Measurement of Mixed Venous Oxygen Tension in Premature Infants by a Rebreathing Method

A. N. KRAUSS^[16], AND P. A. M. AULD

Department of Pediatrics, Cornell University Medical College, New York, New York, USA

Extract

The CO₂ and oxygen tensions of mixed venous blood were determined by the rebreathing method of Cerretelli *et al.* in a group of 21 low birth weight infants. Venous P_{O₂} ranged from 10 to 43 mm Hg, with a mean of 28 mm Hg, and showed no tendency to change with size or age. Cardiac output was calculated from these data according to the Fick principle. Values of 50-100 ml/min/kg were obtained in newborn low birth weight infants; these rise with age to 300-500 ml/min/kg, at which time they are comparable with term infants.

Speculation

The method described herein is practical, simple, and accurate. It provides further quantitative data to characterize healthy and distressed newborns with regard to cardiac output and $\dot{V}A/\dot{Q}$ relations.

Introduction

The recent development of bloodless techniques for measurement of mixed venous oxygen tension is an important development. In this method, the lung is used as an aeronometer to equilibrate alveolar gas and mixed venous blood. The oxygen and carbon dioxide tensions of this gas are continuously sampled. When no further transfer of gas between blood and gas phases occurs, the gas in the rebreathing bag is in equilibrium with the mixed venous blood. The identity between mixed venous oxygen and alveolar gas tensions during rebreathing has been verified by Cerretelli *et al.* [3] and Denison *et al.* [4]. The study reported herein used the method of Cerretelli and co-workers [2] as modified by Farhi and co-workers [8].

Materials and Methods

The subjects were 21 newborn infants ranging in age from 4 hr to 60 days and with birth weights from 1050 g

to 3600 g. Infants 13 and 15 were small for dates; all the others were the appropriate weight for the gestational age. All were healthy at the time of study. Infants 11 and 14 received transfusions because of anemia. The tests were carried out with the infants swaddled in blankets to maintain body temperature. First, arterial blood was obtained from the temporal or right radial artery with the infant at rest, and pH, P_{CO₂}, and P_{O₂} were determined [12]. The values obtained were corrected to the infant's body temperature. Immediately following, end-tidal CO₂ (P_{ACO₂}) was determined with a rapid response infrared CO₂ meter [13].

To obtain mixed venous P_{CO₂} (P $\bar{V}$ CO₂) and P_{O₂} (P $\bar{V}$ O₂), the infant rebreathed from a bag containing 75-125 ml of a gas mixture of 8% CO₂ in nitrogen. During rebreathing, gas was sampled from the bag at a rate of 100 ml/min, first through a microcuvette containing a Clark oxygen electrode [12] and then through an infrared CO₂ analyzer. The two systems were in series and the signals from each were recorded on a Sanborn

recorder. The oxygen electrode was covered with a 3- μ Teflon membrane to increase the response time (90 % response time less than 1 sec). This membrane was stable for at least 30 min at 37°. The linearity of the system was established.

During the test, equilibrium between pulmonary venous blood and alveolar gas was achieved when a plateau was recorded for O₂ and CO₂ (Fig. 1). The values presented for $\bar{P}_{\text{vCO}_2}$ and $\bar{P}_{\text{vO}_2}$ are the average of three runs which varied by less than 0.5 %. A 5-min rest period was allowed between each run, during which time the calibration of the oxygen electrode was rechecked. The entire procedure required less than 30 min and no ill effects were noted. If no plateau for either P_{O₂} or P_{CO₂} was obtained within 10 sec, the run was rejected. This period of time was believed to be well within the recirculation time for these subjects.

