and was subsequently referred to St George's Hospital for biliary reconstruction.

The incidence of bile duct injury at open cholecystectomy is around 1:300 in the United States. Therefore an incidence of 1:53 after laparoscopic cholecystectomy, as found in our survey, represents a considerable increase. Interestingly, of the five surgeons reporting injuries, only two had performed fewer than 20 laparoscopic cholecystectomies. If these injuries are to be put down to the learning curve then either this particular learning curve is much longer than is generally recognised (which has immense training implications) or the operation, as performed at present, is inherently more dangerous than open cholecystectomy. Probably it is a combination of these factors.

Our telephone survey was small and consequently may not be representative of the experience of the entire country, but our figures are comparable to the American experience. If these figures are representative then whether this operation is inherently more dangerous than open cholecystectomy must be considered. This requires comprehensive audit and honesty in reporting. If, alternatively, this increased incidence is reflecting the learning curve then laparoscopic teaching programmes must take this into account.

Minilaparotomy cholecystectomy has recently been proposed as a safer alternative to laparoscopic cholecystectomy.² At present this variation of cholecystectomy is practised mainly by committed biliary surgeons who are unlikely to damage the bile duct whatever the method used to remove the gall bladder. Whether or not the procedure will be safer than laparoscopic cholecystectomy when practised by general surgeons at large is difficult to predict.

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- 2 Baxter JN, O'Dwyer PJ. Laparoscopic or minilaparotomy cholecystectomy? *BMJ* 1992;304:559-60. (29 February.)

SIR,—In suggesting that it is "dangerous if not unethical to accept any new treatment . . . without putting it to the ultimate test—a randomised controlled trial," J N Baxter and P J O'Dwyer imply that surgical operations in current use have been subjected to this ideal scrutiny.¹ As supporters of the clinical trial we wish that this were so. Sadly, examination of the general surgical operative repertoire suggests that this is not the case. Most operations performed by general surgeons have not been accepted into clinical practice as a result of controlled clinical trials for reasons which one of us has elaborated elsewhere.² Worse, when a trial has been performed its conclusions are often ignored. Two randomised trials of highly selective vagotomy versus cimetidine both found in favour of surgery,^{3,4} yet despite this, elective surgery has all but disappeared in favour of treatment with H₂ receptor agonists.

It is unlikely that a controlled trial comparing laparoscopic with minilaparotomy cholecystectomy could be sustained for long enough to show a difference in mortality. In the series reported by Cuschieri *et al* there were no deaths in 1236 patients, and in the audit reported by Dunn there were two deaths in 1653 (0.12%).^{5,6} Similarly, bile duct injury seems unlikely to discriminate between the two techniques now that the lessons of the learning curve have been learnt. Voyles reported no bile duct injuries in 500 patients,⁷ and in our own hospital series there have been no major bile duct injuries after laparoscopic cholecystectomy in over 500 consecutive patients. The criteria used to compare these operations should therefore be postoperative analgesia requirements, postopera-

tive hospital stay, and time to return to work. Our own hospital series has shown a progressive reduction in all of these variables as experience is gained, and it seems inconceivable that minilaparotomy cholecystectomy could prove superior in these areas in any trial.

Laparoscopic cholecystectomy remains unchallenged in one all important respect. It has introduced general surgeons to therapeutic laparoscopy, which seems destined to bring the same benefits to the rest of the gastrointestinal tract as it has already brought to cholecystectomy. Rather than be distracted by learning and testing the technique of minilaparotomy cholecystectomy, surgeons should devote themselves to learning and improving laparoscopic techniques, for it already seems certain that the future of abdominal surgery lies in laparoscopy.

