■ REVIEW ARTICLE ■

Review Series: Non-Invasive Monitoring of Airway Inflammation in Asthma

Lung Sounds in Bronchial Asthma

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ABSTRACT

Modern understanding of lung sounds started with a historical article by Forgacs. Since then, many studies have clarified the changes of lung sounds due to airway narrowing as well as the mechanism of genesis for these sounds. Studies using bronchoprovocation have shown that an increase of the frequency and/or intensity of lung sounds was a common finding of airway narrowing and correlated well with lung function. Broncho-provocation studies have also disclosed that wheezing may not be as sensitive as changes in basic lung sounds in acute airway narrowing.

A forced expiratory wheeze (FEW) may be an early sign of airway obstruction in patients with bronchial asthma. Studies of FEW showed that airway wall oscillation and vortex shedding in central airways are the most likely mechanisms of the generation of expiratory wheezes. Studies on the genesis of wheezes have disclosed that inspiratory and expiratory wheezes may have the same mechanism of generation as a flutter/flow limitation mechanism, either localized or generalized.

In lung sound analysis, the narrower the airways are, the higher the frequency of breathing sounds is, and, if a patient has higher than normal breathing sounds, i.e., bronchial sounds, he or she may have airway narrowing or airway inflammation. It is sometimes difficult to detect subtle changes in lung sounds; therefore, we anticipate that automated analysis of lung sounds will be used to overcome these difficulties in the near future.

KEY WORDS

airflow limitation, asthma, lung sounds, physical examination, wheeze

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INTRODUCTION

The stethoscope was introduced by Laennec almost 200 years ago, and, since then, the relationship between the sounds heard in the chest and the pathological changes in the lungs and airway has become apparent. Bronchial asthma is one of these pathological conditions. The increasing understanding of lung sounds permits a more practical use of the stethoscope in the treatment of bronchial asthma in clinical practice, without replacing new diagnostic tools.[1,2] Auscultation of the chest offers vital and real time information on the pathophysiology of airways readily and is an optimal tool for monitoring rapidly fluctuating diseases, such as bronchial asthma.

Modern understanding of lung sounds started with a historical article by Forgacs.[1] He suggested the same problems, including the terminology of adventitious lung sounds, as we have today. He defined and described the clinical implications and scientific bases for the genesis of lung sounds.

In his article, Forgacs divided wheezes, the best known signs of airway obstruction, into two categories, monophonic and polyphonic. He reported that single and multiple monophonic wheezes were characteristic clinical signs of asthma and polyphonic wheezes were common signs of "all" varieties of chronic obstructive pulmonary disease (COPD). This is a landmark article, but some consideration of the time of its publication is required.

Forgacs' work was published in 1978. At this time, there was no wide agreement on the definitions and classification of COPD,[3] and most pulmonary physicians understood that COPD included emphysema, chronic bronchitis, and even bronchial asthma. Asthma was then defined as a "condition of subjects with widespread narrowing of the bronchial airways, which changes its severity over short periods of time

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Table 1 Nomenclature of lung sounds

1, Breath sounds
    1) vesicular breath sounds
    2) bronchial breath sounds
2, Adventitious sounds
    1) continuous adventitious sounds
        (1) wheezes (high-pitched)
            polyphonic wheezes
            monophonic wheezes
        (2) rhonchi (low-pitched)
    2) discontinuous adventitious sounds
        (1) fine crackles
        (2) coarse crackles
    3) Others
        friction rub, Hamman's sign.

Adapted from Reference 7 and reorganized as in References 1 and 50.

either spontaneously or under treatment." There was no description of airway inflammation. Until the mid-1980s, asthma was not recognized as a bronchial inflammatory disease. Bronchial asthma is now recognized and defined as a chronic inflammatory disorder of the airways.[4-6]

Thus, polyphonic wheezes in Forgacs' article[1] should not be considered to be characteristic of lung sounds in subjects with COPD in the present-day concept. Another problem concerning wheezes is that it is difficult to differentiate multiple monophonic wheezes from polyphonic wheezes either by auscultation or by sound spectrographic analysis despite the advanced computerized analysis of lung sounds that is available today. These are minor points, but they should be considered when reading this historical article.

NOMENCLATURE OF LUNG SOUNDS

Forgacs' suggestion on the terminology regarding adventitious lung sounds was precise. An international agreement was partially reached at an International Symposium on Lung Sounds held in Tokyo in 1986[7] (Table 1). Continuous adventitious sounds were divided into high-pitched (wheezes) and low-pitched (rhonchi) ones. Unfortunately, even after this international agreement, the lung sound terminology used by physicians and co-medical personnel continued to lack uniformity and acceptability.[8-10]

In this review, vesicular breath sounds are breath sounds that are mostly inspiratory sounds with a soft quality. Bronchial breath sounds are those that have a prominent expiratory component and harsher quality.[11,12] Wheezes are continuous adventitious lung sounds and are divided into polyphonic and monophonic ones.[1,13] Rhonchi are low-pitched continuous adventitious sounds, but the definition of this term remains controversial. The implication of these terms in

the management of bronchial asthma will be discussed.

