

3 SHOCK

James W. Holcroft, M.D., F.A.C.S., John T. Anderson, M.D., F.A.C.S., and Matthew J. Sena, M.D.

Management of Shock

In thermodynamic terms, the purpose of the heart is simple enough. Its sole function is to generate useful energy (as opposed to heat, which it also generates) and then transfer that energy into the pulmonary artery and the aortic root as efficiently as possible. The useful energy transferred into the pulmonary artery from the right ventricle moves the blood through the lungs and into the left atrium and ventricle during diastole. The useful energy transferred into the aortic root from the left ventricle moves the blood throughout the body. The blood delivers nutrients (including oxygen) to metabolizing tissues, removes waste products from those tissues, carries heat from those tissues to the skin (where the heat is dissipated into the environment), and transports hormones and intermediate products of metabolism from one part of the body to another. The remaining energy in the blood pushes the blood into the right atrium and ventricle during diastole.

This useful energy has two components: flow and pressure. Flow, in the case of the cardiovascular system, is cardiac output. The pressures of interest are the mean pressures in the roots of the pulmonary artery and the aorta [see Figure 1]. These pressures, like all those we describe in this chapter, are expressed as being above (or occasionally below) atmospheric pressure and are measured with transducers placed at the level of the right atrium.

The formula for calculating the amount of useful energy transferred into the root of the pulmonary artery from the right ventricle (per unit time—typically 1 minute) is the cardiac output multiplied by the mean pressure in the pulmonary artery. The useful energy transferred into the aortic root from the left ventricle (per unit time) is the cardiac output multiplied by the mean aortic root pressure.¹⁻³

If the amount of useful energy transferred into the roots of the pulmonary artery and the aorta is insufficient to meet the body's basic metabolic needs, the patient is said to be in shock. Shock can

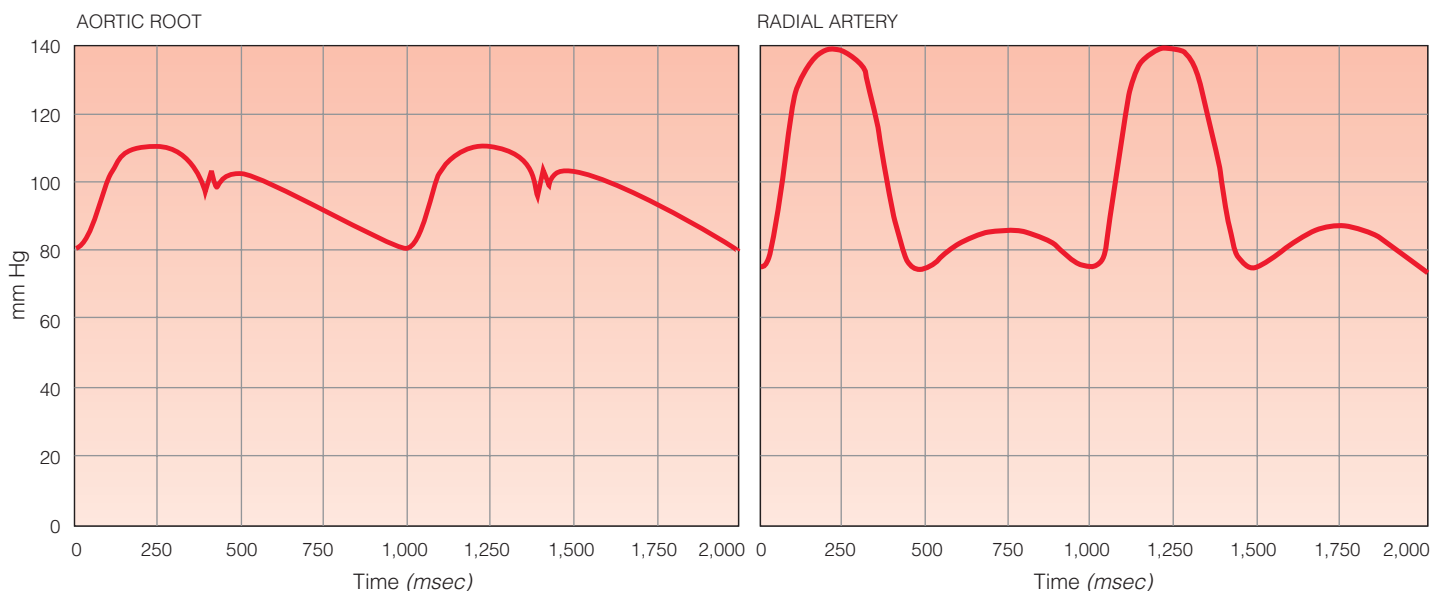
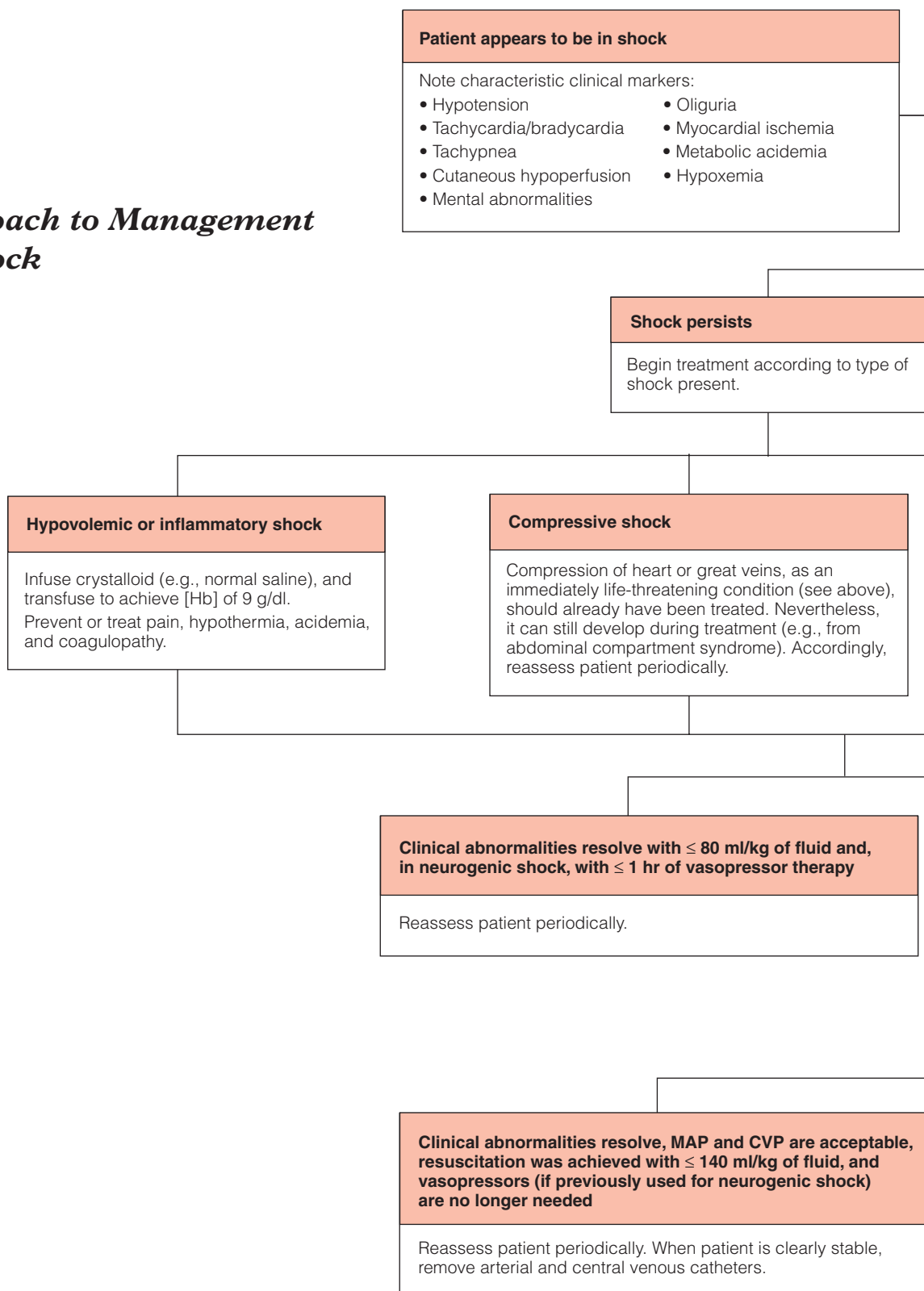
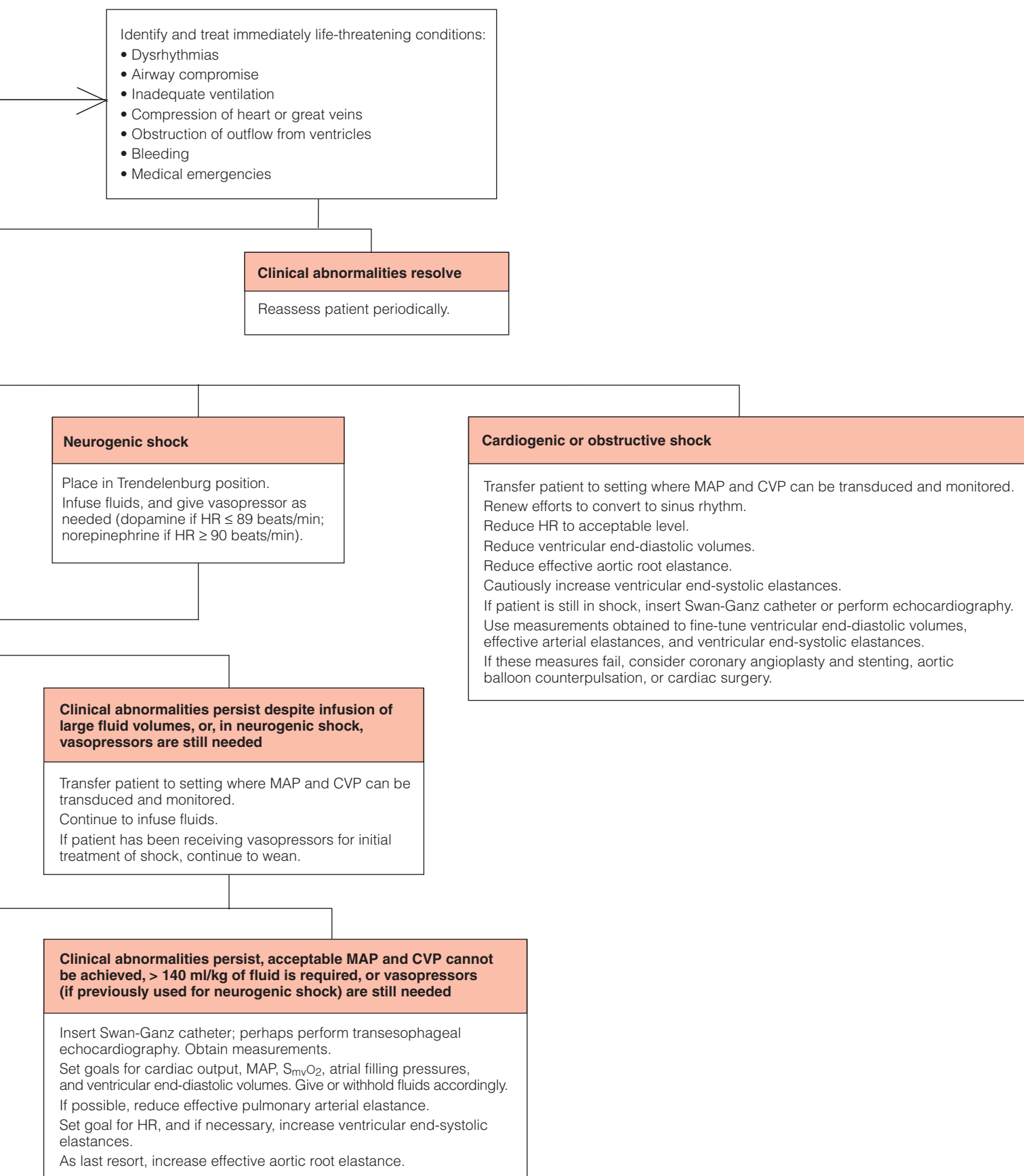


Figure 1 The mean pressure is defined as the area under a pressure tracing divided by the time needed to produce the tracing. A pressure wave in the ascending aorta with a blood pressure of 110/80 mm Hg will have the same mean pressure as a pressure wave in the radial artery of the same patient, even though the radial artery pressure might be 140/75 mm Hg. The systolic pressure in the radial artery is usually inscribed more rapidly. Therefore, even though the peak pressure in the radial artery is greater than that in the aorta, the areas under the tracings will be the same for the two vessels. Sometimes, the mean pressure can be approximated by taking one third of the difference between the systolic and diastolic pressures and adding that value to the diastolic pressure. Frequently, however, the formula does not work. In this example, the mean aortic pressure would be approximated at 90 mm Hg, whereas the mean radial artery pressure would be approximated at 97 mm Hg. Such results would be impossible: if the mean pressure in the radial artery were greater than the mean pressure in the aorta, blood would flow backward. This confusion is avoided by measuring the area under the curve and calculating the mean pressure exactly, which can be done with computer circuits that are available in all modern pressure-monitoring systems. It should also be noted that the systolic pressure in the radial artery is about 30 mm Hg higher than the systolic pressure in the aortic root. In extreme cases, it can be as much as 80 mm Hg higher [see Sidebar Energy Propagation throughout the Arteries and Its Effect on Pressures in Those Arteries].

Approach to Management of Shock





be caused by myriad different clinical conditions, which can be grouped into six broad categories [see Classification, *below*]. In all cases of shock, regardless of the category, one of two things has gone wrong, or else both have: either the cardiac output is inadequate or the mean central arterial pressures are inadequate, or else both are inadequate. When thinking about shock, one must keep these two possibilities in mind, both for assessment of the underlying problem and for treatment.

Classification

HYPVOLEMIC SHOCK

The major physiologic derangement in hypovolemic shock (i.e., shock secondary to loss of blood volume) is a left ventricular end-diastolic volume (LVEDV) that is so small that the heart cannot produce adequate amounts of useful energy. Causes include bleeding, protracted vomiting or diarrhea, fluid sequestration in obstructed gut or injured tissue, excessive use of diuretics, adrenal insufficiency, diabetes insipidus, and dehydration. In severe cases, the hypovolemia is worsened by the loss of sodium, chloride, and water from the plasma to the interstitium and the intracellular space, which occurs as compensation for the intracellular acidosis created by lack of perfusion.

In all cases of hypovolemic shock, the cardiac output will be low. In mild cases, the pressure may be normal, depending on the degree of compensatory arteriolar constriction, but the product of the cardiac output and the pressure will be low. In severe cases, the mean arterial pressure (MAP) will be low, and the product of the output and the pressure will be very low.

INFLAMMATORY SHOCK

Any clinical condition that is associated with ischemia-reperfusion or infection can cause inflammatory shock (which is sometimes called septic shock if caused by an infection). Clinical conditions capable of causing inflammatory shock include pneumonia, peritonitis, cholangitis, pyelonephritis, soft tissue infection, meningitis, mediastinitis, crush injuries, major fractures, high-velocity penetrating wounds, major burns, retained necrotic tissue, pancreatitis, anaphylaxis, and wet gangrene.

This type of shock is caused by inflammatory and coagulatory mediators that are released from the damaged or infected tissues into the systemic circulation. Thus, for the shock state to develop, the infected or traumatized or reperfused tissues must be in proximity to a robust drainage of blood from the tissues. An avascular infection (e.g., a contained abscess), in which the inflammatory mediators do not have access to the circulation, will not cause inflammatory shock, whereas an uncontained abscess (e.g., a ruptured appendiceal abscess or an acutely drained subphrenic abscess), which allows vascular dissemination of the mediators, can do so. Similarly, dry gangrene, because of its poor vascular supply, will not cause inflammatory shock, whereas wet gangrene can.

The cardiovascular derangements in inflammatory shock are caused by three basic mechanisms. The first mechanism arises from the need to keep the body's temperature from becoming excessively high. In the case of inflammatory shock caused by infection, inflammatory mediators released from the infected tissue increase the metabolic rate and heat production by a factor as high as 2. The excess heat is carried by the blood to the skin, where it is dissipated to the environment by convection, conduction, radiation, and evaporation. Under resting, nonseptic conditions, in a thermoneutral environment, the heat can be dissipated and the body temperature controlled with a modest amount of

blood flow to the skin—on the order of 300 ml/min in a 60 kg subject.^{4,5} In an extremely cold environment, however, blood flow can drop to negligible levels, probably as low as 100 ml/min. In the case of extreme hypermetabolism, as occurs during exercise, blood flow can increase to 6 L/min.⁵ In the case of severe sepsis, blood flow is probably on the order of 3 L/min—enough to necessitate increasing the cardiac output by a factor of 1.5.

To maximize the delivery of heated blood to the skin, the cutaneous arterioles dilate. To maximize the surface area of the blood vessels in the skin (and thereby facilitate transfer of heat from the blood to the skin), the cutaneous venules and veins dilate. The blood pressure drops, both because of the arteriolar dilation and because pooling of blood in the cutaneous venous capacitance bed reduces the ventricular end-diastolic volumes (if the patient's blood volume has not been adequately replenished). Small end-diastolic volumes lead to a reduced stroke volume, which, in turn, lowers the cardiac output and exaggerates the fall in the blood pressure.

The second mechanism, also related to the release of inflammatory mediators (either from infected tissue or from tissue that has undergone ischemia and reperfusion), arises from the contraction of actin and myosin filaments in the endothelial cells of the microvasculature, both at the site of infection or ischemia-reperfusion and at distal sites as a consequence of blood-borne mediators. Intercellular gaps open up in the capillaries, venules, and small veins. These gaps give immunoglobulins and inflammatory cells access to the interstitium and allow protein-rich plasma to leak into the interstitium. As a result, blood volume is depleted and the ventricular end-diastolic volumes decreased.

The third mechanism, as in severe hypovolemic shock, is movement of sodium, chloride, and water from the plasma into the interstitium and the intracellular space as a means of controlling intracellular acidosis. Loss of fluid from the plasma into the cells reduces blood volume and thus decreases ventricular end-diastolic volumes.

These three mechanisms give rise to the characteristic clinical findings of inflammatory shock. The blood pressure will be low, for three possible reasons: (1) small ventricular end-diastolic volumes (if the patient has not been resuscitated), (2) lowered hindrance to ventricular ejection (because of the cutaneous arteriolar dilation), and (3) potential myocardial depression.⁶ The heart rate usually rises in an effort to increase the cardiac output; occasionally, it does not increase very much, in an effort to allow more time for ventricular filling and for perfusion of the coronary vasculature during diastole.

If the predominant feature of the shock state is loss of plasma volume into the interstitium through a permeable microvasculature and through intracellular accumulation of sodium, chloride, and water, the patient's skin will be cool and clammy (hence the terms cold septic shock and cold inflammatory shock). The cardiac output and the mean blood pressure will both be inadequate, and the patient's condition will meet the definition of shock—namely, inadequate perfusion because of inadequate generation of useful energy (cardiac output multiplied by mean pressure).

If, however, the blood volume has been restored or the predominant feature of the shock state is cutaneous vasodilatation, the patient's skin will be flushed and warm (hence the term warm inflammatory shock). The cardiac output will be high but the mean pressure will be low, as a consequence of the cutaneous arteriolar dilatation. If the product of the two—that is, the useful energy, or power—is inadequate to provide perfusion for the body, the patient is in shock. If the product of the two is adequate to provide perfusion, the patient will not be in shock, but the prob-

lem causing the systemic inflammatory state will still have to be corrected.

NEUROGENIC SHOCK

The cardiovascular derangements in neurogenic shock arise from the loss of autonomic innervation of the vasculature, caused by conditions such as spinal cord injury, regional anesthesia, administration of drugs that block the adrenergic nervous system (including some systemically administered anesthetic agents), and certain neurologic disorders. In some patients (e.g., those who have a low spinal cord injury or have received a regional anesthetic), the denervation is localized, which means that only the vasculature in the denervated areas will be blocked. In other patients (e.g., those who have a high spinal cord injury or have received a general anesthetic), the heart and the vasculature throughout the body will be blocked.

In all cases of neurogenic shock, the MAP will be low as a consequence of arteriolar dilation. In some cases of denervation, the cardiac output will increase because of the decreased hindrance to ventricular contraction and, in instances where the denervation does not involve the heart, an elevated heart rate. If the increased cardiac output is enough to compensate for the low pressure, the patient will not be in shock.

In most cases of denervation, however, the cardiac output will not increase enough to overcome the adverse effects of the low blood pressure. In some cases, the cardiac output will fall: blood will pool in the denervated venules and small veins; the ventricular musculature will lose its sympathetic tone (in the case of a generalized or high denervation); and the heart rate will not be able to respond with a tachycardia (in the case of a high blockade). When both the MAP and the cardiac output are low, the shock can be profound.

COMPRESSIVE SHOCK

The cardiovascular derangements in compressive shock arise from external forces that compress the thin-walled chambers of the heart (the atria and the right ventricle), the great veins (systemic or pulmonary), or both, compromising the filling of the chambers and resulting in inadequate ventricular end-diastolic volumes. Clinical conditions capable of causing compressive shock include pericardial tamponade, tension pneumothoraces, positive-pressure ventilation with large tidal volumes or high airway pressures (especially in a hypovolemic patient), an elevated diaphragm (as in pregnancy), displacement of abdominal viscera through a ruptured diaphragm, the abdominal compartment syndrome (e.g., from ascites, abdominal distention, abdominal bleeding, retroperitoneal bleeding, or a stiff abdominal wall, as in a patient with deep burns to the torso), and, perhaps, the thoracic compartment syndrome, caused by positive-pressure ventilation, the stiff lungs of the adult respiratory distress syndrome (ARDS), or the elevated diaphragm of the abdominal compartment syndrome.

OBSTRUCTIVE SHOCK

The cardiovascular derangements in obstructive shock arise when excessive stiffness of the arterial walls, compression of the arterial walls, or obstruction of the vasculature imposes an undue burden on the heart, so that the contractile apparatus of the ventricular musculature is no longer matched to the compliance and resistance of the vasculature into which it pumps. The obstruction to flow can be on either the right or the left side of the heart. Causes include pulmonary valvular stenosis, pulmonary embolism, air embolism, ARDS, aortic stenosis, calcification of the systemic arteries, thickening or stiffening of the arterial walls

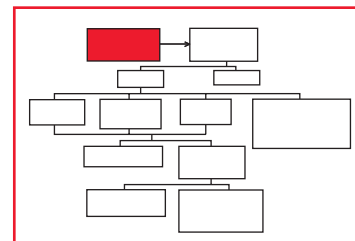
as a result of the loss of elastin and its replacement with collagen (as occurs in old age), and obstruction of the systemic microcirculation as a result of chronic hypertension or the arteriolar disease of diabetes. The mean pressure in the pulmonary artery or the aorta will be high, and the systolic pressures will be disproportionately higher. The cardiac output will be low, and the heart will be working inefficiently.

