# AN OPEN–CIRCUIT HELIUM METHOD FOR MEASURING FUNCTIONAL RESIDUAL CAPACITY AND DEFECTIVE INTRAPULMONARY GAS MIXING [1]

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In pulmonary disease the inspired air is often distributed unequally throughout the lung. The volume of the poorly aerated regions of the lung and their rate of ventilation are of importance to the clinician but quantitation of these values has been difficult.

The situation was much clarified in 1950 by Robertson, Siri, and Jones (1) who demonstrated that an unequally ventilated lung behaves as though it consisted of a number of subdivisions of smaller size, each of which is homogeneously ventilated at its own particular rate. Preliminary work which led to the same concept was also reported at this time by Fowler, Cornish, and Kety (2). By continuously following the course of nitrogen elimination from the lungs of a subject breathing oxygen, it was possible to characterize these lung subdivisions in terms of size and ventilation rate. This information describes an unequally ventilated lung in a way which permits useful, quantitative predictions of its behavior. However, these studies required complex instrumentation.

It is the purpose of the present report to describe a simple method of quantitating unequal pulmonary gas mixing along these lines, and of measuring the functional residual capacity and correcting it for errors resulting from unequal mixing. The method employs an open-circuit arrangement, using helium as the test gas. By this means large, slowly ventilated lung subdivisions have been found in persons with emphysema; in severe cases the mixing inequality seems great enough to interfere seriously with conventional open-circuit residual air measurements.

## METHODS

The subject first breathes a 50 per cent helium, 50 per cent oxygen mixture for 15 minutes, as shown in Figure 1A. This is usually long enough to achieve a steady state with respect to helium concentration throughout the lung. The subject is then switched at the end of a normal expiration to tank oxygen (Figure 1B), and the expired gas is thereafter diverted into a collecting system which has been pre-washed with oxygen. For at least the first 7 minutes all the expired gas is collected in a 100 liter Douglas bag for later measurement of volume and helium concentration. The expired gas stream is continuously analyzed for helium by a katharometer, as shown in Figure 1. Approximately 250 ml. per minute is passed through a drier and carbon dioxide absorber (Ascarite), through the katharometer, through a gas-tight Thiberg pump, and then is returned to the system down-stream from the sampling point.

The katharometer system consists of a Gow-Mac[3] RCT thermal conductivity cell with a sealed reference cell, and an RCT control unit. The output of this system is measured by a Leeds and Northrup potentiometer having a range of 0 to 64 millivolts. This arrangement allows analysis of helium-oxygen mixtures up to about 3 per cent helium. Calibration of the equipment with known mixtures of tank helium and tank oxygen within this range yielded a linear relationship between helium concentration and the electrical potential developed by the katharometer, with a standard deviation from regression of 0.04 per cent helium. After an adequate warm-up period the katharometer is very satisfactorily stable. At the pump rate of 250 ml. per minute and with the Ascarite train, the assembly gives a 95 per cent response to change in helium concentration within 20 seconds. In addition, a few seconds delay is introduced by the volume of gas in the corrugated tubing between mouthpiece and sampling point. This volume amounts to about 1 liter and serves the purpose of mixing expired gas sufficiently to allow a smooth wash-out curve. Because of this slight delay and its sensitive response to helium, the katharometer is suited for measuring relatively slow phases of helium excretion from the lung which may occur after the initial, rapid wash-out. For clinical purposes this terminal, slow phase of helium excretion is of primary importance.
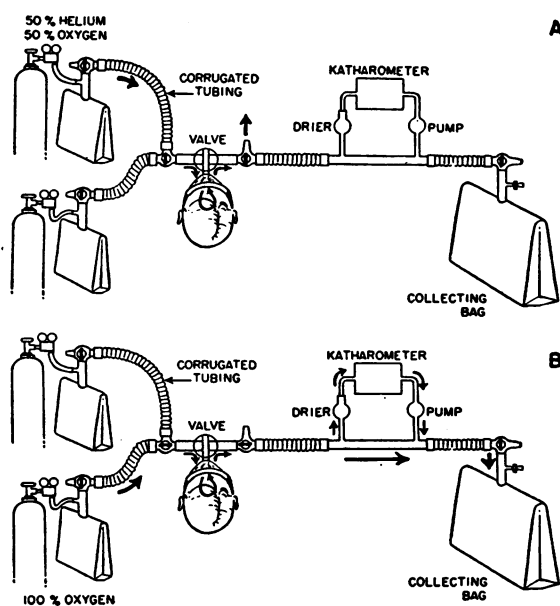
FIG. 1. DIAGRAM OF THE APPARATUS

Section A shows the direction of gas flow during the initial equilibration period. Section B shows the flow during the wash-out period.

