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**Hemodynamic Monitoring**



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**Chapter 8**

## ARTERIAL BLOOD PRESSURE

> It *should be clearly recognized that arterial presmre cannot be meaured with precision by means sphygmomanometers.*
>
> *American Heart Association, Committee for Arterial Pressure Recording_ 1951*

The arterial blood pressure is one of the most popular measurements in modern medicine. However, as emphasized in the introductory quote made *over a half century ago,* the standard method of recording arterial pressure with an inflatable cuff (sphygmomanometer) is not expected to produce accurate results. The imprecision of the indirect blood pressure measurement (which makes one wonder about the diagnosis of hypertension) can be corrected by cannulating a peripheral artery and recording direct intra-arterial pressures. This is a common method of recording arterial blood pressure in the ICU, but direct arterial blood pressure measurements can (like their indirect counterparts) be misleading.

This chapter provides a brief description of both indirect and direct methods of arterial blood pressure recording and highlights the important shortcomings of each method.

### INDIRECT MEASUREMENTS

The indirect method of measuring blood pressure that is used today was first introduced in Italy'in 1896 (by an Italian physician named Riva-Rocci) and was brought to this country at the turn of the century by the famed neurosurgeon, Dr. Harvey Cushing. This method employs a device called a *sphygmomanometer (sphygmos* is a Greek term for pulse, and a manometer measures pressure), which consists of an inflatable bladder covered by a cloth sleeve and a gauge or column to measure pressure. The cloth sleeve is wrapped around the arm or leg in an area that overlies a major artery, and the bladder in the sleeve is inflated until it reaches a pressure that should compress the underlying artery. The bladder is then slowly deflated, allowing the compressed artery to open,

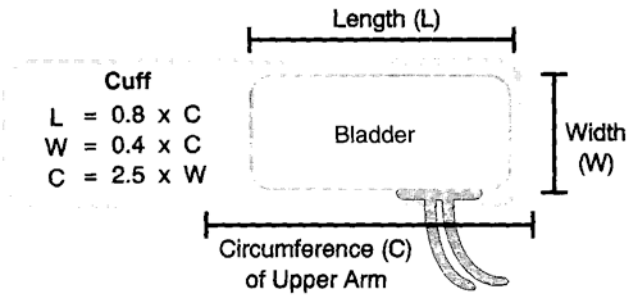


**FIGURE 8.1** Optimal dimensions of the cuff bladder for accurate blood pressure readings. The width ($W$) and length ($L$) of the bladder are expressed in relation to the circumference ($C$) of the upper arm.

and the arterial pressure is determined by recording either the sounds (auscultation method) or the vascular pulsations (oscillometric method) that are generated as the artery opens.

## Influence of Bladder Size

The sounds or vibrations created by the opening of the artery are more reproducible when the artery is compressed uniformly for a short distance, Therefore to ensure a reliable blood pressure recording, the inflatable bladder in the blood pressure cuff should produce a uniform compression of the underlying artery. This is determined by the size of the inflatable bladder relative to the size of the limb being compressed. Figure 8.1 shows the optimal dimensions of the cuff bladder for indirect measurements of brachial artery pressure. The length of the bladder should be at least 80% of the circumference of the upper arm (measured midway between the shoulder and elbow), and the width of the bladder should be at least 40% of the upper arm circumference (1). If the bladder is too small for the size of the arm, the pressure measurements will be falsely elevated (1-5),

### *Miscuffing*

*Miscuffing* is the term used to describe the use of inappropriately sized cuffs for the blood pressure measurement (1). This is considered the most common source of errors in the blood pressure measurement, so it deserves some attention. Table 8.1 shows the appropriate cuff sizes for upper arm circumferences ranging from 22 cm (about 9 inches) to 52 cm (about 21 inches), Since this information is not always available when measuring blood pressures, a simple bedside method of determining
appropriate cuff size is described next. ..

### *Bedside Assessment of Cuff Size*

Before wrapping the cuff around the arm, align the cuff so that the long axis is parallel to the long axis of the arm. Then turn the cuff over so the bladder on the underside is facing you, and wrap the cuff lengthwise around the upper arm, The bladder (width) should encircle half of the upper arm

TABLE 8.1 Appropriate Size of Blood Pressure Cuff in Relation to Upper Arm Circumference

| | Blood Pressure Cuff | |
|---|---|---|
| Upper Arm Circumference | Size | Dimensions |
| 22 to 26 em | Small adult | 12 x 24 em |
| 27 to 34 em | Adult | 16 x 30 em |
| 35 to 44 em | Large adult | 16 x 36 em |
| 45 to 52 em | Adult thigh | 16 x 42 em |

From Reference 1.

(circumference). If the bladder encircles less than half of the upper arm, the cuff is too small, and the blood pressure measurement may be spuriously high. If the cuff encircles most of the upper arm and seems too big for the arm, no change in cuff size is necessary (i.e., a cuff that is larger than needed will not produce spurious pressure recordings) (1),

## Auscultatory Method

The standard method of measuring blood pressure involves manual inflation of an arm cuff placed over the brachial artery. The cuff is then gradually deflated, and the pressure is determined by sounds (called Korotkoff sounds) that are generated when the artery begins to open.

### *The Korotkcdf Sounds*

The Korotkoff sounds are very low frequency sounds (25 to 50 Hz) and are just above the normal threshold for human hearing, which is 16 Hz (6). Human speech is generally in the frequency range of 120 to 250 Hz, and the human ear detects sounds optimally when they have frequencies of 2,000 to 3,000 Hz. (6), What this means is the room should be quiet when listening for Korotkoff sounds (because you will hear people talking more easily than you hear these sounds), and even then, the sounds will be faint to the human ear.

### *Stethoscope Head*

The bell-shaped head of a stethoscope is a low frequency transducer, while the flat, diaphragm-shaped head is designed to detect high frequency sounds. Therefore to optimize detection of the low-frequency Korotkoff sounds, the bell-shaped head of the stethoscope should be used to measure blood pressure (1). This is often neglected, and some stethoscopes are manufactured without a bell-shaped head!

### *Low Flow States*

Because Korotkoff sounds are generated by blood flow, low flow states can diminish the intensity of these sounds. When this occurs, the sounds may not be heard at first (Le., at the systolic pressure), and this will result in falsely low recordings for the systolic blood pressure. The tendency

TABLE 8.2 Discrepancy Between Direct and Indirect Blood Pressure Measurements in Shock

| Systolic BP Difference (Direct BP-Cuff BP) | % |
|---|---|
| 0-10 mm Hg | 0 |
| 11-20 mm Hg | 28 |
| 21-30 mm Hg | 22 |
| >30 mm Hg | 50 |

From Cohn IN. Blood pressure measurement in shock. JAMA 1967;

to underestimate the systolic blood pressure in low flow states is shown in Table 8.2. This is from a study comparing direct and indirect measurements of systolic blood pressure in patients with a low flow state and hypotension (3). In half of the patients, the indirect auscultatory method underestimated the actual systolic blood pressure by more than 30 mm Hg. According to the American Association for Medical Instrumentation, indirect pressure measurements should be within 5 mm Hg of directly recorded pressures to be considered accurate (4), Using this criterion, there was not a single pressure recording with the auscultatory method that could be considered accurate. Observations like these are the reason that direct blood pressure measurements are preferred in hemodynamically compromised patients.

## Oscillometric Method

The oscillometric method uses the principle of plethysmography to detect pulsatile pressure changes (oscillations) in an underlying artery. When an inflated cuff is placed over an artery, the pulsatile pressure changes in the artery will be transmitted to the inflated cuff, producing similar changes in cuff pressure. The periodic changes in cuff pressure (i.e., oscillations) are then processed electronically to derive a value for the mean, systolic, and diastolic blood pressures (5).

### *Peiformance*

Oscillometric devices first appeared in the mid 1970s and since then have gained widespread acceptance for monitoring blood pressure in operating rooms, ICUs, and emergency rooms. However, the accuracy of oscillometric blood pressure measurements is disturbingly low, This is demonstrated in Figure 8.2, which shows a comparison of directly measured systolic pressures with oscillometric measurements in patients undergoing major surgery. The dark line is the line of unity (where the measurements using both techniques would be identical) and the area bounded by the lighter lines (which are 5 mm Hg on either side of unity) is the zone of acceptable accuracy for oscillometric pressure measurements. Note that most of the oscillometric measurements (closed squares) fall outside the zone of acceptable accuracy, indicating that a majority of the oscillometric measurements in this study were inaccurate.

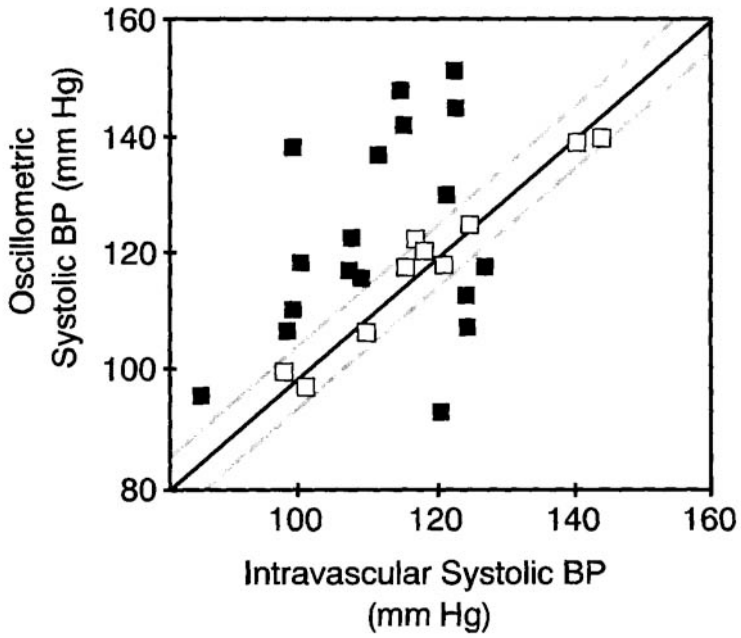


**FIGURE 8.2** Comparison of direct (open squares) and oscillometric (closed squares) measurements of systolic pressure in the brachial artery. (From Gravlee GP, Brockschmidt JK. Accuracy of four indirect methods of blood pressure measurement, with hemodynamic correlations. J Clin Monit 1990;6:284–298.)

5.

Other studies in ICU patients have shown that oscillometric measurements are consistently lower than direct blood pressure measurements (6,7). Some of this discrepancy is due to "miscuffing" (6,7), so attention to proper cuff sizes is important for oscillometric measurements, as it is for auscultatory measurements. However, until accuracy and reliability improve, oscillometric blood pressure measurements should not be regarded as an adequate substitute for direct blood pressure measurements in the ICU.

## DIRECT MEASUREMENTS

Direct recording of intravascular pressures is recommended for all patients in the ICU who are hemodynamically unstable or are at risk for hemodynamic instability. Unfortunately, direct arterial pressure recordings have their own shortcomings, and some of these will be described in the remainder of the chapter,

### Pressure Versus Flow

The distinction between pressure and flow is important to recognize because there is a tendency to equate pressure and flow in certain situations. This is

6.

most evident in the popularity of pressor or vasoconstrictor agents in the management of clinical shock. In this setting, an increase in blood pressure is often assumed to indicate an increase in systemic blood flow, but the opposite effect (a decrease in flow) is also possible.

One of the important distinctions between pressure and flow is the transmission of pressure and flow waves through the circulatory system. Ejection of the stroke volume from the heart is accompanied by a pressure wave and a flow wave, Under normal conditions, the pressure wave travels 20 times faster than the flow wave 00 m/second versus 0.5 m/second), and thus the pulse pressure recorded in a peripheral artery precedes the corresponding stroke volume by a matter of seconds (8). When vascular impedance (Le., compliance and resistance) is increased, the velocity of the pressure wave is increased, while the velocity of the flow wave is decreased, (When vascular impedance is reduced, pressure can be diminished while flow is enhanced.) Thus when vascular impedance is abnormal, the arterial pressure is not a reliable index of blood flow.

## The Arterial Pressure Waveform

The contour of the arterial pressure waveform changes as the pressure wave moves away from the proximal aorta. This is shown in Figure 8.3.

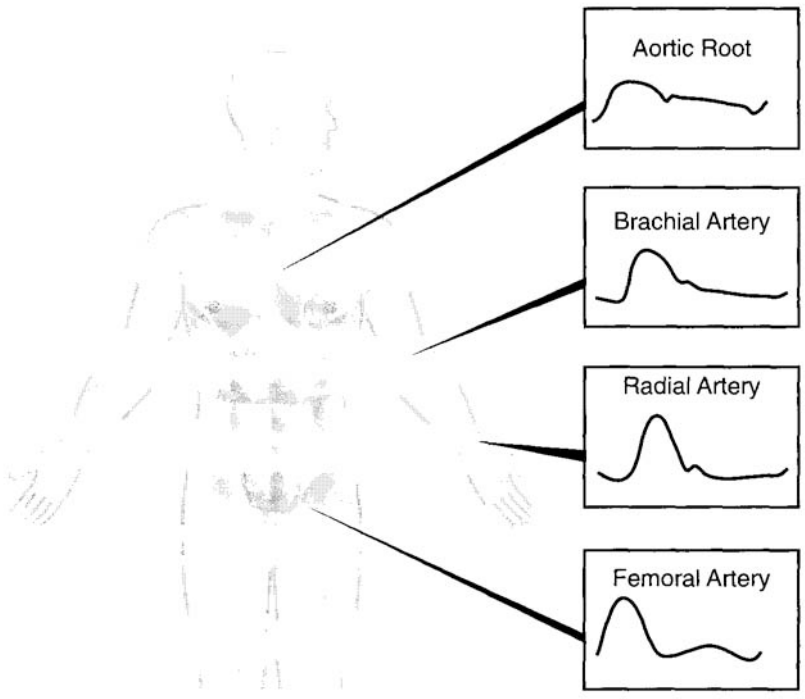


**FIGURE 8.3** Arterial pressure waveforms at designated points in the arterial circulation.

Note that as the pressure wave moves toward the periphery, the systolic pressure gradually increases, and the systolic portion of the waveform narrows. The systolic pressure can increase as much as 20 mm Hg from the proximal aorta to the radial or femoral arteries. This increase in peak systolic pressure is offset by the narrowing of the systolic pressure wave, so that the mean arterial pressure remains unchanged. Therefore, the mean arterial pressure is a more accurate measure of central aortic pressure.

