LETTERS TO THE EDITOR

Atopy, bronchial responsiveness, and symptoms in wheezy 3 year olds

EDITOR,—There is now increasing evidence that most children with recurrent wheeze in the first year of life do not have atopic asthma and that 'wheezy bronchitis' is a distinct entity with a different natural history.¹ Although it is now clear that infants are able to respond to bronchodilators, it is well known that β agonists are rarely effective in this age group during wheezing episodes. Despite this, it is still widely believed that bronchospasm is the main cause of wheeze in these children. The recent paper by Nicola Wilson *et al* suggests that non-atopic infants who wheeze have greater bronchial responsiveness than atopic individuals who wheeze.² In contrast, a recent study from Perth could find no evidence of increased bronchial responsiveness in recurrently wheezy infants when compared with matched controls.³ The group from Perth suggest that their results support the contention that diminished lung function present from birth predisposes infants to lower respiratory tract symptoms.

An alternative explanation may be that excessive mucus production with or without mucosal oedema is predominantly responsible for the symptoms experienced by infants with wheezy bronchitis. This would explain why anticholinergic agents often appear more effective than β agonists. It would also explain why inhaled steroids are frequently of benefit in patients with recurrent or persistent respiratory symptoms as steroids inhibit both the production and release of mucus. Coarse 'ruttly' upper airway noises suggestive of mucus secretions are extremely common in young infants⁴ and many recurrently wheezy children have 'rattles' between exacerbations. 'Noisy breathing' is reported as being always present in 11% of children⁵ and they frequently have symptoms from birth. It may well be that infants with wheezy bronchitis have an increased capacity to secrete mucus in response to stimuli such as virus infections, either because of a tendency from birth or as a response to environmental events such as ventilation in the neonatal period, acute bronchiolitis, or 'passive smoking'. Increased baseline production of mucus might explain the increased airways resistance seen in these infants.³ Anticholinergics will inhibit mucus production from submucosal glands but will have no effect on goblet cell secretion and therefore cannot be expected to relieve totally symptoms in those with prominent goblet cell hyperplasia. These are more likely to be the ones with increased capacity to secrete mucus due to stimuli such as passive smoking and those with 'postbronchiolitic symptoms'. It is possible that treatment of these infants, if any is required, would improve if we consider using drugs which inhibit mucus production or newer mucolytics.

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1 Sporik R, Holgate ST, Cogswell JJ. Natural history of asthma in childhood – a birth cohort study. *Arch Dis Child* 1991; 66: 1050–3.

- 2 Wilson NM, Phagoo SB, Silverman M. Atopy, bronchial responsiveness, and symptoms in wheezy 3 year olds. *Arch Dis Child* 1992; 67: 491–5.
- 3 Stick SM, Arnott J, Turner DJ, Young S, Landau LI, LeSouef PN. Bronchial responsiveness and lung function in recurrently wheezy infants. *Am Rev Respir Dis* 1991; 144: 1012–5.
- 4 Thornton AJ, Morley CJ, Hewson PH, Cole TJ, Fowler MA, Tunnicliffe JM. Symptoms in 298 infants under 6 months old, seen at home. *Arch Dis Child* 1990; 65: 280–5.

Dr Wilson comments:

I was interested in Dr Everard's suggestion that the syndrome of 'wheezy bronchitis' might be explained by increased mucus production rather than bronchospasm. He may well have a point. However, contrary to his implication, we did not propose that the increased bronchial responsiveness found in the non-atopic children in our study¹ was responsible for their virus induced wheeze. We concluded that the episodic wheeze associated with colds in the first three years of life, in this hospital based population, was similar in atopics and non-atopics, apart from the age of onset. Often, early asthma precipitated by viral infections can only be distinguished from wheezy bronchitis retrospectively.

It is therefore very doubtful whether the syndrome of wheezy bronchitis can altogether be explained on the basis of mucus production.

- 1 Wilson NM, Phagoo SB, Silverman M. Atopy, bronchial responsiveness and symptoms in wheezy 3 year olds. *Arch Dis Child* 1992; 67: 491–5.

