Repeated upper gastrointestinal investigations all showed an ulcerative lesion of the duodenum. After a gastroduodenoscopy which confirmed the presence of a duodenal ulcer of linear type, he was on oral cimetidine, 200 mg three times a day and 400 mg at bedtime continuously during the last three months, with only mild relief of his pain. A new endoscopic examination on 6 November showed that the duodenal ulcer had become a roundish lesion (mean diameter 5 mm). Two weeks after beginning this therapy the patient had noted the appearance of gynaecomastia and breast pain and, after a few more days, the development of erythrosis-like skin lesions. These were all over his body but more evident on the trunk, and there was no prurigo. The gynaecomastia and skin manifestations began to disappear within two weeks after he stopped taking cimetidine.

No change in biochemical and haematological values was observed and no other drug was being taken by the patient in this period. There is no evidence to suggest that the erythrosis-like skin lesions were other than a cimetidine-induced phenomenon like gynaecomastia, which is a well-known side effect of the drug and probably due to an increase of serum prolactinaemia.^{1 2}

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¹ Burland, W L, *et al*, *British Medical Journal*, 1978, 1, 717.

² Cavallini, G, *et al*, in abstract of VI World Congress of Gastroenterology, Madrid, June 1978, p 18.

Pyritinol hydrochloride (Encephabol) and senile dementia

SIR,—In the *BMJ* of 3 March, p 601 a reply was made to the question "What is the latest treatment for and the role of vasodilators in treating senile dementia? Has Encephabol/pyritinol hydrochloride/ any part to play?" An opinion was given concerning pyritinol, and at the end of the answer several statements were made which require clarification.

The clinical value of pyritinol is questioned in the article on the basis that Martindale does not list any of the papers demonstrating its efficacy in senile dementia which were published after 1969. In fact the most important body of publications demonstrating clinical efficacy appeared after this date. We are in the process of asking the publishers of Martindale's *Extra Pharmacopoeia* to update the list of references.

Pyritinol is not a vasoactive substance or a vasodilator. However, it has been shown that cerebral blood supply is increased by pyritinol and that this pyritinol-induced increase can be regarded as a consequence of the improvement of nerve cell metabolism.¹ This improvement in nerve cell metabolism has been demonstrated by several authors.²⁻⁴ The clinical efficacy of pyritinol has been demonstrated in more than 20 controlled studies in patients with various forms of organic brain disease (full references available). The results of one such double-blind trial in matched groups of elderly patients with senile dementia showed that pyritinol was significantly superior to placebo in improving their physical activity, alertness, mental power, and interest.⁵

Finally, we should point out that pyritinol is widely prescribed in Eire as well as the countries listed by your contributor. It is not, however, on sale in the UK and therefore it is

not surprising that Hyams does not mention Encephabol in his textbook *Geriatric Medicine and Gerontology*.

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¹ Herrschaft, H, *Münchener Medizinische Wochenschrift*, 1978, 39, 1263.

² Quadbeck, G, *Progress in Brain Research*, 1962, 349.

³ Stoica, E, *et al*, *Neurology*, Minneapolis, 1973, 23, 687.

⁴ Hoyer, S, Oesterreich, K, and Stoll, K D, *Arzneimittel-Forschung*, 1977, 27, 671.

⁵ Hamouz, W, *Pharmatherapeutica*, 1977, 1, 398.

Thrombocytopenia and splenic infarction

SIR,—In reply to the correspondence (17 March, p 748) about our reported case of renal carcinoma (10 February, p 381), we would like to state that we still consider that the patient's thrombocytopenia had no clear cause. In our report the statement that a diffuse intravascular coagulation screen was normal should, in our opinion, leave little doubt that a chronic consumption coagulopathy had been eliminated. Limitations of space prevented us from describing in detail in the report the tests performed—but thrombin time, prothrombin time, partial thromboplastin time, and fibrin degradation products were estimated on a number of occasions while the patient was thrombocytopenic and were always normal. The fibrinogen was consistently slightly raised.

