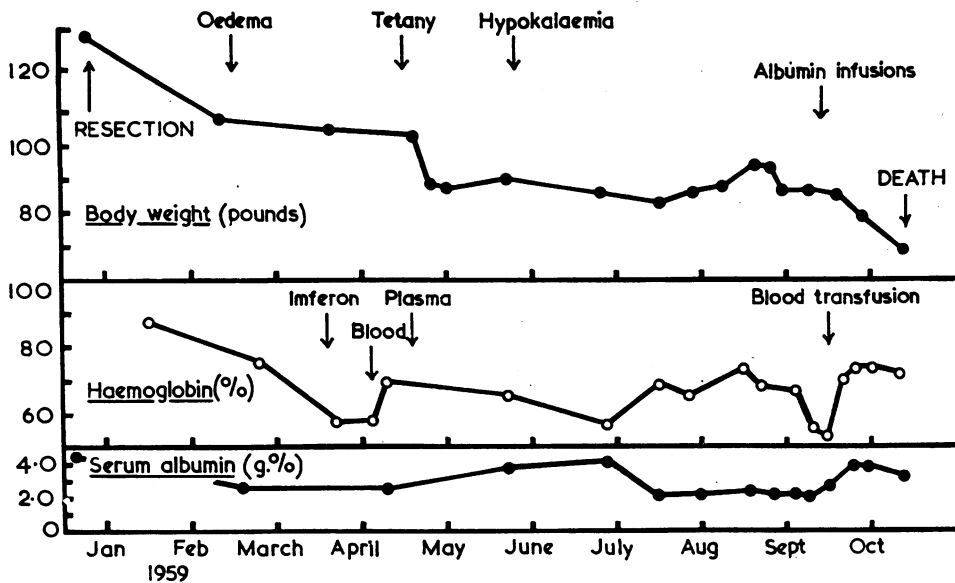
Case 9: RESECTION OF ALL BUT PROXIMAL 8 INCHES JEJUNUM

FIG. 11.—Body weight, hæmoglobin and serum albumin after resection of all but the proximal 8 in. of the jejunum (Case 9). (From Harrison and Booth, 1960.)

CASE 9

The body weight, hæmoglobin level and serum albumin during the nine months that this patient survived after the resection are shown in Fig. 11. At first she had profuse diarrhoea, passing up to 12 watery stools daily. She was given a high-protein, low-fat diet (30 g. of fat daily) and she also received parenteral injections of vitamins A, B₁₂, D and K. Seven weeks post-operatively her weight had fallen by 22 lb. and she had developed hypoproteinaemic oedema. By 12 weeks her hæmoglobin had fallen to 50%, although there was no evidence of deficiency of any known hæmatinic and no evidence of blood loss. She was treated with diuretics, intramuscular iron and crude liver extracts, and subsequently with blood transfusions and infusions of plasma. Her weight continued to fall, but six months postoperatively, despite continued loss of flesh, she was feeling reasonably well. Her dietary fat was restricted to 20 g. daily or less, and she was now passing between one and three stools daily. The most agreeable regime was a high-protein diet, the protein being given as beef steak, chicken or other solid food, and as little fat as possible. A 40-g. fat diet, for instance, produced severe diarrhoea and she had similar trouble when given simply assimilable fluids only, such as glucose and fruit drinks. The more favourable response to a natural than to a synthetic, easily assimilable diet was noted by Althausen and others (1949) in a patient who had only 45 cm. of the proximal intestine remaining. This may be because fluids pass rapidly through the stomach and short length of residual small intestine and there is little opportunity for absorption to occur. On the other hand, if solid food is given, it is likely to be retained longer in the stomach, only being delivered slowly through the pylorus in small amounts which the limited amount of intestine is able to deal with more easily.

Despite all measures, however, this patient's weight continued to decline and she finally died nine months after the operation. The reason for her death was obscure. Although she was losing weight progressively, her serum albumin and electrolytes (including magnesium) were normal and her hæmoglobin was over 70%. Clinically there was no evidence of any specific vitamin deficiency and, apart from the obvious malnutrition, the only significant feature was the development of mental confusion alternating with apathy in the two weeks that preceded her death. Mental changes were also a feature in the patient described by Jackson and his colleagues (1951), who died three and a half years after a similar resection (Jackson and Linder, 1953; Linder, Jackson and Linder, 1953).

