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Abnormalities of lung mechanics in young asthmatic children

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ABSTRACT Measurements of total compliance of the respiratory system by the weighted spirometer technique and of the functional residual capacity by helium gas dilution were attempted in 86 asthmatic children aged 2·2–7·9 years. In all but six of the 86 children reliable measurements could be obtained. Significantly raised functional residual capacity was detected in children with asthma of all degrees of severity. The compliance of the respiratory system was significantly abnormal (reduced) only in children who had symptoms at the time of measurement or who had chronic persistent asthma. The results indicate that these measurements are well tolerated in young asthmatic children. Further work needs to be undertaken to assess the value of this technique in following the response to treatment.

Asthma is a common illness in preschool children; the cumulative prevalence in 2–6 year olds may be as much as 30%.[1] In these children asthma attacks may be more severe,[2] with an increased rate of hospital admission,[3] and the response to medication may be smaller[4] and less predictable[5] than in older children. Thus the ability to assess, by respiratory function testing, the severity of disease and response to treatment is very desirable.

The forced oscillation technique has been used to measure airways resistance in young children,[6] and with practice preschool children can use a peak flow meter.[7] Tests of lung function that depend on forced expiratory manoeuvres or plethysmography are seldom possible in young children. Recently, however, we have adapted the weighted spirometer technique for measurement of compliance of the respiratory system (CRS) for use in such children. This, combined with measurement of functional residual capacity (FRC) by helium gas dilution, can be reliably performed in most children aged 2–7 years.[8] The aim of the present study was to use the combined FRC and CRS technique in young children with asthma, to determine whether the abnormalities of lung mechanics reported in adults[9 10] and older children[11 13] could be detected in this age group.

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Methods

PATIENTS

Studies were attempted in 86 children (29 girls and 57 boys) aged 2·2–7·9 years. All had a history of recurrent wheezing responsive to bronchodilator treatment and were attending the paediatric asthma clinic at King's College Hospital.

For assessing the relationship of FRC and CRS to disease severity, the children were classified in four groups according to the treatment they were receiving at the time of measurement: 1—β adrenergic agonist (β agonist) as necessary (those with the least severe asthma); 2—regular theophylline or sodium cromoglycate; 3—regular inhaled steroids; 4—regular inhaled steroids and theophylline (those with the most severe asthma). Groups 2, 3, and 4 in addition were receiving a β agonist as necessary). A further group (No 5) included any child who had symptoms at the time of measurement, regardless of the treatment previously received.

The study was approved by King's College Hospital's ethical committee and the parents' consent was obtained.

MEASUREMENT OF FRC AND CRS

All children were studied in a sitting position while breathing through a face mask (Medishield) into a water sealed spirometer (Gould Pulmonet 3). The face mask has a semi-inflated diaphragm at its edge to improve the seal and was firmly held in position to prevent leaks. An internal carbon dioxide absorber and adjustable oxygen supply are incorporated in the spirometer, which has a total volume of 6 litres.

Once an apparently good seal had been achieved (no expired gas could be detected escaping around the face mask) the child was switched into the spirometer in FRC mode. FRC was measured by helium gas dilution and a continuous digital readout was displayed.

After the measurement of FRC, CRS was measured by the weighted spirometer technique.[8] After a constant end expiratory level on the spirometric volume recording had been established, a 500 g brass weight was placed on the spirometer bell. This produced a constant positive pressure within the circuit of about 2 cm H_2O and increased the end expiratory level. Airway pressure was measured via a side port (Sanborn pressure transducer 268B). The weight was removed when a new stable baseline had been achieved; on its removal the end expiratory level returned to the previous baseline. This procedure was repeated five times during the study period. The combined compliance of the respiratory system and the spirometer circuit were calculated from the mean volume-pressure changes of the five weighted applications. Compliance of the spirometer circuit alone had been estimated beforehand by applying a series of weights to the spirometer bell with the circuit closed. The compliance of the spirometer was then subtracted from the total compliance to give CRS. Volumes were all corrected to BTPS conditions.

