

Highlights from this issue

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Overall burden of *Helicobacter pylori* on mortality

H. pylori colonisation has been associated with increased risk of peptic ulcer disease and gastric cancer, and reduced risk of asthma and allergy, while the association with cardiovascular disease and lung cancer is inconsistent. In this issue of Gut, Chen *et al* report their interesting data on the influence of *H. pylori* on total and category-specific mortality. They conducted prospective cohort analyses in a nationally representative sample of 9895 participants enrolled in the National Health and Nutrition Examination Survey III (NHANES III) to assess the association

of *H. pylori* status with all-cause and cause-specific mortality. The authors found that *H. pylori* status was not related to overall all-cause mortality. *H. pylori* colonisation was associated with reduced risk of death due to stroke and increased risk of death due to gastric cancer. The data also suggest an inverse association with lung cancer. The authors conclude that *H. pylori* colonisation may have new possibly protective effects (see page 1262).

A little chilli for oropharyngeal dysphagia

Oropharyngeal dysphagia (OD) is a major complaint among the elderly and sadly has no pharmacological treatment. Afferent

areas that trigger a swallowing response are sensitive to mechanical stimuli, to changes in temperature and to chemical stimuli, and express the polymodal Transient Receptor Potential Vanilloid 1 (TRPV1). In this issue of Gut, Rofes *et al* report their clinical videofluoroscopic study that assessed the safety and efficacy of adding capsaicinoid preparations (stimulants of TRPV1) to swallowed boluses. The authors found that natural capsaicinoids added to the alimentary bolus improved safety of swallow of patients with dysphagia and reduced the prevalence of penetrations at the laryngeal vestibule. They also improved efficacy of swallow and reduced the prevalence of pharyngeal residue in such patients. Additionally, natural capsaicinoids improved the swallow response, shortening the laryngeal vestibule closure time and enhancing hyoid motion. Overall, these findings are very promising and suggest that stimulation of TRPV1 might become a pharmacologic strategy to treat OD (see page 1280).

Granulocyte/monocyte apheresis is no better than sham procedure for Crohn's Disease

Granulocytes and monocytes may contribute to the pathogenesis of Crohn's disease (CD) and the therapeutic strategy of removing them is a reasonable approach. The

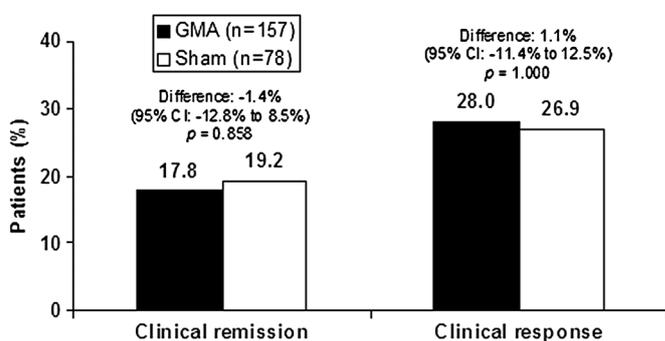


Figure 1 Clinical outcomes in patients treated with granulocyte/monocyte apheresis (GMA) and sham-treated patients.