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- 1 Baxter JN, O'Dwyer PJ. Laparoscopic or minilaparotomy cholecystectomy. *BMJ* 1992;304:559-60. (29 February.)
- 2 Macintyre IMC. Tribulations for clinical trials. *BMJ* 1991;302:1099-100.
- 3 Anderson D, Amdrup E, Sorensen FH, Jensen DB. Surgery or cimetidine? I. Comparison of two plans of treatment: operation or repeated cimetidine. *World J Surg* 1983;7:372-7.
- 4 Gear MWL. Proximal gastric vagotomy versus long term maintenance treatment with cimetidine for chronic duodenal ulcer: a prospective randomised trial. *BMJ* 1983;286:98-9.
- 5 Cuschieri A, Dubois F, Mouiel J, Mouret P, Becker H, Buess G, *et al*. The European experience with laparoscopic cholecystectomy. *Am J Surg* 1991;161:385-7.
- 6 Dunn DC. Voluntary confidential audit of outcome of surgery. *BMJ* 1991;303:1272.
- 7 Voyles CR, Petro AB, Meena AL, Haick AJ, Koury AM. A practical approach to laparoscopic cholecystectomy. *Am J Surg* 1991;161:365-70.

SIR,—It is reassuring that the debate regarding minilaparotomy versus laparoscopy for removal of the gall bladder continues.¹ Less encouraging is J N Baxter and P J O'Dwyer's proposal of a randomised controlled trial to settle the issue. The opportunity to undertake this trial was lost some two years ago when laparoscopic cholecystectomy was still being evaluated in Britain.^{2,3} The almost universal adoption of the laparoscopic approach to the gall bladder over the past two years has been largely patient driven, as a result of media exposure and of surgeons' preference.

Two other factors have fuelled the laparoscopic revolution. The instrument makers have responded quickly to a sudden demand, resulting in large expenditures for the units using laparoscopy. Hospitals have been quick to fund this innovative approach for fear of losing patients to alternative providers.

These factors make it impossible to undertake a randomised controlled trial. Because of the expectations that now exist patients will not accept random allocation to laparoscopic or open treatment, albeit by mini-incision.

The use of the randomised controlled trial in surgery has been criticised.^{4,5} However, alternatives do exist and are being evaluated. One of these is comparative audit, a process which requires large numbers of non-selected participants. This approach may be well suited to studies comparing alternative treatment methods that are considered established practice.⁶ Such a study is currently being undertaken by the comparative audit service of the Royal College of Surgeons of England.

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- 1 Baxter JN, O'Dwyer PJ. Laparoscopic or minilaparotomy cholecystectomy? *BMJ* 1992;304:559-60. (29 February.)
- 2 Russel RCG. Laparoscopic cholecystectomy. *Lancet* 1991;338:1074-5.
- 3 Neugebauer E, Troidl H, Spangenberg W, Dietrich A,

- Lefering R. Cholecystectomy study group. Conventional versus laparoscopic cholecystectomy and the randomised controlled trial. *Br J Surg* 1991;78:150-4.
- 4 Pollock AV. The rise and fall of the random controlled trial in surgery. *Theoretical Surgery* 1989;4:163-70.
- 5 Dudley HAF. Extracranial-intracranial bypass one: clinical trials nil. *BMJ* 1987;294:1501-2.
- 6 Emberton M, Rivett R, Ellis BWE. Comparative audit—a new method of audit delivery. *Ann R Coll Surg Engl* 1991;73 (suppl 6):117-20.

Hazards of tests of growth hormone secretion

SIR,—A Shah and colleagues point out the dangers of insulin induced hypoglycaemia as a pharmacological test of growth hormone secretion.¹ But neither they nor C G D Brook in his editorial² mention a safer, non-invasive investigation for those children thought to be deficient in growth hormone: estimation of overnight urinary growth hormone excretion. Prepubertal children secrete growth hormone predominantly during slow wave sleep at night. Although only approximately 0.1% of the growth hormone in the serum appears in the urine, an immunoradiometric assay exists to detect this amount.³

An early morning collection of all the urine produced overnight is transported to the laboratory in a plain plastic bottle. The volume of urine produced is measured. A sample of this is then preserved by the addition of reagents and frozen for storage until analysis. This is a simple procedure that can be performed in any hospital biochemistry laboratory. The specimens can be transported frozen in dry ice to the nearest suitably equipped endocrine laboratory for analysis.

Walker *et al* have investigated children with short stature and shown that they produce significantly lower overnight urinary growth hormone concentrations than normal children.⁴ Comparison of overnight urinary growth hormone excretion with peak serum response to provocation testing with either clonidine or insulin also showed a highly significant correlation. Those children who were deficient in growth hormone on provocation testing had urinary growth hormone concentrations outside the normal prepubertal range.

