THE MANAGEMENT OF CHRONIC CROHN'S DISEASE

JAMES KYLE, M.Ch., F.R.C.S., F.R.C.S.(I.)
Department of Surgery, Woodend Hospital, Aberdeen

IN NEARLY all patients, Crohn's disease runs a chronic course, usually extending over many years. The thirty-fourth President of the United States, Dwight D. Eisenhower, had the disease for 46 years (Heaton et al., 1964). Without definitive treatment, there is no real evidence that the inflammatory process will ever cease spontaneously and the patient become permanently symptom-free. Progression of Crohn's disease of the colon can often be seen in serial barium enema examinations. It is much more difficult to obtain strictly comparable films of small intestinal changes but progression probably does occur in some untreated patients (Marshak and Linder, 1970). Often, however, it appears that the disease remains active in a short length of lower ileum for years without spreading proximally. Recurrences after inadequate surgical treatment are well known. The very chronic nature of Crohn's disease is a major factor in planning the treatment of any patient in whom the diagnosis has been made.

DIAGNOSIS

The diagnosis of Crohn's disease rests on four main pillars: (i) clinical history and findings; (ii) radiological investigations; (iii) macroscopic appearances, and (iv) histological findings. At least two out of the four must be presented to support the diagnosis. The appearances on X-ray may not always correspond with the clinical state of the patient. When multiple sections are cut, the classical epithelioid cell granulomas and the giant cells will be seen on histological examination in two-thirds of resected or biopsy specimens; their absence does not rule out Crohn's disease. Today more emphasis is placed on the transmural extent of the inflammation and to fissure formation and rather less on Hadfield's (1939) classical criteria. While the diagnosis is usually straightforward, in a quarter of all patients it may only be possible to make the correct diagnosis after observing the behaviour of the disease for several months or even years. On the periphery of any series of patients with Crohn's disease there are always a few cases labelled "Unproven"; prolonged follow-up may elucidate the nature of their illness.

NON-OPERATIVE TREATMENT

The decade of life in which Crohn's disease of the small intestine most often starts is that between 20 and 30 years. This is the time when young men should be earning their living and young women rearing their families - if Crohn's disease has not rendered them infertile. With the cause and cure of the disease still unknown, the doctor must carefully consider what line of treatment will enable each patient to lead as normal and active a life as possible.

Medical therapy is usually tried first. Until recently the results were poor. In Aberdeen, between 1955 and 1968, there were 145 patients with Crohn's disease,
including 30 patients where the colon was the site predominantly affected. Of the 145 patients, 83 had a trial of medical therapy lasting more than one month; only 16 (19 per cent) remain well, most of the others eventually requiring operation. In extenuation, it must be admitted that in some of the failed cases treatment had consisted solely of alleviating symptoms and had not included any concerted attempt to combat infection and inflammation. Crohn’s disease of the colon has only been widely recognised for 10 years (Lockhart-Mummery and Morson, 1960), so that long follow-up results are not available, but it seems that the condition may be more responsive to medical therapy than is ileal Crohn’s disease. Changes in the colon can sometimes regress very rapidly when intensive medical treatment is given.

General Measures

Adequate rest is obviously necessary in a chronic, debilitating illness. Sound sleep at night should be ensured, but during the day the patient is better leading as normal a life as his physical state permits. It is only when a patient sees that he is falling behind his contemporaries that psychological problems arise.

Nutrition

With increased catabolism within the inflamed bowel wall, protein loss from its ulcerated mucosa, and malabsorption from the lumen, the patient’s weight falls rapidly. Many females weigh between 35 and 45 kg. (5.5–7 stones) before treatment. An element of subacute obstruction may make eating difficult. An enthusiastic dietician and close co-operation from the nursing staff are essential if an intake of 2,500–3,500 calories per day is to be ensured (Clark and Lawder, 1969). Most of the intake should consist of carbohydrate and protein. Green vegetables, peas, beans and fruit that leave a considerable residue are better avoided. Mechanical obstruction may have to be corrected before weight gain can be achieved.

Correction of Deficiencies

Resection of excessive lengths of intestine is likely to cause more severe deficiency states than untreated Crohn’s disease. A moderate degree of iron-deficiency anaemia is common and usually responds to oral ferrous sulphate. Megaloblastic anaemia is rare, but in 9 out of 10 untreated patients in Aberdeen the serum folate level was subnormal. Folic acid in a dosage of 5–10 mg./day may be prescribed for these patients. Although the lower ileum is the principal site of absorption of vitamin B₁₂, its uptake and serum level are usually normal unless more than 80 cm. of small intestine have been removed (Schofield, 1965); patients who have had extensive resections may require monthly injections. Other patients unable to eat fruit and vegetables should be given ascorbic acid, 0.5–1 gm./day, and a few require vitamin B complex. When steatorrhoea is marked it is advisable to give supplementary calcium. Magnesium deficiency has been noted in 10–15 per cent of cases; it responds to magnesium hydroxide suspension, 20 ml. daily.

Anti-diarrhoeal agents

One of the most effective agents in reducing the frequency of bowel action is Lomotil (Searle), 5 mg. given several times per day. Codeine phosphate is a useful alternative. In the author’s experience cholestyramine, which lessens colonic irritation by unabsorbed bile salts, and lignin have been less consistently effective.
Sulphasalazine

Salazopyrin (Pharmacia) is the only anti-bacterial drug that has been used in long-term treatment. There have been no controlled clinical trials of its efficacy in Crohn's disease, although one is planned. In addition the mode of action of the drug is not known and even in untreated Crohn's disease remissions and relapses are less clear-cut than in ulcerative colitis. Nevertheless, in a dosage of 1 gm. three or four times per day, sulphasalazine does seem to be beneficial in the more florid stages of the disease.

