150 years of blowing: Since John Hutchinson

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Three recent advances in assessment of routine lung function are reviewed. In both normal subjects and patients with obstructive lung disease, the flows during the forced vital capacity (FVC) manoeuvre depend significantly on the pattern of the preceding inspiratory manoeuvre. Accordingly, the latter should be standardized in clinical and epidemiological studies. Although the nature of this phenomenon is not fully understood, stress relaxation of lung tissues probably plays the primary role. The negative expiratory pressure technique provides a simple and reliable tool for detecting expiratory flow limitation both at rest and during exercise. The method does not require body plethysmography or the patient's cooperation and coordination, and can be applied in any desired body posture. A simple method for monitoring FVC performance has been developed. It allows detection of flow limitation during the FVC manoeuvre.

Key Words: *Chronic dyspnea, Forced vital capacity, Maximum expiratory flow-volume curve, Tidal expiratory flow limitation*

Introduite par John Hutchinson, la spirométrie a 150 ans

RÉSUMÉ : Trois avancées récentes dans l'évaluation systématique de la fonction pulmonaire sont passées en revue. Chez les sujets normaux et chez ceux atteints d'une maladie pulmonaire obstructive chronique, les débits pendant l'exécution d'une capacité vitale forcée (CVF) dépendent de façon significative du profil de l'inspiration qui précède. En conséquence, cette dernière devrait être normalisée dans les études cliniques et épidémiologiques. Bien que la nature de ce phénomène ne soit pas complètement élucidé, le relâchement de la tension des tissus pulmonaires joue probablement un rôle clé. La technique de la pression expiratoire négative fournit un outil fiable et simple pour déceler la limitation du débit expiratoire aussi bien au repos que pendant l'exercice. Cette méthode ne nécessite ni l'utilisation de la pléthysmographie corporelle ni la coopération et la coordination du patient, et peut s'appliquer dans toutes les positions corporelles désirées. On a développé une méthode simple pour surveiller l'exécution de la capacité vitale forcée. Elle permet de déceler la limitation du débit aérien pendant l'exécution de la CVF.

Last year was the sesquicentennial of spirometry, introduced by Hutchinson in 1846 (1). However, this anniversary passed unnoticed, except in the United Kingdom where a symposium, organized by the British Thoracic Society, was devoted to a historical review of spirometry. This article is limited to some recent developments in the field of lung function testing of particular interest to clinicians. First a brief biography of Hutchinson is provided.

JOHN HUTCHINSON (1811-1861)

John Hutchinson was born in 1811 and was brought up in Newcastle-upon-Tyne, United Kingdom. He studied medicine at University College, London. After qualifying, he worked in various posts and was Assistant Physician at the Brompton Hospital, London, United Kingdom when he published his landmark work (1). This work and his other publications (2,3) convey a sense of how physicians were then

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(and perhaps even now) to some extent "showmen". In his landmark paper, Hutchinson described how he asked for a volunteer from a medical audience, estimated the man's vital capacity (VC) to be *x* cubic inches, and when the chap blew into his spirometer he recorded *x*-1 cubic inches. Hutchinson then claimed that with temperature correction it would have been *x* cubic inches, and so his method was proven. Was he able to predict VC so accurately, was the volunteer a 'plant' or did Hutchinson turn off the spirometer as the value *x* approached?

For unknown reasons in 1852 Hutchinson deserted his wife and three children and left for Australia. He practised medicine, probably in the gold fields. The only mention of him during this period is his involvement in a medicolegal wrangle, in which one party took exception to Hutchinson and tore off his beard – this being reported in the press. In 1861, he left Australia and went to Fiji to start up a sheep farm, but within the year he was dead. The exact cause of death is not known.

Hutchinson provided extensive guidelines for the procedure to measure the VC of the lung, as demonstrated by the following excerpt from his 1846 article (1):

> When the vital capacity of the lungs is to be made, let the person to be examined loose his vest, stand perfectly erect, with the head thrown well back, as represented by Figure 1 [Figure 1]; then slowly and effectually fill his chest with air, or inspire as deeply as possible, and put the mouthpiece between the lips (standing in the same erect position), holding it there sufficiently tight as not to allow any breath to escape; the observer in the mean time turns open the tap: immediately the patient empties his lungs, and slowly makes the deepest expiration; at the termination of which the operator turns off the tap ...

The importance of procedures in lung function testing is further underscored in the section of this article that discusses the time dependence of the forced vital capacity (FVC) manoeuvre.

