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UNEVEN PERFUSION AND VENTILATION WITHIN LUNG REGIONS STUDIED WITH NITROGEN-13

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Abstract. The clearance of nitrogen-13 (^{13}N) from the upper, mid and lower zones was measured with a gamma camera during spontaneous breathing in 10 seated subjects. The clearance was monitored after (a) an intravenous injection of ^{13}N dissolved in saline and (b) equilibration with ^{13}N gas in closed circuit. Subjects breathed air first, and then a 30 or 11% oxygen mixture. For any region, the time for 90% elimination (T_{90}) was related to the volume expired by the whole lung during that time (V_{E90}). For the mid and lower zones, the clearance was faster (V_{E90} smaller) after intravenous ^{13}N than after equilibration with ^{13}N gas. This difference persisted when 30% or 11% oxygen was inspired. For the lung overall, the physiological dead space for a mean tidal volume of 884 ml was 277 ml for intravenous ^{13}N clearance, and 384 ml for ^{13}N clearance after equilibration. The conclusions drawn for this study are (1) ventilation in relation to volume is uneven within lung regions (2) intraregional perfusion in relation to volume is also uneven (3) at a local level the well-ventilated units are better perfused (4) these inhomogeneities are not affected by raising or lowering the inspired oxygen concentration.

Dead space
Gas exchange
Gas mixing
Nitrogen washout
Pulmonary circulation
Regional lung function
Stratification in lungs

The use of radioactive gases to detect differences in ventilation and perfusion between lung regions is well established (West and Dollery, 1960; Ball *et al.*, 1962). As monitored by external counting a moderate degree of dispersion of ventilation–blood flow ($\dot{V}A/\dot{Q}$) ratios has been demonstrated, with a threefold difference in $\dot{V}A/\dot{Q}$ between the apex and base of the upright lung. For each region, external detectors record counts proportional to the mean ventilation, perfusion or $\dot{V}A/\dot{Q}$ of a large number of alveolar units (at least 10^7), the distribution of function at a more local level

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being beyond the resolution of the method. Nevertheless, by analysing the regional clearance of radioactivity, after equilibration with insoluble radioactive gases such as nitrogen-13, intraregional inhomogeneity may be revealed (Rosenzweig *et al.*, 1969). In addition, the counting zones can be labelled in proportion to their local blood flow by an intravenous injection of a ^{13}N solution, and the subsequent clearance (*i.e.* the ventilation of perfused units) followed. In this way, intraregional mismatching of ventilation to blood flow can be assessed (Eiser *et al.*, 1977). The dispersion of $\dot{V}A/\dot{Q}$ ratios in the erect lung is greater than that measured by external counting, and at a local level alveolar P_{O_2} may vary from 60–120 mm Hg (Wagner *et al.*, 1974). The lower levels of P_{O_2} within a region may be sufficient to stimulate local hypoxic vasoconstriction which, in turn, would improve the matching of local blood flow and ventilation (Grant *et al.*, 1976).

These experiments set out to detect intraregional inhomogeneity of $\dot{V}A/\dot{Q}$ in the normal lung breathing air, and to assess the effect of high and low inspired oxygen concentration.

Methods

The subjects were medical colleagues who gave informed consent to the study; they were seated upright throughout, breathing normally through a mouthpiece. An insoluble radioactive gas, nitrogen-13 (^{13}N), was used as the marker. This has a short half-life (10 min) and was produced by the M. R. C. Cyclotron by the reaction $^{12}C(d,n)\ ^{13}N$ (Clark and Buckingham, 1975) and pumped to the site of the study. The isotope was initially given as a bolus intravenously, as 1.06–4.5 (mean 2.0) mCi dissolved in 10 ml saline, via a catheter in an antecubital vein with its tip in the axillary or subclavian vein. The injection was made rapidly and the catheter flushed with saline. Radioactivity over the entire lung field was recorded externally by a gamma camera (Nuclear Enterprises) linked via an analogue-to-digital converter to a computer system (Hewlett-Packard 5407). The camera was collimated for the 511 keV γ-emission of ^{13}N. The clearance of the isotope was followed for 7 min; at the end of each run the background counts were negligible (average 12 cps) due to the efficiency of ventilation and the low solubility of the isotope in blood. The subject then breathed ^{13}N gas for 1.5 min in closed circuit from a rebreathing bag filled with an air, oxygen and helium mixture, starting with two or three vital capacity breaths. The initial bag volume ranged from 3.0–3.7 litres and the oxygen concentration was normal at the end of equilibration. The subject was then switched into open circuit, and breathed air, while the clearance of ^{13}N was monitored as before. Tidal volume (V_T) was recorded throughout the study by integrating the signal from a pneumotachograph, and minute ventilation ($\dot{V}E$) was recorded by a gas meter. Functional residual capacity (FRC) was measured by helium dilution during the equilibration phase of the study, or by body plethysmography afterwards. The first part of the study was made breathing air. Each subject then breathed either a high (30%) or

