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Measurement of Functional Residual Capacity during Mechanical Ventilation by Simultaneous Exchange of Two Insoluble Gases

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A precise method for rapid measurement of functional residual capacity (FRC) during mechanical ventilation that uses the simultaneous exchange of argon and nitrogen is described. Circuit leaks were immediately recognizable upon completion of a run, and pneumotachygraphic inaccuracies due to turbulent flows, changes in viscosity, and time delays between pneumotachygraph and mass spectrometer signals were avoided. For 166 duplicate determinations, the first measurement of FRC differed from the second by 0.5 ± 0.5 per cent (mean ± SE). The technique does not affect pulmonary gas exchange. During 35 consecutive determinations of FRC (with an inspired oxygen of 50 per cent), mixed expired oxygen and carbon dioxide tensions varied less than 7 and 1.5 torr, respectively. (Key words: Lung: functional residual capacity; washout. Measurement techniques. Monitoring: ventilation. Ventilation: mechanical).

MOST PATIENTS with acute pulmonary failure have decreased functional residual capacity (FRC), which can lead to progressive alveolar collapse.[1] Prevention or reversal of this collapse often can be accomplished by applying positive airway pressure. An "optimum" airway pressure would prevent alveolar collapse while avoiding significant pulmonary blood flow redistribution or parenchymal lung damage caused by excessive forces or over-distension of alveoli. However, the definition of, or method for, obtaining this optimum pressure has not been determined. Consequently, we investigated the effects of airway pressures on pulmonary gas exchange, lung distension, and regional ventilation. We required a technique that would accurately measure lung volume during positive-pressure ventilation without disturbing important physiologic variables.

For our purposes, the disadvantages of the more standard helium dilution and nitrogen washout techniques include: 1) the possible development of absorption atelectasis and/or pulmonary blood flow redistribution due to changes in alveolar P_{O_2};[2] 2) difficulty in detecting circuit leaks during positive-pressure ventilation, with resulting erroneously large calculated FRC values; 3) inability to make multiple determinations of FRC in rapid sequence; 4) lack of immediate availability of results, which would permit manipulation of FRC according to research or therapeutic protocol; and 5) in washout methods requiring a pneumotachygraph, the possible occurrence of inaccuracies because of varying gas concentrations and, consequently, viscosities, throughout each respiratory cycle.

We present an open-circuit, simultaneous washin/washout technique for measuring FRC that substitutes one insoluble gas for another. Our technique provides immediate results with "on-line" computing, maintains a constant $F_{I_{O_2}}$, avoids inaccuracies due to variable gas viscosities or incompletely compensated time delays in the mass spectrometer, permits immediate detection of circuit leaks, and allows multiple determinations of FRC to be made in rapid sequence.

Methods

The apparatus is illustrated in figure 1. Valves A and B connect the patient through one of two parallel bellows-in-box systems to a ventilator. The two bellows are filled automatically from demand valves (not shown) connected to two compressed gas cylinders, one containing 50 per cent nitrogen and 50 per cent oxygen; and the other, 50 per cent argon and 50 per cent oxygen. During expiration, the weight of the bellows creates the slight negative pressure required to open the demand valves. When valves A and B