RECENT ADVANCES IN LUNG FUNCTION TESTING

An account of time dependence of the FVC manoeuvre and its implications in routine lung function testing is provided. Next a new method for detecting expiratory flow limitation (FL) during tidal breathing is described and the link between tidal FL and chronic dyspnea is discussed. Finally, a simple method for monitoring the performance of FVC manoeuvres is described.

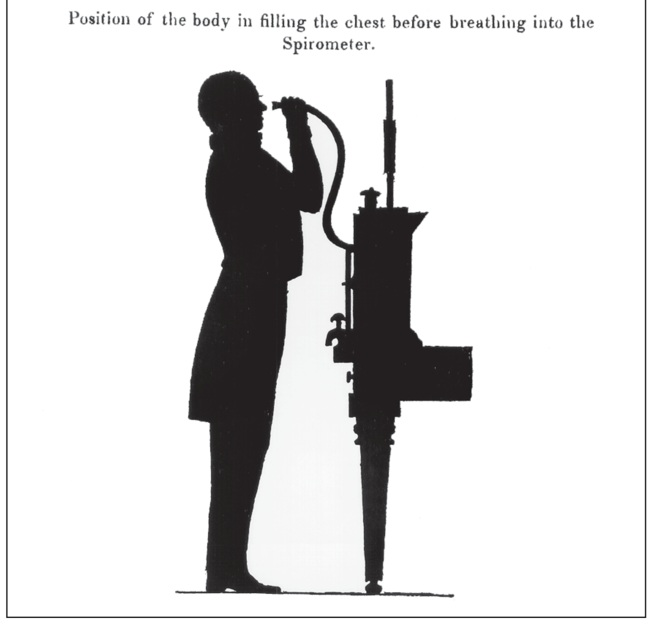

Figure 1) *Silhouette of John Hutchinson and his spirometer, illustrating correct body positioning for performance of the vital capacity manoeuvre (Reproduced from reference 1)*

TIME DEPENDENCE OF FVC MANOEUVRE

Spirometry is the most common pulmonary function test, whose origin can be traced to the measurement of VC introduced by Hutchinson (1). It became apparent, however, that VC measurements did not evaluate the predominant ventilatory defect in diseases characterized by a decreased ability to exhale air at normal rates (eg, asthma and emphysema). In 1947 Tiffeneau and Pinelli (4) made this possible with the introduction of the measurement of volumes exhaled in a given period of time (including 1 s, ie, forced vital capacity in 1 s [FEV_1]) during a FVC manoeuvre. Thus, 1997 marks the 50th anniversary of the FVC manoeuvre, which it is hoped will not go unnoticed. In 1958, Hyatt et al (5) introduced the maximal expiratory flow-volume (MEFV) curve, which emphasized that there is a limit to maximal expiratory flow ($\dot{V}_{max}$) at most lung volumes. The existence of expiratory FL explains why the FVC manoeuvre had proven so useful in clinical testing.

TABLE 1
Average differences in peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV_1) between forced vital capacity manoeuvres 1 and 2 in normal subjects and patients with chronic obstructive pulmonary disease (COPD) and asthma

	Number	Reference	ΔPEF (L/s)	ΔPEF/PEF (2) (%)	ΔFEV_1 (L)	$\Delta FEV_1/FEV_1$ (2) (%)
Normal	13	8	1.28	17	0.19	5
COPD	13	9	0.71	30	0.24	23
Asthma	8	10	1.12	15	0.17	7

Manoeuvre 1 was performed after rapid inspiration from functional residual capacity (usually lasting less than 1.5 s) and with end-inspiratory pauses of less than 0.3 s. For manoeuvre 2, the corresponding values were 3 to 5 s and 4 to 6 s, respectively. Differences are expressed in both absolute units and as percentage changes relative to values obtained with manoeuvre 2

