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# Highlights from this issue

doi:10.1136/gutjnl-2014-307830

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## ACID SUPPRESSION AND BARRETT'S OESOPHAGUS: WHAT DO WE REALLY KNOW?

Although widely believed, the data supporting the premise that suppression of hydrochloric acid exposure to the oesophagus decreases the risk of oesophageal adenocarcinoma is inconsistent at best. In addition, it is known that bile acids may play a role in the formation of Barrett's oesophagus and oesophageal cancer, which would mean medicines like proton pump inhibitors (PPI) may not affect cancer formation in the oesophagus. This led Singh and colleagues to perform a systematic review with meta-analysis of studies evaluating the association between acid-suppressive medications (PPIs and histamine receptor antagonists (H2RA)) and the risk of oesophageal adenocarcinoma or high-grade dysplasia in patients with Barrett's oesophagus. They found seven observational studies that included a total of 2813 patients with Barrett's oesophagus and 317 cases of patients with high-grade dysplasia or oesophageal cancer, of which >80% were PPI users. On meta-analysis, PPI use associated with a 71% reduction in risk of cancer or high-grade dysplasia (adjusted OR, 0.29; 95% CI 0.12 to 0.79) with a trend towards a dose-response relationship with PPI use for >2–3 years. Their study supports the use of PPIs to decrease the risk of high-grade dysplasia or oesophageal cancer in patients with Barrett's oesophagus. The results of ongoing

randomised clinical trials will provide more definitive insight into this potential chemoprevention option for patients with Barrett's oesophagus (figure 1).

## A PROMISING NEW CLASS OF THERAPY FOR UC

There are many factors that appear to influence the occurrence and severity of inflammation in the gut. The activation of enteric glial cells through the enteroglia-specific S100B protein is a particularly interesting mechanism that has been reported to increase intestinal inflammation. This neurotrophin promotes macrophage recruitment in the mucosa and also interacts with toll-like receptors (TLR), which leads to increased colonic inflammation. Based on this knowledge, a research team led by Sarnelli and Esposito investigated whether molecules inhibiting S100B-driven enteric activation might be useful for treating UC. They carried out a series of studies to determine if palmitoylethanolamide (PEA), a drug that blocks astroglial activation in the central nervous system, could suppress intestinal inflammation. They have found that PEA can improve gross findings of inflammation and appears to do so via effects on NF- $\kappa$ B signalling and through PPAR $\alpha$ . They also found no toxicity associated with this treatment suggesting it could be a novel therapeutic approach for the treatment of UC.

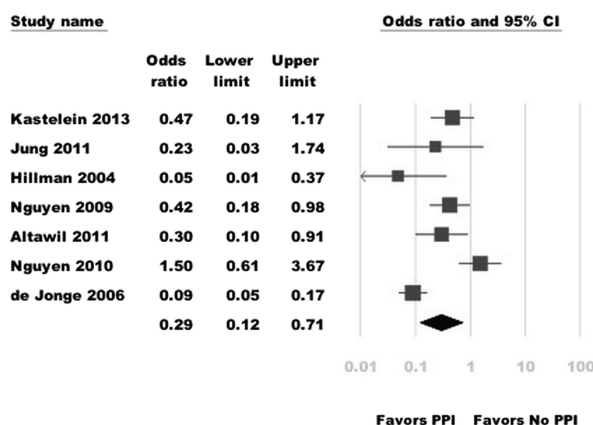
## WHAT SPECIES DEFINE DYSBIOSIS IN PATIENTS WITH UC?

The gut microbiota has important metabolic, protective and trophic functions on the healthy host but the composition and diversity of the microbiota is altered in patients with IBDs. In Crohn's disease (CD) patients, a specific dysbiosis has repeatedly been documented but the data in UC patients remain limited and conflicting. In this excellent study from Leuven, Belgium, Machiels *et al* studied the microbial signature in a large cohort of UC patients. They also assessed the functional impact of dysbiosis by quantifying the bacterial metabolites. The results showed that the CD-dysbiosis signature characterised by *F. prausnitzii*, *B. adolescentis* and *R. gnavus* is not retrieved in UC patients, suggesting different species driving dysbiosis in CD and UC. The microbial composition in UC patients differs from healthy subjects with reduction of *R. hominis* and *F. prausnitzii*, both butyrate-producing bacteria of the Firmicutes phylum. The authors show, for the first time, an inverse correlation between dysbiosis-driving species and disease activity of UC. They conclude that these species may be used to restore and maintain the balance of the microbiota in UC patients with selective probiotics, prebiotics and/or synbiotics.

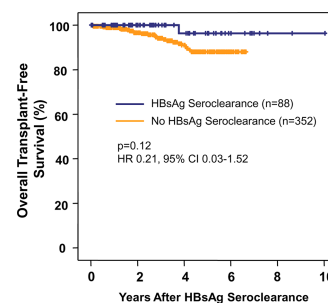
## HEPATOLOGY

### Nucleoside analogue (NUC) treatment for chronic HBV: importance of HBsAg seroclearance

For patients with chronic HBV infection spontaneous or interferon-induced



**Figure 1** Summary of adjusted ORs assessing the risk of oesophageal adenocarcinoma and/or high-grade dysplasia in patients with Barrett's oesophagus with proton-pump inhibitor exposure in all included studies.



**Figure 2** Kaplan-Meier survival curves for overall transplant-free patient survival after nucleoside analogue therapy.

seroclearance (sc) of HBsAg is associated with a decreased risk of hepatocellular carcinoma and with prolonged survival. Currently many patients prefer NUC over interferon therapy, but little is known about the importance of HBsAg sc during NUC treatment. This study from Seoul investigated the long-term effects of NUC-induced HBsAg sc with the largest ever number of patients (*see page 1325*). HBsAg sc was associated with favourable clinical outcomes (*figure 2*). However, in some patients with baseline cirrhosis hepatocellular carcinoma occurrence was

observed even after sc. For these patients long-term surveillance seems useful. Please also read the commentary by M Cornberg on *see page 1208*.

#### **Hepatic stellate cells (HSC) help the liver to regenerate: a ground breaking study**

Liver regeneration after partial hepatectomy is thought to be due to replication of mature hepatocytes. Epithelial-mesenchymal transitions do not play a role during adult liver repair. These two dogmas need to be revisited in the light of the most exciting findings

by A M Diehl and her group (*see page 1333*). This thorough and very elegant study proposes a new concept for liver regeneration after partial hepatectomy: HSC undergo a Hedgehog-dependent transition process to generate myofibroblasts. These give rise to progenitor cells which are pivotal for liver regeneration. In other words scarring is important for liver regeneration and manipulations of the Hedgehog pathway might be a novel therapeutic avenue. This important provocative study will stir debate and stimulate further research.