We also felt that hypersplenism had been eliminated, because although it was possible to palpate the spleen at the time of death this was due to its displacement by the left renal mass. In fact, the spleen weighed 200 g at necropsy and, except for its posterior aspect, where it was involved in the necrotic tissue, the splenic histology was normal. We stated in our report that multiple, small, wedge-shaped infarcts were seen in the spleen, and these were in relationship to the necrotic tissue. Gross splenic infarction did not occur; otherwise as a result we might have seen a raised platelet count, as suggested by Dr D O Ho-Yen.

Since our purpose in describing this case was to draw attention to what we considered to be a unique case, we are not surprised that it does not fit the descriptions seen in standard haematological reference books.

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Suction termination of pregnancy under local anaesthesia

SIR,—Local anaesthesia (about 18-20 ml of 1% lignocaine plus adrenaline, injected at the 12, 4 and 8 o'clock positions) gives adequate relief of pain due to dilation of the cervix. However, it is clear that there is a component of pain caused by uterine contractions, which can be severe in a minority of patients, some of whom find it unacceptable although quite short lived. It is usually described as being similar to dysmenorrhoea.

Mefenamic acid, a powerful inhibitor of prostaglandin synthetase, is highly effective

in the relief of primary dysmenorrhoea.¹ We have tried the effect of 500 mg of mefenamic acid (Ponstan) as premedication about 1½ hours prior to suction termination with a Karman catheter under local anaesthesia. In a series of 25 women I have been impressed by the improved analgesia this provides, particularly during the last few moments of the procedure, when dysmenorrhoea is normally marked. I am in the process of arranging a double-blind randomised study of premedication with this agent, assessing the amount of pain experienced by visual analogue scales and card-sorting procedures; but my colleagues and I are so convinced by the clinical evidence of its efficacy that I felt it justifiable to write this preliminary communication. The combination of mefenamic acid and cervical anaesthesia with lignocaine is so effective that it seems unnecessary to use general anaesthesia up to 10 weeks of gestation for any but the most anxious patients.

Nevertheless, the tradition in most units in this country of using general anaesthesia (and, even more unnecessarily, overnight stay following the procedure) will, I am sure, prove difficult to abandon.

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¹ Anderson, A, *et al*, *Lancet*, 1978, 1, 8060.

Hulka-Clemens clips

SIR,—Mr N R A Trickey's letter (31 March, p 894) cannot go without comment. It is indeed unfortunate that Mr Trickey seeks to damn a method of female sterilisation on such flimsy evidence.

The results of two multicentre prospective trials carried out in the United Kingdom using this method of tubal occlusion reported a failure rate of less than two per 1000.^{1 2} Worldwide experience with this clip confirms its unique safety as it avoids both haemorrhage from the mesentery and diathermy trauma to the bowel.³ For these reasons those working at the Samaritan Hospital were proud to append the hospital's name to the clip applicator.

This method of sterilisation is now being used with increased frequency in the United Kingdom and Europe. Although the operation is quick and easy to perform it does require meticulous attention to detail. For this reason I suggest that those learning the technique should apply two clips to each fallopian tube in their first 100 cases.

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¹ Lieberman, B A, *et al*, *Journal of Reproductive Medicine*, 1977, 18, 241.

² Lieberman, B A, Gordon, A G, and Wright, C S W, in *Endoscopy in Gynecology*, ed J M Phillips, p 182. Downey, California, American Association of Gynecological Laparoscopists, 1978.

³ Hulka, J F, *et al*, *American Journal of Obstetrics and Gynecology*, in press.

Breakage of Falope-ring applicator forceps prongs

SIR,—We have been using the silastic band technique in conjunction with the Falope-ring applicator (KLI Inc, Newtown, USA) for laparoscopic surgery since 1975. So far, we have encountered three instances where the tip of one of the prongs on the applicator forceps has broken at surgery; this unusual complication and its management has not to

the best of our knowledge been reported previously.

