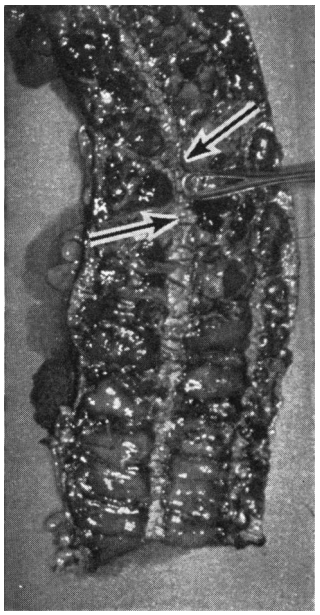

FIG. 1

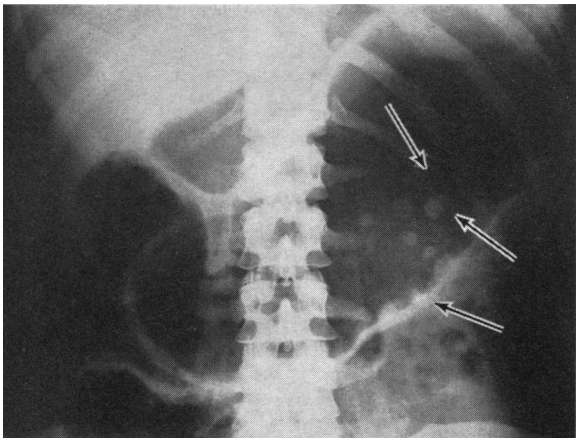

FIG. 2

FIG. 1.—Freshly removed colon at primary colectomy. The longitudinal confluent ulcers are seen to extend so deeply that the fibres of the circular muscle coat are exposed. There is evidence of pseudopolyposis and extensive lacunar sepsis. The radiological picture of this colon is depicted in Fig. 3.

FIG. 2.—Straight radiograph of patient with ulcerative colitis in which large pseudopolyps are demonstrated clearly.

