Epidemiology

Some years before, in another area, the mother was found to have pulmonary tuberculosis and had two 90-day courses of streptomycin and P.A.S. Later, in August, 1952, typical acid-fast bacilli were demonstrated in sputum specimens on two occasions, but no further specimens have yielded acid-fast bacilli. The sensitivity patterns of the strain are not known, since the organism was not grown on culture. The father also was found to have a pulmonary lesion believed to be inactive, though it was still being observed at three-monthly intervals. The only other member of the family in the home, a brother of 19 years, had a lung cavity demonstrated radiologically in 1956, but at no time have acid-fast bacilli been observed or isolated from sputum specimens. The appearance of this lesion is improving on combined streptomycin and isoniazid therapy.

The source of infection of the child is not known for certain. A possible sequence of events is that the brother may have been infected from the mother, and he, in turn, may have infected his sister, since he had probably the most active disease in the family at the time of the baby's infection. Until the patient became ill, the family of four resided in a caravan which, however commodious in itself, was a "single apartment." Since three members of the family had evidence of tuberculosis the ready transference of infection is understandable.

Bacteriology

Isolation.—Paired Löwenstein-Jensen slopes inoculated with spider-web clot and deposit from two specimens of cerebrospinal fluid yielded innumerable discrete colonies after 26 days' incubation. Although it was noted at the time that the colonies tended to appear less craggy and dry than the typical human variety, they were not considered to be bovine in origin.

Sensitivity Pattern.—The strain was sensitive to 10 µg. of streptomycin per ml., 0.2 µg. of P.A.S. per ml., and 0.2 µg. of isoniazid per ml.

Virulence: Catalase Test.—The method used differed from that recommended by Middlebrook *et al.* (1954) in that individual colonies were selected and transferred to tubes containing equal quantities of 20-volume H₂O₂ and 10% "tween 80" solution. Control tubes containing a comparable inoculum of the H₃₇Rv variety of *Mycobacterium tuberculosis* and a selection of recently isolated strains including atypical mycobacteria allowed of a comparison of the enzyme activity to be made. The time of appearance and the amount of oxygen liberated, shown by the bubbles at the surface with the strain under investigation, were similar to that of H₃₇Rv and recently isolated virulent strains.

Animal Inoculation.—Various weighed inocula, 0.1–0.5 mg. of the test strain, were injected intraperitoneally and intramuscularly into four guinea-pigs. Examination at necropsy six to eight weeks later showed progressive generalized tuberculosis. Typical acid-fast bacilli were demonstrated in the spleen, liver, and lung, and, in addition, after intramuscular inoculation caseous lymph nodes were observed in inguinal, lumbar, and tracheo-bronchial sites. Typical cultures were isolated from such lesions. Following intravenous injection the strain did not produce progressive tuberculosis in a rabbit.

Summary

A case of tuberculous meningitis is described occurring in an 11-months-old baby who had been given B.C.G. vaccine nine months previously. The infecting organism was shown to be a virulent strain of *Mycobacterium tuberculosis* of the human variety.

Our thanks are due to Dr. W. H. Findlay, area chest physician, Perth, for details of the medical history of the family.

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HYPOPROTEINAEMIA AFTER PARTIAL GASTRECTOMY CORRECTED BY GLUTEN-FREE DIET

BY

JOHN W. B. FORSHAW, M.D. M.R.C.P.

Senior Medical Registrar, Royal Southern Hospital, Liverpool

The nutritional disturbances following partial (Polya) gastrectomy are usually produced by defective absorption of iron, fat, and the vitamin-B complex (Wollaeger, Comfort, and Weir, 1946; Welbourn, Hughes, and Wells, 1951; Wells and MacPhee, 1954), and although nitrogen absorption is sometimes impaired, this rarely produces hypoproteinaemia (Wollaeger *et al.*, 1946). The deficiency of iron and vitamins may be corrected by giving large doses of these substances either by mouth or parenterally, but in order to correct serious deficiency states the Polya may have to be converted to a Billroth I gastrectomy, in which the blind loop is undone (Bruce, 1955).

It has been established that in most cases of idiopathic steatorrhoea the defective fat absorption is induced by gluten, and that after removal of gluten from the diet fat absorption returns to normal (French, Hawkins, and Smith, 1957). In addition it has been shown that a gluten-free diet corrects the associated faulty absorption of vitamins, minerals (French *et al.*, 1957), and nitrogen (McIver, 1952; Forshaw, 1957). There would appear to be no reason to expect that gluten could be responsible for the malabsorption following partial gastrectomy, and there have been no reports of the trial of a gluten-free diet in such cases.

