Digest

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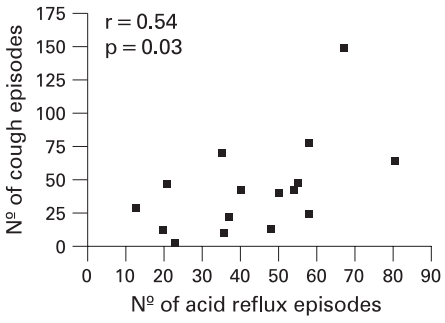
Gastro-oesophageal reflux is common in patients with cystic fibrosis and can lead to poor lung function

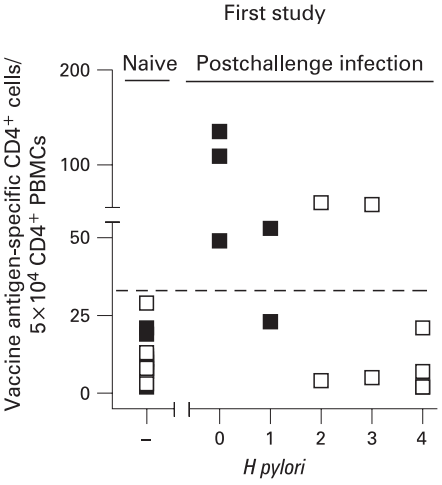
Increased acid gastro-oesophageal reflux (GOR) has been reported in patients with cystic fibrosis (CF). However, its prevalence, characteristics, association with gastric aspiration and impact on respiration are not completely understood. In the study by Blondeau and colleagues, patients with CF underwent: impedance-pH measurement for reflux detection; assessment of the association between reflux and cough; and measurement of bile acids in saliva and bronchoalveolar lavage as surrogate markers for gastric aspiration. Increased GOR was present in 28/33 patients and this was mainly due to acid reflux. However, a small proportion of the patients demonstrated a reflux pattern of mixed acid and weakly acidic reflux, whereas some had mainly weakly acidic reflux. Importantly, reflux did not seem to be secondary to cough because most of the time reflux preceded cough and not the opposite. Gastric aspiration was common, as evidenced by bile acids in saliva in 16/38 patients and in bronchoalveolar lavage fluid in 6/10 patients. Reflux was associated with cough (see fig) and also with poorer lung function. Outcome studies in patients with CF using anti-reflux treatment seem warranted. ***See p 1044***



A significant correlation between acid exposure and number of cough episodes.

Clearance of *Helicobacter pylori* infection in man after vaccination: role of T helper cells

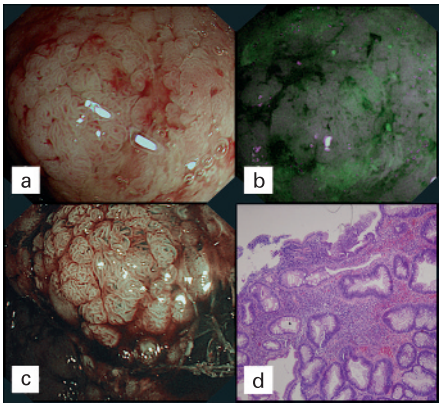
H pylori infection remains a major world health problem and an effective vaccine remains an attractive but as yet unattainable option. Protection against *H pylori* infection in animal models depends on the induction of T helper cells, while natural infection in man induces regulatory T cells that inhibit T cell responses. The study by Aebischer and co-authors tested recombinant live vaccines based on *Salmonella typhi* engineered to express either *H pylori* urease A or B or the protein HP 0231. Two prospective, randomised, double-blind vaccination trials were tested in human volunteers negative for *H pylori* infection who were dosed with either control *S typhi* or the engineered ones. On day 42, volunteers were challenged with *H pylori,* which caused transient dyspeptic symptoms and infection in about 65%. Overall, vaccination did not enhance clearance. However, those who did clear the infection were shown to have a greater proportion of *H pylori* specific T cells (fig). Although efficacy of these vaccines was unsatisfactory, they were safe and the link between *H pylori* clearance and T cell response is encouraging, although plainly further work is required to improve efficacy. ***See p 1060***



Proportion of CD4 T lymphocytes responsive to *H pylori* was inversely related to the *H pylori* score (number of positive tests for *H pylori*).

Endoscopic tri-modal imaging seems to be useful for surveillance in ulcerative colitis

Colonoscopic surveillance with random biopsies is performed in patients with longstanding ulcerative colitis (UC) to detect neoplastic lesions at an early stage, thereby improving the prognosis. However, neoplasia is frequently missed, leading to interval cancers. In this study, van den Broek and co-workers assessed the value of endoscopic tri-modal imaging (ETMI), incorporating white light endoscopy (WLE), autofluorescence imaging (AFI) and narrow band imaging (NBI) for the detection and classification of neoplasia in 50 patients with long-standing UC in a randomised trial. Each colonic segment was investigated twice; once with WLE and once with AFI, in random order. Detected lesions were investigated with NBI (pit pattern analysis) and random biopsies were taken. Neoplasia miss rates for AFI and WLE were 0% vs 50% ($p = 0.036$). Pit pattern analysis by NBI had a moderate accuracy for the prediction of histology. All neoplasias were coloured purple on AFI. Random biopsies detected no additional neoplasias. ETMI seems to be useful for surveillance in long-standing, extensive UC. ***See p 1085***



Images during white light endoscopy (a), autofluorescence imaging (b) and narrow band imaging (c) of a mass revealing low-grade intraepithelial neoplasia on histopathology (d).

