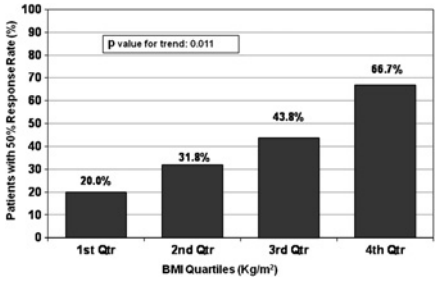
Highlights from this issue

doi:10.1136/gut.2011.240762

Emad El-Omar, William Grady and Alexander Gerbes, *Editor and Deputy Editors*

BMI is a better predictor of response to PPIs in dyspeptics with normal endoscopy

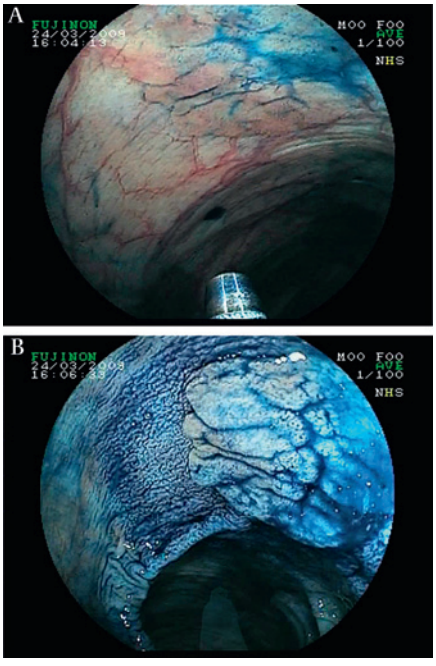
Most dyspeptic patients undergoing endoscopy have normal findings and no evidence of *Helicobacter pylori* infection. Such patients are often prescribed proton pump inhibitor (PPI) therapy, but the value of such treatment and the predictors of response remain unclear. In this issue of *Gut*, Fletcher *et al* carried out a prospective, parallel randomised study comprising 105 *H pylori* negative patients with dyspepsia and normal endoscopy. Full demographic and symptom severity characteristics were assessed, and 24 h oesophageal pH and manometry were performed prior to randomisation to 2 weeks of treatment with lansoprazole 30 mg/day or placebo (2:1). Symptoms were reassessed during the second week of treatment. According to intention to treat analysis, the response was 35.7% for the active group and 5.7% for the placebo group ($p<0001$). The only non-invasive independent predictor of response to PPI in multivariable analysis was the patient's body mass index (BMI) ($p=0.003$). The association of BMI with response to PPI was apparent across the full range of quartiles (see figure). The authors conclude that BMI should be assessed routinely in patients with upper gastrointestinal symptoms and used as a predictor of the response to PPI therapy. ***See page 442***.



Correlation of body mass index (BMI) presented as quartiles with response to proton pump inhibitors.

Pancolonic chromoendoscopy with indigo carmine

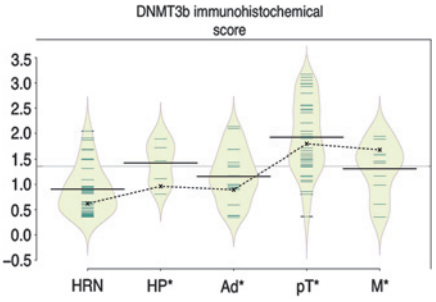
The miss rate for small and flat adenomas during colonoscopy remains unacceptably high. In this issue of *Gut*, Pohl *et al* determined whether enhanced mucosal contrast using pancolonic chromoendoscopy (PCC) allows higher rates of adenoma detection. In a large, prospective, randomised two-centre trial, PCC (with 0.4% indigo carmine spraying during continuous extubation, n=496) was compared with standard colonoscopy (control group, n=512) in consecutive patients attending for routine colonoscopy. Chromoendoscopy increased the overall detection rate for adenomas (0.95 vs 0.66 per patient), flat adenomas (0.56 vs 0.28 per patient) and serrated lesions (1.19 vs 0.49 per patient) ($p<0.001$) (see figure). PCC prolonged the mean extubation time by ~90 s compared with controls ($p<0.001$). The authors conclude that the use of indigo carmine dye spraying during colonoscopy, especially for patients who are at high risk for neoplastic lesions, is useful and practicable. ***See page 485***.



A flat adenoma visualised during withdrawal with indigo carmine spraying (A before and B after spraying).

Too much of a good thing? Is DNMT3B overexpression a cause of cancer-related DNA methylation?

