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Airway Closure during Mechanical Ventilation

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A nitrogen-dilution technique for measurement of airway closing volumes (CV) and functional residual capacity (FRC) not requiring subject cooperation was tested in five healthy, awake, spontaneously breathing subjects and subsequently used in 20 patients during anesthesia with mechanical ventilation. Incomplete exhalation before inhalation of oxygen did not significantly alter CV. Inspiration of a volume of oxygen equal to 75 per cent of vital capacity (VC) did not affect CV, whereas inspiration to 50 per cent VC resulted in a 20 per cent decrease in CV. Expiratory resistance tended to reduce CV. By means of this technique, the validity of which had been thus demonstrated, airway closure could be shown to occur at lung volumes larger than FRC (and thus within a normal tidal volume) in six patients prior to anesthesia, and in a further 11 (total 17 of 20) during anesthesia with mechanical ventilation. FRC decreased by an average of 0.5 liters during anesthesia with mechanical ventilation and was only 0.2 liters above residual volume. Significant hypoxemia was observed in association with airway closure. (Key words: lung, airway closure; Ventilation, mechanical, airway closure.)

WHILE AN INCREASE in the alveolar–arterial oxygen gradient ($P(A\text{-}a)_{O_2}$) associated with anesthesia and mechanical ventilation resulting in relative hypoxemia is well documented,[1,2] it has not been adequately explained. In recent years, it has been shown that small airways tend to collapse at small lung volumes,[3] a phenomenon that may contribute to this relative hypoxemia. Indeed, recent work has shown not only that a large preanesthetic closing volume is associated with a markedly increased $P(A\text{-}a)_{O_2}$ during anesthesia,[4] but also that airway closure occurs more readily postoperatively and may be associated with an increased $P(A\text{-}a)_{O_2}$.[5] However, no data on airway closure during anesthesia have been published. In part this may be because of difficulties inherent in measuring airway closure during anesthesia[4] with available methods.

The aim of this study was to assess the reliability of a method of measuring airway closure applicable to the anesthetized patient, and, using this method, to determine whether relative hypoxemia during anesthesia with mechanical ventilation is associated with an increased tendency to airway closure. The effects of different ventilator settings on the subsequent measurement of airway closure were also investigated.

Material and Methods

Material

The method was first tested in a series of experiments in five healthy, conscious, supine subjects, aged 27–62 years. In a further series, 20 subjects, aged 21 to 72 years, were investigated during general anesthesia prior to operation. Clinical and radiologic examination of the latter group revealed no circulatory or pulmonary disease, although approximately 30 per cent of the patients were moderate smokers. The scope of the investigations was explained to the subjects, and their permission obtained. There were no complications. Information about the subjects is presented in table 1.

Airway Closure, Basis of Method

The method of measuring airway closure we used was based on that described by Anthonisen,[6] using nitrogen as a tracer gas. This method is derived from the concept that with small lung volumes, the alveoli are smallest in the dependent parts of the lungs where the tendency to airway closure is greatest.[7] Thus,

