

Early course of ulcerative colitis

J. McK. WATTS¹, F. T. de DOMBAL², G. WATKINSON, AND
J. C. GOLIGHER

From the Colitis Clinic, General Infirmary, Leeds

EDITORIAL SYNOPSIS The major factors influencing the prognosis in either the first or subsequent attacks of colitis have been found to be the age at onset of symptoms and the severity of disease and extent of involvement of the colon at the time of each attack.

The mortality of this disease under present-day forms of treatment has been found to be low, except in patients with total involvement of the colon and rectum, and in patients over the age of 60 years. Specific recommendations are made for the treatment of patients in these high-risk groups.

The management of a patient with ulcerative colitis still remains a considerable challenge to both physician and surgeon. There is little doubt that with the better understanding of the metabolic requirements of these patients, the introduction of improved, but non-specific drugs, and the acceptance of excisional surgery in selected cases, the outlook for colitic patients has improved during the past decade. However, the results of treatment, both in terms of morbidity and mortality, remain far from satisfactory.

In an attempt to evaluate the course and outcome of patients suffering from ulcerative colitis, we have analysed the progress of a group of 204 patients presenting in the first attack of this disease, admitted urgently to hospital, or referred to a combined medico-surgical colitis clinic during the 12-year period 1952-63.

We have excluded from this study a further 261 patients who presented during this period in a relapse of chronic disease, because our knowledge about the early course of these patients is often incomplete and, in addition, because some of these patients were referred specifically for surgery after medical treatment had been carried out elsewhere.

The majority of these patients have been treated with corticosteroids at some stage in their disease, and a relatively high proportion have undergone excisional surgery. To an extent, therefore, the overall course and mortality in this group of patients can be regarded as the results obtained in the treatment of this disease utilizing all contemporary forms of treatment.

¹Edward Lumley surgical research fellow, Royal Australasian College of Surgeons.

²In receipt of a research grant from the Board of Governors, the United Leeds Hospitals.

CLINICAL MATERIAL AND METHODS

Of 465 patients with ulcerative colitis treated in our clinic or in hospital from 1952 to 1963, 204 presented in the first attack of the disease, within 12 months of the onset of symptoms. The duration of symptoms at the time of presentation for these 204 patients is illustrated in Table I, one-fifth of the patients presenting within two months, two-thirds within three months, and nine-tenths within six months of the onset of symptoms. The group comprised 99 males and 105 females, the age

TABLE I
DURATION OF SYMPTOMS AT TIME OF PRESENTATION

<i>Duration in Months</i>	<i>No. of Patients</i>	<i>Percentage of Total</i>
2	42	20.6
2-3	83	40.7
4-6	59	28.9
7-12	20	9.8
Total	204	100.0

at the onset of symptoms according to sex being illustrated in Table II. The age distribution of the group demonstrates that 17% of the patients were aged less than 20 years, 41% between 20 and 39 years, 28% between 40 and 59 years, and 14% aged 60 years or over at the time of onset of symptoms.

TABLE II
COMPOSITION OF THE SERIES BY SEX AND AGE
AT ONSET OF SYMPTOMS

<i>Age at Onset (years)</i>	<i>Male</i>	<i>Female</i>	<i>Total</i>
0-9	0	2	2
10-19	16	16	32
20-29	16	22	38
30-39	23	22	45
40-49	13	19	32
50-59	17	9	26
60-69	8	13	21
70-79	6	2	8
Total patients	99	105	204

The diagnosis of ulcerative colitis was made in each patient during life, on the basis of characteristic symptoms in association with either or both typical sigmoidoscopic changes in the rectum and radiological changes in the colon. Microscopic examination and culture of the stools was performed in the majority of patients and in no case revealed any specific infective cause for the symptoms.

The information on which this survey is based was obtained by examination of the histories of personally treated patients, the majority having been interviewed and examined by sigmoidoscopy on at least yearly intervals. Examination of the colon by barium enema was performed in most patients at the time of the first attack, and subsequently at two-yearly intervals. All but two surviving patients were personally interviewed and examined by one of the authors during the latter part of 1963; both the remaining patients answered a detailed postal questionnaire. The detailed cause of death has been ascertained for each of the 19 patients who died during the period under review, a detailed necropsy report being available in 12 patients.

THE OUTCOME The outcome of attacks of colitis is expressed according to the following criteria.

1 *Remission* Normal health was regained, with either absent or infrequent and minimal bowel symptoms.

2 *Improved* Normal health was usually regained but bowel symptoms persisted, although these were never incapacitating.

3 *Unchanged* The symptoms were unchanged by medical treatment.

4 *Radical surgery* Total or subtotal excision of the colon and rectum was performed, usually with establishment of an ileostomy, because of the failure of medical treatment to control the disease.

5 *Death, of any cause* These will be further subdivided into (a) deaths related to colitis while the patient was under medical supervision; (b) deaths after radical surgery, during the early post-operative course; (c) deaths incidental to the disease.

The medical failure rate will also be described, being the proportion of patients in whom medical treatment failed, these patients either undergoing radical surgery or dying (of colitis or of causes related to this disease).

THE SEVERITY OF DISEASE The severity of individual attacks of colitis is graded into the following categories, according to the criteria of Truelove and Witts (1955):—

Severe Severe diarrhoea (six or more motions a day) with macroscopic blood in stools; fever (mean evening temperature more than 99.5°F. (37.5°C.), or a temperature of 100°F. (37.8°C.) or more on at least two days out of four; tachycardia (mean pulse rate of more than 90 per minute); anaemia (haemoglobin 75% or less, allowance being made for recent transfusion); E.S.R. much raised (more than 30 mm. in one hour).

Mild Mild diarrhoea (four or less motions a day) with no more than small amounts of macroscopic blood in stools; no fever; no tachycardia; anaemia not severe; the E.S.R. not raised above 30 mm. in one hour.

Moderately severe Intermediate between severe and mild.

THE CLINICAL EXTENT OF DISEASE This is classified thus:—

Rectum Mucosal disease in whole or part of the rectum on sigmoidoscopy. No radiological evidence of disease in the colon.

Substantial involvement Mucosal disease in the rectum at sigmoidoscopy. Radiological evidence of disease in part of the colon, but not extending proximal to the hepatic flexure.

Total involvement Mucosal disease in the rectum on sigmoidoscopy. Radiological evidence of disease throughout the entire colon.

THE OUTCOME OF THE FIRST ATTACK OF COLITIS

The immediate outcome of the first attack of ulcerative colitis in these 204 patients will now be considered in relation to the severity of the attack, the extent and rapidity of onset of the disease, and the age at the onset of symptoms (Fig. 1).

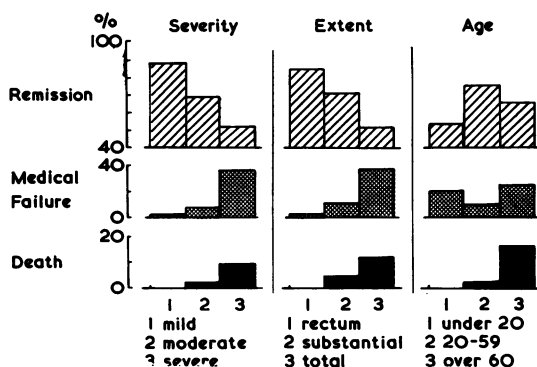


FIG. 1. The factors which modify the outcome of the first attack; the severity of the attack; the extent of the disease, and the age of the patient.