### *Systolic Amplijication*

The increase in systolic pressure in peripheral arteries is the result of pressure waves that are reflected back from the periphery (9), These reflected waves originate from vascular bifurcations and from narrowed blood vessels. As the pressure wave moves peripherally, wave reflections become more prominent, and the reflected waves add to the systolic pressure wave and amplify the systolic pressure. Amplification of the systolic pressure is particularly prominent when the arteries are noncompliant, causing reflected waves to bounce back faster. This is the mechanism for systolic hypertension in the elderly (9). Because a large proportion of patients in the ICU are elderly, systolic pressure amplification is probably commonplace in the ICU.

## RECORDING ARTIFACTS

Fluid-filled recording systems can produce artifacts that further distort the arterial pressure waveform. Failure to recognize recording system artifacts can lead to errors in interpretation.

### Resonant Systems

Vascular pressures are recorded by fluid-filled plastic tubes that connect the arterial catheters to the pressure transducers. This fluid-filled system can oscillate spontaneously, and the oscillations can distort the arterial pressure waveform (10,11).

The performance of a resonant system is defined by the resonant frequency and the damping factor of the system. The resonant frequency is the inherent frequency of oscillations produced in the system when it is disturbed, When the frequency of an incoming signal approaches the resonant frequency of the system, the resident oscillations add to the incoming signal and amplify it. This type of system is called an underdamped system. The damping factor is a measure of the tendency for the system to attenuate the incoming signaL A resonant system with a high damping factor is called an overdamped system,

### Waveform Distortion

Three waveforms obtained from different recording systems are shown in Figure 8.4. The waveform in panel *A,* with the rounded peak and

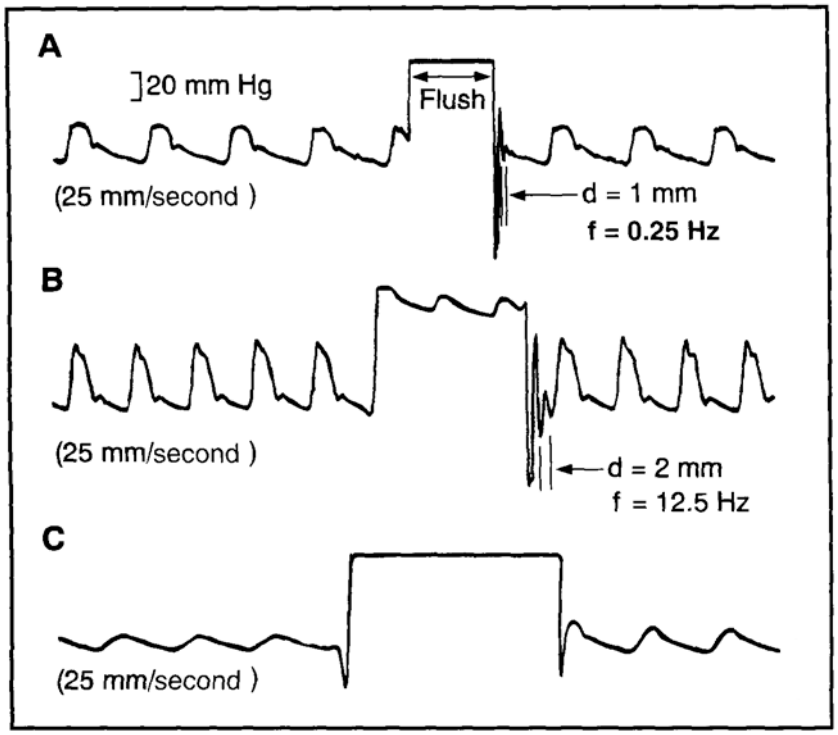


**FIGURE 8.4** The rapid flush test. A, Normal test. B, Underdamped system. C, Overdamped system.

7.

the dicrotic notch, is the normal waveform expected from a recording system with no distortion. The waveform in panel 8, with the sharp systolic peak, is from an underdamped recording system. The recording systems used in clinical practice are naturally underdamped, and these systems can amplify the systolic pressure by as much as 25 mm Hg (12). The systolic amplification can be minimized by limiting the length of the connector tubing between the catheter and the pressure transducer.

The waveform in panel C of Figure 8.4 shows an attenuated systolic peak with a gradual upslope and downslope and a narrow pulse pressure. This waveform is from an overdamped system. Overdamping reduces the gain of the system and is sometimes the result of air bubbles trapped in the connector tubing or in the dome of the pressure transducer. Flushing the hydraulic system to evacuate air bubbles should improve an overdamped signal.

Unfortunately, it is not always possible to identify underdamped and overdamped systems using the arterial pressure waveform. The test described in the next section can help in this regard.

## The Flush Test

A brief flush to the catheter-tubing system can be applied to determine whether the recording system is distorting the pressure waveform (11,13). Most commercially available transducer systems are equipped with a one-way valve that can be used to deliver a flush from a pressurized source. Figure 8.4 shows the results of a flush test in three different situations. In each case, the pressure increases abruptly when the flush is applied. However, the response at the end of the flush differs in each panel. In panel *A,* the flush is followed by a few oscillating waveforms. The frequency of these oscillations is the resonant frequency (f) of the recording system, which is calculated as the reciprocal of the time period between the oscillations. When using standard strip-chart recording paper divided into 1 mm segments, *f* can be determined by measuring the distance between oscillations and dividing this into the paper speed (11); that is, *f* (in Hz) = paper speed (in mm/second) divided by the distance between oscillations (in mm). In the example shown in panel *A,* the distance *(d)* between oscillations is 1.0 mm, and the paper speed is 25 mm/second, so *f* = 25 Hz (25 mm/second divided by 1.0 mm).

Signal distortion is minimal when the resonant frequency of the recording system is five times greater than the major frequency in the arterial pressure waveform. Because the major frequency in the arterial pulse is approximately 5 Hz (14), the resonant frequency of the recording system in panel *A* (25 Hz) is five times greater than the frequency in the incoming waveform, and the system will not distort the incoming waveform.

The flush test in panel *B* of Figure 8.4 reveals a resonant frequency of 12.5 Hz *(f* = 25/2). This is too close to the frequency of arterial pressure waveforms, so this system will distort the incoming signal and produce systolic amplification.

The flush test shown in panel C of Figure 8.4 does not produce any oscillations. This indicates that the system is overdamped, and this system will produce a spuriously low pressure recording. When an overdamped system is discovered, the system should be flushed thoroughly (including all stopcocks in the system) to release any trapped air bubbles. If this does not correct the problem, the arterial catheter should be repositioned or changed.

## Mean Arterial Pressure

The mean arterial pressure has two features that make it superior to the systolic pressure for arterial pressure monitoring. First, the mean pressure is the true driving pressure for peripheral blood flow. Second, the mean pressure does not change as the pressure waveform moves distally, nor is it altered by distortions generated by recording systems (10).

The mean arterial pressure can be measured or estimated. Most electronic pressure monitoring devices can measure mean arterial pressure by integrating the area under the pressure waveform and dividing this by the duration of the cardiac cycle. The electronic measurement is preferred to the estimated mean pressure, which is derived as the diastolic

pressure plus one-third of the pulse pressure. This formula is based on the assumption that diastole represents two-thirds of the cardiac cycle, which corresponds to a heart rate of 60 beats/minute. Therefore heart rates faster than 60 beats/minute, which are common in critically ill patients, lead to errors in the estimated mean arterial pressure.

### *Cardiopulmonary Bypass*

In most circumstances, the mean pressures in the aorta, radial artery, and femoral artery are within 3 mm Hg of each other. However, in patients undergoing cardiopulmonary bypass surgery, the mean radial artery pressure can be significantly (more than 5 rom Hg) lower than the mean pressures in the aorta and femoral artery (15). This condition may be caused by a selective decrease in vascular resistance in the hand, because compression of the wrist often abolishes the pressure difference. An increase in radial artery pressure of at least 5 mm Hg when the wrist is compressed (distal to the radial artery catheter) suggests a discrepancy between radial artery pressure and pressures in other regions of the circulation (16).

## A FINAL WORD

> *I would venture to guess that,of all the procedures done* in *clinical medicine that have important consequences, measurement* ◁f *blood pressure* is *likely the one that* is *done most haphazard'.*
>
> *Norman Kaplan, M.D.*

There are an estimated 50 million people in the United States with the diagnosis of hypertension (17). This represents about 25% of the adult population (210 million) and indicates that hypertension is the number one health problem in this country. Hypertension is clearly an enormous health burden, and the source of this burden is a single diagnostic test: the (indirect) blood pressure measurement. Yet, as indicated by the hypertension expert Dr. Norman Kaplan, this measurement receives little attention and is usually performed haphazardly. This means that a diagnostic test that is performed poorly (i.e., the blood pressure measurement) is responsible for the number one health problem in this country. The implications are obvious.

The consequences of an improperly performed blood pressure measurement are illustrated in the following scenario, About 180 million adults (85% of the adult population) have their blood pressured measured each year. If an improperly performed measurement results in a falsely elevated blood pressure reading in just 1 % of these subjects, 1.8 million new cases of (erroneously diagnosed) hypertension would be created each year. This might explain why there are *so* many people with hypertension in this country.

Regardless of whether you are working in the ICU or elsewhere, it is imperative that you learn all you can about the indirect blood pressure

measurement to obtain the most accurate readings possible. You owe this to your patients and to our overburdened healthcare system,

## REFERENCES

### Chapter 9

## THE PULMONARY ARTERY CATHETER

*A searchlight cannot be used effectively* without *a fairly thorough knowledge of the territory to be searched.*
*Fergus Macartney, FRCP*

The birth of critical care as a specialty is largely the result of two innovations: positive-pressure mechanical ventilation and the pulmonary artery catheter. The latter device is notable for the multitude of physiologic parameters that can be measured at the bedside. Prior to the introduction of the pulmonary artery catheter, the bedside evaluation of cardiovascular function was essentially a "black box" approach that relied on indirect, qualitative markers provided by sounds (e.g., pulmonary rales, cardiac gallops, cuff-based blood pressures), visual cues (e.g., edema, skin color), and tactile cues (e.g., pulse, skin temperature). The pulmonary artery catheter improved dramatically on this approach, allowing physicians to measure quantitative physiologic parameters at the bedside and to apply the basic principles of cardiovascular physiology to the bedside management of patients with cardiovascular disorders.
This chapter describes the multitude of parameters that can be measured with pulmonary artery catheters (1-5). Most of these parameters are described in detail in Chapters 1 and 2, so it may help to review these chapters before proceeding further.
CAVEAT. The value of the pulmonary artery catheter is not determined solely by the measurements it allows but is also dependent on the clinician's ability to understand the measurements and how they are obtained. This deserves mention because surveys indicate that physicians have an inadequate understanding of the measurements provided by pulmonary artery catheters (6,7).

## CATHETER DESIGN

The balloon-flotation pulmonary artery (PA) catheter was conceived by Dr. Jeremy Swan, who was Chief of Cardiology at Cedars-Sinai Hospital when the following experience occurred.

In the fall of 1967, I had occasion to take my (then young) children to the beach in Santa Monica. It was a hot Saturday, and the sailboats on the water were becalmed. However, about half-a-mile offshore, I noted a boat with a large spinnaker well set and moving through the water at a reasonable velocity. The idea then came to put a sail or parachute on the end of a highly flexible catheter and thereby increase the frequency of passage of the device into the pulmonary artery (1).

Three years later (in 1970), Dr. Swan introduced a PA catheter that was equipped with a small inflatable balloon at its tip. When inflated, the balloon acted like a sail to allow the flow of venous blood to carry the catheter through the right side of the heart and out into one of the pulmonary arteries. This "balloon flotation" principle allows a right-heart catheterization to be performed at the bedside, without fluoroscopic guidance.

### Basic Features

The basic features of a PA catheter are shown in Figure 9.1. The catheter is 110 cm long and has an outside diameter of 2.3 mm (7 French). There are two internal channels: One runs the entire length of the catheter and opens at the tip of the catheter (the PA lumen), and the other ends 30 cm from the catheter tip, which should place it in the right atrium (the RA lumen). The tip of the catheter is equipped with a small (1.5 mL capacity) inflatable balloon. When fully inflated, the balloon creates a recess for the tip of the catheter that prevents the tip from coming into contact with (and damaging) vessel walls as the catheter is advanced. The catheter also has a small thermistor (i.e., a transducer device that senses changes in temperature) that is located 4 cm from the catheter tip. The thermistor can measure the flow of a cold fluid that is injected through the proximal port of the catheter, and this flow rate is equivalent to the cardiac output. This is the *thermodilution method* of measuring cardiac output and will be described in more detail later in the chapter.

### Additional Accessories

Other accessories that are available on specially-designed PA catheters include:

An extra channel that opens 14 cm from the catheter tip that can be used to thread temporary pacemaker leads into the right ventricle (8)

A fiberoptic system that allows continuous monitoring of mixed venous oxygen saturation (9)

A rapid-response thermistor that can measure the ejection fraction of the right ventricle (10)

A thermal filament that generates low-energy heat pulses and allows continuous thermodilution measurement of the cardiac output (11)
With such a large variety of accessories, the PA catheter is the Swiss Army knife of the critical care specialist.

CATHETER INSERTION

The PA catheter is inserted into the subclavian or internal jugular veins. A large-bore introducer catheter is inserted first (see Figure 6.4), and the PA catheter is then passed through the introducer catheter. Just before the PA catheter is inserted, the distal (PA) lumen is attached to a pressure transducer, and the pressure is monitored continuously during insertion. When the PA catheter is passed through the introducer catheter and enters the superior vena cava, a venous pressure waveform appears. When this occurs, the balloon is inflated with 1.5 mL of air, and the

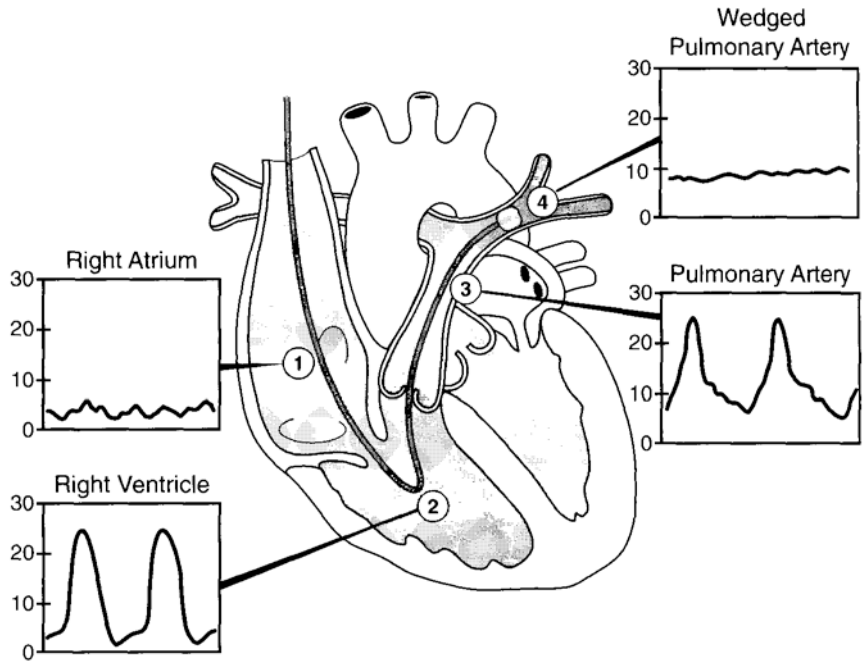


**FIGURE 9.2** The pressure waveforms at different points along the normal course of a pulmonary artery catheter. These waveforms are used to identify the location of the catheter tip as it is advanced.

catheter is advanced with the balloon inflated. The location of the catheter tip is determined by the pressure tracings recorded from the distal (PA) lumen, as shown in Figure 9.2.

