Continuous monitoring of arterial oxygen tension is not sufficiently accurate for practical use in adults. Because of the shape of the hemoglobin dissociation curve, fluctuations at higher levels of oxygen tension are not reflected by corresponding changes in saturation; consequently, measurement of saturation at these levels also lacks sensitivity in detecting physiologic instability. However, at the lower levels of oxygen present in venous blood, a linear relationship exists between saturation and tension. The use of improved fiberoptic oximetry systems in conventional pulmonary artery flotation catheters has made the bedside application of this relationship of practical value in the continuous assessment of mixed venous oxygen saturation. Our own experience with it extends to more than 630 patients. Changes predictive of cardiorespiratory instability and instantaneous response to nursing or therapeutic maneuvers make this technique highly effective in the care of the critically ill.

Mixed venous oxygen levels are dependent on the effectiveness of air-blood gas exchange in the lungs, cardiac output (Qt), oxyhemoglobin dissociation, and tissue oxygen uptake (VO2). Recently, there has been increased interest in the relationship of mixed venous oxygen to cardiorespiratory function in both acute and chronic conditions. Newer technologic advances have overcome the potential errors associated with intermittent measurement in unstable patients, by allowing continuous instantaneous accurate recording of mixed venous oxygen saturation (SVO2). These techniques are of considerable value in the care of the acutely ill.

**Materials and Methods**

**Clinical Physiology**

The partial pressures of arterial blood gases can be rapidly and accurately measured in a blood gas laboratory by suitable electrodes which for this reason are routinely used to assess the presence and severity of cardiorespiratory failure. Comparison of arterial oxygen tension (PaO2) with the calculated level in the alveoli (PAO2) or a derivation of the difference between these provides an index of the severity of the mismatch between ventilation and perfusion in the lung, and appropriate steps may then be taken to correct it. The oxygen tension cascade which begins in the alveoli continues its downward path and eventually reaches the cellular mitochondria where normal function can be maintained at a level of less than 0.5 mm Hg. The high energy phosphate which is needed to maintain cell membrane integrity is produced at this site. If its production is deficient, increased permeability and irreversible fragmentation of cytoplasmic membranes occurs with resulting intracellular edema and death. A capillary-cell tension difference of 5 to 20 mm Hg appears to be sufficient for normal function, and although this cannot be measured directly, consciousness is lost in healthy volunteers, and blood lactate rises as PaO2 falls below 30 mm Hg. Venous oxygen levels provide a closer indication of those existing at end-capillary sites, and sampling from jugular venous blood indicates that unconsciousness occurs at a tension of less than 20 mm Hg, and irreversible brain damage develops rapidly below 12 mm Hg. Similarly, a fall in the oxygen tension of coronary sinus blood from a normal level of 22 to 25 mm Hg to less than 12 mm Hg would be accompanied by severe reduction in myocardial oxygen consumption and cardiac output if coronary artery blood flow could not be selectively increased. It is this increase in oxygen delivery to vital organs which becomes crucial for tissue survival.

While it is not practical to measure the oxygen in venous blood from individual organs, its level in the pulmonary artery is an acceptable index of the effectiveness of cardiac output and of tissue oxygen uptake in the body as a whole. Oxygen transport to the tissues is related to cardiac output and blood oxygen content:

\[
\text{oxygen transport (ml/min)} = Q \times \text{CaO}_2
\]

where Q is cardiac output in liters per minute, and \(\text{CaO}_2\) is arterial oxygen content in milliliters per liter. The latter takes into account the amount of hemoglobin present, its saturation with oxygen, and the fraction in physical solution. This is represented in the standard equation:

\[
\text{CaO}_2 \text{ (ml/dl)} = (\text{SaO}_2 \times \text{Hb} \times 1.34) + (0.0031 \times \text{PaO}_2)
\]

where Hb is hemoglobin concentration in grams per deciliter, 1.34 ml is the quantitatively derived oxygen combining capacity of 1 g of hemoglobin, and 0.0031 is the amount in milliliters of physically-dissolved oxygen for each millimeter of mercury (mm Hg) partial pressure. The \(\text{SaO}_2\) is expressed as a percentage, and \(\text{PaO}_2\) in mm Hg. This conventional oxygen transport to peripheral tissue has recently been referred to as the coefficient of oxygen delivery (COD) and may be used to distinguish diffusional influences due to tension gradients.
The Fick equation establishes the relationship between cardiac output ($Q$) on the one hand, and tissue oxygen uptake (VVO $\text{O}_2$) and arterial-mixed venous oxygen content difference (C(a–v)$\text{O}_2$) on the other. Thus,