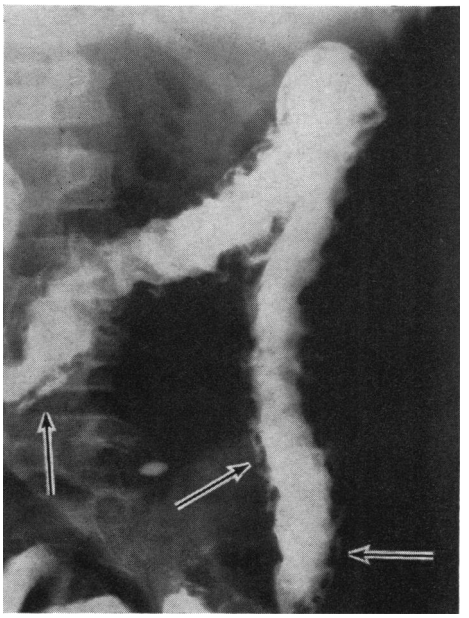

FIG. 3

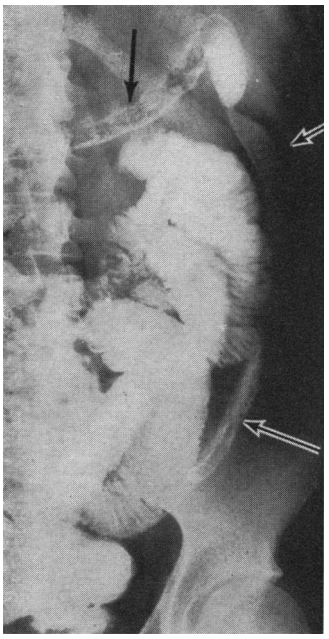

FIG. 4

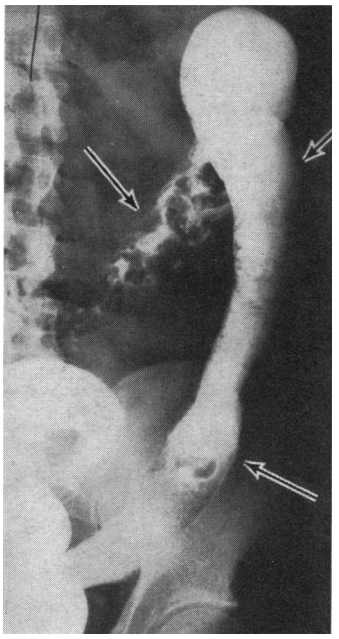

FIG. 5

FIG. 3.—Radiograph of case in which confluent lacunar sepsis is present, separating the mucosa from muscularis of the colon. The fresh specimen is shown in Fig. 1, and it will be seen that the emerging reticular pattern is due to the development of extensive longitudinal ulceration with circumferential extension.

FIG. 4.—A fine reticular pattern is seen in the transverse colon of this patient with ulcerative colitis.

FIG. 5.—Same patient as in Fig. 4 one year later; it is seen that the colonic disorganization has progressed and shows a coarse reticular pattern in transverse colon and more gross disease in descending colon.

FIG. 6.—Reticular pattern is associated with the development of pseudopolyps, which are demonstrated here.

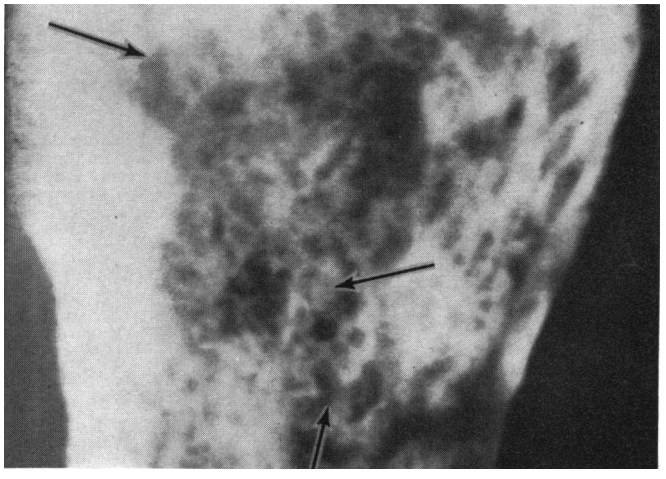

FIG. 6

FIG. 7.—Coarse reticulation developing because of confluence of longitudinal ulcers with lateral extensions occurring in an irregularly dichotomous pattern.

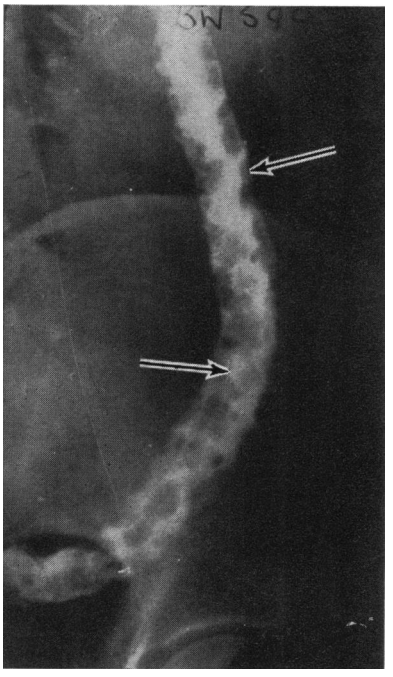

FIG. 7

Irreversible Changes of Ulcerative Colitis

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[WITH SPECIAL PLATE]

Brit. med. J., 1965, **1**, 414–416

Although much has been written of the radiological changes which are associated with ulcerative colitis, little direct correlation has been made between these findings and the gross anatomical and histological changes of the excised bowel following surgical treatment. Dick *et al.* (1955) have provided the only observations of this kind that we can find, and here the problem is considered from the diagnostic viewpoint. It is felt that this correlation has great relevance in the matter of treatment.

