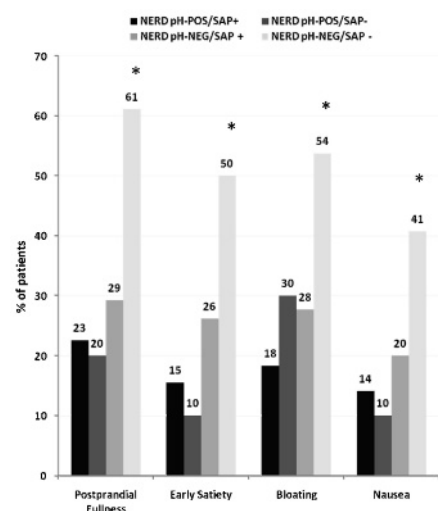


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## Identifying functional heartburn by associated dyspeptic symptoms

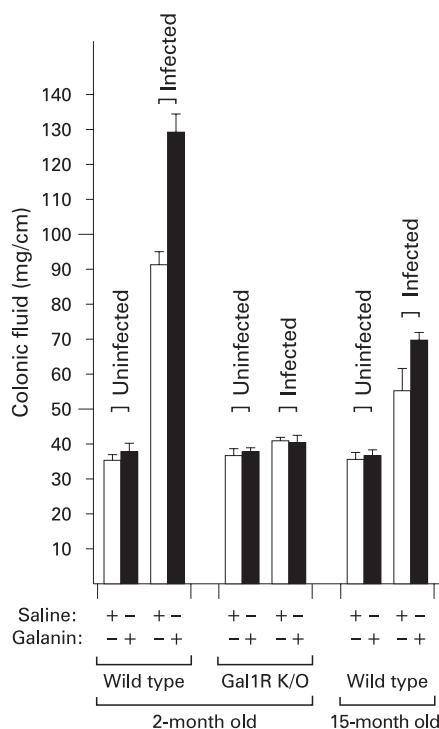
Non-erosive reflux disease (NERD) is the commonest form of reflux, which in some cases is associated with increased acid exposure of the distal oesophagus (NERD pH-POS). Patients with symptoms but normal acid exposure include those with hypersensitive oesophagus with a positive symptom association probability and other cases where there appears to be no temporal link between acid exposure and symptoms. These so called “functional heartburn” (FH) cases are the subject of this study of 200 patients with NERD. Eighty-one patients (41%) had excessive acid exposure, 119 (59%) had normal acid exposure, of which 65 (32%) had hypersensitive oesophagus and 54 (27%) had FH. Patients with FH were more likely to be female (68%) compared with NERD pH-POS (41%) and were characterised by increased prevalence of functional dyspeptic symptoms, including postprandial fullness, early satiety, bloating and nausea (see fig). The proportion of patients with FH reporting a positive response to proton pump inhibitor (PPI) therapy at 29% was significantly lower than the 74% in NERD pH-POS patients. Identifying such patients by their associated dyspeptic symptoms is important since it can avoid fruitless PPI therapy and unnecessary, potentially harmful surgery. **See page 1185**



Prevalence of dyspeptic symptoms in functional heartburn patients (NERD pH-NEG/SAP-).

## Ageing decreases galanin-dependent colonic secretion and may contribute to increased morbidity after Salmonella enteritis

*Salmonella typhimurium* infection is one of the commonest causes of gastroenteritis worldwide. While children get more diarrhoea, they are less likely to die from infection than the elderly. The associated colonic secretion is driven by the neuropeptide galanin, one of whose receptors, Gal1R, is unregulated in salmonella infection. This study examined the age-related differences in this response. Young (2-month-old) wild-type mice gavaged with *S typhimurium* showed increased expression of Gal1R, increased colonic secretion (see fig) and lower rates of bacteraemia compared with infected 15-month-old (elderly) mice who all died by 7 days post gavage. The 2-month-old Gal1R knockout

