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The Effect of Cardiac Output on Arterial Blood Oxygenation

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THE CONCEPT that cardiac output passively affects arterial blood oxygen tension (P_{aO_2}) is widely accepted.^{1,2} In 1967, Kelman *et al.*³ pointed out the theoretical relationship between cardiac output (\dot{Q}_t), per cent venous admixture or intrapulmonary shunt, and the alveolar-to-arterial oxygen tension difference ($A-aD_{O_2}$). These investigators emphasized that a decrease in cardiac output in the face of constant oxygen consumption leads to an increase in oxygen extraction from the blood and a reduction in mixed venous blood oxygen content. Therefore, as the venous blood becomes more desaturated from a reduction in cardiac output, it will decrease P_{aO_2} in a more or less direct relationship to the amount of venous admixture. The greater the venous admixture, the greater the reduction in P_{aO_2} with a reduction in cardiac output. The review of Kelman *et al.*³ was written prior to widespread utilization of pulmonary arterial catheterization in either animal or human studies, so that venous admixture could not be easily determined directly.

The relationships described above are true only assuming venous admixture or shunt remains relatively constant with changes in cardiac output. Subsequent animal and human studies using direct measurement of mixed venous blood oxygen content from pulmonary arterial blood have shown that the assumption of a stable venous admixture or intrapulmonary shunt with a change in cardiac output is usually not valid. In fact, experimental evidence indicates that cardiac output itself has a direct effect on venous admixture in both normal and diseased lungs. To complicate matters further, the effects of cardiac output on venous admixture and oxygenation seem to vary in relation to both acute and chronic changes in cardiac output and whether the lung is normal, or has diffuse

ventilation-perfusion abnormalities or localized disease. This direct effect of cardiac output on gas exchange may have important clinical implications for patients with respiratory failure. The purpose of this review is to focus attention on the relationship of cardiac output to gas exchange, in the light of experimental work that has accrued since the original article of Kelman *et al.*,³ and to stimulate further study of this phenomenon.

Definition of Terms

To avoid confusion, we wish to emphasize at the outset the difference between oxygenation and oxygen transport. The term "oxygenation," as used in this review, refers either to oxygen tension or to the oxygen content of the arterial blood. Oxygen transport is the product of arterial blood oxygen content and cardiac output. Clearly a change in cardiac output will directly affect oxygen transport. This review, however, is concerned with the effect of cardiac output on P_{aO_2} , which is brought about by the interaction of changes in mixed venous blood oxygen content and venous admixture or shunt. The effects of \dot{Q}_t on mixed venous blood oxygen content are well known and easily predicted from the Fick equation:

$$\dot{Q}_t = \frac{\dot{V}_{O_2}}{Ca_{O_2} - C\bar{v}_{O_2}}$$

where \dot{V}_{O_2} = oxygen consumption, Ca_{O_2} = arterial blood oxygen content, and $C\bar{v}_{O_2}$ = mixed venous blood oxygen content.

Venous admixture or "physiologic shunt" is calculated by the formula:

$$\dot{Q}_s/\dot{Q}_t = \frac{C\acute{c}_{O_2} - Ca_{O_2}}{C\acute{c}_{O_2} - C\bar{v}_{O_2}}$$

where $C\acute{c}_{O_2}$ is end-pulmonary capillary blood oxygen content and is directly related to alveolar oxygen tension ($P_{A_{O_2}}$). Normally, venous admixture is 3-5 per cent of \dot{Q}_t and is due to anatomic arteriovenous shunts in the lung and heart, blood flow through atelectatic lung, and blood flow through underventilated lung.