(2) Proximal resections

As shown in Fig. 7, resection of as much as 8 ft. of the jejunum (Case 10) causes no significant malabsorption. A patient with such a resection will therefore develop no nutritional deficiency and no treatment is necessary. If the resection is sufficiently extensive to cause steatorrhœa, dietary management may be important. This is illustrated by the response to dietary treatment in the child who had only the distal half of the ileum remaining (Fig. 12).

CASE 11

This patient, of whom a detailed report has been given by Clayton and Cotton (1961), developed an intussusception complicated by gangrene at the age of 10 months and it was estimated that 135 cm. of the intestine was removed, leaving 38 cm. (15 in.) distally.

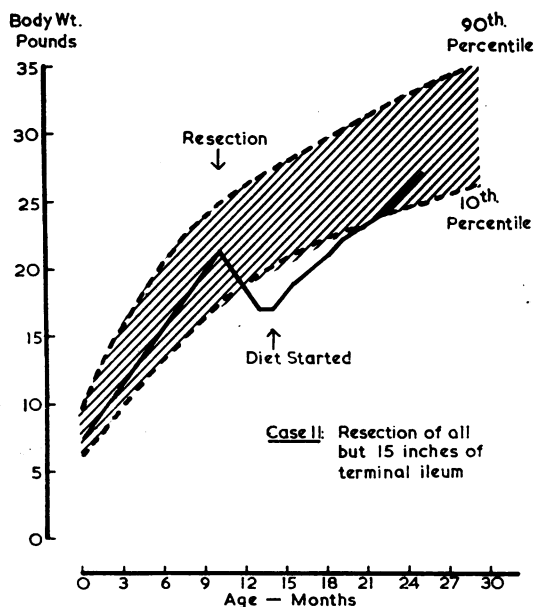


FIG. 12.—Body weight and response to treatment with a solid high-protein, low-fat diet after resection of all but the terminal 15 in. of the ileum (Case 11). (From Clayton and Cotton, 1961.)

The stomach was anastomosed directly to the ileum and the duodenal stump closed. The intestinal function tests were shown in Fig. 7.

He recovered from the resection reasonably well, but diarrhoea was persistent and troublesome. At first he was passing 10 to 14 loose motions daily and by the age of one year he still had marked diarrhoea, passing seven to nine stools daily, and he was losing weight progressively (Fig. 12). At this time it was realized that his diet consisted predominantly of milk and fluid baby foods and his feeds seemed to pass through him rapidly. As in the elderly lady with extensive resection (Case 9), he might be expected to do better on a regime of protein in solid forms, with restriction of fat, for this might be more easily assimilated than his fluid diet. He was therefore changed to a diet high in protein and calories, with fat limited to about 30 g. daily, and the protein was given as chopped meats. His improvement on this regime was immediate (Fig. 12). His motions were reduced to three formed stools daily and he began to put on weight. He rapidly reached the normal weight for his age and has continued to put on weight at the expected rate. In contrast to the patients with distal resections, he absorbed B_{12} normally (Fig. 7). His serum B_{12} level therefore remains normal (445 $\mu\mu\text{g}$. per ml. nine months post-operatively) and he does not require any treatment with this vitamin.

This patient's response provides a further indication of the remarkable intestinal reserve that normally lies dormant in the human terminal ileum.

Summary and Conclusions

This paper seeks to illustrate the importance of physiological principles in guiding effective and rational treatment. If the sites at which absorption normally occurs in the small intestine are known, it is easy to understand what pattern of malabsorption will follow a given resection.

Patients with resections of the distal small intestine may be classified in three groups. A localized resection of the ileum may be associated with an isolated defect of vitamin B_{12} absorption (Group 1) and such a patient therefore requires no other treatment than injections of this vitamin. More extensive resections of the distal small intestine cause steatorrhoea and creatorrhoea in addition to malabsorption of vitamin B_{12} (Group 2). Patients with such resections require a high-protein, low-fat diet in addition to treatment with vitamin B_{12} . Providing sufficient proximal intestine remains to absorb glucose and folic acid normally, no other treatment is usually necessary. Massive distal resections, leaving only a few inches of the proximal jejunum, cause interference with the absorption of glucose and folic acid in addition to steatorrhoea and failure of B_{12} absorption (Group 3). Survival is possible after such resections, but prognosis should be guarded.

The failure of resection of up to 8 ft. of the jejunum to interfere with the absorption of glucose, folic acid or fat indicates that the ileum is capable of taking over the functions of the proximal intestine. Even after a massive proximal resection the terminal ileum is capable of absorbing much of the dietary fat and B_{12} absorption remains normal. However, after such a resection steatorrhoea may be incapacitating unless controlled by a low-fat diet and high-protein feeding is best achieved when the protein is given in solid forms.

