ment in only eight patients (2%). Three have already died within 6 months, of unrelated causes, and five remain well, so far.

We strive not to leave stents in on a permanent basis, believing that most patients can be managed effectively by expert endoscopy, radiology, and surgery, including adjunct techniques such as shock wave lithotripsy. Stenting is useful for a few weeks or months during which the patient's health and options can be reviewed. The King's group are rightly cautious in their recommendations. Stenting has not yet been shown to be a good permanent method for managing difficult stones, and should be used very sparingly.

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1 Cotton PB, Forbes A, Leung J, Dineen L. Endoscopic stenting for the long term treatment of large bile duct stones; 2 to 5 year follow up. *Gastrointest Endosc* 1987; 33: 411-2.

Reply

EDITOR,—In his letter, Dr Cotton raises two important points. The first is the high number of patients that were treated with an endoprosthesis and the second the adequacy of such a treatment in the long term. It is true that the number of patients treated with this approach in our series is high and this is because of two reasons. Firstly, it reflects the referral of some patients who had not responded to treatment in other experienced hands and secondly a conscious decision to achieve immediate drainage and clinical stabilisation in elderly and frail patients in whom we considered a protracted procedure might be more detrimental.

Dr Cotton places great emphasis upon duct clearance, but we would suggest that in some cases this may expose the patient to more risk than an in-dwelling prosthesis. There is a need for controlled data to answer these important points and we are pleased to confirm that we are now well into a multicentre study in a well defined 'high risk' group of patients.

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Assessment of proliferation of squamous, Barrett's, and gastric mucosa in patients with columnar lined Barrett's oesophagus

EDITOR,—I comment on the interesting paper by Iftikhar *et al* on assessment of proliferation in oesophageal squamous, Barrett's, and gastric epithelium by flow cytometric evaluation of Ki67 immunolabelling (*Gut* 1992; 33: 733-7). The authors found that biopsy specimens from squamous lined oesophagus contained cell populations with a higher percentage of Ki67 positive cells than Barrett's, and gastric mucosal biopsy specimens. Barrett's and gastric mucosal biopsy specimens having similar percentages of Ki67 positive cells.

Their results may be misleading as the proportion of stromal cells in Barrett's mucosa greatly exceeds that in gastric and squamous mucosal biopsy specimens, which have over 90% pure epithelial populations; stromal cells are not excluded from the total cell count by their technique and dilute the epithelial cell

population. Thus the finding that Barrett's mucosal biopsy specimens contain a similar percentage of Ki67 cells to gastric biopsy specimens (by this technique) is more likely to imply a considerably higher epithelial Ki67 labelling index in Barrett's than in gastric epithelial cell (as opposed to the total mucosal cell population).

This agrees with the studies performed on stained sections of mucosal biopsy specimens, including our own.¹ In our study of epithelial proliferation in Barrett's oesophagus we used PCNA immunostaining of specialised Barrett's, junctional, and gastric type metaplasia to evaluate proliferation in the epithelial cells only (excluding stromal cells). In our study specialised type Barrett's had a higher proportion of cells in cycle and an expansion of the proliferative compartment out of the crypt and into the luminal and gland cell compartments; implying a higher level of proliferative activity in the specialised Barrett's than in the other types of metaplasia. Our findings are consistent with the proved association of specialised type Barrett's epithelium with malignant change (in smokers).²⁻⁵

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- 1 Gray MR, Hall PA, Lane DP, Nash J, Kingsnorth AN. Epithelial proliferation in Barrett's oesophagus - by PCNA immunolocalisation. *Gastroenterology* 1992; 103: 1769-76.
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Reply

EDITOR,—Thank you for giving us the opportunity to reply to Mr Gray's comments. We share his concern about the increased population of stromal cells in Barrett's oesophagus and it is for this reason that we selected the size of the gate for the epithelial cell populations identified by staining with anticytokeratin. This is clearly stated at the end of the second subsection in the methods section of our paper.

We have not had the opportunity to study the recent paper by Mr Gray and his colleagues² as it has not yet appeared in print. It would seem, however, that they have been examining different types of Barrett's metaplasia rather than comparing Barrett's mucosa with gastric or oesophageal squamous mucosa. The relevance of their results with respect to our findings is therefore difficult to understand.