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TABLE I. Subject Data

	Sex, Age (Years)	Height (cm)	Weight (kg)	Smoking Habits (Cig/Day)	Surgical Diagnosis
Methodologic study					
Subject 1	M, 29	190	85	0	
Subject 2	F, 33	169	57	10	
Subject 3	F, 39	178	64	10	
Subject 4	M, 27	167	67	15	
Subject 5	F, 62	168	76	0	
Clinical study					
Subject 6	M, 56	174	69	0	Cholecystectomy
Subject 7	M, 72	184	64	7 g pipe tobacco	Cholecystectomy
Subject 8	M, 69	184	81	0	Inguinal hernia
Subject 9	M, 52	180	87	20	Varicose veins
Subject 10	M, 62	176	82	0	Inguinal hernia
Subject 11	F, 50	163	64	0	Cholecystectomy
Subject 12	F, 65	169	67	0	Cholecystectomy
Subject 13	M, 51	176	89	15	Varicose veins
Subject 14	M, 62	166	58	7 g pipe tobacco	Inguinal hernia
Subject 15	F, 31	171	65	10	Tumor of the breast
Subject 16	M, 46	185	92	0	Inguinal hernia
Subject 17	F, 32	158	74	0	Cholecystectomy
Subject 18	F, 53	168	62	0	Inguinal hernia
Subject 19	M, 43	174	79	10	Varicose veins
Subject 20	F, 55	174	86	5	Cholecystectomy
Subject 21	M, 64	174	74	0	Varicose veins
Subject 22	F, 61	176	76	0	Inguinal hernia
Subject 23	M, 62	178	88	0	Inguinal hernia
Subject 24	F, 21	163	58	0	Cholecystectomy
Subject 25	F, 60	164	65	0	Cholecystectomy

a deep inspiration of pure oxygen results in a greater dilution of nitrogen in the dependent regions, since alveoli expand to equal dimensions at the end of inspiration. In addition, the nitrogen-rich gas in the large airways and in the apparatus deadspace (150 ml in this study) preferentially goes to non-dependent regions during the inspiration of oxygen. This increases the nitrogen concentration gradient between the upper and lower regions of the lung. During the slow exhalation following oxygen inhalation, expired nitrogen reaches an "alveolar" plateau (phase III) when plotted against exhaled volume. At the end of exhalation nitrogen concentration rises steeply (phase IV), which rise is considered to indicate airway closure in the dependent regions of the lungs. This increase in the nitrogen content of the expirate is due to the continuing emptying of nitrogen-rich gas from non-dependent regions, while the alveoli in the dependent regions with lower nitrogen concentrations have ceased to empty.

The equipment used is shown in figure 1. Nitrogen concentration was analyzed by an ionization method (measuring instrument: Nitralyzer 505, Med. Science). Gas volumes were measured by means of a pneumotachograph with integrator (flow head: Fleisch no. 1, Godart; differential pressure meter EMT 32 and amplifier EMT 31, Siemens-Elema, home-built integrator[8]). Both signals were recorded by means of an X-Y-Y writer (Bryans 26000).

In the *conscious subjects*, airway closure was measured as follows (fig. 2). With the subject breathing air, a normal spirogram was obtained, volume being recorded against time. The subject then breathed out to residual volume (RV) and inspired oxygen to vital capacity (VC). He was then asked to exhale slowly (at a rate of 0.2–0.4 l/sec directed by the examiner) and completely while the nitro-

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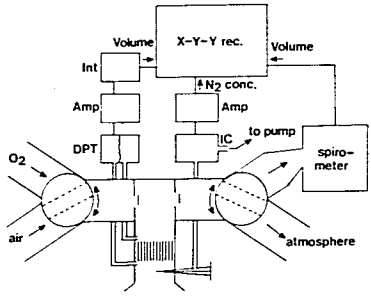

FIG. 1. Diagram of the measuring equipment used. Below, a needle valve is connected to the mouthpiece for continuous gas sampling. Above it is a flowmeter head (pneumotachograph) for measuring gas flow. In the clinical study the spirometer was replaced by a Douglas bag. DPT, differential pressure transducer; IC, ionization chamber; Amp, amplifier; Int, integrator.

gen concentration of the expired gas was recorded instead of time. This was made possible by a switch on the X-Y-Y writer. The commencement of airway closure was taken to be that point on a "best fit" line through the alveolar plateau where a secondary consistent rise in nitrogen concentration commenced (phase IV). The volume at which this secondary rise takes place as measured from RV is closing volume, CV, and the sum of CV and RV is closing capacity, CC (nomenclature according to Anthonisen[9]). Closing volume (or CC) could thus be directly compared with the resting expiratory level (corresponding to functional residual capacity, FRC) on the spirogram.

