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Maintenance azathoprine in Crohn's disease: how long? ►

▲ Lemann M, Mary J-Y, Colombel J-F, *et al*. A randomized, double-blind, controlled withdrawal trial in Crohn's disease patients in long-term remission on azathioprine. *Gastroenterology* 2005;**128**:1812–18.

Thiopurine therapy is known to be an effective maintenance therapy in Crohn's disease. In patients who enter prolonged remission, there is concern about long term therapy because of the potential for bone marrow suppression, opportunistic infection, and the possibility of an increased risk of malignancy, particularly lymphoma. The benefit of continuing therapy has been addressed in this study, from 11 centres, in a double blind withdrawal trial. Patients in remission for more than 3.5 years (mean five years) either continued azathioprine at a mean dose of 1.7 mg/kg (n = 40) or switched to placebo (n = 43) for 18 months. Most of these patients had colonic disease (with or without small bowel involvement). During this time, 3/40 (8%) relapsed in the azathioprine group and 9/43 (21%) on placebo. The difference was 13.4% and the upper limit of the 95% confidence limit for this difference was 26%. The trial was powered to test for non-inferiority of the placebo versus continuing azathioprine, with a difference of more than 20% being considered clinically useful. The upper limit of the difference was greater, and so non-inferiority of stopping azathioprine could not be confirmed.

This study therefore shows that continuation of azathioprine beyond 3.5 years of remission is effective in reducing further relapses. The downside is the one patient on azathioprine who developed fatal myelodysplasia associated with abnormalities in chromosome 7. The annual risk of relapse for those on placebo is low (approximately 14%) but this trial does confirm further reduction in risk of relapse if azathioprine is continued, to be weighed against the inconvenience of monitoring and the (small) risk of toxicity.

A fluid debate ►

▲ Fernandez J, Monteagudo J, Bargallo X, *et al*. A randomized unblinded pilot study comparing albumin versus hydroxyethyl starch in spontaneous bacterial peritonitis. *Hepatology* 2005;**42**:627–34.

Despite a recent clinical trial (including 6997 critically ill patients) confirming unequivocally the safety of albumin (Finfer *et al*. *N Engl J Med* 2004;**350**:2247–56), the cost of albumin justifies a continued debate on its role as a plasma expander. In a previous study including 126 patients with spontaneous bacterial peritonitis (SBP), albumin infusion in addition to antibiotic therapy significantly reduced renal failure and mortality (Sort *et al*. *N Engl J Med* 1999;**341**:403–9). However, this study was criticised for inadequate fluid resuscitation in the control group. Fernandez *et al* have compared the effect of 20% albumin with that of hydroxyethyl starch (Hesteril 6% 200/0.5) in 20 patients with SBP. Patients received two doses of plasma expander, 1.5 g/kg body weight on day 1 and 1 g/kg on day 3. Although the oncotic capacity of albumin is identical to that of hydroxyethyl starch, treatment with albumin (not hydroxyethyl starch) was associated with an increase in arterial pressure and systemic vascular resistance with a reduction in plasma rennin activity. Measures of endothelial dysfunction, including plasma von Willebrand related antigen, serum nitrates, and nitrite were higher in patients treated with hydroxyethyl starch. None receiving albumin, but one of 10 in the hydroxyl ethyl group developed renal failure.

The findings of this pilot study suggest that the beneficial effects of albumin in SBP are due not only to volume expansion but to its potential ligand binding, antioxidant, and anti-inflammatory properties. The conclusions should lead to a large clinical trial investigating the role of a variety of plasma expanders in the management of SBP with clinically relevant end points.

Double standard in the small bowel? ►

▲ May A, Nachbar L, Ell C. Double-balloon enteroscopy (push-and-pull enteroscopy) of the small bowel: feasibility and diagnostic and therapeutic yield in patients with suspected small bowel disease. *Gastrointest Endosc* 2005;**62**:62–70.

Capsule endoscopy leaves us with the problem of obtaining tissue and providing therapy. Push enteroscopy has limited depth of insertion but double balloon enteroscopy (DBE) may allow deeper examination, and in this prospective observational case series the authors undertook DBE in 137 patients with obscure bleeding (90), abdominal pain (11), polyposis syndromes (14), or other suspected small bowel disease, all having undergone extensive negative investigations. The system comprises a 200 cm endoscope with a flexible overtube and latex balloons attached to the tip of the enteroscope and overtube. These allow stabilisation, and sequential pushing and pulling allows segments of small bowel to be examined. The procedure was performed transorally and in 18 patients also via the anal route to visualise the ileum. The procedure was well tolerated and no major complications occurred. Average procedure time was 73 minutes by either route but the oral route allowed almost twice as much small bowel to be examined (240 cm) and problems with bowel preparation, instrument floppiness, and ileal intubation limited success by the anal route. Lesions were found in 70% in patients who underwent oral DBE, rising to 85% if both routes were used. Fifty seven patients (41.5%) underwent endoscopic therapy, including argon plasma coagulation, polypectomy, and dilatation while medical treatment was started or changed in 17%, mostly for Crohn's disease. A decision to operate was made in a further 24 patients on the basis of the findings while no abnormality was discovered in the rest.

These results are clearly impressive and if replicated in randomised controlled studies, DBE may truly usher in a new era of understanding about diagnosis and therapy of small intestinal diseases.