Steroids

Oral prednisone and corticotrophin by injection have an anti-inflammatory effect, but do not cure Crohn's disease. Given in high dosage, e.g. 30-40 mg. prednisone daily for several weeks, these drugs will diminish diarrhoea and lower the E.S.R. They are more effective in younger patients with short histories, but they do not prevent relapses or recurrences. Short courses may be used with advantage to reduce the toxic manifestations of Crohn's disease before elective resection. Nightly retention prednisone enemata are beneficial when the colon is involved. Prior et al (1970) believe that steroid therapy may contribute to the increased mortality in patients with Crohn's disease.

Immunosuppressive Drugs

Azathioprine is the latest drug used in treating Crohn's disease. It works in many but not all cases (Brooke, Hoffman and Swarbrick, 1969). In Aberdeen, eight patients with disease too extensive for resection, or with multiple external fistulae, have been treated to date. Six have responded rapidly. One elderly lady with several associated diseases has not responded at all; in another patient with multiple fistulae arising from partial breakdown of an anastomosis, not unexpectedly the fistulae have remained unhealed. In mid-1970 the optimum dosage and length of treatment with azathioprine are not known. Small doses of 2 mg./kg. per day have been given continuously or 5 mg./kg. daily for 5 days followed by two days' treatment with steroids. While the ill-effects of immunosuppressive drugs were probably over-publicised at the time of the cardiac transplantation failures, undoubtedly they are potent weapons and should only be used when regular supervision is possible.

Surgical Treatment

The need for regular supervision is one of the great disadvantages of conservative management. Very few young people would accept a line of treatment if they realised that it entailed regular attendance at hospital for the next 40 or 50 years. Few people want to be permanent pill-swallowers. The alternative to this type of medicated survival is surgery.

Indications for Operation

The most suitable type of case to operate on is one where there is localised disease which has become quiescent spontaneously or after intensive medical treatment. Inability to enjoy life and the failure of children to thrive are other important considerations. Until the advent of azathioprine, external fistulae would not heal until the underlying disease had been extirpated. Remote toxic manifestations in joints, eyes and skin usually will not subside without intestinal resection.
Mechanical abnormalities such as stenoses and abscesses require surgical treatment. However, if acute intestinal obstruction supervenes emergency operation is better avoided if at all possible – conservative measures should be tried to relieve temporarily the obstruction. The rare complications of free perforation and massive haemorrhage demand urgent surgical intervention.

Operation is not advised when there is very extensive disease, multiple skip areas or rapid progression of the inflammatory process. Further surgery is contraindicated in those unfortunate patients who develop a recurrence after earlier resection; they should be treated by intensive medical therapy.

*Type of Operation*

Resection is the treatment of choice. Eighty per cent of patients have ileal involvement. As well as the thickened ileum, the caecum and about 20 cm. of ileum proximal to the upper macroscopic limit of the disease are excised and the ileum anastomosed to the ascending colon. One short skip area can be ignored. Multiple resections are to be avoided. At the proximal line of section the ends should be opened to make sure no luminal ulcers are present (Atwell, Duthie and Goligher, 1968). Gross rectal and perianal disease may necessitate abdomino-perineal resection. Terminal ileostomy works well after colectomy, but there seems little place for double-barrelled ileostomies and attempts to re-use grossly diseased bowel.

When there is a large inflammatory mass in the right iliac fossa, with dense adhesions to iliac vessels and ureter, short-circuit with exclusion is undoubtedly the safer if less dramatic procedure. This operation will give long-lasting relief of symptoms in almost 50 per cent of cases. Earlier fears about the development of blind-loop syndromes and blown ileal stumps have proved largely unfounded.

*Prognosis*

Crohn’s disease has a high morbidity but a low initial mortality rate. Nevertheless in a series of 300 patients followed for up to 30 years, Prior *et al* (1970) found that the mortality among patients was about double that in an age and sex-matched sample from the general population. Half the deaths were directly attributable to Crohn’s disease. The Aberdeen experience is almost identical.

The disappointing results of earlier medical regimes, and a possible explanation for their failure, have already been referred to. The long-term results of azathioprine are awaited with great interest. It is by no means certain that even a long course of the drug will permanently cure a patient of the tendency to react against his own intestines – if Crohn’s disease is caused by some auto-immunological process. It would be even more naïve to assume that the surgeon’s scalpel could eradicate such a self-destructive propensity. Nevertheless resection offers the patient the best prospect of long periods of normal health.

Because the ileum is the site most often affected, the results of ileal resection are of particular interest. In Aberdeen, 61 patients had primary resections for ileal disease in the years up to 1966. One patient died following operation, an operative mortality of under 2 per cent. The remainder were followed up for at least two years. The chances of recurrence were then calculated according to the actuarial method of Lennard-Jones and Stalder (1967), which is based on the number of patients at risk at the start of each year. After two years the recurrence rate was
13 per cent, rising to 18 per cent after five years. At ten years the symptomatic recurrence rate was 33 per cent. In other words, when it is technically feasible for ileal disease, resection offers two patients out of three some ten years of active, useful life with freedom from the dangers and inconvenience that are inseparable from prolonged drug therapy.

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