

Respiratory problems 2 years after acute bronchiolitis in infancy

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SUMMARY We assessed the clinical progress of 55 children 2 years after admission to hospital with acute bronchiolitis and performed lung function tests on 40. During the 2 year follow up period 75% of the children had wheezed, 36% had 2 or more lower respiratory symptoms lasting more than 2 weeks, 33% had more than 100 days of lower respiratory symptoms, and 13% were readmitted to hospital with acute respiratory disease. In addition 60% of the children were hyperinflated on lung function tests. Many of the children with hyperinflation at the 2 year assessment had not been hyperinflated 1 year earlier, suggesting variable airways obstruction. Reversibility of airways obstruction was also assessed by response to nebulised salbutamol. Nine children had a fall >15% in airways resistance after salbutamol and these children had the highest baseline airways resistances. Airways resistance was higher in the children with a family history of atopy.

Although children often wheeze for some years after acute viral bronchiolitis, the exact relation between bronchiolitis and asthma is unclear.¹⁻⁴ Evidence is also accumulating that bronchiolitis may sow the seeds for chronic obstructive lung disease in adult life⁴⁻⁶ and furthermore asymptomatic children may have abnormalities in lung function many years after an attack,⁷ leaving the possibility that clinical illness will develop subsequently.

We have been collecting information on lung function and symptoms after the acute episode in a cohort of children admitted to hospital with acute bronchiolitis. Our first report on 22 of these infants, all of whom had severe initial disease, showed marked disturbances in lung function in the first year after the acute illness.⁸ We were concerned that these children might not be representative as all were fed via a nasogastric tube and we therefore collected further data on a larger group of children whose only criterion for inclusion was that they had been admitted to hospital with bronchiolitis. The results of the total cohort showed that at follow up after 1 year over 60% had had further wheezing and that 17% had marked hyperinflation on lung function tests.⁹ We aimed to obtain sequential information on children whose progress in the first year after bronchiolitis had been studied⁹ and to report on clinical progress and lung function a year later.

Patients and methods

All 55 children included in this study were admitted to hospital during an epidemic of infection caused by respiratory syncytial virus (RSV). They had a clinical diagnosis of bronchiolitis with tachypnoea, breathlessness, hyperinflation, and widespread crepitations. Viral studies were positive for RSV in 27 patients and adenovirus type 1 was isolated in 1 patient.

The first 24 children studied had severe disease and were fed by a nasogastric tube but our only selection criterion subsequently was that the children had been admitted to hospital for bronchiolitis. Nevertheless, milder cases of acute viral bronchiolitis are probably under represented in the cohort.

Mean age on admission was 96 days (range 29-335 days), and there were 26 boys and 29 girls. Twenty of the children had a first degree relative with asthma, eczema, or hay fever and of these, 9 had a first degree relative with asthma. When information on second degree relatives was included, the numbers rose to 31 and 16 respectively. These figures are comparable with unselected controls.²

Two years after the first admission to hospital we obtained histories regarding the nature, frequency, and duration of lower respiratory tract illnesses after the bronchiolitis. Fifty one of these 55 children had been seen and assessed 1 year earlier.⁹

Lung function tests were performed on 40 of the children on average 25 months after the initial admission (range 23–26 months). Thirty five of these children had been tested 1 year earlier. We measured thoracic gas volumes (TGV),¹⁰ the amount of gas in the lungs at the end of a normal expiration, airways resistance (Raw) using plethysmography,⁸ and total respiratory resistance (R_t) by forced oscillation.¹¹ The total body plethysmograph was a perspex construction of 260 l capacity with a servocontrolled heating system to maintain the face mask, shutter system, and rebreathing bag at 36°C.

Each child after sedation with 100 mg/kg chloral hydrate was nursed supine, and a mask was applied to the face. A bias flow of air, 5 l/minute, passed through the wall of the plethysmograph to the face mask via a wide bore tube, and expiratory gases were conducted out via a similar tube. Signals were relayed to the axes of a cathode ray storage oscilloscope. Measurements of Raw were obtained from the initial part of inspiration when flow is essentially laminar, rather than at 2/3 of maximal inspiratory flow which in these children is under turbulent conditions and will produce much higher values. Readings were obtained and calculations made by standard techniques.⁸ Multiple breaths were sampled in each case.