OVERALL OUTCOME OF THE FIRST ATTACK OF COLITIS Table III demonstrates that the disease went into remission in 70% or was improved after treatment in 16% of the 204 patients. Radical surgery was performed in 23 patients (11.3%), and the total

TABLE III
THE OVERALL OUTCOME OF THE FIRST ATTACK OF COLITIS IN 204 PATIENTS

Outcome	No. of Patients	Percentage of Total
Remission	143	70.1
Improved	33	16.2
Unchanged	2	1.0
Radical surgery	23	11.3
Deaths { medical treatment	2	3.9
after surgery	5	
incidental	1	
Medical failure rate	30	14.7
Mortality due to colitis	7	3.4

mortality of this attack was 3.9%. One patient died of status asthmaticus after rapid improvement of the colitis, making a corrected mortality due to colitis of 3.4%. The overall medical failure rate in the first attack of colitis was 14.7%.

OUTCOME OF THE FIRST ATTACK ACCORDING TO THE SEVERITY OF DISEASE This is illustrated in Table IV and Fig. 1, the severity of disease being classified as mild in 76 patients, moderate in 54 patients, and severe in 73 patients. The severity of attack is shown to have a profound effect on the outcome, the remission rates being 88% and 52% in mild and severe attacks respectively. Similarly, the medical failure rates rise from 1.3% in mild attacks to 35.6% in severe attacks. Only one patient died of 130 with either mild or moderate attacks, whereas six (8.2%) died of the 73 patients with severe attacks. More than one quarter of patients with severe attacks were submitted to radical surgery because medical treatment had failed.

OUTCOME OF THE FIRST ATTACK ACCORDING TO THE CLINICAL EXTENT OF DISEASE Although the assessment of the extent of disease is often very difficult, the extent of disease in the first attack was unknown in only 10 of the 204 patients. Six further patients

were excluded from consideration because the disease was segmental or confined to the right side of the colon.

The outcome of the first attack according to the extent of disease at that time is illustrated in Table V and Figure 1. It can be seen that the extent of disease exerts a considerable effect on the immediate outcome, remission rates falling from 85% in patients with rectal involvement to 51% when the entire colon was involved. Similarly, the medical failure rate increased from 1.4% in patients with rectal involvement to 36% in patients with total rectal and colonic involvement. The mortality due to colitis was 12.2% in patients with total colonic and rectal disease as compared with 2.7% in patients with substantial involvement.

RELATIONSHIP OF SEVERITY OF ATTACK TO THE CLINICAL EXTENT OF INVOLVEMENT It has been demonstrated that the prognosis of the first attack of ulcerative colitis depends to a considerable degree on both the severity of the attack and the extent of involvement of the rectum and colon at that time. The amount to which these two factors are interrelated for the first attack of colitis is illustrated in Table VI.

TABLE IV

THE OUTCOME OF THE FIRST ATTACK OF COLITIS RELATED TO THE SEVERITY OF ATTACK¹

Outcome	Mild (76 Patients)		Moderate (54 Patients)		Severe (73 Patients)	
	No. of Patients	% of Total	No. of Patients	% of Total	No. of Patients	% of Total
Remission	67	88.1	37	68.5	38	53.2
Improved	8	10.5	12	22.2	13	17.8
Unchanged	0	0	2	3.7	0	0
Radical surgery	1	1.3	2	3.7	20	27.4
Deaths {	0	0	1	1.9	1	9.6
medical treatment	0		0		5	
after surgery	0		0		1	
incidental	0		0		0	
Medical failure rate	1	1.3	3	5.6	26	35.6
Mortality due to colitis	0	0	1	1.9	6	8.2

¹Excludes one patient in whom severity of disease was unknown.

TABLE V

THE OUTCOME OF THE FIRST ATTACK OF COLITIS RELATED TO THE CLINICAL EXTENT OF DISEASE¹

Outcome	Rectum (72 Patients)		Substantial Involvement (75 Patients)		Total Involvement (41 Patients)	
	No. of Patients	% of Total	No. of Patients	% of Total	No. of Patients	% of Total
Remission	61	84.7	53	70.7	21	51.2
Improved	10	13.9	13	17.3	9	22.0
Unchanged	0	0	2	2.7	0	0
Radical surgery	1	1.4	6	8.0	10	24.4
Deaths {	0	0	0	2.7	0	12.2
medical treatment	0		1		4	
after surgery	0		0		0	
incidental	0		0		0	
Medical failure rate	1	1.4	8	10.7	15	36.6
Mortality due to colitis	0	0	2	2.7	5	12.2

¹Excludes 10 patients (one death) in whom the extent of disease was unknown, and six patients with right-sided or segmental colitis.

TABLE VI
INCIDENCE OF SEVERE FIRST ATTACKS RELATED TO CLINICAL EXTENT OF DISEASE

Extent of Disease	Total No. of Patients	No. of Patients with Severe Attacks	Percentage Incidence of Severe Attacks
Rectum	72	9	12.5
Substantial involvement	75	28	37.3
Total involvement	41	24	58.5

The incidence of severe first attacks is much greater with increasing involvement of the colon, the incidence of severe first attacks in the totally involved group being 58.5% and only 12.5% when the rectum only was involved.

It may be thought surprising that as many as nine severe attacks occurred in patients with rectal involvement only. However, these patients were recorded as having purely rectal involvement only after radiological examination of the colon had demonstrated no abnormality.

OUTCOME OF THE FIRST ATTACK ACCORDING TO THE AGE AT ONSET OF SYMPTOMS The age at the onset of symptoms is accepted as synonymous with the age at the time of the first attack. In order to evaluate the effect of the age on the outcome of this attack, patients have been classified into the three age groups: less than 20 years old, 20-59 years old, and 60 years and over.

The outcome of the first attack according to these age groups is illustrated in Table VII and Figure 1. The remission rate was greater (75%) in the age group 20-59 years than in the young and the aged. No deaths occurred in the 34 patients under the age of 20 years, but only 53% went into remission and 20.6% underwent radical surgery. The mortality due to colitis in the 29 patients aged 60 years and over was 17.2% although the rate of recourse to radical surgery (13.8%) was lower than that in the under 20 years group. If the mortality due to colitis of the 60 years and over group is compared with the

remainder, the difference is highly significant, illustrating that the age at onset has a profound effect on the outcome of the first attack of colitis.

SEVERITY OF THE FIRST ATTACK OF COLITIS ACCORDING TO THE AGE AT ONSET It has been shown that the age at onset has a profound effect on the outcome of the first attack of colitis. It is interesting, therefore, to relate the incidence of severe first attacks to the various age groups (Table VIII and Figure 1).

Of the patients aged less than 20 years, 58.8% and 44.8% of the patients aged 60 years and over

TABLE VIII
SEVERITY OF THE FIRST ATTACK OF COLITIS ACCORDING TO AGE

Age Groups	Number of Patients	Number of Patients with Severe Attacks	Percentage of Patients with Severe Attacks
Less than 20 years	34	20	58.8
20-59 years	141	40	28.4
60 years and over	29	13	44.8

suffered a severe first attack. On the other hand only 28.4% of patients in the intervening age group suffered a severe first attack of colitis. The difference in the frequency of severe first attacks between the less than 20 years age group, and the age group 20-59 years is significant ($p < 0.01$); the difference between the incidence of severe first attacks in patients 60 years and over and the age group 20-59 years is not quite significant ($0.05 < p < 0.1$).

EXTENT OF DISEASE IN THE FIRST ATTACK OF COLITIS ACCORDING TO THE AGE AT ONSET The frequency of severe first attacks of colitis has been shown to be greater both in patients under 20 years and in patients over 60 years of age. It might be thought that this finding would be related to a greater extent of involvement of the colon in these extreme age groups, but as illustrated in Table IX, the extent of

TABLE VII
OUTCOME OF THE FIRST ATTACK RELATED TO THE AGE AT ONSET OF SYMPTOMS

Outcome	Under 20 Years (34 Patients)		20-59 Years (141 Patients)		60 Years and Over (29 Patients)	
	No. of Patients	% of Total	No. of Patients	% of Total	No. of Patients	% of Total
Remission	18	53.0	106	75.2	19	65.5
Improved	8	23.5	21	14.9	4	13.8
Unchanged	1	2.9	1	0.7	0	0
Radical surgery	7	20.6	12	8.5	4	13.8
Deaths {	0	0	0	2.1	2	17.2
medical treatment	0		1			
after surgery	0		0			
incidental	0		1		0	
Medical failure rate	7	20.6	14	9.9	9	31.0
Mortality due to colitis	0	0	2	1.4	5	17.2

Comparing the mortality due to colitis of the group 60 years and over with the remainder $\chi^2 = 19.46, n = 1, p < 0.001$ (highly significant).

