Adequate tissue perfusion and oxygenation are necessary to maintain or restore homeostasis. When tissue oxygen delivery (\(\text{DO}_2\)) is inadequate to meet metabolic demands, shock ensues. Untreated, shock typically progresses to cellular dysfunction. The prompt recognition of and reversal from an early shock state may prevent the onset of cellular dysfunction. There is renewed interest in quantitative measurements of tissue perfusion in the context of shock detection and resuscitation. However, the interpretation of these measurements in the many clinical conditions that manifest in shock are not well defined. This chapter outlines underlying principles of tissue perfusion and oxygenation and reviews some complexities of making clinically useful measurements with existing monitoring approaches.

There are multiple components of the circulation that contribute to cellular oxygenation, each of which is related to monitoring of tissue perfusion and oxygenation. Tissue perfusion is determined by cardiac output, the distribution of cardiac output to regional tissue beds, and the state of the microcirculation. Tissue oxygenation is determined by perfusion as well as by arterial oxygenation, nutritional blood flow, and cellular extraction of oxygen. This is a complex system, which is highly dynamic: Alteration of any component has physiologic impact upon other components (Fig. 22.1). Moreover, there is enormous heterogeneity within the circulation, both between organs and within organs. Hence tissue perfusion and oxygenation is never uniform between organs, nor even in particular tissue beds. Nonetheless, despite these complexities, there are several principles that allow useful monitoring to occur.

1. Peripheral perfusion and oxygenation monitors are not replacements for other commonly used monitors, but instead provide unique physiologic information.
2. A measured decrease in peripheral tissue perfusion may provide a significant and early warning of circulatory insufficiency.
3. In low-flow shock states (such as hemorrhagic or cardiogenic shock), there is a characteristic redistribution of regional blood flow, such that blood flow to the heart and brain is preserved, while peripheral blood flow is decreased. Blood flow to the skin decreases very early in this process; hence, monitoring skin perfusion is a very sensitive indicator of circulatory shock. Blood flow to other tissues such as the intestinal tract also decreases relatively early in shock, making the gut an alternative sensitive monitoring site. Unfortunately, in high-flow shock states (such as septic shock), the distribution of regional blood flow is less predictable, and interpretation of peripheral perfusion data becomes more complex.
4. A measured decrease in peripheral tissue oxygenation may be a significant warning of decreased tissue oxygenation or perfusion, hemoglobin concentration, arterial oxygenation, or increased cellular utilization of oxygen. Sorting out these alternative explanations for abnormal tissue oxygenation can lead to prompt diagnosis and treatment of the underlying problem.
5. Monitoring changes of tissue oxygenation in response to changes in cardiac output or arterial oxygen may provide meaningful clinical information. The use of these devices in response to physiologic challenges adds another dimension to their potential value.

### Monitoring Techniques

#### Pulse Oximetry

Initially developed to measure oxygen saturation noninvasively, pulse oximetry technology now provides additional useful information in the care of critically ill patients. The incorporation of improved signal processing techniques and sensors has advanced pulse oximetry technology to obtain measurements of total blood hemoglobin, dyshemoglobin levels, and peripheral tissue perfusion. The ratio of the pulsatile to nonpulsatile components of the pulse oximetry waveform, frequently referred to as the perfusion index (PI), may provide a quantitative value of peripheral perfusion. Low values of PI are associated with increased severity of illness and decreased survival in patients with shock (1–4).

Pulse oximetry measurements of oxygen saturation in combination with tissue oxygen monitors can indicate whether low tissue oxygenation is due to arterial hypoxemia or to inadequate circulation. Similarly, oximetry measurements combined with oximetry-derived measurements of total blood hemoglobin and peripheral perfusion may provide an assessment of peripheral perfusion and oxygenation.

