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# Highlights from this issue

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## LUMINAL

### Novel insight into the effect of PPIs on the oesophagus

It is well appreciated that gastric acid can induce oesophagitis and that proton pump inhibitors (PPIs) promote the healing of gastro-oesophageal reflux disease (GORD) through inhibiting gastric acid secretion. More recently, it has been shown that some of the direct, caustic effects of refluxed acid on oesophageal epithelial cells are secondary to chemokines such as interleukin (IL)-8 produced by those cells. It has also been shown that PPIs have a number of potential anti-inflammatory actions independent of their effects on gastric acid secretion, including the ability to inhibit chemokine production in certain epithelial cells. A team led by Spechler and Souza now show that IL-8, a major mediator of inflammation, is induced by acidic bile acid in the oesophagus and that omeprazole can inhibit IL-8 production by suppressing the NF-kappa B signalling pathway. Thus, they have demonstrated novel anti-inflammatory effects of PPIs that are entirely independent of their effects on gastric acid secretion, and that might contribute to the beneficial effects of PPIs in the treatment of GORD.

### An easy-to-use method to identify people at high risk of colorectal neoplasms

Colorectal cancer is one of the most common cancers worldwide, but can be

prevented with available screening methods, like colonoscopy or faecal immunochemical testing. The choice of which screening test to use partly depends on an individual's risk for colorectal cancer. Factors like family history of colorectal cancer and a personal history of colon adenomas or cancer are known to increase that risk. Sung and colleagues now present a validated method that enhances our ability to predict the risk of colorectal cancer. They analysed data from 2 000 asymptomatic screening participants to establish a risk prediction tool and then validated the tool in an independent cohort of 3 200 people. They found that a tool that used age, gender, smoking status, family history, body mass index, and self-reported diabetes successfully predicted the risk of colorectal neoplasia in asymptomatic subjects. High-risk individuals had a 2.37 fold higher risk compared with average risk subjects. Their scoring instrument is easy to use in clinical practice and has the potential to improve the effectiveness of colorectal cancer screening (see [table 1](#)).

## ENDOSCOPY

### Risk scores to define patients with advanced adenomas for colorectal cancer screening—ready for prime time?

Colorectal cancer screening by endoscopy may be regarded as the most effective, but also the most complex and laborious method. Therefore, most countries have employed stool tests as an alternative.

Nevertheless, as with cancer screening in other areas, clinical risk scores are being evaluated to possibly stratify patients into different risk groups, perhaps with different screening methods to be applied or offered. In the March issue of *Gut* (Stegeman *et al*), a Dutch study assessed a clinical risk score together with FIT stool test results in screenees undergoing colonoscopy; this was based on total calcium intake, family history, and age. In this issue, Kaminski *et al* used the Polish screening colonoscopy 7-year registry to arrive at a test and validation set on a total of 35 918 subjects for such risk markers. For the prediction of advanced adenomas (AA), the known risk markers (age, sex, family history, smoking and BMI) were highlighted. Score points 0–1 or 0–2 were ascribed to each of the factors in a simplified risk score, ranging from minimum 0 to maximum of 9, with a rather linear increase between low scores (e.g. score 1–3=AA rate around 5 or lower, 6–8/9=AA rate 15–20%). The results are encouraging thus far. The score would have to be tested in other countries' databases (e.g. Netherlands, Germany, Italy, Spain), but implementation for motivation of higher risk persons or even for stratification would require considerable political work. What would also be needed is outcomes research: do such strategies really lead to improved compliance and enhanced detection of lesions compared to traditional approaches based on invitation systems for everyone? Will insured persons accept being classified into different risk groups? These and other questions arising from the interesting analysis will have to be answered in future studies (see [page 1112](#)).

## HEPATOLOGY

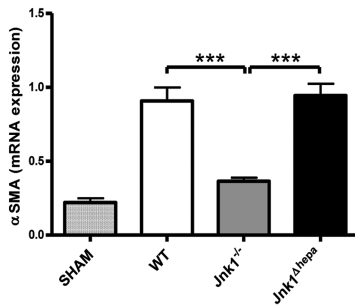
### Understanding liver fibrogenesis remains a challenge

Liver fibrogenesis has a complex pathophysiology. A major role of c-Jun N-terminal kinase-1 (Jnk1) is well known. This experimental study from Germany (see [page 1159](#)) elegantly demonstrates the importance of Jnk1 in hepatic stellate cells, but not in hepatocytes for fibrogenesis ([figure 1](#)). Please also read the insightful commentary on [page 1039](#) which emphasizes the importance of precise, cell specific targeting of molecular pathways to inhibit fibrosis.

**Table 1** Colorectal screening score for prediction of risk for colorectal neoplasia\*

Risk factor	Criteria	Points
Age, years	50–55	0
	56–70	1
Gender	Female	0
	Male	1
Family history present for a first-degree relative	Absent	0
	Present	1
Smoking	No	0
	Current or past	1
BMI	<25	0
	≥25 (obesity)	1
Diabetes mellitus	Absent	0
	Present	1

\*Colorectal neoplasia includes adenoma, advanced neoplasia and cancer. Advanced neoplasia is defined as colorectal cancer, or any colorectal adenoma which has a size of ≥10 mm in diameter, high-grade dysplasia, villous or tubulovillous histologic characteristics, or any combination thereof.  
BMI, Body Mass Index.



**Figure 1** mRNA expression of alpha smooth muscle actin in mouse livers subjected to bile duct ligation.

### Triple therapy with protease inhibitors for HCV in cirrhosis

The therapeutic dilemma for patients with HCV cirrhosis or advanced fibrosis is that they need HCV treatment most, but often cannot receive long-term full dose antivirals due to side effects. If treated outside accepted inclusion criteria severe side effects and high mortality were observed. This prospective, multinational trial with a large number of genotype 1 patients with advanced fibrosis and compensated cirrhosis respectively, provides clinically relevant

information (*see page 1150*). Patients received a combination of the oral protease inhibitor telaprevir, pegylated interferon and ribavirin. On treatment response around 80 percent was remarkable, 12 percent were discontinued due to adverse events. Anaemia was the most frequent adverse event and observed in the majority of patients. Thus for appropriately selected patients triple therapy even in compensated cirrhosis can be performed rather safely.

Please also read the expert commentary by P Ferenci and G Dusheiko on page 1033.