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A METHOD FOR THE DETERMINATION OF THE VOLUME OF AIR IN THE LUNGS: MEASUREMENTS IN CHRONIC PULMONARY EMPHYSEMA *

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The present study is concerned with the measurement of the functional residual capacity (FRC) in chronic pulmonary emphysema by a gas dilution method, i.e., the washout of nitrogen from the lung during prolonged oxygen breathing.

There have been many methods in use to measure the FRC (or the residual volume) since Davy in 1800 measured his own residual volume by rebreathing hydrogen, which he had made himself, from a balloon (1). These methods, both the open circuit (washout) and closed circuit (rebreathing from a balloon or spirometer), have in general followed a consistent historic trend in that longer and longer periods of washout or rebreathing have been required in later methods: Davy in 1800 rebreathed for 20 seconds (1), Gréhan in 1864 for 6 inspirations (2), Van Slyke and Binger in 1923 for 5 minutes (3), Christie and Bates for 7 minutes (4, 5), Darling, Cournand and associates for 7 or 11 minutes (6, 7) and Briscoe, Becklake and Rose for 12 minutes (8, 9). In justice to these earlier workers it should be mentioned that most of those quoted above and others (10, 11) realized that to get the best results in emphysema somewhat longer studies were desirable.

More recent studies of the N₂ or helium washout in patients with chronic pulmonary emphysema have found detectable quantities of these inert gases being washed out of the lungs, distinct from those washed out from tissues, even after 20 to 40 minutes of O₂ breathing (12-18).

The present study describes a method in which all the N₂ eliminated from the lung during 15 minutes, or longer, of oxygen breathing is measured. Moreover, the quantity of N₂ which would be eliminated in a longer study is esti-

mated by integrating the exponential washout function in the least ventilated alveoli. The advantage of this procedure lies in eliminating the need for an alveolar sample to estimate the N₂ remaining in the lung at the end of the study. Such samples are misleadingly low in N₂ in chronic pulmonary emphysema and result in underestimation of the FRC.

METHODS

Functional residual capacities were measured by the conventional method of Cournand, Baldwin, Darling and Richards (7). They were also measured at a different time by a new method to be described here. This method is a development both of that used by Blair, Hickam and Frayzer with helium (14, 15) and by Briscoe and associates with N₂ (19). It utilizes a system of two balloons (Figure 1) which collect the gas expired in alternate 30-second periods. At the end of each 30-second collection, the balloon is emptied into the Tissot spirometer by pressing it between two boards suspended on either side of it. The mixed expired gas expelled from each balloon in turn is analyzed with a N₂ meter. Thus, every 30 seconds the volume expired and the mean concentration of N₂ in that volume are known. The study ends after 15 to 25 minutes.

I. Nitrogen washout curve. Figure 2 shows the data in one study in which there were 32 balloon collections during 16 minutes of O₂ breathing. In each collection the volume measured on the Tissot spirometer and the difference between the inspired N₂ concentration and that of the mixed expired gas in the balloon were measured. Their product yields the quantity of N₂ eliminated from the body in that half minute. By subtracting the quantity of N₂ eliminated from the tissues (\dot{V}'_{N_2}) in each period, the quantity of N₂ eliminated from the lungs (\dot{V}_{N_2}) in each period was determined and plotted on semilogarithmic paper.

At the beginning of O₂ breathing, \dot{V}_{N_2} is momentarily about 81 per cent of expired gas volume (\dot{V}_E). In the first 5 minutes it falls steeply due to the rapid washout of N₂ from the well ventilated groups of alveoli. After about 5 minutes \dot{V}_{N_2} is still considerable and only slowly decreasing. This is due to the extremely small ventilation of a large group of alveoli whose volume and ventilation can be estimated from a straight line drawn through this slow phase. The major part of the total N₂ initially present in

