

drank more than two cups of coffee per day were at approximately half the risk of elevated ALT activity of those who drank no coffee. Compared with those in the lowest quintile for overall caffeine consumption, those in the highest quintile were at less than a third of the risk.

Noting that the observed protective effect of caffeine and coffee was independent of the specific risk of liver injury, the authors discuss possible mechanisms by which the effect is mediated and call for further research in this area.

Original article Ruhl CE and Everhart JE (2005) Coffee and caffeine consumption reduce the risk of elevated serum alanine aminotransferase activity in the United States. *Gastroenterology* **128**: 24–32

Epigenetic markers in the detection of colorectal cancer

Numerous diagnostic markers have been evaluated in ongoing efforts to reduce the considerable morbidity and mortality associated with colorectal cancer. Studies of genetic markers have so far centered on mutations in oncogenes, tumor-suppressor genes and micro-satellite markers. Lenhard and co-workers have extended the search to include epigenetic factors; their recent paper describes the use of promoter methylation as a stool-based DNA marker.

The promoter of the *HIC1* (hypermethylated in cancer 1) gene, a tumor-suppressor gene located on chromosome 17p13.3, is frequently methylated in colorectal cancer but not in normal tissue. Using methylation-specific polymerase chain reaction, Lenhard *et al.* studied *HIC1* promoter methylation status in DNA from stool samples provided by patients with colorectal cancer ($n=26$) or adenomatous polyps of ≥ 1 cm ($n=13$). Samples from healthy individuals ($n=32$), patients with hyperplastic polyps ($n=9$) or chronic inflammatory bowel disease ($n=9$) were used as controls. All the stool samples were also analyzed using the established screening method of fecal occult blood testing.

Sufficient DNA of adequate quality for methylation-specific polymerase chain reaction analysis was isolated from the majority (97%) of stool samples. Eleven patients (42%) with colorectal cancer tested

positive for methylated *HIC1* DNA (95% CI 23%–63%). In addition, samples from 31% of patients with adenomas gave a positive result. None of the samples from healthy controls revealed the presence of methylated *HIC1* DNA, and, except in the case of one patient with ulcerative colitis, samples from patients with non-neoplastic disease all generated negative results. The *HIC1* assay, therefore, was highly specific (98%, 95% CI 92%–100%). Compared with fecal occult blood testing, the new assay was both more sensitive and more specific for the detection of colorectal cancer in this study, although these differences were not statistically significant. Combining the two methods generated a detection rate of 65% (95% CI 44%–83%).

Lenhard *et al.* propose that analysis of *HIC1* methylation, along with a small number of similarly sensitive and specific markers, might provide an accurate stool-based method for use in colorectal cancer screening.

Original article Lenhard K *et al.* (2005) Analysis of promoter methylation in stool: a novel method for the detection of colorectal cancer. *Clin Gastroenterol Hepatol* **3**: 142–149

New toxin treatment for anal fissures

Current treatments for anal fissures focus on reducing the tone of the internal anal sphincter, whether by sphincterotomy, injection of botulinum toxin or the topical application of nitroglycerin or nifedipine. The surgical procedure carries a risk of causing fecal incontinence or other side effects, and reports vary as to the efficacy of the alternative treatments. In their recent paper, Garrido and colleagues from Chile describe the successful use of a new agent, gonyautoxin, in patients with acute and chronic anal fissures.

Gonyautoxin is a paralyzing toxin isolated from shellfish. Garrido *et al.* designed a randomized, double-blind trial in which patients were to receive injections of gonyautoxin or placebo in the internal anal sphincter, on both sides of the anal fissure. Early results indicated that the toxin was highly effective, however, and the treatment was eventually given to all 50 patients.