BRONCHOPROVOCATION TESTS AND LUNG SOUNDS

In 1983, Charbonneau *et al.* recorded and analyzed tracheal sounds in normal and asthmatic subjects and showed that there was a difference of flow-dependent sound spectra between normal and asthmatic subjects.[14] During the 1990s, many lung sound studies using bronchoprovocation tests were conducted to clarify the effects of bronchoconstriction on lung sounds. In most studies, methacholine (MCh), acetylcholine (Ach), or histamine (His) are used to induce bronchoconstriction (Table 2). Acetylcholine (Ach) and MCh mainly act on trachea, and His acts mainly on bronchi.[15]

Anderson *et al.*[16] found that, for a decrease in FEV 1 of 20%, the median frequency of breath sound (F50) increased by 80 Hz in the absence of wheezes. Using computerized lung sound analysis (LSA), Beck *et al.*[17] reported that wheezes were detected by LSA at a half concentration of His of PC20 (the provocation concentration of a bronchoconstrictive agent that produces a 20% fall in FEV1) in five out of six children of age 9 years or older. In six children (age 2 to 5 years), wheezing was detected at a His concentration of 25 to 50% to that of the producing symptoms (cough, subjective wheeze, and chest tightness). Malmberg *et al.*[18] found that the percentage of decrease of FEV1 at PC15 (the provocation concentration of a bronchoconstrictive agent that produces a 15% fall in FEV1) correlated well with the percentage of increase of F50 of expiratory breath sounds by lung sound (= chest wall sound) (r = 0.865) and tracheal sound analysis (TSA) (r = 0.888) in asthmatic children. The decrease of FEV1 at PC15 corresponded to an increase of 8% in expiratory F50 in LSA in asthmatic children. Malmberg *et al.* pointed out that this computerized LSA or TSA during PC15 measurement was applicable to asthmatic children and did not require considerable cooperation, and this bronchial challenge testing with LSA or TSA will be clinically suitable in young children. They also studied adult asthmatics and reported similar findings. The increase of F50 during His challenge was significantly larger in asthmatics than in healthy control subjects. They concluded that a change of F50 in LSA or TSA had good sensitivity and specificity to detect acute airway obstruction.[19] These bronchoprovocation studies using His confirmed that airway narrowing caused an increase of frequency of breath sounds.

Rietveld *et al.*[20] raised the possible efficacy of sound pattern recognition of wheezes during His challenge for detection of airway obstruction. Spence *et al.*[21] reported that wheezing was not heard until FEV1 had fallen by a mean of 35% by the MCh chal-

Table 2 Summary of lung or tracheal sound in bronchoprovocation tests

Author (Ref.)	Year	Bronchocon-stricting stimuli	Subjects (number)	Method: provocation method/sound source	Important findings
Anderson[16]	1990	Histamine	Adult asthmatics (5)	PC20/LSA	F50 increased by 80 Hz at PC20 in the absence of wheezes.
Beck[17]	1992	Histamine	Asthmatic children (12)/control (6)	PC20/LSA	Wheezes were detected at 25% to 50% of the His concentration of PC20 or of producing symptoms.
Malmberg[18]	1994	Histamine	Asthmatic children (11)	PC15/LSA, TSA	% decrease of FEV1 at PC15 correlated with % increase of F50 in LSA and TSA. Decrease of FEV1 at PC15 corresponded with the 8% increase of F50 in LSA.
Malmberg[19]	1994	Histamine	Adult asthmatics (12)/control (6)	PC15/LSA, TSA	% decrease of FEV1 at PC15 correlated with % increase of F50 in LSA and TSA. Decrease of FEV1 at PC15 corresponded 30% increase of F50 in TSA.
Rietveld[20]	1994	Histamine	Asthmatic children (29)	PC20/TSA	Five sound patterns: Increase of pitch, stridor, background buzzing, wheeze (rhonchus), and short wheeze (or rhonchus) indicate airway obstruction.
Spence[21]	1992	Methacholine	Adult asthmatics (6)	PCwheeze/TSA	An audible wheeze appeared after a mean fall in FEV1 of 35%, but the level was not reproducible within patients.
Bohadana[22]	1994	Acetylcholine/carbachol	Asthma (3), Allergic rhinitis (3)	PC20/LSA	Inspiratory breath sound recorded at the lung base decreased markedly at the end point of challenge and reverted completely by salbutamol.
Schreur[23]	1994	Methacholine	Adult asthmatics (9)/control (8)	PC20, PC40/LSA	At similar levels of obstruction, both the pitch and the change in sound intensity with airflow were higher in asthmatics than in normal subjects.
Spence[25]	1996	Methacholine	Adult asthmatics (8)	Symptom-limited Mch challenge/LSA	Expiratory wheeze was observed when airflow limitation was reached. Inspiratory wheeze was observed when the mid- and maximal flow rate was reached.
Pasterkamp[26]	1997	Methacholine	Asthmatic children (15)/control (9)	PC20/LSA (7points), TSA	Decrease in power at low frequencies during inspiration and increase in power at high frequencies during expiration were noted when FEV1 decreased.
Habukawa[27]	2010	Methacholine	Asthmatic children (32)	Astograph/LSA	%change of highest frequency of inspiratory breath sound correlated with rate of increase of respiratory resistance in response to MCh.
Shreur[29]	1996	Antigen	Adult asthmatics (8)	Monitor FEV1/LSI	The change of LSI, frequency content, and extent of wheezing were more prominent in EAR than in LAR despite matched values of FEV1.