In *anesthetized subjects*, the above procedure cannot be performed. First, forced expiration to RV is not possible. Second, the lungs must be inflated with oxygen, which inflation may not invariably be to total lung capacity (TLC). Third, exhalation in the mechanically ventilated subject is not slow and even, but declines exponentially.

Methodologic Study

In order to determine whether airway closure could be measured without subject cooperation, a series of experiments was performed on five healthy, conscious subjects (table 1). Airway closure was measured when 1) the preliminary forced exhalation was halted by the examiner at levels above RV, so that the O_2 administration was commenced either at a point halfway between FRC and RV or at FRC; 2) inspiration of oxygen was similarly halted at levels below TLC at either 75 or 50 per cent of VC; 3) expiration was slowed down by an expiratory resistance or a flow regulator. The resistance used was a spring-loaded valve that opened at a pressure of 3 cm H_2O; the flow regulator, a Servo-ventilator 900 (Siemens-Elema), was set to restrict the flow to 0.4 l/sec; 4) an attempt was made to expel gas from FRC to RV by constricting a sheet wrapped around the chest and abdomen. These maneuvers were facilitated by continuous spirographic recording by the pneumotachograph, which enabled the examiner to direct the subject. Each maneuver was performed four times or more.

The use of a pneumotachograph with integrator for the recording of volumes in both series is not conventional. So its validity was tested in this series by comparing the volumes so recorded with those obtained by means of a dry spirometer (Wedge 570, Med-Science) connected in series. The pneumotachograph was calibrated with air.

Clinical Study

Airway closure, FRC and arterial blood gases were measured prior to and during anesthesia in 20 subjects. The method of measuring *airway closure* in the anesthetized subject was based on the results of the methodologic study. The lungs were inflated, after passive deflation, with a single breath of 2.5–3.5 l O_2, corresponding to more than 75 per cent of VC, and then allowed to deflate passively, the rate of deflation being slowed to approximately 0.2–0.4 l/sec by manual pressure on the reservoir bag used for inflation. Thus, no effort was made to deflate the lungs to RV (*c.f.* fig. 3).

Functional residual capacity was measured by a nitrogen-washout technique, the expirate being collected in a Douglas bag. Oxygen administration was discontinued when the nitrogen concentration was less than 2 per cent. Corrections were made for gas impurities

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(0.2 per cent N_2) and for nitrogen dissolved in body fluids (0.7 per cent N_2). The final end-expiratory nitrogen concentration was assumed to correspond to that in the alveoli. During anesthesia, measurement of FRC was facilitated by having available two inspiratory tubes on the ventilator (Engström 150 or 200, Jungner Instrument), one being flushed with pure oxygen. Thus the inspirate could be changed instantaneously from air to oxygen without being diluted in the ventilator. This technique is further described elsewhere.[10]

Arterial oxygen and carbon dioxide tensions (Pa_{O_2}, Pa_{CO_2}) were measured in blood samples taken from a previously inserted Teflon catheter in the femoral artery. Two samples were taken for each estimation, and blood-gas analysis was performed by means of a Clark oxygen electrode and a Severinghaus carbon dioxide electrode (E5046, E5036, Radiometer). The mean of two estimations was used for a simplified calculation of $P_{(A\text{-}a)_{O_2}}$ according to the following formula:

$$P_{(A\text{-}a)_{O_2}} = Pt_{O_2} - \frac{Pa_{CO_2}}{R} - Pa_{O_2}$$

where Pt_{O_2} is oxygen tension in the inspirate, taken to be 149 mm Hg, and R is the respiratory quotient, taken to be 0.8.

