

INVESTIGATIVE NUCLEAR MEDICINE

Evaluation of a Method for Determination of Mean Transit Time of Xenon-133 in the Lungs

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The purpose of the study was to determine the mean transit time, \bar{t} , for Xe-133 in the lungs and to compare the results with \bar{t} for helium determined simultaneously by the helium-dilution technique. Thirteen normal subjects were studied, and four patients with pulmonary disease.

No significant difference was observed between the mean transit times for Xe-133 and helium obtained in normal subjects during equilibrium as well as during desaturation. The mean washout time for Xe-133 during desaturation, $\rho_{a/h}$ (calculated as the area under the desaturation curve divided by activity at equilibrium), was significantly longer than the mean transit time for He. Similar results were obtained in the patients. Thus it is possible to determine total ventilation per unit volume correctly when the initial washout rate is used, whereas calculations based on $\rho_{a/h}$ underestimate \dot{V}/V . Accordingly, $\rho_{a/h}$ should not be used as equivalent to the mean transit time.

However, $\rho_{a/h}$ might give information of clinical value, especially in patients with chronic obstructive pulmonary disease.

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According to the stochastic tracer theory ("black box" kinetics) the mean transit time, \bar{t} , of a tracer is defined as the first moment of the impulse-response outflow rate (characteristic frequency function), and equals volume of distribution divided by flow (1,2).

In a saturation-desaturation experiment, Lassen (3) has shown that \bar{t} equals the reciprocal of the relative initial slope of the externally monitored desaturation curve (residue curve). Experimental evidence confirming the validity of this calculation has been provided by Sejrsen and Tønnesen (4), and the observed good correlation between ventilation and initial washout rate of Xe-133 in the lungs of dogs (5) is compatible with this. Secker-Walker et al. (6) and Alpert et al. (7) calculated \bar{t} for Xe-133 from the externally monitored desaturation curve, using the area under the curve divided by the average count rate at equilibrium, as proposed in a formula offered by Zierler (8). However, according to this for-

mula, which is derived for a bolus experiment, flow per unit volume equals total input of tracer (dose) divided by the area (to infinity) under the residue curve. The formula was derived later by a convolution of the stimulus-response theorem (9) and by a matrix method (10). The dose of tracer can be determined as the height of the residue curve only if the duration of input is shorter than the shortest transit time in the system. Otherwise it is necessary to determine the total input of tracer with the same efficiency as the externally monitored washout curve, which is difficult.

The purpose of the present study was to test different formulas for calculation of \bar{t} for Xe-133 in the lungs, based on residue curves obtained from saturation-desaturation experiments in healthy subjects. The results were compared with \bar{t} for He determined simultaneously, based on classical spirometry. Furthermore, the "area over height" index (6,7) was compared with the mean transit time for He determined during desaturation.

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EXPERIMENTAL PROCEDURE

The studies were performed in thirteen healthy

TABLE 1. LUNG-FUNCTION VARIABLES FROM FOUR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE*

Patient	Age	VC (1)	FRC (1)	RV (1)	FEV ₁ (1)	Lung-clearance index
A.P.	71	3.19 (85)	3.76 (104)	3.22 (136)	1.30 (51)	14.5
E.G.L.†	62	1.53 (39)	1.85 (49)	1.64 (74)	1.10 (38)	8.2
B.O.C.‡	35	2.07 (56)	4.41 (137)	3.76 (214)	0.93 (32)	—
K.Z.G.	23	5.6 (109)	2.78 (88)	2.02 (103)	3.60 (78)	14.0

* Volumes are expressed at BTPS. Figures in parenthesis denote percentages of values predicted according to J. E. Cotes: Lung function, 3rd ed. pp. 380–381. Lung-clearance index is that volume of oxygen (expressed as a multiple of the functional residual capacity) which, under quiet resting conditions, will lower the concentration of nitrogen in the end-tidal gas by 2%. Ref. J. E. Cotes: Lung function, 3rd ed. p 176.

† Patient suffered from severe alpha₁-anti-trypsin deficiency and could not tolerate the multiple-breath nitrogen washout test.

‡ Patient had ventilation only on left side due to tumor in right main bronchus.

subjects and four patients with lung disease. Results of lung function studies performed in the patients are shown in Table 1. The experimental setup is shown schematically in Fig. 1. The subject was placed in a sitting position with the back against the gamma camera. Xenon-133 in a concentration of 5 mCi/l was inhaled to equilibrium from a spirometer in a closed circuit containing a CO₂ absorber. Oxygen was automatically replaced in order to keep the spirometer volume constant. Equilibrium was assumed to be present when total count rate remained constant (plateau level) for more than 2 min. At equilibrium the subject held his breath for 20 sec at constant end-inspiratory and end-expiratory levels, respectively (Fig. 2). Desaturation was initiated by disconnecting the spirometer and letting the subject inspire from the atmosphere and expire into an empty spirometer (Fig. 1). The total ventilation, \dot{V}_E , was recorded.