## CALCULATIONS

*Calculation of functional residual capacity from volume and helium concentration of gas in collecting bag*

Except for subjects with severe inequalities in intrapulmonary mixing, the functional residual capacity (FRC), which is the lung volume at the end of a quiet expiration, can be calculated from the volume and concentration of helium collected in the Douglas bag during the first 7 minutes. As in other open-circuit methods, the basic procedure consists of determining the total amount of test gas which has been washed out of the lung into the bag, and dividing this volume by the concentration of the test gas in the lung before the wash-out. This quotient, with appropriate corrections for temperature and water vapor, is the functional residual air. In these calculations the following symbols are used in accordance with standard terminology (3):

$F_{He}$ = true fractional concentration of helium in the collecting bag.

$F'He$ = fractional concentration of helium in the collecting bag as indicated by the katharometer after absorption of $CO_2$.

$F_ECO_2$ = fractional concentration of $CO_2$ in expired air. This is assumed to be .025. The error which this assumption may introduce in the measurement of the FRC will be discussed below.

V(ATPS) = Volume, in ml., of gas in the collecting bag at ambient temperature and pressure, saturated.

V(BTPS) = Volume of gas in collecting bag at body temperature and pressure, saturated.

AT = Ambient temperature, Centigrade.

BP = Barometric pressure, mm. Hg.

$P_{H_2O}$ = Water vapor pressure, mm. Hg, at ambient temperature.

FRC = functional residual capacity at BTPS, in ml.

$F_AHe$ = Fractional concentration of helium in alveolar gas after breathing the helium-oxygen mixture for 15 minutes.

$F_AO_2$, $F_ACO_2$, $F_AN_2$ are the respective fractional alveolar concentrations of $O_2$, $CO_2$ and $N_2$.

$F_IO_2$, $F_IHe$ are the fractional concentrations of inspired $O_2$ and He.

R = the respiratory quotient.

The helium concentration in the collecting bag, as determined by the katharometer, is corrected for the error introduced by absorbing $CO_2$ before analysis:

$$F\,He = F'He(1 - F_ECO_2) = 0.975\,F'He \quad (1)$$

The gas volume in the collecting bag is corrected to BTPS:

$$V(BTPS) = \frac{V(ATPS)(BP - P_{H2O})}{(BP - 47)} \cdot \frac{(273 + 37)}{(273 + AT)} \quad (2)$$

The expression for the FRC is:

$$FRC = \frac{(FHe)(V(BTPS))}{F_AHe} \quad (3)$$

To obtain the actual value of the FRC, it is necessary to know the value of $F_AHe$. This can be estimated without serious error for lungs or regions of lungs where gas mixing is good enough to reach virtual equilibrium with the inspired helium mixture by the end of the 15 minute breathing period. Where this is not the case, a correction can be made, as described later. $F_AHe$ is, of course, quite close to $F_IHe$ when mixing is

adequate. The estimation of $F_AHe$ is as follows:

$$F_AHe = 1.00 - F_AO_2 - F_ACO_2 - F_AN_2 \quad (4)$$

From the data of Jones (4) on nitrogen excretion while breathing oxygen, $F_AN_2$ is estimated to be .005 after 15 minutes of breathing the helium-oxygen mixture. $F_ACO_2$ is taken to be .060. Allowing a respiratory quotient of 0.80 and expressing this conventionally in terms of inspired and alveolar gas concentrations (3), it is possible to solve for $F_AO_2$:

$$R = \frac{F_ACO_2(1 - F_IO_2)}{F_IO_2(1 - F_ACO_2) - F_AO_2}$$

Given the specific values of $R = 0.80$, $F_ACO_2 = .060$, and $F_IO_2 = F_IHe = 0.500$, then $F_AO_2 = .432$. Substituting these values in equation (4) yields

$$F_AHe = .503.$$

This value which is very close to $F_IHe$ can be substituted in equation (3) to allow calculation of the FRC.

Several assumptions have been made, but errors in these do not introduce large errors into the determination of the FRC. Specifically, an error of .010 in $F_2CO_2$ introduces a fractional error of about .01 in the FRC; errors of .010 in $F_AN_2$, $F_ACO_2$, and $F_IHe$ (and $F_IO_2$) will each produce fractional errors of approximately .02 in the FRC; and variation in R between 0.70 and 1.00 will result in a fractional error of no more than .01 in the FRC. $F_IO_2$ can, of course, be determined by analysis of the commercially supplied mixture. Errors caused by inexactness in the other assumptions, most of which are concerned with the estimate of $F_AHe$, are not likely to be serious. The helium concentration was measured in 10 "end-expiratory" alveolar samples from eight normal subjects after breathing the same 50 per cent He–50 per cent $O_2$ mixture for 15 minutes. The mean helium concentration was 50.0 per cent with a standard deviation of 0.5 per cent.