PC20 (15, 40), provocative concentration at which FEV1 decreased by 20% (15, 40%); LSA, lung sound (= chest wall sound) analysis; F50, median frequency of breath sound; TSA, tracheal sound analysis; PCwheeze, provocative concentration at which wheeze was induced; LSI, lung sound intensity; EAR, early asthmatic response; LAR, late asthmatic response.

lenge test. In two of their challenges, wheezing was not detected even though the FEV1 fell by 55% and 61% from the baseline. They speculated that FEV1 was dependent on the narrowing of many airways but wheezing required only a critical degree of narrowing in a solitary bronchus.

Bohadana *et al.*[22] reported that inspiratory breath sounds recorded at lung base decreased markedly at the end point of challenge and were completely reverted by salbutamol. Their observation differs from those in other reports,[16-21] which suggested an increase of pitch or intensity of lung sounds in bronchoprovocation tests. The subjects in the study by Bohadana *et al.* were all non-smokers, and the comobidity of emphysema was an unlikely explanation. They speculated that basal airway closure and air

trapping might reduce a regional airflow and produce a noticeable decrease in inspiratory breath sounds. This speculation is possible because, in other reports,[16-20] lung sounds were recorded in the upper anterior chest wall, while Bohadana *et al.* analyzed breath sounds recorded at the lung base.

Shreur *et al.*[23] reported that, at similar levels of airway obstruction, changes in both the frequency and intensity of sound with airflow were higher in asthmatics than in normal subjects. They also found that wheezing was more prominent in asthmatics than in normal subjects. This is the first study in which lung sound characteristics while using airflow and volume standardized sound analysis were examined during acutely induced airways obstruction. These findings suggest that lung sounds in asthmatics do not simply reflect the degree of airway obstruction and that changes in their breath sounds are exaggerated. Morphological changes in asthma, such as increased airway wall thickness,[24] may enhance airflow limitation even at a similar change in FEV1.

Spence *et al.*[25] disclosed a different mechanism of expiratory and inspiratory wheezes by MCh challenge. They found that the severity of airflow limitation at the onset of wheezes was very variable and sometimes wheezing did not occur despite substantial reductions in FEV1. They also found that expiratory wheezing was observed when airflow limitation was reached. Inspiratory wheezing was observed when mid and maximal flow rate was reached (Fig. 1). They carefully suggested that their observation might differ from the bronchoconstriction of asthma because MCh acts directly on the smooth muscles of central airways while asthmatic bronchoconstriction affects airways in a certain diameter range.

Pasterkamp *et al.*[26] analyzed lung sounds at seven points on the chest wall and also at the trachea. Airway narrowing induced by MCh was accompanied by significant changes in chest wall sounds but not in tracheal sounds. In chest wall sounds, a decrease in power at low frequencies during inspiration and an increase in power at high frequencies during expiration were noted when FEV1 decreased by less than 10% from the baseline and were fully reversed after inhalation of salbutamol. Although MCh is known to constrict central airways, the findings of Pasterkamp *et al.* indicate that tracheal sound may not be a sensitive indicator of bronchoconstriction induced by MCh in asthmatic children.

Habukawa *et al.*[27] found that a change in the highest frequency of inspiratory breath sound (HFI) and expiratory breath sound (HFE) corresponded with changes in the forced expiratory parameters, FVC, FEV1, $\dot{V}_{50}$, and $\dot{V}_{25}$. The rate of increase of the change of FEV1 correlated with the rate of increase of respiratory resistance by MCh challenge. HFI and HFE could be used to evaluate severity and response to treatment in the management of children with
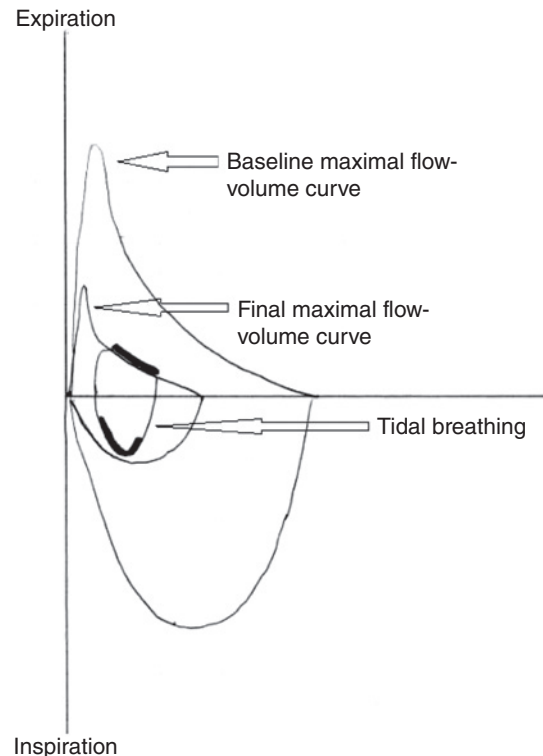