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Strategies for hepatitis B infection

EDITOR,—In their comprehensive leading article Catterall and Murray-Lyon (*Gut* 1992; 33: 576-9) discuss strategies for hepatitis B

immunisation. With regard to the need for booster vaccinations it seems to us that option I (no booster and reliance on immunological memory) has gained additional strength by new in vivo and in vitro data. Some of these have already been mentioned in the addendum. Our own data¹ have been supported by the findings of Jilg's group.^{2,3} To our knowledge, not a single case of clinically evident hepatitis B or carriership following hepatitis B virus infection has been reported in a confirmed serologically to hepatitis B vaccine.

A spot ELISA assay, which visualises the specific immunoglobulin production of either IgG or IgM class by individual mitogenically stimulated B cells in vitro, is able to show latent immunological memory and adds further support to this strategy.⁴ Long term follow up data confirm the presence of persisting circulating B cell memory despite undetectable anti-HBs in the serum seven to nine years after the first vaccination.⁵ Further studies with an even longer interval are in progress. Moreover, follow up data carefully monitoring the course of events after accidental infection (such as needlestick injuries) will give additional information.

Omitting booster vaccinations completely despite theoretical objections, in all those who have been known to react to the initial vaccination series with an anti-HBs titre in excess of 100 IU/l, seems to be a perfectly reasonable alternative to expensive, complicated, and probably unnecessary booster immunisation programmes. This policy is actually being evaluated on a world wide scale at present (be it uncontrolled) because many vaccinees with known responder status will not have received a booster vaccination.

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Overview of screening and management of familial adenomatous polyposis

EDITOR,—In their review article Rhodes and Bradburn (*Gut* 1992; 33: 125-31) emphasise the necessity, and potential benefits, of long term screening of family members and siblings of probands diagnosed as having familial adenomatous polyposis. These screening programmes have identified many affected subjects, usually by identification of rectal polyps at sigmoidoscopy,^{1,2} and reduced the occurrence of invasive colorectal carcinoma to less

than 7%,^{1,4} at the time of diagnosis. The authors note, however, that two patients within the Northern Region Register presented with right sided colonic polyps but no evidence of rectal polyps. Despite this finding, they still advocate rigid or flexible proctosigmoidoscopy as an adequate screening procedure of 'at risk' family members.

We feel it should be emphasised that within this high risk population, a large subset of patients present with 'rectal sparing' at initial diagnosis. As many as 20% of patients with familial adenomatous polyposis present with numerous colonic polyps in the total absence of rectal polyps.⁵ Furthermore, invasive colonic carcinoma has been noted in up to 8% of this group, with no evidence of rectal polyposis.⁵ This was recently reinforced to ourselves, when a young man presented with invasive colonic carcinoma and extracolonic manifestations of the syndrome, but no macroscopic evidence of polyps on rigid proctosigmoidoscopy. As illustrated in our own experience, we believe that rigid proctosigmoidoscopy is too limited an investigation to adequately screen the colorectal mucosa of these at risk family members, as rigid proctosigmoidoscopy alone has a potential false negative diagnostic rate as high as 20%, which may delay prophylactic colectomy and allow progression to colonic malignancy in screened subjects.

We suggest that first degree relatives identified as carriers of the abnormal familial adenomatous polyposis gene (as detected by haematological screening for linked genetic DNA markers), should be screened every 12 months by flexible sigmoidoscopy as a minimum, and colonoscopy as the ideal; and every 3 years in family members with negative linkage markers. The role of rigid sigmoidoscopy should be confined to regular long term follow up of patients at risk of rectal carcinoma following subtotal colectomy and ileorectal anastomosis.

Screening 'at risk' family members with flexible sigmoidoscopy or colonoscopy will minimise delays in diagnosis of affected subjects, and therefore reduce the incidence of colonic carcinoma within the screened population.