CARDIOGENIC SHOCK

The cardiovascular derangements in cardiogenic shock arise from intrinsic cardiac abnormalities that prevent the heart from delivering blood into the vasculature with adequate energy. Sometimes, the problem is with the muscle; sometimes, it is with the rhythm. In all cases, the problem is a mismatch between the contractile or rhythmic characteristics of the myocardial musculature and the compliance and resistance of the vasculature into which the musculature pumps its contained blood. Causes include bradyarrhythmias, tachyarrhythmias, myocardial ischemia, myocardial infarction, cardiomyopathies, myocarditis, myocardial contusion (rare), cardiac valvular insufficiency, papillary muscle rupture, and septal defects. The MAP is usually low, depending on the degree of compensatory constriction of the systemic arterioles; the cardiac output is always low.

Characteristic Clinical Markers

The presence of a shock state is typically signaled by one or more characteristic clinical markers [see Table 1].



HYPOTENSION

The mean aortic root pressure [see Figure 1] is the pressure of consequence for perfusion of noncardiac, systemic tissues. (This pressure is also close to the pressure that perfuses the coronary arteries, though, admittedly, the mean aortic root diastolic pressure is the better descriptor.) The aortic root end-systolic pressure—or, equivalently, the ventricular end-systolic pressure—is the key pressure for assessing the hindrance or impedance that the ventricle faces when it pushes its blood into the vasculature.⁷ The aortic root end-systolic pressure is also the most important pressure for estimating left ventricular myocardial oxygen requirements.^{3,8}

In other words, when one thinks about shock, it is the central pressures, as opposed to the peripheral ones, that one is most interested in knowing. Unfortunately, none of these central pressures will be known during the initial management of a patient in shock, except in those rare instances in which the patient is being managed during cardiac surgery or cardiac catheterization. Instead, in the vast majority of cases, one must use peripheral arterial pressures, typically measured in a brachial artery by means of sphygmomanometry and typically with the emphasis on the systolic pressure. Measurement of the cuff pressures does not require expensive, complicated, or difficult-to-calibrate equipment. The systolic pressure is usually easy enough to hear. Moreover, in the treatment of shock, the brachial peak systolic pressure is the pressure with which most physicians feel most comfortable.

One should, however, keep in mind the problems with using measurements from a peripheral artery, particularly if the measurements are obtained via sphygmomanometry.⁹ The systolic pressure in a peripheral artery is frequently higher than that in the aortic root, sometimes substantially so [see Figure 1 and Sidebar Energy Propagation throughout the Arteries and Its Effect on

Table 1 Clinical Markers of Possible Shock State

Clinical Marker	Value or Findings Indicative of Shock
Systolic blood pressure	
Adult	≤ 110 mm Hg
Schoolchild	≤ 100 mm Hg
Preschool child	≤ 90 mm Hg
Infant	≤ 80 mm Hg
Sinus tachycardia	
Adult	≥ 90 beats/min
Schoolchild	≥ 120 beats/min
Preschool child	≥ 140 beats/min
Infant	≥ 160 beats/min
Cutaneous vasoconstriction	Pale, cool, clammy skin with constricted subcutaneous veins
Respiratory rate	
Adult	≤ 7 or ≥ 29 breaths/min
Child	≤ 12 or ≥ 35 breaths/min
Infant	≤ 20 or ≥ 50 breaths/min
Mental changes	Anxiousness, agitation, indifference, lethargy, obtundation
Urine output	
Adult	≤ 0.5 ml·kg ⁻¹ ·hr ⁻¹
Child	≤ 1.0 ml·kg ⁻¹ ·hr ⁻¹
Infant	≤ 2.0 ml·kg ⁻¹ ·hr ⁻¹
Myocardial ischemia or failure	Chest pain, third heart sound, pulmonary edema, abnormal ECG
Metabolic acidemia	[HCO ₃ ⁻] ≤ 21 mEq/L Base deficit ≥ 3 mEq/L
Hypoxemia (on room air)	
0–50 yr	≤ 90 mm Hg
51–70 yr	≤ 80 mm Hg
≥ 71 yr	≤ 70 mm Hg

Pressures in Those Arteries]; the diastolic pressure in a peripheral artery is almost always lower than that in the aortic root. The approximated MAP, calculated as being one third of the way between the diastolic and systolic pressures, is not a reliable value. The formula is only an approximation to begin with, and the two pressures used in the calculation are unreliable and sometimes hard to obtain, particularly the diastolic pressure. Furthermore, in shock, the flow of blood through the brachial artery can be so minimal that very little turbulence is created and very little sound generated; hearing these faint sounds in a busy emergency department or intensive care unit can be difficult, and hearing their disappearance can be even more difficult.

Assessment of the blood pressure should take into account the patient's age [see Table 1]. In an adult, a low brachial peak systolic pressure (≤ 110 mm Hg) frequently indicates shock; a very low brachial peak systolic pressure (≤ 89 mm Hg) almost always does, especially in a patient who is under stress. (Admittedly, many normal patients, especially young women, may have a systolic pressure of 89 mm Hg or lower when supine, but only when in an unstressed state. The pain or stress associated with an injury or acute illness will drive that normally low pressure to much higher levels.) A sustained (> 30 seconds) systolic pressure drop greater

than 10 mm Hg in a patient who has arisen from a supine to an upright position can also be an indicator of underlying shock.

A normal blood pressure, however, does not rule out shock. Adrenergic discharge and the release of circulating vasoconstrictors (e.g., vasopressin and angiotensin) often sustain blood pressure during shock, especially during its early stages. As a result, visceral hypoperfusion, arising from arteriolar constriction, may precede changes in the supine brachial blood pressure. In addition, some forms of shock can even be associated with hypertension (as in a hypertensive crisis) if the cardiac output is low. Finally, the definition of hypotension can vary, depending on the patient's usual blood pressure, which the physician may not know. A systolic brachial pressure that might be normal for a young healthy patient might be low for an older patient who had severe hypertension before his or her injury or illness.

TACHYCARDIA OR BRADYCARDIA

The pulse rate—perhaps the most evident of all the physical findings in clinical medicine—can increase in shock, and the possibility of shock should be considered in any patient with a tachycardia. An abnormally high pulse rate—with “high” determined in relation to the patient's age [see Table 1]—can serve as an indicator of shock.

A normal or slow heart rate, however, does not rule out shock.^{10–12} On the contrary, a normal or slow rate might indicate severe shock, even imminent decompensation. (The heart rate slows down in severe hypoxemia. In most persons, it also slows down before death; and during childbirth, obstetricians worry about slow heart rates, not rapid ones.) In severe shock, the pulse rate may have to slow down to reduce myocardial oxygen requirements; to allow more time for ventricular filling during diastole; to allow more time for coronary perfusion of the myocardium; and to match the energy-producing capabilities of the ventricles with the compliance and resistance of the vasculatures into which they pump their blood.

TACHYPNEA OR BRADYPNEA

Any patient with tachypnea must be promptly evaluated not only for possible pulmonary insufficiency but also for possible shock [see Table 1]. The rapid respiratory rate may be a response to a metabolic acidemia; it may also be a means of compensating for inadequate filling of the ventricles, in that it will lower the mean intrathoracic pressure and facilitate the diastolic influx of blood into the heart from the capacitance venules and small veins in the periphery. In severe decompensated shock, the respiratory rate may fall to very low levels, perhaps because of ischemia in the muscles providing the ventilation.¹³

CUTANEOUS HYPOPERFUSION

Diminished skin perfusion is often the first sign of shock. In all types of shock other than warm inflammatory shock and neurogenic shock, blood flow to the skin is reduced because of adrenergic discharge and high circulating levels of vasopressin and angiotensin II. The result is the pale, cool, and clammy skin of a person exhibiting the fight-or-flight reaction. Cutaneous hypoperfusion is not specific for shock—it can also be the result of hypothermia, for example—but it can be a warning that the patient may decompensate at any time.

MENTAL ABNORMALITIES

Patients in severe shock frequently exhibit mental abnormalities, which can range from anxiousness to agitation to indifference to obtundation. These findings are not sensitive—indeed, they

Energy Propagation throughout the Arteries and Its Effect on Pressures in Those Arteries

The contraction of a ventricle and the ejection of its blood into a standing column of blood in the root of the pulmonary artery or the aorta create an energy wave that propagates throughout the arterial system. The wave travels distally until it reaches the arterioles, which reflect some of the energy back to the heart. The summation of the antegrade and retrograde energy waves at any given point in the arterial system creates a specific pressure and volume at that point.

Stiff arteries result in increased velocities of wave propagation, both outgoing and returning, and thus early return to the measurement site; compliant arteries result in late return. Distal arteriolar constriction increases the amplitude of the reflected wave; dilation decreases it. Symmetrical spatial distribution of arterioles results in uniform reflection of waves that coalesce in phase with one another; the summed reflected wave is compact with sharp contours and is short in duration. Asymmetrical arteriolar distribution results in reflection of waves that are out of phase with one another; the summed reflected wave is slurred and spread out. Arterioles that are distant from the measurement site create a composite reflected wave that returns late; arterioles that are close create a wave that returns quickly.

If the arterioles distal to the measurement site are constricted, symmetrically distributed, or nearby or if the conducting arteries are stiff, systolic pressures in the peripheral arteries increase and diastolic pressures decrease slightly. In this case, the amplitude of the reflected wave will be large (constricted arterioles), its components will be in phase (symmetrical arteriolar distribution), and the retrograde wave will return quickly (stiff arteries). If the measurement site is close to the arterioles, the reflected wave will return very quickly and will pass through the antegrade wave before diastole begins. The duration of systole will be short. The pressure contour created by the superposition of the antegrade and retrograde waves will be sharp, with a rapid upswing and downswing. The systolic pressure will be increased, sometimes substantially, and the diastolic pressure will be slightly decreased.

The opposite occurs if the distal arterioles are dilated, asymmetrically distributed, or distant from the measuring site or if the conducting arteries are compliant. Under these conditions, the amplitude of the reflected wave will be small, its components will be out of phase, and the retrograde wave will be delayed. Unless the measuring site is very close to the arterioles, the wave will return during both systole and diastole. The duration of systole will be lengthened, and the upswing and downswing of the waveform will be smoothed out. The systolic pressure will be minimized, sometimes substantially, and the diastolic pressure will be slightly augmented.

These general characteristics of the arterial vasculature have specific implications for the pressures in the aortic root and the radial artery. In the aortic root, the typical pressure waveform is blunted (damped) and is characterized by lower systolic pressures and higher diastolic pressures than the distal waveforms. The arterioles in the heart, brain, liver, and kidneys are chronically dilated, diminishing the amplitudes of the reflected waves. The arterioles supplied by the aorta are asymmetrically distrib-

uted: those in the upper part of the body are close to the aortic root, whereas those in the lower extremities are distant. Thus, the reflected waves return to the aortic root at varying times, with the result that some of their pressure oscillations cancel one another out. Finally, the arteries that come off the aorta have varying degrees of stiffness. The arteries supplying the upper body are compliant (slow wave propagation velocities and late return), whereas those supplying the lower body are stiff (high propagation velocities but delayed return because of the long distances the waves must travel). The blunted contour of pressure in the aortic root enhances cardiovascular efficiency: the low systolic pressure results in minimal hindrance to ventricular emptying, and the high diastolic pressure results in maximal perfusion of the coronary vasculature [see Figure 1].

In the radial artery, systolic pressures are almost always higher and diastolic pressures usually somewhat lower than in the aortic root [see Figure 1]. The duration of systole is shorter, with a sharper upswing and a more precipitous downswing. The arterioles in the hand are usually constricted, symmetrically distributed, and close to the measurement site. The normal radial artery is compliant, which decreases the velocity of wave propagation, but its compliance is outweighed by the closeness of the arterioles. Thus, waves return quickly.

The spiked pressure waveform in the peripheral arteries has no adverse effect on distal perfusion. It is the mean pressure in the artery that is important for perfusion, and that pressure is independent of the reflected pulsatile energy wave. The exaggerated peripheral arterial waveform does, however, make it difficult to extrapolate from distally measured systolic pressures back to the central aortic pressures. Such extrapolation must rest on certain assumptions. For example, in a patient with normally constricted arterioles in the hand, the peak systolic pressure in the radial artery is approximately 10 mm Hg higher than that in the brachial artery, which is approximately 10 mm Hg higher than that in the aortic root.

If the arterioles in the hand are constricted more than the arterioles in the central portions of the body (as may be the case in hypovolemic or cardiogenic shock), the peak systolic pressure in the radial artery can be much higher than that in the aortic root because of reflected waves with large amplitudes. On the other hand, severe shock may constrict the arteries between the aorta and the hand sufficiently to decrease all of the distal pressures (mean, systolic, and diastolic).

If the arterioles in the hand are dilated with respect to the central arterioles (as may be the case in inflammatory or generalized neurogenic shock), the peak systolic pressure in the radial artery and that in the aortic root come closer to each other. A warm hand means dilated cutaneous arterioles; accordingly, the reflected waves will have minimal amplitudes.

When managing a patient in shock, one would like to know the pressures in the aortic root, but one must be cautious in trying to estimate those pressures on the basis of pressures in peripheral arteries.

develop only in the late stages of shock—nor are they specific. They are, however, a strong warning to the physician that something must be done quickly. The body protects the blood supply to the brain at all costs. Changes in mental status as a result of severe shock suggest impending circulatory collapse.

OLIGURIA

The stress imposed by all forms of shock—in the absence of diuretic use, high alcohol levels, or administration of radiographic contrast agents—stimulates the release of vasopressin (antidiuretic hormone) and aldosterone (through activation of the angiotensin system).^{14,15} The result is oliguria, which is a sign of stress

at the very least and may be a sign of decreased blood flow to the kidneys in extreme cases [see Table 1].

Whenever the diagnosis of shock is being entertained, a Foley catheter should be placed. Successful treatment should reduce the stress and decrease the plasma levels of vasopressin and aldosterone. It should also increase renal blood flow, if the shock is indeed so severe that inadequate blood flow to the kidneys is compromising their viability. With successful treatment, the urine output should improve; if it does not, further therapeutic measures are necessary.

MYOCARDIAL ISCHEMIA

Electrocardiography is indicated whenever the suspicion of

shock arises. The electrocardiogram may show signs of ischemia, which may be caused either by a primary myocardial problem or by a secondary extracardiac problem (e.g., hypotension resulting from hemorrhage). In either case, the presence of myocardial ischemia should prompt quick action.

METABOLIC ACIDEMIA

Metabolic acidemia, as a sign of shock, may be manifested by an increased respiratory rate. Serum chemistry may demonstrate a decrease in the total concentration of carbon dioxide (bicarbonate plus dissolved CO_2), but analysis of blood gases is usually required for confirmation. The acidosis may take the form of either a low calculated bicarbonate level or a base deficit.¹⁶ Often, it does not become evident until after the shock has been recognized and treatment is under way. In severe, untreated shock, the anaerobic products of metabolism are confined to the periphery; they may not be washed into the central circulation until resuscitation has reestablished some flow to the ischemic tissues. The degree of acidosis after resuscitation can, however, provide information about the duration and severity of the initial insult. This knowledge can be useful in determining how aggressive subsequent management should be.

HYPOXEMIA

Shock may be associated with significant arterial hypoxemia, a finding that, like several of the other variables being discussed, should be evaluated in the context of the patient's age [see Table 1]. Low flow results in marked desaturation of the blood leaving the metabolizing peripheral tissue, which eventually ends up in the pulmonary artery (yielding a low mixed venous oxygen saturation [S_{mvO_2}]). In patients with coexisting pulmonary dysfunction and an intrapulmonary shunt, the markedly desaturated pulmonary arterial blood is only partially saturated as it passes through the lungs, ultimately mixing with fully saturated blood. The increased admixture of oxygen-poor blood results in a reduced oxygen saturation in the systemic arterial blood.

Identification and Treatment of Immediately Life-Threatening Conditions

If the patient shows signs suggestive of shock, the next step is to search for and treat conditions that could be immediately fatal, such as (1) dysrhythmias; (2) airway compromise; (3) inadequate ventilation; (4) compression of the heart, the great veins, or both; (5) acute obstruction of the large arteries into which the ventricles pump their blood; (6) bleeding; and (7) certain life-threatening medical conditions (e.g., anaphylaxis, severe electrolyte disturbances, and life-threatening endocrine abnormalities). Identification frequently requires pattern recognition.

DYSRHYTHMIAS

Given that an ECG is obtained promptly in any case of suspected shock, dysrhythmias will be recognized early in the course of resuscitation. A nonagonal patient should be treated in accordance with standard resuscitation routines [see 8:1 *Cardiac Resuscitation and 8:2 Acute Cardiac Dysrhythmia*]. A sinus rhythm will have to be established, but one can go about this in a deliberate manner.

An agonal patient should undergo cardioversion. In this situation, cardioversion takes precedence even over making a definitive

diagnosis of the particular type of dysrhythmia; one should not even obtain a 12-lead ECG. There are three agonal dysrhythmias that can be treated definitively within seconds: ventricular fibrillation, ventricular tachycardia, and atrial fibrillation. All can be converted to a sinus rhythm with cardioversion. If this measure is successful, patients may reasonably hope for restoration of life with full neurologic function. Admittedly, there are other dysrhythmias besides these three (e.g., asystole) that can produce an agonal state, and cardioversion is of no use for these conditions. There is, however, no treatment for asystole or these other dysrhythmias that is likely to produce survival with reasonable neurologic function. Thus, there is no point in making the differential diagnosis.

Cardioversion also takes precedence over all other potential resuscitative efforts, including gaining airway control, obtaining I.V. access, and performing chest compressions (though if the team taking care of the patient is able to perform cardioversion, secure the airway, and gain I.V. access at the same time, it should do so). The goal is to get blood flowing again to the brain. Even if the initial reperfusion is with partially desaturated blood, it is better than no perfusion at all. Furthermore, perfusion of the brain from a heart in sinus rhythm is many times more effective than perfusion from chest compressions.

COMPROMISE OF AIRWAY

If a patient can talk in a full voice without undue effort, the airway can be assumed to be intact. Supplemental oxygen should be given via a mask or nasal prongs; nothing else need be done.

If the patient cannot talk in a full voice, possible compromise of the airway must be assumed. Causes range from loss of protective reflexes to mechanical obstruction of the trachea or major bronchi. Sometimes, a jaw thrust is all that is needed for diagnosis and treatment of the problem. In cases of profound shock, however, the patient should be intubated and ventilated, either with an Ambu bag or with a mechanical ventilator.

If increasing abdominal distention is apparent, esophageal intubation or displacement of the endotracheal tube into the hypopharynx is a possibility. The tube should be replaced. Reintubation is hazardous in these circumstances, but leaving a tube in the esophagus or hypopharynx is more hazardous.

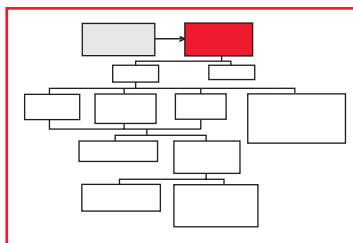
If breath sounds are absent on the left, right mainstem bronchial intubation is a possibility. The tube should be withdrawn into the trachea (or into what one believes to be the trachea).

If the endotracheal tube is obstructed by clotted blood or inspissated secretions, the obstruction can usually be cleared by suctioning. If this measure is unsuccessful, the patient should be reintubated.

Bleeding in the tracheobronchial tree (from injuries or from friable bronchial mucosa or tumor tissue) can eliminate ventilation from the lung segment supplied by the injured or obstructed bronchus and flood the initially uninjured lung with blood. If the bleeding is thought to be coming from the left lung, the endotracheal tube should be advanced into the right mainstem bronchus. Bleeding from the right lung is more problematic. Selective left mainstem intubation is usually impossible under emergency conditions. If selective mainstem intubation is not feasible or substantial bleeding continues on either side, definitive control of the bleeding will have to be obtained by means of either endobronchial techniques or open surgical intervention.

INADEQUATE VENTILATION

In the patient who has just been intubated, ventilation should begin with 100% oxygen, delivered through an Ambu bag. The patient should then be switched over to mechanical ventilation,



again with 100% oxygen. The ventilator should be set up so as to produce a minimal mean airway pressure (mean pressure being defined as the integral of the pressure over time divided by the time over which the pressure is produced [see Figure 1]). The respiratory rate should be set at 15 breaths/min and the tidal volume at 8 ml/kg lean body weight [see Table 2 and Sidebar Expectations for Cardiopulmonary Values in Patients of Different Sizes and Ages]. The end-expiratory pressure should be set at 0 mm Hg. Blood gas values should be obtained, and the settings on the ventilator should be adjusted as needed. The blood should be kept fully saturated. The patient should be mildly hyperventilated if the arterial pH is less than 7.20.

In some respects, these guidelines run counter to those used for long-term support of the mechanically ventilated patient. A fractional concentration of inspired oxygen ($F_{I}O_2$) of 100% can damage the alveolar epithelium and cause absorption atelectasis, and withholding positive end-expiratory pressure can facilitate the formation of atelectasis. A lung-protective ventilation strategy will ultimately be desirable [see 8:5 *Mechanical Ventilation and 8:4 Pulmonary Insufficiency*].¹⁷ In the initial resuscitation of the patient in shock, however, minimizing adverse effects on the cardiovascular system is the goal.¹⁸ Protecting the lungs can come later.

Many problems can arise with the use of mechanical ventilation. Even though modern ventilators are highly reliable, they can malfunction on occasion. If the chest wall does not rise with inspiration, the patient should be removed from the ventilator and ventilation recommenced with the almost foolproof Ambu bag. If ventilation proceeds normally with the Ambu bag, then the ventilator must have been at fault, and it should be replaced.

Pneumothoraces may arise from injuries to the lung, from attempts to place a central venous line, or from positive-pressure ventilation. They are treated with needle decompression followed by insertion of a chest tube.

