Components of the Alveolar-Arterial Oxygen Tension Difference in Anesthetized Man

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Alveolar-arterial oxygen tension difference was measured in twelve anesthetized, paralyzed, artificially ventilated subjects when the inspired gas was halothane in oxygen, and again using 23–30 per cent oxygen, 70–77 per cent nitrous oxide, and halothane as the inspired mixture. During breathing of the high oxygen mixture, mean AaD_{O_2} was 196 mm. of mercury and calculated shunt was 11.0 per cent of cardiac output. When inspired oxygen concentration was in the region of 25 per cent, mean AaD_{O_2} was 49 mm. of mercury and corresponding calculated shunt was 10.4 per cent of cardiac output. These results indicate that the predominant change responsible for the increase in AaD_{O_2} exhibited by anesthetized patients is a significant increase in venous admixture with no detectable change in ventilation-perfusion relations. Values for physiological dead space, oxygen consumption, carbon dioxide production and respiratory exchange ratio during anesthesia obtained in the present study are in good agreement with previously published values for these parameters. Some possible explanations for observed changes in pulmonary gas exchange during anesthesia are considered.

SEVERAL groups of investigators have shown that anesthetized subjects exhibit a marked increase in magnitude of alveolar-arterial oxygen difference (hereafter abbreviated AaD_{O_2}) and calculated total shunt when compared with conscious, spontaneously breathing individuals.[1–6] Table 1 summarizes these observations and includes for comparison selected studies on conscious subjects. The AaD_{O_2} in conscious subjects may be attributed to additive effects of diffusion limitation, ventilation-perfusion abnormalities and venous admixture.[10] It seems quite unlikely that diffusion limitation would contribute appreciably to the AaD_{O_2} at inspired oxygen tensions customarily used during anesthesia.[11] Increase in AaD_{O_2} during anesthesia is therefore due to an increase in ventilation-perfusion abnormalities, to an increase in venous admixture, or to both. Individual contributions of these two parameters to the total AaD_{O_2} may be estimated by studying a subject at two levels of oxygenation.[12]

Although inspired oxygen concentrations have been varied in previous measurements of AaD_{O_2} during anesthesia, any given subject has been studied at only one inspired oxygen concentration. Large variation in AaD_{O_2} among subjects has obscured effects of altering inspired oxygen concentration on magnitude of calculated shunt. The present study was designed to assess relative contributions of ventilation-perfusion abnormalities and of venous admixture to the AaD_{O_2} during anesthesia by measurement of AaD_{O_2} and calculation of shunt during breathing of both 99 per cent oxygen and 20–30 per cent oxygen in nitrous oxide in the same subject.

Methods

Details of subjects of the study are presented in table 2. Each patient was premedicated and subsequently managed by an anesthesiologist who was not involved in conduct of the study. Patients were anesthetized, paralyzed and artificially ventilated through a tightly fitting cuffed endotracheal tube. Two gas mixtures were used sequentially in each patient: halothane in oxygen and halothane, 70–80 per cent nitrous oxide with 20–30 per cent oxygen, and the order in which the mix-

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TABLE 1. Representative Studies from the Literature Illustrating Magnitude of Alveolar-Arterial Oxygen Difference and Total Shunt in Conscious and Anesthetized Man at Different Inspired Oxygen Concentrations

Study and Reference	Respiration	F_{IO_2}	$A_aD_{O_2}$	Shunt
Conscious Man				
Ayers, Criscitiello, Grabovsky (1964)[7]	Spontaneous	0.21	15.2	6.4
		1.0	37.1	3.0
Said and Banerjee (1963)[8]	Spontaneous	0.21	6.6	3.3
		1.0	26.3	1.6
Nunn and Bergman (1964)[9]	Spontaneous	0.21	14.6	5.7
		1.0	14.8	1.3
Anesthetized Man				
Campbell, Nunn, and Peckett (1959)[1]	Artificial	0.21	19.1	10.8
Frumin *et al.* (1959)[2]	Artificial	0.14–0.21	more than 20 mm. Hg in 1/5 of specimens	—
Stark and Smith (1960)[3]	Art. & Spont.	1.0	252	16.0
		1.0	271	17.1
Nunn (1964)[4]	Spontaneous	0.21	26	21
		0.28	42	11
		0.99	184	14
Sykes, Young, and Robinson (1965)[5]	Artificial	0.21	42	9.9
		0.21	51	7.4
Nunn, Bergman, and Coleman (1965)[6]	Artificial	0.25	52	9.3
		0.98	145	10.8

tures were used was varied. Inspired concentration of halothane was adjusted according to clinical requirements and sufficient *d*-tubocurarine or gallamine was administered to prevent spontaneous respiratory efforts. Following initial adjustment of the ventilator no further changes in the controls were made and no hyperinflations of the lung were performed during the study.