Fig. 1 Schematic drawing of flow-volume curve and timing of wheezing (thick lines) during expiration and inspiration after MCh bronchoprovocation challenge. Expiratory wheeze was observed, while tidal breathing flow-volume curve contacted with the final maximal flow-volume curve, implying that wheeze occurred at expiratory flow limitation. Inspiratory wheeze was observed at maximal flow rates were achieved. There was no contact of inspiratory tidal breathing and the inspiratory final maximal flow-volume curve (Adapted and redrawn from Reference 25).

asthma.[28]

Shreur *et al.*[29] found that, during allergen-induced asthmatic response, lung sound intensity (LSI), frequency content, and wheezes were more prominent during a late asthmatic response (LAR) than in an early asthmatic response (EAR). They suggested that LSA was sensitive for the detection of differences in the pathophysiology of airway narrowing in asthma. This finding is in accordance with those in their previous study,[23] which proved the presence of more prominent change of lung sounds in asthmatic subjects than in normal subjects at a similar level of airway obstruction.

These bronchoprovocation studies (Table 2) suggested that an increase of pitch or intensity of lung sounds was common, as was an early finding of airway narrowing. The changes in these sound parameters not only correlated well with forced expiratory parameters in lung function tests but may also reflect pathological changes in the airway. Wheezing is ex-

Table 3 Summary of forced expiration on lung or tracheal sound

Author (Ref.)	Year	Subjects (number)	Method: sound source/ measurement	Primary findings
Kraman[30]	1983	Normal subjects (N) (10)	Mouth sound + LSA (7 points)/ sound analysis	FEW assumed to have come from the same larger airway. Theoretically EPP can be the sound source.
Gavriely[31]	1987	N (6)	TSA/Ptp, flow-volume curve	Flow limitation suggested by sudden change of Ptp preced the onset of FEW. (Note: Please check "preced" and change as appropriate.)
Charbonneau[34]	1987	N (32)	TSA/flow-volume curve	Shape of flow-volume curve affected on-set of FEW.
Gavriely[32]	1989	N (6)	TSA/Ptp, flow-volume curve	Negative Ptp must exist in addition to flow limitation before FEW can be generated.
Beck[33]	1990	N (6)	TSA/Ptp, flow-volume curve	FEW was reproducible and supported the flutter theory as the mechanism of FEW generation.
Shreur[35]	1994	N (8)/Asthma (8)	LSA (3 points)/flow monitoring	Lung sounds were lower in intensity and higher in pitch in asthmatics than in controls.
Fiz[36]	1999	N (15)/Asthma (17)	TSA/effect of bronchodilator	Asthmatics showed more decrease in frequency of FEW at lower expiratory flow than that of control subjects.
Fiz[37]	2002	N (15)/Asthma (16)/ COPD (6)	TSA/automated wheeze analysis	The number of wheezes and percentage of polyphonic wheezes were more frequent in obstructive lung diseases.
Pochektove[38]	2009	N (124)/Asthma (149)	TSA/flow monitoring, body size	Duration of FEW >1.8 sec. was a sensitive index of bronchial obstruction.
Korenbaum[39]	2009	N (54)	TSA/FEW frequency for time domain	The frequency of FEW at sequential time domains fitted with the model of vortex shedding of the bronchial tree.
Korenbaum[40]	2010	N (25)	TSA + LSA-gas mixtures/% spectral similarity	The localization of the FEW source was dependent on the gas density being more distal for heavier gas.
Dynachenko[41]	2011	N (25)	TSA + LSA-gas mixtures/oscillatory acceleration	FEW was gas density-dependent. Thus, vortexes inside the trachea or close to it are the basic mechanisms of FEW.

LSA, lung sound (= chest wall sound) analysis; TSA, tracheal sound analysis; FEW, forced expiratory wheeze; EPP, equal pressure point; Ptp, trans-pulmonary pressure = Pao-Pes, while Pao; airway opening pressure, Pes esophageal pressure.

pected to be a sensitive indicator of childhood asthma. However, wheezing may not be as sensitive as changes of basic lung sounds, especially in the case of acute airway narrowing in adult asthmatic subjects. More care is required concerning the changes of basal lung sounds as a sensitive indicator of airway narrowing than listening exclusively to wheezes.

