Highlights from this issue

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Lymphocytic oesophagitis: pathologists and clinicians look out

Lymphocytic oesophagitis (LyE) has been reported in small series, but no consistent clinical correlations have emerged. In this issue of Gut, Haque and Genta (***see page 1108***) sought to determine the prevalence of LyE in a large US population and define its characteristics. Having established the criteria for the histopathological diagnosis of LyE (see figure 1), the authors then reviewed cases with this diagnosis, collected demographic, clinical and endoscopic data, and compared them with patients with either eosinophilic oesophagitis (EoE) or normal oesophageal biopsies. The study included 129 252 unique patients and controls. A diagnosis of LyE was made in 119 patients (median age 63 years, 40% men; 0.1% of patients with oesophageal biopsies). Dysphagia was as common in these patients as in those with EoE (53% vs 63%; NS), but gastro-oesophageal reflux disease was low in both (18% vs 19%, NS). The clinical and endoscopic characteristics of LyE and EoE overlap considerably although LyE affects predominantly older women. Although the precise clinical significance of oesophageal lymphocytic infiltrates remain to be defined, their association with dysphagia and possibly motility disorders warrants further investigations. More pathologists and clinicians should become aware of this entity and this will no doubt help uncover aetiological associations and therapies.

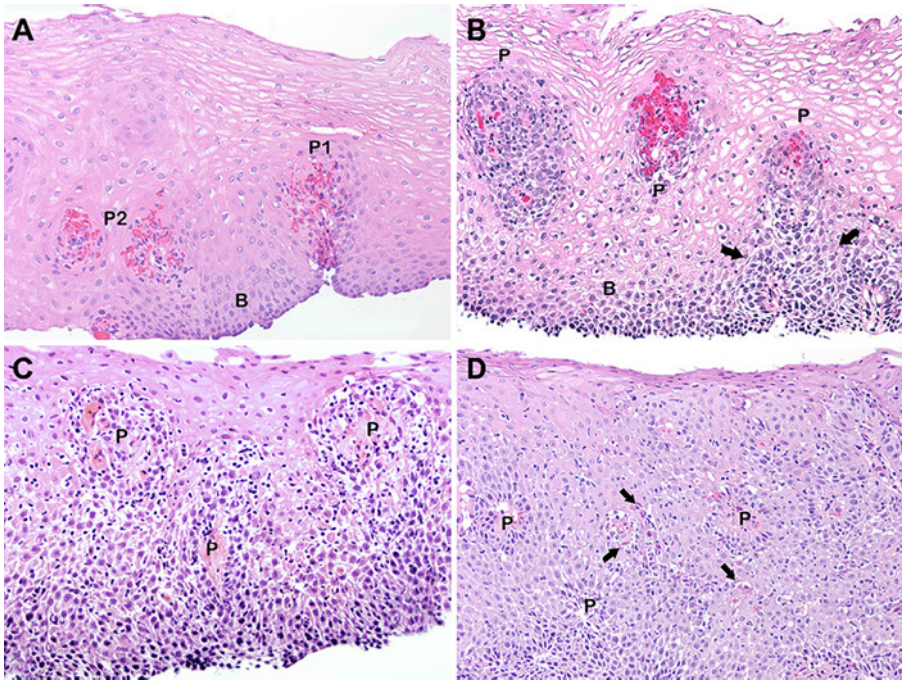

Figure 1 Proposed criteria for the diagnosis of lymphocytic oesophagitis.

The gut microbiota and their hosts

The human gut is home to trillions of bacteria that live in a finely tuned symbiosis with their hosts. Their combined genomes (metagenome), which contain 150-fold more genes compared with our own genome, provide us with functions that we did not have to evolve ourselves. The innate immune system recognises bacteria and other infectious agents by pattern recognition receptors such as Toll-like receptors (TLR). In this issue of Gut, Larsson *et al* studied the influence of innate immunity on microbiota-induced host responses and microbial composition along the length of the murine gut using Myd88 deficiency as a model for the loss of innate immune signalling. They report an extensive survey of host responses to the normal gut microbiota along the length of the gut. They demonstrate that Myd88-deficient mice harbour norovirus in the colonic epithelium, suggesting increased susceptibility to viral infections. The increased understanding of the fundamental factors underlying host-microbial interactions in the mammalian gut is essential for future studies directed at targeting the gut microbiota in order to improve health. The authors provide access to a web-accessible database, http://microbiota.wall.gu.se to investigate whether specific genes are regulated by the gut microbiota and/or MyD88. This resource will facilitate the identification of microbially regulated genes for researchers interested in all aspects of gastroenterology ***(see page 1124)***.

What is the risk of colorectal cancer in people who have a personal history of polyps?

Studies of people who have a personal history of colorectal adenomas have produced discordant results regarding the occurrence of colorectal cancer after colonoscopy with polypectomy. Cottet and colleagues have assessed the risk of

Table 1 Proportion of advanced TNM stage colorectal cancers according to the initial features of first adenomas removed and colonoscopic follow-up

Colorectal cancer diagnosed during follow-up	Total N=87	Among patients with initial advanced adenomas N=53	Among patients with initial non-advanced adenomas N=26
TNM stage III–IV—unclassified	**32 (36.8%)**	**21 (39.6%)**	**9 (34.6%)**
With colonoscopic follow-up	8 (9.2%)	4 (7.5%)	3 (11.5%)
Without colonoscopic follow-up	20 (23.0%)	15 (28.3%)	4 (15.4%)
Unknown colonoscopic follow-up	4 (4.6%)	2 (3.8%)	2 (7.7%)

colorectal cancer after adenoma removal in routine clinical practice and compared this risk to the risk of colorectal cancer in the general population. They conducted a cohort study based on people living in Burgundy (N=5779) and looked at the occurrence of colorectal cancer in people who had colonoscopy and colon adenomas. They found after a median follow-up of 7.7 years, 87 invasive colorectal cancers were diagnosed, whereas 69 cases were expected. Compared to the general population, the overall SIR was 1.26 (95% CI 1.01 to 1.56). The colorectal cancer risk was particularly increased in those people with advanced adenomas (table 1). This study reinforces the recommendation that people with a history of adenomas need a more aggressive surveillance programme than those with no history of colon adenomas ***(see page 1180)***.

