therefore believe that most symptoms were related to the duodenal giardiasis, and that finding *G lamblia* trophozoites in the colon was likely to be an epiphenomenon to the upstream small bowel infection.

Colonic giardiasis has been rarely reported in immunocompetent hosts [1 2] and its contributing factors are speculative. Cholesterol deprivation and exposure to bile acids[3] are demonstrated in vitro as two major stimuli of *G lamblia* encystation. Similarly, in vivo, cholestasis and diet supplemented with cholestyramine have also been shown to dramatically decrease the fecal excretion of *G muris* cysts in mice.[4] We suggest that fibrate treatment, which increases biliary cholesterol excretion and decreases the excretion of bile acids, hampered giardia encystations in our patient, subsequently facilitating *G lamblia* colonic colonisation of trophozoites.

A search through national adverse event databases (Canadian Adverse Drug Reaction Monitoring Program, United Kingdom Medicines and Healthcare products Regulatory Agency: Drug Analysis Prints, United States Food and Drug Administration Adverse Event Reporting System) failed to find any similar report. Changes in bile metabolism induced by hypolipidaemic drugs (not only fibrates but also niacin and statins) or bile acid resins (cholestyramine) may influence the presentation and spreading of *G lamblia*.

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Bone marrow stem cells and liver disease

The review article by Kallies *et al* focuses on the various relationships between bone marrow stem cells (BMSC) and liver diseases (*Gut* 2007;**56**:716–24). It discusses experimental studies with animal models and critically examines the possible role of BMSC in liver repair through the delivery of growth factors, fibrosis resolution and new blood vessel formation.

In addition, the authors examine the development of BMSC treatment of liver diseases and describe three uncontrolled phase 1 clinical trials in humans published up to December 2006. The main end point of these trials was to evaluate the feasibility and safety of BMSC treatment in patients with chronic liver disease. In one trial, human CD34+ stem/progenitor cell populations mobilised into the blood by granulocyte colony-stimulating factor were injected directly into the portal vein or hepatic artery.[1] The study from Terai *et al* transplanted autologous BMSC that were prepared from a large amount (400 ml) of iliac crest aspirate and infused into the peripheral vein of the patients.[2] Feasibility and safety was observed in all studies. Patients' follow-up showed improvement of serum albumin levels and Child–Pugh score.

Our research group has recently published data on 10 patients on a waiting list for a liver transplant who had end-stage chronic liver disease and were enrolled to receive infusion of autologous BMSC.[3] About 50 ml of bone marrow was aspirated under mild sedation and prepared by centrifugation in a Ficoll–Hypaque gradient. A minimum of 100 millions of mononuclear-enriched bone marrow cells were infused into the hepatic artery of the patients by the routine technique used for arterial chemoembolisation of liver tumours. Our results showed that infusion of BMSC into the hepatic artery of patients with advanced chronic liver disease is safe and feasible. In addition, we also observed a decrease of serum bilirubin and an increase in albumin levels.

It seems clear that trials of BMSC treatment in patients with liver disease are still at a preliminary stage and a better understanding of the physiology and mechanism of action of BMSC in animal models of liver disease is needed. Nevertheless, the high death rate of patients on a waiting list for a liver transplant, especially in some areas of the world, and the fact that autologous BMSC treatment is feasible, safe and seems to lead to improvement of the Child–Pugh score and serum albumin levels suggests that randomised controlled studies should be carried out to evaluate the efficacy of BMSC treatment in patients with advanced liver disease.

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Authors' reply

We are grateful to Lyra *et al* for their recently published study showing the apparent safety of bone marrow (BM)-derived mononuclear cell injection for advanced liver cirrhosis.[1] We agree that there is an urgent need to develop alternative treatments for liver cirrhosis given the worsening mismatch between the number of patients requiring a liver transplant and the number of organs available for transplantation.

Stem cell therapy has the potential to benefit this group of patients. However, unlike a defined pharmacological treatment there is additional complexity in selecting BM cells or other stem cells for therapy. There is a wide heterogeneity of cell phenotypes within the BM, and indeed BM stem cells have a wide differentiation potential. Thus different cell isolation and sorting protocols may result in differing cell populations engrafting the liver, with widely varying effects. Initial optimistic reports that BM cells readily differentiated into hepatocytes in vivo have not been substantiated.[2] The case for the clinical use of BM cells in cirrhosis treatment is therefore based on alternative mechanisms of action such as collagen degradation, enhanced vascularisation or secretion of cytokines and growth factors to stimulate liver regeneration.

We agree that given the growing problem of deaths of patients on the liver transplant waiting list and the apparent safety of the use of BM stem cells reported by Lyra *et al*[1] and by other authors,[3] it is ethically justifiable to perform a randomised trial of mononuclear cell therapy for liver cirrhosis. However, many questions remain to be answered such as: Which are the optimal cells to select, and are these cells actually beneficial? If so, what phenotype do the cells eventually adopt in the liver and how do they exert a therapeutic effect? How long does this benefit last, and would you get a longer lasting benefit by injecting more primitive stem cells than more differentiated cells? If a randomised trial was negative should more or different cells have been tried? Of course, the answers to these questions are likely to be found through a combination of preclinical and translational clinical studies that will elucidate mechanism, and randomised trials that will hopefully define a clinical effect. A word of caution should be added though, a population of BM-derived stem cells has been shown to have a fibrotic potential in the liver.[4 5] Furthermore, macrophages, although ''antifibrotic'' in the recovery phase after liver injury, can also be ''profibrotic'' during continuing liver damage.[6] These factors should be borne in mind when planning and implementing new stem cell trials for cirrhosis.

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