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Crohn's disease of the colon

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The fact that Crohn's disease may involve the colon either initially or in association with small bowel disease is now firmly established due largely to the evidence presented by Lockhart-Mummery and Morson (1960, 1964) and Marshak, Lindner, and Janowitz (1966). This entity is clearly distinct from ulcerative colitis and other forms of colonic disease. Our own experience with this disorder reveals many similarities with that published from the U.K. and the U.S.A. Thirty patients with Crohn's disease involving the large bowel were seen at the Royal Prince Alfred Hospital during the last decade, the majority during the past five years. The criteria for inclusion were based on histological examination of operative specimens in 28 and on clinical and radiological features in two patients not submitted to surgery. All had radiological studies of the large bowel and the majority also of the small bowel. This paper presents our clinical experience, management and results, our views concerning the earliest changes, the mechanisms of formation of ulceration, and the basic differences from the pathology of ulcerative colitis.

CLASSIFICATION

Lockhart-Mummery and Morson (1960, 1964) have classified their cases into those with diffuse disease of the colon, strictures or localized disease, and those mainly confined to the rectum. However, their cases with diffuse involvement of the colon varied considerably in the actual anatomical distribution which in fact was often patchy. Their cases described as localized disease often showed many localized areas with healthy bowel intervening. We prefer to group our cases according to whether the lower ileum was involved initially or not. We think that this grouping may have a more practical application.

Our 12 examples of involvement of the lower ileum (ileocolitis) were associated with caecal involvement in three, the right colon in five, the right and transverse colon in two, total involvement with sparing of the rectum in one and the rectum alone in one (Fig. 1). In all the ileal involvement was limited to the terminal 3 to 80 cm. In none was there generalized involvement of the small bowel and the jejunum was never affected unless there had been surgical interference. There was no overt manifestation of malabsorption in any of these patients.

In 18 cases the colon alone was involved. Five had universal involvement, five total involvement with sparing of the rectum, two involvement of the descending colon only, two the transverse colon only, and in the other four there was variable involvement of areas of large bowel (Fig. 2).

CLINICAL FEATURES

The age incidence varied from 6 to 69 years when the patient was first seen, the majority being between the ages of 11 and 50. Taking into account the age of onset, in 23 patients the disease began before the age of 40, and in only seven over 40. There was an equal incidence in the second, third, and fourth decades. The ratio of females to males was 19:11. The frequency and incidence of symptoms and signs are shown in Table I.

TABLE I

PERCENTAGE INCIDENCE OF CLINICAL FEATURES

Symptom	*Percentage Incidence*
Diarrhoea	90
Weight loss	75
Pain	66
Abdominal tenderness	60
Fever	53
Anal involvement	50
Fistulae	30
Palpable abdominal mass	20
Diagnostic sigmoidoscopy	0
Diagnostic rectal biopsy	0

Diarrhoea was the outstanding symptom, being present in all but three and usually for months or even years before a diagnosis was established. Pain was also common, usually of a colicky nature and in the lower or right lower abdomen. Weight loss greater than 2 kg was common and obvious rectal bleeding less so. Abdominal tenderness, particularly in the right lower abdomen but often generalized, and a palpable mass were the important physical signs. Fever was surprisingly common. Erythema nodosum and arthralgia was noted in three and clubbing of the fingers in two patients.

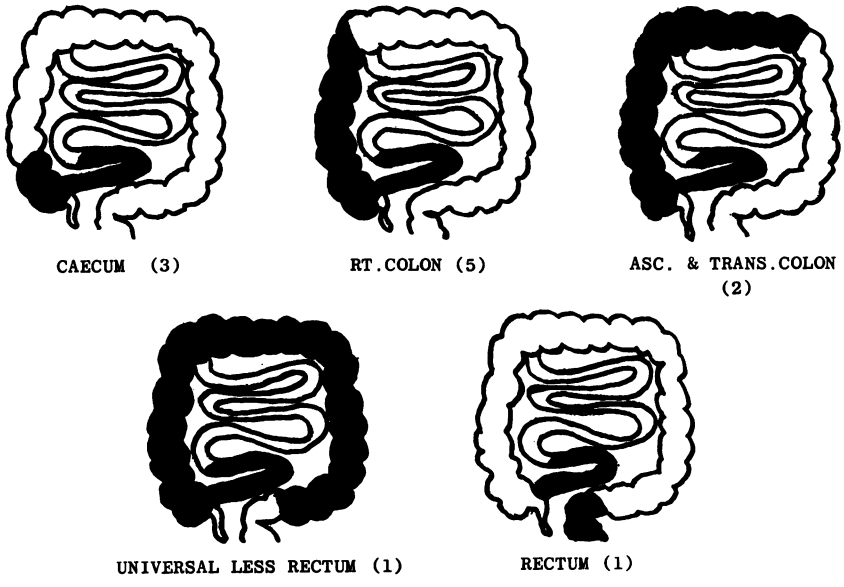

FIG. 1. *Distribution of disease in 12 cases of ileocolitis.*

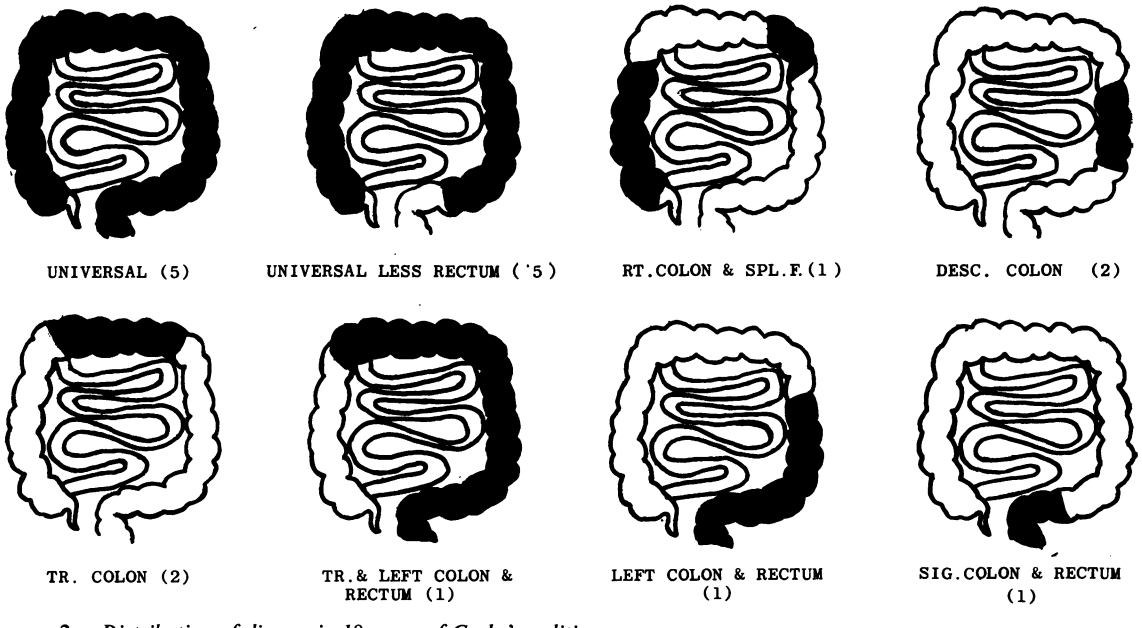

FIG. 2. *Distribution of disease in 18 cases of Crohn's colitis.*

Moderate anaemia and neutrophil-leucocytosis were recorded in half the patients. The erythrocyte sedimentation rate (Wintrobe) generally lay between 30 and 50 mm per hour, the highest reading being 57 mm. Hypoproteinaemia and hypoalbuminaemia were often present. Liver function tests were generally normal. The serum alkaline phosphatase was normal in all except three in whom there were minor elevations. In all patients the zinc sulphate turbidity and gamma globulin levels were within normal limits, and the transaminase levels were not raised.

