LETTERS TO THE EDITOR

Duration of chemotherapy in small cell lung cancer

The lengthy and balanced editorial on treatment duration in small cell lung cancer (January 1990;45:1–2) makes no mention of the first large scale randomised trial specifically addressing this question to be published world wide. In 1986 we reported a randomised trial with over 300 patients, which resulted from collaboration amongst chest physicians, radiotherapists, and medical oncologists in Nottingham and elsewhere in the Midlands.[1] Unlike most subsequent trials we chose not to randomise patients who had clearly demonstrable signs of residual disease after an initial period of induction chemotherapy (that is, partial remissions or failures) as we felt intuitively that these patients (whose tumours were thus not very sensitive to chemotherapy) were very unlikely to benefit from more of the same. The results of the later trials have confirmed that our suspicions were correct. In the Midlands trial limited and extensive stage patients who had responded very well to induction treatment were randomised separately. There were inadequate numbers of limited stage cases for worthwhile conclusions. In extensive disease, however, there was a significant prolongation of survival with maintenance treatment. We concluded that "... patients and their doctors may differ in their views as to whether the quality and duration of the added survival is worth the extra treatment." Our view, like most others now, including the one expressed in your editorial, is that, with currently available treatment the benefit is not worthwhile given treatment toxicity. The distinction between a biological effect and a worthwhile treatment is an important one, which is not developed in your editorial. It would be a shame if this biological effect were forgotten, just because it is currently not applicable. We know that virtually all patients who achieve complete remission have residual disease, and if a less toxic treatment were available maintenance treatment, in the absence of curative treatments, might have a role.

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1 Cullen M, Morgan D, Gregory W, *et al*, and the Midlands Small Cell Lung Cancer Group. Maintenance chemotherapy for anaplastic small cell carcinoma of the bronchus: a randomised, controlled trial. *Cancer Chemother Pharmacol* 1986;17:157–60.

AUTHOR'S REPLY We thank Dr Cullen for his letter and agree with his remarks and perception of the future for the treatment of this disease. The Midland group's paper was well known to us and our failure to include it in the discussion on maintenance therapy was an oversight for which we apologise.

ROBERT SOUHAMI
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Diffuse mengingeal thickening associated with pleural mesothelioma

In a recent report (January 1990;44:70–1) Dr J B Murray and others report an interesting case of diffuse spinal metastases in a patient with pleural mesothelioma. As pointed out by the authors, central nervous system metastases from pleural mesothelioma are rare, with less than two dozen cases published. In addition, only three cases of central nervous system metastases diagnosed before death have been reported. Although the authors mention several studies which document the occurrence of metastases in malignant mesothelioma of the pleura, we would like to mention our 1987 necropsy study, with which the authors may not be familiar.[1] In this report we reviewed 42 cases of pleural mesothelioma and found distant metastases in 32 (76%). Common sites of metastatic spread were the contralateral lung, kidney, liver, and adrenals. No relation between histological type and distant metastases was found.

Recently we also reviewed a case of pleural mesothelioma in a lift mechanic,[2] in which a cerebral metastasis was documented by computed tomography. This patient presented with a right Horner's syndrome of uncertain aetiology and subsequently developed increasing confusion.

Computed tomography of the head showed a metastasis in the left frontal area. The patient died one month later, and necropsy confirmed the diagnosis of mesothelioma. This is the third report of antemortem recognition of a brain metastasis in malignant mesothelioma.

The patient described by Dr Murray and others was noted to be a roofing contractor, as was the patient described by Reichel.[3] These reports suggest the possibility of a mesothelioma hazard in this occupational group. Such reports highlight the need for vigorous investigation of a history of potential asbestos exposure in patients with this tumour as disease risk is recognised as not being confined to asbestos industry workers such as miners and insulators.

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1 Huncharek M, Muscat J. Metastases in diffuse pleural mesothelioma: influence of histological type. *Thorax* 1987;42:897–8.
2 Huncharek M, Capotorto J, Muscat J. Pleural mesothelioma in a lift mechanic. *Br J Ind Med* 1989;46:500–1.
3 Reichel J. A former roofer with chest pain. *Einstein Q J Biol Med* 1988;6:86–90.

Role of histamine released in hypertonic saline induced bronchoconstriction

Dr J P Finnerty's letter (January 1990;45:78) criticises the dose of terfenadine chosen by Dr S P O'Hickey and his colleagues (August 1989;44:650–3). In his reply Dr O'Hickey disputed this criticism and claimed that the dose of terfenadine he chose would have been adequate to interfere with histamine released by hypertonic saline because he found a reduction in histamine responsiveness when this was measured by the topical application of inhaled histamine. Dr O'Hickey's reply shows a basic ignorance of the pharmacology of histamine and antihistamines, such as can be gleaned from perusal of any appropriate textbook.

It has long been recognised that very much higher doses of H_1 receptor antagonists are required to antagonise endogenous ("nascent") histamine: "It is not clear whether it is because these processes occur intracellularly or whether the receptors through which nascent histamine acts are of a different type to those antagonised by the common antihistamines (i.e. H-1 receptor antagonism)."[1]

Dr O'Hickey and his colleagues may have been right in their conclusions but the rejection of Dr Finnerty's criticism is ill based.

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1 Bowman WC, Rand MJ. *Textbook of pharmacology*. 2nd ed. Oxford: Blackwell, 1980:12.10.

AUTHOR'S REPLY I was surprised at the comments of Dr Keaney. There is no evidence that the new non-sedative antihistamines are less effective at antagonising endogenous than exogenous histamines. Reviewing the reference Dr Keaney cited, I note that there is only a dogmatic statement as regards this phenomenon, with no experimental evidence to support the comment.

Furthermore, in studies where endogenous histamine release is thought to be the major mechanism of airways bronchoconstriction, 120 mg of terfenadine has been shown to be as effective as 180 mg in antagonising this response.[1,2]

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1 Chan TB, Shelton DM, Eiser NM. Effect of an oral H_1-receptor antagonist, terfenadine, on antigen-induced asthma. *Br J Dis Chest* 1986; 80:375–84.
2 Patel KR. Terfenadine in exercise-induced asthma. *Br Med J* 1984;ii:1496–7.

A case of necrobacillosis

We were pleased to see the report of a case of *Fusobacterium necrophorum* infection (necrobacillosis) by Dr A J Chippindale and colleagues (January 1990;45:74–5). Over the past four decades the diagnosis seems to have become so unfashionable that in 1984 we entitled our report of five cases "Necrobacillosis: a forgotten disease."[1] Necrobacillosis has subsequently come in from the cold to the extent that it now appears in the *Oxford textbook of medicine*, but it is still largely ignored in respiratory texts.

We suggest that necrobacillosis is still underdiagnosed. Since our report, one of us (JMG), during the course of his own clinical practice, has encountered three more proved cases and one presumptive case of the disease. The other (SJE) has subsequently reported on 40 further cases collected from 20 different hospitals.[2] The report by Dr Chippindale and others is not of an arcane condition, to be read about and then forgotten. The diagnosis may be established infrequently, but necrobacillosis is almost certainly more common than many of the obscure conditions on which final year students and MRCP candidates expend time and effort.

The importance of making the diagnosis is not purely a matter of intellectual satisfaction. A prolonged illness may be expected and the well described complications anticipated and the patient must be carefully observed accordingly; Chippindale's patient was obviously extremely ill, but escaped more lightly than many. Establishing the correct diagnosis will prevent a fruitless search for an underlying