Ventilation-Perfusion Changes During Thoracotomy

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Eleven patients were studied during pulmonary lobectomy and during occlusion of one main bronchus to determine ventilation-perfusion abnormalities, blood gas exchange, and the extent of metabolic acidosis. Anesthesia consisted of intravenous agents plus 100 per cent oxygen. On opening the thorax there was a decrease of *p*H and blood buffer base. The fraction of the lungs which was ventilated but not perfused increased at this time, but returned to control levels when the bronchus to the operated side was occluded. The perfused but unventilated fraction of the lung rose to a lesser degree on thoracotomy, and rose somewhat further on occlusion of the bronchus. The effective (ventilated and perfused) fraction of the lung diminished on thoracotomy, but increased ($P > 0.05$) on occlusion of the bronchus to the operated side. By increasing minute ventilation it was possible to maintain normal blood gas concentrations when only one lung was ventilated.

IT IS well known that severe respiratory acidosis may occur in patients undergoing thoracotomy.[1,2,3] Considerable elevation of arterial P_{CO_2} may occur even with the ventilation increased above normal awake values.[4,5] There must, therefore, be a considerable alteration in the distribution of ventilation and perfusion to various parts of the lungs. Large areas of the lungs may be deprived of blood flow with the development of increased alveolar dead space—a possible contributing factor to the respiratory acidosis.[4] Compatible with this concept is the development of an increase in physiological dead space[3] and an increase in the arterial to end-tidal CO_2 gradient[4] during thoracotomy in man.

There is still question as to the role of metabolic factors in the development of the acidosis associated with thoracotomy. Gibbon, *et al.*[6] found an increase of 2.7 mEq./liter in fixed acids in the blood. Theye and Fowler[7] found a decrease in whole blood buffer base of 2–3 mEq./liter in dogs at the time of thoracotomy. Holaday *et al.*[8] suggested that increased CO_2 retention leads to the development of a metabolic acidosis, but his was contradicted by Gibbon.[6]

Measurements have been made on oxygenation of subjects whose lungs were partially atelectatic during operation, but without calculation of pulmonary blood flows.[9–11] These have shown that oxygenation may be maintained at an adequate level. Measurements have been made in animals to evaluate blood flow through an atelectatic lung.[12–16] These agree that blood flow is decreased through the collapsed lung, although the time required for the change has varied according to conditions. A few data are available on attemps to measure blood flow through the atelectatic human lung.[14,17,18] These reports contain data from only five patients, under widely differing conditions.

This paper will present data on the effects of thoracotomy and occlusion of the bronchus to the operated side, on blood gases and ventilatory changes in patients undergoing lobectomy for tuberculosis. Specifically we have attempted to evaluate (1) the magnitude of ventilation-perfusion abnormalities; (2) whether hyperventilation with the maintenance of lower than normal end-tidal CO_2 tensions can prevent CO_2 retention; (3) the magnitude of the

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Received from Division of Anesthesiology and of Research and Laboratories, National Jewish Hospital, University of Colorado Medical Center, Denver, Colorado; accepted for publication August 24, 1965. Supported in part by a grant H-4308 (C1) from the National Heart Institute, U. S. Public Health Service.

metabolic acidosis; and (4) whether occlusion of the bronchus to the operated side is associated with any significant changes in ventilation or blood gases.

Methods

Eleven patients undergoing lobectomy for pulmonary tuberculosis were studied. Selection was made without consideration of age, sex, extent of disease or pulmonary function; but any case considered unusually complicated by either the anesthesiologists or surgeon was omitted.

Ten of the 11 subjects had routine spirometric studies prior to the operation; six had arterial blood studies on the day preceeding surgery. Preanesthetic drug administration usually consisted of 0.4 mg. of atropine and 100 mg. of secobarbital plus 75 mg. of meperidine per 70 kg. of body weight. A Riley needle was inserted into a brachial artery. The lungs were denitrogenated by breathing high flows of oxygen in a semiclosed CO_2 circle absorption system. Anesthesia was induced with thiopental and maintained with intravenous meperidine. *d*-Tubocurarine was used occasionally for relaxation. In order to avoid interference with blood gas studied, an inhalation anesthetic agent was not used at any time. Succinylcholine was given for endobronchial intubation. A Bonica-Hall[19] tube was used, the specific advantage of which is that the entire lumen may be employed for ventilation of only one lung. This markedly diminishes resistance to breathing (as compared, for example, to the Carlens tube) and allows for ease of aspiration of secretions when required. As soon as the cuff on the tube had been inflated the patient was given "demand" oxygen—about 250 ml. per minute and the system was closed. A Liston-Becker breathe-through cell was connected to the endotracheal tube to monitor end-tidal CO_2 and coupled to a direct writing recorder. The cell had a dead space of 40 ml. A Dräger ventilation meter was placed immediately next to the breathe-through cell on the exhalation side to measure tidal and minute ventilation. Ventilation was performed by intermittent manual compression of the reservoir bag so the oscillosopic readings indicated values less than 30 mm. of mercury P_{CO_2}. This required a minimum of 12 liters per minute ventilation with a frequency of 15 to 20 per minute—often twice this value for only one lung. When ventilation of both lungs was performed the endotracheal tube was placed proximal to the carina. When only one lung was ventilated the tube was inserted into a main stem bronchus and the cuff inflated. Proper placement was ascertained by auscultation. To ventilate both lungs again the cuff was deflated, the tube withdrawn from the bronchus to the trachea, and the cuff reinflated. Throughout operation the only gas administered was 100 per cent oxygen.

Arterial blood samples were drawn in heparinized syringes at the following stages:

(1) Controlled respiration, chest closed, both lungs ventilated.

(2) Controlled respiration, chest open, both lungs ventilated, 30 minutes after opening the chest.

(3) Controlled respiration, chest open, the bronchus to the lung of the operated side occluded. Drawing of arterial blood samples was delayed as long as possible to allow maximum removal of oxygen from the non-ventilated lung. To minimize the effect of ligation of blood vessels, ligation was delayed until the point at which the bronchus of the non-ventilated lung was occluded, immediately before removal of the specimen. Generally, the sample was not taken until lobectomy had been performed.

(4) Controlled respiration, chest open, both lungs again ventilated following lobectomy.

An attempt was made to achieve a steady state before blood samples were taken, in general, at least 30 minutes before a sample was drawn.