The purpose of the present report is to describe the beneficial effect of a gluten-free diet in a patient in whom a low plasma albumin level producing oedema followed a partial gastrectomy; and to emphasize that severe impairment of nitrogen absorption may rarely occur without any apparent disturbance of fat and iron absorption.

Case Report

A man aged 47 was admitted to hospital in October, 1957. He had had a Polya gastrectomy for a duodenal ulcer five years previously. Following the operation he developed attacks of sweating and flushing of the face immediately after food, but otherwise his condition had been satisfactory for four years; he then developed diarrhoea and continued to pass between four and eight pale loose motions daily. During the past three months his mouth and tongue had been sore, and three weeks before admission he developed swelling of both feet and legs and a rash on the legs and abdomen. He thought that he had lost a small amount of weight since the partial gastrectomy, but his weight at the time of operation had not been recorded. There was no history of any significant previous illnesses.

On examination severe glossitis, cheilosis, and angular stomatitis were present. Both feet and legs were moderately swollen, and there was a patchy excoriated erythematous rash on the legs and abdomen. There were no abnormal neurological signs. His weight was 7 st. 2 lb. (45.4 kg.).

Investigations.—Radiographs of the chest and long bones were normal. Radiological examination of the gastrointestinal tract showed that the stoma functioned normally and there was no evidence of stomal ulceration; there was no flocculation of barium in the small intestine, and the barium had been completely evacuated from the bowel

within 24 hours. Barium-enema radiographs showed no evidence of a fistula between the colon and the stomach or small intestine. The blood picture was normal: haemoglobin, 13 g. per 100 ml.; plasma proteins, 4.6 g. (albumin 2 g., globulin 2.6 g.; electrophoresis of globulin, normal); serum calcium, 8.1 mg.; serum sodium, 345 mg.; serum potassium, 18 mg.; serum iron, 105 μ g.; serum bilirubin, 0.4 mg.; serum alkaline phosphatase, 8 King-Armstrong units; serum amylase, 120 units; and thymol turbidity, 2 units per 100 ml. Urea clearance-test was 60% of average normal and urine normal. The glucose-tolerance curve showed a rise of the blood-sugar level to 180 mg. per 100 ml. half an hour after 50 g. of glucose and then a fall to 40 mg. per 100 ml. one hour later. Faeces contained no undigested muscle fibres; faecal fat content, 11.5 g. per 100 g. of dried faeces. A fat-balance test over seven days showed 91% fat-absorption.

Treatment and Progress.—Ascorbic acid, 500 mg., thiamine, 250 mg., nicotinamide, 160 mg., riboflavine, 4 mg., and pyridoxine, 50 mg. ("parenterovite"), were given daily intramuscularly for seven days, and subsequently vitamin-B complex was given by mouth for six weeks. The changes in the mouth and tongue rapidly improved, completely clearing up within three weeks of starting treatment. Treatment with a high-protein diet was given for one month, but during this time the oedema of the feet and legs persisted and the plasma protein level fell to 4.6 g. per 100 ml. (albumin, 1.6 g.; globulin, 3 g.) (see Chart). At this time his

weight was 6 st. 13 lb. (44 kg.). On November 20, 1957, treatment was started with a gluten-free diet. Within a month the oedema had completely cleared up, he had gained 7 lb. (3.2 kg.) in weight, and the plasma proteins had risen to 6.2 g. per 100 ml. (albumin, 3.6 g.; globulin, 2.6 g.).

On April 2, 1958, the improvement was maintained, and the plasma proteins were 6.4 g. per 100 ml. (albumin, 4 g.; globulin, 2.4 g.). He was feeling well and the mouth and tongue were normal. He still had slight sweating and flushing of the face immediately after food, and was passing three or four motions daily.

On July 9 he attended hospital complaining that the rash and swelling of the legs had returned a month previously, and he admitted that during the previous two months he had not been keeping strictly to the gluten-free diet. On examination there was oedema of both legs and the plasma protein level was 5.2 g. per 100 ml. (albumin 2.7 g., globulin 2.5 g.). He agreed to keep strictly to the gluten-free diet, and when seen on August 20 the oedema of the legs had cleared up and the albumin level had risen to 3.2 g. per 100 ml.