Lung activity was recorded continuously in periods

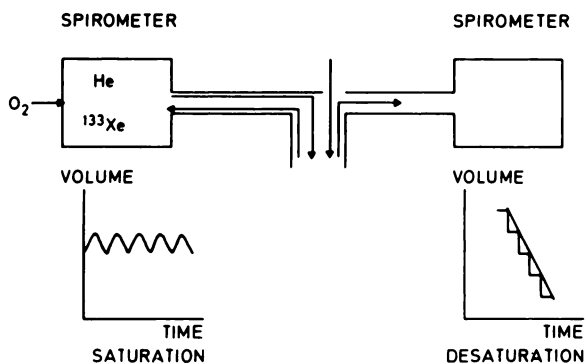


FIG. 1. Diagram showing setup of spirometers. Subject rebreathed, from left-hand spirometer, to equilibrium in a closed circuit, with CO₂ removed and O₂ automatically replaced. At start of desaturation, this spirometer was disconnected and subject inspired from the atmosphere and expired, through a one-way valve, into empty spirometer on right side. \dot{V}_E was determined from activity curves shown below.

of 1 sec by a gamma camera* with low-energy diverging collimator. Data acquisition was controlled by a computer system with magnetic-tape storage.† Correction for background activity was done by fitting a monoexponential function to the count rates measured from 8 to 10 min after start of desaturation; the function was then extrapolated back to the start of desaturation, and the value there taken as the background to be subtracted from the measured count rates.

Calculations. Mean transit time of Xe-133. An idealized time-activity curve is shown in Fig. 2.

Desaturation. Mean transit time during desaturation, \bar{t}_{desat} , equals the reciprocal of the relative initial slope (see Appendix, Eq. 5). In the calculation, \bar{t}_{desat} was approximated as the reciprocal of the initial washout rate constant k_{init} , obtained from the early monoexponential part of the washout curve, i.e.,

$$\bar{t}_{desat} = 1/k_{init}, \tag{1}$$

where k_{init} was determined from the logarithmic transformed count rates using the least-squares method. The mean washout time from a saturated system, $\rho_{a/h}$, was calculated as the area under the desaturation curve divided by q_0 , the average count rate at equilibrium (6,7):

$$\rho_{a/h} = \frac{1}{q_0} \int_0^{\infty} q(t) dt \tag{2}$$

Regional washout rates. For each of three lung regions (basal, central, apical), the washout rate constants were calculated in two ways: k_{init} from $1/\bar{t}_{desat}$, and $k_{h/a}$ from $1/\rho_{a/h}$.

Equilibrium: according to Appendix Eq. 3, is $\bar{t} = q(0)/j_i(0) = q(0)/j_0$, since $j_i(0) = j_0$ at equilibrium. The mean outflux or influx of Xe-133 equals $\Delta q \cdot f$, where Δq is the difference between maximum and minimum lung activity during tidal respiration, and f denotes the respiratory frequency.

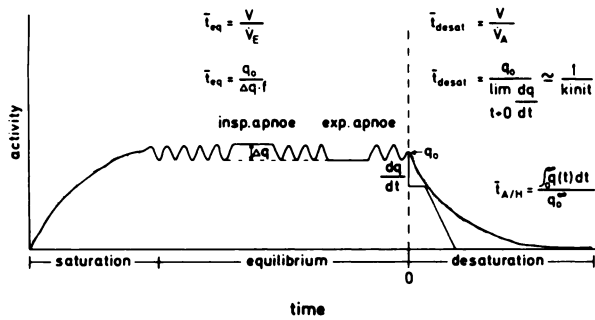


FIG. 2. Showing idealized activity curve versus time, obtained by saturation-desaturation measurements. For details and symbols see text.

Thus at equilibrium, \bar{t}_{eq} can be calculated as

$$\bar{t}_{eq} = q(0) / (\Delta q \cdot f) \quad (\text{see Fig. 2}) \quad (3)$$

Mean transit time of He, \bar{t}_{He} . This will equal volume of distribution divided by ventilation. Mean volume of distribution has been approximated as

$$FRC - V_D + 0.5V_T,$$

where FRC (functional residual capacity) is determined by the helium-dilution technique (11); V_D (dead space) is calculated from age and body weight (11), and V_T (tidal volume) is measured directly.

During desaturation the outflux of He equals alveolar ventilation, \dot{V}_A , times the He concentration:

$$\dot{t}_{desat, He} = (FRC - V_D + 0.5V_T) / (V_E - f \cdot V_D) \quad (4)$$

The flux of He into the alveolar compartment at equilibrium equals total ventilation, \dot{V}_E , times the concentration of He at equilibrium. \bar{t}_{eq} of He can thus be calculated as

$$\bar{t}_{eq, He} = (FRC - V_D + 0.5V_T) / \dot{V}_E \quad (5)$$

Statistics. Student's t-test for paired observations was used to test significance. $P = 0.05$ was used as the limit of significance.

Sources of error and supplementary experiments. Nonlinearity of count rate: Recorded count rates plotted against true count rates were checked by the decay-time method using a phantom 12 cm in thickness containing Xe-133 in aqueous solution to simulate scatter in the subjects. The losses (i.e., percent underestimation referring to true count rate) were less than 6% at 10,000 cps with a 30% window. The recorded count rates never exceeded 10,000 cps in the present study.

Changes in detection sensitivity: Differences in detection sensitivity at different lung volumes might occur, due to changes in radiation absorption characteristics. The relative importance of this error was tested in four subjects. Measurements were performed at equilibrium. Changes in lung activity corresponding to different inspiratory and expiratory volumes, Δq_{V_T} were measured

and the changes in lung activity were expressed relative to the changes observed following maximal inspiration, $\Delta q_{V_T, max}$. These values were compared with the corresponding $V_T/V_{T, max}$ obtained from the spirometer. There was no difference between the relative change in recorded lung activity and lung volume, indicating that counting sensitivity did not change significantly in the present setup.