The following measurements were made on arterial blood: (1) Ca_{O_2} and Ca_{CO_2} in the Van Slyke apparatus; (2) O_2 capacity after equilibration with room air at room temperature and subtracting the amount of dissolved O_2 (estimated from data of

TABLE 1. Preoperative Blood and Respiratory Studies

VC = Vital capacity; FEV_1 = Forced expiratory volume in 1 second; % Pred. = Percentage of predicted volume; FEV% = Percentage of predicted forced expired volume; Pa_{O_2} = Arterial P_{O_2}; Pa_{CO_2} = Arterial P_{CO_2}; $(B_B)_b^+$ = Blood buffer base.

Subject	VC % Pred.	FEV_1 % Pred.	FEV %	O_2 SAT (%)	Pa_{O_2} (mm. Hg)	Pa_{CO_2} (mm. Hg)	$(B_B)_b^+$ (mEq./liter)	*p*H
1	62	48	65	96	64	34	45	7.40
2	72	43	51	93	66	34	46	7.42
3	98	94	81	95	70	40	47	7.37
4	65	68	89	91	63	40	50	7.42
5								
6	104	91	74	94	70	43	48	7.37
7	73	77	89					
8	84	95	96	89	77	45	46	7.33
9	89	87	82					
10	110	96	74					
11	76	54	60					
Confidence limits of normal subjects	74–126	73–127	72.1–97.3	90.8–97.2	78.4–89.6	31.0–39.0	42.8–49.2	7.37–7.45

Sendroy *et al.*[20]; (3) Pa_{CO_2} using a modification of the bubble equilibration technique[21,22]; (4) hematocrit; (5) *p*H and whole blood buffer base $(B_B)_b^+$ from the Singer-Hastings nomogram[23] using Ca_{CO_2}, Pa_{CO_2}, and hematocrit. In some instances *p*H was measured directly with a Cambridge *p*H meter, and the latter values were always within 0.03 of the calculated values with no apparent systematic error.

Estimation of the following parameters to describe ventilation-perfusion relationships in terms of a model: $P^{ac}_{E_{OC_2}}$, $P^{e}_{E_{CO_2}}$, $C^{e}_{a_{O_2}}$, Ca_{O_2}, and $C\bar{v}_{O_2}$. Description of the model is given in the appendix.

The derivations of the equations used for the model are given in considerable detail because of modification of standard terminology.[27]

(1) $P^{ac}_{E_{CO_2}}$ was assumed to be equal to the end-tidal P_{CO_2}.

(2) Ca_{O_2} measured directly from Van Slyke apparatus.

(3) $C\bar{v}_{O_2}$ assumed to be 5 volumes per cent less than Ca_{O_2}. A greater value for $C\bar{v}_{O_2}$ would produce a higher value for the shunt in equation 11 (see appendix). Fuv,p would then be overestimated in equation 15.

(4) $C^{e}_{a_{O_2}}$. Since $FI_{O_2} = 1$, Pa_{O_2} was assumed as the first approximation, to be equal to $P_B - P_{H_2O}$ (47 mm. of mercury) $- Pa_{CO_2}$. The dissolved O_2 in the blood leaving the effective compartment was then calculated from the data of Sendroy *et al.*[20] $C^{e}_{a_{O_2}}$ was considered to be equal to the dissolved O_2 plus the O_2 capacity.

(5) $P^{e}_{E_{CO_2}}$. This measurement is nearly equal to Pa_{CO_2}, but in the presence of a significant right to left shunt, it will be somewhat less than Pa_{CO_2}. $\dot{Q}_a^{salv}/\dot{Q}a$ was calculated from $C^{e}_{a_{O_2}}$, Ca_{O_2}, and $C\bar{v}_{CO_2}$ using equation 11. Substituting Ca_{CO_2} and Cv_{CO_2} in equation 11, $C^{e}_{a_{CO_2}}$ was calculated. $C\bar{v}_{CO_2}$ was assumed to be 4.5 volumes per cent greater than Ca_{CO_2}. $P^{e}_{a_{CO_2}}(P = {}^{e}_{E_{CO_2}})$ was then calculated from the Singer-Hastings nomogram using $C^{e}_{a_{CO_2}}$ and $(B_B)_b^+$. $P^{e}_{E_{CO_2}}$ could then be used to reestimate $P^{e}_{a_{O_2}}$ in the calculation of $C^{e}_{a_{O_2}}$, but there is no difference in the estimate of $C^{e}_{a_{O_2}}$ whether Pa_{CO_2} or $P^{e}_{E_{CO_2}}$ is used in the calculation. The difference between Pa_{CO_2} and $P^{e}_{E_{CO_2}}$ is critical, however, in estimating V_E^{Dalv}/V_E^{ac} with equation 7. If Pa_{CO_2} instead of

TABLE 2. Blood and Respiratory Values at Four Periods During Operation

Subject	Closed					Open					Occluded					Unoccluded				
	Pa_{CO_2} (mm. Hg)	pH	$(B_B)_b^+$ (mEq./liter)	$\dot{V}_E$ (liter/min.)	V_E (liter)	Pa_{CO_2} (mm. Hg)	pH	$(B_B)_b^+$ (mEq./liter)	$\dot{V}_E$ (liter/min.)	V_E (liter)	Pa_{CO_2} (mm. Hg)	pH	$(B_B)_b^+$ (mEq./liter)	$\dot{V}_E$ (liter/min.)	V_E (liter)	Pa_{CO_2} (mm. Hg)	pH	$(B_B)_b^+$ (mEq./liter)	$\dot{V}_E$ (liter/min.)	V_E (liter)
1	29	7.49	47	20.0	.800	45	7.30	43	20.0	.800	46	7.31	44	10.4	.612	40	7.33	43	15.4	.856
2	33	7.40	43	9.5	.594	46	7.28	42	12.0	.706	46	7.31	44	10.0	.667	40	7.35	44	13.9	.662
3	34	7.42	46	14.0	.875	32	7.35	41	11.0	.733	44	7.29	43	12.5	.694	34	7.36	43	12.7	.605
4	50	7.32	46	8.6	.717	77	7.14	41	15.2	.800										
5	21	7.52	43	17.2	.956	28	7.45	44	9.2	.575	21	7.54	44	13.4	.957	22	7.48	42	20.5	1.206
6	55	7.28	46			45	7.28	43	17.2	.956	77	7.10	39	9.9	.495	48	7.24	41	20.0	1.053
7	21	7.56	46	17.6	1.100						27	7.45	43	18.0	.900	29	7.42	43	16.2	.850
8	21	7.53	46			19	7.51	43			25	7.46	44			24	7.47	44		
9	30	7.48	48	13.8	.920	34	7.38	45	13.8	.986	30	7.41	44	14.8	.987	33	7.38	43	13.8	.575
10						30	7.53	51	16.6	.830	24	7.58	50	7.7	1.040	25	7.54	48	10.7	.608
11	28	7.50	49	16.5	.970	34	7.40	45	11.5	.767	31	7.42	47	14.3	.794	33	7.40	45	15.1	1.079
Mean	32.2	7.450	46.0	14.7	.867	39.0	7.362	43.8	14.1	.795	37.0	7.387	44.1	12.3	.794	32.8	7.397	43.6	15.4	.833
S.D.	11.8	.093	1.9	4.0	.159	15.9	.118	3.1	3.5	.125	16.8	.140	2.9	3.2	.188	8.2	.086	1.9	3.2	.223

