lack of vitamin K. Bleeding into the skin is the most common sign, but hæmaturia, melæna, or menorrhagia may occur and, perhaps most dangerous of all from the point of view of the surgeon, there may be massive retroperitoneal hæmorrhage simulating an acute intra-abdominal catastrophe. In others failure to absorb vitamin D and calcium leads to tetany and osteomalacia.

Patients who present with bruising or skeletal pain may have no other symptoms and in the absence of diarrhœa or abdominal distension the underlying cause is easy to overlook. Sometimes, however, the impairment of absorption of fat and other substances gives rise to multiple vitamin deficiencies, to asthenia and muscular weakness from loss of sodium and potassium, to hypoproteinæmia and œdema, and finally to a state of profound cachexia that may prove impossible to relieve even by heroic treatment.

Anæmia is common and may be the presenting symptom. Sometimes it is macrocytic and megaloblastic and indistinguishable from true pernicious anæmia, but usually it is the occurrence of a double picture in the peripheral blood in which some of the cells are macrocytic and hyperchromic, and others small and iron deficient, that arouses the suspicion that the symptoms may be due to a gastro-intestinal lesion. As in idiopathic steatorrhœa, the megaloblastic anæmia may well be the result of a combined deficiency of folic acid and vitamin B_{12}, but in the loop syndrome as Mollin *et al.* (1957) have shown, the deficiency of vitamin B_{12} is usually more important. For this reason it is dangerous to treat the anæmia with folic acid alone, for although the hæmoglobin may return to normal and the anæmia be cured, there is a very real danger of the development of subacute combined degeneration of the cord unless vitamin B_{12} is given at the same time.

Diagnosis

Patients with the blind loop syndrome can be divided into two groups. The first group, which we could call the surgical group, includes all those who have had an intestinal resection or a by-pass operation or indeed any intra-abdominal surgery at some time in the past. In these the occurrence of a megaloblastic anæmia combined with iron deficiency, or more important with free acid in the gastric juice, or the development of diarrhœa with fatty stools should at once arouse suspicion that the patient is suffering from the loop syndrome.

The patients in the second group, the medical group, in which the disease arises spontaneously, are even more difficult to diagnose. In these, if megaloblastic anæmia is the presenting symptom, differentiation from true pernicious anæmia may be very difficult, unless the secretion of acid in the stomach is preserved or the patient is younger than is usual in pernicious anæmia itself. If diarrhœa or steatorrhœa has brought the patient under supervision, confusion with idiopathic steatorrhœa may occur unless an anatomical lesion of the intestine can be demonstrated radiologically, unless occult blood is found in the stools or one of the screening tests, such as the absorption of xylose or radioactive iron, gives an unexpectedly normal result. If the diagnosis is in doubt, per-oral biopsy of the mucosa of the small intestine may be of assistance because the mucosa of the small intestine is often normal in the loop syndrome whereas in idiopathic steatorrhœa the characteristic blunting of the villi and loss of absorptive surface are found.

Whatever the cause of the blind loop syndrome, it is important that an accurate diagnosis be made, for without it the chance of a surgical cure will be denied even to those in whom radical relief is possible, and they may be condemned to a complicated medical regime for the rest of their lives.

REFERENCES

ADDISON, T. (1855) On the Constitutional and Local Effects of Diseases of the Suprarenal Capsules. London.

BADENOCH, J., BEDFORD, P. D., and EVANS, J. R. (1955) *Quart. J. Med.*, **24**, 321.

BARKER, W. H., and HUMMEL, L. E. (1939) *Bull. Johns Hopk. Hosp.*, **64**, 215.

CASTLE, W. B., TOWNSEND, W. C., HEATH, C. W., and STRAUSS, M. B. (1929) *Amer. J. med. Sci.*, **178**, 748.

FABER, K. (1895) *Hospitalstidende*, p. 601.

MOLLIN, D. L., BOOTH, C. C., and BAKER, S. J. (1957) *Brit. J. Haemat.*, **3**, 412.

