unrecognized air swallowing in the aspiration method of treatment. There are no post-operative chest complications, so common after operation for perforation. It may be that the risk of subphrenic abscess will be reduced, if not entirely eliminated, for it is likely that the patient's increased respiratory excursions while under the influence of the anaesthetic can, by suction, fill the subphrenic spaces with peritoneal exudate.

What the ultimate fate of these patients will be it is not possible to say at present. So far only Case 5 has been submitted to operation. All the others left hospital symptom-free, though of course on strict ulcer diet. Case 12 should certainly be subjected to gastrectomy if the gastric ulcer is still present on review. If and when gastrectomy or other operative procedure is required in any of these cases it is to be expected that easier operating conditions will be found than would be the case if a laparotomy had already been performed.

It will be noted from the follow-up that 13 of the 15 cases were seen on the average almost 12 months after perforation, and that their condition was at least no worse than if they had been subjected to an immediate operation. The above series of cases is admittedly a small one, but, even so, I would suggest that immediate operation in simple gastro-duodenal perforation is no longer necessary, and that any operative intervention should be reserved for such complications as may arise. Since this paper was written further cases have been similarly treated with equal success.

I wish to thank Mr. J. C. Jefferson for the watchful eye he kept on the patients and for his help and criticism of this paper; also Dr. T. Benson, house-surgeon, for his enthusiastic co-operation.

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MACROCYTIC ANAEMIA

BY

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The aetiology and treatment of macrocytic anaemia have in recent years been the subject of much investigation, both clinical and experimental. The following case of macrocytic anaemia cured by surgery gives support to the experimental conclusions.

Literature

In 1897 Faber first reported the association of anaemia with gross intestinal disease; many attempts have since been made to relate intestinal disease in human beings, and conditioned disease in animals, to the aetiology of macrocytic anaemia. Anaemia in human beings has long been familiar as a complication of gastrectomy and

of resection of the small bowel. It seemed probable that this anaemia is due to an unaccustomed dietary regime and to the hurried passage of the bowel contents in the changed circumstances. In fact, however, experimental resection of varying lengths of the gut, including in some cases the stomach, failed to produce a macrocytic anaemia in animals. Miller and Rhoads (1935), working on dogs, succeeded in producing only "a mild hypochromic anaemia," while Brown (1938) concluded that "resection alone did not lead to diarrhoea, anaemia, or paralysis." Wintrobe *et al.*, (1939) found that removal of the duodenum with a portion of the jejunum in addition to the stomach resulted in microcytic anaemia. Jensenius (1945) reviewed the literature and carried out a carefully controlled series of experiments on dogs. He concluded that resections of the terminal ileum may be followed by a macrocytic anaemia or a tendency to such.

It therefore seemed that lesions of the proximal gut would tend to produce a microcytic anaemia, and that lesions of the distal bowel would tend to produce a macrocytic type.

Seyderhelm *et al.* (1924), by inducing fibrous strictures of the terminal ileum, were able to produce a macrocytic anaemia in two of seven dogs that survived the operation. They decided that "an abnormal bacterial flora in the small intestine was decisive in the development of the anaemia." Tönnis and Bruns (1931) achieved the same results and attributed the anaemia to autointoxication, which could be relieved by the removal of the affected loop of intestine.

It is to be noted that these experiments introduced a new element, that of partial obstruction as distinct from resection of the bowel. These observations, made by Seyderhelm *et al.* more than twenty years ago, are in accordance with the present belief that a disturbance of the normal fermentative processes in the small intestine and colon results in the failure of production of folic acid and of vitamin B₁₂, with the consequent development of a macrocytic anaemia.

Cartwright *et al.* (1946) produced abnormal intestinal conditions in pigs by withholding folic acid, para-aminobenzoic acid, and inositol, and giving succinylsulphathiazole and a folic-acid antagonist. The four pigs used became weak and listless, with loss of appetite; growth was poor, and diarrhoea developed; in three to six weeks an anaemia, macrocytic in type, with a megaloblastic bone marrow, supervened, which responded to folic acid but not to liver.

In an attempt to find a laboratory animal in which an experimental macrocytic anaemia could be produced at will for assay of therapeutic preparations, Watson, Cameron, and Wits (1948) operated on rats, producing a blind antiperistaltic intestinal loop, and by this means succeeded in inducing a macrocytic (megaloblastic) anaemia.

Since Faber's early observation of the association of anaemia with intestinal disease in humans many clinicians have reported cases in which regional lower-intestinal lesions have been associated with macrocytic anaemia. Barker and Hummel (1939) analysed 51 cases of macrocytic anaemia in which the primary lesion seemed to be intestinal strictures or faulty anastomosis. They suggest that the pathogenesis of this form of anaemia is intimately connected with stagnation and putrefaction of the intestinal contents, resulting perhaps in the absorption of toxins, and that the haemopoietic liver principle may act as a detoxicator of these

substances rather than as a catalyst of red-cell maturation. They point out that the treatment of the syndrome depends on the surgical extirpation of the cause of stagnation.