Two cases occurred at laparoscopic sterilisation. In one the broken metallic bit was retrieved by emergency laparotomy, while in the second case the broken fragment could not be located at laparotomy but was removed with the aid of the x-ray image intensifier five days later, when a repeat laparotomy was performed. There was no obvious peritoneal or omental reaction seen at operation. The third case occurred in mid-December 1978, during application of silastic rings to the round ligaments for ventrosuspension. After unsuccessful attempts at removal with the Palmer forceps, the foreign body was left behind. To date, no adverse effect has been noted.

Since the forceps prongs of the ring applicator are made of surgical grade stainless steel, which should not cause a toxic reaction,¹ removal of the broken metallic fragment by laparotomy is probably unnecessary if laparoscopic retrieval fails. However, the possibility of its migration is an unsettled question.

The metallic prongs are constantly subjected to stress and it would be advisable each time to check their condition prior to use. They should be replaced if the tips are malaligned or are bent as either would indicate excessive strain.²

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¹ Schofield, S R, personal communication.

² KLI Inc, Technical Bulletin 000685-2, Ivyland, PA, USA, KLI Inc, 1976.

Primary screening for visual disorders in children

SIR,—Mrs A V MacLellan and Dr P Harker reported a highly successful method of screening preschool children in a rural area for visual disorders (14 April, p 994). I should like to reinforce their recommendations by relating that a very similar service has been given in the urban London borough of Barnet, with great relief to ophthalmologists in the hospital and to mothers of small children, who for obvious reasons preferred an immediate appointment nearer their homes. A succession of orthoptists over approximately 10 years have had no difficulty in arranging sessions and have proved that "case finding" at an earlier age is more thorough than the orthodox hit and miss.

Mrs MacLellan quotes three very apt histories of children likely to be missed except by such a system as hers and ours. I would draw particular attention to case 1, where near vision was reduced, which is seldom tested in young children, and to case 3, which shows the importance of testing siblings.

The main difficulty in arranging such a service appears to be lack of liaison and interest on the part of the community and hospital administrators and ophthalmologists.

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Continuous narcotic infusions for relief of postoperative pain

SIR,—I was delighted to read the paper on relief of postoperative pain by Dr Jeremy J Church (14 April, p 977). His technique will be a most useful contribution to the problem. But there are two points that I wish to raise.

Firstly, if Dr Church could find the time to titrate his loading doses¹ he would not have to adjust the infusion rates so often. And his results would be even better.²

Secondly, his technique is cheap, effective, and simple; however, it needs at least intensive nursing care. I use a less demanding technique when patients have to return to general surgical wards on operation days. I give buprenorphine (Temgesic), 0.1 mg/20 kg body weight less 0.1 mg for each decade of age over 70 years, intravenously during induction of general anaesthesia. If no more than 0.5% halothane is used and it is stopped 30 minutes before the end of the operation respiration is not depressed and recovery is quick. I give papaveretum, 20 mg intramuscularly, when the patient's reflexes have begun to return but before pain is felt. Neither the level of consciousness, the respiratory system nor the cardiovascular system is depressed. This is due to the antagonist action of buprenorphine. This regimen ensures that patients feel no pain for 2-12 hours after operation, the majority lying within the range 6-8 hours. There is ample time for further injections of analgesics, usually buprenorphine, since pain develops gradually. It is my experience that if pain is prevented during the first 24 postoperative hours by this or any other technique pain on the second and subsequent days is much reduced.

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¹ Fry, E N S, and Desphande, S, *British Medical Journal*, 1977, 2, 870.

² Fry, E N S, *Annals of the Royal College of Surgeons of England*, in press.

Oligoclonal immunoglobulins and multiple sclerosis

SIR,—We read with interest the article by Dr E J Thompson and others (6 January, p 16) entitled "Oligoclonal immunoglobulins and plasma cells in spinal fluid of patients with multiple sclerosis." We would like to draw attention to one aspect of interpretation when looking for the presence of oligoclonal bands in the cerebrospinal fluid (CSF).