FORCED EXPIRATION AND LUNG SOUNDS

Studies using forced expiratory maneuvers and inducing forced expiratory wheezes (FEWs) have analyzed the genesis of wheezing and also tested these procedures for their effectiveness in the detection of airway obstruction (Table 3).

Kraman[30] surmised that each time a FEW was produced, it came from the same airway. Gavriely and colleagues[31-33] measured trans-pulmonary pressure (Ptp) and defined the condition when FEW was pro-duced. Flow limitation suggested by sudden decrease of Ptp preceded the onset of FEW and negative Ptp must exist before FEW could be generated. This phenomenon supported the flutter of airway wall as a feasible mechanism for the generation of wheezing. They also suggested that, during a forced expiratory maneuver, the choke point moves peripherally, and the airway becomes smaller with thinner and softer walls. Reductions in the airway diameter and wall thickness increase the oscillatory frequency, while softer walls decrease the frequency. Thus, the frequency of wheezes tends to change in an inconsistent manner as exhalation proceeds. These findings are important clinical characteristics of wheezes because a stridor, another continuous adventitious sound, shows little fluctuation in frequency.

Charbonneau et al.[34] used the shape in the flow-volume curve to approach FEW and found that the sharp peak and the triangular shape of a flow-volume

curve were more likely to be associated with FEW. Those two different shapes of the flow-volume curve had different timing of generation of FEW, although the clinical implication of these findings is yet to be determined. Shreur *et al.*[35] compared the lung sounds of normal subjects and stable asthmatic patients during standardized quiet breathing and during forced maneuvers. They found that FEW differed little between normal and asthmatic subjects but lung sounds were lower in intensity and higher in pitch in asthmatic than in control subjects, suggesting that the airways of asthmatic patients are different from those of normal subjects even when asthmatic patients are asymptomatic. Fiz *et al.*[36] compared the effect of a bronchodilator on FEW between asthmatics and normal controls. A greater decrease of the frequency of FEW was noted in asthmatics than in normal controls. By computer analysis of lung sounds, which compared FEW in bronchial asthma, COPD, and normal control subjects, they found a linear inverse relationship between FEV1% (% FEV1/FVC) and the log of the wheeze number among all examined subjects.[37]

Recently, Korenbaum and colleague[38] reported that the duration of FEW >1.8 sec. was a sensitive index of bronchial obstruction. They found that this discriminating index was most powerful when the wheeze duration was divided by the squared chest circumference (sensitivity, 93%; specificity, 85%). They further analyzed the frequency of FEW at sequential time domains and concluded that the generation of FEW may be fitted with a model of vortex shedding in the bronchial tree.[39] They also used mixed gas to localize the source of FEW in their subsequent experiments. They used three different gases, i.e., air, helium-oxygen, and krypton-oxygen, and tried to localize the source of FEW. In their studies, the sound source was dependent on the gas density being more distal for heavier gases.[40] They also reported that FEW recorded on the trachea was gas density-dependent, although FEW recorded on the chest wall did not change by the gas density and concluded that vortices inside the trachea or close to it are the basic mechanisms of FEW.[41]

These studies using FEW disclosed that airway wall oscillation and vortex shedding in central airways are possible mechanisms for the generation of expiratory wheeze. FEW may also be useful as an early sign of airway obstruction in patients with bronchial asthma as well as in COPD patients. The author of this review uses FEW as a sensitive and easy-to-perform bedside procedure to detect subtle bronchial narrowing. Further studies will be necessary to clarify FEW as a reliable and useful clinical procedure.

MECHANISM OF WHEEZE GENERATION

Studies using FEW as a tool to understand the mechanism of wheeze generation indicated flow limi-

tation as a necessary condition to produce wheezes, as defined by Ptp.[30-34] Although these studies suggested vortex shedding[39-41] and airway wall oscillation as possible mechanisms of wheeze generation,[30-34] more direct evidence is required to determine the mechanisms of wheeze generation.

Akasaka *et al.*[42] inserted a small microphone in the bronchi of patients with asthma during their asthmatic attack and demonstrated the frequency range of wheezing and their frequency resonances. They also found that there was a good correspondence between wheezing sounds picked up inside the bronchial tree and those recorded on the chest wall.

Gavriely *et al.*[43] analyzed wheezes and compared their spectral shape, mode of appearance, and frequency range with theoretical predictions of five theories of wheeze production: 1) turbulence-induced wall resonator, 2) turbulence-induced Helmholtz resonator, 3) acoustically stimulated vortex sound (whistle), 4) vortex-induced wall resonator, and 5) fluid dynamic flutter. Predictions by theories 4 and 5 matched the experimental observations better than the previously suggested mechanisms. Gavriely *et al.* introduced collapsible tubes as an experimental model of airway collapse and generation of wheezes and measured the pressure-flow relationships and tube wall oscillation.[44] They compared these data with predictions of the fluid dynamic flutter theory and determined that the vortex-induced wall vibration mechanism and viscid flutter in a soft tube were the most probable mechanism for the generation of oscillation and, thus, a possible mechanism of respiratory wheezes.

