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INFLUENCE OF AGE ON ATELECTASIS FORMATION AND GAS EXCHANGE IMPAIRMENT DURING GENERAL ANAESTHESIA

L. GUNNARSSON, L. TOKICS, H. GUSTAVSSON AND G. HEDENSTIERNA

SUMMARY

We have studied the effects of anaesthesia on atelectasis formation and gas exchange in 45 patients of both sexes, smokers and non-smokers, aged 23–69 yr. None of the patients showed clinical signs of pulmonary disease, and preoperative spirometry was normal. In the awake patient, partial pressure of arterial oxygen (Pa_{O_2}) decreased with increasing age ($P < 0.001$) and the alveolar–arterial oxygen partial pressure difference ($PA_{O_2} - Pa_{O_2}$) increased with age ($P < 0.001$). Shunt, assessed by the multiple inert gas elimination technique, was small (mean 0.5%) and uninfluenced by age. However, there was an increasing dispersion (log SD Q) of ventilation/perfusion ratios ($\dot{V}A/\dot{Q}$) and increasing perfusion of regions of low $\dot{V}A/\dot{Q}$ ($\dot{V}A/\dot{Q} < 0.1$) with increasing age ($P < 0.001$ and $P < 0.05$, respectively). No patient displayed any atelectasis as assessed by computed x-ray tomography of the chest. During inhalation anaesthesia (halothane or enflurane) with mechanical ventilation, 39 of 45 patients developed atelectasis and shunt. There was a strong correlation between the atelectatic area and the magnitude of shunt ($r = 0.81$, $P < 0.001$). Atelectasis and shunt did not increase significantly with age, whereas log SD Q and perfusion of regions with low $\dot{V}A/\dot{Q}$ ratios did ($r = 0.55$, $P < 0.001$ and $r = 0.35$, $P < 0.05$, respectively). Awake, the major determinant of Pa_{O_2} was perfusion of regions of low $\dot{V}A/\dot{Q}$ ratios, which increased with age. During anaesthesia shunt influenced Pa_{O_2} most, low $\dot{V}A/\dot{Q}$ being a secondary factor which, however, was increasingly important with increasing age, thus explaining the well-known age-dependent deterioration of arterial oxygenation during anaesthesia.

KEY WORDS

Anaesthesia, general. Complications: age, atelectasis. Lung: atelectasis, gas exchange.

Pulmonary gas exchange is impaired during anaesthesia (for a review see [1]). It is also generally held that the gas exchange impairment in anaesthetized subjects increases with age [1–4]. The causes of the gas exchange impairment during anaesthesia have not been fully understood. However, more recently we have identified at least one mechanism that contributes to impaired arterial oxygenation during anaesthesia — densities in dependent lung regions as assessed by computed x-ray tomography of the chest [5, 6]. These densities have been interpreted as atelectasis [5, 6], and they appear to produce shunt [7]. The dense regions, subsequently termed atelectasis, were independent of the subject's age in a previous report on 28 patients [8]. However, it is not known if shunt increases with age, or if gas exchange is affected by age in another way. In the present study, we have reviewed our previously collected data of clinically lung healthy subjects of different ages. The pooling of these data created a large enough base to allow regression analysis with respect to age.

PATIENTS AND METHODS

During a 2-year period, 45 patients (participating in studies related to the present one from [7, 9, 10 and recently finished studies that have not yet

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TABLE I. *Patient characteristics. *Smokers: mean 16 (SD 8) g tobacco day^{-1} and 18 (14) pack-years. FVC = forced vital capacity; FEV_1 = forced expiratory volume in 1 s*

	Age (yr)	Sex (M/F)	Weight (kg)	Height (m)	Non-smokers /Smokers	FVC (% of expected)	FEV_1/FVC (% of expected)
Mean	46.3	36/9	75	1.77	23/22*	109	94
SD	12.6		8.1	0.07		11.6	8.0

been published]) undergoing elective abdominal surgery were studied immediately before and during general anaesthesia. There were 36 men and nine women, aged 23–69 yr (mean 46 yr). Twenty-three of the patients had never smoked, 18 were smokers (light to moderate), and the remaining four patients were ex-smokers (table I). All patients were clinically healthy, and all had normal body configuration. Spirometry on the day before the study was normal in all: that is, the recorded spirometry data were within 2 SD of expected values [11]. Informed consent to all studies was obtained from the patients concerned and approval was granted by the Ethics Committee of Huddinge University Hospital.

Anaesthesia

All patients received atropine 0.5 mg i.v. before induction of anaesthesia. No other premedication was given. Anaesthesia was induced with thiopentone 300–400 mg and fentanyl 0.10 mg i.v., followed by inhalation anaesthetics (0.8–1.0% enflurane or 0.6–0.8% halothane, inspired maintenance concentration) in oxygen–nitrogen (mean $F_{I_{O_2}}$ 0.40 (range 0.32–0.45)). To facilitate tracheal intubation, the patient received suxamethonium 75–100 mg i.v. Neuromuscular block was maintained by pancuronium given as a priming dose of 6–8 mg followed by intermittent doses of 2 mg i.v. when needed. After tracheal intubation, the lungs were ventilated mechanically at a rate of 12 b.p.m. (Servo 900 C ventilator equipped with an infra-red carbon dioxide analyser, CO_2 Analyzer 930, Siemens). Minute ventilation was adjusted to maintain an end-tidal carbon dioxide concentration of approximately 4%. Ventilatory volumes and airway pressures were obtained from the ventilator.