Tension pneumothoraces sometimes develop in a patient who is breathing spontaneously; more often, however, they are created by the superimposition of positive-pressure ventilation on a previously existing pneumothorax. The tension pneumothorax not only eliminates ventilation on the side of the pneumothorax but also limits ventilation on the uninjured side. In addition, it compresses the heart and great vessels (see below). Characteristic signs include decreased or absent breath sounds on the involved side, a hyperresonant hemithorax, and, if the patient is normovolemic, distended neck veins. (A tracheal shift—a commonly described feature in patients with tension pneumothoraces—is hard to detect and, in our experience, rarely helpful in making the diagnosis.) A tension pneumothorax should be the first diagnosis considered in any patient who suddenly decompensates when placed on positive-pressure ventilation. Treatment consists of needle decompression followed by tube thoracostomy.

Air leaks always signify loss of at least some ventilation on the side of the leak. If they are large, they also signify loss of ventilation on the uninjured side, in that the administered air preferentially exits the airway through the chest wall defect or the chest tube on the injured side. A left-side leak can sometimes be treated by advancing the endotracheal tube into the right mainstem bronchus; a right-side leak usually necessitates surgical intervention, as does any large leak that does not close quickly.

Bleeding into the pleural cavity can eliminate ventilation of the affected side and push the mediastinum into the nonbleeding side. Treatment consists of insertion of a chest tube and, if the bleeding persists, surgical intervention.

COMPRESSION OF HEART OR GREAT VEINS

Acute pericardial tamponade is usually manifested by muffled heart tones and occasionally by an exaggerated (> 10 mm Hg) decrease in systolic blood pressure on spontaneous breathing. If the patient is not hypovolemic, the neck veins are typically distended. Nowadays, the diagnosis is frequently confirmed by echocardiography (if that modality is immediately available). Treatment consists of needle decompression or surgical creation of a pericardial window. Decompression in a patient with a chronic tamponade can also cause shock but may not give rise to the findings characteristic of acute tamponade. The diagnosis usually is made by means of echocardiography. Treatment is the same as for acute tamponade.

Diaphragmatic rupture and the ensuing intrusion of abdominal viscera into the chest can compress the venae cavae, the right side of the heart, the pulmonary arteries, the pulmonary microvasculature, the pulmonary veins, the left atrium, and the lungs. Treatment consists of operative reduction and repair.

The abdominal compartment syndrome can be caused by ascites, intestinal distention, intestinal edema, intra-abdominal or retroperitoneal bleeding, or noncompliance of the abdominal wall (as in patients with deep burns of the torso). The result is compression of the vasculature of the organs within the abdomen and intrusion of the diaphragm into the chest, which compromises ventilation and decreases ventricular end-diastolic volumes. If the patient is hypovolemic, the hemodynamic consequences can be devastating. Infusion of fluid can restore ventricular end-diastolic volumes but can also worsen the underlying problem, either by increasing the central venous pressure (CVP) and encouraging the development of ascites or edema or by exacerbating bleeding.¹⁹⁻²¹ The situation is made even worse because the increased venous pressures further reduce the perfusion pressures (calculated as MAP minus the venous pressure) in the organs at risk.

Initial treatment of ascites consists of paracentesis of just enough fluid to decrease the abdominal pressure, but no more. Treatment of intestinal edema may necessitate opening the

Table 2 Selected Cardiopulmonary Variables in Resting Subjects of Different Age-Adjusted Weights

Height (ft, in)	Lean Weight (kg)	Approximate Lean Weight (kg)	O ₂ Consumption (ml/min)	Cardiac Output (L/min)	Tidal Volume (ml)
5'0"	48.9	50	175	5.0	350
5'6"	59.1	60	210	6.0	420
6'0"	70.4	70	245	7.0	490
6'6"	82.6	83	290	8.3	580

Expectations for Cardiopulmonary Values in Patients of Different Sizes and Ages

Some numerical descriptors of physiologic variables that can be altered in shock (e.g., blood pressure, body temperature, and arterial pH) are independent of the amount of metabolically active tissue the patient has. For example, although it may well be that a large person in a given degree of shock will produce more lactic acid than a small person in a similar degree of shock, the amount of acid produced will be distributed in a larger volume of extracellular water, and the concentration of the acid in the water (and the resulting pH) will be independent of the patient's size. Thus, the interpretation of the arterial pH need not take into account the size of the patient.

Other descriptors, however (e.g., tidal volume, minute ventilation, ventricular end-diastolic volumes, stroke volume, cardiac output, oxygen consumption, carbon dioxide production, and caloric needs) do have to take the patient's size into account.

The question of how to interpret, or index, these size-dependent variables dates back at least to the 1800s. It seemed logical at that time (and still seems so today) to index the variables to body surface area.¹⁰⁷ The area of the body surface, as the site where the body dissipates its heat into the environment, must correlate with the efficiency with which the body offloads its generated heat. (During resting conditions, the amount of heat generated is minimized; during exercise or illness, more heat is generated from the same mass of tissue. Under any conditions, however, the body must be able to dissipate its heat; if it cannot, it will become hyperthermic to the point where its enzyme systems become dysfunctional.) The generated heat must correlate with the mass of oxidizing tissue, which must correlate with oxygen consumption and carbon dioxide production, which must correlate with the caloric needs. Thus, body surface area should correlate with all of these variables.

In the 1920s, when it became possible to measure cardiac output as part of metabolic studies, many investigators began to express cardiac output, as well as metabolic rate, in terms of body surface area, on the grounds that these two quantities should also be correlated. Although it was recog-

nized that the relation was not necessarily a linear one, this approach to indexing worked, in the sense that it minimized some of the inherent variability observed in nonindexed values. By the end of the 1920s, body surface area had become the most commonly used parameter for indexing both metabolic rate and cardiac output to body size.^{108,109}

In the 1930s, however, Max Kleiber made the empirical observation that the metabolic rates—and presumably the cardiac outputs and some of the ventilatory parameters—of members of one species of animals could best be compared with those of another species by indexing to body weight raised to the three-fourths power. Such indexing seemed to reduce variability even more effectively than indexing to body surface area did, though it was difficult to explain why.

Over the ensuing six decades, more and more accumulated evidence came to support Kleiber's contention, but only in the past two decades have his observations been satisfactorily explained. It now seems established that the Kleiber hypothesis can be proved by using a mathematical model that takes into account not only the thermodynamic considerations just described but also the fractal geometry of the vasculature in metabolizing organs and the thermodynamic constraints placed on such systems.

Thus, the problem of correlating size-dependent cardiopulmonary variables between species seems to be settled, and the different metabolic rates, cardiac outputs, and minute ventilations in different species appear to be well explained. However, the practice of using body weight raised to the three-fourths power does not solve the problem of how to make comparisons between members of the same species (e.g., between a large mouse and a small one or between a linebacker and a ballerina). In addressing this second problem, some clinicians, particularly those with a primary interest in the cardiovascular system, continue to index cardiopulmonary variables to body surface area. Others, particularly those with a primary interest in the respiratory system, favor indexing to body weight instead. A few prefer to use body weight raised to the three-fourths power. Still others choose not to index at all.

(continued)

abdomen and leaving it open. Bleeding may be controllable by operative or endovascular means. Treatment of the burned abdominal wall may involve escharotomies.

Pregnancy can elevate the diaphragm and complicate a shock state. If a woman in the late stages of pregnancy is thought to be in shock, she should be turned onto her left side to relieve compression of the right common iliac vein and the inferior vena cava. If shock persists, one should perform a cesarean section. (The goal is to save the mother. In any case, a pregnant woman in shock is of no use to her fetus.)

OBSTRUCTION OF VENTRICULAR OUTFLOW

Obstruction of right ventricular outflow caused by mechanical ventilation, a tension pneumothorax, a ruptured diaphragm, and the abdominal compartment syndrome is treated as previously discussed [see *Inadequate Ventilation and Compression of Heart or Great Veins, above*]. To treat pulmonary thromboembolism, aggressive anticoagulation with heparin, at the very least, is required; fibrinolytics, sometimes infused through a catheter in the pulmonary artery, may also be necessary [see 6:6 *Venous Thromboembolism*].

Right-side air embolism can arise as a complication of insufflation of gas into the peritoneal cavity during laparoscopy.²² It can also arise from penetrating injuries to large veins in the upper part of the body, caused either by trauma or by puncture of a large central vein in the upper body with a large-bore needle (if the needle

is unintentionally left open to atmospheric pressure and air). In the case of penetrating injuries, the air typically gains access to the venous system during spontaneous deep breathing. Patients are particularly vulnerable when upright.

In all of these situations, the air that gains access to the veins can form an obstructing air bubble in the outflow tract of the right ventricle. Treatable sources of air should be searched for and eliminated, and 100% oxygen should be administered to wash out residual nitrogen in the trapped air. The patient should be placed in the Trendelenburg position with the left side down to induce translocation of air from the outlet of the right ventricle to the apex of the chamber. A long central venous catheter should then be advanced centrally into (what is thought to be) the right ventricle to aspirate any air that may be present.

Air in the right atrium can embolize to the left side of the heart if some of the right-side air first embolizes to the pulmonary microvasculature. Obstruction to outflow from the right ventricle causes blood to back up in the right atrium. If the patient has a potentially patent foramen ovale, the increased pressures in the right atrium will push blood containing the residual air into the left atrium and from there into the left ventricle and to the rest of the body. Left-side air embolism can also be the consequence of a penetrating injury to the lung parenchyma (either from trauma or from a needle puncture) in a patient placed on positive-pressure ventilation: the positive airway pressure can push air from an injured bronchus into an adjacent injured pulmonary vein.

Expectations for Cardiopulmonary Values in Patients of Different Sizes and Ages (*continued*)

Not only is there no consensus on the preferred indexing method, but there also is no agreement on how and whether to adjust for obesity and aging. Body surface area is typically calculated on the basis of height and weight. Usually, the measured weight is used, which includes the weight of the fat. Thus, the calculation gives equal emphasis to metabolically active muscle and to metabolically inactive fat. Old age introduces a similar problem: for a given weight, older patients have less lean muscle mass and more fat than younger patients do. Some authors make an adjustment for age; others do not.

Even though there is, at present, no unanimity on how best to deal with these issues, it is obvious that some form of indexing (or nonindexing) is necessary, both for the management of patients and for the creation of written reference sources. Our current practice is to start with the assumption that lean persons (e.g., those with a body mass index [BMI] of 21 or so) do not have very much body fat. Assuming a BMI of 21, we then use the patient's height to assign a weight, which we assume is mostly metabolically active tissue. This assigned weight is employed in interpreting the size-dependent variables. For patients 50 years of age or younger, we use the assigned weight as is. For patients 51 years of age or older, we calculate an age-adjusted lean weight based on the assumption that 1% of lean body weight has been lost each year after the age of 50.¹¹² (Although this loss is in fact exponential in nature, we have not found it necessary to reflect this fact in the calculation.) As an example, with an 83-year old patient, we subtract 33% from the lean weight that the patient would have had at 50 years of age. For older subjects who have kept themselves in particularly good condition, we assume that 0.5% of lean body weight has been lost each year after the age of 50. Finally, we make subjective adjustments if muscle mass appears to be either abnormally large (as in male patients who worked out extensively when young) or abnormally small (as in malnourished patients or patients with a preexisting prolonged critical illness).

This practice means that we do not use the patient's actual weight when setting up the ventilator or when managing the patient on the basis of other size-dependent variables. The weight at the time of measurement can be inflated by fluid resuscitation, the hardware used for fracture fixation, bedclothes, or obesity. It can also be difficult to measure accurately in critically ill patients, who often cannot easily be moved to a bed-

side scale. We also do not adjust for gender. For longevity and freedom from debilitating illnesses, a BMI of 21 is close to ideal for both men and women (though it appears that a higher fat percentage is acceptable or even favorable for women¹¹³). The value we use is also conveniently close to the predicted body weight that has been advocated for use in setting tidal volumes.¹⁷

We have found it useful to assign expected values for size-dependent cardiopulmonary variables in subjects of different age-adjusted lean weights who are resting, fasting, well conditioned, supine, spontaneously breathing, and in a thermoneutral environment [*see Table 2*]. We make three assumptions in assigning these values, using the age-adjusted lean weight for all of the calculations:

1. The normal resting oxygen consumption is $3.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.
2. The normal resting cardiac output is $100 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.
3. The normal resting tidal volume is 7 mL/kg .

In practice, we usually approximate the height to the nearest half-foot [*see Table 2*], then approximate the lean weight for that approximate height. Once this is done, the values for oxygen consumption, cardiac output, and tidal volume tend to come out in a pleasing, almost linear way. We then make any additional adjustments necessary—in particular, for age and cardiovascular variables.

An example will demonstrate how use of the age-adjusted lean weight can influence assessment and treatment. The hypothetical patient is an 83-year-old man with an admission weight of 80 kg and a height of 5 feet 6 inches. If a Swan-Ganz catheter were in place, one would expect a cardiac output of 8 L/min. The patient's age-adjusted lean weight, however, is 40 kg (60 kg was the lean weight at 50 years of age, minus 33% for the subsequent 33 years on the assumption the patient did not work out much over the past few decades). Accordingly, one would expect a resting cardiac output of 4 L/min. (We would accept this value unless the patient had excessive metabolic needs.) This is not an unusual example; one could easily think of more extreme cases. The patient in this example has a BMI of 28, and there are many patients in the ICU today with indices that exceed this level.

The air bubbles in the blood can occlude the vasculature of the brain and heart, as well as that of other organs. The diagnosis should be considered when a patient with a penetrating thoracic injury suddenly and catastrophically decompensates after the initiation of positive-pressure ventilation. The differential diagnosis in this case consists of tension pneumothorax and air embolism. Accordingly, the first therapeutic measure is to insert chest tubes on both the right and the left. If it turns out that the patient has not had a tension pneumothorax, the diagnosis of possible air embolism should be kept in mind as other conditions are ruled out.

Treatment consists of surgical control. In the case of a penetrating injury, the chest should be opened through an anterolateral thoracotomy on the side with the suspected injury. The hilum of the injured lung should be cross-clamped. Then, if the right side was opened first, the incision should be extended into the left chest. The diagnosis may be confirmed if air bubbles are seen in the coronary vasculature. The heart should be massaged while the descending thoracic aorta is compressed. Vasoconstrictors should be given to increase the aortic pressure and to drive the air bubbles through and out of the arterial circulation. If neither side of the chest is known to have had a penetrating injury, the left side should be opened first. If no injury to the lung is detected, yet the diagnosis is certain (based on the finding of bubbles of air in the

coronary arteries), the incision should be carried into the right chest in an effort to find a treatable injury there. One must keep in mind that the primary treatment of air embolism is to eliminate the source of the air.

BLEEDING

Bleeding should be controlled by any means necessary. Compression might suffice, at least initially, if the bleeding is from an easily accessible site in an extremity; immobilization might be enough in the case of a fracture; endoscopic control might be enough for GI hemorrhage; endovascular control might be enough for bleeding from a pelvic fracture. For any kind of bleeding from any site, operative control is usually definitive. In any case, control is paramount: it makes no sense to infuse fluid or blood or to persist with ancillary measures while controllable bleeding continues unabated.

MEDICAL EMERGENCIES

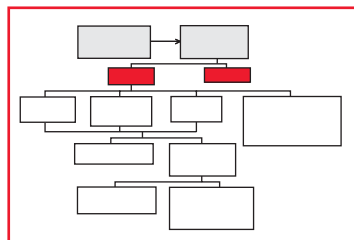
In the appropriate clinical circumstances, early consideration should be given to certain medical conditions that may cause shock. In diabetic patients, severe hypoglycemia should be considered. Rapid assessment with a bedside glucose monitor or empirical I.V. dextrose therapy may prevent the neurologic conse-

quences of prolonged hypoglycemia. Anaphylaxis can be treated with I.V. or subcutaneous epinephrine and antihistamine therapy. In patients with renal dysfunction, life-threatening electrolyte abnormalities should be considered. Finally, whenever standard resuscitative measures are unsuccessful in reversing shock, severe endocrine abnormalities (e.g., addisonian crisis and myxedema), though often difficult to diagnose, should be considered.

Specific Treatment Based on Category of Shock

If shock persists after immediately life-threatening conditions have been treated, the next step is to categorize the shock state on the basis of the underlying physiologic abnormality and treat the patient accordingly.

As a rule, all that is needed to make this preliminary classification is the history, the physical examination, a chest x-ray, an ECG, and, in some cases, a complete blood count, arterial blood gas analysis, electrolyte concentrations, and a glucose level. The categorization is seldom neat: more than one cause of cardiovascular inadequacy is usually present, as when a patient with a myocardial infarction requires mechanical ventilation or when a patient with a ruptured abdominal aortic aneurysm has a distended and tight abdomen. Nevertheless, classification is useful in that it focuses the physician's attention on the primary problem, which should be treated first.



Initial Management of Hypovolemic or Inflammatory Shock

CONTROL OF BLEEDING AND ONGOING INFLAMMATION

Control of bleeding, as the source of the problem in hemorrhagic shock, is the mainstay of treatment for the shock state. In the case of nonhemorrhagic hypovolemic shock or inflammatory shock, however, a temporary delay in source control (e.g., operative management of a bowel obstruction, abscess drainage, or tissue debridement) may be warranted until the patient has been adequately resuscitated. This is a particularly important consideration when the process of source control is likely to result in further cardiovascular compromise. An example is the patient who requires a laparotomy for a hollow viscus perforation. In this situation, briefly delaying administration of a vasodilating inhaled anesthetic while intravascular volume is restored may prevent cardiovascular collapse during anesthetic induction.

In the great majority of cases, source control and resuscitation will be carried out simultaneously. To this end, vascular access is required.

VASCULAR ACCESS

On the assumptions that an airway has been established, that the patient is being ventilated, and that bleeding is being controlled, the next step is to obtain vascular access. If possible, superficial veins in the upper extremities should be percutaneously cannulated with two large-bore catheters. If this is impossible, venous access can be achieved by means of cutdown on veins in the extremities or percutaneous puncture of central veins; access to

the bone marrow can be obtained by means of percutaneous insertion of a thick needle through cortical bone.²³

Cutdowns in the upper extremity cause little morbidity. They sometimes take time to perform, however, and the veins may be thrombosed from earlier use. The cephalic vein at the shoulder is less likely to be thrombosed, but it lies below the deep fascia and is sometimes difficult to isolate. The external jugular vein is deep to the platysma and can be difficult to identify when the lighting is poor. The saphenous vein at the ankle is readily exposed by cutdown and is large and easy to cannulate. It cannot be used, however, if there is extensive trauma to the extremity, and superficial thrombophlebitis is likely to develop if the cannula is left in place for more than 24 hours. The saphenous vein in the groin is large and easy to cannulate, but the end of the catheter inserted through this vein will lie in the external iliac vein. Iliofemoral deep vein thrombosis (DVT) or even septic DVT is common; either can be a potentially fatal complication in a patient who becomes critically ill.

Percutaneous cannulation of the internal jugular vein or the subclavian vein not only affords access for infusion of fluids and drugs but also provides a port for central venous monitoring. Obtaining central venous access with percutaneous techniques, however, can be risky,²⁴ particularly in a hypovolemic patient with collapsed central veins. The puncture can cause a pneumothorax. An artery adjacent to the vein may be punctured. At times, an arterial puncture may not be recognized, and the artery may even be dilated and cannulated. Once the vessel is cannulated, the problem may initially go undetected. Blood drawn from a cannulated artery in a shock patient may be flowing in a nonpulsatile fashion, giving the impression that the targeted vein has been successfully accessed. In severe shock, the arterial blood may be blue, thereby supporting this mistaken impression. A damaged artery can also bleed into the pleural cavity, an untamponaded space. If this occurs in a patient who is already compromised, the patient will probably die.

Percutaneous puncture of the common femoral vein is among the easiest of all venous access techniques and avoids the problems of pneumothorax and bleeding into a pleural cavity. The incidence of both nonseptic and septic DVT is very high, however, with this approach.²⁵⁻²⁷ If this vein is cannulated, the access site should be changed to a vein in the upper body as soon as the patient is stable.

If, in the course of attempting to cannulate the common femoral vein, the adjacent femoral artery is unintentionally cannulated, it is sometimes best to use the artery for vascular access. Intra-arterial infusion of fluids is as effective as I.V. infusion. Care must be taken, however, to ensure that no air enters the system. The catheter should be removed as soon as other access is gained.

In pediatric patients, intraosseous access (e.g., via the proximal tibia, the distal femur, the iliac crest, or the sternum) is a useful means of gaining vascular access under difficult conditions. On rare occasions, this approach may be used in adults when other sites are unavailable.^{28,29}

The first attempts at obtaining vascular access should be made in the upper extremities with a percutaneous technique. If these attempts fail, one should fall back on a technique with which one is comfortable. There is no single best approach.

INITIAL FLUID RESUSCITATION

Once vascular access is obtained, a 20 ml/kg bolus of normal saline should be infused. If the patient is in profound shock, the fluid bolus should be given within 5 minutes; if the situation is less urgent, the bolus may be given over a period of 15 minutes or so. If the shock does not resolve, two more boluses should be given. A rapid infuser might be necessary.

We consider normal saline (NS) the fluid of choice for initial resuscitation in most shock patients. Because it is slightly hyperosmolar, it may have some beneficial effect on the initial perfusion of ischemic tissues by drawing water out of red cells and reducing their rigidity; it may also decrease the swelling of the endothelial cells in the microvasculature of the injured or infected tissues. The chloride concentration of NS (154 mmol/L), however, can induce a hyperchloremic metabolic acidemia. If the patient already has a chloride concentration that exceeds 115 mmol/L, lactated or acetated Ringer solution is used instead. Some favor initial use of lactated Ringer solution to reduce the chance that a hyperchloremic acidosis will develop in the first place. Both lactate and acetate accept a proton to form an organic acid, which is converted in the liver to CO₂ and water. The CO₂ is excreted by the lungs; the water, by the kidneys. As long as hepatic function and pulmonary function are adequate, which is usually the case, the result of this process is buffering of the acidemia that can accompany the shock state. Both lactated and acetated versions of Ringer solution, however, are hyponatremic and hypo-osmotic; the latter is a potential problem in patients at risk for increased intracranial pressure and perhaps for swelling of the endothelial cells in the microvasculature.

Solutions containing glucose should not be used in the initial stages of resuscitation unless the patient is known to be hypoglycemic. Most patients in shock, in fact, are hyperglycemic as a result of high plasma levels of epinephrine, cortisol, and glucagon.³⁰ Excessively high plasma glucose concentrations can induce an inappropriate diuresis.

