

## Changes in Venous Admixture with Alterations of Inspired Oxygen Concentration

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To assess the change in venous admixture during breathing of 100 per cent oxygen ( $F_{I_{O_2}}$ , 1.0), shunt fraction ( $\dot{Q}_s/\dot{Q}_t$ ) was calculated at a maintenance  $F_{I_{O_2}}$  ( $F_{I_{O_2m}}$ : 0.27–0.70) and at  $F_{I_{O_2}}$ , 1.0 in 40 studies of 34 patients with acute respiratory failure. At  $F_{I_{O_2}}$ , 1.0  $\dot{Q}_s/\dot{Q}_t$  increased in 26 studies, but did not increase in 14 studies. Patients in whom  $\dot{Q}_s/\dot{Q}_t$  increased during breathing of oxygen had mild respiratory failure, as indicated by low  $\dot{Q}_s/\dot{Q}_t$  values at  $F_{I_{O_2m}}$  and a low incidence of diffuse parenchymal infiltrates on chest roentgenograms. All patients who had recently had cardiovascular surgical procedures were in this group. Respiratory failure was more severe in those in whom  $\dot{Q}_s/\dot{Q}_t$  decreased with oxygen, as indicated by high  $\dot{Q}_s/\dot{Q}_t$  values at  $F_{I_{O_2m}}$ , evidence of diffuse pulmonary disease by roentgenography, and signs of adult respiratory distress syndrome. The authors conclude that changes in  $\dot{Q}_s/\dot{Q}_t$  in response to  $F_{I_{O_2}}$ , 1.0 in acute respiratory failure are related to the severity of respiratory insufficiency. (Key words: Lung; function; shunting. Oxygen: blood levels. Ventilation: failure; hypoxic response; shunting.)

HYPOXEMIA associated with acute respiratory failure produced by parenchymal pulmonary disease is a reflection of an increase in venous admixture. Normally, venous admixture is primarily composed of small anatomic shunts through the thebesian and bronchial circulations, with a minor contribution from the "shunt-like" effect due to perfusion of alveoli with insufficient ventilation to permit saturation of mixed venous blood. Venous admixture may be increased in acute respiratory failure by anatomic shunting of blood past nonventilated areas of lung, by a larger contribution from "shunt-like" effects, and by perfusion of alveoli with a barrier to diffusion of oxygen.

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The standard shunt equation gives an estimate of total venous admixture.<sup>1</sup> It is derived from a model of the lung which assumes that pulmonary venous blood is a mixture of only two components: mixed venous blood that perfuses well-ventilated alveoli and mixed venous blood distributed to nonventilated alveoli. Although using this model to calculate shunt fraction provides an index of the overall processes in the lung influencing arterial oxygenation, it yields no estimate of the relative contributions of the anatomic and "shunt-like" components. However, changes in shunt fraction as the inspired concentration of oxygen ( $F_{I_{O_2}}$ ) is altered may provide just such an estimate.

It has been suggested that breathing 100 per cent oxygen ( $F_{I_{O_2}}$ , 1.0) eliminates any contribution of "shunt-like" components, and that shunt fraction at  $F_{I_{O_2}}$ , 1.0 should therefore represent only anatomic shunting.<sup>2–4</sup> However, recent studies have shown that shunt fraction may decrease,<sup>5–8</sup> increase, or remain unchanged in response to breathing oxygen.<sup>5,6,8–10</sup> These discrepancies may be due to differences in underlying pulmonary disease,<sup>5–8</sup> but it has also been suggested that artifactual increases in shunt fraction may be a result of measurement errors in the determination of blood oxygen contents.<sup>11,12</sup>

In this study we attempted to minimize measurement errors in the determination of blood oxygen contents, and to investigate whether changes in shunt fraction in response to high levels of inspired oxygen in patients with acute respiratory failure are related to differences in underlying pulmonary disease.