Serum IgG titres against *Pseudomonas aeruginosa*

EDITOR,—*Pseudomonas* specific IgG titres are currently one of the main topics in clinical research in cystic fibrosis.¹ We read with interest the article concerning the value of specific IgG titres in the management of early pseudomonal infection.² From the abstract we understood that most study parameters had improved significantly in the treated group. However, trying to verify such statements from the results in text or tables revealed rather the opposite. Forced expiratory volume in one second (FEV₁) and total serum IgG were not significantly different comparing observation and treated groups after one year, and there was no statistical analysis available comparing longitudinal changes of these parameters throughout the study period. We were also confused by the confidence intervals considered to be significant: p values listed in the table indicate that the authors accepted significance levels of 10% rather than 5% as stated in the instructions to authors.³ Therefore we are still uncertain about the value of the study, and we would like to ask the authors to reveal all the essential data not yet mentioned. Finally we would like to express our concern how an article with inconsistent results could be accepted by the referees for publication in such a highly rated journal.

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- 1 Cordon SM, Elborn JS, Rayner RJ, Hiller EJ, Shale DJ. IgG antibodies in early *Pseudomonas aeruginosa* infection in cystic fibrosis. *Arch Dis Child* 1992; 67: 737–40.

- 2 Brett MM, Simmonds EJ, Ghoneim ATM, Littlewood JM. The value of serum IgG titres against *Pseudomonas aeruginosa* in the management of early pseudomonal infection in cystic fibrosis. *Arch Dis Child* 1992; 67: 1086–8.
- 3 Instructions to authors. *Arch Dis Child* 1992; 67: 156.

Dr Brett and coauthors comment:

We read with interest the comments of W H Nikolaizik and M H Schöni. Their comment that after one year in the trial there was no difference between FEV₁ and total IgG in treated and control groups is quite correct, but the data in table 2 show that on entry to the trial both these values were worse in the treated group than in the observation group, hence during the trial period both these parameters improved in the treated group and deteriorated or remained stationary in the observation group. Other parameters (for example serum IgG titre, white cell count, % neutrophils) showed a similar pattern.

We are unclear about the exact meaning of the comment on longitudinal changes: we give absolute values of parameters on entry and after one year, from which changes can be calculated. The statistics and conclusions are not affected by the method of presentation, although we thought our choice made the results easier to follow. We are also unsure what is meant by the suggestion that we should 'reveal all the essential data not yet mentioned' – the parameters given in tables 1 and 2 (as means with the range) were chosen as being the most meaningful in monitoring the progress of pulmonary infection from the more than 20 which we routinely monitor. We would agree that $p < 0.10$ is not generally considered significant and had no intention of implying otherwise when we included it, for completeness, in table 2.

Audit of screening for congenital hypothyroidism

EDITOR,—We read with interest the audit of a screening programme for congenital hypothyroidism.¹ From the data available the birth prevalence for congenital hypothyroidism in the period of study was calculated to be 1:3770. The authors state 'This level of prevalence is similar to 1:3980 found from 36 centres in 12 European countries and the 1:4200 reported from the USA, which suggest that it is unlikely that a significant number of cases, other than the known false negatives, were missed'. There are a number of problems with this assumption:

(1) In the audit 62 cases were detected out of 228 289 livebirths over a period of seven years, giving a birth prevalence of 1:3682 and not 1:3770 as stated in the article.

(2) If the 95% confidence intervals for the data presented were to be worked out it would give the possible range of birth prevalence as 1:2872 to 1:4803 (using the Poisson distribution). This means, that for 228 289 livebirths, the region could have had between 48 and 79 cases of congenital hypothyroidism. Taking the upper limit would imply that the programme could have missed up to 19 cases – that is, two false negatives that this audit picked up and 17 others that were not.

(3) An examination of the data from European countries mentioned in the statement above showed that 14 European countries (73 centres) had a collective birth prevalence of 1:3598 but there was intercountry variation from 1:2860 in the Netherlands to 1:5770 in Austria.² There is nothing to suggest that the