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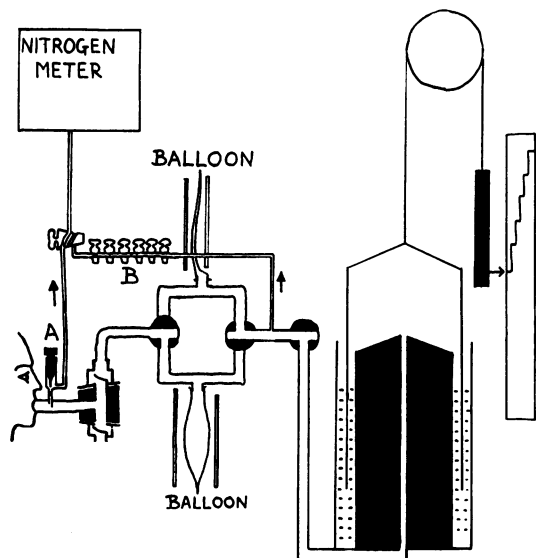


FIG. 1. SCHEMATIC REPRESENTATION OF THE EQUIPMENT USED IN THE PRESENT STUDY. The needle valve (A) samples at the mouth, and the long line, with glass stopcock leak (B), samples mixed expired air; the balloon stopcock assembly is made from anesthesia balloons and standard plumbing fittings. The valve box at the mouth is part of a 5-way stopcock (Respiration Aids, 255 E. 148 St., New York 51, N. Y.) here shown connected for oxygen breathing. When the mouthpiece is connected to air as the inspire, the expirate goes to waste; these two channels used during air breathing are not shown here.

the lungs was determined without assumptions by adding the 32 measurements obtained in 16 minutes ($\int_0^{16} \dot{V}_{N_2} \cdot dt$). The smaller quantity which would have been washed out thereafter was estimated by extrapolating the slow phase and integrating to determine $\int_{16}^{\infty} \dot{V}_{N_2} \cdot dt$ under the straight line in Figure 2.

II. Details of equipment and procedure. The dead spaces of the two anesthesia balloons used were 250 and 330 ml, these being the volumes of the tubes between the mouth and the balloons. To correct for this dead space the midpoint of each collection should be taken to be about 4 seconds earlier than the middle of the 30-second period. This has a negligible effect in studies on patients with chronic pulmonary emphysema. Both balloons were flushed with medical oxygen before each study, until the N_2 meter showed that the gas leaving the balloon contained no more than 0.025 per cent more N_2 than the medical oxygen, this figure being the limit of resolution of our N_2 meter.

The stopcocks controlling admission and displacement of gases alternately to and from the balloons were mechanically linked, so that when either balloon was connected to the Tissot spirometer, the other was automatically connected to the mouth. These stopcocks and their

associated T and L pieces are standard $\frac{3}{4}$ inch plumbing supplies.

Inspired and expired gas were sampled for about 15 seconds in each half-minute period through a needle valve at the mouth. The conventional needle valve type of leak into the vacuum system of the N_2 meter has the advantage of quick response, but it is unreliable for accurate analysis since it is sensitive to changes in hydration and temperature, and to blockage by air-suspended particles. For the analysis of mixed expired gas in the balloons, 6 glass stopcocks connected in series gave a more reliable leak with a line delay of 3 seconds and a 90 per cent response time of half a second, when adjusted to produce a pressure in the vacuum system of 2 mm.

The N_2 meter was calibrated before and at the end of each study with known gas mixtures (air, medical O_2 , and 2.2, 8.6, 16.6 and 42 per cent N_2 in O_2).

Sources of nitrogen other than the lungs were controlled as follows. None of the subjects had perforated ear drums. They were instructed not to belch or to allow leaks at the mouthpiece and their mouths were watched continuously by a second observer. Between balloon analyses the N_2 meter was connected to sample inspired and expired gas at the mouth for about 15 seconds in every half-minute period. The record of N_2 concentration at the mouth obtained via the needle valve showed no leaks.