MONTUSCHI, E. (1949) *Proc. R. Soc. Med.*, **42**, 868.

TAYLOR, G. W. (1930) *New Engl. J. Med.*, **202**, 269.

WHITE, W. H. (1890) *Guy's Hosp. Rep.*, **47**, 149.

WIRTS, C. W., GOLDSTEIN, F., CALARESU, F. R., KRAMER, S., and CONCANNON, J. (1959) Proceedings of the World Congress of Gastroenterology. Baltimore; **1**, 451.

The Blind Loop Syndrome

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IN the previous paper, Dr. Badenoch has indicated the types of intestinal lesion which may be associated with the blind loop syndrome and he has stressed their relationship to megaloblastic anæmia and B_{12} deficiency. This paper describes the defects of intestinal function that may occur in the blind loop syndrome and indicates how these absorption defects may lead to

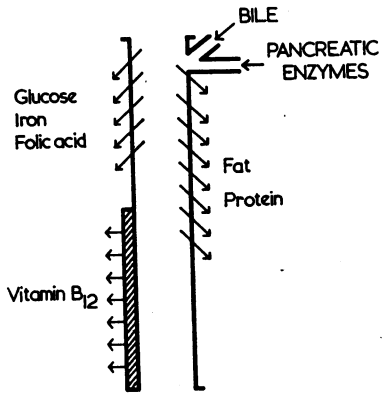

FIG. 1.—Sites of absorption in the small intestine.

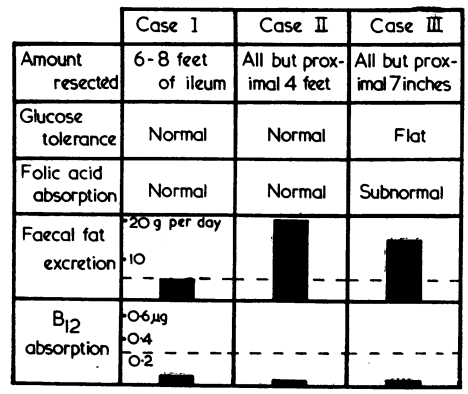

FIG. 2.—The results of glucose, folic acid, fat and vitamin B_{12} absorption tests in patients who had undergone resection of varying amounts of the distal small intestine (Cases I, II and III). In this and subsequent figures, the interrupted lines indicate the upper limit of normal fæcal fat excretion (6 g per day) and the lower limit of normal B_{12} absorption using a test dose of 1·0 µg (Mollin *et al.*, 1957).

deficiency states. The treatment is also discussed.

The pathogenesis of malabsorption and megaloblastic anæmia in jejunal diverticulosis will not be included in this paper, since this condition rarely requires surgical treatment.

Physiological Considerations

Fig. 1 illustrates diagrammatically the sites at which absorption of different substances appears to occur (Booth, 1960). Substances such as glucose, folic acid or inorganic iron, which require no digestion and are absorbed rapidly, are probably absorbed as soon as they reach the absorbing surface of the upper small intestine. Fat and protein require preliminary digestion by bile and pancreatic enzymes and they are absorbed more slowly; the rapid motility of the upper intestine propels them more distally before absorption is complete. The absorption of vitamin B_{12} is remarkable, for under physiological conditions it is only absorbed from the ileum (Booth and Mollin, 1959).

Effects of Intestinal Resection

Since B_{12} absorption occurs in the ileum, resection or disease of this area causes malabsorption of B_{12}. Whether an anatomical lesion of the intestine causes malabsorption of other substances depends on the site and extent of the lesion. This is illustrated first by the results of absorption tests in 3 patients subjected to resection of the distal small intestine (Fig. 2).

The first patient (Case I) had had 6 to 8 ft (2 m) of ileum resected. This caused malabsorption of vitamin B_{12}, but glucose, folic acid and fat, being absorbed proximally, were absorbed normally. In Case II the resection was more extensive, only four feet of the proximal jejunum remaining. Glucose and folic acid were normally absorbed but there was steatorrhœa in addition to malabsorption of vitamin B_{12}. In the third patient (Case III), the resection was so massive that there was not only malabsorption of B_{12} and steatorrhœa, but also interference with the absorption of glucose and folic acid (Fig. 2).