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TABLE 1. Effects of Changes in Cardiac Output on Venous Admixture (\dot{Q}_{VA}/\dot{Q}_t) or Shunt (\dot{Q}_s/\dot{Q}_t) and Pa_{O_2} in Normal Lung

Species	Anesthetic	Pattern of Ventilation	Output Changed by	Direction* of Change in			Reference
				\dot{Q}_t	\dot{Q}_{VA}/\dot{Q}_t or \dot{Q}_s/\dot{Q}_t	Pa_{O_2}	
Dog	Ether Halothane	Controlled	Anesthesia depth	↑↓	↑↓	±	4
Man	Halothane	Controlled	CO ₂	↑↓	±	↑↓	5
Man	Enflurane Oxygen	Controlled	CO ₂	↑↓	±	↑↓	6
Man	Ether Halothane	Controlled	CO ₂ Hemorrhage	↑↓	↑↓	±	7
Dog	Pentobarbital	Spontaneous	Hemorrhage	↓	↓	±	8
Dog	Halothane	Spontaneous	Hemorrhage	↓	↓	↓	9
Dog	Pentobarbital	Controlled	Hemorrhage	↓	↓	±	10
Dog	Pentobarbital	Controlled	Hemorrhage	↓	↓	±	11
Dog	Pentobarbital	Controlled	Hemorrhage	↓	↓	±	12
Dog	Pentobarbital	Spontaneous	Hemorrhage	↓	↓	±	13
Dog	Pentobarbital	Spontaneous	Hemorrhage	↓	↑	↓↓	14
Man	None	Spontaneous	Isoproterenol	↑	↑	↓	17
Dog	Pentobarbital	Controlled	Dopamine	↑	↑	Not reported	18

* Arrows show directions of changes from control values.

During breathing of 100 per cent oxygen ($F_{I_{O_2}} 1.0$), the contribution of underventilated lung or ventilation-perfusion mismatch no longer affects Pa_{O_2} , so any abnormality of oxygenation at $F_{I_{O_2}} 1.0$ is solely due to shunt, which, when increased above normal, is usually the result of alveolar collapse. For the purpose of this review, venous admixture (\dot{Q}_{VA}/\dot{Q}_t) refers to physiologic shunt calculated at $F_{I_{O_2}} < 1.0$ and shunt (\dot{Q}_s/\dot{Q}_t) refers to the same calculation when $F_{I_{O_2}} = 1.0$. In all studies reported below mixed venous blood oxygen tension was measured directly or calculated from the Fick equation with direct measurements of \dot{V}_{O_2} , \dot{Q}_t , and Ca_{O_2} .

Normal Lung

Studies of the effects of cardiac output on gas exchange in dog and man during general anesthesia have yielded disparate results (table 1). Yamamura *et al.*⁴ found a significant positive correlation between shunt and cardiac index in dogs anesthetized with either halothane or ether-O₂. No change in A-aD_{O₂} from the awake state was seen with either agent because, as cardiac output decreased, so did the shunt, and vice versa. Therefore, the reduction in mixed venous blood oxygen content with a decreased cardiac output was offset by the reduction in shunt, so Pa_{O_2} was not affected significantly. Studies of the relationship of cardiac output to gas exchange in

anesthetized man have yielded contradictory results, perhaps because cardiac output was usually altered by changing Pa_{CO_2} (table 1), which may have an independent effect on shunt and/or \dot{V}_{O_2} . Two studies^{5,6} of anesthetized human subjects showed that changes in cardiac output had no effect on shunt, but directly affected Pa_{O_2} . On the other hand, in anesthetized man, Michenfelder *et al.*⁷ found that a change in cardiac output caused by hemorrhage or anesthesia was accompanied by a similar change in shunt and an inconstant relationship between \dot{Q}_t and A-aD_{O₂}.

The effects of hemorrhage-induced changes in \dot{Q}_t on gas exchange have been the more intensively studied in the normal pentobarbital-anesthetized dog⁸⁻¹⁴ than in other models (table 1). The preponderance of evidence indicates that cardiac output does not usually affect Pa_{O_2} because the reduction in mixed venous blood oxygen content is offset by a similar reduction in shunt. Malik and Newell,¹⁴ on the other hand, found a significant decrease in Pa_{O_2} and an increase in \dot{Q}_{VA}/\dot{Q}_t during hemorrhage in spontaneously breathing dogs. The decreased Pa_{O_2} was a result of both increased venous admixture and decreased mixed venous blood oxygen content. The results obtained in Malik and Newell's study differed markedly from those of the other studies, probably as a result of the rapidity and shallowness of respirations of the animals during severe hemorrhage. The authors

postulated¹⁴ that the decreased tidal volume associated with hemorrhage prevented full lung inflation, thus allowing atelectasis. This emphasizes the point that the pattern of ventilation must remain stable in order to make valid determinations of the effect of \dot{Q}_t on \dot{Q}_{VA}/\dot{Q}_t . It should also be noted that the studies mentioned above reflect the immediate effects of hemorrhage and decreased cardiac output on gas exchange. A prolonged reduction in cardiac output due to hemorrhage will cause perivascular pulmonary edema, alveolar collapse, and an increase in shunt.^{15,16}

