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Wheezes

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ABSTRACT: Wheezes are continuous adventitious lung sounds. The American Thoracic Society Committee on pulmonary nomenclature define wheezes as high-pitched continuous sounds with a dominant frequency of 400 Hz or more. Rhonchi are characterized as low-pitched continuous sounds with a dominant frequency of about 200 Hz or less. The large variability in the predominant frequency of wheezes is one of the difficulties encountered with automated analysis and quantification of wheezes. The large variations observed in automated wheeze characterization emphasize the need for standardization of breath sound analysis. This standardization would help determine diagnostic criteria for wheeze identification.

The mechanism of wheeze production was first compared to a toy trumpet whose sound is produced by a vibrating reed. The pitch of the wheeze is dependent on the mass and elasticity of the airway walls and on the flow velocity. More recently, a model of wheeze production based on the mathematical analysis of the stability of airflow through a collapsible tube has been proposed. According to this model, wheezes are produced by the fluttering of the airways walls and fluid together, induced by a critical airflow velocity. Many circumstances are suitable for the production of continuous adventitious lung sounds. Thus, wheezes can be heard in several diseases, not only asthma. Wheezes are usual clinical signs in patients with obstructive airway diseases and particularly during acute episodes of asthma. A relationship between the degree of bronchial obstruction and the presence and characteristics of wheezes has been demonstrated in several studies. The best result is observed when the degree of bronchial obstruction is compared to the proportion of the respiratory cycle occupied by wheeze (t_w/t_{tot}). However, the relationship is too scattered to predict forced expiratory volume in one second (FEV₁) from wheeze duration. There is no relationship between the intensity or the pitch of wheezes and the pulmonary function. The presence or quantification of wheezes have also been evaluated for the assessment of bronchial hyperresponsiveness.

Wheeze detection cannot fully replace spirometry during bronchial provocation testing but may add some interesting information. Continuous monitoring of wheezes might be a useful tool for evaluation of nocturnal asthma and its treatment.

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Wheezes are continuous adventitious lung sounds, which are superimposed on the normal breath sounds. The word "continuous" means that the duration of a wheeze is longer than 250 ms. They are clinically defined as more or less musical sounds and can be characterized by their location, intensity, pitch, duration in the respiratory cycle, and relationship to the phase of respiration.

A standardized nomenclature of lung sounds has been proposed by the American Thoracic Society (ATS) [1], and the Tenth International Conference on Lung Sounds [2]. These nomenclatures define wheezes as high-pitched continuous sounds and qualify low-pitched continuous sounds as rhonchi. Some investigators have proposed that the term rhonchus should be abandoned and the terminology modified by using only the term wheezes and characterizing them as high-pitched or low-pitched wheezes.

However, subjective evaluation of wheezing is not very reliable [3–5] and, despite the nomenclature, the intra-observer agreement on lung sound terminology has been found, a few years ago, to fall somewhere between chance and total agreement [6].

Definition and acoustic characteristics of wheezes

Numerous attempts have been made to better characterize wheezing sounds by analysing them in the time and frequency domain. The development of computer-aided signal processing and analysis has provided more precise information on wheeze characteristics. Using a time-expanded waveform analysis, MURPHY *et al.* [7] have shown that a wheeze produces "continuous" undulating

sinusoidal deflections replacing the normal waveform of lung sounds. The description in the frequency domain of these sinusoidal deflections is usually performed by computing the power spectrum using Fast Fourier Transform (FFT). Wheezes generally produce a well-defined small number of peaks in the power spectrum, with highly variable frequencies ranging 80–1,600 Hz according to GAVRIELY *et al.* [8] and 350–950 Hz according to PASTERKAMP and co-workers [9]. The dominant frequency sets the pitch of the wheeze. The ATS nomenclature of lung sounds defined wheezes as high-pitched continuous sounds with a dominant frequency of 400 Hz or more. Rhonchi are characterized as low-pitched continuous sounds with a dominant frequency of about 200 Hz or less.