Catheterization and gas exchange

Pulmonary artery (Swan–Ganz 7–French gauge, Edward's Laboratories) and brachial artery catheters were inserted for pressure recordings (reference: mid thoracic level) and blood sampling. Cardiac output was measured by thermodilution, and gas exchange was assessed by blood-gas analysis and measurement of the ventilation/perfusion ratios ($\dot{V}_A/\dot{Q}$) by multiple inert gas elimination technique. For this purpose, a solution of six gases (sulphur hexafluoride, ethane, cyclopropane, enflurane or halothane, diethyl ether and acetone) was infused into a vein. After steady state conditions had been obtained, arterial and mixed venous blood samples were taken and mixed expired gas was collected for subsequent analysis by gas chromatography. Arterial and mixed venous oxygen and carbon dioxide tensions (Pa_{O_2}, $P\bar{v}_{O_2}$, Pa_{CO_2}, $P\bar{v}_{CO_2}$) were measured by standard techniques, corrected to a standardized body temperature of 37 °C and the alveolar–arterial oxygen partial pressure difference ($PA_{O_2} - Pa_{O_2}$) was calculated. Venous admixture ("shunt" in a three-compartment analysis—the ideal, the "shunt" and the deadspace compartment) was calculated on the oxygen content in arterial, mixed venous and pulmonary end-capillary blood (the latter assumed to be equal to alveolar PO_2), according to Riley [12]. Deadspace measured by the multiple inert gas elimination technique (V_D, $\dot{V}_A/\dot{Q}$ ratios > 100) includes apparatus deadspace both awake (approximately 20 ml) and during anaesthesia (approximately 40 ml). (For further details, see [7, 9, 10].)

Computed tomography of the chest

The transverse lung area and the structure and density of the lungs were studied by x-ray computed tomography (CT), with the subjects in the supine position on the tomograph table (Somatom 2, Siemens). The arms were raised above the head to allow passage through the gantry (hole) in the CT scanner. This manoeuvre has no effect on FRC as tested in awake volunteers [13]. A frontal scout view covering the chest was obtained initially. Two CT scans in the transverse plane were performed, the lowermost at a level just above the top of the diaphragm and the other 5 cm cephalad. The same scan levels, relative to

the spine, were used during the succeeding measurements during anaesthesia. Densities, considered to reflect atelectasis, were identified in dependent lung regions and were expressed in per cent of the total intrathoracic area (including mediastinum). (For further details, see [7, 9, 10].)

Procedure

The catheters were introduced in the catheterization laboratory, and infusion of inert gases was started. The patient was then moved to the x-ray department and after 20 min of complete rest (40 min of infusion) recordings of central haemodynamic and gas exchange variables were made while the patient was breathing air. CT scans were obtained and the patient was anaesthetized. After 15 min of enflurane or halothane in oxygen–nitrogen anaesthesia and neuromuscular block, the haemodynamic and gas exchange variables were recorded and the CT scans repeated.

After the study the patients, while still anaesthetized, were moved to the operating theatre. All recordings were made with the patient in the supine position, awake or anaesthetized.

Statistics

Mean values and standard deviation (SD) were calculated, except for the variable remaining sum of squares (RSS) where median and range were used because of uneven distribution of values. The significance of a difference was tested by paired Student's *t* test. Correlation and multiple stepwise linear regression were used to analyse relationships between different variables.

RESULTS

Comparison between awake and anaesthesia

Mean data on central haemodynamics, gas exchange and chest dimensions (including atelectasis) for all patients awake and during anaesthesia are shown in table II. Circulatory variables and arterial blood-gas tensions were within normal limits in the awake state [14, 15, local reference values]. Cardiac output and systemic arterial pressures were reduced significantly during anaesthesia to about 70–85 % of the awake value. A small (1–2 mm Hg) decrease in mean pulmonary arterial pressure was observed also.

Shunt (perfusion of regions with $\dot{V}_A/\dot{Q} < 0.005$) increased from 0.5 % of cardiac output awake to about 5 % during anaesthesia (table II). Log SD Q, defined as the logarithmic standard deviation of $\dot{V}_A/\dot{Q}$ around the mean $\dot{V}_A/\dot{Q}$ of the perfusion distribution, increased by almost 50 % during anaesthesia. This indicates an increased dispersion of $\dot{V}_A/\dot{Q}$ (increased $\dot{V}_A/\dot{Q}$ mismatch). Perfusion of regions of low $\dot{V}_A/\dot{Q}$ ($0.005 < \dot{V}_A/\dot{Q} < 0.1$) also increased significantly. Venous admixture was 5.5 % of cardiac output awake and almost doubled during anaesthesia. Awake venous admixture correlated best with perfusion of low

TABLE II. *Haemodynamic, gas exchange and CT data awake and during anaesthesia* (n = 45). *HR = Heart rate;* $F_{I_{O_2}}$ *= inspired oxygen fraction;* $\dot{V}_E$ *= minute volume; Shunt and low* $\dot{V}_A/\dot{Q}$ *= perfusion of non-ventilated* ($\dot{V}_A/\dot{Q} < 0.005$) *and poorly ventilated* ($0.005 < \dot{V}_A/\dot{Q} < 0.1$) *regions, respectively; High* $\dot{V}_A/\dot{Q}$ *= ventilation of poorly perfused regions* ($10 < \dot{V}_A/\dot{Q} < 100$); $\dot{V}_D$ *= ventilation of deadspace* ($\dot{V}_A/\dot{Q} > 100$); *Log SD* Q *= log SD of perfusion;* Pa_{O_2}, Pa_{CO_2} *= arterial partial pressures of oxygen and carbon dioxide, respectively;* ($PA_{O_2} - Pa_{O_2}$) *= alveolar–arterial oxygen partial pressure difference. Significantly different from awake:* *P < 0.05; ***P < 0.001.

