Characteristics and Diagnostic Significance of Wheezes During Exercise-Induced Airway Obstruction in Children With Asthma*

Simon Rietveld, MSc; and Edo H. Dooijes, PhD

The diagnostic significance of wheezes for childhood asthma has not been studied systematically (to our knowledge), even though alternative diagnostic methods are limited, especially with children too young for lung function testing. To fill this gap, tracheal sounds were continuously recorded of 70 school-aged children with and 30 without asthma during standardized physical exercise. Wheezes were digitally analyzed and compared with sound patterns previously recorded after histamine inhalation. Exercise-induced wheezes proved to be indistinguishable from sound patterns associated with histamine. The diagnostic sensitivity and specificity of any wheeze for a fall in FEV₁ greater than 20% after exercise were, respectively, 86% and 99%. The sensitivity and specificity of any wheeze for a diagnosis of asthma were, respectively, 19% and 100%. Wheezes were often audible for a short time only, making traditional (stethoscopic) detection unlikely and thereby restricting clinical diagnostic significance. This suggests that the development of automated detection techniques may be warranted.

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Key words: airway obstruction; asthma; children; diagnostics; lung sounds; physical exercise; wheezes.

Abbreviations: TFP= time-frequency plot

A

ventitious lung sounds or wheezes in children are commonly associated with exacerbations of asthma, especially after physical exercise and exertion. In the classic studies of Bangham and Loudon, significant correlations between wheezes and a fall in lung function were computed. These authors predicted that the proportion of the breath cycle occupied by wheezes corresponds to the severity of airway obstruction. Two studies proposed lung sound analysis as the method of choice for assessment of airway obstruction in children too young for lung function testing. Nevertheless, lung sound analysis as a diagnostic method found little clinical application. This may be related to the lack of information on the diagnostic implications of presence and magnitude of wheezes for (1) degree of airway obstruction and (2) the diagnosis of asthma. There is meager consensus on the statistical relationship between wheezes and lung function in contemporary research. Rietveld et al recorded tracheal sounds of asthmatic children during histamine challenge. Criteria for categorization of wheezes were established and five distinct sound patterns emerged. The presence of any of these patterns predicted a fall in FEV₁ greater than 20% in 23 of 24 children. The discriminative power of wheezes with regard to the diagnosis of childhood asthma has not been established. For adult men, Schreur et al showed that asthmatics in remission could be distinguished from normal control subjects by comparing the mean frequency distribution of digitized lung sounds.

The aim of the present study was to test the diagnostic significance of wheezes in children with and without asthma, for (1) a fall in FEV₁ greater than 20% and (2) the diagnosis of asthma. Tracheal sounds were continuously recorded of children with and without asthma during standardized physical exercise. Since the differentiation of wheezes is a traditional problem, the first step in the analysis consisted of matching exercise-induced wheezes with previously established criteria for classification into sound patterns. Exercise-induced airway obstruction is considered an indirect measure of bronchial responsiveness, and histamine-induced obstruction is considered a direct measure. Accordingly, one might find a distinction between the corresponding wheezing patterns.

Materials and Methods

Subjects

Seventy children with asthma and 30 children without asthma participated (mean age, 11.2 years; range, 7 to 17 years). There were 45 boys with and 15 without
asthma. The children enrolled via referral from general practitioners in Amsterdam or via advertisements in a local newspaper. All parents gave informed consent and the children were financially rewarded. The severity of asthma was evaluated according to the scoring system of the Dutch Society of Paediatricians, section Lung Diseases.11 The children using corticosteroids went into class 3, whereas they would have been divided over classes 3 to 5 according to the international consensus of lung physicians.12 There were 23 children with a diagnosis of severe asthma, treated with oral prednisolone, oral or inhaled corticosteroids, and bronchodilator drugs. Nine children had moderate asthma and used ipratropium bromide, sodium cromoglycate, and bronchodilators. Mild asthma was diagnosed in 38 children; they were treated with bronchodilators. All children underwent medical examination, excluding the possibility of trachea or vocal chord dysfunction. The children were requested to abstain from using bronchodilators on the day of the experiment. All children participated only once in the study, which comprised a 2-month testing period.

**Measurements**

Lung function was expressed in FEV1 and was measured with a pneumotachograph (Pneumoscreen II; Erich Jaeger; Wurtzburg, Germany). The FEV1 was measured preexercise and 5 min postexercise. Only the highest of three FEV1 trials was used for analysis.

