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Is Clinical Wheezing Reliable as the Endpoint for Bronchial Challenges in Preschool Children?

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Summary. The present study was designed to compare the clinical finding of wheeze by auscultation with an objective evaluation by acoustic means at the endpoint of a bronchial challenge in preschool children. Challenges were undertaken using a tidal breathing method in 51 preschool children as part of the investigation of possible asthma. An electronic stethoscope was used for auscultation of each lung and for the simultaneous recording of the acoustic sonogram for analysis. In 24 children, the pediatrician determined that the challenge was positive, and in 22 of these, he heard wheezing at the endpoint of the challenge. In 2 children the challenge was considered positive, based on a modest fall in saturation. The acoustic record was scanned manually for presence of wheeze defined in terms of duration, and power spectrum without reference to auscultatory findings. In positive challenges, the mean wheeze rate was 28.1% (95% CI, 19.5–36.8%), while no wheeze was detected acoustically in negative challenges. Using a cutoff wheeze rate (duration of wheeze/duration of breath phase $\times$100) of 10% for the whole group, clinical wheezing detected by the pediatrician had a sensitivity of 100% (no false negatives) and a specificity of 91%. In conclusion, the clinical observation of wheeze agrees very well with its detection by acoustic measurement at the endpoint of a bronchial challenge in preschool children.
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Key words: bronchial provocation; acoustic analysis; respiratory sounds.

INTRODUCTION

The assessment of bronchial reactivity to inhaled nebulized methacholine and adenosine 5′-monophosphate (AMP) has become an important tool for the diagnosis of asthma in children and young people and its differentiation from other causes of chronic airway diseases.[1] In adults and cooperative children older than about 6 years, the response to these agents is usually assessed by repeated spirometric measurement of lung function, and the endpoint is defined as the concentration of test agent which causes a 20% fall in forced expired volume in 1 sec (FEV_1) from baseline (PC_{20}). In younger children unable to perform spirometry, the response to a challenge can be evaluated by auscultation of the lungs to detect wheezing, with or without mild hypoxia or tachypnea.[1–3] This concentration of challenge agent in this type of challenge has been termed the ''PCwheeze.'' In children old enough to perform spirometry, a good correlation was found between PC_{20} and PCwheeze.[4]

There has been some controversy as to the sensitivity of the auscultation method to detect wheezing after methacholine nebulization in young children. Wilson et al.[5] reported that only 16% of 5-year-old children wheezed at the endpoint concentration of methacholine. Sprikkelman et al.[6] studied children aged 8–15 years and only heard wheeze in 33% with a positive challenge by spirometry, but a subsequent study by these same investigators[7] demonstrated wheeze alone or with other signs in 88% of positive challenges. Yong et al.[8] undertook 56 bronchial challenges in 39 preschool children (mean age, 26.5 months) and heard wheezing at the endpoint in 90%, which agrees closely with our own study of 146 young children with asthma (mean age, 4.3 years) in whom wheeze alone or in combination with other signs appeared in 81%.[9] In these previous studies, the presence or absence of wheezing was determined by a physician either auscultating the chest or listening to a tape recording of breath sounds.

Studies were also undertaken to relate wheezing measured by acoustic techniques to changes in lung function during bronchial challenges in older children. Thus Sanchez et al.[10] found a significant correlation between concentration of methacholine causing acoustic

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wheeze and PC_{20} in subjects in whom both wheeze and a fall in lung function were detectable. Pasterkamp et al.[11] showed that even during quiet breathing without wheeze, there was a correlation between change in frequency of breath sounds and change in lung function during bronchial challenge.

The present study was designed to determine the reliability of the clinical observation of wheezing by auscultation of the lungs by an experienced pediatrician in comparison with the objective evaluation of breath sounds by acoustic means at the endpoint of a bronchial challenge in preschool children.

