Levofloxin-containing sequential therapy for *Helicobacter pylori* infection

Clarithromycin resistance is emerging as a major cause for failure of eradication of *H pylori* infection. Sequential therapy (ST) is a promising alternative to standard triple therapy. Romano et al conducted this randomised trial in a geographical area with >15% prevalence of clarithromycin resistance. They compared the efficacy of a levofloxacin-containing ST versus a clarithromycin-containing ST. 375 infected patients were randomly assigned to one of three treatments: (1) 5 days omeprazole 20 mg bd + amoxicillin 1 g bd followed by 5 days omeprazole 20 mg bd + clarithromycin 500 mg bd + tinidazole 500 mg bd; or (2) omeprazole 20 mg bd + amoxicillin 1 g bd followed by omeprazole 20 mg bd + levofloxacin 250 mg bd + tinidazole 500 mg bd; or (3) same as regimen 2 but with a 500 mg bd of levofloxacin. On an intention-to-treat analysis, the eradication rates for the three groups were 80.8%, 96% and 96.8%, respectively, with high prevalence of clarithromycin resistance. They investigated the role of IAP in the preservation of the normal homeostasis of the gut microbiota. They showed that mice deficient in intestinal alkaline phosphatase (IAP knockout) harboured fewer and different types of intestinal bacteria, compared with wild-type animals. Oral supplementation of IAP rapidly restored commensal gut microbiota lost due to an antibiotic treatment (see figure). In addition, oral supplementation of IAP dramatically reduced colonisation of Salmonella typhimurium. These exciting findings suggest that IAP is involved in the maintenance of normal gut microbial homeostasis and may have therapeutic potential against dysbiosis and pathogenic infections. See page 1465.

Intestinal alkaline phosphatase preserves the normal homeostasis of gut microbiota

Visilizumab is not effective in severe IV steroid-refractory ulcerative colitis patients

Visilizumab, a humanised monoclonal antibody to CD3, has shown efficacy for the treatment of corticosteroid-refractory ulcerative colitis but no placebo-controlled studies were available. This international double-blind, placebo-controlled study evaluated the efficacy of visilizumab (5 mcg/kg intravenously on days 1 and 2) in 127 patients with severe ulcerative colitis despite treatment with five or more days of intravenous corticosteroids. The primary endpoint was response at day 45. Secondary end-points included remission and mucosal healing at day 45, symptomatic response at day 15, and colectomy. The primary endpoint occurred in 55% of patients receiving visilizumab and this was not significantly different from the 47% response observed in placebo treated patients. Also, remission rates, mucosal healing and colectomy rates were not different between both groups. Moreover, there was an excess of cardiac and vascular adverse events in patients treated with visilizumab. The authors conclude that Visilizumab at a dose of 5 mcg/kg for two consecutive days is not effective for severe, corticosteroid-refractory ulcerative colitis and is furthermore associated with important vascular safety problems. See page 1485.

Mannan-binding lectin and intestinal inflammation

Anti-Saccharomyces cerevisiae antibodies are found in up to 60% of Crohn's disease

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**H pylori eradication rates with CLA-ST, LEV250-ST, and LEV500-ST groups.** Per cent and 95% CIs. *p<0.0001 versus LEV250-ST and versus LEV500-ST. CLA, clarithromycin; ITT, intention-to-treat; ST, sequential therapy.

**Oral intestinal alkaline phosphatase (IAP) supplementation enhances the restoration of antibiotic-associated loss of gut microbiota.** Groups of wild-type mice were treated with streptomycin with or without calf IAP (cIAP, 200 U/ml drinking water). Stool culture was performed daily and time of appearance (day) of Gram-negative (E coli) bacteria recorded for each animal. (**p<0.001).
patients, and have been associated with a more severe disease course. Their aetiology remains unknown, although immune cross-reactivity with other intestinal antigens is likely. Mannan-binding lectin (MBL)-deficiency predisposes to ASCA-positivity. Given that the role of MBL in intestinal inflammation is unclear, the authors in this study analysed local MBL expression in the human intestine and studied consequences of MBL-deficiency in DSS colitis and infection with Candida albicans or adhesive/invasive E coli (AIEC). Their experiments show that MBL expression was virtually undetectable in the intestinal mucosa of healthy controls and patients with CD, irrespective of macroscopic inflammation, indicating that systemic MBL must be responsible for the reduced risk for complicated disease in MBL-competent CD patients. MBL-deficient mice but not wild type mice showed enhanced DSS colitis upon oral challenge with C albicans. Remarkably, survival probability was significantly higher in the group randomised to receive clonidine (figure 5A). The investigators then set out to identify predictors of clonidine response. They found baseline norepinephrine concentration and, interestingly, genetic factors related to the effects of clonidine. Certain genotypes for $\alpha_2$ adrenergic receptor subtype, which enhances norepinephrine release and for guanine nucleotide-binding protein 3, were independent predictors of response. Altogether this work suggests a novel approach for an individualised treatment of patients with refractory ascites. See page 1545.

HCV transmission—it is the doctors, not the family

Egypt has the highest HCV prevalence in the world and is thus ideally suited to the study of modes of HCV transmission. This crosssectional study assessed the importance of familial transmission by investigating acute HCV infection in Cairo. Using phylogenetic analysis of the viruses in index cases of acute infection, and of chronic HCV in household members, they found less than 5% of symptomatic HCV was related to familial transmission. However, iatrogenic transmission played a major role; intravenous infusions, stitches or catheter procedures accounted for more than one third of new HCV infections. This study provides important information on household transmission of HCV. Moreover, the high rate of nosocomial infection is alarming. See page 1554.

Clonidine for refractory ascites

Clonidine suppresses the renin-angiotensin-aldosterone system and has been suggested to improve the effects of diuretic treatment in cirrhosis. This study from Taiwan investigated the effects of 0.15 mg clonidine daily in a large group of patients with refractory or recurrent ascites. Clonidine resulted in a decrease in plasma renin, aldosterone and norepinephrine concentrations and increase in urinary sodium excretion (figure 4E). The investigators then set out to identify predictors of clonidine response. They found baseline norepinephrine concentration and, interestingly, genetic factors related to the effects of clonidine. Certain genotypes for $\alpha_2$ adrenergic receptor subtype, which enhances norepinephrine release and for guanine nucleotide-binding protein 3, were independent predictors of response. Altogether this work suggests a novel approach for an individualised treatment of patients with refractory ascites. See page 1493.