Studies reporting the interaction of increased cardiac output with shunting and oxygenation have involved the use of vasoactive agents^{17,18} (table 1). An increase in cardiac output is usually associated with an increased \dot{Q}_{VA}/\dot{Q}_t or \dot{Q}_s/\dot{Q}_t , and P_{aO_2} is unchanged or decreased. It is not clear in these studies whether the direct association of cardiac output and shunt was mediated by the change in cardiac output alone, or by a direct action of the drug on the pulmonary vasculature.

Diffuse Pulmonary Disease

One of the earliest reports of a positive correlation between cardiac index and shunt in patients with respiratory failure was that of Hedley-Whyte *et al.*¹⁰ in 1966. They studied the effects of changing tidal volume on gas exchange and cardiac output in patients with intrapulmonary infection or emphysema who were being treated with continuous mechanical ventilation. Central venous blood, rather than pulmonary arterial blood, was used for calculation of mixed venous blood oxygen content, which may have influenced the results, but their observations have been borne out by subsequent studies. There was a significant correlation between cardiac index and \dot{Q}_s/\dot{Q}_t in each patient, even after the data were adjusted for the effects of tidal volume change on \dot{Q}_s/\dot{Q}_t . The authors concluded that cardiac output is a "major determinant of the percent physiologic shunt."¹⁰ A direct relationship between \dot{Q}_s/\dot{Q}_t and \dot{Q}_t has been found by several groups of investigators in patients with respiratory failure from diffuse parenchymal disease²⁰ and post-traumatic respiratory failure.^{21,22} In one of these studies,²¹ the authors noted that, due to the increased \dot{Q}_s/\dot{Q}_t with the increased \dot{Q}_t , they could find no relationship between P_{aO_2} and \dot{Q}_t . Lemaire *et al.*,²³ in a study of patients with advanced adult respiratory distress syndrome (ARDS) who needed extracorporeal membrane oxygenation, found that there was a direct relationship between the amount of perfusion of the lung and \dot{Q}_s/\dot{Q}_t . As perfusion of the lung was decreased by increasing the amount of veno-arterial flow from the extracorporeal circuit, \dot{Q}_s/\dot{Q}_t decreased and the left ventricular blood P_{aO_2} increased.

In patients with respiratory failure and large shunts, attempts to improve P_{aO_2} by increasing cardiac output with vasopressors have not been successful.²⁴ Mulroy and Fairley²⁴ attempted to increase P_{aO_2} in patients with ARDS by increasing \dot{Q}_t with dopamine. Their rationale was the corollary of the hypothesis of Kelman *et al.*, namely, that the increased mixed venous blood oxygen content brought about by the increased cardiac output would increase P_{aO_2} in these patients with markedly increased shunt. They found, however, that as cardiac output increased, so did the shunt, such that the effect of dopamine on P_{aO_2} was unpredictable and even detrimental in some patients. Similar findings were observed in patients receiving intravenous isoproterenol after cardiac surgery.²⁵ In these patients, isoproterenol increased cardiac output and venous admixture, resulting in a significant decrease in arterial blood oxygen saturation. Lemaire *et al.*,²⁰ studied 28 patients with ARDS and found that when \dot{Q}_t was varied with dehydration, dopamine, isoproterenol, or neosynephrine, shunt was linearly correlated with cardiac index. Values for P_{aO_2} were not reported. Jardin *et al.*^{27,28} found a direct correlation between \dot{Q}_s/\dot{Q}_t and cardiac output in 25 adult patients with severe sepsis treated with dopamine. Cardiac output and oxygen consumption increased with dopamine infusion, but the increased mixed venous blood oxygen tension ($P\bar{v}_{O_2}$) was offset by an increased \dot{Q}_s/\dot{Q}_t , so P_{aO_2} remained unchanged. On the other hand, Hemmer and Suter²⁸ found no change in \dot{Q}_{VA}/\dot{Q}_t when dopamine was administered to patients with acute respiratory failure due to trauma and infection. As a result of the increased \dot{Q}_t in the presence of a fixed \dot{Q}_{VA}/\dot{Q}_t , P_{aO_2} increased significantly in these patients.