SUBJECTS AND METHODS

The children who participated in this study were all those referred to our department for bronchial challenge testing on purely clinical grounds, and suspected of having asthma. The children were admitted consecutively to the study provided they were of a suitable age and were not wheezing clinically before the challenge. They were mostly children with recurrent nonproductive cough without evidence of any other relevant disease. The present study was designed to investigate the reliability of a clinical test and not to study the relationship between bronchial reactivity and lung disease, and therefore the children were neither selected nor classified on the basis of other parameters such as presence or absence of allergy. All tests were undertaken in the previously described fashion,[9] which has been in use clinically in our department for a number of years. No modifications were made to the performance of the test other than the use of a commercially available electronic stethoscope (Meditron, Welch Allyn, Arden, NC) in the place of a regular stethoscope, and the placement of a commercially available inductance belt to record phase of respiration (Respitrace, Ambulatory Monitoring, Inc., Ardsley, NY). The study was approved by our Institutional Ethics Review Board. A total of 51 children with a median age (10–90% CI) of 5.0 (3.5–6.7) years took part in the study. Three children were between 8–9 years old and were studied by the PCwheeze technique because they were unable to perform spirometry. A further 4 children were referred for investigation, but 3 refused to cooperate and the test was abandoned, and one child was found to be wheezing before the challenge, which could not therefore be undertaken.

Bronchial Challenge

The technique for performing a bronchial challenge, using a modification of the original tidal breathing method of Cockcroft et al.[12] with chest auscultation, was fully described previously.[2–4,9] The challenge was performed using fresh solutions of adenosine 5′-monophosphate (AMP) nebulized by a jet-type nebulizer with an output of 0.39 ml/min. Inhalations were performed using a loosely fitting face mask and continued for 2 min of tidal breathing. Doubling concentrations of AMP were used, beginning with 0.39 mg/ml, and increased every 5 min until the maximal concentration (400 mg/ml) or endpoint was reached. Arterial oxygen saturation and heart rate were monitored continuously by pulse oximetry.

Endpoint of a Bronchial Challenge

As in the routine performance of this type of challenge, the endpoint was decided by the pediatrician undertaking the test without reference to the acoustic recording. One pediatrician (K.U.), experienced in this type of test, undertook all challenges. The endpoint of a challenge was defined as the concentration of agent resulting in one or more of the following:

- Wheezing heard with a stethoscope over either or both the right or left upper lobes;
- A fall in oxygen saturation (SaO_2) measured by pulse oximetry of $\geq$5% from baseline (desaturation); and
- An increase in respiratory rate of $\geq$50% or more from baseline (tachypnea).

The challenge was considered positive if the endpoint was reached at a concentration of AMP less than 400 mg/ml. To the best of our knowledge, no population studies in children or adults have been undertaken to determine the normal range of the response to AMP. In our own experience, no child found to be clinically free of asthma has responded to less than 400 mg/ml of AMP, and likewise no healthy adult has responded to less than 200 mg/ml.

Chest auscultation was performed using the electronic stethoscope during the first 30 sec after the end of each period of nebulization. The upper lobe of one lung was auscultated for 3–5 breaths, and then the upper lobe of the other lung was auscultated. In conformity with our normal clinical practice to keep the test as simple and quick as possible, only the upper lobes were auscultated. If the child did not breathe deeply enough for the breath sounds to be heard clearly, he or she was encouraged to take a few deeper breaths, as is our normal practice with this type of challenge. If the pediatrician was unsure of the signs, a similar second or third period of auscultation was performed. The pediatrician recorded the physical signs for each lobe separately on a chart and noted whether wheezing, if present, was inspiratory, expiratory, or both, and whether it was heard for at least 3 breaths. He also recorded the respiratory rate, heart rate, saturation, and whether the child coughed.

Acoustic Recording and Analysis

Before commencing the challenge, a flexible Respitrace inductance belt of suitable size for the child was placed around the midthoracic region. The signal from this

device, together with the acoustic output signal from the electronic stethoscope, was fed into a computer through an analog-to-digital converter with a sampling rate of 11,200 Hz. A simple computer program allowed the simultaneous recording of the two signals during each 30-sec period of chest auscultation and their storage for later analysis, which was undertaken without reference to the opinion of the pediatrician until they were compared for the purpose of this study. Every dose step of the challenge for all 51 children was analyzed from the start up to and including the last step in the challenge. The analysis of the acoustic signal was undertaken using a commercial sound analysis program (Cool Edit Pro, Syntrillium Software Corp., Phoenix, AZ). This program allowed the simultaneous display of the sonogram or a power spectrum along with the Respitrace signal, so that acoustic events could be timed to inspiration or expiration (Fig. 1). The acoustic signal was antialias-filtered before being displayed on a frequency/time plot, as recommended by the European Respiratory Society Task Force for Computerized Respiratory Sound Analysis (CORSA).[13]