Wheezes, which are usually louder than the underlying breath sounds, are often audible at the patient's open mouth or by auscultation over the larynx. In some patients, they may be audible at some distance from the patient. The clinical value of tracheal auscultation in asthma is well-recognized, and the trachea is superior to the lung for detection of wheezing in most asthmatic patients [10–12]. The value of tracheal auscultation in asthma has also been assessed during bronchial provocation challenge by SANCHEZ *et al.* [13]. They found that wheezes were detected over the trachea and over the chest in 12 out of 17 subjects. They were detected only over the chest in two subjects and only over the trachea in three subjects. However, in one study, wheezes were more intense and more frequently detected over the chest than over the neck [14]. The transmission of wheezing sounds through airways is better than transmission through the lung to the surface of the chest wall. The higher frequency sounds are more clearly detected over the trachea than at the chest [15, 16]. The high frequency components of breath sounds are absorbed mainly by the lung parenchyma [17]. The highest frequency of wheezes observed by BAUGHMAN and LOUDON [18, 19], who recorded lung sounds over the chest wall, was 710 Hz. FENTON *et al.* [16] have compared the power spectra of lung sounds recorded simultaneously over the neck and chest of a 16 year old wheezy boy. The peaks at 480 and 650 Hz were seen over both locations, but their relative magnitudes were reversed as a result of the low-pass filtering effect of the lung. Peaks at 870 and 940 Hz seen over the trachea were almost absent on the chest. These observations emphasize that the trachea is important and interesting in asthmatic patients.

The large variability in the predominant frequency of wheezes, the influence of the auscultation site as well as the influence of airflow on the intensity and power spectra of lung sounds in asthmatic subjects [16, 20], illustrate some of the difficulties encountered with automated analysis and quantification of wheezes.

Automated characterization and quantification of wheezes

The automated analysis and quantification of wheezes is usually based on their spectral appearance. For quantification of wheezing in acute asthma, BAUGHMAN

and LOUDON [18] analysed breath sounds recorded over the chest using the FFT technique. Sound segments with wheezes were identified by the presence of sharp peaks, and the duration of wheezes was expressed as a percentage of the respiratory cycle duration (t_w/t_{tot}). In a subsequent study [19], they developed an algorithm to estimate the proportion of the breath cycle occupied by wheezing through the night. Fifty segments of 250 ms per 5 min period of recording were analysed. Wheezes were defined by the presence of a sharp peak in the power spectrum between 150 and 1,000 Hz. PASTERKAMP and co-workers [9, 16] have also developed a technique for automated spectral characterization of wheezing. Wheezes over the trachea as well as over the lung are identified by the presence of a peak in the power spectrum with a frequency above 200 Hz and an amplitude more than 15 times average sound amplitude, in the range 110–1,200 Hz. An amplitude criterion has also been added by BAUGHMAN and LOUDON [14], who considered that a peak was significant when its frequency was greater than 200 Hz and its amplitude three times greater than the baseline signal. Despite different sites of auscultation, similar frequency criteria are used to identify wheezes in all these studies [9, 14, 16]. As there is a difference in breath sound intensity between tracheal and lung sounds [16], it is not clear whether the same amplitude criterion should be used for both sites of auscultation.

PASTERKAMP and co-workers [21] have compared the subjective assessment and the computer analysis of wheezing. Tape recorded breath sounds of asthmatic patients were presented to 40 health professionals. There was a reasonable accord between the mean subjective and the computer analysis wheezing scores.

In their automated analysis of wheezes recorded over the chest, SCHREUR *et al.* [22] defined wheezes as peaks in the power spectrum above 150 Hz with an amplitude three times higher than the baseline level. In this study, a few wheezes were identified by the automated analysis in healthy subjects during quiet breathing. As wheezes do not usually occur in healthy subjects during quiet breathing, these computer-detected wheezes might well be false positive wheezes. BECK and GAVRIELY [23] considered that no common criterion characterizes the spectral appearance of forced expiratory wheezes and defined a list of eight criteria to distinguish them from other noises.

CHARBONNEAU *et al.* [24] have presented a computerized system for monitoring wheezes produced by asthmatic patients during sleep. Respiratory sounds are recorded over the trachea. The system gives the number of wheezing events (>150 ms), the cumulative duration of wheezing time, the number of wheezing episodes longer than 15 s, the mean frequency of all wheezes and the ratio of wheezing duration over recording duration. The detection of wheezes by the computerized system was compared to the human detection in five asthmatic patients during bronchial provocation testing. Two hundred and eighty eight wheezes were heard by subjective listening. The system was found to agree with the human detection in 76% of the cases with a standard deviation of 8%. There were 37 wheezes detected by the automatic analysis, which were not heard by the observer.

An automated system for wheezing analysis and quantification is commercially available. It has been developed by LENS and co-workers [25, 26]. Sounds are recorded over the trachea. This system calculates the proportion of time occupied by wheezing (W%). This system has been validated in seven patients with nocturnal asthma during overnight recording. The correlation coefficient between the W% score and the number of wheezes detected by listening was 0.72 ($p < 0.001$), with a wide scattering. A large number of wheezes detected by the analyser were not detected by listening [27].