Respiratory cycles: The assumption of steady state is not quite realized due to the respiratory cycles. Bassingthwaite (12) has shown that pulsative input and output do not invalidate the calculation of \bar{t} if an adequate number of full cycles is used in the calculation.

Background activity: The "slowest" part of the washout curve, obtained 8–10 min after start of desaturation, was assumed to represent activity located in solid lung tissue, blood, and chest wall (13). The relative slope of this part of the curve is similar to that obtained from an area outside the lungs, as illustrated in Fig. 3. The slope was little influenced by changes in ventilation. In a patient with ventilation only on the left side due to a tumor in the right main bronchus, total and regional washout rates, obtained from the ventilated side 8–10 min after start of desaturation, were equal to those obtained from the corresponding nonventilated areas. However, background activity is underestimated during the initial part of the desaturation, because the washout of Xe-133 from extrapulmonary tissue does not follow a monoexponential course, as is seen in Fig. 3. The intercept of the extrapolated slow part of the washout curve suggests that background activity is initially underestimated by about 40%. As background activity at the start of desaturation amounts to about 20% of total activity, the error in background subtraction is less than 10%. In a patient with severe chronic obstructive pulmonary disease (e.g., BOC, Table 1) the washout rate from the lungs became equal to the washout rate from extrapulmonary tissues at 60 min after start of desaturation (Fig. 4).

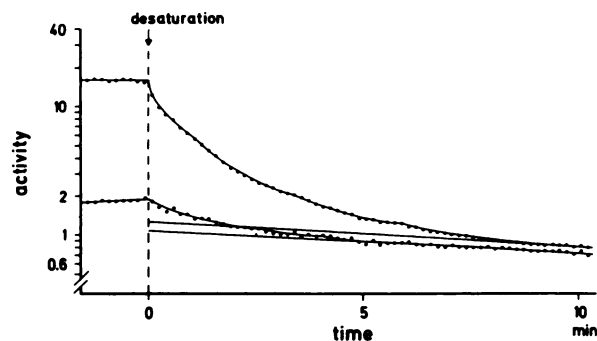


FIG. 3. Example of Xe-133 washout curve obtained from normal subject. Upper curve is washout from lung field, whereas lower curve shows washout from an area below lung fields. Note that after 8 min, washout rates are similar, since curves are parallel. Here washout rates (k_{tail}) are $5.2 \times 10^{-4}/\text{sec}$.

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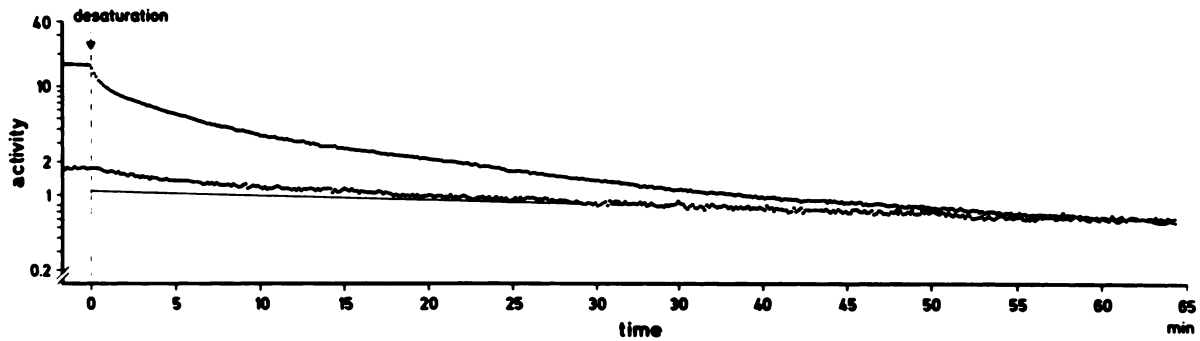


FIG. 4. Total Xe-133 washout curve obtained in patient BOC. Upper curve is from lung field, and lower curve from an area below lungs. Note that after 60 min, washout curve from lungs becomes parallel to curve obtained from extrapulmonary tissue. For upper curve, washout rate after 60 min is 3.2×10^{-4} /sec, and is 3.0×10^{-4} /sec for the lower.

Figure 4 also shows the extrapolation of the activity curve from extrapulmonary tissues, from 60–65 min back to the start of desaturation. At that time the background activity is about 60% of the total, so here again the error in background subtraction will be less than 10%.

Blood-tissue interactions: Interchange of tracer between air, solid tissue, and blood during desaturation might interfere. At the start of desaturation, a net flow of tracer from the air to blood should be expected because saturation of peripheral tissues has not been achieved (14). The relative importance of this expected decrease in lung activity due to washout with blood was tested by measurement of lung activity during apnea following each of the three first inspirations after start

of desaturation. The measurements were performed at maximum lung capacity. The washout rate constant obtained during apnea was less than 1% of k_{init} , indicating that this error is insignificant. This is less than that predicted by Matthews and Dollery (15).

