Ventilation and Perfusion of Each Lung during Differential Ventilation with Selective PEEP

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Lung perfusion was studied in 10 patients (mean age 58 yr) in the lateral position during enflurane anesthesia. They were ventilated through a double-lumen endotracheal catheter: 1) by one ventilator with free distribution of ventilation between the lungs, with no (zero) end-expiratory pressure (ZEEP); 2) as above but with a general positive end-expiratory pressure (PEEP) of 9 cmH₂O; or 3) by two ventilators with equal distribution of ventilation between the lungs and with a selective PEEP of 8 cmH₂O to the dependent lung only. Total ventilation was on average 8 l/min (BTPS) throughout the study. During the first method, 34% of ventilation was distributed to the dependent and 66% to the nondependent lung. Cardiac output (thermodilution) was 4.5 l/min, 57% being distributed to the dependent lung as assessed by iv boli of Xenon 133. During the second method, ventilation was assumed to be distributed equally between the lungs. Cardiac output was decreased to 3.8 l/min, and the dependent lung received 81% of lung blood flow. During the third method, cardiac output was significantly greater than during the second method (4.1 l/min), 51% passing to the dependent lung. Peak and end-inspiratory airway pressures were 5–18 cm H₂O lower during selective than during general PEEP. Arterial oxygen tension was significantly greater during the third method than during either of the other ventilator settings and the alveolar–arterial oxygen tension difference was almost halved compared with the first method. It is concluded that differential ventilation with selective PEEP improves ventilation–perfusion matching and thus oxygenation. (Key words: Lung: blood flow. Ventilation: differential; positive end-expiratory pressure.)

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A GREATER PROPORTION of ventilation is distributed to nondependent regions in the anesthetized subject than in an awake human,[1-3] whereas perfusion, owing to gravitation, is distributed mainly to dependent regions.[4-6] This results in ventilation–perfusion ($\dot{V}/\dot{Q}$) mismatching, with regions with a "low" $\dot{V}/\dot{Q}$ ratio and increased shunt.[7,8]

The impaired dependent ventilation appears to result from a decrease in functional residual capacity (FRC),[9-12] which may promote airway closure in dependent lung units, as shown in several studies,[13-15] although there is one report of contrasting results.[16]

The decrease in FRC can be counteracted by the application of positive end-expiratory pressure (PEEP). However, increase in intrathoracic pressure caused by PEEP decreases cardiac output by impeding venous return[17] and forces the lung blood flow to dependent regions.[4] Moreover, the effect of PEEP on the regional lung volume is distributed unfavorably, dependent lung tissue (where airway closure and any alveolar collapse mainly occur) being less expanded than nondependent tissue.[18,19]

Ideally, mechanical ventilation should distribute inspired gas in proportion to regional perfusion, with the least possible interference with the total lung blood flow. This can be achieved, within certain limits, by the following: 1) positioning the subject in the lateral posture; 2) ventilating each lung separately in proportion to its perfusion (differential ventilation); and 3) applying PEEP only to the dependent lung to ensure the distribution of gas to lower regions within that lung (selective PEEP).[20] Since, with selective PEEP, the overall intrathoracic pressure will be lower, there should be less interference with total lung blood flow and a lower risk of barotrauma than with general PEEP. Preliminary tests of this ventilation concept in patients with acute bilateral lung disease also have shown a dramatic improvement in arterial oxygen tension and a maintained cardiac output.[21,22] However, to create optimum matching between ventilation and perfusion, the perfusion distribution between the lungs has to be known.

In the present study, the distribution of perfusion between the dependent and nondependent lung and the efficiency of regional ventilation were investigated in

TABLE 1. Patient Data

No.	Sex	Age (years)	Height (cm)	Weight (kg)	Smoking (cig/day)	Surgical Diagnosis
1	F	52	—	—	0	Peptic ulcer
2	F	59	164	61	15	Cholecystitis
3	M	29	—	—	0	Peptic ulcer
4	M	65	182	89	0	Hypernephroma
5	F	60	164	64	0	Carcinoma of pancreas
6	M	61	—	—	—	Carcinoma of colon
7	M	52	185	75	0	Carcinoma of liver
8	M	68	180	73	0	Hiatal hernia
9	M	68	178	73	20	Carcinoma of rectum
10	M	61	180	63	0	Colonic diverticulosis

anesthetized subjects in the lateral posture during conventional and differential ventilation with and without PEEP.

