Luminal GI
Omeprazole’s eosinophil-reducing properties
Eosinophilic oesophagitis (EoE) and gastro-oesophageal reflux disease (GORD) share clinical and histological features and it is sometimes difficult to distinguish the two disorders, though some reports suggest that response to PPIs might be a useful test. The premise is that reduced gastric acid secretion is the only important effect of PPIs and, therefore, an acid-peptic disorder like GORD can respond to PPIs. It is also known that oesophageal expression of eotaxin-3 stimulated by Th2 cytokines might contribute to oesophageal eosinophilia in EoE while Th2 cytokine effects on the oesophagus in GORD are not known. In this issue of Gut, Cheng et al measured eotaxin-3 protein secretion stimulated by Th2 cytokines (interleukin (IL)-4 and IL-15) in telomerase-immortalised and primary cultures of oesophageal squamous cells from GORD and EoE patients. Oesophageal squamous cells from GORD and EoE patients expressed similar levels of eotaxin-3 when stimulated by Th2 cytokines, and omeprazole blocked that eotaxin-3 expression. These findings suggest that PPIs might have eosinophil-reducing effects independent of effects on acid reflux and that response to PPIs might not distinguish EoE from GORD. Equally, the findings provide a rationale for the use of PPIs in the management of EoE, irrespective of the presence of GORD (see page 824).

Revised guidelines for the clinical management of Lynch syndrome (HNPCC)
Lynch syndrome (LS) is characterised by the development of colorectal cancer (CRC), endometrial cancer and various other cancers, and is caused by a mutation in one of the mismatch repair genes: MLH1, MSH2, MSH6 or PMS2. In this issue of Gut, Vasen et al present the latest guidelines for the clinical management of LS. The guidelines were formulated by 35 specialists from 13 countries and represent the latest knowledge in this field. Questions addressed by the guidelines include: how to improve the identification of LS; optimal colorectal surveillance protocol for LS; effectiveness of surveillance for endometrial and ovarian cancer; role of prophylactic hysterectomy with or without oophorectomy; effectiveness of surveillance for other cancers; appropriate surgical treatment for CRC; influence of environmental and lifestyle factors on the development of adenoma or CRC in LS; role of aspirin in the management of LS; role of prenatal diagnosis and pre-implantation genetic diagnosis in LS and the psychosocial implications of genetic testing and surveillance. This report is essential reading for all health care providers dealing with LS (see page 812).

Which small polyps should not be ignored
CT colonography is becoming a more widely used method for colon cancer screening; however, there is considerable controversy over the management of small polyps found by this exam. Kolligs and colleagues now present data from a study to identify risk indicators for advanced neoplasm (AN) in subcentimetric polyps. They defined AN as high-grade dysplasia, villous histology, or cancer and studied the results from 1 077 956 colonoscopies. The risk of intermediate (5–9 mm) lesions to carry AN was higher than of diminutive (<4 mm) lesions (OR 3.1). Age ≥85 vs <40 years was associated with an OR of 2.4 (1.8–3.1) for intermediate and an OR of 5.2 (2.3–4.3) for diminutive polyps. Pedunculated versus sessile morphology was associated with ORs of 2.0 (1.9–2.2) and 5.5 (2.9–4.1) for intermediate and diminutive polyps, respectively. This study successfully identified risk factors and established a risk index for subcentimetric lesions. These findings have clear implications for the work-up of individuals with subcentimetric lesions identified using diagnostic imaging (see page 863).

The first steps towards personalised medicine for cancer prevention
CRC results from a combination of environmental and inherited factors. It is believed that approximately 30% of the risk of CRC is secondary to heritable factors. Recent studies have identified over a dozen genetic variants, called single nucleotide polymorphisms and copy number variants, that associate with an increased risk of CRC. The increased risk of any single susceptibility loci is quite small and of little clinical value, which led Dunlop and colleagues to assess the feasibility of using these common genetic variants, combined with other risk factors, to improve our ability to predict an individual’s risk of CRC. They built a risk prediction model that includes age, gender, family history and genotypes at 10 susceptibility loci, and applied it to the Scottish population...
using available data (figure 1). They found that the discriminative performance was poor for the genetic variants alone but that modelling genotype data, family history, age and gender could identify a subgroup with >5% predicted 10-year absolute risk of CRC. Their results suggest that using genetic variant data with other risk factors may lead to more accurate and personalised prevention programmes for CRC (see page 871).

Hepatology
A novel approach to improve survival after liver resection
Cholestasis and liver failure are major problems following extensive partial liver resection. This exciting and comprehensive study from Matias Avila’s group at the university of Navarra provides novel insights into the mechanisms of liver regeneration upon resection. They investigated the role of fibroblast growth factor 15 (Fgf 15) which is a circulating regulator of bile acid homeostasis. Fgf 15 deficient mice had elevated bile acids, impaired liver regeneration and poor survival following partial hepatectomy which was markedly improved by Fgf 15 administration. Importantly Fgf 15 prolonged survival after extensive liver resection also in normal mice (figure 2). In humans Fgf 19 corresponds to murine Fgf 15. This makes it potentially applicable in the clinical management of cholestasis and for the prevention of liver failure following major liver resection (see page 899).

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