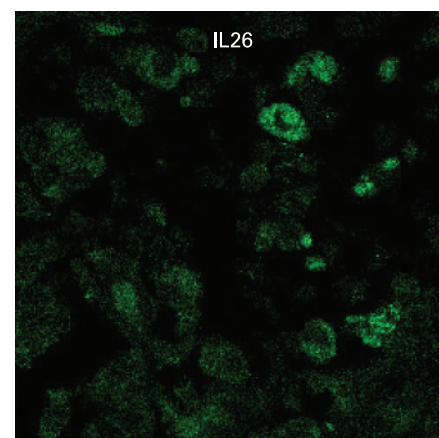


Colonic secretion in closed colonic loops in infected and uninfected 2-month-old wild-type and Gal1R knockout (K/O) mice compared with 15-month-old wild-type. Solid bars show the effect of 1  $\mu$ M galanin compared with saline (clear bars).

mice showed a profile similar to the elderly mice. Adding 6% polyethylene glycol to the drinking water increased colonic secretion, reduced bacterial translocation to the liver and spleen and prevented any deaths. This study clearly shows the protective effect of colonic secretion associated with diarrhoea, lack of which may account for increased mortality in the elderly compared with children. **See page 1201**

## The role of the novel Th17 cytokine IL-26 in intestinal inflammation

Interleukin (IL)-26 is an IL-10-like cytokine expressed in T helper (Th) 1 and Th17 cells. Th17 cells are a newly discovered subset of inflammatory T cells that differentiate in humans under the influence of IL-1, IL-6, IL-21 and IL-23. Th17 cells contribute to the pathogenesis of many inflammatory autoimmune diseases such as multiple sclerosis, rheumatoid arthritis and inflammatory bowel diseases. The function of this novel cytokine IL-26 in human disease is unknown. In this study, the authors investigated its role in intestinal inflammation. IL-26 signals through a receptor pair consisting of the transmembrane proteins IL-20R1 and IL-10R2. The authors showed that all intestinal epithelial cell lines express both IL-26 receptor subunits. Furthermore, IL-26 activates extracellular signal-related kinase-1/2 and

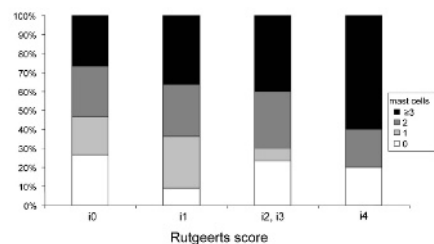


Immunofluorescence analysis of interleukin (IL)-26.

stress-activated protein kinase/c-Jun N-terminal kinase, mitogen-activated protein kinases, Akt and signal transducers and activators of transcription 1/3. Upon stimulation of IL-26, the mRNA expression of proinflammatory cytokines was increased and cell proliferation decreased. IL-26 mRNA expression was increased in the inflamed colon of patients with Crohn's disease (CD). Immunohistochemical analysis demonstrated IL-26 protein expression in colonic T cells including ROR $\gamma$ T-expressing Th17 cells (see fig). There was an increased number of colonic IL-26 expressing cells in active CD. *See page 1207*

### Plexitis as a predictive factor of early postoperative clinical recurrence in Crohn's disease

Many patients suffering from CD need to undergo intestinal resections during the course of their disease. Surgery is, however, no cure and lesions very often recur. In the absence of predictors of postoperative CD recurrence, early endoscopy is proposed to detect early lesions after ileocaecal resection. Previously, the presence of myenteric plexitis in the proximal resection margins was shown to be predictive of early endoscopic recurrence. In the current study, 164 consecutive patients undergoing ileocolonic or ileal resection for active CD were studied. Early clinical recurrence of CD occurred in 28.1%. In multivariate analysis, factors associated with postoperative recurrence were active smoking (hazard ratio (HR) 1.94), submucosal plexitis (HR 1.87) and a disease-free resection margin <5 cm (HR 0.52). The authors conclude that submucosal plexitis is associated with early clinical recurrence. Enteric plexus inflammation (mast cell-associated plexitis) left in place after surgical resection for CD may,