Materials and Methods

Ten patients (seven men and three women, 29–68 years old) were studied during general anesthesia prior to elective surgery. In eight of them, the studies were
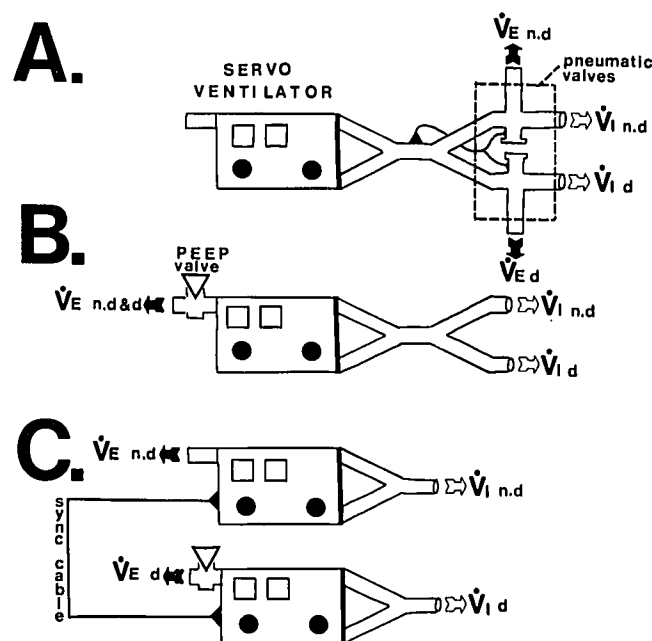

FIG. 1. Technical set-up during the different ventilator settings. *A*) Conventional ventilation with zero end-expiratory pressure and free distribution of inspired gas (VI) to the nondependent (nd) and the dependent (d) lung. Expired gas (VE) from each lung was obtained by means of a pair of pneumatic valves on the expiratory gas line. *B*) General positive end-expiratory pressure (PEEP). During this set-up, the pneumatic valves did not function satisfactorily and they had to be disconnected. Only total ventilation could be measured. *C*) Differential ventilation with selective PEEP administered by two ventilators. Note the synchronization cable between the two Servo-ventilators and that a PEEP valve is applied on the expiratory gas line from the dependent lung only.

performed under similar conditions and these made up the material for statistical analysis. The other two patients were investigated under additional conditions, prompted by the results of the major study (table 1). A criterion for inclusion in the study was that a clinical examination, chest x-ray, and ECG should have revealed no signs of cardiopulmonary disease. Three were current smokers (15–20 cigarettes/day). Informed consent was obtained in each case, and the study had been approved by the local ethical and radioisotope committees.

ANESTHESIA

Premedication consisted of oxycodone 0.10 mg/kg and scopolamine 0.004 mg/kg, given intramuscularly approximately 1 h prior to induction of anesthesia. Anesthesia was induced with a sleep dose of thiopental (2–5 mg/kg) and was maintained with 1–2% enflurane in air–oxygen. The inspiratory oxygen fraction was kept at 0.3 and was checked intermittently by mass spectrometry. Muscular relaxation was secured with pancuronium bromide (0.08–0.1 mg/kg b.w.), and endotracheal intubation was performed with a disposable, double lumen, left main bronchial, plastic catheter with high-volume, low-pressure cuffs (Broncho-Cath®, National Catheter Co.). The resistance to gas flow was fairly similar in the two channels, being approximately 9 and 13 $cmH_2O \cdot s \cdot 1^{-1}$ in each channel at 0.3 and 0.6 l/s, respectively. To check that there was no leakage of gas between the lungs, a small rubber bag was connected to one of the two openings of the tube, while ventilation was being administered through the other. Inflation–deflation of the bag in phase with the ventilation of the contralateral lung, with no successive increase in residual bag volume, indicated a tight airway system. The patient was placed in the left lateral posture and remained so throughout the study. Ventilation was administered by one or two ventilators (Servo-ventilator 900®, Siemens-Elema), depending on which ventilation pattern was being studied (fig. 1). For differential ventilation, the two ventilators were synchronized electronically so that the start of inspiration and of expiration was simultaneous for the two lungs, one of the ventilators (master) commanding the other (slave). Both ventilators were set to deliver a square wave flow with an inspiratory:expiratory ratio of 1:2 and an end-inspiratory pause of 10% of the respiratory cycle. The sum of the two fractional tidal volumes was kept approximately constant during the study and amounted to 7–10 ml/kg b.w. The respiratory frequency was maintained at 12–13 breaths/min throughout the investigation period.

