Ulcerative colitis: one disease or two? (Quantitative histological differences between distal and extensive disease)

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Abstract

Cell counts and measurements of mucosal architecture were made on rectal biopsies from nine patients with total colitis, eight with left sided colitis, 15 with distal colitis, and 11 with proctitis. The mean total lamina propria cell count in proctitis and distal colitis approached twice that of extensive left sided and total colitis ($p < 0.001$) and in distal proctocolitis the cell numbers are further increased in the chronic over the acute phase. This difference was not explained by age, duration, activity, or treatment. The predominantly increased lymphoid and mononuclear cell infiltrate in distal proctocolitis indicates a different pattern of immune response, suggesting a separate process from extensive colitis or a more intense reaction resulting in localisation of disease.

Ulcerative colitis may involve varying lengths of large bowel extending from the rectum. The term idiopathic, or non-specific, proctitis is applied to patients with inflamed rectal mucosa which has an upper limit in the rectum.¹ Similar changes extending into the sigmoid colon are termed proctosigmoiditis or distal proctocolitis.^{2,3} Although a proportion of cases with distal disease on barium enema will have more extensive disease on colonoscopy and biopsy,^{4,5} and it is still unclear whether the general view that all are manifestations of one disease is correct.¹⁻⁹ The gross and microscopic appearances and the medical treatment of localised and extensive colitis are similar^{1,3,6,9} although a small group of cases of 'follicular proctitis' with prominent lymphoid follicles,¹⁰ and a group of young children with allergic proctitis characterised by large numbers of eosinophils¹¹ have been proposed as distinct diseases. Suggestions of an IgE mediated basis for other cases of proctitis have not been confirmed.^{12,13}

Although limited extension of proctitis or distal colitis has been reported in 4-45% of cases, only 10-15% extend to the proximal colon.^{3,4,6-9} There is also only a very low risk of malignancy or systemic complications developing in distal colitis.^{3,9} It is therefore entirely possible that those patients with disease which remains localised are a separate group with a different pathogenesis.

We have previously shown the ability of histological measurements of cell populations and mucosal architecture to identify otherwise undetectable minor changes of inflammatory bowel disease, and to distinguish inflammatory bowel disease from infective colitis.^{14,15} Quantita-

tive histological rectal mucosal biopsy changes in carefully matched groups of patients with proctitis and distal colitis were therefore compared with the changes in extensive ulcerative colitis.

Methods

SUBJECTS

The disease group of 43 patients were all primary referrals to one district general hospital with sigmoidoscopic and biopsy appearances typical of active ulcerative proctocolitis. In none was there evidence of Crohn's disease. All cases were characterised clinically as acutely active, either at onset or exacerbation, or as chronic but still active at the time of the biopsy. Acutely active cases were defined as those with recent (within 12 weeks) onset of diarrhoea either at first onset of disease or during an exacerbation, with endoscopic evidence of inflammation. Chronic activity was defined as symptoms persisting more than 12 weeks, and all had endoscopic abnormality of the mucosa. Patients in complete clinical and endoscopic remission were excluded. The patients were initially divided into four groups on the basis of extent of disease defined by either double contrast barium enema and sigmoidoscopy or by colonoscopy performed at or about the same time as the rectal biopsy examined. Rectal biopsies were taken during the course of routine management.

TOTAL COLITIS

Nine patients, seven men, five acute, with continuous disease extending into the right side of the colon, mostly to the caecum. The median age was 43 years (range 16-70), median duration of the current active state - that is, since first onset or ending of the last remission) was two months (range three weeks to eight years), and median total follow up was 11 years (range three to 35). Four were taking sulphasalazine and none were on steroids.

LEFT SIDED COLITIS

Eight patients, three men, three acute, with continuous disease extending into the descending colon, but not higher than the mid transverse colon. Median age was 35 years (range 19-74), duration one month (range one week to one year), and total follow up nine years (range 3-5-15). Four were taking sulphasalazine and three were also on steroids.

DISTAL COLITIS

Fifteen patients, seven men, six acute, with

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continuous disease extending into the sigmoid colon but not into the descending colon. Median age was 35 years (range 19–55), duration seven months (range two weeks to two years), and total follow up nine years (range 3·5–14·5). None of these patients was known to have progressed to more extensive disease during this time as judged by repeat double contrast barium enema or colonoscopy. Six were taking sulphasalazine and three were also on steroids.