The *procedure* in the clinical study was as follows. All investigations were commenced with the subjects premedicated, supine and breathing air at a rate of 24 breaths/min, determined by a metronome. Two arterial blood samples were drawn, and nitrogen washout performed in order to measure FRC. The subject then breathed air for 10 minutes,

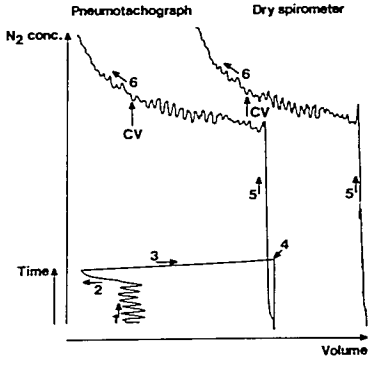

FIG. 2. Measurement of airway closure. The small, numbered arrows indicate the order of events. First, a spirogram is registered (1) (by means of the pneumotachograph). Following expiration to RV (2) the subject inspires O_2 to VC (3). N_2 concentration is now recorded instead of time (4), as slow expiration takes place to RV (5,6). This expiration is also recorded by a dry spirometer (5,6 to the right), hence the two closure curves. Commencement of airway closure is indicated by an arrow with suffix CV. Note the slight difference in volumes recorded.

after which airway closure was measured four to six times in the usual way. The subject was then anesthetized (see below) and ventilated with ambient air for a period of 15 minutes, either with a tidal volume (V_T) of 10 ml/kg bw and 12 breaths/min or with a V_T of 5 ml/kg bw and 24 breaths/min, the setting being chosen randomly. Thus, minute ventilation was constant at either setting. Two

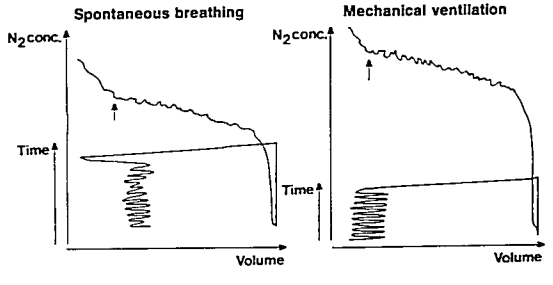

FIG. 3. Measurement of airway closure, with spontaneous breathing (left) and with mechanical ventilation (right). Following exhalation to RV (or passive deflation, with mechanical ventilation) the subject inspires O_2 to VC (or is inflated with 2.5–3.5 l). Commencement of airway closure is indicated by an arrow.

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TABLE 2. Closing Volumes in Awake, Spontaneously Breathing Subjects in the Supine Position under Different Experimental Conditions*

	Normal Method		Point of O_2 Administration		Reduced Inspiration		Expiratory Impedance	
	Spirometer	Pneumotachograph	50 Per Cent of ERV	FRC	75 Per Cent of VC	50 Per Cent of VC	Resistance	Flow Limitation
Closing volume (ml)								
Mean	944	1092	916	928	910	757	891	920
Range	666–1187	690–1244	667–1158	683–1285	750–1058	556–950	612–1075	650–1169
Deviation from "spirometer," per cent	—	5	3	2	4	20	6	3
Significance of deviation, P	—	<0.01	>0.05	>0.05	>0.05	<0.01	>0.05	>0.05

* Calculations are performed on curves obtained by the dry spirometer, except for the column labeled "pneumotachograph." The results in each column are compared with those in the column labeled "spirometer." n = 5. ERV = expiratory reserve volume (FRC–RV).

samples of arterial blood were then withdrawn for analysis, and nitrogen washout performed. Ten minutes later, airway closure was assessed four to six times. The ventilator setting was then changed, and the procedure repeated.

ANESTHESIA

After premedication with diazepam (0.15–0.20 mg/kg) and droperidol (0.35–0.07 mg/kg), both administered intramuscularly approximately one hour previously, anesthesia was induced with a "sleep dose" of thiopental. Succinylcholine (1.5 mg/kg) was then administered, preceded by a small dose of pancuronium (0.5 mg) to minimize postoperative muscular discomfort. Endotracheal intubation, using a wide-bore cuffed Portex endotracheal tube, was performed after ventilating the lungs with oxygen and spraying the vocal cords with a solution of 4 per cent lidocaine. The endotracheal tube was then connected to the ventilator delivering a suitable volume of air. Anesthesia was maintained with fentanyl (0.003 mg/kg) and a thiopental drip (1 mg/ml administered at a rate of approximately 2.0–3.0 ml/min). Further doses of fentanyl (0.02–0.04 mg) were given intravenously as required.