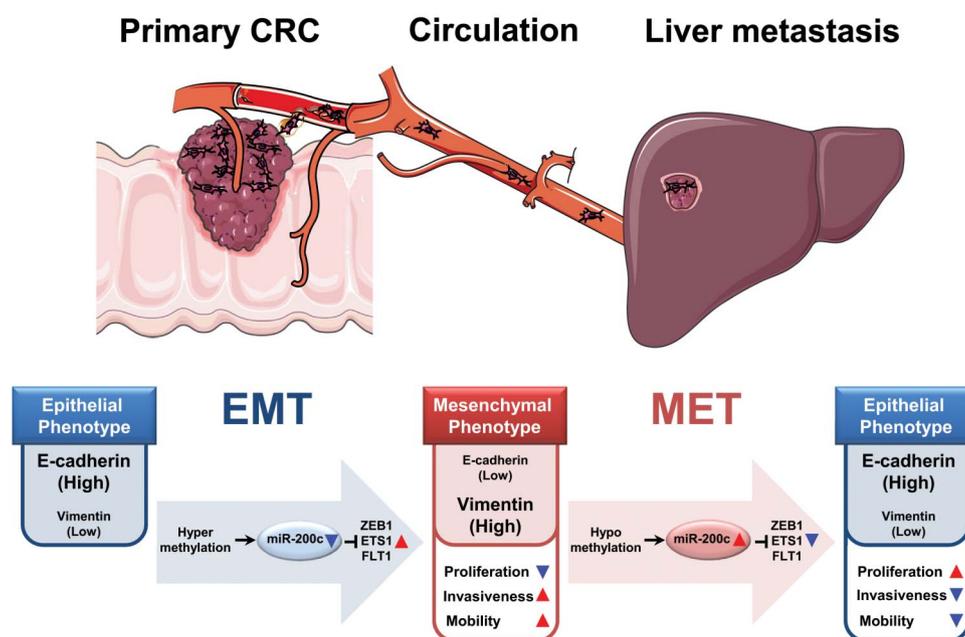


Figure 2 A consolidated model for the role of miR-200c in CRC metastasis.

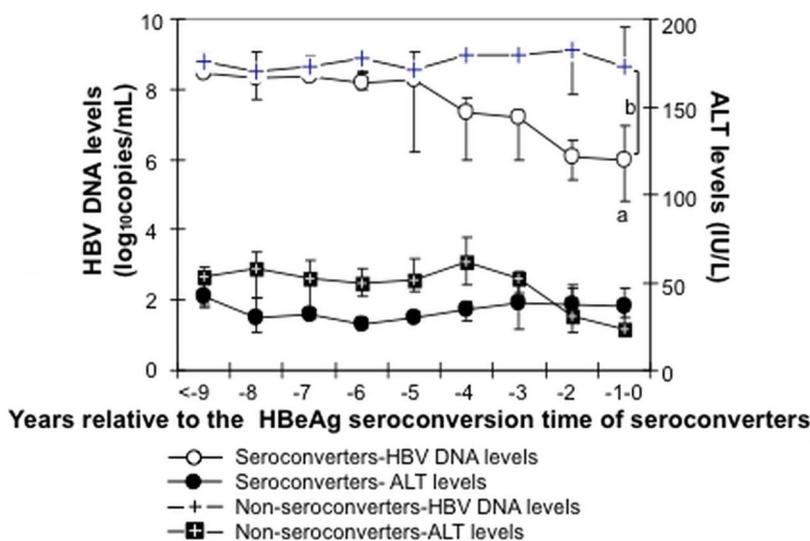


Figure 3 Hepatitis B virus (HBV)-DNA and alanine aminotransferase (ALT) levels in hepatitis B e antigen (HBeAg) seroconverters and non-seroconverters. The HBV-DNA levels of HBeAg seroconverters decrease significantly over time from -4 to 0 (a, $p=0.002$), and are significantly lower than non-seroconverters (b, $p<0.001$). The ALT levels of both groups do not change over time. Minus numbers on the x axis represent the number of years before HBeAg seroconversion, and the corresponding time points in non-seroconverters.

Adacolumn Apheresis System (Adacolumn) is a device that removes activated granulocytes and monocytes from peripheral blood. Granulocyte/monocyte apheresis (GMA) has shown promising efficacy in open-label, uncontrolled studies of patients with CD. In this issue of *Gut*, Sands *et al* report on their randomised, double-blind study comparing GMA with a sham procedure in patients with moderate to severe CD. In essence, the study was negative and while GMA was well tolerated it did not show effectiveness over sham control in patients with moderately to severely active CD (figure 1). These findings are of interest because Adacolumn

apheresis continues to be used to treat both CD and ulcerative colitis in Europe and Asia. Perhaps it is time to pull the plug on this treatment (see page 1288).

