24 changes from another beta agonist to fenoterol as a result of the admission, and 46 changes in the other direction (most of the latter patients were switched to salbutamol). On the other hand, there were substantial changes for other classes of asthma drugs. In particular, as a result of the admission, the proportion of patients prescribed oral corticosteroids increased from 28% to 62%. Thus patients were often prescribed prophylactic medication as a result of their severe attack, but there is no evidence that sicker patients were switched to fenoterol.

The comment about substandard care in the United States among blacks is not relevant to our findings in the Maori. It is well known that Maori have a higher asthma death rate than non-Maori. We have shown something quite different: that the Maori who use fenoterol have a higher death rate than the Maori who do not use fenoterol. The implication that this finding is due to confounding by ethnicity is nonsense as the comparison was made within the one ethnic group.

More generally, are Professors Spitzer and Buist suggesting that the standard of medical care for New Zealand declined so rapidly in 1976 (when fenoterol was introduced) that this accounted for a doubling of the mortality in two years? If so, what evidence do they have for this? Do they also imply that the standard of medical care also declined suddenly in the six countries which had mortality epidemics in the 1960s when isoprenaline forte was introduced? Furthermore, if any bronchodilator can be harmful when prescribed in the context of poor medical care, why did New Zealand not see an epidemic when salbutamol was introduced?

Professors Spitzer and Buist suggest that we have challenged the scientific community with the possibility that good drugs when used poorly may be potentially harmful. We have not. The scientific community already knows this. Rather we have suggested that a poorly selective beta₂ agonist, which is more potent than salbutamol¹ but available by metered dose inhaler at twice the dose of salbutamol, may have been responsible for an epidemic of asthma deaths in young people with severe asthma in New Zealand.

Rather than repeatedly raising the same criticisms of our work, Professors Spitzer and Buist, or Boehringer Ingelheim, should inform the scientific community of the following: (1) Why was fenoterol marketed as a "forte preparation" (200 µg/puff compared with salbutamol at 100 µg/puff) when it was known to be more potent and to have greater cardiac effects than other commonly available beta agonists? (2) Why was the nebuliser formulation made available in New Zealand (5 mg/ml) five times the concentration used in Canada (1 mg/ml)? (3) Why was fenoterol never licensed in the United States? (4) Why was fenoterol marketed as a highly selective beta₂ agonist when Boehringer Ingelheim's own funded experiments had indicated that in the clinical situation it was no more selective than orciprenaline,⁶ the poorly selective agent it was designed to replace?

In conclusion, we concur with the independent report commissioned by the New Zealand Health Department that the evidence proposed by the Boehringer Ingelheim reviewers in favour of the confounding hypothesis is indirect, circumstantial, and considerably subjective.⁷ Although further research would clearly be valuable we also agree with the New Zealand Health Department's conclusion that the current balance

of evidence is now in favour of a causal association between fenoterol use and asthma mortality. As a result, the New Zealand Minister of Health has moved to severely restrict the availability of fenoterol by removing it from the Drug Tariff, and a similar policy has now been adopted in Australia.

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Local anaesthesia for fiberoptic bronchoscopy

Dr AC Davidson and colleagues (March 1990;45:239) were impressed with the local anaesthesia produced by a transcrucoid injection of 4-6 ml 5% cocaine (200-300 mg). They went on to state that they were unaware of a formal comparison of cocaine and lignocaine as local anaesthetics during bronchoscopy but recommended that other centres consider changing to the transcrucoid instillation of cocaine for fiberoptic bronchoscopy.

In a double blind, randomised study of 60 patients we recently compared the local anaesthetic effects of intratracheal injections of lignocaine (4 ml of 4%: 160 mg) with cocaine (4 ml of 2.5%: 100 mg)¹. Local anaesthesia was assessed by numbers of coughs, operator acceptability, and patient discomfort; in all areas cocaine scored only slightly better than lignocaine (for example, there was a mean of eight coughs per procedure with cocaine compared with 11 with lignocaine), none of the differences achieving statistical significance. The impression of Dr Davidson and colleagues of the superiority of cocaine may reflect their use of a dose two to three times higher than in our study. It has been recommended that no more than 1.0-1.5 mg/kg cocaine should be applied to mucous membranes in adults, while others have suggested a maximum dose as low as 50 mg²; the use of higher doses may increase the risks of toxicity.