III. Symbols. It is useful here to comment on the symbols used in this report. They are the same as those used previously in this laboratory (18-20), except in these respects: \dot{V}'_{N_2} is the rate of nitrogen elimination from tissues, and \dot{V}_{N_2} is the rate of nitrogen elimination from

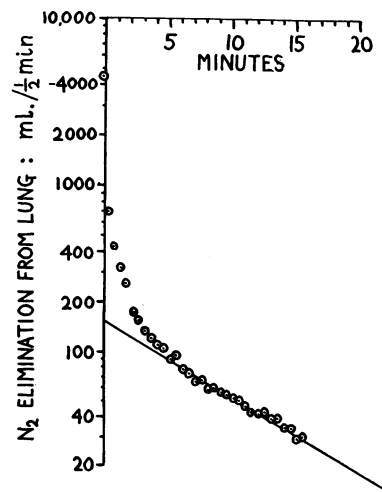


FIG. 2. DATA IN ONE STUDY ON A PATIENT WITH CHRONIC PULMONARY EMPHYSEMA. The abscissa shows the duration of O_2 breathing in minutes. The ordinate shows milliliters of N_2 at BTPS eliminated from the lungs in each half minute collection plotted on a logarithmic scale and corrected for tissue N_2 . The line represents the extrapolated washout from the lungs after 16 minutes. The point before zero time represents the quantity of N_2 expired per half minute while the subject is breathing air.

TABLE I

Quantities of N_2 eliminated by a 70 kg man, in milliliters of N_2 BTPS* during periods ending at the times indicated

Time	Quantity/ 30 sec	Time	Quantity/ 60 sec
<i>min</i>	<i>ml N₂</i>	<i>min</i>	<i>ml N₂</i>
0.5	36	8	22
1.0	24	9	21
1.5	22	10	20
2	21	11	19
2.5	19	12	19
3	18	13	18
3.5	17	14	17
4	16	15	17
4.5	15	16	16
5	13	17	15
5.5	13	18	15
6	12	19	15
6.5	12	20	14
7	12	21	14

* These conditions are applicable to calculations of FRC. Volume (BTPS) = volume (STPD) \times 1.21.

lungs corrected for elimination from tissues, i.e., $\dot{V}_{N_2} = \dot{V}_E(F_E - F_I) - \dot{V}'_{N_2}$. Whenever the symbol F is used for a gas concentration the chemical symbol is omitted, it being understood that we always refer to N_2 concentrations. A superscript refers to the time in minutes at which a rate of elimination or a concentration applies. Subscripts 1, 2 and 3 apply as before to phases or groups of alveoli with decreasing ventilation. M is the number of minutes in which a group of alveoli washes out 90 per cent of its N_2 . \dot{V}' is the flow rate from a group of alveoli at one instant during expiration and \dot{V} is ventilation per minute, integrated over many breaths. F_A' is a gas concentration at the end of a forced expiration and F_A is mean alveolar gas concentration, weighted by the volume of the differently ventilated alveoli.

IV. Tissue N_2 elimination. Thirty-minute washout studies on 5 normal subjects confirmed the rates of tissue N_2 elimination found by Robertson, Siri and Jones (12) and validated the use of our N_2 meter at low N_2 concentrations. Table I shows the rates of N_2 elimination used in calculating our data, which apply for a 70 kg man, and were therefore adjusted in proportion to the weight of each subject. These rates agree with the figures for N_2 elimination in 7 minutes already in use in this laboratory (21, 22).