Anal lesions were found in 15, consisting of proliferative lesions spreading out into the skin, ulceration, abscess formation, fistula and fissure formation, and stricture. Three (25%) of the 12 patients with ileal disease had anal lesions compared with 12 (67%) of the 18 who had colonic disease without ileal involvement.

Fistula formation either internal or external was found in those with ileal involvement to have an incidence of 25% and those without ileal involvement 33%.

Twenty-five patients underwent sigmoidoscopy; 17 were normal and eight abnormal. The eight abnormal were non-diagnostic, the changes being described as non-specific.

Only eight had rectal biopsies and in none could a diagnosis be established. These have been carefully reviewed but not even retrospectively could Crohn's disease of the rectum be confidently diagnosed.

COURSE OF THE DISEASE

The course of the disease was extremely variable. Most cases were subacute or chronic. Many had had the disease for months or even years before the diagnosis was established. There were two examples in which the disease, primarily confined to the colon, was associated with a fulminant episode.

A 21-year-old unmarried girl (case 14) presented in hospital with a history of seven months' continuous diarrhoea and loss of 14 kg in weight. Over the three weeks before her admission on 10 June 1964 the diarrhoea had become much worse and she began passing frank blood. She was febrile and her abdomen was tender in all areas. She rapidly worsened. Her abdomen became markedly distended. Serial plain *x*-ray studies of the abdomen on 10, 14, and 17 June demonstrated increasing gaseous distension of the transverse and left colon (Fig. 3a, b, c). Air fluid levels were also noted and the radiological diagnosis was made of fulminant colitis. Her haemoglobin was 9·7 g, serum iron 9 μg/100 ml, the erythrocyte sedimentation rate 49 mm in one hour, total protein 5·4 g (serum albumin 2·4 g)/100 ml. Serum electrolytes were sodium 130, potassium 3·1, chloride 93 and bicarbonate 25 m-equiv/l when she was dehydrated.

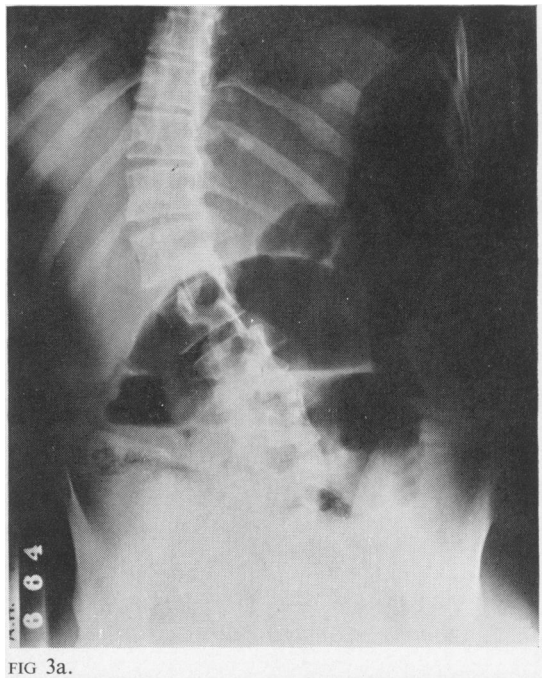

FIG 3a.

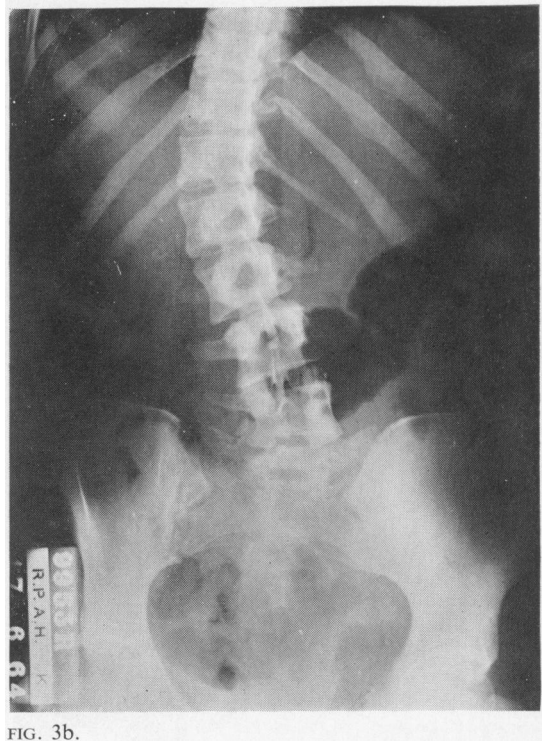

FIG. 3b.

FIG. 3. *a Case 14: plain radiograph of abdomen (14.6.64) showing gross dilatation of transverse and descending colon.*
b Case 14: plain radiograph of abdomen (17.6.64), still showing dilatation of transverse and descending colon.

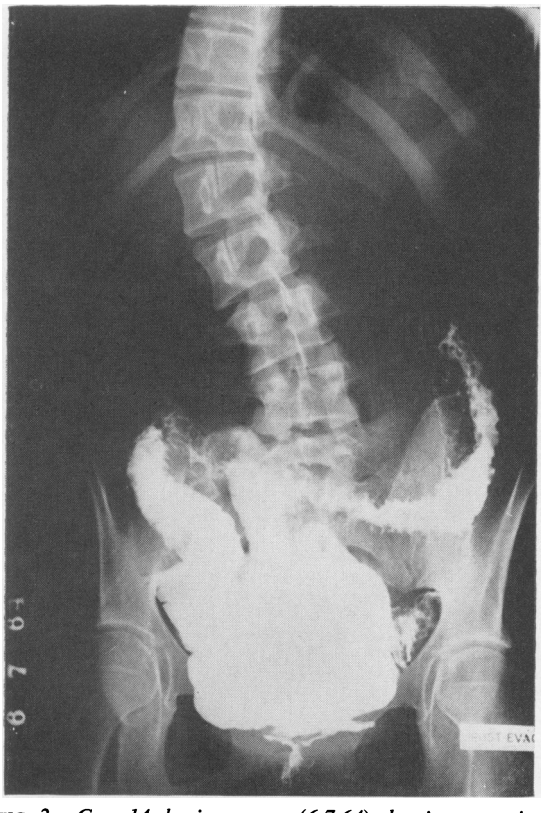

FIG. 3c *Case 14: barium enema (6.7.64) showing extensive involvement of the colon in the post-evacuation film.*

Sigmoidoscopy revealed a granular, oedematous mucosa which bled on contact but the appearances were considered to be non-specific. A rectal biopsy showed inflammatory changes in the mucosa and submucosa but this also was not diagnostic. With the diagnosis of fulminant colitis she was given supportive therapy which consisted of intravenous fluids and electrolytes, albumin, antibiotics, and hydrocortisone. Over the next few days her condition gradually improved and the abdominal distension abated. She was able to leave hospital four weeks later and was maintained on a combination of salazopyrin and corticosteroid therapy. However, the basic condition did not improve and diarrhoea and general ill-health continued. In January 1965 a total colectomy and ileo-rectal anastomosis was performed and at a later date excision of the residual rectum became necessary.