### Methods and Materials

Thirty-four patients who had acute respiratory failure<sup>4</sup> were studied in the medical–surgical intensive care units of the San Francisco General Hospital and the University of California Hospital. Informed consent was obtained according to human research committee guidelines. Six patients had also had chronic obstructive pulmonary disease prior to admission. In most cases, mechanical ventilation was instituted because of respiratory failure resulting from recent cardiovascular operations, severe trauma, or extensive parenchymal pulmonary disease (table 1). All patients were monitored with arterial and pulmonary-artery catheters, and their lungs were ventilated mechanically. The mean initial arterial blood carbon dioxide

TABLE 1. Clinical Data for Patients in Groups I and II

| Major Etiology of Respiratory Failure             | Group I<br>(n = 26) | Group II<br>(n = 14) | Total |
|---|---------------------|----------------------|-------|
| Recent cardiovascular surgery                     | 9                   | 0                    | 9*    |
| Adult respiratory distress syndrome               | 3                   | 10                   | 13*   |
| Sepsis or pneumonia                               | 6                   | 1                    | 7     |
| Heart failure                                     | 2                   | 0                    | 2     |
| Recent major thoracic/abdominal surgery or trauma | 6                   | 3                    | 9     |

\*  $P < 0.05$ .

tension ( $P_{aCO_2}$ ) was 40 torr (range: 23–55 torr). Upon initiation of the study, patients were hemodynamically stable, and maintenance  $F_{IO_2}$ s ( $F_{IO_{2m}}$ , mean: 0.46; range: 0.27–0.70) were such that oxygenation was clinically acceptable (mean  $P_{aO_2}$ : 100 torr, range: 57–153 torr). Five of the 34 patients were studied on more than one occasion, for a total of 40 studies.

For each study, pulmonary arterial and arterial blood samples were drawn at  $F_{IO_{2m}}$  and at  $F_{IO_2}$  1.0. In 22 of the 40 studies, additional blood samples were obtained at two intermediate levels of  $F_{IO_2}$ . In 13 of the 40 studies,  $F_{IO_2}$  was returned to  $F_{IO_{2m}}$ , where a final pair of blood samples was obtained. All blood samples were drawn anaerobically into heparinized syringes, cooled immediately in ice, and analyzed for  $P_{aO_2}$ ,  $P_{aCO_2}$ , pH, and hemoglobin saturation within two hours. Pulmonary arterial blood samples were not drawn at rates exceeding 1 ml/min.  $F_{IO_2}$  was measured at the inspiratory limb of the mechanical ventilator with a paramagnetic oxygen analyzer (Beckman® D2) whose accuracy was verified with a Corning® 175 blood-gas analyzer. At least 15 min were allowed for equilibration before every change in  $F_{IO_2}$ . At  $F_{IO_{2m}}$  systemic and pulmonary arterial phasic and mean pressures were recorded. Additional measurements at  $F_{IO_{2m}}$  included pulmonary-artery occlusion pressure, end-inspiratory and end-expiratory airway pressures, tidal volume, and cardiac output. These measurements were also made at each level of  $F_{IO_2}$  in most studies. An anteroposterior chest roentgenogram obtained on the day of the study was evaluated by one of the authors (SQ or GK) and was considered to manifest diffuse parenchymal infiltration when pulmonary infiltrates were present in at least three quadrants.

Patient outcome (patients eventually discharged from the intensive care unit were considered to be survivors) and ability to resume spontaneous breathing (weaned) were also recorded for each study. The latter was judged on the basis of whether the patient was at any time able to maintain spontaneous breathing for more than 24 consecutive hours after a study and before any subsequent study.

Shunt fraction ( $\dot{Q}_s/\dot{Q}_t$ ) was calculated by use of the standard shunt equation from oxygen contents (ml/dl) of pulmonary end-capillary, arterial, and mixed venous blood.<sup>1</sup> Arterial and mixed venous blood oxygen content values were derived from measurements of hemoglobin, hemoglobin saturation, and oxygen tension, assuming the oxygen-carrying capacity of hemoglobin to be 1.34 ml/g. Pulmonary end-capillary oxygen content was derived in a similar manner using the alveolar oxygen tension ( $P_{A_{O_2}}$ ) computed from the alveolar gas equation, and assuming hemoglobin saturation to be 100 per cent. In five studies where the alveolar oxygen tension was less than 205 torr, hemoglobin saturation was estimated using the  $O_2$  dissociation data of Roughton and Severinghaus.<sup>13</sup>

