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EVALUATION OF LUNG MECHANICS IN EPIDEMIOLOGIC STUDIES *

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ABSTRACT

Recent developments in the field of lung mechanics, with special reference to epidemiologic studies, are reviewed. The relative inability of standard ventilatory tests to detect alterations in the behavior of small intrathoracic airways is noted. Resistance measurements reflect predominantly the pressure-flow behavior of the large intrathoracic and extrathoracic airways in their resting, noncompressed state. Maximal expiratory flows developed during the FVC maneuver reflect a complex interplay among airway geometry, airway compressibility, and lung elastic recoil.

Because of the potential dissociation between measurements of resistance and maximal expiratory flow, we recommend that tests involving both aspects be utilized in epidemiologic studies of obstructive pulmonary disease. Two feasible techniques for measuring the behavior of airways in the noncompressed state are the body plethysmograph and the oscillation method of obtaining respiratory resistance. Flow-volume curves of the FVC maneuver provide the simplest and best current method for evaluating the compressed airway state. Several techniques that give promise of providing important information about the

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peripheral airways are the behavior of the terminal part of flow-volume curves, resistance at lung volumes below functional residual capacity, and nitrogen-washout cruves.

Respiratory function tests ; respiratory mechanics ; airway resistance ; epidemiologic studies.

Epidemiologic studies are designed to measure the frequency and distribution of « disease » and of factors associated with the « disease ». Such studies are usually conducted in situations in which facilities are less ideal than they are in a research laboratory. Thus, it has been customary in studies involving measurement of pulmonary mechanics to select a simple test that can be conveniently applied to large populations.

This emphasis on simplicity and convenience has led to the widespread use of the peak flowmeter and spirometer in epidemiologic studies of obstructive pulmonary disease. Although valuable information has been gained from the use of these tests, recent studies suggest that potentially important information may be missed by not employing a more diversified testing program.

Our purpose will be to review certain recent advances in pulmonary mechanics. Based on these considerations, we shall suggest a testing program that appears both feasible and capable of describing in detail abnormal lung mechanics. Some of the tests require complex equipment, but the feasibility of utilizing such methods in the field has been demonstrated [24]. Because estimation of pleural pressure by an intra-esophageal balloon is not feasible in a population study, only methods that require measurements of volume, airflow, and pressure at the airway or body surface will be considered.

There are two considerations, based on relatively recent observations, that we believe are crucial to the problem. One is the importance of quantifying lung mechanics when the intrathoracic airways are dynamically compressed, as well as when they are not compressed. The other is the realization that standard tests of ventilatory capacity may provide very little information as to the status of the small peripheral airways.

Tests of the Noncompressed and Dynamically Compressed Airways

When the airways are not compressed, the pressure acting on the inner wall of the airways (PI) is greater than the pressure acting on the outer wall (PO). The airways therefore have a diameter at least as large as when lung elastic recoil is zero. This is the condition of the airways when the standard measurements of airway resistance are made. The dynamically compressed airway state implies that maximal expiratory flow has been achieved and that there are intrathoracic airways where the Po is greater than Pi [18]. Such airways are smaller than they would be when the elastic recoil state is zero. This is the situation during the usual forced expiratory vital capacity (FVC) maneuver.

It has been generally assumed that measurements of airway resistance (RA) or pulmonary resistance (RL) made during resting or panting respiration provide the same information regarding pulmonary mechanics as does the FVC, regardless of how the FVC is quantified [10]. In general, changes in the two parameters frequently go together, that is, maximal flow will be decreased when RA or RL is increased. However, some important exceptions to this linkage have been encountered.

Decreased Maximal Flow and Normal Resistance. — This combination has been noted in some patients with chronic obstructive lung disease [9], in several persons with α_1-antitrypsin deficiency (HYATT, R. E.: Unpublished data) and in patients with asymptomatic asthma [17]. PARK and associates [22] found that RA was normal but that maximal flow was decreased in hamsters with papain-induced emphysema. And there are reports [3, 28] of experimental bronchoconstriction leading to little change in RA but to definite decreases in maximal flow.

