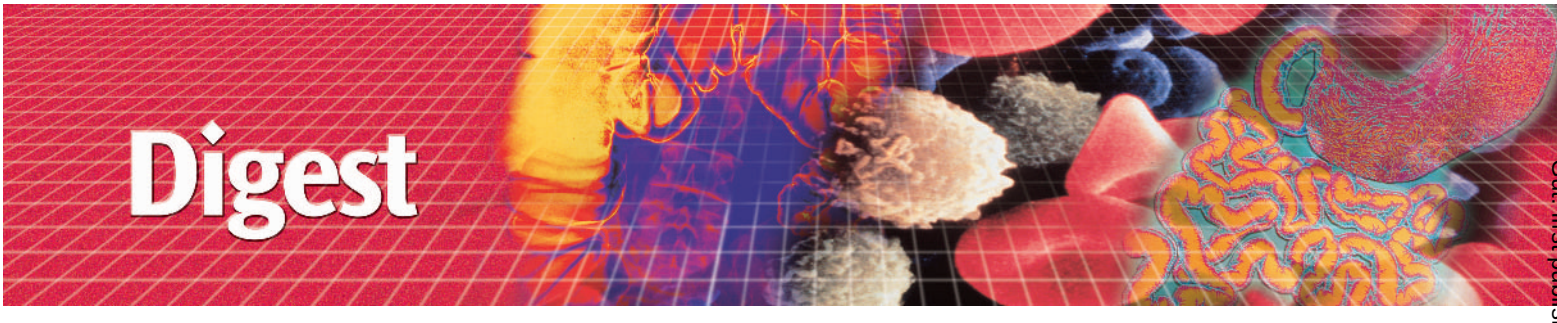

Robin Spiller, *Editor*

PRIORITY FOR GUT FEELINGS

Pain and disturbed function of the oesophagus, stomach and intestine are common symptoms but in many patients, conventional tests are all normal. Recent evidence suggests that the symptoms may arise from a hypersensitivity to stimuli from the gut. This visceral hypersensitivity may be due to either increased signalling from the gut or to altered central processing of such signals. Aziz and colleagues have used functional magnetic resonance imaging to examine central processing. They instructed their subjects to selectively attend to either visual or oesophageal stimuli which were produced by distending a balloon in the mid-oesophagus. They showed that while the visual stimuli activate the visual cortex only, the rather novel oesophageal stimulus activated substantially more areas of the brain, including areas such as the anterior cingulated and prefrontal cortex which are associated with affect and cognition. Furthermore, when both stimuli were presented simultaneously the areas of the brain processing the oesophageal stimulus showed more activation. They hypothesise that "gut feelings" receive priority because they are more likely to signify potential harm to the organism. Whether this selective attention to gut stimuli is enhanced in patients with functional diseases remains to be shown but seems highly likely.

See page 1671

PINPOINTING THE TOXIC PEPTIDES IN GLIADIN

Recent laboratory studies have pinpointed the precise amino-acid sequence believed to be responsible for T cell activation in coeliac disease. The study by Fraser *et al* has tested the putative toxic fragment by directly infusing it into the intestine and performing serial mucosal biopsies in patients with coeliac disease. This demanding protocol was completed in 4 patients. Within 4–6 hours, an infusion containing a peptide corresponding to residues 56–75 of the α-gliadin molecule induced a fall in villous height/crypt depth and an increase in intra-epithelial lymphocytes—strongly supporting the in vitro work indicating that this is the key antigen driving the immune response in coeliac disease. Control peptides from casein with similar amino acids but in different order had no effect. This opens the way to the development of genetically modified wheat which lack this sequence and hence the possibility of flour with the desirable baking properties of normal wheat but lacking toxicity for coeliac patients.

See page 1698

CALCIUM CHANNEL ANTAGONISTS REDUCE THE RISK OF PERFORATION IN DIVERTICULAR DISEASE

Complications of colonic diverticulosis such as haemorrhage, abscess formation or perforation are responsible for more than 22,000 admissions per year in England and Wales. Surprisingly few predictive factors have been identified. Ingestion of non-steroidal anti-inflammatory drugs (NSAIDs) doubles the risk of perforation but the idea that some drugs might be protective is new. The case control study of Morris *et al* suggest that calcium channel blockers, reduce the risk by about 60%. Calcium channel blockers are known to reduce the increase in intracolonic pressure which follows eating providing a plausible mechanism for this epidemiological finding. As the authors suggest, a clinical trial of these well tolerated drugs is a logical extension of this work.

See page 1734

EXTRA COLONIC FINDINGS AT COMPUTED COLONOGRAPHY ARE A CHALLENGE

Computed tomography colonography is an attractive screening tool for colorectal neoplasia as it is minimally invasive. It also examines the entire abdominal cavity and the lower portion of the lungs. However, its exhaustive survey capacity could prove to be something of a mixed blessing in the screening situation. Pedersen and colleagues report that 65% of asymptomatic individuals undergoing polyp/cancer surveillance had extracolonic abnormalities, 12% of whom required additional investigations and 3% of whom required surgery. In some circumstances, this could prove beneficial if, for example, aortic aneurysm or some early cancers are identified. However, it also carries the disadvantage of increasing patient anxiety as lesions are investigated which ultimately prove to be insignificant. The investigation of extracolonic lesions could also play havoc with screening programmes, as agreed criteria would have to be drawn up for every possible extracolonic lesion. This would be essential for both economic reasons and to avoid medicolegal liability. Pedersen's paper is a timely reminder that computed tomography colonography could prove to be a Pandora's Box.

See page 1744

PROGNOSTIC SIGNIFICANCE OF THE ALLELIC LOSS OF BRCA1 GENE IN COLORECTAL CANCER

The question of whether adjuvant treatment for Dukes B colorectal increases survival remains unresolved, with conflicting results from clinical trials. A major confounding factor confronting the clinical assessor is the large variability of prognosis of Dukes B cancers. It has previously been found that 49% of patients with sporadic colorectal cancer have loss of heterozygosity of 21q region of chromosome 17 where the p53 and BRCA1 genes are located. Garcia and colleagues report that BRCA1, but not p53, is an independent prognostic factor conferring a poor prognosis for stage I and II colorectal cancer. BRCA1 plays a role in the repair of double stranded DNA breaks and accounts for the inherited disposition of one third of breast cancer kindreds. The current study establishes that BRCA1 plays an important pathogenic role in intermediate stage colorectal cancer and suggests that patients in future clinical trials of adjuvant therapy for Dukes B/Stage II colorectal cancer should be stratified for loss of heterozygosity of the BRCA1 gene.

See page 1756