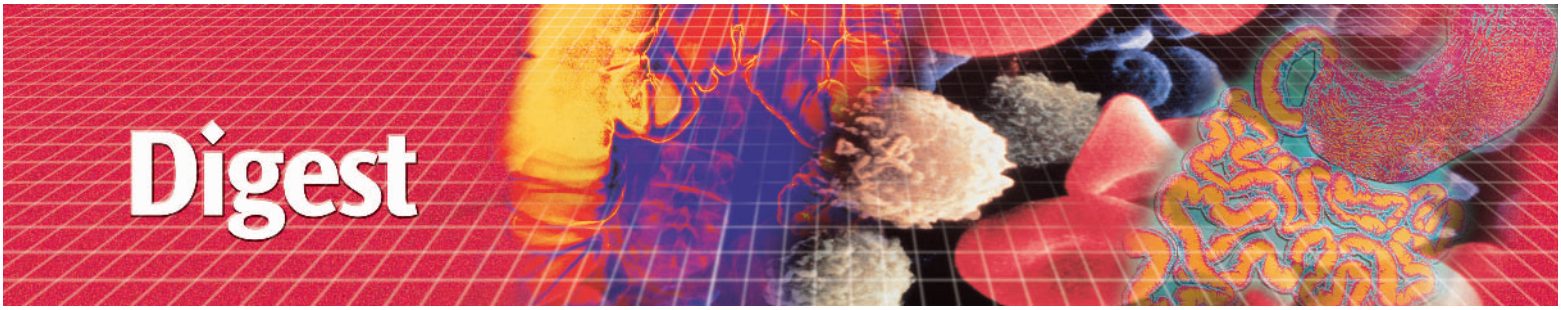

Robin Spiller, *Editor*

ALL THE EXCITEMENT ABOUT HEPCIDIN

In this issue we have an important original article which we felt would be worth supporting with both a leading article focusing on the molecular biology as well as a commentary setting this in context for clinicians. We hope you enjoy reading both, and the article which describes a new assay for prohepcidin which proves to be decreased in haemochromatosis, supporting the idea that hepcidin is a key molecule in regulating iron absorption.
See page 735

ROLE OF TRANSGLUTAMINASE ANTIBODIES IN THE EXTRAINTESTINAL MANIFESTATIONS OF COELIAC DISEASE

While coeliac disease has usually been considered a T cell mediated disorder it is well recognised that coeliac have circulating antibodies to a widely distributed enzyme, transglutaminase 2 (TG2). Whether these antibodies exert important biological effects in vivo is uncertain but in vitro they certainly can. The present issue of *Gut* examined the binding of these antibodies to a wide range of tissues including normal jejunal biopsies from patients who subsequently developed coeliac disease together with biopsies of lymph nodes, liver, skeletal muscle and appendix. Immunofluorescent staining showed IgA deposits to colocalise with TG2 subepithelially along the jejunal basement membrane in patients with normal histology prior to developing villous atrophy and in those with the classic coeliac lesion. This colocalisation was also found in lymph nodes, appendix, liver and muscle from coeliac patients but not in tissue from non-coeliac controls. These antibodies were then eluted from the tissue and the IgA was shown to be TG2 specific. The authors conclude that these TG2 antibodies may be important mediators of the systemic effects of coeliac disease and that they may even be important in the prodromal period before the patient develops the classic jejunal lesion.
See page 641

IMPORTANCE OF EARLY FLEXIBLE SIGMOIDOSCOPY IN DIAGNOSING CLOSTRIDIUM DIFFICILE INFECTION

Early identification and treatment of *C. difficile* is important but often delayed. The present study **[see page 673]** compared the yield from flexible sigmoidoscopy and stool assay for cytotoxin in 252 hospital patients with diarrhoea. Seventy three were identified as due to *C. difficile* on initial cytotoxin assay. One hundred and seventy nine with an initial negative stool cytotoxin assay underwent flexible sigmoidoscopy and 52 were found to have pseudo-membranous colitis in spite of a negative stool cytotoxin assay in 29. Rectal sparing was present in 11%. The important take home message is that clinicians should not be put off by a negative cytotoxin assay in hospitalised patients with clinically significant diarrhoea particularly if they have recently received antibiotics. Under such circumstances an early flexible sigmoidoscopy can prevent a dangerous delay in therapy.
See page 673

VISCERAL SENSITIVITY IN SYMPTOMATIC DIVERTICULAR DISEASE

As our population ages, diverticulosis and its associated complications become increasingly important yet our knowledge base has hardly advanced since the 1960s. The main problem is the very poor correlation between symptoms and objective measures, which so far have been mainly radiological. The investigators from Utrecht **[see page p 101]** used balloon distension of both the diverticular-bearing sigmoid colon and rectum to show that symptomatic patients show a hypersensitivity in both regions. This is an important start but begs the question of where the hypersensitivity lies. Is it in the bowel wall, where altered patterns of innervation have shown or is it more centrally positioned, as is the case in at least some patients with the irritable bowel syndrome? Much remains to be done but at last this very neglected group of patients are starting to be examined with modern techniques.
See page 101

COVERED VERSUS UNCOVERED BILIARY STENTS FOR MALIGNANT BILE DUCT OBSTRUCTION

Self expanding metallic stents have been an important advance but the original uncovered stents often suffer from tumour ingrowth. The first prospective randomised trial of covered versus uncovered stents is reported on page **729**. This shows significantly better patency, in which one year patency of the covered stents in surviving patients was 80% compared with only 52% of uncovered stents. Five patients receiving a covered stent developed acute pancreatitis and 2, whose covered duct overlapped the cystic duct origin, developed acute cholecystitis within 30 days of the procedure. The pancreatitis was mild and was managed conservatively while the 2 cases of acute cholecystitis required percutaneous drainage of the gall bladder. Thus covered stents are clearly superior but endoscopists should be aware of the possibility of these two complications and their optimum management.
See page 729

HEPATOCELLULAR CARCINOMA IS THE MOST FREQUENT COMPLICATION OF COMPENSATED HEPATITIS C-INDUCED CIRRHOSIS

Worldwide viral hepatitis is the commonest cause of cirrhosis. Many such patients present with compensated cirrhosis and knowledge of their prognosis is vital to advise on possible therapy and follow up regime. The study from Italy **[see page 744]** followed up 312 patients with compensated cirrhosis (mostly due to hepatitis C) for a median of 8 years. An alarming 21% developed hepatocellular carcinoma, slightly more than developed ascites while only 5% suffered a GI haemorrhage. Co-infection with Hepatitis B & C viruses was associated with an even higher incidence of HCC (47%). These findings strongly support the idea that routine surveillance for HCC is justified in such patients and provide much needed figures on which to base cost-benefit analyses.
See page 744