Chest closed, after opening, ventilation with one bronchus entirely occluded, and after opening both bronchi.
Pa_{CO_2} = Arterial P_{CO_2}; $(B_B)_b^+$ = Blood buffer base; $\dot{V}_E$ = Exhaled volume per minute; V_E = Volume exhaled per breath.

TABLE 3. Oxygen and Carbon Dioxide Values at Four Periods During Operation for Calculation of Ventilation-Perfusion Indices

Subject	Closed					Open					Occluded					Unoccluded				
	$P_{E\overline{CO_2}}$ (mm. Hg)	$P^{ac}_{E\overline{CO_2}}$ (mm. Hg)	$C^{e}_{aO_2}$ (vol. %)	Cao_2 (vol. %)	Cap. (vol. %)	$P^{e}_{E\overline{CO_2}}$ (mm. Hg)	$P^{c}_{E\overline{CO_2}}$ (mm. Hg)	$C^{e}_{aO_2}$ (vol. %)	Cao_2 (vol. %)	Cap. (vol. %)	$P^{e}_{E\overline{CO_2}}$ (mm. Hg)	$P^{ac}_{E\overline{CO_2}}$ (mm. Hg)	$C^{e}_{aO_2}$ (vol. %)	Cao_2 (vol. %)	Cap. (vol. %)	$P^{e}_{E\overline{CO_2}}$ (mm. Hg)	$P^{ac}_{E\overline{CO_2}}$ (mm. Hg)	$C^{e}_{aO_2}$ (vol. %)	Cao_2 (vol. %)	Cap. (vol. %)
1	27	22	20.07	19.04	18.42	40	27	20.31	19.22	18.70	44	32	20.03	19.29	18.43	39	26	19.58	18.83	17.96
2	33	19	18.29	18.15	16.65	45	23	19.02	18.59	17.42	45	28	19.24	18.53	17.64	39	24	20.37	19.65	18.76
3	32	26	20.64	19.55	19.00	30	20	20.52	19.64	18.88	40	32	20.58	18.82	18.97	33	23	20.45	19.80	18.81
4	49	40	20.62	20.04	19.03	75	34	21.46	20.35	19.33										
5	20	16	19.40	18.62	17.72	26	21	20.37	19.28	18.71	18	16	20.34	18.76	18.66	21	14	20.52	19.98	18.88
6	53	36				43	27				75	40				47	25			
7	20										25	15				28	18			
8	20	15	23.68	23.12	22.00	17	15	23.77	22.80	22.09	22	15	23.35	21.94	21.68	23	13	22.92	22.59	21.25
9	29	21	23.42	22.79	21.77	33	20	23.32	22.87	21.68	29	20	22.83	22.21	21.18	31	20	22.91	21.99	21.27
10						28	18	21.45	20.44	19.80	22	18	21.37	20.38	19.70	24	16	20.91	20.19	19.24
11	26	18	24.16	23.30	22.50	32	18	24.42	23.67	22.78	29	18	24.52	23.54	22.87	32	18	22.88	22.15	21.24
Mean	30.9	23.6	21.29	20.58	19.64	36.9	22.3	21.63	20.76	20.00	34.9	23.3	21.53	20.43	19.89	31.7	19.9	21.32	20.65	19.68
S.D.	11.7	8.8	2.18	2.14	2.18	15.8	5.6	1.82	1.76	1.81	17.0	8.8	1.84	1.91	1.82	8.2	4.6	1.37	1.39	1.35

$P^{e}_{E\overline{CO_2}}$ = Effective exhaled $P_{\overline{CO_2}}$; $P^{ac}_{E\overline{CO_2}}$ = Alveolar $P_{\overline{CO_2}}$ (end-tidal); $C^{e}_{aO_2}$ = Effective arterial oxygen concentration; Cao_2 = Arterial concentration of oxygen; Cap = Oxygen carrying capacity of the blood.

TABLE 4. Ventilation-Perfusion Indices at Four Periods During Operations

Subject	Closed					Open					Occluded					Unoccluded				
	$\frac{V_E^{Dalv}}{V_E^{ac}}$	$\frac{\dot{Q}_a^{Salv}}{\dot{Q}a}$	Fv,p	Fup,v	Fuv,p	$\frac{V_E^{Dalv}}{V_E^{ac}}$	$\frac{\dot{Q}_a^{Salv}}{\dot{Q}a}$	Fv,p	Fup,v	Fuv,p	$\frac{V_E^{Dalv}}{V_E^{ac}}$	$\frac{\dot{Q}_a^{Salv}}{\dot{Q}a}$	Fv,p	Fup,v	Fuv,p	$\frac{V_E^{Dalv}}{V_E^{ac}}$	$\frac{\dot{Q}_a^{Salv}}{\dot{Q}a}$	Fv,p	Fup,v	Fuv,p
1	0.19	0.17	0.70	0.16	0.14	0.33	0.18	0.58	0.29	0.13	0.28	0.13	0.65	0.25	0.10	0.33	0.13	0.61	0.30	0.09
2	0.42	0.03	0.57	0.41	0.02	0.49	0.08	0.49	0.47	0.04	0.38	0.12	0.57	0.35	0.08	0.38	0.13	0.57	0.35	0.08
3	0.19	0.18	0.69	0.16	0.15	0.33	0.15	0.60	0.29	0.11	0.21	0.26	0.62	0.17	0.22	0.30	0.12	0.64	0.28	0.08
4	0.18	0.10	0.75	0.17	0.08	0.55	0.18	0.41	0.50	0.09										
5	0.19	0.13	0.72	0.17	0.11	0.27	0.18	0.63	0.23	0.14	0.11	0.24	0.70	0.08	0.22	0.33	0.10	0.62	0.31	0.07
6	0.32					0.37					0.47					0.47				
7											0.40					0.36				
8	0.25	0.10	0.69	0.23	0.08	0.12	0.16	0.75	0.11	0.14	0.32	0.22	0.58	0.27	0.15	0.36	0.06	0.61	0.35	0.04
8	0.28	0.11	0.66	0.26	0.08	0.39	0.08	0.58	0.27	0.05	0.31	0.11	0.57	0.25	0.18	0.35	0.16	0.58	0.31	0.11
10						0.36	0.17	0.57	0.32	0.11	0.18	0.17	0.71	0.15	0.15	0.33	0.13	0.61	0.30	0.09
11	0.31	0.15	0.61	0.28	0.11	0.44	0.17	0.50	0.40	0.10	0.38	0.16	0.56	0.33	0.11	0.44	0.13	0.51	0.41	0.08
Mean	0.293	0.121	0.674	0.230	0.096	0.405	0.150	0.568	0.331	0.101	0.354	0.176	0.629	0.231	0.150	0.384	0.120	0.594	0.326	0.080
S.D.	0.072	0.048	0.059	0.087	0.041	0.096	0.041	0.096	0.121	0.036	0.084	0.036	0.060	0.092	0.053	0.044	0.029	0.049	0.042	0.020