The superior vena cava pressure is identified by a venous pressure waveform, which appears as small amplitude oscillations. This pressure remains unchanged after the catheter tip is advanced into the right atrium. The normal pressure in the superior vena cava and right atrium is 1 to 6 mm Hg.

When the catheter tip is advanced across the tricuspid valve and into the right ventricle, a pulsatile waveform appears. The peak (systolic) pressure is a function of the strength of right ventricular contraction, and the lowest (diastolic) pressure is equivalent to the right-atrial pressure. The systolic pressure in the right ventricle is normally 15 to 30 mm Hg.

When the catheter moves across the pulmonic valve and into a main pulmonary artery, the pressure waveform shows a sudden rise in diastolic pressure with no change in the systolic pressure. The rise in diastolic pressure is caused by resistance to flow in the pulmonary circulation. The pulmonary artery diastolic pressure is normally 6 to 12 mm Hg.

As the catheter is advanced along the pulmonary artery, the pulsatile waveform disappears, leaving a venous-type pressure

waveform at the same level as the pulmonary artery diastolic pressure. This is the pulmonary artery occlusion pressure, also called the *pulmonary capillary wedge pressure* (PCWP), or simply the *wedge pressure.* This pressure is obtained in the absence of flow between the catheter tip and the left atrium and is a reflection of the venous pressure in the left side of the heart (i.e., left atrial pressure and left-ventricular diastolic pressure). The wedge pressure is equivalent to the pulmonary artery diastolic pressure.
When the wedge pressure tracing appears, the catheter is left in place (not advanced further), and the balloon is deflated. The pulsatile pulmonary artery pressure should reappear when the balloon is deflated. If this occurs, the PA catheter should be secured in place (usually with a single suture that anchors the catheter to the skin), and the balloon should be left deflated.

The Balloon
Sustained periods of balloon inflation creates a risk of pulmonary artery rupture or pulmonary infarction, so the balloon should be deflated at all times while the catheter is in place. Balloon inflation is reserved only for measurements of the wedge pressure. When obtaining a wedge pressure, do not fully inflate the balloon with 1.5 mL air all at once (catheters often migrate into smaller pulmonary arteries, and a fully inflated balloon could result in vessel rupture). The balloon should be slowly inflated until a wedge pressure tracing is obtained. Once a satisfactory wedge pressure is recorded, the balloon should be fully deflated. (Detaching the syringe from the balloon injection port will help prevent undetected balloon inflation while the catheter is in place.)
Trou bleshooting
The following are some common problems encountered during advancement of a PA catheter.

*Catheter Will Not Advance into the Right Ventricle*
Most catheters should enter the right ventricle after they are advanced a distance of 20 to 25 cm (see Figure 6.5). Difficulty advancing a catheter into the right ventricle (which can occur with tricuspid regurgitation or right heart failure) can sometimes be corrected by filling the balloon with sterile saline instead of air (12) and positioning the patient with the left side down. The fluid adds weight to the balloon, and with the left side down, the balloon can fall into the right ventricle. When the right ventricle is entered, the saline should be removed and replaced with air.

*Catheter Will Not Advance into the Pulmonary Artery*
Catheters can become coiled in the right ventricle and fail to enter the pulmonary circulation. This problem is sometimes corrected by withdrawing the catheter into the superior vena cava and re-advancing the catheter using a slow, continuous motion (allowing the venous flow to carry the

catheter into the pulmonary c;irculation) and avoiding rapid thrusts. This problem can persist in patients with pulmonary hypertension.

*Arrhythmias*

Atrial and ventricular arrhythmias can appear in over half of PA catheter placements (13), but they are aln).ost always benign and self-limited and require no treatment. Complete heart block that appears during catheter placement should prompt immediate withdrawal of the catheter and, if necessary, a brief period of transthoracic pacing. Prolonged heart block could indicate injury to the AV node, and might require transvenous pacing.

*Unable to Obtain* a *Wedge Pressure*

In about 25% of PA catheter placements, the pulsatile PA pressure never disappears despite maximum advancement of the catheter in the pulmonary circulation. This can be the result of nonuniform balloon inflation, but in most cases, the phenomenon is unexplained. If this occurs, the pulmonary artery diastolic pressure can be used as a substitute for the pulmonary capillary wedge pressure (in the absence of pulmonary hypertension, the two pressures should be equivalent).

**THERMODILUTION CARDIAC OUTPUT**

The addition of a thermistor to the PA catheter increased the monitoring capacity of the catheter from 2 parameters (i.e., central venous pressure and wedge pressure) to over 10 parameters (see Tables 9.1 and 9.2).

TABLE 9.1 Cardiovascular Parameters

| Parameter | Abbreviation | Normal Range |
|---|---|---|
| Central venous pressure | CVP | 1-6 mm Hg |
| Pulmonary capillary wedge pressure | PCWP | 6-12 mm Hg |
| Cardiac index | CI | 2.4-4 L/min/$m^2$ |
| Stroke volume index | SVI | 40-70 mLlbeaVm$^2$ |
| Left-ventricular stroke work index | LVSWI | 40-60 9 . m/$m^2$ |
| Right-ventricular: | | |
| Stroke work index | RVSWI | 4-8 9 . *m/m$^2$* |
| Ejection fraction | RVEF | 46-50% |
| End-diastolic volume | RVEDV | 80-150 mL/$m^2$ |
| Systemic vascular resistance index | SVRI | 1,600-2,400 dynes· sec' . *cm$^5$/m$^2$* |
| Pulmonary vascular resistance index | PVRI | 200-400 dynes· sec' . *cm$^5$/m$^2$* |

The Method

Thermodilution is an indicator-dilution method of measuring blood flow, and is based on the premise that when an indicator substance is added to circulating blood, the rate of blood flow is inversely proportional to the change in concentration of the indicator over time (14,15). The indicator substance in this case is not a dye but a fluid with a different temperature than blood.

The thermodilution method is illustrated in Figure 9.3. A dextrose or saline solution that is colder than blood is injected through the proximal port of the catheter in the right atrium. The cold fluid mixes with blood in the right heart chambers, and the cooled blood is ejected into the pulmonary artery and flows past the thermistor on the distal end of the catheter. The thermistor records the change in blood temperature with time and sends this information to an electronic instrument that records and displays a temperature-time curve. The area under this curve is inversely proportional to the rate of blood flow in the pulmonary artery. In the absence of intracardiac shunts, this flow rate is equivalent to the (average) cardiac output.

*Thermodilution Curves*

Examples of thermodilution curves are shown in Figure 9.4. The low cardiac output curve (upper panel) has a gradual rise and fall, whereas the high output curve (middle panel) has a rapid rise, an abbreviated peak, and a steep downslope. Note that the area under the low cardiac output curve is greater than the area under the high output curve; that is, the area under the curves is inversely related to the flow rate. Electronic cardiac monitors integrate the area under the temperature-time curves and provide a digital display of the calculated cardiac output.

*Technical Considerations*

The indicator solution can be cooled in ice or injected at room temperature, and the volume of injectate is either 5 mL or 10 mL. In general, higher-volume, lower-temperature injectates produce the highest signal-to-noise ratios and thus the most accurate measurements (16). However, room temperature injectates (which require less preparation than iced injectates) produce reliable measurements in most critically ill patients (17,18). When the indicator fluid is injected at room temperature, the large (10 mL) injection volume produces the most reliable results.

TABLE 9.2 Oxygen-Transport Parameters

| Parameter | Symbol | Normal Range |
|---|---|---|
| Mixed venous oxygen saturation | $Sv0_2$ | 70-75% |
| Oxygen delivery | D02 | 520-570 mUmin/$m^2$ |
| Oxygen uptake | $V0_2$ | 110-160 mUmin/$m^2$ |
| Oxygen-extraction ratio | 02ER | 20%-30% |

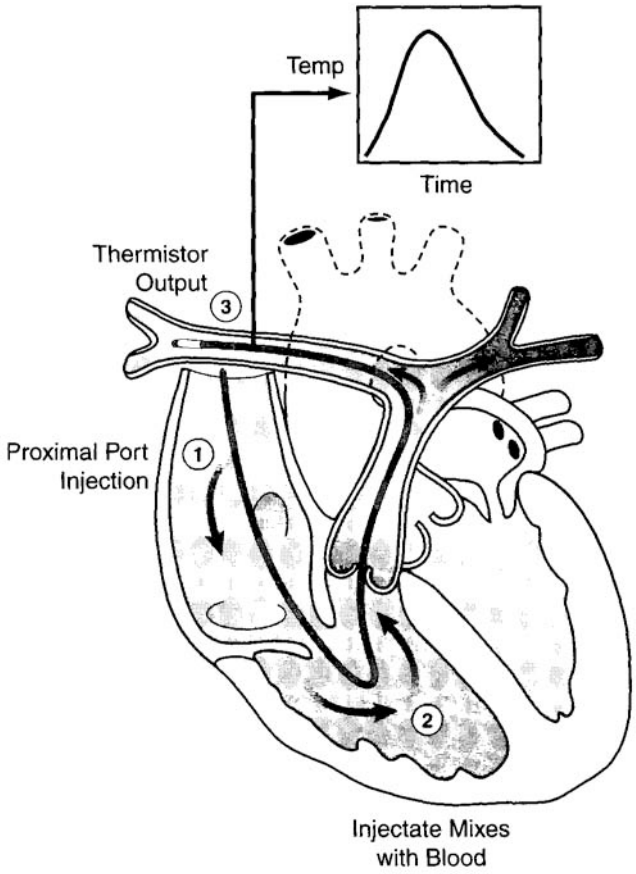


**FIGURE 9.3** The thermodilution method of measuring cardiac output.

Serial measurements are recommended for each cardiac output determination. Three measurements are sufficient if they differ by 10% or less, and the cardiac output is taken as the average of all measurements. Serial measurements that differ by more than 10% are considered unreliable (19).

*Variability*

Thermodilution cardiac output can vary by as much as 10% without any apparent change in the clinical condition of the patient (20). This means that a baseline cardiac output of 5 L/min can vary from 4.5 to 5.5 L/min without the change being clinically significant. A change in thermodilution cardiac output must exceed 10% to be considered clinically significant.

*Other Considerations*

The following clinical conditions can affect the accuracy of thermodilution cardiac output measurements.

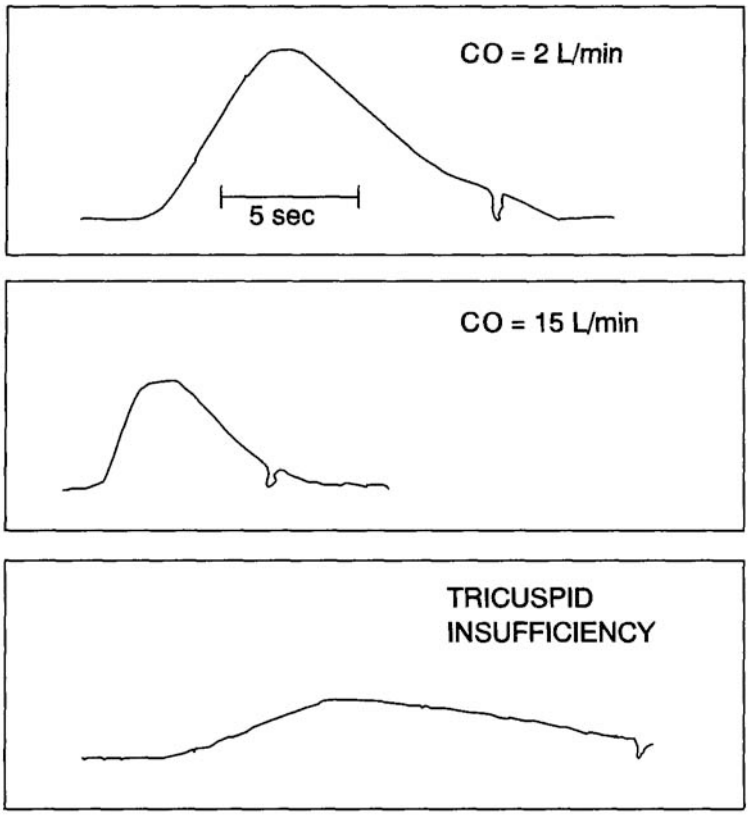


**FIGURE 9.4** Thermodilution curves for a low cardiac output (*upper panel*), a high cardiac output (*middle panel*), and tricuspid insufficiency (*lower panel*). The sharp inflection on each curve marks the end of the measurement period. CO, cardiac output.

TRICUSPID REGURGITATION; This condition may be common during positive-pressure mechanical ventilation. The regurgitant flow causes the indicator fluid to be recycled, producing a prolonged, low-amplitude thermodilution curve similar to the low-output curve in the bottom frame of Figure 9.4. This results in a falsely low thermodilution cardiac output (21).

INTRACARDIAC SHUNTS. Intracardiac shunts produce falsely high thermodilution cardiac output measurements. In right-to-left shunts, a portion of the cold indicator fluid passes through the shunt, thereby creating an abbreviated thermodilution curve (similar to the abbreviated highoutput curve). In left-to-right shunts, the thermodilution curve is abbreviated because the shunted blood increases the blood volume in the right heart chambers, and this dilutes the indicator solution that is injected.