Malabsorption in these resection patients does not appear to be due to flooding of the remaining bowel with bacteria, for oral antibiotics are ineffective in improving absorption.

Blind Loop Syndrome

Intestinal absorption tests.—As in patients subjected to resection, the types of malabsorption in patients with blind loop syndromes depend on the site and extent of the lesion. However, it is likely that bacterial contamination of the small intestine plays the major part in causing malabsorption in these patients. There may be no actual loss of the absorbing surface of the small intestine, but the presence of the anatomical lesion appears to encourage the growth of an abnormal bacterial flora in the small intestine (Seyderhelm *et al.*, 1927; Girdwood, 1959) and this appears to be the factor that causes malabsorption (Badenoch *et al.*, 1955; Mollin *et al.*, 1957). Examples of the intestinal function tests in 3 patients are shown in Fig. 3.

The first patient (Case IV) had a stricture of the terminal ileum and there was only malabsorption of vitamin B_{12}. This situation is analogous to that seen after resection of 6 to 8 ft of ileum (Case I, Fig. 2) with the difference that in this case absorption improved to normal after a four-day course of Aureomycin (Fig. 3).

The lesion in the next patient (Case V) was more extensive. She had had two entero-entero anastomoses performed for tuberculous stric-

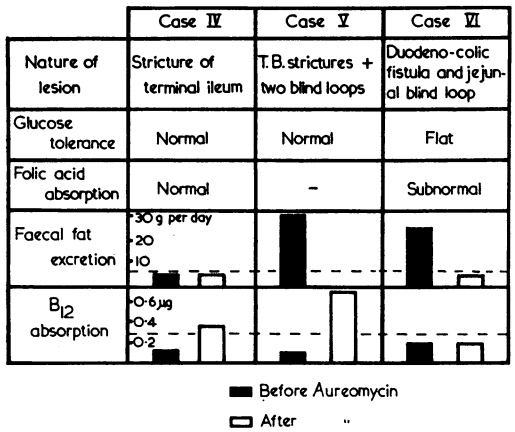

FIG. 3.—The results of similar absorption tests before and after antibiotics in patients with blind loop syndrome (Cases IV, V and VI).

tures and although the proximal few feet of her gut were radiologically normal, the distal intestine was very much dilated and contained several blind loops. She also failed to absorb B_{12}, but the more extensive lesion was associated with steatorrhœa. Glucose tolerance test, however, was normal. The absorption of B_{12} was temporarily improved by Aureomycin (Fig. 3).

The third patient (Case VI) had a duodeno-colic fistula and a large entero-entero anastomosis with an obstructed loop of jejunum. There was steatorrhœa and subnormal B_{12} absorption, but like the patient with the most extensive resection (Case III, Fig. 2) absorption of folic acid and glucose was also abnormal. The steatorrhœa improved after prolonged tetracycline therapy. In her case, however, B_{12} absorption remained subnormal after this treatment.

B_{12} deficiency in the blind loop syndrome.—Patients who have blind loops, strictures, or fistulæ involving the distal small intestine almost invariably fail to absorb vitamin B_{12} normally, for the ileum is flooded with bacteria derived either from stasis within obstructed loops or through fistulæ from the colon. It is therefore not surprising that the predominant and often the only deficiency occurring in these patients is a megaloblastic anæmia due to B_{12} deficiency (Mollin and Ross, 1954; Mollin, 1959). This may sometimes be severe enough to cause subacute combined degeneration of the spinal cord (Hurst, 1933; Wilkinson, 1955; Richmond and Davidson, 1958). Some years may elapse before B_{12} deficiency develops for, as after total gastrectomy, anæmia will only occur when the stores of vitamin B_{12} in the liver have been exhausted. The development of B_{12} deficiency in the patient with tuberculous strictures and blind loops (Case V, Fig. 3) is shown in Fig. 4.

