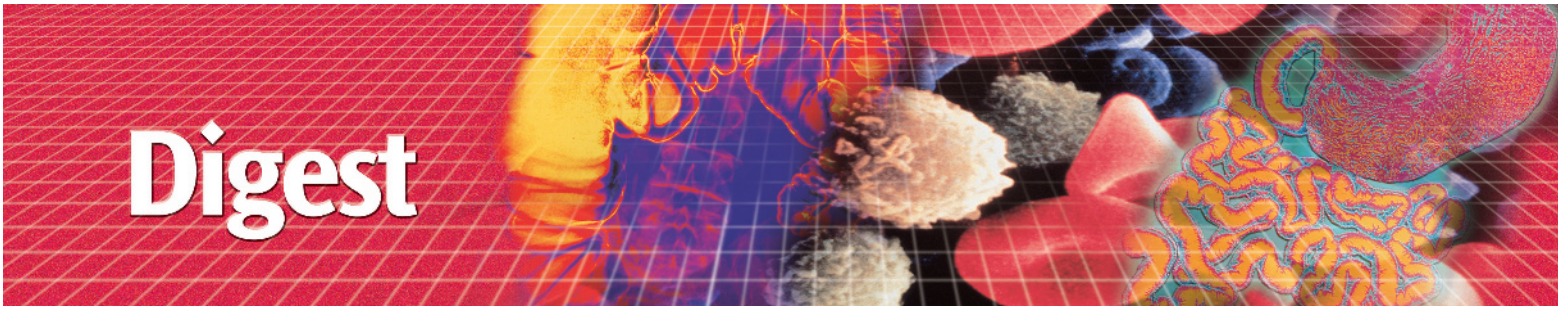


Robin Spiller and Alastair Watson, *Editor and Assistant Editor*

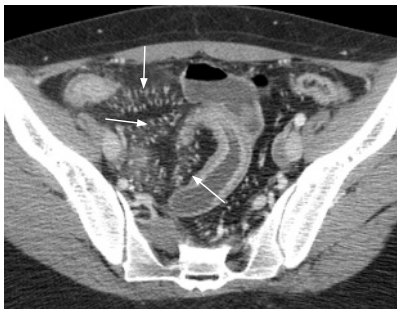
Associations between long term use of acid suppressing drugs and risk of oesophageal adenocarcinoma (OA) compared with non-users stratified by treatment indication

Exposure	Controls	OA	OR (95% CI)
Oesophageal	125 (1.2)	16 (5.6)	5.42 (3.13–9.39)
Other indications	218 (2.2)	10 (3.5)	1.74 (0.90–3.34)

GASTRIC ACID SUPPRESSION AND THE RISK OF OESOPHAGEAL AND GASTRIC CANCER

It has long been suspected that long term gastric acid suppression might be associated with adenocarcinoma of the oesophagus and stomach. This is the first prospective study examining this question. The study is large, including 4 340 207 patient years follow-up from the British General Practitioner's research database. Patients given acid suppressing drugs for reflux symptoms had a fivefold increased risk of oesophageal adenocarcinoma, whereas patients treated for gastroduodenal symptoms were not at increased risk. Similarly, patients given acid suppressing drugs for gastric and duodenal ulceration had a fourfold increased risk of gastric non-cardia adenocarcinoma, whereas those treated for oesophageal or other gastroduodenal symptoms were not. Together, these data suggest that the increased risk is derived from the underlying disease and not the acid suppressing drugs themselves.

See p 1538



Crohn's ileitis. Arrows indicate a moderate ''comb sign''.

CORRELATION BETWEEN CRP AND CROHN'S DISEASE ACTIVITY

Assessment of Crohn's disease is conventionally monitored by a combination of symptoms, clinical signs and the measurement of serological markers of inflammation such as C reactive protein (CRP). However, it is less clear if computed tomography (CT) enterography can assess disease activity and whether CT changes correlate with CRP. In this study small bowel inflammation was assessed by CT enterography in 143 patients with Crohn's disease. Endoscopic scores correlated significantly with CT bowel enhancement, engorgement of the vasa recta (''the comb sign'') and fat density. Correlation was also found with histological evaluation of inflammation. Of particular interest, the strongest correlate with CRP level was the degree of fat density on CT enterography; there was little correlation of CRP with inflammation confined to the bowel wall. This adds to the evidence that mesenteric fat contributes to the immune response in Crohn's disease.