We believe the case here recorded to be of interest in that it provides the analogy, in respect of aetiology, treatment, and results, to the animal experiments of Professor Witts. In both cases a blind antiperistaltic intestinal loop was produced, a macrocytic anaemia resulted, and the anaemia was cured by excision of the loop in the human, without recourse to folic acid or liver.

Case Report

An electrical engineer aged 35 attended hospital on September 3, 1948, complaining of colicky pains in the abdomen of one year's duration. The pain was felt almost immediately after meals and was accompanied by severe

Diagram showing the anatomy found at operation. A = proximal loop of terminal ileum. B = blind end at inguinal ligament. C = blind end of distal loop. D = fistula between proximal and distal loops. E = entero-anastomosis. F = twisted blind loop.

flatulence. There had been no vomiting, and the appetite was about average. The bowels were regular, with no diarrhoea. He also complained of cramps in the legs and of sweating profusely. There had been considerable loss of weight, as evidenced by his clothes.

In 1942 he had been admitted to another hospital with a strangulated inguinal hernia of some days' duration. At operation gangrenous bowel had been found, and, after laparotomy, a Paul-Mikulicz resection had been performed. After prolonged convalescence he had returned to work and had remained in reasonable health until one year before the time of examination.

He was thin almost to the point of emaciation, was pale and listless, and showed clinical evidence of anaemia. His tongue was normal; his finger-nails were brittle, and there was possible early clubbing of the fingers. The abdomen was thin-walled and protuberant, especially in the lower right

quadrant. Coils of distended bowel were palpable in the lower abdomen, and irregular waves of peristalsis could be seen. On September 3 his blood count was: Hb, 76% (10.49 g.%); red cells, 3,090,000 per c.mm.; colour index, 1.2; mean diameter, 7.6 μ ; anisocytosis, ++; M.C.V., 113 μ^3 ; M.C.H.C., 29.99%; leucocytes, 4,800 per c.mm. (polymorphs 40%, lymphocytes 51%, monocytes 9%); E.S.R., 2 mm. in one hour; icterus index, 7 units; blood sugar, fasting, 77 mg. per 100 ml. A test meal showed sustained hyperchlorhydria.

A diagnosis of subacute intestinal obstruction of small-bowel type was made, and on October 31 a laparotomy was performed.

The abdomen was opened through a lower paramedian incision, and distended small bowel presented in the wound. The right iliac fossa was a mass of adhesions, and the anatomy was finally demonstrated only after considerable dissection and with some difficulty. When finally displayed the position was found to be as follows. At about 3 ft. (0.9 metre) from the ileo-caecal valve the proximal loop of the terminal ileum ran down to a blind end at the internal inguinal ring (see Diagram). About 2 in. (5 cm.) above the internal ring a fistulous opening connected the proximal loop to the distal loop of terminal ileum, which also terminated in a blind end at the internal ring. About 6 in. (15 cm.) above this fistula an entero-anastomosis had been performed. In carrying out the anastomosis the proximal loop had been rotated through 180 degrees before being united to the distal loop, thus producing an antiperistaltic anastomosis.

The contents of the intestine therefore passed down the proximal loop of ileum, through the fistula, up the distal loop of ileum to the entero-anastomosis, and so back into the proximal loop in a circus movement. The terminal ileum distal to the anastomosis and the caecum were collapsed. Numerous very large soft glands were present in the mesentery.

After some consideration the entire complex was resected *en masse*, and a side-to-side enterocolostomy performed immediately distal to the caecum. Convalescence was surgically uneventful.

After operation the blood count rose to normal of its own accord. On December 13 the blood picture was: Hb, 98%; red cells, 5,230,000; C.I., 0.94; mean diameter, 7.15 μ .

Up to the time of his last visit to the follow-up clinic, January, 1950, this improvement had been maintained.

Comment

This case differs from those reported by Barker and Hummel and by others in the nature of the causative lesion. In this instance the essential pathology was not a stricture of bowel due to trauma, disease, or an inadequate stoma, but an antiperistaltic anastomosis causing virtually a blind loop, and thus stagnation of the bowel contents. It was in fact precisely the distortion which had been produced deliberately in rats in order to induce a macrocytic anaemia.

All of the 51 cases of lower-intestinal lesions analysed by Barker and Hummel showed anaemia, but 42 presented with gastro-intestinal symptoms; 25 had glossitis, in 4 glossitis was absent, and in 22 glossitis was not mentioned. Macrocytosis was found in 39 cases, and 11 were stated to be suffering from pernicious anaemia; one case showed no macrocytosis. Hyperchromia was recorded in 32 out of 42 cases, while leucopenia was present in 30 cases, absent in 6, and not mentioned in 15. Free hydrochloric acid was present in 17 cases, absent in 19, and not recorded in 15.

Our patient presented with loss of weight and gastro-intestinal symptoms. Anaemia was clinically obvious. Examination showed a macrocytosis with a megaloblastic

bone marrow, neutropenia, and hyperchlorhydria. He stated that his tongue had been sore, but examination showed no abnormality.