V_E^{Dalv} = Volume of alveolar dead space gas; V_E^{ac} = Alveolar component of expired gas; $\dot{Q}_a^{Salv}$ = Blood flow to systemic arteries from the alveolar shunt; $\dot{Q}a$ = Arterial blood flow; Fv,p = Fraction of lung both ventilated and perfused; Fup,v = Unperfused but ventilated fraction of the lung; Fuv,p = Unventilated but perfused fraction of the lung.

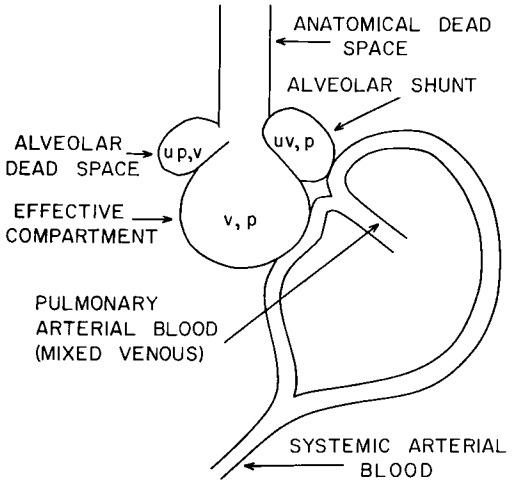

FIG. 1. Alveolar-perfusion relations. uv,p = unventilated but perfused; up,v = unperfused but ventilated; v,p = ventilated and perfused.

$P^{e}_{E_{CO_2}}$ is used in equation 7, the presence of a significant $\dot{Q}_a^{salv}/Q_a$ will cause a considerable overestimation of V_E^{Dalv}/V_E^{ac}. This would also be true if a greater value is assumed for $C\bar{v}_{CO_2}$.

Results

Table 1 lists the preoperative laboratory measurement on the 11 subjects. The figures underlined indicate that the measurement was more than 2 standard deviations removed from the mean value determined on 24 normal subjects, ranging in age from 20 to 67 years, studied in our laboratory (elevation 5,000 feet above sea level) during the same period of time. The vital capacity (VC) and the forced expiratory volume in the first second after full inspiration (FEV_1) are given as percentage of the predicted value from a regression equation relating the measurement to height determined on the 24 normal subjects without consideration of age or sex. FEV percentage is the ratio of FEV_1 to VC times 100. Included in the table are the 95 per cent confidence limits of the measurement on the 24 normal subjects.

Measurements of Pa_{CO_2}, *p*H, $(B_B)_b^+$, $\dot{V}_E$, and V_E are presented in table 2. The data necessary for the estimation of the ventilation-perfusion indices are given in table 3, and the ventilation-perfusion indices are given in table 4.

Differences Among Stages of Operation. To determine whether differences among the various stages of operation were significant and individual changes were considered rather than the pooled data because of the marked differences among subjects. The probability that a mean change occurred by chance alone was estimated by the *t* test for paired variates.

There was a significant decrease in *p*H ($P < 0.01$) and $(B_B)_b^+$ ($P < 0.01$) when the thorax was opened (table 2). No significant changes occurred in these measurements when the bronchus to the operated side was occluded or later opened. No significant changes in Pa_{CO_2} for the group as a whole occurred among the various stages.

Fup,v (fraction of total alveoli ventilated but not perfused) increased significantly when the thorax was opened ($P < 0.05$), decreased significantly when the bronchus to the operated side was occluded ($P < 0.05$), and increased again when the bronchus was opened. Fuv,p (fraction of alveoli perfused but unventilated) showed no change on opening the thorax, but increased significantly when the bronchus to the operated side was occluded ($P < 0.05$) and decreased when it was opened ($P < 0.01$). Fv,p (fraction of alveoli both perfused and ventilated) showed a significant decrease when the thorax was opened ($P < 0.05$), but did not change when the bronchus to the operated side was occluded or later opened.

Blood-gas Relationships as a Whole. There was a highly significant negative correlation between *p*H and Pa_{CO_2}. No subject with a Pa_{CO_2} equal to or less than 30 mm. of mercury had a *p*H less than 7.42; no subject with a Pa_{CO_2} greater than 40 mm. of mercury had a *p*H greater than 7.32. There was a significant negative correlation between $(B_B)_b^+$ and Pa_{CO_2} of -0.43 ($P < 0.01$). A highly significant correlation was found between $P^{ac}_{E_{CO_2}}$ (end-tidal P_{CO_2}) and Pa_{CO_2} (fig. 2), and there was a high degree of correlation between $P^{ac}_{E_{CO_2}}$ and *p*H.

There was no correlation between $\dot{V}_E$ and either Pa_{CO_2} or pH. There was, however, a positive correlation between V_E and pH (+0.40, $P < 0.02$) and a negative correlation between V_E and Pa_{CO_2} (−0.38, $P < 0.05$).

Discussion

Use of the Model. The division of the lung into three compartments representing the extremes of the relations between ventilation and perfusion has been used extensively to evaluate the distribution of perfusion and ventilation.[24,25] Although "percentage alveolar dead space"[25] is quite similar to V_E^{Dalv}/V_E^{ac}, there are two significant differences in our use of the latter term as an index to distribution of blood flow.

