broad-spectrum antibiotics may have a prophylactic effect after upper abdominal surgery, since we found pathogens in the sputum of all the severe cases of postoperative pneumonia.

Pseudomonas was isolated on only 2 occasions and no multiresistant staphylococci were found; had these organisms been prevalent at the time of the trial a different conclusion might have been reached. If the source of the pathogens were known other preventive measures, preferable to chemoprophylaxis, might be taken. There is no general advantage to be gained from giving routine antibiotic 'cover' to bronchitic subjects perioperatively when pathogens are already present in the sputum, as illustrated by I of our bronchitic patients in whom preoperative tetracycline had failed to clear a long-standing pneumococcal infection. Perioperative ampicillin produced a remission without further complications.

Collins and others (1968) stated: 'It is believed that an increase in temperature during the first 48 hours is almost always caused by chest infection.' Infection shown by radiographic changes or purulent sputum accounted for nearly all the pyrexia in the early postoperative period in the present study. Except in 1 patient receiving steroids, the chest radiographs were all normal when the oral temperature was below 37.2°C. in the immediate postoperative period.

Our findings confirm those of Nichols and Howell (1970) that regular twice-daily physiotherapy, including breathing exercises, percussion, and encouragement of coughing, is of no apparent value to non-bronchitic subjects regardless of age, operation, or smoking habits. There is room for investigation of the value of vigorous treatment in the early postoperative period, as suggested by Palmer and Sellick (1962). It is interesting that among the bronchitic subjects who had minor operations, only 1 patient showed collapse radiographically. The more intensive physiotherapy given to this group may therefore have been beneficial, but since the services of trained physiotherapists are always in demand their time should not be spent in useless visits to previously healthy subjects having minor operations.

**Acknowledgements.**—This study was possible because of the co-operation of Miss J. L. Morris and the qualified staff of the Physiotherapy Department, Hammersmith Hospital, who carried out the prescribed treatment and arranged their schedules to fit in with the protocol. We are indebted to Professor R. B. Welbourn for critical reading of the manuscript and advice during the initiation of the study.

**REFERENCES**


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**MALNUTRITION AND MALABSORPTION IN CROHN'S DISEASE WITH REFERENCE TO THE EFFECT OF SURGERY**

**By N. H. DYER AND A. M. DAWSON**

ST. BARTHOLOMEW'S HOSPITAL, LONDON

**Summary**

Sixty-three patients with Crohn's disease showed a high incidence of nutritional deficiencies as judged by laboratory tests. Malabsorption of fat (33 per cent) and vitamin B₁₂ (60 per cent) was not sufficiently severe to account for the malnutrition. Malnutrition was especially severe in unoperated patients with active disease, whereas malabsorption was prominent in patients with recurrent disease after resection although they had less active disease and less severe nutritional deficits. Surgery should not be withheld from a malnourished patient for fear of inducing further malnutrition; excision of toxic inflammatory disease will not only improve the immediate outlook but will also reduce the severity of further recurrences. Xylose-excretion tests give a spurious impression of malabsorption in Crohn's disease, possibly as a result of occult renal impairment, and should be abandoned.

**Nutritional disturbance** is a common complication of Crohn's disease (Cooke, 1955; Ensrud and Sauer, 1957; Kogan, Schapira, Janowitz, and Adlersberg, 1957; Pimparkar, Mourhan, and Bockus, 1960; Tytgat, Vantrappen, Rutgeerts, and Vandenbroucke, 1967; Dotevall and Kock, 1968; Hertzberg, Myren, and Semb, 1969; Krause, Bergman, and Norlen, 1971). Although the number of possible causes are legion (Table I), malnutrition is frequently attributed to malabsorption (Crohn and Yarnis, 1958; Bockus, 1964). However, the role of malabsorption may have been overemphasized because the disease attacks the submucosa rather than the mucosa and frequently
spares the jejunum. Kiefer and Arnold (1950) pointed out that malabsorption which resulted from resection of bowel in Crohn's disease was rarely extensive enough to account for the associated malnutrition, and Hoffbrand, Stewart, Booth, and Mollin