Hemoglobin concentration was measured by the cyanmethemoglobin technique. Hemoglobin saturations were obtained using a Radiometer® OSM2 Hemoximeter. Oxygen tension values were determined with the use of a Corning 175 blood-gas analyzer and were corrected to the patient's temperature.<sup>14</sup> For blood oxygen tension values greater than 350 torr, measurements were obtained after the cuvette was purged with a gas mixture containing 95 per cent oxygen. The oxygen analyzer was calibrated with gases of known oxygen concentration measured by the Scholander technique.<sup>15</sup> The accuracy of the blood-gas analyzer for measuring high oxygen tensions was specifically checked against known gas mixtures. The greatest error occurred using 95 per cent oxygen, where  $P_{O_2}$  was underestimated by 15 torr. For all measurements of oxygen tension in blood, corrections were made for gas-blood differences.<sup>16</sup>

Static total respiratory compliance ( $C_T$ , ml/cm  $H_2O$ ) was calculated from end-inspiratory (measured after no flow for 1 sec) and end-expiratory airway pressures obtained using the aneroid manometer integral to the ventilator, and tidal volume obtained using a Drager® spirometer.\*\* Mean and phasic blood pressures were measured using Hewlett Packard® 78304A or Electronics for Medicine® IR4 oscilloscopes, and Hewlett Packard 1280 pressure transducers. All instruments were calibrated electronically, and the midpoint of the left atrium was assumed to be in the mid-axillary line. Cardiac output values were measured by the thermodilution technique.†† Pulmonary vascular resistance (dynes·sec·cm<sup>-5</sup>) was calculated from the appropriate intravascular pressures and cardiac output. Oxygen consumption (ml/min) was calculated using the Fick equation.

\*\* North American Drager, Telford, Pennsylvania.

†† Edwards Model 9520, Santa Ana, California, and Santa Barbara Technologies Model 1700, Santa Barbara, California, Cardiac Output Computers.

The data were analyzed using Student's *t* tests for paired and unpaired data, chi-square analysis with Yates' correction, one-way analysis of variance, the binomial test, and Wilcoxon's signed rank test with Bonferroni's correction where appropriate. Results are given as mean  $\pm$  standard error.<sup>17</sup>

**Results**

The mean difference between shunt fraction measured at  $F_{I_{O_2}}$  1.0 and that measured at  $F_{I_{O_2m}}$  for all studies was  $+0.03 \pm 0.01$  ( $P < 0.01$ ). More importantly, the shunt fraction increased with  $F_{I_{O_2}}$  1.0 when the shunt fraction at  $F_{I_{O_2m}}$  was relatively small, whereas it decreased or remained unchanged when the shunt fraction at  $F_{I_{O_2m}}$  was large (fig. 1). Although in many patients the shunt fraction increased with  $F_{I_{O_2}}$  1.0, in no patient was  $Pa_{O_2}$  at  $F_{I_{O_2}}$  1.0 less than that at  $F_{I_{O_2m}}$ .

Studies were retrospectively classified into one of two groups, according to the change in shunt fraction in response to  $F_{I_{O_2}}$  1.0. Group I represents 26 studies in which shunt fraction increased. In Group II are 14 studies where it decreased or did not change. All patients with respiratory failure following cardiovascular operations were in Group I (table 1). Most patients with the adult respiratory distress syndrome were in Group II. There was no difference between groups in the proportions of patients with respiratory failure resulting from sepsis or pneumonia, heart failure, and major thoracic/abdominal operations or trauma. Four patients were antecedent chronic obstructive pulmonary disease were in Group I and two were in Group II. Group II had higher values for mean shunt fraction at  $F_{I_{O_2m}}$ , cardiac output, and oxygen consumption, and a greater proportion of chest roentgenograms with diffuse parenchymal infiltrates (table 2).

