Editorial Views

The Black Box Illuminated

It has generally been assumed that the large alveolar-to-arterial oxygen gradients (A-aDO₂) found in patients with acute respiratory failure of nonobstructive origin arise from nonventilated but perfused air spaces, causing a “true physiologic shunt.” Evidence for this conclusion has been based on: 1) the persistence of the shunt even when the inspired oxygen concentration was 100 per cent, a maneuver intended to eliminate the “shunt-like” effect of areas with low, but finite \( V_A/\dot{Q} \)’s; and 2) minimal increases in A-aDO₂ and shunting when the inspired gas mixture contains nitrogen in concentrations of 50 per cent or more.

In this issue, Markello, Winter, and Olszowka present evidence intended to modify these conclusions. In addition to an “oxygen shunt” when \( F_{1\text{O}_2} = 1.0 \), they demonstrate the presence of an even larger “nitrogen shunt” in patients with acute respiratory failure who are ventilated with substantially less than 100 per cent oxygen. Since a “nitrogen shunt” does not arise in lung units with a \( V_A/\dot{Q} \) of zero, the authors postulate that their patients must have had a large lung compartment with a low, immeasurable, but nevertheless finite \( V_A/\dot{Q} \), where perfusion occurred past an open, but essentially nonventilated, terminal air space. Such a low \( V_A/\dot{Q} \) will give rise to an oxygen shunt and yet provide for a sufficient flow of nitrogen to result in a large nitrogen shunt.

The two-compartment lung model used by the authors indicates how an arterial-to-alveolar nitrogen gradient of 13 mm Hg can arise during breathing of air. An occasional reader may not be satisfied that the computer or the model can explain a far larger gradient (reported as high as 120 mm Hg) measured in a group of patients when \( F_{1\text{O}_2} = 0.5 \). A glance at figure 1 will show that an a-ADN₂ of 54 mm Hg is indeed to be expected under the conditions of ventilation and blood flow given by the authors.

What range of \( V_A/\dot{Q} \) values are we dealing with, how plausible is this lung model as an explanation for the findings, and what are the practical implications for the physician charged with the care of the patient? Since shunting persisted, or even increased, during breathing of oxygen, the \( V_A/\dot{Q} \) of the poorly ventilated compartment must have been exceedingly low. In fact, calculation shows that this compartment requires only 50 ml of oxygen inflow to oxygenate fully its allocated blood flow of 1,000 ml per minute, i.e., if \( V_A/\dot{Q} \) falls below 0.05, then shunting must persist during breathing of oxygen. An estimate of the lower limit necessitates calculation of the nitrogen “bulk flow” into the open, nonventilated air space of compartment A needed to raise the \( P_{N_2} \) of mixed venous blood to that obtaining in the alveoli. If \( F_{1N_2} = 0.5 \), according to the figure, “bulk flow” of nitrogen \( V_{N_2} = 1.000 \times 0.0137/760 = 4 \text{ ml} \) (solubility coefficient for \( N_2 = 0.0137 \)). The 4-ml nitrogen flow necessary will carry with it an equal amount of oxygen (since \( F_{1N_2} = 0.5 \), \( F_{1O_2} = 0.5 \)), giving a total unidirectional gas flow of 8 ml/min. Thus, when \( F_{1O_2} = 0.5 \), \( V_A/\dot{Q} \) in compartment A must exceed 0.008 (i.e., 8/1,000) if this air space is to remain open. As \( F_{1O_2} \) increases, so does \( V_{N_2} \) and, at an even faster rate, the total “bulk flow,” until at \( F_{1O_2} \).
1.0 it reaches infinity. This does not mean that an infinite inflow of oxygen is needed to prevent absorption atelectasis. As we have already seen, if 50 ml of oxygen enter compartment A, its blood will be fully oxygenated and absorption atelectasis need not occur.

The authors observed an increase in oxygen shunt in some patients as FIO₂ was increased from 0.5 to 1.0. They explain this observation by absorption atelectasis on the basis of an increased need for "bulk flow" as FIO₂ approaches one. If this explanation is correct, then the shunt should have remained high despite a return of FIO₂ to 0.5, provided no concomitant change in the ventilation pattern and no hyperinflations had been applied to reopen closed air spaces. Since the clinical importance of this proposed mechanism is obvious, we wish the authors had been able to present us with these data as well.

What is the anatomic basis for the postulated physiologic events? It is difficult to accept the persistence of a large, open, essentially nonventilated compartment actually maintaining Vₐ/Q between 0.01 and 0.05. More attractive seems the alternate explanation: brief opening at peak inspiratory pressure of closed small airways or alveoli having a high opening pressure, allowing enough gas to move in and satisfy the need for "bulk flow." In this circumstance, gradients should diminish to some extent with a ventilation pattern which keeps alveoli open during a greater part of the respiratory cycle; an even greater reduction in gradients would be expected if airway or alveolar closure were prevented by use of positive end-expiratory pressure (PEEP). The well-established efficacy with which these ventilatory patterns can reduce oxygen shunting in acute pulmonary edema is reconfirmed in a dog model by Burnham, Martin and Cheney, also in this issue.

Since measurement of the nitrogen gradient (particularly the nitrogen content in whole blood) is a complex procedure which is likely to remain somewhat less than a useful clinical tool, investigators who have mastered this difficult technique might well extend their
studies to a comparison of different ventilatory patterns currently in vogue, in the hope of establishing a clearer physiologic rationale for their proven clinical value.

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References


Circulation

CHRONIC HYPOXEMIA AND IMPAIRED REFLEX VASOCONSTRICTION

Acute hypoxia impairs vasoconstrictor and positive chronotropic responses in normal men. During prolonged hypoxia (more than 36 hours) cardiovascular reflexes in normal men remain impaired and are restored to normal by correction of hypoxia. In the present investigation vasoconstrictor responses were observed in chronically hypoxemic patients to determine whether reflex vasoconstriction is impaired by chronic hypoxemia and whether correction of chronic hypoxemia improves cardiovascular reflexes. Eight hypoxemic patients with a variety of chronic pulmonary diseases were studied. The patients were all ambulatory, and the criteria for selection included arterial P_{O_2} 's and P_{CO_2} 's below 60 mm Hg at rest and a stable clinical situation. With the patient supine, the lower half of the body was enclosed in an airtight box to the level of the iliac crest. The brachial artery was cannulated and blood flow to the forearm was measured with a mercury-in-silastic strain-gauge plethysmograph. Each patient breathed two levels of oxygen: room air and 40 percent oxygen in nitrogen. P_{O_2} was therefore increased from an average of 45 mm Hg to 161 mm Hg. Correction of hypoxemia did not change arterial P_{CO_2} or pH, resting arterial pressure, or forearm vascular resistance, but caused a small increase in resting heart rate. Reflex responses to lower-body negative pressure, i.e., pooling of blood in the lower part of the body similar to the effect of a rapid increase in head-up tilt, were observed when the patients were hypoxic. Lower-body negative pressure caused a decrease in arterial pressure, slight constriction of forearm vessels, and a small increase in heart rate in hypoxemic patients. When hypoxemia was corrected, the same intervention caused marked vasoconstriction and a greater increase in heart rate, but no decrease in arterial pressure. Reflex vasoconstrictor responses are depressed in chronic hypoxemia, indicating that adaptive mechanisms do not include preservation of sympathetic reflexes. (Heistad, D. D., and others: Impaired Reflex Vasoconstriction in Chronically Hypoxemic Patients, J. Clin. Invest. 51: 331-344, 1972.)