TABLE IX

EXTENT OF DISEASE IN THE FIRST ATTACK OF COLITIS ACCORDING TO THE AGE AT ONSET¹

Extent of Disease	Under 20 Years (29 Patients)		20-59 Years (131 Patients)		60 Years and Over (28 Patients)	
	No. of Patients	% of Total	No. of Patients	% of Total	No. of Patients	% of Total
Rectum	10	34.5	48	36.6	14	50.0
Substantial	10	34.5	56	42.8	9	31.2
Total	9	31	27	20.6	5	17.9

¹Excludes 16 patients in whom the extent of disease was unknown or with right sided or segmental colitis.

disease at the time of the first attack shows a tendency to decrease as the age at onset increases. It can be seen that the incidence of total involvement of the colon is 31% in the 29 patients under 20 years old at onset, but only 17.9% in the 28 patients aged 60 years and over at onset, suggesting that the younger group had more extensive disease at the time of the initial attack. These differences, however, while indicating a trend, are not statistically significant.

OUTCOME OF THE FIRST ATTACK ACCORDING TO THE RAPIDITY OF ONSET OF SYMPTOMS One hundred and ninety-nine patients were graded into two groups according to whether the initial symptoms of the disease were gradual or rapid in onset, a rapid onset of disease being defined as symptoms reaching their maximum severity within one month of their commencement.

The outcome of these patients, according to the rapidity of onset, is illustrated in Table X. It can be seen that the rapid development of symptoms implies a worse prognosis in this attack than if the symptoms were slow to develop. In that the medical failure rate in the group with rapid onset was almost twice as great as in the group with gradual onset of symptoms.

The mortality due to colitis in the group with rapid onset of symptoms was 6% but only 1.7% in the group with gradual onset of symptoms. This

difference in mortality, however, is not statistically significant.

Mortality during the course of disease subsequent to the first attack The medical and surgical mortality during the course of 178 patients who survived the first attack on medical treatment is illustrated in Table XI. Seven deaths occurred in patients under medical supervision, three of these deaths (bronchopneumonia, cardiac failure, ruptured Berry aneurysm respectively) were incidental to the disease, as the colitis was inactive at the time. The

TABLE XI

MORTALITY OF MEDICAL AND SURGICAL TREATMENT OF COLITIS DURING COURSE OF DISEASE AFTER FIRST ATTACK IN 178 PATIENTS

	No. of Patients Treated Medically Only	No. of Patients Treated Surgically after Failed Medical Treatment	Total Group
All patients	145	33	178
Died	7 ¹	4	11
% Mortality	4.8	12.1	6.2

¹Only four medically treated patients died of causes due to or related to the disease. Corrected medical mortality is therefore 2.8% and corrected total mortality 4.5%.

other four deaths under medical treatment were attributed to colitis or its complications, two of these patients dying of terminal pulmonary embolism. Of the four surgical deaths, two were due to intra-abdominal sepsis, one to pulmonary embolus, and one to small bowel obstruction.

The overall mortality of 6.2% in this group is an overestimate of the risk to life due to colitis. If only the eight patients dying from causes due to or contributed to by the disease are included, the corrected total mortality becomes 4.5%. Of these eight colitis deaths during the course subsequent to the first attack, three occurred during the first year of follow-up, three during the second year, one during the fourth year, and one during the sixth year of follow-up, illustrating that the risk to life in colitic patients extends well beyond the first year of their disease.

TABLE X

OUTCOME OF THE FIRST ATTACK RELATED TO THE RAPIDITY OF ONSET OF SYMPTOMS¹

Outcome	Gradual Onset (115 patients)		Rapid Onset (84 Patients)												
	No. of Patients	% of Total	No. of Patients	% of Total											
Remission	86	74.8	54	64.3											
Improved	17	14.8	15	17.9											
Unchanged	1	0.9	1	1.2											
Radical surgery	10	8.7	12	14.3											
Deaths { <table border="0" style="display: inline-table; vertical-align: middle;"> <tr> <td>medical treatment</td> <td>1</td> <td rowspan="3" style="font-size: 2em; vertical-align: middle;">}</td> <td>2</td> <td rowspan="3" style="vertical-align: middle;">6.0</td> </tr> <tr> <td>after surgery</td> <td>1</td> <td>3</td> </tr> <tr> <td>incidental</td> <td>0</td> <td>0</td> </tr> </table>	medical treatment	1	}	2	6.0	after surgery	1	3	incidental	0	0		1.7	3	
medical treatment	1	}		2		6.0									
after surgery	1			3											
incidental	0		0												
Medical failure rate	12	10.4	17	20.2											
Mortality due to colitis	2	1.7	5	6.0											

Comparing the mortality of the two groups $\chi^2 = 2.5$, $n = 1$, $0.2 < p < 0.3$ (not significant).

¹Excludes five patients (one death) in whom the rapidity of onset was unknown.

Therefore, with a mortality due to colitis of 4.5% during the average medical follow-up period of 4.3 years, it may be reckoned that approximately 1% of patients with ulcerative colitis will die in each year of causes due to, or related to this disease, a hypothesis supported by subsequent long-term studies (Watts, de Dombal, Watkinson, and Goligher, 1966).

COURSE AND OUTCOME OF PATIENTS UNDERGOING RADICAL SURGERY

Fifty-six of the 204 patients (27.6%) underwent radical surgery, the indications for surgery and the operations performed being shown in Tables XII and XIII respectively.

TABLE XII

INDICATION FOR SURGERY IN THE FIRST ATTACK OF COLITIS AND AFTER THE FIRST ATTACK

Operation	Indication for Surgery	Numbers in First Attack	Numbers After First Attack	Total
Urgent	Deterioration on medical treatment	16	14	30
	Perforation of colon	5	2	7
	Massive haemorrhage	—	1	1
Elective	Chronic invalidism	—	10	10
	Physical retardation	—	1	1
	Colonic stricture	—	1	1
	Ano-rectal complications	2	2	4
	Systemic complications	—	2	2
Totals		23	33	56

TABLE XIII

OPERATIONS PERFORMED IN FIRST ATTACK OF COLITIS AND DURING COURSE OF DISEASE AFTER THE FIRST ATTACK

Operation	Numbers in First Attack	Numbers after First Attack	Total
Proctocolectomy + ileostomy	16	22	38
Colectomy + ileostomy	5	4	9
Colectomy + ileo-rectal anastomosis	1	5	6
Other	1	2	3
Totals	23	33	56

MORTALITY OF RADICAL SURGICAL TREATMENT Nine of the 56 patients died during the early post-operative period, an overall mortality of 16.1% (Table XIV). The risks of surgery are much greater in the presence of severe disease, for all of these nine deaths followed urgent or emergency operations undertaken when medical treatment had failed.

No late deaths occurred among the 47 surgical survivors during the period of follow-up, the

TABLE XIV

MORTALITY IN 56 PATIENTS AFTER RADICAL SURGERY

Operation	Number of Patients	Early Post-operative Deaths		Late Post-operative Deaths
		Number of Deaths	% of Patients	
Urgent	38	9	23.7	0
Elective	18	0	0	0
All	56	9	16.1	0

average duration of which was 3.7 years (range six months to eight years).