The data obtained in man relating cardiac output to shunt and P_{aO_2} in diffuse pulmonary disease are difficult to interpret due to the constraints of patient care. In most instances¹⁰⁻²² no attempt was made to alter cardiac output under controlled conditions, and the association of cardiac output, shunt, and P_{aO_2} was only noted as a casual relationship. Smith *et al.*¹¹ studied the effects of hemorrhage in anesthetized, mechanically ventilated dogs with acute capillary-leak pulmonary edema. During hemorrhage, cardiac output and mixed venous blood oxygen saturation ($S\bar{v}_{O_2}$) decreased significantly, and mean \dot{Q}_s/\dot{Q}_t decreased from 29 ± 4 per cent to 22 ± 3 per cent. P_{aO_2} did not change with hemorrhage, as the decreased \dot{Q}_s/\dot{Q}_t compensated for the marked decrease in $S\bar{v}_{O_2}$. Lynch *et al.*²⁹ varied cardiac output by venous obstruction, pentobarbital overdose, and dopamine infusion in dogs with capillary-leak pulmonary edema. Intrapulmonary shunt fraction, measured with the multiple inert gas elimination technique, varied directly with cardiac

output. As a result of the changes in shunt fraction, Pa_{O_2} did not change significantly during either depression or augmentation of \dot{Q}_t .

It seems, from the observations cited above, that the effect of cardiac output on arterial oxygenation in normal or diffusely injured lung is unpredictable, at best. It is clear from most studies that a change in \dot{Q}_t causes a similar change in \dot{Q}_{VA}/\dot{Q}_t or \dot{Q}_s/\dot{Q}_t , and the resultant effect on arterial blood oxygen content depends on whether the alteration in shunt or venous admixture predominates over the change in mixed venous blood oxygen content. If, for example, cardiac output decreases, Pa_{O_2} will decrease only if $S\bar{v}_{O_2}$ decreases more than the venous admixture.

Mechanism of the Cardiac Output-Venous Admixture Relationship in Normal and in Diffusely Abnormal Lung

What, then, are the possible mechanisms for the relationship between cardiac output and venous admixture as observed in both normal and diffusely abnormal lung? In the absence of any evidence of a change in either functional residual capacity (FRC) or lung volume, the mechanism must somehow relate to alterations in pulmonary blood flow distribution. The normal response of the pulmonary vasculature to localized alveolar hypoxia is vasoconstriction, which diverts blood away from hypoxic areas of the lung.³⁰ Thus, when alveoli are poorly ventilated or totally unventilated, as with alveolar collapse, pulmonary blood flow is, in time, diverted away from these areas of poor alveolar oxygenation. In either normal or diffusely abnormal lung, the hypoxic pulmonary vasopressor response is one of the primary factors responsible for maintaining pulmonary blood flow to well-ventilated alveoli, and any interference with that response would increase venous admixture and decrease Pa_{O_2} . A likely explanation for the direct relationship between cardiac output and venous admixture is the interaction between cardiac output-induced changes in pulmonary arterial pressure and hypoxic vasoconstriction. Colley *et al.*³¹ showed that when pulmonary arterial pressure was decreased by hemorrhage, pulmonary vascular resistance in a hypoxic nitrogen-ventilated lung increased more than that in the contralateral oxygenated lung, indicating that the decreased pulmonary arterial pressure potentiated hypoxic vasoconstriction. It has also been shown that increased pulmonary arterial pressure in the presence³² or absence³³ of increased left atrial pressure inhibits hypoxic pulmonary vasoconstriction. Thus, when cardiac output and pulmonary blood flow increase, the higher pulmonary arterial pressure would inhibit or overcome hypoxic vasoconstriction,

tending to increase perfusion to the hypoxic areas in the lung, thus increasing venous admixture.