Two corrections must be applied to the estimate of FRC as given in equation (3). First, the volume of the instrumental dead space and the connecting tubing which contributes its helium to the collection, in the present case a total of 180 ml., must be subtracted. In the second place, account must be taken of the error

introduced by solution of helium in the body and its subsequent elimination during the wash-out period. Taking into consideration the solubility of helium in body tissues (5, 6), the data of Jones (4) on elimination of inert gases from the body, and the duration of the absorption and excretion periods in the present procedure, it is assumed that about 75 ml. of helium will be excreted from the blood during the wash-out period. This will contribute 150 ml. to the FRC. Accordingly, the quantity of 330 ml. is subtracted from the expression for FRC, and the final expression is:

$$FRC = \frac{(FHe)(V(BTPS))}{0.5} - 330 \quad (5)$$

The reproducibility of the results obtained by the analytical system has been tested by repeated measurements of the volume of a glass bottle which served as a test lung. The bottle was filled with the standard helium-oxygen mixture, and the mixture was then washed into the collecting bag by a stream of oxygen. The volume of the bottle, measured by its water capacity, was 2.20 liters. Eleven successive volume determinations by the helium method yielded a mean of 2.32 liters with a standard deviation of .04 liters. Accordingly, the method gave quite reproducible results, but the mean was slightly above the true value.

### Analysis of the terminal wash-out curve

After the first $1\frac{1}{2}$ to 2 minutes of the wash-out period, the helium concentration in the expired air of most subjects will fall to about 3 per cent and thereby come into the analyzing range of the katharometer system. The concentration is then recorded every 15 or 20 seconds until it has fallen to 0.05 per cent, after which the analysis is abandoned. When intrapulmonary gas mixing is grossly uneven, these data can be used for two purposes: for estimating the volume and ventilation rate of the most slowly ventilated lung spaces, and for applying a correction to the FRC calculated from the 7 minute gas collection.

#### a) Volume and ventilation rate of the "slow component" of the lung volume

As found by Robertson, Siri, and Jones (1) the excretion of an inert gas from lungs with uneven mixing proceeds as though the lung consists of a number of subdivisions each of which is venti-

lated homogeneously at its own rate. The total excretion rate, $R_T$, at a given time will then be the sum of these individual excretion rates:

$$R_T = R_1 + R_2 + R_3 + \cdots R_s,$$

where $R_s$ is the contribution of the subdivision with the slowest excretion rate.

The general behavior of a system of this kind has been described elsewhere (4), but it is convenient to present here the features pertinent to the present situation, specifically the way in which an inert gas will be washed out of a single homogeneously ventilated subdivision:

Let: $\dot{V}_T$ = the total minute ventilation of the subject, in ml.

$V_s$ = volume of the subdivision in ml. (BTPS)

$\dot{V}_s$ = ventilation rate of the subdivision in ml. per min. (BTPS)

$t$ = time in minutes

$Q_s$ = amount of helium, ml., (BTPS), in $V_s$ at time t. At t = 0, $Q_s = Q_{so}$

$k_s = \dfrac{\dot{V}_s}{V_s}$ . This ratio of ventilation to volume is the "turn-over rate"

$R_s$ = excretion rate of helium in ml. (BTPS) per min. from the subdivision at time t

$F_E He_s$ = the fractional concentration in the total expired air of helium from this particular subdivision, or $\dfrac{R_s}{\dot{V}_T}$ .

At t = 0, $F_E He_s = F_E He_{so}$

For present purposes $\dot{V}_s$ can be considered to proceed as a continuous, rather than intermittent flow. Accordingly,

$$\frac{dQ_s}{dt} = - \frac{\dot{V}_s Q_s}{V_s} = - k_s Q_s$$

Integration yields:

$$\ln Q_s = - k_s t + \ln Q_{so} \qquad (6)$$

Since $R_s = k_s Q_s$, equation (6) can be expressed as

$$\ln R_s = - k_s t = \ln R_{so},$$

and since $R_s = (F_E He_s)(\dot{V}_T)$,

$$\ln F_E He_s = - kt + \ln F_E He_{so} \qquad (7)$$

Equation (7) describes the contribution made by the subdivision to the helium concentration of the expired gas from the whole lung at any time t after the start of the wash-out. This time-concentration curve will be a straight line on a semi-logarithmic plot. This property permits a simple graphical solution of the equation when a number of experimental points are available. The points are plotted on semi-logarithmic paper with $F_E H_s$ on the ordinate and time on the abscissa, and a straight line is drawn through the points. The intersection of this line with the ordinate yields $F_E H_{so}$, the concentration of helium at zero time. The value of k is most easily obtained from the "half-time" formula, the half-time (t ½) being the time in minutes required for any given value of $F_E He_s$ to decrease by one-half. This time is determined by inspection of the experimental line. From equation (7), $\ln \dfrac{F_E He_s}{F_E He_{so}} = - k_s t$; therefore at t ½, $\ln \frac{1}{2} = -k_s t \frac{1}{2}$, or

$$k_s = \frac{.693}{t \frac{1}{2}} \qquad (8)$$

If $F_E He_{so}$ and $k_s$ are determined in this way, and in addition the total minute volume of ventilation, $\dot{V}_T$, is known, then the ventilation rate, $\dot{V}_s$, and volume, $V_s$, of the subdivision can be determined.

$$R_{so} = (\dot{V}_T)(F_E He_{so}) = \dot{V}_s \frac{Q_{so}}{V_s}$$

Re-arranging,

$$\dot{V}_s = \frac{(\dot{V}_T)(F_E He_{so})}{Q_{so}/V_s} \qquad (9)$$

The denominator of this expression is the concentration of helium in the subdivision at the beginning of the wash-out period. In the present procedure this is taken to be 0.50 throughout the lung, as noted above. Knowing $\dot{V}_s$, the value of $V_s$ is determined from the relation $V_s = \dfrac{\dot{V}_s}{k_s}$ .