SUBSEQUENT COURSE OF THE 47 SURGICAL SURVIVORS It is difficult to make any assessment of the problems encountered by a patient with a permanent ileostomy after colectomy or proctocolectomy. There are some initial difficulties concerned with adaptation to ileostomy life and in the care of the stoma; however, most of the late complications in this group of patients are either associated with the ileostomy or intraperitoneal adhesions producing small intestinal obstruction. We have, therefore, chosen to measure the post-operative morbidity of these patients, first, by consideration of the re-operations after primary surgery, and, secondly, by an assessment of the general health of these patients at the time of review. This latter aspect will be considered in a later section of the paper.

RE-OPERATIONS AFTER RADICAL SURGICAL TREATMENT OF COLITIS During the period of follow-up (average duration 3.7 years) one or more re-operations have been performed on 15 (31.9%) of the 47 surgical survivors. In all, 26 re-operations have been performed in these 15 patients without mortality. The nature and frequency of the various operations are illustrated in Table XV, it being notable that the majority of operations were performed because of ileostomy complications or small intestinal obstruction.

The steadily decreasing re-operation rate with increasing duration of follow-up is illustrated in

TABLE XV

NATURE AND FREQUENCY OF 26 RE-OPERATIONS IN 15 PATIENTS AFTER RADICAL SURGERY FOR ULCERATIVE COLITIS

Nature of Operation	Number of Operations
Operations on ileostomy	10
Operations for intestinal obstruction	10
Operations on abdominal wound	2
Operations on perineal wound	2
Miscellaneous	2
Total	26

Table XVI. Ten patients (21.3%) required one or more re-operations during the first year after recovery from radical surgery, but no re-operations were performed in the 19 patients followed for more than four years after operation.

OVERALL MORTALITY OF THE GROUP OF 204 PATIENTS

Of the total group of 204 patients, eight died during the first attack and a further 11 died during the course of follow-up. An evaluation will now be made of the factors affecting the subsequent prognosis in this disease by a consideration of the age of the patient, and of the extent and severity of disease, both at the time of the first attack and at the time of death.

OVERALL MORTALITY ACCORDING TO THE SEVERITY OF DISEASE IN THE FIRST ATTACK This is illustrated, separately for the first attack and the subsequent course, in Table XVII and Figure 2.

The severity of disease in the first attack of colitis has a profound effect on the mortality in this attack, which increases from nil in mild attacks, to 1.9% in attacks of moderate severity and to 8.2% in severe

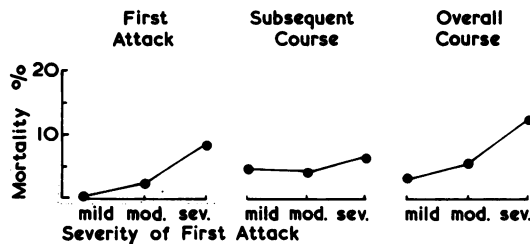


FIG. 2. The influence of the duration of follow-up after the first attack upon the percentage of patients without a second attack of colitis.

attacks. However, this factor has little bearing on the mortality during the subsequent course of the disease, where the mortality in patients who had mild and moderate disease at the time of the first attack is 4.0% and 3.9% respectively and, in those who had a severe attack, 5.9%.

TABLE XVII

EARLY AND LATE MORTALITY DUE TO COLITIS ACCORDING TO SEVERITY OF FIRST ATTACK¹

Percentage Mortality	Severity of First Attack		
	Mild	Moderate	Severe
First attack	0 (76)	1.9 (54)	8.2 (73)
Subsequent course	4.0 (75)	3.9 (51)	5.9 (51)
Overall	3.9 (76)	5.6 (54)	12.3 (73)

¹Excludes one patient in whom the severity of the initial attack was not known. All deaths due to or contributed to by colitis. Figures in brackets indicate numbers of patients followed-up.

The explanation for this is seen when one compares the severity of disease at the time of the first attack with the severity at the time of death in the eight patients who died of colitis during the course of the disease after the initial attack (Table XVIII). It is shown that seven of these eight deaths occurred in the presence of severe disease, the severity of disease at the time of the first attack being mild in three, moderate in two, and severe in only three of these patients.

TABLE XVIII

COMPARISON OF THE SEVERITY OF DISEASE IN FIRST ATTACK WITH THAT AT TIME OF DEATH IN EIGHT PATIENTS DYING OF COLITIS DURING THE COURSE OF THE DISEASE AFTER THE FIRST ATTACK

Severity of Disease	Severity of Disease at Time of First Attack	Severity of Disease at Time of Death
Remission	0	1
Mild	3	0
Moderate	2	0
Severe	3	7

These results indicate that the severity of the initial attack of this disease has little bearing on the risks to the patient after this attack, the prognosis being dependent on the severity of subsequent attacks of the disease.

OVERALL MORTALITY ACCORDING TO THE CLINICAL EXTENT OF DISEASE AT THE TIME OF THE FIRST ATTACK This is shown, separately for the first attack and for

TABLE XVI

RE-OPERATION RATE AFTER RADICAL SURGERY ACCORDING TO TIME AFTER PRIMARY OPERATION

	Years after Primary Operation					
	First Year	Second Year	Third Year	Fourth Year	Fifth Year	Six or More Years
Number of patients	47	39	33	26	19	15
Number of patients with re-operation	10	7	3	1	—	—
Percentage patients with one or more re-operations in year	21.3	17.9	9.1	3.8	—	—

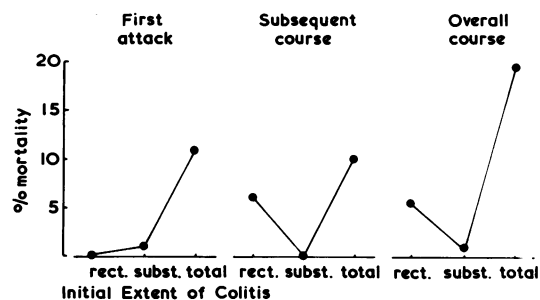


FIG. 3. The influence of the severity of the first attack upon the mortality due to colitis throughout the course of the disease.

the subsequent course in Table XIX and Figure 3. The extent of rectal and colonic involvement at the time of the first attack has a profound effect on the mortality in this attack, increasing from nil in patients with rectal involvement alone to 2.7% in patients with substantial involvement and to 12.2% in patients with total involvement. However, the

TABLE XIX

MORTALITY DUE TO COLITIS ACCORDING TO THE EXTENT OF INVOLVEMENT AT THE TIME OF THE FIRST ATTACK¹

Percentage Mortality	Initial Extent of Involvement		
	Rectum	Substantial	Total
First attack	0.0 (72)	2.7 (75)	12.2 (41)
Subsequent course	7.0 (71)	0.0 (68)	10.0 (30)
Overall	6.9 (72)	2.7 (75)	19.5 (41)

¹Excludes 10 patients (one death) in whom initial extent of colitis was unknown, and six patients with right-sided or segmental colitis. Figures in brackets indicate numbers of patients followed-up.

extent of disease at the time of the first attack has considerably less bearing on the mortality due to colitis during subsequent years, which is 7.0% in patients with rectal involvement, nil in patients with substantial involvement, and 10% in patients with total involvement at the time of the first attack. Of eight patients dying from colitis in the subsequent course of the disease, five showed no evidence of colonic involvement initially. At death, however, all eight patients showed evidence of substantial or total colonic involvement (Table XX).

RADICAL SURGICAL TREATMENT IN THE FIRST ATTACK OF COLITIS Twenty-three patients (11.3%) underwent radical surgery during the first attack of colitis, 21 of these patients having urgent operations in the presence of severe disease after medical treatment had failed, and the remaining two patients under-

TABLE XX

COMPARISON OF EXTENT OF DISEASE IN FIRST ATTACK WITH THAT AT TIME OF DEATH IN EIGHT PATIENTS DYING OF COLITIS DURING THE COURSE OF THE DISEASE AFTER THE FIRST ATTACK

Extent of Disease	Extent of Disease at Time of First Attack	Extent of Disease at Time of Death
Rectum only	5	0
Substantial involvement	0	3
Total involvement	3	5

going surgery because of intractable perirectal complications.

