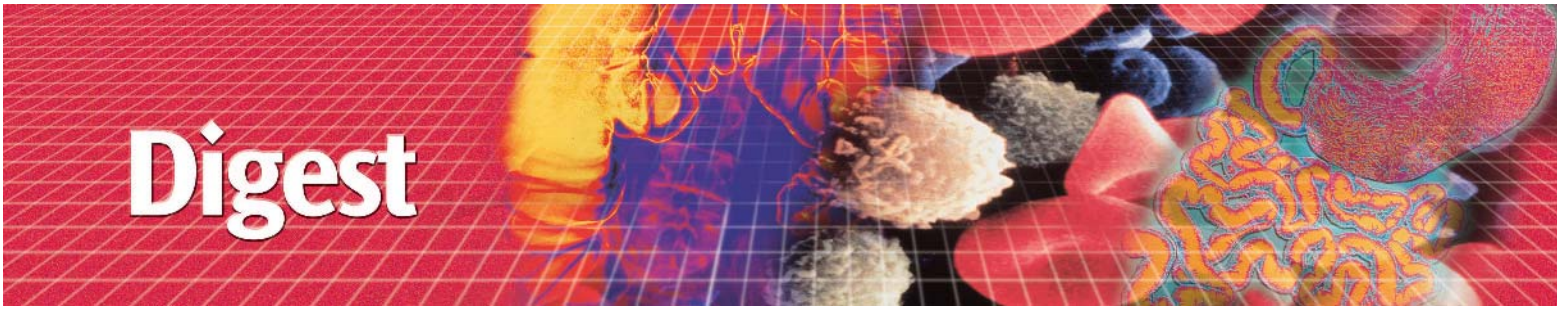

Robin Spiller, *Editor*

BENEFITS OF GHRELIN AFTER GASTRECTOMY

Gastrectomy removes the main source of ghrelin and in man is associated with substantial weight loss, decrease in body fat, and demineralisation. The study by Dornonville de la Cour *et al* examines the effects of replacement therapy with ghrelin in gastrectomised mice. The mice, like men, show a marked fall in basal ghrelin levels, a 15% fall in body weight, and about a 20% fall in bone mineral density. Ghrelin increased body fat and weight, largely abolishing the effect of gastrectomy. It did not alter the decrease in bone minimal density nor did it have a significant effect on lean body mass. In sham-operated animals, the effect of ghrelin was transient, increasing weight only for the first two weeks. This study shows that while in the short term ghrelin stimulates appetite, in the long term its main effect is to promote the deposition of fat, possibly by encouraging metabolism of carbohydrate rather than fat. These results suggest that ghrelin replacement therapy could ameliorate some of the adverse effects of gastrectomy.

See p 907

CONTROL OF HUMAN INTESTINAL MAST CELLS BY TRANSFORMING GROWTH FACTOR B1

Mast cells are important components of many diseases, both those obviously associated with inflammation (such as inflammatory bowel disease, allergic dermatitis, and asthma) and those not so obviously associated (such as irritable bowel syndrome). Mast cell growth and activation is controlled by a number of cytokines including stem cell factor and interleukin-3 and -4. Although transforming growth factor β1 (TGF-β1) inhibits the proliferation of human leukaemic mast cells, animal studies have shown conflicting results, possibly because mast cells from different tissues have a widely varying phenotype. Gebhardt *et al* overcame these obstacles by purifying mast cells from resected human gut, using cell sorting based on magnetic beads bound to antibodies to the *c-kit* receptor. They clearly showed that TGF-β1 enhanced apoptosis and decreased intestinal mast cell proliferation. This was accompanied by a decrease in the expression of the *c-kit* receptor and a decrease in the release of histamine and tumour necrosis factor α (TNF-α). TGF-β1 also changed the phenotype increasing the proportion of mast cells expressing both tryptase and chymase, decreasing the release of histamine and TNF-α, while increasing the production of prostaglandin D2. By teasing out the pathways involved, these studies open the way to therapeutic manipulation of mast cell activation in a wide range of intestinal diseases.

See p 928

ADDITIONAL BENEFITS FROM MESALAZINE ENEMAS IN ACTIVE EXTENSIVE ULCERATIVE COLITIS

Although rectal mesalazine is of proven benefit in distal colitis, its role in more extensive disease is uncertain. Because mesalazine is thought to act mainly locally, rapid transit through the inflamed area is likely to limit the effectiveness of oral treatments. Enemas, however, if retained, are capable of providing much higher concentrations and might improve efficacy. The current study took patients with mild/moderate exacerbations of previously established extensive ulcerative colitis and randomised them to 2 g twice daily oral pentasia combined with an initial 4 weeks of either saline or mesalazine enemas (1 g in 100 ml) at bed time. They showed improved remission rates at 8 weeks of 76% versus 58%, giving a number needed to treat of 5.5. The treatment was patient acceptable, with 84% of patients willing to take such therapy in the future. This study shows that in those with an exacerbation of mild to moderate pancolitis, mesalazine enema treatment, if tolerated, would be a reasonable alternative to corticosteroids.

See p 960

IMMUNE RESPONSE TOWARDS LIPID PEROXIDATION PRODUCTS PREDICT PROGNOSIS OF NON-ALCOHOLIC FATTY LIVER DISEASE

The rising prevalence of the metabolic syndrome means that fatty liver disease is fast becoming the commonest hepatological problem. Oxidative stress combined with steatosis is thought to cause progression to steatohepatitis and ultimately cirrhosis. The resulting lipid peroxidation products form adducts with body proteins. Albano *et al* tested the presence of antibodies to a range of such adducts including human serum albumin complexed with malondialdehyde (MDA-HSA). Antibodies to MDA-HSA were elevated significantly in non-alcoholic fatty liver disease (NAFLD) and elevated levels conferred a 2.8 (1.35 to 5.90) risk of having cirrhosis or advanced fibrosis. Multivariate analysis showed that this effect was independent of the other main predictors, namely presence of diabetes and an AST/ALT ratio greater than 1. If confirmed, this could be a useful non-invasive serum marker, allowing focusing of treatment efforts on those most at risk of progression to cirrhosis.

See p 987

GENOTYPE PREDICTS THE RESPONSE TO INTERFERON IN HEPATITIS B

Although it is well established that the response rate in chronic hepatitis C to interferon treatment is markedly dependant on viral genotype, the picture in hepatitis B has been more confusing. Response rates to interferon are low and worse in those with hepatitis B e antigen (HBeAg) negative status. Eight hepatitis B genotypes have been identified with widely different geographical distribution, which may account for some of the conflicting studies. The study by Erhardt *et al* examined 165 patients of whom 78 had genotype A and 66 had genotype D. The sustained response rate in genotype A was virtually double that for genotype D (49 *v* 26%). This was independent of the HBeAg status. However, HBeAg negative status was much commoner in genotype D, which may explain previous results. As with hepatitis C, it seems that in the future it will be important to genotype all patients undergoing anti-viral therapy.

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