Through a Glass Darkly: the Lung as a Window to Monitor Oxygen Consumption, Energy Metabolism, and Severity of Critical Illness

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Medical diagnosis and therapeutic monitoring for critical illness require adaptation of laboratory analyses to the bedside. These are greatly helped by the modification of physiological and biochemical data-acquisition techniques to increase the number and accuracy of noninvasive variables that can be obtained from the patient. This paper addresses the choice of noninvasive measurements and is largely directed at the assessment of oxygen debt as a measure of the severity of ischemic and septic metabolic processes. Especially considered are those noninvasive measures of cardiorespiratory adequacy, key variables that need to be considered together with the metabolic function to adequately reflect the patient's state of accommodation to critical illness or injury. I describe a noninvasive sensor system linked to a computer work-station that functions in a pattern recognition mode to permit classification of patients as to the type and severity of their physiological adaptation. This system can serve as a sophisticated bedside monitor of the severity of the patient's condition, as a guide to therapy.

Additional Keyphrases: oxygen debt · metabolic acidosis · hypovolemia · shock · sepsis · multiple organ failure syndrome

In health, oxygen consumption is a closely regulated phenomenon, oxygen being the critical carbon acceptor in the generation of energy from metabolic fuel substrates. However, in conditions of altered metabolic states such as are seen in patients after injury or during severe sepsis, oxygen consumption increases, especially when these conditions are associated with an increase in body temperature. Conversely, in hypovolemic ischemic, cardiogenic, or vasodilatory shock states, where oxygen delivery is restricted by low flow, oxygen consumption decreases, falling below the oxidative requirements of the various organ metabolic processes. The oxygen debt produced results in a severe metabolic acidosis. The concept of oxygen debt is illustrated in Figure 1.

Quantifying Severity of Low Flow States by Oxygen Debt

Normal resting oxygen consumption (VO2) in young men has been shown to average 140 mL/min per square meter of body surface area, which is equivalent to approxi-mately 3.5 mL/min per kilogram of body weight, or 250 mL/min in the 70-kg textbook man (1). The normal rate of VO2 is reduced by the restriction in tissue perfusion occurring in hypovolemic shock. This decrease in VO2 below the obligatory oxidative needs produces an oxygen deficit (oxygen debt) over time. If resuscitation occurs early in the process, before a critical level of ischemia has been reached, there is a rapid repayment of the oxygen debt, with an overshoot, in which the unmetabolized metabolic acids (reflected by increases in lactate in plasma and in the base deficit) are oxidized with full recovery from the ischemic insult. If the oxygen debt remains unrepaid or is increased for a longer period of time, critical cellular injuries occur, with intracellular organelle disruption and death of the most vulnerable cells, leaving the individual with significant organ damage—primarily in the organs with high oxidative requirements: brain, liver, kidney, myocardium, and immunologic tissues. These cellular injuries induced by acute ischemia predispose to later complications related to failures of organ function. The specific effects of these failures of cell and organ function are revealed clinically as an altered host defense, which predisposes to sepsis, or as a decompensating organ injury, as is seen in the post-ischemic brain syndrome. Finally, if the oxygen debt is unrepaid for a long enough period, the debt accumulates to a level at which sufficient lethal cell injury is present to prevent recovery, and death may follow, often associated with the so-called multiple organ failure syndrome (MOFS) (2).

The relationship of this oxygen debt to the likelihood of death has been quantified by Crowell and Smith (3) in a canine model, where they found an LD50 at an oxygen debt of 120 mL/min per kilogram. More recently, a precise quantitative study of the relationship of oxygen debt to the
probability of death has been carried out by Dunham et al. (4), using a hemorrhagic shock model that more accurately reproduces the circumstances of patient hypovolemia and resuscitation. Their data (Figure 2) demonstrate the $LD_{50}$ to be at an oxygen debt of 113.5 mL/kg, approximately the same as that by Crowell and Smith (3).