The indications for operation, and the types of operation performed during this first attack, are illustrated in Tables XII and XIII respectively. The operation most commonly performed was ileostomy with colectomy or proctocolectomy.

MORTALITY OF THE FIRST ATTACK OF COLITIS One hundred and ninety-six of the 204 patients (96.1%) survived the first attack of colitis, the overall mortality of this attack therefore being 3.9%. One patient died of status asthmaticus which was unrelated to colitis, so that the corrected mortality due to colitis was 3.4% (Table III).

Five deaths occurred after radical surgery (mortality 21.7%), two of these being due to intra-peritoneal sepsis, one to pulmonary embolus, one to primary haemorrhage, and one due to electrolyte imbalance. All five deaths occurred after an operation in the presence of severe disease, and three of these patients who died were found at operation to have perforation of the colon.

SUBSEQUENT COURSE OF DISEASE IN PATIENTS SURVIVING THE FIRST ATTACK OF COLITIS

One hundred and ninety-six of the original 204 patients survived the first attack of colitis, 18 of these patients having survived after radical surgical treatment, leaving 178 patients who had survived the first attack on medical treatment alone.

SUBSEQUENT COURSE AND OUTCOME OF 178 PATIENTS SURVIVING THE FIRST ATTACK ON MEDICAL TREATMENT ALONE The average length of follow-up in these patients, including the years before radical surgical treatment or death in those concerned, was 4.3 years at the time of review (range six months to 12 years).

Outcome at time of review The outcome for the

TABLE XXI
OUTCOME AT THE TIME OF REVIEW OF 178 PATIENTS SURVIVING FIRST ATTACK ON
MEDICAL TREATMENT ALONE

No. of Patients without Further Attack	Number of Patients with Further Attacks			Deaths		
	Medical Treatment Only	Medical plus Radical Surgical Treatment	Total	Under Medical Treatment	After Surgery	Total
Number of patients	51 ¹	94	127	7	4	11
Percentage of 178 patients	28.7 ¹	52.8	71.2	3.9	2.3	6.2

¹Includes 26 patients with less than one year follow-up after completion of first attack.

whole group at the time of review is illustrated in Table XXI.

It can be seen that 127 (71.2%) of these patients suffered at least one further attack of colitis, and that although 51 patients (28.7%) had suffered no further attack at the time of review, 26 of these patients had less than one year of follow-up from the time of the first attack. Of the 127 patients who suffered further attacks, 33 (18.5% of the 178 survivors of the first attack) have undergone radical surgical treatment, the remaining 94 (52.8%) patients having suffered at least one further attack under medical supervision alone. Eleven patients died during the follow-up period, a total mortality of 6.2% of the 178 survivors of the first attack. Seven of the 11 deaths occurred whilst the patients were under medical supervision and four after surgery.

Duration of freedom from relapse after the first attack of colitis The majority of patients suffer a relapse of colitis, be it mild, moderate, or severe, within a year of their first attack. The numbers of patients without relapse after the first attack is illustrated in Fig. 4, the whole period of follow-up

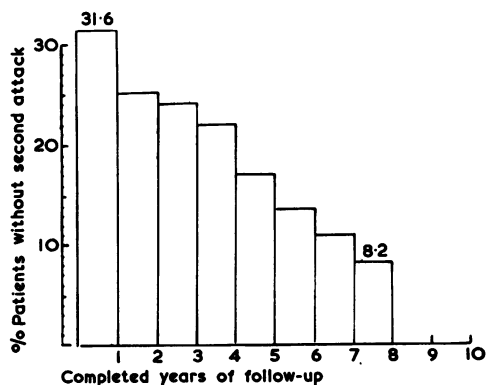


FIG. 4. The influence of the initial extent of colitis upon the mortality due to colitis throughout the course of the disease.

being covered, and all patients with less than one year of follow-up being excluded. In consecutive years the percentage of patients with persisting remission declines from 31.6% in the first year, to 25.2% in the third, 20.1% in the fifth, and 14.7% by the seventh year. Only two patients in this group have had remissions lasting more than seven years after the first attack.

Hospital admissions for treatment of colitis subsequent to the first attack There were 87 hospital admissions in 71 patients during the course subsequent to the first attack; this incidence includes the 33 admissions to hospital culminating in radical surgical treatment but excludes admissions for re-operation. With an average follow-up period of 4.3 years (range six months to 12 years), it can therefore be seen that, on average, 9.3% of these patients were admitted to hospital per year, or that the average yearly admission rate for the treatment of colitis (medical and surgical) in this group of patients was 11.2% after the first attack.

Incidence and outcome of clinically severe attacks Excluding the first attack, there were 51 severe attacks in 39 patients during the period of follow-up (average = 4.3 years). The average annual rate for severe attacks was, therefore, 6.7% in this group of patients. If the 39 patients only are considered, 5% of the group suffered at least one severe attack yearly.

The outcome of the 39 patients who suffered severe attacks, and of individual severe attacks, is illustrated in Table XXII. Twenty-three of the 39 patients who suffered one or more severe attacks were treated by radical surgery after medical treatment had failed, and the remaining 15 patients by medical treatment alone. Seven of these 39 patients died as a result of a severe attack, a mortality rate of 17.9%.

If the 51 individual severe attacks are considered, only 25 (49%) were controlled by medical treatment alone, the medical failure rate being 51%. Radical surgery was necessary in 23 patients (45.1%) of the 51 severe attacks after medical treatment had failed. Four deaths occurred after surgery, a surgical

TABLE XXII

INCIDENCE AND MORTALITY OF CLINICALLY SEVERE ATTACKS IN 178 PATIENTS
(EXCLUDING FIRST ATTACKS)

Method of Treatment	Patients with Severe Attacks	Number of Severe Attacks	Severe Attacks Requiring Surgery	No. of Deaths in Severe Attack	% Patient Mortality	% Mortality per Severe Attack
Medical treatment only	15	16	—	3	20	18.8
Medical and surgical treatment	24	35	23	4	16.7	11.4
All patients	39	51	23	7	17.9	13.7

mortality of 17.4% in severe attacks occurring during the course of the disease after the first attack.

Seven deaths occurred as a result of severe attacks, an overall severe attack mortality of 13.7%.

Subsequent medical course of patients with total colonic involvement Forty-one patients were found to have total colonic involvement at the time of the first attack of colitis. Of these, 10 underwent radical surgery and one died after medical treatment, 30 patients surviving this attack on medical treatment alone.

The subsequent outcome of these 30 patients is illustrated in Table XXIII, the average length of medical follow-up for this group being 3.7 years. Three patients (10%) died during this period. Eight patients (27%) underwent radical surgical treatment because of the failure of medical treatment in a severe relapse.

In addition, a further 16 patients, each with a lesser degree of colonic and rectal involvement at the time of the first attack, developed total rectal and colonic involvement during the period of

follow-up. The outcome of these patients, together with that of the 30 patients with total involvement at the time of the first attack is illustrated in Table XXIV. Of these 46 patients with total involvement during the course of their disease after the first attack, 13 (28.3%) underwent radical surgical treatment because of the failure of medical treatment in a severe attack. Five patients died, an overall mortality of 10.9%.

Surgical treatment subsequent to the first attack of colitis Of the 178 medical survivors of the first attack of colitis, 33 (18.5%) underwent radical surgical treatment during the subsequent course of the disease, the average period of medical follow-up being 4.3 years. The indications for operation in this group, and the operations performed are shown in Tables XII and XIII respectively.