Table I.—Factors Producing Malnutrition in Crohn's Disease

<table>
<thead>
<tr>
<th>Factor</th>
<th>Description</th>
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<tbody>
<tr>
<td>Decreased intake of food</td>
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<tr>
<td>Presence of active inflammation</td>
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<tr>
<td>Increased nutritional requirements</td>
<td></td>
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<tr>
<td>Toxic depression of metabolism</td>
<td></td>
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<tr>
<td>Malabsorption</td>
<td></td>
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<tr>
<td>Loss of bowel</td>
<td></td>
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<tr>
<td>Inflammation</td>
<td></td>
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<tr>
<td>Resection</td>
<td></td>
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<tr>
<td>By-pass</td>
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<tr>
<td>Stagnant-loop syndrome</td>
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<tr>
<td>Stricture</td>
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<tr>
<td>Fistula</td>
<td></td>
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<tr>
<td>Surgical blind loop</td>
<td></td>
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<tr>
<td>Gastro-intestinal loss</td>
<td></td>
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<tr>
<td>Blood</td>
<td></td>
</tr>
<tr>
<td>Protein</td>
<td></td>
</tr>
<tr>
<td>Water and electrolytes</td>
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<tr>
<td>Bile-salts</td>
<td></td>
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<tr>
<td>Minor factors</td>
<td></td>
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<tr>
<td>Rapid intestinal transit</td>
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<tr>
<td>Impaired bowel function above an obstruction</td>
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</table>

(1968) suggested that anorexia was a major factor causing folate deficiency in their patients. The importance of impaired dietary intake, fistulous losses, and sepsis in contributing to undernutrition has been stressed by Clark and Lauder (1969), particularly in the postoperative period.

We have studied an unselected series of patients in order to establish the incidence and severity of malnutrition and malabsorption, as indicated by simple laboratory investigations, and comparisons have been made between patients with active recurrent disease following a bowel resection and those with primary disease.

MATERIALS AND METHODS

Sixty-three patients were studied over a 2-year period; all had symptoms which were sufficiently severe to warrant admission to hospital. The symptoms of those who had suffered a relapse after operation were of comparable severity to the symptoms of patients who had not undergone operation, and the majority of the patients with postoperative recurrences had not been followed up so that they had not been promptly readmitted to hospital. The diagnosis of Crohn's disease was confirmed histologically in 40 patients (63 per cent) and was based on typical clinical and radiological features in the remaining 23, 3 of whom had undergone laparotomy without biopsy. There were 39 females (62 per cent) and 24 males. Their ages ranged from 14 to 71 years with a mean age of 37 years. Only 5 patients were on systemic steroid treatment but 2 others had been given steroid enemata.

The patients were divided into six anatomical groups. Seven patients had diffuse disease which involved the jejunum together with variable amounts of the ileum and colon. Thirteen patients had ileocolic disease, only 1 of whom had more than 30 cm. of terminal ileum involved. Eight patients had ileocolic disease which involved the terminal two or three loops of the ileum and the ascending colon; one patient had disease extending from the proximal ileum to the splenic flexure. Eight patients had colonic disease which was limited to the right colon in 4 and was total in the other 4 cases. Three patients had disease limited to the anorectal region. Twenty-four patients had been operated on previously; most had undergone ileo-colic resections and had developed recurrent disease in the remaining terminal ileum. Seven patients had been operated on for jejuno-ileitis but only 1 had undergone jejunal resection; 11 patients had undergone surgery for ileocolic disease, of whom 9 had had resections but 2 had had 40-60 cm. of ileum by-passed and excluded; 6 patients had ileocolic disease and had received more extensive resections; 1 patient had had local excision of disease limited to the descending colon.

The activity of the disease was arbitrarily graded by a system which awarded points for certain clinical and laboratory characteristics. One point was scored for each of the following (Dyer, 1970): symptoms of disease (pain, diarrhoea in an unresected patient, weight-loss, systemic complications); temperature above 37.2°C. during 3 of the first 10 days; haemoglobin less than 110 g. per 100 ml.; white-cell count above 11,000 per c.mm.; erythrocyte-sedimentation rate (Westergren) above 20 mm. in 1 hour; serum albumin less than 3.5 g. per 100 ml. Thus patients could be separated into seven grades (0-6).

