acupuncture on non-acupuncture points and consequently it is not clear if the effects were due to unspecific effects. Sham acupuncture trials have the disadvantage that the unspecific effect could always be due to some hypothesised unspecific needing effects and hence will always lead to the questions: ‘Was that really a non-acupuncture point? How do you know that acupuncture does not have any effect?’ This was excluded with our study design.

The question arises, why is placebo-acupuncture and placebo in general so effective in irritable bowel syndrome? The second question is whether the results of experimental trials are really due to specific effects. If they are, why is this not reflected in clinical trials? What role does cognitive processing play in this context? Further research is required to shed light on this phenomenon. It was not possible to do a subgroup analysis from a statistical point of view as we had only nine males in our study. This was the same for the clinical subgroups. However, the placebo effect was so strong that almost 526 patients would be necessary to prove an effect. Such an effect could be interesting but may not be clinically relevant.

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References

Infliximab as a treatment for systemic amyloidosis associated with Crohn’s disease
Systemic AA amyloidosis is a serious and potentially fatal complication of Crohn’s disease.7 Although drugs such as azathioprine, colchicines, and dimethylsulphoxide are suggested to delay the progression of renal amyloidosis, the efficacy of these drugs on renal amyloidosis has not been fully elucidated.8 Infliximab is a chimeric anti-tumour necrosis factor a (TNF-a) monoclonal antibody. This drug has been proven to induce clinical response and remission in Crohn’s disease patients with rapid onset of mucosal healing, and improvement of perianal disease, thus increasing quality of life.9 Recent studies provided evidence that infliximab also improved the extraintestinal complications of Crohn’s disease, such as spondyloarthropathy10 and psoriasis.11

Without regard to amyloidosis, recent studies demonstrated the efficacy of infliximab on secondary amyloidosis associated with rheumatic inflammatory diseases.6 However, no clinical report showing the effect of infliximab on amyloidosis associated with Crohn’s disease have been found. Thus, here we present, for the first time, a patient with systemic AA amyloidosis associated with Crohn’s disease that significantly responded to infliximab.

A 34 year old male Crohn’s disease patient was admitted to our hospital with acute
progression of renal dysfunction on 4 April 2004. This patient was diagnosed as having Crohn’s disease with ileocolitis in 1990 based on clinical, endoscopic, and histological criteria. A small amount of proteinuria was observed in 1992, and AA type amyloid deposition was systemically detected in biopsy specimens from his colon, terminal ileum, stomach, duodenum, and kidney.1 Before admission he had been treated with elemental diet,2 prednisolone, and dimethylsulphoxide. After admission, he underwent parental nutrition therapy. However, inflammatory parameters and renal function did not improve in two weeks, and we decided to use infliximab. He received an infusion of infliximab 5 mg/kg on 16 April 2004, and his renal function as well as C reactive protein drastically improved (fig 1). Furthermore, serum amyloid protein level also decreased significantly (from 762 to 30.2 mg/l) in 10 days. The Crohn’s disease activity index (CDAI) of the patient decreased from 235.5 to 76.9 points in eight weeks.

Although the detailed mechanism is unknown, it is noteworthy that infliximab not only decreased serum amyloid protein level but also ameliorated the renal function of our patient with systemic AA amyloidosis associated with Crohn’s disease. Therefore, we hope that clinical trials assessing the efficacy of infliximab in systemic amyloidosis associated with Crohn’s disease will soon be conducted. There have been many patients with Crohn’s disease who have suffered from severe and fatal extraintestinal complications. Infliximab may shed light on therapeutical strategies for such patients.

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References

Do baseline ALT levels predict complications of chronic hepatitis B?

We read with interest the paper by Yuen et al (Gut 2005;54:1610–4). This study included a large patient cohort with chronic hepatitis B and analysed the determinants predicting outcome. The authors concluded that low level viraemia and mildly elevated serum alanine aminotransferase (ALT) levels more commonly led to the development of complications. This conclusion however was not supported by their findings as the independent predictive factors were male sex, age, stigmata of chronic liver disease, and others, whereas serum ALT and hepatitis B virus (HBV) DNA levels were not.

It is questionable if patients with mildly elevated baseline ALT levels are truly associated with a higher risk of complications. As shown in fig 2 of their paper, the incidence of complications in the group with ALT >2–6× upper limit of normal (ULN) and the group with ALT >6×ULN was still significantly higher compared with the group with ALT <0.5×ULN that had the lowest risk of complications. More importantly, serum ALT level was not an independent risk factor predicting poor outcome in the Cox multivariate analysis, suggesting lower serum ALT and/or HBV DNA levels were only associated but not independent factors. Although HBV DNA levels were tested to correlate with clinical course, it should be noted that DNA levels were measured at different time points (21 patients before, nine at, and 80 after the complication developed) and this inhomogeneous information makes the analysis the impact of HBV DNA level on disease course less useful. Interestingly, entirely different conclusions were reported from a recent study that prospectively investigated 41 Taiwanese men who were HBV carriers.1 A higher baseline HBV DNA level was associated with an increased risk of the development of hepatocellular carcinoma (HCC), with a risk ratio of up to 7.3-fold.1 In addition, a positive baseline hepatitis B e antigen consistently predicted a higher risk of HCC.2 The contrast between these studies can be best explained by the fact that patient data were collected at different time points in the natural history of chronic hepatitis B. In this regard, the necessity of serial multiple measurements of clinical parameters in patients with chronic hepatitis B has been emphasised to reveal important information associated with long term outcomes.

Another potential flaw in this study is that the authors defined ascites, spontaneous bacterial peritonitis, and encephalopathy as complications of chronic hepatitis B. It should be noted that these are rather late complications of cirrhosis and may not be directly related to HBV infection. As the time interval from silent cirrhosis to the development of complications may vary widely and many cirrhotic patients never develop significant cirrhosis related complications in their natural history, the complication should be defined as formation of cirrhosis or HCC which is directly linked with chronic HBV infection.

In summary, end points evaluated should be cirrhosis or HCC rather than cirrhosis related complications which are not directly related to HBV infection. Lower serum ALT and HBV DNA levels more likely reflect a later stage of chronic hepatitis B and are possibly associated with increasing age of these patients who may already have severe fibrosis or subclinical cirrhosis.

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References

Authors’ reply
We would like to thank Dr Huo et al for their comments. The following are point by point responses to their comments.

(1) Serum alanine aminotransferase (ALT) levels were not considered in our analysis of prognostic factors because stratification into five groups rendered it too complicated for statistical calculation by multivariate analysis. In addition, we aimed to examine independently the differences in outcome in patients with different ALT levels, as elevated ALT level is the most commonly used criterion for initiation of treatment. As for HBV DNA levels, our conclusion was that development of cirrhosis was related to prolonged low level viraemia up to the time of development of complications. Baseline HBV DNA levels would be of little help in determining whether HBV DNA levels are important. A good example was reported in DNA levels in children, this does not mean that they are at risk of cirrhotic complications when they are young.

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