We do not use colloid solutions in the initial management of hypovolemic or inflammatory shock, and we think that the long-standing crystalloid-versus-colloid debate is now settled.³¹ At the same time, it must be admitted that factors such as the type of colloid used (albumin or hydroxyethyl starch), the timing of administration (early versus delayed), and the environment of care (prehospital, battlefield, or hospital) continue to be explored in laboratory, bedside, and field settings. Colloid solutions, compared with crystalloid solutions, have the advantage of producing a greater intravascular volume expansion for a given volume of fluid infused.³² This advantage may be significant in prehospital, mass-casualty, or battlefield environments.

As for albumin in particular, however, we do not believe it possesses any significant advantages for the purposes of resuscitation, in any environment. It is expensive and at times has been difficult to obtain. Moreover, a study that we consider definitive demonstrated that the use of this agent in critically ill patients provided no benefit and was perhaps even associated with a degree of danger.^{31,33} Accordingly, we see no reason why albumin should be used in any patient. It is possible, however, that other colloid solutions (e.g., hydroxyethyl starch solutions) may be of some use in environments where only limited amounts of fluid can be given. These agents are inexpensive and, in theory, may have some beneficial effects on inflammation and coagulation in the acutely injured patient.³⁴⁻³⁷ At the same time, no large, randomized trials have yet shown these solutions to be of any benefit when used in place of isotonic crystalloid.³⁸

Hypertonic saline solutions containing up to 7.5% sodium chloride (compared with 0.9% for normal saline) show promise for resuscitating patients in situations where large-volume resuscitation with isotonic solutions is impossible (e.g., combat, events involving mass casualties, and prehospital trauma care).^{39,40} Hypertonic solutions provide far more blood volume expansion than isotonic solutions and result in less cellular edema. In addition, they may have favorable effects on the inflammatory

response to injury.⁴¹⁻⁴⁶ These solutions are approved for use and commercially available in Brazil (where the idea originated), Chile, Argentina, and Europe; they are not currently approved for use in the United States or Canada.

TRANSFUSION

The ideal replacement for lost blood is probably fresh, warm, fully crossmatched, whole blood. In some settings (e.g., limited warfare), it is possible to type potential volunteers who are willing to provide the blood.⁴⁷ The volunteers with the appropriate blood type are called in as needed, and the recipients enjoy the benefits of fresh platelets, fresh clotting factors, fresh red cells with good longevity, minimal breakdown products produced by long storage, no cold-induced dysfunction of the infused cells, and no need for reconstitution.

In most settings, however, packed stored red blood cells (RBCs) should be given, supplemented with asanguinous fluids. In an emergency, O-negative cells should be given. There is no need for typing or crossmatching, and in the case of the confusion that can attend the treatment of multiple casualties, there is no danger that a patient will receive the wrong type of blood. If, however, the patient can wait a few more minutes and if there is minimal risk of giving the wrong type of blood, type-specific RBCs should be given. If large amounts of blood are required, as in a patient with extensive injuries or in the setting of multiple casualties, the blood bank will run out of O-negative cells. If the patient has initially been given a large number of O-negative cells and then must be given non-O-negative cells, the newly given cells can react with the initially given cells. Once time is available, typed and crossmatched RBCs should be given.

Transfusion of red cells restores intravascular volume and increases hemoglobin concentration, both of which improve oxygen delivery. On the face of it, it would seem that liberal transfusion of red cells should be ideal for resuscitation of a patient in shock. Unfortunately, allogeneic blood, especially old allogeneic blood, falls short of being the ideal resuscitation fluid.⁴⁸ Allogeneic leukocytes (an unavoidable component of transfused cells), and perhaps soluble factors as well, have been implicated in the observed association between RBC transfusions and poor patient outcomes.⁴⁸⁻⁵³ In critically ill patients who are not in shock, it would appear that limiting transfusions to keep the hemoglobin concentrations no higher than 8 or 9 g/dl might even improve survival, compared with administering transfusions more liberally to yield higher concentrations.⁵⁴

This sort of generalization, while providing useful guidance as to what an appropriate transfusion strategy might be for the average critically ill patient who is euvolemic, may not be applicable to the patient who is in shock. With patients in shock, the first priority is to achieve restoration of intravascular volume with some reasonable level of oxygen-carrying capacity. The second priority is to fine-tune that level of carrying capacity. Generally, in initial resuscitation, the hemoglobin concentration should be on the high side. One usually does not know the magnitude of blood loss in the initial management of shock, nor does one know if the patient is going to continue to bleed. In many cases, one also does not know whether the patient has coronary disease.

The following guidelines provide a reasonable approach to establishing a desirable hemoglobin concentration in the resuscitation of patients in all classes of shock. The key variables are (1) the possibility of a continued decrease in the hemoglobin concentration (from bleeding or hemolysis), (2) the possibility of coronary heart disease, and (3) the estimated or measured values for

the relation between oxygen supply and oxygen demand (determined via mixed venous or central venous oximetry).

1. A hemoglobin concentration of 7 g/dl is adequate in a young patient whose coronary arteries are in good shape and whose bleeding is known to be under control.
2. A hemoglobin concentration of 8 g/dl is adequate in a young patient who may be at slight risk for further bleeding.
3. A hemoglobin concentration of 9 g/dl is required if the risk of bleeding is substantial.
4. A hemoglobin concentration of 10 g/dl should be the goal if overt coronary disease is present or there is a significant risk of occult coronary disease (e.g., in a patient with peripheral vascular disease), even in the absence of ongoing myocardial ischemia.

From a conceptual perspective, the use of blood substitutes for resuscitation should limit the risk of transfusion reactions and could solve the problem of limited availability of allogeneic blood. Multiple preparations of hemoglobin-based oxygen carriers (HBOCs) have been developed, several of which have been tested clinically. Although the results obtained with early preparations have been disappointing, those obtained with newer, polymerized HBOCs have been encouraging. As of fall 2007, however, none had been approved for use.

MANAGEMENT OF PAIN, HYPOTHERMIA, ACIDEMIA, AND COAGULOPATHY

Once blood volume has been at least partially replenished, pain should be treated with small I.V. doses of narcotics. On the one hand, pain relief can reduce the stress response associated with shock and perhaps mitigate the severity of its late sequelae.³⁰ On the other, narcotics can also decrease tone in the venules and small veins, thereby exacerbating the shock state. Accordingly, one should titrate the doses and be ready to reverse the effect with a narcotic antagonist if necessary. A drop in blood pressure after administration of a narcotic suggests that the patient may still be hypovolemic, in which case more aggressive resuscitation may be indicated.

If hypothermia is present initially, it should be corrected; if not, it should be kept from developing. Hypothermia slows metabolic processes. In some situations (e.g., cold-water drowning), this effect may be beneficial, but in most cases, it is better for the patient to have a normal body temperature, normal myocardial function, and intact coagulatory and immune function.

The patient must be unclothed during the initial evaluation but should be covered afterward, with particular attention paid to covering the head. The room should be kept warm, and any fluids administered should be prewarmed either in an oven or with heating devices.

If the arterial pH is low, it should be raised to 7.20 by means of either modest degrees of hyperventilation or administration of bicarbonate. (Although agents other than bicarbonate can be given to correct a metabolic acidemia, it is not clear that they have any more to offer than bicarbonate does.) No efforts should be made to raise the pH above 7.20, other than through resuscitation. Moderate degrees of acidemia are well tolerated, and excessive administration of bicarbonate may worsen intracellular acidosis [see Initial Fluid Resuscitation, *above*].⁵⁵ Instead, efforts should continue to be directed toward managing the underlying cause of shock.

Coagulopathy should be treated with fresh frozen plasma and platelets [see 1:4 *Bleeding and Transfusion*]. The decision whether to use these components should be based on observation of bleeding and clotting in the patient, not on laboratory measurements of

coagulation or platelet counts, which can be normal even during exsanguination.

MODULATION OF INFLAMMATORY RESPONSE

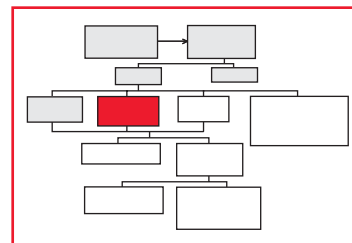
In the case of inflammatory shock, there has long been interest in therapeutic approaches aimed at blocking or counteracting inflammatory and coagulatory mediators released from the inflamed tissues. To date, almost all of these approaches have failed to show any benefit, and some have proved dangerous. A study published in 2001 yielded apparently more promising results, concluding that infusion of activated protein C seemed to improve survival in some patients with severe sepsis.⁵⁶ Since that study was published, several other trials have been carried out in an attempt to define the role of activated protein C in the treatment of severe sepsis with more precision.⁵⁷⁻⁵⁹ Taken as a whole, the current data do not convincingly demonstrate that this product has any real value. What is more, activated protein C is known to be associated with a risk of intracerebral bleeding. Accordingly, we do not use it, even in patients who are in severe sepsis and at high risk of death.

The use of corticosteroids in the treatment of sepsis has been studied extensively over the past several decades. Older regimens involved administering these agents in high doses, and the bulk of the evidence suggested that such regimens probably were, if anything, associated with increased death rates in comparison with placebo.⁶⁰ The authors of a multicenter study published in 2002 concluded that administration of modest doses of hydrocortisone and fludrocortisone to patients in septic shock with impaired adrenal function led to improvements in mortality.⁶¹ These conclusions notwithstanding, we remain unconvinced of the value of this measure, except in those rare patients who are truly addisonian. The possibility of harm is significant, in that corticosteroids have well-established potential side effects in the setting of shock (e.g., kidney damage and perhaps an increased risk of infection). In our view, confirmatory studies are required before this use of steroids in patients with septic shock can be recommended.

Initial Management of Compressive Shock

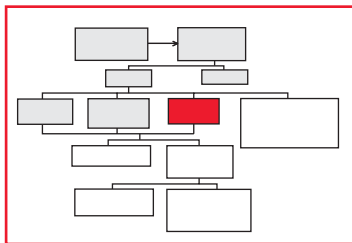
In many cases, extracardiac compressive and extracardiac obstructive shock, being conditions that can kill quickly, will already have been treated by this point in management.

It is wise, however, to keep these two causes of shock in mind as workup proceeds: they often develop secondarily. Examples of problems that can arise as treatment progresses are a tension pneumothorax that develops in a mechanically ventilated patient who is being worked up or treated for some nonpulmonary problem and an abdominal compartment syndrome that develops in a patient who is being resuscitated after a major injury or burn.



Initial Management of Neurogenic Shock

The initial management of neurogenic shock is the same as that of hypovolemic and inflammatory shock. If the shock is compounded by bleeding, the bleeding must



be stopped. Asanguinous fluids should be infused aggressively. Administration of RBCs may prove necessary.

Subsequent management of neurogenic shock, however, differs from that of hypovolemic or inflammatory shock, in that a patient in neurogenic shock may benefit from the use of the Trendelenburg position and the administration of a vasoconstrictor.

TRENDELENBURG POSITION

The Trendelenburg position is of no use in treating hypovolemic or inflammatory shock.⁶² It does increase the pressure in the carotid arteries (provided that the reference point for measurement—the right atrium—is held constant), but it increases the pressure in the internal jugular veins by an identical amount (because there are no valves in the internal jugular veins). The perfusion pressure for the brain, being the difference between these two pressures, is therefore unchanged. Nor, in hypovolemic or untreated inflammatory shock, is the Trendelenburg position of any value in translocating blood from the peripheral venous capacitance system to the heart. The systemic venules and small veins will already be depleted of their blood volume, which means that very little blood is available to be translocated. In the case of cardiogenic shock, the ventricular end-diastolic volumes are already too large; if anything, they must be decreased.

Patients in neurogenic shock, however, can benefit from being placed in the Trendelenburg position, provided that such placement does not compromise other aspects of care (e.g., securing the airway). This position causes blood to be rapidly translocated from the denervated, engorged venules and small veins back to the heart. Ventricular end-diastolic volumes will increase; stroke volumes will increase; the cardiac output will increase; and the blood pressure will rise.

ADMINISTRATION OF VASOCONSTRICTORS

Vasoconstrictors play no role in the initial management of hypovolemic or inflammatory shock, except perhaps for a minute or two in the initial management of a desperately sick patient. For these forms of shock, fluid replenishment is the crucial initial measure. Vasoconstrictors can shut off residual flow to organs already rendered ischemic by the shock state.

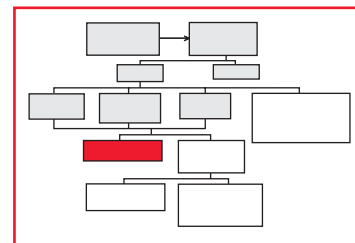
In the management of neurogenic shock, however, vasoconstrictors can be useful. The denervation of the arterioles, venules, and small veins can lead to profound hypotension; if the heart is denervated, the situation will be even worse. All of these ill effects of denervation can be overcome with the use of vasoactive drugs.

If the heart rate is slow, as it may be if denervation extends high enough to block the sympathetic nerves going to the heart, dopamine (in an initial dosage of 5 µg/kg/min) should be given. If the heart rate is rapid, phenylephrine (in an initial dosage of 100 to 180 µg/min, which is then decreased to 40 to 60 µg/min) or norepinephrine (in an initial dose of 0.5 µg/min, which can be increased to 15 µg/min under extreme conditions) should be used.

The danger in giving a vasoconstrictor to a patient in neurogenic shock is that the underlying condition that caused the shock state may also have caused occult bleeding. The vasoconstrictor, by maintaining the blood pressure, may reassure the physician while the patient continues to bleed. It is vital to be aware of this possibility when using vasoactive agents in these patients.

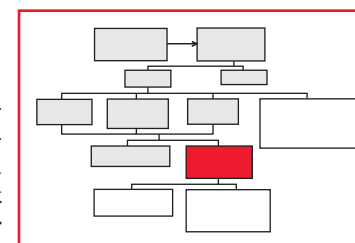
Subsequent Management of Hypovolemic, Inflammatory, Compressive, or Neurogenic Shock

CLINICAL ABNORMALITIES
RESOLVE WITH INITIAL
MANAGEMENT



If these initial maneuvers result in an acceptable blood pressure, heart rate, respiratory rate, skin perfusion, mental status, urine output, myocardial perfusion, acid-base balance, and arterial oxygenation, and if resolution is achieved with the administration of no more than 80 ml/kg of fluid—and, in the case of neurogenic shock, the use of vasopressors for no longer than 1 hour—nothing more need be done, except for periodic reevaluation of the patient for deterioration that might arise from an unexpected problem (e.g., a missed injury) or a complication induced by the initial management (e.g., a tension pneumothorax arising from positive-pressure ventilation).

CLINICAL ABNORMALITIES
PERSIST AFTER INITIAL
MANAGEMENT



Patients whose abnormalities persist despite the administration of 80 ml/kg of fluid and those in neurogenic shock who require vasopressors for longer than 1 hour should be

transferred to a setting in which arterial and central venous pressures can be transduced. Treatment should then be based on resolving the clinical abnormalities in the light of the information obtained via the arterial and central venous catheters.

Insertion of Arterial Catheter and Assessment of Mean Arterial Pressure

Arterial cannulation provides blood for analysis of blood gases and allows reliable measurement of the MAP [see Figure 1], the most useful of all of the peripheral arterial pressures for the assessment and treatment of shock. Morbidity with cannulation is unusual.^{63,64} The radial artery—an artery that usually has abundant collateral circulation—is most often used, at least in adults. The artery can become thrombosed, and portions of the thrombus can embolize distally, but distal tissue loss is rare. At times, larger arteries with less collateral circulation, like the brachial or femoral artery, must be used. The risk of tissue loss is greater when these arteries are cannulated. The perfusion of the limb distal to the insertion site must be assessed every 4 hours. Any suspicion of ischemia mandates removal of the catheter.

If, by chance, one cannot place an arterial catheter or must wait to achieve intra-arterial monitoring, one can use a blood pressure cuff equipped with software that allows measurement of the peripheral MAP using the so-called oscillometric methodology.^{65,66} In patients who are not too unstable, this approach is nearly as accurate as intra-arterial monitoring; however, it does not work well in the setting of hypovolemia, which is precisely where one most often would like to use it.

The mean pressure in the transducer used to monitor the pressure in the artery (or the mean pressure obtained via a properly functioning oscillometric cuff) is the same as the mean pressure in the artery being interrogated. In the absence of proximal obstruc-

tion caused by atherosclerosis in the subclavian or axillary arteries and in the absence of spasm of the proximal conducting arteries, the peripheral MAP is close to the mean pressure in the aortic root, the pressure that drives perfusion of the noncardiac tissues. It is also close to the mean diastolic aortic root pressure and is thus a good approximation for the pressure that perfuses the myocardium.

Thus, knowing the MAP is as close as one can get to knowing the pressure that is providing perfusion for the body. Accordingly, one should focus on the MAP, once it can be accurately determined. Once the MAP is known, there is no reason to pay attention to the systolic or diastolic pressures, as noted earlier [see Characteristic Clinical Markers of Apparent Shock, Hypotension, above]. It is difficult to extrapolate back to the aortic root end-sys-

tolic pressure (the systolic pressure that is of interest) from the peripheral systolic pressure [see *Sidebar* Energy Propagation throughout the Arteries and Its Effect on Pressures in Those Arteries],^{1,67} and the measuring system used to measure peripheral arterial pressures is frequently mismatched to the cannulated artery [see *Figure 2*].^{68,69} Later in the course of management, there will be a reason to try to extrapolate back from the peripheral systolic pressure to the central systolic pressure, but only for the purpose of evaluating the systolic pressure in the context of the stroke volume.

The MAP can be quite low and still be adequate for perfusing most of the tissues of the body. With the exception of the brain and spinal cord, all of the organs in a resting person with no obstructive arterial disease have some degree of chronic resting arteriolar

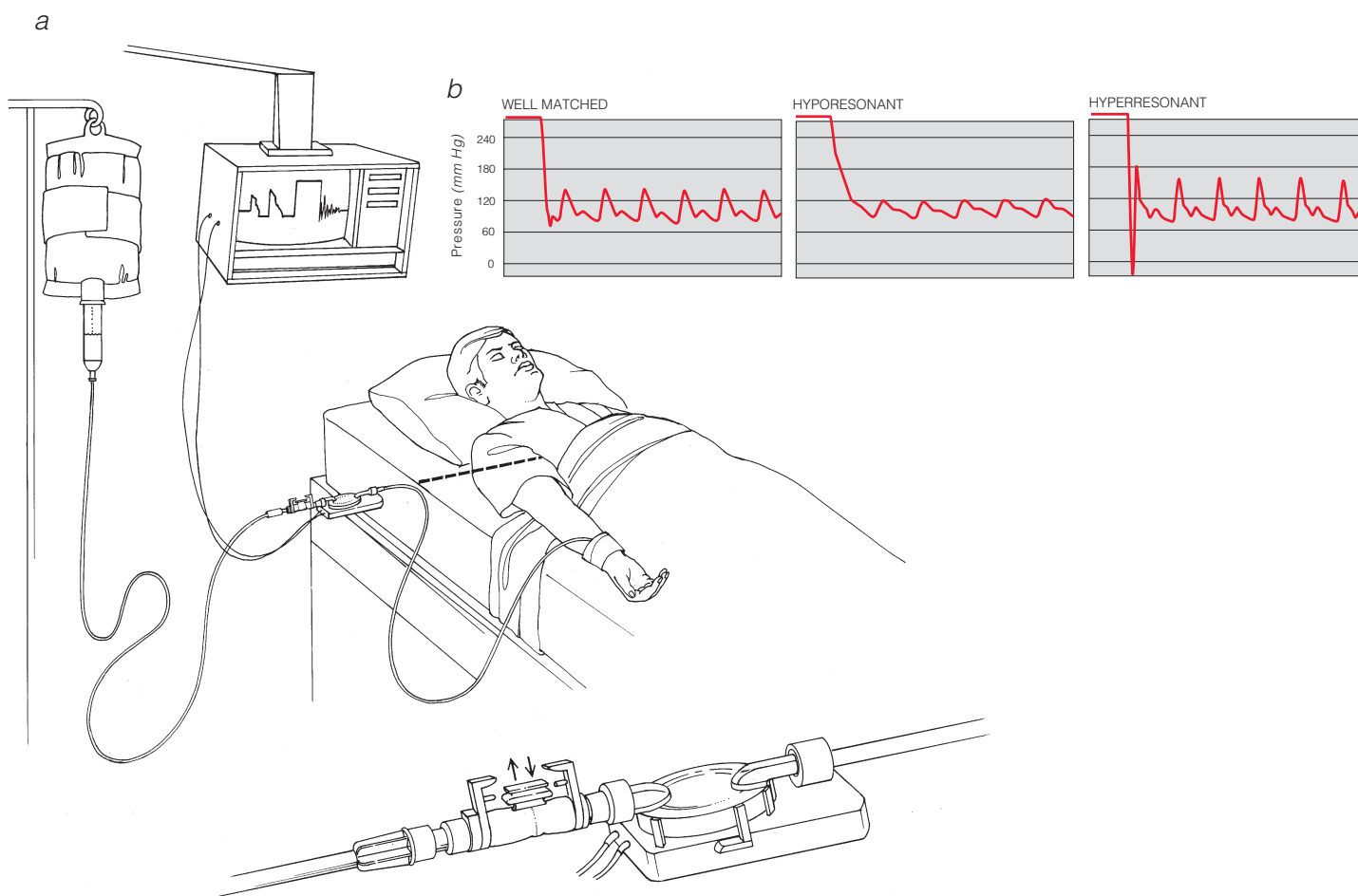


Figure 2 (a) The snap test will indicate if the pressure measured at the transducer is the same as the pressure measured at the tip of the catheter in the vasculature. A pressure of 250 mm Hg is superimposed on the pressure-measuring system by opening the flow-controlling device. The pressure is abruptly removed from the transducer system by snapping the device closed. (b) If the catheter-tubing-transducer system is well matched to the patient's vasculature, a normal arterial tracing (left) should resume promptly with minimal overshoot and oscillation. If the catheter-tubing-transducer system is excessively compliant or obstructed by a clot in the catheter or by a kink in the tubing, sudden closure of the flow-controlling device leads to a slurred, hyporesonant response (center). When the measuring system is excessively stiff in comparison with the vasculature, sudden closure of the device produces a hyperresonant arterial tracing (right), as manifested by an overshoot of the pressure to levels even below 0 mm Hg. In most patients the system used to measure pressures in the pulmonary artery, with a Swan-Ganz catheter, will be adequately matched. The systolic, diastolic, and mean pressures will all be accurately measured. One will be able to use the pulmonary arterial systolic pressure in assessing right ventricular end-systolic elastance, effective pulmonary arterial elastance, and ventricular oxygen requirements, and one will be able to use the mean pressure to assess the amount of useful energy produced by the ventricle. On the other hand, the catheters used to measure systemic arterial pressures will frequently generate a hyperresonant response. In this case, one will not be able to measure the peripheral systolic arterial pressure with adequate accuracy, although one will obtain an accurate measurement of the mean pressure in the artery, which assuming no obstruction or resistance to flow between the aortic root and the monitored artery, will be the mean pressure perfusing the body.

constriction. A fall in the perfusion pressure of an organ at risk in a patient in shock produces local ischemia and accumulation of metabolic waste products. These waste products cause reflex dilation of the arterioles in the organ at risk. Unless the hypotension is extreme, the dilation permits compensatory flow.