Gavriely tried further to clarify the mechanism of generation of inspiratory wheezes using a theoretical model simulation.[45] He calculated trans-mural pressure (Ptm) of airways according to the distance from the alveolar space and airway opening for four different "tube-laws" (normal, constricted, stiff, and floppy). He found that negative Ptm can be induced in constricted airways during inspiration and that intra-thoracic wheezes were generated by the same flutter/flow limitation mechanisms as expiratory wheezes. This theoretical model is in accordance with their findings in collapsible tube experiments.[44] Although the timing of the generation of an inspiratory wheeze is different from that of an expiratory wheeze, as Earis and colleagues[25] reported, it may have the same mechanism of generation as the flutter/flow limitation mechanism. Some localized expiratory wheezes, which are heard only in a limited locus on the chest wall, may also have the same flutter/flow limitation mechanism.

WHEEZING AND RHONCHI

Wheezes are continuous musical pulmonary sounds 1) and have sinusoidal wave appearance on time expanded waveform analysis 2) (Fig. 2). Wheezes gen-
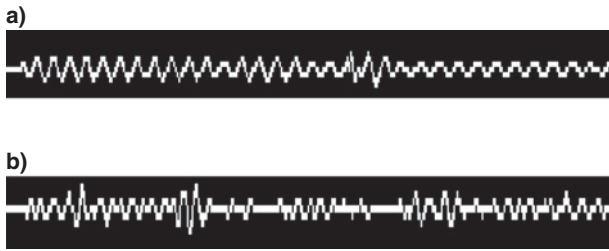
a)

b)

Fig. 2 Amplitude versus time plots of wheezes (**a**) and rhonchi (**b**) by time-expanded wave-form analysis. Tracing of wheezes is recognized as continuous sinusoidal curves, although the amplitude and frequency may change a little, as seen in the middle of trace (**a**). Tracing of rhonchi is recognized as irregular partially continuous delta waves, as seen in trace (**b**).

erally produce a well-defined small number of peaks in the power spectrum with variable frequency ranges[13,20] (Fig. 3). Wheezes with a single peak or with the harmonics of a single basal peak are called monophonic wheezes, and those with variable peaks that differ in harmonics are called polyphonic wheezes.[46] Low-pitched continuous pulmonary sounds with a dominated frequency of about 200 Hz or less are called rhonchi. As a result of the low-pass filtering effect of the lung, wheezes are usually better heard over the trachea, although some localized short wheezes may be missed by tracheal auscultation alone.[47,48] Automated systems for wheezing analysis and quantification[49,50] are now available and will be discussed later.

As discussed in the previous section, the most probable explanation for the genesis of wheezes is airway wall oscillations induced by flow limitation. Most expiratory wheezes are generated by flutter/flow limitation mechanisms in the central airways. Inspiratory and localized expiratory wheezes, which are heard in a localized area on the chest wall, are generated by the same flutter/flow limitation mechanisms but in peripheral airways. Clinically, wheezes are a characteristic sign of airway obstruction, although wheezes are not always a sensitive indicator of degree of airway obstruction.

The term rhonchi has been the cause of much confusion because sometimes this term is used to mean low-pitched wheezes that have whistling characteristics and sinusoidal structures in their time-expanded waveforms (Fig. 2). In other cases, the same term is used to denote rumbling or snoring sounds that have a more complex form than simple sinusoidal time-expanded waveforms and indicate retained secretion in bronchi. The sound analysis of rumbling "rhonchi" is difficult because rhonchi has a low frequency of less than 100 Hz and may be masked by noise, especially when recorded in our daily clinical practice, the outpatient departments, or our hospital wards.

This discrepancy in the terminology of lung sounds makes a lot of confusion in our daily practice in the management of respiratory diseases. When we write "rhonchi" in charts of our patients, some nurses, physiotherapists (PTs), or even physicians understand that this patient has bronchospasm and may need bronchodilator medications. Other nurses, PTs, and physicians may understand this term as a rumbling sound and that this patient has retained secretion. Further discussion on the terminology of rhonchi is necessary.[51]

Care in listening to these low-pitched sounds is essential to the management of asthma. Whether low- or high-pitched, wheezes suggest airway narrowing and flow limitation that cause airway wall oscillation, although the degree of airway narrowing may differ. Rumbling sounds indicate that airway narrowing is fluctuating and, thus, retained secretion, which is a sign of airway inflammation and suggests that anti-inflammatory medication is needed.

VESICULAR AND BRONCHIAL BREATH SOUNDS

Vesicular breath sounds are primarily inspiratory sounds that have a soft quality. Bronchial breath sounds have a prominent expiratory component and harsher quality. Thus, when we listen to the chest, sounds of clearly audible expiratory breath indicate bronchial breath sounds. Although Forgacs[1] discouraged the use of the terms "vesicular" and "bronchial" breath sounds, they are useful for describing the conditions of patients with asthma. When expiratory breath sounds are faintly audible, they are (normal) vesicular breath sounds. Bronchial breath sounds are normally heard over the trachea, in the upper chest close to the trachea, or high back between the scapulae. When we listen to bronchial breath sounds in areas other than these, they are abnormal and suggest stiff lungs or narrowing airways.

