Current Practice

Crohn's Disease

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Brit. med. J., 1968, **3**, 294-298

Though this relatively uncommon but serious and perplexing disease was first described as a clinical entity by Crohn and his associates in 1932, sporadic cases had been previously recorded, probably the first by Morgagni in 1769. Originally designated terminal ileitis, then regional ileitis, and subsequently amended to "regional enteritis," it is now known that the disease can also affect the colon or jejunum, and rarely the stomach or duodenum may be involved. Most British gastroenterologists, therefore, prefer to use the eponymous term Crohn's disease qualified by its site, since this avoids the use of such confusing terms as ileocolitis, granulomatous enteritis, enterocolitis, regional or segmental colitis, and so on to describe the same condition.

Aetiology

The cause of the disease remains unknown. It is not related to sarcoidosis, and there is no convincing evidence that bacterial or viral infections play any part in its aetiology. There is now conclusive evidence that Crohn's disease is not tuberculous in nature, but it must be remembered that ileocaecal tuberculosis still occurs, particularly among the immigrant population, and this possibility must always be considered in the differential diagnosis.

The disease has a definite familial incidence, and a sufficient number of sporadic reports have now appeared in the literature describing its development following severe nonpenetrating abdominal trauma to indicate that this may occasionally be an aetiological factor. The cellular infiltration in the bowel wall in Crohn's disease is a striking feature, consisting predominantly of plasma cells and lymphocytes associated with giant cell systems and sometimes tissue eosinophilia. These are characteristic features of an immune-hypersensitivity reaction, and indeed similar but not identical lesions can be produced experimentally in the alimentary tract of appropriately sensitized animals. However, detailed immunological studies have failed to substantiate the suggestion that Crohn's disease is an autoimmune or hypersensitivity disorder, though the features of the disease and its response to various forms of therapy lead many clinicians to continue to suspect that it probably is. The condition may present clinically as an acute or chronic problem—the latter being much more common.

Acute Regional Ileitis

The patient, usually a child, an adolescent, or a young adult, presents with signs and symptoms resembling those of acute appendicitis—colicky abdominal pain, tenderness in the right iliac fossa, and a fever of 100 to 101° F. (37.8 to 38.4° C.). The terminal ileum is commonly involved, being reddened or purple in colour, swollen, and oedematous, with a marked

regional lymphadenopathy. The segment involved, usually a few inches in length, is sharply demarcated and usually ceases abruptly at the ileocaecal valve. Histologically the submucosa is oedematous and infiltrated with polymorphonuclear leucocytes, monocytes, and plasma cells. The features are essentially those of an acute inflammatory response, and there is no granuloma formation.

In this acute type of disease some 15% of the patients present with a perforation of the affected bowel; this is excessively rare in the chronic disease. The perforations may be single or multiple and usually occur on the antimesenteric border of the terminal 8 to 12 in. (20 to 30 cm.) of the small bowel.

In the majority of instances it is not possible to distinguish between acute regional ileitis and acute appendicitis, and operation is mandatory. In a few patients, however, the history may extend over a period of several days and be associated with diarrhoea, the patient passing four to five loose stools daily. Both these features are unusual in acute appendicitis unless a local or pelvic abscess is present, and in their absence the diagnosis of Crohn's disease merits serious consideration, for nearly all such cases will have positive radiological findings. In the uncomplicated case discovered at laparotomy, nothing further should be done, and the abdomen should be closed; appendectomy should not be performed, as this is meddlesome and predisposes to local abscess formation with the development of an external fistula in approximately 20% of cases so treated. When complications such as a local abscess or perforation have occurred it is probably wisest to drain, divide the bowel proximally, and perform an exclusion ileotransversostomy. This seems to be safer than primary resection and anastomosis, though the number of cases thus treated is so small that no one can be dogmatic on this point. There is now indisputable evidence that half of these acute lesions resolve spontaneously and permanently, but the remaining half develop the classical features of the chronic type of disease, usually within a few years of the acute episode. However, the strong tendency towards spontaneous cure justifies a conservative approach when the patient is first seen.

Segmental lesions closely resembling those of acute regional ileitis may be seen in the collagenoses, polyarteritis nodosa, acute necrotizing jejunitis, or enteritis gravis, and following embolic or thrombotic occlusion of mesenteric segmental arcade vessels. For this reason some have questioned whether acute regional ileitis is a distinct entity. However, the distinctive histological features and the fact that half of the patients with acute lesions subsequently develop classical Crohn's disease have led most gastroenterologists to accept that it is.