By performing the two different measurements a leak in the circuit can always be detected. A leak around the face mask prevents equilibration of helium within the circuit and leads to an upward trend in the spirograph tracing (fig 1). Throughout the measurement of FRC and CRS oxygen is added to the circuit at a rate of 0·15–0·25 l min^{-1}, depending on the size of the child. If oxygen is supplied at a rate in excess of demand this could mask a small constant leak during FRC measurement. After initial adjustment, however, the oxygen flow (indicated by the flow meter) remains constant throughout. A leak would increase and at once become obvious when the weight is added and the circuit pressurised during the measurement of CRS. Thus a leak is exacerbated and may become apparent for the first time as an upward trend in the baseline when the weight is added. If a leak was demonstrated during the measurement of either FRC or CRS the results of both FRC and CRS measurements were discarded.

All calculations of FRC and CRS were performed on coded traces by one observer, who was unaware of the patients' characteristics.

TIME TO EQUILIBRATION

As appreciable airway obstruction was expected in these asthmatic children, we measured the maximum possible equilibration time in four healthy children and five asthmatic children without symptoms. The displayed FRC was recorded every 15 seconds and equilibration was assumed when the display showed a change of less than 20 ml over a 30 second period. Once this had been reached the nine children continued to breathe into the spirometer in FRC mode for at least a further minute and again the displayed FRC was noted at 15 second intervals. This was done to assess whether our assumption of equilibration as defined above was justified.

REPRODUCIBILITY

Reproducibility studies were performed on eight asthmatic children (median age 4·7, range 2·9–7·4 years). Six separate measurements of FRC and CRS were

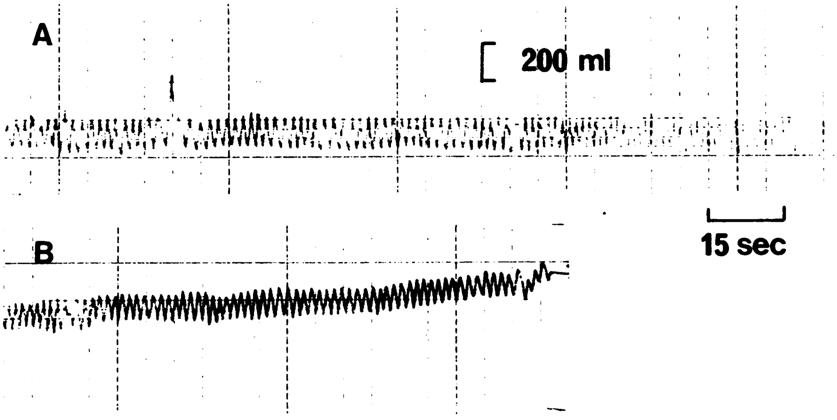

Fig 1 *Typical records obtained during measurement of functional residual capacity. Both traces are taken from a 3 year old asthmatic girl. In the lower record (B) there has been a leak around the face mask, shown by the upward trend of the spirograph tracing. No such leak is seen in trace A even though the child was attached to the spirograph for over two minutes.*

made at the same visit to the laboratory in the four older children, and three measurements on each of two successive days in the four younger children (less than 3·1 years).

In addition to the estimation of FRC and CRS, 40 children were asked to attempt a peak flow (PEF) measurement.

STATISTICAL METHODS

Intrasubject reproducibility was expressed as the coefficient of variation.

To assess the relationship of disease severity to lung function, each measurement was expressed as the number of standard deviations from the mean predicted value (z scores):

$$z\ \text{score} = \frac{\text{measured} - \text{expected (CRS or FRC)}}{\text{SD of normal population}}$$

The expected CRS, FRC, and SD of a normal population were calculated from our previous results in healthy children aged 2–7 years.[8]

Differences between the asthmatic groups were tested for significance with an unpaired Student's t test.