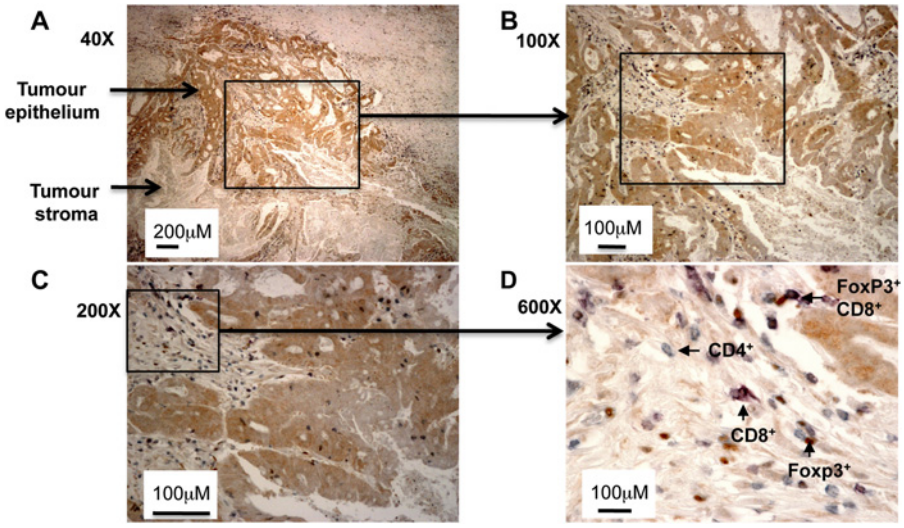

Figure 2 (A—D) Proportions of CD4 cells expressing Foxp3 in tumours and blood of CRC patients. A representative example of a paraffin-embedded human colorectal tumour triple-stained with Foxp3 (brown), CD8 (purple) and CD3 (grey)—specific antibodies.

More insight into what makes colon cancer recur

Colorectal cancer is the second leading cause of cancer-related death, usually as a result of metastatic spread of the cancer to distant organs, like the liver. One factor that may regulate the spread of colorectal cancer is the T cell response to the cancer. It appears that many colorectal cancers have an enrichment of T cells that can suppress anti-cancer immune responses. These cells are characterised by being CD4+Foxp3+ regulatory T cells, which are often referred to as Tregs. Betts *et al* now provide more insight into the role of Tregs in the progression of colorectal cancer. They have found that the presence of colorectal cancer drives the activity of Tregs and suppresses CD4+ T cell responses to tumour-associated antigens (figure 2). Importantly, the suppression of the CD4+ T cell response is associated with recurrence of colorectal cancer at 12 months implying that Tregs contribute to disease progression. These findings suggest that manipulation of Tregs may be another way to prevent the progression of colorectal cancer ***(see page 1163)***.

Hepatology

Importance of HBV recombination in individual patients

Variability of HBV DNA is an important issue for resistance to antiviral treatment. This interesting study from France (***see page 1197***) investigates individual patients with or without HIV co-infection remaining HBV viraemic on antiviral therapy for at least 1 year. Based on near complete HBV sequencing they found in many patients marked changes of HBV quasispecies during a rather short time usually due to recombination events (figure 3). These findings have important implications for diagnosis, monitoring and treatment strategies: genotyping in a single DNA region is not sufficient and should be repeated during treatment in patients remaining viraemic. Furthermore, there seems to be a relation between antiviral drugs and recombination which may play a crucial role in resistance to antiviral treatment. Finally, this paper should stimulate further studies investigating a possible relationship of recombinant mutants and the clinical course of individual patients.

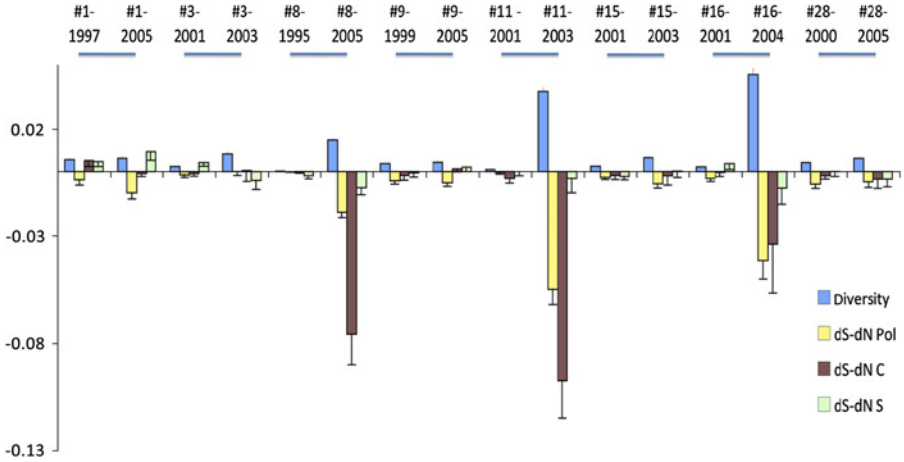

Figure 3 Evolution of diversity in the whole genome and of dS-dN distances in the polymerase, core and surface antigen-encoding regions. Intergenotypic recombinants were found in patients #8, #11 and #16 for whom drastic changes of diversity and dS-dN exist.