Tracheal sounds were recorded with a system for continuous respiratory telemetry (Emco Electronics; Ascendell; the Netherlands). The hardware comprised an electret microphone in a polyester cover (range, 20 to 25,000 Hz within 3 DB), a small transmitter, receiver, and recorder (Hitachi VT-F8200), which took up to 10 h of sound on videotape. The microphone was placed over the suprasternal notch with a double-sided adhesive antiallergic ring (ARBO T08). The transmitter and battery were carried on a waist belt during the exercise task.

**Qualitative Analysis and Scoring of Wheezes**

There were two assessors, experienced in lung sound analysis, who listened independently to each of the sound records. They were free to listen as often as needed for analysis and scoring of wheezes.

The first step consisted of copying segments with wheezes and raised breath sound. The sound segments were given code numbers to allow blind rating. One by one, segments were randomly analyzed and wheezes matched with criteria for categorization into five sound patterns (see below).

The second step included listening to the original 5 min postexercise tracheal sound recording and deciding “asthma” or “no asthma.”

During the final step, the assessors scored the presence of sound patterns in each minute of sound recording.

Categorization followed only with interrater consensus. Disagreement among the assessors was settled after reanalysis of the segments and was expressed in a reliability coefficient.

**Sound Pattern Categories**

Five sound patterns emerged during a previous study2 of histamine-induced wheezes: raised breath sound and four distinct categories of wheezes. For completeness, the descriptions of these patterns are presented in Table 1.

**Signal Processing**

Sound segments of 20 s duration were digitized. The segments were prefiltered by a fourth order Butterworth analog filter with a pass band from 150 to 1,500 Hz. The segments were digitized at 7,500 samples per second by a 12 bits analog-to-digital converter (Keithley model 580), and subsequently processed with a 1,300-Hz low-pass digital filter. This signal was then downsampled by a factor 2 for data reduction. The 150-kB data of each segment were stored on the personal computer’s (80486) hard disk for analysis. The entire signal or its details could be viewed on the personal computer screen graphically while the sound was played back through a headphone. This allowed parallel qualitative and quantitative sound analysis.

Actual digital analysis was conducted with fragments of 6 to 18 s duration at a time, selected by ear from the longer segments. Overall power spectra (the amount of signal power as a function of frequency) were computed, as well as time-frequency representations. For the spectra, the Welch algorithm13 was used. Time-frequency representations were obtained by computing the spectra of a sequence of 50% overlapping frames of 137-ms duration. The resulting 257 spectral values for each frame were combined to form 32 spectral bins. The resulting collection of bin averages was arranged into a regular grid with frequency and time as the row and column coordinates, respectively. A contouring algorithm was used to plot lines of equal power in this grid, at 21 levels equidistantly chosen between zero and overall maximum power. Knowing the absolute value of the power is of no use in this work. Therefore, power was expressed in “arbitrary units” of dimension Vs−2.

**Physical Exercise Task**

Free running was selected for the exercise task because it is less stressful to children and more effective for induction of airway obstruction than home trainer or treadmill running.14,15 The children ran through the empty corridor of the university building until a heartbeat rhythm of 170 beats/min was signaled by a heartbeat-measuring device, strapped around the chest of each child (Polar Edge; Semex Medische Techniek; Nieuwegein, the Netherlands). The building was air conditioned; the temperature at 150 cm above ground level ranged from 20 to 21°C and humidity between 60 and 64%. The children were seated after exercise for 5 min of tracheal sound recording. They were instructed to breathe freely, without specific maneuvers, and to restrain from moving and talking.

**Data Analysis**

1. The children were divided into 4 groups on the basis of fall in FEV1 and group membership (>20%, ≥20%, ≥10%, and no asthma). The significance criterion was p<0.05.  
2. Power spectra and frequency-time representations of selected sound segments were computed.  
3. Wheezes were matched with the criteria for categorization into five sound patterns.

**Table 1—Characteristics and Description of Sound Patterns Recorded During Histamine-Induced Airway Obstruction**

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Raised breath sound; the pitch of the breath sound was clearly raised</td>
</tr>
<tr>
<td>2</td>
<td>Thrill sound or stridor; a high-intensity nonmusical sound, common during the forced inspiration for FEV1 assessment or in the unforced respiration during severe airway obstruction</td>
</tr>
<tr>
<td>3</td>
<td>Background buzzing with or without concomitants; this context sound was audible during or in between inspiration and expiration; it should be present in at least two consecutive respiratory cycles</td>
</tr>
<tr>
<td>4</td>
<td>Series of high-pitched rhonchi; the rhonchi should be present for at least two consecutive inspirations or expirations</td>
</tr>
<tr>
<td>5</td>
<td>Solitary rhonchus; a sudden rhonchus between or during inspiration or expiration</td>
</tr>
</tbody>
</table>
Table 2—Means and SDs of FEV₁ and Percentage of FEV₁ Predicted (%)*