Crohn's Disease

"Chronic regional ileitis" constitutes the chronic manifestation of the disease most commonly seen in clinical practice. The affected segment of bowel becomes thickened and rigid—the

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so-called "hosepipe" appearance—the bowel wall being a centimetre or more in thickness and the lumen narrowed (Fig. 1).

FIG. 1.—Typical Crohn's lesion in ileum—so-called "hosepipe" appearance.

The serosal surface is reddened, and adhesion to neighbouring structures or viscera is common, so that subsequent fistulation is relatively frequent. The mesenteric fat surrounds the bowel to an abnormal extent, the mesentery is markedly thickened, and considerable regional lymphadenopathy is usual. Distally the disease terminates abruptly at the ileocaecal valve in about half the patients, and in 75% of all cases the segment of bowel involved is less than 2 ft. (60 cm.) in length (Fig. 2). Ulcera-

FIG. 2.—Multiple annular Crohn's lesions in jejunum. A relatively rare presentation of the disease.

FIG. 3.—Cobblestone appearance in terminal ileum with rather polypoid mucosa and intervening fissured ulceration.

tion of the mucous membrane is not invariable, but shallow longitudinal ulcers are usually present along the line of the mesenteric attachment; occasionally the ulceration is fissured and deeply penetrating. The remaining mucosa may be atrophic, normal, or polypoid, and sometimes presents a characteristic cobblestone appearance (Fig. 3).

Histologically the submucosa is markedly oedematous and heavily infiltrated with plasma cells, lymphocytes, and eosinophils; interstitial oedema and lymphatic dilatation are often marked (Fig. 4). Noncaseating granulomata may often be seen in all layers of the bowel wall, especially in the submucosa and subserosa (Fig. 5). Giant cells are often present, but they are not specific to regional enteritis. The granulomatous lymphangitis and lymphoedema are striking features and considered by some to be the primary features of the disease, while others consider that submucosal lymphoid hyperplasia is of predominant importance. The local blood vessels in the bowel wall may show endarteritis and perivascular infiltration with plasma cells, but intravascular thrombosis is rare.

FIG. 4.—Lymphatic dilatation in bowel wall in Crohn's disease.

FIG. 5.—Granulomatous response.

Clinical Features

In the majority of patients the predominant and presenting symptom is diarrhoea. Present in about 85% of cases, and initially intermittent, it rarely amounts to more than four to five loose or semiformed stools per day, and is almost never so severe as in ulcerative colitis. The patient may omit to

mention diarrhoea unless specifically asked, though it has often been present for months or years. The presence of recognizable blood in the stools is most unusual unless there is extensive colonic involvement, when the symptoms may closely mimic those of ulcerative colitis.

Pain is the second outstanding symptom. It is usually colicky in nature and characteristically may be relieved by defaecation. It may, however, be constant, particularly if an inflammatory mass is present. Nausea and vomiting are uncommon, and usually denote impending obstruction. Occasionally cases are seen without either abdominal pain or diarrhoea.

A low grade fever may be present, often associated with lassitude and malaise, but while weight-loss is usual it is seldom severe. There is generally a secondary iron deficiency anaemia and a haemoglobin of 65 to 75% ; more rarely the anaemia is macrocytic and usually associated with extensive disease, previous radical surgery, or both these factors.

A third of the patients have a palpable mass, usually in the right iliac fossa, but sometimes midline or confined to the pelvis. Approximately 20% of patients have external or internal fistulae, which are almost pathognomonic of the disease. Spontaneous external fistulae are extremely rare, and usually complicate previous surgery—especially unnecessary appendectomy.

A most valuable and important physical sign from the diagnostic aspect is the presence of anal complications—especially fistulae-in-ano. In about 10% of patients these may be the presenting feature of the disease, and the association of anal abscesses, recurrent fissures, or fistulae-in-ano with mild intestinal disturbance in a young adult should raise strong suspicions of Crohn's disease. Quite apart from their diagnostic significance perianal complications are most unlikely to heal until the primary disease is controlled either by medical or surgical means. In severe cases, especially those with extensive colonic or rectal involvement, perianal suppuration may be so severe that widespread ulceration of the perineum occurs.