RESULTS

Equilibrium. Figure 5 shows $\bar{t}_{eq, Xe-133}$ plotted against $\bar{t}_{eq, He}$. The solid line is line of identity, $y = x$. The slope (b) of the regression line (\pm s.d.) was 1.00 ± 0.07 . The intercept (a) was 0.4 ± 1.8 , and the correlation coefficient, r , was 0.96 ($P < 0.001$). Mean ventilation, \bar{V}_E (\pm s.d.), was 149 ± 44 ml/sec. Average mean transit time for Xe-133, $\bar{t}_{eq, Xe-133}$, was 22 ± 8 sec. Similarly, $\bar{t}_{eq, He}$ was 22 ± 7 sec. This corresponds to a mean ventilation, per unit lung volume, of 0.05 ml/ml-sec. Average $\bar{t}_{eq, Xe-133}$ did not differ significantly from average $\bar{t}_{eq, He}$.

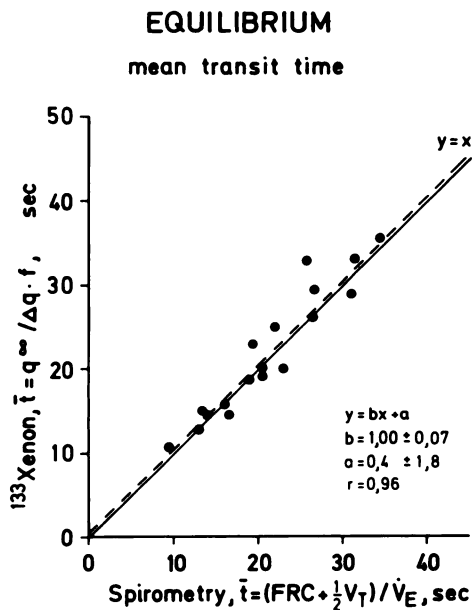


FIG. 5. Mean transit time of Xe-133 ($\bar{t}_{eq, Xe-133} = q(0) \cdot f \cdot \Delta q$, determined at equilibrium) is plotted against simultaneously determined mean transit time of He: $\bar{t}_{eq, He} = (FRC - V_D + \frac{1}{2} V_T) / \bar{V}_E$.

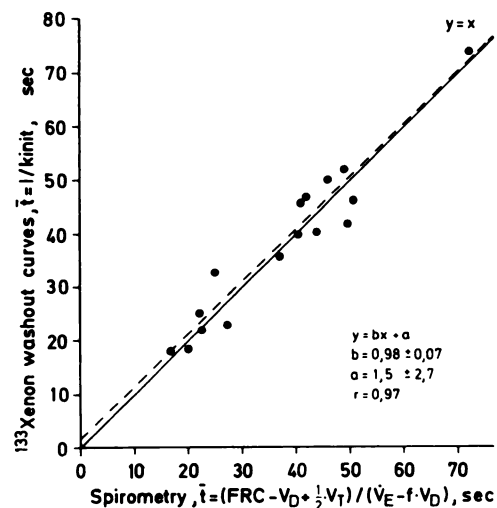


FIG. 6. Mean transit time of Xe-133 ($\bar{t}_{desat, Xe-133} = 1/k_{init}$, determined during desaturation) is plotted against simultaneously determined mean transit time of He: $\bar{t}_{desat, He} = (FRC - V_D + \frac{1}{2} V_T) / (\bar{V}_E - f \cdot V_D)$.

($P > 0.3$). Thus there was good agreement between the calculated mean transit time for Xe-133 and for He in the lungs determined at equilibrium.

Desaturation. In Fig. 6 $\bar{t}_{desat, Xe-133}$ is plotted against $\bar{t}_{desat, He}$. The slope of the regression line was 0.98 ± 0.07 , indicating good agreement between the two methods for determination of \bar{t} in the lungs. Intercept and correlation coefficients were 1.5 ± 2.7 and 0.97 ($P < 0.001$), respectively.

Average ventilation, calculated from the initial part of the desaturation, was 125 ± 46 ml/sec, compared with 132 ± 45 ml/sec as calculated using the whole period of desaturation, ($P > 0.4$).

Average mean transit time for Xe-133, $\bar{t}_{desat, Xe-133}$ was 37 ± 17 sec. Mean transit time of He, $\bar{t}_{desat, He}$, was 35 ± 17 sec ($P > 0.4$). This corresponds to a mean alveolar ventilation per unit lung volume of 0.03 ± 0.001 ml/ml-sec.

Average mean washout time of Xe-133 from a saturated system, $\rho_{a/h}$, calculated as area divided by height (Eq. 2) was 42 ± 11 sec, compared with $\bar{t}_{desat, He}$ of $28 \pm$

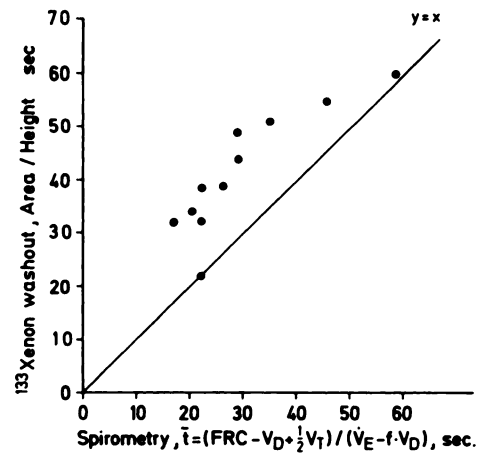


FIG. 7. Mean washout time of a saturated system,

$$\rho_{a/h} = \frac{1}{q_0} \int_0^{\infty} q(t) dt,$$

is plotted against simultaneously determined mean transit time of He, $\bar{t}_{desat, He}$.