Clinical scoring systems might be very different. They may judge the severity of wheezing by its duration and intensity, or they may not specify any particular sound characteristics at all. On the other hand, automated spectral characterization of wheezing, depending on the signal processing and algorithm used, may be less sensitive than the human ear or may be responsible for false positive characterization of wheezing. Obviously, there is a need for standardization of breath sound analysis: pick up locations, type of sensors, amplification and filtration, digitization frequency, FFT technique, averaging of the spectra, use of a standard flow rate. This standardization would help development of diagnostic criteria for wheezes identification. A European project, called Computerized Respiratory Sound Analysis (CORSA), involving a dozen teams has been undertaken in order to propose such a standardization. Results are expected by the end of 1996.

Mechanisms of wheeze production

The mechanisms underlying wheeze production appear to involve an interaction between the airway wall and the gas moving through the airway. Since wheezes are described as musical sounds, their mechanisms of production have been compared with musical wind instruments. The sound of wind instruments is produced either by the oscillations of an air jet (flute) or by a vibrating reed (clarinet). For these wind instruments, the pitch of the sound depends upon the length of the air column that is coupled to the sound source and upon the density of the gas mixture in the resonating column. FORGACS [28] has demonstrated that the pitch of a wheeze does not change when breathing a helium-oxygen mixture. He compared the mechanisms of wheeze production to a toy trumpet whose sound is produced by a vibrating reed [29]. The pitch of a toy trumpet sound is independent of the attached horn, and is determined by the mass and elasticity of the reed. Forgacs states that high-pitched musical sounds are produced when the calibre of the airway is narrowed such that its opposite walls are almost in contact. The acceleration of the gas flow through the narrowed lumen induces oscillation of the airway walls. The pitch of the wheeze is dependent on the mass and elasticity of the airway walls and on the flow velocity. It is not influenced by the length or the size of the airway. Thus, because they are not stationary sounds, high-pitched wheezes are not necessarily produced by peripheral airways and low-pitched wheezes or rhonchi by more central airways, as was initially suggested by Laënnec.

More recently, GROTBORG and DAVIS [30] proposed a model based on the mathematical analysis of the stability of airflow through a collapsible tube. According to this model, wheezes are produced by the fluttering of the airways walls and fluid together. The oscillations begin when the airflow velocity reaches a critical value, called flutter velocity. This flutter velocity is dependent on the mechanical and physical characteristics of the tube and the gas. The model developed by GROTBORG and DAVIS [30], GROTBORG and REISS [31] and GROTBORG and GAVRIELY [32] makes it possible to predict the critical flow velocity inducing airway walls oscillations as well as the frequency of these oscillations. This model shows that wheezes are always accompanied by flow limitation, but that flow limitation is not necessarily accompanied by wheezes. The characteristics in the time and frequency domain of breath sounds measured by GAVRIELY and co-workers [8] in 10 wheezing patients are in agreement with this model.

This fluid dynamic flutter theory has been proposed to explain expiratory wheezes. No theory has yet been proposed to explain inspiratory wheezes, which are often associated with more severe airway obstruction, or to explain inspiratory wheezes associated with upper airways obstruction.

The presence of wheezes during some pulmonary diseases might be explained by this model of flutter of a flattened tube, as these diseases induce changes in the mechanical characteristics of the pulmonary system. The reduction in airway calibre observed in asthma, the decrease in pulmonary elastance accompanying pulmonary oedema, or the reduction in bronchial stiffness associated with some chronic obstructive lung diseases, would result in a lower critical flutter velocity according to this model. Thus, oscillations of the airway walls will start more easily in these situations.

Wheezes can be detected in healthy subjects during forced expirations [33, 34]. These forced expiratory wheezes seem to be associated with airflow limitation. However, they may also be produced by eddy-induced wall oscillations without airflow limitation.

Clinical significance of wheezes

Many circumstances are suitable for the production of continuous adventitious lung sounds. They include all mechanisms narrowing airway calibre, such as bronchospasm, mucosal oedema, intraluminal tumour or secretions, foreign body, external compression by a tumour mass, or dynamic airway compression. Thus, wheezes can be heard in several diseases, not only asthma. Healthy subjects can also produce wheeze during a forced expiratory manoeuvre. The long list of diseases that may be associated with wheezes has been reviewed by WARING *et al.* [35] and YERNAULT *et al.* [36] and is presented in table 1.

