Observer variability in the histopathological reporting of abnormal rectal biopsy specimens

A M Lessells, J Swanson Beck, R A Burnett, S R Howatson, F D Lee, K M McLaren, S M Moss, A J Robertson, J G Simpson, G D Smith, H B Tavadia, F Walker

Abstract

Aims—To study the consistency of reporting of abnormal rectal biopsy specimens, especially in the differentiation of inflammatory bowel disease from other causes of abnormality.

Methods—Sixty rectal biopsy specimens were identified from patients presenting with bloody diarrhoea. These were then circulated to the 11 consultant pathologists in the study who filled in a proforma with a list of 12 diagnostic categories and 22 features.

Results—Forty one of the 60 cases were examples of inflammatory bowel disease. In 33 of these cases nine or more pathologists had made the diagnosis. Further categorisation into ulcerative colitis and Crohn's disease showed better recognition of ulcerative colitis. In the 19 cases of non-inflammatory bowel disease recognition of pseudomembranous colitis and solitary rectal ulcer syndrome was good, but the results were poorer in the case of infective colitis.

Conclusion—The findings suggest that a group of consultant pathologists can differentiate between inflammatory bowel disease and other causes of an abnormal rectal biopsy specimen and can also recognise pseudomembranous colitis and solitary rectal ulcer syndrome satisfactorily.

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In 1985 the Scottish Panel for the Investigation of Consistency of Histopathological Reporting was formed under the chairmanship of Professor Beck. The remit of this group is to look at the robustness of diagnostic terminology as applied in routine histopathology reporting. Many of the terms commonly used by pathologists are applied purely by convention—dividing tumours into well, moderate, and poorly differentiated categories. Until recently, however, there have been relatively few scientific studies which assess whether a group of pathologists can apply such terms consistently. This panel has already carried out several studies in this field, including biopsy specimens of the cervix and bladder.^{1,2} Although the results of the bladder study tended to support the continuation of currently used terminology, the study of cervical biopsy specimen produced findings in favour of a change of cervical intra-

epithelial neoplasia (CIN) grading to high or low grade rather than the present three categories.

We decided to study the consistency of diagnosis of abnormal rectal biopsy specimens concentrating on inflammatory bowel disease. A diagnosis of inflammatory bowel disease may mean long term treatment and follow up by a gastrointestinal unit, so this was felt to be a clinically important area to assess.

Method

The panel consists of 11 consultant pathologists who we regard as a representative cross section of Scottish histopathology practice. All members had undertaken undergraduate or postgraduate training in Scotland, although not exclusively. The members comprise six National Health Service staff and five University staff.

Six pathologists from different centres were each asked to identify 10 examples of abnormal rectal biopsy specimens from patients presenting with bloody diarrhoea. The intention was that this should be the first biopsy specimen, taken at a time when the patient was not receiving treatment. It was the intention that there would be a definite diagnosis established either on the basis of the slide submitted or at a later date when further clinical, radiological, or pathological material was available. The biopsy specimens were probably a fairly representative sample of abnormal rectal specimens. Some of the diagnostic differences encountered undoubtedly related to poor quality, poor orientation, etc, which are common problems. The cases selected were not chosen as good, well orientated, classic examples of the entities. The slides were then sent to the central co-ordinator who gave each case a code number.

A draft proforma was produced which was then tested by circulation of some of the slides among all members of the group. Following the circulation, the final form consisted of two sections—a list of 12 possible diagnostic categories (fig 1), five of which related to inflammatory bowel disease, and a list of 22 histological features. In the second section of the form (fig 2) all 22 features had to be assessed on the basis that they were: (1) present and worthy of comment; or (2) not present or not worthy of comment.

For the circulation of the first batch of 30 slides (in sets of five), a second column sought identification of those features which

Department of Pathology, Western General Hospital, Crewe Road, Edinburgh EH4 2XU Scotland

A M Lessells
J Swanson Beck
R A Burnett
S R Howatson
F D Lee
K M McLaren
S M Moss
A J Robertson
J G Simpson
G D Smith
H B Tavadia
F Walker

Correspondence to:
Dr A M Lessells

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(1)	Normal
(2)	Minor changes
(3)	Non-specific proctitis
(4)	IBD (NOS)
(5)	IBD (UC favoured—active)
(6)	IBD (UC favoured—chronic quiescent)
(7)	IBD (Crohn's disease favoured)
(8)	Definite Crohn's disease
(9)	Pseudomembranous colitis
(10)	Infective colitis
(11)	Ischaemic colitis
(12)	Other (specify) _____

IBD= inflammatory bowel disease; UC= ulcerative colitis.