## Continuous Cardiac Output

The thermodilution method has been adapted to allow automatic, minute-by-minute measurements of cardiac output without the tedium

of intermittent bolus injections of indicator fluid (22). This method uses a specialized PA catheter (Baxter Edwards Critical Care, Irvine, CAl equipped with a 10-cm thermal filament located 15 to 25 cm from the catheter tip. The filament generates low-energy heat pulses that are transmitted to the surrounding blood. The resulting change in blood temperature is then used to generate a thermodilution curve. This method records an average cardiac output over successive 3-minute time intervals.

The continuous thermodilution method provides reliable measurements of cardiac output in critically **ill** patients (23), and it is more accurate than the intermittent bolus-injection thermodilution method (24). Because the continuous method of monitoring cardiac output is less time consuming and more accurate than the intermittent bolus-injection method, this method should be preferred for cardiac output determinations in the ICU.

## HEMODYNAMIC PARAMETERS

The value of the PA catheter is the multitude of hemodynamic parameters that can be generated; there are 10 parameters used to describe different aspects of cardiovascular function (see Table 9.1), and 4 parameters that describe systemic oxygen transport (see Table 9.2). A detailed description of these parameters can be found in the first two chapters of this book.

### Body Size

Hemodynamic variables are often expressed in relation to body size. Instead of mass (weight), the index of body size for hemodynamic measurements is the body surface area (BSA), which can be determined with the simple equation shown below (25).

$$BSA\ (m^2) = [Ht\ (cm) + Wt\ (kg) - 60]/100 \quad (9.1)$$

The average-sized adult has a body surface area of 1.6 to 1.9 $m^2$.

### Cardiovascular Parameters

The parameters used to evaluate cardiovascular function are shown in Table 9.1. Size-adjusted parameters (expressed in relation to body surface area) are identified by the term *index.*

#### *Central Venous Pressure*

When the PA catheter is properly placed, the proximal port of the catheter should be situated in the right atrium, and the pressure recorded from this port should be the right atrial pressure. As mentioned previously, the pressure in the right atrium is the same as the pressure in the superior vena cava, and these pressures are collectively called the *central venous pressure* (CVP). In the absence of tricuspid valve dysfunction, the

CVP should be equivalent to the right atrial pressure (RAP) and the right-ventricular end-diastolic pressure (RVEDP).

CVP = RAP = RVEDP (9.2)

*Pulmonary Capillary Wedge Pressure*

The measurement of the pulmonary capillary wedge pressure (PCWP) is described earlier in the chapter (and the next chapter is devoted almost exclusively to this measurement). The PCWP is measured when there is no flow between the catheter tip and the left atrium (because the balloon on the PA catheter tip is inflated), so the PCWP will be the same as the leftatrial pressure (LAP). When the mitral valve is normal, the LAP should be equivalent to the left-ventricular end-diastolic pressure (LVEDP).

PCWP = LAP = LVEDP (9.3)

*Cardiac Index*

The thermodilution cardiac output is usually corrected for body size as shown below. The size-corrected cardiac output is called the *cardiac index* (CI).

CI = CO/BSA (9.4)

*Stroke Volume*

The stroke volume is the volume of blood ejected by the ventricles during systole. **It** is derived as the cardiac output divided by the heart rate (HR). When cardiac index (CD is used, the parameter is called the stroke volume index (SVD.

SVI = CI/HR (9.5)

*Right- Ventricular Ejection Fraction*

The ejection fraction is the fraction of the ventricular volume that is ejected during systole and is equivalent to the ratio of the stroke volume and the ventricular end-diastolic volume. This parameter provides an indication of the strength of ventricular contraction during systole. The ejection fraction of the right ventricle (RVEF) is the ratio of the stroke volume (SV) to the right-ventricular end-diastolic volume (RVEDV).

RVEF = SV /RVEDV (9.6)

As mentioned earlier, the right ventricular ejection fraction can be measured with a specialized PA catheter that is equipped with a rapidresponse thermistor (see Reference 10 for a description of this technique).

*Right- Ventricular End-Diastolic Volume*

Ventricular end-diastolic volume is the true measure of ventricular preload (see Chapter 1). The end-diastolic volume of the right ventricle can

be determined when the RVEF is measured using the specialized PA catheter mentioned above. The equation below is derived by rearranging the terms in Equation 9.6.

RVEDV = SV /RVEF (9.7)

*Left- Ventricular Stroke Work Index*

Left-ventricular stroke work (LVSW) is the work performed by the ventricle to eject the stroke volume. Stroke work is a function of the systolic pressure load (afterload minus preload), which is equivalent to the mean arterial pressure minus the wedge pressure (MAP - PCWP) and the stroke volume (SV). The equation below is corrected for body size (so LVSW becomes LVSWI), and the factor 0.0136 converts pressure and volume to units of work.

LVSWI = (MAP - PCWP) X SVI (x 0.0136) (9.8)

*Right- Ventricular Stroke Work Index*

The right-ventricular stroke work (RVSW) is the work needed to move the stroke volume across the pulmonary circulation. It is derived as the systolic pressure load of the right ventricle, which is equivalent to the mean pulmonary artery pressure minus the CVP (PAP - CVP), and the stroke volume (SV). The equation below is corrected for body size and includes the same unit correction factor as in Equation 9.8.

RVSWI = (PAP - CVP) X SVI (x 0.0136) (9.9)

*Systemic Vascular Resistance Index*

The systemic vascular resistance (SVR) is the vascular resistance across the systemic circulation. It is directly proportional to the pressure gradient from the aorta to the right atrium (MAP - CVP) and is inversely related to blood flow (CI). The equation below is corrected for body size, and the factor of 80 is necessary to convert units.

SVRI = (MAP - RAP) x 80/CI (9.10)

*Pulmonary Vascular Resistance Index*

The pulmonary vascular resistance index (PVR) is directly proportional to the pressure gradient across the entire lungs, from the pulmonary artery (PAP) to the left atrium (LAP). Because the wedge pressure (PCWP) is equivalent to the LAP, the pressure gradient across the lungs can be expressed as (PAP - PCWP). The PVR can then be derived using Equation 9.11, which is corrected for body size. As in Equation 9.10, the factor of 80 is used to convert units.

PVRI = (PAP - PCWP) X 80/CI (9.11)

Oxygen-Transport Parameters

The transport of oxygen from the lungs to the systemic organs is described using the parameters in Table 9.2. These parameters are described in detail in Chapter 2 and are presented only briefly here.

*Oxysen Delivery*

The rate of oxygen transport in arterial blood is called the *oxygell delivery* ($D0_2$) and is a function of the cardiac output and the oxygen concentration in arterial blood. The determinants of DO, are shown in Equation 9.12. This equation is explained in Chapter 2.

$$002 = CI \times 13.4 \times Hb \times Sa0_2 \qquad (9.12)$$

*Mixed Venous Oxysen Saturation*

The oxygen saturation of hemoglobin in pulmonary artery (mixed venous) blood ($Sv0_2$)can be monitored continuously with a specialized PA catheter, or it can be measured ill *vitro* with a blood sample obtained from the distal port of the PA catheter. (See Chapter 20 for a description of how 02 saturation of hemoglobin is measured.) The $Sv0_2$ is used as an indirect marker of systemic blood flow. A decrease in cardiac output is accompanied by an increase in 02 extraction from the capillaries, and this will decrease the SvO,. Therefore a decrease in SvO, can signal a decrease in cardiac output. **II** 02 extraction is fixed and does not vary with changes in blood flow (which can happen in sepsis), the SvO, is unreliable as an index of blood flow.

*Oxygen Uptake*

Oxygen uptake ($V0_2$), also called oxygen consumption, is the rate at which oxygen is taken up from the systemic capillaries into the tissues. The determinants of $V0_2$ are shown in Equation 9.13. This equation is explained in detail in Chapter 2.

$$V0_2 = CI \times 13.4 \times Hb \times (Sa0_2 - Sv0_2) \qquad (9.13)$$

*Oxygen-Extraction Ratio*

The oxygen extraction ratio (O,ER) is the fractional uptake of oxygen from the systemic microcirculation imd is equivalent to the ratio of 02 uptake to 02 delivery. Multiplying the ratio by 100 expresses it as a percent.

$$02ER = VO/D0_2 \ (X\ 100) \quad (9.14)$$

**HEMODYNAMIC SUBSETS**

The parameters just described can be organized into groups or subsets that are tailored to specific problems. Some examples of hemodynamic subsets are presented below.

*Hypotension*

The mean arterial pressure is a function of the cardiac output and the systemic vascular resistance: MAP = CI X SVRI. The cardiac output, in turn, depends on the venous return. If the CVP is used as an index of venous return, there are three variables that can be used to describe any patient with hypotension: CVP, CI, and SVRI. This 3-variable subset is used below to describe the three classic forms of hypotension.

| Hypovolemic | Cardiogenic | Vasogenic |
|---|---|---|
| Low CVP | High CVP | Low CVP |
| Low CI Low CI | High CI | |
| High SVRI | High SVRI | Low SVRI |

These three hemodynamic parameters can be used to identify the hemodynamic problem in any patient with hypotension. For example, suppose a patient with hypotension has a low CVP, a normal CI, and a low SVRI. This pattern is closest to the vascular dysfunction (vasogenic) category shown above, except that the CI is normal instead of high. Therefore the hemodynamic problem in this patient is a combination of vascular dysfunction and cardiac dysfunction. There are $3^3$ or 27 possible combinations of these 3 variables (CVP, CI, SVRI), and each of these combinations identifies a distinct hemodynamic problem. Therefore this hemodynamic subset of 3 variables will identify the hemodynamic problem in any patient with hypotension.

**Clinical Shock**

The three-variable hemodynamic subset just presented will identify a hemodynamic problem but not the consequences of the problem on tissue oxygenation. The addition of the oxygen uptake ($V0_2$) will correct this shortcoming and can help identify a state of clinical shock. Clinical shock can be defined as a condition where tissue oxygenation is inadequate for the needs of aerobic metabolism. Since a $V0_2$ that is below normal can be used as indirect evidence of oxygen-limited aerobic metabolism, a subnormal $V0_2$ can be used as indirect evidence of clinical shock. The following example shows how the $V0_2$ can add to the evaluation of a patient with a low output state.

| Heart Failure | Cardiogenic Shock |
|---|---|
| High CVP | High CVP |
| LowCI LowCI | |
| High SVRI | High SVRI |
| Normal $V0_2$ | Low $V0_2$ |

Without the $V0_2$ measurement in the above profiles, it is impossible to differentiate a low-output state from cardiogenic shock. This illustrates how oxygen transport monitoring can be used to determine the consequences of hemodynamic abnormalities on peripheral oxygenation. The

uses and limitations of oxygen transport monitoring are described in more detail in Chapter 11.

A FINAL WORD

The PA catheter has been maligned in recent years because of clinical studies showing that mortality is not reduced (26) and can be higher (27) in patients who have PA catheters. As a result of these studies, use of the PA catheter in the western world has dropped about 10% in the past few years (28), and the most zealous critics of the catheter have called for a moratorium on its use.

There are two fundamental problems in the criticism of the PA catheter based on mortality data. The first is the simple fact that the PA catheter is a monitoring device, not a therapy. If a PA catheter is placed to evaluate a problem, and it uncovers a disorder that is untreatable and fatal (e.g., cardiogenic shock), the problem is not the catheter, it is the lack of effective therapy. Mortality rates should be used to evaluate therapies, not measurements.

The second problem is the seemingly prevalent notion that everything we do in the ICU must save lives to be of value. Mortality should not be the dominant outcome measure in ICUs because there are too many variables that can influence mortality in critically ill patients, and also because mortality is an eventual outcome in all patients admitted to the leu. Management decisions should be based on the scientific rationale for an intervention-those who expect their management decisions to consistently save lives are doomed to failure.

**REFERENCES**

**Chapter 10**

**CENTRAL VENOUS PRESSURE AND WEDGE PRESSURE**

*It is what we think we know already that iften prevents* us *from learning.*
*Claude Bernard*

The central venous pressure (CVP) and pulmonary artery occlusion (wedge) pressure, which are clinical measures of right and left ventricular filling pressures, respectively (1-3), have been popularized as hemodynamic measures because of the *Frank-Starling relationship of the heart,* which identifies ventricular filling volume (preload) as the major determinant of cardiac stroke output (see Figure 1.1). Unfortunately, the CVP and pulmonary artery wedge pressure share two major shortcomings: they are often misleading as measures of ventricular preload (4), and the pressure waveforms are often misinterpreted (5-7). Attention to the information in this chapter will help reduce errors in the interpretation of these measurements.

SOURCES OF VARIABILITY

Body Position·

The zero reference point for venous pressures in the thorax is a point on the external thorax where the fourth intercostal space intersects the mid-axillary line (i.e., the line midway between the anterior and posterior axillary folds). This point (called the ph lebo static axis) corresponds to the position of the right and left atrium when the patient is in the supine position. It is not a valid reference point in the lateral position, which means that central venous and pulmonary artery wedge pressures should not be recorded when patients are placed in lateral positions (8).

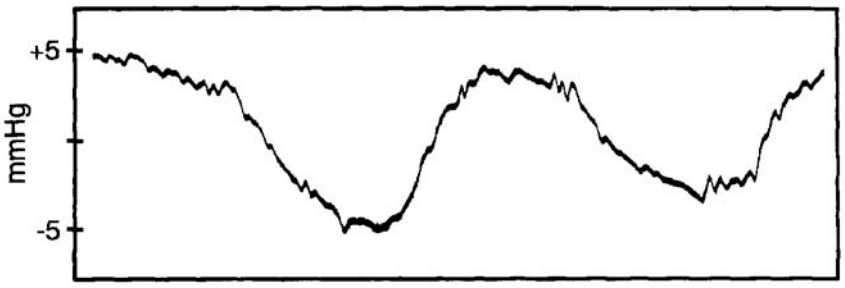


**FIGURE 10.1** Respiratory variations in central venous pressure. The transmural pressure can remain constant throughout the respiratory cycle despite the variations in intravascular pressure.