Evaluation of the Method

The theoretical and practical limitations of measuring $\bar{P}_{\text{vO}_2}$ and $\bar{P}_{\text{vCO}_2}$ have been discussed by Cerretelli *et al.* [2] and Farhi and Haab [7]. A large a-ACO₂ gradient with concurrent large dead space/tidal volume ratios may result in a delayed or elevated plateau for CO₂. This is not a problem with oxygen because of the relative slopes of the dissociation curves for CO₂ and oxygen. Recirculation may occur before a plateau is reached. This occurs in situations in which cardiac output is elevated or in which respiratory rate during rebreathing is slow. If a diffusion barrier exists, the achievement of an oxygen plateau may be delayed. This is important for oxygen because of the low tensions involved.

Cerretelli *et al.* [3] and Denison *et al.* [4] have demonstrated by catheterization studies an identity between blood and gas oxygen tensions when an equilibrium plateau is reached during rebreathing. Gurtner *et al.* [9] and Denison *et al.* [4] have shown that this method overestimates mixed venous CO₂ ($\bar{P}_{\text{vCO}_2}$) by about 5 mm Hg. This results in only a slight underestimation of mixed venous oxygen saturation ($\bar{S}_{\text{vO}_2}$) and oxygen content ($\bar{C}_{\text{vO}_2}$) when Dill's nomogram is used.

The 3- μ Teflon membrane used to improve the response time of the oxygen electrode is delicate and subject to both tearing and drying. Care is needed in handling it. A 90 % response time of 0.3–0.5 sec is obtained with a 3- μ Teflon membrane, however.

Results

Data describing the subjects studied, measured values of mixed venous O₂ and CO₂, and arterial P_{O₂} and P_{CO₂}

appear in Table I. Mixed venous P_{O₂} varied from 10 to 43 mm Hg and showed no relation to postnatal age, body size, or arterial oxygen tension. Data derived from the measured values appear in Table II.

Discussion

The importance of knowledge of the mixed venous P_{O₂} is that cardiac output and venous admixture may then be calculated according to the Fick principle. These calculations may be made from the data in Table I if it is assumed that: (1) a steady state exists during the period of sampling, and (2) the oxygen consumption of these infants is similar to others studied in our laboratory. Derivation of the cardiac output and venous admixture from the data could also be affected by the fact that arterial and venous gas tensions were determined sequentially rather than simultaneously, even though great care was taken to assure a steady state. The assumption of oxygen consumption can introduce an error, but the values used were obtained by us on a similar group of babies [10] under similar conditions and they closely agree with the values of others.

Previous workers have had to assume mixed venous oxygen tension in order to calculate cardiac output and venous admixture. This is more likely to cause a large error than the factors already discussed because of the steep slope of the hemoglobin-oxygen dissociation curve at venous tensions. Small changes in oxygen tension result in large changes of saturation. Blood at arterial P_{O₂} tensions is less susceptible to this effect.

Fig. 1. Alveolar P_{O₂} tension obtained during rebreathing.