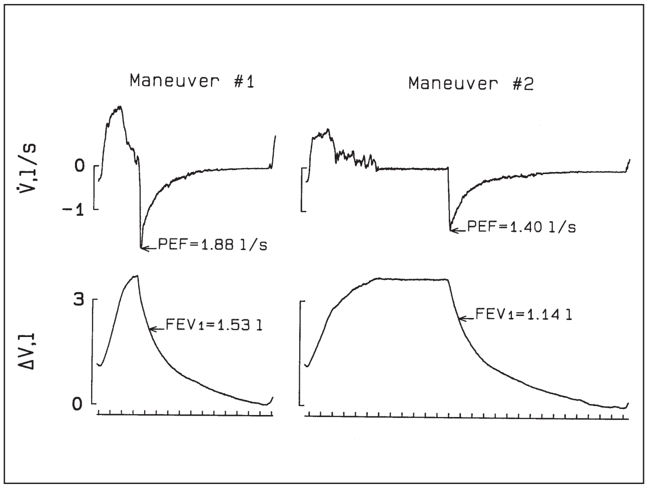

Figure 2) *Tracings showing the time course of changes in lung volume (ΔV, plethysmographic signal) and flow at the mouth ($\dot{V}$) obtained in a chronic obstructive pulmonary disease patient during a forced vital capacity (FVC) manoeuvre preceded by a rapid inspiration without breath hold at end inspiration (manoeuvre 1) and a slow inspiration with a 5 s breath hold (manoeuvre 2). With manoeuvre 2 the peak expiratory flow (PEF) and forced expiratory volume in 1 s (FEV_1) were 23% lower than with manoeuvre 1, while FVC did not change (Modified from reference 9)*

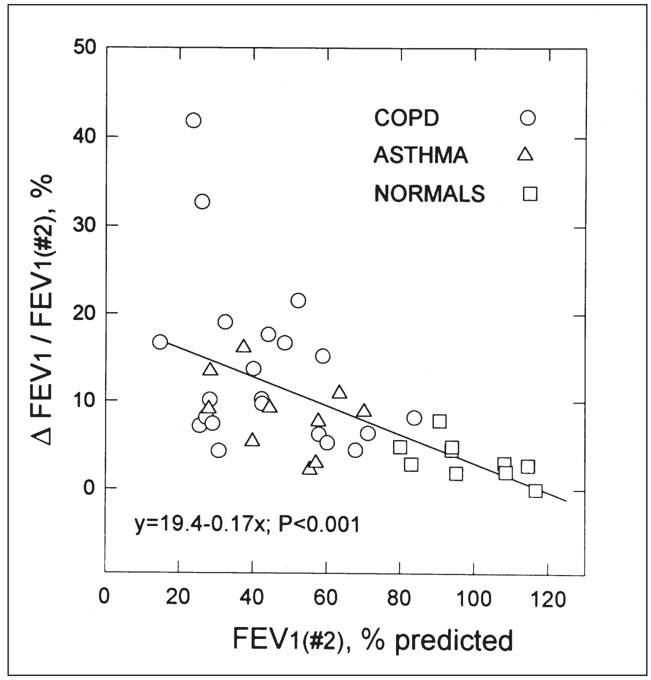

Figure 3) *Relationship between difference in forced expiratory volume in 1 s (FEV_1) between manoeuvres 1 and 2 (ΔFEV_1), expressed as a percentage of FEV_1 with manoeuvre 2, and FEV_1 (% predicted) in normal subjects and patients with chronic obstructive pulmonary disease (COPD) and asthma (Modified from reference 11, used with permission)*

Extensive guidelines have been provided for the measurement procedure of FVC (6,7). In these guidelines, however, the inspiratory manoeuvre preceding the expiratory effort has not been standardized. In practice, the FVC manoeuvre is preceded by maximal inspirations made at different speeds and variable pauses at full inspiration. But the time course of the inspiration preceding the FVC manoeuvre has a marked effect on peak expiratory flow (PEF), FEV_1 and MEFV curves in both normal subjects (8) and patients with obstructive lung disease (9-12).

Figure 2 depicts the time course of flow and volume during two FVC manoeuvres completed by a patient with chronic obstructive lung disease (COPD). The results on the left were preceded by a rapid maximal inspiration without an end-inspiratory pause (manoeuvre 1), and the results on the right were obtained after a slow inspiration with an end-inspiratory pause of several seconds (manoeuvre 2). During manoeuvre 2 there was a marked reduction in both PEF and FEV_1, but not in FVC. Table 1 provides the average differences in PEF and FEV_1 between manoeuvres 1 and 2 of normal subjects and patients with asthma and COPD. These differences are expressed in both absolute units and as percentage changes relative to values obtained with manoeuvre 2. Time dependency of PEF and FEV_1 was found in all instances, while FVC did not change significantly. The absolute values of ΔPEF and ΔFEV_1 were higher in normal subjects and asthmatic patients than in patients with COPD; the opposite was true when differences were expressed as a percentage of the corresponding values obtained with manoeuvre 2. This discrepancy reflects the greater severity of airway obstruction of COPD patients (11). The percentage ratio ΔFEV_1:FEV_1 (2) increases with decreasing FEV_1 (% predicted) (Figure 3).