TABLE 2. RESULTS FROM FOUR PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE.*

Patient:	AP	EGL	KZG	BOC
\dot{V}_E ml-sec ⁻¹	144	207	161	150
Apical k_{init}	$1.8 \cdot 10^{-2}$	$4 \cdot 10^{-2}$	$4.4 \cdot 10^{-2}$	$2.7 \cdot 10^{-2}$
$k_{h/a}$	$1.6 \cdot 10^{-2}$	$3.5 \cdot 10^{-2}$	$3.6 \cdot 10^{-2}$	$1.0 \cdot 10^{-2}$
Central k_{init}	$2.2 \cdot 10^{-2}$	$6.8 \cdot 10^{-2}$	$4.7 \cdot 10^{-2}$	$1.2 \cdot 10^{-2}$
$k_{h/a}$	$1.7 \cdot 10^{-2}$	$2.4 \cdot 10^{-2}$	$3.5 \cdot 10^{-2}$	$0.35 \cdot 10^{-2}$
Basal k_{init}	$2.3 \cdot 10^{-2}$	$8.5 \cdot 10^{-2}$	$4.5 \cdot 10^{-2}$	$0.30 \cdot 10^{-2}$
$k_{h/a}$	$1.6 \cdot 10^{-2}$	$3.3 \cdot 10^{-2}$	$2.1 \cdot 10^{-2}$	$0.15 \cdot 10^{-2}$
Total k_{init}	$2.3 \cdot 10^{-2}$	$7.3 \cdot 10^{-2}$	$4.3 \cdot 10^{-2}$	$1.3 \cdot 10^{-2}$
$k_{h/a}$	$1.5 \cdot 10^{-2}$	$2.6 \cdot 10^{-2}$	$3.0 \cdot 10^{-2}$	$0.36 \cdot 10^{-2}$
k_{tail}	$3.4 \cdot 10^{-4}$	$13.0 \cdot 10^{-4}$	$3.0 \cdot 10^{-4}$	$3.2 \cdot 10^{-4}$
Extrapulm. Tissue k_{tail}	$3.0 \cdot 10^{-4}$	$15.0 \cdot 10^{-4}$	$2.4 \cdot 10^{-4}$	$3.0 \cdot 10^{-4}$
Time for retroplation min	19	7	8	60
Estimated lung volume based on \bar{t}_{desat} (ml BTPS) [†]	4000	2000	2600	5400
Estimated lung volume based on $\rho_{a/h}$ (ml BTPS) [†]	6050	5500	3700	19500
FRC determined by He-dilution technique (ml BTPS) [†]	3760	1850	2780	4410

* Regional values are given as mean value of symmetrical regions in both lungs. k_{init} : initial washout rate constant (sec⁻¹); $k_{h/a}$: height/area index (sec⁻¹); k_{tail} : washout rate constant obtained from late, monoexponential part of washout curve (sec⁻¹); \dot{V}_E : total ventilation, ml(BTPS)/sec.

[†] Volume of air saturated with water vapor at body temperature, ambient pressure.

13 sec. This difference was significant ($P < 0.001$). Figure 7 shows $\rho_{a/h}$ plotted against $\bar{t}_{desat,He}$. There was a significant correlation between the two parameters, $r = 0.78$, $P < 0.01$.

The results obtained in the patients are summarized in Table 2. The washin time varied from 15 to 30 min, and washout from 7 to 60 min. At these times the lung fields were visibly clear of activity. An example of a Xe-133 washout curve is shown in Fig. 4. As in normals, $\rho_{a/h}$ was considerably longer than \bar{t}_{desat} in all patients. Mean lung volume as calculated from \bar{t}_{desat} was of the same order of magnitude as those determined by the He-dilution technique, whereas $\rho_{a/h}$ obviously gave values too large, especially in Patient BOC (see Table 2).

Regional washout rates. Regional distribution of washout rates, k_{init} and $k_{h/a}$, are shown in Fig. 8. Except in the apical regions, $k_{h/a}$ was slower than k_{init} . There was a significant increase in both parameters from apex to basis, but the relative increase in $k_{h/a}$ was considerably less (20%) than the increase in k_{init} (100%), $P < 0.01$.

An example of regional washout curves from the apical and basal regions of the right lung of Patient BOC is shown in Fig. 9. The count rate has reached a constant level before start of desaturation. The time needed for washout of Xe-133 to background level was considerably prolonged in the basal region compared with the apical region. The regional washout rates obtained in the patients are shown in Table 2. There were no differences between symmetrical regions in the right and left lungs. In all cases k_{init} was larger than $k_{h/a}$, which is the washout rate calculated as height divided by the area. Relative distributions of k_{init} and $k_{h/a}$ are shown in Table 3. In two patients (AO,BOC) the gradients from apex to base are qualitatively similar, but the relative differ-

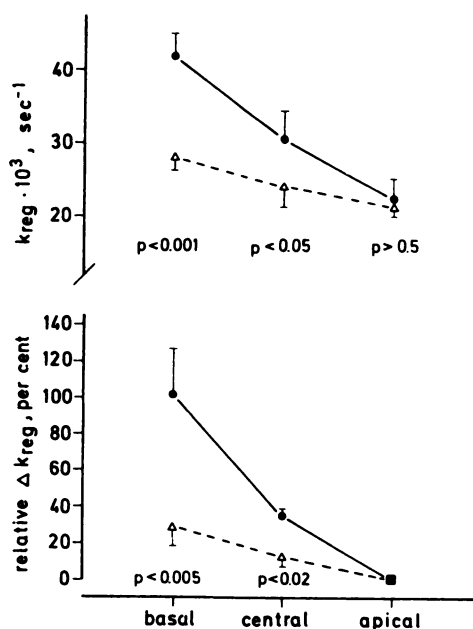


FIG. 8. Washout rate constants for three lung regions in seated normal subjects: k_{init} (solid dots, derived from $\bar{t}_{desat,Xe-133}$) and $k_{h/a}$ (triangles, derived from $\rho_{a/h}$). Vertical lines indicate 1 s.e. Lower graph shows relative increase of k_{init} and $k_{h/a}$ going from apex to base.