Forty patients with ulcerative colitis who have come to surgery in our clinic have had the radiological features of their disease compared with the actual specimen of colon after panproctocolectomy, and in many the opportunity has also been taken to photograph the colon in the fresh state. We have found that certain radiological features indicate a degree of colonic damage so severe that a complete restoration to normal seems so unlikely that they should be considered irreversible. All the changes which we describe have persisted for months or years in spite of all the known medical measures, including the use of adrenocorticosteroids. On many occasions it was possible to see several of the changes in the same colon.

Thirty patients, having been diagnosed as suffering from ulcerative colitis and having had more than one radiological examination, have had their radiographs examined for any sign of regression after the appearance of any of the signs which we consider irreversible, and in no instance has a restoration to normal occurred.

The diagnosis of ulcerative colitis has been made from the clinical features of the case, the character and distribution of the radiological changes in the colon, the histology of a rectal biopsy, and the absence of organisms of typhoid or the bacillary dysenteries, and of ova, cysts, or amoebae. In those treated by surgical excision of the colon the diagnosis has been confirmed by histological examination.

Further studies are in progress, in which it is hoped to perform sequences of barium examinations on all patients treated conservatively.

Pseudopolyposis

When extensive mucosal damage has occurred by digestion or inflammatory ulceration, the surviving mucosa exists as irregularly spaced islands throughout the affected segment of colon. The islands appear radiologically as multiple polyps, and when the bowel is removed and examined in the fresh state it is seen that the ulceration between islets of mucosa extends deeply into the muscularis of the intestine, so that the base is formed by the exposed layer of muscle or even of longitudinal muscle or serosa (Special Plate, Fig. 1). In many places it is possible to demonstrate an extensive undermining of the pseudopolyps, so that even the basal segments of the tubular intestinal glands are separated from the vascular bed, which would be expected to nourish their regeneration. The mucosa and submucosa, and particularly the muscularis, have been found to be so disorganized and the surviving islands so infiltrated with inflammatory cells that a complete restoration to normal has seemed so unlikely, within a reasonable period, that we consider these changes, for all practical purposes, to be irreversible. In our experience, no case exhibiting these changes has resolved radiologically or pathologically, even after the passage of many years with or without corticoid therapy.

In many instances it is possible to demonstrate the presence of large pseudopolyps on straight radiography of the abdomen without recourse to examination by barium enema. This is facilitated when the large bowel contains slightly more gas than is normally present, and this is illustrated in Fig. 2 (Special Plate). It is now our practice to take such an *x*-ray film when pseudopolyposis is seen or suspected on sigmoidoscopic examination. When such changes are seen during the latter examination or on plain *x*-ray examination, the patient is spared any further barium examination and is offered the surgical cure of his condition.

Stricture

A stricture of the colon in ulcerative colitis must always be regarded as sinister, since it cannot be distinguished from a carcinoma. On this account alone it must be considered irreversible, although on strictly pathological grounds the same is true, since it represents the laying down of fibrous tissue which has replaced, for all time, the normal specialized components of that particular segment of bowel. In our experience, where the stricture has proved to be benign there has been an attempt at a compensatory hypertrophy of colon proximal to the stricture; but this has soon become a passive dilatation resulting in incompetence of the ileocaecal valve, so that the more extensive forms of "backwash" ileitis have been seen under these circumstances. It is possible to transect this apparently diseased small intestine, since the ileitis is reversible (Walker and Taylor, 1965), in weeks or months following the cessation of colonic reflux. Where stricture is seen we advise early operation, principally because it must be distinguished from carcinoma, and in any case has proved to represent a truly irreversible change.

