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The influence of microscopic disease at the margin of resection on recurrence rates in Crohn's disease

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Summary

One hundred and forty-two patients with Crohn's disease, undergoing 154 resections and reanastomoses, were reviewed to evaluate the influence of residual microscopic Crohn's disease at the margin of resection on recurrence. Sixty-three cases had microscopic evidence of disease at the resection margin (group I), and 91 cases had disease-free margins (group II). Of the survivors 125 patients undergoing 136 operations were reviewed. Median follow-up was 6.0 years (range 0.25–16 years) in group I, and 5.5 years (range 0.25–14.5 years) in group II. Twenty-two of 57 cases (38%) in group I developed recurrence compared with 23 of 79 cases (29%) in group II (P-NS). Cumulative recurrence rates at 10 years were 66.5% and 58% respectively (P-NS).

The results support the increasing evidence that the presence of microscopic disease at the resection margin does not adversely affect recurrence in Crohn's disease.

Introduction

Recurrence of disease is a serious and often frequent complication occurring in patients who undergo intestinal resection for Crohn's disease *(1–6)*. The extent to which this complication is influenced by residual microscopic disease at the margin of resection is unclear. Surgical opinion differs as to what the margin of clearance beyond apparently diseased bowel should be. Some surgeons remove generous lengths of healthy bowel on either side of the involved segment *(7–10)*, often with the aid of frozen section *(11, 12)*, since they believe that resection margins involved with disease predispose to recurrence. Others *(13–15)* have recently suggested that this complication is unaffected by residual microscopic Crohn's disease and encourage a more conservative policy.

In view of these conflicting opinions the present study was designed to determine if the presence of microscopic Crohn's disease at the resection margin significantly increased the risk of recurrent disease.

Patients and methods

The case records of 620 patients with Crohn's disease, admitted to the General Infirmary at Leeds between 1968 and 1982 were reviewed. Only those patients who had undergone intestinal resection and anastomosis, in whom the histological status of the resection margin was known were included in the study. Nineteen patients (12%) from a total of 161 were excluded. Three patients had macroscopic disease which was unavoidably left behind at the resection margin; eight patients had undergone bypass surgery without resection, and in the remainder, information about the resection margin was inadequate.

Recurrence at or near the site of anastomosis was documented when clinical symptoms were confirmed by radiological or histological evidence. This information was usually determined from the case records since most patients attended regularly at the outpatient clinic. When the required information could not be obtained in this way either the patient or the patient's general practitioner was contacted. Six patients (5%) were lost to follow-up.

The microscopic appearance of the resection margin of each specimen was determined from pathological records, and each case was allocated a category from grade A to C. Grade A was considered to be normal. Grade B was defined as chronic inflammation. This consisted of excessive lymphocytes, plasma cells, and histiocytes within the bowel wall (Fig. 1a). Grade C was more severe inflammation characterised by the presence of fissures, ulceration and granulomas (Fig. 1b). Mucosal and sub-mucosal oedema were not considered to be diagnostic features of Crohn's disease, but were felt to be non-specific signs of distal obstruction or nearby active disease. Where one or both resection margins belonged to grade B or C, the anastomosis was considered to be involved with Crohn's disease, and only when both margins belonged to grade A was it considered to be normal. When a patient had undergone an operation to restore gastro-intestinal continuity, the histological status of the resection margin was taken to be that of the previously resected specimen.

STATISTICAL ANALYSIS

Difference between the groups were compared using the chi-squared test with Yates correction, or Fisher's exact test for small numbers *(16)*. Cumulative recurrence rates were calculated based on life-table methods by Kaplan and Meier *(17)* and comparisons between them were made using the Lee-Desu statistic *(18)*.

Results

One hundred and forty-two patients with Crohn's disease underwent 154 resections and re-anastomoses (112 ileo-colic,