Elevated Resistance With Normal Maximal Flows. — This situation may be encountered in subjects who have obstructing lesions of the major airways [19]. Careful examination of flow-volume relationships often suggests the abnormality, whereas the results of the usual FVC test are often normal.

That such dissociations between resistance and maximal flow may occur is not surprising. Resistance measurements reflect predominately the pressure-flow behavior of the large intrathoracic and extrathoracic airways in their resting, noncompressed state. The maximal expiratory flows developed during the FVC clearly reflect a complex interplay among airway geometry, airway compliance or compressibility, and lung elastic recoil [5].

In view of these considerations, it would appear mandatory to test the airways when they are not compressed as well as when compressed. Only after further experience is obtained will the significance of dissociations between resistance and maximal flow be fully understood.

Two techniques are feasible in epidemiologic studies for measuring the noncompressed state. One is the body plethysmograph, which can be used to provide data on resistance as a function of lung inflation as well as measures of total lung capacity (TLC) ; its use in field studies has already been cited [24].

The other approach is to measure total respiratory resistance (Rrs) by the oscillation technique [6, 7, 12]. This measurement reflects RA primarily [4, 7]. By integrating flow, one can relate Rrs to lung inflation and thence to absolute thoracic gas volume if an independent measurement of TLC is made. One way of accomplishing the latter is by the chest radiograph. Several methods have been described for estimating TLC from full inspiration films [2, 20, 21], and high correlations with independent measures of TLC have been obtained.

The compressed airway state is best evaluated by the use of the regular FVC. The subject inhales to TLC and exhales as hard and fast and completely as possible. We would recommend obtaining -flow-volume curves [11] of this maneuver. If the efforts are stored on an oscilloscope, it is easy to judge if reproducible tests have been obtained (Fig. 1). Superimposing timed pulses on the flow tracing permits easy measurement of the various forced expiratory volumes such as the 1-second forced expiratory volume (FEV_1) (Fig. 1). Measuring the expiratory flow at 50 % of the vital capacity should provide basically the same information as does the maximal midexpiratory flow [14]. One can estimate peak expiratory flow from the loop and also have available the entire curve for any additional measurements that might seem pertinent, such as the slope [10, 13]. Flow-volume data are best evaluated when related to absolute lung volumes [10].

Tests Quantifying the Peripheral Airways

Macklem and Mead [15] have partitioned the resistance of the intrathoracic airways into central and peripheral components. The peripheral component (Rp) includes the resistance from alveoli to airways of approximately the ninth to the twelfth generation. The central component (Rc) measures airways from this level to the intrathoracic trachea. The total resistance (RT) is the sum of Rp and Rc. These authors found that Rp normally accounted for only about 15 % of RT at low lung volumes and was negligible at volumes above 80 % of the vital capacity. They predicted that rather widespread involvement of peripheral airways could occur with little alteration in total airway resistance. Recent studies have proved this prediction correct.

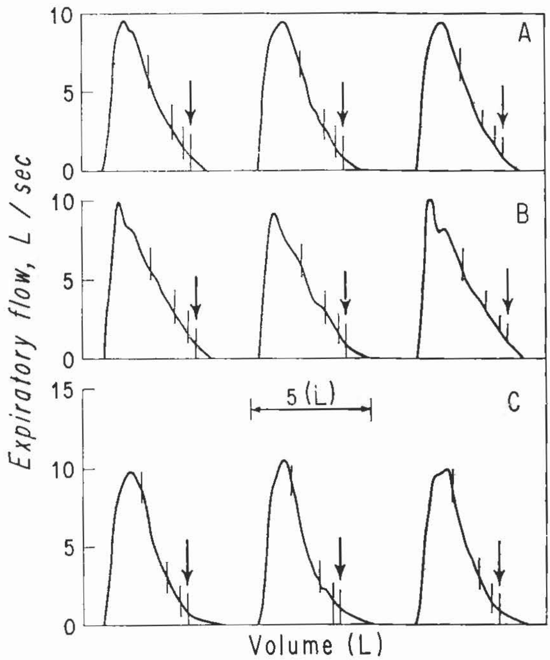

FIG. 1

Flow-volume curves redrawn from face of storage oscilloscope obtained from data on three young males. Time pulses of 0.25 second are superimposed on flow trace. Arrows indicate FEV_1. From left to right, values for FVC and FEV_1 are as follows :