Role of miR-200c in CRC metastasis

Metastasis of colorectal cancer (CRC) to distant organs is the primary cause of death from this common malignancy. There are a number of biological mechanisms that are thought to mediate the invasive and metastatic behaviour of cancer. One of these mechanisms is called epithelial-to-mesenchymal transition (EMT) and it has been implicated in the metastatic behaviour of CRC. One of the molecular factors that

causes EMT in many cancers is increased expression of the miR-200 family of microRNAs. The research team led by Dr. Goel now provides evidence that miR-200 family members also mediate the metastatic behaviour of CRC. Their studies demonstrate a role for the upregulation and hypomethylation of the miR200c/141 cluster in liver metastases. They conducted a systematic analysis of the miR-200 family of miRNAs in primary CRCs and matching liver metastases and discovered a sequence in which the miR-200 members are initially silenced, permitting behaviours that facilitate cellular escape, such as EMT, and then the metastatic cancer cells reverse the EMT phenotype, which facilitates the growth of the metastatic lesions. These results suggest a role for miR-200c in the metastatic behaviour of CRC and suggest that it may be a useful biomarker for this phenotype (see figure 2) (see page 1315).

HEPATOLOGY HBV evolution, HBeAg seroconversion and disease progression

In chronic hepatitis B virus infection HBeAg seroconversion is associated with a marked decrease of viral load and with better clinical outcomes. This interesting study (see page 1347) elucidates cumulative viral evolutionary changes over many years in individual patients. The authors show that an increase in viral diversity precedes reduction of HBV DNA and HBeAg seroconversion, possibly by stimulating the innate immune response (figure 3). This may have implications for treatment aiming at HBeAg seroconversion. Please also read the commentary (see page 1242).

From fatty liver to NASH—a role for mitochondrial epigenetic changes

A considerable proportion of patients with fatty liver develop NASH which may progress to cirrhosis. While a role of mitochondrial dysfunction in this process is generally accepted, the molecular mechanisms behind are not understood. This important paper from Argentina (see page 1356) suggests a critical role of mitochondrial DNA methylation. They found in human liver biopsies that methylation of mitochondrially encoded NADH dehydrogenase 6 was associated with the histological severity of NASH (figure 4). Interestingly, these epigenetic changes were inversely correlated with the patients' physical activity, the lifestyle intervention recommended for NASH. These data suggest an important role of mitochondrial NADH dehydrogenase 6 in the pathogenesis of NASH.

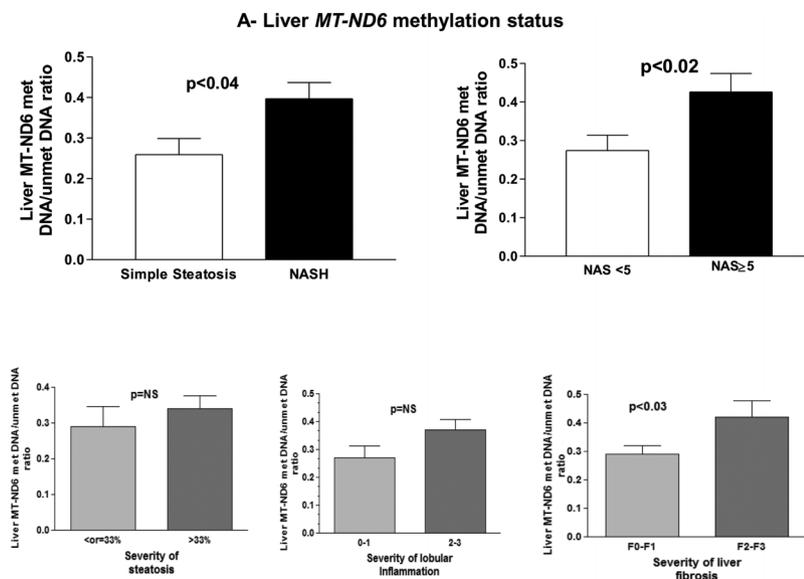


Figure 4 Status of DNA cytosine methylation of mitochondrially encoded NADH dehydrogenase 6 (MT-ND6).

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