The specimen from the first resection consised of the terminal 10 cm of ileum and the entire colon with the exception of the rectum. The mucosa of the terminal ileum was a little irregular. The caecum and first part of the ascending colon had a fairly smooth surface but there were healing longitudinal ulcers of the upper part of the ascending colon with cobble stoned mucosa between them. Throughout the remainder of the colon, there was loss of mucosal pattern with occasional nodularity of the mucosa but no ulcers.

Microscopically the mucosa was normal but raised in a nodular fashion by lymphoid follicles of normal type. The ulcers in the ascending colon were almost completely healed and sections from irregularities of the mucosa elsewhere showed healed ulcers.

The second resected specimen consisted of the rectum, anal canal, and anus. There were deep ulcers throughout the specimen including the anal canal. Lymphoid masses were present throughout in all coats and were particularly dense in the submucosa. Fibroblasts were prominent in the submucosa but fibrosis was very early. Early tuberculoid granulomas were present in the submucosa.

A 19-year-old girl (case 22) was admitted to hospital on 18 June 1966 with a nine months' history of diarrhoea and loss of 16 kg in weight. In the four weeks preceding her admission the diarrhoea had become much more marked and soon she began bleeding profusely from the rectum. She was tender in both iliac fossae but no palpable mass was felt and abdominal distension did not occur. She had subsiding erythema nodosum of the legs, joint pains, and mouth ulceration. Haemoglobin, which on admission was 10·6 g, rapidly fell and she required many transfusions of whole blood. The total white cell count was 20,800 with a neutrophil count of 18,000. The ESR was 54 mm in one hour. Total protein was 5·6 g and serum albumin 2·4 g. Her serum electrolytes were sodium 130, potassium 3·5, chloride 90, bicarbonate 27 m-equiv/l.

A plain radiograph of the abdomen did not show any dilatation. Sigmoidoscopy revealed a normal rectal mucosa but an anal fissure was present. Rectal bleeding continued profusely and her condition deteriorated. On 22 June a laparotomy was performed. Total involvement of the colon but a relatively normal rectum was found at operation and resection of the colon with 17 cm of ileum and a temporary ileostomy was carried out. The proximal end of the rectum was exteriorized.

The specimen consisted of the terminal ileum and 80 cm of the large bowel. Throughout the large bowel there were linear ulcers overlying the tineae with normal mucosa between them (Fig. 4). Microscopically the appearance throughout was that of Crohn's disease. Tuberculoid granulomas were prominent in the submucosa and some were orientated around small blood vessels. There was a patchy arteritis and arteriolitis present in the submucosa. Occasional vessels had undergone fibrinoid necrosis and were surrounded by a granulomatous reaction. In others there was granulomatous inflammation of the vessel wall and in one instance there was a granulomatous reaction within the lumen of the vessel (Fig. 5a, b, c). Sections from the lines of resection showed no lesion in the terminal ileum or in the colon.

Immediately after surgery she was well and the ileostomy began functioning in 48 hours. Four days postoperatively she was passing excessive fluid and her loss of fluid and electrolytes became considerable. In the following few weeks the ileostomy fluid loss climbed to 3 litres a day. There was no evidence either clinical or radiological of any obstruction in the region of or proximal to the stoma. Antibiotics and corticosteroid therapy in full dosage did not improve the situation. During this time she

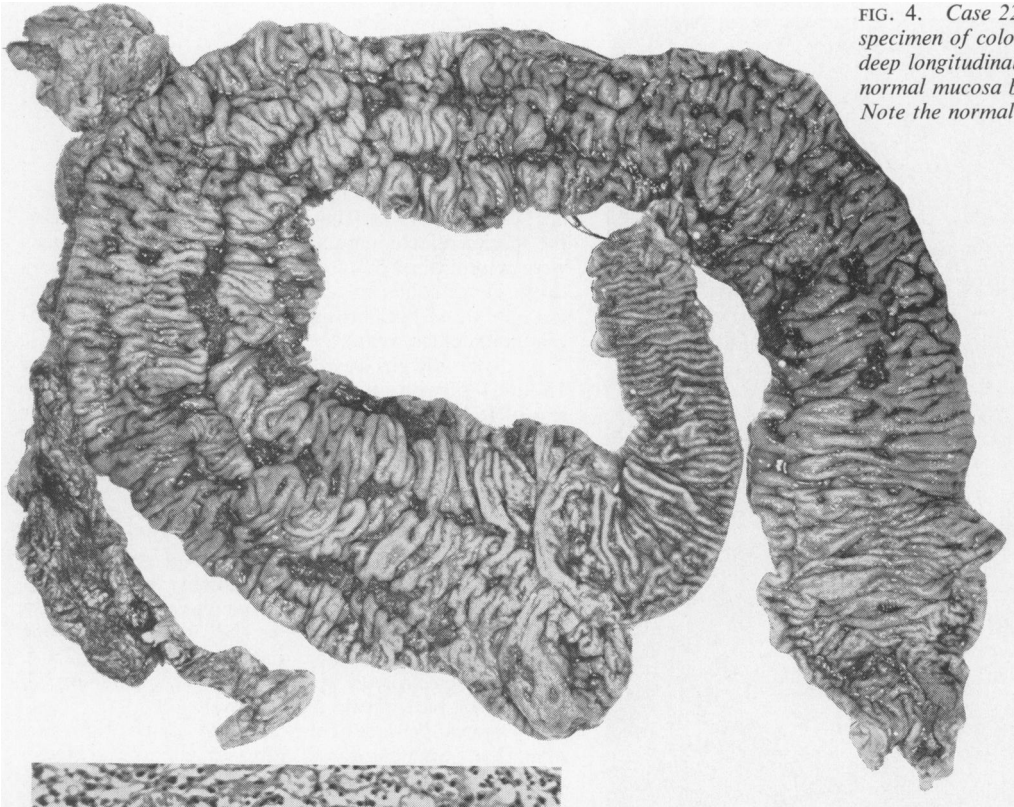

FIG. 4. *Case 22: resected specimen of colon showing the deep longitudinal ulcers with normal mucosa between them. Note the normal ileum.*

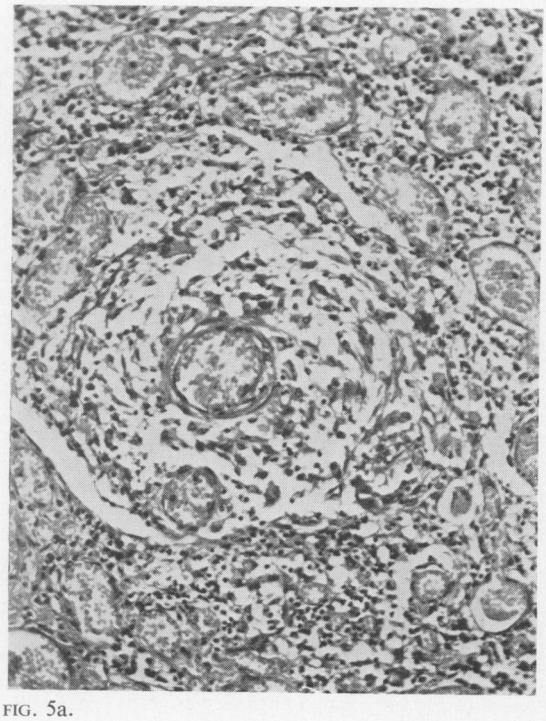

FIG. 5a.