Haemoglobin and serum albumin were estimated by routine laboratory techniques. Serum folate was measured by the method of Waters and Mollin (1961). Serum vitamin B₁₂ was measured by the method of Anderson (1964). Xylose absorption was estimated after an overnight fast followed by the oral administration of 25 g. of D-xylose and 600 ml. of water; urine was collected for the next 5 hours and a blood-sample was taken at 1½ hours. Xylose was measured by the method of Roe and Rice (1948). Faecal fat was estimated by the method of Van der Kamer, Ten Bokkel Huinink, and Weyers (1949). Vitamin B₁₂ absorption was measured by the method of Schilling (1953); after an overnight fast 0.5 μg. of the labelled vitamin was administered with 150 mg. of hog intrinsic factor and a flushing inject of 1000 μg. of unlabelled vitamin was given subcutaneously 2 hours later. Not every patient had every investigation.

RESULTS

Evidence of Malnutrition (Fig. 1).—

Haemoglobin.—Seventy-five per cent of the males had a haemoglobin concentration of less than 12.5 g. per 100 ml. and 54 per cent of the females had a concentration below 11.5 g. per 100 ml. The incidence and degree of anaemia were similar in operated patients regardless of the main site of disease. In females the haemoglobin levels were significantly higher in those admitted with recurrent disease after operation (t = 2.38, P < 0.025); in males there was no such difference. There was a progressive fall in haemoglobin associated with increasing activity of the disease (P < 0.001).

Serum Albumin.—Forty-four per cent of 59 patients had values below 3.5 g. per 100 ml. Patients with unoperated disease involving the colon with or without associated ileal lesions had a mean level of 3.0 g. per 100 ml. which was significantly lower than the 3.6 g. per 100 ml. which was found in patients whose disease was confined to the small bowel (t = 2.15,
Although operated patients had a higher mean level than unoperated ones, this did not quite achieve significance \((t = 1.84, P < 0.1)\). There was a progressive fall in serum albumin with increasing activity of disease \((P < 0.005)\). No direct correlation could be demonstrated with blood-urea levels, although subnormal urea concentrations (less than 20 mg. per 100 ml.) were only found in active disease. There was a significant correlation with serum-calcium levels \((r = +0.64, P < 0.001)\), the few patients with divergent results all having steatorrhoea.

**Serum Folate.**—Sixty-four per cent of the patients had levels below 4.0 ng. per ml. Significant differences could not be demonstrated between patients

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**Fig. 1.**—Scatter diagrams comparing the levels of (A) haemoglobin (in males and females), (B) serum albumin, (C) serum vitamin B₁₂, and (D) serum folate in patients with unoperated Crohn’s disease against levels in patients with recurrent disease after operation. Dotted lines indicate normal limits. •, Patients with an ileal by-pass. ■, Patients who had had a jejunal resection.
with disease at different sites except that unoperated patients had lower values than patients admitted with recurrent disease after surgery \((t=2.42, P<0.02)\). There was a progressive fall in folate levels with increasing disease activity \((P<0.002)\).

Serum Vitamin \(B_{12}\).—Sixteen per cent of the patients had levels below 160 pg. per ml. Although the mean vitamin \(B_{12}\) values were significantly lower in patients who had undergone ileal resection \((t=2.63, P<0.02)\), 3 unoperated patients had values below the normal range. These patients all had evidence of disease in the ileum and the lowest value occurred in a patient who had had symptoms for over 20 years. Four patients with resections of less than 30 cm. of ileum were not vitamin-\(B_{12}\) deficient, whereas 2 of the 3 with resections of more than 100 cm. developed very low levels within 3 years; the third patient appeared to be protected by preservation of the ileo-caecal valve and a small cuff of the terminal ileum.

Xylose Tolerance.—This test is an indirect assessment of jejunal function which depends not only on the intestinal absorption of the sugar but also on the excretion of xylose in the urine. Although 43 per cent of 42 patients excreted less than 4.2 g. per 5 hours and 23 per cent of 39 patients had serum levels of less than 32.5 mg. per 100 ml., only 1 patient had both abnormalities (Fig. 2), which by these strict criteria indicates that malabsorption of xylose is rare even in the presence of jejunal disease.

Because impaired urinary excretion of xylose is the usually accepted criteria of jejunal dysfunction we have analysed our data further. The mean excretion of xylose for patients with ileocolic or colonic involvement was greater than that for patients with disease confined to the small bowel \((t=2.22, P<0.05)\), but jejunal disease did not result in a greater impairment of excretion than ileocaecal disease and 3 patients raised blood-urea levels and only 2 were aged over 65 years, so that neither ureaemia nor old age was influencing the results. There was no correlation with faecal fat excretion or with the level of serum folate, a vitamin which is absorbed in the jejunum.