Variable	Awake	Anaesthesia
Cardiac output (litre min^{-1})	6.3 (1.1)	5.3 (0.8)***
HR (beat min^{-1})	67 (10)	79 (10)***
Vascular pressures (mm Hg)		
Systemic arterial, mean	99.1 (13.3)	72.0 (12.7)***
Pulmonary artery, mean	14.2 (3.0)	13.5 (2.7)***
Pulmonary capillary wedge	8.1 (2.4)	7.3 (2.2)*
Right atrial	5.1 (2.5)	5.3 (1.9)
Cross-sectional chest area (cm^2)		
Scan 1 (top of diaphragm)	377 (41)	358 (41)***
Scan 2 (5 cm cephalad of 1)	355 (45)	318 (46)***
Atelectatic area (% intrathoracic area)		
Scan 1 (top of diaphragm)	0	1.9 (2.1)***
Scan 2 (5 cm cephalad of 1)	0	1.4 (1.7)***
Gas exchange		
$F_{I_{O_2}}$	0.21 (0.0)	0.40 (0.05)***
$\dot{V}_E$ (litre min^{-1})	8.4 (2.9)	6.2 (1.1)***
Shunt (% $\dot{Q}t$)	0.5 (1.0)	4.8 (4.1)***
Low $\dot{V}_A/\dot{Q}$ (% $\dot{Q}t$)	1.7 (3.3)	5.0 (4.9)***
High $\dot{V}_A/\dot{Q}$ (% $\dot{V}_E$)	0.1 (0.3)	1.8 (3.8)*
$\dot{V}_D$ (% $\dot{V}_E$)	34.8 (14.1)	35.0 (9.9)
Log SD Q	0.67 (0.28)	1.04 (0.36)***
Venous admixture	5.5 (4.4)	9.2 (4.9)***
Arterial blood-gas values		
Pa_{O_2} (kPa)	12.5 (1.7)	21.4 (6.4)***
Pa_{CO_2} (kPa)	4.9 (0.6)	4.9 (0.7)
($PA_{O_2} - Pa_{O_2}$) (kPa)	1.4 (1.2)	10.8 (6.6)***