ence between base and apex is less for $k_{h/a}$ than for k_{init} . In the other two patients, the apical-basal gradients for k_{init} and $k_{h/a}$ go in opposite directions, since k_{init} increased from apex to base whereas $k_{h/a}$ decreased.

DISCUSSION

The main result of the present study is that the mean transit times of Xe-133, determined at equilibrium as

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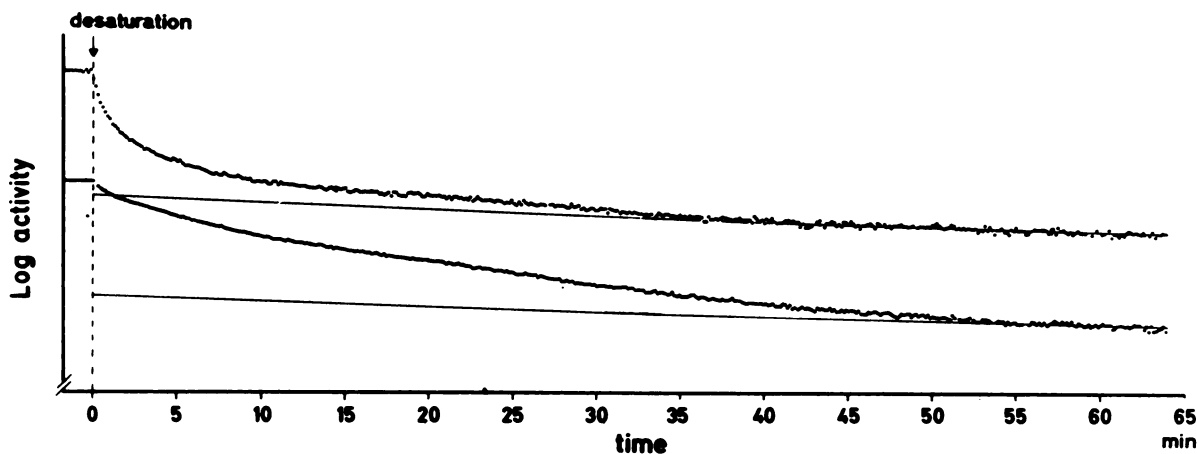


FIG. 9. Xenon-133 washout curves obtained from apical region (upper curve) and basal region (lower curve) of right lung in patient BOC. Note that time needed for washout of tracer from basal part is considerably prolonged: 60 min basal vs 45 min apical. After 60 min the two curves are parallel and similar to that obtained from extrapulmonary tissue (see Fig. 4).

TABLE 3.

Patient	AP		EGL		KLG		BOC	
	k_{init}	$k_{h/a}$	k_{init}	$k_{h/a}$	k_{init}	$k_{h/a}$	k_{init}	$k_{h/a}$
Apical*	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Central	1.24	1.08	1.70	0.68	1.13	0.96	0.46	0.35
Basal	1.25	1.10	2.13	0.74	1.16	0.85	0.03	0.15

* Relative distribution of regional washout rates, normalized to apical region = 1. k_{init} : initial washout rate constant (sec^{-1}); $k_{h/a}$: height/area index (sec^{-1}).

well as during desaturation, corresponded, respectively, with the simultaneously determined mean transit times of He. The $\rho_{a/h}$ was significantly longer than $\bar{t}_{\text{desat, He}}$, but there was a significant correlation between the two parameters. The results obtained in the patients are compatible with this, since lung volumes calculated by way of \bar{t}_{desat} corresponded with those obtained by the He-dilution technique, whereas those calculated from $\rho_{a/h}$ were obviously too large. The differences between \bar{t}_{desat} and $\rho_{a/h}$ cannot be explained by error in background subtraction. As argued previously, this error seems to be less than 10% even in the patients.

Secker-Walker et al. (16) similarly found a significant correlation between ventilation and height/area index ($1/\rho_{a/h}$) in normals. The mean value was about 0.03 min^{-1} , like that obtained by the "initial slope" in this study, but in their study average ventilation was much higher (200 ml/sec) than in our study (132 ml/sec). Calculation of mean lung volume based on the average values obtained by Secker-Walker et al., and assuming a dead space of 200 ml, gives a mean lung volume of 5500 ml. This is too high, indicating that height/area index underestimates the fractional ventilation. The problem seems more pronounced in the patients with chronic obstructive pulmonary disease, since there was no significant correlation between ventilation and height/area index, as there is in normals (16). Calculation of mean lung volume in the patients, based on the average data obtained by Secker-Walker et al., gives a mean value of 13 l, which is more than three times the expected value. This is in agreement with the findings in the present study. Thus $\rho_{a/h}$ does not give the mean transit time of the system, and consequently the height/area index does not give alveolar ventilation per unit volume. The reason is that the washout curves do not follow a monoexponential course, even in normals. The basic assumption that activity at equilibrium may represent the distribution of the dose in a bolus experiment for the desaturation that follows is not valid because, at equilibrium, concentration of tracer is equal in all parts of the lung—including regions with long transit times—whereas concentration of tracer is lower in these "slower" parts of the lung following a bolus injection, (cf. bolus fractional principle). Therefore, in a desaturation