In addition, the Dunham study (4) showed that not only can an accurate prediction of the probability of mortality ($P_{\text{death}}$) be made from the accumulated oxygen debt, but also if the oxygen debt rate can be ascertained, then the time remaining from any given oxygen debt until the estimated $LD_{50}$ is reached also can be estimated as a guide to the urgency of resuscitation.

The consequence of the ischemic restriction of oxygen availability is to prevent the oxidative metabolism of energy fuel substrates, most prominently glucose, as well as various amino acids and lipids. As a result, the magnitude of the oxygen debt is directly proportional to the degree of the metabolic acidosis, reflected by the magnitude of the total base deficit (negative base excess), and by the increase in plasma lactate (4). The relationship between $P_{\text{death}}$, and base deficit in hemorrhagic hypovolemia also has clinical importance. Similarly, my coworkers and I (5), studying 408 patients with blunt multiple trauma, also have shown that in humans the probability of death can be predicted from the magnitude of the metabolic acidosis (Figure 3).

Moreover, our studies (5) have shown that the severity of the ischemic shock process (quantified by the base deficit) interacts with the physiological severity of any direct contusive organ injury to the brain (as reflected by a decrease in the patient’s Glasgow Coma Scale). These two factors appear to be the primary determinants of outcome in injured patients. From the extracellular base excess and Glasgow Coma Scale data obtained at admission, a more comprehensive linear logistic model also has been developed by which the probability of death can be estimated in post-trauma patients (5).

Evaluation of the Post-Injury Hyperdynamic Response from Measurement of Oxygen Consumption

In the post-injury period, trauma induces an altered metabolic state characterized by a hyperdynamic circulation. The main effect of this response appears to be an increase in the delivery of oxygen to tissues whose demand for oxygen consumption has been increased by the sequence of eicosanoid, cytokine, and hormonal mediator interactions initiated by the trauma, and its shock-induced ischemic response (6, 7). The mean magnitude of oxygen consumption in post-trauma patients is increased (Table 1), but the limit of the post-injury stress response is age dependent (1). To a large extent, this age dependence is undoubtedly related to the decrease in lean body mass that also occurs as a function of age, as demonstrated by Moore et al. (8) in their classic studies of the body cell mass. However, regardless of age, the adequacy of the post-injury response to a period of traumatic ischemic shock is reflected in the ability of the hyperdynamic cardiovascular response to increase oxygen consumption above the pre-injury baseline to compensate for the altered metabolic response to injury.

Because the primary function of the cardiac output is the adequate delivery of oxygen to meet the oxygen-consumption needs of the body, one can monitor the degree of severity and the rate of recovery from hypovolemic or

| Table 1. Oxygen Consumption in Post-Trauma Patients* |
|-----------------|---------------|---------------|-----------------|
| Age range, years | $\text{VO}_2$ mL/min per m² | $\text{VO}_2$ mL/kg per min | Estimated $\text{VO}_2$, mL/min² |
| 13–30           | 283           | 173           | 4.28            | 299           |
| 31–49           | 166           | 152           | 3.76            | 263           |
| 50–65           | 98            | 136           | 3.36            | 235           |
| >65             | 98            | 129           | 3.19            | 223           |

* Based on 645 observations in 165 patients. Data from Tacchino RM, Siegel JH, Emanuele T, et al., cited by Siegel et al. (7).

* Estimated for a 70-kg man with 1.73 m² body surface area.
low-perfusion shock states by evaluating the oxygen consumption (VO₂). This can be done indirectly through the direct measurement of cardiac output by indicator dilution techniques, computing the oxygen consumption by multiplying the flow by the arteriovenous oxygen content difference (Cₐ₋V₀₂), adjusted for body surface area or body mass (Table 2).