## Changes in Thoracic Pressure

The pressure recorded with a vascular cannula is the intravascular pressure [i.e., the pressure in the vessel lumen relative to atmospheric (zero) pressure]. However, the physiologically important vascular pressure (i.e., the one that determines distention of the ventricles and the rate of edema formation) is the *transmural pressure* (i.e., the difference between the intravascular and extravascular pressures). The intravascular pressure is an accurate reflection of the transmural pressure only when the extravascular pressure is zero (atmospheric pressure). When vascular pressures are recorded in the thorax, changes in thoracic pressure can be transmitted across the wall of blood vessels, resulting in a discrepancy between intravascular and transmural pressures. This is illustrated by the respiratory variations in the CVP tracing shown in Figure 10.1. The intravascular pressure changes in this tracing are caused by respiratory variations in intrathoracic pressure that are transmitted into the lumen of the superior vena cava. In this situation, the transmural pressure (i.e., the cardiac filling pressure) may be constant despite the phasic changes in intravascular pressure. (It is not possible to determine how much of the change in thoracic pressure is transmitted into the blood vessel in an individual patient, and thus it is not possible to determine whether transmural pressure is absolutely constant.) Thus respiratory variation in intravascular pressures in the thorax is not an indication that the transmural pressure (the cardiac filling pressure) is also changing (9).

### *End-Expiration*

Intravascular pressures will be equivalent to transmural pressures when the extravascular pressure is zero. In healthy subjects breathing at normal rates, this occurs at the end of expiration, when intrathoracic (extravascular) pressure returns to atmospheric or zero pressure. Therefore intravascular pressures should be measured at the end of expiration, when they are equivalent to the transmural pressure (1,9). Intravascular and

transmural pressures will differ at end-expiration only if there is positive intrathoracic pressure at the end of expiration, as explained next.

POSITIVE END-EXPIRATORY PRESSURE (PEEP). There are two situations, where the intrathoracic pressure is above atmospheric pressure at the end of expiration. In one situation, positive end-expiratory pressure (PEEP) is applied during mechanical ventilation to prevent alveolar collapse. In the other situation, incomplete alveolar emptying (e.g., due to airflow obstruction) does not allow alveolar pressure to return to atmospheric pressure at the end of expiration. These two conditions are referred to as *extrinsic PEEP* (see Chapter 25) and *intrinsic PEEP* (see Chapter 26), respectively. In both conditions of PEEP, intravascular pressures measured at the end of expiration will exceed the transmural pressure.

When external PEEP is applied, intravascular pressures should be measured at end-expiration when the patient is briefly disconnected from the ventilator (10). In the presence of intrinsic PEEP, accurate recording of intravascular pressures can be difficult (11). See Chapter 26 for a description of how the CVP and wedge pressure can be corrected in the presence of intrinsic PEEP.

*Pressure Monitors*

If the bedside monitors in the ICU have oscilloscope display screens with horizontal grids, the CVP and wedge pressures should be measured directly from the pressure tracings on the screen. This provides more accurate measurements than pressures that are digitally displayed (12). Most ICU monitors have a digital display that includes systolic, diastolic, and mean pressures; each measured over successive 4-second time intervals (the time for one sweep across the oscilloscope screen). The systolic pressure is the highest pressure, the diastolic pressure is the lowest pressure, and the mean pressure is the integrated area under the pressure wave in each time period. During spontaneous breathing, the pressure at the end of expiration is the highest pressure (i.e., systolic pressure), and during positive-pressure mechanical ventilation, the end-expiratory pressure is the lowest pressure (i.e., diastolic pressure). Therefore systolic pressure should be used as the end-expiratory vascular pressure in patients who are breathing spontaneously, whereas diastolic pressure should be used in patients receiving positive-pressure mechanical ventilation. The mean pressure should never be used as a reflection of transmural pressure when there are respiratory variations in intravascular pressure (9).

*Units oj Measurement*

Most intravascular pressures are measured with electronic transducers that record the pressure in millimeters of mercury (mm Hg). Waterfilled manometers that record pressure in cm $H_20$ are occasionally used to measure CVP (13). Because mercury is 13.6 times more dense than water, pressures measured in cm $H_20$ can be divided by 13.6 X 1/10 = 1.36 to be expressed in mm Hg (the factor 1/10 converts cm to mm;) i.e.,

pressure in em $H_2O$ + 1.36 = pressure in mm Hg. A table of conversions for these units is included in Appendix 1.

### Spontaneous Variations

Like any physiologic variable, vascular pressures in the thorax can vary spontaneously, without a change in the clinical condition of the patient. The spontaneous variation in wedge pressure is 4 mm Hg or less in 60% of patients, but it can be as high as 7 mm Hg in any individual patient (14). In general, a change in CVP or wedge pressure of less than 4 mm Hg should not be considered a clinically significant change.

## PULMONARY ARTERY WEDGE PRESSURE

Few pressures in the ICU are misinterpreted as frequently, and as consistently, as pulmonary capillary wedge pressure (5-7,15). Probably the most important feature of the wedge pressure is what it is *not:*

Wedge pressure is *not* left-ventricular preload.

Wedge pressure is *not* the pulmonary capillary hydrostatic pressure. Wedge pressure is *not* a reliable measure for differentiating cardiogenic from noncardiogenic pulmonary edema.

These limitations are explained in the description of the wedge pressure that follows.

### Wedge Pressure Tracing

When the pulmonary artery catheter is properly positioned, inflation of the balloon at the tip of the catheter causes the pulsatile pressure to disappear. This is demonstrated in Figure 10.2. The non pulsatile or "wedged" pressure is equivalent to the pulmonary artery diastolic pressure, and represents the pressure in the venous side of the pulmonary circulation. The magnified section of the wedge pressure in Figure 10.2 shows the individual components of th~ pressure: the a wave is produced by left atrial contraction, the c wave is produced by closure of the mitral valve during isometric contraction of the left ventricle, and the v wave is produced by systolic contraction of the left ventricle against a closed mitral valve. These components (which are also present in the central venous pressure tracing) are often not distinguishable in a normal wedge pressure tracing, but they can become evident in conditions where one component is magnified (e.g., mitral regurgitation produces large v waves, which can be identified in a wedge pressure tracing).

### Principle of the Wedge Pressure

The wedge pressure is a measure of the filling pressure in the left side of the heart, and the basis for this is shown in Figure 10.3 (13). Inflation of the balloon at the tip of pulmonary aretery catheter creates a static column of blood between the catheter tip and the left atrium. In this

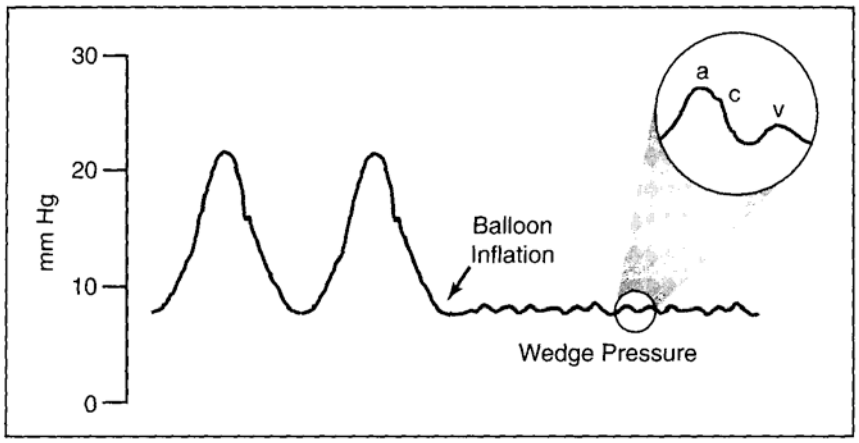


**FIGURE 10.2** Pressure tracing showing the transition from a pulsatile pulmonary artery pressure to a balloon occlusion (wedge) pressure. The magnified area shows the components of the wedge pressure: a wave (atrial contraction), c wave (mitral valve closure), and v wave (ventricular contraction).

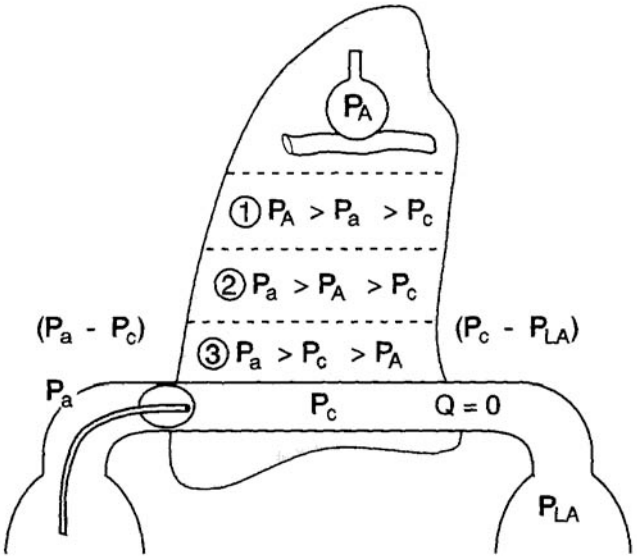


**FIGURE 10.3** The principle of the wedge pressure measurement. When flow ceases because of balloon inflation ($Q = 0$), the pressure at the catheter tip ($P_c$) is the same as the pressure in the left atrium ($P_{LA}$). This occurs only in the most dependent lung zone. The lung is divided into three zones based on the relationship between alveolar pressure ($P_A$), mean pulmonary artery pressure ($P_a$), and pulmonary capillary pressure ($P_c$). Wedge pressure is an accurate reflection of left-atrial pressure only in zone 3, where $P_c$ is greater than $P_A$.

situation, the pressure at the tip of the pulmonary artery catheter is the same as the pressure in the left atrium. This can be demonstrated using the simple hydraulic relationship $Q = \Delta P/R$, which indicates that steady flow in a tube *(Q)* is directly proportional to the pressure drop along the tube *(Delta P)* and is inversely proportional to the resistance to flow in the tube *(R).* Rearranging terms yields the following relationship: $\Delta P = Q \times R$. This relation is expressed below for the venous side of the pulmonary circulation, where *Pc* is capillary pressure, $P_{LA}$ is left-atrial pressure, Q is pulmonary blood flow, and Ry is pulmonary venous resistance.

$$Pc - P_{LA} = Q \times Rv \qquad (10.1)$$

if $Q = 0$, $Pc - P_{LA} = 0$, and $Pc = P_{LA}$

Thus when the balloon is inflated, the pressure at the tip of the pulmonary artery catheter *(PC>* is equal to the pressure in the left atrium *(P* LA)' Because left-atrial pressure is normally the same as the left-ventricular enddiastolic pressure (LVEDP), the pulmonary capillary wedge pressure can be used as a measure of left-ventricular filling pressure. What the wedge pressure *actually* measures is the focus of the remainder of this chapter.

## Wedge Pressure as Preload

The wedge pressure is often used as a reflection of left-ventricular filling during diastole (i.e., ventricular preload). In Chapter 1, preload was defined as the force that stretches a muscle at rest, and the preload for the intact ventricle was identified as end-diastolic volume (EDV). However, the pulmonary capillary wedge pressure (like the CVP) is a measure of end-diastolic pressure, and end-diastolic pressure may not be an accurate reflection of preload (BOV). The graph in Figure 10.4 shows the relationship between pulmonary capillary wedge pressure and left-ventricular end-diastolic volume in a group of normal subjects (4). Note the poor correlation between the two measurements *(r* = 0.04). In fact, only 7 of the 12 wedge pressure measurements (58%) are within the normal range (shaded area). This shows that the pulmonary artery wedge pressure is not an accurate reflection of left-ventricular preload (4,16). Similar results have also been reported with the central venous pressure (4).

## Wedge Pressure as Left-Atrial Pressure

The following conditions can influence the accuracy of the wedge pressure as a measure of left-atrial pressure.

### *Lung Zones*

If the pressure in the surrounding alveoli exceeds capillary (venous) pressure, the pressure at the tip of the pulmonary artery catheter may reflect the alveolar pressure rather than the left-atrial pressure. This is illustrated in Figure 10.3. The lung in this figure is divided into three zones based on the relationship between alveolar pressure and the pressures in the

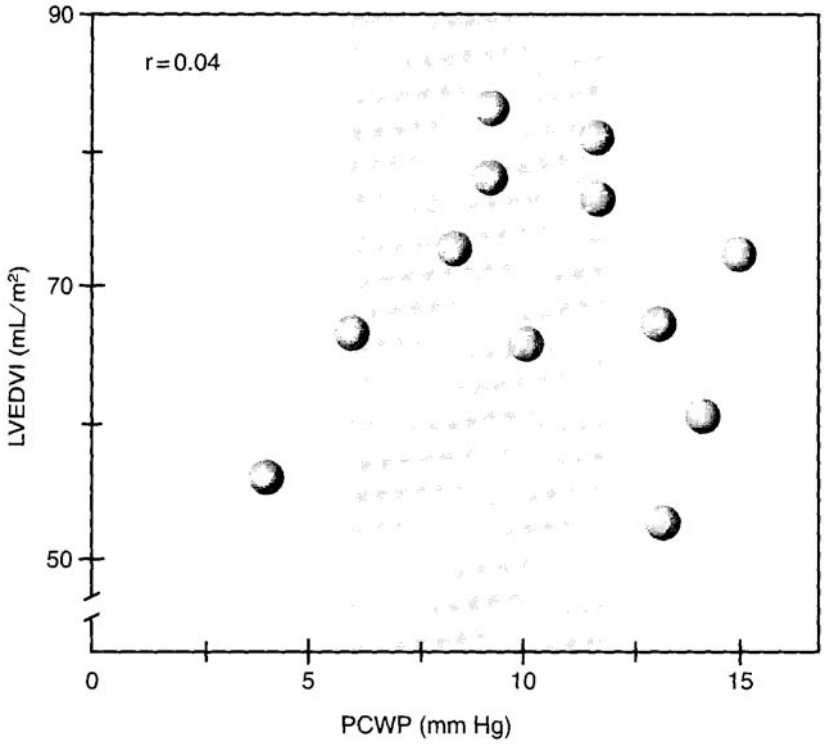


**FIGURE 10.4** The relationship between the pulmonary capillary wedge pressure (PCWP) and the left-ventricular end-diastolic volume index (LVEDVI) in 12 normal subjects. The *shaded area* represents the normal range for PCWP, and the r value is the correlation coefficient. (From Kumar A, Anel R, Bunnell E, et al. Pulmonary artery occlusion pressure and central venous pressure fail to predict ventricular filling volume, cardiac performance, or the response to volume infusion in normal subjects. Crit Care Med 2004;32:691.)

pulmonary circulation (1,3). The most dependent lung zone (zone 3) is the only region where capillary (venous) pressure exceeds alveolar pressure. Therefore, wedge pressure is a reflection of left-atrial pressure only when the tip of the pulmonary artery catheter is located in zone 3 of the lung.