a low (11%) oxygen concentration from a Douglas bag filled from pre-mixed gas cylinders for a period of 10–15 min, after which the intravenous and inhalation studies were repeated. The same inspired oxygen concentration was maintained throughout.

The intravenous bolus of ^{13}N produced peak counts for the whole lung field of 500–1500 cps. The peak activity in the upper zones after i.v. ^{13}N was 100–400 cps. A mean of 5 mCi activity was given for each equilibration study, resulting in peak activities of 1250 cps for the total lung field and 350 cps for the upper zones.

The summed radioactivity for the lungs for each run was displayed as an image on an oscilloscope screen and divided into upper, middle and lower regions, which included both lungs, with a light pen. Time activity curves, corrected for radioactive decay and initial background, were generated for each zone and for the whole lung field, with radioactive counts accumulated over 4-sec intervals. The time taken for radioactivity to fall by 60 or 90% from the peak (after the i.v. bolus) or from the plateau (after the equilibration manoeuvre) was calculated (T_{60}, T_{90}). The volume expired (VE) during this time was measured from the pneumotachograph or gas meter trace and designated VE_{60} or VE_{90}. For the lung as a whole, the clearance was expressed in terms of turnovers of lung volume where turnover (TO) equals the volume expired divided by average lung volume in litres (FRC + 0.5 VT). This was related to the turnover of an ideal system, with a small corection for respiratory frequency, as described by Cumming and Jones (1966). For example, an ideal system, without dead space and at a stroke frequency of 15 min^{-1}, needs 2.45 turnovers of its volume for the activity of a uniformly distributed marker to fall by 90%. If a lung requires 4.9 turnovers, its efficiency for 90% elimination ($efficiency_{90}$) will be 0.5 or 50%. Knowing the mean tidal volume (VT), the wasted ventilation (or dead space) per breath can be calculated in ml as (VT − VT · efficiency). To the extent that the ^{13}N clearances are alinear, the choice of the 90% elimination point gives undue weight to the poorly ventilated units, but in normal subjects the error will be small.

The distribution of blood flow per unit alveolar volume was estimated in the usual fashion by relating the peak count in any region after i.v. injection (as a percent of total counts) to the fractional count rate for the same zone in the plateau at equilibration.

Results

Anthropometric data and smoking history of the subjects is given in table 1. Typical regional clearance curves following equilibration with inhaled ^{13}N or after an intravenous ^{13}N bolus are shown in fig. 1. The insolubility of ^{13}N means that virtually all of the i.v. bolus evolves into alveolar gas as it passes through the capillary bed. (In supine anaesthetized dogs only 2–4% of the activity of dissolved ^{13}N in the pulmonary artery can be recovered from the aorta (Ronchetti *et al.*, 1975) and in awake erect man the proportion is probably less). Subsequent clearance reflects the specific ventilation of the perfused units in the counting regions. The equilibration