Oxygen consumption also can be measured directly through quantifying the oxygen mass balance obtained from pulmonary gas exchange. This can be done either on a breath-by-breath basis, taking into account the dynamic flow and compositional changes in the inspired and expired gas, or through an oxygen-balance methodology involving use of a mixing chamber to provide a mean VO₂ over a period of several minutes. The latter method has an advantage for use in patients who are not intubated or ventilated, because a flow-through head tent can be used. However, either of these noninvasive methodologies also can be used in association with a ventilator at an increased fraction of inspired oxygen (FIO₂) in patients who are severely ill or injured, when mechanical ventilation is required for control of respiration.

Relation of Oxygen Delivery to Oxygen Consumption

Under normal conditions, nearly all of the oxygen-carrying capacity of the blood is provided by the hemoglobin. Thus, when hemoglobin concentration is decreased, the cardiac output must be increased to permit oxygen delivery great enough to allow the mandated oxygen consumption (Table 2). Therefore, the maintenance of an adequate concentration of hemoglobin becomes a critical factor in optimizing oxygen delivery at an efficient magnitude of cardiac output, i.e., one that does not require excessive cardiac work.

Finally, I emphasize that oxygen consumption is related not only to the rate of flow throughout the body, which is in turn a function of the quality of cardiac ejection and the hemoglobin concentration, but also to the adequacy of the total blood volume, so that a maximum volume perfusion of the metabolizing capillary beds with an adequate oxygen delivery can be achieved. Studies of the regulation of oxygen consumption in 165 post-trauma patients of all ages (1) (Figure 4) showed that the VO₂ is a function not only of the cardiac ejection fraction, which sets the magnitude of cardiac output, but also of the magnitude of the blood volume, as reflected in the pulmonary reservoir blood volume (DV). An adequate blood volume not only ensures a maximization of pulmonary capillary blood flow distribution to improve oxygen exchange, but also allows for distention and perfusion of the body capillary beds. Figure 4 also demonstrates that a significant negative factor reducing oxygen consumption is the patient's age, which, as noted earlier, has its effect primarily through the decrease of lean body mass. Intercept (INT) is the unexplained effect.

**Quantifying the Effectiveness of Therapy for Shock by Measuring Oxygen Consumption**

As noted earlier, the main function of the cardiac output is to achieve a magnitude of oxygen consumption at which all metabolic needs are compensated. Consequently, determination of an adequate stable volume of oxygen consumption can be substituted for quantification of optimum total blood flow. In various types of pathophysiological conditions (cardiogenic shock, traumatic shock, or severe sepsis, with or without liver disease), the patient attempts to increase flow until a steady-state maximum effective volume of oxygen consumption is achieved (Figure 5). Thus, in the iatrogenic resuscitation from one of these shock states, volume infusion and cardiac inotropic support are increased until the patient reaches his or her steady-state maximum oxygen consumption, i.e., a condition that cannot be further increased by additional support measures. This therapeutic technique also allows the physician to use the noninvasively obtained VO₂ to monitor the effectiveness of the patient's hyperdynamic cardiovascular response to achieve optimum steady-state physiological compensation after a major low-flow shock state (Figure 5).

An example of the interaction of the cardiac output and blood volume in regulating oxygen consumption during and after human traumatic hypovolemic shock is shown in Figure 6. This case demonstrates that the use of oxygen consumption is a better single variable for quantifying the adequacy of perfusion than is blood pressure or heart rate.

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**Table 2. Effect of Hemoglobin Reduction on Circulatory Oxygen Delivery**

<table>
<thead>
<tr>
<th></th>
<th>Arterial: 100 g/L × 90% satn. × 1.39 = 125 mL/L O₂</th>
<th>Venous: 100 g/L × 40% satn. × 1.39 = 58 mL/L O₂</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cₐ₋V₀₂ difference</td>
<td>69 mL/L O₂</td>
<td></td>
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</table>

For a cardiac output of 4.00 L/min:

