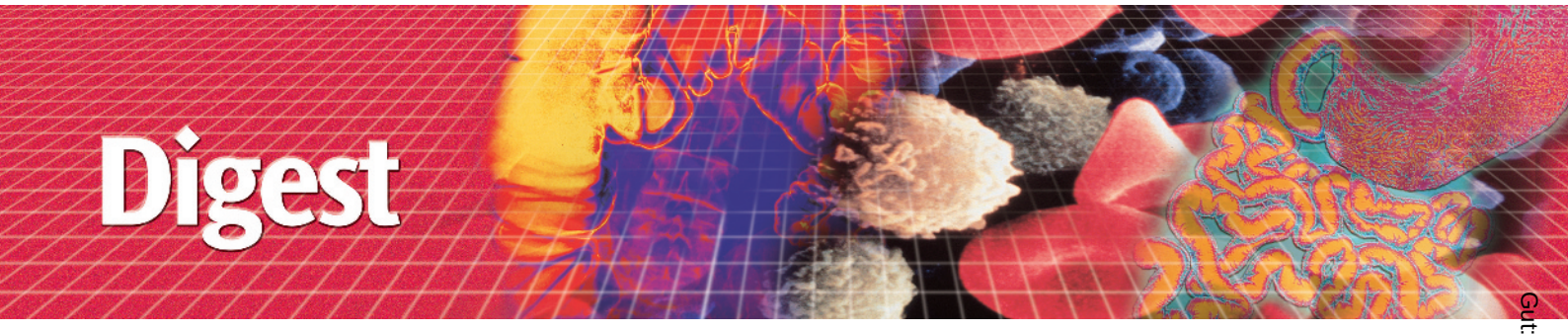
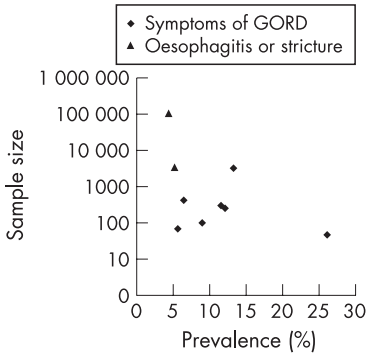
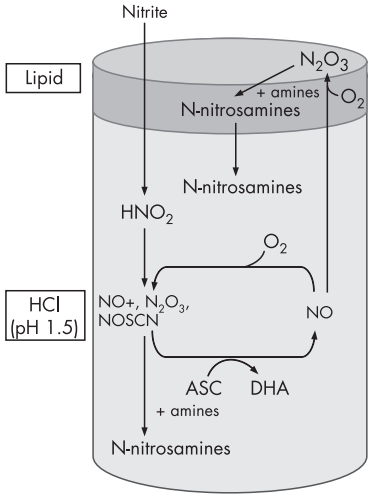


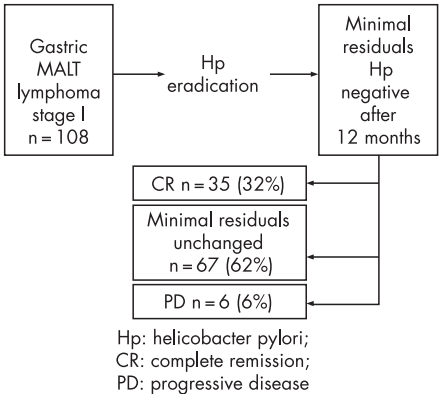
Robin Spiller and Emad M El-Omar, *Editor and Deputy Editor*



Funnel plot showing the prevalence of asthma in patients with gastro-oesophageal reflux disease against sample size.



Proposed mechanism of N-nitrosamine formation in a dual phase system with ascorbic acid present in the aqueous phase.



Hp: helicobacter pylori;
CR: complete remission;
PD: progressive disease

Outcome of patients with minimal histological residuals of gastric mucosa associated lymphoid tissue lymphoma after successful eradication of *Helicobacter pylori*.

THE ASSOCIATION BETWEEN GASTRO-OESOPHAGEAL REFLUX DISEASE AND ASTHMA: A SYSTEMATIC REVIEW

Gastro-oesophageal reflux disease (GORD) is associated with significant extra-oesophageal complications including asthma but the strength and direction of this association is not clear. Havemann *et al* attempt to clarify this issue by systematically reviewing all published studies that examined prevalence or incidence of asthma in patients with GORD or GORD in patients with asthma. The average prevalence of asthma in patients with GORD was 4.6%, compared with 3.9% in controls (see fig). Pooling the odds ratios gave an overall ratio of 5.5 (95% CI 1.9 to 15.8) for studies reporting the prevalence of GORD symptoms in patients with asthma, compared with 2.3 (95% CI 1.8 to 2.8) for those studies measuring the prevalence of asthma in patients with GORD. One longitudinal study showed a significant association between a diagnosis of asthma and a subsequent diagnosis of GORD (relative risk 1.5; 95% CI 1.2 to 1.8). The two studies that assessed whether GORD precedes asthma gave inconsistent results. This analysis suggests that there is a significant association between GORD and asthma but the direction of causality requires further studies.