The experimental apparatus is illustrated in figure 1 and is a modification of the system devised by Nunn for measurement of gas exchange during anesthesia.[13] The desired gas mixture from an anesthesia machine was saturated with water vapor at room temperature by bubbling through two humidifier bottles and then was introduced into the box of a box-bag system. A pump removed gas from the box and delivered it to the Manley Ventilator. The Manley Ventilator (Blease Anesthetic Equipment Company of England) has a non-rebreathing circuit which permits quantitative collection of uncontaminated exhaled gas, and the minute volume of the patient is the flow of gas delivered to the respirator. A 10-liter waterless spirometer ("Wedge" Spirometer, Med Science Electronics, St. Louis) communicated with the box. During the period of equilibration flow of fresh gas into the box was in excess of that from box to ventilator. The spirometer therefore filled, and when a preset volume was achieved was periodically emptied to atmosphere by the Spirometer Recycling Device (Med Science Electronics). In this manner the spirometer-box system was flushed with fresh gas and gas in the system gradually attained the desired composition. During the equilibration period the bag was empty and exhaled gases escaped to atmosphere. Pressure in the airway was detected with a Statham PM5TC Pressure Transducer which was calibrated against a water manometer. Output of this transducer and also output of the volume transducer of the Wedge spirometer were recorded with a Minneapolis-Honeywell Visicorder. Expired tidal volume was measured with a Wright Respirometer. Since reading of this instrument is known to

TABLE 2. Details of Patients Studied

Patient	Age	Sex	Height (cm.)	Weight (kg.)	BSA (sq. m.)	Pre-medication	Operation	Medical Status	Control	
									Pa_{O_2}	Pa_{CO_2}
1	69	M	178	90	2.08	A, H	Femoral artery graft	Diabetes		
2	62	M	163	62	1.67	A, H, P	Aortic graft	Chronic bronchitis		
3	44	F	152	67	1.64	A, H, P	Cholecystectomy	Hypertension	70	34.2
4	49	M	180	91	2.11	A, H, M, P	Small bowel Resection	Asthma, inactive	64	33.9
5	34	M	178	71	1.88	A, H, M, P	Vagotomy, pyloroplasty	Healthy		
6	52	M	174	76	1.90	A, H, M	Vein ligation	Healthy		
7	43	M	168	75	1.84	A, M, P	Vagotomy, pyloroplasty	Healthy		
8	31	M	173	68	1.81	A, H, M	Vagotomy, pyloroplasty	Healthy	74.8	36.5
9	48	M	173	72	1.85	A, H, P	Vagotomy, pyloroplasty	Diabetes		
10	45	M	165	55	1.60	A, H, P	Vagotomy, pyloroplasty	Remote pneumonitis		
11	41	M	160	54	1.54	A, H, P	Vagotomy, pyloroplasty	Healthy	82.4	37.0
12	58	M	170	64	1.74	A, H, P	Vein ligation	Hypertension	66.4	37.8

Premedication: A = Atropine, H = Hydroxyzine, M = Meperidine, P = Pentobarbital.

vary with minute volume, gas composition and respiratory pattern, the respirometer was calibrated against a spirometer after each study using conditions which prevailed during the experiment.[14] Respiratory frequency was measured by timing ten respiratory cycles with a stopwatch.

Measurements were made after a 30–45 minute period of equilibration and when respiratory frequency and exhaled tidal volume had become constant. Temperature in the box was noted and the two three-way taps were simultaneously rotated stopping delivery of fresh gas to the box and diverting exhaled gas into the bag. Thus, a closed box-bag system was attained. Inspired gas flowed from box through pump to ventilator and patient and exhaled gas was returned to the bag. Any change in volume of the system was recorded by the spirometer. At the end of the measurement period, the three-way taps were returned to their original positions and box temperature was again noted.

