

## GLP-2 ANALOGUE IMPROVES SHORT BOWEL SYNDROME PATIENTS

While short bowel syndrome is fortunately rare, patients who have it develop numerous complications, many of which relate to their need for total parental nutrition (TPN). If the colon remains intact in short bowel syndrome then compensatory secretion of certain gut hormones, including glucagon-like peptide 2 (GLP-2), leads to mucosal hypertrophy, compensation of absorptive defects, and in some cases cessation of the need for total PN. This study examined the effect of an analogue of GLP-2 given subcutaneously once daily for 21 days. Ten of the patients had an end jejunostomy (group 1) while five had > 50% of the colon remaining (group 2). GLP-2 induced an increase in villous height in group 1 and eight out of 10 showed clinical benefit with about a 10% fall in faecal calorie loss and a 1.4 kg rise in weight. Four out of five of those in group 2 also showed a fall in faecal energy excretion. Although the effect appeared transient, with most parameters returning to pre-treatment levels 2–3 weeks later, this treatment may well be of value in such patients who are both difficult to treat and severely disabled.

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## PANCREATITIS ASSOCIATE PROTEIN (PAP) INHIBITS PROINFLAMMATORY CYTOKINES

Mucosal inflammation in inflammatory bowel disease (IBD) is a complex balance of proinflammatory and anti-inflammatory factors. PAP is part of the REG gene family, initially discovered in experimental pancreatitis. The current study shows a specific elevation in IBD but not infectious gastroenteritis. The source appears to be Paneth cells, commonly increased in IBD. The authors show not only increased production of PAP in IBD, but also a close correlation between blood levels and endoscopic and histological markers of inflammation. They also show that PAP

inhibits cytokine production from IBD biopsies and prevents the translocation of NF $\kappa$ B p65 into the nucleus in isolated cell lines. This effect is more marked in Crohn's disease than ulcerative colitis, perhaps in keeping with the greater role of TNF- $\alpha$  in this condition. The authors conclude that synthetic PAP might be a useful and specific anti-inflammatory treatment in IBD.

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## A NEW CLINICAL SIGN IN COLORECTAL CANCER

Fordyce granules are ectopic sebaceous glands seen in the mouth as small white/yellow macules, 1–3 mm in diameter. Recent studies of the "hedgehog" pathway (a crucial signalling pathway in organogenesis that is involved in colorectal cancer) suggest its activation causes an increase in the size and number of sebaceous glands. The current article shows that 13 of 15 individuals with hereditary non-polyposis colorectal cancer syndrome had Fordyce granules versus 6 of 630 controls, giving a relative risk of 61. The commonest site for these granules was the lower lip. The authors suggest that this could be a new clinical sign of value in identifying affected families and improving the accuracy of genetic counselling.

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## METHYLATION OF THE OESTROGEN RECEPTOR GENE PREDICTS CANCER RISK IN ULCERATIVE COLITIS

Those doing surveillance colonoscopy for ulcerative colitis often long for a means of improving the targeting of this expensive procedure. Methylation of genes is part of the ageing process and common in sporadic colorectal neoplasms, possibly because it inactivates tumour suppressor genes. The present study compared methylation of the oestrogen receptor gene in 30 patients with long standing ulcerative colitis, 13 of whom had associated colorectal neoplasia. Oestrogen receptor gene methylation was found in the rectal biopsy of 92% of those with neoplasia, versus 31% of those without. This age related change appeared accelerated in those with neoplasia and undoubtedly shows potential as a biomarker to assist selection of high risk individuals for colorectal cancer surveillance.

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## BACTERIAL TRANSLOCATION OCCURS FREQUENTLY IN ACUTE PANCREATITIS

Sepsis is a much-feared complication of acute pancreatitis that may account for up to half the total mortality. Experimental models of pancreatitis in animals suggest that bacteraemia is common, owing to altered gut permeability. The current study showed that using a sensitive polymerase chain reaction method, bacterial DNA could be detected in 6 out of 31 individuals who were admitted with acute pancreatitis. Blood cultures were negative in all cases, suggesting that in most patients the bacteria were inactivated by the immune system. C reactive protein levels tended to be higher in those with circulating bacterial DNA. The frequency of its occurrence emphasises the importance of vigilance in detecting sepsis in these patients.

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## GENE THERAPY FOR HEPATOMA?

Extensive work over the past decade has shown the key importance of p53 tumour suppressor gene, mutations of which lead to lack of apoptotic signals in cancer cells. Mutation or absence of p53 has been associated with adverse prognosis and resistance to both radio- and chemotherapy. Hepatocellular carcinoma (HCC) has a high incidence of p53 mutations and in this case report a 23 year old male who had already had a partial hepatectomy for HCC was treated with p53 using an adenovirus vector. As the images show, there was a dramatic reduction in tumour size and 7 months later his  $\alpha$ -fetoprotein levels were normal, with minimal evidence of recurrent tumour on the CT scan. Although not necessarily representing a cure, this is indeed a dramatic response and gives hope for future use of this novel therapy in a disease that affects many young people in their prime of life.

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