Table I. Mixed venous oxygen and carbon dioxide data¹

Case no.	Birth wt, g	Study wt, g	Study age, days	Length, cm	Body surface area, m ²	Hematocrit, %	O ₂ capacity, vol/100 ml	PaO ₂ , mm Hg	PaCO ₂ , mm Hg	PvO ₂ , mm Hg	PvCO ₂ , mm Hg	CaO ₂ , vol/100 ml	CvO ₂ , vol/100 ml	a-vO ₂ , vol/100 ml
1	1300	1300	1	39	0.118	52	23.9	70.0	42.0	30	43	22.5	15.0	7.5
		1240	2	39	0.118	44	20.3	79.1	27.3	27	41	19.5	11.5	8.0
		1520	21	42	0.141	27	12.4	84.5	31.5	27	38	12.0	7.8	4.2
		1520	22	42	0.141	28	12.9	86.5	34.5	24	46	12.3	5.7	6.6
		1900	34	44	0.157	25	10.5	83.6	34.9	18	44	10.2	3.7	6.5
2	2480	3460	28			29	13.4	76.9	32.0	37	43	12.5	10.6	1.9
3	1900	2470	30	43	0.152	33	15.2	89.0	29.0	31	44	14.5	9.8	4.7
4	2600	2400	8	40	0.126	32	14.7	84.9	30.0	33	45	14.0	8.8	5.2
5	1616	1510	1.5	41	0.135	36	16.6	57.1	35.2	27	50	15.0	8.7	6.3
		1580	8	41	0.135	43	19.8	50.6	38.8	24	52	17.0	9.0	8.0
6	1440	1440	6 hr	40	0.126	45	20.7	48.1	32.8	16	49	17.5	5.5	12.0
		1350	6	40	0.126	45	20.7	82.0	32.7	21	53	19.7	8.0	11.7
		1490	13	40	0.126	40	18.4	55.5	37.8	20	46	16.5	7.0	9.5
7	2200	2200	4 hr	45	0.166	51	23.7	62.0	37.0	26	44	21.8	11.8	10.0
		2140	1	45	0.166	43	19.8	74.6	31.5	27	47	18.5	10.8	7.7
8	1060	1070	35			31	14.8	63.0	36.0	32	45	13.5	9.7	3.8
		1320	60	41	0.135	20	9.2	78.0	33.0	33	39	8.8	6.4	2.4
9	1160	1520	34			26	12.0	71.0	41.0	29	45	11.1	7.2	3.9
10	1050	970	8	38	0.113	42	19.4	56.6	40.4	29	42	17.0	12.0	5.0
		1250	29	40	0.126	27	12.4	93.0	34.0	30	41	11.9	7.9	4.0
		1440	40	43	0.149	23	10.6	78.8	30.6	31	47	10.0	6.5	3.5
		1690	47	43	0.149	20	9.2	80.0	32.0	26	45	8.8	4.9	3.9
11	1390	1530	34			19	8.8	63.0	36.0	19	46	8.0	3.1	4.9
		1780	40			18	8.3	69.5	31.1	18	42	7.8	3.0	4.8
		1810	43			24	11.1	67.6	33.0	37	34	10.4	7.9	2.5
12	1440	1690	29			21	9.7	68.6	40.0	29	44	8.9	5.9	3.0
		2160	47	44	0.157	21	9.7	52.0	36.0	28	55	8.5	5.1	3.4
13	1560	1560	1	38	0.112	63	29.0	84.0	28.5	24	43	28.0	14.0	14.0
		1880	21	42	0.141	40	18.4	85.3	31.2	30	42	17.7	11.5	6.2
14	1660	1900	24			21	9.7	53.0	37.0	41	43	8.5	7.5	1.0
		1960	27			32	14.7	57.0	32.0	41	44	13.3	11.3	2.0
15	1800	1800	2	43	0.149	55	25.3	77.1	34.4	34	42	23.5	17.7	5.8
		2130	12	45	0.166	39	17.9	79.0	32.0	10	49	17.0	10.2	6.8
16	2880	2880	2	49	0.200	55	25.3	69.9	32.8	18	36	24.0	9.7	14.3
17	1790	1680	3	42	0.141	46	21.2	79.0	36.6	22	51	20.5	8.8	11.7
		1680	4	42	0.141	44	20.2	100.8	26.3	40	37	20.0	15.7	4.3
		1680	10	42	0.141	45	20.7	65.0	35.4	28	44	19.5	12.0	7.5
18	1700	1640	3	43	0.149	58	26.7	77.0	33.6	41	40	25.0	8.2	16.8
		1640	4	43	0.149	56	25.8	65.5	36.0	26	38	23.5	14.5	9.0
		1590	10	43	0.149	57	26.2	76.9	34.9	27	42	24.5	14.7	9.8
19	1330	1310	24	38	0.112	32	14.7	53.0	37.6	27	64	13.0	7.1	5.9
		1560	34	39	0.118	27	12.4	72.0	37.5	26	44	11.6	6.8	4.8
20	3600	3560	1	46	0.174	54	25.0	80.9	30.5	34	42	24.0	17.5	6.5
21	2540	2300	6	44	0.157	35	16.2	69.6	29.2	43	45	15.2	12.5	2.7

¹ PaO₂: Arterial oxygen tension. PaCO₂: Arterial carbon dioxide tension. PvO₂: Mixed venous oxygen tension. PvCO₂: Mixed venous carbon dioxide tension. CaO₂: Arterial oxygen content. CvO₂: Venous oxygen content. a-vO₂: Arteriovenous oxygen difference.