Concentration of oxygen in inspired and exhaled gas was determined on samples collected from the box and bag, respectively, using a Servomex DCL 101 paramagnetic analyzer. In a previous evaluation sensitivity, reproducibility, and probable accuracy of this device was found to be comparable to that obtainable with the Haldane apparatus.[15] During the period of measurement, blood samples were withdrawn from a needle in the brachial or radial artery and were analyzed for oxygen

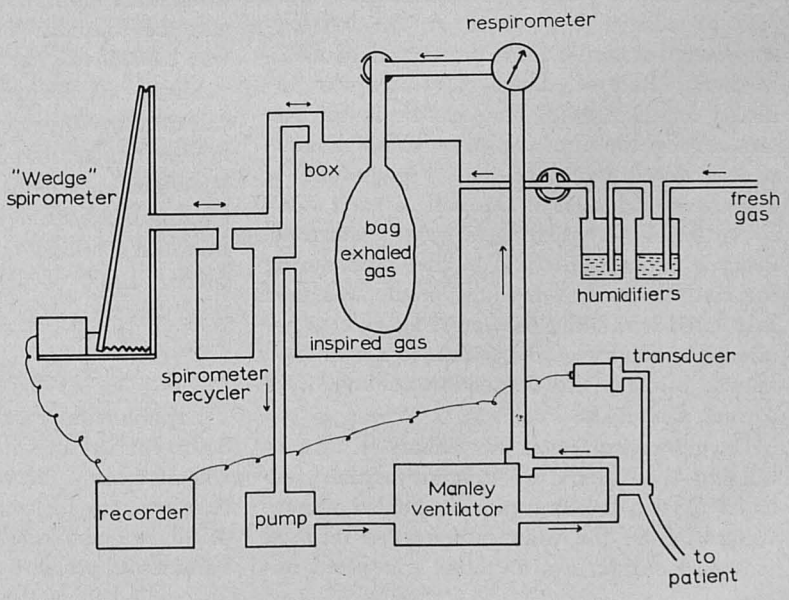

FIG. 1. Diagram of experimental apparatus. (See text for explanation.)

and carbon dioxide tensions using an Instrumentation Laboratory System. Electrodes were calibrated both before and after each determination. The oxygen electrode was calibrated with oxygen-free nitrogen, room air or commercial oxygen (assumed to be 99.8 per cent oxygen). The carbon dioxide electrode was calibrated with carbon dioxide-air mixtures whose exact composition had been determined by Scholander analysis. Instrument readings were corrected for metabolic changes in blood on standing (Nunn and Capel, unpublished observations), and for differences between patients' esophageal temperature and electrode temperature.[16] In addition, oxygen tension readings were corrected for the 5 per cent difference in reading of blood and gas of identical oxygen tension previously established by tonometric studies in our laboratory. Blood analyses were started immediately after obtaining the sample and were completed within 10–12 minutes. Hemoglobin concentration was determined on each subject using the cyanmethemoglobin method..[17] Carbon dioxide tension of mixed exhaled gas collected from the bag was measured with the carbon dioxide electrode.

Exhaled minute volume was calculated by multiplying exhaled tidal volume, obtained from the respirometer, by respiratory frequency. Differences between inspired and expired minute volume was calculated from rate of change of volume in the box-bag-spirometer system during the period of measurement. Rate of change of volume was corrected for changes of temperature in the system during the run and also for small leaks which were usually present. Magnitude of leaks was evaluated at the end of each study by artificially ventilating a ten gallon steel drum at a pressure equal to that used during the study. Inspired minute volume was then calculated by adding the corrected change per minute in volume of the system to the exhaled minute volume. All ventilation volumes were corrected to BTPS.

Oxygen consumption was calculated by subtracting the volume of oxygen exhaled (exhaled oxygen concentration × exhaled minute volume) from the volume of oxygen inspired (inspired oxygen concentration × inspired minute volume), and was also expressed as percentage of predicted normal basal oxygen consumption.[18] Carbon dioxide production was calculated from exhaled minute volume and concentration of carbon dioxide in exhaled gas. Respiratory exchange ratio (R) was calculated as the ratio of carbon dioxide production to oxygen consumption. Inert gas exchange was that portion of the difference between inspired and expired minute volume which was not due to the difference between oxygen consumption and carbon dioxide production, and under varying circumstances represented nitrogen elimination and/or uptake or elimination of nitrous oxide and halothane. All gas exchange volumes were corrected to STPD.