For diagnostic features below:		
	1 = Present and worthy of comment 2 = Not present and not worthy of comment (all boxes to be completed)	5 = Contributing to diagnosis (only selected boxes to be completed)
LUMEN: Pus	☐	☐
Pseudo-membrane	☐	☐
MUCOSAL CRYPTS:		
Normal architecture	☐	☐
Crypt irregularity (branching/atrophy/dilatation segmental destruction)	☐	☐
Crypt atrophy	☐	☐
Cryptitis	☐	☐
Crypt abscess	☐	☐
LAMINA PROPRIA:		
Normal	☐	☐
Neutrophils present	☐	☐
Increase in chronic inflammatory cells? (lymphocytes/plasma cells/eosinophils)	☐	☐
If present—(1) generalised or (2) focal	☐	☐
?Increase in lymphoid aggregates	☐	☐
Granuloma	☐	☐
Pericryptal aggregate of epithelioid histiocytes	☐	☐
Fibrosis	☐	☐
Muscle fibres	☐	☐
Oedema	☐	☐
Giant cell(s) without granuloma	☐	☐
Haemorrhage	☐	☐
Thrombosis	☐	☐
Thickened subepithelial collagen	☐	☐
SUBMUCOSA:		
Chronic inflammatory reaction	☐	☐
Granuloma	☐	☐
PATHOLOGIST CODE:	☐	

Figure 2 Assessment of all 22 features

Table 1 Final diagnosis in 19 cases of non-IBD

Pseudomembranous colitis	5
Infective colitis	5
Solitary rectal ulcer syndrome	4
Ischaemic colitis	1
Collagenous colitis	1
Graft versus host disease	1
Intestinal spirochaetosis	1
Radiation changes	1

Table 2 IBD score in 41 cases of inflammatory bowel disease

IBD score	No of cases
11	20
10	9
9	4
8	4 (3 CD)
7	1 (1 CD)
6	1
5	1 (1 CD)
3	1 (1 CD)

Table 3 IBD score in 19 cases of non-IBD

IBD score	No of cases
0	3
1	4
2	4
3	3 (1 infective)
5	4 (3 infective)
9	1 (infective)

the pathologist thought contributed to the diagnoses. The second column was deleted from the form used for the second set of 30 slides. One of the members of the panel (FDL) provided a helpful guide outlining the diagnostic features likely to be present in each of the diagnostic groups. It was up to each individual to make use of this guide as appropriate. This guide was not intended to be prescriptive, and it was not part of the study to assess its use by the individual pathologists.

A discriminant analysis was carried out using the SPSS computer program, to examine the combinations of histological features which best identified the diagnostic categories ulcerative colitis, Crohn's disease, and other non-inflammatory bowel disease diagnoses. All the diagnostic features included on the form (fig 1) were included in the analysis with the exception of lumen: pseudomembrane, giant cells without granuloma, and the last four on the form, which were mentioned infrequently. Variables were entered or removed using a stepwise method which selected the variable that maximises the smallest F ratio between pairs of groups. The discriminant functions were calculated using data from the first circulation and the eventual diagnosis of these cases, and then used to classify the cases in the second circulation.

Results

The 60 rectal biopsy specimens included 41 cases of inflammatory bowel disease (IBD): 23 ulcerative colitis; 17 Crohn's disease; and one inflammatory bowel disease (not otherwise specified). The other 19 cases consisted of a wide variety of conditions associated with an abnormal rectal biopsy specimen (table 1). An IBD score was calculated, which was taken as the number of individuals who had placed cases in categories 4–8. In 33 (80%) of the 41 cases of inflammatory bowel disease an IBD score of 9–11 was obtained (table 2). In 39 out of the 41 (95%) cases a majority favoured a diagnosis of inflammatory bowel disease. Of the eight cases with a score of eight or less, the eventual diagnosis in six was Crohn's disease.