<table>
<thead>
<tr>
<th></th>
<th>FEV₁</th>
<th>SD</th>
<th>%</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>2.19</td>
<td>0.75</td>
<td>92</td>
<td>14</td>
</tr>
<tr>
<td>Post</td>
<td>1.47</td>
<td>0.61</td>
<td>61</td>
<td>16</td>
</tr>
<tr>
<td>Group B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>2.22</td>
<td>0.91</td>
<td>89</td>
<td>14</td>
</tr>
<tr>
<td>Post</td>
<td>1.55</td>
<td>0.81</td>
<td>74</td>
<td>18</td>
</tr>
<tr>
<td>Group C</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>2.15</td>
<td>0.80</td>
<td>90</td>
<td>16</td>
</tr>
<tr>
<td>Post</td>
<td>2.01</td>
<td>0.17</td>
<td>84</td>
<td>17</td>
</tr>
<tr>
<td>Group D</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre</td>
<td>2.35</td>
<td>0.71</td>
<td>97</td>
<td>15</td>
</tr>
<tr>
<td>Post</td>
<td>2.27</td>
<td>0.78</td>
<td>94</td>
<td>18</td>
</tr>
</tbody>
</table>

*Separately for children with a postexerciise fall in FEV₁ >20% (group A, n=14); ≤20% (group B, n=17); ≤10% (group C, n=36), and children without asthma (group D, n=30). Pre=preexercise; Post=postexercise.

4. Sound patterns were scored as present or absent in minutes of sound recording.
5. The dependence between sound patterns and a fall in FEV₁ greater than 20% was tested with Pearson’s χ² and the phi association coefficient. Diagnostic sensitivity and specificity percentages were calculated.
6. The sound records were judged to be associated either with asthma or no asthma. Diagnostic sensitivity and specificity percentages were calculated.
7. The interrater reliability was tested using Cohen’s kappa criterion.

RESULTS

Lung Function

The preexercise lung function of 3 children did not allow physical exercise (FEV₁ <55% of predicted) leaving 67 asthmatic children for further investigation. Fourteen children (21%) achieved a fall in FEV₁ greater than 20% after exercise (group A) and another 17 children (25%) a fall between 10% and 20% (group B). Most children with asthma did not achieve airway obstruction (group C) and neither did children without asthma (group D). The lung function data are summarized in Table 2.

Signal Analysis

Various phenomena can be observed in the time-frequency plots (TFP, defined in the previous section).

Table 3—Total Number (#) and Percentage (%#) of Wheezes Categorized Into Sound Patterns, and Total Number (ch) and Percentage (%ch) of Sound Patterns Observed in Children*

<table>
<thead>
<tr>
<th>Sound Pattern</th>
<th>#</th>
<th>%#</th>
<th>ch</th>
<th>%ch</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>7</td>
<td>7</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>22</td>
<td>23</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>4</td>
<td>38</td>
<td>40</td>
<td>5</td>
<td>7</td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>30</td>
<td>4</td>
<td>6</td>
</tr>
</tbody>
</table>

*Here and in the tables to follow, sound pattern 1 has been abandoned.

Figure 1 is derived from a baseline recording from a girl subject A with severe asthma. In the baseline plot, the spectrum extends over the full measurement range, corresponding to the white-noise-like quality of the sound. Notice, however, the relatively narrow-band and short-duration “satellites,” that indicate the presence of wheezes even in the preexercise stage. In the postexercise plot (Fig 2), the signal power appears to be restricted to a 600-Hz wide band, typical for sound pattern 3. It is all but impossible to discern the respiration cycle in this plot.

Figure 3 is a snapshot taken from subject B, a boy with severe asthma, 4 min postexercise. In this case, high-pitched wheezes at approximately 650 and 980 Hz dominate the sound pattern, which was rated to belong to classes 3 and 4. In Figure 4, the corresponding power spectrum is shown. The peaks visible herein approximately correspond to the observed wheezing pitches and suggest a harmonic relationship between them (the frequency ratio of the relevant spectral peaks being about 1:2:3). Unlike the TFP, this plot obscures the fact that these harmonically related components do not necessarily occur at the same time. This observation could be of importance for the physical explanation of the phenomena.

In Figure 3, a pattern of activity is observed around 200 Hz, which is explained by the presence of some background noise, probably generated by the air-conditioning system. This type of disturbance can be expected in recordings taken under real-life conditions.