In addition to the mechanical effects of pulmonary arterial pressure and pulmonary blood flow on hypoxic pulmonary vasoconstriction, mixed venous blood oxygen may also affect the pulmonary vasculature. In areas of alveolar collapse or poor ventilation, the highest blood oxygen content achieved in the pulmonary vasculature of that area may be that of the mixed venous blood. A decrease in $S\bar{v}_{O_2}$ resulting from a decreased cardiac output may potentiate hypoxic vasoconstriction, thus causing a decrease in venous admixture. This hypothesis was tested by Smith *et al.*,¹¹ who altered mixed venous blood oxygen content independent of cardiac output and oxygen consumption with use of extracorporeal veno-venous bypass in anesthetized dogs with normal and with edematous lungs. Mixed venous oxygen content was varied by adding 95 per cent oxygen plus 5 per cent CO_2 or 95 per cent nitrogen plus 5 per cent CO_2 to a disc oxygenator, through which a portion of the dog's venous blood passed. Cardiac output, pulmonary arterial pressure, and pulmonary vascular resistance remained stable throughout the experiment. Decreasing $S\bar{v}_{O_2}$ in animals with normal lungs and pulmonary edema caused a small but significant decrease in \dot{Q}_s/\dot{Q}_t . Because of the changes in \dot{Q}_s/\dot{Q}_t , there was no significant change in Pa_{O_2} with the wide variations in $S\bar{v}_{O_2}$. The authors concluded that changes in mixed venous blood oxygen content may contribute a small but constant amount to the regulation of pulmonary blood flow during alterations in cardiac output.¹¹ From the small changes found in this study, the effect of mixed venous blood oxygen content must be very minor in comparison with the blood flow and pressure effects.

Sawa *et al.*³⁴ have suggested that cardiac output exerts its effect on calculated \dot{Q}_s/\dot{Q}_t by alteration of the oxygen-receiving capacity of the mixed venous blood. Varying the flow through an artificial lung (bubble-type oxygenator), they observed that the calculated shunt decreased as mixed venous blood oxygen saturation decreased, and vice versa. They concluded that there was no change in the oxygenating function of the artificial lung; rather, as $P\bar{v}_{O_2}$ changed so did the affinity of hemoglobin for oxygen as blood passed through the artificial lung. They hypothesized that *in vivo* a reduction in the $P\bar{v}_{O_2}$ would increase the affinity of hemoglobin for oxygen in the pulmonary capillaries so that Pa_{O_2} would remain unchanged. It would then appear that the shunt had decreased, where in fact no change in lung function had occurred. Their experimental data, however, may have reflected only the diffusion limitation of the bubble oxygenator, rather than an *in vivo* effect. Colley *et al.*³¹ showed that