Carcinoma

In ulcerative colitis carcinoma may present in the form of a stricture, although when it occurs in the diseased rectum it may assume the character of a large malignant ulcer. Early surgical excision offers the only prospect of cure. It is significant that cases of carcinomatous degeneration in long-standing cases of ulcerative colitis are being reported at a time when the disease is thought to be clinically quiescent (Slaney and Brooke, 1959). In our experience it is difficult, if not impossible, to distinguish the occurrence of this complication at an early stage from a recrudescence of ulcerative colitis. The five-year survival figures following colectomy for ulcerative colitis complicated by carcinoma are only of the order of 18.6% (Slaney and Brooke, 1959).

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Confluent Lacunar Sepsis

Confluent lacunar sepsis is the term we apply to an extensive undermining of the mucosa, submucosa, and often of the circular muscle layer (Special Plate, Fig. 3). Many lacunar or crypt abscesses have become confluent by their enlargement and have permeated in many directions, with a degree of undermining which amounts to nearly complete dissection of the lining of large parts of the colon from its underlying muscularis. Many of the abscesses penetrate beyond the muscular coat of the intestine, and we have seen instances where only the serosal coat prevents overt perforation and peritonitis. Since corticoid therapy, under these conditions, is fraught with the danger of precipitating this disaster, and the intestinal disorganization is such that resolution seems improbable, we advise early operation, and our experience has been that the intestinal damage is always more extensive than has been demonstrated radiologically. Our feeling is that the condition is analogous to the more severe forms of ischiorectal fistulation, that fresh infection occurs from time to time, and that the abscesses permeate and burrow in all directions, seeking fresh pathways along which to point.

Loss of Mucosal Haustration

Loss of muscular haustration of the colon appears to be a reversible sign, and we have seen instances of its reappearance after weeks or months of absence. However, the disappearance of those radiologically apparent haustra which are due to permanent elevations of the submucosa of the colon seem always to indicate such a degree of mucosal damage and derangement that we believe this to be an irreversible sign. On examination of the fresh colon we have found that it is lined either by granulation tissue without epithelium or by a debased form of epithelium which lacks evidence of functional specialization. There is always evidence of extensive fibrosis, and the large bowel has become nothing more than an inert conduit for the passage of ileal contents. Few of these patients have a stool frequency of less than six or seven times a day, which in most instances restricts their domestic and social activities considerably. We advise these patients to undergo panproctocolectomy and to accept an ileostomy.

Reticulation

Various reticular patterns of the colonic mucosa are apparent on barium-enema examination and are associated with the presence of pseudopolyps, although on many occasions the polyps themselves cannot be visualized. We have classified these as fine, medium, and coarse reticulations, and we have found that a steady and relentless progression occurs whenever these patterns are seen. When cases of ulcerative colitis are kept under observation and repeat barium studies are made at intervals it is possible to demonstrate the transition from fine through to coarse reticulation (Special Plate, Figs. 4 and 5) and finally to the demonstration of actual polyps (Fig. 6). This demonstration of the progressive destruction of the lining and wall of the bowel occurs so regularly that we regard the appearance of even fine reticulation as evidence of an irreversible stage of the disease. The features which are responsible for the radiological pattern are demonstrated when the fresh specimen of colon is opened. Longitudinally placed ulcers with a floor formed by the circular muscle coat become confluent in the long axis of the colon, and at the same time runnels of destruction pass from these confluent ulcers in an irregularly dichotomous pattern which becomes increasingly evident with the passage of time. Fig. 1 is the freshly removed colon which radiologically showed both extensive lacunar sepsis and coarse reticulation (Fig. 3). Fig. 7 (Special Plate) demonstrates more clearly the radiological appearances of the longitudinal ulcers and their lateral extensions.

Acute Toxic Dilatation of Colon

It is only in the last decade that the complication of a rapid and striking dilatation of the colon, associated with extreme intoxication of the patient, has been recognized as evidence of imminent perforation of the colon. It has been suggested that this is due to the destruction of the myenteric plexus (Bockus *et al.*, 1958), but the integrity of this system has been demonstrated by Sampson and Walker (1961). It is more probable that the smooth-muscle cells are so damaged that they become unable to be influenced by their chemical environment. The extensive damage to the muscle cells leads to a loss of intestinal motility over such a length of the colon that the proximal bowel is physically unable to project its content through the paralysed segment. The disintegrating colon becomes transformed into a large reservoir of gas and fluid faeces, and, because the intestinal wall is so friable and soft, it is probably the mere weight of its fluid content and distension by associated gas which causes it to give way.