Shunt fraction was calculated at two intermediate

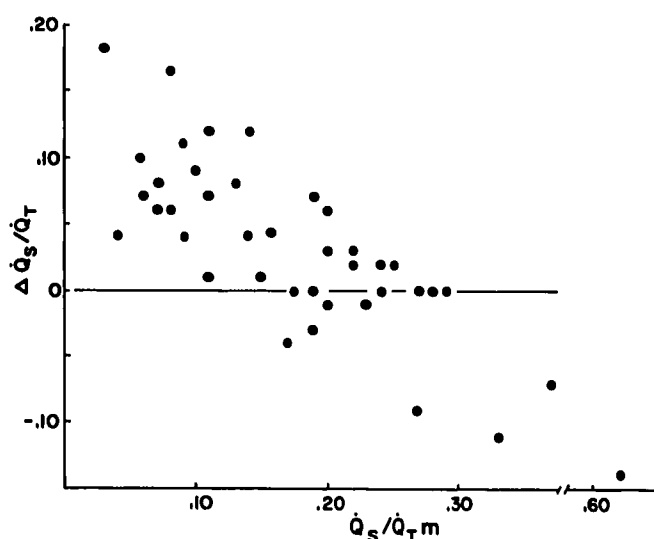


FIG. 1. Change in shunt fraction ( $\Delta Q_s/Q_t$ ) during breathing of 100 per cent oxygen as a function of the initial shunt fraction ( $Q_s/Q_{tm}$ ). Low values of  $Q_s/Q_{tm}$  are associated with a  $+\Delta Q_s/Q_t$ , whereas with higher values of  $Q_s/Q_{tm}$ ,  $\Delta Q_s/Q_t$  is negative or zero.

levels of  $F_{I_{O_2}}$  in 14 studies in Group I and eight in Group II. In Group I, shunt fraction progressively increased as  $F_{I_{O_2}}$  increased. At each higher level of  $F_{I_{O_2}}$ , the shunt fraction was greater than that at  $F_{I_{O_2m}}$  ( $P < 0.02$ ; fig. 2). For Group II, shunt fraction initially declined as  $F_{I_{O_2}}$  increased and then remained unchanged as  $F_{I_{O_2}}$  approached 1.0 ( $P < 0.05$ ; fig. 2).

The change in shunt fraction with increasing  $F_{I_{O_2}}$  was not related to respiratory compliance, cardiac output, pulmonary vascular resistance, mean pulmonary arterial pressure, or pulmonary-artery occlusion pressure when all patients were analyzed together or separately as Groups I and II. In those 13 studies where  $F_{I_{O_2}}$  1.0 was followed by  $F_{I_{O_2m}}$ , the initial and final shunt fractions at  $F_{I_{O_2m}}$  were not significantly different.

TABLE 2. Characteristics of Patients in Group I Compared with Group II

|  | Group I<br>(n = 26)* | Group II<br>(n = 14)*        |
|--|----------------------|------------------------------|
| Shunt fraction at maintenance $F_{I_{O_2}}$ ( $F_{I_{O_2m}}$ )             | $0.13 \pm 0.01(26)$  | $0.28 \pm 0.03(14)\ddagger$  |
| Change in shunt fraction with 100 per cent oxygen ( $\Delta Q_s/Q_t$ )     | $+0.06 \pm 0.01(26)$ | $-0.04 \pm 0.01(14)\ddagger$ |
| Maintenance $F_{I_{O_2}}$ ( $F_{I_{O_2m}}$ )                               | $0.44 \pm 0.02(26)$  | $0.50 \pm 0.03(14)$          |
| Cardiac output ( $l \text{ min}^{-1}$ )                                    | $5.1 \pm 0.3 (22)$   | $7.4 \pm 0.5 (12)\ddagger$   |
| Oxygen consumption ( $ml \text{ min}^{-1}$ at STPD)                        | $233 \pm 13 (22)$    | $298 \pm 12 (12)\ddagger$    |
| Pulmonary vascular resistance ( $dynes \cdot sec \cdot cm^{-5}$ )          | $249 \pm 36 (22)$    | $171 \pm 24 (12)$            |
| Total static lung thoracic compliance ( $ml \text{ cm H}_2\text{O}^{-1}$ ) | $45 \pm 3 (25)$      | $46 \pm 5 (14)$              |
| Pulmonary-artery occlusion pressure (torr)                                 | $13.2 \pm 1.0 (25)$  | $10.4 \pm 1.3 (14)$          |
| Patients weaned†   | 18/26                | 6/14                         |
| Patients surviving†  | 17/26                | 5/14                         |
| Patients with roentgenographic diffuse parenchymal infiltration            | 8/26                 | 10/14‡                       |

\* Data given as means  $\pm$  SEM were applicable. Number of patients for each variable is given in parentheses.