Insulin-like growth factor 1 promoter polymorphism markedly influences risk for colorectal cancer in Han Chinese

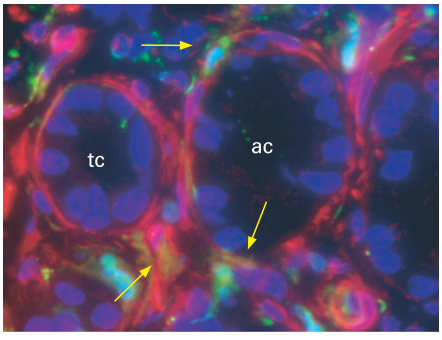
Colorectal cancer (CRC) rates have doubled in South East Asia in the past two decades, possibly related to the adoption of a Western diet, which significantly increases serum insulin-like growth factor 1 (IGF1). Population studies suggest elevated IGF1 levels are associated with an increased risk of CRC. The study by Wong and colleagues explored the evolutionary conserved regions of the IGF1 gene and identified a common (minor allele frequency = 0.36) single nucleotide polymorphism SNP *IGF-2995* C/A. This polymorphism was predicted to be functional, the A allele preventing the binding of the transcription factor octamer binding factor (OCT-2), which is over expressed in CRC. This polymorphism is common in Han Chinese but rare in Europeans and Asians. Possession of the A allele markedly reduced the risk of CRC by 41% (see table). An even larger effect was seen in those who were physically active, where the reduction was 70%. Surprisingly, there was no link between the polymorphisms and serum IGL1 but these may not be a good marker of local tissue exposure. This study makes it clear that the relative importance of various genes in CRC will vary by ethnic group and will interact with environmental and lifestyle factors, which should now be looked for in other populations. ***See p 1092***

Odds ratios for developing colorectal cancer in Han Chinese. Possession of the A allele reduced the risk by 41%

Genotype	Controls (%)	Cases (%)	OR (95%CI)
CC	482 (42.2)	160 (53.7)	1.00 (referent)
CA	532 (46.6)	106 (35.6)	0.56 (0.42,0.75)
AA	128 (11.2)	32 (11.7)	0.68 (0.43,1.07)
CA + AA vs CC			0.59 (0.45,0.77)

Bone marrow-derived cells contribute to the pancreatic stellate cell population in chronic pancreatitis

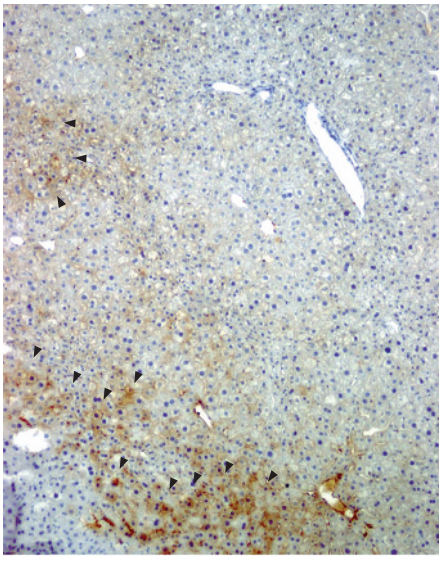
Chronic inflammation is a risk factor for cancer development and bone marrow-derived progenitor cells (BMDCs) seem to have a major role in chronic inflammation-based carcinogenesis. In the study by Marrache and co-authors, the role of BMDCs in chronic pancreatitis in mice was evaluated. After bone marrow transplantation, chronic pancreatitis was induced by repeated cerulein injections. The fate of BMDCs was followed using two different bone marrow markers and the phenotype of engrafted BMDCs was based on co-expression of bone marrow and pancreatic markers. BMDCs did engraft the pancreas after induction of pancreatitis and mainly contributed to the pancreatic stellate cell pool (see fig) and, to a lesser extent, to pancreatic duct cells. Importantly, pancreatic stellate cells derived from BMDCs could be activated, as shown by α-smooth muscle actin expression. These data suggest a potentially important role for BMDCs in tissue repair in the pancreas during inflammation. As no preneoplastic lesions developed, the role of BMDCs in pancreatic carcinogenesis could not be evaluated in this study. ***See p 1110***



Bone marrow-derived pancreatic cells surrounding an acinus (ac) and a tubular complex (tc).

Isolating hepatic progenitor cells from adult human liver for transplantation treatment

Harnessing the legendary regenerative properties of hepatic progenitor cells to overcome the shortage of liver donors is an attractive option. A key step in making this possible is the isolation of progenitor cells from adult liver and their expansion prior to retransplantation. The study by Weiss and co-workers digested human liver tissue and isolated hepatic progenitor cells using an immuno-magnetic activated cell sorting based on a monoclonal antibody to a stem cell marker CD90 (Thy-1). Thy-1 expression was found in the portal tract area and scattered in the surrounding parenchyma. Fluorescence-activated cell sorting analysis showed about 60% of Thy-1 cells were positive for liver progenitor markers, including M2PK the fetal isoform of pyruvate kinase, the biliary marker CK19 and HepPAR1, a hepatocyte specific marker, thereby demonstrating their pluripotential nature. After partial hepatectomy and treatment of the recipient mice with an inhibitor of regeneration these cells were injected intrasplenically. Human hepatic cells were detected in the mouse liver 7 weeks later and were seen to be functioning normally producing human albumin (see fig). At present, repopulation efficiency is low and ways are needed to improve the regenerative potential, a topic which should be the focus of further research. ***See p 1127***



Engrafted cells (arrows) expressing human albumin in the transplanted mouse liver.