Progress in Ulcerative Colitis

D. G. BURNS, M.B., CH.B., D.PHIL. (OXON.), F.C.P. (S.A.), S. BANK, M.B., CH.B., M.R.C.P. (LOND.) AND I. N. MARKS, B.SC., M.B., CH.B., F.R.C.P. (EDIN.), *Gastro-intestinal Clinic and Department of Medicine, Groote Schuur Hospital and University of Cape Town*

SUMMARY

The prognosis and course of ulcerative colitis in Cape and other centres are discussed and a short resumé of the results of various forms of treatment is presented.

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Idiopathic ulcerative colitis has been defined as an acute and chronic inflammatory and ulcerative disease of the rectum and colon, of unknown aetiology. Since the first description as a separate entity by Wilks and Moxan in 1875, there has been a disproportionate amount of time and energy spent on the study of this intriguing disease. Despite this, it continues to be a dangerous disease without absolutely satisfactory treatment, and a recent review of the subject concluded, 'there have been no major advances

during the past few years either in treatment or in our knowledge of the cause of ulcerative colitis'.[1]

However, there have been many notable contributions, mainly of a clinical nature. These have undoubtedly increased our understanding of the epidemiology and natural history of this condition, providing a better guide to treatment. A major advance in knowledge has been the distinction of this disease from granulomatous colitis (Crohn's disease of the colon) and its possible relationship to it.[2-4] Clinically, the emphasis on diarrhoea, weight-loss, anal lesions and fistula formation, rather than on rectal bleeding, suggests granulomatous colitis. On barium enema examination, a discontinuous lesion, often with sparing of the rectum and associated with fistulae, fissuring, caecal deformity and a cobblestone appearance, distinguish it from ulcerative colitis. It has also become apparent that the majority of such patients will require surgery at an earlier stage in the disease in contrast to many patients with ulcerative colitis.

In recent years one has become more aware of other forms of colitis which may simulate non-specific ulcerative colitis: namely ischaemic colitis,[5] amoebic and postdysenteric colitis[6] and lymphoma of the colon.[7] An interesting report on the cytological diagnosis of the precancerous state in ulcerative colitis came recently from Morson and Pang.[8] These workers stressed the diminution in amount of mucus secreted, irregularity in size and shape of cells, increase in size and irregularity of nuclei, and irregularity of epithelial tubules. This work remains to be confirmed and critically evaluated.

It is not the purpose of this article to review these or other aetiological concepts, but rather to confine discussions to epidemiological and clinical advances with their therapeutic implications.

PREVALENCE

Most epidemiological studies have reflected hospital incidence. Evans and Acheson in Oxford found a prevalence rate of 79·9/100 000 population at the end of 1960.[9] In Copenhagen County it was found to be 44·1/100 000.[10] In a study of residents in a Baltimore area between 1960 and 1963, a total annual prevalence rate of 16·48/100 000 of hospital admissions was found.[11] In all studies, a higher incidence and prevalence rate has been found in Whites than non-Whites, Jews than non-Jews and females than males. It has also been shown that although the peak incidence of the disease is in early adult life, the elderly are also at risk. The Oxford studies showed a second incidence peak in the over-60-year age-group, while the Baltimore study showed a similar trend for females. In the Cape Town cases the peak incidence for all races was similar. Of interest have been descriptions of the disease in Africans from the Baganda tribe[12] and Bedouin Arabs[13]—both primitive communities. In Cape Town, 28·5% of a series of 178 cases were Coloured, while only 1 case in a Bantu was included. The latter case was also very atypical in that there was segmental non-specific colitis, cured by partial colectomy.

PROGNOSIS AND COURSE OF THE DISEASE

It must be emphasized that studies of this nature are usually centred on patients referred to hospitals and inpatients, as a result of which data are influenced by selection and the incidence of radical surgery, which itself may modify subsequent course and prognosis. Two excellent studies over prolonged periods of time have been published. The first is from Oxford with a study of 624 patients over a period of 20 years,[14,15] and the other from Leeds with a study of 465 patients over 10 years.[16] In both studies the follow-up of cases was complete. The records of 178 patients satisfying criteria for diagnosis of this disease at Groote Schuur Hospital have also been studied retrospectively. Most of these cases were referred to the Gastro-Intestinal Service of this hospital during the past 10 years, and some of these results are included for comparison.

In the Oxford and Leeds surveys, the severity of the disease was graded according to similar criteria, and incidence of severe, moderately severe and mild cases was essentially the same (Table I). Likewise, the extent of the disease was similar in both series (Table II). Both groups agree that the prognosis in the first attack is worse in the elderly, in a severe attack, and in patients with extensive colonic involvement. The mortality rates for severe attacks in the second part of the Oxford series and Leeds series were 26·8% and 9·6% respectively. In both series, the mortality for a severe attack in patients over the age of 60 years was extremely high. By comparison, in the Cape Town cases, 11% of patients with a severe attack died.

