of bioequivalence of metered dose inhalers, some research evidence relating the cost of treatment of asthma to the quality of patients' lives, and a more appropriate method of educating health professionals than such unreferenced reports.

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- 1 Prescription Pricing Authority. *Asthma and inhaler therapy*. Newcastle upon Tyne: PPA, 1994.
- 2 Saarelainen P, Sovijarvi ARA. Comparison of acute bronchodilation effects of two preparations of salbutamol aerosol in asthma. *Current Therapeutic Research* 1991;50:224-30.
- 3 Food and Drug Administration. *Interim guidance for documentation of in vivo bioequivalence of albuterol inhalation aerosols*. Washington: FDA, 1994.

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Virtual reality surgery in otorhinolaryngology

EDITOR,—Anthony Hinton and Victoria Moore-Gillon mention that virtual reality surgery could well be the next development in otorhinolaryngology.¹ Since 1992 we have used a Viewing Wand (ISG Technology, Mississauga, Ontario, Canada) to aid ear, nose, and throat surgery.² The wand is an intraoperative image guidance system with a proprioceptive robot-like arm attached to a standard three pin Mayfield head rest. Using preoperative computed tomograms or magnetic resonance imaging scans, the wand creates almost instantaneous three dimensional or triplanar (sagittal, coronal, and axial) computerised reconstructions, showing the exact position of the tip of the arm on the reformed images.

The wand has proved extremely useful in aiding preoperative navigation, in identifying the relation and proximity of important anatomical structures, and in the assessment of the extent of resection of lesions. We have used it to aid the resection of many lesions in ear, nose, and throat surgery, including large primary cholesteatomas, glomus jugulare tumours, acoustic neuromas, and clivus chordomas. With a special bayonet probe, it has been used to fenestrate the sphenoid and create a minimally invasive approach to the pituitary fossa (M I Torrens, D R Sandeman, proceedings of the second international skull base symposium, St Petersburg, 1994). We also plan to use it to aid orientation during functional endoscopic sinus surgery, in which it should prove invaluable in identifying the lamina papyracea and the floor of the anterior cranial fossa. We have little doubt that such technology will prove to be of benefit in many more aspects of otorhinolaryngology.

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- 1 Hinton A, Moore-Gillon V. Recent advances: otorhinolaryngology. *BMJ* 1994;309:651-4. (10 September.)
- 2 Zinreich SJ, Robles HA, Long DM, Bryan RN. 3D imaging for neurosurgery. In: Tos M, Thomsen J, eds. *Acoustic neuroma*. Amsterdam, New York: Kugler, 1991:109-18.

Appropriateness of referrals to hospital

EDITOR,—In their study of the appropriateness of referrals Glyn Jones Elwyn and Nigel CH Stott used the concept of avoidable referrals.¹ They found that 38% of the referrals studied over one year had been avoidable, whereas in a larger study Fertig *et al* found 15.9% of referrals to have been possibly inappropriate when judged against locally determined guidelines.² Thirty two of the avoidable referrals in the authors' study were considered to have been due to lack of resources, and it is perverse to judge the decision on referral in these cases as inappropriate. If these cases were included in the appropriate group the proportion of inappropriate or avoidable referrals would fall to 15.5%, almost exactly the same as Fertig *et al*'s finding and well within their 95% confidence interval (11.8% to 20%).²

Since inappropriate referrals do not seem to explain variation in referral rates the authors' approach, which classifies the reason for referral, may offer a way forward; perhaps the proportions of the types of referral vary between doctors with high and low referral rates.^{1,2} Unfortunately, it is not clear how significant was the agreement between the referrer's assessment and that of his collaborator, and it would be interesting to know what they disagreed about (nor are we told the referral rate per 100 consultations in this study). It would have been helpful if at least two other general practitioners had assessed the referrals so that we could know both how closely they agreed with the published assessments and whether the referrer's assessments were significantly different from those of the others; the degree of agreement can be measured by calculating κ for each pair.³

Two important points made by this study are the extent to which referrals in general practice are necessitated by lack of resources and inadequate communication with hospitals. The second point clearly needs to be addressed, but the first is not so clear cut as may be assumed. For example, if general practitioners were able to carry out upper gastrointestinal endoscopy in their surgeries they would not have to refer patients for this investigation; the costs in terms of equipment and time, however, are so great that it is almost certainly more economical for endoscopy to continue to be done in the secondary sector. We should be wary of the suggestion that a reduction in referral to hospital is necessarily desirable.

