Our experience with these investigations has been largely restricted to adolescents with suspected hypogonadotropic hypogonadism, often in combination with growth hormone deficiency. Although hepatic, renal, and adrenocorticotrophic reserves are expectedly higher in this age group, we still observe appreciable adverse manifestations, including nausea, sweating, and tachycardia, with the standard doses of thyrotrophin releasing hormone, luteinising hormone releasing hormone, and soluble insulin that we use in our unit. When concomitant deficiency of gonadotrophin and growth hormone is suspected interpreting the total pituitary function profile becomes far more complicated and frustrating. Often results are unsatisfactory with minimal clinical value in the overall management of the patient.

Inconclusive results may erroneously be attributed to an "inadequately" stressed pituitary gland, which may result in an overwhelming desire to repeat the investigation with higher doses of pituitary stimulants. Our view is that such temptations must be firmly overruled. Even for this age group the hazards associated with such higher doses outweigh any potential clinical benefits.

In such circumstances obtaining the growth hormone profile after exercise may be beneficial. Above all, clinical sense and competence must prevail above potentially dangerous laboratory investigation. In a considerable proportion of our patients with confirmed growth hormone deficiency fusion of epiphyseal cartilage would have been completed. Growth hormone replacement therapy seems immaterial in such patients. Gonadotrophin deficiency is treated with the combined contraceptive pill, pulsatile ovarian stimulation with luteinising hormone releasing hormone, or nothing.

The safety guidelines recommended by the authors are valuable. But the fact that two of their cases occurred in dedicated endocrine units and one presumably in a district general hospital hardly justifies their conclusion that the risks must be much higher in non-specialist units. The unpredictable nature of complications of pituitary stress tests is well recognised.

In our district general hospital all procedures are performed in a day central treatment unit, with flexibility for extended admission on demand, that is located close to the intensive therapy unit. The nursing staff have considerable experience; we believe that both their early recognition of potential complications and their intervention are paramount with regard to optimal outcome. In addition, we strictly observe our unit's policy of giving the intensive therapy unit early warning that the test is imminent. We consider that these factors deserve far more emphasis irrespective of the location of the clinical setting, and they certainly seem possible in every district general hospital providing laboratory services of this nature.

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Failed hip replacements

SIR,—We endorse several of the sentiments expressed by R N Villar in the editorial on failed hip replacements.¹ The apparent success of total hip replacement has extended its indications, and as a result we can expect ever increasing numbers of revisions.

At our centre the probability of survival of a Charnley hip replacement after 10, 15, and 20 years is 91%, 87%, and 82% respectively.² These

results are comparable with those in other published series. The consequence of such figures, taking into account patients' survival, is at least five revision procedures per 100 primary arthroplasties. In 1991 we performed 56 revision hip arthroplasties at an estimated mean unit cost three times that of a primary arthroplasty. Extrapolation of these figures suggests that every 100 primary arthroplasties will result in a minimum potential extra expenditure equivalent to 15 primary arthroplasties. The Swedish experience of two less successful prostheses gave probabilities of survival of 63% and 28% at 10 years.³ The burden of revision accruing from such poor results has worrying financial implications, especially under market constraint.

The wide range of currently available prostheses tempts surgeons with new design features, but follow up data sufficient for analysis of survival are available for only a few prosthetic designs. Undoubtedly, technical skill and choice of prosthesis at primary arthroplasty determine outcome. These factors are even more relevant at revision.

While revisions increase in numbers, complexity, and expense we believe that some financial provision should be made at primary arthroplasty for the likelihood of revision surgery, which may be performed at a specialist centre. This figure can be calculated only for prostheses with a documented probability of survival and surgery of certain quality. We conservatively estimate this to be an addition of about 15% to the cost of a primary total hip arthroplasty.

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- 1 Villar R. Failed hip replacements. *BMJ* 1992;304:3-4. (4 January.)
- 2 Carter SR, Pynsent PB, McMinn DWJ. Greater than ten year survivorship of Charnley low friction arthroplasty. *J Bone Joint Surg [Br]* 1986;68(suppl 1):71.
- 3 Ahnfelt L, Herbert SP, Malchau H, Andersson GB. Prognosis of total hip replacement. *Acta Orth Scand [Suppl]* 1990;61:1-26.

