

Highlights from this issue

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Luminal GI

H1N1 influenza vaccination and IBD

The global pandemic of novel influenza A (H1N1) affected 70 countries in 2009. There was particular concern for infection in immunocompromised patients, including those with IBD. The 2009 H1N1 influenza vaccine produced seroprotection rates of >85% in the general population but there are no data on the immunogenicity of the vaccine in patients with IBD. In this issue of *Gut*, Cullen *et al* report their observational prospective open-label study which examined the immunogenicity of the 2009 H1N1 influenza vaccine in IBD patients. Patients with IBD vaccinated with the 2009 H1N1 influenza vaccine had a low rate of seroprotection, particularly those who were immunosuppressed or received combination immunosuppression (see table 1). An assay of T lymphocyte function may indicate those at risk of low rates of vaccine response. The work highlights the need for studies of the clinical benefit of vaccines in this population and patients with IBD need to be aware of this reduced immunogenicity (see page 385).

Visceral hypersensitivity in endometriosis

Patients with minimal to mild endometriosis often have symptoms that are out of proportion to the laparoscopic findings. The reason for this observation is unknown. IBS is also common in this setting and it feasible that the visceral

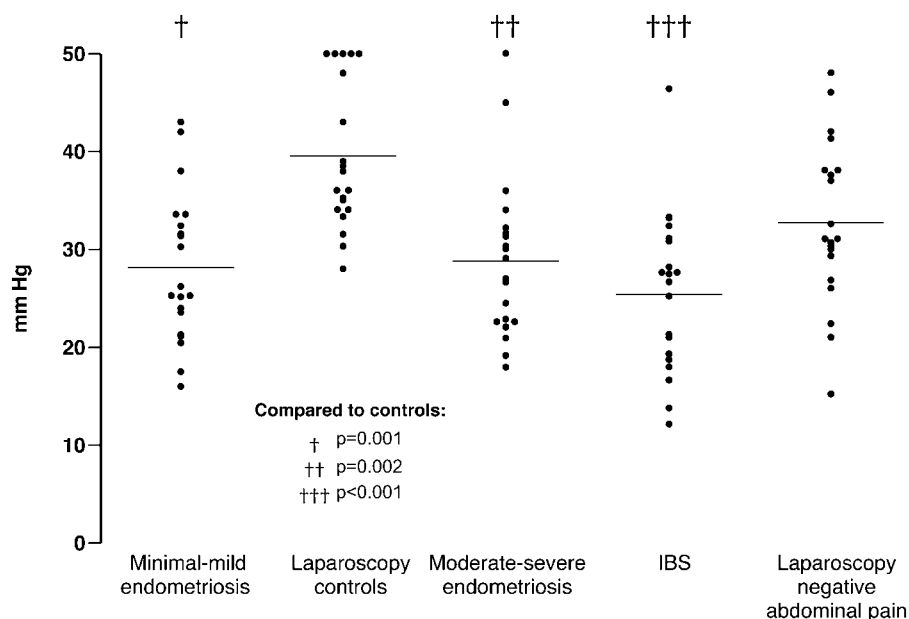


Figure 1 Comparison of individual sensory thresholds and group means between laparoscopy controls and patients with minimal to mild endometriosis, moderate to severe endometriosis, laparoscopy negative abdominal pain and irritable bowel syndrome (IBS).

hypersensitivity associated with this condition might be amplifying the symptoms of endometriosis. In this issue of *Gut*, Issa *et al* assessed visceral sensitivity to balloon distension, symptoms and psychological status following laparoscopy in women with minimal to mild endometriosis, moderate to severe endometriosis, laparoscopy negative abdominal pain and asymptomatic women undergoing laparoscopic sterilisation who acted as controls, and compared with women with IBS. They show that visceral hypersensitivity is common in patients with endometriosis and especially those with minimal to mild disease (see figure 1). They speculate that this might be the underlying mechanism that explains the paradoxical discrepancy between symptoms and extent of disease. This study has introduced a completely new concept into the understanding of pain in endometriosis and could open up new opportunities for treatment (see page 367).