Subject A		Subject B		Subject C	
FVC	FEV_1	FVC	FEV_1	FVC	FEV_1
4.44	3.55	4.61	3.84	5.03	3.52
4.41	3.55	4.46	3.60	5.03	3.48
4.45	3.58	4.61	3.73	4.90	3.52

HOGG and associates [8] partitioned resistance in the manner of MACKLEM and MEAD in lungs in which evidence of chronic obstructive disease was obtained at autopsy. In two cases, significant disease verified by pathologic examination showed little increase in RT but a fourfold increase in Rp. These investigators concluded that « It is thus entirely possible for a patient with chronic cough and sputum to have considerable small-airway obstruction and an increase in Rp and yet have virtually normal total airway resistance ». Similarly experiments by Ann WOOL-

COOK and her co-workers [29], studying the effects of vagal stimulation in the dog, suggest that RT may give very little information about the caliber of small airways.

There are additional studies that indirectly suggest the importance of predominant small-airway involvement. ROSSING [25] studied the effects on dogs of chronic exposure to phosgene. The pathologic changes involved primarily the terminal bronchiole and respiratory bronchiole [26]. In some animals, abnormalities in the nitrogen washout preceded elevations of pulmonary resistance, and these abnormalities persisted after resistance had returned to normal. WOOLCOCK and associates [30] suggested that when resistance and lung static recoil are normal, frequency dependence of dynamic compliance (CL) is strong evidence for peripheral airway involvement. Five subjects with clinical chronic bronchitis showed definite frequency dependence of CL despite relatively normal results of ventilatory studies. HOGG and associates [8] emphasized the potentially adverse effects of small-airway disease on gas exchange. ANTHONISEN and co-workers [1], studying a similar group of bronchitic patients with the Xenon-133 technique, found evidence of decreased ventilation and depressed ventilation-to-perfusion ratios in some lung regions and most commonly in the basal areas. Their patients showed frequency dependence of compliance but preservation of ventilatory capacity. And McFADDEN and LYONS [16], studying asymptomatic asthmatic subjects, demonstrated frequency dependence of CL and maldistribution of ventilation despite normal RA and FEV_1.

Therefore, the premise that measures of total airway resistance may not reflect the state of peripheral airways seems well established. In addition, primary involvement of these small airways is associated with significant pulmonary disease. However, because the retrograde-catheter technique or partitioning resistance into Rp and Rc cannot be employed in man, are there practical ways that the epidemiologist may evaluate these airways ?

Although no definitive answer can be given at this time, there are several techniques that give promise of providing the necessary information. Since the predominant effect of Rp is seen at low lung volumes [15], resistance data should be measured over the entire vital capacity volume, with special attention paid to the resistance at volumes below functional residual capacity.

The work of SCHILDER, ROBERTS, and FRY suggests that [27] the terminal portion of the expiratory flow-volume curve, that is, the part near residual volume, may predominantly reflect small-airway behavior. This suggestion is supported by the study of PETERS and FERRIS [23], which showed that decreases in maximal expiratory flow over the lower 25 % of the vital capacity correlated well with the level of cigarette consumption. Maximal flows at greater lung volumes did not show as high a correlation.

Other methods worthy of consideration are the nitrogen-washout technique [25] and the Xenon-133 method [1] for the reasons noted previously.

Although certain of the procedures we are suggesting are expensive, they can be adapted to field studies. We believe there is sufficient evidence pointing to the importance of the peripheral airways that every effort should be made to quantify their behavior in any serious epidemiologic study of respiratory disease. In addition, it will be extremely important to conduct more studies such as those described by ANTHONISEN and associates [1] and Ann WOOLCOCK and co-workers [30]. Such studies should include, however, detailed data on the resistance-thoracic gas volume relationship, especially at low lung volumes, the behavior of the terminal portion of the flow-volume curve, and the nitrogen-washout curve. Eventually, it may be possible to develop simple tests that quantify the status of the peripheral airways.