This list shows that wheezes may be much more frequent than asthma. In an epidemiological study, wheezes have been perceived at some time by more than 25% of a population sample, whereas the prevalence of asthma

Table 1. – Clinical conditions associated with wheezes

Infections, such as croup, whooping cough, laryngitis, acute tracheobronchitis
Laryngo-, tracheo- or bronchomalacia
Laryngeal or tracheal tumours
Tracheal stenosis
Emotional laryngeal stenosis
Foreign body aspiration
All causes or large airway compression or stenosis
Asthma
Chronic obstructive pulmonary disease
Bronchorrhoeal states, such as chronic bronchitis, cystic fibrosis, bronchiectasis
Interstitial fibrosis, hypersensitivity pneumonitis
Pulmonary oedema
Forced expiration in normal subjects

in this population was 7% [37]. Wheezes are usual clinical features in patients with chronic obstructive airway disease. However, they are not always present in bronchial obstruction, and GODFREY *et al.* [4] found that only 70% of patients with severe airflow obstruction (forced expiratory volume in one second (FEV₁) <1L) wheeze. Wheezes are more frequent in patients with asthma than in patients with chronic obstructive pulmonary disease (COPD) [38]. They are heard particularly during acute episodes of asthma [39].

The continuous musical respiratory sound heard in patients with upper airway obstruction is usually called stridor. The frequency of stridor is similar to the frequency of wheezes. It is heard during inspiration and is more prominent over the neck than over the chest [14]. A functional laryngeal disturbance might be associated with expiratory wheezing resembling that of asthma [40, 41]. These expiratory wheezing sounds are heard over the neck and appear to be transmitted to the chest [41, 42]. This "vocal cord dysfunction" usually has a psychogenic basis and should be distinguished from asthma to avoid unnecessary treatment [43].

In hypersensitivity pneumonitis and other pulmonary fibrosing diseases, inspiratory wheezing or "squawking" has been reported. These squawks are late inspiratory sounds in hypersensitivity pneumonitis and are heard in the early to mid-inspiration in other types of fibrosing disease [44].

Relationship between wheezes and the severity of airway obstruction

MARINI *et al.* [38] studied the relationship between wheezing intensity and the severity of bronchial obstruction in 83 patients with chronic airflow obstruction. They established wheezing scores after auscultation in several areas, in the seated and then supine position, during forced and unforced expirations. Wheezes were detected during unforced breathing in 48 out of 83 patients. Wheezing patients differed from nonwheezing subjects by their bronchodilator response. In wheezing patients, there was an independent relationship between the wheezing score and degree of obstruction, the bronchodilator

response and asthmatic history. Although high wheezing scores were only observed during quiet breathing in patients with FEV₁ lower than 40% predicted, FEV₁ ranging 15–90% predicted might be associated with similar moderate wheezing scores. Thus, the presence or absence of wheezes did not allow the degree of airflow obstruction to be predicted.

SHIM and WILLIAMS [45] found a relationship between the characteristics of wheezing and the severity of airways obstruction. Bronchial obstruction was more severe in patients with both inspiratory and expiratory wheezes than in patients with only expiratory wheezes. It was also more severe in patients with high-pitched wheezes than in patients with low-pitched wheezes. There was a progressive decrease in peak expiratory flow rate (PEFR) from patients with minimal wheezing to patients with severe wheezing. Although the difference between groups was significant, there was a large overlap in PEFR between groups.

McFADDEN *et al.* [39] compared the degree of airways obstruction and the clinical manifestations of asthma in 22 patients with acute exacerbation of asthma. On initial observation, all patients had at least expiratory wheezes. One of these patients did not report symptomatic wheezing. During bronchodilator therapy, the absence of symptoms reported by the patients did not guarantee normalcy. When 90% of the patients considered themselves asymptomatic, 40% still had expiratory wheezes and their mean FEV₁ was below 50% of predicted value. When objective wheezes disappeared, the FEV₁ was only 63% of predicted value. In another study on patients with acute exacerbations of asthma, wheezing was one of the less discriminating factors to predict relapse or need for hospitalization [46].

Using spectral analysis of pulmonary sound recordings in patients with an acute exacerbation of asthma, BAUGHMAN and LOUDON [18] calculated the proportion of the respiratory cycle occupied by wheeze (t_w/t_{tot}). Pulmonary function tests and recording of pulmonary sounds were repeated after bronchodilator treatment. They found a loose but significant relationship between FEV₁ and t_w/t_{tot} . There was no correlation between the intensity of wheezing and the degree of airflow obstruction.

PASTERKAMP and co-workers [9] recorded breath sounds in patients with exercise-induced asthma. Automated spectral characterization was also used to measure wheezing as a proportion of respiratory time. Wheezing as % t_{tot} correlated with airway obstruction measured by FEV₁, forced expiratory flow at 50% of forced vital capacity (FVC) and specific conductance. Wheezes were detected in all subjects when FEV₁ was <45% pred. Conversely, no wheezing occurred with FEV₁ >84% pred. There was no correlation between the pitch of wheezing and the pulmonary function.