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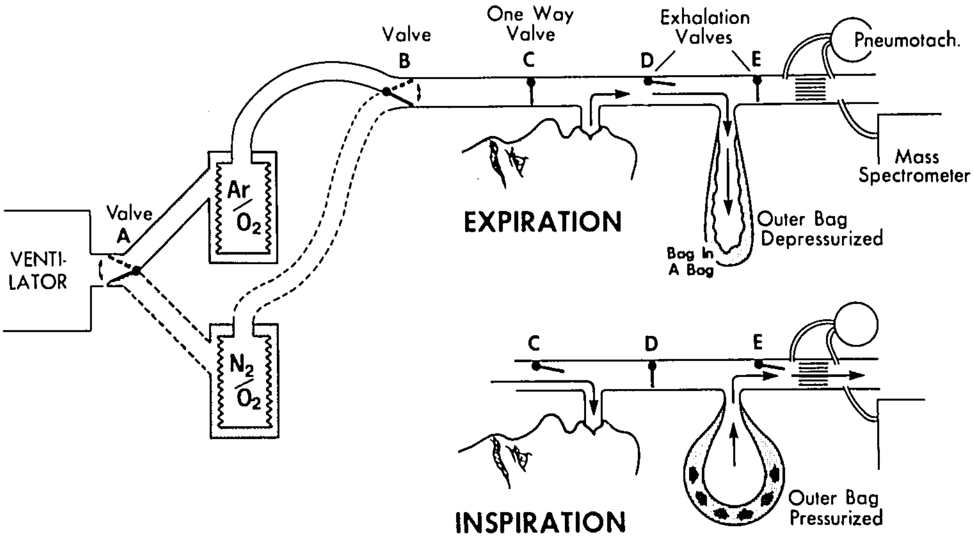

FIG. 1. Diagram of apparatus used for determination of FRC illustrating operation of valves during expiration and inspiration. Valves A and B are turned simultaneously by hand. Valves C, D, and E and the pressure between the two bases are controlled pneumatically and are timed relative to the ventilator cycle.

are turned simultaneously during expiration, the patient can be switched to either one of the bellows-in-box systems. To begin a measurement, the patient is first equilibrated with one of the insoluble gases. When the washout/washin is to begin, the patient is switched to the other bellows-in-box system, causing argon to be washed in while nitrogen from the patient is washed out (or vice versa). Instead of using the ventilator directly for the nitrogen equilibration cycles, one of the bellows-in-box systems is used so that the system compliance and tidal volume remain constant throughout the measurement. The collection, mixing, and ejection of expired gas for measurement are timed by the ventilator cycle and controlled pneumatically‡ as follows: during expiration, valve E closes 0.2 s before valve D opens, and expired gas passes into a previously emptied bag-in-bag (a one-way valve, C, prevents reflux of expiratory gas back into the inspiratory ventilator tubing). On inspiration, valve D closes, pneumatic pressure is applied between the two bags, and valve E opens. A homogeneous, expired gas mixture is thereby emptied through a heated pneumotachygraph (Fleisch® No. 2). Resistance to expiratory flow is 0.1 cm $H_2O \cdot l^{-1} \cdot min^{-1}$ at 80 l/min. Tidal volumes are obtained by analog integration of the flow signal with respect to time. The sampling port for a mass spectrometer (Chemetron,® Medspec II) is located distal to the pneumotachygraph in order to avoid producing an artifactual drift of the volume signal due to aspiration of gas into the mass spectrometer. Each set of values for tidal volume and gas concentration is converted to digital signals by a computer (Digital Equipment Corporation, LSI 11/03). The computer stores, calculates, and, at the completion of a run, displays (on a terminal at the bedside) values for breath-by-breath mixed expired gas concentrations, tidal volume, and washin and washout FRC values. Positive end-expiratory pressure was applied by placing an Emerson PEEP assembly between the patient and valve D (fig. 1). When a run is completed, the patient's lung is already equilibrated with the insoluble gases, and another determination of FRC can be started immediately by switching the patient to the opposite bellows.

‡ Using components from Bird Corporation, Palm Springs, California. Parts list available on request from authors.

The equation used for computing FRC is derived below by totaling the net gas exchange within the apparatus and lungs. The quantity of gas returned to the lungs in the mixed venous blood is assumed to be insignificant.[3]

$$(V + DS)CE_N - (V + DS)CI = \text{net change of insoluble gas in } (V + DS).$$

ABBREVIATIONS

V = lung volume at FRC (including patient dead space)
DS = volume of apparatus (including volume of collapsed expiratory bag)
CI = concentration of insoluble gas equilibrated in lung (V) and apparatus (DS) just prior to the washin/washout exchange
CF = concentration of the insoluble gas inspired during the exchange
CE_i = mixed expired concentration of the i'th breath
N = the number of the breath at which CE_i first is within one per cent of CF
VI_i = inspired volume of the i'th breath
VE_i = expired volume of the i'th breath
CE_N = final concentration of insoluble gas in lung (V) and apparatus (DS); (i = N)