First, we used *effective* P_{CO_2} rather than arterial P_{CO_2} in the calculation of V_E^{Dalv}/V_E^{ac}. When arterial P_{CO_2} is used, nonventilated alveoli contribute "percentage alveolar dead space,"[25] the result of shunting mixed venous into arterial blood.

Since Pa_{CO_2} is approximately equal to P_{ECO_2}, equation 7 (see appendix) can be written

$$Pa_{CO_2} \cong \left[\frac{1}{1 - V_E^{Dalv}/V_E^{ac}}\right] P_{ECO_2}^{ac} \quad (16)$$

If V_E^{Dalv}/V_E^{ac} has a relatively normal distribution, which is not an unlikely assumption (fig. 3), the regression line through the data in figure 2 is estimated by taking the mean values of $V_E^{Dalv}/V_E^{ac} \pm 2$ standard deviations in equation 16. The scatter of the points suggests that $P_{ECO_2}^{ac}$ is a much more reliable indicator of Pa_{CO_2} when $P_{ECO_2}^{ac}$ is low than when it is high.

Equation 16 can be arranged to

$$Pa_{CO_2} - P_{ECO_2}^{ac} \cong \left[\frac{V_E^{Dalv}/V_E^{ac}}{1 - V_E^{Dalv}/V_E^{ac}}\right] P_{ECO_2}^{ac} \quad (17)$$

This equation suggests that the difference between Pa_{CO_2} and $P_{ECO_2}^{ac}$ (the so-called aA CO_2 difference) should be correlated with $P_{ECO_2}^{ac}$. Such a relationship was indeed found (fig. 4) with a correlation coefficient of 0.61 ($P < 0.001$). Again the

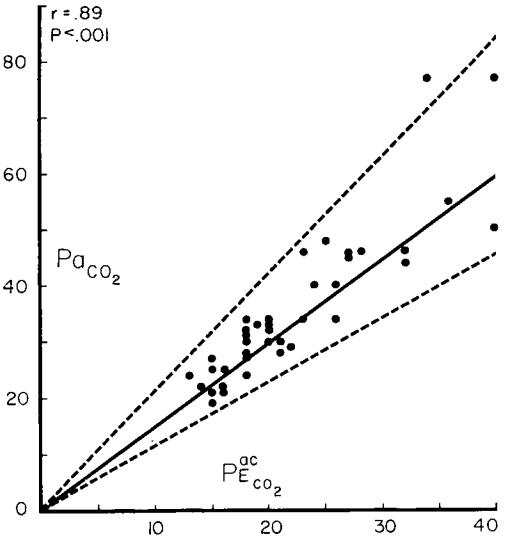

FIG. 2. Comparison of end-tidal versus arterial P_{CO_2}. Pa_{CO_2} = Arterial P_{CO_2}; $P_{ECO_2}^{ac}$ = P_{CO_2} from the alveoli contained in exhaled gas.

regression line and confidence limits were calculated by substituting mean $V_E^{Dalv}/V_E^{ac} \pm 2$ standard deviations in equation 17. The scatter of the points suggests that the aA CO_2 difference cannot be used as an indicator of the degree of alveolar dead space ventilation without consideration of the level of the $P_{ECO_2}^{ac}$. A small difference can be compatible with a large alveolar

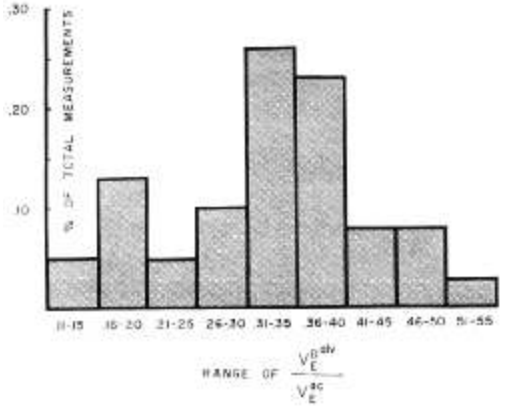

FIG. 3. Distribution of ratios of alveolar dead space to alveolar component. V_E^D = Dead space component of exhaled air; V_E^{ac} = Alveolar component of exhaled air.

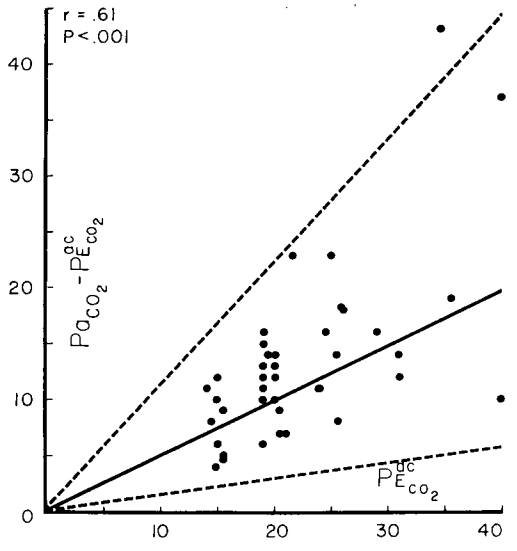

FIG. 4. aA CO_2 difference correlated with end-tidal P_{CO_2}. Pa_{CO_2} = Arterial P_{CO_2}; $P^{ac}_{ECO_2}$ = P_{CO_2} from alveoli which is found in exhaled air.

dead space ventilation when $P^{ac}_{ECO_2}$ is low and vice versa.

Second, we did not use V_E^{Dalv}/V_E^{ac} itself as the index of the fraction of total alveoli which are unperfused with blood, but considered V_E^{Dalv}/V_E^{ac} as the ratio of unperfused alveoli to total alveoli minus the unventilated alveoli. If the fraction of unperfused alveoli remained constant, but there was a significant decrease in the fraction of unventilated alveoli, V_E^{Dalv}/V_E^{ac} would decrease (and "percentage alveolar dead space even more so), and one would be in error to interpret this decrease as the result of a change in the distribution of blood flow. Therefore, our estimation of Fup,v takes into consideration both V_E^{Dalv}/V_E^{ac} and $\dot{Q}_a^{salv}/\dot{Q}a$. Similarly, estimation of Fuv,p takes into consideration both ratios. Workman[26] suggests that these considerations have importance in relating changes in blood flow to changes in ventilation.