The use of the present analytical system in measuring ventilation rate and volume of a slow subdivision from the helium wash-out curve was tested on bottles which served as model lungs. The volume and "ventilation rates" of the bottles were known.

Figure 2 shows the wash-out points obtained from two bottles of known volumes and "venti-

lation rates," and Figure 3 shows the result of combining the emergent gas streams and analyzing them together. From the wash-out curve and the total "ventilation rate" a reasonable estimate can be made of the volume and flow rate of the slow bottle.

In the case of an unevenly ventilated lung, the contribution of the most slowly ventilated subdivision is identified as the terminal, straight-line portion of the wash-out curve on semilogarithmic paper. If desired this can be subtracted from the remaining curve and the next slowest subdivision identified.

The question arises whether excretion of helium from the blood significantly affects the terminal portion of the wash-out curve. Since half the

HELIUM WASHOUT FROM COMBINED BOTTLES



FIG. 3. THE EFFECT OF COMBINING THE EMERGENT STREAMS FROM THE BOTTLES OF FIGURE 2

Volumes and ventilation rates are as before. The straight lines are the calculated contributions of the two bottles to the helium concentration of the combined outflow which is represented by the curved line. The points are the experimental values found for helium concentration in the combined stream. Graphical analysis, as described in the text, predicts for the slow bottle a volume of 2500 ml. and a ventilation of 910 ml. per minute. The actual values are 2300 ml. and 800 ml. per minute.
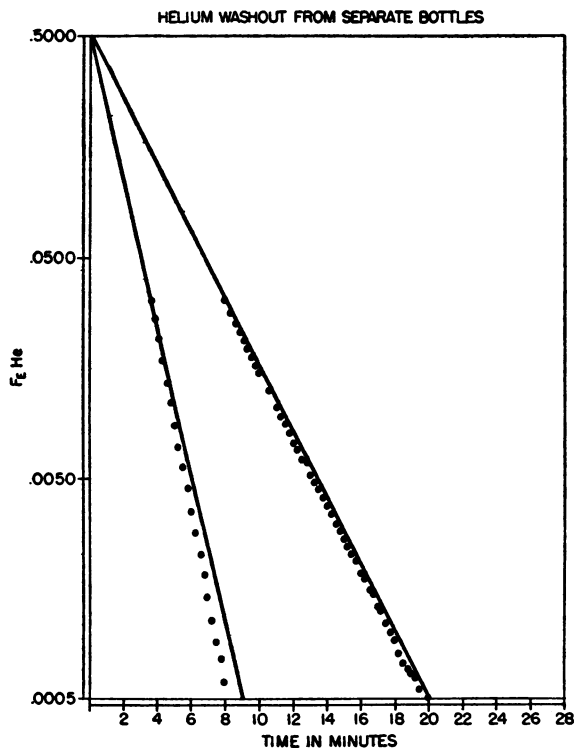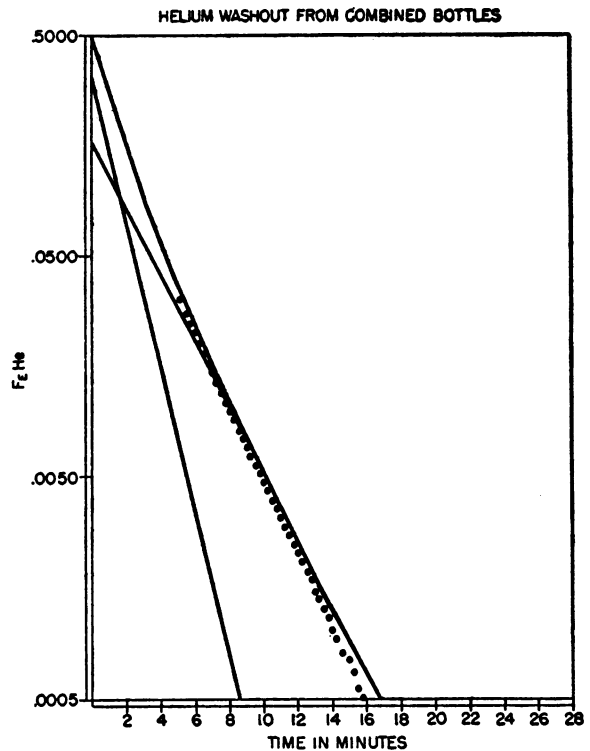
HELIUM WASHOUT FROM SEPARATE BOTTLES



FIG. 2. COMPARISON OF THEORETICAL WITH ACTUAL COURSE OF HELIUM WASH-OUT FROM BOTTLES VENTILATED AT A CONSTANT RATE BY A STREAM OF OXYGEN