STATISTICS

Statistical analysis consisted of calculation of mean, range, SD, and SE, and of a regression equation according to the least-squares method. Student's t test was used to assess the significance of the differences between the results.

Results

METHODOLOGIC STUDY (TABLES 2 AND 3)

Incomplete exhalation before the inspiration of oxygen did not significantly alter CV, but if the inspiration of oxygen commenced at FRC, the transition from phase III to phase IV was less well defined (the change in nitrogen concentration was smaller and less abrupt), resulting in greater intraindividual variation.

When inspiration of oxygen was halted at a level corresponding to 75 per cent of VC, the ensuing measured value of CV was not significantly altered. Inspiration of oxygen to 50

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TABLE 3. Standard Deviation of Four Consecutive Closing Volume Determinations for Each Subject under Different Experimental Conditions, Mean and Range for Five Subjects (Volume in ml)

	Normal Method		Point of O_2 Administration		Reduced Inspiration		Expiratory Impedance	
	Spirometer	Pneumotachograph	50 Per Cent of ERV	FRC	75 Per Cent of VC	50 Per Cent of VC	Resistance	Flow Limitation
Mean	115	117	118	205	130	131	123	107
Range	43–175	38–170	35–184	89–307	63–241	47–224	56–213	28–203

per cent VC resulted in a measured value of CV that was 20 per cent lower.

Exhalation against resistance caused a small, non-significant reduction in CV, while exhalation through a flow regulator did not alter CV at all.

Compression of the chest and abdomen resulted in the expulsion of less gas than did active exhalation. A rapid increase in the nitrogen concentration of the expirate occurred simultaneously.

Closing volume recorded with the pneumotachograph was consistently 5 per cent larger than that recorded with the spirometer. Accordingly, the volumes measured by the pneumotachograph in the subsequent clinical study were divided by 1.05.

CLINICAL STUDY (TABLE 4, FIGS. 4–6)

Functional residual capacity was within normal limits for conscious subjects in the supine position.[11] On the average, FRC was 0.5 l less during anesthesia and mechanical ventilation at either rate, and only 0.2 l above RV. Closing capacity (CV + RV) was approximately the same with anesthesia and mechanical as it was with the patient awake and breathing spontaneously. However, the reduction in FRC associated with anesthesia and mechanical ventilation resulted in a markedly higher incidence of airway closure above FRC (and thus within a normal tidal volume). Thus, airway closure occurred above FRC in six awake subjects during spontaneous breathing and could be demonstrated in a further 11 (total 17 of 20) during anesthesia with mechanical ventilation. On the average, CC was 0.2 l less than FRC during spontaneous breathing and 0.3 l more than FRC during mechanical ventilation. The three subjects in whom closure could not be demonstrated during mechanical ventilation were all women, nonsmokers, and young or middle-aged (Subjects 17, 18, and 24 in table 1).

With spontaneous breathing, Pa_{O_2} was within normal limits.[12] It was significantly lower during anesthesia and mechanical ventilation, and slightly though significantly lower still on reducing V_T and increasing the frequency of ventilation. With spontaneous breathing, $P_{(A\text{-}a)_{O_2}}$ was fairly large,[12] and it was significantly greater with anesthesia and mechanical ventilation. There was no significant difference in the values obtained at the different V_T's and frequencies of ventilation. $P_{(A\text{-}a)_{O_2}}$ correlated with CC, but poorly. With spontaneous breathing, Pa_{CO_2} was within normal limits, and it was approximately the same during mechanical ventilation. The value