Case V.—This patient first presented at Hammersmith Hospital in 1943 with tuberculous peritonitis. In 1944 and 1946 recurrent bouts of intestinal obstruction necessitated entero-entero anastomoses as life-saving procedures. She had diarrhœa following these operations and then, four years later, in 1950, developed a megaloblastic anæmia. This was associated with a subnormal serum B_{12} concentration (70 $\mu\mu$g per ml).[1] She was treated first with a single injection of 20 μg of vitamin B_{12} and there was an excellent reticulocyte response and rise in her red cell count (Fig. 4). For four years she continued to receive 40 μg of B_{12} monthly and since 1954 has been given 200 μg monthly. Apart from a recurrence of her intestinal tuberculosis in 1957 she has remained well without other treatment. Her diarrhœa has been controlled

[1] Normal range 140 to 960 $\mu\mu$g per ml (Mollin and Ross, 1957).

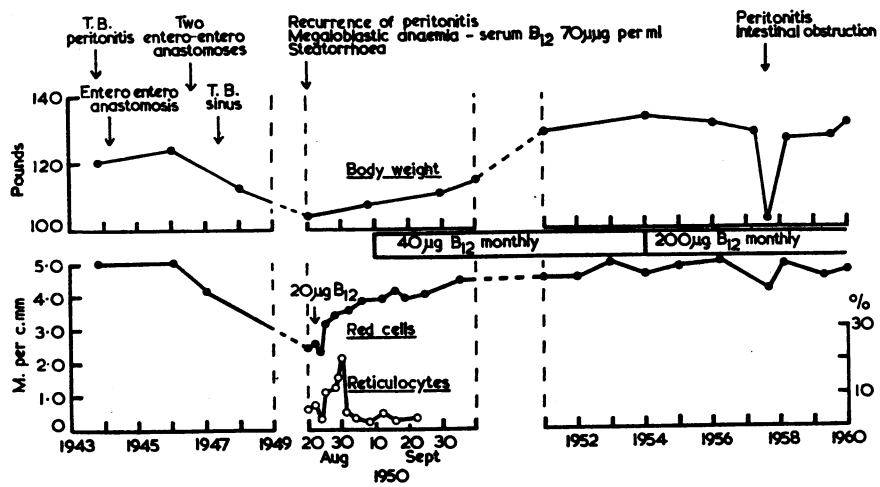

FIG. 4.—The changes in body weight, red cell count and reticulocytes in a patient with blind loop syndrome associated with tuberculous peritonitis, treated with vitamin B_{12} (Case V).

by a low fat diet and despite marked steatorrhœa she has no osteomalacia or evidence of any other deficiency. This is an example of a distal intestinal lesion causing a pure B_{12} deficiency state.

In this patient the megaloblastic anæmia was an incident during the course of prolonged and irreparable intestinal disease, associated with obvious intestinal symptoms and gross steatorrhœa. In contrast, patients with a localized lesion of the ileum may have minimal intestinal symptoms, and it may be the anæmia that first draws attention to an intestinal lesion. This type of presentation is illustrated by a patient who initially attended Hammersmith Hospital (Professor J. McMichael) with complaints of general malaise and shortness of breath (Case VII).

Case VII.—Her hæmoglobin was 9·6 g per cent and stained blood films showed macrocytes and signs of iron deficiency. Sternal marrow was megaloblastic and her serum B_{12} concentration (45 $\mu\mu$g/ml) was subnormal. She had occult blood in her stools. Since she had free acid in the gastric juice, it was unlikely that she had Addisonian pernicious anæmia, and for this reason attention was directed to the small intestine. A barium follow through (Dr. J. Laws) revealed gross dilatation of the terminal ileum which was interpreted as indicating chronic intestinal obstruction. After treatment with iron, vitamin B_{12}, and oral antibiotics, laparotomy was performed by Mr. R. H. Franklin who discovered a grossly dilated segment of terminal ileum. It was obstructed by a congenital vascular band a few inches proximal to the ileocæcal valve (Fig. 5). Resection of the stricture and end-to-end anastomosis was performed and the result has been excellent in this patient.