See p 1561

Table 2 Probiotic pretreatment prevents bacterial translocation to mesenteric lymph nodes in rats subjected to water avoidance stress

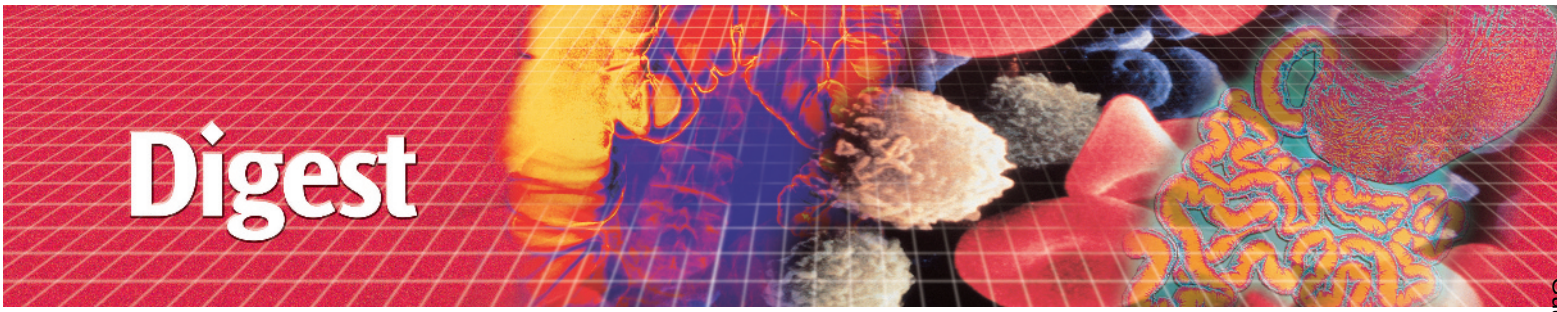
Group	No of rats affected/total no of rats in group	No of CFU/MLN of rats (median (range))
Control	0/4	0
Probiotics	0/4	0
WAS	4/6	1381 (360–2012)
Probiotics +WAS	0/4	0

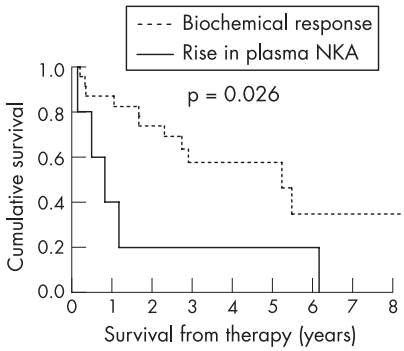
PROBIOTIC *LACTOBACILLUS* PREVENTS BACTERIAL TRANSLOCATION AND IMPROVES BARRIER FUNCTION IN RATS AFTER PSYCHOLOGICAL STRESS

Probiotics are non-pathogenic bacteria that promote health. They have been shown to improve a variety of inflammatory conditions of the intestine. Stress is a risk factor for inflammatory bowel disease. The effect of the probiotic species *Lactobacillus* on bacterial translocation and intestinal barrier function was studied in stressed rats, induced by placing them in warm water. This stimulus increased bacterial translocation and reduced barrier function as measured by transepithelial conductance. Pretreatment with *Lactobacillus* completely prevented bacterial adhesion and translocation to mesenteric lymph nodes. The treatment also increased the short circuit current (a measure of ion transport) but had no effect on transepithelial conductance. The mechanisms of these effects are currently unknown. These data emphasise the importance of luminal bacterial ecology in the regulation of intestinal epithelial function.

See p 1553

Gut: first published as on 17 October 2006. Downloaded from http://gut.bmj.com/ on April 23, 2024 by guest. Protected by copyright.



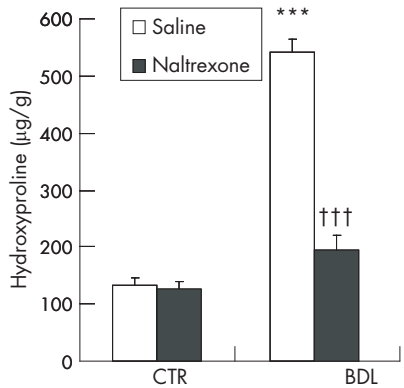


Kaplan-Meir plot showing the effect of rise in plasma NKA on survival.