TABLE 4. Lung Volumes in 20 Healthy Supine Subjects Awake, Breathing Spontaneously, and Anesthetized, Ventilated Mechanically

	Conscious				Anesthetized
	Vital Capacity	Functional Residual Capacity	Expiratory Reserve Volume	Residual Volume	Functional Residual Capacity
Lung volume (liters)					
Mean	3.96	2.68	0.72	1.96	2.20
SD	0.89	0.62	0.20	0.43	0.55

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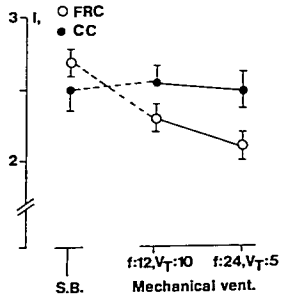

FIG. 4. Functional residual capacity (FRC) and closing capacity (CC) with spontaneous breathing (S.B.) and mechanical ventilation (M.V.) at f = 12/min, V_T = 10 ml/kg bw, and f = 24/min, V_T = 5 ml/kg bw. ● = mean; I = standard error. Student's t test: FRC: S.B. – M.V. f = 12, V_T = 10, $P < 0.01$; S.B. – M.V. f = 24, V_T = 5, $P < 0.001$; M.V. f = 12, V_T – M.V. f = 24, V_T = 5, $P > 0.05$. CC: no significant difference.

obtained with the smaller V_T and higher rate of ventilation was slightly higher than that obtained with the larger V_T and lower rate.

Discussion

Methodologic Study

Our results show that the modifications of the conventional method of measuring airway closure used need not vitiate the results. Thus, neither oxygen inflation of the lungs commencing above RV, nor its stopping short at volumes less than VC, nor limiting the rate of expiration by means of a flow regulator alters the position of the commencement of phase IV, and thus the measured value of CV. These findings, taken in conjunction with that of a low FRC during anesthesia (average 0.2 l above RV) indicate that airway closure can be measured, using the nitrogen-dilution method, in the absence of patient cooperation. Clearly, no closure will be demonstrated below FRC, unless gas is somehow further expelled from the lungs. This, however, is unacceptable, since it was accompanied by a large artifact.

Oxygen administration. Dollfus *et al.*[13] and Holland *et al.*[14] have shown that the regional distribution of ventilation varies with lung volume. Thus, it might have been expected that the administration of oxygen above RV would adversely affect the ensuing closure measurements. Our results showed that this is not so. Even when oxygen administration was commenced at FRC, the mean CV was unaltered, although the scatter was greater. On the other hand, inspiration of oxygen to 50 per cent VC resulted in the tardy appearance of phase IV. Thus, CV will be underestimated. This has been reported previously by Holtz *et al.*,[15] who attribute it to the hysteresis of the volume–pressure curve during the inspiration–exhalation cycle (personal communication; *c.f.* Glaister *et al.*[16]).

Flow limitation. According to Hyatt *et al.*,[17] the position of phase IV is a function of the expiratory flow rate, and its appearance due to dynamic compression of the dependent airways. Although this hypothesis has not been widely accepted, it is customary to measure airway closure during slow exhalation (approximately 0.3–0.5 l/sec) to minimize any effect of dynamic compression. Since the expiratory flow rate in the anesthetized, mechanically ventilated subject has an exponential decay, an expiratory resistance will

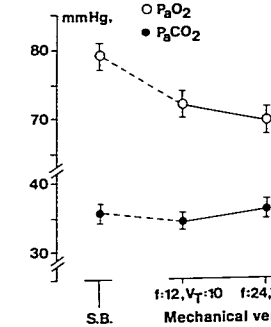

FIG. 5. Arterial blood gases during spontaneous breathing (S.B.) and mechanical ventilation (M.V.) at f = 12/min, V_T = 10 ml/kg bw, and f = 24/min, V_T = 5 ml/kg bw. ● = mean; I = standard error. Student's t test: Pa_{O_2}: S.B. – M.V. f = 12, V_T = 10, $P < 0.01$; S.B. – M.V. f = 24, V_T = 5, $P < 0.001$; M.V. f = 12, V_T = 10 – M.V. f = 24, V_T = 5, $P < 0.01$; Pa_{CO_2}: S.B. – M.V., no significant difference, M.V. f = 12, V_T = 10 – M.V. f = 24, V_T = 5, $P < 0.01$.

