Hypomagnesaemia due to malabsorption is not always responsive to oral magnesium oxide supplementation alone

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We read with interest the Gut File report by Dr Ross and colleagues of hypomagnesaemia due to malabsorption, eventually responding to oral magnesium oxide supplementation (Gut 2001;48:857–8). Our experience however has been different. For the past seven years we have managed a 65 year old woman with short bowel syndrome (right hemicolectomy after a terminal ileal resection for abscess formation) who have managed a 65 year old woman with short-bowel syndrome (right hemicolectomy) have managed a 65 year old woman with short-bowel syndrome (right hemicolectomy) after a terminal ileal resection for abscess formation. They were unable to malabsorption, eventually responding to oral magnesium oxide supplementation but despite this the frequency of intravenous magnesium “top ups” were not reduced. Compliance was not deemed to be an issue with our patient.

Since then we have managed this woman while still taking magnesium oxide supplements with almost 3–6 monthly (fig 1) intravenous magnesium replacement through a peripheral line and have avoided insertion of a Hickman line and all its associated complications.’ While we agree that a trial of magnesium oxide is prudent and until the pharmacokinetics are better understood, this preparation may not be sufficient, especially in patients with extensive resection of the small bowel, as demonstrated in our patient.

Figure 1 Serum magnesium levels in our patient over the course of treatment with magnesium oxide supplements and intravenous magnesium replacement.
Authors’ reply

We appreciate Dr Beales’ interest in our study describing the effects of gastrin releasing peptide (GRP) and its antagonist BIM26226 on gastric acid secretion in healthy male subjects. One can only speculate on the mechanisms of endogenous GRP on acid output were independent of plasma gastrin in humans. These results are clearly in contrast with findings in animals and suggest species differences. Thus the molecular mechanism of GRP stimulated acid production has not directly been substantiated in humans. This is not likely to be investigated in the near future because the antagonist BIM26226 is no longer available for human use.

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Osteoporosis is not a specific complication of primary biliary cirrhosis (PBC)

Newton et al (Gut 2001; 49: 282–7) described a retrospective study on bone mineral density (BMD) in a large cohort of patients with primary biliary cirrhosis (PBC). The authors concluded that osteoporosis is not a specific complication of PBC, but certain weaknesses in the study design do not support this conclusion.

(A) The authors did not include age and sex matched controls from the general population, or control groups with different types of liver disease.

(B) A proper methodological design comparing osteoporosis in PBC and in a normal population should calculate the standardised incidence ratio of osteoporosis for the two cohorts by comparing the observed incidence versus the expected incidence. The calculation should include 95% confidence intervals according to exact Poisson limits.

(C) A logistic regression analysis including risk factors for osteoporosis (that is, age, menopausal status, smoking habits, alcohol consumption, etc) should have been performed.

The major drawback however is the lack of control population matched to other types of liver disease. New data are emerging in the literature concerning this field. In particular, several recent studies (including one of our own1) have demonstrated that PBC in itself does not exert a negative influence on BMD. Thus we agree with Newton et al that osteoporosis in PBC should be revisited. In fact, analysis of the literature enables the following conclusions to be drawn. There are several osteoporosis risk factors common to liver disease, aging processes, or genetic variability, as well as cholestasis related risk factors, that are obviously not specific for PBC (table 1).

The pathogenesis of osteoporosis is multifactorial, increasing with advancing age, and influenced by genetic factors, and it may be that liver disease accelerates bone resorption through various mechanisms.

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References

Authors’ reply

We read with interest the letter of Professor Floreani in which she agrees that it is timely to revisit the perceived dogma that patients with primary biliary cirrhosis (PBC) are predisposed to osteoporosis. It was pleasing to note that our findings compare favourably with work from her group. We would also like to take this opportunity to draw attention to two further studies which have been presented in abstract form since the submission of our manuscript, which confirm that there is no increase in prevalence of osteoporosis and no increase in fracture risk in PBC populations taken as a whole compared with appropriately matched normal controls. A further study has also been published recently describing bone mineral density in a selected series of patients with PBC in whom the proportion of osteoporosis (defined by T score) was comparable with that seen in our series. We were pleased to note that in this prospective series other risk factors for osteoporosis were examined. They concur with our finding that increased age is an independent risk factor, although they do not present mean Z score data (bone mineral density data controlled for both sex and age). Their group, we would argue, was younger and had more severe disease than patients in our series, whom we would regard as more representative of the whole PBC population.