Discussion

Following both total and partial (Polya) gastrectomy the absorption of nitrogen is rarely impaired sufficiently to pro-

duce hypoproteinaemia. Blake and Rechnitzer (1953) found that the plasma protein level was invariably normal in nine patients at an interval between nine months and three years after total gastrectomy, and Welbourn *et al.* (1951) found that the plasma protein level was below 5.5 g. per 100 ml. in only one out of seven patients following a Polya gastrectomy, and this patient did not have oedema. Wollaeger *et al.* (1946) have shown, however, that after partial gastrectomy there is occasionally a slight excess of nitrogen in the faeces, and in one of their patients who developed hypoproteinaemia and oedema the nitrogen excess was considerable. Furthermore, they noted that excess faecal nitrogen did not tend to occur more often in those patients who lost the most fat in their stools.

The factors which have been thought to be responsible for the absorptive disorders following gastric operations are as follows: (1) impairment of the mechanism which stimulates the flow of pancreatic secretions and bile; (2) imperfect mixing of the food with digestive ferments owing to the shunting of the gastric contents away from the duodenum; (3) intestinal hurry: Wells and Welbourn (1951) decreased the amount of fat excreted in the faeces by slowing the rate of peristalsis with ganglion-blocking drugs; and (4) growth of bacterial flora in the stagnant loop may compete with the host for vitamins and damage the intestinal mucosa (Witts, 1955). Baird and Dodge (1957), however, found slight abnormalities in the jejunal mucosa in only 8 out of 31 patients following partial gastrectomy, and they conclude that the impaired absorption of fat and iron following partial gastrectomy cannot regularly be attributed to structural alteration in the jejunal mucosa. Most probably the relative importance of these aetiological factors varies considerably, thus accounting for the variation in the relative degree of absorption of fat, nitrogen, vitamins, and minerals in different cases.

In the case described here the correction of the low plasma albumin level by a gluten-free diet was unexpected, but the explanation that the impaired nitrogen absorption was primarily induced by gluten and unrelated to the partial gastrectomy seems too coincidental to be readily accepted. It will be necessary, however, to try the effect of a gluten-free diet on a number of such cases before a conclusion can be reached. If it is assumed that the impaired nitrogen absorption was produced by the partial gastrectomy, then the mechanism by which gluten contributes towards the absorptive disorder remains to be discussed. French *et al.* (1957) have suggested two possible explanations for the mechanism of defective absorption in cases of idiopathic steatorrhoea. Firstly, that gluten may produce an allergic reaction in the intestinal mucosa resulting in an increased secretion of mucus which delays absorption. Secondly, that there may be a failure to digest gluten which may lead to the development of toxic substances by intestinal bacteria. Although there is no evidence as yet to support either of these explanations, it is tentatively suggested that partial gastrectomy may occasionally produce a disturbance of gluten digestion, thus leading to the production of toxic substances capable of damaging the jejunal mucosa.

Summary

A case is described in which severe impairment of nitrogen absorption following a partial (Polya) gastrectomy was corrected by a gluten-free diet. The impaired nitrogen absorption produced a selective fall in the plasma albumin level, the globulin level remaining within normal limits.

Severe impairment of nitrogen absorption occurs only rarely after partial gastrectomy, and the nutritional disturbances are more usually produced by impaired absorption of iron, fat, and the vitamin-B complex. In the present case, although there were clinical manifesta-

tions of riboflavine and nicotinamide deficiency, there was no anaemia, and fat absorption was only slightly impaired.

My thanks are due to Dr. E. N. Chamberlain for permission to publish this case.

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Medical Memorandum

Arthropathy due to Gastric Carcinoma

Certain gastro-intestinal diseases are recognized causes of arthropathy or of finger-clubbing; for instance, ulcerative colitis (Schlicke and Bagen, 1940), steatorrhoea (Bennett *et al.*, 1932), and amoebic or bacillary dysentery (Rappaport *et al.*, 1951). Arthropathy may also be the presenting symptom in carcinoma of the bronchus (Berg, 1949; Holmes *et al.*, 1950; Ellman, 1953), but carcinoma of the alimentary tract associated with arthropathy is very rare, although finger-clubbing has been described in cases of carcinoma of the small bowel and colon (Mendlowitz, 1942) and of the stomach (Willemse, 1922).

There is no report of gastric carcinoma causing arthropathy, and so a case with this association is worthy of record.

