developing an increased incidence of cancer elsewhere remain speculative: the increased permeability of the intestinal mucosa to carcinogens and the immunological disorders [15–17] often associated with coeliac disease might play an important role.

The prevalence of the disease, which has been estimated at 0.03% of the general population, is not really known, as it may be present in apparently asymptomatic individuals [18]. The incidence appears to vary in different parts of the world: the highest incidence, (1/300), has been reported in West Ireland [19]. As malignancy might develop in as many as 14% of patients with coeliac disease [11], this would justify investigation in order to identify coeliac disease in patients with cancer occurring at an unusual young age, and the evaluation of preventive measures for family members of patients with established coeliac disease.

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Comments on *Costs of Treating Advanced Colorectal Cancer*, *Ross* et al., Eur J Cancer 1996, 32A, 513–517

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Ross and associates [1] presented a detailed analysis of the relative total costs of four different palliative chemotherapy regimens for the treatment of colorectal cancer. They conclude that the pattern of costs is such that high drug costs, for example those associated with raltitrexed therapy, are partially offset by reductions in hospital visits and stays, making it a cost-effective alternative. The De Gramont regimen [2] was shown to be considerably more expensive than any of the other three treatments. A large proportion of the cost was for inpatient stays of 48 h every 2 weeks.

In our department, patients on the De Gramont regimen are all treated as outpatients. The chemotherapy is administered through a Hickman Line with a continuous pump over 48 h and patients attend the chemotherapy day unit for pump connection and to receive their leucovorin and 5-fluorouracil bolus doses. This reduces the staff and fixed costs of this regimen to two attendances with increased pharmacy time for filling the pump. There is, therefore, a considerable cost saving and we would estimate that this brings the De Gramont regime into the cost bracket of the other three treatments. The patient spends less time in hospital.

Our centre now administers several other regimens, as day-case procedures, which previously would have been delivered as an inpatient. For example, cisplatin is delivered as an 8–10 h day-case procedure. This entails problems of bed occupancy in the day unit and also of scheduling of nursing staff. Nevertheless, this has increased our chemotherapy capacity and is a practice that has been undertaken for a decade in the United States where cost pressures have always been more marked [3]. Such treatment delivery has been facilitated by the 5HT3 antagonist anti-emetics. As far as costings in colorectal carcinoma are concerned, this will be one of the major end-points of the MRC CR06 trial which is comparing the De Gramont regimen with continuous 5-fluorouracil and with raltitrexed. The main end-points are survival and quality of life, but a subgroup of patients will have extensive assessment of their costs including drugs, staff (medical, nursing and pharmacy), consumables, investigations and patient borne

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costs. This analysis will need to take account of the potential to move care from the inpatient ward to the day-case unit as we have done. It is only when this and other similar comparisons have been made that we will be able objectively to compare the cost benefit outcomes of the different regimens.

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Possible Prognostic Significance of P53 Immunoreactive Status of Hepatic Colorectal Cancer Metastases Following Surgical Resection

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THE EXPRESSION of the mutant p53 protein has been demonstrated to have poor prognosis significance following surgical resection of colorectal adenocarcinoma [1]. These data have been recently confirmed by immunohistochemical analysis of the p53 antigen in paraffin slides [2]. The prognostic significance of *Tp*53 mutation in liver metastases from colorectal cancer has not been evaluated. We report here a retrospective study with the aim of assessing the possible relationship between p53 status of hepatic metastases from colorectal cancer and outcome following hepatectomy.

102 patients who underwent liver resection for colorectal metastases in our unit from 1983 to 1989 (at least a 6-year follow-up) were reviewed. We excluded all patients for whom liver resection had not been curative and/or patients who had received pre-operative chemotherapy. Pre-operative chemotherapy was considered to change the immunohistochemical results due to necrosis of the tumour.

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Table 1. *Nuclear overexpression of p53 in colorectal hepatic metastases according to the clinical outcome*

	p53+++	p53++	p53+	p53+/+++	p53−
DFS ($n=10$)	3 (30%)	1 (10%)	0 (0%)	4 (40%)	6 (60%)*
HR ($n=11$)	2 (18%)	3 (27%)	4 (36%)	9 (82%)	2 (18%)

DFS, disease-free; HR, hepatic recurrence; +++, nuclear staining above 60%; ++, 30–60%; +, 5–30%; −, absence of nuclear staining or below 5%. *$P=0.08$ (Fisher's exact test).

As a preliminary approach, two groups of patients with opposite outcomes following liver resection were evaluated. One group consisted of 10 patients alive and disease-free for more than 4 years following resection (DFS group), whilst the second group consisted of 11 patients who demonstrated intrahepatic recurrence within 1 year from resection leading to death within 2 years from surgery (HR group).

An immunohistochemical evaluation was performed by a single pathologist unaware of the medical history and outcome of patients. Formalin-fixed paraffin-embedded sections of liver metastases were studied for expression of p53 protein using the antibody DAKO-p53, DO7.

Results were expressed in a semiquantitative manner (Table 1). Other prognostic factors such as age, sex, latency of liver metastases, pre-operative serum carcinoembryonic antigen (CEA), number and maximum size of metastases as well as margin of resection were correlated to ultimate patients' outcome following surgery.

Patients' survival was significantly different between the two groups (7.2 ± 1.9 years for the DFS group compared with 1.1 ± 0.6 years in the HR group). The maximum size of metastases was higher in the HR group than in the DFS group (59.7 ± 25.7 versus 36.0 ± 21.6 mm; $P=0.03$, test *t*). Serum levels of CEA were also increased in the HR group (112 ± 163 versus 11 ± 14 ng/ml) ($P=0.07$). The other factors were comparable between groups.

Positive immunohistochemical staining for p53 was more frequently observed in the HR group (82%) than in the DFS group (40%), but the difference was not significant ($P=0.08$). Sensitivity of p53 immunohistochemical expression for predicting early liver recurrence was 6/10 (60%) while specificity was 9/11 (82%). The positive predictive value was 6/8 (75%) while the negative predictive value was 9/13 (69%).

The small number of patients evaluated in these series does not allow a definitive conclusion that p53 wild-type status is an independent prognosis factor. However, the encouraging results observed provide a basis for further investigation as the p53 status determined by immunohistochemistry could be part of the decision-making process of adjuvant therapy following curative resection of colorectal liver metastases.

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