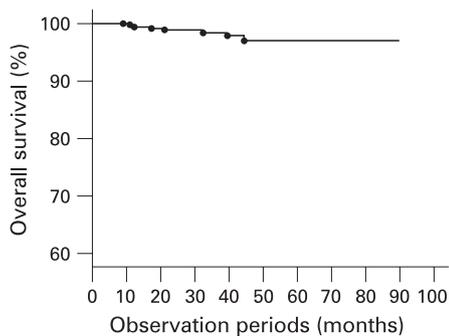


## Excellent prognosis for patients with early gastric cancer treated with endoscopic submucosal dissection

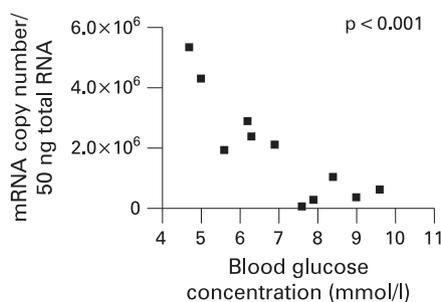
Early gastric cancer (EGC), that is, gastric cancer confined to the mucosa or submucosa, is prevalent in Japan. Endoscopic mucosal resection (EMR) is widely accepted as standard treatment for EGC, but it is not reliable for larger lesions or for EGC with ulcer findings. In preliminary studies, endoscopic submucosal dissection (ESD) has been proposed to be superior to EMR for removing larger or ulcerated EGC in an en bloc manner. In this large follow-up study, including 551 patients with EGC, Isomoto *et al* demonstrate excellent prognosis following ESD, with 5-year overall and disease-specific survival rates of 97.1% and 100%, respectively (see fig). They were able to perform en bloc resection in the majority of cases (94.9%), and 94.7% of the lesions were deemed to have undergone curative resection based on the histopathological evaluation. During follow-up, a small, but significant, number of patients developed local recurrence, as well as metachronous gastric cancers. From this study it can be concluded that the prognosis after ESD for EGC seems to be excellent, but continued surveillance for recurrent tumours is necessary. See page 331.



Overall survival curve of patients with early gastric cancer treated by endoscopic submucosal dissection.

## Taste molecules in the small intestine in mice and men

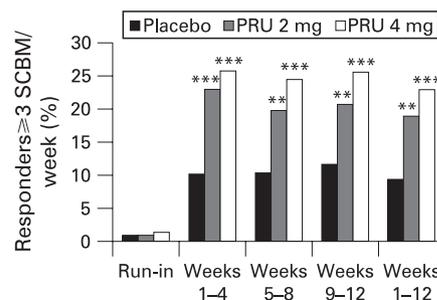
Nutrients in the small intestine generate signals that regulate absorption, gastric emptying and appetite, and give rise to symptoms modulating food intake. The molecular mechanisms by which the small intestine senses different nutrients, such as glucose, are incompletely known. Recent studies have demonstrated taste molecules in the rodent and human small intestine, similar to those found in the tongue. In this issue of *Gut*, Young *et al* present a study in which they assessed the quantitative regional expression of taste molecules in the human upper GI tract and evaluated changes in their expression in patients with type 2 diabetes and in the jejunum in mice after glucose perfusion. The taste molecules were preferentially expressed in the proximal small intestine, that is, in “nutrient detection regions”, which is consistent with a role in “tasting”. Moreover, expression of the taste molecules were inversely correlated with blood glucose concentration in the diabetic patients (see fig), and the transcript levels were reduced after jejunal glucose perfusion in mice. This interesting study will definitely be followed by other studies evaluating the role of taste molecules in different metabolic disorders. See page 337.



Expression of the taste G-protein  $\alpha$ -gustducin was reduced in subjects with type 2 diabetes with increased blood glucose concentrations.

## Benefit of a 5HT<sub>4</sub> receptor agonist in chronic constipation

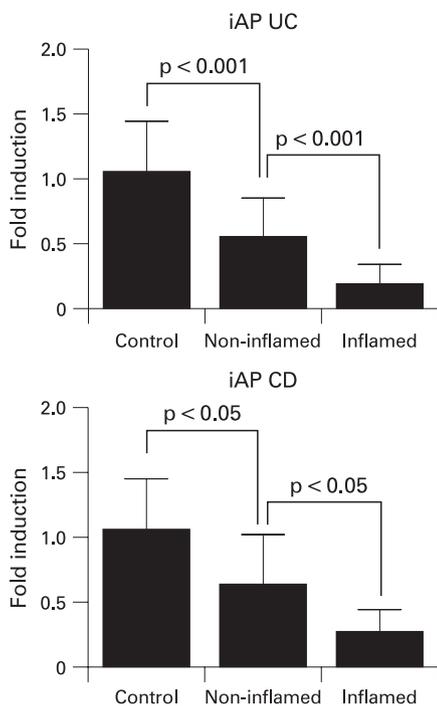
Osmotically acting and bulking agents are currently the most often prescribed medications for chronic constipation but these often cause bloating and discomfort, and around half of patients report dissatisfaction with lack of predictability of their action. Constipation is associated with slow transit through the colon and infrequent propulsive motor patterns. Prucalopride is a highly selective 5HT<sub>4</sub> receptor agonist that increases propulsive motility and accelerates colonic transit. This trial randomised 713 patients with chronic constipation to either placebo or prucalopride 2 mg or 4 mg daily. As the figure shows, prucalopride increased the percentage of patients with  $\geq 3$  spontaneous complete bowel movements (SCBM) per week significantly more than placebo. This represents on average a 14% difference in responder rate, giving a number needed to treat of 7. The most frequent side effects differing significantly from placebo were headache and nausea, and 7%, 6% and 15% of patients discontinued treatment in placebo, 2 mg and 4mg prucalopride treatment arms respectively. Prucalopride may benefit a small but important subgroup of patients who are dissatisfied with standard therapy. See page 357.