Further analysis of the cases of ulcerative colitis and Crohn's disease was performed by dividing the IBD category into three groups— inflammatory bowel disease (NOS) or category 4, ulcerative colitis (category 5 and 6), and Crohn's disease (category 7 and 8). This showed that in 17 (74%) of 23 cases of ulcerative colitis there was a score of five or more in favour of that diagnosis and that the score for ulcerative colitis was greater than that for Crohn's disease in 22 (96%) of the 23 cases. In the case of Crohn's disease a similar analysis showed that only 10 (59%) out of 17 had a score of 5 or more for Crohn's disease and in 12 out of 17 (76%) the score for Crohn's disease was greater than that for ulcerative colitis.

Analysis of the non-IBD group (table 3) showed in only one case a majority in favour of a diagnosis of inflammatory bowel disease.

Table 4 Diagnostic categories in 14 cases of non-IBD

	1-3	4-8	9	10	11	12
Pseudomembranous colitis (9)		2	3	3	3	
		2	9			
		1	9	1		
		3	8			
			9	1		1
Infective (10)	2	7		2		
	4	1		4		
	2	5		4		2
	1	5		5		
	2	3		6		
	1	1				9
Solitary rectal ulcer syndrome (12)	1	1				9
		2				9
	2					9

Table 5 Feature recognition by all 11 pathologists in ulcerative colitis (23 cases) and Crohn's disease (17 cases)

Feature	Ulcerative colitis	Crohn's disease
Increased chronic inflammatory cells	76	72
Increased neutrophils	63	55
Cryptitis	64	52
Crypt irregularity	73	50
Mucin depletion	67	29
Crypt abscess	41	19
Luminal pus	40	25
Normal anatomy	6	23
Pericryptal aggregate	15	57
Granuloma	2	37

Table 6 Comparison of majority diagnosis with eventual diagnosis

Majority	Eventual diagnosis						
	IBD (NOS)	Ulcerative colitis	Crohn's disease	PSMC	Infective	ISCH	Other
2	0	0	1	0	0	0	1
4	1	4	2	0	1	0	0
5 + 6	0	19	2	0	0	0	1
7 + 8	0	0	11	0	0	0	0
9	0	0	0	4	0	0	0
10	0	0	0	1	4	0	0
11	0	0	0	0	0	1	0
12	0	0	1	0	0	0	6
Total	1	23	17	5	5	1	8

Table 7 Comparison of final diagnosis of all pathologists with eventual diagnosis

Final opinion	Eventual diagnosis						
	IBD (NOS)	Ulcerative colitis	Crohn's disease	PSMC	Infective	ISCH	Other
1	0	0	1	0	0	2	2
2	0	3	9	0	2	2	6
3	0	6	11	0	9	0	4
4	4	54	33	0	14	0	0
5 + 6	2	144	30	6	5	5	9
7 + 8	4	36	93	2	2	0	0
9	0	2	1	38	0	0	0
10	0	5	3	5	21	0	1
11	0	3	1	3	0	13	4
12	1	0	5	1	2	0	51
Total	11	253	187	55	55	22	77

Table 8 Range of diagnostic categories used by 11 pathologists

Final opinion								
Reader	Minor changes	IBD (NOS)	Ulcerative colitis	Crohn's disease	PSMC	Infective	ISCH	Other
1	5	17	10	10	5	6	3	4
2	1	15	21	6	5	4	1	7
3	12	3	14	16	4	1	5	5
4	0	11	19	16	3	2	1	8
5	11	5	19	16	0	3	5	1
6	2	7	18	14	4	7	1	1
7	11	13	13	9	4	2	2	6
8	4	10	24	8	3	2	2	7
9	6	9	15	13	5	3	1	8
10	0	7	29	16	4	2	1	1
11	5	8	19	13	4	3	2	6
Final diagnosis	1	23	17	5	5	1	8	

Four of the five cases with a score of 5 or more were also cases of infective colitis. In this group of 19 there were three conditions with small but adequate numbers for analysis—pseudomembranous colitis (five cases); solitary rectal ulcer syndrome (four cases); and infective colitis (five cases). All four cases of solitary rectal ulcer syndrome had a significant majority in favour of that diagnosis, while four of the five cases of pseudomembranous colitis also had a strong majority (table 4). In the case of infective colitis there were almost equal numbers favouring inflammatory bowel disease, infective colitis, or non-specific changes. This group also included a single case of ischaemic colitis, which was correctly categorised by all the group and a case of collagenous colitis which had a majority in favour of that diagnosis.

