disease, and both had had evidence of malabsorption for up to 10 years before the diagnosis of idiopathic chronic ulcerative enteritis.⁵

The mean age at the onset of symptoms from ulcerative enteritis is about 50, and women slightly preponderate. Patients usually present with chronic symptoms—diarrhoea, steatorrhoea, abdominal pain, and loss of weight. They may have a low grade fever, finger clubbing, evidence of wasting and nutritional deficiencies, and abdominal distension. Complications of small intestinal ulceration, such as haemorrhage, perforation, or obstruction, are common. Investigation invariably shows malabsorption of fat, and most patients have radiological abnormalities of the small intestine. These abnormalities may be non-specific, such as dilatation or thickened valvulae conniventes, or there may be strictures or ulceration. Jejunal biopsy specimens show a variable degree of villous atrophy and may even be normal. A finding of frank ulceration in a jejunal biopsy specimen appears to be rare.⁹ Many patients have anaemia, usually due to iron deficiency, a neutrophil leucocytosis, hypoalbuminaemia, and immunoglobulin abnormalities.

Diagnosis of chronic ulcerative enteritis is usually not too difficult except in the occasional patient in whom there are no specific radiological features.¹⁰ In these cases diagnosis is often delayed unless laparotomy is undertaken. Once the diagnosis has been made there are few guidelines for treatment. All patients with an abnormal small intestinal mucosa should be given a gluten free diet and, if no histological response occurs, withdrawal of soy protein or even enteral feeding with an elemental diet may be worth while. Bacterial overgrowth of the small intestine should be looked for and treated with antibiotics. Steroids are often used, but the evidence that they are beneficial is limited and entirely anecdotal. Tight strictures and perforations require surgical management. Whatever treatment is employed the prognosis is poor: of the 40 patients described in published reports, two thirds were dead within three years of diagnosis.

The aetiology of chronic ulcerative enteritis remains unknown. The exact relation to coeliac disease is also not clear. There is often a strong clinical suspicion of coeliac disease, as discussed above, even though definitive proof is lacking. Furthermore, many patients have shown evidence of hyposplenism³ and six patients from Leeds⁷ had the HLA-B8 phenotype. Perhaps the most controversial contention is the nature of the underlying disease process. Isaacson and Wright suggested that malignant histiocytosis may be responsible for most, if not all, cases of ulcerative enteritis.⁶ Only three of the eight patients from Leeds, however, were shown to have malignant histiocytosis.⁵ On present evidence, therefore, malignant histiocytosis seems to account for only a minority of cases of ulcerative enteritis. Now that pathologists are much more aware of this diagnosis and special stains are available,¹¹ the pathological features of idiopathic chronic ulcerative enteritis should be examined more critically than has previously been possible.

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Recurrent cancer of the large bowel

Cancer of the large bowel causes some 17 000 deaths each year in England and Wales and is the second most common cause of death from malignant disease. Many patients who die from cancer of the bowel have previously undergone what was hoped to have been a "curative" resection, only to return with lethal recurrent or metastatic disease; some patients in whom surgical cure has been successful will later develop a second, metachronous cancer elsewhere in the large bowel.

Is the picture one of complete gloom, or can painstaking follow up identify these lesions at a stage where further surgical resection is possible and rewarding? Once colorectal cancers could be removed successfully it soon became clear that the remaining large gut might be the site of development of a second tumour.¹ In 1951, Rankin and Conger described seven patients whose second tumours had been resected successfully.² By 1958 Moertel and his colleagues could report 261 multiple colorectal cancers among 6012 cases at the Mayo Clinic (4%), of which 157 were simultaneous, 95 metachronous, and nine both.³ Interestingly, 21 of these 261 patients had, in addition, another tumour elsewhere as well as their two or more colorectal growths.

A review from St Mark's Hospital, London, of 4884 survivors from operations for cancer of the large bowel showed that 83 patients (2%) had operations for metachronous cancers.⁴ Eighteen patients had their second cancer diagnosed in the first two years after initial operation, and some of these might have been synchronous tumours missed at the first operation; but among the remainder the average interval between the first and second operations was just over 11 years. The St Mark's report points out the difference in prognosis in patients who developed a second cancer of the large bowel while attending the follow up clinic regularly compared with those who had defaulted or had been discharged. The 41 tumours in the "follow up" group were diagnosed apparently earlier than in most series, and no fewer than 70% were at Dukes stage A or B. By contrast, eight of the 17 patients who were not attending the clinic had inoperable growths at the time of diagnosis. The policy at St Mark's was that patients should be examined by a double contrast barium enema every two years combined with sigmoidoscopy every six months—but that was at a time before the routine use of the

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fibreoptic colonoscope, which permits a much more complete examination of the whole of the remaining large bowel.

