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 hypothalamo-pituitary-adrenal axis with sensitive tests such as the measure-
tment of overnight urinary cortisol excretion, this is likely to have little clinical significance. There is no date to 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.12 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).1 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.

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Lipworth BJ, Clark DJ, McFarlane LC. Adreno-
cortical activity with repeated twice daily dos-

Timothy DG, Reed CE, Nelson HS, Oxford KP. Aerosol beclometasone dipropionate compared with theophylline as primary treat-


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 urin-
ary cortisol was associated with a blunted vasoconstrictor response in children. 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. Further-
more, inhaled corticosteroids did not appear to exert any effect on final height achieved in adult-
hood.2

I therefore remain firmly of the opinion that, at conventional doses of up to 400 μg/
day, inhaled corticosteroids have a high thera-
pic 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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2 Brodie J, Soferman R, Kivity F, et al. Low dose adrenocorticotropic tests reveal impaired ad-

3 Clark DJ, Clark RA, Lipworth BJ. Adrenal sup-
pression with inhaled budesonide and flu-
ticasone propionate given by a large volume spacer to asthmatic children. Thorax 1996;51:
941–3.


6 Agertoff L, Pedersen S. Effects of long-term treat-


Fenoterol and asthma deaths

After reading the correspondence on this vex-
atious topic published in the August issue of Thorax1,2 I am more deeply puzzled than ever by the acrimony displayed by the Wellington and Auckland medical journals 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-
ovitation of its Asthma Foundation which 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 Ifo Forte, had a high degree of iso-
prenealin that had been implicated in the earlier UK “epidemic” might be responsible. Thus, when I was informed that vast numbers of beclometasone dipropionate (BDP) patients were using this preparation in excess by patients with severe asthma anxiously to avoid or at least defer the payment of doctors’ fees, I felt it was unreasonable for me to blame the indiscriminate and un-
controlled use of this nebuliser for the in-
creased asthma mortality. My views on this matter were published in both the British and New Zealnd medical journals,1,4 evoked heated criticism to which I responded vigorously.1 I gave no further thought to the controversy until it was claimed by the Wellington medical school in 1989 that fenoterol by inhalation was the principal cause of that “epidemic” of asthma deaths. That may or may not be the case, but in retrospect I find it incom-
prehensible that the words “fenoterol” or “Iso Forte” 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 pres-
cription 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 terbutaline. 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 safety of 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 Ifo 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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1 Pearce N, Burgess C, Crane J, Beasley R. Fen-
oterol, asthma deaths, and asthma severity: confounding or confusion? Thorax 1997;52:
750.

2 Garrett JE, Lanes S, Rea HH, Kelbye J. Fenoterol, asthma deaths, and asthma severity: con-


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 dom-
ic indoor exposure that appeared to explain a 20% increase in the population prevalence odds of wheeze in children in the 1980s.10 By 1978 and 1991 this extends their previous epidemiological studies on synthetic material-filled pillows as a risk factor for severe asthma in adolescence. In the study they hoped that synthetic material-filled pillows may release volatile or-
ganic 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 p1 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 p1 between 1979 and 1989. However, in that study Der p1 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 p1 allergen than feather pillows. Given that people spend many hours in close contact with pillows, it could be argued that exposure to higher levels of Der p1 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. 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: e.pick@int.azg.nl or c.w.verver@int.azg.nl.

CORRECTION

Survival of patients with severe \( \alpha_1 \)-antitrypsin deficiency

In a paper entitled “Survival of patients with severe \( \alpha_1 \)-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.

1 Seersholm N, Kok-Jensen A, Dirksen A. Survival of patients with severe \( \alpha_1 \)-antitrypsin deficiency with special reference to non-index cases. Thorax 1994;49:695–8.

Figure 1 Cumulative probability of the survival time of index cases and non-index cases with 95% confidence intervals. Survival of the normal Danish population is shown for comparison.