Also,

$$\sum_{i=1}^{N} (CF_i \cdot VI_i)$$

= amount of insoluble gas entering (V + DS) during N breaths,

and

$$\sum_{i=1}^{N} (CE_i \cdot VE_i)$$

= amount of insoluble gas leaving (V + DS) during N breaths.

Since the net change of gas in (V + DS) is equal to the difference between the amount of gas entering and leaving (V + DS), the following equation may be written:

[Net change of gas in V + DS]

= [Total gas entering] − [Total gas leaving]

or as follows:

$$[(V + DS)CE_N - (V + DS)CI] = [\sum_{i=1}^{N} (CF \cdot VI_i)] - [\sum_{i=1}^{N} (CE_i \cdot VE_i)] \quad \text{(equation 1)}$$

Solving for V in equation 1 produces the following:

$$V = \frac{\sum_{i=1}^{N} (CF \cdot VI_i - CE_i \cdot VE_i)}{(CE_N - CI)} - DS \quad \text{(equation 2)}$$

This is a general equation that is applicable for both washin and washout, and for step changes in the concentration of a single gas. We do not measure inspired volumes and assume that $VI_i = VE_i$. If CF is zero for one of the gases (the "washout gas"), then the determination of V is unaffected by inaccurate values for VI_i's and, therefore, may be used to verify the value of V obtained from the washin gas. If $VI_i = VE_i$, equation 2 may be rewritten as follows:

$$V = \frac{\sum_{i=1}^{N} (CF - CE_i)VE_i}{(CE_N - CI)} - DS \quad \text{(equation 3)}$$

Gas concentrations are measured dry, and volume measurements must therefore be corrected from BTPD to BTPS.

Each exchange is terminated when CE_i is within one per cent of CF for both argon and nitrogen. (The number of breaths required to meet this condition for each gas was not statistically different.)

For measuring volume, a pneumotachygraph is preferable to a spirometer-Douglas bag combination because of its small size and its ability to provide breath-by-breath volume information. The pressure drop across the pneumotachygraph is directly proportional to both flow and viscosity when the gas flow is laminar. However, when the pneumotachygraph is placed directly in the patient's airway, its accuracy is limited by the development of turbulent gas flows and variations in exhaled gas concentrations, which require continuous correction for viscosity. Patients mechanically ventilated for diseases causing decreased compliance may have expiratory flow rates above the laminar range of the pneumotachygraph (180 l/min). To eliminate these problems and to obtain precise volume measurements (table 1), we placed the pneumotachygraph after the expiratory gas collection system. At that location, the pneumotachygraph would have more constant laminar flow rates, independent of tidal volume. The gases used in our system have viscosities (relative to air) of 1.22 for argon, 1.08 for oxygen, 0.98 for nitrogen, and 0.83 for carbon dioxide. Depending on the oxygen concentration, the viscosity may vary more than 15 per cent during a determination of FRC; therefore, the pneumotachygraph signal must be corrected to permit an accurate volume measurement. With this system, only one correction for viscosity per breath is required, since for each breath only homogeneous gas mixtures pass through the pneumotachygraph. Therefore, it is not necessary to correct the pneumotachygraph signal for viscosity throughout exhalation.