Analysis of the data related to specific features of diagnostic importance showed that only one—the presence of muscle fibres in the lamina propria—was specific for solitary rectal ulcer syndrome. A pseudomembrane was also highly suggestive of pseudomembranous colitis and a well formed epithelioid cell granuloma was almost diagnostic of Crohn's disease. Table 5 indicates the number of occasions a feature was reported as being present and worthy of comment by all 11 pathologists combined, in the 23 cases of ulcerative colitis and 17 cases of Crohn's disease. This is expressed as a percentage of the maximum possible total, 11–253 (11 × 23) in ulcerative colitis and 187 (11 × 17) in Crohn's disease. In the area of inflammatory bowel disease three of the commonest features, in both ulcerative colitis and Crohn's disease, were an increase of inflammatory cells, presence of neutrophils, and cryptitis. It was only in the less common features observed that a pattern emerged with mucin depletion, crypt abscess, crypt irregularity and luminal pus favouring ulcerative colitis, while a normal anatomy and pericryptal histiocyte aggregates favoured Crohn's disease.

Table 6 compares the majority diagnosis of the group with the eventual diagnosis. In 46 of the 60 (77%) cases the diagnostic category was correct. In four cases of ulcerative colitis and two further cases of Crohn's disease the majority diagnosis was also inflammatory bowel disease (NOS). Table 7 compares the final opinion of all 11 pathologists with the eventual diagnosis. Even there, 55% of diagnoses were in exactly the same category as the final "correct" diagnosis.

Table 9 Classification of cases in second circulation by discriminant analysis, using individual reports

Actual group	Predicted group (%)		
5-6	69	21	10
7-8	24	71	6
9-12	2	34	64

Total correctly classified 67.6%.

Table 8 shows the variation between the 11 pathologists in the diagnostic categories assigned to the 60 cases. This shows that there was a considerable variation in the number of cases categorised under 1-4—non-specific changes and inflammatory bowel disease (NOS) with the range varying from 7-24. There was one pathologist who failed to recognise pseudomembranous colitis, although the overall results showed that this was an entity well recognised in four of the five cases. Two pathologists failed to recognise the entities included in category 12 which included four cases of solitary rectal ulcer syndrome, another condition recognised well by the majority.

The discriminant analysis identified one function with which cryptitis, crypt irregularity, crypt abscess, increase in lymphoid aggregates, mucin depletion and presence of neutrophils were most highly correlated, and one function correlated with increase in chronic inflammatory cells, pericryptal aggregate of epithelioid histiocytes, absence of luminal pus, granuloma and Paneth cell metaplasia. Table 9 shows that these functions classify 68% of the cases in the second circulation into the correct diagnostic group.

Discussion

As in most organs, a limited number of patterns of abnormality are possible in the rectum, and yet a large number of diseases may be associated with an abnormal appearance of the rectal mucosa. One skill of the pathologist lies in the ability to recognise consistently that certain patterns are often associated with certain clinical conditions. This study has shown that a group of consultant pathologists can distinguish, with acceptable accuracy, inflammatory bowel disease from other causes of an abnormal biopsy specimen and more specifically, ulcerative colitis, pseudomembranous colitis, solitary rectal ulcer syndrome, ischaemic colitis and collagenous colitis, although the latter two conditions included only a single example of each. The results for Crohn's disease are poorer, but this is understandable, considering the wide range and focal nature of histological appearances which may be seen in this condition. As a group we were poorer at recognising infective colitis.

In previous studies from this group^{1,2} we have used κ statistics for analysis of the data. In those studies there was no assumption concerning the "correct" diagnosis, but in the present study a gold standard was available in the form of the diagnosis made at the time based on the clinical history and information, and in some cases further material at a later

date which confirmed or modified the initial diagnosis. In a number of cases, especially four initially allocated to the category of inflammatory bowel syndrome (NOS), retrieval of the notes indicated quite clearly that three of these were examples of ulcerative colitis, while one was an example of infective colitis. The cases of ulcerative colitis had been diagnosed some years earlier, but this information had not been available to the reporting pathologist at the time of the biopsy specimen included in the study.