The record from each lung was analyzed separately, although the investigator could see the record from both lungs simultaneously. The acoustic record was scanned for the presence of wheeze, which was defined in accordance with the CORSA report on computerized breath sounds[13–15] as musical monophonic or polyphonic sounds with a duration of at least 100 msec. These sounds were further classified as asthmatic wheeze in the frequency range of 150–800 Hz, provided these were inspiratory or expiratory polyphonic or expiratory monophonic in character. For each lung, the first two consecutive breaths with clear acoustic and Respitrace records were analyzed. In approximately 10% of instances, the pattern varied from breath to breath, and 2 representative breaths were chosen instead of 2 consecutive breaths. Wheeze rate was defined

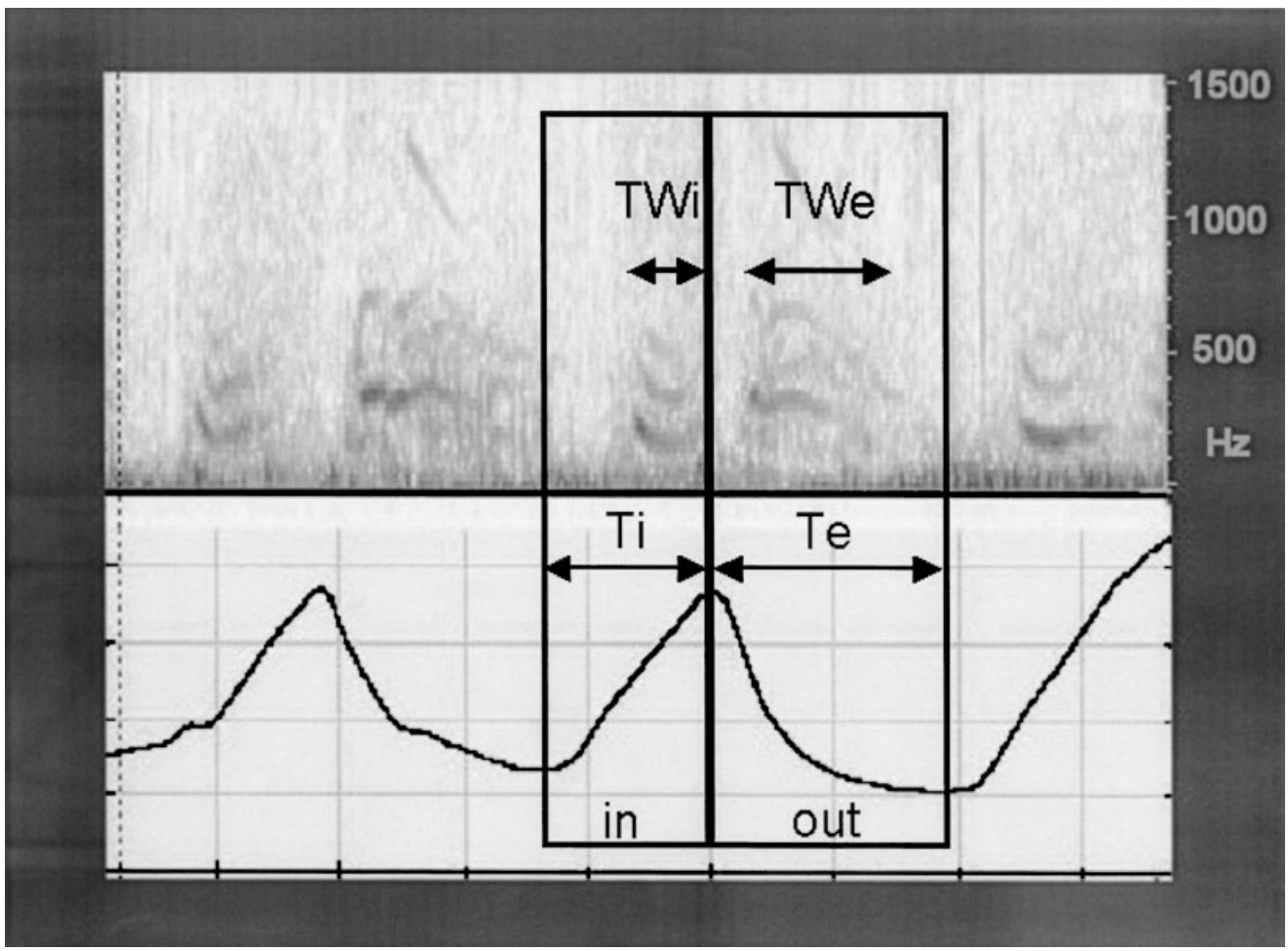

Fig. 1. Record from a positive bronchial challenge, showing sonogram in spectral form (above) and respiratory movement (below). Respiratory movement was recorded simultaneously with sound signal, using an analog-to-digital card, and stored as an acoustic (wav) file which enabled it to be displayed by Cool Edit. Boxes outline inspiration and expiration for one breath. Dark bands in sonogram show wheezes. Total durations of inspiratory wheeze (TWi) and expiratory wheeze (TWe) are indicated. Durations of inspiration (Ti) and expiration (Te) are also indicated.