The reason why the brain and the spinal cord are exceptions is that their arterioles are chronically dilated. Under ordinary circumstances, this is not a problem, in that the cardiovascular system is designed to maintain a normal pressure for the brain. It is no accident that the primary baroreceptors for the system are placed at the carotid bifurcations. In severe shock, however, the body's cardiovascular reflexes may not be able to provide a MAP that is adequate for perfusion for the brain and the brain stem.

If the patient is awake and alert and there is no sign of spinal cord ischemia, one can be sure that the MAP is adequate for perfusion of the central nervous system. If the patient is obtunded, sedated, or anesthetized, however, assessing the adequacy of perfusion can be a challenge. In certain cases, one might know that at some previous point, perhaps during the same hospitalization, the patient was alert and neurologically intact with a given MAP (e.g., 50 mm Hg). If so, one can assume that the same pressure would still be adequate now. If, however, one does not have this information, one must err on the side of giving more fluids to keep the blood pressure high. In the case of an obtunded patient with no indications of possible carotid disease or of obstructed blood supply to the spinal cord, an arbitrary value can be assigned. A reasonable MAP might be 60 mm Hg for a younger patient (or somewhat higher for an older patient). In the case of a patient with possible carotid disease or compromised blood flow to the spinal cord, the pressure will have to be higher yet.

Determining the adequacy of the MAP for perfusion of non-CNS organs supplied by obstructed arteries is also a challenge. The microvasculature of the gut is maximally dilated in a patient with an occluded superior mesenteric artery. The same is true in a patient who has a kidney with an obstructed renal artery, an extremity with obstructed proximal arteries, or a heart with obstructed coronary arteries. In the face of hypotension, these organs cannot compensate with arteriolar dilation. A fall in the perfusion pressure can lead to a profound loss of flow.

In the case of a patient with possible obstruction of the arterial supply to susceptible organs, one must do one's best to assess the perfusion to the particular organ in question. For the heart, the absence or resolution of chest pain with resuscitation and the absence of ischemic changes on the ECG suggest that pressure and perfusion are adequate. For the gut, the absence of a history of cigarette smoking, the absence of pain, and the presence of bowel activity are reassuring. For the kidneys, adequate urine output and excretion of creatinine are generally indicative of acceptable pressure and perfusion. For the extremities, physical examination of the skin usually suffices.

Insertion of Central Venous Catheter and Assessment of Mean Central Venous Pressure and Right-Ventricular End-Diastolic Volume

The catheter used to measure the central venous pressure (CVP) is typically inserted percutaneously into either the subclavian vein or the internal jugular vein. As a rule, the tip of the catheter ends up in either the superior vena cava or the right atrium. The pressures at these sites vary both with the cardiac cycle and with ventilation. These variations can be substantial, depending on atrial activity and on the pressures produced by the labored breathing of the critically ill patient or by the effects of mechanical ventilation. Dealing with these fluctuations can be a challenge.^{70,71}

Nowadays, when considering the CVP, most physicians use the mean value, obtained over several ventilatory cycles [see Figure 1]. Typically, the number is read directly off the digital readout on the monitor. If the transducer is calibrated and zeroed properly (at the midaxillary line), interobserver variation should be nonexistent. The mean CVP gives a direct measure of the pressure that is most important in producing edema in the peripheral tissues. It is also close to the mean right ventricular end-diastolic pressure (RVEDP) (in the absence of tricuspid valvular stenosis) and thus can be used to derive a rough estimate of the right-ventricular end-diastolic volume (RVEDV) (i.e., for making an initial assessment of the adequacy of volume restoration).

Care must be exercised, however, in extrapolating from the CVP to the RVEDV. The CVP (or the RVEDP) is an intracavitary pressure, measured with respect to the atmospheric pressure present outside the body. To extrapolate from the intracavitary pressure to the cavity volume, one must consider that pressure with respect to the stiffness of all of the tissues from the inside of the chamber to the outside of the body. Many factors can increase the stiffness of these tissues. The stiffness of the ventricular wall itself during diastole (at this point, we are only considering diastolic volumes) will be increased by hypertrophy, scarring, and stretching. Ischemia, especially in association with a tachycardia, will also increase the stiffness of the ventricular wall during diastole. In addition, various factors can increase the stiffness of the tissues surrounding the ventricular cavity. The ventricle can be compressed by stiff, edematous lungs, lungs inflated with positive-pressure ventilation, or an elevated diaphragm. An edematous chest wall, in turn, can compress the lungs. All of these conditions will necessitate a high intracavitary pressure to produce an adequate end-diastolic volume.

Perhaps only one factor can actually reduce the stiffness of the tissues surrounding the ventricle. Spontaneous ventilation, with expansion of the chest wall and dropping of the diaphragm into the abdomen during inspiration, typically decreases the stiffness of the tissues around the lungs and thereby creates a negative pressure (with respect to atmospheric pressure). The result is a ventricle that fills easily with a low pressure.

Thus, in extrapolating from the intracavitary CVP to the RVEDV, one must do one's best to assess the stiffness of the ventricular wall and of the tissues surrounding the heart. For a normal subject breathing spontaneously, a CVP of 3 mm Hg is usually enough to support a normal RVEDV. For a healthy patient who is undergoing an elective operation and is on mechanical ventilation, a CVP of 6 mm Hg should be sufficient. For a modestly ill patient who has some edema in the lungs or chest wall and is on positive-pressure ventilation, a CVP of 9 mm Hg should be enough. For the usual patient sick enough to be in an ICU, who typically has more edema and perhaps an element of diaphragmatic elevation, the CVP should probably be around 12 mm Hg. For a patient who has ventricular ischemia, substantial edema, or greater than usual intrusion of the diaphragm into the chest, the CVP may have to be as high as 18 mm Hg.

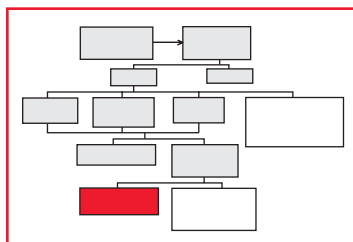
Treatment

Once the patient is in an environment where arterial and central venous monitoring is available, treatment consists of infusing more fluid. The goals are severalfold: to resolve the clinical abnormalities; to generate a MAP that appears to be adequate for perfusion of the brain and organs that might have an obstructed blood supply; to generate a CVP that is high enough to suggest an adequate RVEDV but is not unnecessarily elevated (we are aware of the potential conflict here); and, in the setting of neurogenic

shock, to wean the patient from vasopressors (which could shut off blood flow to the kidneys, the gut, or other organs with a high basal metabolic rate).

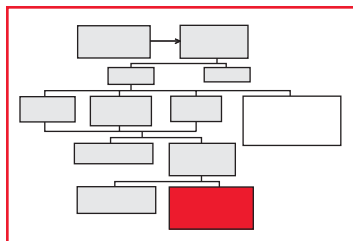
This fluid infusion can cause problems. On the one hand, it is important to be sure that at least the RVEDV is adequate to support ventricular production of useful energy. The values given (see above) can provide some guidance in this regard. On the other hand, it is also important to ensure that the CVP is no higher than necessary. High pressures create edema, and this edema can impair wound healing, make it difficult for tissues to fight off infection, and produce compartment syndromes in the brain, the liver, the kidneys, the abdomen, the chest, or an injured extremity. Furthermore, unnecessarily large end-diastolic ventricular volumes can increase ventricular oxygen requirements to an unacceptable extent.

CLINICAL ABNORMALITIES
RESOLVE AFTER ADMINIS-
TRATION OF ≤ 140 ML/KG OF
ADDITIONAL FLUID, WITH
ACCEPTABLE MEAN ARTERIAL
PRESSURE AND CENTRAL
VENOUS PRESSURE



If infusion of fluid of reasonable amounts of fluid (defined as no more than 140 ml/kg of crystalloid) leads to resolution of the clinical abnormalities with an acceptable MAP and an acceptable CVP (that is, with a CVP that should not produce edema unnecessarily and that should be associated with an estimated RVEDV that does not increase ventricular oxygen requirements unnecessarily), nothing more need be done. If the patient recovers completely from the problems that caused the shock, he or she might even be able to undergo diuresis—with the caveat that waiting for spontaneous mobilization of the administered fluid is usually safe, whereas giving a diuretic prematurely has the potential for pushing the patient back into a state of inadequate perfusion.

CLINICAL ABNORMALITIES
PERSIST DESPITE ADMINIS-
TRATION OF 140 ML/KG OF
ADDITIONAL FLUID



If, however, the clinical abnormalities do not resolve with the infusion of a reasonable amount of fluid, or if it is not clear that the patient has an acceptable MAP and CVP, or if vasopressors (in the case of neurogenic shock) are still thought to be necessary, then either insertion of a Swan-Ganz catheter or, in some cases, transesophageal echocardiography is indicated. Using the measurements obtained via a Swan-Ganz catheter (or from transesophageal echocardiography) can help one strike the optimal balance among fluid administration, use of drugs, edema formation, myocardial oxygen requirements, and peripheral perfusion.

There are few risks associated with transesophageal echocardiography, but the attendance of a physician is mandatory when the equipment is in use. Many anesthesiologists are comfortable with the technique, which can be very helpful in monitoring anesthetized patients. In the ICU, however, the required level of physician involvement is not likely to be available for any great length of time.

Insertion of a Swan-Ganz catheter requires gaining access to a central vein, which can cause problems [see Clinical Abnormalities

Persist after Initial Management, Insertion of Central Venous Catheter and Assessment of Mean Central Venous Pressure and Right-Ventricular End-Diastolic Volume, above].^{24,72} In addition, there are problems associated with passage and maintenance of a pulmonary arterial catheter [see Sidebar Problems Associated with Use of the Swan-Ganz Catheter].

The information obtained from a Swan-Ganz catheter, however, can give a nearly complete description of the status of the right ventricle. In some patients, it will give a good description of the left ventricle as well; in others, the Swan-Ganz information combined with the information obtained by means of echocardiography will yield a sufficiently good description.⁷³ In all patients, such monitoring will add significantly to the data that were already available [see Figures 3, 4, 5 and 6 and Sidebar Measurements That Can Be Obtained from Invasive Monitoring]. Understanding how this information is obtained and how it should be put into context is the most challenging part of treating the patient who is ill enough to need this sort of monitoring. Armed with the information obtained from invasive monitoring, one can set specific goals beyond that of resolution of the clinical abnormalities. Developing specific goals will help one strike the balance between generating power and minimizing edema formation and myocardial oxygen requirements.

Set Goals of Resuscitation, and Give or Withhold Fluids to Achieve Desirable Ventricular End-Diastolic Volumes

The goal in shock resuscitation is to achieve resolution of clinical abnormalities without creating excessive amounts of edema or imposing excessive demands on the heart. The first step is to decide on acceptable values for the cardiac output, the blood pressure, and the mixed venous oxygen saturation (S_{mvO_2}) in the context of the atrial pressures and the ventricular end-diastolic volumes.

In patients with major injuries or overwhelming infections, we aim for slightly higher than normal (but not excessively high) cardiac output values. Hyperthermia or systemic inflammation can raise oxygen consumption to values as high as twice those encountered in normothermic, uninjured, or uninfected persons [see 8:25 *Metabolic Response to Critical Illness*]. (To put these changes in perspective, oxygen consumption in a strenuously exercising young subject can increase by a factor of 15 to 20.) If the environment is cold enough to induce shivering, oxygen consumption can rise to levels several times higher than those observed in a thermoneutral environment. In these situations, a higher cardiac output is to be expected and presumably is desirable. By way of contrast, hypothermia in the absence of shivering decreases oxygen consumption. In this situation, the cardiac output can fall to quite low levels with no detrimental effect on survival. Efforts to increase cardiac output in severely cold patients can even induce fatal ventricular arrhythmias.

We also set different goals for the cardiac output, depending on the patient's premorbid cardiovascular capabilities. For example, cardiovascular conditioning increases the blood volume, increases the ventricular end-diastolic volumes, increases the stroke volume, and decreases the resting heart rate⁷⁴—that is, it prepares the cardiovascular system for stress. Accordingly, if we know that a patient was in good cardiovascular condition before the acute problem developed, we aim for a higher cardiac output. We do the same for pregnant patients, whose cardiovascular systems have adapted to deal well with hemorrhage and stress. With respect to age, we set higher goals for younger patients than for older ones.

Finally, we sometimes set goals for the cardiac output on the basis of trial and error. For example, if a supranormal cardiac output causes an abnormality (e.g., metabolic acidosis) to resolve when a normal output did not, we make an effort to keep the car-

Problems Associated with Use of the Swan-Ganz Catheter

Passage of a Swan-Ganz catheter can induce ventricular dysrhythmias, particularly in patients who have suffered recent myocardial infarctions or who have an irritable myocardium (as indicated by a preexisting arrhythmia or conduction defect). For some of these patients, prophylactic administration of lidocaine is indicated. Usually, the dysrhythmia subsides when the end of the catheter finally passes through the ventricle and enters the pulmonary artery. Sometimes, however, it can be eliminated only by complete removal of the catheter; in rare instances, aggressive pharmacologic treatment or even cardioversion is required. The balloon on the end of the catheter should be kept inflated during passage to cushion the tip and minimize myocardial irritability.

Passing a Swan-Ganz catheter in a patient with left bundle branch block can be particularly hazardous. The catheter can eliminate conduction through the right ventricle, producing complete heart block. If this condition does not resolve upon prompt withdrawal of the catheter, insertion of a transvenous pacemaker or the use of external pacing may be necessary. The time required to establish a rhythm, however, can be so long that the patient may die first. Swan-Ganz catheters should be placed in patients with left bundle branch block only when absolutely necessary.

Lodging of the catheter tip in the trabeculae of the right ventricle is a common problem during catheter passage. On rare occasions, the end of the catheter may puncture the right ventricular wall. The puncture site may not be immediately obvious and may in fact seal by itself; it is more likely, however, to lead to pericardial tamponade and, possibly, death. Measurements from the Swan-Ganz catheter will indicate pericardial tamponade, which mandates emergency operation.

Passage of the catheter through the tricuspid and pulmonic valves can damage them, especially if the device is roughly pulled back through the valves with the balloon inflated. In addition, if the catheter is left in place for more than a few days, valvular damage may result. Besides minimizing long-term use of the catheter, little can be done to prevent this problem.

A problem unique to the Swan-Ganz catheter is intracardiac knotting, which is most likely to develop during placement. The knot can occasionally be untied by manipulating the catheter under fluoroscopic guidance.

Passage of a J-wire into the right side of the heart from the groin can also be effective. If these approaches do not work, the catheter must be withdrawn to the site of entry and then removed, usually under direct surgical control.

Swan-Ganz catheters can migrate distally and cut off the blood supply to the pulmonary parenchyma, resulting in pulmonary infarction. This complication can usually be prevented by continuous monitoring of the pulmonary arterial waveform. Development of a permanently wedged wave pattern mandates immediate withdrawal of the catheter into a more proximal portion of the pulmonary vasculature. The catheter should never be allowed to have a wedge tracing (except, of course, when the wedge pressure is being measured); the tracing seen on the monitor should look like a tracing from the pulmonary artery or one of its large branches.

On rare occasions, the catheter can perforate the pulmonary artery. This event typically presents with hemoptysis but may present with acute cardiopulmonary collapse during or immediately after measurement of the wedge pressure. Risk factors include advanced age, pulmonary arterial hypertension, warfarin anticoagulation, clotting deficiencies, distal migration of the catheter into the pulmonary vasculature, and balloon overinflation. Patients with tumors surrounding the pulmonary artery are also at increased risk. The balloon itself may disrupt the pulmonary artery directly, or inflation of the balloon may force the tip of the catheter through the vessel wall.

Prevention consists of continuous monitoring of pulmonary arterial pressure tracings. The catheter location should be confirmed by chest x-ray at least once daily. Wedge pressures should be measured only when needed. The degree of balloon inflation necessary to obtain a wedge tracing should be noted and overinflation avoided. The balloon inflation port should be identified so that infusions are not misdirected into the balloon. The catheter should never be left in the wedge position. Rupture associated with mild hemoptysis can be treated by removing the catheter; rupture associated with cardiovascular collapse calls for lobectomy or pneumonectomy, which occasionally permits patient salvage.

diac output high for a while. Once the abnormality is resolved, we see whether the resolution can be maintained with a more normal cardiac output.

The goal for the systemic arterial pressure is one that is sufficient to perfuse the CNS and any organs that might have an obstructed arterial supply. In some cases, we might accept a lower value than the initial assessment if the cardiac output turns out to be high. Useful energy, in this context, is cardiac output multiplied by MAP. Thus, if the cardiac output is high enough, it is possible to maintain the desired level of energy with a low MAP.

In all cases, we aim for an $S_{mv}O_2$ of 60% or higher. As noted (see above), high $S_{mv}O_2$ values are not necessarily reassuring, but low values suggest that the heart, an organ that normally consumes a large amount of the oxygen delivered to it, is dangerously close to becoming hypoxic. Low $S_{mv}O_2$ values warrant immediate attention.

The initial goal with fluid infusion should be to achieve an RVEDV and an LVEDV that are at least normal. If either volume is less than normal, it will be close to impossible for the heart to generate adequate power for perfusion in an efficient manner. A CVP in the low teens with a pulmonary arterial wedge pressure (PAWP) in the midteens (on the assumption that the patient is undergoing mechanical ventilation) is a good start. As noted (see above), however, this is a complicated issue. On the one hand, one hopes that the filling pressures will be adequate to generate a sat-

isfactory cardiac output and an acceptable MAP. On the other hand, one does not want to raise these pressures any higher than necessary.

On the right side, the end-diastolic volume will be known. In a normal 60 kg subject who is breathing spontaneously, an RVEDV of 150 ml is enough to ensure adequate filling of the heart [see Table 3]. In a critically ill patient on mechanical ventilation, a larger volume is needed—closer to 200 ml. If possible, the RVEDV should not be too much larger than that figure: excessive volumes increase oxygen consumption unnecessarily, and perhaps right atrial pressure as well. In some patients, however, one has no choice. One must ensure that the ventricle has an adequate end-diastolic volume, even if the value turns out to be higher than desired. An inadequate volume will make it impossible for the ventricle to do its job, no matter how well tuned the rest of the cardiovascular system may be. No cardiovascular adjustment can overcome the problems produced by an inadequate end-diastolic volume.

On the left side, the judgment is far more complicated. The LVEDV will not have been directly measured and must therefore be estimated [see Sidebar Measurements That Can Be Obtained from Invasive Monitoring]. Trial infusions can sometimes help. If necessary, one can obtain echocardiography. In all cases, the goal is the same: an end-diastolic volume that is at least normal.

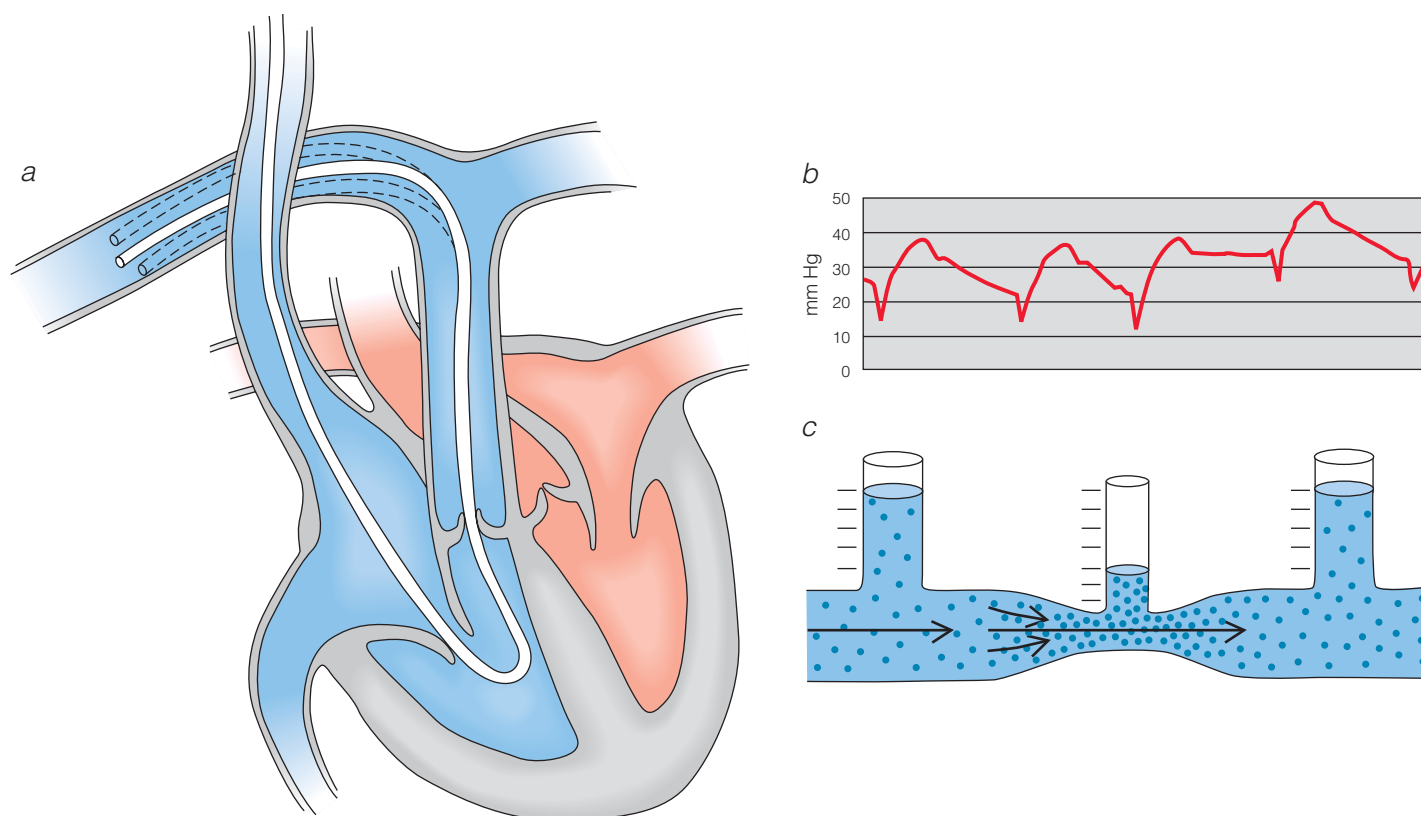


Figure 3 Catheter whip (or fling) results from movement of a catheter within the vasculature (a) that produces hydrostatic pressure changes at the tip of the catheter that are independent of any changes in hydrostatic pressure within the vessel itself. Pressure drops during diastole that are the result of catheter whip could be falsely interpreted as true vascular diastolic pressure. In the pressure tracing shown (b), the true diastolic pressure in the pulmonary artery is 24 mm Hg; catheter fling produces the lower pressure of 12 mm Hg at the tip of the catheter.

