Lung function after acute bronchiolitis

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SUMMARY We performed 211 lung function measurements on 93 children in the first year after they had been admitted with acute bronchiolitis. During the convalescent phase of the illness, 77% of the infants were hyperinflated with a thoracic gas volume greater than 40 ml/kg and 3 months later 43% were hyperinflated. Twelve months after the initial illness, 17% still had lung function abnormalities and most of these children have had lower respiratory tract symptoms. For the group as a whole about 60% have had at least one episode of wheezing. Specific conductances were significantly lower in children from atopic families, indicating worse lung function, but the significance of this finding is unclear.

The medical consequences of bronchiolitis extend beyond the acute viral illness. It is well known that bronchiolitis is associated with wheezing in subsequent months, although the exact relationship between bronchiolitis and asthma remains unclear.¹⁻⁴ Evidence is also accumulating that it sows the seeds for chronic obstructive lung disease in adult life.⁴⁻⁶ Furthermore asymptomatic children may have abnormalities in lung function many years after a single attack,⁷ leaving the possibility that clinical illness will develop subsequently.

In view of the potential long-term effects of bronchiolitis, it is important to obtain prospective information on symptoms and lung function after the initial episode. A preliminary report on a small cohort of infants admitted to hospital with severe bronchiolitis showed marked disturbances in pulmonary function in the first year after the acute illness.⁸ These findings conflict with those of Phelan *et al.*⁹ who reported normal lung function within 3 months of an attack. One explanation for this dichotomy is that the children in our initial study were a selected group who were particularly ill and in whom data in the acute phase had indicated gross lung function abnormalities.¹⁰ The Australian infants were chosen on the basis that their disease was mild or moderate.⁹

In this report we have set out to study lung function in a less selected group in an attempt to elucidate prognostic features, including history of atopy and severity of illness, and to delineate the frequency of physiological sequelae. Our aim was also to collect data on a larger cohort which would form the basis for a long-term prospective study.

Patients and methods

The 93 children studied in this project were admitted to hospital during an epidemic of infection due to respiratory syncytial virus (RSV). All had a clinical diagnosis of bronchiolitis with tachypnoea, dyspnoea, hyperinflation, and widespread crepitations. In addition, viral studies were positive for RSV in 48 infants and there were single isolates of adenovirus type 1 and adenovirus type 6.

The first 22 children studied, who were the basis of our first report,⁸ had severe disease requiring nasogastric feeding but subsequently we had no deliberate selection bias, apart from requiring admission to hospital. However, if we were not certain that a child had bronchiolitis that child was not tested. It is likely that milder cases of acute viral bronchiolitis are under-represented in the cohort.

The mean age on admission was 116 (range 25-388) days and there were 52 boys and 41 girls. Nineteen of the children had a first-degree relative with asthma and 34 a first-degree relative with asthma, eczema, or hay fever. If information on second-degree relatives is included, these numbers are increased to 36 and 56. These figures are comparable with unselected children.²

Lung function tests were performed at convalescence (before discharge from hospital), at a mean time of 3.5 months after admission (range 2.3-5.4), and 12.6 months after admission (range 11.0-15.2). The number of studies performed at each period was 53, 83, and 75 respectively. Forty of the 93 children had lung function tests on all three occasions.

We measured thoracic gas volume (TGV), the amount of gas in the lungs at the end of a normal expiration, and airways resistance (RAW), using techniques described in detail previously.^{8 11-13} The total body plethysmograph had a 260 litre capacity, was of Perspex construction, with a servocontrolled heating system maintaining the facemask, shutter system, and rebreathing bag at 36°C.

Each child, after sedation with 80-100 mg/kg chloral hydrate, was nursed supine and a mask applied to the face. A bias flow of air, 5 litres/minute, passed through the wall of the plethysmograph to the facemask via a wide bore tube and expiratory gases passed out via a similar tube. Signals were relayed to the axes of a cathode ray storage oscilloscope, readings were obtained and calculations made by standard techniques.¹¹⁻¹³ Multiple breaths were sampled in each case. Specific conductances (sGAW) were calculated using the formula $sGAW = 1/(TGV \times RAW)$.

At the one year follow-up visit, we obtained histories regarding the nature, frequency, and duration of lower respiratory tract illnesses after the bronchiolitis.

Statistics used were unpaired *t* test and χ^2 analysis.

The local ethics committee approved the study, and all children were tested after informed parental consent had been obtained.

Results

Table 1 shows the lung function results for the total number of children tested on each occasion, and for those tested all three times. Available data on normal children indicate that a TGV greater than 40 ml/kg is abnormal at all weights.^{12 14 15} Table 2 gives the number of children with TGVs greater than 40 ml/kg.

