

PHARMACOLOGICAL CONTROL OF GASTRIC DISTENSION REDUCES TRANSIENT LOWER OESOPHAGEAL SPHINCTER RELAXATION

Most gastro-oesophageal reflux events occur because of transient lower esophageal sphincter relaxations (TLESRs). The present treatment of this ubiquitous problem leaves these TLESRs unaltered and replaces the abnormality of reflux with another, namely achlorhydria. Opiates reduce TLESRs but until now the mechanism was unknown. Penagini and colleagues studied the lower oesophageal sphincter of healthy volunteers whose stomachs were distended with a barostat balloon. When the distension was held at a constant pressure, morphine decreased the size of the stomach and the incidence of TLESRs. However, when the distension was at a constant volume, no such effect was seen. Thus, the authors conclude that morphine acts by reducing the gastric volume and suggest that this approach might lead to the development of more specific treatment for reflux.

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VALUE OF EXAMINING THE LARYNX DURING UPPER GI ENDOSCOPY

For most endoscopists the larynx is something one tries to avoid on the way to the stomach, but the evidence in this month's *Gut* suggests that we should all take a closer look. These authors systematically examined the larynx in 1191 patients undergoing upper GI endoscopy and found 3% had a significant abnormality. The commonest one was chronic laryngitis, others included retention cysts, Reinke's edema, and in one case an early cancer was detected. As it adds very little to the duration of the endoscopy, it would seem sensible to incorporate this as part of a routine. Interestingly, there appears to be something of a learning curve and in the first half of the study they suspected pathology in 7%, whereas in the second half it was just 4%. It would be worth noting that before starting

this study, all the endoscopists were taught how to examine the region by an ENT expert, which would probably be useful to avoid an excess of false positives.

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TNF ENHANCES GUT BARRIER FUNCTION BY INHIBITING EPITHELIAL APOPTOSIS IN CROHN'S DISEASE

Impairment of epithelial barrier function in Crohn's disease is well recognised and thought to be due to actions of the pro-inflammatory cytokine tumour necrosis factor- α (TNF- α). In vitro studies on cell lines indicate that TNF- α increases permeability by increasing epithelial apoptosis and weakening tight junctions. The study attempted to examine the effects of TNF- α antibody treatment on these parameters in Crohn's disease. As expected, Crohn's patients had decreased epithelial resistance and increased epithelial cell apoptosis rates. Both abnormalities were corrected by TNF- α antibody treatment, although, interestingly, the expression of the tight junction proteins occludin and claudin did not change. Further cell line work confirmed that inducing apoptosis to a similar degree to that found in Crohn's disease patients induced a similar decrease in epithelial resistance. This effect of TNF- α antibody on epithelial cells should be contrasted with the known acceleration of lymphocyte apoptosis it induces.

The authors suggest that the early onset anti-diarrhoeal effects seen in some patients undergoing infliximab treatment maybe due to this effect on gut permeability.

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CANCER AND MORTALITY IN INFLAMMATORY BOWEL DISEASE—THE IMPORTANCE OF NOT SMOKING

For many inflammatory bowel disease patients a gastroenterologist is their main point of contact with the health service and as this study shows it is very important that we take a global view. Crohn's disease patients have a standardised mortality ratio (SMR) of 1.5 compared with the normal population, while ulcerative colitis patients have a SMR of 0.7, an effect that the authors argue is likely to be due at least in part to the increased frequency of smoking in Crohn's disease. Ulcerative colitis patients showed no excess mortality from GI disease along with the expected reduction in risk of lung and cardiovascular disease associated with a low incidence of smoking. By contrast, Crohn's disease showed a SMR of 4.5 for GI diseases with an increased incidence of colon and stomach cancer. They also showed a fourfold risk of dying from lung disease. It seems likely that the stopping smoking will have a far bigger effect on overall life expectancy than any drug treatment or surveillance programme that a gastroenterologist could offer. It follows that this should be one of the most important targets for a gastroenterologist treating such patients.

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SUCCESSFUL TREATMENT OF HCV TYPE 1b INFECTION DEPENDS ON THE NUMBER OF MUTATIONS IN THE NS5A GENE

While patients infected with HCV genotype 2 and 3 can be cured by a combination of interferon and ribavirin, those with the more common genotype 1b are much more difficult to treat. On page 1345 there is a meta-analysis that examined data on 1230 patients from both Europe and Japan. NS5A is a gene that spans the interferon (IFN) sensitivity determining region (ISDR). In this meta-analysis the sustained virological response (SVR) was only 10% in those with the wild type gene in Japan compared with 79% in those with four or more mutations. A similar though less striking pattern is seen in Europe, with a 6% v 43% SVR, respectively. The normal NS5A protein blocks the antiviral effect of IFN, something the mutant version does not do so well. Thus, by measuring the number of ISDR mutations it should be possible to predict the response rate to treatment and prevent unnecessary and potentially toxic treatments that have no chance of success.

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