TABLE 1
Anthropometric data on 10 normal male subjects

Subject	Age (yr)	Height (cm)	FEV_1/VC l (BTPS)	FRC (air) l (ATPS)	$F_{I_{O_2}}$	Smoking history
JR	26	172	4.5/5.1	4.5	0.30	0
EJ	35	182	4.0/4.7	5.1	0.30	+
JM	34	181	5.9/6.0	4.0	0.30	0
DO	28	173	4.8/5.3	3.9	0.30	0
DL	29	179	4.7/6.7	3.5*	0.30	0
AD	26	182	5.4/6.3	3.5*	0.30	0
IG	31	185	5.8/6.5	3.8	0.11	0
NP	43	184	5.1/6.1	2.95	0.11	0
AM	30	175	4.8/5.4	2.8*	0.11	+
JO'K	26	172	4.4/5.0	3.0	0.11	0

* FRC measured afterwards, breathing air, by body plethysmography.

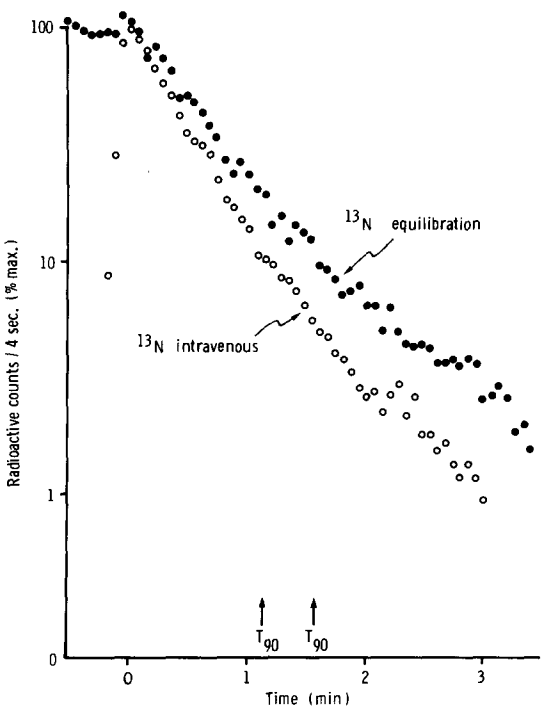

Fig. 1. Radioactivity (summed counts per 4 sec) on log scale plotted against time for lower zone clearance in JO'K breathing air, after an intravenous bolus of ^{13}N and after 1.5 min equilibration with ^{13}N gas. Activity is expressed as a percentage of peak counts. T_{90} indicates the time for 90% elimination of ^{13}N. Note slower and less linear clearance after ^{13}N equilibration which labels all patent ventilatory units.

procedure, on the other hand, labels the gas containing spaces of the lung uniformly, and the clearance is related to the mean ventilatory performance of all patent units. Figure 1 shows that breathing spontaneously on air, the perfused units within a region have a faster clearance than all patent alveoli. Table 2 shows that in terms of T_{90}, breathing air, the lower zone clearance of ^{13}N given intravenously relative to that after equilibration is faster in seven out of ten subjects, though there are no differences for the upper zones or when high or low oxygen concentrations are breathed. For conciseness, only the upper and lower zone clearances are shown. Because of

TABLE 2

Time in seconds for 90% elimination of ^{13}N for upper and lower zones, after intravenous and equilibration with ^{13}N, breathing air and oxygen (30% for JK–AD, 11% for IG–JO'K)

Subject	Lung zone	Air		Oxygen	
		^{13}N i.v.	^{13}N equilibration	^{13}N i.v.	^{13}N equilibration
JK	Upper	172	224	193	166
	Lower	127	206	145	142
EJ	Upper	78	59	95	72
	Lower	58	41	69	54
JM	Upper	136	138	154	
	Lower	116	116	112	
DO	Upper	191	212	233	171
	Lower	134	210	167	150
DL	Upper	183	188	187	182
	Lower	132	148	112	151
AD	Upper	110	115	140	100
	Lower	85	98	82	85
IG	Upper	154	144	148	146
	Lower	101	119	121	118
NP	Upper	138	105	161	139
	Lower	95	75	104	110
AM	Upper	144	140	119	122
	Lower	79	90	66	82
JO'K	Upper	135	142	113	101
	Lower	92	125	79	71