A further feature of great significance occurs which may be misleading. Where the patient previously had a marked frequency of motions, the number becomes markedly reduced as the dilatation advances. On some occasions this has progressed to a complete cessation of the passage of stools and flatus. This reduction in the frequency of stools has sometimes been misinterpreted as a favourable response to the drug which was currently being prescribed. If the diminution in the number of stools is not accompanied by improvement in the general condition of the patient, operative intervention may be urgently indicated. The clinical suspicion of the condition can be confirmed by a straight radiograph of the abdomen in the supine position, which demonstrates gaseous distension of the large bowel that can sometimes reach remarkable proportions. Resort to routine barium-enema examination is unnecessary, and it may be dangerous since it can precipitate rupture of the friable bowel. At this time it is impossible to decide whether perforation has occurred, as it may be clinically silent in this disease. These patients are too ill *not* to be operated on, but intervention should be restricted to a primary colectomy. The manipulations necessary for ileostomy or caecostomy alone have in many cases resulted in rupture of the friable bowel, which cannot be repaired by suture. Under these circumstances colectomy becomes obligatory. In a series of 14 cases of acute dilatation of the colon reported by Sampson and Walker (1961), only four patients died—a survival rate of 70%. This compares favourably with any published alternative regime of management.

Discussion

Granulomatous disease of the intestine is not an uncommon cause of diarrhoea associated with the passage of blood, pus, and mucus in patients of 20 to 40 years of age. Initially there must be a stage of the disease where it is restricted to mucosa or submucosa and without the extensions into muscularis which make a radiological diagnosis possible. No extensive structural damage has occurred, and specialized elements may yet survive without being replaced by the less mature epithelial elements or by extensive fibrosis. However, at the present time it is not possible, at this stage, to distinguish between the varieties of non-specific granulomata which may affect the colon, since the diagnostic radiological features have not yet appeared. The brunt of ulcerative colitis appears to affect the mid-descending colon, which suggests its differentiation from Crohn's colitis, in which the maximal changes occur in the ascending colon. In some instances, however, the distribution of the radiological changes makes such a distinction most difficult, and on occasion impossible. Granular proctitis or proctosigmoiditis seems to be restricted to rectum and pelvic colon. On sigmoidoscopic examination the red, granular, bleeding surface of the mucosa

of rectum and lower sigmoid colon will be visible in proctosigmoiditis, but unless the viewer is able to see the line of demarcation between diseased and normal tissue he cannot distinguish this from an ulcerative colitis without certain typical radiological features demonstrated in the bowel at a higher level. Biopsy will distinguish Crohn's granuloma from the last two, but is of no more help.

When the pathological processes have extended so that the radiological changes typical of ulcerative colitis have appeared, it has been our experience that the disorganization of the bowel is invariably more extensive than is radiologically apparent.

Search of the literature in pursuit of reports and demonstrations of cases positively diagnosed on radiological examination as ulcerative colitis which completely resolved after the appearance of any of the signs we describe reveals a surprising sparsity of such claims. Those which demonstrate *some* resolution seem always to make some reservation in respect of clinical recrudescence or of some segment not yet fully resolved. Of reports demonstrating the final and prolonged resolution of these last cases there are none.

Our studies in which correlation has been made between the radiological features of the disease and the condition of the freshly excised colon have suggested that certain features represent a degree of mucosal and mural disorganization so great that for all practical purposes the condition has become irreversible, so that the clinician should now be properly weighing up the advantages which surgical ablation would confer against the continuing morbidity and risk with which his patient is saddled.