In view of its non-invasive nature, its low cost, and the lack of need for admission to hospital urinary growth hormone analysis is a screening test that should be more widely advocated.

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- 1 Shah A, Stanhope R, Matthew D. Hazards of pharmacological tests of growth hormone secretion in childhood. *BMJ* 1992;304:173-4. (18 January.)
- 2 Brook CGD. Who's for growth hormone? *BMJ* 1992;304:131-2. (18 January.)
- 3 Evans AJ, Wood PJ. Development of an assay for human growth hormone in urine using commercially available reagents. *Ann Clin Biochem* 1989;26:353-7.
- 4 Walker JM, Wood PJ, Williamson S, Betts PR, Evans AJ. Urinary growth hormone excretion as a screening test for growth hormone deficiency. *Arch Dis Child* 1990;65:89-92.

SIR,—We were interested to read in D A Price's letter that Manchester growth clinic avoids using insulin tolerance tests.¹ Such a policy does not eradicate the hazards of pharmacological tests of growth hormone secretion as one of the deaths reported by Shah and colleagues occurred after a glucagon stimulation test.² Certainly, interpreting any test of growth hormone secretion, either physiological or pharmacological, is problematical.³ Moreover, growth velocity is a more accurate predictor of response to growth hormone treatment.⁴

The product licences for growth hormone state that it is for use in growth failure in children due to deficiency of endogenous growth hormone secre-

tion as verified by tests of pituitary function. Most tests of growth hormone secretion are performed to satisfy this condition of the product licences. Although such tests are of dubious value in selecting patients for growth hormone treatment,⁴ occasionally pharmacological tests may still be indicated to assess the hypothalamic-pituitary-adrenal axis.

A recent letter from the chief medical officer to all paediatricians stating that insulin tolerance tests are being restricted to specialised centres has been a helpful guideline.⁵ Before Price's hope is realised and the insulin tolerance test and other pharmacological tests can become obsolete,¹ however, a change is necessary in the conditional clause requiring pituitary function tests before growth hormone is given.

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- 2 Shah A, Stanhope R, Matthew D. Hazards of pharmacological tests of growth hormone secretion in childhood. *BMJ* 1992;304:173-4. (18 January.)
- 3 Brook CGD, Hindmarsh PC. Tests for growth hormone secretion. *Arch Dis Child* 1991;66:85-7.
- 4 Darendeliler F, Hindmarsh PC, Brook CGD. Dose-response curves for treatment with biosynthetic growth hormone. *J Endocrinol* 1990;125:311-6.
- 5 Calman KC. *Insulin tolerance test: a potential hazard in children*. London: Department of Health, 1991.

Drug treatment for acute upper gastrointestinal bleeding

SIR,—Colin Brown and W D W Rees's editorial highlights current morbidity and mortality from upper gastrointestinal bleeding related to ulcers.¹ This is despite the adoption of team approaches and audit of different strategies for managing such bleeding. The continuing problem of rebleeding associated with ulcers owes much to the failure of potent acid inhibitory drugs such as H₂ antagonists and proton pump inhibitors, which might have been expected to offer therapeutic benefit.

Consequently, we wish to draw attention to two double blind studies with the analogue of prostaglandin E₁ misoprostol, which indicate potential therapeutic benefit in preventing upper gastrointestinal rebleeding associated with ulcers.^{2,3} The first study was a multicentre comparison of misoprostol and placebo in 377 patients.² It assessed prevention of rebleeding over the first four days after admission to hospital for endoscopically proved upper gastrointestinal bleeding due to gastric or duodenal ulceration. On an intention to treat basis the rebleeding rates were 16% in the misoprostol group and 23.9% in the placebo group ($p=0.059$). The difference was significant in the predetermined evaluable cohort ($n=307$), the rebleeding rates being 14% and 24% respectively ($p=0.016$, using χ^2 for treatment differences and a log linear model that included effects of treatment and centre and their interaction).