CATHETERIZATION AND CARDIAC OUTPUT

A triple-lumen thermodilution catheter (Swan-Ganz® no. 7 F; Edwards Laboratory) was introduced percuta-

neously by a sleeve technique into a medial cubital vein and was advanced to the right ventricle and pulmonary artery during continuous monitoring of ECG and intravascular pressure (recording equipment: Philips Medical System). Intravascular pressures were related to atmospheric pressure, the level of the transducer being 10 cm above the lowermost point of the chest wall. This position was assumed to correspond to the vertical level of the left atrium. Cardiac output was determined by thermodilution, with injection of 10 ml boli of ice-cold 5% glucose solution into the superior vena cava and measurement of the temperature in the pulmonary artery (CO computer 9520A; Edwards Laboratory). Cardiac output values presented in the text and tables are mean values of four to five determinations. A short Teflon® cannula was introduced percutaneously into a radial artery for blood sampling.

REGIONAL PERFUSION

It was assumed that the maximum activity in each lung of a poorly soluble gas, about 200 MBq (5 mCi) of 133-Xe, injected into the superior vena cava, would reflect the perfusion distribution between the lungs. The maximum activities in each lung were summed, and division of the individual value by the sum gave the percentage flow in each lung. To create as long a period as possible for the isotope to distribute and to accumulate in the alveolar gas before its elimination via the airways began, the bolus was injected through the side hole of the Swan-Ganz® catheter exactly at the start of an expiration and the respiratory rate was kept low at 12–13 breaths/min. This technique will not take into account, or will grossly underestimate blood flow that does not come into contact with gas-filled alveoli, and can thus be considered to measure "nonshunted blood flow." In order to reduce any shunt, alveolar collapse was prevented as far as possible by intermittent deep sighs and two "near vital capacity" inflations 1–2 min before the perfusion measurement.

Starting at the time of injection, four exposures were made every second for 15 s with a gamma camera (General Electric, Giga 535). Thereafter, 5-sec exposures were made over a period of 5 min. By adding consecutive exposures (after subtraction of background activity), periods of 5 s could be selected to find the period of maximum uptake for each lung. Before the peak activity was determined, the outlines of each lung had to be defined. Since the boundaries varied during the period of analysis, the approximate period of maximum activity was determined from the raw activity data and the outlines of each lung were established. This was done by a computer (PDP 11/34 with Gamma 11 software), using a nine-point smoothing procedure and the 10%

isocount of the maximum for each lung as the border limit. When the lung fields had been established, the 5-s period of peak activity again was determined. This finally determined period differed from the initial trial period by at most 3–4 s and usually by less than 2 s. It was found that the peak activities in the two lungs did not coincide, stressing the importance of determining the peaks independently. The outlining of the lungs was repeated under each condition of the study.

TOTAL VENTILATION

Ventilation of each lung was measured by collecting the expired gas in a bag during 1 min and measuring its volume with a spirometer (Bourns Medical System Inc.). This procedure was repeated three to four times, and the mean value was computed. Total ventilation was obtained by adding dependent and nondependent lung ventilation. The separation of lung ventilation was ensured by incorporating pneumatic valves in the expiratory lines between the double-lumen endotracheal catheter and the ventilator ("free" distribution with zero end-expiratory pressure (ZEEP), or by using two ventilators (various forms of differential ventilation and selective PEEP) (fig. 1). General PEEP was administered with one ventilator, and the pneumatic valves initially were used for separating the ventilation of each lung, however, the valves did not function satisfactorily during PEEP and had to be disconnected. Thus, only total ventilation could be measured during general PEEP. The addition of pneumotachography was considered but was rejected because of the complexity of the study and the time limits imposed.

REGIONAL VENTILATION

The elimination of the isotope via the airways was determined independently for six horizontal slices of equal thickness (nine picture elements, corresponding to 7.5 mm on the image). The slices were positioned above each other, three covering most of the dependent and the other three most of the nondependent lung. The lung volumes covered by each slice were not measured, but most probably they differed, the lung tissue within each slice being of different width and depth. However, these differences would have no effect on the calculated ventilation efficiencies (see below and "Discussion"). Background activity was subtracted in the same way as for the perfusion measurements. The activity was measured for each slice during 5-s periods corresponding to the time of peak activity, and also during 5-s periods starting 15, 30, 45, and 115 s after the injection of the bolus. A plot of activity against time was constructed, and the time taken for washout of the isotope to 50% of the initial level (T50) was calculated by an interpolation technique. These washout times