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RÉSUMÉ

Les récents développements dans le domaine de la mécanique pulmonaire, en particulier dans le domaine des études épidémiologiques, sont passés en revue. La relative impuissance des tests de ventilation standard à détecter les altérations du comportement des petits conduits aériens intrathoraciques est soulignée. Les mesures de résistance reflètent surtout le comportement pression/débit dans les gros conduits respiratoires intrathoraciques et extrathoraciques dans leur état de repos non comprimé. Les débits expiratoires maximaux développés pendant la manœuvre d'expiration forcée (FVC) reflètent une interaction complexe entre la géométrie des voies aériennes, leur compressibilité et les forces de rétraction élastique pulmonaire.

A cause de possibles discordances entre les mesures de résistance et de débit expiratoire maximum, nous recommandons que des tests comportant ces deux aspects soient utilisés dans les études épidémiologiques des maladies pulmonaires obstructives. Les deux méthodes utilisables pour mesurer le comportement des voies aériennes dans l'état non comprimé sont le pléthysmographe corporel et la méthode des oscillations appliquée à la mesure des résistances respiratoires. Les courbes débit/volume, les résistances mesurées aux volumes pulmonaires inférieurs à la capacité résiduelle fonctionnelle, et les courbes de rinçage de l'azote.

ZUSAMMENFASSUNG

Es werden neuere Entwicklungen auf dem Gebiet der Atemmechanik mit spezieller Bezugnahme auf epidemiologische Gesichtspunkte besprochen. Es ist bekannt, dass die atemphysiologischen Standardtests zum Nachweis von Veränderungen im Verhalten der tieferen intrathorakalen Luftwege wenig geeignet sind. Resistance-Messungen geben vor allem das Druck-Fluss-Verhalten der grösseren intrathorakalen und extrathorakalen Atemwege im Ruhezustand und bei Fehlen einer Kompression wieder. Die maximale exspiratorische Strömungsgeschwindigkeit bei der Bestimmung der forcierten Vitalkapazität (FVC) ist das Ergebnis eines komplexen Zusammenspiels der Geometrie der Luftwege, ihrer Kompressibilität und des elastischen Zuges des Lungengewebes.

Da zwischen den Bestimmungen der Resistance und der maximalen exspiratorischen Strömungsgeschwindigkeit ein diskordantes Verhalten möglich ist, empfehlen wir für epidemiologische Untersuchungen des obstruktiven Syndroms Untersuchungsmethoden, die beide Aspekte berücksichtigen. Zwei brauchbare Methoden zur Untersuchung des Verhaltens der Luftwege im nichtkomprimierten Zustand sind die Ganzkörperplethysmographie und die Unterbrechermethode zur Bestimmung der Resistance. Fluss-Volumen-Kurven bei der Durchführung der FVC-Bestimmung liefern die einfachste und beste Aussage über das Verhalten der Atemwege bei Kompression. Einige Untersuchungsverfahren, die wesentliche Informationen über die peripheren Luftwege versprechen, sind die Endstücke der Fluss-Volumen-Kurven, Bestimmungen der Resistance bei Lungenvolumina unterhalb der funktionellen Residualkapazität und Stickstoffauswaschungskurven.

RESUMEN

Se pasa revista de las novedades que respectan a la mecánica pulmonar en particular en el terreno de los estudios epidemiológicos. Se resalta la relativa impotencia de los tests de ventilación standard para detectar las alteraciones de comportamiento de los pequeños conductos aereos intratorácicos. Las medidas de resistencia reflejan sobre todo el comportamiento presión/débito en los gruesos conductos respiratorios intratorácicos y extratorácicos sin compresión y en estado de reposo.

Los débitos espiratorios máximos desarrollados durante la maniobra de espiración forzada (FVC) reflejan una interacción compleja entre la geometría de las vias aereas, su compresibilidad y los fuerzas de retracción elástica pulmonares.

Con motivo de las posibles discordancias entre las medidas de resistencia y del débito espiratorio maximum, nosotros recomendamos que sean utilizados en los estudios epidemiológicos de las enfermedades pulmonares obstructivas los tests que abarquen esos dos aspectos.