The time dependency of PEF has also been studied in children with asthma (12). Contrary to the results in Table 1, no difference in PEF was found between manoeuvres 1 and 2. This discrepancy, however, merely indicates that in the asthmatic children PEF was measured with a peak flow meter, which was inserted into the mouth *after* inhalation to total lung capacity (TLC). This necessarily involves an obligatory end-inspiratory pause even with manoeuvre 1, which may last several seconds depending on the coordination of the children and on the instructions that they have received. As a result of this 'spurious' obligatory pause, the difference in PEF between manoeuvres 1 and 2 is necessarily reduced or may even be abolished, depending on the duration of the pause. In this connection it should be stressed that routine FVC measurements involve equipment inserted in the mouth either before the maximal inspiration or after inhalation to TLC. In the latter instance, the manoeuvres are never of type 1.

Figures 4 and 5 depict the average MEFV curves obtained with manoeuvres 1 and 2 in 13 normal subjects and 13 COPD patients. In both instances the values of $\dot{V}_{max}$ were significantly higher with manoeuvre 1.

Nature of time dependence of MEFV: Although several factors may contribute to the time dependency of MEFV (8,9), this phenomenon is mainly due to the fact that in manoeuvre 1 the effective elastic recoil pressure of the lung (Pel,L) is higher as a result of viscoelastic (*stress adaptation*) behaviour of lung tissue (11,13,14). Because the values of

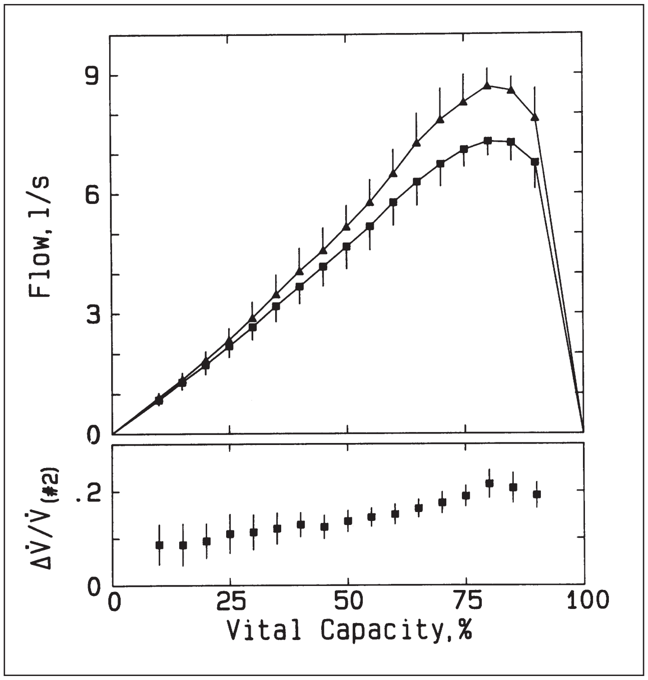

Figure 4) Top *Mean values of maximal expiratory flow volume ($\dot{V}$) curves of 13 normal subjects during manoeuvres 1* (▲) *and 2* (■) **Bottom** *Mean differences in flow ($\Delta\dot{V}$) between manoeuvres 1 and 2, expressed as a fraction of the corresponding flows with manoeuvre 2. Bars indicate SD (Reproduced from reference 8, used with permission)*

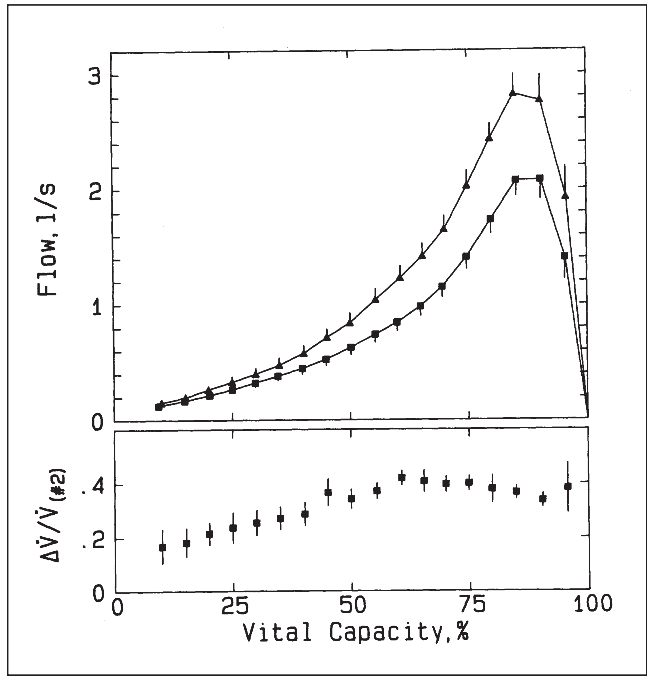

Figure 5) *Mean values of maximal expiratory flow ($\dot{V}$) volume curves of 13 chronic obstructive pulmonary disease patients, whose average ± SD forced expiratory volume in 1 s was 56±15% predicted, during manoeuvres 1* (▲) *and 2* (■)*. Bars indicate SD*

