

3. Kaslick RS, Bernstein HC: Epidermolysis bullosa. Review of the literature and report of a case. *Oral Surg* 14:1315-1330, 1961
4. Lewis IC, Stevens EM, Farquhar JW: Epidermolysis bullosa in the newborn. *Arch Dis Child* 30:277-284, 1955
5. Wheeler CE: Pemphigus, Cecil and Loeb Textbook of Medicine, Twelfth edition. Philadelphia, Saunders, 1967, pp 481-483
6. Dundee JW, Riding JE: Barbiturate narcosis in porphyria. *Anaesthesia* 10:55-58, 1955
7. Hamman RA, Cohen PJ: Anesthetic management of a patient with epidermolysis bullosa dystrophica. *ANESTHESIOLOGY* 34:389-390, 1971
8. Jeyaram C, Torda TA: Anesthesia management of cholecystectomy in a patient with buccal pemphigus. *ANESTHESIOLOGY* 40:600-601, 1974
9. Marshall BE: A comment on epidermolysis bullosa and its anaesthetic management for dental operations. A case report. *Br J Anaesth* 35:724-727, 1963
10. Katz RL, Matteo RS, Papper EM: Injection of epinephrine during general anaesthesia. *ANESTHESIOLOGY* 23:597-600, 1962

Extrapulmonary Influences on A-aD_{O₂}^{1.0} Following Cardiopulmonary Bypass

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Pulmonary insufficiency is one of many diagnostic and therapeutic challenges posed by postoperative or traumatically injured patients. The alveolar-arterial oxygen tension gradient calculated during inhalation of 100 per cent oxygen (A-aD_{O₂}^{1.0}) has been used widely for assessment of pulmonary dysfunction.¹⁻³ Changes in A-aD_{O₂}^{1.0} also have been used to dictate oxygen therapy,¹ initiation or withdrawal of mechanical ventilatory support,² application of positive end-expiratory pressure (PEEP),⁴ administration of diuretic and colloid therapy,³ and initiation of extracorporeal membrane oxygenation.⁶ The purpose of this investigation was to assess the accuracy of A-aD_{O₂}^{1.0} in estimating intrapulmonary right-to-left shunting (Q_p/Q_t) of blood in patients following extracorporeal circulation.

METHODS AND MATERIALS

Twenty-one consecutive patients admitted to the Surgical Intensive Care Unit following

cardiopulmonary bypass for myocardial revascularization procedures were studied. § Anesthesia was induced with pentothal, followed by nitrous oxide supplemented with morphine (1-3 mg/kg), halothane, or ketamine. All patients had thermistor-tipped, flow-directed pulmonary-artery⁵ and radial-artery catheters inserted percutaneously prior to operation. Proper positioning of pulmonary-artery catheters was confirmed by chest roentgenogram.

Following operation, patients were assigned randomly to receive controlled ventilation, intermittent mandatory ventilation (IMV),⁷ or IMV with 6 cm H₂O PEEP, in order to assess the effects of different ventilatory patterns on cardiopulmonary function. One, 4, 8, and 16 hours following initiation of mechanical ventilation, simultaneously drawn samples of blood from the radial and pulmonary arteries were analyzed for hemoglobin concentration (cyanmethemoglobin method),⁸ oxygen content by the galvanic cell method,⁹ and blood-gas tensions and pH by standard electrode techniques.** Appropriate values

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§ The voluntary fully informed consent of the subjects used in this research was obtained as required by AFR 169-8.

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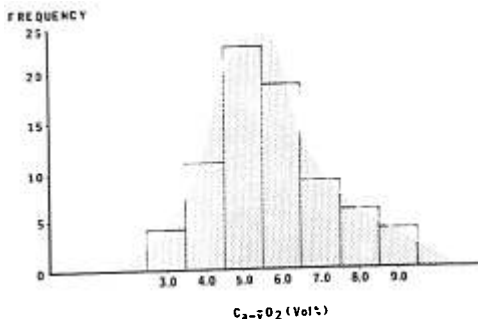


FIG. 1. Frequency distribution of arterial-mixed venous oxygen content differences ($Ca-\bar{v}O_2$).

were corrected to the patient's body temperature.¹⁰ All patients breathed 100 per cent oxygen for 20 minutes prior to each determination. Cardiac output was measured by the thermodilution method.¹¹ This value was divided by body surface area for determination of cardiac index. Oxygen consumption was measured with a modified 13-l water spirometer^{††} in a closed system with carbon dioxide absorption, corrected to BTPS and body surface area. $A-aD_{O_2}^{1.0}$ was determined by the formula:

$$A-aD_{O_2}^{1.0} = PA_{O_2} - Pa_{O_2} \quad (\text{ref. 14})$$

where

$$PA_{O_2} = P_b - P_{H_2O} - Pa_{CO_2}$$

Intrapulmonary right-to-left shunting was calculated by the formula:

$$\dot{Q}_s/\dot{Q}_t = \frac{Cc_{O_2} - Ca_{O_2}}{Ca_{O_2} - C\bar{v}_{O_2}} \quad (\text{ref. 14})$$