V. Check on the method. In determining, by the use of balloons, the quantity of N_2 eliminated from the lungs over any given period, it is necessary to add the quantities in many balloon collections. The sum of so many quantities, each being a product of a volume and a concentration read from a calibration curve, might have a large error were there a small systematic error in each collection. Therefore, in 3 patients, as well as in a group of normal subjects not described here, the volume of lung N_2 eliminated both between 0 and 7 and between 7 and 15 minutes of O_2 breathing was simultaneously measured in three different ways as a check on the method: 1) by summing the quantities of N_2 measured every half minute in the balloon collections by N_2 meter analysis and Tissot volume record

between 0 and 7 and between 7 and 15 minutes; 2) by collecting expired gases between 0 and 7 and 7 and 15 minutes in two different Tissot spirometers and analyzing the mixed gas in each spirometer by means of the N_2 meter; and 3) by analyzing gas samples from the same two spirometers with the Van Slyke apparatus.

Thus, in each subject there were two gas collections in which the quantity of N_2 eliminated from the lungs in 7 minutes was measured in three different ways. These three different methods of measurement agreed: the standard deviation of the various methods from the mean for all three was 99 ml N_2 BTPS in the 0 to 7 minute collection when the total quantity of N_2 averaged 3,479 ml, and 87 ml N_2 in the 7 to 15 minute period when the total quantity averaged 1,035 ml.

An additional check on the method is afforded by measurement of the quantities of N_2 eliminated in 7 minutes at different times by methods 1 and 3 in all 11 cases. Here, too, as is apparent from Table III, there is agreement within 10 per cent.

RESULTS

All 11 patients were disabled by severe chronic pulmonary emphysema with or without a bronchitic element. Their physical characteristics and maximal breathing capacity (MBC) are given in Table II. The results in this group will be presented under two main headings: 1) the quantities of N_2 eliminated, as measured by different methods at various times during O_2 breathing, and the estimates of the FRC derived therefrom; 2) the relative volume and ventilation of the least ventilated alveoli and their gas composition after 7 minutes of O_2 breathing.

I. Quantities of N_2 eliminated from lungs and FRC measurement. The FRC is the quantity of N_2 initially present in the lungs at the end of a resting expiration divided by 81 per cent, a

TABLE II

Physical characteristics and maximal breathing capacity (MBC) in 11 patients with chronic pulmonary emphysema

Subject	Age	BSA	MBC
	<i> yrs</i>	<i> m²</i>	<i> L/min</i>
W.D.	61	1.64	16
M.L.	40	1.35	15
W.H.	58	1.50	20
A.Mc.	54	1.48	18
O.H.	66	1.85	18
S.G.	55	1.50	19
J.J.	67	1.57	14
L.L.	52	1.59	19
C.Gy.	56	1.46	16
C.Gi.	60	1.77	46
T.L.	58	1.53	19
Mean	57	1.57	20

TABLE III
*Quantities of N₂ eliminated and the FRC: Comparison between new method and conventional method
 in 11 cases of chronic pulmonary emphysema*

Subject	Quantities of N ₂ eliminated*				FRC	Differences between two estimates of FRC	
	0-7 min	7-15 min	15-∞ min	0-∞ min		ml	%
W.D.	3,623 [3,823]	1,324	669	5,616	6,933 [5,245]	1,688	32
M.L.	2,335 [2,125]	686	383	3,404	4,202 [2,847]	1,355	48
W.K.	3,752 [3,725]	932	225	4,909	6,060 [5,094]	966	19
A.Mc.	2,517 [2,313]	433	173	3,123	3,856 [3,052]	804	26
O.H.	4,190 [4,215]	1,224	816	6,230	7,691 [6,222]	1,469	24
S.G.	2,687 [2,485]	663	350	3,700	4,567 [3,396]	1,171	34
J.J.	3,449 [3,461]	1,089	326	4,864	6,005 [4,873]	1,132	23
L.L.	2,740 [2,610]	826	537	4,103	5,065 [3,505]	1,560	45
C.Gy.	4,429 [3,995]	948	612	5,989	7,393 [5,368]	2,025	38
C.Gi.	2,497 [2,637]	999	533	4,029	4,974 [3,600]	1,374	38
T.L.	2,903 [2,985]	836	545	4,284	5,289 [4,053]	1,236	30
Mean	3,192 [3,125]	905	470	4,568	5,639 [4,296]	1,344	32

* All quantities of N₂ are at BTPS and corrected for N₂ from tissues. Figures in brackets are those obtained by the conventional method.

figure considered to correspond to the initial concentration of N₂ in the lungs. The quantity initially present theoretically corresponds to the quantity collected during the washout with O₂. This quantity, and hence the FRC, were determined by the conventional and by the new method. These determinations are summarized in Table III.