In the second, single centre study, of 150 patients, the same design of reduction in rebleeding was seen (25% to 15% in the intention to treat analysis), although the difference did not achieve significance in either the intention to treat or evaluable cohorts owing to the smaller sample size.³ There was, however, a significant reduction in the amount of fluid required for transfusion and a trend towards earlier discharge from hospital in the group who received misoprostol.

These positive effects have not been seen with other agents and are in contrast to results of studies of famotidine and omeprazole.^{4,5} The differences between the results obtained with misoprostol and those obtained with other agents suggest that misoprostol exerts its beneficial effects through

actions other than, or in addition to, inhibition of acid. The underlying mechanism may be the effect misoprostol exerts on epithelial repair, which is not seen with omeprazole⁶ and could be related to the action that misoprostol is known to have on mucosal blood flow. Obviously, detailed scrutiny of the data must await full publication of the results, but further investigation seems to be warranted in the light of these promising results.

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- 1 Brown C, Rees WDW. Drug treatment for acute upper gastrointestinal bleeding. *BMJ* 1992;304:135-6. (18 January.)
- 2 Robinson GC, Shield MJ, Fenn GC. Misoprostol versus placebo in prevention of recurrence of acute upper gastrointestinal haemorrhage: a randomised double-blind study. *Gut* 1991;32:A572.
- 3 Birnie CG, Fenn GC, Shield MJ, Robinson GC. Double-blind comparative study of misoprostol with placebo in acute upper gastrointestinal bleeding. *Gut* 1991;32:A1246.
- 4 Walt RP, Cottrell J, Mann SG, Freemantle N, Langman MJS. Randomised double blind controlled trial of intravenous famotidine infusion in 1005 patients with peptic ulcer bleeding. *Gut* 1991;32:A571.
- 5 Daneshmend TK, Hawkey CJ, Langman MJS, Logan RFA, Long RG, Walt RP. Omeprazole v placebo for acute upper gastrointestinal bleeding: a randomised double blind controlled trial in 1154 patients. *Gut* 1990;31:A1206.
- 6 Daneshmend TK, Hawkey CJ, Langman MJS, Logan RFA, Long RG, Walt RP. Omeprazole versus placebo for acute upper gastrointestinal bleeding: randomised double blind controlled trial. *BMJ* 1992;304:143-7. (18 January.)
- 7 Levi S, Goodlad RA, Lee CY, Stamp G, Walport MJ, Wright NA, et al. Inhibitory effect of non-steroidal anti-inflammatory drugs on mucosal proliferation associated with gastric ulcer healing. *Lancet* 1990;336:840-3.

SIR,—We appreciate the difficulty that Colin Brown and W D W Rees had in covering such a vast topic as gastrointestinal haemorrhage comprehensively but thought that the section of their editorial dealing with somatostatin and octreotide was inadequate and partly incorrect.¹

We agree that in clinical trials in which all patients with upper gastrointestinal haemorrhage have been included neither somatostatin nor octreotide has had a significant effect on bleeding, the need for surgical intervention, or mortality. These observations are not surprising because of the heterogenous source of the bleeding and the natural course of gastrointestinal haemorrhage. Thus the need for surgical intervention and death (mortality 10-15%) are largely confined to a high risk group of patients (about 20%) who continue to bleed, show signs of early recurrent haemorrhage, or are bleeding from multiple sites. Any possible beneficial effects of somatostatin in controlling haemorrhage could therefore be masked in trials in which all patients with haematemesis or melaena are included.

This suggestion is supported by two controlled trials in high risk patients in which somatostatin was shown to be significantly more effective than ranitidine or placebo in controlling the bleeding and reducing the need for surgical intervention.^{2,3} Furthermore, we have found somatostatin and octreotide to be effective in controlling severe upper gastrointestinal haemorrhage in patients in whom operation is hazardous because of bleeding from multiple peptic lesions, further complicated in some by intercurrent disease, age, or previous surgery.⁴ Clearly, further controlled trials are necessary to establish the role of somatostatin and octreotide in managing upper gastrointestinal bleeding in high risk patients.