There have been surprisingly few similar published studies. Several studies in the late 1970s reported the histological appearances in infective colitis due to salmonella, campylobacter, etc.^{3,4} Over the next five years there followed a number of papers from North America and this country describing the appearances of acute self-limiting colitis and the differentiation of this condition from inflammatory bowel disease.⁵⁻⁷ Acute self-limiting colitis is a condition where the clinical course resembles infective colitis, but in which a pathogen is identified in less than 50% of cases.^{5,7} Nostrant⁶ showed that in a series of 168 biopsy specimens (84 active chronic ulcerative colitis; 36 ulcerative colitis in first attack; and 48 acute self-limiting colitis) all 48 cases of acute self-limiting colitis could be distinguished from the cases of ulcerative colitis.

In an earlier study Surawicz⁵ compared 44 cases of acute self-limiting colitis with 104 cases of inflammatory bowel disease which in this study included both ulcerative colitis and Crohn's disease. They also looked at specific features which could help to differentiate these two conditions. Seven features had a high predictive probability (87-100%) of diagnosing inflammatory bowel disease—distorted crypt architecture; increased acute and chronic inflammatory cells in the lamina propria; a villous surface; epithelioid cell granulomas; crypt atrophy; basal lymphoid aggregates and basally located giant cells. One or more of these features was present in just under 80% of cases. The third study⁷ from the United Kingdom compared 27 cases of acute self-limiting colitis with 37 cases of inflammatory bowel disease—all biopsy specimens being the initial biopsy from that individual. This showed that distorted crypt architecture, crypt atrophy, basal lymphoid aggregates and dense lymphocytic infiltrates were features with a 76-86% probability of predicting inflammatory bowel disease, but their discriminant value was reduced by interobserver disagreement. Isolated basal giant cells, epithelial surface erosions, and epithelioid granulomas were the most reliable features and these were associated with good interobserver agreement.

The study⁸ which most closely resembles ours compared 238 patients presenting to an acute infectious unit, of which 42 patients were identified as cases of transient colitis syndrome—cases of acute self-limiting colitis where no pathogen is identified. In that paper the pathologist in the study reported the cases

"blind" without clinical data. The categories used were similar to ours—ulcerative colitis (5 and 6); Crohn's disease (7 and 8); inflammatory bowel disease (4); infective (10); minor changes (2 and 3); normal (1). In that study 77% of cases of ulcerative colitis were correctly assigned to that category compared with 83% in our study. In the case of Crohn's disease 50% were correctly classified with a wide spread amongst the other categories, again in a pattern very similar to our own results.

A study looking at observer variation among three pathologists⁹ who examined 40 rectal biopsy specimens from cases of inflammatory bowel disease showed that only five abnormalities were sufficiently reproducible with a κ of >0.4 . These were ulceration, villous surface, epithelioid cell granulomas, severe mucin depletion and crypt abscesses. Our own data showed similar results, with six features having a κ of >0.4 —luminal pus, cryptitis, crypt abscess, mucin depletion, granuloma and neutrophils in the lamina propria.

There was considerable variation between pathologists in the categories used (table 8). In particular, the use of the non-specific categories 1-4 ranged from 7-24. This could partly be explained by individuals' differing approaches. If it is assumed that in most cases a specific diagnosis had been established, even if not on that biopsy specimen alone, then a case with mild focal inflammatory changes could be Crohn's disease, because of the wide spectrum recognised in that condition. However, in normal daily practice, it may have been reported in a non-specific way using words equivalent to categories 2 or 3. One problem with a study like this, is that it is not directly comparable with daily practice. We also had no opportunity to indicate our degree of certainty of the category chosen. It must be remembered, however, that in this study the only information we could assume was that the patient had presented with bloody diarrhoea. It is also important to emphasise that the biopsy specimens were not in any way selected as good examples of the various entities, nor were

cases restricted to well orientated, adequate biopsy specimens. They were in all probability a fairly representative set of rectal biopsy specimens similar to those encountered in daily pathological practice. We did not know the age, sex, clinical features, length of history or the sigmoidoscopic findings, all of which are important in the formulation of the final report issued on rectal biopsy specimens in daily practice. If all this information had been available, together with subsequent biopsy specimens, the results would probably have been even better.

This study has pinpointed areas of diagnostic difficulty, but its overall findings are reassuring as they show that the areas of strength reside in recognition of those categories which have major clinical impact. The identification of inflammatory bowel disease and its distinction from other inflammatory processes means appropriate management, careful follow up, and further investigations to permit more specific categorisation. The recognition of pseudomembranous colitis and solitary rectal ulcer syndrome are also of great clinical importance.

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