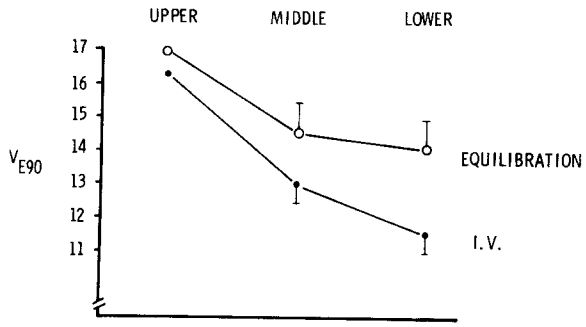

Fig. 2. Expired volume in litres for 90% elimination of ^{13}N (V_{E90}) after intravenous ^{13}N and after equilibration with ^{13}N. Mean results for 10 subjects for upper, middle (±1 SE) and lower (±1 SE) zones.

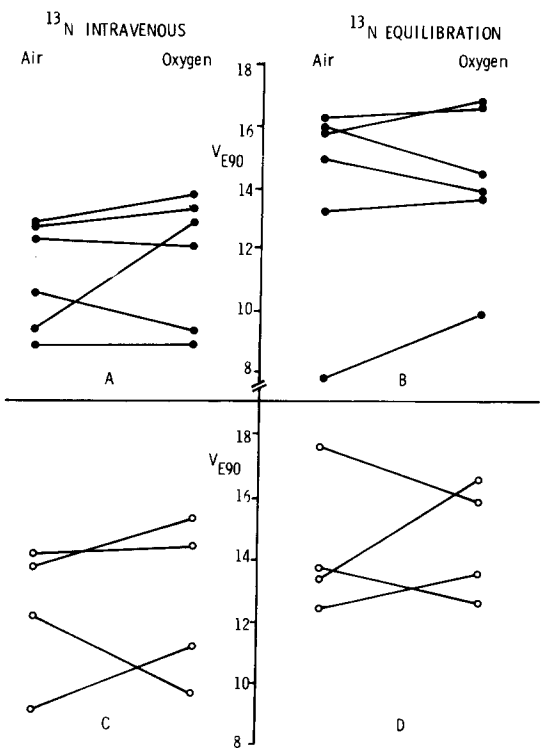

Fig. 3. Expired volume in litres for 90% elimination of ^{13}N after i.v. and equilibration manoeuvres in 6 subjects breathing air and 30% oxygen (A and B) and 4 subjects breathing air and 11% oxygen (C and D). Results for individual subjects and lower zones only. For both groups, the V_{E90} is less after ^{13}N i.v. than ^{13}N following equilibration, but there is no effect on changing the inspired oxygen concentration.

differences in minute volume between measurements, the results for T_{90} have been re-expressed in fig. 2 in terms of the expired volume required to reduce the peak activity by 90% (VE_{90}). The clearance of the i.v. ^{13}N bolus is faster (VE_{90} smaller) than the equilibrated ^{13}N in the mid ($P < 0.2$) and lower ($P < 0.05$) zones but not in the upper zone. Figure 3 shows that no significant change in i.v. ^{13}N clearance occurs on changing from air to either 30 or 11% oxygen breathing but, for the lower zones the difference between i.v. and equilibrium in ^{13}N clearance at either level of inspired oxygen remained ($P < 0.001$). There were no important changes in the pattern of breathing between i.v. and equilibration clearances or between air and oxygen breathing (table 3).

The initial slope of the clearance curves on a semi-logarithmic plot after equilibration is a measure of specific ventilation (Briscoe and Cournand, 1959). The values breathing air are similar to those reported by Rosenzweig *et al.* (1969), being 1.25 ± 0.2 (SEM), 1.58 (± 0.2) and 1.72 (± 0.4) $l \cdot min^{-1} \cdot l^{-1}$ for the upper, middle and lower zones respectively.