With these limitations, cardiac output may be calculated according to the Fick equation:

$$\dot{Q}_s = \frac{\dot{V}_{O_2}}{Ca_{O_2} - Cv_{O_2}} \times 100$$

where $\dot{V}_{O_2}$ = oxygen consumption, milliliters per minute (standard temperature and pressure, dry); CaO₂ = pre-

ductal arterial O₂ content; CvO₂ = mixed venous oxygen content; and $\dot{Q}_s$ = systemic flow, milliliters per minute. Oxygen content was derived from Dill *et al.*'s nomogram [5] as modified for fetal blood by Edwards and Ross [6]. Oxygen capacity was determined by using Peters' factor [11], hematocrit $\times$ 0.46. Pulse rate taken at the end of the experiment was used to calculate stroke vol-

Table II. Calculation of cardiac output and venous admixture¹

Case no.	$\dot{Q}_s$, ml/min	$\dot{Q}_s$, ml/min/kg	$\dot{Q}_s$, ml/min/m ²	$\dot{V}_{O_2}$ [10] (assumed), ml/min, STPD ²	Venous admixture, %	Pulse beats/min	SAO ₂ , %	SvO ₂ , %
1	116	81	985	8.7	16	148	94	63
	109	88	925	8.7	9		96	58
	291	191	2050	12.2	9	160	97	63
	185	122	1310	12.2	8		95	44
	234	123	1440	15.2	4	156	97	35
2	1600	440		30.4	32		93	79
3	462	187	3039	21.7	13		95	64
4	405	169	3214	21.1	14		95	66
5	161	107	1190	10.1	20	140	90	58
	149	95	1200	11.9	25		86	45
6	79	54	630	9.4	21	136	85	32
	85	63	675	9.9	11		95	39
	116	78	920	11.0	17	136	90	38
7	147	67	885	14.7	16	160	92	50
	214	97	1290	16.5	14	140	93	55
8	214	199		8.1	26	148	91	66
	443	336	3280	10.6	14		96	70
9	298	196		11.6	19		93	60
10	140	143	1240	7.0	32	145	88	62
	250	200	1980	10.0	11		96	64
	311	216	2040	10.9	15	150	94	61
	328	194	2201	12.8	8	150	96	56
11	250	164		12.2	14	158	91	35
	310	174		14.9	9		94	36
	580	321		14.5	18		94	71
12	450	267		13.5	21	130	92	61
	509	236	3240	17.3	26		88	53
13	80	53	705	11.2	7	138	97	48
	266	141	1900	16.5	10	170	96	63
14	2170	1125		21.7	55	192	88	77
	1085	554		21.7	41		90	77
15	225	125	1510	13.0	24	130	93	70
	266	125	1600	18.1	12	150	95	57
16	151	52	755	21.6	8	150	95	38
17	108	64	754	12.6	6		97	42
	293	174	2080	12.6	4	128	99	78
	175	104	1240	13.1	14	144	94	58
18	73	45	490	12.3	9		94	31
	137	84	920	12.3	20	144	91	56
	127	80	850	12.4	15	156	94	56
19	178	136	1590	10.5	22		88	48
	260	167	2200	12.5	14	172	94	55
20	368	103	2115	23.9	13	150	96	70
21	663	288	4220	17.9	27	144	94	77

¹ $\dot{Q}_s$: Systemic flow, $\dot{V}_{O_2}$: Oxygen consumption, SAO₂: Arterial oxygen saturation, SvO₂: Venous oxygen saturation.