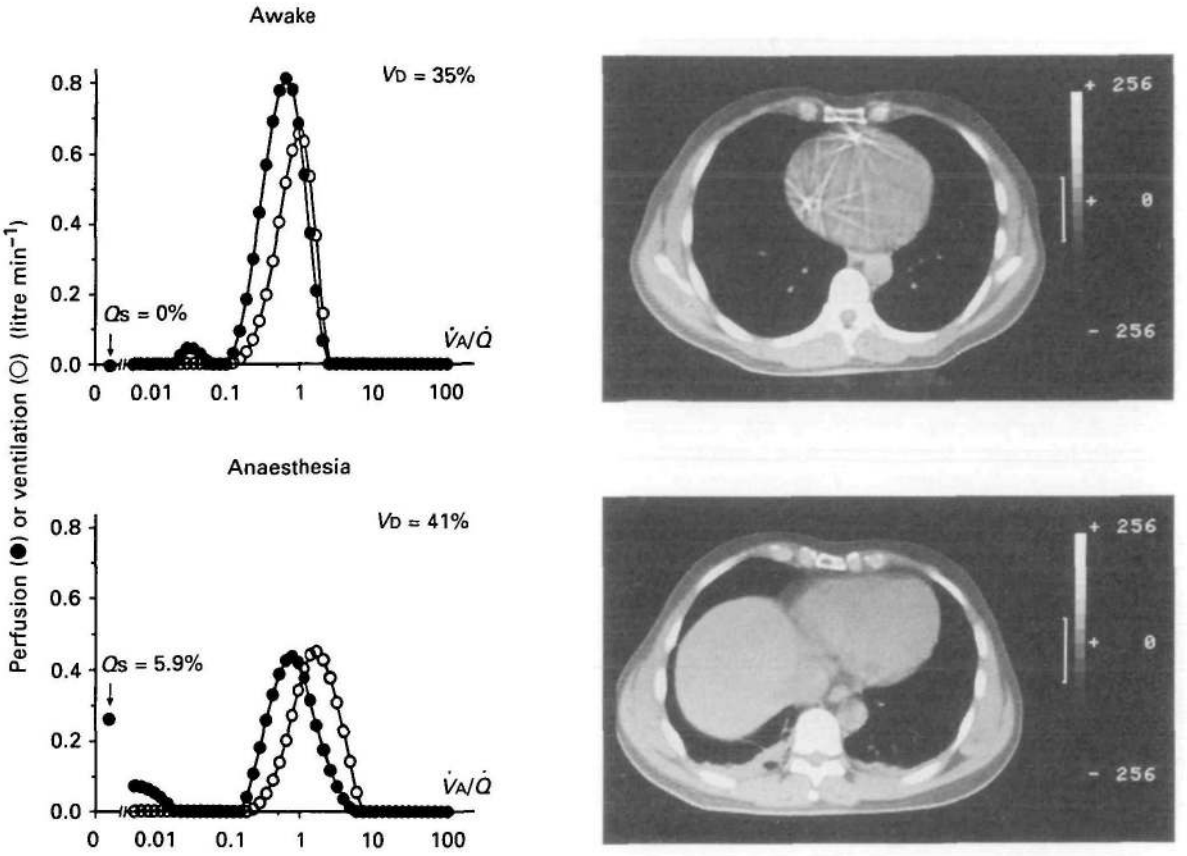

FIG. 1. Normal pattern of gas exchange and CT scans (caudal level) awake and during anaesthesia. Ventilation–perfusion distribution to the left; CT scan of the chest to the right. Note the increase in shunt, log SD Q (widened $\dot{V}_A/\dot{Q}$ mode), and low $\dot{V}_A/\dot{Q}$, in addition to the atelectatic areas in the dorsal part of the CT scan during anaesthesia. The large white area in the middle of the right hemithorax (lower CT scan) is the diaphragm that has moved cranially during anaesthesia.

$\dot{V}_A/\dot{Q}$ regions (venous admixture = 0.54 (low $\dot{V}_A/\dot{Q}$) + 4.65; $r = 0.40$; $P < 0.01$), and during anaesthesia the best correlation was with the sum of both shunt and perfusion of low $\dot{V}_A/\dot{Q}$ regions (venous admixture = 0.67 (shunt + low $\dot{V}_A/\dot{Q}$) + 2.73; $r = 0.83$; $P < 0.001$). Arterial oxygenation was impaired during anaesthesia, as demonstrated by the increased $(P_{A_{O_2}} - P_{a_{O_2}})$. (However, the increased $F_{I_{O_2}}$ during anaesthesia is an additional confounding factor.)

A decrease in the cross-sectional thoracic area of approximately 5 % was noted after induction of anaesthesia. Awake, no patient had evidence of atelectasis. During anaesthesia, 39 of 45 patients developed densities in dependent lung regions, interpreted as atelectasis (fig. 1). In patients with atelectasis in the caudal CT scan, more than 80 % also had atelectasis in the cranial scan. No patient displayed atelectasis solely in the cranial scan, but always in combination with atelectasis in the caudal scan. The atelectatic area was slightly larger in the caudal CT scan than in the cranial (table II). The magnitude of shunt correlated strongly with the atelectatic area, and calculations made on the caudal CT scan are shown in figure 2.

When the data were classified into smokers (including the four ex-smokers) ($n = 22$) and non-smokers ($n = 23$), no difference in any variable could be disclosed. Also, smoking was not a significant factor in a multivariate analysis which also included age. Separate data for the two groups have therefore not been presented in this paper. There was also no significant difference in any circulatory or gas exchange variable between the two anaesthetics (halothane and enflurane).

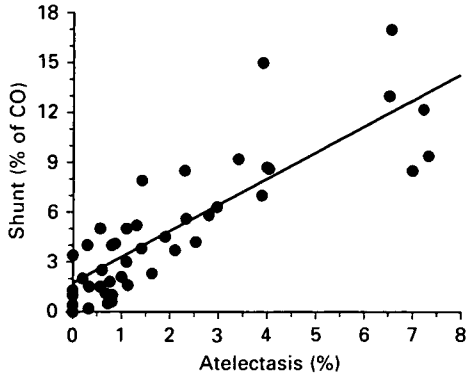

FIG. 2. Atelectatic area (% of intrathoracic area, caudal scan level) and shunt (% of cardiac output (CO)) during anaesthesia. Regression equation: Shunt = 1.6Atelectatic area +1.7; $r = 0.81$, $P < 0.001$.

Influence of age

Circulation. Awake, both systemic and pulmonary artery pressures increased with age (correlations and regression line equations in table III), but pulmonary capillary wedge and right atrial pressures, in addition to cardiac output, were not affected significantly. During anaesthesia, systolic pulmonary artery pressure increased significantly with age ($r = 0.46$, $P < 0.05$), but no other age-dependent correlations were found.

Gas exchange. There was no significant correlation between age and shunt. There were positive correlations for the awake state between age and log SD Q and age and perfusion of regions of low $\dot{V}A/\dot{Q}$ ($r = 0.55$, $P < 0.001$ and $r = 0.39$, $P < 0.01$, respectively) (fig. 3, regression equations in table III). Venous admixture increased with age at the same rate as perfusion of regions of low $\dot{V}A/\dot{Q}$. A fair correlation between age and Pa_{O_2} ($r = -0.44$, $P < 0.01$) was found (fig. 4, regression line equation in table III). If the analysis was extended to the combination of age, perfusion of regions with low $\dot{V}A/\dot{Q}$, $P\bar{v}_{O_2}$ and Pa_{CO_2} on the one hand, and Pa_{O_2} on the other, the correlation increased further ($r = 0.83$, $P < 0.001$) (regression equation in table III). $(PA_{O_2} - Pa_{O_2})$ also showed a correlation with age ($r = 0.50$, $P < 0.001$). The correlation increased if not only age, but also $P\bar{v}_{O_2}$ and perfusion of regions with low $\dot{V}A/\dot{Q}$ ratios were included in the analysis ($r = 0.71$, $P < 0.001$) (regression equation in table III).

