

## SAFETY OF LONG TERM OMEPRAZOLE

Omeprazole is one of the most widely prescribed medications, being used both for the symptomatic treatment of gastro-oesophageal reflux and also to prevent NSAID associated peptic ulcer. The results of the recent survey of mortality in 18 000 people treated with omeprazole is therefore of great interest. While there is a modest increase in mortality from circulatory, respiratory, and musculoskeletal disorders in the first year after initiating treatment, this fell to the expected level by year 4, strongly suggesting that the observed increased mortality was due more to the underlying disease for which omeprazole was prescribed, than the drug itself. A different pattern was observed in neoplasms of the oesophagus and cirrhosis, conditions which both showed a continuing excess over a period of four years from commencing treatment. When examined more closely, the risk for oesophageal cancer was only increased in those with Barrett's oesophagus, a condition known to be pre-malignant. This strongly suggests that the excess mortality in this group is due to the underlying disease. Reassuringly, there was no increase in gastric cancer but the length of follow up is insufficient to allay all fears since the delay between vagotomy and the observed increase in gastric cancer was >10 years. Plainly therefore, surveillance will need to continue for sometime yet.

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## FEATURES OF UNDETECTED COELIAC DISEASE

The availability of sensitive and specific serological tests for coeliac disease has facilitated numerous population surveys which indicate a population prevalence of the coeliac condition of around 1%. However, as the survey in this month's issue indicates this cannot be called a "dis-ease" since the affected individuals are more likely to report their health as good or excellent than the controls. This "feel good factor" may relate to a lower than average weight and cholesterol together with a reduced proportion of smokers. These apparent benefits were only slightly offset by an increased risk of osteoporosis, which did not however translate into a statistically significant difference in wrist fractures. While the advantageous cardiovascular risk profile of diagnosed coeliac has been attributed to increased health consciousness after the diagnosis, the reduced risk of smoking in undiagnosed coeliacs suggests a more interesting hypothesis, namely that duodenal pathology somehow reduces the pleasures of smoking. This is plainly worth exploring.

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## ADVANCES IN IMAGING COLONIC DYSPLASIA

Anyone who has spent a long afternoon doing surveillance colonoscopy in colitis will realise the potential value of a method which will highlight dysplastic areas within macroscopically normal looking mucosa. Endoscopic fluorescence imaging using 5 amino- laevulonic acid (5-ALA) as a sensitizer appears a promising technique to address this problem. Tumour cells have a defect in metabolism, which allows

the accumulation of protoporphyrin IX after dosing with 5-ALA. Fluorescence endoscopy shows this accumulation as a red patch when the mucosa is illuminated by a blue light. Topical rather than oral sensitizer was associated with a much improved sensitivity though the positive predictive value remained low. Importantly, the negative predictive value was high, which would allow one to make considerable savings in histology costs and surveillance programmes. This technique plainly needs a randomised control trial to evaluate its economic significance.

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## INCREASED TNF PRODUCTION IN CIRRHOTICS WITH ASCITES

Animal models of cirrhosis indicate a range of insults causing bacterial translocation increase tumour necrosis factor (TNF) production. Several authors have hypothesised that TNF mediated up-regulation of endothelial forms of nitric oxide synthase (NOS) might underlie the splanchnic arterial vasodilation characteristic of cirrhosis. The hepatology team from Val d'Hebron in Barcelona have succeeded in obtaining mesenteric lymph nodes from cirrhotics at the time of liver transplant. The lymph nodes have been analysed for TNF and confirm the animal models results indicating that, in this setting, the presence of ascites is a strong predictor of abnormal TNF production. The availability of specific TNF antagonists to allow the manipulation of TNF pathways for therapeutic benefit is already an active area of research, and these findings give it a further impetus.

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## MAGNETIC RESONANCE SPECTROSCOPY TO ASSESS CIRRHOSIS

One of the major problems in evaluating and managing chronic liver disease is the lack of a reliable non-invasive way of assessing the progression of cirrhosis. Liver biopsy is an invasive procedure with recognised morbidity and even occasional mortality, which is poorly suited to monitoring disease progress. Surrogate markers are often used which are crude and relatively insensitive. It is therefore exciting to read of a new non-invasive test involving magnetic resonance imaging of phosphorus. This allows analysis of the concentration of hepatic ATP levels. These correlated strongly with a histological index of cirrhosis, the liver cell volume per unit of tissue in all three animal models of cirrhosis studied. This decline in ATP may not only reflect loss of function in liver cells but a decline in hepatic concentrations in the remaining cells which are attempting to compensate for the loss of liver function. Lesions involving periportal hepatocytes appear to deplete ATP more markedly, suggesting that the absolute MR value may be of diagnostic value. This study suggests potential application in man and further results are awaited with interest.

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