We agree with Kinnear *et al*³ that transcrucoid injections of local anaesthetic are well tolerated and produce effective local anaesthesia for fiberoptic bronchoscopy. When used

in the doses recommended above cocaine and lignocaine appear equally effective.

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- 1 Teale C, Gomes PJ, Muers MF, Pearson SB. Bronchoscopic local anaesthesia: intratracheal cocaine and lignocaine appear equally effective [abstract]. *Thorax* 1990;45:333P.
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- 3 Kinnear WJM, Reynolds L, Gaskin D, Macfarlane JT. Comparison of transcrucoid and bronchoscopic routes for administration of local anaesthesia before fiberoptic bronchoscopy [abstract]. *Thorax* 1988;34:805P.

AUTHOR'S REPLY We are grateful to Dr Teale and colleagues for drawing our attention to their study of local anaesthesia for bronchoscopy, which we had overlooked. The main point that we were making was that patient tolerance is dependent on the effectiveness of local anaesthesia and two studies now attest to the superiority of the transcrucoid route.^{1,2} Our impression of the greater effectiveness of cocaine may be the result of our use of a higher dose (200-300 mg) than that used by Dr Teale and colleagues in their study (100 mg); it is interesting that a trend towards a superiority of cocaine is apparent in their abstract. The question of the safe maximum dose of topical anaesthetic agents is controversial and surveys of practice in the UK suggest the use of more lignocaine at bronchoscopy than many authorities recommend. That this is safe practice is suggested by a study demonstrating serum concentrations well below the toxic range with topical doses in excess of 500 mg,³ presumably because only a proportion of the administered dose is actually absorbed through mucus membranes. The recommended doses quoted by Dr Teale are unrealistically low and the *British National Formulary* recommends a maximum topical dose of 3 mg/kg for cocaine. We now aim to measure serum cocaine levels to ensure that the doses we employ do not produce toxicity. An internal audit of complications in nearly 1000 bronchoscopies has, however, shown no evidence of cocaine induced neurological or cardiac toxicity.

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BCG vaccination of schoolchildren in England and Wales

One aspect of discontinuing routine BCG not discussed by Drs V H Springett and I Sutherland (February 1990;45:83-8) is the possible increase in mortality which may result.

Using published data^{1,2} from the Office

Extra deaths expected from stopping BCG in given five year periods

Year stopped	1995-9	2000-4	2005-9	2010-4	2015-9
1991	1	2	3	2	2
1996	0	1	2	2	1

of Population Censuses and Surveys, we calculate that in the last 10 years the ratio of the number of deaths from tuberculosis per 100 notifications in the 15-29 age group is 0.75. In other words, one death apparently results from 140 notified cases.

On the basis of the figures of Drs Springett and Sutherland for the increased numbers of notifications which are likely to result from discontinuing BCG, the table above shows an estimate of the number of "preventable" deaths in the 15-29 age group which may result in the next 30 years.

The possible increase in mortality is obviously another important factor which should be borne in mind when we are considering discontinuation of routine BCG vaccination.

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1 Office of Population Censuses and Surveys. *Mortality statistics (cause)*. London: HMSO, 1975-88.

2 Office of Population Censuses and Surveys. *Communicable diseases*. London: HMSO, 1975-88.

Posture and nocturnal asthma

The mechanisms that underlie nocturnal bronchoconstriction in asthma remain elusive. Among possible pathogenetic factors posture per se has been considered potentially important because some studies have found the supine body position to be a stimulus to bronchoconstriction in patients with asthma.^{1,2} Drs K F Whyte and N J Douglas have recently challenged these observations (July 1989;44:579-81). They found that FEV₁ recorded in the upright posture declined to the same extent in nine asthmatic patients after they had been supine for four hours as it did after the patients had been upright for the same time interval. They then draw the conclusion that the horizontal body position is not an important cause of overnight bronchoconstriction. In our opinion this conclusion is premature with respect to the design and results of their study.

Firstly, Drs Whyte and Douglas limited their measurements to the upright posture and therefore missed important information. We found the peak flow (PEF) response to posture in asthmatics to be dual: an immediate decrease on lying down (also present in healthy persons) and a progressive decrease in the lying position, which is specific for asthmatic patients.^{1,2} Peak flow rate measured supine tends to decrease in direct proportion to the time spent supine. When the upright position is assumed once more there may be an immediate or a more gradual recovery, with a sustained decrease of lung function in the latter case.