TABLE 2. Airway Pressures and Ventilation during Zero, General, and Selective Positive End-expiratory Pressure
(ZEEP, Gen. PEEP and Sel. PEEP, Respectively) (n = 8)

| | Airway Pressures, cmH₂O | | | | | | Ventilation, l/min BTPS | | |
| | P_{max} | | P_{ei} | | P_{ee} | | | | |
	DEP	N.-DEP	DEP	N.-DEP	DEP	N.-DEP	TOT	DEP	N.-DEP
ZEEP									
x̄	13.8	12.5	7.1	8.3	0	0	8.18 ± 0.48	2.75 ± 0.29	5.43 ± 0.30
±SEM	0.8	0.7	0.5	0.6	0	0			
GEN. PEEP									
x̄	31.4*	31.4*	25.0*	25.0*	9.3*	9.3*	7.98 ± 0.25	(3.84)†	(4.15)†
±SEM	2.6	2.6	2.0	2.0	0.6	0.6			
SEL. PEEP									
x̄	26.7‡§	12.0‡	19.9*‡	7.3‡	7.8*	0‡	8.08 ± 0.25	4.12 ± 0.17*	3.96 ± 0.12*
±SEM	3.6	2.3	2.2	1.1	0.7	0			

DEP = dependent and N.-DEP = nondependent lung. P_{max}, P_{ei}, and P_{ee} = maximum, end-inspiratory and end-expiratory pressures.
* Significantly different from ZEEP, $P < 0.001$.

† Assumed distribution according to Rehder *et al.*[2] and Bindslev *et al.*[3]
‡ Significantly different from GEN. PEEP, $P < 0.001$.
§ Significantly different from ZEEP, $P < 0.01$.

depend not only on the magnitude of regional ventilation ($\dot{V}r$) but also on the regional volume (Vr), *i.e.*, on the ventilation volume ratio ($\dot{V}r/Vr$), and thus can be considered a measure of the efficiency of ventilation.

ARTERIAL BLOOD GASES

Arterial oxygen and carbon dioxide tensions (PaO_2, $PaCO_2$) were measured by a conventional electrode technique (ABL 2, Radiometer). Alveolar oxygen tension (PA_{O_2}) was calculated as: $PA_{O_2} = PI_{O_2} - PaCO_2/R$, where PI_{O_2} is inspired oxygen tension and R the respiratory quotient, assumed to be 0.8.

STATISTICS

Standard statistical methods were employed, using the paired t test when applicable. All data are presented as means ± SE.

TABLE 3. Washout Times of the Isotope (in seconds) to Reduce the Activity to 50% of the Maximum Level, in Six Horizontal Lung Slices, Located One above Another, Three Covering Most of the Dependent and Three Most of the Nondependent Lung (n = 8)

| | Dependent | | | Nondependent | | |
	Lower	Middle	Upper	Lower	Middle	Upper
ZEEP						
x̄	52.6	46.9	53.1	42.1	42.0	68.6
±SEM	11.4	12.2	14.6	6.8	5.2	7.9
GEN. PEEP						
x̄	24.9*	28.8*	38.1	44.5	63.5*	97.4*
±SEM	3.4	5.2	6.7	5.8	7.4	10.7
SEL. PEEP						
x̄	31.6*†	33.4	40.2	41.5	50.0	67.4†
±SEM	3.7	4.4	4.3	4.9	6.9	7.1

* Significantly different from ZEEP, $P < 0.01$.
† Significantly different from GEN. PEEP, $P < 0.01$.
Significantly different from the region below, during the same ventilator setting, $P < 0.05$.

Results

ZERO END-EXPIRATORY PRESSURE

Ventilation (tables 2 and 3): The average total ventilation was 8.2 l/min (BTPS), 34% being distributed to the dependent and 66% to the nondependent lung, respectively. The peak airway pressure, measured at the proximal end of the double-lumen catheter, was approximately 13 cm H_2O in both channels, and the end-inspiratory pressure was around 7–8 cm H_2O.

The half time (T50) of the washout of the injected 133-Xe varied between 42 and 69 s (fig. 2). The longest T50 was seen in the uppermost lung field in the nondependent lung. There was no continuous decline in T50 down the lungs, but the lower region in the nondependent lung had a shorter washout time than the uppermost region in the dependent lung ($T < 0.05$). The majority of the plots proved to be close to monoexponential decay curves. However, in three of the eight subjects, some of the washouts displayed a bi-exponential pattern. The same observations also were made during general and selective PEEP.