Unevenness of ventilation-perfusion ratios will create a rise in calculated Fuv,p and Fup,v even though there are no areas of the lungs not perfused or ventilated. Nevertheless, a recent theoretical analysis[28] suggests that the magnitude of the calculated Fuv,p is principally determined by the degree of unevenness of ventilation in different parts of the lungs and is affected very little by unevenness of perfusion. On the other hand, the magnitude of the calculated Fup,v is determined principally by the degree of the unevenness of perfusion and is affected little by unevenness of ventilation. From the standpoint of maintenance of normal Pa_{CO_2} during anesthesia it is irrelevant whether there is a true alveolar dead space or whether there is marked variability in distribution of blood flow. In ether case total ventilation must be increased, and there is no practical need for distinguishing between these two situations.

In this study the problem of the interpretation of Fuv,p is somewhat less complicated than Fup,v since the subjects were breathing 100 per cent O_2. Under these conditions, the magnitude of the calculated Fuv,p is essentially determined only by the number of atelectatic alveoli which are perfused. A spectrum of ventilation-perfusion ratios throughout the lungs should not give rise to a measurable Fuv,p. In addition, an area completely unventilated, but still containing O_2, will not affect the calculated Fuv,p.

Influence of Type of Patient and Effect of Anesthesia and Controlled Respiration. Although it was not the aim of this investigation to study the effects of anesthesia and controlled ventilation *per se*, the analysis of the data suggests that the subjects of this study while on controlled respiration had marked abnormalities of distribution of blood flow and ventilation even before operation began. It is likely that anesthesia, controlled ventilation, and the lateral decubitus position contributed to these findings.[29–32] It must be emphasized, however, that the patients as a group were not normal subjects when studied in the unanesthetized state. Five of the 10 patients with spirometric studies preoperatively gave data outside the normal range. All 6 patients who had arterial blood studies prior to operation had abnormally low oxygen tensions, and 4 of the 6 had abnormally high CO_2 tensions.

Effect of Thoracotomy on Bronchial Occlusion. The abnormalities of distribution of blood flow and ventilation prior to operation became more marked when thoracotomy was performed. The increases in Fup,v and Fv,p suggest that there was an increase in poorly perfused areas of the lung at the time of thoracotomy. These findings are compatible with those of Rehder (32) in healthy dogs and Nunn *et al.*[33] in human subjects with minimal pulmonary disease. Stead *et al.*[3] observed greater changes at thoracotomy in patients who were more nearly comparable to ours. The ratio of dead space to tidal volume of 0.46 in their subjects rose to 0.62 on thoracotomy. A ratio of greater than 0.30 is probably the result of alveolar dead space added to normal anatomical dead space.[34]

Our findings of a significant decrease in Fup,v when the bronchus to the exposed side was occluded and the subsequent increase when the bronchus was opened indicate that the increased alveolar dead space may be principally on the exposed side. Nunn[30] made a similar suggestion. Thoracotomy is associated with increased ventilation of the exposed as compared to the unexposed side.[35–37] Although the blood flow tends to increase with ventilation in thoracotomized dogs, it does not do so to the same extent as the ventilation, leading to a greater ventilation-perfusion ratio in the exposed side.[37] To account for the magnitude of the findings in the present study one must postulate the presence of a significant proportion of the lungs with little perfusion.[34] Recent studies by West and Dollery[38] and a theoretical analysis by Permutt *et al.*[39] suggest that conditions exist in which an increase in alveolar pressure can cause cessation of perfusion of the upper portions of a lung, even when total blood flow is unchanged or increased. The combination of increaaed alveolar pressure and the situation in the uppermost position of the exposed lung of our subjects could combine to produce this situation.

The increase of Fuv,p on occlusion of the bronchus was unquestionably the result of development of atelectasis in the occluded lung. The increase was small even though an entire lung was not ventilated. One cannot assume that the lung was entirely atelectatic at the time the blood samples were obtained. It has already been pointed out that nonventilated but nonatelectatic areas would not cause an alveolar shunt in the presence of pure oxygen as the inspired gas. Even if the occluded lung were entirely atelectatic, it is quite likely that the blood flow may have been considerably reduced, thereby tending to reduce the magnitude of the alveolar shunt.[13] The increased shunt was of no clinical significance; 3 subjects showed mild desaturation of arterial blood, but even in these cases the saturation was greater than 96 per cent, higher than the preoperative values for these patients.

It would appear that there are no untoward effects of bronchial occlusion during breathing of 100 per cent oxygen so long as the total volume of ventilation is maintained. In fact, it is possible that some improvement in gas exchange can occur if the occluded lung contributes more than 50 per cent of the alveolar dead space. Indeed, since the Fup,v diminished on occlusion of one bronchus, a patient might have, better ventilation throughout operation if he had only one lung ventilated, *i.e.*, if endobronchial rather than endotracheal intubation were employed continuously. This would appear to be true even though Fuv,p increased on occlusion of the bronchus to the operated side.

There was a significant reduction in $(B_B)_b^+$ accompanying thoracotomy. Eight of 9 subjects in which paired observations could be made showed a decrease. This decrease was not great and in no instance was it greater than 5 mEq./liter, on the average was only 2.2 mEq./liter. The present study shed no light on possible causes of the decrease at the time of thoracotomy. There was a significant negative correlation between $(B_B)_b^+$ and Pa_{CO_2} for the study as a whole, compatible with the findings of Holaday *et al.*[8]; but the change in Pa_{CO_2} at the time of thoracotomy appears insufficient to account for the $(B_B)_b^+$ change.

Summary

Eleven patients undergoing lobectomy were studied to determine ventilation-perfusion abnormalities, the extent of metabolic acidosis, and the blood gas changes which might occur during the procedure including period when one main bronchus was occluded. Anesthesia was maintained with intravenous agents so that the lungs could be ventilated with 100 per cent oxygen.

A discussion of the lung as a three-compartment system was presented, the three compartments being: (1) ventilated-unperfused, (2) ventilated-perfused, and (3) perfused unventilated sections, and calculations of blood gas exchanges were made on this basis.

When the thorax was opened a decrease in *p*H (7.45 to 7.36) ($P < 0.01$) and blood buffer base (46.0 to 43.8, $P < 0.01$) occurred. The fraction of the lungs which were ventilated but not perfused increased on opening the thorax (0.23 to 0.33, $P < 0.5$), but this diminished significantly (0.33 to 0.23, $P < 0.05$) when the bronchus to the operated side was occluded. The perfused but unventilated fraction of the lungs rose from 0.096 to 0.101 ($P < 0.05$) on opening the chest, and increased further to 0.15 ($P < 0.01$) on occlusion of the bronchus; this fell to 0.08 on release of occlusion. The ventilated and perfused (effective) fraction of the lung dropped from 0.67 to 0.57 ($P < 0.05$) on thoracotomy. There was an increase to 0.63 on occlusion of the bronchus ($P > 0.05$).