The first four columns of this table give the respective quantities of N₂ eliminated from the lungs: from 0 to 7 minutes, $\int_0^7 V_{N_2} \cdot dt$; from 7 to 15 minutes, $\int_7^{15} V_{N_2} \cdot dt$; from 15 to ∞ minutes, $\int_{15}^{\infty} V_{N_2} \cdot dt$; and from 0 to ∞ minutes, the total amount of N₂ eliminated from the lungs if the study had continued indefinitely. These figures are corrected for the N₂ elimination from tissues and are based on the half-minute balloon

collections. The lower figures in the first column are the quantities of N₂ eliminated from lungs as measured in the Tissot spirometer by the conventional method. Although measured on a different occasion, these data agree well with the results of the balloon collection. The data in column 3 are derived from the plotted N₂ washout curve by algebraic integration of the extrapolation of the slow phase from the end of the study to infinity:

$$\int_{15}^{\infty} V_{N_2} \cdot dt = {}^{15}V_{N_2} \cdot M_3 / 2.3$$

where M₃ is the time taken for the slow phase to fall through one logarithmic cycle, 2.3 is log₁₀ 10, and ${}^{15}V_{N_2}$ is the rate of N₂ elimination from the lungs at 15 minutes.

It can be seen from the mean values that in patients with severe emphysema only 70 per cent of the lung's N₂ is eliminated in the first 7 min-

utes of O₂ breathing, 20 per cent between 7 and 15 minutes and the remaining 10 per cent thereafter.

The FRC determined by the quantity of N₂ eliminated during prolonged washout is $\int_0^{\infty} V_{N_2} \cdot dt / 0.81$. It has an average value of 5,639 ml. The FRC determined by the conventional method is $\left(\int_0^7 V_{N_2} \cdot dt \right) \div (0.81 - {}^7F\bar{A})$ and has an average value of 4,296 ml. The new method gives an FRC which ranges between 0.804 and 2.025 L higher than the conventional method, with a mean difference of 1.344 L; the percentage difference ranges between 19 and 48 per cent, with a mean difference of 32 per cent.

In Table IV are given some other lung volumes which are derived from the FRC. Values based on the conventional method are listed between parentheses. Significantly, the residual volume/total lung capacity (RV/TLC) ratio is relatively little affected by these large changes in both volumes (1.4 L), its average value increasing

TABLE IV
Residual volume (RV) and total lung capacity (TLC)

Subject	RV*	TLC*	RV/TLC*
	L	L	%
W.D.	6.2 [4.4]	8.6 [6.8]	72 [64]
M.L.	3.1 [1.7]	5.2 [3.8]	59 [45]
A.Mc.	3.5 [2.6]	5.2 [4.3]	67 [61]
O.H.	6.9 [5.4]	9.0 [7.5]	77 [72]
J.J.	5.4 [4.2]	7.0 [5.9]	77 [72]
L.L.	3.9 [2.8]	5.7 [4.6]	69 [62]
C.Gy.	6.7 [4.7]	8.4 [6.3]	80 [73]
C.Gi.	4.3 [2.9]	7.9 [6.4]	63 [44]
T.L.	4.2 [2.9]	6.6 [5.4]	62 [54]
Mean	4.9 [3.5]	7.0 [5.7]	70 [62]

* The upper figures are derived from the FRC determined by the method described in this paper. The figures in brackets are based on the conventional method.