PROCTITIS

Eleven patients, four men, four acute, with continuous disease confined to the rectum. Mean extent was 8·5 cm and the maximum 15 cm. Median age was 34 years (range 24–75), duration four months (range eight weeks to 2·5 years), and total follow up 12 years (range eight to 20). Only one patient was known to have progressed to left sided colitis on repeat colonoscopy and this patient's biopsy was used only as a test case. Six patients were taking sulphasalazine and three were also on steroids.

The control group comprised 23 patients, nine men, median age 38 years (range 20–73) who had no evidence of organic gastrointestinal disease and were considered to have irritable bowel syndrome.

PROCEDURE

Rectal biopsies were immediately fixed in formalin. Well oriented biopsies of adequate size were cut at 1µ thickness perpendicular to the mucosal surface, and sections were stained with haematoxylin and eosin for counts of polymorphs and total cellularity and for architectural measurements. IgA, IgM, and IgG plasma cells were shown using a peroxidase-antiperoxidase technique. Measurements were carried out using a MOPPET image analyser. The method has

been described previously;¹⁴ the variables are shown in Table I.

STATISTICAL ANALYSIS

Variables were transformed where necessary to normalise the distribution. The Mann-Whitney U test was used to compare age and duration of disease, and χ^2 numbers on drug treatment, with colonoscopy and with acute and chronic disease in each group.

All other analyses were carried out using the BMDP computer package (University of California) on the Amdahl computer at the University College, London, Computer Centre. A one-way analysis of variance (ANOVA) was carried out across the four groups using the program BMDP7D, which also performs pairwise Student's *t* tests. When multiple groups were compared, the appropriate Bonferroni significance values were used to compensate for the number of groups, to reduce the probability of detecting spurious differences. Groups were only regarded as not showing significant differences, however, when the nominal probability of each significance test was greater than 0·05.¹⁶ Student's *t* tests were also used in the program BMDP3D to compare the means for each variable in the combined groups, and to examine the effects of drug treatment within each group.

Stepwise discriminant analysis was carried out using the program BMDP7M with a 'jack knife' procedure to reduce any bias resulting from classifying a data set with a discriminant function produced from the same set.

Results

There were no significant differences between the four groups for age, duration of disease, number of patients receiving drug treatment, investigated by colonoscopy, or degree of disease activity. Variables for which the one way ANOVA was significant (*p*<0·05) are shown in Table II, with the Bonferroni significance values for the *t* tests made between each pair of groups. There were no significant differences between biopsies from patients with total colitis and those with left sided colitis for any of the variables. Similarly there were no significant differences between distal colitis and proctitis. The other four pairs of comparisons showed two to five significant differences each. Five of the six differing variables were lamina propria cell counts, reflecting total cellularity (CELLEN), cell density (CARE), and cell densities at differ-

TABLE I Variables measured or computed and used in the analyses

IGM	Plasma cells/mm mucosal length
IGG	Plasma cells/mm mucosal length
IGA	Plasma cells/mm mucosal length
SIE	Surface intraepithelial polymorphs/mm mucosal length
CIE	Crypt intraepithelial polymorphs/10 crypts
CLUM	Crypt lumen polymorphs/10 crypt lumens
LPP	Lamina propria polymorphs/mm mucosal length
CELLEN	Total lamina propria cells/mm mucosal length
CARE	Total lamina propria cells/mm ² mucosa
HCDENS1,2,3	Total cell densities in superficial, middle and basal bands of lamina propria respectively
HCDRAT	Ratio of total cell density in superficial horizontal band of lamina propria to that in basal band
SLR	Measured surface length: smoothed surface length
MLA	Lamina propria area/mm mucosal length
CAMM	Total crypt area/mm mucosal length
CRYPTS	Number of crypts/mm surface length
CRYPTEQV	Number of crypt profiles/mm mucosal length, weighted by length
CRYVOLI	Percentage of a line, superimposed on the mucosa one-third down from the surface, occupied by crypt
CRYVOL2	Percentage of a line, superimposed on the mucosa two-thirds down from the surface, occupied by crypt
CRYVOLT	Percentage of whole mucosa occupied by crypt
MHMEAN	Mean of mucosal height measurements
CLMEAN	Mean of crypt length measurements
CDMEAN	Mean of mucosal diameter measurements
SEWMEAN	Mean of surface epithelial width measurements
CEWMEAN	Mean of crypt epithelial width measurements
ICDMEAN	Mean of intercrypt distance measurements
MHCOEFF	SDMH/MHMEAN
CLCOEFF	SDCL/CLMEAN
CDCOEFF	SDCD/CDMEAN
SEWCOEFF	SDSEW/SEWMEAN
CEWCOEFF	SDCEW/CEWMEAN
ICDCOEFF	SDICD/ICDMEAN
MUCLRAT	MHMEAN/CLMEAN
SCHEWRAT	SEWMEAN/CEWMEAN

SD=Standard deviation.