For the lung as a whole, the ventilatory efficiency was calculated by relating the VE_{90} for the total lung field to the lung volume and minute ventilation (see Methods). The efficiency with which the lung achieved 90% elimination of ^{13}N is shown in table 4. Efficiency is equal to $1 - V_D/V_T$ where V_D/V_T is an index of wasted ventila-

TABLE 3

Minute ventilation ($\dot{V}_E$) in litres/min and tidal volume V_T (ml) in 10 subjects, following injection or inhalation of ^{13}N, breathing air or oxygen (30% for JK–AD, or 11% for IG–JO'K)

Subject	Air				Oxygen			
	^{13}N Intravenous		^{13}N Equilibration		^{13}N Intravenous		^{13}N Equilibration	
	$\dot{V}_E$	V_T	$\dot{V}_E$	V_T	$\dot{V}_E$	V_T	$\dot{V}_E$	V_T
JK	4.6	–	4.27	–	5.6	–	5.95	–
EJ	9.43	1240	12.85	2300	7.32	1340	11.62	2070
JM	6.28	660	7.78	700	7.0	550	8.4	603
DO	5.66	710	4.57	720	4.68	930	5.85	870
DL	5.43	800	6.32	1010	6.27	800	6.48	822
AD	7.7	715	8.15	700	7.18	717	9.32	843
Mean	6.52	825	7.32	1086	6.34	867	7.94	1042
IG	8.5	900	8.7	780	7.47	690	8.68	717
NP	8.77	675	10.75	545	8.64	610	9.02	550
AM	9.15	615	8.5	620	9.3	670	9.9	660
JO'K	6.1	635	6.7	580	8.24	693	10.86	810
Mean	8.13	706	8.66	631	8.41	666	9.62	684

TABLE 4

Tidal volume (VT), whole lung ventilatory efficiency for 90% ^{13}N elimination ($Efficiency_{90}$) and calculated washed ventilation per breath or dead space (VD)

Subject	^{13}N intravenous			^{13}N equilibration		
	VT (ml)	$Efficiency_{90\%}$	VD (ml)	VT (ml)	$Efficiency_{90\%}$	VD (ml)
JK	–	–	–	–	–	–
EJ	1240	66	375	2300	59	895
JM	600	68	167	700	53	285
DO	710	55	275	720	49	322
DL	800	60	275	1010	48	480
AD	715	66	198	700	54	277
IG	900	56	351	780	51	337
NP	675	43	340	545	43	271
AM	615	42	312	620	39	333
JO'K	635	61	203	580	48	257
Mean	772	57	277	884	51	384

tion per breath or equivalent dead space. By averaging the tidal volume during the clearance, the volume of wasted ventilation per breath was calculated as VD (table 4).

The interzonal distribution of blood flow is plotted in fig. 4. There was a small but insignificant effect of high or low oxygen concentrations on the interzonal distributions. This is in agreement with the findings of Holley *et al.* (1966) breathing high oxygen mixtures. Dawson (1969) found a small increase in apical blood flow with 14% inspired oxygen; this might have been present in our subjects had a more detailed interzonal analysis been performed.

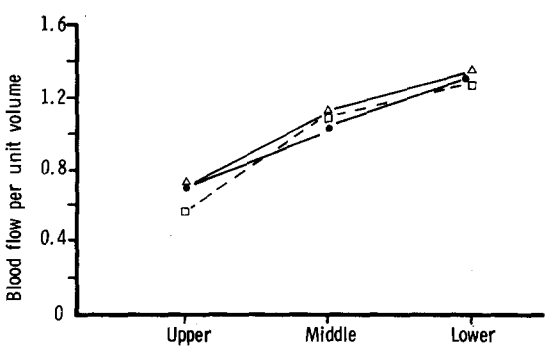

Fig. 4. Distribution of blood flow per unit alveolar volume in arbitrary units for 10 subjects breathing air (□), 6 subjects breathing 30% oxygen (Δ) and 4 subjects breathing 11% oxygen (●).