TABLE V

Relative volume (L_3/LT) and ventilation (\dot{V}_{A_3}/\dot{V}_E) of the least ventilated alveoli, and alveolar nitrogen concentrations

Subject	L_3/LT	\dot{V}_{A_3}/\dot{V}_E	Alveolar N ₂ concentrations*		
			$FA_3\uparrow$	$F\bar{A}\uparrow$	$FA'\uparrow$
	%	%	%	%	%
W.D.	84	11	32	28	8.1
M.L.	67	6	39	26	6.3
W.H.	68	9	23	16	7.8
A.Mc.	64	6	24	15	5.2
O.H.	74	6	36	27	13.2
S.G.	74	7	30	22	7.8
J.J.	74	10	29	22	9.9
L.L.	76	5	36	27	6.5
C.Gy.	58	5	37	21	6.6
C.Gi.	76	3	40	30	7.7
T.L.	67	3	37	24	7.4
Mean	71	6	33	23	7.9

* After 7 min of O₂ breathing.

† FA_3 , alveolar N₂ concentration in least ventilated alveoli; $F\bar{A}$, mean alveolar N₂ concentration in all alveoli; FA' , alveolar N₂ concentration estimated by forced expiration.

from 62 per cent with the conventional method to 70 per cent with the new method.

II. Characteristics of the least ventilated alveoli and their effects upon alveolar gas composition after 7 minutes of O₂ breathing. Table V gives two parameters determined by the slow phase of the washout curve (19): L_3/LT is the fraction of the FRC which is very poorly ventilated and \dot{V}_{A_3}/\dot{V}_E is the fraction of expired ventilation which comes from these spaces. On the average, 71 per cent of the FRC was ventilated by 6 per cent of the minute ventilation. These characteristics have a profound effect upon the significance and validity of alveolar gas sampled after 7 minutes of O₂ breathing.

The concentration of N₂ in the least ventilated alveoli after 7 minutes of O₂ breathing (7FA_3) is estimated from the washout rate of the slow phase:

$${}^7FA_3 = 0.81 \times e^{-(7 \times 2.3) / M_3}$$

It ranges from 23 to 40 per cent with a mean of 33 per cent. The true mean alveolar N₂ concentration (${}^7F\bar{A}$) at this time, when the more ventilated alveoli contain negligible concentrations, is ${}^7FA_3 \times L_3/LT$. This ranges from 15 to 30 per cent with a mean of 23 per cent. The forced mixed alveolar sample (FA') at this time ranges from 5.2 to 13.2 per cent with a mean of 7.9 per cent.

DISCUSSION

I. The magnitude of the discrepancy. There is a large discrepancy, up to 2.0 L, in the FRC measured by the two methods in patients with emphysema. It is worthwhile to establish this firmly, since some earlier studies found that the N₂ washout curve yielded essentially the same FRC, even in emphysema, as did the conventional method (13). This discrepancy is not due to differences in measurements of quantities of N₂ eliminated from the lungs as shown by Table III. Furthermore, measurements in normal subjects, not described here, showed good agreement between the two methods. This discrepancy is largely due to the fact that the conventional method uses a forced expiration to estimate the average concentration of N₂ remaining in the lung after 7 minutes of O₂ breathing. Moreover, it has been shown that the least ventilated alveoli, which constitute on the average 71 per cent of the FRC, are ventilated by only 6 per cent of the minute ventilation (Table V). In order that the forced alveolar sample be representative for the measurement of the FRC, it is necessary that these alveoli contribute 71 per cent of the gas in this sample. If they did so, this sample (⁷FA) would, on the average, contain 23 per cent N₂. The forced alveolar sample (⁷FA'), with a mean composition of 7.9 per cent N₂, therefore grossly underestimates the mean N₂ concentration in the lungs after 7 minutes of O₂ breathing.