It was assumed that arterial and pulmonary capillary hemoglobin were 100 per cent saturated with oxygen and that:

$$Cc_{O_2} = Ca_{O_2} - (Pa_{O_2} \times 0.0031) + (Pa_{O_2} \times 0.0031).$$

RESULTS

Cardiac indexes ranged from 1.2 to 4.5 l/min/m². Oxygen consumption indexes ranged

from 87 to 234 ml/min/m² and hemoglobin, from 9 to 15 g/100 ml. The large variability in cardiac and oxygen consumption indexes was reflected by a wide variability in $Ca-\bar{v}O_2$ (fig. 1). The $A-aD_{O_2}^{1.0}$ was 251 ± 70 torr (mean \pm SD; range 55-519 torr) and \dot{Q}_s/\dot{Q}_t was 0.115 ± 0.025 (range 0.02-0.23).

The pooled correlation coefficient for within-subject determinations of \dot{Q}_s/\dot{Q}_t and $A-aD_{O_2}^{1.0}$ was 0.862 ($P < 0.0001$). The correlation coefficient for 77 separate paired determinations of $A-aD_{O_2}^{1.0}$ and \dot{Q}_s/\dot{Q}_t was 0.737 ($P < 0.01$). There was a better relationship between $A-aD_{O_2}^{1.0}$ and \dot{Q}_s/\dot{Q}_t for each patient than for the group of patients as a whole. Since the coefficient of correlation between two variables (r) equals

$$\sqrt{\frac{\text{Explained variation}}{\text{Total variation}}},$$

we found that only 54 per cent of the variation ($r = 0.74 = \sqrt{.54}$) in $A-aD_{O_2}^{1.0}$ was secondary to \dot{Q}_s/\dot{Q}_t and 46 per cent was secondary to $Ca-\bar{v}O_2$.

The standard deviation of intrapulmonary shunt adjusted to the mean $A-aD_{O_2}^{1.0}$ for all determinations was 0.02458. Therefore, the width of a 95 per cent confidence band (± 2.09 SD) to include a patient's true shunt for any given $A-aD_{O_2}^{1.0}$ was 0.1028. The regression line obtained from the 77 paired determinations of $A-aD_{O_2}^{1.0}$ and \dot{Q}_s/\dot{Q}_t was described by the equation:

$$\dot{Q}_s/\dot{Q}_t = -0.01091 + 0.0004993 (A-aD_{O_2}^{1.0}) \quad (\text{fig 2}).$$

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Mechanical ventilation with or without PEEP had no significant effect on $Ca\bar{v}O_2$ or the relationship between \dot{Q}_s/\dot{Q}_t and $A-aD_{O_2}^{1.0}$.

DISCUSSION

While it frequently is assumed that the $A-aD_{O_2}^{1.0}$ accurately assesses \dot{Q}_s/\dot{Q}_t ,^{3,4,15} this measurement is affected by cardiac output and by total-body oxygen consumption.¹⁴ Problems in sampling mixed venous blood have led investigators to assume an approximate arterial-mixed venous oxygen content difference ($Ca\bar{v}O_2$) to simplify calculation of intrapulmonary shunt.¹⁵ The classic shunt equation listed earlier may be simplified by assuming 100 per cent saturation of the arterial hemoglobin (which was the case in all measurements in this series), and rearranging the equation to the following form:

$$\begin{aligned} \dot{Q}_s/\dot{Q}_t \\ = \frac{(A-aD_{O_2}^{1.0}) \times 0.0031}{(A-aD_{O_2}^{1.0}) \times 0.0031 + Ca\bar{v}O_2} \quad (\text{refs. 1,14}) \end{aligned}$$

Assumption of constant arterial-to-venous

oxygen content difference allows intrapulmonary shunt to be calculated from measurement of $A-aD_{O_2}^{1.0}$ alone. However, the factors mentioned earlier—cardiac output and oxygen consumption—bear crucially on venous oxygen content.

We found assumption of a constant $Ca\bar{v}O_2$ is not justified. Variability in intrapulmonary shunting for any given $A-aD_{O_2}^{1.0}$ was such that accurate estimation of intrapulmonary shunting was not possible (fig. 2). Percutaneous insertion of a flow-directed pulmonary-artery catheter can be accomplished within minutes in most patients,^{16,17} and allows direct measurement of arterial-venous oxygen content difference and determination of intrapulmonary shunting, cardiac output and oxygen consumption.¹¹

Therapeutic intervention based on $A-aD_{O_2}^{1.0}$ may be inappropriate. For instance, a patient with low cardiac output secondary to intravascular hypovolemia may be hypoxicemic in the absence of elevated levels of intrapulmonary shunting. Application of PEEP and/or vigorous diuresis in an attempt to improve arterial oxygenation could impede thoracic venous inflow of blood, resulting in further

