LETTERS TO THE EDITOR

Adrenocortical activity in children

I read with interest the report on adreno-
cortical activity in children receiving inhaled corticosteroids by Lipworth and colleagues, but am perplexed by the relevance to clinical practice. Although it is possible to dem-
strate biochemical evidence of suppression of the hypothalamic-pituitary-adrenal axis with sensitive tests such as the measurement of overnight urinary cortisol excretion, this is likely to have little clinical significance. There is to date no evidence that inhaled cortico-
steroids taken at recommended doses have caused clinically significant adrenal sup-
pression.

The major side effect of inhaled cortico-
steroids in childhood is growth suppression.1 In a group of children aged 7-9 years who received beclometasone dipropionate at a dose of 400 μg/day there was no significant effect on overnight urinary cortisol. Despite this, there was clinically relevant growth sup-
pression in those children who received beclometasone dipropionate (difference of 1 cm in growth over seven months of study). I therefore feel that the authors' conclusions are premature as no conclusions on the safety profile of either budesonide or fluticasone propionate can be derived from this study.

AUTHOR’S REPLY Adrenal suppression, and particularly overnight urinary cortisol, is a sensitive marker of potential systemic bio-
activity with inhaled corticosteroids.1 It has been shown that suppression of 24 hour urinary cortisol was associated with a blunted dynamic response to a low dose (0.5 μg) ACTH in children receiving inhaled corticosteroids. Inhaled fluticasone propionate is licensed to be used in children at doses up to 200 μg/day although many practitioners are now using higher doses which have been shown to ex-
hibit significant adrenal suppression.2

The observed effects of beclometasone dipropionate on growth in the study reported by Doull et al. over a seven month period are rather short term and do not take into account intermittent growth spurts which occur in the longer term over several years during normal childhood. Indeed, in a meta-analysis of studies with inhaled beclometasone dipropionate there was no association between its use and the adverse effect of diurnal cortisol.3 This is supported by a large six year cohort follow up study with budesonide where there was no significant effect on growth velocity at doses up to 400 μg/day. Furthermore, in-
haled corticosteroids in children do not appear to exert any effect on final height achieved in adult-
hood.4

I therefore remain firmly of the opinion that, at conventional doses of up to 400 μg/ day, inhaled corticosteroids have a high ther-
apeutic ratio with little if any long term risk for significant systemic toxicity in children. The potential for any degree of systemic bio-
activity will be minimised by stepping down in order to achieve the lowest possible main-
tenance dose required to achieve effective asthma control and quality of life.

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3 Clark DJ, Clark RA, Lipworth BJ. Adrenal suppression with inhaled budesonide and flut-

Fenoterol and asthma deaths

After reading the correspondence on this vex-
atious topic published in the August issue of
Thorax5.6 I am more deeply puzzled than ever by the acrimony displayed by the Wellington and Auckland medical schools over the role played by fenoterol in the 1977/82 “epi-
demic” of asthma deaths in New Zealand. I visited that country in 1982 at the in-
vitation of its Asthma Foundation which had hoped I might be able to shed some light on the cause of the “epidemic” that had given rise to serious public concern. I suspected that a therapeutic innovation, available without prescription, analogous to that of Medihaler Iso Forte, would lead to a high prevalence of iso-
prene inhaler which had been implicated in the earlier UK “epidemic” – might be responsible. Thus, when I was informed that vast numbers of nebulisers delivering large doses of sal-
butamol were being used in excess by patients with severe asthma anxiously to avoid or at least defer the payment of doctors’ fees, I felt it was not unreasonable for me to blame the indiscriminate and un-
controlled use of these nebulisers for the in-
creased asthma mortality. My views on that matter were published in both the Lancet and NZ medical journals,7,8 evoked heated criticism to which I responded vigorously.9 I gave no further thought to the controversy until it was claimed by the Wellington medical school in 1989 that fenoterol by inhaler was the principal cause of that “epidemic” of asthma deaths. That may or may not be the case, but in retrospect I find it in-
comprehensible that the words “fenoterol” (or “Berotec”) did not cross the lips of any of the many respiratory physicians I met dur-
ing my visit to New Zealand in 1982. I was clearly given to understand that the only β2 agonists used in the treatment of asthma at that time were salbutamol and terbutaline. Had I been informed of the widespread pre-
scription of fenoterol inhalers during the 1977/82 “epidemic” I would certainly have questioned its safety.