$$Q_1 = \frac{V_{\text{O}_2}}{C(\text{a–v})\text{O}_2}$$

in which $V_{\text{O}_2}$ is expressed in ml/minute and $C(\text{a–v})\text{O}_2$ as ml/liter, or by transposition,

$$C(\text{a–v})\text{O}_2 = \frac{V_{\text{O}_2}}{Q_1}$$

Equation 1

From this, it is apparent that a fall in mixed venous oxygen content (CVO $\text{O}_2$) reflects an increase in tissue oxygen uptake or a fall in cardiac output, or both. These factors can be separated by determining cardiac output using thermodilution or other methods not dependent on the Fick equation. When a steady state oxygen uptake is assumed, changes in mixed venous oxygen content can be accepted as indicating alterations in cardiac output and arterial oxygen content. This is frequently done in clinical practice.

It is a particular virtue of measuring the partial pressure of oxygen in arterial blood that variations can be detected at high levels where the horizontal slope of the oxyhemoglobin dissociation curve prevents corresponding changes in saturation (Fig 1). Partial pressure also takes account of physically dissolved oxygen which can make a significant contribution to arterial oxygen content when a high inspired oxygen fraction (FI$\text{O}_2$) is breathed. In mixed venous blood, these characteristics are not present since the low partial pressure results in a negligible amount of oxygen in solution, and the values for saturation (SVO$\text{O}_2$) fall on the steep slope of the dissociation curve. Between the normal SVO$\text{O}_2$ of 75 percent (PVO$\text{O}_2$ = 40 mm Hg) and a level of 35 percent (PVO$\text{O}_2$ = 20 mm Hg) below which tissue oxygen extraction is not usually effective, the relationship of saturation to tension is linear. Alterations in blood oxygen are readily detectable by measurement of saturation in this range in which there is approximately a 2 percent fall in SVO$\text{O}_2$ for each 1 mm Hg drop in PVO$\text{O}_2$. In the virtual absence of a physically dissolved fraction and a known constant hemoglobin concentration, saturation closely reflects the content present. These considerations make measurement of mixed venous oxygen saturation a valuable tool, particularly since technical advances have made it possible to do so continuously and in real time.

Oximetric Measurement

Transmission and reflection spectrophotometry have been used for many years in the diagnosis and quantitation of intracardiac shunts, both by direct measurement of oxyhemoglobin saturation and with the use of dye dilution curves. Dye curves have also been used for estimation of cardiac output, central blood volume, and less accurately, valvular regurgitation. All photometric methods for the determination of blood oxygen saturation depend on the difference in light absorption between hemoglobin and oxyhemoglobin. As a general statement, it can be said that of the two, hemoglobin is more photosorbent so that there is an increase in transmitted and reflected light when oxyhemoglobin is present. Within narrow spectral bands, spectrophotometry measures light absorption usually from an incandescent source. The reflection method permits the light source and sensing photocell to be on the same side of the blood sample in contrast to transmission spectrophotometry in which the blood is interposed between them. The influence of hemoglobin concentration present in transmission oximetry is not a critical factor with the reflection method and because of this, an infrared filter and photocell are not necessary.

Intermittent sampling methods necessary with these techniques result in average values obtained over varying time intervals, comparable to those for arterial blood gas levels derived from repeated withdrawals through a needle or cannula. Continuous estimation of arterial oxygen saturation can be obtained using an earpiece oximeter. Those presently in use have a high degree of accuracy and a rapid response time. Because of the flatter upper portion of the normal oxyhemoglobin dissociation curve, oxygen tension must fall to less than 60 mm Hg before saturation is reduced below 90 percent. For a patient breathing supplemental oxygen, this represents significant hypoxemia from any cause. This problem and the difficulty of keeping an earpiece in place on a restless patient have made this type of oximetry of less value in the care of the unstable or critically ill than for observations in the cardiac or pulmonary function laboratory.