Ideal alveolar oxygen tension was calculated by substituting appropriate values for inspired and exhaled oxygen tension and expired and arterial carbon dioxide tension into an alveolar air equation.[19] Total shunt was calculated from alveolar and arterial oxygen tensions and hemoglobin concentrations using a shunt equation [20] and the following assumptions: (1) No alveolar-end capillary diffusion gradient existed. (2) Arterial-mixed venous oxygen content difference was 5 vol. per cent.[21] (3) The form of the oxygen dissociation curve is that presented by Severinghaus in the "Blood Gas Calculator" slide rule [22] and base excess in all patients was 0. (4) Each gram of hemoglobin when fully saturated carried 1.34 ml. oxygen and the solubility of oxygen in whole blood was 0.0031 vol. per cent/mm. of mercury.

Physiological dead space was calculated by substituting appropriate values for exhaled tidal volume, arterial and mixed exhaled carbon dioxide tensions in Bohr's equation. Apparatus dead space of 20 ml. was subtracted from the resulting value to obtain patient dead space. Ratio of physiological dead space to tidal volume (V_D/V_T) was also calculated.

Results

Experimental results are presented in table 3 for ventilation with 23–30 per cent oxygen and in table 4 for ventilation with 95–97 per cent oxygen. Elevation of our laboratory is 4,780 feet above sea level and average total barometric pressure is 640 mm. of mercury.

TABLE 3. Experimental Results During Breathing of 23–30 Per Cent Oxygen

Subj.	Time from Induct.	F (Br./min.)	V_E (ml.)	$\dot{V}$ (ml./min.)	P_{IO_2} (mm. Hg)	P_{AO_2} (mm. Hg)	P_{aO_2} (mm. Hg)	$A_aD_{O_2}$ (mm. Hg)	Shunt (% CO)	P_{aCO_2} (mm. Hg)	V_D/V_T: (%)	$\dot{V}_{O_2}$ (% basal)	$\dot{V}_{CO_2}$ (ml./min.)	R	Inert Gas Exch. (ml./min.)
1	135	9.7	840	8,148	168	139	76	64	10.4	28.5	33.6	84	169	0.786	131
2	75	10.2	828	8,448	156	117	71	46	8.9	27.0	37.2	128	159	0.600	36
	245	10.7	788	8,433	142	119	53	66	19.5	29.1	44.5	79	150	0.920	160
3	105	12.7	603	7,661	143	123	63	60	15.0	26.2	27.5	88	161	0.920	213
4	70	9.6	851	8,167	137	111	49	62	27.7	31.5	44.3	60	159	0.975	140
5	45	10.1	903	9,120	176	150	109	41	4.2	30.0	38.8	78	187	0.930	132
	140	10.6	837	8,863	176	150	128	23	2.2	25.6	37.8	76	157	0.801	92
6	115	8.1	664	5,380	160	125	73	52	11.2	36.7	35.7	70	140	0.828	161
7	45	11.5	701	8,058	145	127	74	54	12.9	28.9	30.8	70	179	1.05	263
8	75	10.2	768	7,831	143	112	81	31	6.7	29.4	40.1	96	158	0.666	216
9	120	9.0	849	7,641	145	121	68	53	10.9	25.7	37.2	75	147	0.817	129
10	45	10.2	896	9,136	179	142	90	51	8.3	31.1	45.1	118	174	0.710	58
	150	10.4	878	9,134	173	144	100	44	5.8	28.8	40.8	92	174	0.906	52
11	125	10.0	710	7,098	149	121	97	24	3.7	25.0	33.5	92	131	0.693	112
12	90	10.6	840	8,907	171	144	79	65	9.4	25.5	47.0				
	195	11.0	830	9,135	168	145	85	61	8.9	25.2	50.8	66	125	0.862	97
Mean		10.3	799	8,199	158	129	81	49	10.4	28.4	39.0	84	156	0.831	133
S.D.								14.0	6.4		6.2	18.6		0.125	
S.E.								3.5	1.6		1.6	4.8		0.032	