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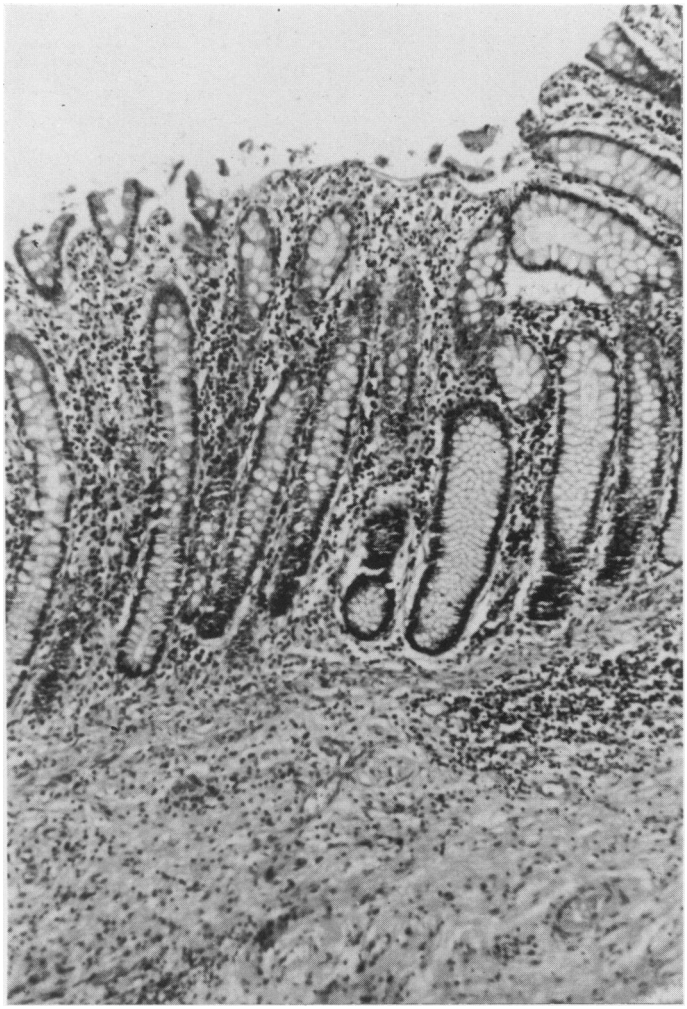

FIG. 1a The colonic mucosa shows a diffuse moderate increase in chronic inflammatory cells and some autolytic detachment of the surface epithelium but no fissures, no acute inflammatory activity, and no granulomata. These features are interpreted as 'non-specific chronic inflammation', grade B. (HE × 100.)

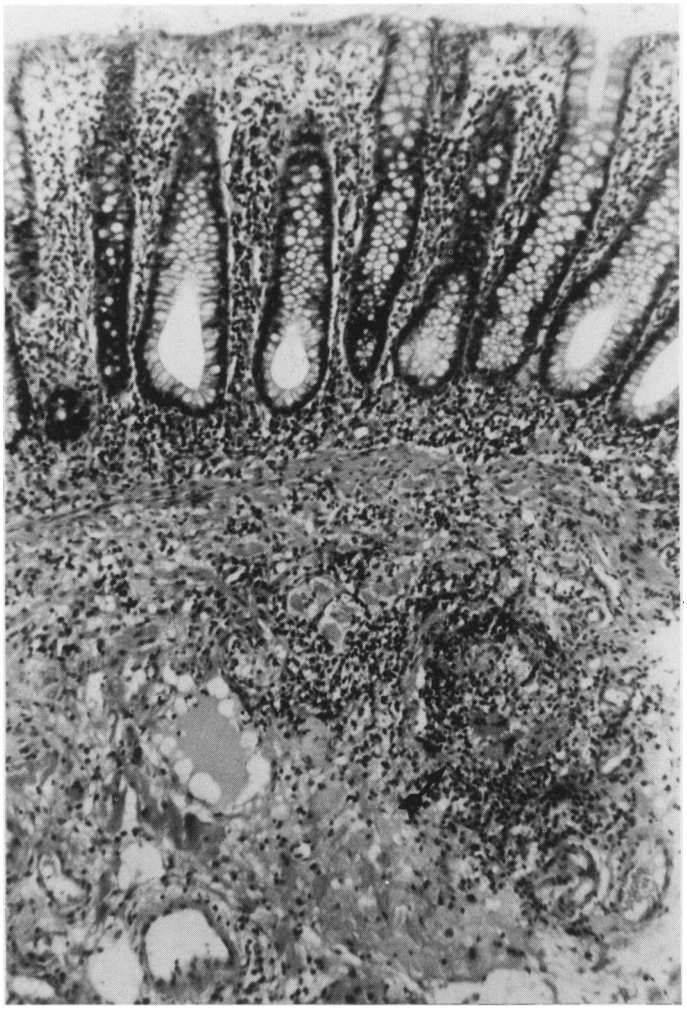

FIG. 1b In this resection margin, the colonic mucosa also shows a moderate chronic inflammatory cell infiltrate but in the submucosa there is a granuloma (arrowed) and lymphangectasia. The appearances indicate involvement by Crohn's disease, grade C. (HE × 100.)

30 ileo-rectal, 10 jejuno-ileal and 2 colo-colic). Sixty-three cases (mean age 39.5 years, range 16–71 years; m:f 19:44) had microscopic evidence of Crohn's disease at the resection margin (group I), and 91 cases (mean age 38.0 years, range 12–77 years; m:f 35:56) had disease free margins (group II). These two groups were similar with regard to the mean duration of Crohn's disease prior to surgery, the number of patients on systemic steroids, and those undergoing emergency resection (Table I). Mean haemoglobin and serum albumin concentrations were also similar. The number of patients, however, who underwent ileo-rectal anastomosis in group I (19 of 63) was significantly greater than the number in group II (11 of 91: chi-square 6.6, $P<0.01$). The operative mortality in group I was 6% (4/63), compared with 4% (4/91) in group II.