Breath sound are generated in the large airway and turbulence in the airstream are believed to be the source of breath sounds.[52] In turbulent flow, energy is transferred between colliding packets of gas, and transient pressure fluctuations occur and generate sound. Turbulence begins at a critical flow velocity, when the Reynolds number exceeds approximately 2,000. The Reynolds number is defined by the tube diameter and length, flow velocity, dynamic viscosity, kinematic viscosity, and density of the flowing substance. In quiet breathing, the Reynolds number exceeds 2,000 only in the trachea and the main and first few branches of the bronchus.[53] Although unproved, the Karman vortex or similar mechanism is a possible sound source and explanation for the fact that inspiratory breath sounds are louder than expiratory breath sounds in normal vesicular breath sounds.
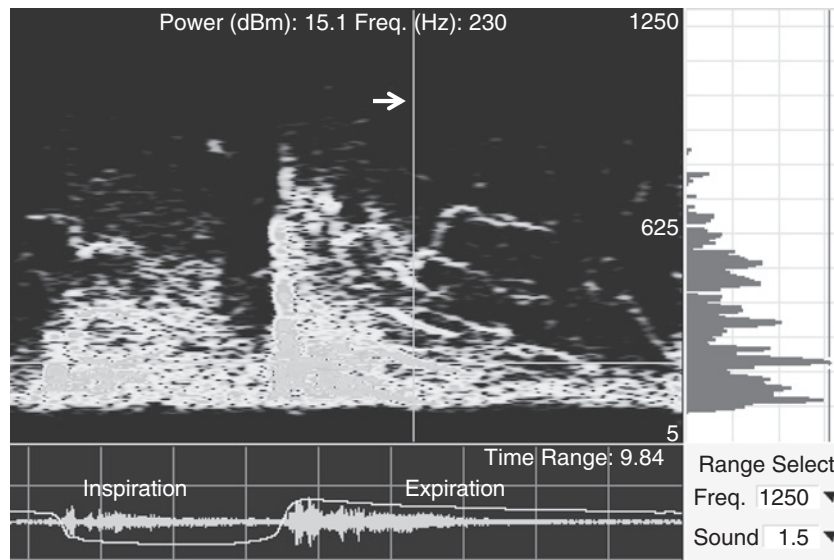
Fig. 3 Sound spectrogram (left) and power spectrogram (right) of polyphonic expiratory wheezes. The upper panel of the sound spectrogram shows the time vs. frequency of the sound. The intensity is expressed as brightness. Following a peak expiratory breath sound, a few declining power bands (wheezes) are observed. The lower left panel shows the time vs. respiratory cycle and the sound power expressed as amplitude. The power spectrogram in the right panel shows the power distribution according to the sound frequency (ordinate) at a moment shown on a vertical line in the sound spectrogram (arrow). The fundamental tone of the major wheeze was 230 Hz, shown as the longest horizontal line (peak) in the power spectrum. The harmonics of the fundamental tone was observed at 460 Hz and 690 Hz. Several peaks other than those harmonics are observed at 510 Hz and 620 Hz. The presence of sound peaks other than harmonics of major wheezing suggests that this is a polyphonic wheeze.

IMPLICATION OF VESICULAR AND BRONCHIAL BREATH SOUNDS IN ASTHMA

As shown in the section of bronchoprovocation tests (Table 2), an increase in the frequency or intensity of breath sounds is a good index of acute bronchospasm.[16,18-20,22,26,27] When there is airway narrowing, the breath sounds become harsher and are expressed as bronchial breath sounds. A commonly used term, prolongation of expiration is almost synonymous with bronchial breath sounds.

We measured the intensity and frequency of these breath sounds in adult asthmatics.[54] We found expiratory (E)/inspiratory (I) ratio of sound intensity was 0.27 and 0.72 in vesicular and bronchial breath sounds, respectively. The highest audible frequency of inspiratory (HFI) and expiratory (HFE) breath sounds was 250 Hz (HFE)/420 Hz (HFI) in vesicular breath sounds and 470 Hz (HFE)/490 Hz (HFI) in bronchial breath sounds (Table 4).