Results

EQUILIBRATION TIME

The maximum time to equilibration in the four healthy and five asthmatic children was 105 seconds (range 40–75 seconds in healthy children and 75–105 seconds in asthmatic children). The five asthmatic children, aged 3–7 years, had values of FRC ranging from 110% to 150% of the predicted value. All nine children remained attached to the spirograph in the FRC mode for at least two minutes after equilibration time was achieved; within that period the change in volume never exceeded 20 ml. For the remainder of the study the equilibration time was therefore defined in terms of a volume change of less than 20 ml within 30 seconds.

Asthmatic patients with symptoms (group 5) required a significantly longer time to reach equilibration (mean 96 seconds, range 90–105 s) than those with the mildest asthma (group 1: mean 76, range 60–90 s; $p < 0·01$). The time to equilibration was also affected by the severity of disease, groups 3 and 4 requiring a longer time to equilibration (mean 85 s) than group 1 (mean 76 s); but this difference did not reach statistical significance.

REPRODUCIBILITY

Six of the eight children in whom reproducibility studies were performed were symptom free at the time of measurement. The intrasubject coefficient of variation in six successive measurements in each child ranged from 2·7% to 8·4% (FRC) and from 4·9% to 8·9% (CRS). Reproducibility in the two youngest children (2·9 and 3·0 years) was similar to that in the older children (table 1).

Two of the children, twins aged 3·1 years, developed symptoms by the second day. Their results therefore were excluded from the reproducibility study. They showed deterioration in lung function when they had symptoms. In one twin compliance decreased from 50 to 23 ml/cm H_2O and FRC increased from 674 to 985 ml and in the other CRS decreased from 57 to 38 ml/cm H_2O while FRC increased from 693 to 837 ml.

CRS AND FRC

Measurements of both FRC and CRS were obtained in 27 girls (median age 5·2, range 2·5–7·9 years) and 53 boys (median age 4·7 years, range 2·2–7·9). In six children only FRC measurements were made. These six children in whom measurements of CRS were not possible were all boys aged 6·0–7·5 years; they either would not remain attached to the spirometer long enough to perform both measurements or breathed irregularly on addition of the weight.

Most of the asthmatic children had higher FRC values (fig 2) than our previous normal population. There was a trend for increasing severity of asthma, as reflected by an increased need for medication, to be associated with increasing mean FRC (fig 2). Comparisons between groups showed significantly greater values of FRC in those with the most severe and symptomatic asthma (groups 3, 4, 5) than in the children in treatment group 1 ($p < 0·01$).

The mean values of CRS in treatment groups 1, 2,

Results of reproducibility studies, with coefficients of variation in parentheses

Patient details			*Results of measurements*	
Age (y)	*Height (cm)*	*Treatment score**	*FRC (ml)*	*CRS (ml/cm H_2O)*
2·9	94	2	543 (6·7)	20·5 (8·9)
3·0	92	4	590 (2·7)	32·9 (4·9)
4·9	110	1	801 (8·4)	53·4 (7·0)
5·2	111	2	846 (8·3)	55·2 (8·7)
5·7	110	3	930 (4·7)	44·5 (7·6)
6·1	119	2	943 (5·9)	40·2 (7·8)

*See under "Patients."