Perfusion and $\dot{V}/\dot{Q}$ (table 4): The mean cardiac output was 4.5 l/min, the stroke volume and heart rate falling within the ranges observed in earlier studies on subjects of comparable age during similar anesthesia.[23] The perfusion distribution was 57% to the dependent and 43% to the nondependent lung (fig. 3). Peak activity occurred 1–2 s earlier in the dependent than in the nondependent lung, and the first appearance of the isotope also was noted in the dependent lung. (This also was the case with general and selective PEEP.) Pulmonary arterial and capillary wedge pressures were comparable to those recorded in previous studies on normal subjects

during similar anesthesia and mechanical ventilation.[2] The average $\dot{V}/\dot{Q}$ ratio was 1.1 for the dependent and 2.8 for the nondependent lung.

Blood Gases (table 5): Arterial P_{O_2} and P_{CO_2} fell within normal limits. The alveolar–arterial oxygen tension difference, $P(A-a)_{O_2}$, was on an average 83 mmHg.

GENERAL PEEP

Ventilation (tables 2 and 3): The general PEEP applied was on an average 9 cmH_2O, and total ventilation was kept essentially unaltered in comparison with that during ZEEP. Individual lung ventilation could not be measured for technical reasons (see above). Compared with ZEEP, peak airway pressure was more than doubled, and end-inspiratory pressure was 3–3.5 times higher. The end-inspiratory minus end-expiratory pressure was, on the average, almost 16 cmH_2O, which was twice that during ZEEP, indicating a much less compliant lung–thorax.

The washout of the injected 133-Xe bolus was less uniform than during ZEEP. T50 decreased successively from top to bottom of the lungs and was longer in the nondependent and shorter in the dependent regions than during ZEEP (fig. 2). In three patients there was virtually no elimination of the isotope at all from the uppermost lung field.

Perfusion and $\dot{V}/\dot{Q}$ (table 4): Cardiac output was reduced significantly by an average of 0.7 1/min, a consequence of a reduced stroke volume and an unaltered heart rate. As much as 81% of lung blood flow was distributed to the dependent and no more than 19% to the nondependent lung (fig. 3). Pulmonary arterial mean pressure was increased by 42%, and pulmonary capillary wedge pressure was more than doubled. Assuming even distribution of ventilation between the lungs,[2,3] the calculated $\dot{V}/\dot{Q}$ ratio increased in both lungs, but more in the nondependent than in the
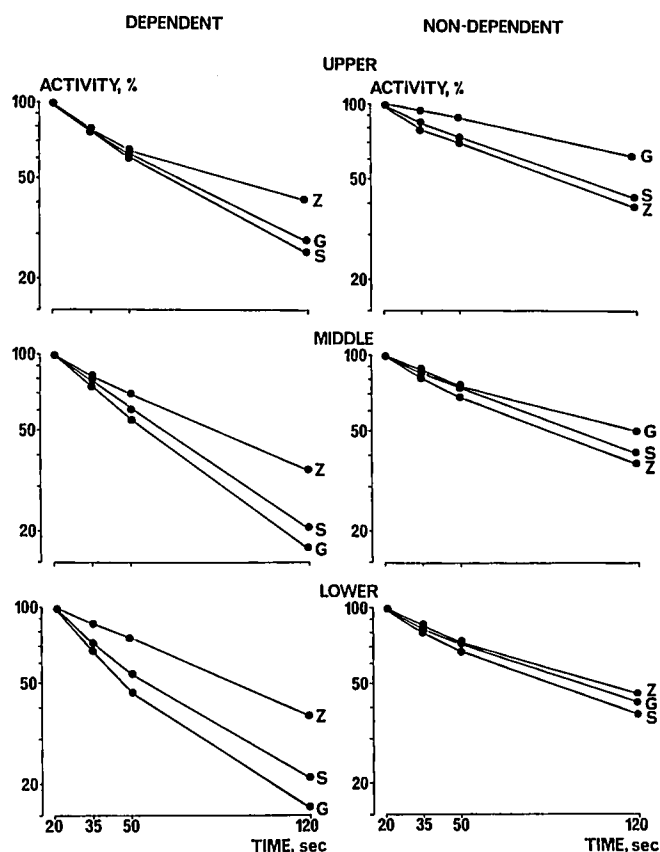

FIG. 2. Washout times (T50, see text) of the injected xenon gas in the upper, middle, and lower segments of the dependent and nondependent lungs (example from one patient; for mean data, see table 2). Z = ZEEP; G = general PEEP; S = selective PEEP. Note the "slow washout" in the lower segment of the dependent lung during ZEEP and in the upper segment of the nondependent lung during general PEEP.

dependent lung, resulting in a fivefold difference between them.