#### Transcutaneous Oxygen

In 1956 Clark developed a practical polarographic electrode to measure oxygen tension (5). Since then, the Clark electrode has become the standard for blood gas analysis. When the Clark electrode is placed into a heated probe, it can be used to measure transcutaneous oxygen. Heating the skin to 44°C or higher rapidly (over minutes) melts the lipoprotein barrier and allows diffusion of oxygen across the stratum corneum. Transcutaneous oxygen tension (\(\text{PtO}_2\)) values may be site specific, sometimes with lower values in the extremities of patients with peripheral vascular disease. For critical care monitoring, most studies utilize the torso. Despite several confounding issues, transcutaneous oxygen monitoring provides useful physiologic data that are meaningfully related to tissue oxygenation.
Experimental studies have shown that transcutaneous oxygen monitoring is sensitive to arterial oxygen tension (PaO₂) during normal cardiac output, but is more sensitive to perfusion in low-flow shock (6). In adult patients, PtcO₂ is approximately 80% of the PaO₂ during normal hemodynamic conditions. However, when blood flow is diminished, PtcO₂ also decreases. PtcO₂ is therefore related to both perfusion and oxygenation. When perfusion is normal, PtcO₂ varies with arterial oxygenation. When perfusion is inadequate, PtcO₂ varies with cardiac output. Hence, a normal PtcO₂ value indicates that both oxygenation and perfusion are relatively normal. A low PtcO₂ indicates that either oxygenation and/or cardiac output are inadequate. If arterial oxygenation is normal (as indicated by blood gases or pulse oximetry), low PtcO₂ indicates low-flow shock (7).

The relationship between PtcO₂ and PaO₂ can be quantitated, utilizing the PtcO₂ index, which is simply defined as PtcO₂/PaO₂. In a study that simultaneously measured cardiac index, PtcO₂, and PaO₂ in a large number of critically ill surgical patients, it was found that when cardiac output was relatively normal (cardiac index >2.2 L/min/m²), the PtcO₂ index averaged 0.79 ± 0.12. In individual patients with these normal cardiac outputs, PtcO₂ varied linearly with PaO₂. When cardiac output decreased, however, the PtcO₂ index decreased as well. For patients with a cardiac index between 1.5 and 2.2 L/min/m², the PtcO₂ index averaged 0.48 ± 0.07. For patients with a cardiac index below 1.5 L/min/m², the PtcO₂ index was 0.12 ± 0.12 (7). These data confirm that when blood flow is relatively normal, PtcO₂ varies with arterial oxygenation. However, with low-flow shock, PtcO₂ becomes very sensitive to changes in cardiac output.

Clinical studies have demonstrated the usefulness of transcutaneous oxygen monitoring in detecting shock. When PtcO₂ monitors are placed during acute emergency resuscitation, low PtcO₂ values detect both hypoxemia and hemorrhagic shock. Moreover, the response of PtcO₂ during fluid infusion is a sensitive indicator of the efficacy of shock resuscitation (8,9).

Transcutaneous oxygen monitoring thus has benefit both as an early detector of shock and as a monitor to titrate resuscitation to a physiologic end point. It is noninvasive and inexpensive, and is therefore widely applicable for patients at risk, such as during emergency resuscitation of trauma and acute surgical emergencies, in the perioperative and postanesthesia period, and in the intensive care unit (ICU). However, while end points of successful resuscitation utilizing transcutaneous oxygen monitoring have been suggested, such values have not been validated in large prospective studies.

**Tissue Oxygen Monitors**

In addition to transcutaneous oxygen probes, alternative direct tissue oxygen monitoring techniques have been developed. An advantage of such tissue probes is that heating of the skin is not necessary. In addition, specific tissues can be monitored to provide organ-specific information. Probes may be placed into the subcutaneous tissue, which is very sensitive to low flow. They may also be placed into muscle, which is perhaps less sensitive to low flow, but more rapidly responsive to resuscitation. Probes may also be placed directly into organs. For example, specific probes are now available for placement in the brain to provide a measure of cerebral oxygenation.