See p 1654

FAT TRANSFORMS ASCORBIC ACID FROM INHIBITING TO PROMOTING ACID-CATALYSED N-NITROSATION

Carcinogenic N-nitroso compounds are generated from salivary nitrite upon acidification in the proximal stomach. A major factor protecting against this nitrosative chemistry is gastric juice ascorbic acid, which reduces acidified nitrite to nitric oxide. However, nitric oxide can also generate nitrosating species, particularly when it is generated in high concentrations close to lipids. This could have a major relevance to the alarmingly rising rate of junctional cancers. Combet *et al* investigated the effect of lipid and ascorbic acid on the nitrosative chemistry under in vitro conditions simulating the human proximal stomach. They measured the nitrosation of four secondary amines and found that in the absence of lipid, nitrosative stress was inhibited by ascorbic acid through conversion of nitrosating species to nitric oxide. In contrast, when 10% lipid was present, ascorbic acid increased the amount of nitrosated secondary amines compared with its absence. Thus, the presence of lipid overcomes the protective effect of ascorbic acid and transforms it from an inhibitor to a promoter of nitrosation (see fig). Understanding the role of lipids in this process is very relevant to the in vivo situation and will enhance our understanding of proximal cancers.

See p 1678

OUTCOME OF GASTRIC MUCOSA ASSOCIATED LYMPHOID TISSUE LYMPHOMA AFTER ERADICATION OF *HELICOBACTER PYLORI*

Helicobacter pylori eradication leads to complete remission of gastric mucosa associated lymphoid tissue lymphoma in approximately 80% of cases. Patients who have successful eradication but retain minimal persisting lymphoma infiltrates are currently classified as treatment failures and referred for aggressive oncological treatment. Fischbach *et al* conducted a study to see if a strategy of watch and wait could be a safer option. They selected 108 patients from a larger series treated at various European institutions. All patients had successful *H pylori* eradication and normalisation of the endoscopic findings but had lymphoma infiltrates present histologically at 12 months. No oncological treatment was given and the patients had regular follow up with endoscopies and multiple biopsies. After 42.2 months (2–144) of follow up, 102 patients (94%) had a favourable disease course. Of these, 35 (32%) went into complete remission, 67 (62%) showed no changes to their minimal histological residuals and 6 patients (6%) showed local lymphoma progression (see fig). The authors conclude that a watch and wait strategy with regular endoscopies and biopsies appears to be safe and may become the approach of choice in this situation.

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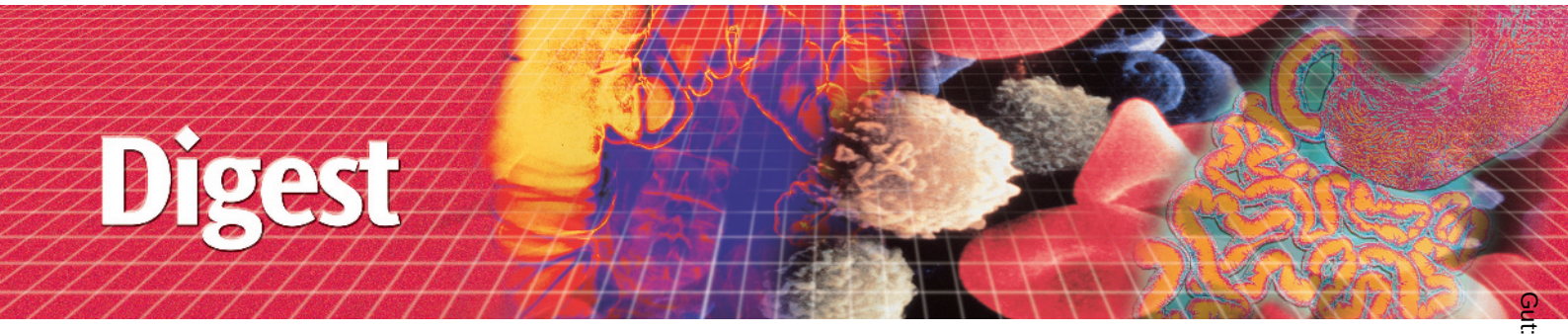

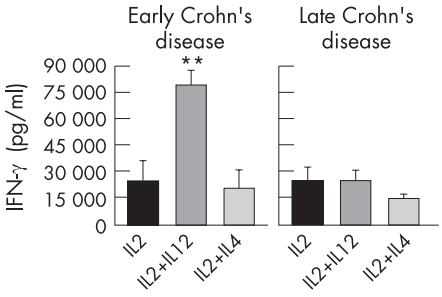

Interferon γ response to interleukin (IL) 12 is significantly greater in early rather than late Crohn's disease.