$\dot{V}_{max}$ depend on Pel,L (15), the maximal flows are necessarily higher with manoeuvre 1 than with manoeuvre 2. In this context, it should be stressed that the higher Pel,L obtained with fast inspiration can be completely dissipated during a 5 s breath hold at TLC; hence, to achieve the highest expiratory flows it is necessary to inhale as fast as possible and exhale without pausing at end inspiration (8).

Implications of time dependence of MEFV curves: In normal subjects the differences in PEF and FEV_1 between manoeuvres 1 and 2 averaged 1.28 L/s and 0.19 L, respectively. In normal nonsmoking adults such a change in PEF and FEV_1 would, on average, be expected over an age span of about 30 years (8). Clearly, in epidemiological studies the inspiratory manoeuvre before FVC needs to be standardized. The same is valid for patients with COPD and asthma. However, in this case the time dependence of $\dot{V}_{max}$ also has an important bearing on the assessment of the FEV_1 response to bronchodilators. According to the American Thoracic Society recommended criteria for response to bronchodilator drugs, a greater than 12% increase in FEV_1 relative to baseline represents a meaningful response (16). In view of the marked time dependency of FEV_1 (Table 1) with these criteria, correct delineation of responders *versus* nonresponders to bronchodilator (or bronchoconstrictor) drugs becomes problematic unless the inspiratory pattern before the FVC manoeuvre is standardized (11). Similar considerations apply to the measurement of PEF and MEFV curves.

In the past, MEFV curves obtained with the subject breathing air or 80% helium-20% oxygen have been compared to elucidate the mechanisms of reduced flows in patients with airway obstruction, and to detect obstructive disease at a time when maximal flows are still in the normal range but small airway resistance is increased (17). However, within-subject variability of responses was found to be so great (18) that the clinical use of this helium test was discontinued. If properly standardized, however, this test may well turn out to be more reliable than previously thought.

In conclusion, in normal subjects and patients with obstructive lung disease, the flows during the FVC manoeuvre depend significantly on the pattern of the preceding inspiratory manoeuvre. Accordingly, the latter should be standardized in clinical and epidemiological studies. If the highest flows and FEV_1 are desired, manoeuvre 1 should be used. For assessment of the evolution of lung disease or of the effects of treatment (eg, bronchodilators) either manoeuvre may be used, but should be used consistently (11). Although the nature of the time dependence of FVC is not fully understood, stress relaxation of viscoelastic units within the lung during manoeuvre 2 plays a primary role (11).

DETECTION OF TIDAL EXPIRATORY FL

The highest pulmonary ventilation that a subject can achieve is ultimately limited by the highest flow rates that can be generated. Most normal subjects do not exhibit expiratory FL even during maximal exercise. In contrast, patients with COPD may exhibit FL even at rest, as first suggested by Hyatt (19). This was based on his observation that patients with severe COPD often breathe tidally along their MEFV curve. The presence of expiratory FL during tidal breathing promotes dynamic pulmonary hyperinflation and intrinsic positive end-expiratory pressure (PEEP), with concomitant increase of inspiratory work, impairment of inspiratory muscle function and adverse effects on hemodynamics (20). This, together with flow-limiting dynamic compression during tidal breathing, may contribute to dyspnea (21,22).

Conventionally, FL is assessed by comparison of the tidal expiratory flow volume ($\dot{V}$- V) curves with the corresponding MEFV curves: patients in whom, at comparable lung volumes, flows are similar or higher than those obtained during the FVC manoeuvre are considered FL (19). This approach, however, has limitations because, as a result of thoracic gas compression during the FVC manoeuvre, the tidal and maximal $\dot{V}$- Vcurves have to be measured with a body plethysmograph (23). This implies that such measurements are confined to resting breathing in the sitting position. Apart from this, other factors make assessment of FL based on comparison of tidal and maximal $\dot{V}$- Vcurves problematic. These factors include volume-dependent changes in airway resistance and lung recoil during the maximal inspiration before the FVC manoeuvre, and time-dependent viscoelastic behaviour of pulmonary tissues and time-dependent lung emptying due to time constant inequality (14,24). These mechanisms imply that the maximal flows that can be reached during expiration depend on the volume and time history of the preceding inspiration (see above). Because, by definition, the previous volume and time history vary between resting and maximal inspiration, it follows that assessment of FL based on comparison of tidal and maximal $\dot{V}$- V curves may lead to erroneous conclusions, even if the measurements are done with body plethysmography (25,26). Recently, however, an alternative technique, the NEP method, has been introduced to detect expiratory FL during tidal breathing. It does not require performance of FVC manoeuvres on the part of the patient, nor a body plethysmograph (27,28). The negative expiratory pressure method has been validated by concomitant determination of isovolume flow-pressure relationships (28).