Fiberoptic reflectometry for direct oximetric measurement of oxyhemoglobin saturation in the right heart and great vessels was introduced in 1968. Progressive modification overcame initial problems associated with the rapid direct readout systems used and made it possible to measure oxygen saturation instantaneously and continuously from intracardiac sites without the need for withdrawal of blood samples. This catheter-oximeter system had particular merit for the study of intracardiac shunts by continuous registration of both blood oxygen saturation and dye dilution curves. The increasing experience of a number of investigators indicated that the system was stable, linear over the range of saturations encountered in clinical practice, rapidly responsive, and simple to operate. It was also accurate and reliable and permitted thorough exploration of the right side of the heart and great vessels in a much shorter period of time than had been previously possible. Frommer et al pointed out that the system made it theoretically feasible to obtain continuous calculation of cardiac output.

Although problems were encountered with this new form of oximetry, they have not proved to be insurmountable. Proximity to or contact with vascular endothelium may produce "wall artifact" which interferes with the accuracy of recorded results. So too does the formation of fibrin or platelet thrombi at the catheter tip. Introduction of an artifact meter into the system allows these problems to be readily detected at their onset by the presence of a pulsatile response through the catheter. Appropriate changes in catheter tip design and simple repositioning and flushing of the catheter have provided corrective answers. The breakage of fiberoptic bundles has not been frequent and has been of more theoretical than practical importance since intermittent sampling of SVO$\text{O}_2$ can be done if necessary. Similarly nonlinearity below 30 percent oxyhemoglobin saturation in some catheter-oximeter systems exaggerates rather than diminishes the hypoxemia present, and the error has not been a serious one. Furthermore, these levels are not usually compatible with prolonged survival. Intervial spectrophotometric calibration ensures correction for hemodilution or shift of the dissociation curve, although in practice, neither of these potential problems has caused difficulty.

Acceptance of commercial systems for clinical use was delayed largely by unmanageable catheter stiffness, which made it difficult to advance the instrument into the pulmonary artery. Other problems of calibration and drift were also troublesome. Within the last few
years, however, these drawbacks have been overcome, and in presently-available catheter-oximeter systems, the use of three wavelengths instead of two has improved sensitivity.4 Flexibility of the original polyvinyl chloride instrument has also been improved by the addition of aramid fibers along the full length of the catheter. This has been accomplished despite the incorporation of two fiberoptic channels in a conventional 7F French balloon-tipped catheter, which has thermodilution capabilities and proximal (right atrial) and distal (pulmonary artery) lumens. It can be directed through a No. 8 French introducer into a central vein by way of subclavian or internal jugular vein access.

In this system, three light-emitting diodes send alternating pulses of three different wavelengths down one fiberoptic channel at a frequency of 244 times per second. This is absorbed and refracted by the hemoglobin constituents and reflected down the receiving channel. Oxyhemoglobin saturation is computed, averaged over a five-second interval, and updated each second on a two-speed paper recorder. In our own practice, calibration is carried out before insertion from a standard reference or after insertion by four wavelength spectrophotometric analysis. Heparinized lactated Ringer’s solution is infused continuously at a rate of 3 ml/hour to prevent clotting. For purposes of calculation, 5 percent dextrose and water is used during thermodilution cardiac output measurement but is otherwise avoided because of facilitated contamination of equipment and hyperglycemia in diabetic patients. Cardiac output determinations and pressure recordings are made in conventional fashion.

This system has proved to be accurate in clinical use.44 Our early experience with it has been previously reported and has now been extended to 630 patients at the time of writing.30 Regression analysis of 124 paired in vivo and in vitro SvO₂ measurements showed a good correlation between them (r = 0.9016, Sy.x = 3.562). It was stable for up to 102 hours of continuous use with an observed drift of less than 1 percent in 24 hours. Consequently, for clinical purposes, recalibration was not found to be necessary at any greater frequency than once daily. The accuracy of the system remained unaffected by body temperature, hemoglobin concentration, cardiac index, or the method of calibration.3 Increasing clinical experience and improvements in design have greatly reduced the incidence of catheter failures to where ease of introduction, monitoring performance, and simplicity of management are comparable to those of conventional Swan-Ganz type.