*Catheter-tip Position*

Although the lung zones shown in Figure 10.3 are based on physiologic rather than anatomic criteria, the lung regions below the left atrium are considered to be in lung zone 3 (1,3). Therefore the tip of the pulmonary artery catheter should be positioned below the level of the left atrium to ensure that the wedge pressure is measuring left-atrial pressure. Because of the higher blood flow in dependent lung regions, most pulmonary artery catheters are advanced into lung regions below the level of the left atrium. However, as many as 30% of PA catheters are positioned with

TABLE 10.1 Criteria for Wedge Pressure Validation

| |
|---|
| Wedge $P0_2$ - Arterial $P0_2$ 2': 19 mm Hg |
| Arterial $PC0_2$ - Wedge $PC0_2$ 2': 11 mm Hg |
| Wedge pH - Arterial pH 2': 0.008 |

From Morris AH, Chapman RH, Gardner RM. Frequency of wedge pressure ICU. Crit Care Med 1985; 13:705-708, with permission.

their tips above the level of the left atrium (3). When patients are supine, routine portable (anteroposterior) chest x-rays cannot be used to identify the catheter-tip position relative to the left atrium. Rather, a lateral view of the chest is needed. An alternative approach is to assume that catheter tips are in zone 3 of the lung in all but the following conditions: when there are marked respiratory variations in the wedge pressure and when PEEP is applied and wedge pressure increases by 50% or more of the applied PEEP (3).

*Wedged Blood Gases*

As many as 50% of the nonpulsatile pressures produced by balloon inflation represent damped pulmonary artery pressures rather than pulmonary capillary wedge pressures (17). Aspiration of blood from the catheter tip during balloon inflation can be used to identify a true wedge (capillary) pressure using the three criteria shown in Table 10.1. Although this is a cumbersome practice that is not used routinely, it seems justified when making important diagnostic and therapeutic decisions based on the wedge pressure measurement.

Wedge Pressure as Left-Ventricular End-Diastolic Pressure Even when wedge pressure is an accurate reflection of left-atrial pressure, there may be a discrepancy between left-atrial pressure and leftventricular end-diastolic pressure (LVEDP). This can occur under the following conditions (3).

*Aortic insufficiency:* LVEDP can be higher than PCWP because the mitral valve closes prematurely while retrograde flow continues to fill the ventricle.

*Noncompliant ventricle:* Atrial contraction against a stiff ventricle produces a rapid rise in end-diastolic pressure that closes the mitral valve prematurely. The result is a PCWP that is lower than the LVEDP.

*Respiratory failure:* pCWP can exceed LVEDP in patients with pulmonary disease. The presumed mechanism is constriction of small veins in lung regions that are hypoxic (18).

Wedge Pressure as Capillary Hydrostatic Pressure

The wedge pressure is often assumed to be a measure of hydrostatic pressure in the pulmonary capillaries. The problem with this assumption

is the fact that the wedge pressure is measured in the absence of blood flow. When the balloon is deflated and blood flow resumes, the pressure in the pulmonary capillaries will remain the same as the left-atrial (wedge) pressure only **if** the resistance to flow in the pulmonary veins is negligible. This is expressed below, where *Pc* is capillary hydrostatic pressure, Ry is the hydraulic resistance in the pulmonary veins, Q is blood flow, and wedge pressure (PCWP) is substituted for left-atrial pressure.

$$Pc - PCWP = Q \times Rv \qquad (10.2)$$

**If** Rv = 0, $Pc - PCWP = 0$, and $Pc = PCWP$.

*Pulmonary Venous Resistance*

Unlike the systemic veins, the pulmonary veins contribute a significant fraction to the total vascular resistance across the lungs. (This is a reflection more of a low resistance in the pulmonary arteries than of a high resistance in the pulmonary veins.) As shown in Figure 10.5, 40% of the pressure drop across the pulmonary circulation occurs on the venous side of the circulation, which means that the pulmonary veins contribute 40% of the total resistance in the pulmonary circulation (19). Although this is derived from animal studies, the contribution in humans is probably similar in magnitude.

The contribution of the hydraulic resistance in the pulmonary veins may be even greater in critically **ill** patients because several conditions that are common in ICU patients can promote pulmonary venoconstriction. These conditions include hypoxemia, endotoxemia, and the acute respiratory distress syndrome (18,20). These conditions further magnify differences between wedge pressure and capillary hydrostatic pressure, as demonstrated below.

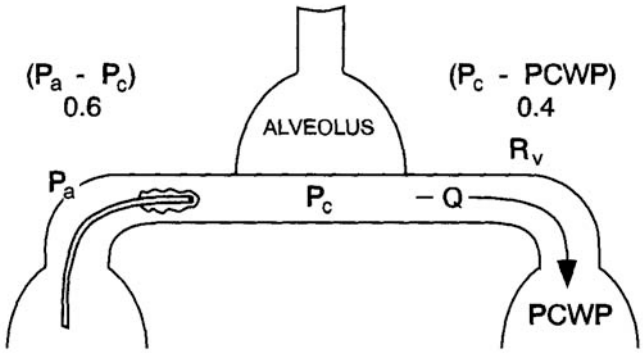


**FIGURE 10.5.** The distinction between capillary hydrostatic pressure ($P_c$) and wedge pressure (PCWP). When the balloon is deflated and flow ($Q$) resumes, $P_c$ and PCWP are equivalent only when the hydraulic resistance in the pulmonary veins ($R_v$) is negligible. $P_a$ = pulmonary artery pressure. If the pulmonary venous resistance ($R_v$) is greater than zero, the capillary hydrostatic pressure ($P_c$) will be higher than the wedge pressure.

*Wedge-Hydrostatic Pressure Conversion*

Equation 10.3 can be used to convert wedge pressure (PCWP) to pulmonary capillary hydrostatic pressure (Pc). This conversion is based on the assumption that the pressure drop from the pulmonary capillaries to the left atrium (Pc - *P* LA) represents 40% of the pressure drop from the pulmonary arteries to the left atrium *(*Pc – P LA*)* Substituting wedge pressure for left-atrial pressure (i.e., $P_{LA}$ = PCWP) yields the following rela tionship:

Pc - PCWP = 0.4 *(Pa* - PCWP)

Pc = PCWP + 0.4 *(Pa* - PCWP) (10.3)

For a normal (mean) pulmonary artery pressure of 15 mm Hg and a wedge pressure of 10 mm Hg, this relationship predicts the following:

Normal lung: Pc = 10 + 0.4 X (15 - 10) *(1004)*

Pc = 12 mm Hg, Pc - PCWP = 2 mm Hg.

Thus in the normal lung, wedge pressure is equivalent to capillary hydrostatic pressure. However, in the presence of pulmonary venoconstriction and pulmonary hypertension (e.g., in acute respiratory distress syndrome), there can be a considerable difference between wedge pressure and capillary hydrostatic pressure. The example below is based on a mean PA pressure of 30 mm Hg and a venous resistance that is 60%of the total pulmonary vascular resistance.

ARDS: Pc = 10 + 0.6 X (30 - 10) (10.5)

Pc = 22 mm Hg, Pc - PCWP = 12 mm Hg.

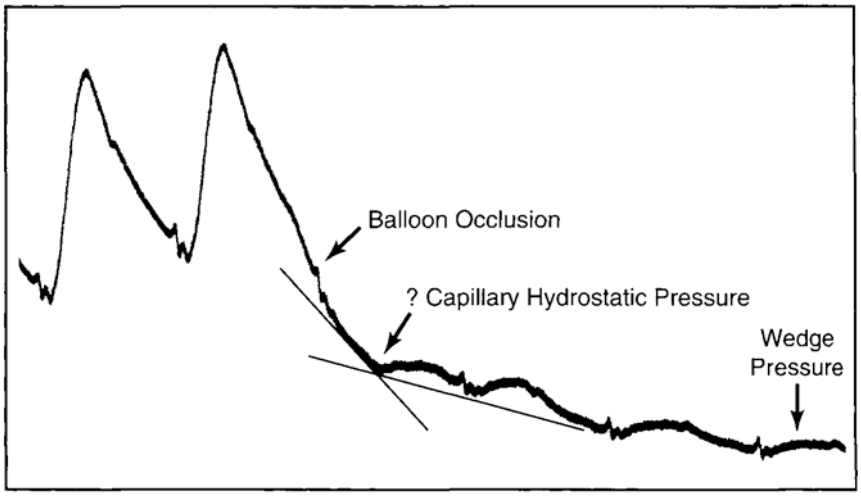


**FIGURE 10.6** Pulmonary artery pressure tracing showing a rapid and slow component after balloon occlusion. The inflection point may represent the capillary hydrostatic pressure, which is higher than the wedge pressure.

Unfortunately, pulmonary venous resistance cannot be measured in critically ill patients, and this limits the accuracy of the wedge pressure as a measure of capillary hydrostatic pressure.

### Occlusion Pressure Profile

The transition from pulsatile pulmonary artery pressure to nonpulsatile wedge pressure in Figure 10.6 shows an initial rapid phase followed by a slower, more gradual pressure change. The initial rapid phase may represent the pressure drop across the pulmonary arteries, while the slower phase may represent the pressure drop across the pulmonary veins. If this is the case, the inflection point marking the transition from the rapid to the slow phase represents the capillary hydrostatic pressure. Unfortunately, inflection points are often not recognizable following balloon occlusion (21,22).

### A FINAL WORD

Despite their popularity, the central venous pressure and pulmonary artery wedge pressure provide limited and often misleading information about intravascular volume, cardiac filling volumes, and capillary hydrostatic pressure. What this means is that these pressures should not be used (at least in isolation) to determine if a patient is dehydrated or fluid overloaded (23), and the wedge pressure should not be used to diagnose hydrostatic pulmonary edema. The pulmonary artery catheter provides much more important measurements, particularly cardiac output and systemic oxygen transport variables, and these, together with other methods of assessing tissue oxygenation (see next chapter) make the CVP and wedge pressures outdated measures that are not necessary in the hemodynamic assessment of critically ill patients.

**REFERENCES**

**Chapter 11**

# TISSUE OXYGENATION

*People say life can't exist without air, but it does under water; in fact, it started in the sea.*
*Richard Feynman*

The management of critically ill patients has one universal goal: to maintain adequate levels of tissue oxygenation and sustain aerobic metabolism. However, much of what is done in the name of aerobic support is based on traditional beliefs rather than documented need because there is no direct measure of tissue oxygenation. This chapter describes some 'indirect measures of tissue oxygenation used by critical care specialists .

## TISSUE OXYGEN BALANCE

The adequacy of tissue oxygenation is determined by the balance 'between the oxygen delivered into the tissues and oxygen required to ~ustain aerobic metabolism. This balance is illustrated in Figure 11.1. 'The $VO_2$ is the rate of oxygen delivery into the tissues, and the *MRO2* is the metabolic requirement for oxygen. When the $VO_2$ is equivalent to the $MRO_2$' glucose is completely oxidized to yield 36 ATP molecules -(673 kcal) per mole glucose. When VO2 cannot match *MRO*2 some of the glucose is diverted to form lactate, with an

energy yield of 2 ATP (47 kcal) molecules per mole glucose. Thus an inadequate supply of oxygen limits the energy yield from substrate metabolism. The condition in which metabolic energy production is limited by the supply or utilization of oxygen is called *dysoxia* (1), and the clinical expression of this condition is known as *shock.* Dysoxia can be the result of an inadequate supply of oxygen, as occurs in hypovolemic shock and cardiogenic shock, or it can be caused by a defect in mitochondrial oxygen utilization, as occurs in septic shock. Monitoring the $VO_2$ can help to identify the tissue dysoxia that results from an inadequate supply of oxygen (2), as described next.

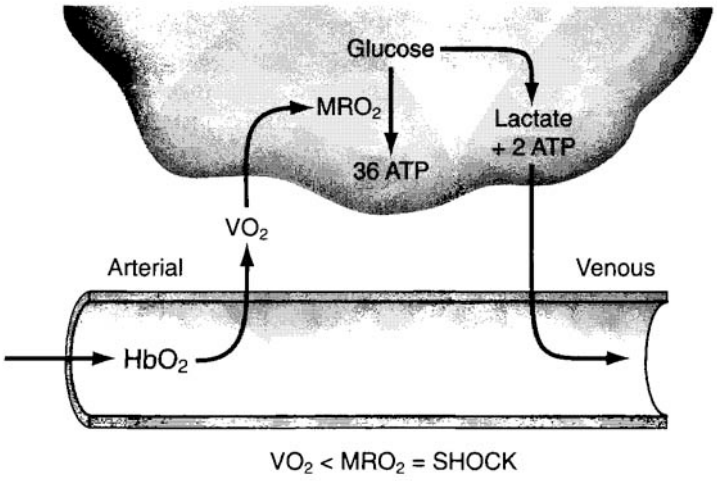


**FIGURE 11.1** Illustration showing the relationship between oxygen uptake into tissues ($VO_2$) and the metabolic requirement for oxygen ($MRO_2$). When the $VO_2$ is equivalent to the $MRO_2$, oxidative metabolism proceeds unimpeded. Shock is defined as the condition in which the $VO_2$ is unable to match the $MRO_2$.

OXYGEN UPTAKE

The rate of oxygen uptake from the systemic capillaries ($VO_2$) is a measure of oxygen availability in the tissues, as just described. Because oxygen is not stored in tissues, the $V0_2$ is also a measure of tissue oxygen consumption.

Calculated Versus Measured $V0_2$

The VO2 can be calculated by using a modification of the Fick equation (Equation 11.1), or it can be measured directly as the rate of oxygen disappearance from the lungs. Each of these methods is described in Chapter 2. The directly measured VO2 is more accurate and more reliable than the calculated $V0_2$, as described next.

VT *2*= Q X (CaT *2*- CvT *2*) *(11.1)*

*Whole-Body VO2*

The calculated VO2 is not a measure of whole-body VO2 because it does not include the $V0_2$ of the lungs. This distinction is of little importance in healthy subjects because the $V0_2$ of the lungs is normally less than 5% of the whole-body $V0_2$ (3). However, in patients with inflammation in the lungs (e.g., from pneumonia or acute respiratory distress syndrome), the VO2 of the lungs can be 20% of the whole-body VO2 (4). Therefore when lung inflammation is present, the calculated $V0_2$ will underestimate the whole-body $V0_2$ by as much as 20%. This is one reason to avoid using the calculated $V0_2$ if possible in patients with inflammatory

TABLE 11.1 Variability of Calculated and Measured $V0_2$

| Parameter | Variability |
|---|---|
| Thermodilution cardiac output | :±:10% |
| Hemoglobin concentration | :±:2% |
| % Oxyhemoglobin | :±:2% |
| Oxygen content of blood | :±:4% |
| CaO2 – CvO2 | :±:8% |
| Calculated $V0_2$ | :±:18% |
| Measured $V0_2$ | :±:5% |

conditions in the lungs. As you will learn a little later, the VO2 determined by either method (i.e., calculated or measured) may not be a worthwhile measure in patients with widespread inflammation.