CASE REPORT

A single woman aged 64 had had periodic blood-stained vomits for 10 months, and for five months she noticed that food seemed to "stick" at about mid-sternal level, though she was able to eat solids normally. She had lost a few pounds in weight. For four months she had had pains in her knees, ankles, wrists, and small joints of the fingers. The pains in the fingers were so bad that she could not make a fist or grip with either hand, and had been taking 8 or 10 aspirin tablets daily.

Examination showed her to be well nourished, with moderate pallor. There was grade 1 finger-clubbing. The proximal interphalangeal joints and metacarpophalangeal joints of both hands were swollen and tender, and movements were limited in these joints. The wrists, ankles, and knees were not swollen, but movements were painful, and the ankles were tender. The dorsum of each hand appeared swollen. There was no bony tenderness.

Investigations.—Hb, 7.7 g./100 ml. (52%); M.C.H.C., 26%; M.C.V., 71 cubic microns; P.C.V., 30%; W.B.C., 11,200/c.mm.; E.S.R., 29 mm. fall in one hour (Wintrobe). C-reactive protein, +++; Rose's test (D.A.T.), 1 in 8. Serum proteins, total 5.8 g./100 ml. (albumin, 3.6 g.). Barium-meal examination showed a new growth of the cardiac end of the stomach close to the oesophageal opening.

Mr. D. Ioan-Jones removed the carcinoma, a well-differentiated adenocarcinoma with one lymph node involved. The joint pains disappeared two days after operation, and the swollen joints became normal within three weeks. Five weeks after operation the C-reactive protein was +; Rose's test (D.A.T.), 1 in 2.

DISCUSSION

Pathogenesis.—The mechanism of a carcinomatous arthropathy is not clear. Removal of the primary tumour is known to relieve arthropathy at once (Clagett *et al.*, 1952;

Ellman, 1953), and simple section of the vagi, which is thought to abolish a "neural reflex," has also caused instant relief of arthropathy (Flavell, 1956). The vagi were cut at gastrectomy in the present case, and so the prompt relief of her joint pains could have been due either to interruption of a vagal reflex arc or to removal of the gastric carcinoma. Our patient showed no signs to support two other hypotheses—"dyspituitarism" (Fried, 1943), and "toxic absorption" (Wooler, 1948) due to delayed gastric emptying (Preble, 1898; Dennig, 1901), and so the pathogenesis of her arthropathy cannot be defined.

Incidence and Sex.—Arthropathy is said to occur in 50% of cases of pleural tumours (Clagett *et al.*, 1952), but it has not been reported in carcinoma of the stomach, although Willemse (1922) described two cases with marked finger-clubbing and solitary gastric cancers. Analysis of the case records of the last 200 patients with a proved gastric carcinoma at this hospital has shown that not one had joint pains, only four had finger-clubbing, and two of these four had chronic lung disease more than likely to cause such finger-clubbing. The patient described above is a female, whereas osteoarthropathy associated with intrathoracic neoplasms (Bamberger-Marie syndrome) is much commoner in males (Gall *et al.*, 1951; Shapiro, 1956).

Joints Involved.—The joints which are involved most often in an arthropathy associated with carcinoma are the ankles, knees, wrists, and interphalangeal joints. Only these joints were affected in our patient, and the distribution of her arthropathy could well have been mistaken for early rheumatoid arthritis. Craig (1937), Berg (1949), and Frank (1952), have all stressed that rheumatoid arthritis may be confused with arthropathy due to carcinoma, especially when the primary tumour itself causes no symptoms.

Investigations.—Many workers stress that the E.S.R. is very high in patients with arthropathy due to carcinoma; for instance, Hansen (1952) and Holmes *et al.* (1950) report values of 70–120 mm. fall in one hour. This is not always the case, however, as Pattison *et al.* (1951) report values of 23–32 mm., which accord with the E.S.R. of 29 mm. (Wintrobe) in our patient. It is interesting to note that in our patient the Rose test (D.A.T.) titre fell from 1:8 to 1:2 after operation, and as 1:16 is the lowest significant titre for rheumatoid arthritis (Kellgren, 1957), this test might be useful in differentiating from the arthropathy due to carcinoma. A fever, often reaching 101 to 102° F. (38.3 to 38.9° C.) (Fischl, 1950), and a normocytic anaemia (Temple and Jaspin, 1948) may occur in pulmonary osteoarthropathy, but our case had different features: a low-grade fever, to 99° F. (37.2° C.) only, and a hypochromic anaemia due to blood loss.

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E. H. O. PARRY, M.B., M.R.C.P.,
Late Resident Medical Officer, Cardiff Royal Infirmary.

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