As was reported in the section of bronchoprovocation tests and lung sounds, acute airway narrowing results in an increase in frequency and inten-

Table 4 Numerical characteristics of vesicular and bronchial breath sounds

	E/I Power Ratio	HFE/HFI	HFE	HFI
Vesicular breath sounds	0.27	0.6	250	420
Bronchial breath sounds	0.62	1.0	470	490

E/I, expiratory/inspiratory; HFE/HFI, highest frequency of inspiratory sounds/highest frequency of inspiratory sounds.

sity of lung sounds.[16-19,23-28] These changes in breath sounds were also observed in sustained airway obstruction. Habukawa *et al.*[28] measured HFI and HFE of lung sounds in asymptomatic stable asthmatic children. They observed an inverse correlation between HFI and forced expiratory parameters. They treated those cases that showed lower than normal $\dot{V}_{50}$ with inhaled corticosteroids (ICS) and found an increase in $\dot{V}_{50}$ correlated with a decrease in HFI. There were similar correlations of HFE with those forced expiratory parameters, but they were not as significant as those of HFI. Habukawa *et al.* speculated that this

small difference was most likely due to the inspiratory breath sounds, which are more prominent than those in expiratory breath.

We[55] reported that markers of airway inflammation, such as eNO (concentration of nitric oxide in exhaled air) and percentage of inflammatory cells in induced sputum, were higher in asthmatic patients who had bronchial breath sounds than in patients who had vesicular breath sounds. These findings raised the possibility that the degree of airway inflammation can be assessed by auscultation of the asthmatic patients.

Our observations are in accordance with reports presented in bronchial provocation tests, namely, that the narrower the airways are, the higher the frequency of breath sounds is. Therefore, these results are applicable to clinical practice. When expiratory breath sounds are clearly heard in an asthmatic patient, this patient may have airway narrowing or airway inflammation. However, sometimes it is difficult to tell exactly whether the sounds detected are vesicular or bronchial in clinical settings. Automated analysis of lung sounds is expected to overcome these difficulties.

COMPUTERIZED AUTOMATED ANALYSIS OF LUNG SOUNDS

In 1983, Charbonneau et al.[14] raised the possibility of computerized automated analysis of tracheal sounds to discriminate asthmatics from normal subjects. They found that the sound spectral features, i.e., frequency (Hz) vs. amplitude of asthmatic subjects, were different from those of normal subjects. In 1991, Tinkelman et al.[56] used computer digitized airway phonography (CDAP) and tried to differentiate asthmatic from normal children by analyzing the intensity of lung sounds. They were able to differentiate wheezing from non-wheezing subjects and postulated that CDAP was a reproducible and quantifiable method to detect airway obstruction. In 1996, Malmberg et al.[57] evaluated lung sounds of a few typical lung diseases by a computerized method called self-organizing map (SOM). They found that SOM was useful to differentiate subjects with emphysema from normal controls but not very effective to differentiate subjects with asthma and fibrosing alveolitis from normal controls. Lenclud et al.[58] studied the usefulness of the tracheal sound analyzer ELEN-DSA, which allows automatic detection of wheezes from recorded sounds, but this was shown to have relatively poor characteristics for detecting wheezing. In 1999, Rietveld et al.[59] recorded the tracheal sound of normal and asthmatic subjects and detected wheezes by the computerized recognition of differences in the breath sound spectrum. They found that wheezes detected by this method were observed when there was a decrease of more than 20% in the peak expiratory flow rate (PEF) (sensitivity, 88%; specificity, 92%). Those studies published before 2000 aimed at computerized monitoring of breath sounds and/or wheezes in asthmatic patients but were not automated yet.

Gavriely published a technological approach to automated digital data acquisition and processing of breath sounds[60] in 1995, and he developed a commercial device (PulmoTrack®) that enabled the automated and continuous monitoring of wheezes. Several reports have suggested the usefulness of PulmoTrack®.[50,61-63] Prodhan et al.[61] used this monitor in a pediatric intensive care unit and reported that PulmoTrack® was better than the staff at detecting wheezing. Boner et al.[62] reported that monitoring wheezing during sleep was useful when treating asthmatic children and that Tw/Ttot (= duration of wheeze/duration of recording) correlated with changes in the peak expiratory flow rate (PEF). Bibi et al.[63] reported on the usefulness of cough and wheeze monitoring in pediatric asthma and found that some asthmatic children who had increased cough rates after Albuterol inhalation experienced longer hospital stays.

Recently, Habukawa et al.[64] reported that the airflow and body size of children can be estimated by analyzing tracheal and chest wall breath sounds. These researchers are planning to develop an automated lung sound analyzer that will detect changes in basic breath sounds. Their study enables the automated correction of breath sounds by body size and airflow by analyzing breath sounds alone and will make automated analysis of breath sounds easier.

The studies described above, which will analyze basic breath sounds, are expected to improve the sensitivity and specificity of automated breath sound analysis in the management of asthma.

SUMMARY

The results from bronchoprovocation studies and forced expiratory wheezes have shown that an increase in the frequency and intensity of breath sounds is observed. This change in breath sounds is sometimes more sensitive than the appearance of wheezing, although wheezing is more characteristic and much easier to identify by auscultation. Flow limitation and flutter of the airway wall are believed to be the mechanism behind the genesis of wheezing. Changes in breath sounds in airway narrowing are explained by an increase in the flow, which increases the Reynolds number and airflow turbulence. Automated and computerized analysis of lung sounds is expected to make lung sounds more useful in the management of bronchial asthma.

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