Crohn's disease may be accompanied by generalized manifestations such as polyarthritides, spondylitis, iridocyclitis, erythema nodosum, iritis, and clubbing of the fingers, and generalized features such as hypocalcaemia or hypoalbuminaemia due to secondary malabsorption syndromes may also be present.

FIG. 6.—Classical "string-sign" in terminal ileum.

In the majority of cases the diagnosis can be made on these clinical features and confirmed by the radiological appearances. Sigmoidoscopy and rectal biopsy may sometimes provide confirmatory evidence.

Radiological Appearances

In the acute phase these may be slight and easily missed, but the intestinal mucosa loses its delicate feather pattern and the folds become oedematous, swollen, and coarse, producing a characteristic saw-toothed appearance.

In the patient with classical Crohn's disease the radiological appearances are striking, and often more advanced than the clinical features would suggest. As the disease progresses and fibrosis develops organic stenosis of the bowel lumen occurs, ultimately involving several centimetres of bowel and producing a rigid contracted tube resulting in the classical string-sign of Kantor (Fig. 6). When there is extensive disease areas of stenosis alternate with segments of dilatation and sometimes saccululation; evidence of obstruction or fistulation into neighbouring bowel loops or viscera may be seen. Ulceration of the mucosa may be evident and if marked produces a cobblestone effect, while skip-areas, due to intervening segments of normal intestine interposed between diseased segments, are a characteristic feature when present.

Usually the disease stops at the ileocaecal valve, but involvement of the caecum is not uncommon, and sometimes other segments of the colon are affected (Fig. 7). More rarely the colon may be the sole site of the disease, when the radiological features are distinctive; these cases are becoming more frequently recognized. Diffuse colonic involvement can cause diagnostic difficulty, as the appearances may simulate those of ulcerative colitis.

FIG. 7—Segmental Crohn's colitis affecting descending colon.

While the radiological features of Crohn's disease are usually diagnostic, intra-abdominal inflammation, tuberculosis, lymphoma, sprue, idiopathic steatorrhoea, and postmesenteric infarction can all produce similar x-ray appearances.

Metabolic Disorders Associated with Crohn's Disease

Absorption Defects

Both carbohydrate and protein absorption are usually normal unless there is extensive involvement of the small bowel, but there may be a significantly increased daily protein loss in the stools. This usually accounts for the low serum albumin figures

commonly seen, which on occasion may cause the patient to present with hypoproteinaemic oedema. Crohn's disease should certainly be considered in the differential diagnosis of such a patient below the age of 30 in the absence of renal disease.

Disorders of fat absorption with hypovitaminosis A, D, K, and E occur more often in Crohn's disease than is generally appreciated. Clinically, fat absorption constitutes a good guide to the degree of involvement of the small intestine, in that patients with well-localized disease and no significant obstruction seldom have an appreciable degree of steatorrhoea. Conversely with extensive disease of the small bowel steatorrhoea is almost invariable, though severe steatorrhoea and vitamin deficiency may occur with relatively localized disease if fistulation or previous surgery have produced a blind loop syndrome. Generally, however, severe steatorrhoea indicates the presence of widespread disease with a poor prognosis, and, as might be expected, such patients usually do badly after surgery, which has a formidable recurrence rate.

There may be markedly defective calcium absorption associated with steatorrhoea; varying degrees of hypocalcaemia occur, and rarely these absorption defects may be sufficiently severe to produce metabolic bone disease with subsequent structural changes, including pathological fractures.

Anaemia

Mild degrees of iron-deficiency anaemia are not uncommon, owing to protracted oozing from areas of ulcerated mucosa, but when the colon is involved the anaemia may be severe. Macrocytic anaemia usually due to deficiency of B₁₂ and sometimes of folic acid occurs occasionally, and despite current controversy concerning B₁₂ absorption there is no doubt that clinically it is particularly associated with extensive ileal disease or numerous surgical resections. It may, however, be present even with well-localized disease in the terminal ileum.

Electrolyte Depletion

Though often mild, disturbances of electrolytes can on occasion be severe and extremely serious. Some degree of dehydration and sodium and chloride deficiency is usual, and long-continued diarrhoea imposes a very severe drain on the potassium reserves of the body, which can be decreased by 20 to 30%, even though the serum potassium remains normal; indeed, if the latter is low a serious degree of potassium depletion probably exists. Clinically this results in lassitude, weakness, and disturbances in acid base and nitrogen metabolism. Potassium depletion is of particular importance surgically, for it impairs intestinal peristalsis and produces atony of the gut. This biochemical ileus commonly precipitates an obstructive episode, and prompt restoration of potassium reserves by intravenous therapy usually results in resolution of the obstructive phase. This is of fundamental importance, for the vast majority of such patients can be managed on conservative lines, thus enabling them to be brought into better physiological and metabolic balance should definitive surgery subsequently be deemed necessary.