experiment with residue detection, the washout of tracer from less ventilated regions is fully represented in the initial part of the washout curve, being proportional to the relative volume of distribution. Using height/area index, the washout from the slow parts of the lungs is weighted too much. Obviously the error is greater when the time-weighted area under the externally monitored desaturation curve (first moment) is used (17). In patients with chronic obstructive pulmonary disease with increased inhomogeneity of ventilation, the error seems to be augmented, as indicated by the calculations above. However, by including the slower parts of the desaturation curve, the height/area index might give information of clinical value about the poorly ventilated volumes in these patients.

As concluded previously, "height over area," obtained from a saturation-desaturation experiment, does not equal ventilation per unit volume, but the regional height/area index might still give a correct estimate of relative regional distribution of ventilation per unit

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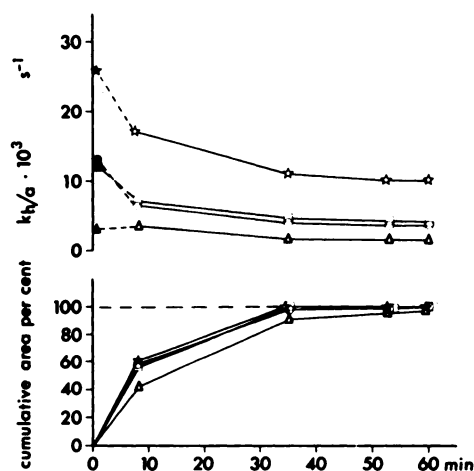


FIG. 10. Showing influence of integration time upon calculated height/area index (upper panel), and calculated area (lower panel), obtained in patient BOC. O: total lung field; ☆: apical region; □: central region; Δ: basal region. Filled-in symbols denote initial washout rate constants, k_{init} . Note especially first 40 min, where results are very much influenced by time of integration.

volume. The known gravity-dependent increase in ventilation per unit volume (18–20) is clearly demonstrated by the results based on initial slope, whereas this is much less pronounced when height/area index is used. The relative increase in height/area index of 20% from apex to base is in agreement with the findings of Secker-Walker et al. (16). Similarly, in two patients the apex-base difference was less for $k_{h/a}$ than for k_{init} . It should be emphasized, however, that in the two other patients k_{init} increased from apex to base whereas $k_{h/a}$ decreased. Distribution of regional k_{init} , obtained in the normals and the patients, seems to be correct, since k_{init} for both lungs corresponded to the overall alveolar ventilation per unit lung volume based on the spirometer data. Furthermore, Fig. 10 shows clearly that the obtained $k_{h/a}$ and the relative regional distribution—especially in the first 20 min—vary with the integration time. Thus, height/area index seems to underestimate the relative regional differences in ventilation per unit volume, and may in some patients even give a false picture of the relative distribution of regional ventilation per unit volume.

In conclusion, it is permissible to apply the stochastic tracer theory to lung function studies, and to determine ventilation per unit volume, without making any assumptions about the composition of the system or the precise nature of the washout of tracer. In patients with chronic obstructive pulmonary disease, longer washin times are needed to get full saturation of the lung volume. Similarly, longer washout times are needed—to the point where the washout rate from the lungs is similar to that obtained from extrapulmonary tissue—in order to minimize the error in background subtraction. The washout should be continued 5 min after the lung fields appear cleared of activity. The $\rho_{a/h}$ reflects a “mean washout time” from a saturated system and should not be used as equivalent to the mean transit time, defined as the first moment of the bolus-response outflow rate. Half-time index (7, 21, 22) might well give a better indication of the distribution of ventilation per unit volume than $\rho_{a/h}$. In a bolus experiment, ventilation per unit volume can be determined as the height of the externally monitored residue curve divided by the area (23), but distribution of tracer must represent the distribution of inspiratory air, which may raise difficulties because this varies throughout the inspiratory phase (24). However, this error is probably smallest with respiration around FRC.

FOOTNOTES

* RADI CAMERA II

† Nuclear Data 50/50

APPENDIX

Consider the saturation-desaturation experiment as an interaction between the lungs and a spirometer, neglecting the contribution of blood and tissue. Assuming linearity (9), complete mixing, and steady state (i.e., invariant lung function), let $j_i(t)$

denote the mean rate of tracer input (activity/time) and $h(t)$ the characteristic frequency function (impulse-response function). The corresponding mean output flux, $j_o(t)$, can then be written:

$$j_o(t) = \int_0^{\infty} j_i(t - \tau)h(\tau)d\tau \quad (1)$$

where τ is the integration variable with dimensions of time varying between 0 and ∞ . If steady-state saturation has been reached, and desaturation starts at $t = 0$, then

$$j_i(t) = \begin{cases} j_i(0) & \text{for } t \leq 0 \\ 0 & \text{for } t > 0 \end{cases}$$

The activity of the tracer in the lungs at equilibrium, $q(0)$, can be calculated as the time integral of the output flux during desaturation, i.e.,

$$q(0) = \int_0^{\infty} j_o(t) dt = j_i(0) \int_0^{\infty} \left[\int_t^{\infty} h(\tau)d\tau \right] dt \quad (2)$$

