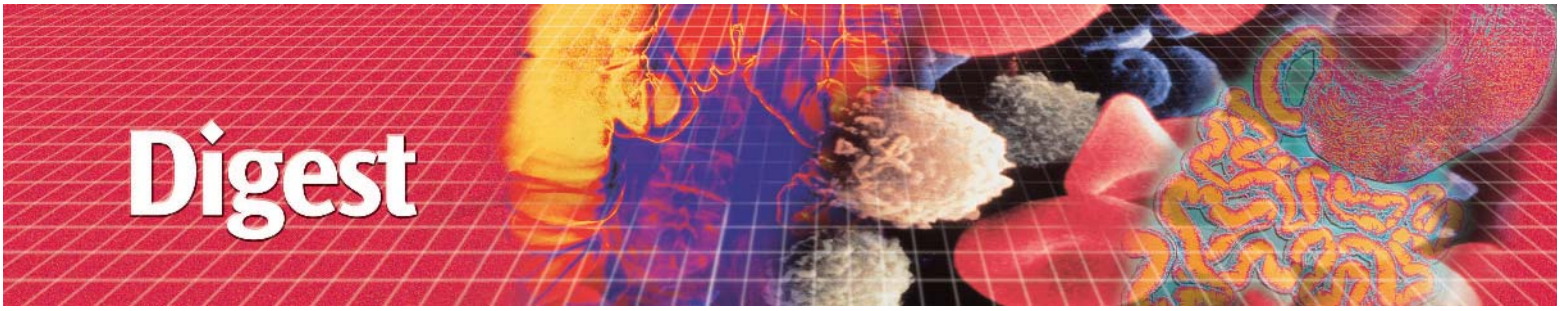

Robin Spiller, *Editor*

Could this be reflux induced cough?

Gastroenterologists are often referred patients with persistent cough from their ENT colleagues with the question ''Could this be reflux induced cough?'' Traditional pH recordings demonstrate a strong association between reflux and cough in some, but others remain a mystery. The study from Leuven of 22 such patients shows that oesophageal impedance monitoring can detect non-acidic reflux, which is missed by traditional pH monitoring. Ten patients were shown to have reflux induced cough and three of these would have been missed using traditional pH monitoring alone. Because this leads to significantly different treatment, patients with unexplained chronic cough should have oesophageal impedance monitoring if clinical impressions are not supported by 24 hour pH recordings.
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Detecting hereditary defuse gastric cancer by chromoendoscopy

Hereditary diffuse gastric cancer is a rare but devastating genetic condition caused by a mutation that inactivates the cell to cell adhesion molecule E-cadherin. Those with this mutation have a 70% chance of developing gastric carcinoma in their early 30s. Because prophylactic gastrectomy is associated with considerable morbidity and even mortality, a reliable endoscopic surveillance method would have some appeal. Shaw and colleagues describe 33 patients with the relevant mutation who underwent yearly chromoendoscopy using the congo red/methylene blue method. Congo red was given after an injection of gastrin to stimulate acid secretion, which turns the dye from red to dark blue. Early gastric cancers that do not secrete acid show up as a pale area. Fifty six such lesions, not visible on standard endoscopic examination, were identified and biopsies were taken, 41% of which proved to be signet ring cancers. During the five years of study, 10 of the 33 CDH-1 mutation carriers underwent gastrectomy, all of whom showed early gastric cancer with no lymph node spread. Because 100% of mutation carriers will have microscopic foci, endoscopy may allow identification of disease progression and gastrectomy once larger lesions appear.
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Osteoprotegerin and IBD bone loss

Many factors influence the severity of bone loss in IBD patients. Mouse models of IBD have shown that one factor, so far ignored by gastroenterologists, may be a ligand (RANKL) that stimulates bone osteoclastic activity by binding to its receptor (RANK). Osteoprotegerin (OPG) is a natural decoy receptor for RANKL and can reverse osteopenia in mice with colitis due to IL-2 deficiency. In mouse models, bone loss appears to be mediated via the RANKL/RANK system with the rise in OPG representing a later compensatory response. Moschen *et al* studied 180 IBD patients and found colonic biopsies from IBD patients secreted nearly double the amount of OPG than controls did, with a tripling of the OPD to soluble RANKL ratio. Significantly, this ratio was much increased in those with osteoporosis. Increased release of OPG was demonstrated ex vivo in cultured colonic biopsies from inflamed but not uninflamed colon. Immunofluorescence suggested that OPG originates mainly from macrophages while RANKL comes from T lymphocytes. Plasma levels of soluble RANKL were significantly increased in untreated IBD patients although normal in those on treatment. The real interest here is in the possibility of the use of RANKL antagonists as a novel approach to inhibit osteopenia in IBD patients.
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Endocannabinoids mediate selective splanchnic vasodilatation in cirrhosis

Recent studies have shown that cirrhotic patients' circulating monocytes overproduce anandamide (AEA), one of the natural ligands for the cannabinoid CB1 receptor, which mediates systemic vasodilatation. Using rats with carbon tetrachloride induced cirrhosis, the authors show that cirrhotic rats' mesenteric arteries were hypersensitive to AEA. This effect was reduced by specific CB1 and TRPV1 receptor antagonists. CB1 receptor mRNA was increased in the mesenteric but not the femoral circulation of cirrhotic rats and immunofluorescence staining confirmed increased levels in peri-vascular sensory nerves and adventitial cells. AEA also acts on TRPV1 receptors, found only on afferent nerves, to release CGRP, which is a known vasodilator. These studies point the way to new ways of pharmacologically controlling portal hypertension.
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Hepatocellular carcinoma—another manifestation of the metabolic syndrome?

The incidence of hepatocellular carcinoma (HCC) has nearly tripled since the 1980s. While a proportion of this is due to hepatitis C virus (HCV), up to half of all cases have no obvious cause. The Surveillance Epidemiology and End Result (SEER) programme in the United States identified 2061 cases of HCC and compared them with 6183 controls, all over the age of 65 years. Diabetes was found in 43% of HCC patients. Because HCC patients get intensively investigated this might reflect an ascertainment bias; however, the incidence remained high (32%) even when those in whom diabetes was identified within two years of HCC diagnosis were excluded. Multiple logistic regression indicated that diabetes trebled the risk of HCC. Even after excluding patients with known risk factors for HCC (HCV and HBV, alcoholic liver disease, and haemochromatosis) the relative risk was 2.9 (2.5 to 3.3). Although this risk is much lower than that associated with haemochromatosis (odds ratio (OR) 8.9), and HCV (OR 24) diabetes is much commoner and appeared to be the only factor in 32% of HCC patients. This provides yet one more example of how controlling the rising tide of obesity and its associated diseases might improve public health.
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