as the duration of wheeze measured from the spectral display of the acoustic record divided by the duration of the breath phase (inspiration, expiration, or both as the case may be) measured from the Respitrace record. The wheeze rate was calculated for each breath for inspiration and expiration separately (Twi/Ti, Twe/Te) and for inspiration plus expiration combined (Tw/Ttot). The results from the two breaths were averaged and recorded separately in a data base for each lung and for each phase of respiration. All acoustic measurements were checked by one of the investigators (S.G.) familiar with this type of analysis.

Analysis of Results

The data were initially analyzed separately for those children in whom the pediatrician determined that the challenge was positive because the endpoint had been reached before the highest concentration of AMP had been administered, and for those in whom he determined that the challenge was negative. Since the data were normally distributed, unpaired *t*-tests and chi-square analyses were used to compare these groups. Subsequently, comparisons were made between the opinion of the pediatrician and the results of the acoustic analysis in terms of the presence or absence of wheezing for the whole group of children. Calculations were made of sensitivity, specificity, and predictive values, accepting that the presence of wheeze detected acoustically was ''truth.'' Differences were considered as significant if $P < 0.05$.

RESULTS

Endpoint Determination by the Pediatrician

The pediatrician decided that the bronchial challenge was positive in 24 children and negative in 27 children. There were no significant differences between these two groups in terms of age, sex distribution, proportion with a personal or family history of atopy, baseline respiratory rate, O_2 saturation, or heart rate (Table 1). The median (range) concentration of AMP at which the test was halted in the positive group was 25.0 (6.25–100.0) mg/ml. In this group, the mean fall in O_2 saturation at the endpoint of the challenge (Table 1) was significantly greater than that after the final step in children with a negative challenge ($P < 0.0001$). Likewise, the mean rise in respiratory rate at the endpoint of the challenge in the positive group was significantly greater than that after the final step in children with a negative challenge ($P < 0.0001$).

The endpoint of the challenge in the positive group was determined by the pediatrician hearing wheeze in 22 of 24 children (91.7%). Of these 22 children, he reported wheeze over the right lung in all 22, and over the left lung in 19. Of the children with wheeze heard over the right lung, it was heard during inspiration in 18 (81.8%) and during expiration in 20 (90.9%). Of the children with wheeze heard over the left lung, it was heard during inspiration in 15 (78.9%) and during expiration in 18 (94.7%). Unilateral wheeze at the endpoint was noted by the pediatrician in 2 of 24 children with positive challenges.

Of the 22 children in whom wheeze was heard at the endpoint, desaturation ($\geq$5% fall in SaO_2) was also present in 16, tachypnea ($\geq$50% rise in respiratory rate) in 7, and both desaturation and tachypnea in 5. In the 2 children in whom no wheeze was heard at the endpoint, the challenge was terminated by the pediatrician because of a fall in saturation of 7.1% together with a rise in respiratory rate of 55% in one child, and by a fall of saturation of 5.1% together with a rise of respiratory rate of 58% in the other.

Of the 27 children with a negative challenge, 25 reached the endpoint with no clinical wheeze, desaturation, or tachypnea. In 2 children, the pediatrician noted transient wheeze for one breath which disappeared, never to return in subsequent breaths. This occurred only at the highest concentration, and therefore the challenge was considered

TABLE 1—Comparison of Children Judged by Pediatrician to Have a Positive Challenge With Those Judged to Have a Negative Challenge[1]

