genotypes were identified had genotype II alone or in combination with other types, and the high frequency of type II genotype is in keeping with the prevalence in Italy.11 Thus, HCV infection in patients with IPF is not associated with specific genotypes. Thirdly, in two patients a combination of two and three genotypes was present, a rare association in a single patient and almost exclusively confined to cases who have received multiple transusions.12

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Characteristics of patients and results of lung function testing

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>FEV1/VC (%)</th>
<th>Methacholine (mg/ml)</th>
<th>Lung sounds</th>
</tr>
</thead>
<tbody>
<tr>
<td>no.</td>
<td></td>
<td></td>
<td>PD20</td>
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<tr>
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<td></td>
<td></td>
<td>PDwheeze</td>
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<tr>
<td>1</td>
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<td>1.2</td>
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<td>&gt;39-3</td>
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</table>

FEV1 = forced expiratory volume in one second; VC = vital capacity; PD20 = dose of methacholine causing a 20% fall in FEV1; PDwheeze = dose of methacholine at which change in lung sounds was heard.

(FEV1) after inhaling methacholine (PC20) and the occurrence of wheeze. It was reported recently that the auscultation method is potentially dangerous because significant falls in transcutaneous oxygen tension sometimes occur in the absence of wheeze.4

Since the results of studies that use audible wheeze as an indicator of bronchial responsiveness during challenge tests are controversial, we investigated in a pilot study whether a change in lung sounds corresponded to a 20% fall in FEV1 after methacholine challenge in asthmatic children, and whether the occurrence of wheeze was the most important change.

Methods

SUBJECTS

Fifteen asthmatic children (eight boys) aged 8–15 years (mean 10.8 years) were recruited from our outpatient clinic. The mean baseline Tiffeneau index (FEV1/VC) before the methacholine challenge test was 79% of predicted (range 60–93). All children had normal chest auscultation before the challenge test. Bronchial challenge with methacholine was requested as part of their routine evaluation and consent of the child and parents was obtained. Symptomatic bronchodilator therapy was withheld for at least eight hours (short acting) or 24 hours (long acting) before testing and antihistamines for one week. Inhaled corticosteroids and sodium cromoglycate were continued. The study was approved by the medical ethics committee of our hospital.

INHALATION CHALLENGE TEST

The children performed spirometric tests using a water sealed spirometer (Lode, Groningen, The Netherlands). The best result of three FEV1 attempts was used for analysis. Methacholine inhalation challenge was preceded by baseline lung function measurements, followed immediately by inhalation of saline control. After inhalation of saline doubling concentrations of methacholine (beginning with 0.15 mg/ml to a maximum of 39.3 mg/ml) were delivered during four inhalations via a gauged Devilbiss nebuliser model 646, with a calibrated output of 5.0 μl per puff. The Devilbiss nebuliser was attached to a French Rosenthal dosimeter. During each inhalation of the aerosol a deep breath was taken and held for 10 seconds. The aerosol was delivered into the mouth piece and a nose clip was applied. Three minutes after the fourth inhalation of the diluent FEV1 measurements were performed. Each methacholine concentration was given at five minute intervals. The tests were discontinued if FEV1 decreased by 20% or more from the baseline or when the maximum dose of methacholine was reached. Bronchial responsiveness was defined as the total cumulative dose of methacholine inducing a 20% or more fall in FEV1 (PD20).

TRACHEAL AUSCULTATION

A microphone (Wip en Broos, Winsum, The Netherlands) was placed in the suprasternal notch and lung sounds were recorded over the trachea for one minute starting two minutes after administration of each dose of methacholine during quiet respiration. The microphone was attached to the skin with two sided adhesive tape rings. Lung sounds were stored on tape (DT-120 Rn, Sony), using a digital audio tape recorder (DTC-59 ES, Sony) and were analysed by headphone (Beyer Dynamic DT 801). The lung sounds were scored directly as wheeze, cough, prolonged expiration, and increase in respiratory rate. Cough was scored if it was persistent, and prolonged expiration was scored when the duration of expiration exceeded the duration of inspiration. Increase in respiratory rate was defined as an increase of 50% or more from baseline respiratory rate. A second analysis of the lung sounds was blindly scored from the audio tape recordings by another physician who was unaware of patient characteristics, baseline lung function, and the methacholine concentrations. During this second analysis lung sounds of all children were successively recorded on one tape and no indication of the start and ending of the challenges was given. The total cumulative methacholine dose at which a change in lung sounds was heard was defined as PDwheeze.

Results

The results of the study are presented in the table. In 12 of the 15 children the methacholine PD20 was detected by the change in lung sounds – in four by wheeze and in eight by cough, prolonged expiration, and/or increased respiratory rate. In two children lung sounds were detected one dose step before the PD20 was reached. In three of 15 children in whom no change in lung sounds could be detected there was no fall in FEV1 on the highest methacholine dose.

Total agreement was found between the lung sounds scored directly and the lung sounds scored blindly during the subsequent audio tape recording analysis.
Discussion
Changes in lung sounds were found to correspond well with a 20% fall in FEV₁ after methacholine challenge. In contrast with earlier studies, in which wheeze was the indicator of bronchial responsiveness, we found wheeze by itself to be a poor indicator for assessing bronchial responsiveness. Cough, increase in respiratory rate, and prolonged expiration were more frequently found.

Noviski et al. observed that transient coughing, increase in respiratory rate, mild wheezing over the lung fields, and localized crepitations in some patients did not correlate with either the concentration of methacholine causing wheezing or the concentration causing the FEV₁ to fall by 20%.

Avital et al. concluded that wheeze was present in almost every child who was challenged and had a fall in FEV₁ of more than 20%. The discrepancies between our results and the observations of this group may be explained by the fact that they do not state what the real fall in FEV₁ was after the challenge. It might well be that the actual fall in FEV₁ was far greater than 20%.

Our observation that wheeze by itself is not sensitive for assessing the response to a methacholine challenge is in accordance with Wilson et al. who compared three techniques for measuring bronchial responsiveness in young children. They also reported that most of the children coughed after methacholine at doses which were associated with a fall in transcutaneous oxygen tension. Because Wilson et al. did not investigate FEV₁, it is not clear whether this coughing would have corresponded with a fall in FEV₁ of 20%. In contrast with our findings, Wilson et al. stated that the auscultation method is unreliable and potentially dangerous. They observed that significant falls in transcutaneous oxygen tension sometimes occurred in the absence of wheeze. However, four of their children showed signs of respiratory distress. In our study none of the children showed signs of dyspnoea, cyanosis, or intercostal retractions. The differences in the results could thus be due to differences in study populations. Only 11 of the 30 children studied by Wilson et al. were considered to have asthma, whereas our group consisted only of asthmatic children.

In conclusion, changes in lung sounds are easy to detect over the trachea and correspond well with a 20% fall in FEV₁ after methacholine challenge. Computerised analysis of changes in lung sounds may provide a more objective method in situations where this warrants the cost. For routine clinical assessment of bronchial responsiveness in asthmatic children, changes in lung sounds can be used provided that attention is paid, not only to the occurrence of wheeze, but also to cough, increase in respiratory rate, and a prolonged expiration.

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Use of tracheal auscultation for the assessment of bronchial responsiveness in asthmatic children.

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