Notice the slight differences in time duration between the TFPs, resulting in a relative horizontal compression of the contour patterns in the longer-duration plots.

Diagnostics

Wheezes and raised breath sounds from recordings of 97 children were matched with the criteria for categorization into 5 sound patterns. A total of 156 distinct sounds was matched with the criteria for categorization, 60 segments with a raised pitch and 96 with wheezes. The raised breath sound (sound pattern 1) was not easy to distinguish from postexercise sighing and its rating was the subject of interrater disagreement. The sound pattern was lacking strict criteria and hence was excluded from further analysis. All 96 wheezes matched with criteria for categorization into the four remaining sound patterns (Table 3). The only disagreement among the raters occurred when different types of wheezes were audible simultaneously, eg. series of high-pitched ronchi with background buzzing.

Sound peculiarities not fitting the existing criteria were observed only in two children who were excluded from exercise because of severe airway obstruction.
One boy with 30% FEV1 of the predicted value presented a soft squeaking and another boy with 52% FEV1 of predicted presented a moist, “sticking” sound of low frequency.

Wheezes in the children who finished the exercise usually commenced 2 to 3 min after running and faded before the fifth minute. Since a maximum fall in lung function would be expected after 5 min, this observation emphasized a temporal distinction between the commencement of wheeze and a fall in lung function. The solitary rhonchi (sound pattern 5) were observed over a wide range of time, shortly after running in some children and 10 min after running in others. The thrill sound or stridor (sound pattern 2) was observed in 4 children during forced inspiration for postexercise FEV1 assessment.

Wheezes were present in the sound records of 13 children, 12 with a fall in FEV1 greater than 20% (86% of all children with a fall in FEV1 >20%) and 1 with a fall of 16% (7%); this child had a solitary rhonchus (sound pattern 5). A raised breath sound (pattern 1) was audible in the 2 children with no wheezes during a fall in FEV1 greater than 20%. Wheezes were not observed in sound records of children without asthma (Table 4).

The dependency calculations between individual sound patterns and a fall in FEV1 greater than 20% were not significant. The sensitivity of the individual sound patterns for a fall in FEV1 greater than 20% was 29 to 36% and the specificity was 98 to 100%. The sensitivity and specificity of the sound patterns together, that is for any wheeze, were 86% and 99%, respectively. The results are presented in Table 5.

Of the 97 sound records, both raters correctly judged 13 to be associated with asthma (19%) and

![Figure 1. TFP, subject A, sample e4712g, baseline recording. The lower portion of the diagram represents the instantaneous signal power in arbitrary units.](image-url)

### Table 4—Presence of Sound Patterns*

<table>
<thead>
<tr>
<th>Group</th>
<th>sp2</th>
<th>sp3</th>
<th>sp4</th>
<th>sp5</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>4</td>
<td>4</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>B</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>C</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>D</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*Separately for children with a fall in FEV1 >20% (group A, n=14), ≤20% (group B, n=17), ≤10% (group C, n=36), and children without asthma (group D, n=30). sp=sound pattern.
these were all records with audible wheezes (Table 3). Finally, Cohen's kappa was 0.86 (p=0.013).

**DISCUSSION**

Tracheal sound analysis revealed that wheezes recorded after physical exercise resembled sound patterns associated with histamine-induced airway obstruction. The wheezes were similar in frequency distribution and timing. Sound patterns of wheezes were present in 12 of 14 children with significant airway obstruction and in 1 child with moderate obstruction. This demonstrated that wheezes were sensitive symptoms of exercise-induced airway obstruction. Wheezes were never observed in children without airway obstruction, hence showing perfect specificity. Lack of significance among the dependency computations between sound patterns and lung function was obviously related to the small number of individual sound patterns observed. Confirmation of a diagnosis of asthma by means of auditive sound analysis was successful only when wheezes were present.

Simple statistics (percentiles of the power distribution, for instance) derived from individual power spectra did not contribute to the discrimination between asthmatics and normal control subjects; visual inspection of time-frequency diagrams did, however. The presence of wheezes was not sufficiently sensitive for a diagnosis of asthma, although very specific. Intensity of wheezes was irrelevant for the diagnostic significance. Soft background buzzing (sound pattern 3) was equally informative as loud high-pitched wheezes or a combination of wheezes. These results highlighted the diagnostic information from wheezes: presence of any wheeze implied moderate and probably significant airway obstruction and a diagnosis of asthma. The absence of wheezes provided a less clear