Effects of surgery.—Where possible, blind loops should be corrected surgically and the results are usually good provided that extensive resection is not required. The main operative hazard is often the associated malnutrition and patients who are severely undernourished are bad operation risks. For this reason preparation for operation is important. Anæmia and other deficiencies should be corrected and a preliminary course of oral antibiotics is advisable.

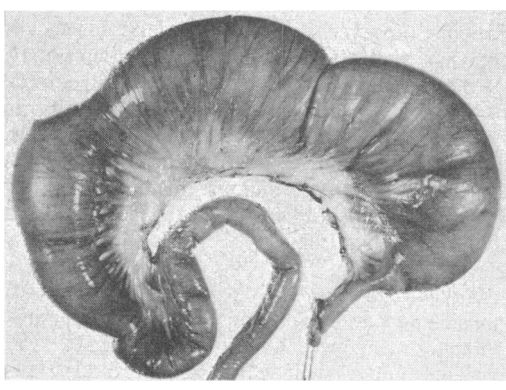

FIG. 5.—Operation specimen showing gross dilatation of the terminal ileum caused by a congenital stricture a few inches proximal to the ileo-cæcal valve (Case VII).

In some patients, such as those who have chronic adhesive tuberculous peritonitis, surgical correction may not be technically possible. However, as Fig. 4 shows, such patients may remain well if their anæmia is treated with vitamin B_{12} and they are given a low fat diet.

Blind Loop Syndrome with Intestinal Resection

Intestinal function tests.—Blind loops, stricture, or fistulæ may be complicated by intestinal resections. In patients with such lesions, the type of malabsorption depends on the extent of the resection which has been carried out. Two extreme examples are shown in Fig. 6.

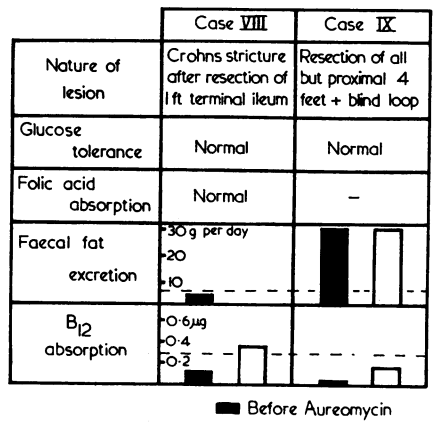

FIG. 6.—The results of absorption tests before and after antibiotics in patients with resection associated with stricture (Case VIII) and blind loop (Case IX).

The first patient (Case VIII) had only lost 12 in. (30 cm) of the terminal ileum but a stricture had occurred at the site of the anastomosis. Her malabsorption was predominantly due to her stricture for she failed to absorb B_{12} and this was corrected by Aureomycin.

In the second patient (Case IX) the resection was very much more extensive and only about 4 ft (120 cm) of the jejunum remained. A side-to-side anastomosis to the colon had been performed and as often happens after this operation, the terminal small intestine had blown up to form an enormous blind loop. However, the malabsorption in this patient was predominantly due to the resection, not to the blind loop, for in