*Variability*

Another shortcoming of the calculated $V0_2$ is its variability. The equation used to derive $V0_2$ includes four separate measurements (cardiac output, hemoglobin concentration in blood, and the percent oxyhemoglobin saturation in arterial and mixed venous blood), and each has its own inherent variability. These are shown in Table 11.1 (5-7). The variability of the calculated $V0_2$ is 18%, which is equivalent to the summed variability of its components (see Equation 11.1). As a result of this variability, the calculated $V0_2$ must change by at least 18 or 20% for the change to be considered significant. The measured $V0_2$ has a variability of less than 5% (6,7) and thus is much more reliable than the calculated $V0_2$•

*Availability*

The calculated $V0_2$ is readily available in patients who have an indwelling pulmonary artery catheter (used to measure cardiac output and the percent oxyhemoglobin saturation in mixed venous blood). The directly measured $V0_2$, on the other hand, requires speciali2ed equipment (i.e., a device such as a metabolic cart that is equipped with an oxygen sensor) and trained personnel to operate the equipment. For this reason, the measured $V0_2$ is not readily available, at least on a 24-hour basis, in most ICUs.

Using the $V0_2$

The $V0_2$ can be used to identify a global (whole-body) state of tissue dysoxia due to impaired tissue oxygenation, as described in the next section.

*$V0_2$* Deficit

An abnormally low $V0_2$ (less than 100 mL/min/m2) can be the result of hypometabolism or tissue dysoxia due to impaired tissue oxygenation.

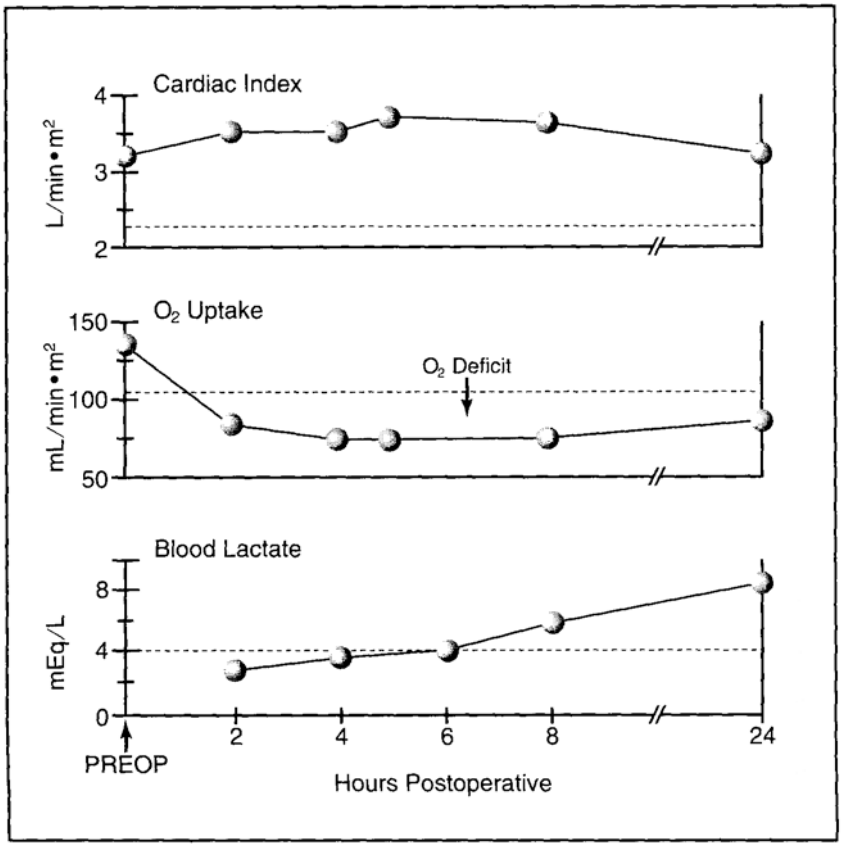


**FIGURE 11.2** Serial measurements of cardiac index, systemic oxygen uptake, and blood lactate levels in a patient who underwent abdominal aortic aneurysm repair. The *dotted lines* indicate the lower limits of normal for each measurement. The *shaded area* represents the oxygen debt.

Because hypometabolism is uncommon in critically ill patients, a $V0_2$ that is below the normal range (below 100 mL/minute/$m^2$) can be used as evidence of impaired tissue oxygenation. An example of this is shown in Figure 11.2. The measurements in this figure are from a patient who underwent an abdominal aortic aneurysm repair. The first set of postoperative measurements (at 2 hours following surgery) show a normal cardiac index and blood lactate level along with an abnormally low $V0_2$• The low $VO_2$ persists, and the blood lactate level begins to rise, steadily, reaching 9 mEq/L at 24 hours after surgery. The abnormally low $V0_2$ is evidence of a generalized oxygen deficit, as confirmed by the eventual rise in blood lactate levels. Monitoring the $VO_2$ in this case therefore provided early evidence of impaired tissue oxygenation. Note that the cardiac index remains in the normal range despite the evidence of impaired tissue oxygenation. This illustrates the non value of cardiac output monitoring in the assessment of tissue oxygenation.

**OXYGEN DEBT**. The shaded area in the $V0_2$ curve in Figure 11.2 shows the magnitude of the $V0_2$ deficit in the early postoperative period. The cumulative deficit is called the *oxygen debt*. Clinical studies have shown a direct relationship between the magnitude of the oxygen debt and the risk of multiorgan failure and death (8,9). This indicates that $V0_2$ deficits should be corrected, if possible, to prevent progressive organ injury and avoid a fatal outcome.

*Correcting VO2 Deficits*

Interventions designed to correct a $VO_2$ deficit can be identified using the determinants of VO2 in the equation shown below.

$$VT\ 2 = Q \times 13.4 \times Hb \times (SaT\ 2 - SvT\ 2) \qquad (11.2)$$

This equation is derived from Equation 11.1 by removing the common term in the O2 content ($CaO_2$ and $CvO_2$) equations (see Chapter 2). This equation identifies three determinants of $V0_2$: cardiac output (Q), hemoglobin concentration in blood (Hb), and the difference in oxyhemoglobin saturation between arterial and venous blood ($Sa0_2$ - $Sv0_2$). The following interventions are designed to augment each of these determinants.

AUGMENT CARDIAC OUTPUT. If the cardiac output is low (i.e., cardiac index < 2.4 L/min/m2), the next step is to measure the ventricular filling pressure [i.e., the central venous pressure (CVP) or the pulmonary capillary wedge pressure (PCWP)]. If the CVP is below 4 mm Hg or the PCWP is below 6 mm Hg, volume resuscitation is indicated until the CVP rises to about 10 mm Hg, or the PCWP rises to about 15 mm Hg (these values are slightly above the normal range for each pressure). If the ventricular filling pressures are normal or etevated, the cardiac output should be normali2ed by using dobutamine (a positive inotropic agent described in Chapter 16).

CORRECT ANEMIA. If the hemoglobin is below 7 g/ dL, consider blood transfusion. This approach is problematic in low output states because an increase in hematocrit will increase blood viscosity, and this can decrease the cardiac output (see Figure 1.8). .

CORRECT HYPOXEMIA. If the arterial oxyhemoglobin saturation ($Sa0_2$) is below 90%, the concentration of inhaled oxygen should be increased until the $SaO_2$ rises above 90%.

This approach is designed to correct VT *2* deficits in patients with impaired tissue oxygenation due to hypovolemic shock or cardiogenic shock. It may not be appropriate for patients with septic shock, where tissue dysoxia may be the result of a defect in oxygen utili2ation rather than oxygen availability, as explained next.

*The VOl* in *Sepsis*

The $VO_2$ may not be an appropriate parameter to monitor in patients with severe sepsis or septic shock because the VO2 may not reflect the rate of aerobic metabolism in sepsis. Activation of neutrophils and macrophages is accompanied by a marked increase in cellular oxygen consumption,

TABLE 11.2 Oxygen-Transport Variables, Blood Lactate, and Survival in Septic Shock

| Measurement | Survivors | Nonsurvivors | Difference |
|---|---|---|---|
| Cardiac index (Umin/$m^2$) | 3.8 | 3.9 | +2.6% |
| Oxygen uptake (mUmin/$m^2$) | 173 | 164 | -5.2% |
| Arterial lactate (mmol/L) | 2.6 | 7.7 | +296% |

Measurements in nonsurvivors are the last ones before death.
From Reference 23.

called the *respiratory burst.* The oxygen consumed in this process is used to generate toxic oxygen intermediates (e.g., superoxide radical and hydrogen peroxide) that are released as part of the inflammatory process (O). This oxygen consumption contributes to the VO2 measurement but is unrelated to aerobic metabolism. This means that in sepsis, there is a *non-metabolic VO?!* which is the contribution of the respiratory burst in phagocytes, that adds to the metabolic $V0_2$, or the rate of aerobic metabolism.

As just described, in patients with severe sepsis or a systemic inflammatory condition, the measured $V0_2$ is not a true reflection of aerobic metabolism (i.e., the metabolic $V0_2$). The measured VT *2* is expected to overestimate the metabolic VT *2* in sepsis by an amount that is equivalent to the non-metabolic VT 2 in phagocytes. The magnitude of the non-metabolic VT *2* in sepsis is unknown, but it may be considerable (11).

The non-value of the measured VT 2 in sepsis is demonstrated in Table 11.2. In this study of patients with septic shock, the VT *2* was slightly above the normal range (100 to 160 mL/min/m2) in both survivors and nonsurvivors. However, the metabolic VT *2* should be lower than normal (reflecting anaerobic metabolism) in patients with shock, especially in patients who do not survive. The higher-than-expected $V0_2$ in Table 11.2 may then be a reflection of the added contribution of the non-metabolic VT *2* in activated phagocytes. In fact, the elevated $V0_2$ that is often observed in sepsis may not represent true hypermetabolism but may be a reflection of the added $O_2$ consumption in activated phagocytes.

*Tissue Oxyoenation* in *Sepsis*

The graph in Figure 11.3 shows the *pO2* recorded with an oxygen electrode placed in a forearm muscle in a group of healthy subjects and a group of patients with severe sepsis (2). Note that the tissue $P0_2$ is *increased* in the septic patients, indicating that tissue oxygenation is not impaired in sepsis. Similar results have been reported in the bowel mucosa of animals injected with endotoxin (13). Despite the improved tissue oxygenation, aerobic metabolism is challenged in sepsis because there is an apparent defect in oxygen utili2ation in mitochondria (14). Nevertheless, because tissue oxygen levels are not impaired in sepsis, therapy designed to improve tissue oxygenation does not seem warranted in patients with severe sepsis or septic shock.

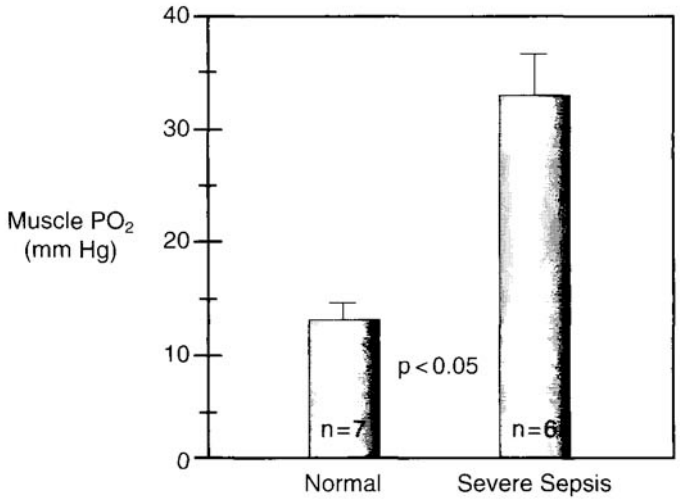


**FIGURE 11.3** Tissue $PO_2$ (mean) recorded in the forearm muscles of 6 healthy volunteers and 7 patients with severe sepsis. *Crossbars* represent the standard error of the mean. (From Sair M, Etherington PJ, Winlove CP, et al. Tissue oxygenation and perfusion in patients with systemic sepsis. Crit Care Med 2001;29:1343.)

*Clinical Outcomes*

The value of the oxygen transport variables (i.e., oxygen delivery and oxygen uptake) as therapeutic end-points in critically ill patients is a matter of considerable debate. Some studies show improved outcomes with this approach (15), whereas others do not (16). One source of confusion may be the fact that many of these studies included septic patients (16), who are not expected to have impaired tissue oxygen levels and are not expected to improve with interventions designed to promote tissue oxygenation.

*Summary*

To summarize, an abnormally low $\dot{V}O_2$ (less than 100 mL/min/$m^2$) can be a marker of impaired tissue oxygenation, but only in patients who are free of sepsis or systemic inflammation (see Chapter 40 for a description of the sepsis and inflammatory syndromes). Furthermore, management designed to improve tissue oxygenation may not be appropriate in sepsis because tissue oxygenation does not seem to be impaired in this condition.

## VENOUS $O_2$ SATURATION

The oxygen saturation of hemoglobin in mixed venous (pulmonary artery) blood can be used to evaluate the balance between systemic oxygen delivery and systemic oxygen uptake. This concept is described

in Chapter 2 (see the section, Control of Oxygen Uptake) and is briefly reviewed here.

### Control of $0_2$ Uptake

The oxygen transport system operates to maintain a constant rate of oxygen uptake into tissues ($V0_2$) in the face of variations in systemic oxygen delivery (DO). This is accomplished by varying the oxygen desaturation of hemoglobin in capillary blood as the $00_2$ varies. This relationship is expressed in Equation 11.3.

$$VT\ 2 = DT\ 2\ X\ (SaT\ 2 - SvT\ 2) \qquad (11.3)$$

The SaT 2 and SvT 2 represent the oxygen saturation of hemoglobin (Le., the percentage of total hemoglobin that is fully saturated with oxygen) in arterial and mixed venous blood, respectively. The difference (SaT 2 - SvT 2) represents the degree of oxygen desaturation of hemoglobin as it passes through the capillaries, also known as the *oxygen extraction* from hemoglobin in capillary blood.