In the anaesthesia state, there were correlations between age and log SD Q ($r = 0.52$, $P < 0.01$) (fig. 3, regression equation in table III), between age and perfusion of regions of low $\dot{V}A/\dot{Q}$ ($r = 0.35$, $P < 0.05$) (table III), and between age and venous admixture ($r = 0.42$, $P < 0.05$) (table III). The age coefficients (slopes of the regression lines) were similar to those in the awake state, but the intercepts were higher during anaesthesia. Shunt did not show any correlation with age. Pa_{O_2} decreased with age, and did so faster than in the awake state (however, FI_{O_2} differed between awake and anaesthesia, as mentioned earlier) ($r = -0.50$, $P < 0.01$) (fig. 4, regression equation in table III). There was a corresponding increase in $(PA_{O_2} - Pa_{O_2})$ with age ($r = 0.34$, $P < 0.05$) (table III). An extension of the analysis, taking into account not only age but also perfusion of regions of low $\dot{V}A/\dot{Q}$ shunt, $P\bar{v}_{O_2}$, FI_{O_2} and Pa_{CO_2} on the one hand, and Pa_{O_2} on the other, increased the correlation to such an extent that 75% of the variation in Pa_{O_2} could be explained ($r = 0.88$, $P < 0.001$). The same variables, except Pa_{CO_2}, explained the variation in $(PA_{O_2} - Pa_{O_2})$ to a similar degree ($r = 0.91$, $P < 0.001$) (regression equations in table III). Mixed venous oxygen tension did not correlate with age, nor did arterial–mixed venous oxygen partial pressure difference.

Atelectasis and chest dimensions. Age did not influence the amount of atelectasis, or the decrease in cross-sectional chest area during anaesthesia.

DISCUSSION

The large data base used in the present study enabled us to demonstrate that both atelectasis and shunt developed to a substantial degree during anaesthesia, but that neither atelectasis nor shunt increased with increasing patient age. On the other hand, the dispersion of the $\dot{V}A/\dot{Q}$ distribution, indicating the degree of $\dot{V}A/\dot{Q}$ mismatch, increased with increasing age, both in the awake state and during anaesthesia. Thus increasing $\dot{V}A/\dot{Q}$ mismatch with age adds to the age-independent formation of atelectasis and shunt, to produce the well known gas exchange impairment during anaesthesia.

Methodological aspects

Two complicated techniques have been used: the multiple inert gas elimination technique in order to enable separation of shunt from $\dot{V}A/\dot{Q}$ mismatch and formation of low $\dot{V}A/\dot{Q}$ regions,

TABLE III. *Correlations and regression lines for arterial pressures and gas exchange variables* (n = 45). FI_{O_2} = *inspired oxygen fraction; Shunt and low* $\dot{V}_A/\dot{Q}$ = *perfusion of non-ventilated* ($\dot{V}_A/\dot{Q} < 0.005$) *and poorly ventilated* ($0.005 < \dot{V}_A/\dot{Q} < 0.1$) *regions, respectively; Log SD Q = log SD of perfusion;* Pa_{O_2}, Pa_{CO_2} = *arterial partial pressures of oxygen and carbon dioxide, respectively;* $(PA_{O_2} - Pa_{O_2})$ = *alveolar–arterial oxygen partial pressure difference*

Age and arterial pressures

Systemic arterial pressures (mm Hg)

Awake			
Systolic = 0.5Age + 115		$r = 0.37$	$P = 0.05$
Mean = 0.3Age + 83		$r = 0.33$	$P < 0.05$

Pulmonary artery pressure (mm Hg)

Awake			
Systolic = 0.2Age + 14		$r = 0.49$	$P < 0.01$
Mean = 0.01Age + 10		$r = 0.38$	$P < 0.05$
Anaesthesia			
Systolic = 0.1Age + 12		$r = 0.46$	$P < 0.05$

Age and gas exchange

Pa_{O_2} *(kPa)*

Awake	$Pa_{O_2} = -0.06\text{Age} + 15.3$	$r = -0.44$	$P < 0.01$
Anaesthesia	$Pa_{O_2} = -0.25\text{Age} + 33.3$	$r = -0.50$	$P < 0.001$

$(PA_{O_2} - Pa_{O_2})$

Awake	$(PA_{O_2} - Pa_{O_2}) = 0.05\text{Age} - 0.83$	$r = 0.50$	$P < 0.001$
Anaesthesia	$(PA_{O_2} - Pa_{O_2}) = 0.18\text{Age} + 2.40$	$r = 0.34$	$P < 0.05$

Log SD Q

Awake	Log SD $Q = 0.012\text{Age} + 0.12$	$r = 0.55$	$P < 0.001$
Anaesthesia	Log SD $Q = 0.015\text{Age} + 0.35$	$r = 0.52$	$P < 0.001$

Low $\dot{V}_A/\dot{Q}$ *(% of cardiac output)*

Awake	Low $\dot{V}_A/\dot{Q} = 0.14\text{Age} - 3.0$	$r = 0.39$	$P < 0.05$
Anaesthesia	Low $\dot{V}_A/\dot{Q} = 0.14\text{Age} - 1.5$	$r = 0.35$	$P < 0.05$