With respect to variceal haemorrhage some of the information on somatostatin is incorrect and does not reflect adequately the efficacy and safety of the drug in this important indication. Of the two placebo controlled trials of somatostatin,^{5,6} only

one⁶—not both as Brown and Rees state—showed any significant benefit of the drug in controlling variceal bleeding. In addition, the results of these two trials and eight other controlled studies indicate that somatostatin or octreotide controls variceal bleeding in about 70% of patients and no major complications have been associated with use of the drugs.⁷

Finally, somatostatin has also been shown to be effective in controlling haemorrhage after injection sclerotherapy—from the varices themselves⁸ or from oesophagitis and oesophageal ulceration.⁹ Our recent experience with octreotide suggests that it is as good as somatostatin for these indications. In conclusion, therefore, if the controlled clinical trials currently under way in the United Kingdom confirm the efficacy of somatostatin and octreotide in controlling acute variceal bleeding, thereby facilitating subsequent sclerotherapy and preventing early haemorrhage after injection, there would be a good case for recommending their routine use in all patients presenting with variceal bleeding.

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- 1 Brown C, Rees WDW. Drug treatment for acute upper gastrointestinal bleeding. *BMJ* 1992;304:135-6. (18 January.)
- 2 Corragio F, Scarpato P, Spina P. Somatostatin and ranitidine in the control of iatrogenic haemorrhage of the upper gastrointestinal tract. *BMJ* 1984;289:224.
- 3 Magnusson I, Ihre T, Johansson C, Seligson U, Torngren S, Unvas-Moberg K. Randomised double blind trial of somatostatin in the treatment of upper gastrointestinal haemorrhage. *Gut* 1985;26:221-6.
- 4 Jenkins SA, Taylor BA, Nott DM, Ellenbogen S, Haggi J, Shields R. Management of massive upper gastrointestinal haemorrhage from multiple sites of peptic ulceration with somatostatin and octreotide—a report of 5 cases. *Gut* (in press).
- 5 Valenzuela JE, Schubert T, Fogel MR, Strong RM, Levine J, Mills PR, et al. A multicentre randomised double-blind trial in the management of acute haemorrhage from oesophageal varices. *Hepatology* 1989;10:958-61.
- 6 Burroughs AK, McCormick PA, Hughes MD, Sprengers D, D'Heygere F, McIntyre MN. A randomised double-blind placebo-controlled trial of somatostatin for variceal bleeding: emergency control and prevention of early variceal bleeding. *Gastroenterology* 1990;99:1388-95.
- 7 Burroughs AK. Somatostatin and octreotide for variceal bleeding. *J Hepatol* 1991;13:1-4.
- 8 Jenkins SA, Shields R, Jaser N, Ellenbogen S, Makin C, Naylor E, et al. The management of gastrointestinal haemorrhage by somatostatin after apparently successful injection sclerotherapy for bleeding oesophageal varices. *J Hepatol* 1991;12:296-301.
- 9 Jenkins SA, Shields R, Jaser N, Ellenbogen S, Naylor E, Baxter JN. The management of persistent or recurrent variceal bleeding after injection sclerotherapy by somatostatin. *World Journal of Hepatic, Pancreatic and Biliary Surgery* (in press).

Swimming and grommets

SIR,—M B Pringle discusses whether children with grommets should be allowed to swim.¹ Certainly, most patients with grommets are advised to avoid getting water in their ears and diving significantly increases the risk of getting a middle ear infection,² though Chapman and Smelt and Yeoh found that the rate of otorrhoea was lower in those who swam than in non-swimmers.^{3,4} If penetration of water into the ear canal is the main factor leading to otorrhoea in patients with grommets the rate of infection will increase with the number of baths. To our knowledge few authors have attempted to correlate the risk of otorrhoea with the amount of swimming done.

We conducted a study last summer to assess the risk of swimming for patients with grommets. To minimise any bias due to social class or regional differences the study was performed by five independent ear, nose, and throat surgeons in France. All our patients had T tubes, which are ventilation tubes with long shafts. They were allowed to swim, bathe, and shower without protecting their ears. During a follow up visit in September or October the child or parent was asked how many times the child had swum in the Atlantic or in a pool and