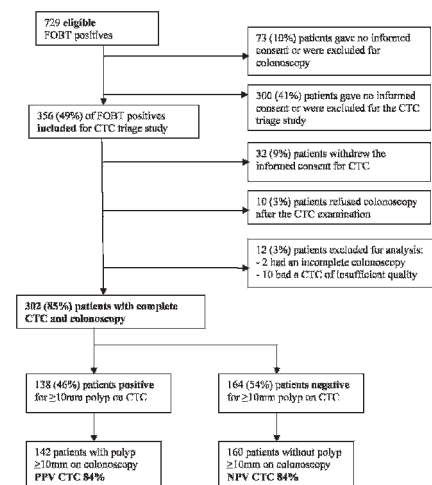


Correlation between mast cells submucosal plexitis and postoperative endoscopy (Rutgeerts score).

therefore, lead to early gut inflammation and early clinical recurrence. Further studies should now establish whether a more aggressive treatment of patients with proctitis after surgery could reduce their risk of recurrence. *See page 1218*

### CT colonography after positive faecal occult blood test in colorectal cancer screening

The lifetime risk for colorectal carcinoma (CRC) is in the order of 6% and it represents a major cause of cancer deaths. Early detection of CRC and adenomas could reduce mortality. Screening with faecal occult blood test (FOBT) has been demonstrated to reduce CRC-related mortality by 14–16% over 10–18 years. However, false positive FOBTs are not infrequent and lead to unnecessary colonoscopies. In this study, the authors investigated the introduction of CT colonography (CTC) as a triage instrument for patients presenting with a positive FOBT. A total of 302 FOBT-positive patients underwent CTC before colonoscopy. In 22 patients (7%), a CRC was found and 211 (70%) had a lesion  $\geq$  6mm. The sensitivity for CTC was 91% and specificity 69% for the detection of colonoscopy lesions  $\geq$  6 mm. The positive predictive value of CTC was 87% and the negative predictive value was 77%. Using CTC as a triage technique in 100 FOBT-positive patients would mean that colonoscopy could be avoided in 28 patients but lesions  $\geq$  10 mm would be missed in 2 patients. The authors conclude that CTC

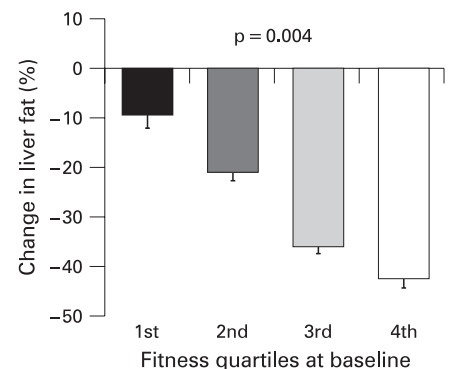


Flowchart of FOBT-positive participants.

has reasonable predictive values in a FOBT-positive population. However, given the high prevalence of relevant lesions in FOBT-positive patients, CTC is unlikely to be an efficient triage technique. *See page 1242*

### Diet and exercise programmes reduce liver fat most in those who are capable of the greatest exertion

Non-alcoholic fatty liver disease (NAFLD) is a major health concern, being a risk factor for developing insulin resistance, type II diabetes and cardiovascular disease. Weight loss is the main treatment but there is a wide variation in the reduction of hepatic fat for any given weight loss. Exercise is also an important factor and physical fitness—as assessed by maximal aerobic capacity (VO $_{2,max}$ )—inversely correlates with hepatic fat, although the underlying mechanism is uncertain. The present study examined the effect of a 9-month diet and exercise programme in 50 adults with NAFLD and 120 controls at risk from metabolic disease. Total fat, visceral and hepatic fat were assessed by proton magnetic resonance and fitness from VO $_{2,max}$  during exercise to exhaustion on a bicycle ergometer. VO $_{2,max}$  was the strongest predictor of reduction in liver fat (see fig). Cardiovascular fitness is closely associated with mitochondrial function, which may determine the loss of hepatic fat in response to exercise. Patients with lower levels of cardiovascular fitness may well require drug treatment rather than exercise to normalise hepatic fat. *See page 1281*



Increasing fitness as assessed by maximal aerobic capacity was associated with increasing reduction in liver fat.