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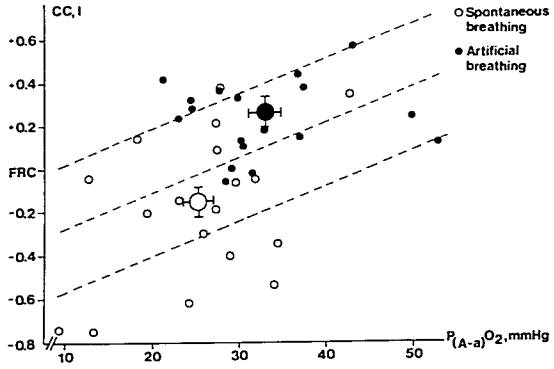

FIG. 6. $P_{(A-a)_{O_2}}$ and CC (expressed as volume greater or less than FRC). ○ = spontaneous breathing; ● = mechanical ventilation (f = 24/min, V_T = 5 ml/kg bw); $\overset{+}{\underset{+}{\oplus}}$ = mean and standard error for the clinical material, spontaneous breathing; $\overset{+}{\underset{+}{\oplus}}$ = mean and standard error, mechanical ventilation. Mean $P_{(A-a)_{O_2}}$ was 32.5 mm Hg, mean CC was FRC + 0.25 l with mechanical ventilation at f = 12/min and V_T = 10 ml/kg bw.) Regression line with residual standard deviation is drawn according to the equation: CC − FRC = 0.016 × $P_{(A-a)_{O_2}}$ − 0.426 n = 36, r = 0.46, $P < 0.01$. Student's t test: $P_{(A-a)_{O_2}}$; S.B. − M.V. f = 12, V_T = 10, $P < 0.001$; S.B. − M.V. f = 24, V_T = 5, $P < 0.001$. M.V. f = 12, V_T = 10 − M.V. f = 24, V_T = 5, $P > 0.05$.

reduce the flow rate but not alter its exponential character. Exhalation will cease at a higher lung volume. Flow regulation, on the other hand, whether performed manually or by means of a regulator, limits flow to a certain maximum, but does not alter the lung volume at which exhalation ceases. The present results showed insignificant variations in CV measured with either method of expiratory impedance, although CV measured in the presence of an expiratory resistance tended to be smaller.

Pneumotachograph. We used the pneumotachograph for volume recordings because of its convenience, obviating the need for taps and valves. In addition, a direct comparison of a spirogram and the ensuing recording of airway closure is immediately available. However, the pneumotachograph is sensitive to zero-drift, to pressure changes, and to changes in gas viscosity.[18] Corrections can be made for these factors. Gas compression resulting from the inflationary pressures will result in an underestimation of VC by approximately 2 per cent and of CV by less than 1 per cent. The smaller error in the determination of CV than of VC is due to the lower pressure in the flowmeter head at the end of exsufflation. We have neglected this small error. The viscosity of oxygen is 11 per cent greater than that of air. This means that in a subject with a RV of 1.96 l and a VC of 3.96 l (mean values of 20 subjects studied, *c.f.* table 4) the pneumotachograph will overestimate the expired volume, as well as CV, by 7 per cent. A comparison between volumes recorded by a pneumotachograph and those recorded by a spirometer showed that the former overestimated volumes of the oxygen-enriched expirate by 5 per cent. Thus, in subjects with normal lung volumes, dividing the volumes of the oxygen-enriched expirate recorded by a factor of 1.05 will make the pneumotachographic recordings sufficiently accurate.