VO₂ + 69 mL/L O₂ x 4.00 L/min = 276 mL/min O₂

**Fig. 4. Relative effect, in units of VO₂/m² of ejection fraction (EFx), pulmonary dispersive blood volume (DV/m²), and age on oxygen consumption per body surface area (VO₂/m²), as derived from regression equation of 654 results for 165 post-trauma patients from data of Tacchino RM, Siegel JH, Emanuele T, et al., as reported in Siegel et al. (1); used with permission.**

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**Fig. 5. Relative effect, in units of VO₂/m², of ejection fraction (EFx), pulmonary dispersive blood volume (DV/m²), and age on oxygen consumption per body surface area (VO₂/m²), as derived from regression equation of 654 results for 165 post-trauma patients from data of Tacchino RM, Siegel JH, Emanuele T, et al., as reported in Siegel et al. (1); used with permission.**

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**Fig. 6. Relative effect, in units of VO₂/m², of ejection fraction (EFx), pulmonary dispersive blood volume (DV/m²), and age on oxygen consumption per body surface area (VO₂/m²), as derived from regression equation of 654 results for 165 post-trauma patients from data of Tacchino RM, Siegel JH, Emanuele T, et al., as reported in Siegel et al. (1); used with permission.**

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the conventional cardiovascular measures used to evaluate the adequacy of circulation in ordinary clinical practice. Figure 6 shows two phases in the physiological pattern of adaptation to hemorrhage shock and resuscitation in a

24-year-old man, body surface area = 1.79 m², who was involved in a motor vehicle accident. The patient sustained a ruptured spleen, a fractured pelvis, hemorrhagic hypovolemia, and chest contusion with myocardial depression. His physiological response pattern, obtained by the use of invasive measurement techniques, is shown before (Figure 6A) and after (Figure 6B) the institution of adequate volume resuscitation and cardiac inotropic support to help him achieve an adequate hyperdynamic response (I).

Figure 6A illustrates that the cardiac output was markedly depressed (1.9 L/min) because of a marked decrease in blood volume. The pulmonary dispersive blood volume (DV = 223 mL) was lower than the 356 mL (DV = 200 mL/m²) normally expected for this patient. His hemoglobin concentration was essentially normal at 116 g/L. As a result of his low pulmonary blood volume, which was compounded by severe myocardial depression (cardiac ejection fraction of only 44%), the normalized body flow was reduced to a cardiac index of 1.1 L/min per square meter. Even though his body tissues showed a maximum attempt to extract oxygen, an arteriovenous oxygen content difference of 90 mL/L, the oxygen consumption was only 98 mL/min per square meter and there was a significant base deficit of −2.9 mmol/L. Despite this severe hypovolemic ischemia, the use of the blood pressure measurement as an index of severity would have been totally misleading in this patient, because his blood pressure was 107/65 mmHg, with a mean arterial pressure of 93 mmHg, owing to a markedly increased arterial vasoconstrictor response, as evidenced by an increased total peripheral resistance (TPR) of 38.11 mN·cm·s⁻².

Fig. 5. Oxygen consumption/flow relationships in the critically ill: regression lines derived from 758 studies of patients with cardiogenic shock, post-trauma, or with major chronic sepsis or cirrhotic hyperdynamic liver disease.

Source: same as in Fig. 4; used with permission from Churchill Livingstone, New York, NY.
After treatment was instituted (Figure 6B), the blood volume increased to a DV of 409 mL, the cardiac contractility was improved by the addition of continuous intravenous inotropic support (a combination of dopamine and dobutamine), and as a result the cardiac ejection fraction was increased to 82%. As a consequence of both the increased blood volume and the improved myocardial function, the cardiac output rose to 8.8 L/min (cardiac index = 4.9 L/min per square meter). The increased body perfusion resulted in an increased oxygen consumption to 165 mL/min per square meter, which is close to the age-corrected post-stress mean value expected for this patient (Table 1). This was achieved at a relatively normal arteriovenous oxygen content difference (34 mL/L). The combination of more adequate perfusion with an improved oxygen consumption corrected the base deficit. Of considerable clinical interest with regard to the use of blood pressure as a measure of hypovolemic shock, his high diastolic blood pressure despite the ischemic shock state was actually lowered to 118/53 mmHg and the mean arterial pressure was reduced to 69 mmHg, with the decrease in TPR to 6.28 mN·cm·s⁻¹. This decrease in peripheral vascular resistance reflects the abolishment of the previous pathophysiological vasoconstrictor response to trauma as flow and blood volume were increased.