Blood Gases (table 5): There were no significant changes in blood gases.

TABLE 4. Pulmonary Vascular Pressures, Blood Flow, and Ventilation/Perfusion Ratios ($\dot{V}/\dot{Q}$) during Zero, General, and Selective Positive End-expiratory Pressure (ZEEP, GEN. PEEP and SEL. PEEP, Respectively (n = 8)

	Pulmonary Vascular Pressures (mmHg)						Cardiac Output (l/min)			($\dot{V}/\dot{Q}$)		
	Syst	Artery Diast	Mean	Wedge Mean	HR beats/min	SV ml	Total	DEP	NON-DEP	Total	NON-DEP	DEP
ZEEP												
x̄	21.05	9.95	14.37	6.37	73	67	4.46	2.53	1.93	1.84	2.82	1.09
±SEM	1.75	0.81	1.00	0.67	5	7	0.38	0.26	0.15	0.11	0.13	0.07
GEN. PEEP												
x̄	26.25*	16.62*	20.28*	14.27*	75	52	3.78*	3.05	0.73*	2.1*	(5.69)†	(1.26)†
±SEM	1.10	1.27	1.32	0.83	4	3	0.26	0.24	0.11	0.16		
SEL. PEEP												
x̄	22.11‡	11.43*‡	16.25‡	8.29*‡	74	58	4.06*‡	2.05*‡	2.01‡	1.99*‡	2.01‡	1.97*‡
±SEM	1.22	0.65	1.27	0.62	5	4	0.25	0.22	0.15	0.11	0.13	0.09

NON-DEP = nondependent lung; DEP = dependent lung; HR = heart rate; SV = stroke volume.
* Significantly different from ZEEP, $P < 0.01$.

† Assumed ventilation distribution according to Rehder *et al.*[2] and Bindslev *et al.*[3]
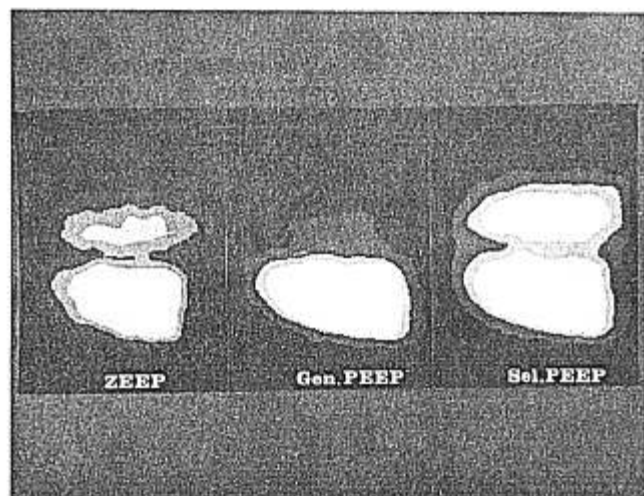‡ Significantly different from GEN. PEEP, $P < 0.01$.

FIG. 3. Distributions of pulmonary perfusion as recorded with a gamma camera in subject 4. Note the greater perfusion of the dependent lung during conventional ventilation with ZEEP (*left panel*) and the further fractional increase in dependent perfusion during general PEEP (*middle panel*). Also note the almost even perfusion distribution between the lungs during differential ventilation with selective PEEP (*right panel*).

DIFFERENTIAL VENTILATION AND SELECTIVE PEEP

Ventilation (tables 2 and 3): Total ventilation was maintained at the same level as during ZEEP and general PEEP. Ventilation was administered deliberately so that half of the tidal volume was delivered to the dependent and the other half to the nondependent lung. The peak and end-inspiratory airway pressures in the dependent lung, subjected to a mean PEEP of 8 cmH_2O, were higher than without PEEP but lower than with general PEEP. The average difference between end-inspiratory and end-expiratory pressure in the dependent lung was 12 cmH_2O and thus smaller than with general PEEP. The peak and end-inspiratory airway

TABLE 5. The Alveolar–Arterial Oxygen Tension Difference (P(A-a)$_{O_2}$) and Arterial Blood Gases (Pa$_{O_2}$, Pa$_{CO_2}$) during Conventional Ventilation with Zero End-expiratory Pressure (ZEEP) and General PEEP of 9 cmH_2O (gen. PEEP) as Well as During Differential Ventilation with Selective PEEP of 8 cmH_2O (sel. PEEP). Left Lateral Position (O$_2$ and CO$_2$ tensions in mmHg; n = 8)