Symbols are in accord with the recommendations of the Committee for Standardization of Definitions and Symbols in Respiratory Physiology.[34]

TABLE 4. Experimental Results During Breathing of 95–97 Per Cent Oxygen

Subj.	Time from Induct.	F (Br./min.)	V_E (ml.)	V (ml./min.)	P_{IO_2} (mm. Hg)	P_{AO_2} (mm. Hg)	P_{aO_2} (mm. Hg)	A_{aDO_2} (mm. Hg)	Shunt (% CO)	P_{aCO_2} (mm. Hg)	V_D/V_T: (%)	$\dot{V}_{O_2}$ (% basal)	$\dot{V}_{CO_2}$ (ml./min.)	R	Inert Gas Exch. (ml./min.)
1	75	10.0	903	9,033	578	555	328	212	11.8	29.4	35.4	103	188	0.718	−47
	170	10.3	866	8,919	578	546	333	213	12.0	31.6	38.9				
2	175	11.0	795	8,741	588	561	421	140	7.9	28.7	51.2	122	135	0.536	−127
3	60	13.5	574	7,750	577	545	266	279	15.3	27.4	33.4	87	155	0.891	−25
	140	13.5	618	8,357	577	541	237	304	16.6	25.0	32.7	121	155	0.638	−65
4	115	10.3	835	8,597	568	524	246	278	15.5	29.6	40.2	69	169	0.894	−81
5	100	11.2	923	10,340	570	533	481	52	3.3	24.1	35.6	99	180	0.706	−96
6	60	7.0	797	5,577	578	536	431	105	6.0	37.7	37.6	91	146	0.664	−19
7	100	13.9	583	8,091	572	557	295	262	14.7	25.8	35.3				
8	30	10.7	771	8,243	580	546	299	247	13.9	30.2	32.6	112	185	0.668	−16
9	60	9.5	850	8,079	577	552	248	304	16.6	24.6	36.7	69	140	0.848	41
	175	9.8	826	8,100	575	546	450	96	5.5	24.8	35.8	88	144	0.690	−24
10	100	11.6	840	9,747	573	524	411	113	6.9	28.8	40.7	119	185	0.746	−128
11	65	11.5	739	8,498	585	564	465	99	5.8	21.1	28.6	100	143	0.701	−19
12	60	11.5	840	9,663	569	540	353	187	10.7	25.5	49.4	81	138	0.775	−18
	160	11.4	837	9,546	570	532	284	248	13.9	24.2	44.3	79	143	0.827	−79
Mean		11.0	786	8,580	576	544	347	196	11.0	27.4	38.0	95	159	0.736	−50
S.D.								84	4.5		6.1	18		0.102	
S.E.								21	1.1		1.5	5		0.027	

Mean minute volume was 8,390 ml./minute. Minute volume, respiratory rate and tidal volume were identical during breathing of both high and intermediate oxygen mixtures. This level of ventilation resulted in moderate hyperventilation of patients in this series; mean arterial carbon dioxide tension was 27.9 mm. of mercury, and did not vary significantly with inspired oxygen concentration. Inflating pressure remained constant throughout the duration of each study, and there was no tendency for tidal volume to decrease during the period of constant pressure ventilation.

Mean dead space to tidal volume ratio (V_D/V_T) was 38.0 during breathing of high oxygen and 39.0 during administration of intermediate oxygen concentrations. This difference is not significant. There was no recognizable change of V_D/V_T with time.

In some subjects arterial blood was obtained after premedication and before induction of anesthesia. Results of analysis of these samples for oxygen and carbon dioxide tension are included in table 2.

When halothane in oxygen was administered, inspired oxygen concentration varied from 95.4 to 97.4 per cent. Mean alveolar oxygen tension was 544 mm. of mercury, mean arterial oxygen tension was 347 mm. of mercury and mean AaD_{O_2} was 196 mm. of mercury (range 52 mm. to 304 mm.). Corresponding calculated total shunt was 11.0 per cent of cardiac output (range 3.3–16.6 per cent). At intermediate levels of oxygen, inspired oxygen concentration ranged from 23.0 to 30.1 per cent. Mean alveolar oxygen tension was 129 mm. of mercury, mean arterial oxygen tension was 81 mm. of mercury and mean AaD_{O_2} was 49 mm. of mercury (range 23–66 mm. of mercury). Corresponding calculated total shunt was 10.4 per cent of cardiac output (range 2.2–27.7 per cent). There was no correlation between magnitude of calculated shunt and V_D/V_T at either inspired oxygen level. There was also no systematic tendency for either AaD_{O_2} or shunt to change with time (fig. 2).