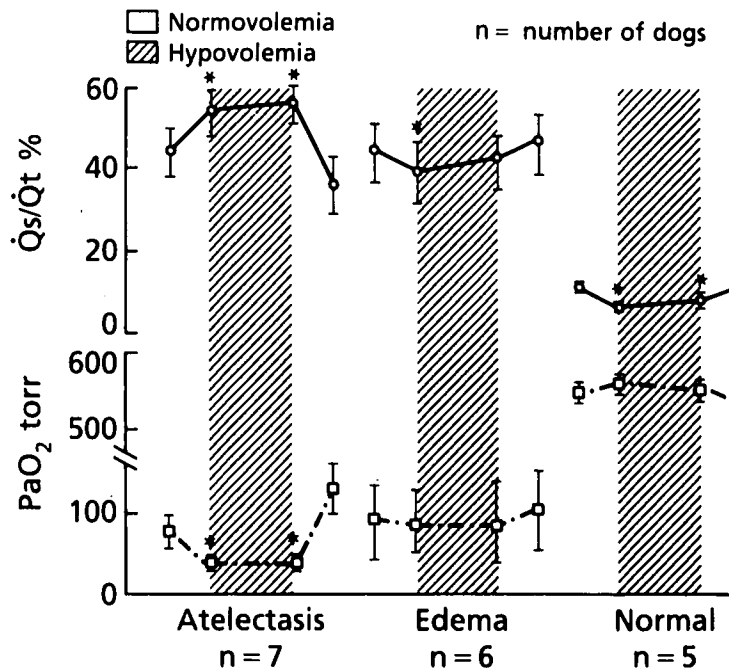


FIG. 1. Mean changes in \dot{Q}_s/\dot{Q}_t and Pa_{O_2} when cardiac output is reduced by 25 per cent during acute hemorrhage (30 min duration) in dogs with normal lungs, diffuse pulmonary edema, or atelectasis of one lung. Values are means \pm SE. * indicates $P < 0.05$ compared with prehemorrhage control values Colley, P. and Cheney, F.: (unpublished data).

a hemorrhage-induced decrease in cardiac output resulted in a decreased $P\bar{v}_{O_2}$ and decreased Pa_{O_2} in dogs with one lung ventilated with 100 per cent oxygen and the other lung ventilated with 100 per cent nitrogen. Calculated flows to the two lungs were about equal with the decreased flow and pulmonary arterial pressure associated with acute hemorrhage, so there was no change in calculated \dot{Q}_s/\dot{Q}_t . These results indicate that variation in the affinity of oxygen for hemoglobin is not a significant factor in the *in-vivo* cardiac output-venous admixture relationship.

In those studies wherein vasoactive agents were used to increase cardiac output, the effect of these agents on the pulmonary vasculature was a factor that undoubtedly affected the results. Catecholamines such as isoproterenol cause pulmonary vasodilatation, which antagonizes hypoxic vasoconstriction.³⁵ As isoproterenol also increases cardiac output, it cannot be definitely concluded whether the increased venous admixture seen in studies with isoproterenol^{17,25} is due to increased total pulmonary blood flow or interference with hypoxic vasoconstriction, or both. From the evidence cited above, the mechanical factors of the alterations in cardiac output, pulmonary blood flow, and pulmonary arterial pressure would seem to be the predominant factors.

Another hypothesis that has been invoked to explain the changes in venous admixture with changes in cardiac output is the possibility of small precapillary pulmonary arteriovenous shunts opening and closing in response to changes in pulmonary arterial pressure.¹⁰ Such anatomic connections have been found in the

dog³⁶ and man.³⁷ However, Cheney *et al.*³⁸ were unable to find any change in anatomic shunt in dogs with a fourfold increase in pulmonary arterial pressure. It appears unlikely that the change in anatomic shunt flow through arteriovenous anastomoses contributes anything significant to the relationship between cardiac output and venous admixture.

Regional Atelectasis

In the previous discussion, the decrease in \dot{Q}_{VA}/\dot{Q}_t or \dot{Q}_s/\dot{Q}_t observed with an acute decrease in cardiac output was seen in both normal and diffusely abnormal lungs and in both man and animals. This effect was mainly attributed to potentiation of hypoxic vasoconstriction as pulmonary arterial pressure (PAP) decreased. There are no comparable studies in man in the presence of regional atelectasis. However, in animals with regional atelectasis just the opposite relationship between \dot{Q}_t and \dot{Q}_s/\dot{Q}_t has been found. Both Wahrenbrock *et al.*³⁹ and Colley *et al.*³¹ have demonstrated that a hemorrhage-induced decrease in cardiac output markedly increases \dot{Q}_s/\dot{Q}_t in animals with lobar³⁹ or one-lung atelectasis,³¹ causing a marked reduction in Pa_{O_2} . The results of a study comparing the effects of hemorrhage on gas exchange in dogs with normal lungs, edematous lungs, and lungs with regional atelectasis are shown in figure 1.