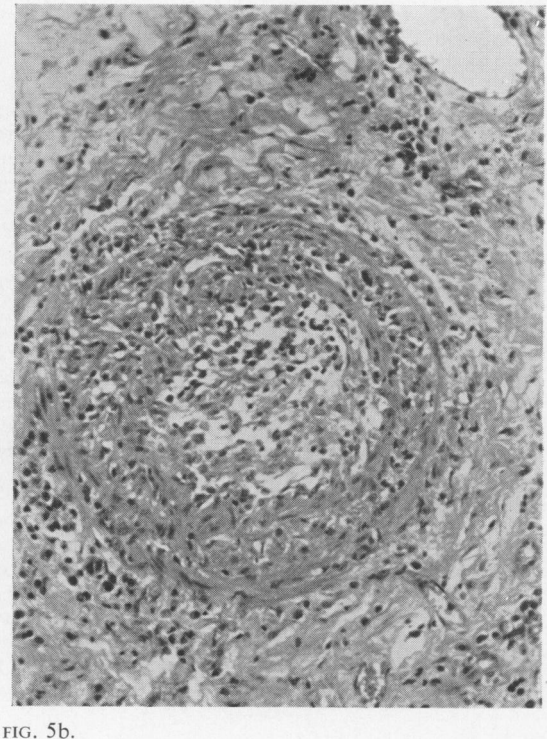

FIG. 5b.

FIG. 5. *Case 22: (a) Perivascular granuloma formation; (b) arteritis with intravascular granuloma. Haematoxylin and eosin × 150.*

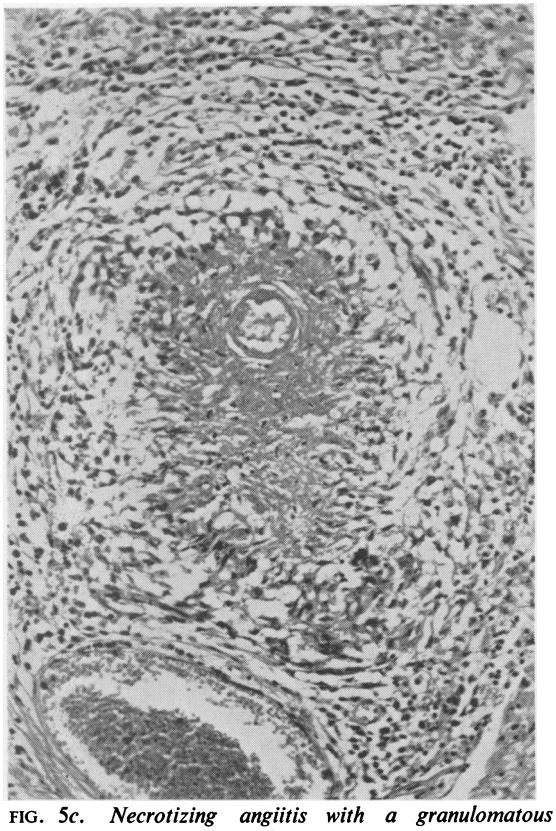

FIG. 5c. *Necrotizing angiitis with a granulomatous reaction. Haematoxylin and eosin* × *150.*

again had a marked fever and began to pass blood through the ileostomy. Despite strenuous efforts to maintain her fluid and electrolyte balance she failed to improve and a further laparotomy was performed on 22 July. The acutely inflamed ileum was removed and a new ileostomy fashioned. No obstruction was found at or proximal to the stoma and the jejunum appeared healthy. Several ileal perforations occurred while the bowel was being handled.

The specimen consisted of 127 cm of small bowel. The mucosa of the distal half of the specimen was ulcerated, mainly in relation to the mesenteric attachment. The ulcers were progressively larger and deeper towards the distal end of the specimen where they measured up to 5 cm in length and some penetrated the serosa. In the distal 10 cm the mucosa had a jelly-like exudate adherent to it. The unulcerated mucosa elsewhere appeared normal.

Microscopically the appearance was that of Crohn's disease with vasculitis similar to that in the first specimen. There was no fibrosis but oedema was prominent in the affected portions. The distal portion showed typical pseudomembranous enteritis (Figs. 6 and 7).

After this procedure the patient recovered and seven months later an ileorectal anastomosis was performed.

There were three examples of involvement of the ileum following colonic surgery.

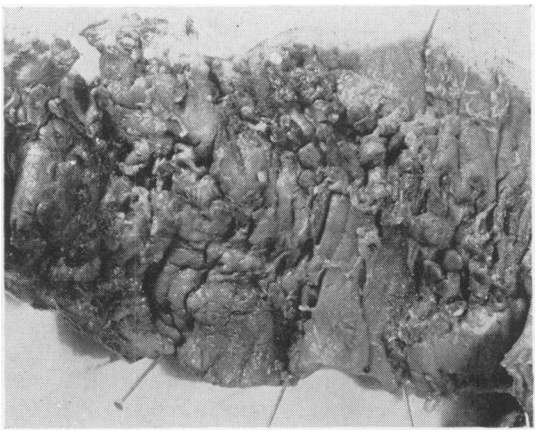

FIG. 6. *Case 22: pseudomembranous enteritis. The membrane has been partially rubbed off the oedematous mucosa.*

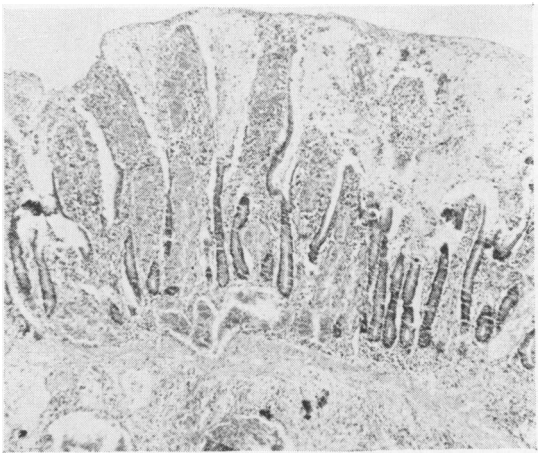

FIG. 7. *Case 22: pseudomembranous enteritis illustrating the fusion of a layer of mucus and exudate with the necrotic mucosal surface. Haematoxylin and eosin* × *44.*

The patient already quoted (case 22), with primary colonic disease, had a secondary and severe involvement of the ileum after surgery.

A young girl aged 9 (case 21) who had total involvement with sparing of the rectum had a bypass ileosigmoid anastomosis performed. Three months later a subtotal colectomy and ileostomy was carried out because of continuing activity of the disease. This was followed after some months by a postoperative ileorectal fistula with involvement of the ileum and rectum at the anastomosis and finally she required an abdominoperineal resection and permanent ileostomy.