Mean carbon dioxide production was 158 ml./minute and did not vary with changes in inspired gas composition. Oxygen consumption during high oxygen administration was 95

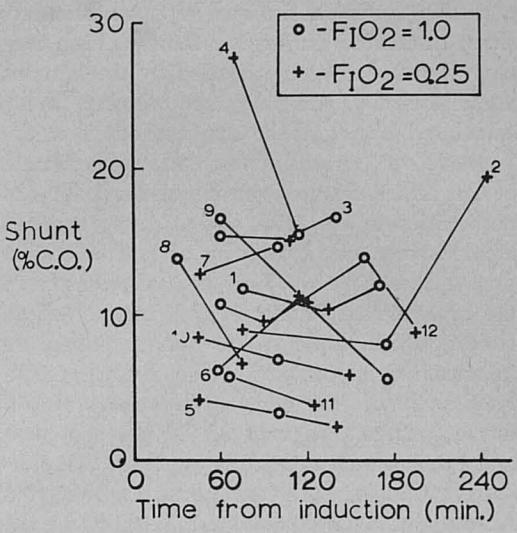

FIG. 2. Changes in total calculated shunt with time.

per cent of predicted basal value while at the intermediate concentration of oxygen the value was 84 per cent. This difference does not approach the customary level of significance ($0.2 < P < 0.1$). Mean respiratory exchange ratio was 0.784. Due to the variation in sequence of administration of the different gas mixtures values for inert gas exchange cannot be interpreted precisely. Measurements made during administration of nitrous oxide-halothane-oxygen mixtures showed that significant volumes of anesthetic gas were being taken up while those made during administration of halothane and oxygen generally indicated elimination of inert and anesthetic gases from the body.

Discussion

Magnitude of alveolar-arterial oxygen differences and calculated shunts in the present report are in good agreement with those of previous studies in anesthetized man summarized in table 1. It is emphasized that in the absence of measurements of mixed venous oxygen content, calculation of total shunt merely offers an expedient method for comparing different individuals and different experimental conditions but can only indicate orders of magnitude and not precise values.

Shunt calculated during breathing of 25 per cent oxygen is attributable to both ventilation-

perfusion abnormalities and venous admixture, shunt calculated during breathing of high concentrations of oxygen is caused by true venous admixture only, and difference between shunts calculated during these two conditions is the "relative" or "virtual" shunt and is an estimate of the contribution of ventilation-perfusion abnormalities to the total AaD_{O_2}. Average calculated shunt of 11 per cent of cardiac output during breathing of 95–97 per cent oxygen in the present study indicates the presence of an abnormally high degree of venous admixture in anesthetized patients. The average calculated shunt of 10.4 per cent of cardiac output during administration of 23–30 per cent oxygen is not significantly different from that during breathing of high concentrations of oxygen. Absence of a detectable virtual shunt in the present study, however, does not necessarily indicate absence of ventilation-perfusion abnormalities and uniform distribution of inspired gas with respect to pulmonary capillary blood in anesthetized patients. Measurements of inert gas exchange showed that at the time experimental observations were made during nitrous oxide administration appreciable amounts of anesthetic gas were being taken up, and in some subjects uptake of nitrous oxide equaled or exceeded oxygen uptake. Each volume of nitrous oxide taken into pulmonary capillary blood is replaced in the alveolus not by pure nitrous oxide but by a volume of the inspired mixture of nitrous oxide and oxygen. Hence, in alveoli which are perfused in excess of their ventilation, the fall in oxygen tension will be minimized by inward diffusion of inspired gas to replace nitrous oxide which is taken up by blood, and the distribution component of the AaD_{O_2} will be minimal. This is a "second gas effect" produced by nitrous oxide.[23] Under these conditions this phenomenon might be called "diffusion hyperoxia." It has been previously demonstrated by Heller and Watson [24] and is exactly the reverse process of "diffusion anoxia" described by Fink as occurring on emergence from nitrous oxide anesthesia.[25] In addition, theoretical considerations indicate that contribution of ventilation-perfusion abnormalities to total shunt is maximum when alveolar oxygen tension is about 80 mm. of mercury and becomes less as alveolar oxygen tension increases.[12] Because of the second gas effect of nitrous oxide and because mean alveolar oxygen tension was 129 mm. of mercury small degrees of ventilation-perfusion abnormality were not detected in the present study.

