They’re bugs, Jim, but not as we know them ▶

A theme is evolving in the pathogenesis of chronic inflammation seen in colitis and Crohn’s disease and it points to bacterial flagellin. The dependence of inflammatory bowel disease (IBD) on intestinal microbes is increasingly clear but the molecular mechanisms are not. CD4+ T cell lymphocytes directed against enteric microbiota are crucial effector cells in experimental models of IBD. Enteric bacterial antigen reactive CD4+ T cells are able to induce colitis when transferred to immunodeficient recipients. There is a relatively small number of immunodominant antigens that stimulate pathological T cell responses and attention was drawn in a previous issue of JournalScan to a paper in PNAS that identified an epitope on the flagellar hook protein of Helicobacter hepaticus as a precipitant of colitis. The current paper from Birmingham Alabama and Los Angeles initially identified specific bacterial antigens driving experimental IBD by a technique called serological position cloning which screens DNA libraries with defined antisera. Strong reactivity against specific flagellins was seen in many models of colitis. They then demonstrated that flagellin specific CD4+ T cells induced colitis when transferred into SCID mice. The two flagellins tested were CBir1 and Fla-X, possibly derived from bacteria in the Clostridium and related genera but different to Salmonella species or E coli flagellin. Remarkably, serum IgG to CBir1 flagellin was then found to be elevated in patients with Crohn’s disease (p<0.0001) but not in ulcerative colitis or infective colitis, or normal controls. Antibodies to Salmonella species flagellin were not elevated in Crohn’s disease or other conditions.

The same investigators presented serological data at DDW on 211 patients, showing that 50% of patients with Crohn’s disease had anti-CBir1 antibodies compared with 8% of healthy controls. Anti-CBir1 antibodies discriminated patients with Crohn’s when other serological tests (ASCA, pANCA, anti-I2) were unhelpful. This remarkable observation means that a bacterial flagellin antigen identified in experimental CBir1/He8Bir mice (hence CBir1) could have a pathogenic role and that human anti-CBir1 could have a clinical application in discriminating Crohn’s from other colitides. It all has a ring of credibility because it is not difficult to conceive how a specific bacterial antigen, but not a bacterium, might cause colitis and account for epidemiological or genetic associations and lack of response to antibiotics. Watch this space.

Upper endoscopy is painless—except for patients ▶

Oesophago-gastroduodenoscopy (OGD) is considered safe, yet published complication and death rates vary widely and some data predate modern video endoscopes and sedation practices. The authors prospectively audited OGD and patient preferences, comparing midazolam sedation with pharyngeal anaesthesia. A total of 1287 consecutive outpatients (mean age 60 years) undergoing OGD in a high quality endoscopy unit were studied and 91% of patients were contacted at 30 days by structured questionnaire interview about adverse effects and sedation preferences. No immediate complications occurred during endoscopy although one patient required transfusion after a duodenal biopsy taken while on warfarin. In total, 119 patients (10%) reported 134 problems at 30 days, most occurring in the first seven days and lasting an average of eight days. The commonest were sore throat and abdominal pain and 25 patients (2%) sought medical attention for their problems. Some of these complaints might have related to the underlying condition triggering the endoscopy and so this value may be an overestimate. There were no differences between those having sedation and those having throat spray, nor were there any differences related to patient age or endoscopist experience. While 95% of patients having sedation would opt for the same method again, only 79% of pharyngeal anaesthesia patients would repeat the experience: in particular, 25% of women in this group would prefer sedation if undergoing a further endoscopy. Thus in good units with modern equipment, diagnostic endoscopy remains a safe procedure but, from the patient’s perspective, is associated with a significant minor morbidity rate, which we (and patients) should recognise.