Mean transit time can be calculated as $\bar{t} = \int_0^{\infty} [1 - H(t)] dt$ where $H(t) = \int_0^t h(\tau)d\tau$ is the cumulative frequency function (8). Thus,

$$q(0) = j_i(0) \int_0^{\infty} (1 - H(t))dt = j_i(0) \cdot \bar{t}, \quad (3)$$

since $h(t)$ is a normalized frequency function. For $t > 0$ the time derivative of the activity in the lungs is given by

$$\frac{dq}{dt} = -j_o(t) = -j_i(0) \int_t^{\infty} h(\tau)d\tau, \quad (4)$$

yielding $q(0)$

$$\bar{t} = - \frac{q(0)}{\lim_{t \rightarrow 0^+} \frac{dq}{dt}}, \quad (5)$$

REFERENCES

- STEPHENSON JLL: Theory of the measurement of blood flow by the dilution of an indicator. *Bull Math Biophys* 10: 117–121, 1948
- MEIER P, ZIERLER KL: On the theory of the indicator-dilution method for measurement of blood flow and volume. *J Appl Physiol* 6: 731–744, 1954
- LASSEN NA: On the theory of the local clearance method for measurement of blood flow including a discussion of its application to various tissues. *Acta Med Scand Suppl* 472: 136–145, 1967
- SEJRSEN P, TØNNESEN KH: Inert gas diffusion method for measurement of blood flow using saturation techniques: Comparison with directly measured blood flow in the isolation gastrocnemius muscle of the cat. *Circ Res* 22: 679–693, 1968
- GOODRICH JK, JONES RH, COULAM CM, et al: Xenon-133 measurement of regional ventilation. *Radiology* 103: 611–619, 1972
- SECKER-WALKER RH, HILL RI, MARKHAM J, et al: The measurement of regional ventilation in man: A new method of quantitation. *J Nucl Med* 14: 725–732, 1973
- ALPERT NM, MCKUSICK KA, CORREIA JA, et al: Initial assessment of a simple functional image of ventilation. *J Nucl Med* 17: 88–92, 1976
- ZIERLER KL: Equations for measuring blood flow by external monitoring of radioisotopes. *Circ Res* 16: 309–321, 1965
- PERL W, EFFROS RM, CHINARD FP: Indicator equivalence theorem for input rates and regional masses in multi-inlet steady-state systems with partially labeled input. *J Theoret Biol* 25: 297–316, 1969

10. PERL W, LASSEN NA, EFFROS RM: Matrix proof of flow, volume and mean transit time theorems for regional and compartmental systems. *Bull Math Biol* 37: 573-588, 1975
11. COTES JE: *Lung Function, Assessment of Lung Function Studies in Medicine*. London, Blackwell Scientific Publications, 1975, pp 113-117, 253
12. BASSINGTHWAIGHTE JB, KNOPP TJ, ANDERSON DU: Flow estimation by indicator dilution (bolus injection). Reduction of errors due to time-average sampling during unsteady flow. *Circ Res* 27: 277-291, 1970
13. MILIC-EMILI J, HENDERSON JAM, DOLOVICH MB, et al: Regional distribution of inspired gas in the lung. *J Appl Physiol* 21 (3): 749-759, 1966
14. SUSSKIND H, ATKINS HL, COHN SH, et al: Whole-body retention of radioxenon. *J Nucl Med* 18: 462-471, 1977
15. MATTHEWS CME, DOLLERY CT: Interpretation of ^{133}Xe lung wash-in and wash-out curves using an analogue computer. *Clin Sci* 28: 573-590, 1965
16. SECKER-WALKER RH, ALDERSON PO, WILHELM J, et al: The measurement of regional ventilation during tidal breathing: a comparison of two methods in healthy subjects, and patients with chronic obstructive lung disease. *Br J Radiol* 48: 181-189, 1975
17. NOSIL J, HUGHES JMB, HUDSON FR, et al: Functional imaging of lung ventilation using the concept of mean transit time. *Phys Med Biol* 21: 251-262, 1976
18. WEST JB, DOLLERY CT: Distribution of blood flow and ventilation-perfusion ratio in lung measured with radioactive CO_2 . *J Appl Physiol* 15: 405-410, 1960
19. BRYAN AC, BENTIVOGLIO LG, BEEREL F, et al: Factors affecting regional distribution of ventilation and perfusion in the lungs. *J Appl Physiol* 19(3): 395-402, 1964
20. GLAISTER DH: The effect of posture on the distribution of ventilation and blood flow in the normal lung. *Clin Sci* 33: 391-398, 1967
21. DE ROO MJK, GORRIS M, VAN DER SCHUEREN G, et al: Computerized dynamic scintigraphy of the lungs. *Respiration* 26: 408-424, 1969
22. TAM CH, MANSELL AL, LEVISON H, et al: Dynamic regional lung function studies in patients with asthma and cystic fibrosis. *Am Rev Resp Dis* 108: 283-293, 1973
23. MCKENZIE SA, GODFREY S, PAL SINGH M: A new method for investigating regional lung function in children with localized lung disease. *J Pediatr Surg* 12: 177-181, 1977
24. KANEKO K, MILIC-EMILI I, DOLOVICH MB, et al: Regional distribution of ventilation and perfusion as a function of body position. *J Appl Physiol* 21(3): 767-777, 1966

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