	Positive challenge (n = 24)			Negative challenge (n = 27)		
Personal atopy	8			5		
Family atopy	8			9		
	Mean	Upper 95% CI	Lower 95% CI	Mean	Upper 95% CI	Lower 95% CI
Age (years)	5.0	5.5	4.4	5.0	5.6	4.4
Baseline SaO_2 (%)	98.1	98.4	97.8	98.1	99.0	97.0
Baseline RR (/min)	21.1	22.8	19.7	21.8	23.6	20.0
Baseline HR (/min)	101.5	109.4	93.6	94.4	102.0	86.8
Change in SaO_2 (%)	−5.4	−4.6	−6.3	−0.5	0.2	−1.2
Change in RR (%)	39.2	49.0	29.4	−0.2	5.7	−6.0

[1]Only significant differences were in change in saturation and respiratory rate ($P < 0.0001$). RR, respiratory rate; HR, heart rate; SaO_2, saturation.

negative. Cough was noted at the endpoint in 22 (91.7%) children with a positive challenge and 6 (22.2%) with a negative challenge, the difference being significant ($P < 0.0001$), but coughing was often heard at concentrations of AMP before wheezing or desaturation occurred. Thus, in 6 children with a positive challenge, the cough appeared 3 or more dose steps before the endpoint was reached, and in 3 children, cough was heard at one level but not at the next highest concentration.

Acoustic Findings at Endpoint Determined by the Pediatrician

In the 24 children with a positive challenge determined by the pediatrician, the mean total wheeze rate of both breath phases and both lungs together (Twz/Ttot) was 28.1% (95% CI, 19.5–36.8%), while in all but one of the children with a negative challenge, no wheeze was detected acoustically. In this child, in whom the pediatrician had also noted wheeze, there was unilateral acoustic wheezing at an AMP dose of 400 mg/ml, but the test was considered negative because the highest dose had been reached. No other acoustically determined wheezing was found in the records from children with a negative challenge, even though the pediatrician had recorded one other child as having transient wheeze at the endpoint.

The acoustic and clinical findings in the children with a positive challenge and the observations of the pediatrician are detailed in Table 2. While there were no significant differences in wheeze rates during inspiration or expiration or between the two lungs, it is obvious from Table 2 that there was considerable variability in wheezing. The mean duration of inspiration (Ti) at the endpoint in children with a positive challenge was 0.87 sec, and the mean duration of expiration (Te) was 1.27 sec. Given that the minimum duration of wheeze accepted by CORSA as detectable[13–15] is 100 msec, the average minimal detectable wheeze rate during inspiration would be 11.5% ($0.1/0.87 \times 100$), and during expiration, 7.9%. For simplicity in further analysis, it is assumed that a minimal wheeze rate of 10% was needed for detection of acoustic wheezing. From Table 2, it can be seen that acoustic wheeze rate $\geq$10% was detected in 11 of 24 children during inspiration and 17 during expiration over the right lung, and similarly in 11 and 14 children, respectively, over the left lung. Unilateral acoustic wheezing (either

TABLE 2—Individual Results of Wheeze Rates for Each Lung and for Inspiration and Expiration Separately, Together With Opinion of Pediatrician as to Presence of Wheeze Clinically for 24 Children With Positive Bronchial Challenge[1]

	Right lung				Left lung			
Patient initials	Twi/Ti (%)	MD Iw (y/n)	Twe/Te (%)	MD Ew (y/n)	Twi/Ti (%)	MD Iw (y/n)	Twe/Te (%)	MD Ew (y/n)
S.M.	71.8	y	87.8	y	71.8	y	87.8	y
F.C.	37.0	y	19.6	y	0.0	y	0.0	y
B.Y.	61.7	n	72.2	y	0.0	n	43.9	y
R.N.	46.2	y	55.1	y	62.5	y	58.7	y
B.D.	0.0	y	22.9	y	21.9	y	45.7	y
T.F.	30.0	y	0.0	y	0.0	y	55.7	y
G.R.	47.2	n	15.9	y	59.4	n	12.4	y
R.N.	0.0	y	63.5	y	30.9	y	75.7	y
W.Y.	0.0	y	52.4	y	23.1	y	63.7	y
S.N.	65.5	y	98.2	y	0.0	n	0.0	n
T.J.	0.0	n	0.0	n	0.0	n	0.0	n
N.A.	0.0	n	0.0	y	0.0	n	24.3	y
K.G.	0.0	n	0.0	y	30.3	n	30.1	y
K.M.	0.0	y	50.6	y	0.0	y	0.0	y
L.E.	0.0	y	39.7	y	47.2	y	75.5	y
S.B.	58.8	y	59.5	y	84.7	y	63.0	y
B.T.	0.0	y	52.8	y	0.0	y	0.0	y
F.C.	70.1	y	0.0	y	74.0	y	0.0	y
Y.N.	61.4	y	39.9	y	0.0	n	0.0	n
S.L.	0.0	y	39.4	y	0.0	y	0.0	y
C.G.	0.0	n	0.0	n	0.0	n	0.0	n
B.R.	0.0	y	20.1	n	0.0	n	0.0	n
G.H.	0.0	y	65.0	y	0.0	y	45.8	y
S.Y.	65.6	y	0.0	n	76.3	y	53.0	n
Mean	25.6		35.6		24.3		30.6	
+95% CI	37.6		47.8		36.7		42.9	
−95% CI	13.7		23.4		11.9		18.3	