Faecal Fat.—Thirty-three per cent of 48 patients excreted more than 6.0 g. of fat per 24 hours. Although severe steatorrhoea was commoner after resection (Fig. 4), faecal fat excretion was not significantly greater in unoperated patients in this study \((t=1.97, P<0.05)\). There were no differences in mean faecal fat excretion in unoperated patients with disease at different sites although no patient with disease apparently confined to the colon or rectum had steatorrhoea. The 2 patients with an ileal by-pass did not have steatorrhoea. There was no direct correlation between faecal fat excretion and disease activity or with the serum levels of calcium, magnesium, and cholesterol, nor did urinary excretion of xylose or vitamin \(B_{12}\) correlate with fat excretion. The degree of fat excretion did not correlate with the amount of ileum resected, but 1 patient whose ileocaecal valve had been left in situ after a large resection appeared to be protected from steatorrhoea (Fig. 5).

Vitamin-\(B_{12}\) Absorption.—Sixty per cent of 42 patients had subnormal absorption and operated patients absorbed significantly less vitamin \(B_{12}\) than unoperated ones \((t=4.08, P<0.001)\). However, the incidence and degree of malabsorption did not differ.
amongst unoperated patients with different primary sites of disease, 48 per cent of whom had subnormal results including 2 of the 4 patients with disease apparently confined to the colon (Fig. 6). Only 3 of the 18 operated patients excreted more than 15 per cent of the vitamin; 2 had resections of less than 30 cm. and the third had an intact ileocaecal valve (Fig. 7). There is a tendency for vitamin B₁₂ absorption to decrease with increasing amounts of ileal resection provided that the ileocaecal valve is removed, although an intact valve does not guarantee normal absorption. Severe malabsorption may also occur with minor resections or even in the absence of operation, but there was no correlation of vitamin B₁₂ malabsorption and disease activity.

**DISCUSSION**

This study not only confirms that there is a high incidence of nutritional abnormalities in Crohn's disease but relates the degree of disturbance to a measurement of disease activity. Although previous workers have noted an association of malnutrition with active disease, the degree of activity has not been defined (Tytgat and others, 1967; Hoffbrand and
others, 1968). Our measurements have shown that active or severe disease is not confined to patients with diffuse jejuno-ileitis (Bockus, 1964); since activity and malnutrition are especially liable to complicate colonic disease; the finding of severe hypoalbuminaemia and the less marked tendency to folate deficiency and anaemia in colonic disease also suggests that malabsorption is not a major cause. Patients with active disease frequently also have profound anorexia and so malnutrition may be the result of starvation. There may also be increased demands for essential nutrients owing to excessive production and loss of inflammatory and other cells so that decreased blood levels may merely represent rapid clearance. Hypoalbuminaemia may result from decreased protein synthesis, hypercatabolism of serum proteins, or loss of protein into the bowel (Waldmann, 1970). Our results support the theory of enteric protein loss; the lack of correlation between serum-albumin and blood-urea levels suggests that neither starvation nor decreased protein synthesis is of major importance and that the presence of hypoalbuminaemia is not a reliable index of total protein deficiency. Moreover, some nutritional parameters are interdependent and results should be interpreted with care; hypocalcaemia is usually associated with hypoalbuminaemia because of the loss of the binding protein and rarely indicates malabsorption of calcium with its attendant risk of osteomalacia. Osteomalacia may erroneously be suspected if there is a coincidental increase in serum alkaline phosphatase; this disturbance, however, is usually due to abnormal liver function rather than to disturbed bone metabolism in such patients (Dyer and Dawson, 1972).

The less severe degree of malnutrition in patients who have developed recurrent disease after resection should not be dismissed as the result of selection of patients, because similar indications for admission obtained in all the cases. Moreover, the majority of the patients were often living at a distance from the hospital so that they were not seen at an earlier stage of their illness. Kalser, Roth, Tumen, and Johnson (1960) found that incomplete resection in patients with jejuno-ileitis led to a great improvement in health in spite of the effects of the disease left behind and the malabsorption resulting from surgery. When our patients are graded for disease activity, significantly more unoperated patients have active disease compared with operated ones (Fig. 8). Thus, it appears that the total amount of inflamed tissue determines the degree of malnutrition and that reduction of this 'toxic mass' is of prime importance. However, these results should not encourage indiscriminate surgery since adrenocorticotropic hormone and azathioprine therapy can also dramatically reduce the activity of Crohn's disease within a few days.