CLINICAL STUDY

Anesthesia with mechanical ventilation and $P_{(A-a)_{O_2}}$. The alveolar–arterial oxygen gradient is increased with anesthesia and mechani-

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cal ventilation. An attempt has been made to explain this increase by postulating the appearance of small areas of atelectasis.[19] This explanation would appear unlikely since the increase in gradient has been demonstrated shortly after the induction of anesthesia.[1] Nunn[20] has suggested that this increase may reflect changes in ventilation or perfusion patterns of the lungs. The demonstration that gas distribution is even during anesthesia and mechanical ventilation[10,21,22] suggests that changes in the pattern of ventilation are unlikely to explain this phenomenon. A contributing factor may be the reduction in cardiac output associated with mechanical ventilation.[23] This, however, postulates the existence of a significant right-to-left shunt, which has not been demonstrated. It may also be that airway closure is the cause of the increase $P_{(A-a)_{O_2}}$, which possibility is further discussed below.

Anesthesia with mechanical ventilation and airway closure. It has recently been shown that small airways tend to collapse at small lung volumes.[3] In the supine position, FRC is reduced so that airway closure may occur at lung volumes near to or indeed larger than FRC.[24,25] FRC is reported to be further reduced by anesthesia[26,27,28] (a finding confirmed in our study), although contradictory results have been presented.[4] The reduction in FRC may be due to trapped gas, thoracic gas volume remaining unchanged. However, Westbrook *et al.*,[28] using a body plethysmograph to measure thoracic gas volume, found a reduction of the same magnitude as demonstrated using tracer gas methods. We therefore assume that the diminished FRC during anesthesia indicates a true reduction in lung volume. This reduction in FRC increases the tendency to airway closure despite an unchanged CC. Thus, CC prior to anesthesia was above FRC in six of 20 subjects apparently free of pulmonary disease and in a further 11 (total 17) during anesthesia with mechanical ventilation. The three subjects without airway closure during anesthesia with mechanical ventilation of a total of 20 all belonged to that category least prone to airway closure during spontaneous breathing (young non-smokers).[4,6,29]

$P_{(A-a)_{O_2}}$ and airway closure. If changes in $P_{(A-a)_{O_2}}$ occurring during anesthesia and mechanical ventilation are to be explained by the closure of small airways, it must be assumed that blood-flow continues to the connected alveoli. There is evidence to suggest that this may not be so in the conscious subject breathing spontaneously (West, personal communication). However, it may well be that such a control of the pulmonary blood flow, if it exists, is inhibited during anesthesia and mechanical ventilation. Moreover, Nunn *et al.*[30] have shown that hypoxemia can be demonstrated in normal subjects breathing at lung volumes below FRC. Further evidence for the contribution of airway closure to the increase in $P_{(A-a)_{O_2}}$ is our finding of a relationship between $P_{(A-a)_{O_2}}$ and CC-FRC (*c.f.* fig. 6). In addition, in the three subjects in whom airway closure could not be demonstrated during anesthesia and mechanical ventilation, no increase in $P_{(A-a)_{O_2}}$ occurred.

$P_{(A-a)_{O_2}}$ and ventilator setting. Changing the ventilator setting from a large V_T with low frequency to a small V_T with high frequency, or *vice versa*, did not significantly alter either CC or $P_{(A-a)_{O_2}}$. That $P_{(A-a)_{O_2}}$ was unchanged may appear anomalous, since it would be expected that the lower the V_T, the greater the period of airway closure during the respiratory cycle. However, it has been shown that increasing the frequency of ventilation and reducing V_T (the respiratory minute volume being kept constant) is associated with an increase in cardiac output.[31] This increase presumably compensates for the increase in venous admixture, resulting in an unchanged $P_{(A-a)_{O_2}}$.

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