Discussion

The most remarkable finding in this study was the faster lower zone clearance for ^{13}N introduced intravenously compared to ^{13}N rebreathed in closed circuit (fig. 1). This difference was statistically significant when overall ventilation was taken into account (fig. 2). For greater accuracy, changes of regional or overall lung volume should also be assessed when comparing two clearance curves. This underlies the concept of efficiency. Computation of ventilation (in $l \cdot min^{-1}$) and lung volume (in l) for each zone from the total flow and volume would have involved unjustifiable assumptions about the relative efficiency of radioactive counting over different parts of the lung. Secondly overall FRC could only be measured accurately *before* and not *during* each clearance. In a separate series we measured FRC, with the same rebreathing circuit, in 7 subjects, at 10-min intervals for 70 min. The first three measurements were on air and the last four on 30% oxygen. There was no systematic variation of FRC with time or with oxygen breathing. Only two subjects showed a variation of more than 500 ml.

It is unlikely that the difference between the ^{13}N intravenous and ^{13}N gas equilibration clearances is an artefact caused by a relatively greater proportion of ^{13}N in the chest wall or returning in mixed venous blood during the post equilibration clearance (Matthews and Dollery, 1965). First, nitrogen is extremely insoluble in tissue and blood with a blood gas partition coefficient of approximately 0.017, so very little would enter the blood during the 2-min equilibration phase. Second, after equilibration for 4 min with ^{13}N, the expired air VE_{90} (which excludes the chest wall) is the same as the lung VE_{90} (Ronchetti *et al.*, 1975) whereas there was 100% increase in lung VE_{90} compared to expired air when the measurement was repeated with the much more soluble gas, $^{133}Xenon$.

From the difference between the i.v. and equilibrated clearance of ^{13}N in terms of VE_{90} for the mid and lower zones the following conclusions can be drawn. First, the distribution of ventilation to volume within the zone must be uneven otherwise the clearances would have been the same, irrespective of the initial distribution. Second, the distribution of perfusion in relation to volume must be uneven otherwise the zone would have been labelled identically after the i.v. bolus and after equilibration. Again, the clearances would have been similar. Third, on a local basis, blood flow is preferentially distributed to the better ventilated units.

INTRAREGIONAL INHOMOGENEITY OF VENTILATION

Intraregional differences in specific ventilation (in $l \cdot min^{-1} \cdot l^{-1}$ or as volume to ventilation ratio ($Vo/\Delta V$)) are well recognized in normal subjects. Suda *et al.* (1970) sampled nitrogen concentrations from small catheters (1–1.7 mm o.d.) placed in the subdivisions of lobes in upright and supine man. During a multi-breath nitrogen washout, the $Vo/\Delta V$ in younger subjects in subsegments of lobes, taking 1 SD around

the mean, ranged from 7.99 to 21.47. This dispersion was approximately the same for segments, lobes and lungs. Our data has not been analysed in the same way, *i.e.* by a 6-compartment computer reconstruction of the washout curves, but the alinearity in fig. 1 and in similar curves analysed by Rosenzweig *et al.* (1969) is consistent with this dispersion of $V_O/\Delta V$ within each region. In anaesthetized dogs, Engel *et al.* (1974) found that most of the slope of the alveolar plateau in the trachea following a single breath of oxygen was also present in samples taken from a 3-mm airway. From the peripheral cardiogenic oscillations they calculated a 2 : 1 variation in ventilation to volume ($\Delta V/V_O$) ratios, similar to the dispersion calculated by Suda *et al.* (1970). Rosenzweig *et al.* (1969), using ^{13}N and tightly collimated detectors, found 3 and 4 : 1 variations in specific ventilation within regions.

Considerable controversy surrounds the mechanisms underlying the intraregional inhomogeneity of ventilation. Inhomogeneity of mechanical properties (Sugihara *et al.*, 1971), uneven distribution of dead space gas (Horsfield and Cumming, 1968) and incomplete mixing between inspired and residual gas (stratified inhomogeneity) (Sikand *et al.*, 1976; Okubo and Piiper, 1974) may all play a part. There is certainly stratification of gas concentrations in the periphery during inspiration (Paiva, 1973) but whether these gradients persist during the subsequent expiration is less clear. On the other hand, the asymmetrical anatomy of the lobule (Parker *et al.*, 1971) can be invoked to explain the existence of parallel and series inhomogeneities within the same region.