TABLE I. SEVERITY OF ATTACKS

	Oxford (%)	Leeds (%)	Cape Town (% 178 patients)
Severe	**17·7**	**14·6**	**29·0**
Moderate	**24·0**	**23·9**	**31·5**
Mild	**58·3**	**61·5**	**39·5**

TABLE II. EXTENT OF THE DISEASE

	Oxford (%)	Leeds (%)	Cape Town (% 154 patients)
Distal	**23·1**	**19·2**	**29·9**
Substantial	**43·2**	**47·6**	**31·8**
Total	**33·7**	**33·2**	**38·3**

Methods of analysis of long-term prognosis differed in the Oxford and Leeds surveys, which may partly account for the different conclusions reached. The Oxford work has shown that the severity of the attack and extent of colonic involvement affected not only the outcome of the initial attack, but also subsequent prognosis. Thus, patients with mild disease or the distal type of the disease had survival curves not differing greatly from expected values, while those with severe attacks or major involvement of the

colon had a bad prognosis throughout the entire length of follow-up. The Leeds workers failed to show this long-term effect on prognosis, and found that prognosis was more related to the severity of individual attacks. However, both groups were in agreement that the majority of patients suffer from a chronic intermittent course of the disease. In the Oxford series, 7 out of 8 patients had experienced 1 or more recurrences by 5 years, while in the Leeds series, 69% of all patients relapsed within 1 year of the attack.

The tendency for the disease to extend and involve a substantial length of colon when it was initially confined to the rectum, was different in the two series. This occurred in less than 10% of the Oxford cases and the mortality was low. In the Leeds cases the incidence of extension was 36% with 5 deaths. However, subsequent studies from other centres have substantiated the conclusions of the Oxford workers, who found the incidence of extension to be low.

One may therefore conclude that, whereas most cases recur, it is only in patients with substantial colonic involvement, who often also have severe attacks, that the expectancy of life is significantly reduced. It follows that, unless complications supervene, there should be little indication for radical surgery outside this group of patients.

MANAGEMENT

Controlled clinical trials have shown that local and systemic corticosteroid treatment is effective in the acute attack, and that Salazopyrin may prevent relapse, certainly over a trial period of 1 year. Many physicians are reluctant to treat patients in an acute attack or in a relapse, with systemic corticosteroids. It should be borne in mind that many of these relapses may develop into severe attacks, and that the risks of a short course of systemic steroids are trivial in comparison with the risks of a severe attack of ulcerative colitis. It is therefore of great importance that patients be treated with Salazopyrin and cortisone retention enemas early in an attack or relapse. If there is no improvement within a week, a short course of systemic steroids should be commenced and, if response is not satisfactory, the patient should be admitted to a hospital or specialized unit without delay. Patients with severe or fulminating attacks are best treated in hospital and should be given intensive treatment with large doses of intravenous corticosteroids and a broad-spectrum antibiotic. The bowel should be rested by allowing nothing orally save sips of fluid for the first few days, while strict attention is paid to protein loss and electrolyte depletion.

There is some evidence that certain patients have a lower relapse rate when treated on a milk-free diet, but at the present time there is no way of telling in advance whether a patient will respond to such a diet. In refractory attacks, or in patients with frequent relapses, exclusion of milk from the diet is nevertheless worth an empirical trial. Supportive psychotherapy, in addition to other therapeutic measures, is important. However, few physicians would agree that this should constitute the major therapeutic approach and most regard it as an important but secondary form of treatment. Immunosuppressive drugs have been used in an uncontrolled fashion with varying degrees of enthusiasm. In some cases response has been good, but in others severe bone-marrow depression has ensued and patients have tended to relapse when the drugs are withdrawn.

Statistics from many centres have shown a high mortality for emergency colectomy (15% - 30%), as opposed to elective colectomy (2% - 3%). Whereas in some cases perforation or other complications favour emergency surgery, in many cases it is difficult to judge when conservative measures should be abandoned in the management of an acute attack. By reducing the initial period of conservative management in an acute attack to 3 - 4 days, the Leeds group of workers have reduced the mortality of emergency surgery from 20% to 2%. This has been achieved at the expense of a very high rate of surgery in the acute attack, and by subjecting a number of patients in their first acute attack of the disease to total colectomy and the ileostomy life.

In the chronic continuous or chronic intermittent form of the disease, surgery should rarely be required unless there is substantial or total colonic involvement. There is ample evidence of considerable morbidity associated with any operative procedure, and surgery should be reserved for those patients whose symptomatology and general debility demands it, in those with complications such as fistulae, or in those with a significant risk of developing a carcinoma. The main factors associated with a high risk of colonic carcinoma complicating ulcerative colitis appear to be (*i*) a severe first attack, (*ii*) total colitis, (*iii*) chronic continuous symptoms, and (*iv*) onset of colitis in childhood. Furthermore, the risk only becomes appreciable after the initial few years of the illness and it should rarely be necessary to consider surgery on these groups until 6 - 8 years have elapsed.

In conclusion it should be stressed that in areas where amoebiasis is endemic, it is essential to exclude this disease which can mimic non-specific ulcerative colitis in its entirety. This should be done by frequent examination of rectal scrapings and resorting to a therapeutic trial with metronidazole in any case where doubt exists, no matter how slight.

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