LETTERS TO THE EDITOR

BCG vaccination by multipuncture method

I write in response to the article by Al Jarad et al1 on this topic. The first study to compare the efficacy of BCG vaccination and its side effects using the Bignall multipuncture device with the reusable handle and disposable heads was the pilot study of neonatal BCG vaccination carried out in 1992 for the tuberculosis Health Authority in the borough of London.2

In previous studies in neonates and children under two, referenced in the paper by Al Jarad et al,1 an 18–20 needle percutaneous head gave approximately the same degree of tuberculin conversion as did intradermal vaccination but, to achieve this in older children and adults, 36–40 punctures were required. This would require either a 40 needle head or a double vaccination with two × 18–20 needles. This is why percutaneous BCG is currently only licensed for children aged under two years. Although in neonates3 and in Al Jarad’s study1 in older children the rate of tuberculin conversion was lower with percutaneous than with intradermal vaccination, tuberculin conversion does not necessarily equate to lower efficacy. In the early studies on BCG the protective efficacy of the vaccination was related to the presence of a scar after vaccination, but not to the tuberculin test result after vaccination. Those with a BCG scar but a negative post vaccination tuberculin test—that is, no tuberculin conversion—had the same degree of protection against tuberculosis over the 15 years following vaccination as did those with a scar and a positive post vaccination tuberculin test.4

The multipuncture method is undoubtedly easier to use in neonates because their very thin skin makes intradermal vaccination difficult. The skin is also thinner in those children who are a risk group, as is the skin in premature infants. Further multipuncture studies on large numbers of subjects would be required to determine whether the technique using only 18 needles in older children is as effective as intradermal vaccination. Such studies may well prove to be unnecessary. The PHL system for enhanced tuberculin surveillance begun this year should, with sufficient cooperation, be able to give the relevant information by the end of 2001 to show whether England and Wales meet the internationally recommended criteria for discontinuation of unselective BCG vaccination in low prevalence countries.5 BCG vaccination of selective at risk groups, however, would still be required.

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Respiratory care units for non-invasive mechanical ventilation in motor neurone disease

We read with interest the review by Polkey et al6 pointing out the need to use all means possible to enable patients with motor neurone disease to achieve the best quality of life.

The authors state that, in order to maintain 24 hour ventilatory support, nasal ventilation must be complemented with alternative strategies during the day that are not suitable for widespread use in district general hospitals. They consider it is possible to maintain 24 hour non-invasive ventilation in patients with motor neurone disease if nasal ventilation is combined with other non-invasive techniques such as mouth piece ventilation or a pneumobelt, and with manual or mechanical expiratory muscle aids to clear secretions in those patients whose weakness makes spontaneous coughing ineffective.7 It is important to provide these aids because they can delay tracheostomy and additional problems in most patients with motor neurone disease and are the only way for those patients who reject tracheostomy but need ventilatory support. However, we are in agreement with Polkey et al that this treatment must be performed by trained staff in respiratory care units. Moreover, these units are the best place to prevent respiratory morbidity and mortality, to enhance cooperation between patients, relatives and caregivers, and to manage clinical and psychological problems during the terminal phase of the disease.

In our experience the care of patients with motor neurone disease outside respiratory care units needs to be improved. These patients must not be negatively discriminated against compared with other chronic patients receiving even more expensive but socially accepted treatment. We must therefore try to ensure that all patients with motor neurone disease have access to management in a respiratory care unit in order to receive standardised quality care both in hospital and at home.

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AUTHOR’S REPLY
We thank Dr Servera and colleagues for their interest in our paper. We agree that patients with motor neurone disease have to access to specialist expertise where this is necessary. However, we are also conscious that travel can be difficult for some patients with advanced disease and our experience is that, in many cases, satisfactory palliation can be achieved using non-invasive positive pressure ventilation alone. This treatment could theoretically be applied in a significant proportion of patients with motor neurone disease.
Asthma deaths in Scotland and in Wales

It is surprising to say the least that, although the two inquiries into asthma deaths published recently in *Thorax* 

1 made the point that most asthma deaths occurred outside hospital and the “relative rarity” of deaths in hospital, neither addressed the question as to whether more prompt admission to a hospital with respiratory intensive care facilities could have prevented some, or even many, of the domestic deaths. 

The Respiratory Unit at the Northern General Hospital in Edinburgh first addressed that question as long ago as 1968 when it inaugurated a self-admission scheme for patients known by the unit to be subject to severe attacks of asthma, whereby delays inherent in conventional admission procedures were bypassed with the willing cooperation of their general practitioners. The scheme was more fully described that question as long ago as 1968 when it inaugurated a self-admission scheme for patients known by the unit to be subject to severe attacks of asthma, whereby delays inherent in conventional admission procedures were bypassed with the willing cooperation of their general practitioners. The scheme was more fully described in 1975 and reports on 10 year and 15 year reviews of its progress were published in 1979 and 1987. These showed that the death rate in patients admitted under the scheme was only 0.3%, substantially lower than that recorded in asthmatic patients who relied on conventional admission procedures. 

The asthma self-admission scheme was widely welcomed as a measure which could save lives and was copied in many other countries, including Australia. Yet in neither of the studies reported in the November 1999 issue of *Thorax* was this important initiative even mentioned. May I ask the authors why?