TABLE I *Clinical features of the two groups*

	Group I Microscopic disease n = 63	*Group II Disease-free n = 91*
Age (years)	39.5	38.0
M:F	19:44	35:56
Duration CD prior to surgery (years med (range))	5.5 (0.1–25)	4.5 (0.1–19)
Systemic steroids	19 (30%)	33 (36%)
Emergency operations	9 (14%)	19 (21%)
Primary anastomosis	53 (84%)	84 (92%)
Haemoglobin conc (g/dl) (mean ± SD)	12.6 ± 1.8	12.7 ± 1.8
Albumin conc (g/dl) (mean ± SD)	39.3 ± 5.9	38.7 ± 4.0
Ileo-rectal anastomosis*	19 (30%)	11 (12%)
Ileo-colic anastomosis†	39 (62%)	73 (80%)
Jejuno-ileal anastomosis	5 (8%)	5 (5.5%)
Colo-colic anastomosis	—	2 (2.5%)

*$P<0.01$.
†$P<0.02$ (chi square test).

RECURRENCE

Of the 131 patients available for follow-up with an intact anastomosis, 125 were reviewed. These patients underwent 136 anastomoses. There were 45 recurrences, an overall rate of 33%. Median follow-up was 6.0 years (range 0.25–16 years) in group I (57 cases), and 5.5 years (0.25–14.5 years) in group II (79 cases). The median time to documented recurrence was 2.5 years (0.5–6 years) and 2.0 years (0.5–9 years) respectively.

Twenty-two of 57 cases (38%) in group I developed recurrence compared with 23 of 79 cases (29%) in group II ($\alpha^2 0.9$, *P*-NS). The cumulative recurrence rate at 10 years for group I was 66.5%, and for group II was 58% (*P*-NS, Fig. 2). Furthermore, the number of cases requiring surgery for their recurrence was also similar—10 of 22 cases in group I (45%) compared with 13 of 23 cases in group II (56%).

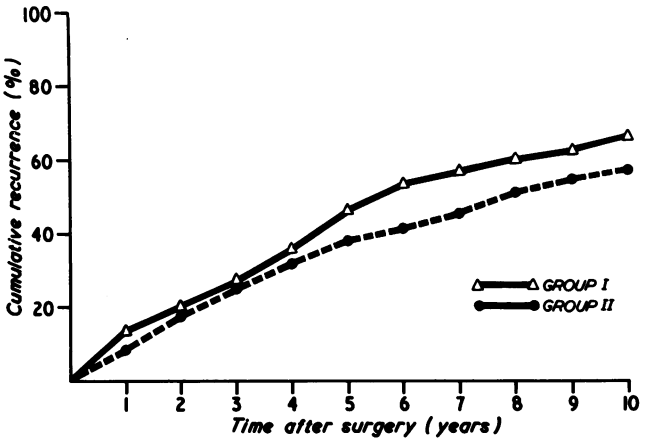

FIG. 2 Cumulative recurrence rates after resection for Crohn's disease in patients with diseased margins (group I) and disease free margins (group II). (*P*-NS.)

Discussion

There are now several reports which suggest that the majority of patients with Crohn's disease have diffuse involvement of the gastro-intestinal tract from the outset. Both biochemical and histological abnormalities have been demonstrated in apparently normal mucosa of patients with Crohn's disease elsewhere in the gastro-intestinal tract *(19–22)*. If one accepts this as evidence that Crohn's disease is pan-enteric in distribution, it would seem logical to believe that surgery, however, radical, would be unlikely to produce a cure in most patients. Indeed, based on recent evidence *(13–15)*, there is now an increasing belief that residual microscopic disease at the margin of resection does not adversely affect the development of recurrence following intestinal resection for Crohn's disease. The results of our study lend support to this belief. The cumulative recurrence rates, which correct for variation in follow-up between patients, and the median time to documented recurrent disease, were almost identical between the two groups. The number of those who required surgery for their recurrence was also similar.

These findings are in agreement with those of Pennington *et al. (13)* who reported an incidence of 41% recurrence at the suture line in patients with margins involved by microscopic disease, compared with 35% in patients in whom the resection margins were clear of disease. Two more recent studies *(14, 15)* have also failed to show any adverse effects, in terms of recurrence, of leaving behind microscopic disease.