Studies of the alveolar N₂ concentration after a single breath of O₂ have clearly shown that the least ventilated alveoli contribute more to the expirate at the end of the forced expiration (23, 24). From such data it is not possible to determine how much more they contribute, since the N₂ concentration within the differently ventilated alveoli is not measured. The N₂ washout method permits an estimate of the N₂ concentration in the least ventilated alveoli after 7 minutes of O₂ breathing. Hence, we can determine how much these alveoli contribute to the sample taken at the end of a forced expiration.

$$FA' = (\dot{V}'_3FA_3 + \dot{V}'_2FA_2 + \dot{V}'_1FA_1) / (\dot{V}'_1 + \dot{V}'_2 + \dot{V}'_3)$$

where \dot{V}' refers to an instantaneous flow rate at the end of the expiration, and the subscripts re-

fer to groups of alveoli. Since FA₂ and FA₁ are practically zero at 7 minutes of O₂ breathing

$$FA' / FA_3 = V'_3 / (V'_1 + V'_2 + V'_3).$$

Using our mean values, this ratio is 7.9/33 = 24 per cent. In other words, the poorly ventilated alveoli, which in this study constitute 71 per cent of the FRC, contribute only 24 per cent of the gas expired at the end of a forced expiration.

While this is four times as much as the 6 per cent which these alveoli contribute to mixed expired gas, it is not enough to make the forced expiratory sample a valid one. The better ventilated alveoli, which constitute only 29 per cent of the lung volume, still contribute 76 per cent of the gas expired, even at the end of a forced expiration. The use of such an alveolar sample to estimate the quantity of N₂ remaining in an unevenly ventilated lung must lead to an underestimate of the FRC. The only question is as to the degree of underestimation. This, in severe chronic pulmonary emphysema, is as indicated in Table III.

II. Validity of high FRC's in the literature. Determination of the FRC by mixing an inert gas into a spirometer of decreasing volume (due to oxygen consumption) tended to overestimate the FRC in patients with chronic pulmonary emphysema (4). This was due to the "N₂ lag" phenomenon (25, 26). However, from time to time, very high estimates of the FRC by valid methods in the hands of careful workers are found in patients with chronic pulmonary emphysema, and published. This applies both to the closed (27) and the open circuit methods (12, 14, 15, 18, 19) and especially when the studies are prolonged. In the past, values over 6 L have sometimes been presented apologetically by their authors and subject to a certain amount of skepticism. They have, for example, been attributed to leaks at the mouth or in the equipment used, to belching of abdominal gas, or to perforated ear drums. It was believed that the FRC in emphysema could not exceed the TLC of a normal lung (28). It now seems that some of these very large FRC's may, in fact, be acceptable measurements.

III. The concept of trapped gas. DuBois, Bedell and associates (29, 30), in comparing the thoracic gas volume measured by a body plethys-

mographic method (31) with the FRC measured by the conventional method, found that the latter was less by an amount which varied between 0.69 and 2.38 L in emphysematous subjects. At that time they attributed their higher values by the plethysmographic method to trapped gas. They conceived that there were alveoli which were closed and which therefore did not wash out N₂, although they did, like freely communicating alveoli, affect the compressibility of the lung by the chest wall when the shutter at the mouth was closed. It now seems that if great care is taken to collect and measure all the N₂ washed out of the alveoli in prolonged O₂ breathing, a discrepancy of the same order of magnitude is observed. In the present study, the new method gave values which exceeded those of the conventional method by between 0.828 and 2.082 L. This suggests that the present method is measuring the same lung spaces as did the plethysmographic method.

That these spaces are included in the FRC, as measured in the present study, indicates that their gas is not completely trapped. Any gas-filled space in the body must be replenished from time to time if it is not to collapse; the spaces we measure must also contribute to expired gas, not necessarily at every breath but at some times during 15 minutes. In some patients with large cysts in otherwise normal lungs, we have observed that there are variations in the N₂ wash-out curve, suggesting that some pulmonary spaces empty intermittently at intervals of several minutes. This has been observed by others also (32). We regard these spaces as ventilated, not as reservoirs of trapped gas, even though they do not contribute to expired gas at every breath.