Because oxygen consumption can be adequately measured noninvasively, this type of therapeutically induced major transition from hypovolemic ischemic shock to a state of physiological adequacy clearly can be monitored equally effectively by the indirect invasive measure of cardiac output and arteriovenous oxygen content difference used here, or by the direct noninvasive measurement of oxygen consumption by using the inspired–expired oxygen mass balance obtained from the pulmonary gas exchange.

Use of \( \dot{V}O_2 \) and \( \dot{V}CO_2 \) to Monitor Altered Metabolic Fuel Utilization in Sepsis

The physiological response in the post-injury period is manifested by a hyperdynamic cardiovascular state, which becomes greater in patients who develop severe sepsis or MOFS (9, 10). As part of this normal post-stress response, oxygen consumption rises and remains increased, or increases further as sepsis develops (9). However, when sepsis occurs, the metabolic fuel control is apparently altered, so that there is a relative inhibition of glucose oxidation by peripheral tissues (11, 12), even though the body's total glucose turnover and uptake may be greatly increased (12–14). Under septic conditions, lactate concentrations in skeletal muscle and plasma increase even in the presence of adequate oxygen delivery and high oxygen consumption. This increase is secondary to a post-insulin-receptor inhibition of glucose oxidation at the point of control of pyruvate dehydrogenase (14, 15). This makes the septic increase in plasma lactate different from that seen in low-flow perfusion states, where decreased oxygen delivery rather than altered metabolic fuel control is the limiting factor in oxygen consumption (16).

At the same time as this alteration in glucose oxidation is induced, the down-regulation of pyruvate dehydrogenase activity shifts the pattern of metabolic fuel utilization, so that lipid fuels and branched-chain keto acids are oxidized in preference to glucose, especially in skeletal muscle and heart tissue (9, 11, 17). During the adaptation to sepsis, the ratio between oxygen consumption and carbon dioxide production is altered so that the respiratory quotient (RQ) decreases (11). This alteration in the metabolic utilization of oxygen (\( \dot{V}O_2 \)) and in CO₂ production (\( \dot{V}CO_2 \)) in septic patients is shown in Table 3A. Septic patients have significantly greater oxygen consumption than do nonseptic patients, but with no significant change in carbon dioxide production. Thus the RQ decreases.

Analyzing the change in the RQ over the entire range of caloric intake (Figure 7) indicates that, although there is a wide spread in the data, the mean RQ rises as total calories are increased. However, for any given amount of caloric intake, the septic patients had a lower RQ than the nonseptic patients, this difference in the \( \dot{V}CO_2/\dot{V}O_2 \) relationship being highly significant (11). Table 3B summarizes the preferential utilization of lipid fuels in sepsis. Compared with nonseptic patients, in whom lipid infusion produces little or no significant \( \dot{V}O_2 \) effect, in septic patients the preferential utilization of administered lipid fuels increases oxygen consumption as well as carbon dioxide production, while maintaining the lower \( \dot{V}CO_2/\dot{V}O_2 \) ratio. As a result, in sepsis the RQ generally remains <0.9, unless extremely large quantities of calories are given, in excess of metabolic needs. Under those conditions, a net lipogenesis occurs that is in excess of the increased lipid oxidation capacity of the peripheral muscle and heart (11). The mass balance of CO₂,