NEP method for detection of expiratory FL: FL is a term often used to indicate that, in a given patient, the flows during the FVC manoeuvre are below the predicted normal. In this account the term is used to indicate that the expiratory flow rates achieved during the entire or part of the tidal expiration are the maximal achievable under the prevailing conditions.

Figure 6 depicts the experimental set-up used to detect expiratory FL with NEP. It consists of a pneumotachograph and a Venturi device capable of generating a negative pressure when connected to a source of compressed air. The Venturi device is activated by opening a rapid solenoid valve (22).

The NEP method consists of applying negative pressure at the mouth during tidal expiration and comparing the ensuing $\dot{V}$- V curve with that of the previous control expiration. Therefore, with this technique, the volume and time history before the expiration with NEP is the same as that of the preceding control breath. If the application of NEP elicits increased flow over the entire range of the control tidal volume, the patient is not flow limited (Figure 7, left). In contrast, if with NEP the subject exhales along the control $\dot{V}$- V curve over part or the entire range of the control tidal expiration, FL is present (Figure 7, middle and right). The FL portion of the tidal expiration can be expressed as a percentage fraction of the control tidal volume (%V_T). In the two FL subjects depicted in Figure 7, the FL position amounted to 45% and 68% V_T, respectively. If expiratory FL is present when NEP is applied, there is a transient increase of flow (Figure 7, spike in right panel), which mainly reflects enhanced dynamic airway compression and sudden reduction in volume of the compliant oral and neck structures (27,28). Such spikes are useful markers of FL.

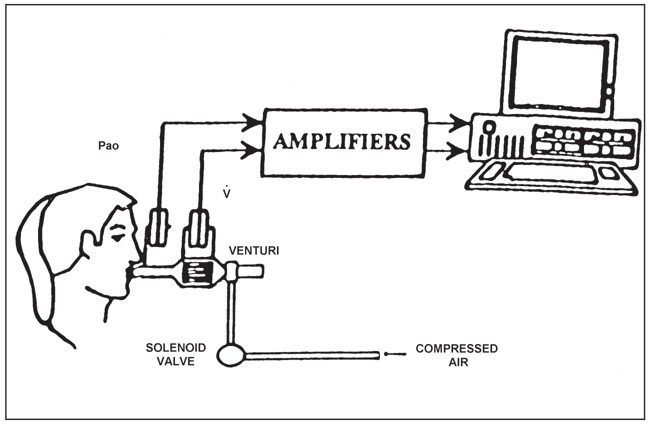

Figure 6) *Schematic diagram of equipment set-up for negative expiratory pressure test. Volume is obtained by numerical integration of flow ($\dot{V}$) signal. During the study, the time course of flow, volume and pressure are continuously monitored on the screen of the computer, together with the corresponding flow-volume curves. Pao Pressure at airway opening (Reproduced from reference 22, used with permission)*

Relationship of FEV_1 to FL: Figure 8 depicts the relationship between FEV_1 (% predicted) and FL in 117 stable COPD patients. Expiratory FL was determined during resting breathing in sitting and supine positions. Although, on average, the patients who were FL in both seated and supine positions had a significantly lower FEV_1 (% predicted) than those who were not FL ($P<0.001$), there was considerable scatter of the data. Indeed, 60% of the non-FL group had a FEV_1 below 49% predicted and would be classified as having severe to very severe airway obstruction (29). Thus, FEV_1 is not a good predictor of tidal expiratory FL.

FL and chronic dyspnea: Intuitively, one would expect patients with the most severe airway obstruction, as assessed with routine lung function measurements, to be the most dyspneic. However, some patients with severe airway obstruction are minimally symptomatic, whereas others with little objective dysfunction appear to be very dyspneic (30). Many studies have shown that the correlation between chronic dyspnea and FEV_1 is weak (22). In contrast, FL as measured with the NEP technique is a much better predictor of chronic dyspnea (22,25,26).

Assessment of FL with conventional method: Assessment of FL based on comparison of tidal with maximal $\dot{V}$– V curves (19) has been found to be inaccurate even when volume was measured with a body plethysmograph in order to avoid thoracic gas compression artefacts (25,26).

