

## LETTERS TO THE EDITOR

### Relation of urinary cotinine concentrations to cigarette smoking and to exposure to other people's smoke

Dr Simon Thompson and his colleagues measured urinary cotinine in 184 self reported non-smokers (May 1990;45:356-61). Taking 10-30% of average smokers' concentrations to indicate occasional smoking and over 30% to indicate regular smoking, they found two (1.1%) occasional smokers and no regular smokers among their non-smokers. In an earlier study,<sup>1</sup> based on 808 self reported non-smokers, I found 1.1% occasional smokers and 1.4% regular smokers and, on the basis of these data and evidence from other sources on the extent to which self reported never smokers were ex-smokers, I calculated that bias caused by misclassification of smoking habits could completely explain reported excesses in lung cancer risk in non-smokers married to smokers. Thompson and colleagues argue that the lack, in their study, of typical smokers misreporting themselves as non-smokers "strongly suggests" that my hypothesis is "untenable."

Their conclusion is unreasonable for several reasons. Firstly, their study is much smaller than mine. Secondly, unlike mine it was not nationally representative, being based on men and women attending BUPA. Thirdly, the number of regular smokers observed (zero) is not different from that expected (2.6) were the underlying misclassification rate in fact 1.4%. Fourthly, they ignore evidence from several other relevant studies. Elsewhere, in a detailed review of possible health effects of environmental tobacco smoke,<sup>2</sup> I cite data from 10 studies (including Dr Thompson's and my own) of more than 100 subjects, all carried out in a context in which subjects were not actively persuaded to give up smoking (which increases misclassification rates<sup>3</sup>). Among a total of 12 948 subjects 245, or 1.9%, were found to have cotinine concentrations consistent with regular smoking. The 10 studies gave rates ranging up to 2.7%, with a median of 1.4%, only the Thompson study and the earlier study of Wald and Ritchie<sup>4</sup> reporting a rate of zero.

Although it is the existence of true smokers among the self reported non-smokers that causes bias in estimates of the effect of a smoking spouse on lung cancer risk, defining rate with self reported non-smokers as the denominator may be somewhat misleading. For a given proportion of smokers claiming to be non-smokers, calculated in this way the misclassification rate depends to a substantial extent on the proportion of smokers in the population (low in those attending BUPA), and it may be better to use true smokers as the denominator when estimating misclassification for a study. On the basis of results from those eight of the 10 studies used earlier that provide relevant data, I found that 3.2% of smokers claimed to be a non-smoker while having cotinine concentrations consistent with regular smoking. Clearly Dr Thompson's data, being based on only 49 self

reported smokers, are not inconsistent with this overall finding.

Estimating the true extent of bias due to misclassification of smokers as non-smokers is a complex issue, made more difficult by a lack of information on rates in Oriental populations and on the extent to which current smokers misclassify themselves as lifelong never smokers (rather than as non-smokers).

An up to date review of the evidence<sup>2</sup> underlines its importance, however, and apparently—but not actually—discrepant results from one small study can scarcely change this.

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- 1 Lee PN. Lung cancer and passive smoking: association an artefact due to misclassification of smoking habits? *Toxicol Lett* 1987;35: 517-24.
- 2 Lee PN. A detailed review of epidemiological evidence relating environmental tobacco smoke (ETS) to the risk of cancer, heart disease and other causes of death in adults who have never smoked. Basel: Karger (in press).
- 3 Lee PN. *Misclassification of smoking habits and passive smoking. A review of the evidence.* Heidelberg: Springer, 1988.
- 4 Wald NJ, Ritchie C. Validation of studies of lung cancer in non-smokers married to smokers. *Lancet* 1984;i:1067.

### Life threatening haemoptysis in cystic fibrosis: an alternative therapeutic approach

We think that a number of important aspects of the report by Dr Bilton and colleagues (December 1990;45:975-6) merit further comment. The first is that this is not the first report of the use of pressor agents in managing patients with haemoptysis as they claimed.<sup>1</sup>

Secondly, omitting to correct the gross thrombocytopenia ( $8.2 \times 10^9/l$ ) must have contributed to the severity of the recurrent haemoptysis and is in itself not compatible with simple hypersplenism. Although the administration of vitamin K will correct clotting factor deficiencies linked to vitamin K malabsorption, it takes 24-48 hours to be effective; it is not appropriate treatment for correcting coagulation defects in actively bleeding patients, where fresh frozen plasma is the treatment of choice. We presume that the stated prothrombin time of 1.4 seconds was a typographical error.

Thirdly, the failure to instigate specific measures to protect the airway and prevent asphyxiation during the episodes of rebleeding was somewhat disconcerting and, although it was stated that there was no difficulty in distinguishing between a large haemoptysis and a haematemesis in this patient, more precise quantification of his cardiovascular and respiratory state (for example, arterial oxygen tension, blood pressure, heart rate, and respiratory rate and the appearance of the chest radiograph) would have been helpful, especially in view of his previous variceal bleeds and the recent sclerotherapy.

Finally, discussion of the more important and potentially fatal consequences of intravenous administration of desmopressin and vasopressin apart from water retention and bronchoconstriction (see *Martindale*<sup>2</sup> and references therein) should have been included as this report may prompt more

widespread recourse to the use of these agents in other, perhaps older, patients presenting with severe haemoptysis from other causes.

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- 1 Magel G, Williams MH Jr. Treatment of massive haemoptysis with intravenous pitressin. *Lung* 1982;160:165-9.
- 2 Anonymous. *Martindale. The extra pharmacopoeia*. 29th ed. London: Pharmaceutical Press, 1989:1138.

### AUTHORS' REPLY

We commend Drs Chilvers and colleagues for finding a report that had eluded ourselves, the pharmaceutical company and recent editorials on the subject. Our report was clearly timely in reawakening interest in a therapy that had been forgotten and may be useful in carefully selected patients.

We have used vasopressin since our report was published to control profuse haemoptysis in a further patient with cystic fibrosis. Side effects were those of fluid retention that required diuretics as previously mentioned. Our case report was specific to cystic fibrosis and discussion of other serious side effects (detailed in the *British National Formulary*) did not seem relevant as they are well known from the use of vasopressin for oesophageal variceal bleeding in older patients.

With regard to protection of the airway, the patient was sucked out. It is difficult for a patient to retain a mouthpiece while coughing blood and the insertion of an endotracheal tube was contraindicated in this patient as it would have required sedation and assisted ventilation. Intravenous pressor agents resolved this problem.

The platelet count was a typographical error: it should have read  $82 \times 10^9/l$ ; and the prothrombin measurement was a ratio [1.4].

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## BOOK NOTICES

**Electron Microscopy of the Lung.** Vol 48. Dean E Schraufnagel. (Pp 612; \$210.) New York: Dekker, 1990. ISBN 0-8247-8319-0.

This is an excellent reference book, of interest to the research scientist and clinician alike. It is illustrated with 290 micrographs of normal and abnormal lung. Divided in two parts, the first part focuses on most of the electron microscopic methods currently available and the results of their application to study normal airway cilia, surface epithelium, lung interstitium, vasculature, permeability, and variations in human or experimentally induced lung disease, including pneumoconiosis. The second section summarises the applications of the electron microscope as a clinical tool in the diagnosis of neoplastic and