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- 1 Jones Elwyn G, Stott NCH. Avoidable referrals? Analysis of 170 consecutive referrals to secondary care. *BMJ* 1994;309:576-8. (3 September.)
- 2 Fertig A, Roland M, King H, Moore T. Understanding variation in rates of referral among general practitioners: are inappropriate referrals important and would guidelines help to reduce rates? *BMJ* 1993;307:1467-70.
- 3 Sackett DL, Haynes RB, Guyatt GH, Tugwell P. *Clinical epidemiology—a basic science for clinical medicine*. New York: Little, Brown, 1991:24-34.

Therapeutic use of bisphosphonates in oncology

EDITOR,—Juliet E Compston's review of the therapeutic use of bisphosphonates understates their value in oncology.¹ In addition to their efficacy in hypercalcaemia they are effective in relieving bone pain and in preventing some of the skeletal complications associated with both advanced breast cancer and multiple myeloma.

High doses of intravenous pamidronate have consistently been shown to relieve pain in around half of patients with bone metastases from breast

cancer and induce healing of lytic bone lesions in 20-25%.² Intravenous pamidronate also prolongs the time to progression in bone when patients with advanced breast cancer are treated with palliative combination chemotherapy.³ Randomised controlled clinical trials of oral bisphosphonates in breast cancer⁴ and multiple myeloma⁵ have shown that long term administration reduces pathological fractures, the incidence of hypercalcaemia, requirements for palliative radiotherapy, and the severity of pain. Numerous animal and laboratory studies have indicated that bisphosphonates may prevent bone metastases, and clinical trials investigating this are in progress.

Metastatic bone disease is the most clinically important skeletal disorder after osteoporosis. The bisphosphonates are an important new modality of treatment with useful effects on quality of life and skeletal morbidity.

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- 1 Compston JE. The therapeutic use of bisphosphonates. *BMJ* 1994;309:711-5. (17 September.)
- 2 Coleman RE, Purohit OP. Osteoclast inhibition for the treatment of bone metastases. *Cancer Treat Rev* 1993;19:79-103.
- 3 Conte PF, Giannesi PG, Latreille J, Mauriac L, Koliren L, Calabresi F, *et al*. Delayed progression of bone metastases with pamidronate therapy in breast cancer patients: a randomised phase III trial. *Ann Oncol* 1994;5(suppl 7):41-4.
- 4 Van Holten-Verzantvoort AT, Kroon HM, Bijvoet OLM, Cleton FJ, Beex LVAM, Blijham G, *et al*. Palliative bone treatment in patients with bone metastases from breast cancer. *J Clin Oncol* 1993;11:491-8.
- 5 Lahtinen R, Laakso M, Palva I, Virkkunen P, Elomaa I, for the Finnish Leukaemia Group. Randomised, placebo-controlled multicentre trial of clodronate in multiple myeloma. *Lancet* 1992;340:1049-52.

Imported falciparum malaria

EDITOR,—A television programme during the summer (*World in Action*, "Dying for a Holiday," Granada TV, 18 July 1994) that reported on cases of falciparum malaria in tourists returning from tropical holidays mirrored experience that we have reported in British troops.¹ The programme relayed criticism from bereaved relatives about general practitioners' inadequate advice and awareness of the condition.

The striking difference between our cohort of troops and most tourists is that before duty in tropical areas the troops receive a briefing on effective antimosquito measures, are issued with nets and repellent, and are supervised in taking chemoprophylactic tablets. Unfortunately, even these measures were not adequately followed in our disciplined group. Seven of 150 British soldiers on a five week exercise in central Kenya developed symptomatic falciparum malaria while taking proguanil-chloroquine chemoprophylaxis. Symptoms started between two and 10 days before the soldiers' return to Britain, and the diagnosis was made between five and 13 days after the first symptoms developed. The index patient was severely ill with 50% parasitaemia: he required intensive care, exchange blood transfusion, and haemofiltration for acute renal failure.

We did not measure compliance with chemoprophylaxis biochemically. The army's policy with regard to chemoprophylaxis, however, was amended in June last year so that mefloquine will be used in future rather than proguanil-chloroquine. This should improve compliance and thus effectiveness.

The index patient made us aware that others in his group were at risk owing to common exposure in an area with a high rate of transmission. Subsequently 21 men were traced and screened. This detected two further cases and enabled earlier and definitive treatment of this potentially fatal condition.