Venous admixture (% of cardiac output)

Awake	Ven. admixt = 0.15Age − 1.5	$r = 0.43$	$P < 0.01$
Anaesthesia	Ven. admixt = 0.17Age + 1.6	$r = 0.42$	$P < 0.01$

Multiple regression for Pa_{O_2} and $(PA_{O_2} - Pa_{O_2})$

Pa_{O_2} *(kPa)*

Awake	$Pa_{O_2} = -0.04\text{Age} - 0.11$ (low $\dot{V}_A/\dot{Q}$) $+ 1.05\, P\bar{v}_{O_2} - 1.60 Pa_{CO_2} + 16.45$	$r = 0.83$	$P < 0.001$
Anaesthesia	$Pa_{O_2} = -0.08\text{Age} - 0.99\text{Shunt} - 0.47$ (low $\dot{V}_A/\dot{Q}$) $+ 2.63 P\bar{v}_{O_2} - 2.00 Pa_{CO_2} + 56.26 FI_{O_2} - 4.11$	$r = 0.88$	$P < 0.001$

$(PA_{O_2} - Pa_{O_2})$ *(kPa)*

Awake	$(PA_{O_2} - Pa_{O_2}) = 0.03\text{Age} + 0.10$ (low $\dot{V}_A/\dot{Q}$) $- 0.82 P\bar{v}_{O_2} + 4.39$	$r = 0.71$	$P < 0.001$
Anaesthesia	$(PA_{O_2} - Pa_{O_2}) = 0.08\text{Age} + 0.94\text{Shunt} + 0.45$ (low $\dot{V}_A/\dot{Q}$) $- 2.63 P\bar{v}_{O_2} + 42.27 FI_{O_2} - 1.60$	$r = 0.91$	$P < 0.001$

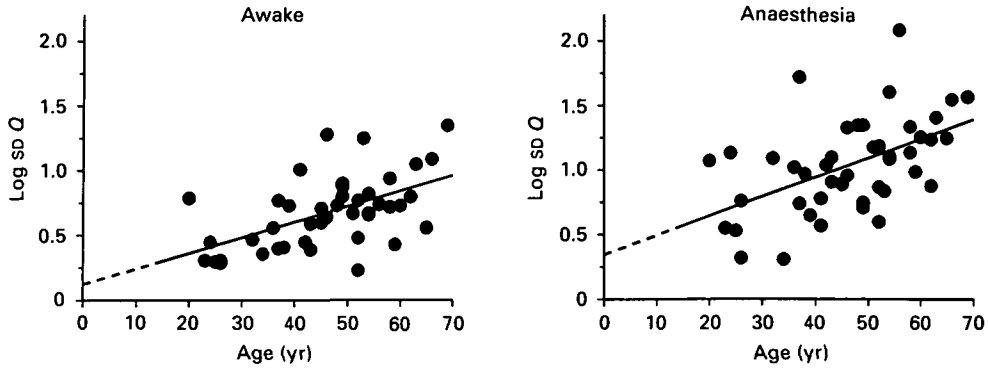

FIG. 3. Age and log SD Q awake and during anaesthesia. A significant difference was found in intercept, but not in slope, between the awake state and during anaesthesia ($P < 0.01$). For regression equations and correlations, see table III.

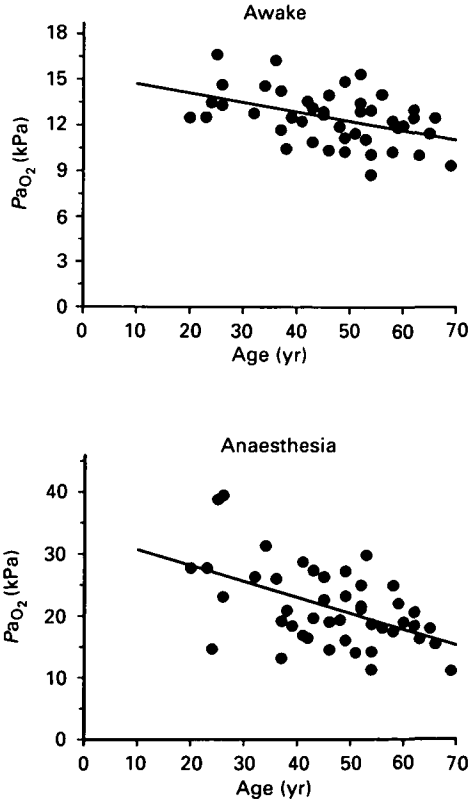

FIG. 4. Pa_{O_2} against age in the awake state ($FI_{O_2} = 0.21$) and during anaesthesia ($FI_{O_2} = 0.40$). For regression equations and correlations, see table III.

and computed x-ray tomography of the chest to demonstrate and quantify atelectasis.

Ventilation–perfusion distribution in the lungs has been analysed with several different techniques, from the initial three-compartment analysis of venous admixture, physiological deadspace and the ideal compartment by Riley and co-workers [12], to the multi-compartment analysis by multiple inert gas elimination technique by Wagner and co-workers [16, 17]. The theoretical and methodological aspects of the multiple inert gas elimination technique have been investigated extensively. It has been concluded that up to three distinct $\dot{V}_A/\dot{Q}$ modes and shunt can be detected [16–18], and the reliability of the ventilation–perfusion distribution has been studied by linear programming [19, 20]. A more cautious approach to the multiple inert gas elimination technique has also been advocated [21].