The total energy in a hydraulic system, such as the vasculature, is the sum of hydrostatic pressure and kinetic energy. The kinetic energy depends on the square of the velocity of the fluid. Because the velocity—and thus the kinetic energy—is greater the narrower the system (c), and because the total energy measured at any point in the system is constant, the hydrostatic pressure must be less in the narrow portion of the tube, where the velocity of flow is higher.

If a femoral or pulmonary arterial catheter moves within the vasculature as the heart beats, the velocity of blood across its orifice will increase; as the velocity increases and the kinetic energy increases, the hydrostatic pressure as measured at the tip will fall. This transient decrease in hydrostatic pressure at the tip of the catheter (as seen in the tracing) does not reflect the true hydrostatic pressure in the artery.

The radial artery catheter is best for determining the total energy in the systemic arterial vasculature. The catheter will not whip, because the artery is small and the catheter has no room to move about, and there will be no kinetic energy component in the blood, because the radial artery catheter is end-on (i.e., it faces into the direction of the flow), and thus, the velocity of the blood as it runs into the end of the catheter is zero. Therefore, the hydrostatic pressure will represent the total energy of the blood at that point of the arterial system. A catheter placed in the ascending aorta will be buffeted by the rapidly accelerating blood in the aorta, and catheter whip will be introduced. A pulmonary arterial catheter potentially has both the problem of catheter whip and the problem that it measures pressure in the direction of flow rather than end-on. The latter problem cannot be avoided. The problem of catheter whip can be dealt with by advancing the tip of a catheter that seems to be in the main pulmonary artery distally, into one of the branches of the artery. This will minimize whip and will be safe, as long as care is taken to be sure that the catheter is not placed so far distally that it becomes permanently wedged.

Minimize Effective Pulmonary Arterial Elastance

Once end-diastolic volumes that appear to be adequate but not excessive have been achieved, the next step is to determine whether the effective pulmonary arterial elastance can be decreased. In many surgical patients, the pulmonary arterial elastance is elevated as a consequence of stiff pulmonary arteries, a compressed pulmonary microvasculature,¹⁸ or a stiff left atrium. It can be measured quite accurately by means of the Swan-Ganz catheter (with some qualifications [see *Sidebar* Measurements That Can Be Obtained from Invasive Monitoring]). In general, the pulmonary arterial elastance should not exceed the right ventricular end-systolic elastance. This latter value will not be obtainable from the

Swan-Ganz catheter data, because the end-systolic unstressed volume will not be available, but it is known that the maximal end-systolic elastance for the right ventricle in a 60 kg subject is on the order of 0.8 mm Hg/ml [see *Table 4*]. As a rule, therefore, if the effective pulmonary arterial elastance exceeds 0.8 mm Hg/ml in a 60 kg patient, one should try to reduce it.

Treatment includes (1) adjustment of the ventilator to minimize compression of the vasculature and the atrium; (2) alteration of the patient's position so that the better of the two lungs is dependent (the goal being to maximize flow to the microvasculature that is least obstructed and to minimize flow to the microvasculature that is most obstructed); (3) diuresis, if possible, to decrease dis-

tention of the vasculature and atrium; and (4) decompression of the abdomen if the patient has a compartment syndrome (the elevated diaphragm of the syndrome and the resultant stiffness of the tissues in the chest are bad not only for the heart but also for the pulmonary vasculature).

In our experience, pharmacologic treatment of an elevated effective pulmonary arterial elastance has rarely worked, at least in adult surgical patients. In particular, we have not had much success with metabolites of arachidonic acid or analogues of these metabolites, nor have we had much success with inhaled nitric oxide. In the past few years, there have been several reports on the use of enteral sildenafil, 25 to 100 mg, in medical patients that appear to give grounds for optimism.⁷⁵ In surgical patients, however, the problem underlying elevated effective pulmonary arterial elastance is frequently mechanical. In such circumstances, one

cannot hold out too much hope for an intervention that works primarily on smooth muscle spasm. Admittedly, we do not have much experience with this use of sildenafil.

Set Goal for Heart Rate, and Increase Ventricular End-Systolic Elastances If Necessary

The next step, if necessary, is to increase the ventricular end-systolic elastances while taking into account the heart rate. Digoxin is a good choice for the occasional patient who is in atrial fibrillation, exhibits a rapid ventricular response, and also happens to be in shock. It can be given in a 0.5 mg loading dose, followed by increments of 0.25 mg every hour until the atrioventricular node is blocked sufficiently to yield the desired ventricular response. A guideline for an acceptable ventricular response might be a heart rate lower than 120 beats/min in a young

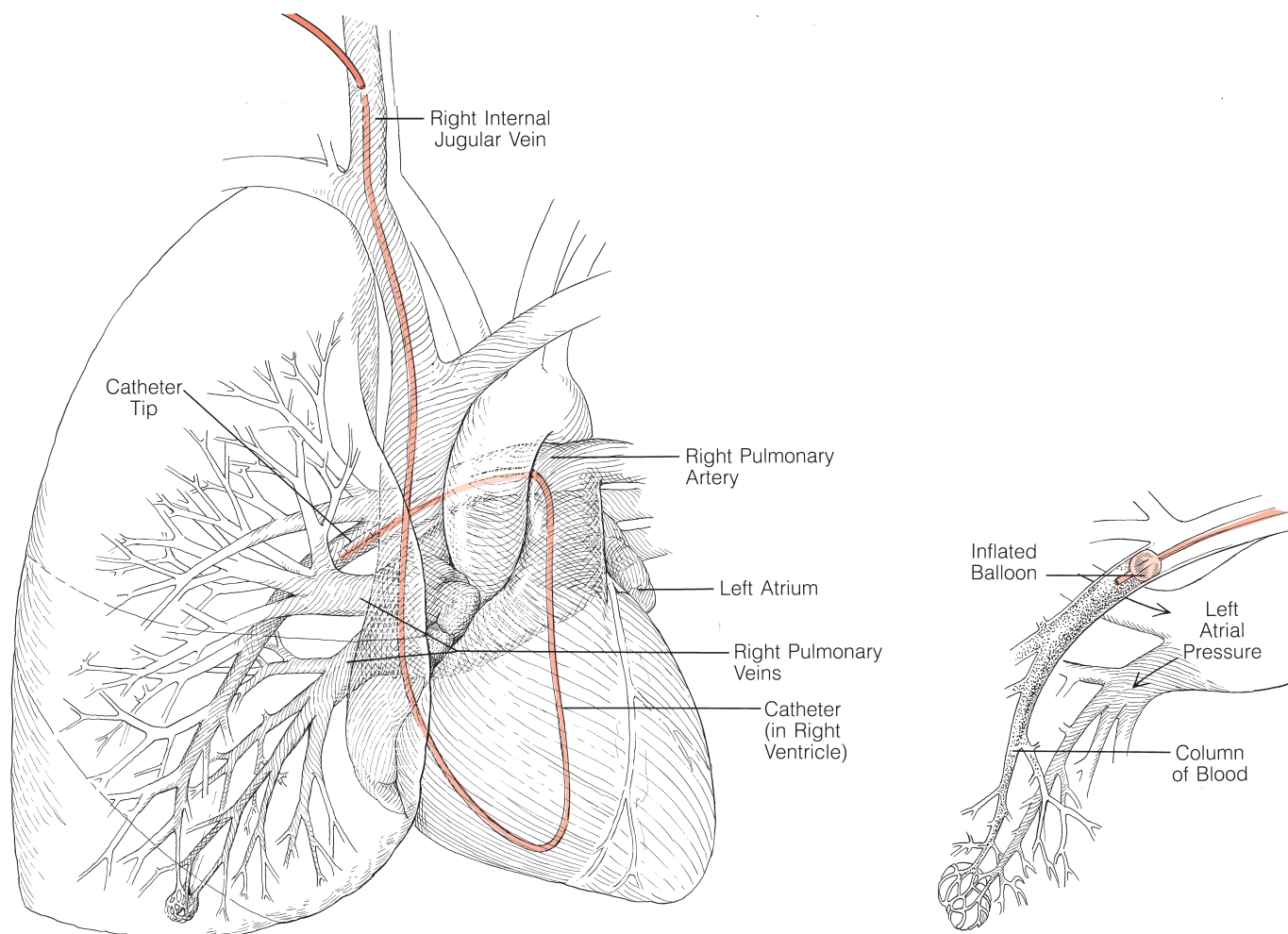


Figure 4 The pulmonary arterial catheter measures pressure in the pulmonary artery when the balloon is deflated. Because flow in the vascular system generates a pressure drop as the blood passes through the microvasculature, the pressure in the pulmonary artery has to be greater than that in the left atrium. When the balloon is inflated, flow in the vasculature distal to the tip is eliminated; therefore, there is no pressure drop. Because there is no pressure drop and because there are no valves between the left atrium and the pulmonary artery, the pressure in the pulmonary artery distal to the point of occlusion must equal the pressure in the left atrium, provided that there is an open column of blood between the end of the catheter and the left atrium. That is, pulmonary arterial wedge pressure will equal left atrial pressure as long as the catheter is in a dependent portion of the lung with a vasculature that remains open during ventilation. Because the catheter is flow directed, it usually will end up in such a dependent, well-perfused area. This is not a certainty, however. If inflated alveoli occlude the microvasculature, wedge pressure will equal alveolar pressure. This inaccuracy might not be easily detected.

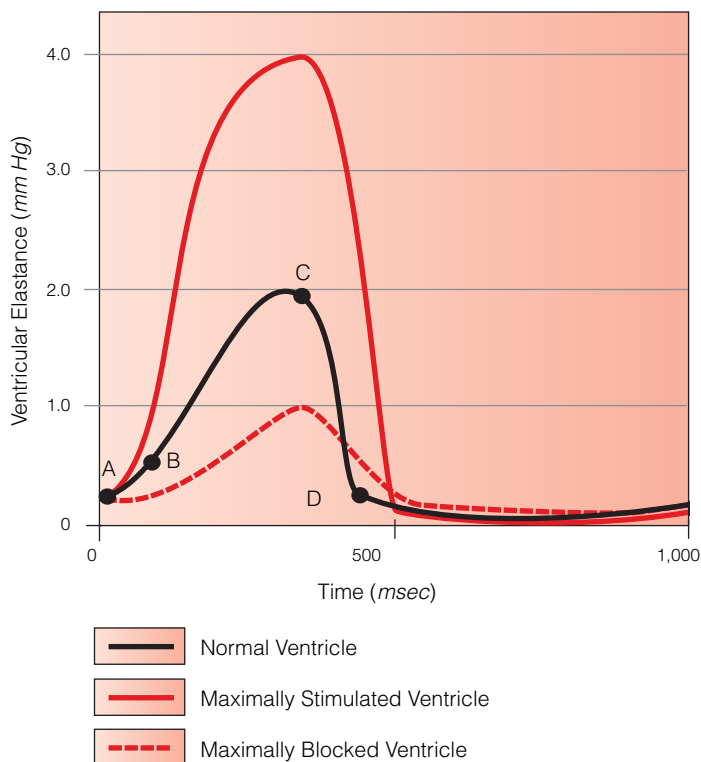


Figure 5 Illustrated is the elastance (stiffness) of the left ventricle over a cardiac cycle in a 60 kg person, as seen in a normal person under resting conditions, a person with a maximally contractile ventricle, and a person with profound beta blockade or congestive heart failure. Point A is the beginning of systolic contraction; point B is the opening of the aortic valve; point C is end-systole; and point D is the beginning of diastolic filling. During diastole, the stiffness typically increases from a minimum of 0.1 mm Hg/ml, in a 60-kg subject, at the beginning of diastolic filling, to a maximum of 0.2 mm Hg/ml at the end of diastole. The stiffness of the ventricle then dramatically increases, from the beginning of systole to the end of systole, where the stiffness under resting conditions is typically 2.0 mm Hg/ml. With maximal contractility, elastance rises more quickly than normal, and maximal stiffness, at end-systole, is twice the normal value. With congestive failure, elastance rises more slowly, and maximal stiffness is half the normal value. The elastance during diastole is lowest under conditions of maximal contractility, in the normal heart, leading to the ideal situation in which diastolic filling is maximized at the same time as maximum contractility. In the ischemic heart, diastolic stiffness increases under stress, so that filling is compromised at the same time that contractility is hampered.

patient, or lower than 90 beats/min in an older patient, or lower than 75 beats/min in a patient with coronary artery disease. Blood levels should not be monitored. The ventricular response will serve as a bioassay both for efficacy and for toxicity. Digoxin should not be used in patients who have any dysrhythmia other than atrial fibrillation: the toxicity will be unpredictable and difficult to monitor.

Dobutamine is the usual choice for most patients who might benefit from increases in ventricular end-systolic elastances. The dosage should be $5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ initially. It can then be increased as needed, to an upper limit of $20 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. If necessary, milrinone may be added, first administered in a $50 \mu\text{g}/\text{kg}$ loading dose over 10 minutes and then infusion at a dosage of 0.375 to $0.75 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. The two agents increase intracellular systolic calcium concentrations by different mechanisms. Neither has any vasocon-

strictor effects, and both are safe, at least for a short time. The usage of these drugs should be governed by consideration of the heart rate. As a rule, the heart rate will not increase very much with administration of either agent, but if it does rise to unacceptably high levels, one will have to reduce the dosage.

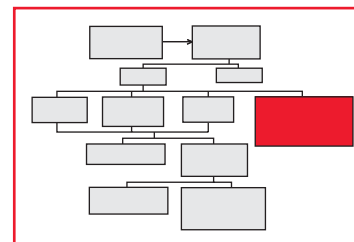
Last Resort: Increase Effective Aortic Root Elastance

As a rule, increasing the blood pressure is a trivial matter, except in the preagonal patient. One can always administer a vasoconstrictor, and one can almost always achieve any pressure desired. If the heart rate is not too rapid, dopamine can be given; if the rate is too fast, norepinephrine can be given. With either drug, the addition of vasopressin in low doses can facilitate its actions and allow one to minimize the doses.

A more difficult problem is knowing when one has no choice but to use a vasoconstrictor. In this situation, the Swan-Ganz catheter is invaluable. On occasion, use of dopamine or norepinephrine results in an increased cardiac output. If the increase in the blood pressure is caused primarily by an increase in the cardiac output, then the drugs are safe. If, however, the cardiac output is not increased, then the increased blood pressure must be the result of vasoconstriction. This means that at least some of the organs in the body must be experiencing reduced blood flow. Some organs (e.g., skin and fat) can withstand ischemia for a while, but no part of the body is expendable. Necrotic skin in an extremity means amputation of the limb; a necrotic gut means death.

The question of when to use a vasoconstrictor arises quite frequently in the treatment of warm inflammatory shock. There are no easy answers. We follow the guidelines described earlier [*see Insertion of Arterial Catheter and Assessment of Mean Arterial Pressure, above*]. In many cases, we find that a quite low MAP is adequate for perfusion, especially when associated with a generous cardiac output. We do everything we can to avoid using constrictors, resorting to them only when every other possible treatment has failed.

Management of Cardiogenic or Obstructive Shock



Many patients in hypovolemic, inflammatory, compressive, or neurogenic shock can initially be treated without invasive monitoring. Their problems may be manageable with fluid administration alone. Patients in cardiogenic or obstructive shock, however, probably have more complicated problems. These patients should be transferred to a unit where the cardiac rhythm can be monitored and arterial and central venous catheters can be used.

Treatment of cardiogenic or obstructive shock begins with renewed attempts to correct dysrhythmias (if this has not already been done). Every effort should be made to achieve a normal sinus rhythm. If myocardial damage is unlikely, as in a patient with uncomplicated valvular problems, the heart rate should not be allowed to reach or exceed 90 beats/min. If myocardial ischemia is a possibility, the heart rate should not be allowed to exceed 75 beats/min.

As noted earlier (see above), digoxin is excellent for controlling an unacceptably high heart rate in a patient in atrial fibrillation (in cases where the patient cannot be converted to sinus rhythm). Occasionally, it may be supplemented with a calcium channel blocker (e.g., diltiazem, 5 to 15 mg/hr).

For all other patients with an unacceptably high rate, a beta blocker should be given instead. Esmolol is a good first choice, in that it has a rapid onset of action and a short duration of action. A 500 $\mu\text{g}/\text{kg}$ loading dose is given, followed by a 50 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ infusion, which is increased as necessary. Metoprolol, 5 to 15 mg every 6 hours, may be given later if it is clear that beta blockade was needed and still is. If the heart rate is still excessively high, a calcium channel blocker should be added.

If the ventricular end-diastolic volumes seem excessively large, diuresis should be initiated or morphine sulfate, 1 to 4 mg/hr, should be given, both to relieve pain and stress and to allow pooling of blood in the systemic capacitance vessels.

If the effective aortic elastance is thought to be excessive, the stiffness of the arteries should be decreased by performing further diuresis, by adding an angiotensin-converting enzyme (ACE) inhibitor (e.g., enalaprilat, 1.25 to 5 mg every 6 hours), or by adding nitroglycerin, 5 to 200 $\mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Nitroprusside is occasionally indicated, if the problem is believed to be exclusively on the arterial side of the circulation. As a rule, hydralazine should not be used. Because its principal effects are on the arterioles, not the arteries, it lowers the MAP but has substantially less effect on the stiffness of the arteries (which is more important for decreasing the ventricular oxygen requirements). Hydralazine can also increase the heart rate and thereby increase myocardial oxygen

requirements, thus defeating the very purpose for which it was originally given. The use of clonidine should also be avoided if possible. It, too, works mainly on the arterioles instead of the arteries, and it can cause nightmares and disorientation, side effects that can be a major problem in critically ill patients. With all of these drugs, dosages should be titrated as necessary.

If the energy-producing capabilities of the ventricles are still in question, an inotrope (e.g., dobutamine or milrinone) should be tried—albeit cautiously, in view of the effect these agents have on myocardial oxygen requirements. The inotrope can be added to digoxin if the patient is already receiving digoxin for treatment of a rapid ventricular response in atrial fibrillation.

The hemoglobin concentration should be kept at 10 g/dl or perhaps even higher, especially if the higher hemoglobin concentrations are associated with alleviation of symptoms. If transfusion is required, more aggressive diuresis will be needed as well.

If the clinical abnormalities still have not resolved, a Swan-Ganz catheter should be inserted. The measurements obtained from the catheter will allow more precise management of the ventricular end-diastolic volumes. Adjustments to these volumes can be directly correlated with their effects on the stroke volumes. The measurements might indicate that some of the problem is on the right side of the heart. If the effective pulmonary arterial elastance is excessively high, treatment should proceed in the same manner

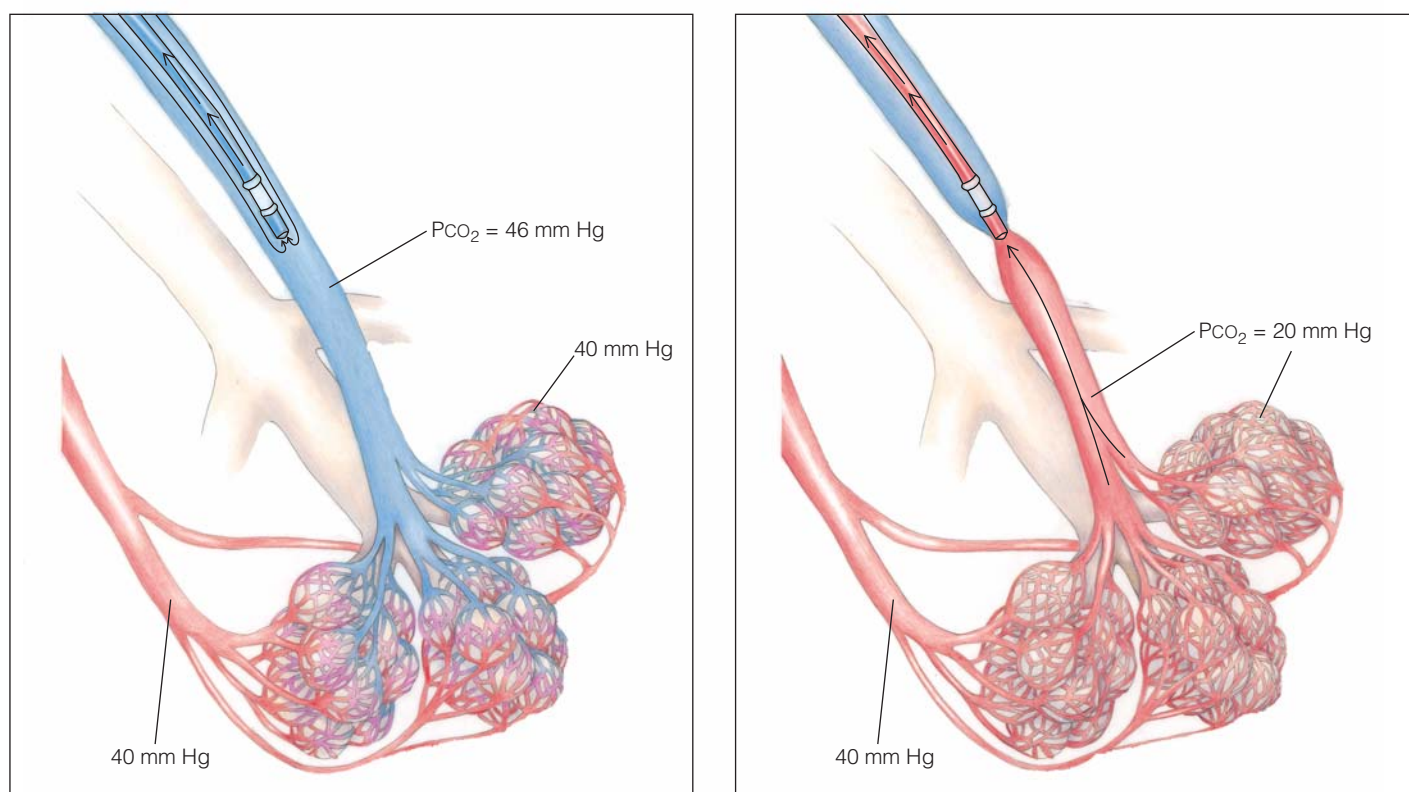


Figure 6 The Swan-Ganz catheter allows collection of mixed venous blood for measurement of S_{mvO_2} (left). If blood from the pulmonary artery is withdrawn through the catheter too forcefully, however, arterial walls can collapse around the tip of the catheter (right). The sample will in that case consist of blood from the distal pulmonary vasculature that has been pulled back past ventilated alveoli. To determine whether this has happened, the PCO_2 in the sample should be checked. P_{mvCO_2} is typically about 5 mm Hg greater than P_{aCO_2} . If the arterial walls have collapsed around the catheter, the sample will consist of blood from which much of the CO_2 will already have been removed by the ventilating alveoli, and the P_{mvCO_2} in the recovered blood may be as much as 20 mm Hg lower than a simultaneously obtained P_{aCO_2} . Specimens of this sort should be discarded and new specimens obtained. Taking care in obtaining true mixed venous blood is equally important when using a catheter with an oximeter mounted on its tip. Calibration of the oximeter requires direct measurement of S_{mvO_2} in a correctly obtained specimen.