A 45-year-old woman (case 27) had involvement of the transverse colon, left colon, and rectum. A resection of the left portion of the transverse colon, hepatic flexure, and descending colon was performed. This was followed

by an anal stricture, necessitating removal of the rectum and sigmoid colon. This in turn was followed by a jejunocolic fistula requiring excision of the right half of the transverse colon and the involved jejunum, and a colostomy was made in the proximal ascending colon.

In these last two examples the involvement of the small bowel occurred in the neighbourhood of the anastomosis.

PATHOLOGY

The material for this study consisted of resection specimens from 27 and biopsy material from one patient at exploratory laparotomy. The main pathological features are summarized in Table II. As a result of a close study of this material the following observations and conclusions concerning the pathology of Crohn's disease of the colon were made.

TABLE II

SUMMARY OF MAIN PATHOLOGICAL FEATURES

Lesion			*Total No. of Cases* 28	
Lymphocytic aggregates				
	Submucosa	28		(100%)
	Muscle	20		
	Subserosa	25		
Fibrosis				
	Submucosa	28		(100%)
	Muscle	19		
	Subserosa	12		
Tuberculoid granulomas			21	(75%)
	Mucosa	2		
	Submucosa	15		
	Muscle	9		
	Subserosa	9		
	Anal	6		
	Lymph nodes	6	(17 cases examined)	
Fissures			17	(60%)

ULCER FORMATION Ulcer formation followed a distinct pattern. It was always preceded by an accumulation of lymphocytes without follicle formation beneath the mucosal tubules, sometimes entirely within or sometimes extending into the lamina propria from the submucosa. The first stage in the development of an ulcer appeared to be degeneration of the basal cells of the mucosal tubules immediately overlying a lymphocytic accumulation. If the lymphoid mass was small only a few tubules degenerated. When the lymphoid aggregates were extensive a correspondingly larger ulcer resulted. Once the lymphocytic aggregation was established, ulceration appeared to occur in one of the following three ways and in any individual specimen each of the three types of ulceration might be present.

Failure of normal tubule regeneration Normally there is a continual replacement of intestinal epithelium by proliferation of basal cells in the depths of the crypts. In Crohn's disease this normal type of intestinal regeneration appears to be retarded and tubules may disappear from the lamina propria rendering it vulnerable to infection and ulceration. This mode of ulcer formation is also seen in ulcerative colitis but the lymphocytic aggregations that characterize Crohn's disease are absent.

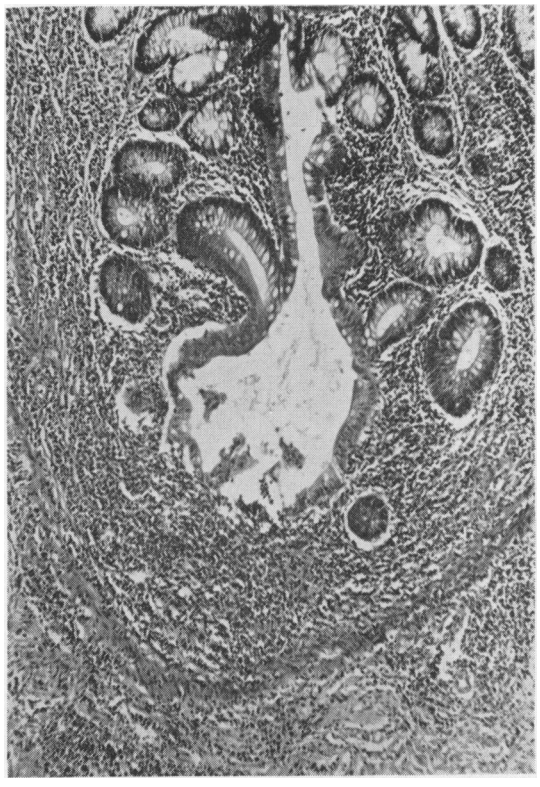

FIG. 8. *Early ulcer formation. There is a collection of lymphocytes in the lamina propria between the tubules and the muscularis mucosae. The bases of the tubules have been destroyed but proliferated epithelium is attempting to cover the defect. Haematoxylin and eosin* × *150.*

Mucosal abscess formation with undermining of the mucosa In ulceration of this type the basal cells of the tubules immediately overlying a lymphocytic aggregation undergo degeneration, their mitotic rate is reduced, and they disintegrate. Some regeneration occurs and the cells of adjacent tubules may join one another at their base. This results in a shallow cavity beneath the mucosa with normal tubules arising from it (Figs. 9, 10, 11). Polymorphonuclear leucocytes may accumulate beneath the affected tubules and abscesses so formed further undermine the musosa, or in more severe cases penetrate more deeply through the submucosa or even through the muscle coats. When the mucosa is extensively undermined it sloughs off leaving an ulcer.

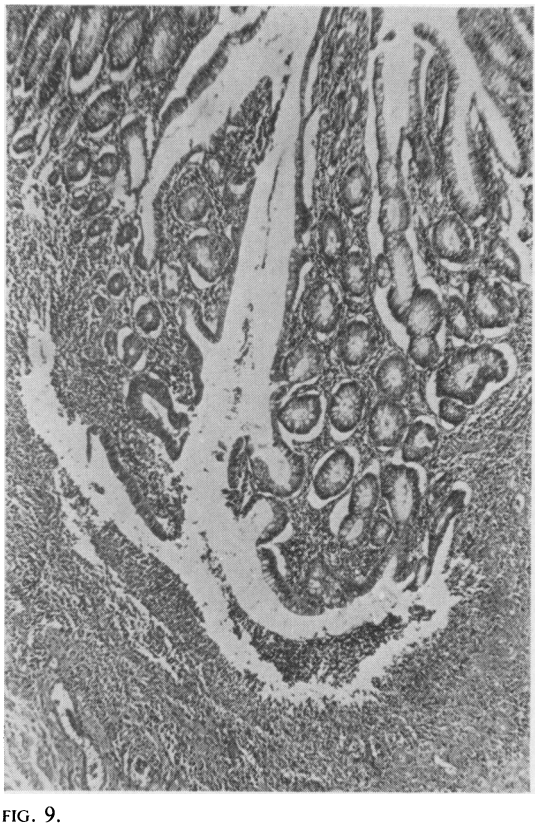

FIG. 9.

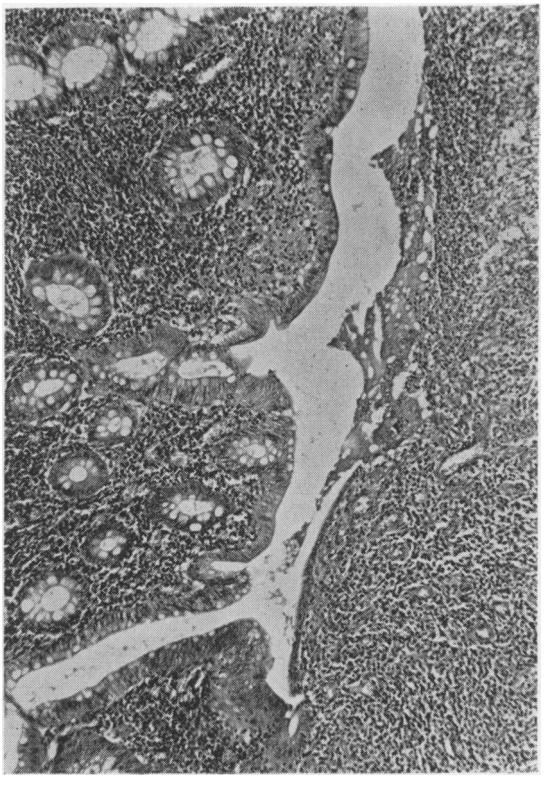

FIG. 10.