Results of the present study indicate that as a group, anesthetized patients exhibit a marked increase in true venous admixture and no detectable increase in nonuniformity of distribution of pulmonary capillary blood flow relative to inspired gas. Nunn and co-workers tentatively offered the same conclusions on the basis of measurements of AaD_{O_2} at two levels of oxygenation in two different groups of patients.[6] Inspection of data for individual patients, however, indicates that although the majority of subjects have an abnormally large degree of venous admixture, an occasional patient has a small total shunt which would be considered in the normal range for a conscious individual. Also, occasionally suggestion of a significant distribution component contributing to a large total shunt is encountered.

Pulmonary atelectasis is the most obvious and simple explanation for the large degree of venous admixture in anesthetized patients. Bendixen and associates have demonstrated progressive increases in veno-arterial shunting and decreases in thoracic compliance during anesthesia with normal tidal ventilation lacking in periodic deep breaths.[26] Incidence of these changes was minimal if large tidal volumes were used and changes were reversible by hyperinflation of the lung imitating the spontaneous deep breath. These changes were attributed to progressive atelectasis during anesthesia. Although there is no doubt that atelectasis does occur during anesthesia there are several facts that lend support to the thesis that atelectasis is not the fundamental abnormality responsible for increased venous admixture in the anesthetized patient. Both in the present study and in that of Nunn *et al.*[6] a minority of patients exhibited progressive increase of shunting or fall in effective compliance with time, and in those in whom these phenomena were demonstrated, changes were most frequently not dramatic. In addition, spontaneous decreases in shunt during constant pressure ventilation also occurred. High

degrees of venous admixture have been observed as soon after induction of anesthesia as it has been possible to make measurements. The 16–17 per cent shunt reported by Stark and Smith was measured approximately four minutes after induction of anesthesia,[3] and Nunn *et al.* found large shunts 10–20 minutes following induction.[6] Although lung collapse occurs rapidly during breath-holding with oxygen [27] it is unlikely that atelectasis sufficient to account for the magnitude of observed shunts could develop in a relatively short time during cyclic ventilation of the lungs.[28] Furthermore, measures which are designed to re-expand atelectatic lung rarely alter magnitude of venous admixture in patients who are being moderately hyperventilated. Nunn *et al.* were unable to decrease shunt by hyperinflation of the lungs or by imposition of an expiratory resistance.[6] Data of Bendixen and co-workers indicate that in subjects who had exhibited progressive fall in arterial oxygen tension, hyperinflation of the lungs was only partially effective in reducing the alveolar-arterial oxygen difference indicating that a sizeable shunt remained after re-expansion of atelectatic lung.[29] Thus, there is little objective evidence for attributing the marked increase in venous admixture in anesthetized subjects to atelectasis. The large shunts frequently observed in these individuals would seem to be an as yet unpreventable consequence of induction of anesthesia, the mechanism of which remains unknown. Superimposed on this, as a consequence of relative hypoventilation may be progressive decreases in arterial oxygen tension secondary to atelectasis.

The present study again confirms that physiological dead space is increased in anesthetized subjects. V_D/V_T ratios of 38.0 and 39.0 are in good agreement with published values of previous investigators. Progressive increase in V_D/V_T ratio with time reported by Askrog *et al.* was not confirmed.[30] Values for oxygen consumption, carbon dioxide production, and respiratory exchange ratio are also in good agreement with previously published values, and confirm the conclusions of Theye and Tuohy that there is no remarkable reduction in oxygen consumption during light halothane anesthesia.[31]

Salient findings of the present study in anesthetized patients are a marked increase in true venous admixture without evidence of increase in ventilation-perfusion abnormalities and an increase in physiological dead space. These observations are consistent with the hypothesis that during anesthesia in most subjects pulmonary blood flow is diverted away from some alveoli, which remain open and ventilated, and is shunted through or across the lungs by way of some as yet undefined channel. Previous demonstration that no detectable change in distribution of inspired gas occurred following induction of anesthesia with artificial ventilation supports this conclusion.[32] The undefined shunt pathway does not include Thebesian veins, since flow through these channels has been shown to change very little with anesthesia.[33]