Two techniques for direct tissue oxygen monitoring are available. Polarographic electrodes incorporated into needles have been most widely utilized. In addition, a technique utilizing the phenomenon of fluorescence quenching is available. Tissue oxygen probes contain a fluorescent compound that is O₂ sensitive, such that its fluorescent emission is diminished in direct proportion to the amount of O₂ present. Energy from the monitor is transmitted through fiberoptic elements to the fluorescent compound in the probe, resulting in the emission of light, which is then measured by sensors in the tissue probe. The intensity of the emitted light is inversely proportional to the tissue pO₂ (10).

Another method of tissue oxygen monitoring is transconjunctival. The conjunctiva of the eye does not have a stratum corneum, so oxygen is freely diffusible. Transconjunctival probes are placed against the eye, and allow continuous tissue oxygen monitoring without heating; the technology has been utilized both during anesthesia and shock (11).

Direct tissue oxygen monitoring devices offer alternatives to transcutaneous monitoring, with the potential advantages of more rapid initial readings, a variety of monitoring sites, and no heating necessary. However, there are little clinical data to determine the relative sensitivities and specificities of these various techniques.

**Near-Infrared Spectroscopy**

Near-infrared spectroscopy (NIRS) has been developed as a noninvasive measure of tissue oxygenation (12–15). NIRS measures the ratio of oxygenated hemoglobin to total hemoglobin (SO₂) in the microcirculation of the underlying muscle by measuring the absorption and reflectance of light. Using cutaneous probes placed upon the thenar eminence, values of 87% ± 6% have been measured in normal volunteers. Early clinical experience suggests that SO₂ values decrease during shock and increase with successful resuscitation. A recent multicenter trial in trauma patients suggested that a SO₂ value of 75% may be a therapeutic goal. This monitoring approach has potential value, as it provides convenient, continuous, noninvasive measurements. However, clinical data are limited. Tissue edema may be
a confounding factor, as the distance between the probe and the underlying muscle affects measurements. Again, the sensitivity and specificity of this device compared to other tissue oxygen monitoring devices has not been studied. NIRS has been demonstrated to have a close relationship to base deficit in critically injured patients (15) as well as predicting development of organ failure in traumatic shock patients (16).

**Gastric Tonometry**

The mesenteric circulatory bed, particularly the gut mucosa, is prone to hypoperfusion and ischemia during shock. Tonometry has been developed as a technique to detect adequacy of gastrointestinal mucosal perfusion (17). The technique is based upon calculation of the gastrointestinal intramucosal pH (pHi). The basis of this measurement is that the gastrointestinal mucosal pCO₂ equilibrates with the gastric luminal pCO₂. Measurement of luminal pCO₂ was originally accomplished by placing a tube diffusible than is O₂, heating of the probe is not necessary. The CO₂ to diffuse; measuring pCO₂ in the balloon, assuming that luminal pCO₂ equals mucosal pCO₂; and then calculating pH by the Henderson–Hasselbalch equation as follows:

\[
\text{pHi} = 6.1 + \log([\text{HCO}_3^-]) / ([\text{HCO}_3^-] \times 0.031)
\]

Gastric pH monitoring has recently been improved by utilizing gas tonometry without the need for balloons, utilizing capnography. This improvement decreases the lag time necessary for equilibration of carbon dioxide, and allows for more continuous measurements.

The potential usefulness of gastric tonometry has been suggested in clinical studies, in which pH has been reported to reflect the severity of shock and to increase during successful resuscitation (17). However, the technique has not gained widespread acceptance, in part because the accuracy of the pH measurement has been questioned. Utilization of arterial bicarbonate as an estimate of mucosal bicarbonate concentrations may be inaccurate. Measurements can also be altered by gastric acid secretion, because buffering of gastric acid by bicarbonate can produce CO₂ in the gastric lumen, which will confound the estimate of mucosal pCO₂. Enteral feeding may also affect pH, although this effect is variable. To minimize these errors, it has been suggested that gastric feeding be withheld and antacid medication given prior to pH monitoring. However, the variation and inaccuracies of gastric tonometry have limited its widespread application. Moreover, clear treatment end points have not been validated.