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- 1 Bulow S. Familial adenomatous polyposis. *Ann Med* 1989; 21: 299-307.
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Reply

EDITOR.—We thank Tate *et al* for highlighting the problems of routine screening in familial adenomatous polyposis. We appreciate that there is a definite incidence of rectal sparing in familial adenomatous polyposis although the current experience in the Northern Region Register is not as high as the 20% quoted by Bess *et al*.¹ The two patients with rectal sparing

in the Northern Region Register referred to by the authors have now been fully reported.²

We nevertheless feel that flexible or rigid proctosigmoidoscopy is an adequate screening procedure for most at risk family members and do not consider colonoscopy necessary for all 'at risk' individuals. This more invasive investigation should be reserved for selected patient groups. Those patients who have congenital hypertrophy of the retinal pigment epithelium and unfavourable DNA markers but have not developed polyps by the late teens or early twenties should have proximal polyposis or carcinoma excluded by colonoscopy. Similarly the small group of patients with established but mild polyposis in whom it is considered desirable to delay colectomy must have colonoscopic surveillance. We feel that this selective usage will minimise the number of patients receiving an investigation, which has a definite associated risk of morbidity and death, at no detriment to their care.

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- 1 Bess MA, Martin AD, Elveback LR, Moertel CG. Rectal cancer following colectomy for polyposis. *Arch Surg* 1980; 115: 460-6.
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Bleeding varices in the elderly

EDITOR.—I read with interest the leading article by Triger (*Gut* 1992; 33: 1009-10) on the management of bleeding oesophageal varices in the elderly. I was surprised that he did not mention transjugular intrahepatic portosystemic shunting (TIPS), a new, minimally invasive interventional radiological technique for the treatment of bleeding varices. A tract is created between the hepatic vein and portal vein and patency is maintained by placement of an expandable metallic stent. The procedure is performed through a 10 French (3.3 mm diameter) sheath sited in the internal jugular vein. Early results using this procedure have been very encouraging.

Unlike surgical portosystemic shunting, TIPS has low procedure related morbidity and mortality. Five patients of the first 59 reported have died in the first thirty days following the procedure; three had Child's Stage C disease and two had sepsis unrelated to the TIPS procedure.¹⁻⁵ The oldest patient to undergo a successful TIPS procedure was 78 years old.² Encephalopathy following TIPS has been reported in one patient.³ A recent editorial in the *Lancet* advocates a controlled trial of TIPS v injection sclerotherapy for the treatment of bleeding oesophageal varices.⁶ All gastroenterologists should be aware of this procedure.

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- 1 Zemel G, Katzen BT, Becker GJ, Benenati J, Sallee DS. Percutaneous transjugular portosystemic shunt. *JAMA* 1991; 266: 390-3.
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Reply

EDITOR.—I am grateful to Dr McDermott for drawing attention to my omission of transjugular portosystemic shunting (TIPS) in my editorial. While this technique offers exciting prospects for a new therapeutic approach to variceal haemorrhage, I would urge some caution against its uncritical adoption. Reports to date have been based on relatively limited experience from the few specialist centres and, as McDermott points out, no controlled trials have yet been undertaken to compare it with endoscopic sclerotherapy. It is somewhat naive to describe the technique as being 'minimally invasive'; the procedure frequently takes as long as three hours to perform, and there have been several reports of fatal haemoperitoneum because of traumatic rupture of the portal vein/liver.

Anecdotal reports of TIPS being successfully used in elderly patients should not be taken as evidence that the procedure should be readily adopted as an alternative treatment without careful evaluation. Whereas the elderly should not be denied any form of treatment simply on account of their age, it is equally important to ensure that new therapeutic manoeuvres are adequately assessed before being applied to them.

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NOTES

Liver Disease

The XVIIIth International Update on Liver Disease will be held at the Royal Free Hospital School of Medicine, London from 8-10 July 1993. Further information from Professor Neil McIntyre, University Department of Medicine, Royal Free Hospital, Pond Street, London NW3 2QG. (Tel: 071 794 0500 extn 3969; fax: 071 435 5803.)

Gastrointestinal Motility

The 14th International Symposium on Gastrointestinal Motility will be held on 29 August to 3 September 1993 at Minett, Muskoka, Ontario, Canada. Further information from Dr N E Diamant, Chairman, c/o Mrs Diana Valdez, Symposium Co-ordinator, Toronto Hospital (Western Division), 12-419 McLaughlin Pavilion, 399 Bathurst Street, Toronto, Ontario, Canada, M5T 2S8. Tel: 416 369 5075; fax: 416 369 6204.