The theoretical courses are indicated by the lines and the experimentally found values by the points. $F_EHe$ is the fractional concentration of helium in the wash-out gas. In both cases the bottles contained .50 helium in oxygen at the start. The right-hand line is that of a bottle with a volume of 2300 ml. and a ventilation rate of 800 ml. per min. The left hand line is that of a bottle with a volume of 2100 ml. and a ventilation rate of 1600 ml. per minute.

normal subjects show no evidence of a slow subdivision, it appears that the present method is not sensitive enough to be much affected by excretion from the blood. In four normal subjects attempts were made to measure helium excretion from the blood after equilibration periods of 15 and 60 minutes followed by 2 minutes of hyperventilation to clear the lungs. After the 15 minute period, the mean excretion rate was 3.3 ml. at 5 minutes and 2.0 ml. at 7 minutes; after the 60 minute period, the rates were about 30 per cent greater. The rates are less than expected from Jones' data (4), but the present method is inexact for these quantities. Such amounts will not significantly affect the present measurement of slow lung spaces.

*b) Correction of the slow subdivision and the FRC*

Where intrapulmonary mixing is grossly uneven, the slowest ventilated subdivision will not fill completely with the helium mixture in 15 minutes, nor empty completely in 7 minutes. Corrections for the resultant errors in $V_s$, $\dot{V}_s$ and FRC can be made from the wash-out line of the slow subdivision. These corrections embody the assumption that helium enters and leaves the lungs with equal facility. The fraction of full equilibration which $V_s$ will attain with a new inspired gas composition by any time t after beginning to breathe the mixture is $\dfrac{F_E He_{so} - F_E He_{st}}{F_E He_{so}}$. Accordingly, the extent to which the subdivision could fill with the helium mixture in 15 minutes is obtained from this fraction, and the correction factor for $V_s$ (and $\dot{V}_s$) is its inverse. Denoting the corrected volumes as $V_{sc}$:

$$V_{sc} = (V_s) \frac{F_E He_{so}}{F_E He_{so} - F_E He_{s15}}$$

The FRC is corrected by subtracting the fraction of $V_s$ which would have been delivered into the bag in 7 minutes and adding $V_{sc}$. Denoting the corrected FRC as $FRC_c$:

$$FRC_c = FRC + V_s \left( \frac{F_E He_{so}}{F_E He_{so} - F_E He_{s15}} - \frac{F_E He_{so} - F_E He_{s7}}{F_E He_{so}} \right)$$

Much the greater part of the error in FRC results from failure to wash well in 7 minutes, rather than from poor filling in 15. The method of correcting the 7 minute FRC has been tested in several subjects with impaired mixing by collecting the expired gas for prolonged periods. The results, presented in Table I, appear to support the procedure.

*Sample calculation*

The wash-out curve of a 50 year old man with emphysema is presented in Figure 4.

*FRC:* V(BTPS) = 92,500 ml.

FHe = .0312

$$FRC = \frac{(.0312)(92,500)}{0.50} - 330 = 5450 \text{ ml.}$$

$V_s$:

$$\dot{V}_T = \frac{V(BTPS)}{7} = 13,200 \text{ ml.}$$

$t_s = 3.5 \text{ minutes}$

$$k_s = \frac{.693}{3.5} = 0.20$$

$F_E He_{so} = .0300$

$$\dot{V}_s = \frac{(13,200)(.0300)}{0.50} = 790 \text{ ml. per min.}$$

$$V_s = \frac{790}{0.2} = 3950 \text{ ml.}$$

$V_{sc}$, $FRC_c$:

$F_E He_{s15} = .0016$

$F_E He_{s7} = .0075$

$$V_{sc} = 3950 \frac{.0300}{.0300 - .0016} = 4170 \text{ ml.}$$

$$\dot{V}_{sc} = (0.2)(4170) = 830 \text{ ml. per min.}$$

$$FRC_c = 5450 + 3950 \left( \frac{.0300}{.0300 - .0016} - \frac{.0300 - .0075}{.0300} \right) = 6630 \text{ ml.}$$

The correction has added approximately 1200 cc. to the 7 minute FRC, of which only about 200 ml. $(V_{sc} - V_s)$ is required for failure to fill with helium in 15 minutes. About two-thirds of the lung volume has an effective ventilation of only 0.8 liters per minute, while the remaining third gets approximately 12 liters per minute.

## RESULTS

Measurements of the FRC in the seated position were made on 15 normal males 22 to 28 years of age. The results, presented in Table II, are similar to those obtained by other methods (7).

Typical normal wash-out curves are shown in Figures 5 and 6. Ventilation appears homogeneous in Figure 5, within the limitations of the method, but a small slow space is apparent in Figure 6. The prolonged wash-out curve of a subject with emphysema is presented in Figure 4.

The ventilation pattern may change strikingly in some subjects. This is particularly evident in asthmatic patients following treatment with bronchodilator drugs or on spontaneous improvement.

