# Gut Digest

**Robin Spiller,** *Editor*

## GENETIC INFLUENCES ON REFLUX

Reflux is a disease which doctors tend to blame on their patient's lifestyle. However this month we publish a study which may force a reappraisal of this approach. 4480 pairs of twins from the St Thomas' Adult UK Twin Registry were sent a questionnaire concerning reflux symptoms. Subjects were considered to be refluxers if they had symptoms at least weekly. Most of the twins are female so their conclusions are strictly only valid for females. By comparing the case wise concordance in monozygotic (46%) and dizygotic twins (26%), the authors were able to estimate the heritability of gastro-oesophageal reflux disease (GORD). After adjusting for body mass index (BMI), the heritability of GORD was estimated to be 43%. The hunt is now on for the genes, which are likely to be multiple.

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## NITRITES AND GASTRIC CARDIA CANCER

The incidence of adenocarcinoma of the gastric cardia is increasing in developing countries but the pathogenesis of cancer at this site is unknown. Suzuki *et al* hypothesise that it is caused by high levels of carcinogenic nitroso-compounds (derived from dietary nitrate). In the current study they show, in healthy volunteers given nitrate, that nitrite levels are high at the gastric cardia and that levels of protective ascorbic acid are low. Their data suggest that the high nitrite levels are probably due to entero-salivary circulation of nitrate. Suzuki *et al* speculate that high levels of nitrite and low levels of ascorbic acid at the gastric cardia will lead to rapid generation of nitroso-compounds as nitrite contacts gastric acid. The data are consistent with their hypothesis for carcinogenesis at this site, and should encourage further mechanistic studies as well as studies in patients.

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## PERIANAL CROHN'S DISEASE AND IBD 5

It has been recently postulated that different genotypes may be responsible for the different phenotypes found in both chronic inflammatory bowel diseases, ulcerative colitis, and Crohn's disease. The authors investigated the association of one of the known IBD susceptibility loci, IBD 5, in an UK population with 330 Caucasian Crohn's disease and 457 ulcerative colitis patients. They used three different single nucleotide polymorphisms (SNPs) to define haplotypes in this susceptibility region. In addition they analysed possible interactions with the recently found NOD2/CARD 15 gene. They found susceptibility for CD but not for UC associated with homozygocity of a common haplotype and showed in addition that this association was particularly strong in patients with perianal disease. This study is among the first to test the influence of other susceptibility loci known to confound risks for IBD regarding their association with clinical phenotypes. This and a other recent studies will undoubtedly lead to a more differentiated approach to treating patients with IBD.

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## HOW SHOULD WE RESPOND TO LOW GRADE DYSPLASIA FOUND DURING SURVEILLANCE OF COLITICS?

How to manage dysplasia identified during annual colonoscopic surveillance in ulcerative colitis remains a thorny and contentious issue. The recent BSG guidelines have recommended discussing surgery with patients with low grade dysplasia, however, the Leeds follow up data reported in this issue introduces a discordant note. After 10 years follow up, the incidence of high grade dysplasia or colorectal cancer was 10% in low grade dysplasia compared with 4% in those without dysplasia, a non-significant difference. Furthermore, histopathological review showed demonstrated substantial disagreement between histopathologists in making the diagnosis of low grade dysplasia, indicating clearly that better methods of identifying cancer risk in ulcerative colitis patients are needed. Only once these are available will we be able to provide rational advice to our colitis patients.

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## ANTI-TNF ANTIBODY REDUCES HEPATIC VENOUS PRESSURE GRADIENT IN ALCOHOLIC HEPATITIS

Many recent studies implicate TNF in the pathogenesis of portal hypertension, mainly in animal models. The availability of anti-TNFα antibody for use in humans has allowed this to be tested directly in man. In the current issue, 10 patients with alcoholic hepatitis were given anti- TNFα antibody infusion. This induced a significant decrease in hepatic venous pressure gradient with a reduction in both cardiac output and intrahepatic resistance. This is strong evidence for an important role for TNFα in the control of portal hypertension. Critically, the fall in cardiac output was not mirrored by a fall in renal blood flow, which was well maintained, implying that this approach may have some therapeutic value.

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## PREDICTING THE PRESENCE OF VARICES NON-INVASIVELY?

The increasing incidence of cirrhosis and the evidence that pharmacological prophylaxis is effective in preventing variceal haemorrhage has increased the number of patients requiring endoscopy to identify those with varices. The study by Gainnini *et al* proposes a simple, non- invasive, and readily available test which could markedly reduce the burden on endoscopic services. Previous studies have shown that varices are more likely to occur in patients with indirect evidence of portal hypertension such as thrombocytopaenia and splenomegaly, and the current study assessed the predictive value and the reproducibility of a simple ratio of platelet count to spleen size measured by ultrasound. Using multivariate analysis, the ratio of platelet count to spleen diameter was found to be independently associated with the presence of varices, and a cut off level of 909 for platelet count:spleen diameter ratio had 100% negative and 71% positive predictive values for the presence of varices. This needs to be confirmed in another series since such a simple test, which could replace the need for endoscopy to diagnose varices, would lead to substantial cost savings.

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