It is notable that there has been a considerable change in the indications for operation in these 33 patients, compared with the indications for operation in the first attack; almost one half of these patients underwent elective operations because of chronic disease or its complications.

Figure 5 shows how the initial extent of colitis alters over a period of time in a considerable proportion of our patients. Of 50 patients with involvement limited initially to the rectum, the disease had

TABLE XXIII

OUTCOME OF 30 PATIENTS WITH TOTAL COLONIC INVOLVEMENT SURVIVING FIRST ATTACK ON MEDICAL TREATMENT ALONE¹

Treatment	Number of Patients	Died	Mortality (%)
Medical alone	22	1	4.5
Radical surgery after failed medical treatment	8	2	25
Total	30	3	10

¹Average follow-up was 3.7 years.

TABLE XXIV

OUTCOME OF 30 PATIENTS WITH TOTAL COLONIC INVOLVEMENT SURVIVING FIRST ATTACK ON MEDICAL TREATMENT AND 16 PATIENTS DEVELOPING TOTAL INVOLVEMENT DURING FOLLOW-UP

	Number of Patients	Radical Surgery	Total Deaths
Total involvement at time of first attack	30	8	5
Total involvement developing subsequent to first attack	16	5	2
All patients	46	13 (28.3%)	5 (10.9%)

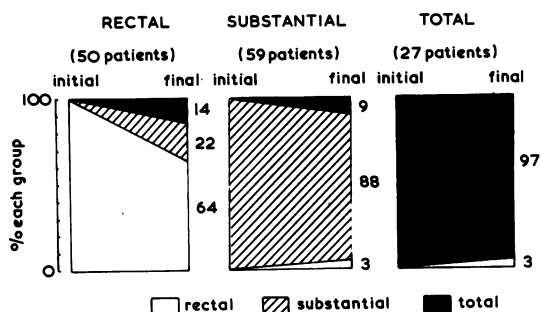


FIG. 5. The change in extent of disease, showing the extension and regression of colitis in a group of 128 patients. (Excludes patients whose initial or final extent of disease was unknown, and patients with under one year of completed follow-up.)

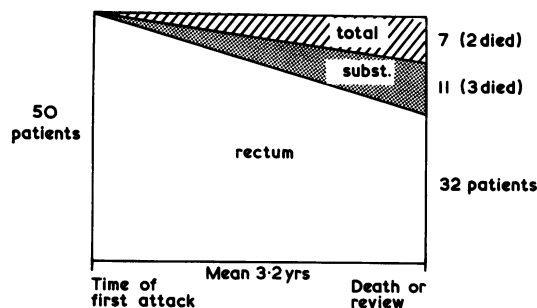


FIG. 6. The progress of a group of 50 patients with disease initially confined to the rectum, showing the proximal spread of colitis, and the mortality due to colitis. (Excludes patients whose final extent of the disease was unknown, and patients with less than one year of completed follow-up.)

spread proximally in 36% at the time of review, surgery, or death. In 59 patients with substantial involvement of the colon initially, progression to total involvement occurred in six patients (9%) and regression of the disease to involvement of the rectum alone in two patients (3%). All but one of the patients with initial total involvement remained with total involvement throughout the course of their follow-up.

Figure 6 illustrates that changing extent of disease in our patients implies a changed prognosis. Fifty patients with disease limited to the rectum at the time of the first attack were followed for a mean period of 3.2 years until they died or came to review. Disease remained limited to the rectum in 32 patients and among this group of patients the prognosis remained excellent. None died and only one came to radical surgery. However, the disease extended to involve part or all of the colon in 18 patients, and in this group, the subsequent prognosis was surprisingly poor; medical treatment failed in no less than 12 patients, and five patients died.

These findings illustrate that it is the extent of the disease present at any particular time that affects the prognosis, the extent at the time of the first attack being a somewhat misleading index, because of the propensity of this disease to extend and involve greater areas of the colon with the passage of time.

OVERALL MORTALITY ACCORDING TO THE AGE AT ONSET OF THE DISEASE It has been shown that the mortality of colitis during the first attack is greatly influenced by the age at the onset of symptoms. This factor similarly affects the mortality during the subsequent early course of the disease (Table XXV and Fig. 7), when the mortality rises from 3.7%

and 2.3% in the patients aged below 20 years and from 20 to 59 years respectively, to 21.1% in the patients aged 60 years and over. Unlike the variable factors of severity of attack and extent of disease, the broad age groups studies are relatively constant during the first attack and subsequent early course. The age at onset is therefore a particularly reliable index on which to base prognosis in such a study of the early course of colitis.

TABLE XXV

MORTALITY DUE TO COLITIS ACCORDING TO AGE AT ONSET Percentage Mortality	Age at Onset (years)		
	Less than 20	20-59	60 and Over
First attack	0.0 (34) ¹	1.4 (141)	17.2 (29)
Subsequent course	3.7 (27)	2.3 (132)	21.1 (19)
Overall	2.9 (34)	3.5 (141)	31.0 (29)

¹Figures in brackets indicate numbers of patients followed-up.

The overall mortality due to colitis of 31% in the patients aged 60 years and over suggests that the age at onset is probably the single most important factor in determining the prognosis during the first few years of this disease.

COMBINATION OF POOR PROGNOSTIC FACTORS As might be expected, if more than one poor prognostic factor occurs in the same patient, then the outlook for that patient is appalling. Severe attacks in patients over 60 carried a 50% mortality rate, and total involvement in patients over 60 implied a mortality rate of 83%. Of the small group of unfortunate patients over 60 with severe colitis and total involvement, none survived for more than six months.

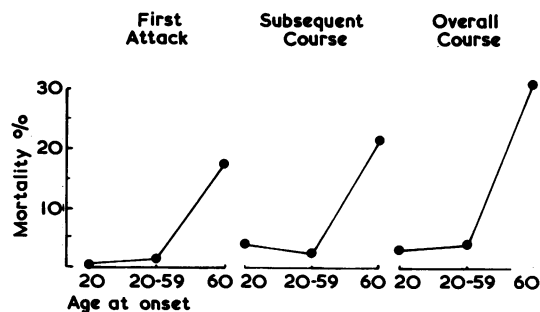


FIG. 7. The influence of the age at the onset of colitis upon the mortality due to colitis throughout the course of the disease.

CLINICAL STATE OF SURVIVORS
AT THE TIME OF REVIEW

One hundred and eighty-five patients were alive at the time of review during the latter part of 1963. All patients were traced and all but two of the survivors interviewed, these two patients answering a detailed postal questionnaire.

GENERAL HEALTH OF SURVIVORS AT REVIEW The following criteria have been used to evaluate the general health of the survivors, this being reported separately for both the survivors after medical treatment and the survivors after surgery (Table XXVI and Fig. 8):—(1) Excellent, leading a normal

TABLE XXVI

GENERAL HEALTH OF THE 185 SURVIVORS AT THE TIME OF REVIEW

General Health	Medical Survivors	Surgical Survivors
	No. of Patients	No. of Patients
Excellent, leading a normal life	59 (42.8%)	36 (76.6%)
Good, occasional curtailment of work and recreation	77 (55.8%)	10 (21.3%)
Poor, working capacity reduced	—	1 (2.1%)
Chronic invalid, unable to work	2 (1.4%)	—
Total	138 (100%)	47 (100%)
Patients receiving maintenance/medical treatment	72 (52.2%)	4 (8.5%)

life; (2) good, occasional curtailment of work or recreation; (3) poor, working capacity reduced; and (4) chronic invalid, unable to work.

It is remarkable that approximately 98% of the surviving patients experienced either good or excellent general health. However, the incidence of excellent general health is much greater in the

surgical (76.6%) than in the medical survivors (42.8%).

The low incidence (1.4%) of poor general health or chronic invalidism in the medical survivors is somewhat misleading because in 12 such patients the outcome of an attack of colitis was awaited before this review was undertaken.