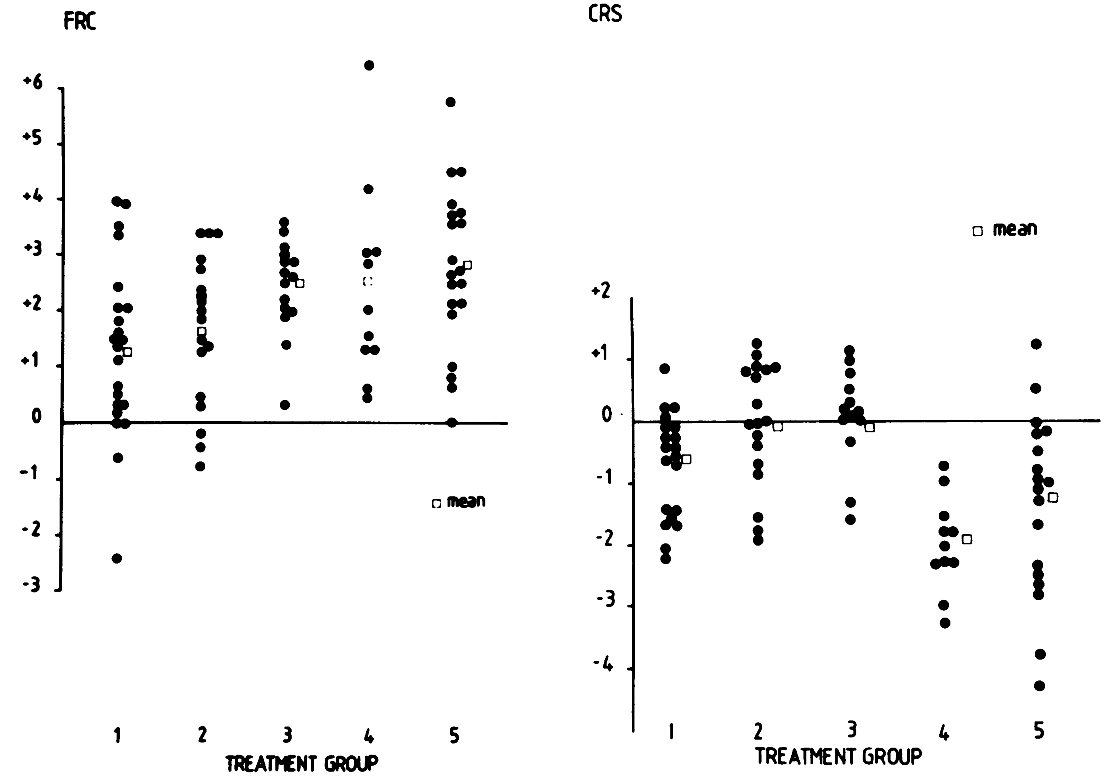

Fig 2 *Measurements of functional residual capacity (FRC) and compliance of the respiratory system (CRS) system for each patient, represented as z scores, plotted according to treatment group. The open squares represent the mean values for each group. All treatment groups had a higher mean FRC than the normal population.[8] CRS values for treatment groups 1, 2, and 3 are similar to values for the normal population; in groups 4 and 5, however, CRS was significantly less than normal.*

and 3 did not differ significantly from our previous normal population.[8] Between group comparisons showed a significantly lower CRS in those with the most severe (group 4, $p < 0{\cdot}001$) and symptomatic asthma (group 5, $p < 0{\cdot}01$) than in the children in treatment groups 1, 2, and 3 (fig 2).

PEAK FLOW MEASUREMENTS

Ten of the 20 children aged 4–6 years and 16 of 20 aged 2–4 years were unable, even with practice, to perform reproducible peak flow manoeuvres. We could not therefore make a useful comparison of peak flow with FRC and CRS.

Discussion

About 11% of British schoolchildren suffer from asthma.[14] In children and adults lung function studies are extremely useful in establishing the diagnosis of asthma by showing variability of airways obstruction, describing the pattern and severity of asthma, and monitoring the response to treatment. Unfortunately, traditional methods of measuring lung function in asthma become increasingly unreliable in children aged less than 7 years, but by this age most of those with childhood asthma will have had their first attack.[15]

Peak flow has been used in young children to assess bronchodilator response and confirm reversibility. Its main advantage is simplicity, which means that the test can be performed repeatedly, and at home.[13] Peak expiratory flow, however, is influenced mainly by the calibre of the larger airways and may not detect abnormalities of small airway function.[16] Although children as young as 2 years can perform a peak flow manoeuvre, they require practice and some tend initially to close the glottis, producing an inaccurate recording.[17] At least one author has suggested that peak flow recordings are unlikely to be sufficiently reliable under the age of 5 years.[18] We found that children under 5 years rarely perform this manoeuvre successfully on their first visit to the laboratory. Most who were successful had already taken part in other asthma studies and had been educated in the performance of the manoeuvre over several months.