FIG. 9. *Lateral extension of the early ulcer undermines the adjacent normal mucosa. The floor of the ulcer has a granulomatous appearance. Haematoxylin and eosin* × *75.*

FIG. 10. *Lateral extension of an ulcer showing proliferated cells from the remaining intact cells of the mucosal tubules covering the undersurface of the undermined mucosa. Haematoxylin and eosin* × *150.*

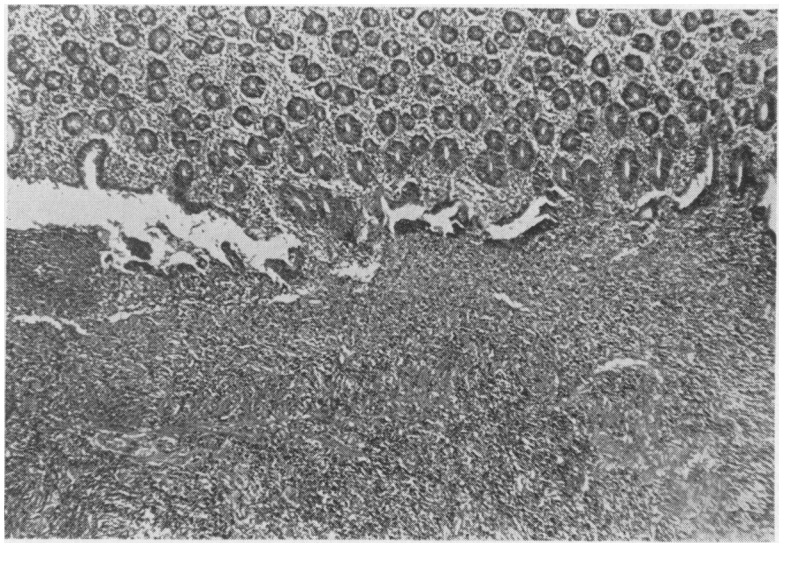

FIG. 11. *Extensive undermining of the mucosa. Haematoxylin and eosin* × *54.*

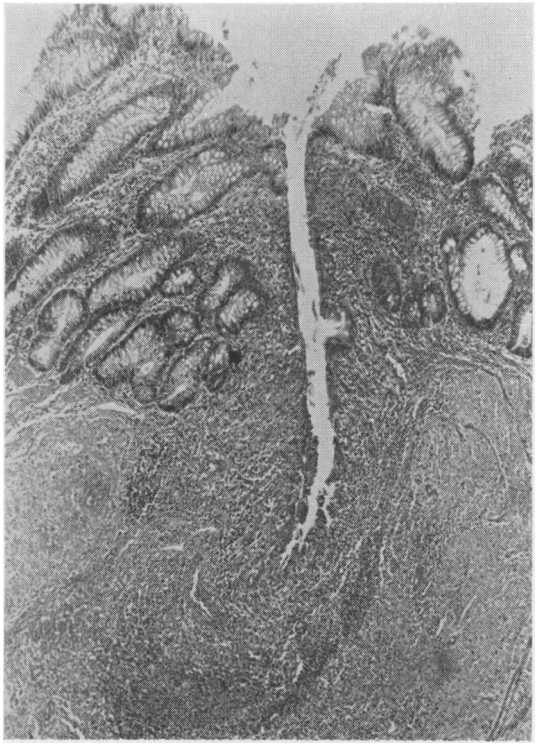

FIG. 12. *Cleft-like ulcer. Haematoxylin and eosin* × *44.*

Fissured ulcers The cleft-like ulcers which are so characteristic of Crohn's disease may occur longitudinally as well as in a transverse direction. The lymphocytic infiltrate that precedes this type of ulcer is usually related only to one or two tubules but the inflammatory reaction which follows the breach in the tubules may be quite intense, extending well into the submucosa (Fig. 12). The cleft then extends from the damaged tubule into the abscess zone and continues to extend, even to the serous layer. This is the mechanism of perforation and of fistula formation. The abscess often tracks obliquely through the submucosa and consequently in histological sections may appear to have no connexion with the mucosal surface. Sometimes too, when the acuteness has subsided, mucosal epithelial cells succeed in growing down such a cleft and one may then find colonic epithelium partially lining a chronic abscess cavity in the submucosa while the overlying mucosa appears normal.

It has been emphasized by Lockhart-Mummery and Morson (1960, 1964) that the mucosa between the ulcers of Crohn's disease is normal. There are occasions, however, when the microscopic pattern of the mucosa is quite irregular and is then liable to be mistaken for that of ulcerative colitis.

When the muscularis mucosa has been destroyed or is fibrotic from previous ulceration, the normal mucosal pattern is not re-established when healing occurs. In such cases, fibrosis often extends into the mucosa also. Consequently, in stating that the mucosa between the ulcers of Crohn's disease is normal, one must point out that this is so only when the muscularis mucosae is normal.

In summary, ulcer formation follows certain patterns depending upon the intensity of the process, loss of tubules from the lamina propria being the least severe and fissure formation representing the most severe type of reaction. In every case ulcer formation was preceded by lymphocytic aggregations which may even have initiated the process.

FIBROSIS Oedema of the submucosa was sometimes quite prominent but in most cases the thickening of the submucosa was due not so much to oedema as to fibrosis.

Fibrosis is a characteristic of Crohn's disease and in every case there was fibrosis of the submucosa. Involvement of the other coats of the gut wall was not always seen and seldom was it of severe degree.

LYMPHOCYTIC AGGREGATIONS The normal lymphoid follicles of the large intestine are found mainly in the superficial portions of the submucosa. Sometimes they extend into the lamina propria, displacing the mucosal tubules which otherwise remain normal. Lymphoid aggregations without germinal centres, however, were distributed throughout the submucosa and their intrusion into the lamina propria was associated with destruction of the basal cells of the tubules and ulceration at that site.

Lymphoid aggregations were invariably present in the submucosa and if enough blocks of tissue were examined they would probably have been found in the muscle coat and serosa in every case.

GRANULOMAS Tuberculoid granulomas were found most commonly in the submucosa but occurred in all coats of the intestinal wall. The granulomatous reaction was not confined to the formation of miliary follicles but was found in the floor of ulcers, around blood vessels, and even on rare occasions within blood vessels.

VASCULITIS In one case (case 22) there was a patchy vasculitis consisting of a granulomatous infiltrate around small vessels, in their walls and even within the lumen of some, while a few vessels exhibited fibrinoid necrosis surrounded by a granulomatous collection of epithelioid cells and Langhan's cells. There was no suggestion in this case that the

vasculitis was anything more than an unusual accompaniment of the disease.

PSEUDOMEMBRANOUS ENTERITIS In case 22, as well as vasculitis, acute involvement of the small intestine followed colectomy, and superimposed upon Crohn's disease were the changes of pseudomembranous enteritis. A firm membrane consisting of mucus, fibrin, and a few leucocytes was fused with the mucosa.

Finally we would stress that in every case we found lymphoid aggregates and fibrosis in the submucosa. Each of these may extend to other coats of the intestinal wall, but their presence in the submucosa is regarded as a *sine qua non* for the diagnosis of Crohn's disease. Other features which are diagnostic but are not invariably present are tuberculoid granulomata and fissure-like ulcers extending into the submucosa and beyond.