There are, however, conflicting reports in the literature. In 1977 Bergman *et al. (7)* presented a long term study of 186 patients who had undergone intestinal resection and re-anastomosis for Crohn's disease, and suggested that a wide resection margin, involving 10 cm of microscopically normal bowel, reduced the incidence of recurrence. Radical resection resulted in a recurrence rate of 29% whereas with a more conservative approach recurrence occurred in 84% of cases. It is not clear, however, whether the two groups of patients in this latter study were comparable. Moreover, the data were compiled from several different hospitals and variations in the interpretation of recurrence may have occurred. In contrast, the present study was performed not only in one hospital but also in one unit.

Wolff *et al. (8)* recently reporting their experience from the Mayo Clinic, also found a higher recurrence rate when the margins were involved with microscopic disease. Their criteria for involvement by disease were more stringent than our own in that their patients were only considered to have involved margins if they fulfilled our Group A criteria. Nevertheless, when the patients in our study were categorised according to Wolff's criteria, no significant differences between the groups emerge.

In conclusion, the results of this study support the growing feeling that surgery for Crohn's disease should be conservative rather than radical. On this basis we would advise that only macroscopic Crohn's disease be resected and that the anastomosis be made in bowel which appears macroscopically normal.

We would like to thank Dr M F Dixon (Leeds University Department of Pathology) for his help and advice regarding the pathological records and for providing the photomicrographs, and to Mrs Lorna McQuade for secretarial assistance. We are also grateful to Professor D Johnston for allowing us to study patients under his care and for his interest and helpful criticism.

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Robert John McNeill Love 1891–1974

Robert McNeill Love, Hamilton Bailey's surgical 'twin', was born in Devonport, son of an Ulsterman who had built up a highly successful warehousing firm in Plymouth and who was mayor of that town at the time of Robert's birth. A cherished childhood memory of Robert's was of being held up to see Queen Victoria during her Diamond Jubilee visit to Devonport.

Having qualified from the London Hospital in 1914, he served in the RAMC throughout the Great War in India, the Dardanelles and Mesopotamia, latterly as a surgical specialist. He always expressed his deep indebtedness to George Grey Turner who was his commanding officer in Mesopotamia. After the War he was house surgeon at The London Hospital and R.S.O. at Poplar before completing his final fellowship and mastership. As a first assistant at The London he acknowledged the inspiration of Hugh Lett, Malcolm Rigby and Russell Howard. During that period Hamilton Bailey was a fellow chief assistant at The London thought neither of them became consultants there. However, the staff of the Royal Northern Hospital were astute enough to invite them both to join them in 1930. There followed a long and fruitful collaboration heralded by publication of the *Short Practice of Surgery* in 1932, a book which was to reach its sixteenth edition by the time of Love's death. He also published a book on the appendix and *Surgery for Nurses* which ran to three editions.

'Robbie', as he was affectionately known, was a born teacher and enthusiastic surgical tutor throughout his professional life. He welcomed postgraduates and undergraduates at his clinics, and in the theatre, making much use of mneomonics and broad classifications to simplify the learning process. He was very much a general surgeon and was one of the first to use operative cholangiography in this country. But he regarded himself as one of the old school brought up to complete an abdominal operation within the hour, and he found it hard to adjust to the slower and more precise technique permitted by modern anaesthesia. I shared a registrar and house surgeon with him for several years. When he retired from the Royal Northern staff in 1956, and following the untimely death of Hamilton Bailey, two reconstructed theatres were named after them.

Robert was on the Court of Examiners for six years, latterly as its chairman. He was on Council from 1945–1953, declining to serve for a second term so as to make way for younger men. He was Hunterian professor and Erasmus Wilson demonstrator, and instituted a prize for College staff who had served for 40 years. He also founded awards for those who had served for 15 and 25 years. He was a keen scoutmaster at Poplar in his younger days when he spent his entire savings of £500 to puchase Goffs Oak, a delightful camp site in Hertfordshire which is still used by Scouts and Guides.

He was twice married. There were two children by the first marriage. The daughter trained as a nurse and later became head of the sociology department at the North London Polytechnic. In 1982 she was awarded a life peerage in the name of Baroness Cox.

A lover of the country, having inherited a farm from his mother's family in Devon, he later bought Seward's farm in Hertfordshire which his son, but for his early death from Hodgkin's disease, would have taken over. Robert himself was no mean farmer and had a reputation as the quickest and slickest gelder in Hertfordshire. Former members of Court and Council, as well as his hospital colleagues, will remember his celebrated farm suppers for he was a most kindly and hospitable man. He died of an inoperable carcinoma of the stomach which first manifested itself by hepatic secondaries. He sensibly declined investigation and with characteristic consideration kept the true nature of his illness from his relatives until a short time before his death.

REGINALD MURLEY PPRCS