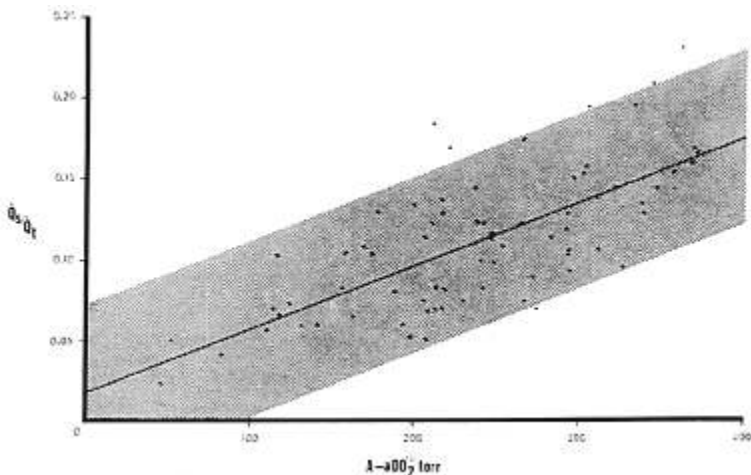


FIG. 2. Alveolar-arterial oxygen gradient during breathing of 100 per cent oxygen ($A-aD_{O_2}^{1.0}$) vs. intrapulmonary right-to-left shunt (\dot{Q}_s/\dot{Q}_t) with 95 per cent confidence band (stippled area).

depression of cardiac output and, therefore, further deterioration of systemic oxygenation.

Changes in $A-aD_{O_2}$ ^{1,9} following therapeutic interventions or clinical occurrences that could alter any of the other variables affecting $A-aD_{O_2}$ ^{1,9} should not be attributed to intrapulmonary shunting unless all of the other variables have been measured. Investigations that equate changes in arterial oxygenation with improvement or deterioration of pulmonary function must be interpreted with caution and in context with other factors that may modify these values.

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REFERENCES

- Pontoppidan H, Geffin B, Lowenstein E: Acute respiratory failure in the adult. *N Engl J Med* 287:690-698, 743-752, 799-806, 1972
- Bendixen HH, Ebert LD, Hedley-Whyte J, et al: *Respiratory Care*. St. Louis, C. V. Mosby, 1965
- Skillman JJ, Parikh BM, Tanebaum BJ: Pulmonary arteriovenous admixture: Improvement with albumin and diuresis. *Am J Surg* 119:440-447, 1970
- Tumbull KW, Miyagishima RT, Gerein AN: Pulmonary complications and cardiopulmonary bypass: A clinical study in adults. *Can Anaesth Soc J* 21:181-194, 1974
- Laver MB, Morgan J, Bendixen HH, et al: Lung volume, compliance, and arterial oxygen tensions during controlled ventilation. *J Appl Physiol* 19:725-733, 1964
- Hill JD, DeLeval MR, Fallat RJ, et al: Acute respiratory insufficiency. Treatment with prolonged extracorporeal oxygenation. *J Thorac Cardiovasc Surg* 64:551-562, 1972
- Downs JB, Perkins HM, Modell JH: Intermittent mandatory ventilation: An evaluation. *Arch Surg* 109:519-523, 1974
- Davidsohn I, Henry JB: *Todd-Sanford Clinical Diagnosis by Laboratory Methods*. Philadelphia, WB Saunders, 1974
- Kusumi F, Butts WC, Ruff WL: Superior analytical performance by electrolytic cell analysis of blood oxygen content. *J Appl Physiol* 35:299-300, 1973
- Severinghaus JW: Blood gas calculator. *J Appl Physiol* 21:1108-1116, 1966
- Ganz W, Donoso R, Marcus HS, et al: A new technique for measurement of cardiac output by thermodilution in man. *Am J Cardiol* 27:392-396, 1971
- McMahon SM, Halprin GM, Sieker HO: Positive end-expiratory airway pressure in severe arterial hypoxemia. *Am Rev Resp Dis* 108:526-535, 1973
- Suter PM, Schlobohm RM: Determination of functional residual capacity during mechanical ventilation. *ANESTHESIOLOGY* 41:605-607, 1974
- Colgan FJ, Mahoney PD: The effects of major surgery on cardiac output and shunting. *ANESTHESIOLOGY* 31:213-221, 1969
- Bendixen HH, Hedley-Whyte J, Laver MB: Impaired oxygenation in surgical patients during general anesthesia with controlled ventilation. *N Engl J Med* 269:991-996, 1963
- Swan HJ, Ganz W, Forrester J, et al: Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. *N Engl J Med* 283:447-451, 1970
- Civetta JM, Gabel JC: Flow directed-pulmonary artery catheterization in surgical patients: Indications and modifications of technique. *Ann Surg* 176:753-756, 1972

Sulfhemoglobinemia and Methemoglobinemia— Uncommon Causes of Cyanosis

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Cyanosis has long been stressed as a sign of inadequate oxygenation. The alert anesthetist observing cyanosis immediately makes diligent efforts to determine and cor-

rect the cause of the hypoxia. Occasionally cyanosis is produced by causes other than hypoxia, as the following case report illustrates.

REPORT OF A CASE

A 56-year-old white man was admitted for an esophagogastrectomy for carcinoma of the distal esophagus. Physical examination revealed "bronzed"

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