### Table 3. Metabolic Gas Exchange

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>( \dot{V}O_2 ) mL/min per m²</th>
<th>( \dot{V}CO_2 ) mL/min per m²</th>
<th>RQ</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>A: In sepsis, all cases, regardless of full mixture</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonseptic</td>
<td>128</td>
<td>133 ± 27</td>
<td>129 ± 29</td>
<td>0.98 ± 0.12</td>
</tr>
<tr>
<td>Septic</td>
<td>246</td>
<td>144 ± 19*</td>
<td>126 ± 19</td>
<td>0.87 ± 0.10*</td>
</tr>
<tr>
<td><strong>B: Effect of lipids and sepsis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nonseptic (no lipid infusion)</td>
<td>94</td>
<td>136 ± 28</td>
<td>130 ± 29</td>
<td>0.97 ± 0.12</td>
</tr>
<tr>
<td>(0.09)</td>
<td></td>
<td></td>
<td>(0.08)</td>
<td></td>
</tr>
<tr>
<td>Septic (no lipid infusion)</td>
<td>132</td>
<td>142 ± 19</td>
<td>123 ± 19</td>
<td>0.87 ± 0.10</td>
</tr>
<tr>
<td>Nonseptic (lipid infusion)</td>
<td>34</td>
<td>124 ± 18</td>
<td>125 ± 22</td>
<td>1.01 ± 0.12</td>
</tr>
<tr>
<td>Septic (lipid infusion)</td>
<td>114</td>
<td>151 ± 14</td>
<td>134 ± 19</td>
<td>0.89 ± 0.09</td>
</tr>
</tbody>
</table>

* Significantly different from nonseptic group (P<0.0001; Student’s t-test of differences between means).

** Table 3: Metabolic Gas Exchange**

Adapted from Nanni et al. (11).
as a measure of $\text{VCO}_2$, can also be obtained noninvasively from the pulmonary gas exchange and the RQ can be computed as a means of quantifying shifts in metabolic fuel utilization and caloric needs compatible with the posttraumatic hyperdynamic state or with the transition to a septic response.

Altered Oxygen Consumption in the Septic Multiple Organ Failure Syndrome

Finally, in severe end-stage sepsis, there is evidence of impairment of a wide range of oxidative processes in association with the development of MOFS (9, 10). The end-stage metabolic failure associated with MOFS appears to involve marked abnormalities in peripheral muscle metabolism, with greatly accelerated proteolysis (septic autocannibalism) (18) as well as severe impairment in skeletal muscle utilization of glucose as an oxidative fuel and profound alteration in hepatic gluconeogenesis (16), ketogenesis (19), and lipogenesis (20). Conjugative detoxification processes in the liver are inhibited, and there is a marked reorganization of hepatic acute-phase protein synthetic function (21). Under these circumstances of septic MOFS, actual oxygen consumption may decrease, despite the maintenance of a persistent exaggerated cardiovascular hyperdynamic state. This deterioration in the $\text{VO}_2$ in the presence of a pathophysiologic high-flow/low-resistance state (the septic B state) is the characteristic feature of end-stage septic MOFS (9, 10).