**DISCUSSION**

Ventilation-perfusion imbalance in cardiorespiratory failure results in hypoxemia, and since there are no body stores of usable oxygen, rapid compensation or correction is needed. When it is sufficiently severe that cellular metabolic needs are not being adequately met, the principal response is either an increase in tissue oxygen uptake or in cardiac output or both. A similar response occurs in anemia or during exercise. A fall in mixed venous oxygen indicates that the delivery system has become impaired, but compensation for its abnormal components can be effected for as long as increased cardiac output is maintained. When this is no longer possible, a reduction occurs in intracellular oxidative metabolism with accumulation of lactic acid and eventually cell death. Because only a small oxygen tension gradient is needed to maintain adequate mitochondrial function, in most circumstances, this is due to failure of convective rather than diffusion mechanisms. Consequently, when arterial oxygenation and hemoglobin concentration are normal, the mixed venous oxygen level is regarded as a reasonable reflection of cardiac output. In general, it is an acceptable index of respiratory exchange at central and peripheral levels and of cardiac function. These relationships are illustrated in equation 1.

In normal circumstances, an athlete may increase oxygen consumption more than tenfold during exercise, but this depends not only on lowering SvO₂, but principally on an adequate increase in cardiac output.10 In severely ill patients, myocardial function is often sufficiently depressed from primary or secondary causes that a low flow state persists. The accompanying increase in respiratory muscle work also necessitates higher oxygen consumption. The influence of muscle activity on oxygen uptake is significant, and marked falls in SvO₂ occur during shivering, convulsions, rewarming after hypothermia, and movement during routine nursing procedures (Fig 2). It has been suggested that in these circumstances, there may be ineffective distribution of oxygen to vital organs because maximum possible oxygen transport has already been achieved (Fig 3).17

Many of the observations on which these concepts are based have come from postoperative studies of patients who have undergone open heart surgery. When arterial oxygen is normal and no detectable reason for increased oxygen uptake is present, changes

![Figure 2. Fall in SvO₂ from simple turning of a patient during nursing care. The degree and duration are noteworthy.](Downloaded From: http://journal.publications.chestnet.org/pdaccess ashx?url=/data/journals/chest/21401/ on 04/02/2017)
in \( \text{SVO}_2 \) and cardiac output have been found to fulfill theoretical expectations by closely paralleling each other, particularly in low flow states.\(^9\) In our own experience and that of others, cardiopulmonary instability is seldom seen at an \( \text{SVO}_2 \) above 60 percent.\(^9\) A rapid or prolonged fall from this level is indicative of a significant deterioration in the patient's clinical condition. A value of less than 40 percent reflects a poor convection state, and based on a normal hemoglobin dissociation curve, a marginal diffusion capacity also.\(^9\) These levels have frequently been associated with the onset of such hemodynamic problems as hypotension, vasoconstriction, ventricular dysrhythmias, respiratory distress, and cardiac arrest.\(^9,10\) As would be expected from the shape of the oxyhemoglobin dissociation curve, the level of \( \text{SVO}_2 \) has been found to vary frequently even when there has been no change in simultaneously recorded arterial oxygen saturation (\( \text{SaO}_2 \)) (Fig I), and our own experience confirms this finding.\(^8\) The rapidity with which these changes develop emphasizes the advantages of continuous monitoring over repetitive sampling.\(^9\) The predictive value of mixed venous oxygen measurements is well established.\(^9\) Alarm limits can be set so that a fall below an optimum saturation will alert attending personnel to institute corrective measures promptly.

The distinctive combination of an increase in cardiac output and low arteriovenous oxygen difference in the early stages of septic shock results in a high \( \text{SVO}_2 \) and may be the first indication of its onset. It has been suggested that these changes in the initial hyperdynamic phase of this syndrome may be due to preferential redistribution of vascular flow to areas of sepsis in which regional vasodilatation is present, or to local arteriovenous shunting.\(^9\) Another possibility is that cellular damage occurs early, and as a consequence, oxygen is no longer taken up by the affected tissues. This is similar to the inhibition of cellular oxidative metabolism due to cyanide poisoning.\(^9\) An unusually high \( \text{SVO}_2 \) should alert the physician to the possibility of commencing sepsis or cyanide intoxication, which can be identified by an elevated blood thiocyanate or plasma cyanide level, particularly when large doses of sodium nitroprusside are being given to

![Figure 3](Image)

**Figure 3.** A small and then a larger drop in \( \text{SVO}_2 \) accompanied turning and tracheobronchial suctioning respectively. Level remained depressed and preceded cardiac arrest by 15 to 20 minutes.