TABLE II Comparison of means for variables showing significant differences by Analysis of Variance (ANOVA)

Variable	ANOVA	Student's <i>t</i> *			
		Total colitis v: Dist col	Proct	Left-sided colitis v: Dist Col	Proct
CELLEN	<0·001	<0·001	<0·005	<0·05	NS
CARE	<0·001	NS	<0·005	<0·05	<0·005
HCDENS1	<0·001	NS	<0·005	NS	<0·005
HCDENS2	<0·005	NS	<0·05	<0·05	<0·005
HCDENS3	<0·01	NS	<0·05	NS	NS
MLA	<0·005	<0·005	NS	NS	NS

*Bonferroni significance levels; dist col=distal proctocolitis; proct=proctitis.

TABLE III Extensive and distal colitis and controls: (Derived) means and 95% confidence limits for all variables

Sample size	Controls 23		Extensive colitis 17		Distal colitis 25		EC v DC p
	Mean	95% CL	Mean	95% CL	Mean	95% CL	
IGM	78	62-98	181†	85-387	245‡	166-360	0.024
IGG	34	24-51	336‡	226-500	455‡	317-653	
IGA	250	219-286	593‡	431-816	889‡	721-1096	
SIE	4	3-6	5	2-11	6	4-10	
CIE	1	0-2	18‡	8-41	46‡	24-88	
CLUM	0	0-0	1*	0-2	4‡	1-8	<0.001
LPP	11	8-14	123‡	73-208	202‡	135-304	
CELLEN	1368	1255-1490	2710‡	2195-3347	4898‡	4327-5544	
CARE	5902	5140-6778	8185‡	7382-9074	11350‡	10310-12480	
HCDENS1	7727	6695-8915	7568	6694-8557	10910‡	9736-12240	
HCDENS2	5370	4587-6287	8531‡	7658-9504	11430‡	10290-12690	<0.001
HCDENS3	4198	3656-4820	8375‡	7482-9376	11300‡	10080-12670	
HCDRAT	1.87	1.73-2.01	0.92‡	0.82-1.03	1.00‡	0.98-1.12	
SLR	1.05	1.04-1.06	1.17‡	1.09-1.24	1.09‡	1.07-1.12	
MLA	0.236	0.211-0.261	0.331‡	0.291-0.371	0.447‡	0.399-0.495	<0.001
CAMM	0.213	0.186-0.241	0.230	0.183-0.277	0.244	0.192-0.296	
CRYPTS	6.6	5.8-7.5	4.2‡	3.5-5.1	3.8‡	3.2-4.4	
CRYPTEQV	10.3	9.1-11.6	7.6‡	6.4-8.9	7.4‡	6.4-8.5	
CRYVOL1	49	44-54	42	37-47	40‡	36-45	0.014
CRYVOL2	61	57-65	49‡	42-56	36‡	28-44	
CRYVOLT	47	44-51	40*	35-46	34‡	31-38	
MHMEAN	398	369-427	526‡	458-594	598‡	524-657	
CLMEAN	356	333-378	452‡	389-515	458‡	400-516	
CDMEAN	77	71-84	96‡	86-106	91*	81-100	0.039
SEWMEAN	38	35-41	27‡	21-32	20‡	17-24	
CEWMEAN	24	22-25	26	23-29	23	21-25	
ICDMEAN	32	28-38	53‡	45-63	63‡	53-75	
MHCOEFF	0.10	0.09-0.12	0.11	0.10-0.13	0.10	0.07-0.12	
CLCOEFF	0.12	0.10-0.14	0.16*	0.12-0.19	0.14	0.12-0.17	0.027
CDCOEFF	0.15	0.13-0.17	0.28‡	0.21-0.35	0.29‡	0.22-0.36	
SEWCOEFF	0.18	0.15-0.20	0.24*	0.19-0.30	0.27‡	0.24-0.30	
CEWCOEFF	0.22	0.20-0.24	0.31‡	0.27-0.35	0.31‡	0.27-0.36	
ICDCOEFF	0.87	0.76-0.98	0.91	0.83-0.99	0.95	0.85-1.05	
MUCLRAT	1.12	1.09-1.14	1.17	1.10-1.24	1.32‡	1.22-1.42	0.027
SCEWRAT	1.63	1.49-1.78	1.07‡	0.88-1.26	0.90‡	0.77-1.02	

p values for significance of difference of means from control group: * <0.05; † <0.01; ‡ <0.001.