	P(A-a)$_{O_2}$	Pa$_{O_2}$	Pa$_{CO_2}$
ZEEP			
x̄	83	94	35
±SEM	29	24	5
GEN. PEEP			
x̄	71	109	32*
±SEM	38	32	3
SEL. PEEP			
x̄	47†‡	132†‡	32*
±SEM	24	31	3

* Significantly different from the ZEEP value, $P < 0.05$.
† Significantly different from the ZEEP value, $P < 0.01$.
‡ Significantly different from the gen. PEEP value, $P < 0.05$.

pressures in the nondependent lung did not differ from those during ZEEP. The washout of the injected bolus from the lowermost region in the dependent lung was slightly longer than during general PEEP but still shorter than during ZEEP. In the nondependent lung, the washout was faster than with general PEEP (fig. 2). Thus, none of the patients displayed the slow or almost nonexistent washout in uppermost lung regions observed during general PEEP.

Perfusion and $\dot{V}/\dot{Q}$ (table 4): Cardiac output increased significantly, by 0.3 l/min, in comparison with that during general PEEP, but was lower than with ZEEP. Cardiac output was distributed almost equally between the two lungs, 51% passing to the dependent and 49% to the nondependent lung (fig. 3). The pulmonary arterial pressures were lower than during general PEEP; the systolic and mean pressures were no longer significantly different from those during ZEEP. The $\dot{V}/\dot{Q}$ ratio was approximately 2.0 in both lungs.

In one patient, the selective PEEP was increased from 8 to 16 cmH_2O, which reduced the fractional perfusion of the dependent lung from 52% to 35% of the total lung blood flow. Cardiac output in this patient was reduced from 3.1 l/min during conventional ventilation with ZEEP to 3.0 and 2.6 l/min with differential ventilation and selective PEEP of 10 and 16 cmH_2O, respectively.

In another patient, conventional ventilation with ZEEP was replaced by differential ventilation with even distribution of the tidal volume to the lungs, first with ZEEP and then with selective PEEP of 10 cmH_2O. The fractional perfusion of the dependent lung was reduced from 57% during conventional ventilation to 45% during differential ventilation with ZEEP, and to 37% on commencement of selective PEEP.

Blood Gases (table 5): Pa$_{O_2}$ increased significantly by 38 and 24 mmHg in comparison with ZEEP and general PEEP, respectively. Pa$_{CO_2}$ did not change. P(A-a)$_{O_2}$ was reduced to almost half of that seen during ZEEP and also was reduced significantly to two-thirds of the value recorded during general PEEP.

Discussion

This study has shown that ventilation and perfusion can be distributed evenly between dependent and nondependent lung units in anesthetized subjects if the subject is in the lateral position, ventilation is distributed so that 50% of the tidal breath is administered to each lung, and a PEEP of 8–10 cmH_2O is applied solely to the dependent lung. This results in significant improvement of the arterial oxygenation in comparison both with ZEEP and with general PEEP. It should be stressed that differential ventilation is not a new technique and that it has been proposed in the treatment of unilateral lung disease and during thoracic surgery (one-lung

ventilation).[24] The concept presented here is aimed at counteracting the *gravitational* disturbance of ventilation–perfusion matching that regularly occurs in the lung-healthy, anesthetized subject and presumably in an acute bilateral lung disease necessitating ventilator treatment.[25,26] In the following discussion, methodologic aspects and the perfusion and ventilation distributions will be considered in further detail.

PERFUSION

Methodologic Aspects: Perfusion measurements by bolus techniques frequently are done during breath holding to prevent early elimination of the bolus via the airways. Ventilation was, however, not interrupted in our patients, since its influence on perfusion was the principal aim of the study. It was observed in preliminary tests that the peak activity of 133-Xe over a 5-s collection period coincided with the second breath after injection, and thus only one breath may have caused some elimination of 133-Xe via the airways before peak activity had been reached. This elimination was calculated to be, at most, 6–10% of the xenon, on the basis of the presently measured washout time of xenon from the alveoli and assuming a cardiac ejection fraction of 0.6. Moreover, the ratio of activity between the two lung fields will be determined even more accurately than the activity of each individual lung, since the sources of error will affect both lungs and thus tend to be cancelled out.