TABLE 1. Calibration of Pneumotachygraph System Using a Jumbo Syringe

Tidal Volumes Delivered by a Jumbo Syringe (ml)	Volumes (Mean ± SD) Determined by Pneumotachygraph Collection System (ml)	Coefficient of Variation (Per Cent)	n
500	504 ± 4.5	±0.89	25
1000	993 ± 5.2	±0.52	25
1500	1478 ± 8.5	±0.58	25

Oxygen, carbon dioxide, nitrogen, argon, and helium are measured with a mass spectrometer, which has a 5 to 95 per cent full-scale response time of 180 ms, a resolution of 1 torr, and a degree of accuracy of within 1.4 torr/760 torr. Such precision is more than sufficient for this application. However, if the pneumotachygraph and mass-spectrometer port are placed immediately adjacent to the patient's endotracheal tube, the quantity of a gas exhaled per breath must be obtained by integrating the instantaneous product of concentration and flow with respect to time. Although the pneumotachygraph signal occurs almost instantaneously, the signal from the mass spectrometer is altered both by delays in washout

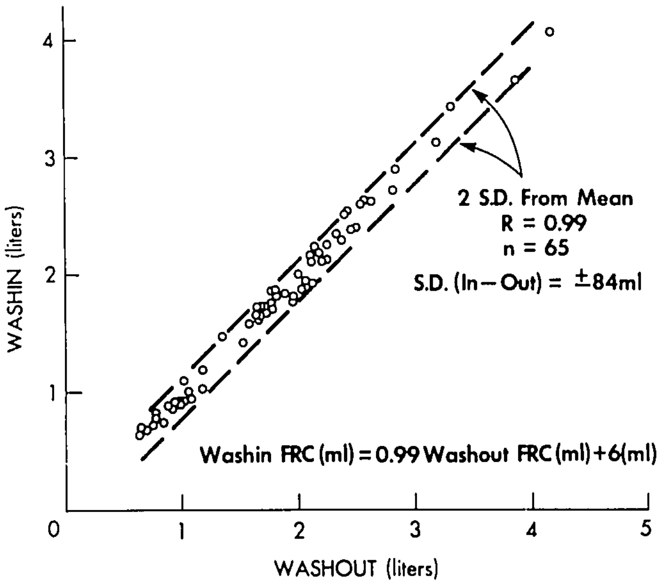

FIG. 2. Plot of washin *vs.* washout FRC values for 65 determinations in 20 patients. The dashed lines represent two standard deviations from the mean. The linear regression equation has a slope of 0.99 and an intercept of 0.006 l.

through the sampling catheter and delays in the electronic response. Precise correction of these effects would require using complex deconvolution or difference equation methods.[4,5] Our technique of first mixing the expired gases and then measuring their concentrations avoids the problems of intrabreath integration of concentration and flow, and provides several seconds during which the concentrations may be measured. Additionally, all gas concentrations are measured at atmospheric pressure, a practice that eliminates the airway pressure artifact on the mass spectrometer reading (as much as one per cent error with 20 cm H_2O). The accuracy of the mixed-expired gas concentrations was verified by comparing the average of breath-by-breath P_{CO_2} values with the P_{CO_2} of gas collected simultaneously in a Douglas bag. The average breath-by-breath P_{CO_2} for 120 breaths was within 0.25 torr of the P_{CO_2} in the Douglas bag, a degree of accuracy well within that of the mass spectrometer.

For a determination of FRC, it is necessary to know the quantity (*e.g.*, moles) of gases that have been washed into or out of the lungs. Since no lung is homogeneous, methods based on "end-tidal" concentrations are inherently inaccurate. There is no single alveolar gas concentration within the lung, and the error resulting from using the product of mid-tidal (or end-tidal) concentrations and tidal volume is increased in those disease states that increase inhomogeneity of ventilation.

The difference between simultaneous washin and washout FRC values is used to test for system leaks. If a washin FRC value is larger than the washout value by more than 168 ml, two standard deviations determined in a preliminary study (see results), a leak is presumed, the system is checked, and the run is repeated using the reverse gas exchange sequence. If washin and washout values are within the two standard deviations, the average is taken as the patient's FRC.

The exchange of one insoluble gas for another and maintenance of the same system compliance for both bellows permit the mixed expired P_{O_2} and P_{CO_2} to remain essentially constant throughout the determination of FRC.