Forced oscillation, on the other hand, requires little or no cooperation from the child. With this technique total respiratory impedance (or resistance) can be calculated from the relationship between pressure and flow at the mouth when flow is produced by a sinusoidal wave. In older children this method gives reproducible results with a coefficient of variation of 12% but there is a wide scatter of results in 4 and 5 year olds.[6] The technique has been used to investigate response to treatment in preschool asthma.[19 20] It is, however, influenced by upper respiratory tract infections, which are common in young children, and it gives a value of resistance unrelated to lung volume. A major criticism is that in the presence of respiratory disease, such as asthma, the lung may not act as a single unit and therefore there is no one resonant frequency. As a consequence, flow resistance will be underestimated.

The present results show that the combined technique of helium gas dilution and weighted spirometry is not only well tolerated in such young asthmatic children but also reproducible. Despite the impairment of gas mixing[21] that occurs in asthma, we found that the time to equilibration during the measurement of FRC by helium gas dilution was only about twice that quoted in most studies for normal subjects (for example, 20–60 seconds[22] and 45 seconds[23 24]), only one study giving a longer equilibration period of three minutes.[25] In children with symptoms we found that the time to equilibration was significantly longer, but still considerably less than the time (over five minutes) observed in a study on adults with severe asthma.[26] This last study, however, used a more stringent definition of equilibration, less than 0·01% of change over one minute.

In the present study measurement of FRC was well tolerated in all the children tested, no practice was required, and the level of reproducibility was well within the range quoted for other methods in normal children.[6 7] A possible source of error is the problem of leaks, but by combining the two techniques as described leaks are easily detected (fig 1). Another possible source of error, especially in smaller children, is that the circuit volume is relatively large in comparison with the FRC. The spirometer bell always resets to a constant volume at the beginning of each test. The addition of a child's FRC of 600 ml would make a change of about 10% to the total circuit volume. We have shown, however, both in normal[8] and in young asthmatic children that the measurement of FRC is very reproducible.

Measurement of CRS by weighted spirometry assumes relaxation of the chest wall at the end expiration during positive pressure breathing. Electromyographic studies during application of this technique have been reported for only one infant, but in this child no expiratory muscle activity was detected.[27] In our previous study attempts to obtain electromyographic recordings had to be abandoned because of the difficulty of obtaining interference free signals and because of poor tolerance of the increased duration of the test.[8] Traces were inspected therefore for changes in respiratory pattern that would indicate active expiration. In this study, on the basis of such criteria, results from three of the 86 children had to be excluded. In three other children it was impossible to make measurements of compliance because of their limited cooperation.

From these measurements we have been able to show that some of these very young asthmatic children have a significantly raised FRC and reduction in respiratory compliance. Similar observations have been made in older asthmatic subjects by several groups.[11 28–30] During an acute attack of asthma FRC may be greater than the total lung capacity after recovery.[10] Compliance, which may dimish during an acute episode in adults and older children,[31–34] may revert to normal after resolution of symptoms.[35] Using this combined technique, we have been able to demonstrate improvements both in FRC (decrease) and in compliance (increase) after bronchodilator treatment during an acute asthma attack.[36]

This study has shown that mean FRC progressively increases with increasing severity of asthma. A significant reduction in CRS, however, was seen only in children with chronic persistent disease. We have also shown that these two techniques are well tolerated and reproducible in most young asthmatic children.

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