Measurements That Can Be Obtained from Invasive Monitoring

Cardiac Output

Thermistor-tipped Swan-Ganz catheters can measure cardiac output by means of thermodilution [see Table 2].^{114,115} Originally, these values were obtained by injecting a known quantity of a cool solution into the right atrium and analyzing the temperature drop in the pulmonary artery as the cooled blood flowed past the thermistor. Nowadays, a heater coil is used to heat the blood in the right ventricle, and the resulting rise in temperature in the pulmonary artery is used to calculate the output. The temperature pulses are generated randomly. The measured outputs are obtained over the entirety of the respiratory cycle. Commercially available computers make the calculations on the basis of indicator dilution theory. Stroke volumes, obtained by echocardiography, can also be used to calculate the cardiac output, but cardiac outputs measured via the Swan-Ganz catheter are more accurate than those calculated from echocardiographic measurements.

Stroke Volume

The stroke volume is calculated as the cardiac output (measured by thermodilution) divided by the heart rate [see Table 3].

Right Ventricular End-Diastolic Pressure and Volume

The right ventricular end-diastolic pressure (RVEDP) is essentially the same as the central venous pressure, provided that there is no tricuspid stenosis. The proximal port on a Swan-Ganz catheter can be used to transduce that pressure.

The right ventricular end-diastolic volume (RVEDV) can be approximated from the end-diastolic pressure, but the introduction of pulmonary arterial catheters equipped with fast-response thermistors now allows direct measurement of the RVEDV.¹¹⁶ The measurements are accurate as long as the patient has a regular rhythm and a heart rate lower than 140 beats/min.

Measuring right ventricular volumes with echocardiography is difficult. The chamber is typically crescent-shaped; therefore, mathematical formulae based on linear measurements of the chamber will not be able to generate reliable estimates.

Right Ventricular End-Systolic Pressure and Volume

The right ventricular peak systolic pressure is the same as the peak pulmonary arterial pressure, provided that the pressures from the catheter are being accurately measured [see Figures 2 and 3]. The right ventricular end-systolic pressure (RVESP), which is the key pressure for evaluating the energy-producing capabilities of the ventricle and assessing the hindrance that the ventricle faces when it expels its blood into the root of the pulmonary artery (see below), can be approximated as 90% of the peak systolic pressure.³

The right ventricular end-systolic volume (RVESV) can be obtained by subtracting the stroke volume from the end-diastolic volume [see Table 3].

Left Ventricular End-Diastolic Pressure and Volume

The pulmonary arterial wedge pressure, measured with a Swan-Ganz catheter, will approximate the left atrial pressure, provided that there is no significant bronchial blood flow entering the vasculature distal to the end of the catheter and that the catheter is placed in a portion of the vasculature that is open to the left atrium throughout the ventilatory cycle [see Figure 4]. If no mitral valvular stenosis is present, the left atrial pressure will approximate the left-ventricular end-diastolic pressure (LVEDP). Thus, the wedge pressure will usually be close to both the left atrial and the left ventricular end-diastolic pressure. Knowing the left atrial pressure can be very helpful in making an estimate of the pulmonary microvasculature hydrostatic pressure. One will not be able to assign a specific number to that pressure on the basis of the left atrial or wedge pressure, but one will know that the microvascular pressure must be greater than the wedge

pressure. From the standpoint of preventing pulmonary edema, one would like to keep the wedge pressure as low as possible.

One can also use the wedge pressure—cautiously—to estimate the left-ventricular end-diastolic volume (LVEDV), but only if the ventricular wall is not abnormally stiff during diastole and if the tissues surrounding the left ventricle are not abnormally stiff.

Many different factors may influence the stiffness of the ventricular wall during diastole. A distended right ventricle under high pressure (a common finding in ARDS) can push the ventricular septum into the left ventricle during diastole and thus increase the diastolic stiffness of the walls of that chamber. (This situation will result in a large RVEDV in association with a small LVEDV—a frequent finding in patients in inflammatory shock. The situation can also go the other way: in patients with left-side congestive heart failure, left ventricular values can be substantially larger than right ventricular values.) The possibility of septal shift into the left ventricle can be ruled out if the measured RVEDV is reasonably small and the measured CVP is reasonably low.

The diastolic stiffness of the left ventricle can also increase if the wall is (1) thick (which can be ruled out with reasonable certainty if it is known that the patient has no aortic valvular disease and is not chronically hypertensive), (2) ischemic (which might become a problem with a tachycardia; a normal electrocardiogram usually suffices to rule out the possibility); or (3) scarred, as from an old myocardial infarction (which can be ruled out with a history and an electrocardiogram). If the left ventricular wall is none of these things, one can assume that it is probably normally compliant during diastole.

To assess the possibility of increased stiffness of the tissues surrounding the left ventricle, one can compare the RVEDV (measured with the Swan-Ganz catheter) with the CVP. If a low CVP is associated with a reasonably large end-diastolic volume, then it is clear that the tissues surrounding the heart cannot be excessively stiff (if they were, the low intracavitary CVP would not be able to produce a reasonable volume).

If the clinical assessment suggests that the walls of the left ventricle are normally compliant during diastole and if the assessment of the CVP and the RVEDV suggests that the tissues surrounding the ventricle are not excessively stiff, one can extrapolate from the wedge pressure to the ventricular end-diastolic volume. If, however, there is a question about the stiffness either of the left ventricular wall during diastole or of the tissues surrounding the ventricle, one cannot make this extrapolation.

Under these circumstances, one can make a rough estimate of the LVEDV by giving a fluid bolus in an amount that is sufficient to increase the wedge pressure by at least several mm Hg. If this measure increases the stroke volume, especially if the increase is associated with increased systemic arterial pressure, the initial LVEDV was probably small. If, however, increasing the wedge pressure has minimal effects on the stroke volume and the arterial pressure, there are two possibilities. The first is that the LVEDV was already generous. To test this possibility, a diuretic can be given; if the stroke volume and blood pressure do not decrease, one can assume that the left ventricular volume was probably adequate, perhaps even more than adequate. The second possibility is that the volumes were small but the diastolic compliance was poor.

In a 60 kg subject, a normal LVEDV is on the order of 150 ml (the same as for the right ventricle) for a wedge pressure of 6 mm Hg. If an essentially normal subject undergoes mechanical ventilation, as for an elective operation, a wedge pressure of 9 mm Hg is usually enough to produce an adequate LVEDV. If the patient is moderately ill, the pressure will probably have to be 12 mm Hg; if he or she is seriously ill, it will have to be 15 mm Hg, if not higher. Under no circumstances, however, should the pressure exceed 24 mm Hg: that level of left atrial pressure will give rise to fulminant pulmonary edema, even in a patient with completely normal pulmonary microvascular permeability.

(continued)

Measurements That Can Be Obtained from Invasive Monitoring (continued)

It must be kept in mind, however, that these generalizations are only that. Their accuracy suffers from the effort to extrapolate from an intracavitary pressure to a volume without any sure knowledge regarding the stiffness of the structures around the volume being considered. For accurate measurements of the LVEDV, transesophageal echocardiography is necessary.

Left Ventricular End-Systolic Pressure and Volume

Estimating the peak aortic root pressure is as difficult a process as estimating the LVEDV. Nevertheless, the effort is worth making. The systolic pressures in the aortic root and the left ventricle are the same. To have at least some idea of what these pressures are would be useful if one is to make an estimate of the energy-producing capabilities of the left ventricle and if one wants to know the hindrance that the ventricle faces when it pushes its blood into the aortic root.

One approach in estimating the systolic pressures in the aortic root is to measure the peak systolic pressures in the radial artery and then to cautiously extrapolate back to the corresponding pressures in the root of the aorta [see *Sidebar Energy Propagation throughout the Arteries and Its Effect on Pressures in Those Arteries*]. Another approach is to estimate the peak aortic root pressure by extrapolating from the MAP. In young patients with compliant arteries and no abnormal arteriolar constriction, the peak systolic pressure in the aortic root is usually about 20 mm Hg higher than the MAP.¹ In patients with stiff or calcified arteries, the central peak systolic pressure can be much higher than the MAP. In patients who are in warm inflammatory shock or neurogenic shock, the central systolic pressure may be only 10 mm Hg higher than the MAP. Usually, the aortic root end-systolic pressure is about 90% of the peak aortic root pressure.³

The left ventricular end-systolic volume (LVESV) (end-diastolic volume minus stroke volume) cannot be obtained with any reasonable accuracy from measurements obtained via the Swan-Ganz catheter. Estimates of the end-diastolic volume on the basis of the wedge pressure are very rough; at times, there might be some inaccuracy in measuring the stroke volume from the thermodilution cardiac output. If one needs to know the end-systolic volume, it is necessary to use echocardiography, which is usually quite accurate. Alternatively, one can use echocardiography to measure the end-diastolic volume and then subtract the stroke volume calculated from the heart rate and the cardiac output obtained by thermodilution.

Effective Arterial Elastances

Of the many cardiovascular descriptors that can be derived from the variables just described, four are of particular importance in considering how to treat a patient in shock: the two effective arterial elastances (one for the pulmonary artery and one for the root of the aorta) and the two ventricular end-systolic elastances. It is also valuable to have some feeling for the concept of the ventricular end-systolic unstressed volume.

The so-called effective arterial elastance is a single number used to describe the total hindrance that the ventricle faces as it ejects its blood during systole. It is calculated as the proximal arterial (or ventricular) end-systolic pressure divided by the stroke volume and is expressed in mm Hg/ml. In the case of the pulmonary vasculature, the effective arterial elastance can be calculated quite accurately, provided that a pulmonary artery catheter is in place and that the system used to measure the pulmonary arterial pressures is satisfactorily matched to the vasculature [see *Figures 2 and 3*]. In the case of the systemic vasculature, however, the calculation becomes problematic because of the difficulty in determining the pressures in the root of the aorta [see *Figure 2 and Sidebar Energy Propagation throughout the Arteries and Its Effect on Pressures in Those Arteries*]. Nevertheless, the effective arterial elastance for the aortic root remains the best single-number approximation for the hindrance faced

by the left ventricle. The values for the elastances depend on the patient's size [see *Table 4*].

The effective arterial elastance takes into account the stiffness of the arteries faced by the ventricles, the resistance of the arterioles in the circuit, the stiffness of the atrium and ventricle into which the blood is driven during diastole, and the interaction of all of these elements in conjunction with the heart rate. The systemic vascular resistance, as one part of this hindrance, can be calculated as the difference between the mean aortic pressure and the right atrial pressure divided by the cardiac output. One can also calculate a resistance for the pulmonary vasculature, but the calculation depends on the difference between two small numbers. In our view, calculated pulmonary vascular resistance is too unreliable to be a useful clinical descriptor.

The units used to express vascular resistances vary from hospital to hospital. It is simplest, as well as perfectly acceptable scientifically, to use arbitrary units. We prefer mm Hg·L⁻¹·min. That is, we use the number obtained through the simple calculation described without making any further corrections. Some multiply this raw number by 80 to convert the resistances to units in the centimeter-gram-second (CGS) system.

Ventricular End-Systolic Unstressed Volumes

The unstressed volume of a chamber is the minimal volume in the chamber that will generate a positive pressure. In the case of a cardiac ventricle, the end-systolic unstressed volume is the unstressed volume in the chamber when the ventricle is maximally stiff, at the end of systole. These volumes cannot be determined with currently available ICU monitoring, but one must nonetheless be mindful of the concept of end-systolic unstressed volume when assessing the energy-producing capabilities of the ventricles.

In normal subjects, the left ventricular end-systolic unstressed volume, measured with sophisticated echocardiography or in the cardiac catheterization laboratory, is on the order of 0.1 ml/kg lean weight. In patients with congestive heart failure, it can increase by a factor of 10, to 1.0 ml/kg. That is, left ventricular end-systolic unstressed volume is close to zero in a normal human heart, compared with other heart volumes (e.g., the end-diastolic volume, which is on the order of 2.5 ml/kg), but it can become substantial in a flabby heart.

To our knowledge, the right ventricular end-systolic unstressed volume has not yet been satisfactorily measured in human beings, even in the catheterization laboratory. This volume is very small in normal dogs, and there are reasons why it should be small in normal human beings as well. There are also reasons why the right ventricular end-systolic unstressed volume is likely to be very large in a patient with a failing right ventricle—probably even larger than the unstressed volume in the left ventricle of a patient in left-side failure.

Ventricular End-Systolic Elastances

The ventricular end-systolic elastance is a single number that represents the maximal stiffness of a ventricle, which occurs at end-systole. (The ventricles are quite compliant during diastole; they become much stiffer during systole [see *Figure 5*].) It is expressed in mm Hg/ml. Nowadays, ventricular end-systolic elastances are the most frequently used single-number approximations for describing the energy-producing capabilities of the ventricles. Large elastances correlate with good capabilities for energy production; low elastances correlate with poor capabilities.

Ventricular end-systolic elastances do not provide a complete description of energy-producing capabilities; for that, one also needs the ventricular end-systolic unstressed volumes. Nonetheless, they are good descriptors and are ideally suited for analysis of how a ventricle interacts with its vasculature.

(continued)

Measurements That Can Be Obtained from Invasive Monitoring (continued)

The right ventricular end-systolic elastance, in a patient who does not have unusually large end-diastolic volumes, can be approximated as the ventricular (or pulmonary arterial) end-systolic pressure divided by the end-systolic volume. The left ventricular end-systolic elastance cannot be approximated very well in the ICU, but studies done in the catheterization laboratory have yielded known values for both normal subjects and patients in congestive heart failure. One can sometimes assign a number to a patient if the clinical circumstances make it obvious that the patient's heart is clearly in good condition or clearly failing. These numbers can then be used in making decisions about adjustment of the effective aortic elastance.

Values for ventricular end-systolic elastance in a spontaneously breathing normal subject depend on body size [see Table 4]. In a maximal state of ventricular function, the values can double; in profound beta blockade or profound heart failure, the values can fall to 50% of normal.

Mixed Venous Oxygen Saturations

The mixed venous oxygen saturation (S_{mvO_2}) can be measured with appropriately equipped Swan-Ganz catheters [see Figure 7]. It will be

high if the cardiac output is high, if the hemoglobin concentration is high, if the arterial oxygen saturation is high, and if the oxygen consumption is low. It may be the best single-number descriptor of the adequacy of shock resuscitation.

Saturations lower than 60% should always be considered grounds for concern. The heart consumes much of the oxygen delivered to it. Low mixed venous values raise the possibility that the heart might not be receiving the oxygen it needs. Saturations higher than 80% are reassuring, in the sense that they suggest that it is not necessary to increase the oxygen delivery to the body (because the body, as a whole, is only using 20% of the oxygen delivered to it). On the other hand, there are situations in which a high S_{mvO_2} can be worrisome. The high value might arise from excessive amounts of blood being shunted to the skin, as in the case of sepsis, or it might arise from failure of metabolic activity either generally or in specific organs, resulting in minimization of oxygen consumption. As with all of the cardiovascular descriptors discussed, S_{mvO_2} values must be considered with respect to the specific clinical context in which they are determined.

as for hypovolemic or inflammatory shock (see above). If the effective aortic elastance still seems excessively high in relation to the estimated left ventricular end-systolic elastance, more aggressive efforts either to reduce the effective aortic elastance or to augment the left ventricular end-systolic elastance are warranted. The goal is to manage the patient so that the estimated effective aortic elastance is approximately one half of the estimated left ventricular end-systolic elastance—in other words, to achieve as much efficiency as possible.⁷⁶⁻⁷⁸

In some patients with acute myocardial ischemia and shock, all of the aforementioned treatments will fail. Such patients should undergo emergency coronary angiography, as should any patient with an acute coronary syndrome that becomes unstable

or that is associated with ST-T segment elevation. The purpose of the angiography is to find a correctable lesion that can be treated with coronary angioplasty, stenting, or surgical revascularization. If necessary, an intra-aortic balloon pump may be placed before or at the time of angiography, angioplasty, or stenting; it can then be left in place while the underlying problem awaits possible surgical correction (if indicated). The pump can be extraordinarily effective: there is no better means of dealing with the reflected energy waves generated by the transmission of energy into these vessels. It does, however, put the perfusion of the limb with the cannulated artery at risk. Furthermore, the pump is only a short-term solution: eventually, the underlying problem will have to be dealt with.

Discussion

To the best of our knowledge, the thermodynamic characterization of the cardiovascular system was first described in the 1880s, by Otto Frank in Germany. Frank compared the ventricles to Carnot engines and used that analogy to account for how the heart generated its energy. He was unable, however, to confirm his theory experi-

mentally—it was too complex to be evaluated with the measurements available at the time—and he was unable to account for how the ventricles transferred their generated energy into their respective vasculatures.

In the early 1900s, Ernest Starling, who had worked in Germany in his younger days and was aware of Frank's work,

Table 3 Influence of Body Size on Selected Cardiovascular Parameters in a Resting Subject*

Lean Weight (kg)	Cardiac Output (L/min)	Stroke Volume (ml)	End-Diastolic Volume (ml)	End-Systolic Volume (ml)
50	5.0	83	125	42
60	6.0	100	150	50
70	7.0	117	175	58
80	8.0	133	200	67

*On the assumptions that (1) cardiac output is 100 mL·kg⁻¹·min⁻¹, (2) heart rate is 60 beats/min (or, equivalently, stroke volume is 1.67 mL/kg), and (3) end-diastolic volume for the two ventricles is 2.5 mL/kg.

Table 4 Derived Descriptors of Energy-Producing Capabilities of Ventricles and of Hindrance That Ventricles Face When Injecting Blood into Their Respective Vasculatures*

Lean Weight (kg)	Right Ventricular End-Systolic Elastance (mm Hg/ml)	Effective Pulmonary Arterial Elastance (mm Hg/ml)	Left Ventricular End-Systolic Elastance (mm Hg/ml)	Effective Aortic Root Elastance (mm Hg/ml)
50	0.52	0.26	2.4	1.2
60	0.44	0.22	2.0	1.0
70	0.38	0.19	1.7	0.85
80	0.33	0.17	1.5	0.75

*On the assumptions used in Table 3 and on the additional assumptions that (1) right ventricular end-systolic pressure is 22 mm Hg, (2) left ventricular end-systolic pressure is 100 mm Hg, and (3) ventricular end-systolic unstressed volumes are zero.

expanded on that work both experimentally and theoretically. Using isolated muscle strips contracting against a suspended weight, he was able to demonstrate that the resting length of a muscle was a determinant of the amount of work that the muscle could produce. Going on to experiments in anesthetized dogs, he introduced the concepts of contractility and afterload and was then able to describe the energy produced by a ventricle and transferred into the vasculature as the result of the interaction between the ventricular end-diastolic volume, the contractility of the ventricle, and the afterload facing the ventricle.

This Frank-Starling model of the heart was elegant and parsimonious and could qualitatively describe much of normal cardiovascular physiology, but for a long time, two of its variables—contractility and afterload—could not be satisfactorily described in mathematical terms. As a consequence, the model could not deal with quantitative problems like heat dissipation throughout the system, nor could it address the issue of ventricular-arterial coupling.

These problems have now been solved. Modern models, using engineering concepts developed in the midportion of the 20th century and applied to the cardiovascular system in the latter part of the century, have succeeded in mathematically describing how a ventricle interacts with its vasculature. Like Frank's original description, these models begin by comparing a ventricle (either the right or the left) to a Carnot engine (or to an oscillating electrical energy source). They then compare the vasculature (including the contralateral atrium and the contralateral ventricle during its diastole) into which the ventricle pumps its blood to a system of pipes with compliant and resistive elements (or to an electrical circuit with capacitive and resistive elements). The interaction between the pulsatile energy source and the hindrance or impedance imposed by the vasculature determines the amount and type of energy that is transferred from a ventricle into its vascular bed.

The modern models use five variables to account for generation and transfer of energy in the cardiovascular system: (1) ventricular end-diastolic volumes, (2) ventricular end-systolic unstressed volumes, (3) ventricular end-systolic elastances, (4) effective elastances of the roots of the pulmonary artery and the aorta, and (5) heart rate. These variables determine how the ventricles interact with their complex vasculatures. They determine the pressures that will be generated in the system; the stroke volumes that will be produced; the cardiac output that will be produced (as the product of the heart rate and the stroke volume); the work that will be done by the heart on the vasculature; the total, mean, and oscillatory power that will be delivered into the vasculature; the heat that will be dis-

sipated into the walls of the heart during the cardiac cycle; the heat that will be dissipated in the walls of the arteries as the arteries expand and recoil during the cardiac cycle; the heat that will be dissipated in the arterioles of the microvasculature; the amount of oxygen that myocardium will require to produce all of this energy; and the efficiency with which the heart generates and transfers the energy into the vasculatures. In other words, by reasoning from the modern models, one should be able to predict, at least theoretically, all that one needs to know about managing a patient in shock. Thus, a knowledge of cardiovascular thermodynamics is not only of intellectual interest (to some) but also of therapeutic value. The goal of studying this material is to reach an informed understanding of how to deal with the basic problem of managing the patient in shock—that is, the problem of helping the heart produce and transmit energy without producing too much edema and without putting excessive demands on the myocardium.