The anaemia was undoubtedly due to stagnation of bowel contents interfering with the normal fermentative processes in the ileum, affecting folic acid and/or vitamin-B₁₂ production. The recent work of Dyke *et al.* (1950) would seem to support this contention, more particularly if it can be assumed that the effects of the stagnation would extend to include the colon with consequent folic acid and vitamin-B₁₂ deficiency.

Summary

A case is presented of a man aged 35, with loss of weight, gastro-intestinal symptoms, and a macrocytic anaemia, which seems to give clinical support to experimental work on the aetiology of macrocytic anaemia. It is noteworthy that the condition developed after surgical procedures which led to small-bowel stasis, and was cured by surgical removal of the lesion, without recourse to liver, folic acid, or vitamin B₁₂, which were not necessary in order to effect a readjustment of the normal intestinal metabolic processes and of the normal relationship between host and intestinal bacteria.

This case and a study of the literature emphasize again the necessity for a complete intestinal investigation in all cases of macrocytic anaemia which do not fall into well-recognized clinical groups, such as Addisonian anaemia, the macrocytic anaemia of pregnancy, or those associated with diagnosed constitutional disease.

It seems that short-circuit operations below the stomach are unsound except as a temporary measure. This is particularly the case when an antiperistaltic anastomosis is fashioned. There is a danger of the development of a macrocytic anaemia in such procedures as ileo-colostomy, in which a blind length of bowel is left.

The literature is reviewed.

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In the annual report for 1949 of the Medical Department of the Uganda Protectorate there is a description of the methods by which information is obtained about the state of public health in the Protectorate. Some of the notifications of deaths and of infectious diseases are made by chiefs of tribes, and, though the total deaths notified in this way are reasonably accurate, the allocation of deaths to the primary cause leaves much to be desired. The compiler of the report writes: "While the infectious diseases are generally diagnosed accurately, many deaths from 'old age,' 'chest,' or 'njoka' (literally, a snake in the stomach) afford little information about the real cause of death. Less than one-twentieth of all deaths occur in Government hospitals, and it is rare for deaths outside to be attended by medical practitioners."

Medical Memoranda

Pericardial Effusion as a Sequel to Subphrenic Abscess

The rarity of pericardial effusion as a sequel to subphrenic abscess has prompted the recording of this case. Of 182 cases of subphrenic abscess reviewed by Harley (1949), none were complicated by pericarditis. Ochsner and De Bakey (1938), reviewing the world literature, recorded pericarditis as a complication in 5% of 1,380 cases. This incidence, which largely results from one series of cases, is probably above the average.

Case Report

On June 4, 1948, a boy aged 11 was admitted to hospital with a 36-hours history of abdominal pain. Operation revealed a gangrenous appendix with pus in the peritoneal cavity. Appendicectomy was performed and the peritoneum drained. During the next three weeks two further abdominal abscesses were evacuated. As his fever persisted he was screened, and this showed the right dome of the diaphragm to be raised and immobile. An anterior sub-costal incision was made and two pints (1.14 litres) of pus were obtained from the lateral and superior aspects of the liver. On culture this grew coliform organisms, non-haemolytic streptococci, and *Staphylococcus albus*.

On August 17, as these measures were not entirely successful, 6 in. (15 cm.) of the tenth rib was resected posteriorly. The diaphragm was incised through a trans-pleural approach. Adhesions were broken down and a cavity was found lying well towards the midline. Thick pus was removed and the site drained. His condition steadily improved, and on September 27 he was discharged. While in hospital he had received 18,200,000 units of penicillin and 64 g. of sulphadimidine.

Three weeks after discharge he vomited and complained of headache, which was later associated with severe upper substernal pain. After one week in bed he felt better.

Three weeks later he was readmitted to hospital following a recurrence of the pain. Clinical findings suggested the presence of a pericardial effusion. In particular, the apex beat could not be seen or felt and the area of cardiac dullness was greatly increased. The heart sounds were notably faint. An electrocardiogram showed no abnormality. Screening revealed a grossly enlarged heart shadow with little movement. The lung fields were clear. A needle was inserted in the fifth left intercostal space, 1 in. (2.5 cm.) medial to the anterior axillary line, and 300 ml. of greenish-yellow opalescent fluid removed. This contained lymphocytes and polymorphonuclear leucocytes in equal numbers and was sterile on culture. The effusion recurred during the next three days, but by the end of a week had receded to normal.

Three weeks later he complained of substernal pain and the effusion was found to have recurred. A small right-sided pleural effusion was also noted—a new feature. The pericardial fluid had the same characteristics as before. The symptoms and signs gradually receded over the next five days.

He remained well until the beginning of February, 1949—an interval of two months. On this occasion the effusion appeared on the day after he had been allowed up for the first time. Bilateral small pleural effusions were also present. He improved with rest. At this point he was given 1 g. of streptomycin daily for eight days. He has had no episodes of pericarditis since.

He was last seen on December 19, 1949, when there was no clinical or radiological evidence of pericardial or subphrenic disease.