This change also can be monitored noninvasively by demonstrating a decrease in oxygen consumption when the noninvasive measures of cardiac output are showing an excessive increase in flow and an associated widened pressure pulse dynamic, together with the characteristic physical diagnostic features of hyperdynamic skin perfusion. The likelihood of a transition towards septic MOFS can also be suggested by a progressive increase in lactate and triglycerides in plasma, accompanied by a decrease in base excess to negative values while the $\text{VO}_2$ remains high or normal and the RQ is <1.0. High probability of a fatal septic deterioration is suggested when oxygen consumption becomes insufficient to meet the metabolic needs in hyperdynamic septic MOFS. This abnormality in $\text{VO}_2$ is accompanied by a metabolic acidosis with an excessive increase in plasma lactate (to >5 mmol/L) and in the metabolic base deficit (to exceed –6 mmol/L), despite a high cardiac output. These features can also serve as quantitative indicators of the severity of the organ failure process and, in some cases, as predictors of outcome. Thus, the oxygen consumption and carbon dioxide production, as well as the relationship between them, are noninvasive information of considerable clinical value. Measurements of these variables can be used to assess the presence of a hyperdynamic septic shock state as well as the likelihood of an altered nutritional fuel utilization characteristic of sepsis and the pathophysiological deterioration of the septic MOFS. Also, by using a modification of Weir's methodology (22) with these determinations, the metabolic utilization of carbohydrates, fats, and proteins for oxidation can be determined. Consequently, by utilizing the measurement of oxygen consumption and the change in RQ, one can follow the degree of severity of the septic process and quantify the metabolic fuel needs, as guides to the magnitude, quality, and adequacy of nutritional support measures.

Abnormalities of Oxygen Exchange in the Adult Respiratory Distress Syndrome

In cases of severe respiratory insufficiency following injury or sepsis, the severity of the post-traumatic lung syndrome known as adult respiratory distress syndrome (ARDS) can be quantified by computing the alveolar to arterial oxygen gradient, normalized by the arterial oxygen tension (A – $\text{aO}_2$/PaO$_2$), at a known fraction of inspired oxygen. This so-called respiratory index (RI), when compared with the percentage of pulmonary veno-arterial mixture (Qsp/Qt), provides an index of the availability of ventilatory alveolar oxygen delivery to the perfusing blood whereby the magnitude of the respiratory exchange dysfunction can be quantified (23, 24). Figure 8 shows that not only the respiratory index but also the slope of the respiratory index to pulmonary shunt relationship [RI/(Qsp/Qt)] are higher in those patients who developed severe, eventually fatal ARDS, compared with those patients who had only septic or post-traumatic hyperdynamic states without ARDS, or those with minimal ARDS who survived (24). The respiratory index also can be estimated noninvasively from transcutaneous $\text{PaCO}_2$ measurements (TcO$_2$), adjusted by an empirically derived regression that relates the TcO$_2$ to the $\text{PaCO}_2$ at a known fraction of inspired oxygen (25). The respiratory index relationship can be used not only to quantify the severity of the ARDS process, but also to predict the likelihood of death and severity of ARDS in post-trauma and septic patients (24).

Use of Pattern-Recognition Techniques in Noninvasive Quantifications of Human Pathophysiologic States

The use of pattern recognition techniques to facilitate the interpretation of noninvasive measurements is shown in Figures 9 and 10. Figure 9 shows the graphic output of an on-line computer-based system connected to a set of totally noninvasive sensors used to develop a physiological pattern that is characteristic of various cardiogenic states.

Panel A illustrates a pattern for either hypovolemic or cardiogenic low-flow states (cardiogenic D state). This pattern can be compared with that manifested by a patient with a compensated high-$\text{VO}_2$ post-traumatic or compensated septic state (septic A state, panel B) or that charac-
teristic of a decompensated hyperdynamic septic MOFS (septic B state, panel C). In Figure 10 the pattern seen in severe ARDS respiratory insufficiency (Cp state) is shown together with the individual sensor measures over time, as the prototype changes successively from the D to A to B state patterns shown in Figure 9.

In this noninvasive system, oxygen consumption is measured by a direct oxygen-consumption monitoring device (Delta Track; SensorMedics, Yorba Linda, CA); the transcutaneous $p_{\text{aO}}$ and $p_{\text{aCO}}$ are also measured noninvasively (SensorMedics), and these skin measurements are corrected by use of the algorithms previously described, so that a noninvasive RI can be computed (25). Measures of blood pressure are obtained noninvasively from an oscillometric cuff device, and heart rate is derived from an electrocardiogram. Cardiac output and cardiac ejection velocity are estimated from impedance cardiography (NCCOM), which is corrected by an empirically derived correlation between the noninvasive impedance measures and invasive determinations of cardiac output with use of cardiogreen dye dilution (Siegel et al., unpublished data). In intubated patients, one can also obtain the ventilatory flow dynamics and airway pressures (26).