Wahrenbrock *et al.*³⁹ postulated that \dot{Q}_s/\dot{Q}_t increased in the lobar atelectatic model because hemorrhage produced acidosis and catecholamines, which together inhibited hypoxic vasoconstriction in the atelectatic lung. Yet, as we have just seen, hemorrhage appears to

potentiate hypoxic vasoconstriction and reduce \dot{Q}_s/\dot{Q}_t in normal and diffusely injured lungs. Furthermore, Colley *et al.*³¹ found that hemorrhage did not inhibit hypoxic vasoconstriction or alter relative flow to a lung in which hypoxic vasoconstriction was induced by ventilation with nitrogen. Instead, they found that hemorrhage increased pulmonary vascular resistance in the nitrogen-ventilated lung, indicating that hypoxic vasoconstriction was potentiated. Using radioactive microspheres injected into the right ventricle, Colley *et al.*³¹ measured the change in pulmonary blood flow distribution between ventilated and atelectatic lung caused by hemorrhage. They found that hemorrhage increased \dot{Q}_s/\dot{Q}_t by causing a disproportionate reduction in flow and an increase in pulmonary vascular resistance in the ventilated lung. Pulmonary blood flow and pulmonary vascular resistance in the collapsed lung were essentially unchanged from the control state. The mechanism for these observations during hemorrhage would appear to be due to differences in alveolar intravascular pressures, alveolar perivascular pressures, and alveolar structure that exist between ventilated and collapsed lungs. First, hemorrhage decreases flow to the apex or nondependent part of the ventilated lung because of progressive closure of vessels as intravascular pressure in vessels exposed to alveolar pressure falls below alveolar pressure. At the base or dependent part of the ventilated lung and in the collapsed lung, vessel closure should not occur, because intravascular pressure remains higher than alveolar pressure. Second, with lung collapse, gas is absorbed from alveoli and so alveolar pressure decreases. Thus, the net vascular pressure is greatest in the collapsed lung, making the vessels perfusing collapsed alveoli less likely to close with hemorrhage. Third, Assimacopoulos *et al.*⁴⁰ have shown that when alveoli collapse, the air-blood tissue barrier folds into the capillary space, forming intercommunicating chambers. These folds of tissue resemble pillars and may make the capillary bed in collapsed lung more resistant to vascular collapse from a reduction in intravascular pressure.

In simple terms, the effect of hemorrhage on gas exchange with one-lung ventilation is similar to that of overinflation of one lung in the presence of collapse of the other. Finley *et al.*⁴¹ showed that in the presence of one-lung intubation increased transpulmonary pressure in the ventilated lung caused increased perfusion of the nonventilated lung. The net result was an increased \dot{Q}_s/\dot{Q}_t and decreased Pa_{O_2} . Blood was effectively "squeezed" from the ventilated lung to the nonventilated lung as alveolar pressure increased relative to pulmonary arterial pressure in the ventilated lung.

TABLE 2. Effects of an Acute Reduction in Cardiac Output Induced by Hemorrhage on Venous Admixture or Shunt and Pa_{O_2}

	Direction* of Change in		
	\dot{Q}_t	\dot{Q}_{VA}/\dot{Q}_t or \dot{Q}_s/\dot{Q}_t	Pa_{O_2}
Normal lung	↓	↓	±
Pulmonary edema	↓	↓	±
One lung collapsed	↓	↑	↓↓

* Arrows show directions of changes from control values.

In the case of hemorrhage, alveolar pressure stays constant in the ventilated lung while pulmonary arterial pressure decreases, thus giving rise to a relative increase in perfusion of the collapsed lung.

