university-affiliated medical center were twice as likely to undergo colonic biopsy than those being assessed at community sites (odds ratio 2.1, 95% CI 1.5–3.0). In addition, patients over 50 years of age were less likely to undergo biopsy than their younger counterparts (odds ratio 0.7, 95% CI 0.6–0.8). This observation was surprising given the higher rate of microscopic colitis among older patients. In the Veterans Affairs Medical Centers, the odds that biopsy specimens were obtained were 4.1 times higher in women than in men (95% CI 1.6–10.5). Although a gender difference was also seen in the community setting (odds ratio 1.4, 95% CI 1.2–1.6, for women vs men), there was no such disparity at university-affiliated sites.

Harewood *et al.* discuss the possibility that physicians included in the Clinical Outcomes Research Initiative cohort might not be representative of the "average GI specialist" in some respects. Nevertheless, say the authors, the study reveals "a reasonably good understanding" of the need to perform colonic biopsy in patients with diarrhea and normal endoscopic findings. Defined guidelines are needed, they note, to avoid the observed disparity between different settings and patient groups.

Original article Harewood GC *et al.* (2005) Colonic biopsy practice for evaluation of diarrhea in patients with normal endoscopic findings: results from a national endoscopic database. *Gastrointest Endosc* **61:** 371–375

New molecular markers in hepatocellular carcinoma

Survival is highly variable in patients with hepatocellular carcinoma and new prognostic markers are needed. A recent study by Schöniger-Hekele and colleagues in Austria has investigated the potential role of several molecular histologic markers involved in proliferation, cell cycle, metastatic potential and immunogenicity.

The expression of Ki-67, HER2/neu, p53, mdm2, p21, CD81, and HLA-DR was investigated in tumor tissue samples from 81 patients with hepatocellular carcinoma. These results were correlated with patient survival using the Kaplan–Meier method. In addition, associations were sought between expression of the various markers and clinical characteristics, including tumor size and grade, portal-vein invasion and lymph-node metastasis.

Associations were shown between two cell-cycle markers and survival. Tumors showing nuclear accumulation of p53 were associated with worse survival than those that did not accumulate p53 (median survival 4.1 months vs 9.3 months, $P = 0.018$). An inverse relationship was found between tumor expression of mdm2 and survival; patients with low levels of mdm2 expression survived for a median period of 9.4 months, compared with only 3.9 months for those with high expression. In addition, patients with enlarged lymph nodes were more likely to have HLA-DR-positive tumors, and tumors expressing CD81 were less frequent in patients with distant metastases.

In summary, the study revealed several markers that might be useful, in combination with information on patient and tumor characteristics, in the development of new prognostic models for hepatocellular carcinoma.

Original article Schöniger-Hekele M *et al.* (2005) Hepatocellular carcinoma—survival and clinical characteristics in relation to various histologic molecular markers in Western patients. *Liver Int* **25:** 62–69

Mutation screening in colorectal cancer

Mutation analysis in patients with inherited forms of colorectal cancer generally relies on genomic DNA sequence analysis, but certain types of mutation can be missed using this method. Large genomic deletions, for example, are masked by the presence of the normal allele. Casey *et al.* have investigated conversion analysis—based on the separation of the chromosomes into hybrid cell lines and analysis at the mRNA level—as an alternative means of detecting mutations in these families.

Using the Colon Cancer Family Registry, the team identified 89 patients with colorectal cancer who were judged likely to carry a germline mutation in a mismatch repair gene. These included 64 cases of hereditary nonpolyposis colorectal cancer (HNPCC), 8 HNPCC-like cases, and 17 cases of colorectal cancer in patients aged <50 years.

Conventional genomic DNA sequence analysis of the mismatch repair genes *MLH1*, *MSH2*, or *MSH6* revealed 28 pathogenic coding-domain mutations, 16 missense mutations, 4 inframe deletions, and 22 putative splice-site