By increasing the minute volume of ventilation it was possible to maintain normal blood gas concentration when only one lung was being ventilated.

Appendix

Symbols

General Variables

V	gas volume
$\dot{V}$	gas volume per unit time (gas flow)
$\dot{Q}$	blood volume per unit time (blood flow)
P	gas pressure or partial pressure
F	fraction; fractional concentration of gas in dry gas phase or fraction of total alveoli.
C	concentration of gas in blood
N	total number of alveoli
$(BB)_b^+$	whole blood buffer base

Subscripts

p	alveoli which are perfused with blood
v	alveoli which are ventilated
up	alveoli which are unperfused with blood
uv	alveoli which are unventilated
E	expired gas
I	inspired gas
a	arterial blood
O_2	oxygen
CO_2	carbon dioxide
$\bar{v}$	mixed venous blood (blood from pulmonary artery)
B	barometric

Superscripts

ac	alveolar component
D	dead space
anat	anatomical
alv	alveolar
e	effective
i	individual alveolus
s	shunt

Model for Analysis of Ventilation-Perfusion Relations

Consider a lung divided into alveoli and anatomical dead space. Consider the alveoli further divided into three distinct compartments; a compartment in which alveoli are ventilated, but not perfused with blood; a compartment in which alveoli are evenly ventilated and perfused; and a compartment in which alveoli are perfused, but not ventilated (fig. 1). Let each ventilated alveolus have equal ventilation and each perfused alveolus have equal perfusion. Let Fup,v = fraction of total alveoli which are ventilated, but unperfused; Fv,p = fraction of total alveoli which are both perfused and ventilated; and Fuv,p = fraction of total alveoli

which are perfused, but unventilated. Thus

$$F_{up,v} + F_{v,p} + F_{uv,p} = 1 \quad (1)$$

The v,p compartment is called the *effective* compartment since this is the only area in which gas exchange can occur. It is assumed that the gas expired from this compartment has *effective* partial pressures ($P^e_{E\bar{C}O_2}$ and $P^e_{E\bar{C}_2}$) and that these partial pressures are exactly equal to the mean partial pressures in the blood which reaches the systmic arteries from the effective compartment ($P^e_{a\bar{C}O_2}$ and $P^e_{a\bar{O}_2}$). Thus no end gradient for diffusion is present and cyclical changes with respiration are ignored.

During a single expiration, the first air to leave the mouth or nose is from the anatomical dead space, and its composition is virtually the same as that of inspired air. When inspired air has been washed out of the dead space, the alveolar component of the expired gas follows. The volume expired in a single breath (V_E) is thus made up of an alveolar component (V_E^{ac}) and an anatomical dead space component (V_E^{Danat}). Thus

$$V_E = V_E^{ac} + V_E^{Danat} \quad (2)$$

The alveolar component of the expired gas is itself a mixture of gas from the effective compartment and from the compartment which is ventilated but unperfused. Hence

$$V_E^{ac} = V_E + V_E^{Dalv} \quad (3)$$

where V_E^{Dalv} = volume of "alveolar dead space" gas contributed to the expired volume from the up,v compartment and V_E^e = volume of gas contributed to the expired gas from the *effective* compartment.

The amount of CO_2 per breath contributed from all alveoli to the expired gas must be the product of the fractional concentration of CO_2 in the alveolar component of the expired gas and the volume of the alveolar component of the expired gas. Furthermore, this product must be equal to the total amount of CO_2 expired per breath, since no CO_2 is expired from the anatomical dead space (assuming inspired CO_2 = 0). Thus

$$V_{E\bar{C}O_2} = V_E^{ac} F^{ac}_{E\bar{C}O_2} \quad (4)$$

On the other hand, the only source of CO_2 in the expired gas is from the effective compartment,* since all alveolar-capillary gas exchange takes place here, and it follows that

$$V_{E\bar{C}O_2} = V_E^e F^e_{E\bar{C}O_2} \quad (5)$$

From equations 4 and 5

$$V_E^{ac} F^{ac}_{E\bar{C}O_2} = V_E^e F^e_{O\bar{C}_2} \quad (6)$$

Substituting V_E^e from equation 3 in equation 6 and rearranging terms yields

$$\frac{V_E^{Dalv}}{V_E^{ac}} = \frac{P^e_{E\bar{C}O_2} - P^{ac}_{E\bar{C}O_2}}{P^e_{E\bar{C}O_2}} \quad (7)$$

Let V_E^1 = volume of gas that an individual alveolus contributes to the expired gas and N = total number of ventilated alveoli. It follows that

$$\frac{V_E^{Dalv}}{V_E^{ac}} = \frac{V_E^{Dalv}}{V_E^e + V_E^{Dalv}}$$

$$= \frac{(F_{up,v})(N)(V_E^1)}{(F_{v,p})(N)(V_E^1) + (F_{up,v})(N)(V_E^1)}$$

$$= \frac{F_{up,v}}{F_{v,p} + F_{up,v}}$$

Hence

$$\frac{V_E^{Dalv}}{V_E^{ac}} = \frac{F_{up,v}}{F_{v,p} + F_{up,v}} \quad (8)$$

The arterial blood, like the expired gas, is a mixture. It is made up predominantly of blood from the alveolar capillaries called the alveolar component of the arterial blood. To this is added a small amount of venous blood from the bronchial and Thebesian vessels. In the model shown in figure 1, we have assumed that the arterial blood comes only from alveolar capillaries; hence, $\dot{Q}_a = \dot{Q}_a^{ac}$, where $\dot{Q}_a$ equals volume of blood entering systemic flow per unit time and $\dot{Q}_a^{ac}$ equals

* Even though all gas exchange with the blood takes place in the effective compartment, some of the alveolar component of the expired gas is inhaled from the anatomical dead space into the unperfused compartment at the beginning of each breath. Thus, the expired gas contains a small amount of CO_2 from the unperfused compartment. We shall neglect this small contribution from the alveolar dead space and assume that all the CO_2 in the expired gas comes from the effective compartment.

that part of the systemic blood flow derived from alveoli. The alveolar component of the arterial blood is a mixture of blood leaving the effective compartment and the compartment which is perfused, but unventilated. Therefore,

$$\dot{Q}a = \dot{Q}_a^{ac} = \dot{Q}_a^{e} + \dot{Q}_a^{Salv} \quad (9)$$

where $\dot{Q}_a^{e}$ equals blood flow contributed to the systemic arteries from the effective compartment and $\dot{Q}_a^{Salv}$ equals blood flow contributed to the systemic arteries from the "alveolar shunt."

