and had osseous metastases. The histology of the tumour was that of a non-argentaffin carcinoid. Many patients with these tumours excrete excessive amounts of uropepsinogen (they have a high incidence of duodenal ulcers), but we have found that their acid secretion varies; perhaps the acid estimation is affected by the strong motor contractions of the stomach leading to rapid emptying. With regard to the question of œdema, 5-HT has been shown by Hulet and Perera (1956) to cause sodium retention. Most often the cardiac condition seems to explain the occurrence of œdema. I think it unlikely that many patients will have cardiac surgery for pulmonary stenosis, since it tends to develop late in the disease.

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"Blind Loop" Syndrome

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THE term "blind loop" is an unsatisfactory descriptive title which may be extended to cover a number of apparently diverse intestinal conditions, such as massive diverticulosis and intestinal stricture, all of which may present with a similar clinical picture of malnutrition, anæmia, steatorrhœa, &c.

Historically there was early surgical recognition of the complications of side-to-side anastomosis with subsequent pouch formation (Cannon and Murphy, 1906) and possible ulceration and perforation. There followed the observation by Meulengracht (1929) that the clinical picture of pernicious anæmia might be associated with certain intestinal abnormalities, in particular benign strictures. While it is no longer possible to accept all these early cases of pernicious anæmia as due to intestinal strictures, his paper undoubtedly stimulated work on the relation of anæmia to intestinal function.

In the early accounts the concept of intestinal auto-intoxication was predominant and, as early as 1920, Seyderhelm (1922) treated pernicious anæmia with ileostomy on the theory that bacterial poisoning might be responsible. In 2 out of 5 patients so treated he obtained a remission, with great improvement in the blood picture and gain in weight. A relapse which ended in death occurred following the closure of the ileostomy. The failure of this treatment in another patient was ascribed to the continuation of infection in the small intestine. These results were confirmed elsewhere (Dixon *et al.*, 1925).

In 1924, Seyderhelm and others were able to produce artificially a hyperchromic anæmia in a dog with an intestinal stricture, and related this anæmia, not to the degree of narrowing produced, but to the infection of the intestinal canal above the stricture which followed. Where this infection did not occur, no anæmia resulted. Other experimenters (Tönnis and Brusis, 1931, 1932) constructed in dogs blind loops which were arranged to fill by peristalsis. Anæmia was produced and extirpation of the loop greatly improved the clinical condition. Life was prolonged by the giving of liver injections. Other experiments showed that the use of intestinal antiseptics such as trichlorcresol (Horster, 1935) greatly lengthened life and prevented the onset of loss of weight and anæmia.

It should be noted that the production of blind loops does not necessarily result in anæmia. Pearce (1934) confirmed in dogs that when the segment of intestine was so arranged that it emptied, the animal remained normal, and appetite and activity was unimpaired. Only when the loop was so arranged that it filled did symptoms appear of weakness, lethargy, and loss of weight, and unless the loops were resected the animals died. He reported no significant changes in the blood.

The most recent animal work has been that of Cameron *et al.* (1949) who, after forming blind sacs under certain conditions in rats, succeeded in producing a macrocytic anæmia and confirmed and extended earlier experimental observations. They were able to prolong life and cure anæmia by using chlortetracycline and folic acid. Since some of their rats died without anæmia, they emphasized that the deficiency must be multiple. All this experimental work may be summarized by saying that the production of intestinal blind loops, sacs or strictures may profoundly affect an animal, but only when stasis has been produced; that these effects include malnutrition, anæmia, loss of weight, and may terminate in death; that the effects may be abolished by extirpation of the blind loop or sac, or the resection of the stricture; and that improvement of the animal's condition may be achieved by intestinal antiseptics, more recently by antibiotics, and also by giving folic acid, liver injections, &c.