It is important to recognize that remarkably little residual small intestine is necessary for life and survival is possible after even the most massive resection.

I am particularly grateful to Dr. D. L. Mollin for much stimulating discussion and for permission to quote details of the B_{12} studies, and to Dr. I. Chanarin for carrying out the folic acid absorption tests. I also wish to thank Dr. F. Avery Jones, Dr. N. F. Coghill, Dr. Barbara Clayton, Dr. P. R. Evans, Dr. R. J. Harrison, Mr. D. P. van Meurs and the physicians and surgeons of Hammersmith Hospital for kindly allowing studies on patients who were under their care; and I am indebted to Dr. Ian McIntyre for the magnesium studies in Case 4.

Figs. 3 and 4 are reproduced through the courtesy of Dr. J. W. Laws and the Editor of the *British Journal of Radiology*, and Figs. 8 and 11 with the permission of the Editor of *Gut*. Figs. 9 and 12 are modified from illustrations previously published in the 'Archives of the Diseases of Childhood'.

REFERENCES

- ALCOCK, N., MCINTYRE, I., and RADDE, I. (1960): The Determination of Magnesium in Biological Fluids by Flame Photometry, *J. clin. Path.*, **13**, 506.
- ALTHAUSEN, T. L., UYEVAMA, K., and SIMPSON, R. G. (1949): Digestion and Absorption after Massive Resection of the Small Intestine: I. Utilization of Food from a 'Natural' versus a 'Synthetic' Diet and a Comparison of Intestinal Absorption Tests with Nutritional Balance Studies in a Patient with only 45 cm. of Small Intestine, *Gastroenterology*, **12**, 795.
- , DOIG, R. K., UYEVAMA, K., and WEIDEN, S. (1950): Digestion and Absorption after Massive Resection of the Small Intestine: II. Recovery of the Absorptive Function as Shown by Intestinal Absorption Tests in Two Patients and a Consideration of Compensatory Mechanisms, *Ibid.*, **16**, 126.
- ANNEGERS, J. H., BOUTWELL, J. H., and IVY, A. C. (1948): Effect of Dietary Fat on Fecal Fat Excretion and Subjective Symptoms in Man, *Ibid.*, **10**, 486.
- BERK, L., CASTLE, W. B., WELCH, A. D., HEINLE, R. W., ANKER, R., and EPSTEIN, M. (1948): Observations on the Etiologic Relationship of Achylia Gastrica to Pernicious Aemia: X. Activity of Vitamin B₁₂ as Food (Extrinsic) Factor, *New Engl. J. Med.*, **239**, 911.
- BOOTH, C. C. (1958): A Clinical and Experimental Study of the Intestinal Absorption of Vitamin B₁₂, M.D., Thesis St. Andrew's University.
- , and MOLLIN, D. L. (1959): The Site of Absorption of Vitamin B₁₂ in Man, *Lancet*, **i**, 18.
- , — (1960a): The Effects of Resection on the Small Intestine in Man, *Proc. Int. Conference of Gastroenterology*, Leyden, 1960, p. 249.
- , — (1960b): The Blind Loop Syndrome, *Proc. roy. Soc. Med.*, **53**, 658.
- , EVANS, K. T., MENZIES, T., and STREET, D. F. (1959): Intestinal Hypertrophy following Partial Resection of the Small Bowel in the Rat, *Brit. J. Surg.*, **46**, 403.
- , READ, A. E., and JONES, E. (1961): Studies on the Site of Fat Absorption: 1. The Sites of Absorption of Increasing Doses of ¹³¹I-labelled Triolein in the Rat, *Gut*, **2**, 23.
- , ALLDIS, D., and READ, A. E. (1961): Studies on the Site of Fat Absorption: 2. Fat Balances after Resection of Varying Amounts of the Small Intestine in man, *Ibid.*, **2**, 168.
- , and BRAIN, M. C. (1961): The Absorption of Tritium-labelled Pyridoxine in the Rat. In preparation.
- BORGSTRÖM, B., DAHLQVIST, A., LUNDH, G., and SJOVALL, J. (1957): Studies of Intestinal Digestion and Absorption in the Human, *J. clin. Invest.*, **36**, 1521.