In our study we demonstrated that although 85/272 (31%) patients had osteoporosis, as defined by the World Health Organization at the time of their first DEXA scan, mean Z score at the neck of femur was −0.1 and at the lumbar spine 0.1. As Z scores represent bone mineral density compared with an age and sex matched population, this suggests that the prevalence of osteoporosis seen in PBC is a reflection of the fact that this is predominately a disease of postmenopausal women who show a generalised increased prevalence of osteoporosis. The use of Z scores implicitly controls our data for age and sex norms. We agree with Professor Floreani that redressing the question of osteoporosis prevalence in other chronic liver diseases (both cholestatic and non-cholestatic) would be of interest but we feel that this is not relevant to the current study.

Given the very real problems experienced by some PBC patients as a result of osteoporotic fracture (particularly in the early post-transplant period), further study of the aetiology is appropriate (although the retrospective nature of the current study makes the suggested logistic regression analysis inappropriate). The message that we (and more recently others) have been communicating is that the search for risk factors for osteoporosis should not be focused on liver disease specific factors but could more usefully be directed at more generalised population risk factors.

Acknowledgements
We would like to take this opportunity to acknowledge the support of the National Institute for Health Research, Centre for Global Health Research, Guy’s and St Thomas’ Foundation Trust, London.

Table 1 Risk factors for osteoporosis in liver diseases

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<th>Common risk factors</th>
<th>Cholestasis related risk factors</th>
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<tr>
<td>• Cirrhosis</td>
<td>• Calcium malabsorption</td>
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<td>• Female sex</td>
<td>• Vit D malabsorption</td>
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<tr>
<td>• Old age</td>
<td>• Hypogonadism</td>
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<td>• Alcohol consumption</td>
<td>• Hypothyroxinaemia</td>
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Expression of isofoms of nitric oxide synthase in collagenous colitis

We read with interest the study by Perner et al (Gut 2001;49:387–94) investigating expression of various isofoms of nitric oxide synthase (iNOS, eNOS, and nNOS) in non-inflamed colon, collagenous colitis, and ulcerative colitis. Inducible NOS (iNOS) was identified by immunohistochemical analysis in the epithelium of patients with non-inflamed colon. The authors concluded that this might be a result of bowel preparation with bisacodyl. Increased synthesis of nitric oxide has been detected by a number of different methods in bowel preparation with bisacodyl.

We have previously found a physiological expression of iNOS in histologically normal colon using reverse transcription-polymerase chain reaction (RT-PCR), immunohistochemistry, and immunoblotting. Tissue from three different sources was studied. Surgical specimens were obtained from patients undergoing colectomy for colorectal cancer who had undergone bowel preparation with sodium picosulphate, colonic mucosal biopsies from patients who had received no bowel preparation. This last group of patients also underwent colonoscopy with and without bowel preparation and again 12 hours after rectal administration of an enema consisting of bisacodyl (100 mg) or polyethylene glycol 3000 (6.4 g in 100 ml of water) in randomised order. Expression of iNOS protein was quantified by western blot analysis and localised by immunohistochemistry. iNOS was expressed in the colonic mucosal biopsies from all subjects and localised in epithelial cells, particularly at the luminal border of the epithelial cells and more pronounced in the crypt epithelium. Expression of iNOS was unaffected by bowel preparation with bisacodyl or polyethylene glycol (fig 1).

Hence we agree with Cameron et al that expression of iNOS in epithelial cells is possibly a result of physiological expression of iNOS rather than a secondary phenomenon as a result of the bowel preparation per se or the effect of the secretagogue laxative bisacodyl.

For the reasons given above, we also agree that nitric oxide may be important in maintaining the epithelial barrier and may represent a link between dietary or other luminal factors and the development of colorectal cancer, as hypothesised by Cameron et al, although high iNOS expression in collagenous colitis is not associated with an increased risk of malignancy.

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References
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