The quality of the inert gas data may be tested by calculating the remaining sum of squares (RSS) between measured (arterial and mixed venous samples) and calculated (from the derived $\dot{V}_A/\dot{Q}$ distribution) retentions. RSS had a median of 2.5 (range 0.1–22.9) and it was less than 6 in 74 of a total of 90 measurements made both awake and during anaesthesia. This should be compared with a suggested requirement that 50% of the $\dot{V}_A/\dot{Q}$ measurements should have a fit with an RSS less than 6 [22]. Thus the quality of the inert gas data seems to be satisfactory.

However, a good fit does not rule out other possible $\dot{V}_A/\dot{Q}$ distributions from a given set of inert gas data. To test that a derived $\dot{V}_A/\dot{Q}$ distribution is compatible with the measured oxygenation of the blood, the measured Pa_{O_2} may be compared with that obtained from the derived $\dot{V}_A/\dot{Q}$ distribution. This requires measurement of cardiac output, mixed venous oxygen tension and the slope of the haemoglobin dissociation curve.

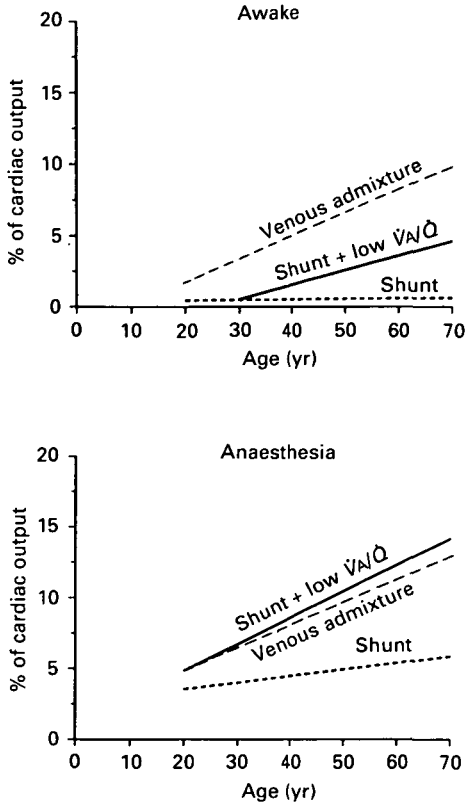

FIG. 5. Schematic drawing of shunt, the sum of shunt and perfusion of regions with low $\dot{V}_A/\dot{Q}$, and venous admixture against age awake and during anaesthesia. Note the appearance or increase of shunt during anaesthesia and the increasing perfusion of low $\dot{V}_A/\dot{Q}$ regions with age both awake and during anaesthesia. Also note the close similarity between venous admixture and the sum of shunt and low $\dot{V}_A/\dot{Q}$ during anaesthesia. Regression equations and correlations (see also table III): *Awake*—Shunt = 0.004Age + 0.36, $r = 0.04$, ns; Shunt + low $\dot{V}_A/\dot{Q}$ = 0.104Age − 3.0, $r = 0.41$, $P < 0.05$. *Anaesthesia*—Shunt = 0.047Age + 2.6, $r = 0.14$, ns; Shunt + low $\dot{V}_A/\dot{Q}$ = 0.187Age + 1.1, $r = 0.38$, $P < 0.05$.

These were measured or assumed (the dissociation curve) and, by using the algorithms of Kelman [23, 24], Pa_{O_2} was estimated. The measured ($Pa_{O_2,meas}$) and calculated ($Pa_{O_2,calc}$) oxygen tension agreed well according to the equation:

$$Pa_{O_2,\,calc} = 1.07\ Pa_{O_2,\,meas} - 1.2\ (Pa_{O_2}\text{ in kPa})$$

$r = 0.96$; $P < 0.001$. The minor deviation from the identity line is to be expected, as the calculation of $Pa_{O_2,calc}$ does not take into account Thebesian blood flow (veins emptying in the left atrium). The good correlation is further support for the reliability of the $\dot{V}_A/\dot{Q}$ distributions found here.

The other complicated technique that deserves comment is analysis of atelectasis by computed tomography of the chest. The atelectatic area was identified by eye as a dense area in dependent lung regions. The area was encircled by hand and calculated by a computer. For comparative purposes, an analysis was made afterwards in 50% of patients, by defining the atelectatic area as picture elements (pixels) with an attenuation of −100 to +100 Hounsfield units (HU). The computer-based analysis still required careful delineation of the lung tissue from the soft tissues of the chest wall, which have an attenuation factor which does not differ by more than 30–40 HU from that of the atelectatic lung. Computer analysis and manual analysis produced similar results for atelectatic areas (per cent of intrathoracic area: manual = 1.04 (computer analysis) − 0.39; $r = 0.99$, $P < 0.001$). The variability between different measurements, expressed as coefficient of variation of duplicate measurements of the same scan, was no larger than 6%.

Influence of age

Central circulation. The correlations between age and systemic artery and pulmonary artery pressures in the awake state are in accordance with earlier observations [14]. During anaesthesia, familiar decreases in systemic vascular pressures and cardiac output were observed. In addition, a small but significant reduction of pulmonary artery pressure was found, which is in accordance to the findings of Price and colleagues [25]. However, no or only weak correlations with age were noted during anaesthesia.