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3 Grant IWB. Deaths from asthma. *BMJ* 1986;1:575.

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Nebulised fluticasone

The place of nebulised inhaled corticosteroids in the treatment of patients with asthma is difficult to assess, but Dr J M Hill’s editorial in *Thorax* was inaccurate and below acceptable standards for a major medical journal.

Nebulised fluticasone is frequently referred to, yet all the studies referenced 

1 have now been published as abstracts (sponsored by the manufacturers of fluticasone) in supplements to journals. There are insufficient details for these papers to be properly scrutinised. They have not been subject to proper peer review and should have no place as the sole references for a new treatment for asthma in the editorial of a major medical journal.

Dr Hill states that “it is clear from a number of studies that fluticasone is twice as potent as budesonide at a mg for mg dose” but references this with a study which compares fluticasone with beclomethasone and not budesonide.

This is clearly incorrect. She forgets that different inhaling devices influence potency ratios. Thus, fluticasone in a Diskhaler may be equipotent with budesonide in a Turbolizer and a more diluted dose inhaler may be equipotent with beclomethasone in the newer, smaller particle, CFC free inhaler (Qvar). 

As far as nebulised steroids are concerned, she seems unaware that different nebuliser systems may affect the amount delivered to the lung by a factor of four or more. Is this not important to mention? Also, the respirable fraction of nebulised steroid depends on the physical properties of the steroid molecule. For example, beclometasone might be equipotent with budesonide in metered dose inhalers, but beclometasone solution nebulises poorly and has been withdrawn from use. So, what is the potency ratio between nebulised fluticasone and budesonide? The answer is unknown, simply because there are no comparative studies. Yet Dr Hill confidently assumes a 1:2 potency ratio when giving the costs of each treatment—and fluticasone appears to be one half the price of budesonide.

Finally, any article, editorial or otherwise—and especially one that makes unfavourable comparisons between drugs—should be accompanied by a declaration of competing interests. There is nothing wrong with having a competing interest but it should be declared. Dr Hill should have stated these interests (if any) in the same detail as reported recently in a review article on asthma drugs in the *BMJ*.

Conflict of interests: neither Dr Todd nor his spouse have shares in any pharmaceutical company. He has received payment from Astra, Boehringer, 3M, Forest Laboratories (USA), Glaxo/Wellcome, MSD and Zeneca for presentations/lectures in the past five years. He has only received payment from research from Glaxo/Wellcome (fluticasone).

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Tending meetings in the last three years.

There are few published randomised controlled trials of nebulised fluticasone or budesonide in the treatment of asthma. Despite this, these agents are being actively marketed by the pharmaceutical industry so it is vital that the debate about the place of these agents in the treatment of asthma should continue. The author therefore thinks that it is justifiable to review what evidence is available, accepting its limitations in abstract form.

The author apologises for incorrectly quoting a paper comparing the potency of budesonide and fluticasone. The correct reference is cited below. However, the author had presumed that the readers of Thorax would be well aware that data comparing different inhaled corticosteroids apply only to the type of inhaler used in any comparison, and that this basic principle did not require explanation.

Dr Todd’s comments about different nebuserum systems and drug solubility are well taken. However, this was a short review of the available clinical evidence for the use of nebulised corticosteroids in the treatment of patients with asthma. It was not possible to, nor did I, review nebuserum pharmokinetics and, as Dr Todd states, there are no comparative studies of the potency ratio of nebulised budesonide and fluticasone.

Finally, neither Dr Hill nor her spouse has shares in any pharmaceutical company manufacturing asthma treatments. She has received payment from GlaxoWellcome, manufacturing asthma treatments. She has no personal or financial conflicts of interest.

AUTHOR’S REPLY The author thanks Dr Todd for his constructive comments on her review article.

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studies, the highest value for C_{max} was used. A significant difference in lung dose between devices will remain the same and is related to the bronchodilator response.\textsuperscript{14} Measurement of the lung bioavailability of salbutamol in healthy subjects may therefore represent a simple in vivo method for preliminary quantification of the relative lung dose from different inhaler devices to select rational doses for subsequent clinical equivalence studies in asthmatic patients.

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NOTICE

International Pediatric Respiratory and Allergy Congress

The International Pediatric Respiratory and Allergy Congress will be held on 1–4 April 2001 at the Prague Congress Center, Prague, Czech Republic. For further information contact the Congress Secretariat at the Congress Centre, Czech Medical Society, JEP Sokolská 31, CZ-120 26 Prague, Czech Republic. Telephone +4202 296889 or +4202 297271; fax +4202 294610 or +4202 2416836. Email: lonekova@cls.cz

\textsuperscript{1} Hughes DA, Woodcock A, Walley T. Review of therapeutically equivalent alternatives to short-acting \beta\_2 adrenoceptor agonists delivered via chlorofluorocarbon-containing inhalers. \textit{Thorax} 1999;54:1087–92.
\textsuperscript{2} Clark DJ, Lipworth BJ. Dose-response of inhaled drugs in asthma. \textit{Clin Pharmacokinetics} 1997;32:58–74.
\textsuperscript{3} Lipworth BJ, Tan S, Devlin M, et al. Effects of treatment with formoterol on bronchoprotec-
Asthma deaths in Scotland and in Wales

IAN W B GRANT

Thorax 2000 55: 345
doi: 10.1136/thorax.55.4.345b

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