[1]Twi/Ti, inspiratory wheeze rate; Twe/Te, expiratory wheeze rate; MD Iw, presence (y) or absence (n) of clinical inspiratory wheeze as determined by pediatrician; MD Ew, presence (y) or absence (n) of clinical expiratory wheeze as determined by pediatrician.

inspiratory, expiratory, or both) was detected in 9 children. In both children (T.J., C.G.) in whom the pediatrician determined the endpoint without clinical wheezing, the acoustic analysis also did not detect any wheeze. Of 27 children in whom the pediatrician determined that the challenge was negative, no acoustic wheeze was detected either on inspiration or expiration before the highest concentration of AMP in any child.

Comparison of Acoustic Findings With Wheeze Reported by the Peditrician

Comparisons were made of the objective measurement of wheezing by acoustic analysis with that of the pediatrician using values for a cutoff wheeze rate between 5–100% in order to calculate sensitivity, specificity, and predictive values at different cutoff levels. All measurements from both lungs of all 51 children were used for this analysis, yielding a total of 102 comparisons. The sensitivity, specificity, positive predictive value (PPV = percentage of pediatrician positive observations which were true positives acoustically), and negative predictive value (NPV = percentage of pediatrician negative observations which were true negatives acoustically) were calculated for whole breaths, inspiration, and expiration. The highest values for the sum of sensitivity and specificity (equivalent to the best value in a receiver operating characteristic (ROC) analysis) for total wheeze rate was found with a Tw/Ttot of 10%, and at this level, the sensitivity was 100% (no false negatives), specificity was 91%, PPV was 100%, and NPV was 91%. If a higher cutoff value for Tw/Ttot as ''truth'' was used, the sensitivity remained at 100% (the pediatrician was very unlikely to miss wheeze which lasted longer), but specificity fell (because the pediatrician reported wheeze even though the cutoff level had not been reached, i.e., a ''false-positive'' result), as shown in Figure 1. A similar analysis of inspiratory wheeze and expiratory wheeze separately yielded rather lower values for sensitivity (82%, 86%) and specificity (89%, 86%) with ideal cutoff values of wheeze rates up to 20%.

DISCUSSION

This study confirmed that a trained pediatrician can reliably determine the presence of wheezing by auscultation at the endpoint of a bronchial challenge in preschool children (''PCwheeze'' technique). Because the endpoint was determined by the clinician, the results could have been biased in favor of hearing wheeze, but we did employ the additional safeguards of detecting desaturation or tachypnea, and these only came into play in 2 children before wheeze was heard. Had we chosen a lesser degree of desaturation or tachypnea to indicate the endpoint, it is possible that more studies would have been halted before wheeze occurred, but we know of no data suggesting that such lesser changes would be reliable as endpoints. The incidence of physician-diagnosed wheezing at the endpoint of a positive challenge in the present study was very similar to that in two previous studies using this technique in preschool children,[8,9] but this is the first to objectively confirm the reliability of the clinical observation of wheeze with acoustic measurements. In a study in children with cystic fibrosis using a different technique to measure wheeze, Sanchez et al.[16] noted that ''wheeze detected by respirosonography was also noted on auscultation by the physician in the laboratory.''