Arterial oxygenation and ventilation/perfusion. The decrease in Pa_{O_2} with age in the awake state is in accordance with the results of Marshall and Whyche [26] who, in a review, calculated a regression line:

$$Pa_{O_2} = -0.04\ \text{age} + 13.6\ (\text{age in years and } Pa_{O_2}\text{ in kPa})$$

(*cf.* our regression line in table III). Correlation analysis of the present data showed that age, as inferred from r^2, accounted for approximately 15–20% of the changes in Pa_{O_2} awake. Multiple regression analysis showed that 67% of the alterations in Pa_{O_2} were explained by age, perfusion of regions with low $\dot{V}_A/\dot{Q}$ ratios, Pa_{CO_2} and $P\bar{v}_{O_2}$. Shunt was minor or absent, and had no significant influence on Pa_{O_2}.

During anaesthesia, most patients developed atelectasis, and they also developed shunt, which accounted for approximately 20% of the variation in Pa_{O_2} ($r = 0.46$) and almost 50% of that in ($P_{A_{O_2}} - Pa_{O_2}$) ($r = 0.69$). The dispersion of $\dot{V}A/\dot{Q}$ distribution (log SD Q) explained another 15–20% ($r = 0.37$–0.45) of these variations.

Neither atelectasis nor shunt increased with age, whereas both log SD Q and low $\dot{V}A/\dot{Q}$ did. It is also worth noting that both log SD Q and perfusion of low $\dot{V}A/\dot{Q}$ regions increased with age at the same rate during anaesthesia as in the awake state, but at greater values. Thus there was a parallel shift of regression lines. The effect of these parallel shifts was that anaesthesia increased the dispersion of $\dot{V}A/\dot{Q}$ ratios (log SD Q) to the same extent as an increase in age by approximately 20 yr, and it increased perfusion of low $\dot{V}A/\dot{Q}$ regions as much as an increase in age by 10 yr.

The effect of age on shunt, perfusion of low $\dot{V}A/\dot{Q}$ regions and venous admixture has been presented schematically in figure 5. It may be seen that shunt was the major cause of impaired arterial oxygenation during anaesthesia in younger patients but, around 45 yr, the amount of perfusion of low $\dot{V}A/\dot{Q}$ regions equals the shunt and, at greater ages it becomes larger than the shunt. However, the scatter around the regression line (age *vs* low $\dot{V}A/\dot{Q}$) was large, precluding the use of these relations for predictions in any individual. Also, it should be remembered that shunt blood flow has a greater impact on arterial desaturation than perfusion of low $\dot{V}A/\dot{Q}$ regions, in particular when the patient undergoes ventilation of the lungs with oxygen-enriched gas mixtures (for a review, see West [27]). Calculation of venous admixture from blood-gas values and alveolar partial pressure of oxygen according to the standard equation, includes both shunt ($\dot{V}A/\dot{Q} < 0.005$) and $\dot{V}A/\dot{Q}$ mismatch (in particular "low $\dot{V}A/\dot{Q}$"), but to a varying extent depending on, among other things, FI_{O_2}. There was a close similarity between venous admixture and the sum of shunt and low $\dot{V}A/\dot{Q}$ during anaesthesia, whereas venous admixture was larger than shunt and low $\dot{V}A/\dot{Q}$ in the awake state. This difference may be attributed to larger influence of $\dot{V}A/\dot{Q}$ mismatch (not only low $\dot{V}A/\dot{Q}$) when breathing air (awake state), than breathing oxygen-enriched gas (anaesthesia) [27].

There is also support in the literature of an increasing $\dot{V}A/\dot{Q}$ mismatch with increasing age during anaesthesia. Thus Rehder and co-workers [28] found only a small log SD Q in anaesthetized young healthy volunteers, and also very little shunt. Prutow and colleagues [29], however, found a larger shunt in similarly young group of patients, the mean shunt being around 8%. In middle-aged subjects, Bindslev and colleagues [30] found a widened $\dot{V}A/\dot{Q}$ distribution with a greater log SD Q than that reported by Rehder and co-workers in young volunteers [28]. Shunt averaged 8%, similar to that reported by Prutow and co-workers. Finally, Dueck and colleagues detected even larger broadening of the $\dot{V}A/\dot{Q}$ distributions and increases in shunt in old patients with varying degrees of pulmonary disease [18]. Thus there appears to be an increase in the $\dot{V}A/\dot{Q}$ mismatch with increasing age, when data from these four studies are combined. This is in accordance with earlier observations of increasing gas exchange impairment (increasing venous admixture) with age during anaesthesia [1–4].

While shunt appears to be explained by the formation of atelectasis in dependent lung regions during anaesthesia, the cause of increased log SD Q and increased perfusion of regions with low $\dot{V}A/\dot{Q}$ ratios is unexplained. One possible explanation is airway closure in lung regions just above the atelectatic zone. Increased airway closure, as assessed by single breath nitrogen washout and bolus techniques, has been demonstrated by several groups [31–33], but conflicting results have also been reported [34, 35]. Moreover, the techniques used can not easily differentiate between airway closure and atelectasis if collapsed tissue is recruited during the vital capacity manoeuvre that is part of the airway closure measurement. Airway closure during anaesthesia is therefore still an open question. Further studies are required to answer this question.

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