MANAGEMENT

All but one patient with involvement of the terminal ileum and part of the colon had a resection performed and the details are shown in Table III. The 11 patients on whom resection was performed were followed up for six months to six years. Three required further resections for recurrences at the site of anastomosis after right hemicolectomy. There were no deaths and all the results were good, the patients living normal lives. The patient treated conservatively has active disease and surgery is being considered. The details and results of treatment in the 18 patients with colitis alone are shown in Table IV. Two were treated medically, with one remission, and one has continued active disease and is awaiting operation. The remission occurred in case 18, a man with acute disease involving the whole colon apart from the rectum. The diagnosis was made at exploratory laparotomy and he was kept on corticosteroid therapy for three months. Sixteen patients required surgery and there were two postoperative deaths, one (case 19) from intestinal obstruction and one (case 24) from peritonitis. These 16 patients had a total of 30 separate operations. The rectum was involved in eight patients and in each required resection. When there was total colonic involvement with sparing of the rectum, ileorectal anastomosis was attempted four times and was only successful in two. It is evident that piecemeal resection for colonic disease always resulted in recurrence, requiring further resections. Often the colonic disease was more extensive than was realized at the time of surgery.

Five patients received corticosteroid therapy. Case 18, a man aged 39, with total colonic involvement but rectal sparing underwent an exploratory laparotomy and the diagnosis was established by biopsy. He received corticosteroid therapy for three months, had a clinical remission, and has remained well for three years. Two others had temporary improvement lasting a short time and two failed to respond. All four required surgery.

DISCUSSION

Our clinical experience is similar in most respects to that reported by Lockhart-Mummery and Morson (1960, 1964), Marshak *et al.* (1966), and Jones, Lennard-Jones, and Lockhart-Mummery (1966). The age group involved is the same, with emphasis on the second and third decades, but we noted distinctly more females than males in contrast to the other series in which there was little difference between the sexes. We found diarrhoea the most common symptom, often unrecognized by the doctor and even by the patient for some months. We agree with Cornes and Stecher (1961) that arthropathy and erythema nodosum may precede or accompany the diarrhoea. Certain symptoms and signs were found more commonly than those quoted in the literature.

TABLE III

MANAGEMENT OF CROHN'S ILEOCOLITIS

Site	*Case No.*	*Operation 1*	*Operation 2*	*Follow Up (Yr.)*	*Result*
Ileum, caecum (3)	1	Local excision ileum R hemicolectomy		3	Good
	2	R hemicolectomy		3	Good
	3	R hemicolectomy		1	Good
Ileum, R colon (5)	4	Local excision ileum, R hemicolectomy		5	Good
	5	R hemicolectomy	Resection at the anastomosis	5	Good
	6	R hemicolectomy	Resection at the anastomosis	6	Good
	7	R hemicolectomy	—	5	Good
	10	R hemicolectomy	Resection at the anastomosis	4	Good
Ileum, R & Tr. colon (2)	8	Local excision ileum R. hemi- and transverse colectomy	—	18 months	Good
	9	R hemi and transverse colectomy	—	3	Good
Ileum, rectum (1)	11	Local excision ileum, abdominoperineal	—	6 months	Good
Ileum, universal colon without rectum (1)	12	—	—	1	Unsatisfactory

TABLE IV

MANAGEMENT OF CROHN'S COLITIS

Site	Case No.	Operation 1	Operation 2	Operation 3	Operation 4	Follow up (Yr.)	Result
Universal (5)	13	L inguinal colostomy	Procto colectomy, ileostomy	—	—	3	Good
	14	Subtotal colectomy, ileorectal anastomosis	Abdominal-perineal ileostomy	—	—	3	Good
	15	Resection splenic flexure	Subtotal colectomy, ileostomy	—	—	5	Good
	16	Abdominal drainage, ileostomy	Subtotal colectomy ileostomy	Abdominal perineal	—	10	Good
	17	R hemicolectomy	Proctocolectomy, ileostomy	—	—	4	Good
Universal without rectum (5)	18	Exploratory laparotomy, biopsy	— —	—	—	4	Good
	19	Subtotal colectomy, ileorectal anastomosis	Intestinal obstruction, peritonitis	—	—	—	Died
	20	Subtotal colectomy, ileorectal anastomosis	—	—	—	1	Good
	21	Bypass ileosigmoid anastomosis	Subtotal colectomy, ileostomy	Abdominal perineal	—	10	Good
	22	Subtotal colectomy, ileostomy	Excision 3 ft ileum	Ileorectal anastomosis	3 months	3 mths	Fair
Descending colon (2)	23	Local resection	—	—	—	—	Died
	24	Local resection	—	—	—	—	Good
Transverse colon (2)	25	Local resection	—	—	—	2 mths	Good
	26	Local resection	—	—	—	1	Good
Transverse left colon rectum (1)	27	Local resection	Local resection	Abdominal perineal	Local resection R colostomy	5	Good
Descending sigmoid colon and rectum	28	Resection L colon and rectum	—	—	—	3	Good
R colon, splenic flexure	29	—	—	—	—	1	Unsatisfactory
Sigmoid colon, rectum	30	Abdominal perineal	—	—	—	8	Good

Pain was prominent in 60%, weight loss greater than 7 kg in 55%, local abdominal tenderness in 60%, and a palpable mass in 24%. A moderate anaemia and neutrophil leucocytosis were almost invariable and the erythrocyte sedimentation rate was always raised, usually moderately to levels between 30 and 50 mm in one hour. None of our patients had clinical or biochemical evidence of liver disease but no liver biopsies were done. The incidence of anal lesions was 50% and fistulae 30%, lower than that reported by Lockhart-Mummery and Morson (1964), Cornes and Stecher (1961), or Marshak *et al.* (1966). We did not find sigmoidoscopy diagnostic or particularly helpful unless the rectum was normal, which served as an important clinical distinction from ulcerative colitis in which the rectum is invariably involved. In our hands rectal biopsy was uninformative. The eight rectal biopsies were non-specific. This is in marked contrast to the report by Lockhart-Mummery and Morson (1964) who found sarcoid reactions in 16 of 19 biopsies.

Crohn's disease of the colon can become an extremely acute and fulminant disease, as in two of our patients in whom all the clinical, biochemical, and radiological features of fulminant ulcerative colitis were mimicked. Toxic dilatation was documented in case 14. Janowitz and Present (1966) commented that toxic dilatation had yet to be described in this form of inflammatory disease of the large bowel, and Marshak *et al.* (1966) concurred.

Hawk and Turnbull (1966), however, stated that toxic dilatation of the colon occurred as a complication of regional enteritis in 14 of 87 patients (16%) with the same alarming suddenness as seen with ulcerative colitis, and Morson (1966) agreed that he had observed it. We regard toxic dilatation as a rare event in Crohn's disease of the colon and associate it with severe and fulminant disease. This observation is not surprising as colonic dilatation has been described in amoebiasis (Wruble, Duckworth, and Rothschild, 1966) and can be associated with ischaemic enterocolitis or mesenteric vascular occlusion.