ent levels in the lamina propria (HCDENS1,2,3) and the other (MLA) measures lamina propria volume and thus affects cell density. The consistent difference in cellularity indicated that the four groups could be combined into two: extensive ulcerative colitis which comprised patients

with total and left sided colitis, and distal proctocolitis which included proctitis and distal colitis. The variables for these groups are compared in Table III. There were no significant differences in age, duration, activity, or drug treatment between the two combined groups. None of the variables which differed significantly between the two groups were significantly affected by treatment.

Comparison of the acute and chronic phases of extensive ulcerative colitis and distal proctocolitis is shown in Table IV. In extensive disease (Table IVa) the measures of total cellularity (CELLEN, CARE, HCDENS1,2,3) remained similar between the acute and chronic phases, but there was a very significant one third decrease in the number of crypts (CRYPTS). Crypt length (CLMEAN), total crypt area (CAMM), and mucosal height (MHMEAN) were also reduced. Surface epithelial cell height (SEWMEAN) increased to normal in the chronic phase in many cases. In distal disease (Table IVb) the most significant differences between acute and chronic cases were increased cell densities at all levels in the lamina propria (CARE, HCDENS1,2,3), although the only specifically measured cell population to increase significantly was IgG plasma cells. There was a reduction in crypt numbers (CRYPTS) in the chronic phase similar to that in extensive disease and there was a significant increase in variability of crypt length (CLCOEFF) and crypt diameter (CDCOEFF). When the acute phases of each were compared (Table V), in distal disease the total lamina propria cellularity (CELLEN) and mucosal volume (MLA) were increased compared to extensive disease, but measures of cell density were not significantly different. In the

TABLE IVa Acute and chronic extensive colitis: (derived) means and 95% confidence limits

Sample size	Acute extensive colitis 8		Chronic extensive colitis 9		t test: p
	Mean	95% CL	Mean	95% CL	
IGM	274‡	155-485	125	45-347	0.015
IGG	386‡	282-530	296‡	133-657	
IGA	724‡	537-977	496*	273-901	
SIE	6	1-19	5	1-14	
CIE	15‡	3-63	22‡	6-72	
CLUM	1	0-3	1	0-4	0.001
LPP	135‡	44-407	114‡	62-211	
CELLEN	3083‡	2244-4229	2410‡	1711-3394	
CARE	8414‡	6907-10250	7998*	6944-9212	
HCDENS1	7261	5665-9307	7870	6923-9212	0.007
HCDENS2	9099‡	7597-10900	8072‡	6893-9450	
HCDENS3	8831‡	7127-10940	8017‡	6885-9335	
HCDRAT	0.84‡	0.69-1.00	1.00‡	0.84-1.15	
SLR	1.18	1.04-1.32	1.15	1.04-1.27	
MLA	0.356‡	0.312-0.400	0.309	0.233-0.385	0.022
CAMM	0.285*	0.204-0.366	0.182	0.135-0.229	
CRYPTS	4.7*	3.6-5.8	3.9‡	2.6-5.3	
CRYPTEQV	9.4	7.6-11.2	6.0‡	5.0-7.1	
CRYVOL1	43	37-50	41	32-49	
CRYVOL2	52*	41-63	47‡	35-58	0.002
CRYVOLT	43	34-52	38‡	31-46	
MHMEAN	611‡	554-668	451	348-554	
CLMEAN	539‡	451-626	375	313-437	
CDMEAN	87	73-100	104‡	88-121	
SEWMEAN	21‡	15-28	32	24-41	0.022
CEWMEAN	23	20-26	28*	23-33	
ICDMEAN	46*	36-60	60‡	48-76	
MHCOEFF	0.10	0.07-0.14	0.13	0.10-0.15	
CLCOEFF	0.13	0.08-0.19	0.18‡	0.13-0.22	
CDCOEFF	0.27	0.13-0.40	0.29‡	0.20-0.37	0.022
SEWCOEFF	0.26‡	0.19-0.34	0.23	0.13-0.33	
CEWCOEFF	0.29‡	0.22-0.35	0.33‡	0.26-0.39	
ICDCOEFF	0.89	0.80-0.99	0.93	0.78-1.07	
MUCLRAT	1.15	1.04-1.26	1.19	1.07-1.31	
SCEWRAT	1.94‡	0.64-1.24	1.18‡	0.90-1.46	

p values for significance of difference of means from control group: * <0.05; † <0.01; ‡ <0.001.