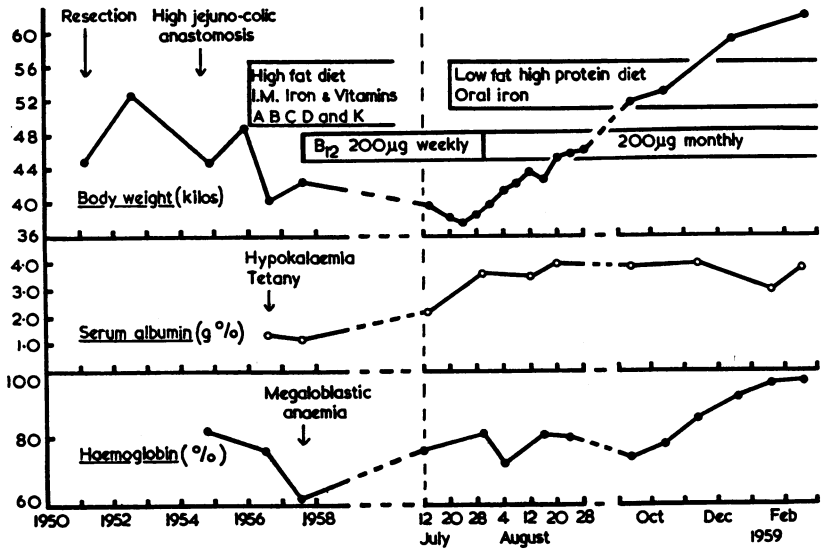

FIG. 7.—The changes in body weight, serum albumin and hæmoglobin in a patient with Crohn's disease (Case X), treated with a low fat diet.

contrast to the blind loop patients, no improvement in absorption occurred when Aureomycin was given (Fig. 6). In such patients surgery is not usually curative for the patient's resection itself often causes malabsorption (Fig. 2). Although the blind loop in this patient did not contribute to his malabsorption, it did cause anæmia from chronic blood loss. The mucosa of blind loops often becomes ulcerated and bleeds and in this case bleeding only ceased when the blind loop was corrected by further surgery.

Dietary management.—The commonest condition causing the mixed type of lesion, resection together with blind loops, is Crohn's disease. Vitamin B_{12} deficiency occurs almost inevitably in such patients and they usually require treatment with this vitamin (Meynell *et al.*, 1957). However, their diet is also important. A low fat diet is necessary if there is steatorrhœa, for large amounts of dietary fat may cause incapacitating diarrhœa. This is shown in Fig. 7, which illustrates the course of a patient with extensive Crohn's disease (Case X) whose clinical condition improved greatly when she was given a low fat diet.

Case X.—This patient first developed symptoms in 1950 and in early 1951 required a resection of the terminal ileum. In 1954, there was an extensive recurrence and a high jejuno-colic anastomosis was necessary, leaving approximately 4 ft (120 cm) of jejunum proximal to the anastomosis. After this operation she had severe diarrhœa, developed hypoproteinæmia and her legs became œdematous. By 1956 she was very ill and grossly undernourished. She was being treated with injections of iron and most of the vitamins, an injection of some sort being given every day of the week except Sundays during this time. In 1957 she developed megaloblastic anæmia and she was also given vitamin B_{12}. Throughout this period, however, she had been treating herself with a high fat diet in a vain attempt to fatten herself up. When the dietary fat was reduced in August 1958 she made a remarkable recovery. She now only requires one injection parenterally, vitamin B_{12} once monthly, and remains well.

Conclusion

Blind loop syndromes are less frequently encountered to-day, for surgeons are aware of the potential hazards of the entero-entero anastomosis or of side-to-side operations. In some patients, however, it may not be possible to avoid creating such lesions. If such patients have steatorrhœa, their diarrhœa may be controlled by a low fat diet, and if megaloblastic anæmia develops, they require vitamin B_{12}. Their anæmia should never be treated with folic acid alone for, as in pernicious anæmia, this may precipitate subacute combined degeneration of the cord (Best, 1959).

Acknowledgments.—We wish to thank the physicians and surgeons of Hammersmith Hospital who have kindly allowed us to study patients under their care. We are also particularly grateful to Dr. F. Avery Jones, Dr. N. F. Coghill and Dr. R. J. Harrison for their collaboration in the study of patients described in this paper.

REFERENCES

BADENOCH, J., BEDFORD, P. D., and EVANS, J. R. (1955) *Quart. J. Med.*, **24**, 321.

BEST, C. N. (1959) *Brit. med. J.*, ii, 862.

BOOTH, C. C. (1960) *Brit. J. Radiol.*, **33**, 201.

——, and MOLLIN, D. L. (1959) *Lancet*, i, 11.