The present study was designed to duplicate as closely as possible the manner in which the auscultation technique is performed in clinical practice, and moreover, for safety reasons, it was decided that the endpoint would be determined by the pediatrician alone using the criteria established in our previous studies.[2–4,9] It is true that we used a commercially available electronic stethoscope rather than a traditional stethoscope, but we feel it unlikely that this could have materially altered what the pediatrician heard. More problematic is the fact that the clinical impression of the breath sounds was based on 3–5 breaths from each lung, while the acoustic analysis was usually based on 2 breaths because the repositioning of the diaphragm of the stethoscope generated artifacts in the signal, thus reducing the number of breaths available for analysis. Again, we feel that this was unlikely to influence the results, because the 2 breaths were sampled randomly from the 3–5 breaths auscultated by the physician. The way in which the present challenges were undertaken also accounts for the similarity of results in comparison with the study of 146 young children with asthma (mean age, 4.3 years) by Springer et al.[9] In that study, auscultatory wheeze alone or in combination with desaturation or tachypnea appeared in 81% of children, although the incidence of desaturation ($\geq$5%) and tachypnea ($\geq$50%) in combination with wheeze was a little higher in the present study. Likewise, no adverse effects occurred in the present study, and the lowest oxygen saturation recorded was 89% (a fall of 9.2% from baseline). The major difficulty in evaluating methods for bronchial challenge tests in preschool children is that there is no absolute ''gold standard'' with which to compare them, since these children are unable to undertake tests of lung function reliably and repeatedly. We chose to use acoustically documented wheeze as our ''gold standard'' because, using the electronic stethoscope, there was no way that the pediatrician could hear a breath sound that was not recorded by the computer, and the computer could not mistake the side or breath phase. The converse is not true, and human error could cause the pediatrician to fail to detect or misinterpret the sound. There is no absolute agreement about the acoustic definition of wheeze, although Sovijarvi et al.[13–15] went a long way toward

clarifying the issue in recent reports of the European Respiratory Society Task Force for Computerized Respiratory Sound Analysis (CORSA). The definition used in the present study was even more stringent than the CORSA recommendations based on frequency and duration alone, in that we took note in addition of the phase of breathing and the mono- or polyphonic characteristics of acoustic events. This was because monophonic inspiratory continuous adventitious sounds in isolation are impossible to distinguish acoustically from stridor or even some types of vocalization originating in the region of the larynx. The fact that the cutoff wheeze rate which yielded the most positive results in comparison with the physician was 10%, approximately equivalent to a wheeze duration of 100 msec, is completely in line with the CORSA definition of minimal requirement for wheeze,[13–15] and suggests that the pediatrician was able to detect even very brief wheezing.

While the agreement between the detection of wheeze by the pediatrician and the acoustic record was good, with a sensitivity of 100% and specificity of 91%, it was not perfect. Of inspiratory acoustic wheezes, the pediatrician correctly identified the wheeze as inspiratory in 82% and mistook the phase in 18%. The results for expiratory acoustic wheeze were a little better (94% and 6%, respectively). There were also false-positive observations in which the pediatrician reported wheeze which was not apparent from the acoustic record, although this always occurred in children in whom acoustic wheeze was present at another site or phase of respiration. Why was the agreement not perfect? The respiratory belt only recorded from the chest, and could have mistimed the breath phase if there was paradoxical breathing. None of these children developed severe airways obstruction, and we have never noticed paradoxical breathing during this type of challenge. The pattern of breathing and respiratory rate in small children during bronchial challenge makes it difficult to be certain of the breath phase in every instance. It is also possible that under the pressure of the study, the pediatrician simply did not have enough time to listen carefully and time the respiration properly. It is highly unlikely that there was ''computer error'' rather than ''human error,'' because when there was no wheeze detected acoustically, there were still acoustic and Respitrace signals of the breaths seen on the computer display. We subsequently amplified and listened to each of the negative records, and in no instance was a wheeze found. While it is traditional to consider the predictive values of a challenge, we do not feel this to be particularly helpful. PPV and NPV are greatly influenced by the proportion of positive results in the population studied, which in this case was 22/51 = 43%. Different values would have been obtained had there been more or fewer children with positive challenges, even if the ability of the pediatrician to detect wheeze was unchanged.

In conclusion, in this type of bronchial challenge whose endpoint is determined by a clinician hearing wheeze, mild desaturation, or tachycardia, the very large majority of preschool children are wheezing at the endpoint of a positive bronchial challenge, and the clinical observation of wheeze agrees very well with its detection by acoustic measurement. The auscultatory (''PCwheeze'') technique for bronchial challenges in preschool children is reliable and safe when undertaken in the manner used in this and previous studies. The ability to measure wheeze by acoustic means opens the possibility for the future automatic performance of this type of bronchial challenge, which would undoubtedly be an improvement on the manual technique, provided a reliable algorithm for the detection of wheeze can be developed.

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