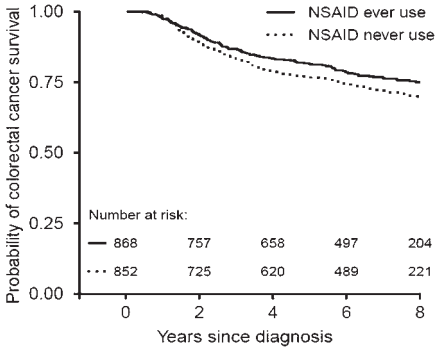
Although the aberrant methylation of genes in the progression of colorectal neoplasia has been previously reported, no model-based analysis of the incremental changes through the intermediate adenoma stage has been described. In addition, the biological drivers for these methylation changes have yet to be defined. In this issue of *Gut*, Ibrahim *et al* have provided more insight into the epigenetic alterations in colon cancer by addressing these unresolved issues. They have used linear mixed-effects modelling to study the onset and patterns of the methylation changes in the polyp to cancer sequence in the colon and have correlated these results with DNA methyltransferase 3B (DNMT3B) levels of expression. They have found that the onset and pattern of methylation changes during colorectal neoplastic progression are gene specific and that two loci, *SFRP2* and *IGF2*, are particularly specific for colon neoplasms. They have also found that these cumulative changes are closely correlated with a gain of DNMT3B expression, suggesting a causal relationship. These results have significant implications for the use of methylated genes as biomarkers for colon adenomas and/or cancer. ***See page 499***.



Bean-plot representing levels of immunohistochemical expression of DNMT3B in high-risk normal mucosa (HRN), hyperplastic polyps (HP), adenomatous tissue (Ad), primary (pT) and metastatic (M) adenocarcinoma tissue.

NSAIDs and colorectal cancer: not just for breakfast anymore

Non-steroidal anti-inflammatory drug (NSAID) use is well known to decrease both the incidence of colorectal cancer and recurrence of adenomas among patients with prior colorectal neoplasia. However, few studies have investigated the association between NSAID use and colorectal cancer-specific survival. This led Coghill *et al* to assess the role of prediagnostic NSAID use in relation to colorectal cancer-specific survival among cases from the Seattle Colon Cancer Family Registry. They found that NSAID use prior to colorectal cancer diagnosis was associated with a 20% lower rate of colorectal cancer mortality after diagnosis compared with never use (HR 0.79; 95% CI 0.65 to 0.97). Importantly, this relationship was duration dependent and significant. Pronounced reductions in mortality were observed only among proximal colon cancer cases (HR 0.55; 95% CI 0.37 to 0.82). Their findings suggest that regular use of NSAIDs prior to diagnosis is associated with improved colorectal cancer survival, particularly among cases diagnosed with proximal disease and in longer term NSAID users. These results suggest that NSAIDs may be important in the post-treatment care of patients with proximal colon cancer. ***See page 491***.

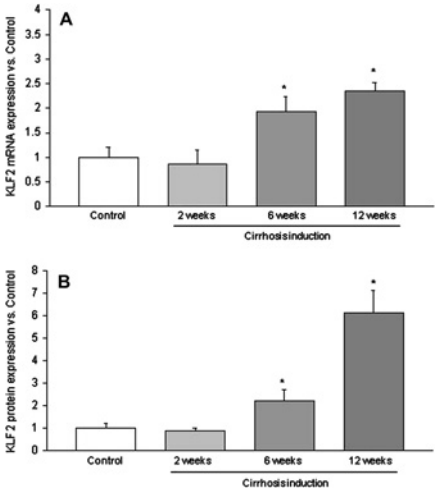


Colorectal cancer survival according to prediagnostic non-steroidal anti-inflammatory drug (NSAID) use.

Hepatology

A new player in portal hypertension

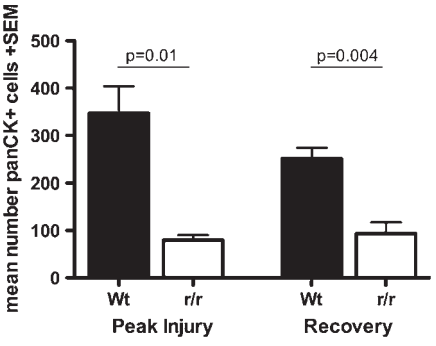
Krupple-like factor 2 (KLF 2) is a transcription factor of the vascular endothelium which protects against inflammation and thrombosis. Moreover, KLF 2 is a potent activator of vasodilators such as C-type natriuretic peptide or endothelial nitric oxide synthase. In their interesting work, J Bosch and his group demonstrate expression of KLF 2 in sinusoidal endothelial cells of the liver. Importantly, rats with cirrhosis show an upregulation of KLF 2 (see figure) and of several of its vasoprotective target genes. To further elucidate the role of KLF 2 they investigated the effects of statins, which were recently shown to reduce portal hypertension in patients with cirrhosis. Simvastatin further increased KLF 2, suggesting it as an important mediator in this respect. Thus, the present work is another step forward in our understanding of portal hypertension in cirrhosis. ***See page 517.***



KLF 2 mRNA (A) and protein (B) expression are increased in cirrhotic liver.

Liver regeneration by hepatic progenitor cells (HPCs) depends on fibrosis

Regeneration is pivotal following acute and chronic liver injury. HPCs reside in niche structures (see *Gut* 2010;**59**:645–54) and play an important role in liver regeneration. In their important study, the groups of S Forbes and J Iredale investigated the role of HPCs in mouse models of chronic liver injury. Interestingly, degradation of the collagen matrix and fibrosis resolution were a prerequisite for activation of HPCs (see figure) and for regeneration. Consequently, remodelling of the extracellular matrix must be considered for strategies to improve liver regeneration. ***See page 525***.



The response of hepatic progenitor cells is markedly reduced in mice with excessive fibrosis (r/r).