INTRAREGIONAL INHOMOGENEITY OF BLOOD FLOW

On the basis of measurements of expired P_{O_2} and P_{CO_2} and P_{argon} in man, Read (1966a, b) argued that the blood supply of regions emptying late in expiration was less than that of better ventilated regions. Wagner *et al.* (1967) injected radio-labelled albumin particles (< 20 μm diameter) into the pulmonary circulation of rats, and found a gradient of diminishing radioactivity from the proximal to distal parts of lobules. In saline-filled dog lungs, surrounded by saline to eliminate gravity effects, and uniformly labelled with ^{133}Xe, West *et al.* (1972) found that a brief period of blood flow caused a rise in the terminal part of the expired ^{133}Xe alveolar plateau. They calculated that the lung regions emptying last had 16% less blood flow than those emptying earlier.

LOCAL INHOMOGENEITY OF VENTILATION–PERFUSION RATIOS

Inhomogeneity of blood flow between and within adjacent alveolar septa is well recognized (Warrell *et al.*, 1972) and contributes to the phenomenon of vascular recruitment. Nevertheless, inhomogeneity between arteriolar domains was not seen and the way in which terminal units with the better ventilation are better perfused

is not clear. Inequalities in local alveolar oxygen tension and local hypoxic vasoconstriction do not play a part on the basis of the experiments reported here when 30% oxygen was breathed. Wagner *et al.* (1967) similarly found no effect of oxygen breathing on the local distribution of blood flow. Again, putting all pulmonary vessels in a moderately hypoxic environment by breathing 11% oxygen did not make the distribution of local blood flow more uniform.

This contrasts with the situation in patients with chronic bronchitis and emphysema, where regional clearance of intravenous ^{13}N is considerably faster than that after equilibration with ^{13}N. Breathing 30% oxygen slowed the intravenous clearance but did not affect the other (Eiser *et al.*, 1977), as if hypoxic vasoconstriction to poorly ventilated units had been relieved. Anthonisen *et al.* (1968) made similar measurements in bronchitic patients using ^{133}Xe. In the more normally ventilated areas, their fig. 1 shows a tendency for intravenous clearance to be faster than that after rebreathing, but the reverse occurred in the poorly ventilated zones. The effect of oxygen breathing was not studied. ^{133}Xe is more soluble in blood than ^{13}N, which complicates the analysis.

The failure of changes of oxygen concentration to alter intraregional $\dot{V}_A/\dot{Q}$ mismatching requires some comment. Haab *et al.* (1969), from an analysis of arterial–alveolar nitrogen gradients, found no improvement in $\dot{V}_A/\dot{Q}$ distribution when normal subjects moved to a high altitude. On the other hand, there is some evidence that increasing the inspired oxygen concentration worsens $\dot{V}_A/\dot{Q}$ distribution by releasing hypoxic vasoconstriction. With an inert gas technique, Wagner *et al.* (1974) found that the $\dot{V}_A/\dot{Q}$ variance in young subjects did not increase when 100% oxygen was breathed; nevertheless, a 0.6% venous admixture (exclusive of anatomic shunt) developed. Harris *et al.* (1974) showed increase in $A\text{-}a\ D_{O_2}$ when breathing 40% oxygen which was equivalent to a 0.5% increase in venous admixture. It is unlikely that the regional clearance of ^{13}N could detect such small changes.

In the absence of any anatomical basis for parallel differences of blood flow and ventilation in which better ventilated units are also better perfused, we follow Read (1966a, b) and put forward a series model (fig. 5) as an explanation for our results. The basis of the scheme is that the dissolved ^{13}N, on its arrival in the lung, meets the better-ventilated units first. There is some support for this notion because the pulmonary arteries accompany the airways down to the level of respiratory bronchioles. To take an extreme example, if there was no limit to the diffusion of inert gases between arteries and airways, all the i.v. bolus of ^{13}N would be evolved into the bronchi and would be rapidly cleared from the lung. A second possibility, illustrated in fig. 5, is that the alveoli or alveolar ducts in the immediate vicinity of precapillary vessels, are the best ventilated ones.