SIR,—In an editorial R N Villar drew attention to the increasing number of revision hip arthroplasties being performed in the United Kingdom.¹

The need for a considerable proportion of these revision procedures could be delayed or avoided. Any measure or technique proved clinically to reduce the rate of complications in hip arthroplasty should be used at the primary intervention. Uncemented components have not been shown to improve the long term results of hip arthroplasty, and many designs have caused considerable early morbidity. With cemented total hip replacement improved techniques are frequently not used by the operating surgeon.² Prophylactic measures taken against early complications such as deep infection or venous thrombosis are often not optimal. Likewise, although it is known that the surgical technique used at operation will affect the longevity of the prosthesis,³ improved methods are often not practised.²

Fractures of acrylic cement and loss of bone stock are mentioned in the editorial as causes of loosening¹ whereas they are often a consequence of the failure of mechanical fixation of the implant. Refinements in surgical technique such as cleaning the bone, intramedullary plugging, and applying pressure to the cement have been shown clinically to improve mechanical interlock and longevity of the prosthesis.⁴ They should be used routinely.

At 10 year follow up there is a 20-fold difference in the incidence of loosening of the femoral component after cemented hip arthroplasty in the absence of sepsis.^{4,5} Reports from a surgeon's personal series of operations⁶ are generally better than those reflecting collective experience at institutions.^{7,8} Results from centres with a special-

ised interest in hip arthroplasty are comparable with those from a single surgeon.^{9,10}

Villar should be supported in the call for revision hip surgery to be carried out by specialists. The need for revision surgery would be diminished if a greater proportion of the more complex primary hip arthroplasties and operations on patients under 60 were also performed in specialist centres or by surgeons with a specific interest in the technique.

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- 1 Villar RN. Failed hip replacements. *BMJ* 1992;304:3-4. (4 January.)
- 2 Timperley AJ, Jones PR, Roosen R, Porter ML. Their hip in your hands—what is the contemporary total hip? *J Bone Joint Surg [Br]* 1991;73:71-2.
- 3 Lee AJC, Ling RSM. Loosening. In: Ling RSM, ed. *Complications of total hip replacement*. Edinburgh: Churchill Livingstone, 1984:110-45.
- 4 Sutherland CJ, Wilde AH, Borden LS, Marks KE. A ten year follow-up of 100 consecutive Muller curved-stem total hip arthroplasties. *J Bone Joint Surg [Am]* 1982;64:970-82.
- 5 Older J. Low-friction arthroplasty of the hip. A 10-12 year follow-up study. *Clin Orthop* 1986;211:36-42.
- 6 Eftekhar NS, Tzitzikalakis GI. Failures and re-operations following low-friction arthroplasty of the hip. *Clin Orthop* 1986;211:65-78.
- 7 Stauffer RN. Ten-year follow-up study of total hip replacement. *J Bone Joint Surg [Am]* 1982;64:983-90.
- 8 Dall DM, Grobelaar CJ, Learmonth ID, Dall G. Charnley low-friction arthroplasty of the hip. Long term results in South Africa. *Clin Orthop* 1986;211:85-90.
- 9 Eftekhar NS. Charnley low friction "torque" arthroplasty. *Clin Orthop* 1971;81:93.
- 10 Charnley J, Cupic Z. The nine and ten year results of the low-friction arthroplasty of the hip. *Clin Orthop* 1973;95:9.

Voice after laryngectomy

SIR,—In his editorial on voice after laryngectomy Michael Gleeson refers to the inferiority of radiotherapy compared with primary surgery in locally advanced (T_3, N_0, M_0) disease.¹ We disagree for several reasons.

T_3, N_0, M_0 laryngeal cancer is a heterogeneous entity including disease ranging from small glottic lesions fixing the vocal cords to large transglottic tumours fixing the entire hemilarynx. Therefore no single treatment is necessarily appropriate for all cases. In this and many other British centres the primary management of almost all laryngeal cancer including T_3, N_0, M_0 disease is with radical radiotherapy. The patient is then followed up closely at a combined otolaryngology and oncology clinic, and salvage laryngectomy is performed if indicated. Gleeson supports his preference for primary surgery by referring to a retrospective study by Kaplan *et al* of just 10 cases of T_3, N_0, M_0 laryngeal cancer treated with primary radical radiotherapy.² It is clearly preferable to base policy decisions on larger studies. In a recent large unselected series of 376 cases from this centre the five year cause specific survival for all stages was 75.5% (J M Heywood *et al*, unpublished observations). Of the 99 patients with T_3 tumours (83 were T_3, N_0), 23 subsequently required salvage laryngectomy, with a five year cause specific survival of 66% (R P Crellin *et al*, unpublished observations).

Harwood *et al*, in a review of 144 selected cases of T_3, N_0, M_0 glottic cancer, showed that local control and cause specific survival after primary radiotherapy with surgical salvage did not differ significantly from those after primary surgery.³ This policy was particularly effective for female patients, with a local control rate of 92%.