† Criteria defined in text.  
‡  $P < 0.05$ .

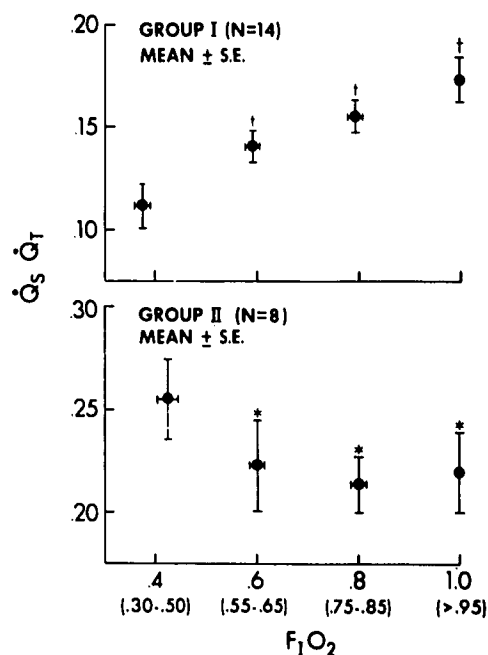


FIG. 2. Shunt fraction ( $\dot{Q}_s/\dot{Q}_t$ ) as a function of inspired oxygen concentration ( $F_{I_{O_2}}$ ). In patients of Group I (upper),  $\dot{Q}_s/\dot{Q}_t$  progressively increased with increasing  $F_{I_{O_2}}$ . In Group II (lower), there was an initial decline in  $\dot{Q}_s/\dot{Q}_t$  as  $F_{I_{O_2}}$  increased from 0.4 to 0.6, but no further change as  $F_{I_{O_2}}$  increased from 0.6 to 1.0. \*Significant difference ( $P < 0.05$ ) compared with value at  $F_{I_{O_2}} = 0.4$ . †Significant difference ( $P < 0.02$ ) compared with value at next-lowest  $F_{I_{O_2}}$ .

### Discussion

The net change in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0 is a result of those effects that increase and those that decrease  $\dot{Q}_s/\dot{Q}_t$ . Two mechanisms have been suggested for the increase in  $\dot{Q}_s/\dot{Q}_t$  with an increasing  $F_{I_{O_2}}$ . First, resorption atelectasis may be produced by the removal of the stabilizing effects of nitrogen in very poorly ventilated alveolar units, resulting in a decrease in functional residual capacity (FRC) and an increase in  $\dot{Q}_s/\dot{Q}_t$ .<sup>9,10,18,19</sup> The quantity of nitrogen necessary to prevent this process has not been determined. Dantzker *et al.*<sup>20</sup> theorize that as  $F_{I_{O_2}}$  increases the number of critically unstable, poorly ventilated alveoli also increases, resulting in progressive atelectasis and larger shunt fractions. Resorption atelectasis has not been demonstrated in normal subjects when  $F_{I_{O_2}}$  is less than 0.95.<sup>21</sup> In a clinical study of patients with acute respiratory failure whose lungs were mechanically ventilated, Suter *et al.*<sup>9</sup> observed increases in  $\dot{Q}_s/\dot{Q}_t$  at  $F_{I_{O_2}}$  0.90 and 1.0, but FRC decreased at  $F_{I_{O_2}}$  1.0 only.