Below 100 μm diameter, arterial vessels rapidly lose their muscular coat, becoming indistinguishable from capillaries, and therefore capable of gas exchange (Reid, 1968). The summed cross-sectional area of vessels from 140 to 30 μm is about 120 cm^2 (Singhal *et al.*, 1973) and although this is a mere fraction of the total cross-sectional area of the capillary bed, significant exchange of very insoluble gases such as nitrogen

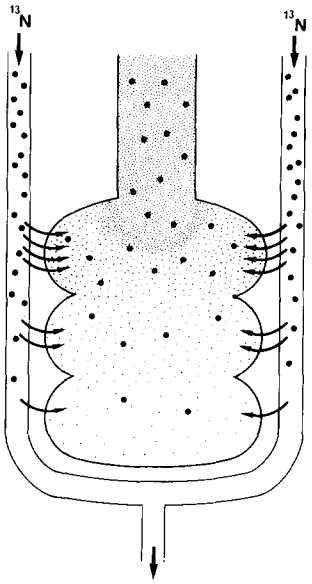

Fig. 5. Schematic diagram of terminal ventilatory unit with group of alveoli, supplying bronchiole, incoming arterial vessels containing dissolved ^{13}N, capillary bed and venous outflow. Ventilation is stratified in accordance with density of fine stippling. Location of ^{13}N molecules (●) and their evolution from blood to gas is shown.

might occur because of their fast rate of diffusion (Wagner, 1977). Staub (1961) has claimed, from rapidly frozen lung sections, that raising the inspired oxygen from 21 to 100% in cats leads to oxygenation of the blood in pulmonary arterial vessels up to 200 μm in diameter. On the other hand, Sackner *et al.* (1964) calculated that the evolution of ether from 50-μm vessels would account for only 0.2% of the total evolved, though the proportion rose to 9% for the precapillaries (10–20 μm diameters). These calculations are heavily dependent on the value chosen for wall thickness, *i.e.* 0.5 μm for capillaries, 1.4–3.0 μm for 10–20 μm and 5 μm for the 50 μm vessels. To the extent that a proportion of precapillary vessels are as thin as capillary vessels, as suggested by Reid (1968), ^{13}N evolution from their lumen into adjacent bronchioles or alveolar ducts might be substantial.

EFFECTS OF GRAVITY

With the lungs divided into only three zones, there was sufficient height in each region for the parallel differences of ventilation and perfusion caused by gravity to play a part. For example, by interpolation the more dependent parts of each zone received more blood flow (fig. 4) and were better ventilated (fig. 2). Therefore the i.v. bolus preferentially labelled the dependent part which was also better ventilated. This effect should be greatest in the upper zone because the change of blood flow

per cm of distance is greater than over the lower half of the lung. In fact, the upper zone showed the least difference between the i.v. and equilibrated ^{13}N clearances. On the other hand, the explanation offered in terms of the model (fig. 5) should apply equally well to all zones. The different behaviour of the upper zones may reflect a preferential distribution of common dead space gas to them (Grant *et al.*, 1974). In the upper zone the clearance of the i.v. ^{13}N bolus would be delayed by re-inspiration of dead space gas from the lower zone where there was a higher concentration of ^{13}N. Nevertheless, the possibility that local inhomogeneities are gravity-dependent and related, perhaps, to differences in parenchymal expansion remains.

DEAD SPACE

The mean efficiency of clearance for all units within the lung was 51% and for the units labelled with i.v. ^{13}N 57% (table 4). This gives rather high values for *physiological* dead space or wasted ventilation – 384 and 277 ml respectively, especially when compared to the Fowler anatomic dead space (ca. 150 ml) or the Bohr physiological dead space for CO_2 (approximately 175 ml for VT of 750 ml (Harris *et al.*, 1973)). The Fowler dead space is probably a minimum value, and the Bohr would be larger if the P_{CO_2} of the anatomic dead space was taken into account in the estimate of the inspired CO_2 concentration. Nevertheless, for gas exchange the preferential matching of ventilation and perfusion means some reduction in dead space, if the clearance of i.v. ^{13}N reflects the situation for oxygen and carbon dioxide.

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