IV. The time needed between studies. The quantity of N₂ eliminated in successive conventional FRC determinations in this laboratory indicates that in chronic pulmonary emphysema the second study showed a smaller quantity of N₂ eliminated. This review applied to paired studies in each of 15 consecutive cases with emphysema both in 1940 and in 1958. The mean differences were 8.6 per cent of the total quantity of N₂ in 1940, and 9.0 per cent in 1958. A waiting period of half an hour between studies was usually allowed. This seems to be inadequate in emphysema, and a waiting period of at

least 1 hour between duplicate determinations of FRC is now being used with the new open circuit method.

V. Relative merits of various methods used for the measurement of FRC. The open circuit method described here has the advantage of giving a more accurate estimate of the volume of the lungs in emphysema than the conventional method, which is in error by as much as 48 per cent in this series. It should be pointed out that when Cournand and co-workers (7) developed the conventional method, they were very much aware of the possibility of such an error in patients with emphysema. They measured the discrepancy between wash-in and wash-out FRC determinations, which is due to poor distribution and inadequate representation by the terminal forced expiration sample. In their subject, M.K., there was a discrepancy of 865 ml at 7 minutes, which fell to 590 ml when the study was continued for 11 minutes (6). This is in the lower part of the range of the discrepancies discussed here.

The mean values in Table II show that in a typical case of severe chronic pulmonary emphysema about 70 per cent of the lung's nitrogen has been washed out in 7 minutes and about 90 per cent is washed out in 15 minutes. If the 7-minute alveolar sample were in fact representative, it should indicate that 30 per cent of the nitrogen initially present still remains in the lungs, i.e., it would have a value of about 24 per cent in a typical case. In fact, this is more than the highest values which are actually observed. Alveolar samples at the end of a 7-minute wash-out can lead to large errors; but if a 15-minute collection were made, at which time a typical case has washed out 90 per cent of the nitrogen initially present, a low alveolar sample could cause an error of, at most, 10 per cent of the FRC. However, if 15-minute washouts were done with the conventional Tissot method of collecting the gas, it would be necessary to use more, or larger, collecting spirometers and to analyze for very low concentrations of N₂.

The method described here requires considerably more time, skill in handling of equipment, and calculation than the conventional method, and it may therefore be unsuitable for routine use. An alternative procedure is the body ple-

thysmographic method (31). This requires more instrumentation and more skill in maintenance and testing of equipment, but the duration of the study and the time spent in calculation is less. Good as this method is, however, it must underestimate, by about 30 per cent, the volume of lung spaces too large to allow rapid heat exchange between gas and tissue (33). To attain comparable accuracy in severe emphysema by the closed circuit helium dilution method, prolonged studies are necessary and the leakage or diffusion of helium from the circuit must be considered. It seems then that the measurement of the volume of air in the lungs of patients with severe chronic pulmonary emphysema presents an even greater challenge to our ingenuity than has been suspected heretofore. However, the method which at present seems the least open to objection is the one described here, which measures the total quantity of N₂ initially present in the variously ventilated parts of these lungs, and washed out of them during O₂ breathing.

SUMMARY

A method is described for collecting and measuring the quantity of N₂ washed out of the lungs every half minute during oxygen breathing. The total quantity of N₂ eliminated in 15 minutes of O₂ breathing was measured in 11 patients with chronic pulmonary emphysema. The quantity of N₂ which would have been eliminated in more prolonged studies was estimated by extrapolating the N₂ washout curve. The functional residual capacity (FRC) so determined exceeded that obtained by conventional FRC measurements by between 0.804 and 2.025 L. The magnitude of this discrepancy agrees well with that seen when body plethysmographic estimates are compared with conventional measurements of the FRC. It is suggested that this new method measures the volume of the same intrapulmonary spaces as does the body plethysmograph.

The composition of forced expiratory gas samples in chronic pulmonary emphysema is discussed.

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