TABLE I

*Effect of correcting FRC in severe emphysema*

| Subject | Total collecting time (min.) | FRC at 7 minutes (liters) | FRC, Total time (liters) | Corrected FRC (FRCc) (liters) | $V_{sc} - V_s$* (liters) | $k_s$ | $V_{sc}$ (liters) |
|---|---|---|---|---|---|---|---|
| C. L. | 18 | 3.64 | 3.87 | 3.93 | 0.00 | 0.20 | 1.10 |
| B. S. | 15 | 4.49 | 5.16 | 5.48 | 0.21 | 0.15 | 1.92 |
| H. B. (1) | 32 | 3.44 | 4.07 | 5.16 | 0.69 | 0.09 | 2.56 |
| H. B. (2) | 27 | 3.65 | 4.37 | 5.07 | 0.44 | 0.12 | 2.74 |
| G. H. | 20 | 3.98 | 5.75 | 6.43 | 0.68 | 0.14 | 5.30 |
| A. T. | 28 | 4.10 | 4.90 | 5.49 | 0.43 | 0.13 | 2.78 |
| W. W. | 41 | 3.77 | 5.59 | 6.69 | 1.10 | 0.10 | 4.75 |

* $V_{sc} - V_s$ is the estimated error resulting from failure of the lung to fill completely with helium in the 15-minute equilibration period. Prolonging the wash-out time cannot correct this error. Subtracting the quantity $V_{sc} - V_s$ from the corrected FRC, which appears in the column immediately preceding, yields the FRC value which should be obtained by a very prolonged wash-out. Inspection of the table indicates that the values actually obtained ("FRC, Total time") approach the predicted value quite closely in most cases.
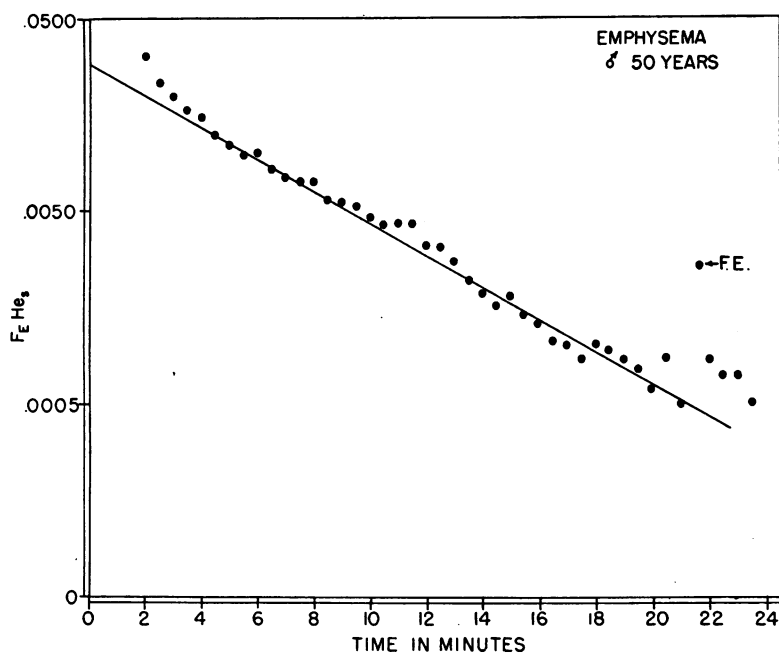


FIG. 4. HELIUM WASH-OUT CURVE OF A 50 YEAR OLD MAN
WITH EMPHYSEMA

The increased concentration marked "F.E." resulted from a forced expiration. The wash-out line of the slow component is drawn in. $F_E He_{s0}$, the intersection of this line with the ordinate, is .0300. The values for $F_E He_{s7}$ and $F_E He_{s15}$ are .0075 and .0016, respectively.

TABLE II

*FRC and other lung volumes in normal seated males*

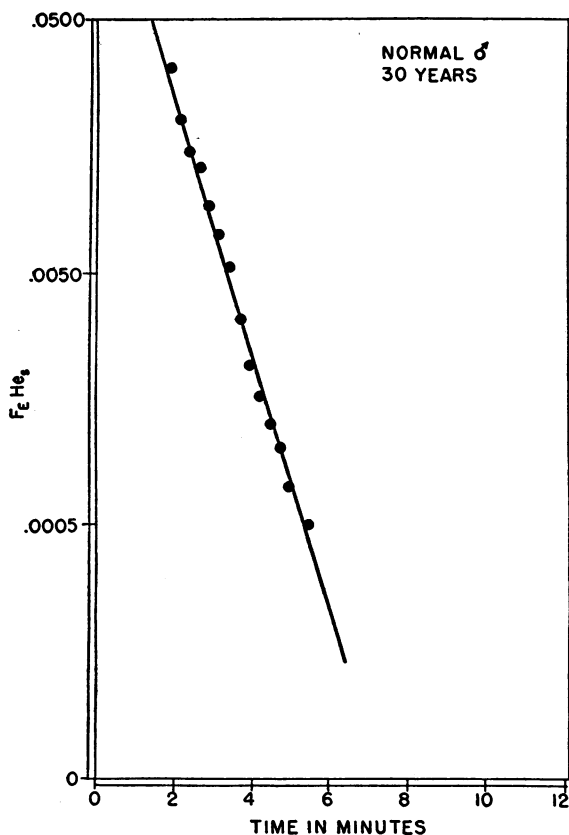| Number subjects | Age (years) | Surface area ($M^2$) | Vital capacity (liters) | FRC (liters) | Total capacity (liters) | Residual capacity (liters) | RC/TC |
|---|---|---|---|---|---|---|---|
| 15 | 25.3 ± 2.6* | 1.92 ± .14 | 4.80 ± .70 | 3.03 ± .37 | 6.16 ± .60 | 1.37 ± .34 | 22.3 ± 6.0 |

* Standard deviation.