<table>
<thead>
<tr>
<th>Sound Pattern</th>
<th>%1</th>
<th>%2</th>
<th>$\chi^2$</th>
<th>p</th>
<th>phi</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>29</td>
<td>100</td>
<td>2.22</td>
<td>0.19</td>
<td>0.47</td>
</tr>
<tr>
<td>3</td>
<td>29</td>
<td>100</td>
<td>2.04</td>
<td>0.23</td>
<td>0.38</td>
</tr>
<tr>
<td>4</td>
<td>36</td>
<td>100</td>
<td>3.02</td>
<td>0.13</td>
<td>0.38</td>
</tr>
<tr>
<td>5</td>
<td>29</td>
<td>98</td>
<td>2.04</td>
<td>0.23</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*With respect to an alpha level of p=0.05, none of these statistics are statistically significant, a consequence of the small number of observations per individual sound pattern. Also, sensitivity percentage of children with presence of sound pattern and a fall in FEV$_1$ >20% (%1) and specificity percentage of children with absence of sound pattern with a fall in FEV$_1$ <20% (%2). Statistics calculated over all subjects.
picture, although it probably indicated no airway obstruction. Wheezes were often only audible for short periods of time, making traditional (stethoscopic) detection unlikely and thereby restricting the clinical diagnostic significance. The development of automated detection techniques may be warranted. A follow-up project will be dedicated to this issue.

A raised breath sound was abandoned as a diagnostic sound pattern. The specificity was insufficient and the raters disagreed about many records. Although Pardee et al.\textsuperscript{10} observed fairly good interrater agreement for sound intensity, the rating of breath sounds without clear criteria seems unreliable, especially with children sighing after running. The inspiratory and expiratory wheezes in the study were not separately scored, in view of the robust correlations found between inspiratory and expiratory sound patterns in a previous study.\textsuperscript{7} Differentiating between inspiration and expiration sounds, especially during postexercise sighing, can also be very difficult. Because inspiratory and expiratory sound patterns possibly refer to differences in pulmonary abnormalities (central vs peripheral airway obstruction), the legitimacy of averaging inspiratory and expiratory sound patterns remains questionable.\textsuperscript{17}

Only a minority of children achieved airway obstruction after exercise. Anderson et al.\textsuperscript{18} reported that 89% of asthmatic children achieved a fall of more than 10% in lung function after bicycle riding; other researchers reported likewise.\textsuperscript{19-21} The modest percentage of exercise-induced obstruction in the present study was possibly related to medication or test circumstances. The children were requested to abstain from using bronchodilators before exercise but this could not be checked. The circumstances during the task were optimal with regard to temperature and humidity.

The expected peak of exercise-induced airway obstruction is 3 to 5 min postexercise.\textsuperscript{14,15} In the current study, wheezing never commenced in the fifth minute postexercise. Although recording was continued until after posttest FEV\textsubscript{1} assessment, this period would not have provided additional information with regard to the aims of the study.

In several studies,\textsuperscript{22-24} it has been emphasized that wheezes are common in the general population or that subjects can provoke wheezes themselves. However, this was not confirmed in the present study: children without asthma simply did not wheeze.

The following discussion pertains to the digital analysis of the recorded sounds. In their laboratory
Figure 4. Power spectrum corresponding to the signal shown in Figure 3.

experiments, Schreur et al. have used the instant of maximum airflow (as measured by a spirometer) as a point of reference for determining the timing of wheezes in the course of a respiration cycle, and for the purpose of averaging many cycles to obtain a stable spectrum. In the present study, where only a sound signal was recorded, this was not possible. However the cycle boundaries can be determined rather accurately by detecting the instants of minimal activity in a TFP. Moreover it is readily observed that there exists an appreciable variability in cycle duration, especially in the postexercise plots, making the validity of the averaging approach questionable.

A possible objection against this detailed frequency-time plot representation is that it might emphasize statistically irrelevant events. The authors' point of view is, however, that it is just this type of events that can contribute to the physical understanding of the sound patterns under study. Generally speaking, techniques that are not based on any physical model, like averaging followed by the determination of simple statistics, such as mean and variance, are liable to mask vital information from the available data. Before statistics can be meaningfully applied, a model giving a rough explanation of the structures observed has to be constructed. Certainly much work has to be done toward attaining this goal and improving the diagnostic applicability of digitized sounds.

The problems with the quantified information from power spectra stimulate development of new methods for lung sound analysis, possibly using self-learning systems for identifying the relevant features of the pulmonary sounds. Finally, it would be necessary to compare wheezes during induced airway obstruction with wheezes during spontaneous exacerbations of asthma.

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