In human pernicious anæmia, Castle's hypothesis, which fitted so many of the facts, might have been expected to destroy the theories which saw bacterial intestinal infection as in some way causative (Castle *et al.*, 1930). But Castle wrote prophetically: "Next to a defect of the original formative process within the stomach, the loss of the absorptive power of the intestinal tract, either mechanically or by way of bacterial invasion, or the destruction in the bowel of the effective principle after formation would be the most obvious ways in which a deficiency of the

final effective substance could be brought out." By 1936 Minot could write: "Occasionally, a patient with an intestinal short circuit, maintained with difficulty on liver extract administered orally, is able to maintain his blood without taking liver extract after the intestines have been returned to essentially their normal state by operative procedure." There is here the clear recognition, even if it was then not widespread, of one form of the "blind loop" syndrome.

Parallel to these clinical observations, there was another line of enquiry. By 1939, animal physiologists had pointed out that vitamin synthesis of several members of the B complex took place in the rumen of the sheep (McElroy and Goss, 1939). This was evidence that the animal's requirements of vitamins could to some extent be supplied by synthesis within the gut. These conclusions are probably true of man, so that we depend to a variable extent on the presence of bacteria in our own gut to supply our needs. There is therefore justification for thinking that the supplanting of bacteria which normally synthesize vitamins, or the growth of bacteria which themselves utilize substances required by the host, might result in a deficiency state.

There is other evidence to support this concept. The discovery that sulphonamides can alter bacterial growth in the intestine was soon followed by the observation that antibiotics can improve the utilization of food in treated animals and promote more rapid growth. These effects can be produced by a series of chemical substances which have nothing in common, apart from their antibacterial action. While there seems no clear relationship between the feeding of an antibiotic and the establishment of any particular type of bacterial growth, the empirical results are unquestioned, so that this device has proved one of the major advances in livestock husbandry. On human subjects only a few observations on the action of antibiotics in hastening growth have been carried out. There are, however, several papers which suggest that growth in children may be improved by their administration. Even in young men at the end of their growth period, significant increases in weight were observed in an antibiotic-treated group. In a more specific study, there is evidence that blood formation may be aided in patients deficient in folic acid or cobalamin by giving antibiotics which are presumed to act by promoting the bacterial synthesis of these substances (Jukes, 1955).

Evidence of a different kind is supplied by parasitology. There is no doubt that parasitized animals grow at a slower rate than parasite-free animals and that on the same food intake the weight gain is less. Why is this? There is no evidence that the parasites act by diverting calories, and the most promising hypothesis is that the parasites act by using essential trace food factors necessary for the adequate nutrition of the host.

There are therefore good grounds for thinking that malnutrition might arise from an altered flora in the intestine resulting in a deprivation of essential trace food factors. There is evidence that an altered flora may occur in blind loops or sacs of the intestine and in intestinal diverticula (Girdwood and Doig, 1957). If this general theory is accepted, then we should distinguish between those sacs or loops which, though anatomically blind, are not stagnant. For example, there is no account in the literature of the "blind loop" syndrome arising with a Meckel's diverticulum, and this is consistent with the experimental work which shows that if the sac readily empties, no untoward symptoms appear. Some writers have hinted that the afferent loop of a Polya-type anastomosis following gastrectomy in which the duodenum is closed can act as a "blind loop". It is of course blind anatomically but this particular piece of gut is extremely active, empties itself readily, and is normally washed through by pancreatic juice and bile after each meal. It is therefore not comparable to the "blind loop" formed by surgical short-circuiting of an obstruction.

If we accept as an essential condition an alteration of flora, it is somewhat difficult to see how bacteria, growing in loops or sacs and by definition out of the main intestinal current, can obtain these food factors and so deprive their host. The abnormal bacterial growth may, of course, spread throughout the bowel, but there is another explanation which deserves consideration. I refer to the concept, adopted by some parasitologists as a working hypothesis, of the exocrine-enteric circulation (Read, 1950).