We are not claiming that each of these changes represents a completely irreversible state in the strictly pathological sense, although this may be the case, but that for all practical purposes no resolution will occur within a reasonable number of months or years, whatever medical measures are used.

In 5% to 10% of cases of ulcerative colitis severe colonic complications may be expected—perforation, pericolic abscess, diffuse peritonitis, massive haemorrhage, and toxic dilatation (Korelitz and Janowitz, 1960). With greater experience of the use of adrenal cortical hormones it is becoming increasingly evident that they are not without their own inherent dangers. Adrenocortical hormones are most effective in inducing remissions in acute first attacks, and less so in subsequent recrudescence. They certainly impair the capacity to resist infection.

Numerous series of cases of ulcerative colitis have now been reported, drawing attention to the sinister changes which may be associated with the unstable mucosa resulting from repeated hyperplasia to make good recurrent ulceration. Weckesser and Chinn (1953), while noting a colon-cancer rate in a normal population of 0.06%, indicate that a thirtyfold increase (1.9%) exists among those with ulcerative colitis. A study of 20 reported series of significant size (Slaney and Brooke, 1959) has established the overall incidence of carcinoma to be of the order of 4%. Closer investigation, however, reveals that the duration of the disease is related to the development of carcinoma. Figures as high as 50% (Dukes and Lockhart-Mummery, 1957), 36% (Lyons and Garlock, 1951), and 30% (Cattell and Boehme, 1947) have been recorded when the disease has been present for ten years or more. Our own experiences have been similar.

Where carcinoma does develop in a thinned previously diseased bowel, by the time this is recognized to be something other than a further recrudescence of the original disease it is often not only incurable but unresectable. These considerations have suggested to us the pattern of treatment of ulcerative colitis which we regard as rational since our recognition of signs that we have found to be irreversible. The method we advocate is to treat symptomatically the diarrhoea of unknown cause, to use cortisone and other supportive measures while changes that may be reversible are present, but to advise surgery when evidence of irreversibility appears. When the cancer period is entered at about the tenth year, we advocate surgical ablation provided there is positive radiological evidence of ulcerative colitis, since there is no way in which to detect the development of a cancer in such a diseased bowel. On a number of occasions, because of an acute exacerbation or because of toxic megacolon, we have performed laparotomy only to find widespread carcinomatosis present. How much happier would the anguished husband or wife have been had his or her partner been fit and well—even with an ileostomy ? In some patients irreversible signs may appear within weeks or months, while in others an interval of several years may occur.

The generally accepted indications for the surgical treatment of ulcerative colitis are where there has been a steady and continued deterioration in spite of medical treatment ; chronic illness of such a degree that the patient is unlikely to return to normal life unless treated surgically ; the presence of anorectal complications and those complications remote from the gut, such as arthritis, skin affections, and iritis ; and chronic continued or massive bleeding. To these we would add that surgery should not be unduly delayed when radiological evidence of an irreversible degree of damage to the colon becomes evident.

Summary

Forty patients with ulcerative colitis have had the radiological features of their disease compared with the actual specimen of colon removed by panproctocolectomy. Where the changes of pseudopolyposis, stricture, carcinoma, confluent lacunar sepsis, loss of mucosal haustration, acute toxic dilatation, and certain reticular patterns are evident, it has been concluded that these represent irreversible stages of the disease. Thirty patients who have had more than one radiological examination, and in whom any of these features have been seen, have failed to show any evidence of subsequent regression of these radiological changes after months or years of full medical treatment. The recognition of a stage at which the damage to the colon is irreversible suggests to us that surgery should not be unduly delayed and that when the disease has been present for ten or more years the carcinoma hazard is such as to justify a prophylactic colectomy.

We would like to thank Professor A. G. R. Lowdon for his help and advice in the preparation of this paper, Dr. C. K. Warrick for his encouragement, and the physicians of the Royal Victoria Infirmary for permission to examine *x*-ray films of their patients. Our thanks are also due to the department of photography, University of Newcastle upon Tyne, for the photographs.

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