Using Thompson's modification of polyacrylamide gel electrophoresis¹ and staining with Coomassie Blue, we have examined the CSF of 131 patients whose provisional diagnoses on admission included multiple sclerosis, and 33 control CSF samples from patients who clinically had no neurological disease. Of the 33 control samples, 10 showed one or more oligoclonal bands in the γ region following electrophoresis. In five of these 10 a serum sample (100 μ g protein) was run with the CSF sample (100 μ g protein) and the bands present in the CSF were found to correlate in position with bands in the serum sample. In eight other control samples where serum and CSF samples were run simultaneously, oligoclonal bands present in the serum were not found in the CSF, which showed only a diffuse pattern. The remaining 15 control CSF samples showed only a diffuse pattern. Over one-third of our 131 patients CSF samples have shown bands which correlated with bands in their serum. These patients, with two exceptions, have subsequently not been diagnosed clinically as having multiple sclerosis. We therefore assume that in these cases the discrete bands found in the CSF are due to diffusion into the CSF of immunoglobulins or other proteins present in the plasma.

As a consequence of these findings, we routinely perform electrophoresis on CSF and serum from each patient and disregard (for diagnostic purposes) those oligoclonal bands in the γ region of the CSF

electrophoretogram which correlate in position with those of serum. It has also been found that CSF samples left more than 24 hours at 4°C are not suitable for electrophoretic analysis, as the bands become indistinct.

In summary, to avoid false positive results, it is necessary to run a fresh serum sample simultaneously with each fresh, red-cell-free CSF sample. Only those bands in the CSF which do not have a corresponding band in the serum should be called abnormal oligoclonal immunoglobulins.

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Beta-blockers and renal function

SIR,—The letter from Dr R Wilkinson (3 March, p 617) commenting on the paper by Dr A D Wright and others (20 January, p 159) regarding reduction in renal function with beta-blockers aligns with observations that propranolol caused a reduction in renal plasma flow from 213 to 184 ml/min/100 g in 12 patients with essential hypertension.¹ However, such studies and the controversy over the relative effects of cardioselective and non-cardioselective agents only tend to highlight the fact that all beta-blockers studied to date have been shown to reduce renal function.

Recent studies with nadolol,² using a xenon-133 washout technique have shown maximal increases in renal blood flow compared with control ranging from 16% to 26%. Eight volunteers on a low-sodium diet were studied, three normotensive and five hypertensive. Dosage ranged from 0.3 to 10 μ g/kg. Mean renal blood flow increased from 270 ± 19 ml/100 g/min in the control state by a mean of 46.9 ± 9 ml/100 g/min at 1.0 μ g/kg, by 72 ± 4 ml/100 g/min at 3 μ g/kg, and 70 ± 5 ml/100 g/min at 10 μ g/kg—an increase of 26%. In addition, a dose-ranging clinical study of the treatment of hypertension with nadolol³ showed an increase in 24-hour sodium excretion from a pretreatment average of 203 mmol(mEq) to 258 mmol after 14 weeks' treatment.

As Dr Wilkinson points out, such an effect on renal function may well be of importance in patients with renal disease on treatment with beta-blockers.

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¹ Sullivan, J M, Adams, D F, and Hollenberg, N K, *Clinical Research*, 1976, 39, 532.

² Hollenberg, N K, et al, *British Journal of Clinical Pharmacology*, 1979, 7, 219.

³ Frithz, G, *Current Medical Research and Opinion*, 1978, 5, 383.

Treatment of exophthalmos and pretibial myxoedema with plasmapheresis

SIR,—The observations of Dr Dandona and others (10 February, p 374) on treatment of exophthalmos and pretibial myxoedema by plasmapheresis are certainly interesting, but the emphasis on attributing the beneficial result to a drop in the concentration of thyroid-stimulating immunoglobulins (or ophthalmogenic IgG or dermatogenic IgG) is not justified by the data.

Plasmapheresis obviously could lower the concentration of many different proteins present in plasma—for example, thyroglobulin