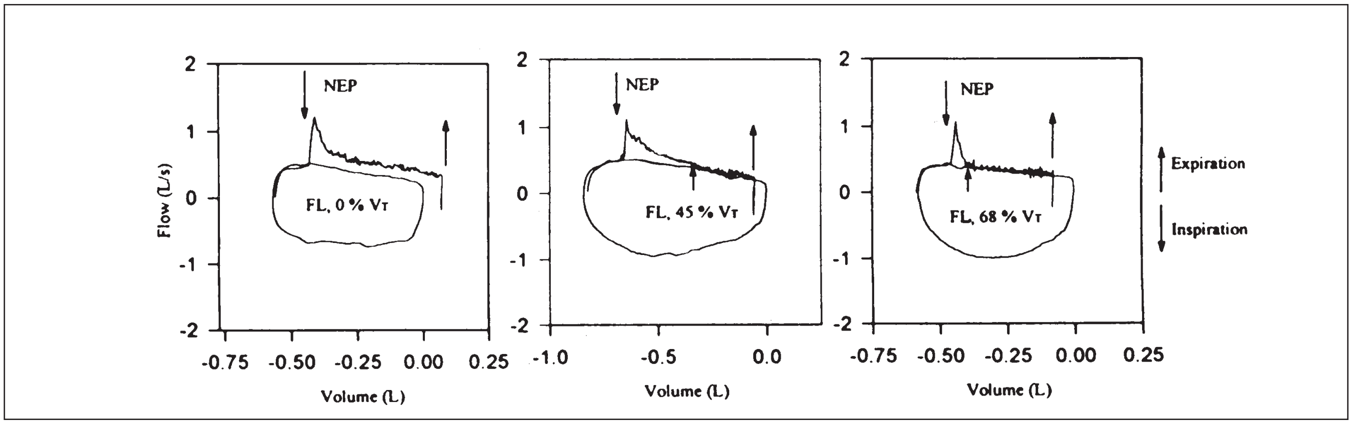

Figure 7) *Flow-volume loops of negative expiratory pressure (NEP) test breaths and preceding control breaths in three representative chronic obstructive pulmonary disease patients seating at rest. No flow limitation (FL) (***left***), FL over last 45% of control expired tidal volume (V_T) (***middle***), FL over 68% V_T (***right***). Long arrows indicate onset of NEP. Short arrows indicate onset of FL. Zero volume is end-expiratory lung volume of control breaths (Reproduced from reference 22, used with permission)*

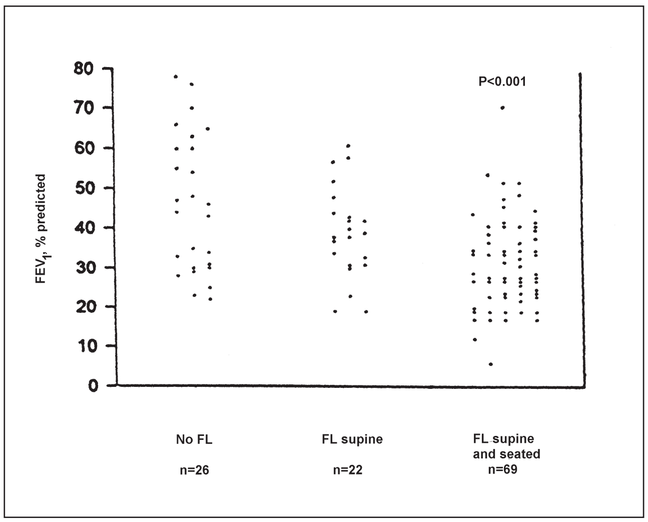

Figure 8) *Individual values of forced expiratory volume in 1 s (FEV_1) (% predicted) and tidal flow limitation (FL) of 117 chronic obstructive pulmonary disease patients while seated and supine at rest. Twenty-six patients were not FL either seated and supine, 22 were FL only supine, and 69 were FL both seated and supine; P refers to difference between no FL and FL both seated and supine. (Reproduced from reference 22, used with permission)*

In conclusion, the NEP method provides a simple and reliable method for detecting expiratory FL both at rest and during exercise (31). The method does not require body plethysmography, does not depend on patient cooperation and coordination, and can be applied in any desired body posture. In COPD patients, FL at rest is associated with impaired exercise capacity (31).

