mortality, is deliberately misleading: the excess deaths were due to distant metastases. These deaths were inevitable even before the patients entered the flawed trial. We know that this was the basis for the rejection of the study as totally inappropriate by the Radiation Therapy Oncology Group's fast neutron group in the US. So why waste time, precious resources, and the trust of patients?

Yet Dr Errington and colleagues have persevered and delivered another antineutron headline. Such a headline might have been critical to the project to get a cyclotron where it would be used effectively for the benefit of patients. But this had already been torpedoed—after a brilliant, well orchestrated campaign—by the withdrawal of what has been represented as the infamous Thatcher £6 million repayable loan—which was not a grant for cancer research, as is so often misreported, but a repayable loan for treatment.

Happily, one important message that can be gleaned from this study is the absence of excess normal tissue morbidity in the pelvis of patients treated with 19·2 Gy of high energy neutrons in 12 fractions over 28 days. Further studies—sadly, probably elsewhere—will identify the true role for neutrons in treating advanced cancer.

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1 Errington RD, Ashby D, Gore SM, Abrams KR, Myint S, Bonnett DE, *et al.* High energy neutron treatment for pelvic cancers: study stopped because of increased mortality. *BMJ* 1991;**302**:1045-51. (4 May.)

AUTHORS' REPLY,—Dr Bates's comments are inappropriate as far as the detail of the design and subsequent analysis of the Clatterbridge trial of high energy neutrons versus photons in advanced pelvic cancers are concerned.[1] The trial featured informed consent, no exclusions from analysis, randomisation from the first patient, and the same investigations and follow up procedures for patients treated with neutrons and photons. It lacked power to detect moderate benefit for high energy neutrons from the point of view (that is, equipoise) reflected in the prior opinion of peers—a problem common to all trials of neutrons because of the cost of cyclotrons and need for all patients to be assessed by the same doctors. There was, however, no lack of power to exclude modest benefit for high energy neutrons from the prior position reflected in the results of trials of low energy neutrons. A priori, peer opinion moderated pessimism about low energy neutrons. A posteriori, the relevance of the results obtained with low energy neutrons had to be reassessed.

Randomisation should preclude imbalance of patients with occult metastases between neutron and photon treatment. It will not do so in every trial. The issue of fortuitous imbalance is addressed by retrospective proportional hazards adjustment of major prognostic factors ascertained before randomisation and themselves related to metastatic risk. Retrospective adjustment should not be made for metastatic state as ascertained after randomisation because the ascertainment process or the metastases, or both, could be related to treatment. With respect to the data on morbidity, Dr Bates has overlooked the caution we advocated in their interpretation because of the small number of patients at risk of developing later severe reactions.

The statement concerning the rejection of our study by colleagues in the Radiation Therapy Oncology Group is misleading.[1] The paper was presented at meetings of the group's Neutron Collaborative Working Group in the US in March and October 1990 and March 1991. At no time did the working group question the merits of our trial or reject its findings. At the time that the cyclotron controversy started[2] the studies at Clatterbridge were still recruiting patients. This continued despite the difficulties caused by the extreme views expressed by the protagonists and antagonists of neutron treatment. These certainly were a betrayal of the trust of patients and restricted the use of a precious resource primarily carrying out objective clinical research.

As far as other studies are concerned, the cyclotron at Clatterbridge has been a major contributor to the Radiation Therapy Oncology Group and Medical Research Council neutron head and neck trial (data validated by a site visit by the Radiation Therapy Oncology Group in November 1990). The role of neutrons in locally advanced salivary gland[3] and air sinus tumours[4] is acknowledged, with treatment available at Clatterbridge since July 1987. Alternative approaches to trials of neutron treatment have been suggested.[5] Until these can be put into practice the results of randomised studies and their objective appraisal[6] are a more appropriate guide to the correct application of neutron treatment than clinical anecdotes and subjective views, which have been such a feature of the cyclotron saga.

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1 Errington RD, Ashby D, Gore SM, Abrams KR, Myint S, Bonnett D, *et al.* High energy neutron treatment for pelvic cancers: study stopped because of increased mortality. *BMJ* 1991;**302**:1045-51. (4 May.)
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What determines the age at the menopause?

SIR,—Though I agree with Dr Jean Ginsberg that parity, race, and smoking are factors that influence the age at the menopause, a link with nutrition is not clear cut.[1] Genetic and racial factors and high parity are probably the most important determinants. The connection may lie in "genetic programming," to which Dr Ginsberg refers. This causes some women to ovulate longer, which may lead to higher parity and possibly a later menopause. It is difficult to understand why multiple pregnancy should lower the age at the menopause when there is a correlation between high parity and multiple pregnancy.

Viable pregnancy is rare in women beyond the age of 50. This has been presumed to be a result of increasing anovulation. Nevertheless, Novak found a surprising number of women—23% in his study of 200 women above 50—showing histological evidence of recent ovulation.[2] In a recent study (paper in preparation) of pregnancies in seven women confirmed as being aged over 50 conducted over two years at Dudley Road Hospital, Birmingham, some fascinating features emerged. Four are worthy of consideration.

Firstly, all the women were Asian. Four came from the Mirpur district of Pakistan and three from the Sylher district of Bangladesh. Both these regions are underdeveloped and overpopulated. Secondly, the average age at the time of the latest delivery was 52·8 years (oldest 59, youngest 51). The age was checked from birth certificates or passports and cross checked with that on the birth certificate of the first child. Thirdly, all these women were highly parous with an average of 8·8 children. Two of the seven women had also delivered twins. Finally, the average age at the first pregnancy had been 31. Every one of these women was a grandmother.

Such examples of ovulation continuing well beyond the average age of the menopause may indeed be due to genetic programming. As well as a late age at the menopause the effect of this is, more importantly, prolonged fertility well into the sixth decade. Understanding and perhaps regulating the factors determining the age at the menopause could have important effects in controlling fertility, particularly in already overpopulated countries.

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1 Ginsburg J. What determines the age at the menopause? *BMJ* 1991;**302**:1288-9. (1 June.)
2 Novak ER. Ovulation after fifty. *Obstet Gynaecol* 1970;**36**: 903-10.

SIR,—In her editorial[1] Dr Jean Ginsberg has omitted to mention that left handed women have earlier menopauses than right handed women. This association may be related to possible correlations between left handedness and autoimmune disorders, which may include reactions against hormone receptor sites and oocytes.[2]

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Increasing the uptake of cervical smear testing among Asian women

SIR,—Dr Brian R McAvoy and Rabia Raza's recent article about the effectiveness of personal visits in increasing the uptake of cervical smear testing among Asian women[1] prompted a letter of response[2] that raised once again the issue of the availability of the target population for screening and the inaccuracy of recorded addresses in the databases of family health services authorities. We agree that studies to assess the effectiveness of efforts to promote screening are dogged by the problem of women not being resident at the address on the invitation and no access being possible at the address.

The discrepancies between the findings of Dr McAvoy and Rabia Raza and Drs Joyce M Carter and Susan E Ellerby with regard to the proportion of women who were contactable at the address on the screening invitation may be accounted for by the different populations that were being studied. Dr McAvoy and Rabia Raza visited randomly selected Asian women who had never been tested previously whereas Drs Carter and Ellerby visited any women who had not responded to the call-recall scheme for cervical cytology: Dr McAvoy and Rabia Raza found that 159 of 482 declined to participate or were not contactable whereas Drs Carter and Ellerby found that at 58-68% of 1273 addresses no access was possible and 12-13% of addresses were incorrect.

In following up women who do not attend for