As I pointed out in a letter to the New Zealand Medical Journal published on 11 April 1990, one metered dose (then 200 μg) of fenoterol was equivalent to four metered doses (400 μg) of salbutamol or a fenoterol inhaler would be four times more dangerous in terms of adverse cardiac and metabolic side effects than similar use of a salbutamol inhaler. In effect, the use of a fenoterol inhaler in patients with severe acute asthma must have carried a simi-
lar risk to that of overuse of other β2 agonists delivered by nebuliser and overuse of Medi-
haler Iso Forte in the 1970s which must all have contributed to “epidemics” of asthma deaths.

I would urge my colleagues in New Zealand to accept that view, which may seem simplistic but carries more conviction with practical clinicians than the sterile semantics that have occupied so much space in medical journals during the past few years.

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5 Grant IWB. Asthma in New Zealand. BMJ 1983;286:718.

Home environment and asthma

Butland and colleagues found that increased use of non-feather pillows was the only domestic indoor exposure that appeared to explain a 20% increase in the population prevalence odds of wheeze in children living in Croydon, London between 1978 and 1991.9 This extends their previous epidemiological studies on synthetic material-filled pillows as a risk factor for severe asthma in adolescence. In the study they hypothesised that synthetic material-filled pillows may release volatile organ-
ic compounds, possibly influencing the airway response to inhaled allergens.
In their latest study no hypothesis for the association between wheezing and the use of non-feather pillows is put forward. Environmental exposures to allergens were not directly examined and, in particular, levels of the major house dust mite allergen Der p 1 in feather and non-feather pillows were not available. They discard the possibility that house dust mite allergens could be a reason for the increased prevalence of wheeze based on a study that showed no change in domestic reservoir levels of Der p 1 between 1979 and 1989.1 However, in that study Der p 1 levels were measured in dust samples from mattresses, bedroom floors, and living room carpets, not from pillows.

We have recently demonstrated and confirmed in a follow up study that synthetic pillows contain a mean of eight times more total Der p 1 allergen than feather pillows.41 Given that people spend many hours in close contact with pillows, it could be argued that exposure to higher levels of Der p 1 in non-feather pillows may explain the findings of Butland and colleagues relating the increased use of non-feather pillows with an increase in the prevalence of wheeze. Recent evidence shows clear correlations between exposure to house dust mite allergens in the bed and the severity of various parameters used in the measurement of asthma severity.6

We agree with Butland and colleagues that further studies are required to explain the link between increased wheeze and the use of non-feather pillows — not only toxicological and epidemiological studies, as suggested by the authors, but further investigations of allergen levels in different types of pillows to determine whether our New Zealand based findings are applicable in the UK and elsewhere.

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NOTICES

Sixth Bronchitis Symposium

The Sixth Bronchitis Symposium on the link between asthma and COPD will be held in Groningen, The Netherlands on 24–26 August 1998. For further information contact the Secretariat Department of Pulmonary Diseases, PO Box 30,001, 9700 BB Groningen, The Netherlands. Telephone: +31 50 361 2357 or 3532. Fax: +31 50 361 9320. E mail: c.w.verver@int.agz.nl.

CORRECTION

Survival of patients with severe α₁-antitrypsin deficiency

In a paper entitled "Survival of patients with severe α₁-antitrypsin deficiency with special reference to non-index cases" by Seersholm, Kok-Jensen and Dirksen published in Thorax in 1994 it has been pointed out by Dr James K Stoller of the Cleveland Clinic, Cleveland, Ohio, USA that the labels on the key of figure 1 on page 696 were transposed. A correct version of the figure is shown below.