TABLE IVb Acute and chronic distal colitis: (derived) means and 95% confidence limits

Sample size	Acute distal colitis		Chronic distal colitis		t test: p
	Mean	95% CL	Mean	95% CL	
Variable					
IGM	329‡	202-537	205‡	116-362	0.005
IGG	250‡	133-471	652‡	443-958	
IGA	989‡	761-1 283	836‡	609-1147	
SIE	9*	4-18	5	3-9	
CIE	43‡	14-129	48‡	19-119	0.001
CLUM	3*	1-7	4*	1-14	
LPP	237‡	114-491	186‡	106-322	
CELLEN	4 539‡	3 651-5 644	5 117‡	4 326-6 050	
CARE	9 462‡	8 213-10 900	12 560‡	11 320-13 930	0.001
HCDENS1	9 290	7 678-11 240	11 970‡	10 420-13 740	0.022
HCDENS2	9 354‡	8 164-10 720	12 790‡	11 420-14 330	0.001
HCDENS3	9 484‡	7 711-11 660	12 500‡	11 000-14 220	0.012
HCDRAT	1.02‡	0.81-1.22	1.00‡	0.84-1.15	0.049
SLR	1.08*	10.5-1.11	1.10*	1.06-1.14	
MLA	0.490‡	0.414-0.566	0.423‡	0.357-0.489	
CAMM	0.271*	0.207-0.335	0.229	0.152-0.306	
CRYPTS	4.6‡	3.4-6.0	3.4‡	2.8-4.1	0.049
CRYPTEQV	9.2	7.4-11.0	6.5‡	5.2-7.8	
CRYVOL1	41	32-50	40*	34-46	
CRYVOL2	43*	27-58	32‡	22-43	
CRYVOLT	36‡	29-42	34‡	28-39	0.043
MHMEAN	603‡	546-659	582‡	478-686	
CLMEAN	502‡	430-575	432	348-517	
CDMEAN	79	68-90	97‡	85-110	
SEWMEAN	20‡	15-26	20‡	16-26	0.049
CEWMEAN	23	20-26	24	21-26	
ICDMEAN	51‡	38-70	72‡	58-88	
MHCOEFF	0.07*	0.04-0.11	0.11	0.08-0.14	
CLCOEFF	0.09*	0.07-0.10	0.17‡	0.14-0.21	<0.001
CDCOEFF	0.21	0.14-0.27	0.34‡	0.24-0.43	
SEWCOEFF	0.30‡	0.25-0.36	0.25‡	0.21-0.29	
CEWCOEFF	0.32*	0.22-0.41	0.31‡	0.26-0.36	
ICDCOEFF	0.97	0.73-1.21	0.94	0.82-1.06	0.047
MUCLRAT	1.22	1.07-1.37	1.38‡	1.24-1.51	
SCEWRAT	0.92‡	0.73-1.11	0.88‡	0.70-1.07	

p values for significance of difference of means from control group: *<0.05; ‡<0.01; †<0.001.

chronic phase there were highly significant increases in cell density at all levels (CARE, HCDENS1,2,3) as well as total cellularity (CELLEN) in distal proctocolitis compared with extensive ulcerative colitis.

Discriminant analysis and jack knife testing achieved 93% separation of distal proctocolitis from extensive ulcerative colitis, using four variables which measured cell density and distribution of cells in the lamina propria, and mucosal volume: CELLEN, HCDRAT, MLA, and HCDENS3. Overall lamina propria cell density (CARE) and a measure of surface irregularity (SLR) could be substituted for the measures of cell density in the basal third of the lamina propria (HCDENS3) and of mucosal volume (MLA) respectively with 88% discrimination. For the acute cases only complete discrimination was achieved using mucosal volume (MLA), IgG plasma cell count (IGG), and numbers of crypt profiles (CRYPTEQV), while for the chronic cases only, cell density in the lamina propria (CARE) and mucosal volume (MLA), gave 92% discrimination.