MEDICAL TREATMENT OF THE SURVIVORS AT REVIEW Seventy-two of the 138 medical survivors (52.2%) were receiving some form of specific maintenance medical treatment at the time of review (Table XXVI) Forty-four of these patients were receiving corticosteroids in some form.

On the other hand, only four of the 47 surgical survivors (8.5%) were receiving medical treatment, three of these patients receiving steroids and/or Sulphasalazine because of persistent symptoms after ileo-rectal anastomosis. The other patient was receiving high doses of prednisone for the control of persistent iritis and arthritis after procto-colectomy.

OVERALL OUTCOME OF THE WHOLE GROUP AT THE TIME OF REVIEW The general health of all survivors and the combined medical and surgical mortality for the group is illustrated in Table XXVII. Nineteen patients (9.3%) died during the overall course of the disease, the average period of follow-up for the 196 patients surviving the first attack of the disease being 4.8 years (range six months to 12 years) for the combined medical and surgical follow-up).

If the four patients dying of causes unrelated to colitis are excluded, the overall mortality due to colitis in this group of patients is 7.4% throughout this period.

TABLE XXVII

OVERALL OUTCOME OF WHOLE GROUP OF 204 PATIENTS AT TIME OF REVIEW

General Health	Number of Patients
Excellent	95 (46.6%)
Good	87 (42.6%)
Poor	1 (0.5%)
Invalid	2 (1.0%)
Deaths ¹	19 (9.3%)
Total	204 (100%)

¹Includes four deaths incidental to colitis so that corrected overall colitis mortality is 7.4%.

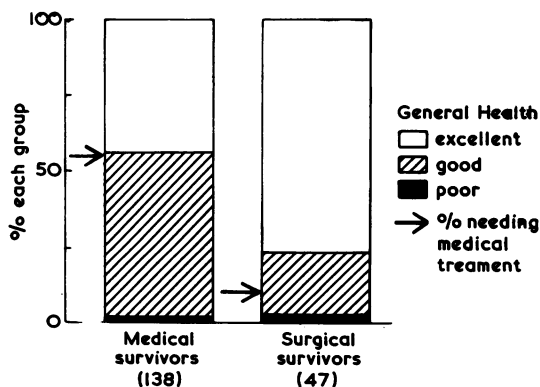


FIG. 8. The general health of all medical and surgical survivors at the time of review.

DISCUSSION

The unpredictability of the course of patients suffering from idiopathic ulcerative colitis has been the stimulus for a large volume of literature on the factors affecting the prognosis in this disease. Unfortunately, most of these studies, with the

notable exception of those of Rice-Oxley and Truelove (1950) and Edwards and Truelove (1963), have failed to distinguish between those patients presenting in the first attack of the disease and those initially coming under treatment with a relapse of established chronic disease. Similarly, the lack of precise definition of the severity of attacks, and the loss of large numbers of patients to follow-up has sometimes undermined the validity of their conclusions.

These objections have been obviated in the present survey by the inclusion of only those patients presenting in the first attack of their disease within a year of the onset of symptoms. With few exceptions, this group of patients has been reviewed yearly or more often in a combined medical and surgical colitis clinic, and, during the latter part of 1963, all surviving patients in the group were traced. Apart from two patients who answered detailed postal questionnaires, all survivors were personally interviewed and examined. Detailed information about all attacks of colitis was obtained from an examination of the case histories, the severity of all attacks being classified according to the criteria of Truelove and Witts (1955).

An obvious criticism of our study is that it reveals the disease as seen by a group of physicians and surgeons particularly interested in colitis, and not as it occurs in the general population (Hurst, 1935; Nefzger and Acheson, 1963). Evidence that this may be so can be adduced from the fact that in our group of patients there was a high incidence, both of severe initial attacks, and of patients with total colonic involvement. The mortality in this series, at least for the initial attack, is therefore likely to be greater than that of colitis as encountered by general practitioners.

THE FIRST ATTACK OF ULCERATIVE COLITIS This study confirms that the mortality of this disease is always greatest during the year of the first attack (Hurst, 1935; Rice-Oxley and Truelove, 1950; Sloan, Borgen, and Gage, 1950; Demole, 1956; Banks, Korelitz, and Zetzel, 1957; Kellock and White, 1957; Nefzger and Acheson, 1963; Edwards and Truelove, 1963). This high mortality in the year of the first attack is understandable, because this is the only year in which all the patients surveyed have an attack of colitis.

It has been clearly shown that the outcome of this attack is influenced by a number of factors, namely, the rapidity of onset of symptoms, the severity of the attack, and the extent of rectal and colonic involvement (Fig. 1). The most striking factor influencing the outcome was the age of the patient, and no fewer than five of the eight deaths

in this attack occurred in the group of 29 patients aged 60 years or more. The overall mortality of the first attack in this series is 3.9%, or only 3.4%, if the death incidental to colitis is excluded. Furthermore, if the 29 patients aged 60 years and over are excluded, the mortality of the 175 remaining patients is only 1.7%.

To an extent some of these factors which affect the outcome of the first attack are interrelated. As expected, there is a correlation between the amount of colon involved and the severity of the attack, there being a greater incidence of severe first attacks with increasing colonic involvement. Severe attacks were also commoner in the young and in the old, as shown by the fact that medical treatment failed in 20% of the patients aged less than 20 years old and in 31% of those aged 60 years and over, but only in 9% of the remainder. Although the incidence of severe attacks is greatest in these two extreme age groups, it can only be explained in terms of great extent of colonic involvement in the group of patients aged less than 20 years. For, of the patients aged 60 years and over, no less than one half had rectal involvement only, without radiological evidence of disease in the colon, and only 17.8% of this group had total colonic and rectal involvement. Yet it is this group of patients that has such a high incidence of severe attacks, suggesting that the systemic reaction to this disease is much greater in the aged, even with minimal degrees of colonic and rectal involvement. They are therefore less likely to withstand the onslaught of this disease unless treatment is immediately effective.

Rice-Oxley and Truelove in 1950 reported a mortality of 22% in patients presenting to hospital in the first attack of colitis. A subsequent report from Oxford (Edwards and Truelove, 1963) confirms our finding that there has been a marked reduction in the mortality of the first attack of this disease during the past decade. It is suggested by these authors that this reduction is due to a larger proportion of patients being seen with mild attacks and to the sharp decline in fatality associated with attacks of moderate severity, the mortality from severe attacks having remained fairly constant throughout.

We are unable to make such a comparison in our series, except to report that of the 130 patients with mild or moderate disease only one patient died. On the other hand, the mortality of the 73 patients with severe first attacks was 9.6%. Further analysis of these patients dying in a severe attack shows that there were only two deaths in the 60 patients aged under 60 years at the time of a severe first attack (mortality 3.3%), but that of 13 patients with severe first attacks aged 60 years and over no less than five died, a mortality of 38.5%.

It must be concluded therefore that modern methods of medical treatment, supplemented by radical surgery when required, can achieve a low mortality in the first attack of this disease if the patient is aged less than 60 years. On the other hand, the mortality of a severe attack in patients over this age is still alarmingly high, so much so that we would feel compelled to consider a change in the regime of management of this older, severe type of case in the future. Admittedly many of these patients over 60 eventually came to emergency operation, when medical treatment had failed to secure remission, and most of the deaths occurred after operation. It may be that operations of this kind in elderly patients are inseparable from a considerable mortality, but it is at least arguable that delay in the application of surgery might have been an important contributory factor, and that a speedier resort to operation might have avoided some of these deaths.

An analogy may perhaps be drawn between colitis and haematemesis, for in haematemesis Avery Jones (1947) and Tanner (1950) have clearly shown that the mortality is highest in patients over 60, and, further, that this mortality can be reduced by early surgical intervention.