The relationship between wheezes and the severity of airflow obstruction has also been studied during induced bronchoconstriction [47–49]. BAUMANN *et al.* [47] found no relationship between the degree of airway obstruction induced by specific or nonspecific challenge tests and the presence of wheezes. Bronchial provocation testing with methacholine was undertaken in 15 children with

obstructive lung disease by NOVISKI *et al.* [50]. They found a correlation between the concentration of methacholine causing a 20% fall in FEV₁ (PC₂₀) and the concentration at which wheezing was first heard over the trachea (PC_w). PC_w was higher than PC₂₀ in all children, with the exception of one who did not have asthma but an immotile cilia syndrome. A relationship between PC₂₀ and PC_w has also been found by AVITAL *et al.* [51] and by SANCHEZ *et al.* [13].

Wheezes for the diagnosis of bronchial hyperresponsiveness

Bronchial provocation tests are usually performed to assess the presence of bronchial hyperresponsiveness, either to evaluate individuals with symptoms suggestive of asthma or for epidemiological studies. The bronchial response is assessed by the PC₂₀, concentration of the provocative agent inducing a 20% fall in FEV₁. Determination of the PC₂₀ requires repeated measurements of pulmonary function and, thus, patient co-operation. These measurements are not possible in patients with limited co-operation who are unable to perform good forced expiratory manoeuvres. Therefore, breath sound analysis and wheezes identification has been proposed to evaluate bronchial responsiveness, especially in children.

SANCHEZ *et al.* [13] found a sensitivity of 68% and a specificity of 85% for wheezes as an indicator of bronchial hyperresponsiveness during methacholine challenge in asthmatic children. When compared to the measurement of PC₂₀, the reproducibility of acoustic measurement between two challenges was good, whilst PC₂₀ was variable. Whereas some children with positive spirometric response did not present wheezes, three children with a negative spirometric response to methacholine presented wheezes. This indicates that some variation in airway calibre has occurred, but it was not sufficient to induce a 20% fall in FEV₁. In children with cystic fibrosis and normal children, SANCHEZ and co-workers [52] found that wheezing was a specific indicator of bronchial hyperresponsiveness, but was absent in 50% of children with cystic fibrosis whose methacholine challenge was considered as positive on the PC₂₀ measurement. Thus, if wheeze detection cannot fully replace spirometry in bronchial provocation testing, it may add some interesting information.

Wheezes for monitoring nocturnal asthma

Nocturnal asthma or asthma worsening during the night is a common complaint of asthmatic patients [53–55]. Recognition and evaluation of nocturnal asthma and of its therapy is usually performed by waking asthmatics at intervals during the night and measuring their pulmonary function, for example their PEF_R or FEV₁ [53, 56]. Such a method disturbs the patient's sleep and might interfere with the natural evolution of asthma symptoms during the night.

Wheezes are very often reported by patients who wake up at night with nocturnal asthma symptoms [55]. Thus, the noninvasive monitoring of wheezes has been proposed to assess changes in airway obstruction during sleep without disturbing the patient. MARTIN *et al.* [57] have documented the wheezing episodes occurring night and day in hospitalized asthmatic children. They found that children with oesophageal reflux had more wheezes at night than children without reflux. ISSA and SULLIVAN [58] recognized asthma attacks during sleep by the presence of loud continuous audible inspiratory and expiratory wheezing. After spontaneous awakening, the exacerbation of asthma detected by the presence of audible wheezing was confirmed by measuring a lower FEV₁/FVC ratio than the values recorded before sleep.

MESLIER *et al.* [59] recorded 48 episodes of wheezes in eight stable asthmatic patients. Thirty two episodes did not induce arousal. Thus, monitoring wheezes during sleep in asthmatic patients brings more information on the changes in airways obstruction than measurements of pulmonary function indices during spontaneous awakening induced by asthma exacerbation. BAUGHMAN and LOUDON [19] used an estimate of tw/t_{tot} to evaluate nocturnal asthma. More wheezes were observed from 4–4.30 a.m. than earlier in the night. They also used monitoring of wheezing during the night to evaluate the efficacy of a long-acting sympathomimetic agent to prevent nocturnal exacerbation of asthma [60]. In this study, the fall in FEV₁ and PEF_R found at 4 a.m. during the night with placebo was associated with an increase in the amount of wheezing in most patients. During the night with procaterol, the small fall in FEV₁ and PEF_R was not associated with a significant change in the amount of wheezing. These studies show that analysis of breath sounds might be useful for evaluation of nocturnal asthma and its treatment.

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