FIG. 5.  NORMAL HELIUM WASH-OUT CURVE

Data relating to ventilation and lung volume in 16 normal subjects and 16 patients with pulmonary emphysema are summarized in Figure 7. Half of the normal subjects had no detectable slow space. When a slow space was found in a normal subject it comprised a relatively small fraction of the functional residual volume and had a relatively good ventilation compared to the slow spaces found in the subjects with emphysema. In the latter, the slowest spaces constituted a large part of the FRC and were very poorly aerated. In some of these subjects the greater part of the lung volume is almost without ventilation, and at least part of the remaining lung must therefore be ventilated at a much greater than normal rate.

### DISCUSSION

In developing the open circuit method for estimating residual air, Darling, Cournand, and Richards (8) made allowance for nitrogen still remaining in the lungs at the end of a 7-minute

wash-out period by measuring the nitrogen concentration in an alveolar air sample. This was used to represent nitrogen concentration throughout the lung, although it was well recognized that the estimate might be in error where ventilation was grossly uneven, as in severe emphysema. Such patients had 7-minute alveolar nitrogen concentrations as high as 10 or 11 per cent (9). Gilson and Hugh-Jones (10) found a concentration of 15 per cent in one subject. The present method allows an estimate of the error which may be involved in taking a 7-minute alveolar air sample to be representative of mean gas concentration in the lung. The fraction of the original quantity of helium which remains in the slow space, $V_{sc}$, at 7 minutes is

$$\frac{F_E He_{s7}}{F_E He_{s0}} = e^{-7k_s}$$

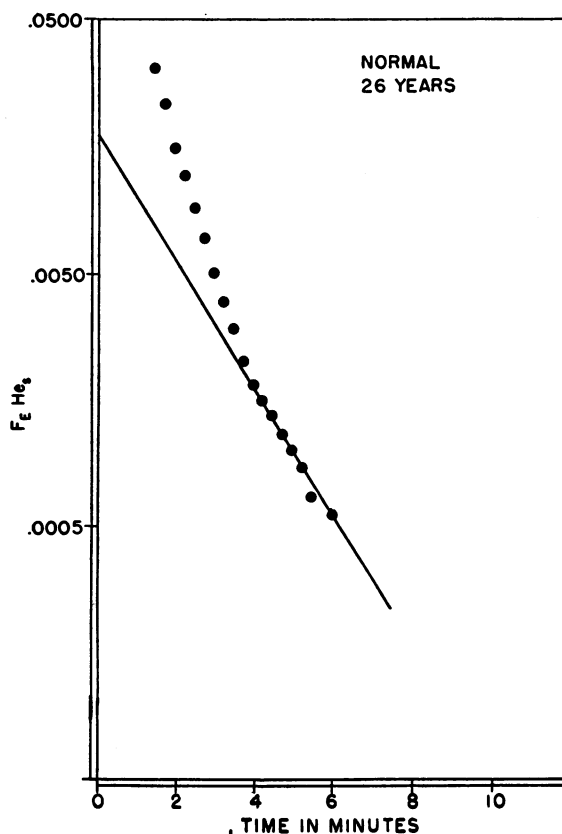The assumption is made that nitrogen would wash out at the same rate, though it may in



FIG. 6.  NORMAL HELIUM WASH-OUT CURVE

There is a small slow space.

RELATION BETWEEN SIZE AND VENTILATION RATE OF
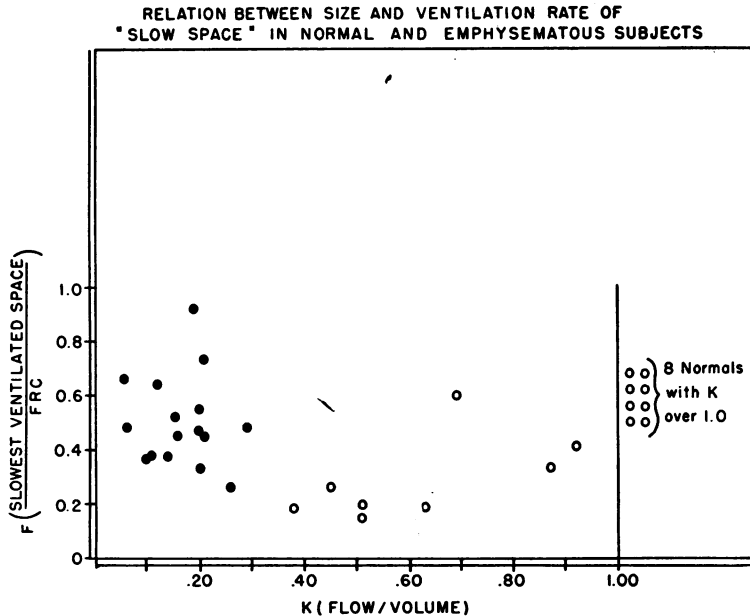"SLOW SPACE" IN NORMAL AND EMPHYSEMATOUS SUBJECTS