Clinical Implications

The effect of an acute alteration in cardiac output on oxygenation in the clinical situation would appear to depend upon whether the lung is normal or has diffuse disease or regional atelectasis (table 2). In patients who have diseased lungs, changes in shunt or venous admixture may not reflect changes in the intrinsic disease process, but may simply reflect changes in pulmonary blood flow. One of the more frequent causes of decreased cardiac output during anesthesia is hypovolemia. In this circumstance, Pa_{O_2} will not be affected significantly with normal or diffusely abnormal lungs. On the other hand, if the animal data can be extrapolated to man, decreased cardiac output induced by acute hemorrhage in a patient with lobar or one-lung atelectasis may cause a profound reduction in Pa_{O_2} because of the combined effects of decreased mixed venous blood oxygen content and increased venous admixture. Another clinical situation where a decreased cardiac output may be associated with increased venous admixture is pulmonary edema associated with increased left atrial pressure. With left ventricular failure accompanied by a significant increase in left atrial pressure, the pulmonary vessels in the dependent portions of the lung will be mechanically dilated by the high left atrial pressures. These pulmonary vessels would not respond to hypoxic vasoconstriction,³³ so \dot{Q}_{VA}/\dot{Q}_t is likely to remain the same or even increase with a decrease in cardiac output, irrespective of changes in pulmonary edema. In this case, the decreased mixed venous blood oxygen content associated with the decreased \dot{Q}_t would not be offset by a decreased \dot{Q}_{VA}/\dot{Q}_t , so a significant decrease in Pa_{O_2} would result.

Iatrogenic manipulations of cardiac output will probably not affect Pa_{O_2} in patients who have diffuse pulmonary disease. The patients will clearly be better

off with a high cardiac output because of the improvement in oxygen transport, but Pa_{O_2} may not be affected. On the other hand, patients with regional pulmonary disease affecting one lobe or one lung should have marked increases in Pa_{O_2} when cardiac output is increased because \dot{Q}_{VA}/\dot{Q}_t decreases. These patients would benefit not only from increased oxygen transport with a higher cardiac output, but also from increased Pa_{O_2} . It should be recognized that all vasoactive agents that are currently used to increase cardiac output will also affect the pulmonary vasculature and interfere with hypoxic vasoconstriction. This is even true of vasoactive agents that do not primarily affect cardiac output. For example, we have shown that sodium nitroprusside increases \dot{Q}_s/\dot{Q}_t in the presence of regional atelectasis⁴² and increases \dot{Q}_{VA}/\dot{Q}_t in the presence of pulmonary edema,⁴³ both in the absence of change in cardiac output. These changes were presumably due in part to the interference of sodium nitroprusside with the hypoxic vasoconstrictor mechanism in both lung models, and were associated with marked decreases in Pa_{O_2} .

It is hoped that future investigations in man will answer some of the following questions. What are the effects of various anesthetic agents on the relationships of cardiac output and venous admixture to Pa_{O_2} ? What are the effects of some of the adjunct vasoactive agents used during anesthesia on the gas exchange-cardiac output relationships in patients with normal and abnormal lungs? Similar studies should be done in patients in respiratory failure in the intensive care unit. For example, it would be attractive to find pharmacologic agents that increase cardiac output and mixed venous oxygen content without increasing venous admixture in patients with ARDS and large fixed shunts. Alternatively, pharmacologic agents that decrease shunt or venous admixture without affecting cardiac output would also be most useful.

Summary

Although classic teaching suggests that changes in cardiac output and mixed venous blood oxygen content will cause similar changes in Pa_{O_2} , most experimental evidence indicates otherwise. The effects of changes in cardiac output on Pa_{O_2} are variable, ranging from essentially no effect in normal or diffusely diseased lung to a marked direct effect in regional lung collapse. The reason for this phenomenon is that a change in cardiac output itself causes a change in venous admixture or the shunt fraction in the lung. Venous admixture or shunt varies directly with cardiac output in normal or diffusely abnormal lung and indirectly with cardiac output in regional atelectasis.

The net result of the cardiac output-induced changes in mixed venous blood oxygen content and venous admixture is that Pa_{O_2} is significantly affected by cardiac output only in the presence of regional atelectasis, where Pa_{O_2} is directly related to cardiac output. In the normal or diffusely diseased lung, the cardiac output-venous admixture relationship is probably due to the mechanical effects of changes in the magnitude of pulmonary blood flow and pulmonary arterial pressure. These pressure and flow changes alter the hypoxic vasoconstrictive response, which in turn results in changes of the distribution of pulmonary blood flow to areas with low ventilation-perfusion ratios or alveolar collapse. With regional atelectasis, the effects are probably due to the mechanical effects produced by differences in lung heights and pressures acting on vessels, rather than any major effect on hypoxic pulmonary vasoconstriction.

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