If we consider the movement of substances across the intestinal wall, we all agree that a fluid secretion occurs into the gut, and that the water is absorbed elsewhere. The extent of this transfer is known to be very great. There is equally no doubt that electrolytes circulate in a similar way. No one questions that bile salts circulate with a time cycle of the order of eight to sixteen hours. Bile salts are synthesized and destroyed, but the body seems to economize by using them again and again. If this mechanism exists for bile salts, may it not occur for other substances, particularly if they play a catalytic role in biochemical reactions and so can be used repeatedly? The simplicity of the hypothesis is very attractive. There is, at any rate, a good deal of evidence to make it likely that there is such a

circulation which includes various vitamins (Read, 1950).

If this is accepted as a working hypothesis, then it is easy to see how bacteria in a stagnant loop or diverticulum can interrupt this recirculation, since these food factors may appear in all intestinal secretions. It would also explain why quite small collections of bacteria might give rise to symptoms of malnutrition, since these bacteria do not have to consume a fraction of the ingested factor, but have only to remove part of a very much smaller amount, which is being constantly recirculated. There is one other phenomenon which may be explained by this theory, and that is the reported observation (Halsted *et al.*, 1956), that the anæmia in the "blind loop" syndrome is unaffected by neomycin which is not readily absorbed, whereas it may be cured by chlortetracycline which is readily absorbed, and may therefore appear in sufficient concentration in the "blind loop".

Clinical Considerations

The frequency with which the "blind loop" syndrome follows a short-circuiting operation is unknown. Though it is probable that examples may be missed, especially if they have no severe anæmia, it seems likely that the condition is rare and this suggests that the conditions for bacterial growth in the loop, sufficient to impair nutrition, are critical and not easily attained. The symptoms of the general "blind loop" syndrome may be considered under two headings:

(1) Symptoms from the purely structural abnormality in the gut, such as the anatomical arrangement of the "blind loop", the extent of the diverticulosis, or the presence of strictures producing intestinal obstruction.

(2) Symptoms arising from intestinal dysfunction. These comprise malnutrition, which includes loss of weight, anæmia, deficiencies of essential food factors, and their resulting neuropathies. There may also be steatorrhœa, diarrhœa or colicky pain. We cannot pretend that the origin and mechanism of all these symptoms is clear.

The explanation of the anæmia, which may be due to cobalamin or folic acid deficiency, or both, has been fully reviewed and will not be discussed further (Foy and Kondi 1954; Badenoch, 1958). Deficiencies of essential food factors may lead to vitamin deficiency syndromes or to loss of weight. Steatorrhœa, which is frequently seen, is not easily explained and appears to be due to malabsorption. In the case of blind loops high up, which involve the duodenum, inadequate mixing of food with pancreatic juice is a conceivable explanation in some cases. It should also be remembered that, in any severe state of malnutrition, the pancreas may become secondarily affected and therefore the steatorrhœa becomes partly pancreatic in origin. In a case described by Brock (1939), with multiple intestinal strictures, the steatorrhœa showed only 20% splitting, suggesting a pancreatic fibrosis as responsible. Diarrhœa in a mild form is a common symptom and may be due to several causes. Occasionally it appears in a very severe form. In one patient we saw, the only complaint was of a profuse, watery diarrhœa, which came on paroxysmally, particularly at night. This description strongly recalled the diarrhœa occasionally seen with severe diabetes and which, it has been suggested, may be due to a neuropathy of the abdominal autonomic nervous system (Joslin *et al.*, 1952). His only abnormality, apart from absent ankle-jerks, was a multiple diverticulosis throughout the entire gut. There was no anæmia, and all biochemical tests were normal. In 5 cases of extensive diverticulosis, described by Badenoch *et al.* (1955), all had diarrhœa. In one of these cases there was mental change, in another there were paræsthesiæ, and in a third there was gross peripheral neuritis. The possibility that in such cases the diarrhœa is an expression of a neuropathy of the autonomic system, due to some nutritional defect, ought seriously to be considered.