The analysis of the perfusion distribution was restricted to the partitioning between the lungs, and no regional analysis within the lung was undertaken. This was because the regional activity could not be related to regional lung volume, rendering a regional perfusion analysis rather meaningless. Regional lung volume determinations by a rebreathing technique were not performed for ethical (dose) and time reasons.

Clinical Implications: The smaller reduction in total blood flow with selective PEEP than with general PEEP is similar to the findings in patients with acute, severe bilateral lung disease necessitating ventilator treatment.[21,22] Indeed, in the severely ill patients cardiac output remained the same with selective PEEP as with no PEEP. The redistribution and the maintenance or smaller reduction of lung blood flow with selective as compared with general PEEP may be attributed to smaller increases in intrathoracic pressure and pulmonary vascular resistance. As to the first point, general PEEP increases the volume of both lungs, and the chest wall is expanded. With selective PEEP, only the dependent lung volume is increased, the volume of the nondependent lung being reduced and the chest wall being less expanded.[22] Accordingly, selective PEEP generates a lower intrathoracic pressure than general PEEP and can be expected to impede venous return and cardiac output to a lesser degree.[17] Concerning the second

point, general PEEP has been shown to increase the pulmonary vascular resistance,[27] and mostly so in non-dependent lung units.[4] With selective PEEP, the non-dependent lung volume is maintained or even diminished to some extent (the exact reduction depending on the compliances of the lungs and the chest wall).[22] The vascular resistance of the nondependent lung thus need not be increased, and the perfusion will not be forced away from that lung as with general PEEP.

VENTILATION

With ZEEP, there were only moderate differences in washout times between the six lung fields. This may seem unexpected in view of the much greater ventilation of the nondependent than of the dependent lung. However, the volume of the nondependent lung is larger than that of the dependent lung,[2,18] resulting in a fairly similar ventilatory efficiency ($\dot{V}r/Vr$) for the two lungs. The discontinuity of washout times over the mediastinum is similar to the discontinuity of regional volumes observed by Roussos *et al.*[28] in awake subjects in the lateral posture.

With general PEEP, the washout times were longer for the nondependent than for the dependent lung. This was presumably an effect of the larger volume increase of the nondependent than of the dependent lung caused by general PEEP[18,19] and a more homogeneous ventilation distribution between the lungs, as shown in previous studies.[2,3]

With differential ventilation and selective PEEP, the washout times in the nondependent lung were similar to those during ZEEP, even though the nondependent lung ventilation was approximately 25% smaller. The maintenance of ventilatory efficiency may be compatible with a decreased nondependent lung volume, this lung being squeezed between the expanded dependent lung (selective PEEP) and the chest wall.[22] By the same token, the slightly longer washout time in the lowermost region of the dependent lung during selective than during general PEEP with similar ventilation volumes, may be in line with a larger dependent lung volume with selective PEEP, as has been observed in a previous study.[22]

Another interesting finding was the much smaller transthoracic pressures with selective than with general PEEP. Assuming that the end-inspiratory airway pressure equaled the alveolar pressure, it is evident from table 1 that the nondependent lung was subjected to no greater stress (in this sense) than during ZEEP and also that the alveolar pressure in the dependent lung was significantly lower with selective than with general PEEP, despite the fact that the lung was (probably) more inflated.[29] This lower stress is presumably of clinical importance, in reducing the risk of barotrauma. The effects on the vertical perfusion distribution have been discussed previously.

Arterial Oxygenation: The lack of any significant improvement in the arterial oxygenation with general PEEP has been observed earlier in lung-healthy subjects during anesthesia[30,31] and led Hewlett and co-workers to conclude that "general PEEP has no place in routine anesthesia."[30] On the other hand, differential ventilation with selective PEEP, as executed here, resulted in a 40% increase in Pa_{O_2} and a 43% decrease in $P(A-a)_{O_2}$ in comparison with baseline data during ZEEP. These findings conform with the considerable improvement in arterial oxygenation that has been observed in preliminary tests on patients with acute respiratory failure due to bilateral, severe lung disease.[21,22] The observations clearly underscore the beneficial effects of improving the overall matching of ventilation and perfusion in each lung.

In conclusion, differential ventilation with equal distribution of ventilation between the lungs, together with selective PEEP of about 8–10 cmH_2O, applied solely to the dependent lung, results in equal distribution of perfusion between the lungs. This $\dot{V}/\dot{Q}$ matching promotes gas exchange. The lower intrathoracic pressures than with general PEEP offer less impedance to cardiac output and presumably reduce the risk of barotrauma.

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