which is certainly no better than the results achieved by more conventional treatment, although, of course, they may have been seeing the worst end of the spectrum of disease. The patient is not overly concerned with response rates; what he or she desires is life, and the fact that there may have been response to treatment is no consolation to the relatives if the final result is death. Furthermore, the varying histologies, each with a different clinical course and with a limited follow up, make it difficult to draw any positive conclusions about the efficacy of fast neutrons in the treatment of upper jaw tumour.

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**The authors reply below.—ED, *BMJ*.

SIR,—We are able to reassure Mr Narula and his colleagues that we are aware of the long clinical course of adenoid cystic tumours from which six of our patients suffered. However, 5 and 10 years survival rates of 74% and 25% are figures taken from a point years earlier in the disease than that at which our patients were referred for neutron therapy. Our patients had such advanced disease that they would, in general, have been dead within months if an effective treatment had not been given. Since this applied to all the histological types reported we felt justified in presenting the results together.

We regret that we fail to understand the sentence about controlled trials. Any agreed protocol for such a trial would obviously select the relevant points for follow up.

These authors and Mr Shaheen express concern that neutron therapy did not prevent death from metastases. However, we would point out that neutron therapy was given by beams of radiation directed precisely to the primary tumour as a local treatment having local effects. Complete regression was achieved in 29 patients, in four of whom disease recurred, leaving 25 with local control. The efficacy of neutrons in controlling the primary tumour meant that most of those patients who eventually died of metastases were made free of malignancy in their faces for the remainder of their lives. That generalised metastases are a common cause of death is well recognised, and an effective systemic treatment is needed. When this is available and is combined with neutron therapy for the primary tumour a significant advance could be achieved.

Of the 10 complications, three followed treatments given for recurrence after radical x ray treatment that had devascularised the tissues before neutrons were given. Three other patients had temporal lobe damage, which was controlled by the use of steroids, giving a good quality of life. Neutron complications which did occur were therefore certainly no worse than the sequelae of every radical surgical procedure for these tumours.

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SIR,—While appreciating the excellence of the small series of patients with head and neck cancers surviving after neutron treatment by Dr Mary Catterall and others it is important that your readers should know about the other side of the coin.

For the past 50 years trials of neutrons have been strewn with complications, such as the loss of an eye in the present series. It is not as if there is no alternative for difficult anoxic tumours. Although hyperbaric therapy has come to a halt, it still has some enthusiastic adherents. A good vascularity is associated with good responses to radiation. Intra-arterial chemotherapy may be administered in conjunction with non-toxic antidotes delivered to the venous circulation and so timed that a barrier of neutraliser meets the cytotoxic drug emerging from the tumour circulation.[1] This results in some leucocytosis instead of leucopenia, possibly suggesting an improved immunological effect. Two cases may illustrate the usefulness of this method.

Case 1—This patient had a painful, large, stony hard, fixed squamous carcinoma of the side of the back of the tongue. There were small shotty nodes in the neck. The patient was initially refused radiotherapy. Infusion was followed by softening and improved vascularity, as shown by a repeat angiogram. Radical radiation was followed by survival beyond 20 years.

Case 2—This patient had a huge fibrosarcoma of the upper thigh. An infusion was followed by regression and softening. Radiotherapy produced flattening. The whole muscle group was removed by radical electrocoagulation and showed only dead cells on histological examination. The patient survived for over 15 years.

A series of similar patients has confirmed the value of the method. Tracking radiotherapy so that the treatment is confined to the spread of the disease, thus sparing normal tissue and increasing the dose to this small volume, also gives most encouraging results.[2-4]

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Luteinising hormone releasing hormone analogue for prostatic cancer

SIR,—There are no data to support the statement by Mr Gordon Williams and his colleagues (8 December, p 1580) that luteinising hormone releasing hormone analogues have revolutionised the care of prostatic carcinoma. Previous delivery systems for these drugs and the frequency of administration required have so far made them quite unsuitable for routine use. In a previous leading article (8 September, p 571) Mr Williams himself states that they have unreliably suppressed testosterone concentrations. He has also advocated combination with large, expensive, and almost certainly toxic doses of ketoconazole to reduce androgen secretion still further. Cyproterone acetate already performs this function, but there is little evidence to show superiority over orchidectomy and oestrogens.

Most cases of prostatic carcinoma are advanced on presentation and tumours contain many anaplastic, hormone independent cells. Surely the future management of this disease does not lie in tinkering with the margins of endocrine control.

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**Mr Williams replies below.—ED, *BMJ*.

SIR,—Most patients with metastatic carcinoma of the prostate are treated with oestrogens, orchidectomy, or antiandrogens. About 70% will show an initial response, of whom half will relapse within two years, and half of these will die within six months of this relapse. In addition, the side effects of such treatments seriously limit patient compliance and acceptability. There is thus a clear need for a more acceptable, well tolerated, and, one hopes, more efficient form of treatment.

Our paper described a completely new form of administration of a luteinising hormone releasing hormone (LHRH) analogue, which at present only has to be given every 28 days and, as clearly stated in the paper, reliably suppresses testosterone throughout the 28 days (present follow up 12 months), with none of the testosterone blips seen with other LHRH analogues. Some patients are administering the agent themselves, and in many large series using LHRH analogues no side effects related to the drug, apart from hypoandrogenicity, have been seen. The results of combination therapy using an LHRH analogue and a pure antiandrogen[1 2] in stage D2 carcinoma of the prostate have shown an initial 100% objective response (National Prostate Cancer Project criteria). The normalisation of bone scans in 26% of patients and of acid phosphatase values in all patients in whom they were raised within four months, and a mortality at two years of 3·3%, may not be revolutionary, but these results are certainly impressive when compared with current treatment and provide very strong supportive evidence for the concept of total androgen ablation for the treatment of this disease.

We have used ketoconazole, a drug which blocks both testicular and adrenal androgen production, in 26 patients with progressive prostatic cancer who had relapsed after conventional endocrine therapy. Seven out of 11 patients alive at six months have shown objective evidence of response, suggesting that these cells do still retain androgen dependence. No patient treated for this period shows any abnormality of liver function. The only other option in these patients would have been combination chemotherapy. Most would have had severe side effects, and few would have responded.

Cyproterone acetate, which is more expensive than ketoconazole, is not a pure antiandrogen, nor when given alone does it reduce testosterone to castration levels. It is therefore hardly surprising that it is not better than orchidectomy or oestrogens. Man is unique in having adrenals that secrete androgens and precurser steroids that are converted, in the periphery, to androgens.[3] After surgical or medical castration the intraprostatic concentration of the active androgen dihydrotestosterone remains as high as 40-50% of the value in intact patients.[4] It appears to me that the concept of total androgen ablation is not tinkering with the margins of endocrine control but making a positive attempt to improve the results of treatment of this condition.

As Mr Taylor is unable to suggest any alter-