It is misleading to state that only up to one in five patients choose radiotherapy in preference to surgery, particularly as in McNeil *et al*'s study the subjects were not patients but healthy people.⁴ Although all patients are theoretically able to make an informed choice of alternatives, most will be guided by their specialist, whose personal preferences or prejudices will inevitably influence

the final choice of treatment. In a recent survey on the management of laryngeal cancer in the United Kingdom and Ontario, Canada, Gaze *et al* found that 84% of otolaryngologists and 96% of clinical oncologists would recommend primary radiotherapy for T₃,N₀,M₀ laryngeal cancer.¹

The recent advances in stomal valves and speech buttons are excellent news for patients in whom laryngectomy is inevitable, but we should still strive to allow as many patients as possible to retain their larynges with good speech function.

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- 1 Gleeson M. Voice after laryngectomy. *BMJ* 1992;304:2-3. (4 January.)
- 2 Kaplan MJ, John ME, Clark DA, Cantrell RW. The roles of surgery and irradiation. *Cancer* 1984;53:2641-8.
- 3 Harwood AR, Bryce DP, Rider WD. Management of T3 glottic cancer. *Arch Otolaryngol* 1980;106:697-9.
- 4 McNeill BJ, Weichselbaum R, Pauker SG. Speech and survival. Tradeoffs between quality of life in laryngeal cancer. *N Engl J Med* 1981;305:982-7.
- 5 Gaze MN, Mackillop WJ, O'Sullivan B, Gilbert R, Maki E, Lundgren J. The management of laryngeal cancer. A comparison of practice in the United Kingdom and Canada. *Clin Oncol* 1991;3:296.

SIR,—As a speech and language therapist working primarily with patients with head and neck cancer, and particularly patients who have had a laryngectomy, I wish to respond to Michael Gleeson's editorial on voice after laryngectomy.¹ I work in one of the British centres for surgical voice restoration (the technical term for voice valving). We offer this as the first option for communication after laryngectomy, except in rare cases in which the prognosis is particularly poor. It is important to note that the voice valve merely allows lung air to produce the sound for speech. As with normal speakers, this sound is modified by the oropharyngeal tract and the articulators. Voice is a small but fundamental part of speech. The editorial does not distinguish clearly between voice and speech.

Voice valves can also be offered to patients who have had a laryngectomy who have undergone more extensive resection with, for example, gastric pull up repair. Valves have been especially successful in those with jejunum grafts, where the quality of voice afforded is more acceptable than that with gastric pull up. These are patients who, as Gleeson says, would have had little chance of attaining satisfactory voice with traditional methods.

With regard to cost, maintenance may not be too expensive, but, especially in the early stages, the call on the time of medical staff and speech therapists is great.

No one can overestimate the far reaching effects that loss of voice has on lifestyle and personality. The availability of voice valves goes some way towards minimising these and providing successful rehabilitation.

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SIR,—In his editorial on the quality of speech after laryngectomy Michael Gleeson is less than fair when reviewing the evidence for the effectiveness of non-surgical treatments.¹

At least two substantial British prospective randomised studies of radiotherapy with or without chemotherapy have shown that many patients with advanced laryngeal cancer (T₃,N₀,M₀ and

upwards, by Gleeson's chosen classification of stage) can be cured.² Not only is this clearly contrary to his statement that "Others present with advanced disease, and for these unlucky patients total laryngectomy provides the only hope of long term survival" but analysis of "salvage" surgery—that is, total laryngectomy after failure of non-surgical treatment—has confirmed that avoiding early surgery does not seem to prejudice overall survival (H R Grant *et al*, 5th European conference on clinical oncology, London, September 1989). This study showed conclusively that over half of the patients, particularly those with T₃ rather than T₄ laryngeal cancers, never required surgical treatment and were therefore cured, particularly if the tumour had not spread to lymph nodes in the neck, without laryngectomy and consequent loss of voice.