MONITORING OF FVC PERFORMANCE

One of the largest sources of within-subject variability of FVC is the performance of the test with insufficient expiratory effort to reach expiratory FL (32). In the past, no online method was available to assess whether the flows during the FVC were maximal. Recently, however, a simple method to assess FVC performance has been developed (33). It is based on application of short pulses of negative pressure (–10 cm H_2O) during the FVC manoeuvre. If during the FVC manoeuvre expiratory flow increases during the application of the negative pressure pulse, then expiratory flow is submaximal. In contrast, if flow does not increase with the negative pressure, expiratory FL has been reached. Thus, with this method it is possible to determine whether the maximal flows are low as a result of insufficient expiratory effort (eg, weak expiratory muscles, subject cannot produce a sustained forced expiratory effort because of lack of coordination or comprehension, or subject is malingering). This study has also demonstrated that, at least in normal subjects, PEF is in the effort-independent range of FVC (33), and not in the effort-dependent range as previously thought (5).

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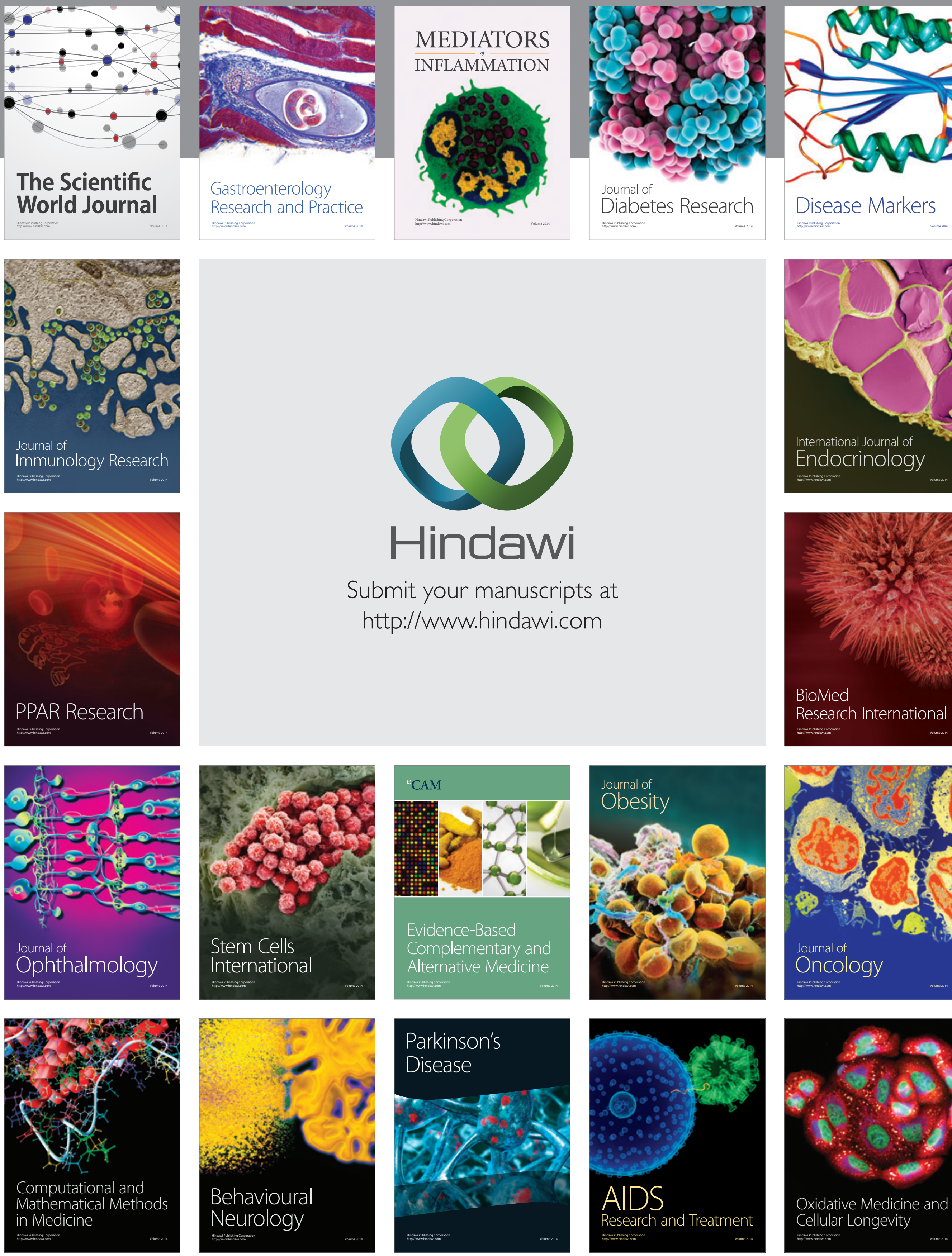
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