FIG. 7. SIZE AND VENTILATION RATE OF THE SLOWEST SPACE IN NORMAL PERSONS (OPEN CIRCLES) AND PATIENTS WITH EMPHYSEMA (SOLID CIRCLES)

The size of the space is expressed as the ratio between ventilation and volume of the slow space. The emphysematous subjects have relatively large and poorly ventilated slow spaces. The "normal" subject with the largest space had had bronchial asthma in childhood. Eight normal subjects have no slow space detectable by this method.

fact be much slower. Taking the starting alveolar nitrogen to be 81 per cent and assuming that nitrogen has been completely eliminated from all regions but the slowest space, the predicted mean alveolar nitrogen percentage at seven minutes would be:

$$\text{Alveolar } N_2\% = \frac{(81)(e^{-7k_s})V_{sc}}{FRC_c}$$

Applying this formula to the subjects in Table I yields the following predicted 7-minute alveolar nitrogens: C. L., 5.7 per cent; B. S., 9.9 per cent; H. B. (1), 21.3 per cent; H. B. (2), 18.9 per cent; G. H., 24.3 per cent; A. T., 16.5 per cent; and W. W., 28.6 per cent. Inspection of Figure 4 suggests that an average member of this group would have a slow component constituting about 0.5 of the FRC, with a $k_s$ of about 0.15. The predicted 7-minute mean alveolar nitrogen would be 14.2 per cent. These high values for routinely encountered cases of pulmonary emphysema suggest that the alveolar air sampling method considerably underestimates the amount of nitrogen remaining in the lung at 7 minutes

in such patients. This would result in a considerable underestimation of the FRC by the Darling method. Gilson and Hugh-Jones (10) found that the Darling method yielded lower FRC values than the closed circuit helium method in severe emphysema.

Fowler, Cornish, and Kety (11) made somewhat similar calculations of mean alveolar nitrogen in the course of their study of nitrogen wash-out and compared these with the concentration in alveolar samples. Although the concentrations in the samples were a little below the predicted values, the differences were not enough to affect seriously the Darling method. Analysis of expired nitrogen concentration during the wash-out was performed continuously by the nitrogen meter, which has so rapid a response and covers so great a concentration range that the wash-out can be followed from the very beginning. However, the analysis was abandoned when the mean expired nitrogen fell below 1 per cent, which would correspond to 0.63 per cent of helium in the present method. At this point the slowest space in most of our subjects

with greatly impaired mixing has not yet become adequately defined on the graph, and abandoning the analysis would result in missing the slowest space. In turn the amount of helium left in the lungs at 7 minutes would be very much underestimated. For the detection and measurement of these very slow spaces it is important to use an analytical method which is accurate at very low concentrations, at least when helium is used as the test gas. It seems quite possible that the same considerations may apply to nitrogen.

There is some uncertainty in predicting the behavior of nitrogen from results obtained with helium. Helium is a much more diffusible gas than nitrogen, and this should favor its wash-out rate. A slow space by the present method would probably be even slower in terms of nitrogen elimination. For this reason the helium method may underestimate to some extent the mixing inequality of the ordinary respiratory gases in severe emphysema.

The present method does not provide an over-all view of intrapulmonary mixing because it cannot describe the behavior of the rapidly ventilated lung spaces. It does allow comparison of the size and ventilation rate of the worst, and sometimes next worst, ventilated regions with the total ventilation rate and FRC.

Using a closed circuit helium method, Briscoe (12) has been able to divide the lung into a well and a poorly ventilated space in cases of mixing inequality, and to calculate the ventilation rate of the slow space. Distinguishing more than one slow space by means of a closed circuit system, however, appears to involve rather complex calculation.

## SUMMARY AND CONCLUSIONS

1. A convenient open-circuit method using helium is described for measuring the functional residual capacity of the lungs. After an initial period of equilibration on a helium-oxygen mixture, the subject begins to breathe oxygen, and the expired gas is collected for measurement of helium. Continuous analysis of the helium concentration in the expired gas allows calculation of the volume and ventilation rate of slowly ventilated lung spaces in patients with defective intrapulmonary gas mixing.

2. Eight of sixteen normal subjects had unequal intrapulmonary gas mixing by this method. In emphysematous subjects there were very large lung spaces with very slow ventilation rates.

3. The findings suggest that the conventional open-circuit nitrogen method may significantly underestimate the functional residual volume in patients with severely impaired intrapulmonary mixing.

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