Total respiratory resistances during inspiration (R_t insp) and expiration (R_t exp) were measured using a modification of the forced oscillation technique.¹¹ A pressure manometer connected to the inflated flange of the face mask ensured that the mask was applied to the face with the same amount of pressure during each measurement of R_t .¹²

After baseline recordings were obtained of TGV, Raw, and R_t , each child was given 2 ml of a solution containing 5 mg salbutamol through a Sandoz nebuliser driven by compressed air at a flow rate of 6 l/minute. Ten minutes later TGV, Raw, and R_t were measured again.

Statistical analysis employed Student's *t* test and χ^2 analysis. Our coefficient of variation for R_t is 8.9%.¹¹ We calculated the coefficient of variation for TGV and Raw by comparing lung function before and after nebulised water in 18 children. The values were 8.0% and 15.8% respectively. The local ethical committee approved the study and informed parental consent was obtained for all tests.

Results

The frequency of lower respiratory tract symptoms experienced by the 55 children in the 2 years after their initial admissions with bronchiolitis is shown in Table 1. Cough rather than wheeze was the predominant symptom in many children with lower

Table 1 Incidence of reported lower respiratory symptoms in 55 children during the 2 years after the initial attack of bronchiolitis

| | Positive No (%) | Negative No (%) | Unclear No (%) |
|---|--------------------|--------------------|-------------------|
| Any episode of wheezing | 41 (75%) | 11 (20%) | 3 (5%) |
| Two or more episodes of cough or wheeze, or both, lasting more than 2 weeks | 20 (36%) | 31 (56%) | 4 (7%) |
| More than 100 days of cough or wheeze, or both | 18 (33%) | 32 (58%) | 5 (9%) |
| Readmission to hospital with lower respiratory illness | 7 (13%) | 48 (87%) | 0 (0%) |
| Lower respiratory illness lasting more than 2 weeks or any episode of wheeze, or both | 45 (82%) | 8 (15%) | 2 (4%) |

Table 2 Lung function data on 40 children before and after nebulised salbutamol

| | Initial (mean (SD)) | After salbutamol (mean (SD)) |
|--|------------------------|---------------------------------|
| TGV (ml/kg) | 33.9 (5.9) | 32.5 (5.9) |
| TGV (% predicted for weight) ¹⁴ | 125 (21) | 120 (21) |
| TGV (% predicted for length) ¹⁴ | 125 (19) | 118 (18) |
| Raw (cmH ₂ O/l/s) | 9.9 (5.2) | 9.9 (5.3) |
| R_t insp (cmH ₂ O/l/s) | 47.7 (21.5) | 46.2 (29.0) |
| R_t exp (cmH ₂ O/l/s) | 50.3 (21.5) | 50.7 (33.7) |

TGV = thoracic gas volume; Raw = airways resistance; R_t insp = total respiratory resistance during inspiration; R_t exp = total respiratory resistance during expiration.

respiratory disease lasting more than 2 weeks. Fifteen children had fewer reported respiratory problems in the second year of follow up, compared with the first, 17 had more, and 23 were essentially unchanged. We found no notable relation between a family history of asthma or of other atopy and the prevalence of symptoms. Height and weight percentiles of the 55 children were within normal limits.¹³

Lung function data on the 40 children tested are documented in Table 2. Thirty five of these 40 children had been tested 1 year earlier. Analysis of the sequential data shows minor changes in both TGV and Raw for the group as a whole. Thoracic gas volume fell from mean (SD) 35.4 (9.9) ml/kg to 34.0 (5.9) ml/kg and Raw fell from 11.3 (7.5) cmH₂O/l/s to 9.9 (5.3) cmH₂O/l/s. We noted considerable variations, however, in Raw and TGV in some children. Twenty two children had a TGV greater than 120% predicted for weight¹⁴ at 2 year follow up but only 11 of these (50%) had a TGV greater than 120% predicted 1 year earlier, and 6 of the 11 children with a Raw greater than 10.0 at 2 year follow up had had a similar Raw previously.