Intestinal colicky pain, where obstruction is not present, may possibly be due to paroxysmal cramps of the intestine as may also occur in a diabetic neuropathy and diarrhœa.

Diagnosis

The diagnosis of a true "blind loop" or sac may be difficult if intestinal fistulous formation has occurred spontaneously. More frequently the "blind loop" follows some previous surgical operation, such as the short-circuiting of an obstruction. Provided the suspicions of the surgeon or physician are aroused when a patient shows some symptoms or signs of malnutrition following a previous abdominal operation, the diagnosis is likely to be made sooner or later. It is more easily made if the patient has a macrocytic anæmia, since an identification of its cause can now be made with considerable precision. Cases are more liable to be missed if they have no overt anæmia, or if the stools do not obviously suggest a steatorrhœa. The radiological investigation may prove difficult, or may fail, since barium will not readily enter a "blind loop", and the post-operative conditions under which "blind loops" arise make radiological interpretation difficult.

Intestinal diverticulosis may be discovered by accident radiologically; probably the majority

of cases are symptomless. It may also be found on radiological examination of a patient with malnutrition, anæmia, steatorrhœa, &c. Diverticula may fail to fill and their number and extent are always likely to be underestimated.

As a further diagnostic aid in all doubtful cases of this syndrome, an absorbable antibiotic such as chlortetracycline should be given. If clear improvement results in the blood picture or clinical state, the diagnosis is strongly supported.

Treatment

Operation may be necessary if "blind loops" are suspected, to judge the extent of intestinal diverticulosis, or, in rare instances, to resect a stricture. Before operating, it should be possible in most patients to improve their general condition and the anæmia can nearly always be ameliorated. A low-fat diet may be necessary, and mineral and vitamin deficiencies will need replacement. If a "blind loop" can be resected, and normal continuity restored, there should be a complete and dramatic recovery. If the bowel is the seat of multiple diverticulosis, this may prove at operation to be far more extensive than was anticipated, and resection may be impossible. If radical treatment is not possible, the patient can usually be greatly improved by medical measures.

If the general ætiology of all these conditions is accepted, that is, that there exists under certain conditions in the intestine an altered flora such that essential trace food factors are lost to the host, then the purely descriptive name of "blind loop" should be abandoned, to be replaced by some name which describes the functional state of privation. The concept of this privative state may then be extended. Dare we regard for instance, the fatty liver which proceeds to fibrosis, seen in some patients with severe ulcerative colitis, as, in part, a nutritional disease of the liver due to involvement of the cæcum and ascending colon, that is, that part of the gut which is said to be the main site of vitamin synthesis? Our attention was directed to this possibility when, a year ago, we saw a patient with œdema and hypoproteinæmia, who was found to have a carcinoma of the cæcum, with a fatty liver, and amblyopia. The carcinoma was successfully resected; the liver is now progressing to fibrosis. Such a possibility should receive consideration.

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Massive Intestinal Resection

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The term "massive intestinal resection" has by convention come to mean the loss of more than 200 cm., or approximately 7 feet, of small bowel. The early reports were content with short-term survival and in the rivalry of the early years of the century surgeons competed in the magnitude of their resections. Of more interest to the patient is the amount of small bowel that remains and recent emphasis has shifted to the investigation of the effects of resection in survivors.

Normal Length of Small Bowel

This is extremely variable and increases with stature and in races taking a diet containing much roughage. Bryant (1924) found lengths varying between 10 ft. and 28 ft. 4 in.; Treves (1885) between 15 ft. and 33 ft., while Kallio (1932) found a mean of 22½ ft., or 675 cm., in 1,161 individuals measured *post mortem* or at operation. Alvarez (1948), however, gives a length of 8 to 10 ft. in the live state.

Measurements vary with the tone of the muscle, or the presence of the mesentery or the manner of its detachment, and should be made in the unfixed state. The length of remaining intestine cannot be deduced by a simple subtraction of the