The graph in Figure 11.4 shows the relationship between 02, delivery (OT 2)' $O_2$ uptake (VT 2)' and $O_2$ extraction (SaT 2 - SvT 2) when $O_2$ delivery is progressively decreased. The normal SaT 2 and SvT 2 are 95%

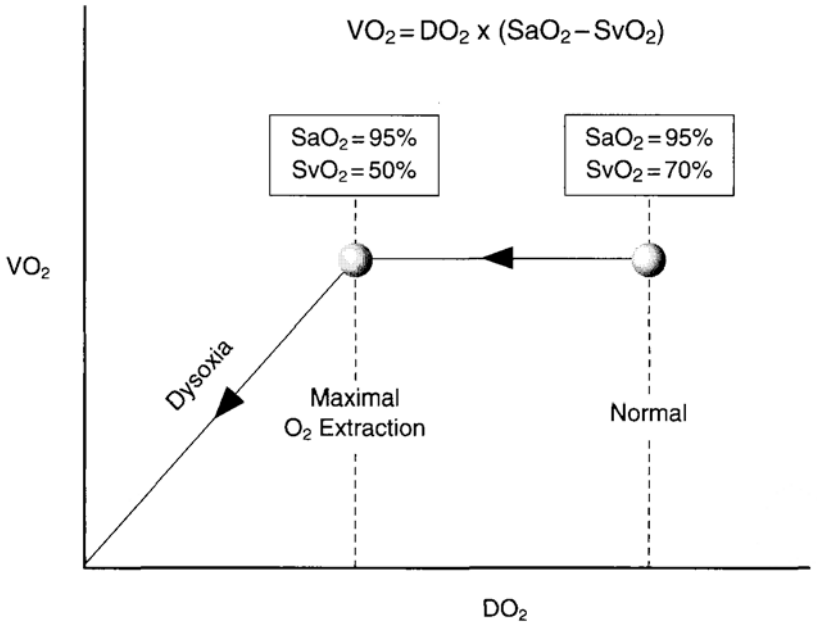


**FIGURE 11.4** The relationship between systemic oxygen delivery ($DO_2$), systemic oxygen uptake ($VO_2$), and oxygen extraction ($SaO_2 - SvO_2$) in capillary blood. $SaO_2$ and $SvO_2$ represent the oxygenated hemoglobin expressed as a percentage of total hemoglobin in arterial and mixed venous (pulmonary artery) blood, respectively.

and 70%, respectively, indicating a normal $O_2$ extraction of 25%. This means that 25% of the hemoglobin molecules desaturate as they pass through the capillaries. As the $00_2$ begins to decrease below normal, the $V0_2$ remains constant, indicating that the $O_2$ extraction is increasing. At the point where $O_2$ extraction is maximal, the $Sa0_2$ is unchanged at 95%, but the $Sv0_2$ has decreased to 50%. The maximum $O_2$ extraction is thus 45%, or almost twice normal. When *O2* extraction reaches its maximum level, further decreases in $00_2$ are accompanied by similar decreases in $V0_2$. This condition of delivery-dependent $V0_2$ is a sign of tissue dysoxia (i.e., oxygen-limited aerobic energy production).

### Using the $Sv0_2$

According to the relationships shown in Figure 11.4, monitoring the $SvO_2$ can provide the following information.

A decrease in $SvO_2$ below 70% indicates that systemic $O_2$ delivery is impaired. The possible sources of impaired $O_2$ delivery are identified by the determinants of $D0_2$ in Equation 11.4 (which is described in more detail in Chapter 2). A decrease in $00_2$ can be the result of a low cardiac output (Q), anemia (Hb), or hypoxemia ($Sa0_2$).

$$D0_2 = Q \text{ X } 13.4 \text{ X Hb X SaT } 2 \qquad (11.4)$$

A decrease in $SvO_2$ to 50% indicates a global state of tissue dysoxia or impending dysoxia.

The $Sv0_2$ measurement requires a pulmonary artery (PA) catheter (described in Chapter 9) because blood from the pulmonary artery is considered to be a mix of venous blood from all tissue beds (hence the term "mixed" venous blood). The measurement is usually performed on a blood sample taken from the distal lumen of the PA catheter. There is also a speciali2ed PA catheter that is capable of performing continuous *in vivo* measurements of the $Sv0_2$ in pulmonary artery blood. The methodology for the measurement of $O_2$ saturation in blood (which is called *oximetry)* is described in detail in Chapter 20.

*Variability*

Continuous monitoring of $SvO_2$ with speciali2ed pulmonary artery catheters has revealed a spontaneous variation that averages 5% but can be as high as 20% (17). In general, a greater than 5% change in $Sv0_2$ that persists for longer than 10 minutes is considered a significant change (18).

### Central Venous 02 Saturation

For patients who do not have a pulmonary artery catheter, blood from the superior vena cava (drawn through a central venous catheter) has been recommended as a suitable alternative to mixed venous (pulmonary

artery) blood for the measurement of *O2* saturation (19). The agreement between *central venous* 02 *saturation* ($ScvO_2$) and mixed venous $O_2$ saturation ($Sv0_2$) is reasonable (within 5%) if multiple measurements are averaged, but single measurements of $Scv0_2$ can differ from $Sv0_2$ by as much as 10% (absolute difference) (20). Therefore multiple measurements of $Scv0_2$ are recommended before making diagnostic and therapeutic decisions based on the measurement.

The ScvT 2 is gaining popularity as a surrogate measure of mixed venous *O2* saturation because it obviates the cost and morbidity associated with pulmonary artery catheters. Recent guidelines for the early management of patients with severe sepsis and septic shock includes an ScvT *2* of greater than 70% as a therapeutic end-point (19).

**LACTATE LEVELS IN BLOOD**

As indicated in Figure 11.1, lactate accumulation in tissues and blood is an expected consequence of dysoxia (21). Monitoring blood lactate levels is the most widely used method of evaluating tissue oxygen balance and detecting global (whole-body) tissue dysoxia. Lactate can be measured in whole blood or plasma (22), and concentrations above 2 mEq/L are considered abnormal. Increasing the threshold to 4 mEq/L may be more appropriate for predicting survival (22).

### Blood Lactate and Survival

As demonstrated in Figure 11.2, lactate accumulation in blood can be a delayed finding in patients with impaired tissue oxygenation. However, once elevated, blood lactate levels show a direct correlation with mortality in patients with circulatory shock. This is demonstrated in Figure 11.5. Note that most patients survive when the blood lactate concentration is below 2 mmol/L, while most patients do not survive when the blood lactate level approaches 10 mmol/L. In patients with circulatory shock (e.g., hypotension, oliguria, etc.), the likelihood of a fatal outcome is 60% when the blood lactate is above 2 mmol/L, and 80% when the blood lactate exceeds 4 mmol/L (22). In patients with septic shock, an elevated blood lactate level is more predictive of a fatal outcome than the oxygen transport variables. This is demonstrated in Table 11.2 (23). Neither cardiac output nor systemic oxygen uptake (VT 2) differs significantly in survivors and nonsurvivors, whereas the lactate levels are three times higher in patients with a fatal outcome.

### Other Sources of Lactate

Unfortunately, lactate accumulation in blood is not specific for global tissue dysoxia. Other causes of hyperlactatemia include hepatic insufficiency (which impairs lactate clearance from the blood), thiamine deficiency (which inhibits pyruvate dehydrogenase activity and blocks pyruvate entry

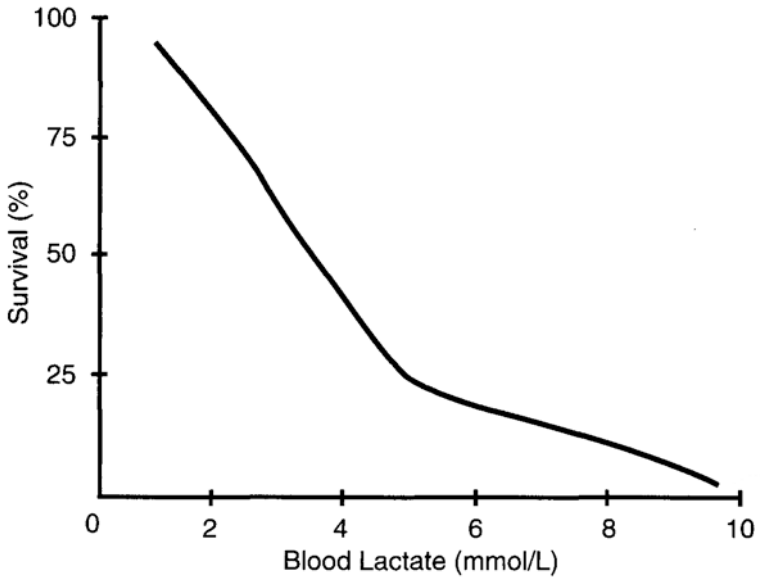


**FIGURE 11.5** The relationship between blood lactate and survival in patients with circulatory shock. [From Weil MH, Afifi AA. Experimental and clinical studies on lactate and pyruvate as indicators of the severity of acute circulatory failure (shock). Circulation 1970;16:989.]

into mitochondria), severe sepsis (same mechanism as thiamine deficiency, as described below), and intracellular alkalosis (which stimulates glycolysis) (21,24). For more information on these disorders, see Chapter 29.

*Sepsis*

Lactate accumulation in sepsis may not be the result of tissue oxygen deprivation. The culprit may be endotoxin, which blocks the actions of the pyruvate dehydrogenase enzyme that moves pyruvate into mitochondria. Pyruvate is allowed to accumulate in the cell cytoplasm, where it is converted to lactate. The ability of endotoxin to promote lactate formation is shown in the graph in Figure 11.6 (25). In this animal study, a one-hour infusion of endotoxin was associated with a progressive rise in blood lactate. The animals were then given dichloroacetate, a substance that activates pyruvate dehydrogenase in the presence of oxygen. This causes a progressive decline in lactate levels to normal, indicating that pyruvate dehydrogenase was activated and oxygen was present in cells to permit activation. Finally, when the animals were subjected to hypoxemia by breathing a low-oxygen gas mixture, blood lactate levels failed to rise. These findings suggest that impaired tissue oxygenation is not the source of blood lactate accumulation in sepsis.

The combination of elevated tissue oxygen levels (Fig. 11.3) and lactate accumulation in sepsis is consistent with the notion that dysoxia in sepsis may be the result of a defect in the cellular utilization of oxygen.

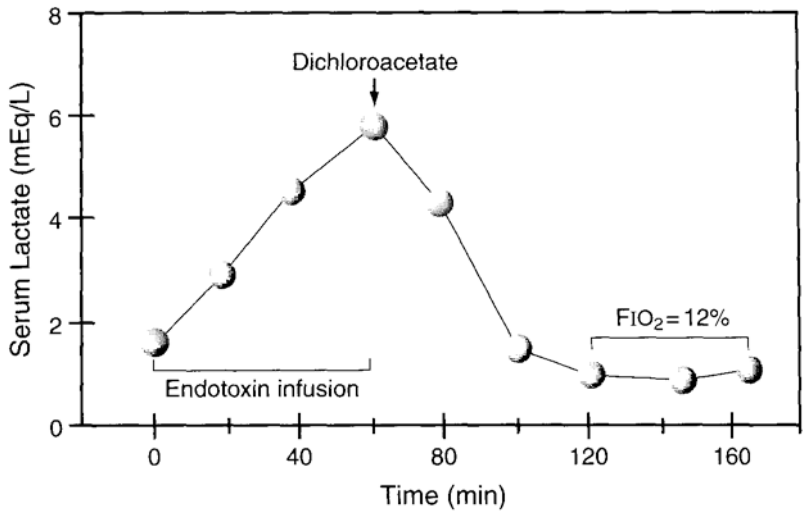


**FIGURE 11.6** Influence of endotoxin, dichloroacetate, and hypoxic challenge on arterial lactate levels. Response to dichloroacetate indicates that endotoxin-associated lactic acidosis is not caused by anaerobic conditions. (From Curtis SE, Cain SM. Regional and systemic oxygen delivery/uptake relations and lactate flux in hyperdynamic, endotoxin-treated dogs. Am Rev Respir Dis 1992;145:348–354.)

Lactate as a Fuel
One feature of lactate that is often overlooked is its ability to serve as an oxidative fuel. The energy yield from the oxidation of both glucose and lactate is shown in Table 11.3. The energy yield from glucose oxidation is twice that of lactate, but each mole of glucose produces 2 moles of lactate. Therefore the energy yield from glucose metabolism is about the same when glucose is directly oxidi2ed and when glucose is converted to lactate and the lactate is oxidi2ed.
Lactate can serve as an oxidative fuel in several organs, including the heart, brain, liver, and skeletal muscle (26,27). If the lactate generated by tissue dysoxia can undergo oxidation in these organs at a later time, when aerobic metabolism is restored, then the energy yield of glucose oxidation will be preserved. In this context, lactate production could

TABLE 11.3 Lactate as an Oxidative Fuel

| Substrate | Molecular Weight | Heat of Combustion | Caloric Value |
|---|---|---|---|
| Glucose | 180 | 673 kcal/mole | 3.74 kcal/g |
| Lactate | 90 | 326 kcal/mole | 3.62 kcal/g |

Glucose→oxidation→673 kcal

or
Glucose→Lactate→oxidation→652 kcal

serve as a means of preserving the nutrient energy supply during limited periods of tissue dysoxia.
ALIMENTARY TRACT HYPERCARBIA
Dysoxia promotes intracellular acidosis from enhanced lactate production and hydrolysis of high energy phosphate compounds. Bicarbonatebased buffering of this intracellular acidosis leads to enhanced $CO_2$ production and an increase in tissue $PCO_2$ (28). In cases of circulatory shock, increases in tissue $PCO_2$ are prominent in the wall of the gastrointestinal tract (29), which seems particularly vulnerable to ischemic injury. Such injury in the bowel wall may occur early in circulatory shock and may playa role in the development of multiple organ failure (via translocation of microbes and inflammatory cytokines) (30).
Two methods have been developed to detect hypercarbia in the alimentary tract: gastric tonometry (31) and sublingual capnometry (32). Despite initial enthusiasm for these methods, neither has gained widespread acceptance, and sublingual capnometry is not currently available. The reader is directed to references 31 and 32 for information on these methods.

A FINAL WORD
There are three take-home messages in this chapter. First, it is not possible to reliably assess tissue oxygenation in the clinical setting, and thus all interventions aimed at promoting tissue oxygenation are performed without justification and without a measurable end-point. Second, tissue oxygen levels are

apparently not depressed in patients who are septic or have systemic inflammation, and thus efforts to promote tissue oxygenation are not warranted in these patients. And finally, the consensus view that tissue oxygenation is an important determinant of viability in critically **ill** patients is without proof.

**REFERENCES**