We also assessed the reversibility of airways

Table 3 Airways resistance in children with and without a family history of atopy (mean (SD))

| | No | Present Raw (cmH ₂ O/ l/s) | No | Absent Raw (cmH ₂ O/ l/s) | P value |
|--------------------------------------|----|--|----|---|------------|
| Asthma in 1st degree relative | 7 | 13.2 (8.8) | 33 | 9.2 (4.0) | NS |
| Atopy in 1st degree relative | 15 | 12.1 (6.3) | 25 | 8.5 (4.1) | < .05 |
| Asthma in 1st or 2nd degree relative | 10 | 12.8 (7.6) | 30 | 8.9 (3.9) | < .05 |
| Atopy in 1st or 2nd degree relative | 22 | 11.6 (5.9) | 18 | 7.8 (3.2) | < .05 |

obstruction by means of nebulised salbutamol (Table 2). For the group as a whole we found a small decrease in TGV from mean (SD) 33.9 (5.9) ml/kg to 32.5 (5.9) ml/kg ($P < .01$) but no significant changes in Raw or R_t . Nine children responded to salbutamol with a fall in Raw of more than 15%. These children had higher initial airways resistances than those who did not respond. Five of the 7 highest values for Raw were obtained from children who had a response to salbutamol ($P < 0.01$). Four children, 3 of whom had an initial TGV greater than 120% predicted, had a fall in TGV of greater than 15%.

Higher airways resistances were found in children with a family history of atopy (Table 3). Each of the lower respiratory tract symptoms documented were individually more likely to occur in children with either higher baseline airways resistances or a 15% fall in Raw after salbutamol. These associations did not, however, reach statistical significance.

Discussion

As is shown in Table 1, further lower respiratory tract symptoms were observed in at least 82% of our children who had been admitted to hospital with bronchiolitis 2 years previously. These symptoms were often prolonged and severe, sometimes leading to hospital admission. Although none of the children were re-admitted to hospital in the second study year compared with 7 in the first year of follow up, there was little other evidence of general improvement in respiratory symptoms and 17 children were undoubtedly worse. These findings are in conflict with the conclusion drawn by Sims *et al.* that 'the wheezing episodes experienced subsequently by the children who had had bronchiolitis were neither severe nor frequent enough to have resulted in hospital out-patient or in-patient referral'.¹⁵ One explanation for this may be that in long term retrospective studies the passage of time has blurred the memories of problems experienced in the first few years after

bronchiolitis. At the 2 year assessment in our study some parents had only a sketchy recall of respiratory problems that had occurred in the first year of life. The studies which have reported that most children are clinically well 8–10 years after the initial illness^{2 15} overlook the considerable morbidity caused by respiratory disease that we have found in the first years after bronchiolitis.

Another possible explanation for the optimistic outlook given by Sims *et al.*¹⁵ is that their report focused on the frequency of wheezing rather than lower respiratory tract disease in general. In our study, however, wheeze was not responsible for all the respiratory problems and many children had prolonged episodes of cough as their primary symptom. Mok and Simpson have reported that 'tendency to cough' was a symptom in 34.5% of 200 children some time in the first 7 years after bronchiolitis and that 3.5% had 'established bronchitis'.¹⁶

Two years after admission to hospital with acute bronchiolitis, hyperinflation on lung function testing was common. Considerable variations were observed in some children when we compared TGV, R_t , and Raw results 2 years after admission with those obtained when the children were younger. We believe that these changes are real and not caused by technical problems. Our techniques are standardised and one of us has participated in all of the more than 250 lung function studies we have performed on the cohort of children. The logical reason for the changes in lung function is variable airways obstruction. This is supported by the correlation between high Raw and response to salbutamol. Many children, however, remain hyperinflated after nebulised salbutamol—a finding also observed by Lenney and Milner in asthmatic children of similar ages.¹¹ They were able to show a fall in Raw of greater than 18% in 6 of 7 children over the age of 20 months, but although these children were hyperinflated, only 1 had a fall in TGV of greater than 15% after salbutamol treatment. The fact that we have been able to show the reversibility of hyperinflation in the longer term, but often not after salbutamol, suggests that mucosal oedema and mucous plugging, rather than just muscle spasm, may be important in these children. No attempt was made to postpone lung function tests until 6 weeks after a respiratory illness had resolved and some of the changes may reflect transient after effects of viral infections.¹⁷

A family history of atopy was associated with increased airways resistance but the study design did not allow a definitive statement on the relation between atopy, post-bronchiolitic wheezing, and asthma. Nor can we state how many of the lung function abnormalities we documented are reversible given more time and further lung development.

Comparisons with other reports on children who have been symptom free for a prolonged period^{2 7} make it probable that some of the defects are permanent. We are following this cohort of children to try to resolve this question.

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