It should be emphasised again that loss of voice is a majority penalty of laryngectomy, however effective the rehabilitation, follow up, and supportive care. Every effort should be made to avoid this tragedy by offering the most powerful form of non-surgical treatment as the primary treatment. Fortunately, this message seems to have filtered through to most British specialist centres, although it is apparently not yet widespread in the United States, even though a recent American based randomised study again showed that only about one third of patients with advanced laryngeal cancer required laryngectomy for relapse after maximum non-surgical treatment.³

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- 1 Gleeson M. Voice after laryngectomy. *BMJ* 1992;304:2-3. (4 January.)
- 2 SECOG Participants. A randomised trial of combined multi-drug chemotherapy and radiotherapy in advanced squamous cell carcinoma of the head and neck. *Eur J Surg Oncol* 1986;12:289-95.
- 3 Gupta NL, Pointon RCS, Wilkinson PM. Randomised clinical trial to contrast radiotherapy with radiotherapy and methotrexate given synchronously in head and neck cancer. *Clin Radiol* 1987;38:575-81.
- 4 Department of Veterans Affairs Laryngeal Cancer Study Group. Induction chemotherapy plus radiation compared with surgery plus radiation in patients with advanced laryngeal cancer. *N Engl J Med* 1991;324:1685-90.

Appropriate chemotherapy for palliating advanced cancer

SIR,—R D Rubens and colleagues' suggestion that a consensus view on good clinical practice for the management of a particular cancer should be published¹ is to be applauded, provided the consensus view includes the best available treatments validated by research and is not just a restatement of traditional treatments, which will do little to improve the treatment of cancer.

Although the treatment of multiple myeloma remains palliative, considerable prolongation of good quality life is possible, and the Medical Research Council's fifth myeloma trial, which compared melphalan with combination chemotherapy, showed a clear survival advantage for combination chemotherapy. This large randomised trial is the first Medical Research Council myeloma trial to show a significant improvement in survival with the new regimen of adriamycin, carmustine, cyclophosphamide, and melphalan over the well established melphalan regimen. At four years 31% of patients treated with the combination were alive as opposed to 16% in the melphalan group.²

A second important advance has been the prolonged duration of the plateau phase in patients treated with interferon alfa as shown in a smaller randomised study³; this is the subject of a larger Medical Research Council study of interferon alfa-2b given during the plateau phase, which was started in April 1989.

These two well documented advances surely

deserved a mention in Rubens and colleagues' brief discussion of the treatment of myeloma, in preference to trials of high dose chemotherapy with bone marrow transplantation, which are at present too small or in which long term follow up is insufficient to determine outcome. Multiple myeloma is perhaps an example of a cancer for which achieving an accurate consensus view of optimal management from published reports required more detailed and wider consultation than was undertaken.

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- 1 Rubens RD, Towson KE, Ramirez AJ, Coltart S, Slevin ML, Terrell C, *et al*. Appropriate chemotherapy for palliating advanced cancer. *BMJ* 1991;304:35-40. (4 January.)
- 2 MacLennan ICM, Kelly K, Crockson RA, Czuzik J, Chapman C. Results of the MRC myelomatosis trials for patients entered since 1980. *Hematol Oncol* 1988;6:145-58.
- 3 Mandelli F, Tribalto M, Avvisati G, Cantonetti M, Petrucci MT, Boccadoro M, *et al*. Recombinant interferon alfa-2b (Intron A) as post induction therapy for responding multiple myeloma patients. M84 protocol. *Cancer Treat Rev* 1988;15(suppl A):43-8.

SIR,—As a director of public health, I welcome efforts by the *BMJ* to provide practical help to health authorities and general practitioners in their new purchasing role. Given the breadth of health authorities' remit, the advice given in R D Rubens and colleagues' review of appropriate chemotherapy for palliating advanced cancer is most useful.¹

What this and similar articles do not do is help authorities to make decisions when resources are scarce. Though Rubens and colleagues acknowledge that the costs of such services need to be weighed against potential benefits, no evidence is presented to support this aspect of decision making. As well as considering the utility of any treatment or intervention, as the authors suggest, it is important to assess its cost effectiveness. How else will public health directors and their health authorities be able to make informed choices about whether to spend money prolonging the quality of life of patients with lung cancer or to shift more resources into preventing smoking related disease?

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Overheads for clinical research

SIR,—University departments are encouraged by the Committee of Vice Chancellors and Principals to charge realistic overheads when engaging in contract research with the pharmaceutical industry. Practices still vary widely, but non-itemised proposals for overheads of as much as 100% on research contracts are now being made in Britain.

The practice in continental Europe, according to a survey performed by the Association of the British Pharmaceutical Industry, is different. In Belgium, Switzerland, Finland, and Sweden overhead charges have never been incurred. In Norway, Germany, Ireland, the Netherlands, and Spain less than a quarter of institutions request such overheads, and invariably at a rate of less than 25%. In the United States overhead charges are not always added to research grants, but the practice is more variable than in Europe. The highest rate encountered in the survey was 70%, and in most cases the rate was less than 25%.

There can be no objection to itemised expenses, which can be debated directly by the institution and the company concerned. High demands that