Prucalopride increased the percentage of patients with  $\geq 3$  spontaneous complete bowel movements (SCBM). \*\*  $p < 0.01$ , \*\*\*  $p < 0.001$  versus placebo.

### Alkaline phosphatase—a future treatment option for patients with IBD?

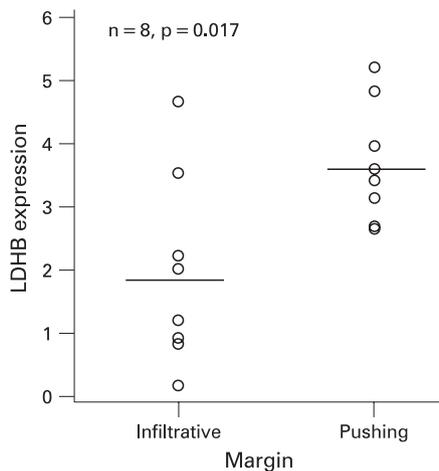
Deficiencies in mucosal response mechanisms against bacterial products, in particular lipopolysaccharide (LPS), are thought to be important in inflammatory bowel disease (IBD). Alkaline phosphatase (AP), an enzyme present along the microvilli in the small intestine, dephosphorylates and detoxifies LPS. This study, assessing the intestinal AP (iAP) expression in intestinal biopsies of control subjects and patients with IBD as well as the effect of iAP tablets on dextran sodium sulfate-induced colitis in rats, is therefore highly interesting. The mRNA levels and enzyme activity of iAP were high in the ileum relative to the colon in healthy subjects, and reduced in patients with IBD, especially in inflamed areas of the colon (see fig). Moreover, iAP tablets significantly reduced the inflammatory activity and improved the morphology of the intestinal wall in the rat model of colitis. These results provide new important insight into the pathophysiology of IBD and suggest that oral administration of iAP in IBD patients may be therapeutically effective. A proof of concept study in IBD patients seems warranted. See page 379.



Intestinal alkaline phosphatase (iAP) mRNA expression in control subjects and non-inflamed and inflamed intestinal tissue of patients with ulcerative colitis (UC) and Crohn's disease (CD).

### Shift in lactate dehydrogenase isoenzymes in infiltrating margin of Duke's C colorectal cancer suggests enhanced lactate production

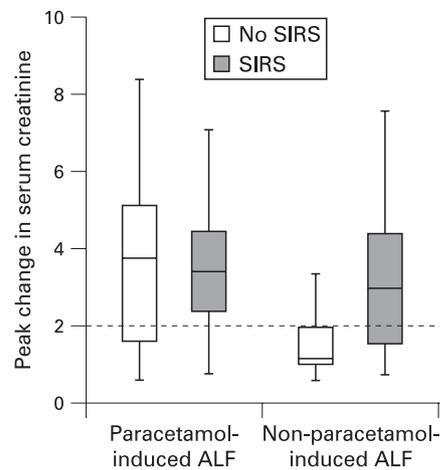
An infiltrating margin in a colorectal cancer (CRC) indicates a poor prognosis, but its underlying molecular characteristics are unknown. Laser-capture microdissection (LCM) allows study of the tumour uncontaminated by stroma, making interpretation of results simpler. The current study used LCM in 16 Dukes B CRC, 8 with an “infiltrative” and 8 with a “pushing” margin, and compared these with 16 normal mucosal samples. mRNA was assessed using a microarray technology and 794 genes identified as differentially expressed in CRC compared with normal, of which 39 were different between the two types of CRC. Microarray results for lactate dehydrogenase B (LDHB), cyclinD2 and serine protease 23 were validated using RT-PCR. As the figure shows, LDHB expression was significantly lower in the infiltrating type. This would be predicted to lead to formation of more of the LDHV isoenzyme, which generates more lactate, a feature that has been shown in other studies to be linked to aggressive histological features of CRC. By furthering our understanding of tumour biology this study may allow better targeting of treatments for this common condition. See page 404.



Reduced lactate dehydrogenase B (LDHB) expression in infiltrating margin of Duke's C colorectal cancer.

### Systemic inflammatory response syndrome predicts renal impairment in patients with acute liver failure not due to paracetamol

Patients with acute liver failure (ALF) commonly develop renal failure, a feature that adversely affects survival. This large retrospective study evaluated predictors of renal injury in 308 non-ventilated patients with ALF admitted to the Scottish Liver Transplant Unit in Edinburgh. At some time during their admission 67% of patients met the criteria for acute renal injury (AKI). Paracetamol overdose was the cause in 70% of patients and these patients were more likely to develop AKI. They were also more likely to develop the systemic inflammatory response syndrome (SIRS), which was diagnosed in 77%, significantly more than in those with non-paracetamol-induced injury (54%). Multivariate analysis showed that AKI was associated with increasing age, SIRS, superimposed infection, hypotension and fulfilling the Kings College Hospital poor prognostic criteria. SIRS was associated with worse renal impairment in those with non-paracetamol-induced ALF but did not appear to alter renal impairment in paracetamol-induced ALF (see fig). The authors argue that the impact of SIRS is due to the toxicity of associated systemic cytokines and advocate a range of measures aimed at reducing SIRS to reduce mortality of ALF. See page 443.



Peak change in serum creatinine in patients with acute liver failure (ALF), with and without SIRS. SIRS was associated with worsening of renal impairment in non-paracetamol-induced ALF but not paracetamol-induced ALF.