A better way to do colonoscopy?

It is well known that standard colonoscopy misses adenomas, especially those

located on the proximal aspects of haustral folds. So, there has been a lot of effort put into developing more accurate endoscopic methods for polyp detection. Cap assisted colonoscopy is one of these methods. It uses a transparent plastic cap attached to the tip of the colonoscope that can help flatten and depress the colonic folds, thereby decreasing the blind mucosal areas. Although conceptually appealing and technically straightforward, the results from prior studies have shown variable success rates with this method. In this issue, Amit and colleagues report on a randomised controlled trial on cap assisted colonoscopy in a western cohort. In this well-designed study, they found cap assisted colonoscopy detected a significantly higher proportion of subjects with at least one adenoma as well as higher number of adenomas per subject compared to standard colonoscopy. Perhaps most importantly, they found cap assisted colonoscopy also detected significantly more right sided adenomas and flat adenomas compared to standard colonoscopy (see page 402).

Table 1 Post-vaccination seroprotection rates (defined as HI \geq 40) for the 2009 H1N1 influenza vaccine shown as percentages in all subjects (n=105)

	All subjects (n=105)
All subjects	52/105 (50%)
Non-immunosuppressed, based upon medication	18/28 (64%)
Immunosuppressed, based upon medication	34/77 (44%)
Corticosteroid monotherapy	2/3 (67%)
Imod/MTX monotherapy	11/26 (42%)
Biological monotherapy	16/34 (47%)
Combined Imod/biological/steroid	5/14 (36%)

HI, haemagglutinin inhibition; Imod, immunomodulators (azathioprine or 6-mercaptopurine); MTX, methotrexate.

New molecular markers for high-risk GISTs

Gastrointestinal stromal tumours (GIST's) are the most common mesenchymal tumours of the gastrointestinal tract. They are often cured by surgical resection alone, but a subset of these tumours will metastasize. There are two predominant prognostic features (tumour size and mitotic index) of primary GISTs that are currently used for risk stratification. Although clinically of some value, these features misclassify a subset of cases as low risk that nonetheless metastasize. Okamoto and colleagues have now used state of the art genome-wide DNA methylation analysis to find more accurate molecular markers for determining

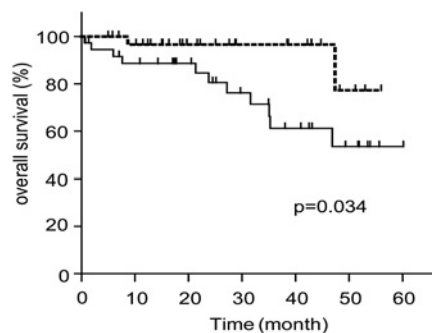
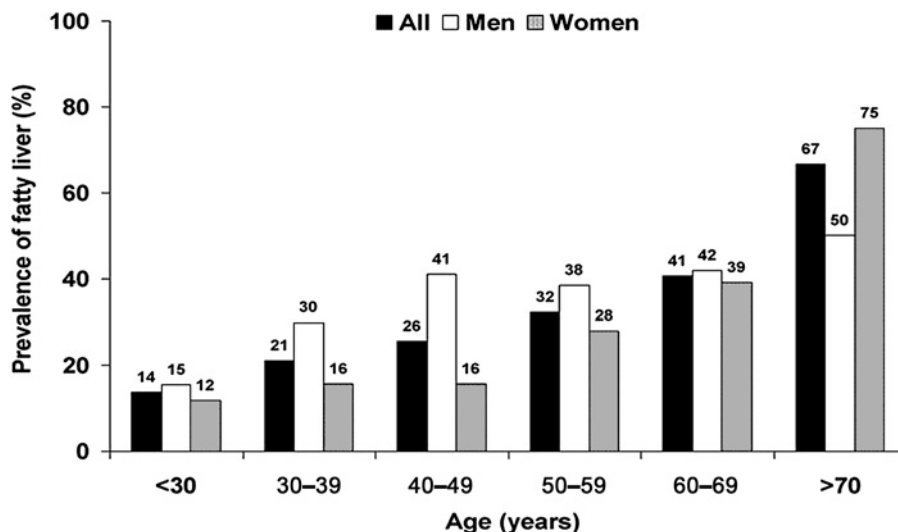


Figure 2 Kaplan-Meier analysis of overall survival in cases of GIST with and without DNA methylation in at least one of the *REC8*, *PAX3* or *p16* genes. Broken and solid lines indicate GIST without (n=32) and with methylation (n=37), respectively (p=0.034).