Associated Visceral Disturbances

It is now known that secondary disturbances of both pancreatic and liver function can occur in association with Crohn's disease. However, these occur much less commonly than in ulcerative colitis, and seldom constitute serious problems in management.

Management of Crohn's Disease

The problems posed by this serious disease are numerous, and occasionally they may tax clinical ingenuity to the utmost. The best results are obtained when treatment is supervised by surgeons and physicians with a common interest in this disorder, for the management of the individual patient demands a nicety of clinical judgement where there is no place for tardy conservatism on the one hand or over-enthusiastic surgical buccaneering on the other. Regular consultation and supervision remains a most important, possibly the most important, principle in the management of a patient with Crohn's disease, since there is no specific treatment for this disorder. While it is convenient to discuss management from the medical and surgical aspects it is of the utmost importance to appreciate that these are complementary and not antagonistic, though one or the other may predominate during various phases of the disease in the individual patient.

Medical Aspects

The general principle of management should be to advise a reasonable way of life with adequate rest and a high-calorie, high-protein, low-fat type of diet. It is important to treat the patient rather than the x-ray appearances, and when symptoms are mild empirical general measures usually suffice. When diarrhoea is a problem it may be minimized by codeine preparations, Isogel, propantheline bromide, or Lomotil, and the old-fashioned belladonna preparations together with chalk and kaolin mixtures still have a useful role. If diarrhoea is appreciable potassium supplements should be given, but it is prudent not to prescribe potassium chloride because of its association with ulceration and stricture formation in the ileum. If there is definite malabsorption it is wise to prescribe calcium and vitamin supplements.

Regular blood counts safeguard against the development of anaemia, and estimations of the erythrocyte sedimentation rate and serum mucoids are useful non-specific indicators of active disease. Anaemia is usually of the iron-deficiency type responding readily to iron therapy, which sometimes has to be given parenterally. When extensive disease is present, or more than 3 to 4 ft. (0.9 to 1.2 m.) of ileum has been removed, vitamin B₁₂ deficiency is likely, and if serum levels are low regular monthly supplements of B₁₂ should be given.

Antibiotics seldom do good and may do harm, though they may temporarily reduce the severity of the steatorrhoea and diarrhoea when a blind loop syndrome has developed as a complication of the disease or previous surgery. The non-absorbable sulphonamide preparations, especially salicylazosulphapyridine 1.5 g. q.d.s., may be useful during an acute flare-up, but generally their long-term use has been disappointing.

Experience with the corticosteroid drugs and corticotrophin has been varied, but generally disappointing. These drugs are usually prescribed as A.C.T.H. 40 units daily or prednisone 20 to 40 mg. daily for three to four weeks, reducing to 10 to 15 mg. daily for maintenance therapy. There is no real evidence that A.C.T.H. is more or less efficacious than prednisone. Traditionally these drugs are prescribed for severe initial disease, extensive or progressive disease not amenable to surgical treatment, and recurrent disease following previous surgery. There is often a dramatic initial improvement, but later relapse is common and permanent improvement unusual; occasionally, however, some patients remain in good health after stopping treatment. As a general principle it is wise to avoid long-term steroid therapy, as the majority of patients show their maximal improvement within three months or so. In a few patients therapy may have to be continued for long periods, but it must be remembered that steroid therapy has its own real dangers, particularly the increased tendency to infection and the possible need for steroid supplements if surgery is undertaken within 12 months.

Surgical Aspects

Indications and Limitations

For a decade or so after the recognition of regional enteritis as an entity the almost universal method of treatment was surgical excision of the affected segment of bowel. This was followed by various types of short-circuiting operation culminating in exclusion ileotransversostomy, which puts the diseased area at rest by completely excluding the faecal stream from it. The initial results suggested that short-circuiting procedures had both lower mortality and recurrence rates than excision. Subsequent experience has not, however, confirmed this view, and the pendulum of surgical opinion continues to oscillate between those who favour resection and those who believe that exclusion is the better method of management; many British surgeons wholeheartedly favour resection. Further confusion has arisen following the recognition of Crohn's colitis as an entity, for it poses different problems and has a different prognosis. It is therefore essential to be absolutely clear whether one is considering predominantly small-bowel disease, Crohn's colitis, or a mixture of both.