The second mechanism proposed is that of dilation of pulmonary arterioles which had been constricted by local hypoxia, thereby increasing pulmonary blood flow to poorly ventilated or nonventilated areas of lung. This has been described as a release of hypoxic

pulmonary vasoconstriction (HPV). In acute respiratory failure, HPV occurs in areas of the lung with low alveolar ventilation, resulting in a more favorable distribution of pulmonary blood flow. Pulmonary arteriolar vasoconstriction has been shown to decrease with either a high  $P_{A_{O_2}}$  or a high mixed venous oxygen tension,<sup>22</sup> which may occur as  $F_{I_{O_2}}$  is increased. It is, therefore, possible that with enhanced oxygenation pulmonary arterioles in close proximity to, but not perfusing, the alveoli will increase their blood flow, resulting in an increase in  $\dot{Q}_s/\dot{Q}_t$  without a change in FRC.<sup>9,10,23</sup>

The influence of mechanisms that increase  $\dot{Q}_s/\dot{Q}_t$  is demonstrated by the increase in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0 in Group I patients. These patients had lower  $\dot{Q}_s/\dot{Q}_t$  values at  $F_{I_{O_2m}}$  and a lower incidence of diffuse parenchymal infiltrates on chest roentgenograms than did patients of Group II. Group I also included all patients who had respiratory failure following cardiac surgical procedures, in whom extensive parenchymal pulmonary disease would not be expected. Prior studies of similar patients also demonstrated increases in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0.<sup>6,9</sup>

The present study was unable to differentiate between the effects of resorption atelectasis and those of regional changes in pulmonary blood flow. Three arguments, however, suggest that resorption atelectasis was not the major cause of the observed increases in  $\dot{Q}_s/\dot{Q}_t$  during breathing of oxygen. First, as demonstrated by the 14 patients in Group I studied at intermediate levels of  $F_{I_{O_2}}$ , there was a progressive increase in  $\dot{Q}_s/\dot{Q}_t$  at  $F_{I_{O_2}}$  levels well below 1.0, and resorption atelectasis is not observed in this type of patient until the  $F_{I_{O_2}}$  approaches 1.0.<sup>9</sup> Second, there was no difference in  $\dot{Q}_s/\dot{Q}_t$  values obtained at the initial  $F_{I_{O_2m}}$  and upon return to  $F_{I_{O_2m}}$ . Since there was no deliberate attempt to reexpand atelectatic alveoli, any atelectasis resulting from resorption would have been expected to produce a higher  $\dot{Q}_s/\dot{Q}_t$  upon return to  $F_{I_{O_2m}}$ . Third, increases in  $\dot{Q}_s/\dot{Q}_t$  were not associated with changes in  $C_T$ . Suter *et al.*<sup>9</sup> demonstrated a decrease in  $C_T$  corresponding to a decrease in FRC and an increase in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0. While change in  $C_T$  is not a sensitive indicator of change in FRC, the lack of any decrease in  $C_T$  with increasing  $\dot{Q}_s/\dot{Q}_t$  in this study argues against resorption atelectasis as a major cause of an increase in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0.

A decline in  $\dot{Q}_s/\dot{Q}_t$  with increasing  $F_{I_{O_2}}$  has been attributed to a decrease in "shunt-like" effects produced by poorly ventilated areas of lung or impairment of diffusion. As  $F_{I_{O_2}}$  and thus  $P_{A_{O_2}}$  are increased, more oxygen enters poorly ventilated areas of lung. Although the significance of diffusion impairment in producing arterial hypoxemia is unclear, the increase in  $P_{A_{O_2}}$  offers a more favorable oxygen diffusion

gradient across the alveolar capillary surface. In both cases, "shunt-like" effects are minimized.<sup>2-4</sup>