Discussion

The results suggest that it is not correct to regard all ulcerative colitis as an identical process differing only in extent. It appears appropriate to group proctitis and distal colitis as 'distal proctocolitis', and to distinguish this from 'extensive ulcerative colitis'. The mean total lamina propria cellularity, measured per millimetre of mucosal length, in distal proctocolitis approaches twice that of extensive colitis. This highly significant increase cannot be explained by differences in age, duration, activity, or drug

usage, and the difference is still present when only untreated cases are compared.

In acute distal proctocolitis there is excess total cellularity with a high lamina propria volume, and cell density is not increased. In the chronic active cases the cell density and total cell numbers are increased compared with the acute cases. This contrasts with the chronic, but still active, phase of extensive colitis. The surface epithelial height parallels the inflammatory infiltrate and is reduced in both groups in the acute phase; in the chronic phase it returns to normal in extensive disease but remains low in distal proctocolitis. Very little of the difference in cellularity can be explained by any changes in the measured specific cell populations. The only significant difference was in IgG plasma cells in chronic disease. Eosinophils and IgE plasma cells were not counted in this study, but none of the cases showed the heavy eosinophilia described for allergic proctitis in children under two years old,¹¹ and in a previous study no difference was found in IgE plasma cell counts between proctitis and other ulcerative colitis.¹³ It therefore appears that the major difference is in the number of lymphocytes, histiocytes, or other mononuclear cells in the lamina propria.

Further studies are needed to establish whether the increased lamina propria cell infiltration found in distal proctocolitis represents a quantitative or a qualitative difference from more widespread colitis. The similarity of the crypt damage suggests that the two might be related diseases, differing in intensity or pattern of immune response. The failure of conventional histology to detect the differences in cell populations is not surprising as subjective judgment of cellularity is not highly reproducible.¹⁷

The differences identified do not conflict with the observation that there is variation in extent of ulcerative colitis with time. Most of the variation in extent is confined to the distal colon and rectum, with the cumulative probability of extension of proctitis to the sigmoid colon at 20 years approximately 29% (SD of 6%) using a combination of rigid sigmoidoscopy and barium enema.⁷ Colonoscopic study has suggested that the rate of this extension may be up to 45%.⁴ The rate of extension of localised proctosigmoiditis to involve the proximal colon is much lower, about 10-15% in the same studies. Extensive ulcerative colitis also appears to vary in extent at different times.⁴ The cases studied here were assessed by both colonoscopy and double contrast barium enema, but there is no evidence of any systematic bias which could have affected the demonstration of a relationship between quantitative histological changes and extent.

The variation in extent could be accounted for by the existence of two disease processes, distal proctocolitis variably involving the rectum and sigmoid with time, and more extensive ulcerative colitis which could sometimes present as a proctitis and may also regress to involve only the rectum during remission. The low rate of progression of distal proctocolitis to extensive disease and the finding that over 90% of distal proctocolitis can be identified as a histological entity by discriminant analysis support this. The correct prediction of subsequent progression of

TABLE V Extensive colitis v distal colitis: variables for which the difference of means is significant

Variable	p values for t tests between:	
	Acute cases	Chronic cases
IGG	NS	0.034
CELLEN	0.026	<0.001
CARE	NS	<0.001
HCDENS1	NS	<0.001
HCDENS2	NS	<0.001
HCDENS3	NS	<0.001
MLA	0.003	0.026
SEWMEAN	NS	0.009

one patient in this study, who presented with rectal disease, to extensive ulcerative colitis provides some support for this hypothesis. It may be possible to quantitatively predict those cases of distal proctocolitis at risk of progression to extensive disease.

Other differences support a two disease hypothesis. The difficulty of inducing complete remission is consistent with the finding that cell counts increase with transition of distal proctocolitis to a chronic phase.^{18,19} The similar duration of disease before presentation and similar age at presentation for patients with limited disease and those with total colitis, suggests that these, in general, are not sequential processes.²⁰ In proctitis the risk of systemic complications is low and associated with progression and few patients require surgery.^{1,8,9} Many patients may not have recurrent disease after a single attack, even with long follow up.¹ There is also a low risk of developing carcinoma compared with extensive ulcerative colitis.^{3,8}

Recognition of two different patterns in pathological process related to extent of disease may resolve some of the confusion and uncertainty, clinical and scientific, over inflammatory bowel disease.

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