The results of the xylose test give very little evidence that jejunal malfunction is important in the genesis of the nutritional disturbance. Thus, although the sugar is predominantly absorbed in the jejunum (Fordtran, Soergel, and Ingelfinger, 1962) changes in renal function and urinary xylose excretion may be of equal importance in giving an abnormal result. This factor has been disregarded by previous workers who have reported variable degrees of 'malabsorption' in Crohn's disease (Benson, Culver, Ragland, Jones, Drummey, and Bougas, 1957; Christiansen, Kirsner, and Ablaza, 1959; Fowler and Cooke, 1960; Shiner, Volk, and Wilcox, 1962; Dotevall and Kock, 1968; Hertzberg and others, 1969). The recent studies by Kendall (1971), who has shown that intravenously administered xylose is poorly excreted in Crohn's disease, confirm our suspicions of occult renal dysfunction; only 1 of 39 patients had low levels of xylose in both blood and urine whereas active disease was associated with falling urine and rising blood levels. The indiscriminate application of this urinary excretion test is to be deprecated and the presence of a normal blood-urea level is no safeguard against a spurious result.

Malabsorption of fat and vitamin $B_{12}$ was attributed to the presence of extensive disease or massive resection (Cooke, 1955; Bockus, 1964). However, our results confirm that malabsorption may also follow relatively small ileal resections and is sometimes a feature of unoperated localized disease of the ileum (Ensrud and Sauer, 1957); this has recently been explained by the discovery that the terminal ileum is the main site of absorption of vitamin $B_{12}$ and conjugated bile-salts (Booth and Mollin, 1959; Lack and Wiener, 1967). The role of bacteria in the production of malabsorption of fat and vitamin $B_{12}$, as in the stagnant loop syndrome, has been overemphasized, since bacterial overgrowth is variable in Crohn's disease and cannot be directly correlated with malabsorption (Vince, Dyer, O'Grady, and Dawson, 1972). We did not find the severe degrees of steatorhoea that have been reported by some American workers (Kalser and others, 1960; Pimparkar and others, 1960), possibly because our surgeons have tended to conserve as much bowel as feasible at operation. However, the incidence of malabsorption
in our patients was similar to that reported by Hertzberg and others (1969), but their patients were all investigated after operation and there was often no evidence of active recurrent disease. The clinical importance of mild steatorrhoea associated with unresected ileal disease has yet to be established, although the development of megaloblastic anaemia due to malabsorption of vitamin B₁₂ is well documented. However, the present study has confirmed that vitamin-B₁₂ deficiency occurred only after ileal resections of more than 100 cm. and was not a feature of small resections or unoperated disease, but his conclusions were based on serum vitamin-B₁₂ levels which usually only become abnormal after massive resection. The results of the Schilling test are unlikely to be abnormal owing to subtle dysfunction such as obtains for the xylose test, because similar results have been found in Crohn’s disease using a whole-body counter (Dyer, 1972). Not only may this vitamin-B₁₂ malabsorption lead to megaloblastic anaemia in unoperated patients (Dyer, Child, Mollin, and Dawson, 1972), but an abnormal absorption test may also be a valuable sign of early Crohn’s disease at a stage when radiography of the ileum is normal.

The relatively minor degrees of malabsorption noted in our patients were insufficient to account for the nutritional disturbances observed and the lack of correlation of malabsorption with disease activity also suggests that malabsorption and malnutrition are unrelated. Our studies suggest that malabsorption is of little clinical significance except in the genesis of vitamin-B₁₂ deficiency. On the other hand, it may account for the symptom of diarrhoea which is sometimes due to either steatorrhoea or the cathartic action of unabsorbed bile-salts on the colon (Hofmann, 1967).

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REFERENCES


— (1972), unpublished observations.
— and Dawson, A. M. (1972), Digestion, 5, 317.
Hoffmann, A. F. (1967), Gastroenterology, 52, 752.