Similarly, for colitis, a good case can certainly be made out for the trial, in elderly severely ill patients, of a combined medico-surgical approach. Such an approach would involve a short course of intensive medical treatment, which, unless an immediate response occurs, is followed by early radical surgery, as practised so successfully by Gallagher, Goulston, Wyndham, and Morrow (1962) in a younger group of patients.

COURSE OF THE DISEASE AFTER THE FIRST ATTACK

Some measure of the morbidity of patients after their first attack of colitis can be obtained by a consideration of the number of subsequent hospital admissions for the treatment of colitis, and the duration of freedom from further attacks. In fact the annual rate of hospital admissions in our series was 11.2%, and it was found to be uncommon for a patient to escape a further attack of colitis, the incidence of patients without further attacks steadily decreasing with increasing length of follow-up.

The annual incidence of clinically severe attacks of disease has been estimated at 6.7% or, if patients are considered, 5% suffered one or more severe attacks annually. The mortality of severe attacks during the period of follow-up (13.7%) is greater than that of severe first attacks (9.6%), and, although this difference in mortality is not statistically significant, it suggests that present forms of medical and surgical treatment may be less satisfactory in the treatment of severe relapses, particularly in view of

the small number of patients at risk in the age group 60 years and over at this stage.

Total involvement of the colon was found to influence the prognosis adversely during the first attack; it is therefore interesting to note that the risks to these patients were carried into the subsequent course of their disease. There was a 10% mortality in this group of patients during the average medical follow-up period of 3.7 years, the annual mortality rate therefore being just under 3% (Table XXIII). If we consider our experience with the 41 patients presenting initially with total involvement of the colon and rectum, it is evident that medical treatment has failed in 20 patients (49%) over the period of the first attack and for 3.7 years' average follow-up. This experience would seem to indicate that patients with total involvement of the rectum and colon have an annual risk to life which is only just less than the mortality of elective surgery. On these grounds it would seem that radical surgery should be recommended to any patient found to have total involvement of the colon, either at the time of the first attack, or during the subsequent course of the disease, even before any appreciable risk of carcinoma developing has arisen.

The overall mortality due to colitis of the group of 178 patients surviving the first attack on medical treatment is 4.5%, and it has been shown that approximately 1% of patients will die each year from the disease or its complications. An analysis of the extent and severity of attacks at the time of death illustrates that this mortality is almost entirely sustained by patients suffering a severe attack of the disease and manifesting total, or subtotal, colonic involvement.

SURGICAL TREATMENT The results of surgical treatment in this series confirm that the risks of this form of treatment are much greater in the presence of a severe attack than when performed as an elective procedure. Actually there were no deaths after 18 elective procto-colectomies in this series, which is gratifying, but obviously underestimates the risk of operation at this stage. But, of 38 patients submitted to operation during severe attacks, nine died. This difference in fatality rate can only partly be explained by the relatively high mortality of surgery in patients aged 60 years and over, for although four of six patients in this age group died after operation, one of 12 patients under 20 years of age and four of 32 patients aged 20 to 59 years also succumbed following surgical treatment.

The high mortality rate after operation in severe attacks is clearly unsatisfactory and poses a difficult problem. On the one hand, realization of the hazards of emergency operation encourages the clinician to

persist with conservative measures as long as possible; on the other hand, it could be said that, if operation were undertaken much earlier before the patient's general condition had deteriorated significantly, at least some of the hazards of surgery might be obviated. Such early intervention has been practiced by Gallagher *et al.* (1962) with reduction of their operative mortality to 9% in 'fulminating' cases. In the light of our results, we propose to give a thorough trial to this policy of invoking surgical aid at a very early stage of severe attacks, unless there is unequivocal evidence of rapid improvement on medical treatment.

Radical surgical treatment in colitis usually involved inflicting on the patient a permanent ileostomy with its attendant disadvantages, for most surgeons have been unable to secure the excellent results reported by Aylett (1963) with ileo-rectal anastomosis. As has been shown in this study, patients may have to face further relatively minor operations for a variety of sequelae following radical surgery, and these are clearly a nuisance to the patient and carry some risk to life. But ileostomy is certainly compatible with good general health and minimal restrictions. Yet, there are strong psychological reasons why a patient should be averse to accepting an artificial anus. The decision in favour of surgical treatment is therefore often extremely difficult, for it can only justifiably be reached when the risk to life or the invalidism due to the disease clearly outweigh the disadvantages of this form of treatment.

THE PROGNOSIS IN ULCERATIVE COLITIS It has been shown that the prognosis of the first attack of colitis is dependent on a number of factors, in particular the age at the onset of symptoms (Table I). Edwards and Truelove (1963) have based their studies on the long-term prognosis in this disease on the severity and extent of the disease at the time of the first attack. However, an analysis of the mortality in our series of patients during the subsequent course of their disease has shown that the prognosis during this period is related to the severity and extent of disease at the time of the attack, which are often quite unrelated to the severity of the first attack and the initial extent of disease. For example, the majority of deaths during the period of follow-up occurred in the presence of a severe attack, but the first attack in these patients was just as commonly mild as severe (Table XVIII). Similarly, deaths during the course of follow-up occurred almost entirely in patients with total involvement of the colon, but the majority of these patients had only rectal involvement at the time of the first attack

(Table XX). The only factor we have found to affect the prognosis equally in the first attack and during subsequent years is the age at the onset of symptoms. It can therefore be seen that the outcome of this disease subsequent to the first attack is unpredictable on the basis of the severity and extent of disease in the first attack and that this unpredictability is produced by the group of patients in whom the extent of disease either regresses, or, more commonly, progresses with the passage of time (Palmer, 1948; Sloan *et al.*, 1950; Kirsner, Palmer, and Klotz, 1951; Bockus, Roth, Buchman, Kalser, Staub, Finkelstein, and Valdes-Dapena, 1956; Banks *et al.*, 1957; Texter, 1957).

CLINICAL STATE OF THE SURVIVORS AT REVIEW One of the most remarkable findings in this survey was that, at the time of review, no fewer than 98% of the 185 medical and surgical survivors were in good or excellent health (Fig. 4). There was a much greater proportion (76.6%) of the 47 surgical survivors enjoying excellent health than in the medical group (42.8%) of the 138 survivors. As already explained the invalidism in the medical group would have been a little greater if the outcome of an attack had not been awaited on 12 occasions before review. In addition, it has been our policy not to persist with medical treatment for long periods in the face of chronic disabling symptoms, and no less than 52% of the medical survivors were receiving some form of therapeutic or maintenance treatment when reviewed.

Nevertheless, these findings illustrate that, with modern forms of medical and surgical treatment, it is possible in most cases to keep a patient in reasonable health between attacks of colitis.

In conclusion it can be said that modern methods of treatment in ulcerative colitis have transformed the outlook for patients suffering with this disease. The risks to life have been shown to be not very great unless there is total or near total involvement of the colon, or the patient is aged over 60 years at the time of onset of symptoms. The results reported here are those pertaining to the first few years of the disease, these patients not having yet reached the duration of symptoms when malignant change affects the prognosis.

SUMMARY

This paper presents the results of a survey into the course and results of treatment of 204 patients with ulcerative colitis who presented at the time of their first attack to hospital or to a combined medico-surgical colitis clinic between 1952 and 1963. A complete follow-up has been obtained and a com-

prehensive analysis is presented of the factors influencing the prognosis in this disease. Details are provided, both of the morbidity and mortality due to colitis in medically treated patients, and of the early and late results of the patients in this group who required radical surgical treatment.

We wish to express our gratitude to Dr. Felicity Edwards and Dr. S. C. Truelove for their assistance with the planning of this follow-up study, to Mrs. Joan King for secretarial assistance, and to Miss Elaine Smith for assistance in tracing every one of our patients; and to numerous medical practitioners who supplied details and case histories of those of our patients who subsequently came under their care.

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