In recent years there has been considerable interest in the use of serial estimations of carcinoembryonic antigen for detecting early asymptomatic recurrent disease. The hope has been that effective second look surgery might be employed as a result of such early detection. Martin and his colleagues from Columbus, Ohio, reported a prospective study on 17 patients after resection of colorectal cancers (and one who had had a hepatoma removed) who were followed up with frequent serial determinations of carcinoembryonic antigen and in whom there was a rise in titre.⁵ Re-exploration of these 18 patients showed that 13 had localised recurrent disease and four disseminated cancer. There was only one negative exploration. Steele and his colleagues in Boston, however, found that they could perform only four potentially curative resections in 18 patients monitored by serial carcinoembryonic antigen estimations.⁶ Wanebo points out that in four reported series the proportion of positive explorations ranged from 78% to 94% and of resectable disease from 7% to 72%.⁷

Without doubt a rising carcinoembryonic antigen titre after curative resection of cancer of the large bowel indicates the likelihood of recurrent or metastatic disease, but it remains to be seen whether second look surgery based on these findings will give better results than surgery on patients with clinical evidence of localised, resectable recurrent disease. Obviously only a carefully controlled clinical trial can answer this important problem, and such a trial, coordinated by the Cancer Research Campaign, is now in progress at several centres in Britain.

Hitherto, recurrences in the pelvis after abdominoperineal excision of the rectum have tended to present only at a late and incurable stage. Gualdi and his colleagues have used computed tomography in routine follow up of such patients.⁸ In 16 cases extraluminal recurrences were detected in four patients, and in three these deposits were between only 2 and 3 cm diameter. Radical excision of these deposits was possible in all four.

For most the diagnosis of liver metastases is a death sentence, and, indeed, the mean survival from diagnosis in patients with colorectal cancer ranges from five to nine months. Admittedly every now and then a brilliant cure is obtained by surgical resection; for example, Jurewicz and Everett have recently reported a patient who survived 10 years after right hemihepatectomy for multiple metastases, which is the longest survival for multiple deposits yet reported in a patient with colorectal cancer.⁹ Morrow and his colleagues have carried out an aggressive surgical policy in the treatment of secondary hepatic neoplasms and reported a five year survival of 27% for their patients with colorectal primary tumours.¹⁰ These workers consider that better diagnostic procedures using scanning and tumour markers might provide a substantial increase in the numbers of patients potentially available for hepatic resection.

Against these optimistic reports the results of a recent study by Beart and O'Connell cast considerable gloom.¹¹ They reported 168 patients followed up at the Mayo Clinic after curative resection of cancers of the large bowel of Dukes stage B or C. All patients were seen at least every 15 weeks, with a detailed clinical examination on each occasion together with chest x ray films, liver function tests, a complete blood count, and estimation of carcinoembryonic antigen. Endoscopy was carried out every six months, and a barium enema

and liver scan were done yearly. Additional studies included CT scans, laparoscopy, liver biopsy, and surgical exploration when indicated. Despite what can only be described as the most scrupulous follow up, the results were far from happy. Within four years 48 of the 168 patients developed histologically confirmed recurrent cancer. Despite having been seen at least every 15 weeks no fewer than 41 of these 48 patients had symptoms before or at the time of detection of the recurrent tumour by physical examination or the presence of biochemical or radiological abnormalities. Even more disappointingly, despite this vigorous postoperative follow up, probably as detailed as could be carried out in any centre, only one of the 48 recurrences was potentially resectable. These workers conclude: "From a clinical stand point, our study does not demonstrate any value to a vigorous postoperative follow up for the detection of recurrences at the earliest possible time in as much as most lesions so detected were surgically unresectable. A pertinent medical history and physical examination accompanied by periodic assessment with proctoscopy and barium enema remain the most effective means of identifying potentially resectable recurrent or metachronous tumors. The CEA test is the most sensitive non-invasive method of detection of the recurrence at a therapeutically advantageous stage."

We must maintain a certain degree of optimism in this pessimistic subject. From time to time an altogether benign lesion may mimic recurrent or metastatic disease to perfection.¹² Such lesions include benign ovarian or hepatic cysts, anastomotic strictures, subacute obstruction due to adhesions, or a chronic intra-abdominal abscess. In a personal series of 108 patients undergoing "second look" explorations for suspected recurrent disease due to a variety of abdominal primary cancers, no fewer than 16 had this happy state of affairs.¹³

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