Several alternatives to gastric tonometry have been studied. Sublingual capnography is a less invasive technique, which shows promise as a sensitive indicator of tissue acidosis in shock models and in early clinical reports (18). This device was recalled in 2004 for infectious complications and may be reinstated in the future. Alternative luminal monitoring sites, such as the small intestine, rectum, and bladder, have also been proposed as monitoring sites for pH monitoring (19).

**Transcutaneous and End-Tidal Carbon Dioxide**

Transcutaneous carbon dioxide may be measured using the Severinghaus carbon dioxide electrode. Because CO₂ is more diffusible than is O₂, heating of the probe is not necessary. In analogy with PtcO₂ monitoring, transcutaneous CO₂ parallels arterial values when cardiac output is relatively normal, although transcutaneous values are normally 10 to 30 mmHg higher than arterial. During low-flow shock, transcutaneous pCO₂ is increased, due to accumulation of carbon dioxide in the tissues due to inadequate perfusion (20). Increased transcutaneous pCO₂ may thus be utilized as an indicator of inadequate circulation, particularly if arterial pCO₂ is normal. In combination with low PtcO₂, increased transcutaneous pCO₂ gives additional evidence of circulatory shock. End-tidal CO₂ may also be utilized as a measure of perfusion; end-tidal CO₂ is decreased during low-flow states due to decreased pulmonary flow (21). Decreased end-tidal CO₂ values in combination with increased transcutaneous pCO₂ and normal arterial pCO₂ values are strong evidence of circulatory shock. This is an example of how combining noninvasive monitoring data can provide additional information.

**TISSUE BLOOD FLOW**

Measuring tissue blood flow can provide an indication of the adequacy of both cardiac output and regional blood flow. In critical illness, blood flow measurement has the particular potential to be combined with tissue oxygen monitoring to help determine if inadequate tissue oxygenation is due to perfusion deficits. Hence, a reliable tissue perfusion monitor has great appeal.

Many technologies have been developed to measure tissue perfusion. The best studied of these is laser Doppler. Laser Doppler utilizes analysis of scattering of light to determine quantitative blood flow in a small area around the probe (22). A variety of probes have been developed, which can be placed noninvasively onto the skin, or into tissues with needle probes. Laser Doppler measurements have been shown to be useful in detecting changes in blood flow under many experimental conditions. However, clinical utility has been limited due to the large variation in blood flow within tissues (23). Because of these variations, no normal values, no optimal values, and no therapeutic goal values for blood flow have been determined.

Numerous alternative approaches to monitoring tissue perfusion have also been developed. Measurement of local blood flow by thermal diffusion has been developed as an alternative to light scattering, and implantable probes using this technology are available. In addition, magnetic resonance imaging, positron emission tomography, and contrast-enhanced ultrasonography have been used to measure tissue perfusion, although these are not available as continuous monitoring devices. Videomicroscopy techniques such as fluorescence microangiography, orthogonal polarization spectral imaging, and sidestream dark field imaging can provide both visual imaging of the microcirculation and measurements of local blood flow (24–26). As with laser Doppler monitoring, validated clinical applications for these technologies have yet to be defined.