Secondly, if there is a decline in FEV₁ on the upright day also, as in the experiment of Drs Whyte and Douglas (due to a tapering

effect of medication?), it might be difficult to detect a modest effect of posture if recordings are performed upright only. Lung function remained unchanged during the control day in our study, thus enabling us to link the decline in PEF on the other days to the change in posture.¹

Thirdly, it is evident from figure 1 of the study by Drs Whyte and Douglas that the fall of FEV₁ after four hours supine was rather abruptly converted into a rising trend after the patient assumed the upright position—thus indicating that posture was important also in these patients.

Recent studies have shown that nocturnal increases in airway resistance in asthmatic patients are modified by sleep stage—that is, the deepest sleep is associated with the largest increases in resistance.³ This has been interpreted as a decreased responsiveness to resistive loads during deep sleep.³ What is then the cause of this increased resistive loading during the night? To our minds, it seems probable that resting body position, possibly through increased vagal tone, causes bronchoconstriction in hyperreactive airways. If so, there is no need to incriminate endogenous circadian rhythms to explain nocturnal asthma.

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1 Jönsson E, Mossberg B. Impairment of ventilatory function by supine posture in asthma. *Eur J Respir Dis* 1984;65:496-503.

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3 Bellia V, Cuttitta G, Insalco G, Visconti A, Bonsignore G. Relationship of nocturnal bronchoconstriction to sleep stages. *Am Rev Respir Dis* 1989;140:363-7.

AUTHOR'S REPLY We do not wish to extend our criticisms of the studies of Jonsson and Mossberg, which are already well documented,^{1,2} and are essentially that their studies are inadequately controlled and analysed and that many of the reported changes are mechanical effects on the efficiency of forced expiration when supine. Our reply to their points is:

1 Our study clearly showed no difference in peak flow (PEF) after four hours erect compared with supine. Our study addressed the possibility of nocturnal airway narrowing—which persists on assuming the erect posture—resulting from prolonged airway narrowing after lying down. Our data strongly suggest that it does not.

2 There are other explanations. We would suggest that the lack of decline in lung function in the seated posture reported by Jonsson and Mossberg reflects their patients' less severe asthma, producing both less circadian variation and less bronchodilator use before the study, with less airway narrowing as this wears off.

3 No. There was no significant rise in PEF

after they had resumed the upright posture, nor was there any difference in the change in PEF after the period in the trial posture between the erect and supine day.

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1 Catterall JR, Douglas NJ. Effect of sleep deprivation on overnight bronchoconstriction in nocturnal asthma. *Thorax* 1987;42:319-20.

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BOOK NOTICES

High Altitude Medicine and Pathology. 3rd ed. D Heath, DR Williams. (Pp 352; £65.) Guildford: Butterworth, 1989. ISBN 0-407-00499-8.

The third version of this popular book has been rewritten to emphasise the state of clinical knowledge of man at high altitude. The coverage is impressively wide, covering climatology, geography, social and physical anthropology, and even comparative zoology, and examines every aspect of life at high (3000 m), and extreme (5800 m) altitude. The bulk of the book covers the clinical effects of hypobaric hypoxia and other features of altitude, such as ultraviolet radiation and exposure to cold. It describes the scientific advances that have occurred through the study of highland populations, natural experiments like the Mexico Olympiad, the anecdotes of climbers, and genuine scientific expeditions. There are also full descriptions of the clinicopathological features of benign and malignant acute mountain sickness, along with the theoretical discussion of the basis for chronic mountain sickness through failure of acclimatisation or loss of adaptation. The importance of sleep and ventilatory control is clearly defined as a productive area for further research. Other chapters, including those on fertility, exercise, and psychology, cover all conceivable aspects of life at altitude. The authors themselves have clearly made a major contribution to knowledge on the subject, particularly in pathology, where the writing is most confident. In other areas the presentation is more cautious and, for example, the physiology topics are described without a single formula. This is no disadvantage, however, as it makes the book more accessible and could be recommended to others. The style is clear, thorough, and slightly repetitive, but in an avuncular fashion that does not give offence. The book is well illustrated with standardised diagrams and interesting photographs and there is an extensive bibliography. The book will appeal to most libraries, respiratory specialists, and climbers as an obligatory reference book. It also makes an excellent read for those with even a passing interest.—MDLM