The volume of O_2 entering the systemic arteries per unit time must be the product of the arterial blood flow and the concentration of oxygen in the systemic arteries; hence,

$$\dot{V}a_{O_2} = \dot{Q}aCa_{O_2}$$

The oxygen entering the systemic arteries comes from two sources (assuming no anatomical shunt): (1) from the uv,p compartment in an amount equal to $\dot{Q}_a^{Salv}C\bar{v}_{O_2}$, where $C\bar{v}_{O_2}$ equals concentration of oxygen in the mixed venous blood, and (2) from the effective compartment in an amount equal to $\dot{Q}_a^{e}Ca_{O_2}^{e}$, where $Ca_{O_2}^{e}$ equals concentration of oxygen entering systemic arteries from the effective compartment. Hence,

$$\dot{V}a_{O_2} = \dot{Q}_a^{Salv}C\bar{v}_{O_2} + \dot{Q}_a^{e}Ca_{O_2}^{e}$$

and

$$\dot{Q}aCa_{O_2} = \dot{Q}_a^{Salv}C\bar{v}_{O_2} + \dot{Q}_a^{e}Ca_{O_2}^{e} \quad (10)$$

Since $\dot{Q}_a^{e} = \dot{Q}a - \dot{Q}_a^{Salv}$ (equation 9), equation 10 can be written

$$\dot{Q}aCa_{O_2} = \dot{Q}_a^{Salv}Co\bar{v}_2 + (\dot{Q}a - \dot{Q}_a^{Salv})Ca_{O_2}^{e}$$

and rearranging terms becomes

$$\frac{\dot{Q}_a^{Salv}}{\dot{Q}a} = \frac{Ca_{O_2}^{e} - Ca_{O_2}}{Ca_{O_2}^{e} - C\bar{v}_{O_2}} \quad (11)$$

If $\dot{Q}_a^{l}$ equals blood flow contributed to the systemic arteries from an individual alveolus,

$$\frac{\dot{Q}_a^{Salv}}{\dot{Q}a} = \frac{\dot{Q}_a^{Salv}}{\dot{Q}_a^{e} + \dot{Q}_a^{Salv}}$$

$$= \frac{(Fuv,p)(N)(\dot{Q}_a^{l})}{(Fv,p)(N)(\dot{Q}_a^{l}) + (Fuv,p)(N)(\dot{Q}_a^{l})}$$

$$= \frac{Fuv,p}{Fv,p + Fuv,p}$$

Hence,

$$\frac{\dot{Q}_a^{Salv}}{\dot{Q}a} = \frac{Fuv,p}{Fv,p + Fuv,p} \quad (12)$$

Fuv,p, Fup,v, and Fv,p can now be specified by solving simultaneously equations 1, 8, and 12:

$$Fv,p = \frac{1 - V_E^{Dalv}/V_E^{ac} - \dot{Q}_a^{Salv}/\dot{Q}a + (V_E^{Dalv}/V_E^{ac})(\dot{Q}_a^{Salv}/\dot{Q}a)}{1 - (V_E^{Dalv}/V_E^{ac})(\dot{Q}_a^{Salv}/\dot{Q}a)} \quad (13)$$

$$Fup,v = \frac{V_E^{Dalv}/V_E^{ac} - (V_E^{Dalv}/V_E^{ac})(\dot{Q}_a^{Salv}/\dot{Q}a)}{1 - (V_E^{Dalv}/V_E^{ac})(\dot{Q}_a^{Salv}/\dot{Q}a)} \quad (14)$$

$$Fuv,p = \frac{\dot{Q}_a^{Salv}/\dot{Q}a - (V_E^{Dalv}/V)_E^{ac}(\dot{Q}_a^{Salv}/\dot{Q}a)}{1 - (V_E^{Dalv}/V_E^{ac})(\dot{Q}_a^{Salv}/\dot{Q}a)} \quad (15)$$

Thus, Fv,p, Fup,v, and Fuv,p can be calculated when V_E^{Dalv}/V_E^{ac} and $\dot{Q}_a^{Salv}/\dot{Q}a$ are given. These two ratios can be calculated from equations 7 and 11 when $P_{ECO_2}^{ac}$, $P_{ECO_2}^{e}$, Ca_{O2}, $Ca_{O_2}^{e}$, and $C\bar{v}_{O_2}$ are given. Equations 13, 14 and 15 are applicable only when FI_{CO_2} equals 0 and $\frac{\dot{Q}_a^{Sanat}}{\dot{Q}a}$ is negligible.

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HYPERBARIA In 107 infants with congenital heart disease undergoing operation under hyperbaric conditions, a decrease in lactate-pyruvate ratio occurred in the majority of patients if systemic pressure and cardiac output were maintained. This change was indicative of an increase in the available molecular oxygen, permitting combustion of anaerobic substrates to carbon dioxide and water. Following a return to normobaric conditions, final values for plasma lactate and pyruvate depended entirely upon the maintenance of adequate circulation and tissue oxygenation. Patients who developed ventricular fibrillation during operation maintained a high lactic acid concentration despite hyperbaric oxygenation. Increased arterial oxygen tension under hyperbaric conditions is of little value without the maintenance of satisfactory central and peripheral circulation. (*Bernhard, W. C., and others: Metabolic Alterations Noted in Cyanotic and Acyanotic Infants During Operation Under Hyperbaric Conditions, J. Thor. Cardiov. Surg. 50: 374 (Sept.) 1965.*)

HEPATIC TOXICITY Wide pH variation occurred with spontaneous respiration in patients anesthetized with methoxylflurane. Excess base decreased with low tidal exchange, but returned to normal within 3 days after operation. During methoxyflurane nitrous oxide anesthesia, 70 per cent retention of bromsulphaphthalein was observed at 30 minutes and 5 per cent at 120 minutes. Changes in alkaline phosphatase levels were minimal during and after surgery. Liver biopsies showed slight changes. However, S.G.O.T. and G.P.T. values increased significantly in some cases after surgery. Therefore, hepatic failure might possibly be induced by methoxyflurane administration. In 50 cases of methoxyflurane anesthesia, 6 per cent evidenced acute hepatitis among 67 cases of halothane anesthesia, 1 case (1.5 per cent) showed evidence of hepatic failure. (*Kawashima, K., and others: Influence of Methoxyflurane and Halothane Anesthesia on Liver Function and Acid-base Balance (Japanese), Jap. J. Anaesth. 140: 380, 1965.*)