Crohn's Disease of the Small Bowel.—This is the common situation where the small bowel, usually the ileum, is maximally affected and colonic involvement, if any, is minimal. In recent years it has become increasingly obvious that whatever method of surgical treatment is employed the recurrence rate is disturbingly high and directly proportional to the length of the follow-up period. In this country the recurrence rate is about 50% at five years, rising to 70% or so at ten years. While the majority of the recurrences develop within three years of operation, sporadic recurrences can occur 25 years or so later. The management of recurrent lesions presents even more serious problems, because in patients given surgical treatment for their first recurrence the subsequent recurrence rate is 80%, and after surgery for a second recurrence it is 90%. In spite of this, with a good overall management many of these patients continue to live happy and productive lives.

It is obvious, therefore, that surgery is not the optimal treatment for Crohn's disease of the small bowel, and initial management should be along medical lines. This is not to say that surgery does not have a most important, and sometimes life-saving, role to play in the management of these difficult problems, but it should be reserved largely for the treatment of the complications of the disease or when it is clear that medical measures alone are failing to control the situation. Continued ill-health, retardation of growth and sexual development, recurrent obstructive episodes, fistulae, persistent inflammatory masses, and intractable perianal suppuration are all strong indications for surgical intervention. If surgery is undertaken it should be as conservative as possible compatible with performing an adequate procedure. Certainly extensive resections should be avoided at all costs, since there is no evidence that they in any way lessen the tendency to recurrence but merely add to the degree of alimentary insufficiency already present. There remains a divergence of opinion whether a short-circuiting procedure or excision is the better operation. When the disease is strictly localized and at the fibrotic quiescent stage, excision is preferable. If, however, the disease is extensive or in the active florid stage a short-circuiting procedure with exclusion may be indicated; sometimes it may be advisable to do nothing and close the abdomen. For the reasons already given recurrence following surgical excision should be managed conservatively whenever possible and for as long as possible. While this should certainly remain a guiding principle it is not

uncommon for further surgery to become mandatory following the development of additional mechanical problems or intractable complications.

Crohn's Colitis.—While similar general principles apply, Crohn's disease of the large bowel is worthy of separate consideration, because the problems and prognosis are somewhat different. Crohn's colitis may occur in association with disease in the small bowel—commonly the terminal ileum—or the colon alone may be involved. Though usually chronic, Crohn's colitis can follow an acute and fulminant course resembling acute ulcerative colitis, including the development of so-called toxic dilatation. Increasing experience has shown that most cases of Crohn's disease affecting the large bowel do badly on conservative or medical treatment, and 80 to 90% of cases in published series ultimately required surgical treatment, usually within a relatively short time after the onset of the disease. Thus when the disease is predominantly or entirely confined to the colon some surgeons tend to intervene at an earlier stage than when the disease is confined to the small bowel alone. The type of operation performed depends entirely on the site and extent of the disease, but the principle should be to excise the affected segment of bowel whenever possible. The results of diversion type operations for colonic disease are abysmally poor, for the disease progresses unabated in the defunctioned colon, and in almost all instances a further operation has to be undertaken.

If the entire colon is involved proctocolectomy and ileostomy produces good results, but there is always the danger that Crohn's disease may develop subsequently in the small bowel, and should this be the case the consequences are likely to be catastrophic. However, experience has shown that while instances of this undoubtedly occur it is relatively infrequent, and the majority of cases continue to do well five years or more postoperatively. When the rectum is normal colectomy and ileorectal anastomosis also produce good long-term results. Conversely, when the rectum and anal canal alone are involved, with the remaining colon being normal, excision of the rectum and the establishment of a permanent colostomy is indicated. For patients with well-localized colonic involvement segmental excision or hemicolectomy with end-to-end anastomosis produces good results.

To summarize, therefore, when Crohn's disease predominantly affects the small bowel the initial management should be along conservative lines with well-supervised medical treatment, recognizing that the majority of patients will at some time ultimately require an operation for the complications of the disease. When the site of the disease is predominantly colonic, though the same general considerations apply, these cases tend to do much less well on conservative management, and surgery should be considered at an earlier stage.

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