CHANGING NATURE OF T CELL RESPONSIVENESS IN THE EVOLUTION OF CROHN'S DISEASE

Studying the first attack of irritable bowel disease (IBD), as in the study by Kugathasan *et al*, offers a unique opportunity to separate out primary immunological abnormalities from those secondary to chronic mucosal injury or treatment. Mucosal T cells from children with early IBD (0–6 months from onset, before any treatment) responded to a combination of interleukin (IL) 2 and IL12 with high levels of interferon, similar to that seen in T cells from patients with infective gastroenteritis. By contrast, T cells from those with more chronic disease (5–10 years from onset) failed to show this response (see fig). Increased responsiveness of T cell clones to IL12 correlated with increased expression of high affinity IL12 receptor (IL12Rβ2) mRNA, which was also elevated in mucosal biopsies in early but not late Crohn's disease (CD). These data suggest that treatment of early CD with blockade of the IL12 would have benefits that would not be seen when given in the chronic phase.
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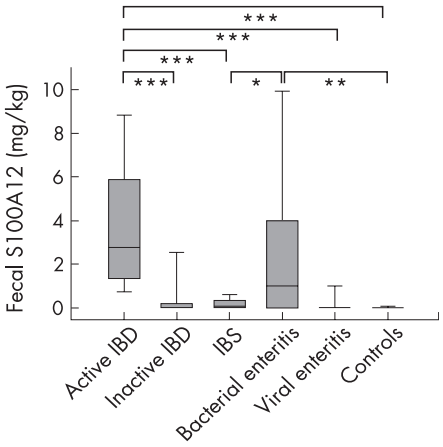
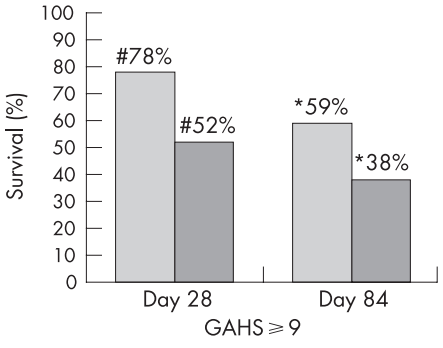


Faecal S100A12 is increased in active inflammatory bowel disease (IBD) and bacterial enteritis but not in irritable bowel syndrome, inactive IBD or viral gastroenteritis, compared with controls. *** $p<0.001$, ** $p<0.01$, * $p<0.05$.

VALUE OF S100A12 AS A MARKER OF ACTIVATION OF INFLAMMATORY BOWEL DISEASE

Simple, non-invasive tests to distinguish acute infection or irritable bowel syndrome (IBS) with diarrhoea from flares in inflammatory bowel disease (IBD) would be of great value in enabling better targeting of investigations and treatment. The study by Kaiser *et al* examines the performance of a novel faecal marker, S100A12. This is secreted by granulocytes and activates NFκB via the receptor for advanced glycation endproducts (RAGE). However, unlike its related molecule calprotectin, S100A12 is not secreted by enterocytes. As the figure shows, S100A12 was elevated in IBD during relapse and less so in bacterial enteritis but not elevated at all in viral gastroenteritis, controls, IBS or inactive IBD. The authors also calculated a histological inflammation score combining endoscopic and histological inflammation and these correlated well with faecal S100A12 in both ulcerative colitis and Crohn's disease. The receiver operating curves showed better sensitivity and specificity of faecal S100A12 in distinguishing IBD from IBS than calprotectin. S100A12 appears to be a simpler and superior technique for assessing gut inflammation than current measures.
See p 1706



Beneficial effect of steroid treatment in those with a Glasgow alcoholic hepatitis score ≥9.

WHICH PATIENTS WITH ALCOHOLIC HEPATITIS BENEFIT FROM CORTICOSTEROID TREATMENT?

Alcoholic hepatitis is an increasing cause of hospital admission with high associated morbidity and mortality. Corticosteroid treatment is of disputed efficacy, hence the value of the study by Forrest *et al*. The authors describe 225 patients admitted to hospital with jaundice (bilirubin >80 mmol) owing to alcohol excess, in whom other causes were excluded and who had a Madrey Discriminate Function score >32 and hence were eligible for corticosteroid treatment according to current guidelines. The Glasgow alcoholic hepatitis score (GAHS) was also calculated. Overall, treatment with steroids was associated with a better 28-day survival, 79% vs 62% compared with those not receiving steroids. Subgroup analysis showed that those with a GAHS <9 showed no benefit, while in those with a GAHS ≥9, survival at 28 days was increased in the group treated with steroids to 78% vs 52% compared with those not treated (see fig). The GAHS is a simple score that can be readily used to predict who would benefit from steroid treatment.