Men	N =	39	30	122	146	50	2
Women	N =	34	51	192	201	51	4

Figure 3 Prevalence of fatty liver by age and gender.

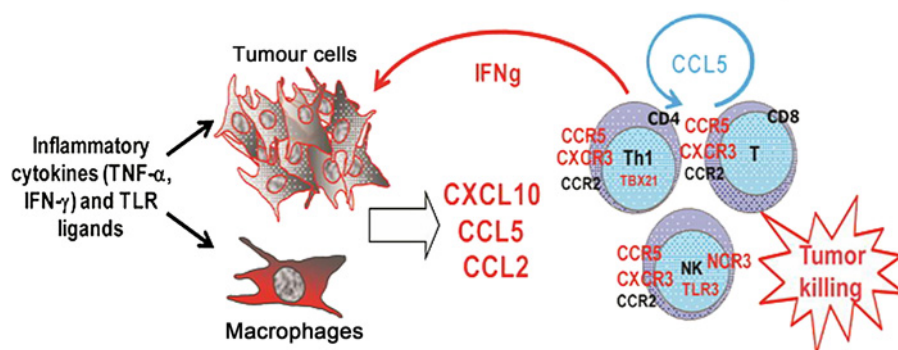


Figure 4 Model showing that the inflammatory cytokines TNF- α and IFN- γ and TLR ligands stimulate cancer cells or macrophages to produce the key chemokines CXCL10, CCL5 and CCL2. These chemokines induce tumour-infiltration by Th1, CD8⁺ T and NK cells which induce cancer cell killing and tumour control.

the prognosis of GISTs. They found more genes were methylated in advanced GIST than small GIST, suggesting a link between the accumulation of DNA methylation and disease progression. In one of the largest series of GISTs published to date, they found three methylated genes, *REC8*, *PAX3* and *p16/CDKN2A*, significantly correlated with a worse prognosis, suggesting that these may be used in the clinic in the near future to identify those patients who may be candidates for adjuvant therapy (see page 392).

Hepatology

MR spectroscopy for detection of NAFLD in a Chinese population

This interesting paper describes a prospective, cross-sectional study on the prevalence of non-alcoholic fatty liver disease (NAFLD) in a large cohort randomly selected from the Hong Kong population. Just recently Clavien's group suggested MR imaging as new reference standard for quantifying hepatic steatosis (*Gut* 2012;61:117–27). Interestingly, by use of proton MR spectroscopy the present study found a 27% prevalence of NAFLD which was clearly age dependent and to some extent also gender dependent (see figure 3). Advanced fibrosis as determined by elastography was found in only 4%. Modest alcohol consumption was not associated with neither fatty liver nor with fibrosis. These results indicate that MR spectroscopy might be a useful tool to screen for NAFLD (see page 409).

An intra-tumoral gene signature focusing on inflammation predicts survival in patients with early HCC

This intriguing study investigated the importance of inflammation in the tumour microenvironment for progression of hepatocellular carcinoma (HCC). The authors identified a signature of 14 immune genes expressed in resected HCC tissue as predictor of survival in training and independent validation cohorts, respectively. This was striking for patients with early stages of HCC. The thorough and comprehensive work also demonstrates a functional correlation between the expression of some of these genes coding for chemokines and the infiltration by lymphocytes or NK cells. The authors propose a model (figure 4) to explain the immune mechanism underlying survival probability in early HCC (see figure 4) (see page 427).