In addition to the abnormalities in lung function, lower respiratory tract symptoms were common.

Table 2 Children with thoracic gas volume greater than 40 ml/kg after acute viral bronchiolitis

	No tested	With TGV > 40 ml/kg	
		No	%
Convalescent period	53	41	77
3 months after bronchiolitis	83	36	43
1 year after bronchiolitis	75	13	17

One year after the attack of bronchiolitis, 49 of the 75 children tested at this time had each suffered at least one episode of wheezing. The clinical progress of the 18 children who did not have lung function tests one year after admission was similar to that of their colleagues. Four were lost to follow-up but 6 of the remaining 14 experienced attacks of wheezing.

We compared lung function abnormalities with frequency of subsequent lower respiratory tract symptoms. Eleven of the 13 children, each with a TGV greater than 40 ml/kg one year after the initial illness wheezed, compared with 38 of the 62 whose TGV was less than 40 ml/kg. Although this difference is not statistically significant using χ^2 analysis, we believe it likely that there is a true correlation between marked hyperinflation on lung function and lower respiratory tract symptoms.

No relationship was found between hyperinflation and prematurity, age on admission, severity as judged by the need for nasogastric feeding or oxygen, or family history of atopy. However, as shown (Table 3) specific conductances were lower (worse lung function) in children from families with atopic disease. Wheezing was also more common in the children with a family history of atopy, although the trends did not reach statistical significance.

The 48 infants from whom RSV was isolated had similar thoracic gas volumes, airways resistances, and specific conductances to the 45 children in whom RSV infection was unproved. These results, together with the clinical findings, age of the children, and seasonal pattern of admission to hospital suggest that

Table 1 Lung function results showing means and standard deviations for the total number of children tested on each occasion, and for those tested on all three occasions

	Thoracic gas volume		RAW (cmH ₂ O/l per second)	sGAW (cmH ₂ O/l per second)
	ml/kg	% expected for weight ¹⁴		
Convalescent period				
Total number on each occasion	53.5 (±18.4)	167.1 (±56.3)	24.8 (±11.5)	0.19±0.09
Tested on all 3 occasions	55.3 (±19.6)	172.7 (±59.7)	24.1 (±10.9)	0.19±0.10
Three months after acute illness				
Total number on each occasion	39.6 (±9.2)	136.8 (±30.5)	13.7 (±5.8)	0.28±0.12
Tested on all 3 occasions	39.7 (±10.1)	136.7 (±32.5)	14.5 (±6.5)	0.28±0.14
One year after illness				
Total number on each occasion	32.8 (±8.8)	117.4 (±30.3)	13.7 (±8.0)	0.29±0.16
Tested on all 3 occasions	34.5 (±9.6)	122.9 (±32.6)	10.0 (±6.8)	0.37±0.17

Table 3 Specific conductances in children with and without a family history of atopic disease

	3 months after acute illness		One year after acute illness	
	Number	Mean $\pm$ 1 SD (cmH ₂ O/l per second)	Number	Mean $\pm$ 1 SD (cmH ₂ O/l per second)
Asthma in 1st-degree relative	19	0.23 $\pm$ 0.11	18	0.22 $\pm$ 0.10
Not present	63	0.29 $\pm$ 0.12 P=0.05	57	0.31 $\pm$ 0.17 P<0.05
Atopy in 1st-degree relative	31	0.24 $\pm$ 0.10	29	0.27 $\pm$ 0.15
Not present	51	0.30 $\pm$ 0.13 P<0.05	46	0.30 $\pm$ 0.16 P>0.05
Asthma in 1st- or 2nd-degree relative	34	0.23 $\pm$ 0.10	32	0.23 $\pm$ 0.13
Not present	48	0.31 $\pm$ 0.13 P<0.01	43	0.33 $\pm$ 0.16 P<0.01
Atopy in 1st- or 2nd-degree relative	51	0.26 $\pm$ 0.11	47	0.27 $\pm$ 0.16
Not present	31	0.31 $\pm$ 0.14 P<0.05	28	0.32 $\pm$ 0.15 P>0.05

the children represented a fairly homogeneous group that had been the victim of a virus infection.

Discussion

Disturbances in lung function were large just before discharge from hospital with acute viral bronchiolitis. Three months later we found reductions in both TGV and RAW accompanied by a rise in sGAW indicating improved lung function. One year after the initial insult to the lungs, there was further reduction in TGV for the group as a whole, but 17% of the children still had a TGV greater than 40 ml/kg, suggesting that in these cases at least, bronchiolitis was not an acute self-limiting illness. The abnormalities were less frequent than in our initial study,⁸ in which all the infants had severe bronchiolitis, findings which are consistent with the hypothesis that disturbances of lung function are more common in those with worse disease initially. However, we have no other data to support this.