![Figure 4](Image)

**Figure 4.** Sodium nitroprusside infusion was started at the time marker. \( \text{SVO}_2 \) and cardiac output rose as blood concentration increased.

![Figure 5](Image)

**Figure 5.** Muscle paralysis with pancuronium bromide led to improvement in \( \text{SVO}_2 \) as oxygen extraction was reduced.

Continuous Monitoring of Mixed Venous O₂ Saturation (Diversie, McMichan)
hemodynamically-compromised patients. This should not be confused with the rise in SVO₂ to more normal values which occurs when afterload reduction by this drug has allowed cardiac function to improve and which can be used to titrate its effectiveness in bringing this about (Fig 4). A similar improvement in mixed venous oxygen saturation can be seen when muscle relaxants are employed for better surgical access during anesthesia, or to permit adequate synchronization between patient and machine for effective mechanical ventilation (Fig 5).

Positive end-expiratory pressure (PEEP) is an accepted method of improving pulmonary gas exchange during mechanical ventilation. At higher levels, usually above 10 cm H₂O, there may be interference with cardiac output, and consequently, of convective oxygen delivery to tissue sites. Measurement of cardiac output after an increase in the level of PEEP can determine its optimum value, but in practice, a mixed venous oxygen sample has been found to be an acceptable substitute with occasional confirmation by Qt determination. The ability to monitor SVO₂ continuously has made this a simple matter (Fig 6), and in our own experience has effectively reduced the time needed for a "best PEEP" study and the need for cardiac output measurements for this purpose, not only in the care of the critically ill, but also during management of anesthesia.

During therapeutic maneuvers which may interfere with the concentration of inspired oxygen, such as interrupting mechanical ventilation for measurement of pulmonary artery wedge pressure and tracheobronchial suctioning, or weaning from high levels of FIO₂, reduction of the amount of oxygen in the alveoli can result in a fall in its level in mixed venous blood particularly when air-blood gas exchange in the lungs is compromised by an underlying disease process (Fig 7). The physiologic instability which this reflects has led us to modify our approach to these procedures. Similarly, when fiberoptic bronchoscopy is required in a mechanically ventilated patient, the continuous monitoring of SVO₂ has marked benefit in quantitating the interference with oxygenation which frequently results. The increasing use of bronchoalveolar lavage in ventilator-supported patients makes these measurements additionally valuable.

Extremes of ventilation-perfusion (Vₐ/Q) scatter have either a dead space (Vₑ/D⁰) or shunt (Qₛ/Qₜ) effect. It has been shown that the hypoxemia of the adult respiratory distress syndrome is due to increased intrapulmonary venoarterial shunting or areas of low Vₐ/Q. The best available method for separating these physiologic changes is by multiple inert gas elimination. Although of great value, this technique has disadvantages for evaluation of the critically ill. For this purpose, the use of respiroly gases remains the most clinically applicable in spite of its recognized drawbacks. For patient care at the bedside, the two fractions are considered together as shunt effect. Uninterrupted measurement of SVO₂ makes continuous monitoring of Qₛ/Qₜ within sight of practicality, although a number of assumptions are necessary for doing so. The greatest impediment at the present time is the lack of a dependable method for continuous assessment of arterial oxygen tension in adult patients. When this becomes feasible, the long-sought goal of
automated management of cardiorespiratory support will be more readily achieved.

It is now established practice to use right heart catheterization in the management of critically ill or unstable patients, and continuous monitoring of intravascular pressures from the right heart and great vessels is a routine function of intensive care units. This allows assessment of hemodynamic variables so that appropriate therapy can be started and later adjustments made according to the physiologic response.

A recent study has indicated that clinical prediction of functional derangement and its degree is not accurate when these observations are compared with measurements of intravascular pressures and cardiac output obtained from right heart catheterization. The ability to measure mixed venous oxygen saturation uninterruptedly through a pulmonary artery catheter has recently become a practical matter, and its accuracy has been established. Growing experience indicates its sensitivity to cardiorespiratory instability and its predictive capabilities. Because it has reduced the need for repeated estimates of cardiac output and arterial oxygen tensions, it is no more expensive than conventional right heart catheterization, and in our practice has become established as a valuable addition to the care of the unstable patient in coronary and other critical care units and in the operating room.

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