Although the increase in magnitude of AaD_{O_2} during anesthesia in the present study has been attributed entirely to increase in true shunt, other possible causes for increases in AaD_{O_2} should be considered. The equation used for calculating shunt in the present study was [20]:

$$\frac{Q_s}{Q_t} = \frac{C_cO_2 - C_aO_2}{C_cO_2 - C\bar{v}O_2}$$

Where Q_s/Q_t is the ratio of quantity of blood flowing through the shunt to total quantity of blood flow (cardiac output) and Cc_{O_2}, Ca_{O_2} and $C\bar{v}_{O_2}$ are oxygen contents of pulmonary capillary, arterial and mixed venous blood, respectively. When oxygen is breathed and arterial hemoglobin is fully saturated the following simplified form of the shunt equation is applicable:

$$\frac{Q_s}{Q_t} = \frac{0.0031\ AaDo_2}{0.0031\ AaDo_2 + (Cao_2 - C\bar{v}o_2)}$$

The Fick equation relates cardiac output, oxygen consumption, and arterio-venous oxygen difference:

$$\text{C.O. (l./min.)} = \frac{\dot{V}o_2\ \text{(ml./min.)}}{Cao_2 - C\bar{v}o_2\ \text{(ml./l.)}}$$

When the Fick equation is solved for arterio-venous oxygen difference and the result substi-

tuted into the simplified shunt equation the following expression is obtained:

$$\frac{Q_s}{Q_t} = \frac{0.0031\ AaDo_2}{0.0031\ AaDo_2 + (\dot{V}o_2/C.O.) \times 0.1}$$

Solving this expression for AaD_{O_2} results in the following equation:

$$AaDo_2 = \frac{0.1 \times \dot{V}o_2 \times Q_s}{0.0031 \times C.O. \times (Q_t - Q_s)}$$

Thus, magnitude of AaD_{O_2} varies not only with ratio of blood shunted to blood not shunted, but also varies directly with oxygen consumption and inversely with cardiac output. Possible contribution to the large AaD_{O_2} in the present study by increases in oxygen consumption is excluded by the observation that in these patients oxygen consumption was slightly below predicted basal value. The role of decreases in cardiac output and increases in arterio-venous oxygen differences is more difficult to assess since neither was measured. Possibly a portion of the abnormally large AaD_{O_2} is attributable to decrease in cardiac output with anesthesia, and probably much of the variation of AaD_{O_2} with time in individual patients may be explained by variation in cardiac output. However, as a group, patients in the present study exhibited an AaD_{O_2} four to six times greater than that anticipated in a comparable group of conscious subjects. If this magnitude of AaD_{O_2} is to be explained by decrease in cardiac output, it must be postulated that cardiac output fell to less than one quarter of its preanesthetic value. A fall in cardiac output of this magnitude was not consistent with the clinical status of the patients, and is not compatible with previously published studies on hemodynamics during halothane anesthesia.[35] It is therefore believed that the greatest portion of the large AaD_{O_2} observed in the present study may be attributed to increase in true shunt.

Summary and Conclusions

Average alveolar-arterial oxygen tension difference in twelve anesthetized, paralyzed subjects was 196 mm. of mercury during artificial ventilation with 95–97 per cent oxygen, and total calculated shunt was 11.0 per cent of cardiac output. In these same subjects when inspired gas contained 23–30 per cent oxygen, mean alveolar-arterial oxygen tension difference was 49 mm. of mercury and corresponding calculated total shunt was 10.4 per cent of cardiac output. These results indicate that the predominant cause for the abnormally large alveolar-arterial oxygen difference exhibited by most anesthetized subjects is increase in true shunt (venous admixture) without detectable change in relative distribution of inspired gas and pulmonary capillary blood flow. Observed changes in pulmonary gas exchange during anesthesia are consistent with the hypothesis that in most subjects during anesthesia, pulmonary blood flow is diverted away from some alveoli, which subsequently remain open and ventilated, and is shunted through or across the lungs by way of some as yet undefined channel.

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