The only published data on airways resistances in normal infants which used a heated shutter system¹⁶ gave values of 16.9 cmH₂O/l per second. The first impression of our results (Table 1) is that the RAW at 3 and 12 months was normal. However, our measurements of RAW are obtained from the initial part of inspiration,⁸ when flow is essentially laminar, rather than at two-thirds of maximal inspiratory flow, which in these children is under turbulent conditions, and will produce much higher values. In the absence of appropriate normal data it is difficult to say if the mean airways resistances are increased outside the convalescent period, although we suspect that they are.

About two-thirds of the group experienced episodes of wheezing, with a non-significant trend that symptoms were associated with a family history of atopy. However, lung function was worse in children who came from atopic families. Since the

study design did not include a control group, we cannot make precise comments about the possible interrelationships between atopy, bronchiolitis, and postbronchiolitis wheezing. However, it does show that one year after bronchiolitis, an appreciable number of children remain grossly hyperinflated as judged by lung function tests, and that most such children are symptomatic. We are following up these children to establish whether the airways obstruction is reversible, whether permanent lung damage has been caused by the virus, or whether, as we suspect, there is a combination of the two.

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References

- 1 Rooney J C, Williams H E. The relationship between proved viral bronchiolitis and subsequent wheezing. *J Pediatr* 1971; **79**: 744-7.
- 2 Pullan C R, Hey E N. Wheezing, asthma, and pulmonary dysfunction 10 years after infection with respiratory syncytial virus in infancy. *Br Med J* 1982; **284**: 1665-9.
- 3 Laing I, Riedel F, Yap P L, Simpson H. Atopy predisposing to acute bronchiolitis during an epidemic of respiratory syncytial virus. *Br Med J* 1982; **284**: 1070-2.
- 4 Kattan M. Long-term sequelae of respiratory illness in infancy and childhood. *Pediatr Clin North Am* 1979; **26**: 525-35.
- 5 Colley J R T, Douglas J W B, Reid D D. Respiratory disease in young adults: influence of early childhood lower respiratory tract illness, social class, air pollution, and smoking. *Br Med J* 1973; **iii**: 195-8.
- 6 Burrows B, Knudson R J, Lebowitz M D. The relationship of childhood respiratory illness to adult obstructive airway disease. *Am Rev Respir Dis* 1977; **115**: 751-60.
- 7 Kattan M, Keens T G, Lapierre J, Levison H, Bryan A, Reilly B J. Pulmonary function abnormalities in symptom-free children after bronchiolitis. *Pediatrics* 1977; **59**: 683-8.

- ⁸ Stokes G M, Milner A D, Hodges I G C, Groggins R C. Lung function abnormalities after acute bronchiolitis. *J Pediatr* 1981; **98**: 871-4.
- ⁹ Phelan P D, Williams H F, Freeman M. The disturbances of ventilation in acute viral bronchiolitis. *Aust Paediatr J* 1968; **4**: 96-104.
- ¹⁰ Stokes G M, Milner A D, Groggins R C. Work of breathing, intrathoracic pressure, and clinical findings in a group of babies with bronchiolitis. *Acta Paediatr Scand* 1981; **70**: 689-94.
- ¹¹ Dubois A B, Botelho S Y, Bedell G N, Marshall R, Comroe J H, Jr. A rapid plethysmographic method for measuring thoracic gas volume: a comparison with a nitrogen washout method for measuring functional residual capacity in normal subjects. *J Clin Invest* 1956; **35**: 322-6.
- ¹² Radford M. Measurement of airway resistance and thoracic gas volume in infancy. *Arch Dis Child* 1974; **49**: 611-5.
- ¹³ Stocks J, Levy N M, Godfrey S. A new apparatus for the accurate measurement of airway resistance in infancy. *J Appl Physiol* 1977; **43**: 155-9.
- ¹⁴ Hatch D J, Taylor B W. Thoracic gas volume in early childhood. *Arch Dis Child* 1976; **51**: 859-64.
- ¹⁵ Taussig L M, Harris T R, Lebowitz M D. Lung function in infants and young children. *Am Rev Respir Dis* 1977; **116**: 233-9.
- ¹⁶ Stocks J, Godfrey S. Specific airway conductance in relation to postconceptional age during infancy. *J Appl Physiol* 1977; **43**: 144-54.

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