FALLING PLASMA NEUROKININ A IS A MARKER OF IMPROVED SURVIVAL IN CARCINOID PATIENTS TREATED WITH SOMATOSTATIN ANALOGUES

Carcinoid tumours are rare, making randomised placebo controlled trials difficult. Somatostatin analogues (SS), which give symptomatic relief, are widely used although their effect on survival is uncertain. The team in Belfast studied 139 such patients over the past 22 years using a range of markers, including liver imaging, plasma neurokinin A (NKA) and urinary 5HIAA, in an attempt to predict survival. Eighty per cent had liver metastases at presentation and median survival was 53% (95% CI 44 to 62%) at 5 years. Both NKA and 5HIAA increased with tumour progression. Thirty three patients had complete data before and after treatment with somatostatin analogues. Changes in urine 5HIAA did not predict survival; however, 1-year survival was 81% in the 22 patients with a fall in NKA, but just 40% in the 5 whose NKA rose (see fig). The authors conclude that serial NKA can be used for early detection of those failing to respond to somatostatin analogues, allowing an earlier switch to more aggressive treatment.

See p 1586

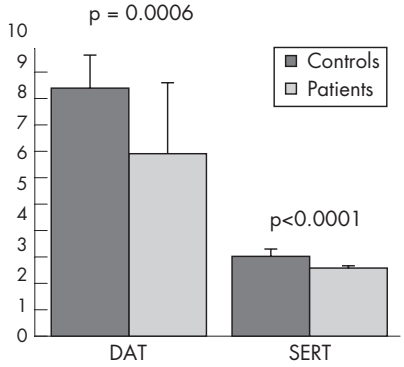


Bile duct ligated (BDL) rats showed significantly increased hepatic hydroxyproline compared with controls (CTR), an effect which naltrexone largely prevented.

BRAIN–LIVER INTERACTIONS

The importance of brain–gut interactions have long been recognised, but emerging evidence suggests there are also important brain–liver interactions. Plasma opioids increase in liver disease and intracerebral opioid agonists decrease hepatic glutathione (GSH) synthesis. Recent evidence suggests that naltrexone, an opioid antagonist, can attenuate hepatic fibrosis, something this study confirmed using bile duct ligated rats, showing a significant reduction in fibrosis (see fig). This was associated with a 40% reduction in activated hepatic myofibroblasts as assessed by α-smooth muscle actin staining. Naltrexone blocked the fall in hepatic GSH and largely prevented the alteration in redox state resulting from bile duct ligation. Activated rat hepatic stellate cells were shown to express opioid receptors while opioid ligands increased procollagen 1 and tissue metalloproteinase expression, providing evidence of the mechanism whereby opioids contribute to hepatic fibrosis. Whether opioid antagonists can reduce hepatic fibrosis and prevent disease progression in humans remains to be proven.

See p 1606



Dopamine transporter binding (DAT) and serotonin transporter binding (SERT) in patients and controls.

ABNORMAL BRAIN AMINES IN HEPATITIS C VIRUS (HCV) INFECTED PATIENTS WITH CHRONIC FATIGUE

Chronic fatigue and cognitive dysfunction are frequent symptoms in HCV which surprisingly do not correlate with liver dysfunction but do respond to the serotonin receptor antagonist, ondansetron. Several studies have shown there is altered cerebral metabolism thought to be caused by HCV infected macrophages entering the brain. This study examined 20 HCV infected patients with normal liver function but debilitating chronic fatigue and cognitive decline. I-123-β-CIT, a radiolabelled ligand for the 5HT (SERT) and dopamine transporter (DAT) was used to perform single photon emission tomography (SPECT) to create a 3D image of the binding sites in the brain. Figure shows abnormally low DAT binding at 24 h in the patients. Psychometric tests showed greater impairment in those with reduced ligand binding, particularly when both transporters were reduced. The results suggest that treatment of such patients should focus on altering serotonin and dopamine neurotransmission rather than just the liver.

See p 1624

Gut: first published as on 17 October 2006. Downloaded from http://gut.bmj.com/ on April 23, 2024 by guest. Protected by copyright.