² STPD: Standard temperature and pressure, dry.

ume. Venous admixture was calculated using the Berggren shunt equation [1]:

$$\dot{Q}_s/\dot{Q}_t = (Cc_{O_2} - Ca_{O_2})/(Cc_{O_2} - C\bar{v}_{O_2})$$

The results of these calculations are seen in Table II. Systemic cardiac output was lowest during the 1st week of life, ranging from 50–100 ml/min/kg or 500–1500 ml/min/m². An increase in calculated systemic output was noted as the infants became older. Venous admixture was under 30% in most cases, but showed no

tendency to rise or fall with time. The cardiac output calculations are recorded as systemic blood flow because the presence of a right-to-left shunt through the foramen ovale is a possibility, particularly in the first days of life. A right-to-left ductus shunt would appear to be excluded because of a sampling site (right radial or temporal artery) proximal to its origin.

References and Notes

- BERGGREN, S. M.: O₂ deficit of arterial blood caused by non-ventilatory parts of the lung. *Acta Physiol. Scand.* (Suppl. 11), 4: 1 (1942).
- CERRETELLI, P., CRUZ, J. C., FARHI, L. E., AND RAHN, H.: Determinations of mixed venous O₂ and CO₂ tensions and cardiac output by a rebreathing method. *Resp. Physiol.*, 1: 258 (1966).
- CERRETELLI, P., DI PRAMPERO, P. E., AND RENNIE, D. W.: Measurement of mixed venous oxygen tension by a modified rebreathing method. *J. Appl. Physiol.*, 28: 707 (1970).
- DENISON, D., EDWARDS, R. H. T., JONES, G., AND POPE, H.: Direct and rebreathing estimates of the O₂ and CO₂ pressures in mixed venous blood. *Resp. Physiol.*, 7: 326 (1969).
- DILL, D. B., EDWARDS, H. T., AND CONSOLAZIO, W. V.: Blood as a physicochemical system. XI. Man at rest. *J. Biol. Chem.*, 118: 635 (1937).
- EDWARDS, M. J., AND ROSS, B.: Graphical representation of respiratory gas dissociation characteristics of fetal and maternal blood. *J. Appl. Physiol.*, 14: 454 (1959).
- FARHI, L. E., AND HAAB, P.: Mixed venous blood gas tensions and cardiac output by "bloodless" methods: recent developments and appraisal. *Resp. Physiol.*, 2: 225 (1967).
- FARHI, L. E., CHINET, A., AND HAAB, P.: Pression partielle d'oxygene du sang veineux mele chez l'homme, en plaine et en haute altitude. *J. Physiol. (Paris)*, 58: 516 (1966).
- GURTNER, G. H., SONG, S. H., AND FARHI, L. E.: Alveolar and mixed venous P_{CO₂} difference under conditions of no gas exchange. *Resp. Physiol.*, 7: 173 (1969).
- KRAUSS, A. N., AND AULD, P. A. M.: Metabolic requirements of low birth weight infants. *J. Pediatr.*, 75: 952 (1969).
- PETERS, J. P., BIELGAR, H. A., AND EISENMAN, A. J.: Studies of the CO₂ absorption curve of human blood. IV. The relation of the hemoglobin content of blood to the form of the CO₂ absorption curve. *J. Biol. Chem.*, 58: 749 (1924).
- Instrumentation Laboratory Ultramicro system, Instrumentation Laboratory, Inc., Lexington, Mass.
- Beckman Instruments, Inc., Palo Alto, Calif.
- Dr. P. A. M. Auld holds an Investigatorship of the Health Research Council of the City of New York, under Contract no. I-236.
- Supported by Public Health Service Research Grants nos. HD-02644 and HE-09410.
- Requests for reprints should be addressed to: A. N. KRAUSS, M.D., Department of Pediatrics, Cornell University Medical College, 525 East 68th Street, New York, N. Y. 10021 (USA).
- Accepted for publication July 9, 1971.