- BRAIN, M. C., and BOOTH, C. C. (1961): The Absorption of Tritium-labelled Pyridoxine in man. In preparation.
- CHANARIN, I., ANDERSON, B. B., and MOLLIN, D. L. (1958): The Absorption of Folic Acid, *Brit. J. Haematol.*, **4**, 156.
- CLARK, A. C. L., and BOOTH, C. C. (1960): Deficiency of Vitamin B₁₂ after Extensive Resection of the Distal Small Intestine in an Infant, *Arch. Dis. Child.*, **35**, 595.
- CLAYTON, B. E., and COTTON, D. A. (1961): A Study of Malabsorption after Resection of the Entire Jejunum and the Proximal Half of the Ileum, *Gut*, **2**, 18.
- COGSWELL, H. D. (1948): Massive Resection of the Small Intestine, *Ann. Surg.*, **127**, 377.
- COX, E. V., MEYNELL, M. J., COOKE, W. T., and GADDIE, R. (1958): The Folic Acid Excretion Test in the Steatorrhœa Syndrome, *Gastroenterology*, **35**, 390.
- CUMMINS, A. J., and JUSSILA, R. (1955): Comparison of Glucose Absorption Rates in the Upper and Lower Human Small Intestine, *Ibid.*, **29**, 982.
- DAWSON, A. M., and ISSELBACHER, K. J. (1960): The Esterification of Palmitate-I-C¹⁴ by Homogenates of Intestinal Mucosa, *J. clin. Invest.*, **39**, 150.
- FLETCHER, R. F., HENLY, A. A., SAMMONS, H. G., and SQUIRE, J. R. (1960): A Case of Magnesium Deficiency following Massive Intestinal Resection, *Lancet*, **i**, 522.
- FLINT, J. M. (1912): The Effect of Extensive Resections of the Small Intestine, *Bull. Johns Hopk. Hosp.*, **23**, 127.
- FRAZER, A. C. (1943): Differentiation in the Absorption of Olive Oil and Oleic Acid in the Rat, *J. Physiol. (Lond.)*, **102**, 306.
- GLASS, G. B. J., BOYD, L. J., and STEPHANSON, L. (1954): Intestinal Absorption of Vitamin B₁₂ in Humans as Studied by Isotope Technique, *Proc. Soc. exp. Biol. (N. Y.)*, **86**, 522.
- HAHN, P. F., BALE, W. F., ROSS, J. F., BALFOUR, W. M., and WHIPPLE, G. H. (1943): Radioactive Iron Absorption by Gastrointestinal Tract: Influence of Anemia, Anoxia and Antecedent Feeding Distribution in Growing Dogs, *J. exp. Med.*, **78**, 169.
- HARRISON, R. J., and BOOTH, C. C. (1960): Massive Resection of the Small Intestine after Occlusion of the Superior Mesenteric Artery, *Gut*, **1**, 237.
- JACKSON, W. P. U. (1958): Massive Resection of the Small Intestine, in 'Modern Trends in Gastroenterology', ed. Avery Jones, F., second series, p. 243. London: Butterworth.
- , LINDER, G. C., and BERMAN, S. (1951): Small Gut Insufficiency following Intestinal Surgery, *S. Afr. J., clin. Sci.*, **2**, 70.
- , — (1953): Influence of Malnutrition on Pancreas: Report of Case following Small Gut Resection, *Metabolism*, **2**, 563.
- JENSENIUS, H. (1945): 'Results of Experimental Resections of the Small Intestine on Dogs'. London: H. K. Lewis.
- KINNEY, J. M., GOLDWYN, R. M., BARR, J. S., and MOORE, F. D. (1961): Management of a Patient after Loss of the Entire Jejunum, Ileum and the Right Colon. In press.
- KREMEN, A. J., LINNER, J. H., and NELSON, C. H. (1954): An Experimental Evaluation of the Nutritional Importance of Proximal and Distal Small Intestine, *Ann. Surg.*, **140**, 439.
- KOGAN, E., SCHAPIRA, A., JANOWITZ, H. D., and ADLERSBERG, D. (1957): Malabsorption following Extensive Small Intestinal Resection, including Inadvertent Gastro-ileostomy, *J. Mt Sinai Hosp.*, **24**, 399.
- LACK, L., and WEINER, I. M. (1961): *In vitro* Absorption of Bile Salts by Small Intestine of Rats and Guinea Pigs, *Amer. J. Physiol.*, **200**, 313.
- LAWS, J. W., and PITMAN, R. C. (1960): The Radiological Investigation of Malabsorption Syndrome, *Brit. J. Radiol.*, **33**, 211.