The condition for which Crohn's disease of the colon is most likely to be mistaken is ulcerative colitis. In ulcerative colitis the mucosa between the ulcers is not normal. Even before ulceration, the

mucosa is abnormal. There is usually prominent congestion and oedema, and tubules appear emptied of mucus. When a crypt abscess forms, the whole of the affected tubule degenerates and leucocytes appear within it at any level, whereas in Crohn's disease leucocytes appear in the tubule only after its base has disintegrated. Oedema is mainly responsible for thickening of the submucosa in ulcerative colitis while in Crohn's disease the prominent thickening of the bowel is due mainly to fibrosis.

Lymphocytic aggregations similar to those of Crohn's disease do not occur in ulcerative colitis though follicles of normal type with germinal centres may be increased in number in the upper zones of the submucosa and also in the mucosa itself, particularly in relation to a chronic ulcer or after healing of an ulcer.

In general ulcerative colitis affects the superficial zones of the bowel wall, and before ulceration is characterized by apparent diminished secretion of the mucosal tubules and by congestion and oedema of the mucosa and to some extent of the submucosa. In Crohn's disease the mucosa is normal before ulceration but even at that stage lymphocytic aggregates are present in all coats of the bowel, the submucosa is greatly thickened and fibrotic, and granulomas may be present in any portion of the bowel wall.

Crohn, Ginzburg, and Oppenheimer (1932) pointed out that tuberculoid granulomas in the intestinal wall do not necessarily mean tuberculosis and when they first delineated terminal ileitis as a clinico-pathological entity, their main concern was to distinguish the condition from tuberculosis.

Hadfield (1939) considered the pathology of Crohn's disease in more detail and emphasized the lymphoid aggregations and the tuberculoid granulomas which often appear in the centres of lymphoid nodules. Warren and Sommers (1954) regard Crohn's disease as the result of a granulomatous lymphangitis causing lymphatic obstruction with consequent oedema and cicatrization of the bowel wall. They noted sudanophilic droplets in the giant cells of the granulomas and implied that they might have been aetiologically concerned in the process.

We feel that granulomas are a reaction to some product of the inflammatory process of Crohn's disease rather than a part of the initial process, and that they are part of the reaction to injury. The fact that granulomas may be absent or sparsely present indicates that they are not an essential part of the process. The invariable presence of lymphoid aggregates and fibrosis, on the other hand, suggests that they are products of whatever may be the prime cause.

The recognition of Crohn's disease of the colon and its distinction from ulcerative colitis has been due largely to Lockhart-Mummery and Morson (1960, 1964). They point out that the pathological changes in Crohn's disease of the colon are similar to those of Crohn's disease in the small intestine and the features they stress are transmural distribution of the inflammation as compared with the superficial inflammation in ulcerative colitis, tuberculoid granulomas, submucosal fibrosis, cleft-like transverse ulcers which are responsible for the fistula formation, and essentially normal mucosa between ulcers. Notwithstanding such excellent criteria, there are still examples of Crohn's disease in which the histological diagnosis is not clear cut. We have not included other cases which we think are examples of Crohn's disease but which do not conform sufficiently well to the histological criteria we have established.

We feel that not enough emphasis has been given to the manner in which ulceration occurs, in particular the lymphocytic aggregates preceding the degeneration of the basal cells of related tubules. We concur with all other writers in the diagnostic significance of granulomas, and we agree with Lockhart-Mummery and Morson (1960, 1964) that cleft-like ulcers are diagnostic, but above all we insist that without lymphoid aggregates and submucosal fibrosis the diagnosis of Crohn's disease of the colon cannot be made.

We have not found Lockhart-Mummery and Morson's (1964) classification of colonic involvement particularly useful. They divide their cases into three groups: those with diffuse disease of the whole colon, localized strictures, and disease localized to the rectum. Thirty per cent of their cases had involvement of the terminal ileum. Lindner, Marshak, Wolf, and Janowitz (1963) and Marshak *et al.* (1966) make no attempt at grouping. It may be more useful to classify patients into those with associated terminal ileum involvement and those without. The former, in our experience, seem to behave in a more benign manner. The ileal involvement is always short and is confined to the terminal 80 cm of ileum. We have not had any patient demonstrating malabsorption due to small bowel involvement. The incidence of anal involvement in this group was 25% compared with 66% in cases involving the colon alone. The results of surgery were more satisfactory. In only three out of 12 cases was a second resection necessary due to failure to remove all the involved ileum at the first operation.

Our 18 patients with colonic involvement alone presented much more serious disease and 16 patients required 30 operative procedures. From this experience it seems clear to us that if there is extensive involvement of the large bowel it is wiser to perform subtotal colectomy with or without removal of the rectum, depending upon its involvement.

Diversion operations were undertaken in three patients (cases 13, 16, and 21). All were failures. A left inguinal colostomy was performed in case 13 and the second operation required was proctocolectomy. An ileostomy in case 16 was soon followed by a subtotal colectomy and later by an abdominoperineal resection. An ileosigmoid bypass procedure (case 21) was unsuccessful and subtotal colectomy and ileostomy was required a month later.

Partial resections leaving diseased colon *in situ* have not met with success. In our hands, corticosteroid therapy, used sparingly, was associated with success in only one patient. Jones *et al.* (1966) presented an extensive review of treatment and prognosis in 96 patients and their much greater experience with corticosteroids was identical to ours. They gave corticosteroids to 24 patients and 20 came to surgery in one year. Lindner *et al.* (1963) report initial benefit in 17 of 31 patients with corticosteroid therapy but the majority of these patients apparently came to surgery.

It seems clear that the great majority of patients with colonic involvement in Crohn's disease will require surgery. Resection of all involved tissue should be the aim. Corticosteroid therapy is likely to be most helpful when the process is acute and as a prelude to surgery.

SUMMARY

The clinical features, pathology, and management of 30 cases of Crohn's disease of the colon have been reviewed. Patients with ileal involvement were found to have a better prognosis than those with colonic involvement alone.

In the great majority, the disease began before the age of 40, there being an equal incidence in the second, third, and fourth decades. The ratio of females to males was 19:11. Diarrhoea was the outstanding symptom, pain and weight loss less so, and rectal bleeding uncommon. Fever, abdominal tenderness, and a palpable mass were the most valuable physical signs. A moderate anaemia and leucocytosis were frequent. Small intestinal malabsorption and liver disease were not seen. Sigmoidoscopy and rectal biopsies were not helpful in diagnosis.

Although granulomas and fissures are characteristic of Crohn's disease we feel that lymphocytic aggregates and submucosal fibrosis are essential for the diagnosis. Ulceration was preceded by the accumulation of lymphocytic aggregations beneath the tubules in contrast to ulcerative colitis in which the initial changes are in the mucosal tubules.

All except three patients required surgical resection of the involved area. There were two postoperative deaths. In all, 27 patients had a total of 44 major operations. Corticosteroid therapy was successful in one patient out of five. The surviving 28 patients are reasonably well.

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ADDENDUM

While this paper was in preparation two further cases of Crohn's ileocolitis have been seen by one of us (S.J.M.G.). A boy aged 13, with five years' history, presented with involvement of half the ileum and the whole colon less the rectum, and a woman aged 50 with a 10-year history with involvement of 35 cm of ileum and the whole colon less the sigmoid and rectum with fistulous tracks between ileum and colon. The latter has had a successful resection of the diseased areas and an ileosigmoid anastomosis performed. In both cases the jejunum was uninvolved.