The influence of a decrease in "shunt-like" effects was observed in Group II, where  $\dot{Q}_s/\dot{Q}_t$  decreased or remained unchanged during breathing of 100 per cent oxygen. The higher mean  $\dot{Q}_s/\dot{Q}_t$  at  $F_{I_{O_2m}}$ , the greater incidence of diffuse parenchymal infiltrates on chest roentgenograms, and the larger proportion of patients with adult respiratory distress syndrome in Group II patients are indicative of respiratory disease more severe than that in Group I. Previous studies involving patients with large shunt fractions have also demonstrated no change or a decrease in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0.<sup>7,8</sup> In some patients of Group II in whom  $\dot{Q}_s/\dot{Q}_t$  did not change or was slightly lower with  $F_{I_{O_2}}$  1.0, the influence of mechanisms that decrease  $\dot{Q}_s/\dot{Q}_t$  may have equalled that of those that increase it. This argument is supported by an increase in  $\dot{Q}_s/\dot{Q}_t$  at high intermediate levels of  $F_{I_{O_2}}$  observed in several patients in Group II. Alternatively, a large contribution to the shunt fraction from a nonresponsive pathologic shunt may explain the lack of change in  $\dot{Q}_s/\dot{Q}_t$  in some patients of Group II.

The explanation for finding both increased and decreased shunt fractions may reside in the ability of the pulmonary vasculature to react to changes in  $P_{A_{O_2}}$ . In patients with moderate respiratory insufficiency, an intact pulmonary vasoregulatory mechanism may facilitate a favorable regional redistribution of pulmonary blood flow to well-ventilated alveoli. It has been suggested that this redistribution is abolished at high  $F_{I_{O_2}}$ ,<sup>24,25</sup> producing an increase in  $\dot{Q}_s/\dot{Q}_t$ . With more severe parenchymal pulmonary disease, this reactivity may be impaired or absent. Alternatively, there may be large regions where ventilation is absent; hence,  $P_{A_{O_2}}$  will have no effect on the vascular tone in these regions. These conditions may favor a decrease in  $\dot{Q}_s/\dot{Q}_t$ . Since change in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0 appears to be related to the severity of underlying respiratory failure, it may be another indicator of the severity of underlying parenchymal pulmonary dysfunction.

Errors in the measurement of oxygen tension at high levels of  $F_{I_{O_2}}$ <sup>11,12</sup> can artifactually increase  $\dot{Q}_s/\dot{Q}_t$ , but it is unlikely that this is the explanation for the increase in  $\dot{Q}_s/\dot{Q}_t$  in Group I of this study. Rapid cooling of the blood samples, minimal exposure of the samples to air, and purging of the cuvette of the blood-gas analyzer with a gas mixture containing 95 per cent oxygen<sup>††</sup> all minimized error in measuring  $P_{O_2}$ .

Additional findings in this study were higher initial values for cardiac output and oxygen consumption

in Group II patients. It has been suggested that  $\dot{Q}_s/\dot{Q}_t$  may increase with cardiac output.<sup>26</sup> Patients with more severe respiratory failure, as in Group II, may have greater metabolic demands, requiring higher cardiac output to provide adequate oxygen delivery. A higher cardiac output may increase perfusion of nonventilated or poorly ventilated areas of the lung, resulting in a larger  $\dot{Q}_s/\dot{Q}_t$ .

This study has demonstrated that changes in  $\dot{Q}_s/\dot{Q}_t$  with  $F_{I_{O_2}}$  1.0 are related to the severity of underlying respiratory insufficiency as manifested by the level of initial shunt fraction. An increase in  $\dot{Q}_s/\dot{Q}_t$  is more likely to occur when  $\dot{Q}_s/\dot{Q}_t$  at  $F_{I_{O_2m}}$  is small, whereas no change or a decrease may be seen when  $\dot{Q}_s/\dot{Q}_t$  at  $F_{I_{O_2m}}$  is large. In clinical situations, therapeutic interventions are sometimes initiated to minimize  $\dot{Q}_s/\dot{Q}_t$  at  $F_{I_{O_2}}$  1.0. This study indicates that use of  $F_{I_{O_2}}$  1.0 to compute  $\dot{Q}_s/\dot{Q}_t$  in patients with mild to moderate respiratory failure may result in an overestimation of the shunt fraction, which may lead to therapeutic maneuvers directed at abnormalities induced by the method of measurement rather than at changes in patient condition. However, calculation of  $\dot{Q}_s/\dot{Q}_t$  at both  $F_{I_{O_2m}}$  and at  $F_{I_{O_2}}$  1.0 may be useful, and may provide important information about the pathophysiology of the underlying pulmonary disease without inducing harm to the patient.

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