GIRDWOOD, R. H. (1959) *Proc. R. Soc. Med.*, **52**, 37.

HURST, A. F. (1933) *Guy's Hosp. Rep.*, **83**, 47.

MEYNELL, M. J., COOKE, W. T., COX, E. V., and GADDIE, R. (1957) *Lancet*, i, 901.

MOLLIN, D. L. (1959) Lectures on the Scientific Basis of Medicine (Brit. Postgrad. Med. Fed.). London; **7**, 94.

——, BOOTH, C. C., and BAKER, S. J. (1957) *Brit. J. Hæmat.*, **3**, 412.

——, and ROSS, G. I. M. (1954) *Proc. R. Soc. Med.*, **47**, 428.

——, —— (1957) Vitamin B_{12} und Intrinsic Factor. I Europäisches Symposion, Hamburg. Ed., H. C. Heinrich, Stuttgart; p. 417.

RICHMOND, J., and DAVIDSON, L. S. P. (1958) *Quart. J. Med.*, **27**, 517.

SEYDERHELM, R., LEHMANN, W., and WICHELS, P. (1927) *Krankheitsforschung*, **4**, 263.

WILKINSON, R. W. (1955) *Lancet*, i, 74.

The Natural History of Achalasia of the Cardia [*Abridged*]

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THE natural history of achalasia of the cardia has been studied by tracing the progress of 85 unselected patients in whom the diagnosis was first established between 1933 and 1948. In 1958 33 of these patients were found to be alive and were investigated clinically and radiologically. 24 were known to have died and the cause of death was established. Of the remaining 28 patients, 8 were untraced, 4 known to have died were excluded because the cause of death could not be established, and 16 were excluded because of uncertainty in the diagnosis of achalasia.

Patients No Longer Alive (24)

Duration of disease.—Fig. 1 shows the age of onset of the disease and its duration in the group of 24 patients who died from known causes. While those patients in whom the disease started at an early age failed to achieve their expectation of life by many years, a calculation of the expectation of life from the Life Tables of the Registrar-General of the remainder shows that the majority died before their expected age of survival. 5 patients exceeded their expectation of life.

Cause of death.—Of these 24 patients, 7 died

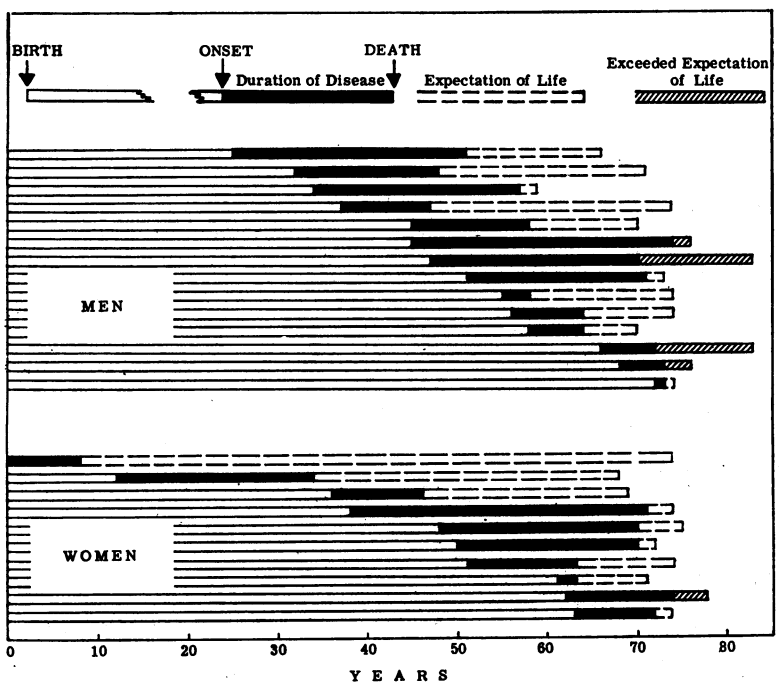

FIG. 1.—Duration of life.