We verified our method, in part, by comparing the determinations of the FRC of a mechanical lung analog using both helium dilution and nitrogen/argon exchange.

Approval was received from the Committee on Human Research of the University of California, San Francisco, and informed consent was obtained for each patient. Statistical analysis was performed using a Student *t* test, two-factor analysis of variance, and method of least-squares for linear regression.

Results

The helium dilution and nitrogen/argon exchange values for FRC obtained from the mechanical lung analog were not significantly different. Using helium dilution, FRC (mean ± SD) was 1863 ± 30 ml (n = 5); using nitrogen/argon exchange, FRC (mean ± SD) was 1862 ± 29 ml (n = 10).

The mixed expired P_{O_2} and P_{CO_2} were essentially constant throughout 35 consecutive determinations of FRC in five patients. The maximum variation in mixed expired P_{O_2} and P_{CO_2} for all exchanges was less than 7.0 and 1.5 torr, respectively (maximum minus minimum value).

A preliminary study was performed using 65 FRC values for simultaneous washin and washout exchange in 20 patients during mechanical ventilation for respiratory failure. The range of FRC values was 632 to 4117 ml. The mean difference (±SD) between pairs of washin and washout data was 25 ± 84 ml (fig. 2). The variance was independent of lung volume, and the mean difference between pairs of data for washin and washout was independent of whether nitrogen or argon was used as the washin gas. (We anticipated that we would observe a constant difference between values for FRC calculated from the two gases, since argon is approximately twice as soluble in water as nitrogen.) However, within runs, no consistent (or statistically significant) difference was observed. Thus, the magnitude of the difference in gas volume absorbed by the body for the two gases was less than the error of the measurement.

In subsequent studies utilizing the criteria that acceptable washin and washout FRC values be within 168 ml of each other, 166 duplicate determinations of FRC were made in 21 patients requiring mechanical ventilation for acute pulmonary failure. The first measurement of volume (mean ± SD) differed from the second by 0.5 ± 0.5 per cent, the range of values for FRC being 710 to 4488 ml.

Discussion

We desired a safe, accurate, and rapid method for measuring FRC without altering the alveolar P_{CO_2} or P_{O_2} that would provide breath-by-breath washout concentrations of the insoluble gas. Several of the advantages of our technique over helium dilution or standard nitrogen washout methods result from the exchange of one insoluble gas with another.

First, when positive-pressure ventilation is used with other methods for measuring FRC, leaks in the apparatus circuitry are very difficult to detect. However, with our technique, leaks would cause a loss primarily of the washin gas (since the inspired concentration of the washout gas is zero). Therefore, the washin FRC value would be significantly greater than the washout value. Because the computer provides immediate values for FRC, the leak can be quickly recognized and corrected, and the run repeated.

Second, since the patient's lung is equilibrated with the alternative gas mixture at completion of a run, another determination can be begun immediately. This advantage has made possible clinical studies that require extensive and rapid measurement of FRC with minimal disruption in patient care.

Third, many measurements of FRC can be made without significantly altering mixed expired (and presumably, alveolar) P_{O_2}. Therefore, uncertain effects due to absorption atelectasis or pulmonary blood flow redistribution are avoided.

Fourth, since a washout value is equivalent to a washin value (in a mathematical sense), each exchange provides duplicate measures of the mixed expired gas concentrations (argon and nitrogen). This duplication improves the accuracy of the measurements of FRC.

An additional advantage of our method over helium dilution methods arises from the breath-by-breath mixed expired concentrations of the insoluble gases. Although the clinical applicability has yet to be demonstrated, mixed expired concentrations may be used to provide extensive descriptions of regional ventilatory performance.[6,7]

The major disadvantage of our technique stems from the relative complexity of the equipment required to obtain accurate, mixed expired gas concentrations. Once the equipment is in place at the patient's bedside, a series of FRC determinations may be made very quickly. However, the time required for equipment setup and calibration precludes the application of this method for routine clinical measurements.

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