**The Oxygen Challenge Test**

An approach to utilize tissue oxygen monitoring in a more dynamic manner was proposed by Dr. Hunt’s group in San Francisco (27,28). Endeavoring to assess adequacy of tissue
perfusion in postoperative patients, they measured subcutaneous PO2 before and after patients breathed high-inspired O2 concentrations. The expected response in well-perfused patients was a rapid increase in tissue PO2. Many postoperative patients failed to demonstrate this response, which was, however, restored with intravenous fluid infusion. A physiologic explanation for the responses of tissue PO2 to inspired O2 is interesting. If there is no cellular O2 deficit, then additional dissolved O2 supplied after breathing O2 is not required nor utilized by cells, and therefore results in increased tissue PO2. However, if there is a cellular O2 deficit (shock), then any additional dissolved O2 would be rapidly utilized, and would thus not result in increased tissue PO2. The tissue PO2 response to inspired O2 may then be a relatively rapid and minimally invasive method to detect cellular hypoxia. This approach, named the O2 challenge test, was evaluated in trauma patients (29–31) (Table 22.1). The O2 challenge test had 100% sensitivity and specificity in detecting flow-dependent O2 consumption in invasively monitored patients in the ICU. It also appeared to be a very sensitive indicator of shock during acute resuscitation. This method, utilizing either transcutaneous or direct tissue O2 monitors, has potential to detect which patients require fluid resuscitation, to provide a physiologic end point for resuscitation, and to detect the patients in whom initial resuscitation is inadequate and who therefore require additional monitoring and therapy. Using a noninvasive transcutaneous (PtcO2) monitor, Yu et al. have studied the O2 challenge test in patients in the ICU and have validated the sensitivity and specificity of the test in identifying patients in occult shock. In addition, their data have defined an increase in PtcO2 of greater than 20 to 25 mmHg in response to a FiO2 of 1.0 as a therapeutic end point (30,31). In a prospective randomized trial using the oxygen challenge test as an end point of resuscitation compared to the DO2 variables from the pulmonary artery catheter, an improved survival was reported (31). Monitoring and treating the peripheral tissue oxygenation state does not exclude utilization of central hemodynamic parameters such as cardiac output and DO2, but does allow manipulation of DO2 to reach a specific goal of tissue perfusion rather than aiming for a general DO2 value.

**SUMMARY**

Monitoring tissue perfusion and oxygenation provides important physiologic information. Increasing interest and use of noninvasive monitoring systems continue to demonstrate utility in the detection and treatment of shock. Great potential exists to develop these devices, which will provide sensitive and specific indications both of the severity of shock and end points for resuscitation. Such systems would provide a minimally invasive approach to improve the treatment of shock. To achieve acceptance and application of such systems will require quality clinical studies to determine and validate optimal treatment goals.

**Key Points**

- In addition to arterial oxygen saturation, pulse oximetry–derived measurements can provide noninvasive estimates of tissue perfusion and total hemoglobin. Low values of peripheral pulse index are associated with increased illness severity and mortality.
- A decreased transcutaneous oxygen value may be an early warning of decreased arterial oxygenation, decreased hemoglobin, or decreased cardiac output.
- The ratio of transcutaneous oxygen to arterial oxygen may be utilized as an end point of resuscitation, with a goal of 0.8.
- NIRS devices placed on the thenar eminence provide a measure of tissue oxygenation, with a normal value of 87% ± 6% saturation. Values less than 75% may indicate shock.
- Increased transcutaneous pCO2 is an indicator of tissue acidosis.
- The presence of decreased end-tidal pCO2 in the face of normal arterial pCO2 is an indicator of low cardiac output.
- The response of transcutaneous or tissue oxygen monitors to an increased FiO2 is an indication of the presence or absence of flow-dependent oxygen consumption. An increase in tissue oxygen of greater than 25 torr may be utilized as an end point of resuscitation.

**TABLE 22.1 Oxygen Challenge Test (29–31)**

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Select patients who have baseline arterial O2 saturation over 90% on FiO2 less than 0.6–0.8.</td>
</tr>
<tr>
<td>2.</td>
<td>Obtain baseline transcutaneous (or tissue) PO2 value.</td>
</tr>
<tr>
<td>3.</td>
<td>Increase FiO2 to 1.0.</td>
</tr>
<tr>
<td>4.</td>
<td>After 5 min, repeat transcutaneous (or tissue) PO2 measurement.</td>
</tr>
<tr>
<td>5.</td>
<td>If transcutaneous (or tissue) PO2 increases greater than 20–25 torr, patient can be assumed to have no flow-dependent oxygen consumption.</td>
</tr>
<tr>
<td>6.</td>
<td>If transcutaneous (or tissue) PO2 increases less than 20 torr, provide therapy to increase oxygen delivery until step 5 is met.</td>
</tr>
</tbody>
</table>

**References**