- LINDER, A. M., JACKSON, W. P. U., and LINDER, G. C. (1953): Small Gut Insufficiency following Intestinal Surgery: Further Clinical and Autopsy Studies of Man Surviving 3½ years with 7 inches of Small Intestine, *S. Afr. J. clin. Sci.*, **4**, 1.
- MEYER, H. W. (1946): Acute Superior Mesenteric Artery Thrombosis: Recovery following Extensive Resection of Small and Large Intestines, *Arch. Surg. (Chicago)*, **53**, 298.
- (1954): Discussion on paper by Kremen, Linner and Nelson (1954), *Ann. Surg.*, **140**, 447.
- MOLLIN, D. L., and ROSS, G. I. M. (1956): The Pathophysiology of Vitamin B₁₂ Deficiency in the Megaloblastic Anæmias: Vitamin B₁₂ and Intrinsic Factor. I. Europäisches Symposion über Vitamin B₁₂ und Intrinsic Factor, p. 413. Stuttgart: F. Enke.
- , BOOTH, C. C., and BAKER, S. J. (1957): The Absorption of Vitamin B₁₂ in Control Subjects, in Addisonian Pernicious Anæmia and in the Malabsorption Syndrome, *Brit. J. Hæmat.*, **3**, 412.
- MONTO, R. W., REBUCK, J. W., and BRENNAN, M. J. (1953): Crystalline B₁₂ Inhalation Therapy in Pernicious Anæmia, *Amer. J. med. Sci.*, **225**, 113.
- PARKINS, R. A., DIMITRIADOU, A., and BOOTH, C. C. (1960): The Rates and Sites of Absorption of ¹³¹I-labelled Albumin and Sodium ¹³¹I in the Rat, *Clin. Sci.*, **19**, 595.
- REYNELL, P. C., and SPRAY, G. H. (1956): The Simultaneous Measurement of Absorption and Transit in the Gastro-intestinal Tract of the Rat, *J. Physiol. (Lond.)*, **131**, 452.
- ROSENTHAL, H. L., and HAMPTON, J. K. (1955): The Absorption of Cyanocobalamin (Vitamin B₁₂) from the Gastro-intestinal Tract of Dogs, *J. Nutr.*, **56**, 67.
- ROSS, G. I. M., MOLLIN, D. L., COX, E. V., and UNGLEY, C. C. (1954): Hæmatological Responses and Concentration of Vitamin B₁₂ in the Serum and Urine following Administration of Vitamin B₁₂ Without Intrinsic Factor, *Blood*, **9**, 473.
- (1956): Vitamin B₁₂ in Tissues in Pernicious Anæmia and Other Conditions: Vitamin B₁₂ and Intrinsic Factor. I. Europäisches Symposion, Hanbury, p. 437. Stuttgart: F. Enke.
- SCHWARTZ, M. K., MEDWID, A., ROBERTS, K. A., SLEISENGER, M., and RANDALL, H. T. (1956): Fat and Nitrogen Metabolism in Patients with Massive Small Bowel Resections, *Surg. Forum*, **6**, 385.
- SHELTON, E. L., and BLAINE, M. H. (1954): Massive Small Bowel Resection in Post-gastroectomy Patients: Report of Two Cases, *Tex. St. J. Med.*, **50**, 96.
- SHONYO, E. S., and JACKSON, J. A. (1950): Massive Resection of the Small Intestine, *Arch. Surg. (Chicago)*, **61**, 123.
- SPENCER, R. P., and ZAMCHECK, N. (1961): Intestinal Absorption of Riboflavine by Rat and Hamster, *Gastroenterology*, **40**, 794.
- STEWART, J., and BOOTH, C. C. (1961): Unpublished observations.
- TURNER, D. A. (1958): The Absorption, Transport and Deposition of Fat: Application of a New Method for the Determination of ¹³¹I-lipid Activity in Dogs and Man, *Amer. J. dig. Dis. n.s.*, **3**, 594, 682.
- VERZAR, F., and McDUGALL, E. J. (1936): 'Absorption from the Intestine'. London: Longmans, Green.
- WOLLAEGER, E. E., COMFORT, M. W., and OSTERBERG, A. E. (1947): Total Solids, Fat and Nitrogen in the Feces: A Study of Normal Persons Taking a Test Diet Containing a Large Amount of Fat, *Gastroenterology*, **9**, 272.
-