The physiological picture of a specific patient’s adaptive pattern is compared with the prototype states (shown in Figures 9 and 10), which have been derived from a previous analysis of multivariable data from a large number of critically ill patients classified by their disease pattern (10, 27, 28). The likelihood or similarity of the studied patient to each of these prototype states is compared by using a covariance matrix derived from a bayesian statistical analysis (29). Because the physiological pattern presentation is in terms of standard deviations from a normal resting state (R state), one patient can be compared with another, or with his or her own previous pattern as a state change occurs, and the likelihood of the patient being in a partic-
in the C2 state is a high cardiac index (CI) and heart rate (HR) with increased VO2 and VCO2, but decreased lung tidal volume (TV) and a markedly reduced pulmonary compliance (cmH2O). The PI is increased and the PaO2 (corrected from TCO2) falls despite a very high fraction of inspired oxygen (FIO2). VCO2 is normal or high, with a reduced TV and a decreased minute ventilation (VE), and there is a marked disparity in respiratory gas exchange, as evidenced by an increased PI. The degree of respiratory insufficiency has reached the point at which CO2 elimination is impaired and PaCO2 (corrected from TCO2) increases. This C2 state demonstrates failure of gas exchange for both oxygen and CO2 at high VO2 and VCO2.

The Lung as a Window for Noninvasive Viewing of Physiological Adaptation in Critical Illness

In summary, in hypovolemic shock and in low-flow cardiogenic failure states, the measurement of VO2 can provide a quantitative guide to the adequacy of tissue perfusion, and the likelihood of an oxygen deficit can be evaluated by comparing the noninvasively obtained VO2 with the normally expected stress-increased values of VO2, and with the determinations of plasma lactate and base excess. In critically ill hyperdynamic patients managed in the post-injury or septic phases of their disease process, the adequacy of and need for disease-specific types of nutritional support can be evaluated by analysis of VO2 and VCO2 and the relationship between them, as manifested in the RQ. The measurement of oxygen consumption gives an indication of the total caloric need, and the CO2 production and RQ indicate the required nutritional fuel mixture. The relationship between oxygen consumption and CO2 production provides an estimate of the caloric utilization of carbohydrates and lipids, and the magnitude of protein oxidation can be estimated from a modification of the Weir equation (22), if the daily urinary urea nitrogen excretion is also obtained. Thus, from the dynamics of oxygen consumption and carbon dioxide production, giving the qualitative aspects of metabolic fuel utilization, and the measures of the effectiveness of lung gas exchange (quantified by the respiratory index), the state of physiological adaptation of critically ill patients can be quantitatively assessed by a set of noninvasive sensors whose output is analyzed in real time. From these data, and with use of a diagnostic pattern-recognition technique implemented on a bedside computer work-station, appropriate therapeutic measures can be devised and their response quantified on an ongoing basis, so that appropriate tailoring of cardiodynamic, respiratory, and metabolic therapies can be done to fit the patients' needs.

In conclusion, to succeed in critical care, as to be successful in business, one must follow Marshall Field's law: "Give
the customer [the patient] what she wants [physiologically as well as psychologically]". To understand these physiological requirements [wants], the physician must have a rapid and dynamic means of observing the critical variables and a methodology to facilitate the recognition of the patient's specific pattern of pathophysiological adaptation. The newer developments in noninvasive sensor methodology and computer data analysis make it possible to utilize the respiratory gas-exchange data as well as transcutaneous blood gas and cardiodynamic measurements in a real-time information-generating system. From these data, processed into an information-rich format, a physiologically compatible therapeutic program can be devised and its effects monitored to achieve the optimum possible response.

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References