We begin our discussion of cardiovascular thermodynamics by describing the various types of power generated by the heart and transferred into the vasculature. On the assumption that some useful energy is present in the cardiovascular system, we then describe how that energy accounts both for the distribution of blood in the various parts of the system and for the flow of blood through the various organs in the system. Next, we describe more specifically how a ventricle interacts with the root of its vasculature (either the root of the pulmonary artery or the root of the aorta) to generate and transfer its energy into the blood vessels. Finally, we describe the factors that determine how much energy is produced and how efficiently it is produced.

Analysis of Cardiovascular Thermodynamics

TYPES OF POWER PRODUCED BY HEART AND TRANSFERRED INTO VASCULATURE

The total power generated by a ventricle and transferred into its vasculature over time can be calculated as the cardiac output multiplied by the end-systolic pressures in the ventricle.^{2,79} It typically is expressed in units of volume divided by time multiplied by pressure. (It can also be expressed in units of heat divided by time or in terms of amounts of oxygen used for oxidation divided by time.) The total power is the major determinant of the ventricle's oxygen requirement.³

The total power has two components: the mean power and the oscillatory power. The mean power transferred into the vascula-

Table 5 Influence of Interventions on Goals of Shock Resuscitation, as Determined by Graphical Mathematical Analysis

Goal	Interventions
To increase stroke volume	Increase ventricular end-diastolic volume Increase ventricular end-systolic elastance Decrease effective arterial elastance
To increase arterial pressures	Increase ventricular end-diastolic volume Increase ventricular end-systolic elastance Increase effective arterial elastance
To increase work done by ventricle on its vasculature	Increase ventricular end-diastolic volume Increase ventricular end-systolic elastance Adjust effective arterial elastance so that it equals the ventricular end-systolic elastance
To decrease ventricular oxygen requirements	Decrease ventricular end-diastolic volume Decrease ventricular end-systolic elastance Decrease effective arterial elastance
To optimize efficiency*	Increase ventricular end-diastolic volume Adjust effective arterial elastance so that it is approximately one half the ventricular end-systolic elastance

*Defined as work done on the aortic root per heart beat divided by the sum of work done plus heat dissipated during isovolumetric relaxation.

ture is the useful power. The mean power generated by the heart and delivered into the roots of the pulmonary artery and the aorta is the power that moves the blood throughout the cardiovascular system, as described earlier (see above). The oscillatory power is an unavoidable consequence of coupling a pulsatile energy source with a circuit containing stiff and resistive elements. It is dissipated as heat in the walls of the arteries as the arteries expand and recoil during the cardiac cycle. It does no useful work and hence is not considered useful power.

Just as the mean power generated by the left side of the heart and delivered into the aortic root can be calculated as the cardiac output multiplied by the mean aortic root pressure, the oscillatory power generated by the left ventricle and delivered distally can be calculated as the difference between the total power generated (the cardiac output multiplied by the left ventricular end-systolic pressure [LVESP]) and the mean power. A similar calculation can be used for the right side of the heart.

In a well-conditioned normal person, one third of the total power generated and transmitted by the right ventricle into the pulmonary artery is in the form of oscillatory power; two thirds is in the form of mean power. (The right ventricular end-systolic pressure [RVESP] is on the order of 22 mm Hg; the mean pressure in the pulmonary artery is on the order of 15 mm Hg.) This level of efficiency (defined, in this case, as mean power divided by total power) is good, compared with that of most mechanical systems. (There are many definitions of efficiency [see Table 5].) Because the load faced by the right ventricle is usually minimal, an efficiency of two thirds is more than adequate to allow the ventricle to move the blood through the pulmonary vasculature and into the left side of the heart during diastole.

On the left side of the circulation in a normal person, the efficiency is extraordinarily good. Only 10% of the power transferred into the aortic root of a young individual is in the form of oscillatory power; 90% is in the form of mean power. (The LVESP is on

the order of 100 mm Hg; the mean pressure in the aortic root is on the order of 90 mm Hg.) The load imposed on the left ventricle is substantial, but the strength of the ventricle and its excellent matching with its vasculature allow it to carry out its functions easily and enable it to do far more than meet basal needs at times (as during exercise).

DISTRIBUTION AND FLOW OF BLOOD WITHIN AND THROUGH COMPONENTS OF CARDIOVASCULAR SYSTEM

Working on the assumption that the ventricles are capable of generating and transferring some mean power into the pulmonary and systemic arterial vasculatures, one can deduce how the blood volume is distributed throughout the vasculature and can determine the blood flow to the various parts of the vasculature. To make these deductions and determinations, however, one must understand the engineering concepts of unstressed volume, elastance, and resistance.

The unstressed volume of a hollow structure is the volume within the structure that is just large enough to generate a positive pressure (in reference to the atmosphere). The unstressed volume of the systemic venules and small veins is on the order of 1,000 ml; the unstressed volume of the right atrium during most of its cycle is probably on the order of 50 ml; the unstressed volume of the right ventricle at the end of diastole is probably on the order of 30 ml; the unstressed volume of the right ventricle at the end of systole is probably on the order of 5 ml; the unstressed volume of the left atrium is probably on the order of 30 ml; the unstressed volume of the left ventricle at the end of diastole is on the order of 30 ml; and the unstressed volume of the left ventricle at the end of systole is on the order of 5 ml. Whereas a quite large volume of blood is necessary to produce energy in the venules and the small veins, a quite small volume is adequate in the normal left ventricle at end-systole. The unstressed volumes in the other parts of the cardiovascular system fall between these two extremes.

The deformation of a hollow structure with changes in volume can be described in terms of compliance, capacitance, distensibility, elasticity, stiffness, or, to use the engineering term, elastance. All of these terms refer to the same mechanical characteristic of the structure, though some of them refer to changes in volume divided by changes in pressure, whereas stiffness and elastance refer to changes in pressure divided by changes in volume. A large elastance denotes a stiff structure; a small elastance, a compliant structure. Arteries have a large elastance; veins, a small elastance. The ventricles have a large elastance during systole and a small elastance during diastole.

The elastances of hollow structures (e.g., blood vessels) are usually thought of in terms of changes in pressure (referenced to the atmosphere) divided by changes in volume. The typical unit for the cardiovascular system would be mm Hg/ml. The pressure measured will be the pressure generated by the interaction of the energy inside the structure with the components of the structure itself and the components of the tissues surrounding the structure out to the body surface.

In mathematical terms, the elastance of a chamber with a given volume and pressure is the slope of the line that is drawn tangentially to the pressure-volume relation in the chamber around that point. In terms of the calculus, it is the first derivative with respect to volume of the pressure-volume relation. If the pressure-volume relation in the chamber is a straight line, the elastance is equivalent to the difference between the pressures at any two points on the line divided by the difference between the volumes associated with those two pressures.

Traditionally, in plotting the pressure-volume relation, physiologists, engineers, and cardiovascular physiologists have preferred to assign volume to the x-axis as the independent variable and to assign pressure to the y-axis as the dependent variable. Pulmonary physiologists, however, have generally preferred to reverse this assignment. Neither way is right or wrong: the assignment of variables to axes is arbitrary. Nevertheless, for the purposes of consistency and clarity, one must make a decision about how these concepts are to be represented. Accordingly, in the ensuing discussion, we will treat volume as the independent variable and, for the most part, will address stiffness or elastance rather than compliance, distensibility, or elasticity.

Many factors influence the elastances of the different parts of the cardiovascular system—activation of receptors in the walls of the vessels for adrenergic agonists, angiotensin, and vasopressin; the thickness of the walls; the amount of collagen in the walls versus the amount of elastin or scar; stretching of the walls; calcification of the walls (as in diabetes); compression of the vessels by surrounding tissues; linking of actin and myosin in contracted muscle in the walls; viscoelasticity of the walls; and ischemia.

The resistance of a conduit in a dynamic system refers to the hindrance to flow (as opposed to the elastance of the conduit, which refers to the hindrance to changes in shape). The resistance offered by a vessel in the cardiovascular system depends on its cross-sectional area, its length, and the viscoelasticity of the blood (which, in turn, depends on the temperature of the blood, the hematocrit, the fibrinogen concentration, and the velocity of the blood within the vessel).

On the arterial side of the systemic circulation, the great majority of the resistance present in a normal person with no obstructive arterial disease comes from the arterioles. The total cross-sectional area of the arterioles is smaller than that of the arteries. In contrast, on the venous side of the circulation, the great majority of the resistance comes from the great veins—namely, the superior and inferior vena cavae, the hepatic veins, and the pulmonary veins. The total cross-sectional area of these vessels is smaller than that of the venules and the small veins. In the pulmonary circulation, the majority of the resistance to flow comes from the microvasculature of the lungs, and the majority of the resistance to drainage of blood from the lungs comes from the pulmonary veins.

The resistance in the systemic arteries, the large systemic veins, the pulmonary microvasculature, and the pulmonary veins depends on a number of factors, many of which are the same as those that affect the elastance of the arteries. These factors include responses to adrenergic agonists, angiotensin, vasopressin, thromboxane, endothelin, and nitric oxide; external compression, as in a compartment syndrome; and mechanical blockage, as in embolism.

On the basis of these concepts, one can begin to consider the distribution of blood within the various parts of the cardiovascular system and the variation in flow to different organs under different conditions. A good initial example is the distribution of blood between the venous side of the systemic circulation and the right atrium and ventricle during diastole. The portion of the blood contained within the venules and the small veins that exceeds the unstressed volume of these vessels interacts with the elastance to create a pressure. This pressure drives the venous blood through the resistance posed by the hepatic veins, the inferior vena cava, and the superior vena cava and into the right atrium and right ventricle during diastole. If both the resistance of the large veins and the elastance of the right atrium and ventricle are low during diastole, a large amount of blood will end up in the

heart at this point. If the pressure in the venules and the small veins is low (as, for example, in hypovolemic shock), it will not be strong enough to drive the blood centrally. If the large veins are compressed and acquire a high resistance (as typically happens to the inferior vena cava and the hepatic veins in the abdominal compartment syndrome), filling of the right side of the heart will be slowed. If the right side of the heart is stiff during diastole (as, for example, in a patient with a pericardial tamponade or an ischemic right ventricle or even a patient on high levels of positive-pressure ventilation), its capacity for accepting blood from the venules and small veins will be limited.

Similar reasoning can be applied to the filling of the coronary vasculature during diastole. The volume of blood in the aortic root over and above the unstressed volume interacts with the elastance to create a pressure in the root. This pressure drives the blood through the coronary vasculature and into the coronary sinus. If there is minimal resistance in the ostia of the coronary arteries, if the thickness of the ventricular wall through which the arteries pass is not excessive, and if the elastance of the coronary sinus and right atrium is low, a large amount of blood will flow through the vasculature during diastole. If the ostia of the arteries are obstructed or if the arterial resistance is high because of ventricular hypertrophy, blood flow will be slow and there will not be adequate time for perfusion of the myocardium. In addition, there will be insufficient time for myocardial perfusion if the right atrium is stiff during diastole (as in the case of overdistention, external compression, or ischemia).

In the case of organs that are perfused evenly throughout the cardiac cycle (i.e., all of the noncardiac organs), blood flow depends on the difference between the pressures on either side of the organ (the MAP minus the pressure in the veins draining the organ) divided by the resistance of the arterioles in the organ. A large pressure differential creates a large flow, as does a low resistance.

Under ordinary, resting circumstances, a minimal pressure differential is adequate for perfusion of all of the noncardiac organs, provided that their arterial inflow is unobstructed. All of these organs, with the exception of the brain and the spinal cord, have at least some chronic constriction of their arterioles. All of them, again with the exception of the brain and the spinal cord, will be protected if the MAP falls for some reason. If the pressure falls, the arterioles will dilate and the resistance to steady-state flow will decrease. Flow will thus be maintained. The brain and the spinal cord will be protected because the cardiovascular system is designed to maintain normal perfusion of the CNS. The baroreceptors for the cardiovascular system are not placed in the origins of the internal carotid arteries for no reason.

If an organ is supplied by an obstructed artery (as in atherosclerosis), it becomes vulnerable. Chronic preexisting ischemia leads to chronic arteriolar dilation. The arterioles in the organ thus lose their option of dilating in the face of hypotension. The arteries at particular risk for this adverse development are those supplying the heart, the brain, the kidneys, the viscera, and the lower extremities.

In the case of organs confined within a rigid structure or a capsule (e.g., the brain, the kidneys, the liver, the muscle in a patient with compartment syndrome, or the gut in a patient with abdominal compartment syndrome), swelling will increase the resistance of the microvasculature (through compression of the vessels) and will raise the pressures in the veins draining the organs (also through compression). This combination—a high resistance with a low perfusion pressure as a consequence of a high venous pressure—is particularly ominous: it may lead to obliteration of all flow into the swollen space.

GENERATION OF ENERGY BY VENTRICLES AND TRANSFER OF ENERGY INTO VASCULATURE

To describe the energy-producing capabilities of the heart, the modern models start by considering the unstressed volumes and elastances of the chambers of the heart throughout the cardiac cycle. In the case of a ventricle, the unstressed volume is the volume of blood that would be left behind in the chamber at any given time if the ventricle could empty itself against no hindrance. Large unstressed volumes and small elastances describe a chamber that will fill well during diastole; small unstressed volumes and large elastances during systole describe a chamber with a good capacity for generating energy.

The elastances of the ventricles depend on many of the same factors that determine the elastances of the rest of the cardiovascular system, such as myocardial wall thickness, scar tissue, and ischemia. They also depend, however, on the influx of calcium into the myocytes and the linking of actin and myosin within the cells. The greater the concentration of ionized calcium in the cytosol during systole, the greater the linking and the greater the systolic elastance. Factors increasing systolic ionized calcium concentrations include stimulation of beta₁ receptors in the myocardium, inhibition of the sodium-potassium adenosine triphosphatase (ATPase) in the cell membranes (as with digitalis compounds), inhibition of phosphodiesterase within the cells (as with milrinone), and elevation of the extracellular calcium concentration (as with administration of calcium chloride or gluconate). The influx of calcium into a cardiac myocyte during systole requires no energy: the calcium easily goes down its electrochemical gradient, traveling from the outside to the inside of the cell. During diastole, however, it is necessary to pump the calcium out of the cell, and this step does require energy. Thus, any process or drug that increases ventricular end-systolic elastance will also increase ventricular oxygen requirements.

The elastances of a ventricle during a cardiac cycle can be mathematically described through analysis of ventricular pressure-volume loops.^{1,3} This is done by simultaneously measuring ventricular volume (with implanted microsonographic crystals, conductance catheter techniques, contrast ventriculography, or echocardiography) and intraventricular pressure. These measurements are then repeated while either the end-diastolic volumes or the hindrances against which the ventricle contracts are altered, thereby yielding a “family” of pressure-volume relations. From this family, the elastances of the ventricle during an entire cardiac cycle can be calculated.

How ventricular elastance varies during a single cardiac cycle can be illustrated by considering typical values for the left ventricle in a normal 60 kg woman in a resting state [see Figure 5]. At the end of diastole (or the beginning of systole), the elastance is 0.2 mm Hg/ml. When systole begins, the elastance increases rapidly (within about 50 milliseconds) to 1.0 mm Hg/ml. At this point in the cardiac cycle, the pressure inside the ventricle is high enough to open the aortic valve. The elastance continues to increase as the ventricle pushes its blood into the aortic root, reaching its maximum at the end of systole. Typically, the end-systolic elastance is some 10 times greater than the end-diastolic elastance, or about 2.0 mm Hg/ml. The elastance rapidly decreases during isovolumic relaxation until the beginning of diastolic filling of the ventricle; it then gradually and slightly increases until the end of diastole, returning to the initial value of 0.2 mm Hg/ml.

It is worthwhile to compare these variations in elastance with those seen in a person with maximal adrenergic stimulation of the heart and in a person with profound beta blockade [see Figure 5]. In the former, the end-systolic elastance is double the normal

value, or 4.0 mm Hg/ml, and the ventricle reaches its maximal elastance more quickly. In the latter, the end-systolic elastance is half the normal value, or 1.0 mm Hg/ml, and the ventricle reaches its maximal elastance more slowly.

Thus, the end-systolic elastance can serve as a reasonably complete and simple measure of ventricular systolic function.^{3,80} It can be precisely measured, at least in the catheterization laboratory; it has been shown to be independent of end-diastolic volumes and the hindrance imposed on the ventricle by the vasculature in experimental animals; and it is ideally suited for dealing with one of the fundamental problems in managing critically ill patients—namely, the problem of predicting how a ventricle with a given capacity for energy generation will interact with a vasculature with a given hindrance [see Ventricular-Arterial Coupling, below].

The hindrance that the contracting ventricle encounters during systole is probably best described as the impedance of the vasculature.^{7,81} It is a quantifiable descriptor and can be determined by making measurements of flow and pressure in the aortic root in the cardiac catheterization laboratory. Vascular impedance is a concept that is ideally suited for dealing with the problem of ventricular-arterial coupling. It can, with reservations, be expressed as a single number. On the right side of the heart, it can, again with reservations, be approximated from values obtained from measurements made with a Swan-Ganz catheter; on the left side of the heart, it can, with further reservations, be approximated by using the stroke volume taken from use of the catheter and estimating the aortic root end-systolic pressure.

The impedance (hindrance) faced by the ventricle during emptying has three components, which then interact with one another in various ways, depending on the heart rate. (We use the left ventricle as an example here, but the same concepts apply to the right ventricle.) The first component is the elastance (stiffness) of the named arteries, including the aorta, which hinders the accommodation of blood in the arteries as the ventricle empties during systole. The second component is the resistance to steady-state flow offered by the arterioles throughout the body. The third component is the resistance to flow offered by the large veins as they enter the chest, coupled with the stiffness of the right atrium and ventricle as they accept blood returning from the body.

At first glance, the way in which these components relate to impedance appears simple. The stiffer the arteries, the higher the impedance; the greater the arteriolar constriction, the higher the impedance; and the greater the hindrance to the filling of the contralateral heart, the higher the impedance. The concept becomes more complex, however, when one tries to understand how these components interact with one another, as they do when connected to a pulsatile energy source (e.g., a contracting ventricle). One way of exploring this interaction is to consider the energy wave that is propagated throughout the vasculature when the ventricle pumps blood into the aortic root.

When the left ventricle contracts, it pushes the blood it contains into a standing column of blood in the aortic root. Initially, this column of blood remains stagnant; however, the energy impulse imparted to it by the inrush of ventricular blood generates an energy wave that propagates throughout the arteries until it reaches the arterioles, which are situated throughout the body at differing distances from the heart. Part of the propagated wave bounces off the arterioles, generating reflected waves that return to the aortic root and the heart.^{1,82,83}

The amplitude of the reflected waves that return to the root of the aorta depends on the degree to which the arterioles are constricted: the greater the constriction, the larger the amplitude. Some of the reflected waves return during systole, some during

diastole. The timing, as one might expect, depends to a large extent on the spatial distribution of the arterioles: waves from nearby arterioles return sooner, and waves from distant arterioles return later. The timing also depends on the propagation velocity of the waves, which depends on the elastance of the walls of the arteries through which the waves pass: compliant arterial walls generate waves with a slow (desirable) velocity, and stiff walls generate waves with a rapid velocity. Finally, the timing depends on the viscoelastic properties of the conducting medium (i.e., the blood), but aside from limiting blood transfusions and keeping the patient warm, there is little that one can do to influence these properties. There is, however, a great deal that one can do to influence arterial elastance (see below).

The velocity of the propagating energy wave can be measured quite simply in humans by means of Doppler technology. The velocities in the upper part of the body are slower than those in the lower part because the arterial walls in the upper extremities are thinner and more compliant than those in the lower extremities. The velocities are faster if arterial wall receptors for norepinephrine, vasopressin, or angiotensin II are activated; if the arteries are stretched; or if the walls are calcified (as in diabetes).

The pulse velocities on the left side of the heart are, on average, about 4 m/sec in young children and 18 m/sec in octogenarians.⁸⁴⁻⁸⁶ (The increased velocities in older persons are a result of stiffened arterial walls, caused by the replacement of elastin in the walls with collagen as part of the aging process.)

These propagation velocities are much faster than the velocities with which the blood moves through the arteries. Blood flow velocity is fairly constant throughout all of the arteries in the body and does not differ substantially between human beings of different sizes or animals of different species. The velocities at which blood flows during a cardiac cycle typically range from 0 to 50 cm/sec, depending on many factors (e.g., the stage in the cardiac cycle and the presence of pulse wave reflections from the organ or organs that the artery supplies). In most arteries, whether the ascending aorta of a human being or the common iliac artery of a wombat, the mean blood flow velocity is approximately 15 cm/sec. This value is determined by the amount of blood flowing through a vessel per unit time and the cross-sectional area of the vessel. Unlike the propagation velocity of the energy wave, it is not affected by arterial wall elastance.

Thus, for a child, the energy wave propagation velocity (4 m/sec) is more than 25 times faster than the mean blood flow velocity, whereas for an 80-year-old, the energy wave propagation velocity (18 m/sec) is more than 100 times faster. The differences between energy wave propagation velocity and blood flow velocity indicate that although the blood is indeed moved by the energy waves generated by ventricular contraction, it has inertia. The blood does accelerate and gain speed as the energy wave moves through it, but it cannot be expected to keep up with the wave.

As a general rule, a patient is better off with compliant arteries and slow propagation velocities for the energy wave.^{1,82,83} With high velocities, the waves return too rapidly to the aortic root, arriving even before the ventricle has finished contracting; as a result, the ventricle fights itself, pumping against the very pressure wave that it generated. Another problem with high propagation velocities is that the waves die out before diastole, and thus, pressure that could have been used for perfusion of the coronary vasculature is lost. The mean aortic root pressure may even fall, compromising peripheral perfusion.

In a young, unstressed patient, the propagation velocities are slow, and the waves return during diastole. The heart benefits enormously. Because the waves arrive back at the heart after the

aortic valve has closed, the ventricle does not have to pump against its own energy impulse, and the perfusion pressure of the coronary arteries is maximized. The augmented diastolic and mean pressures maintain peripheral perfusion.

The behavior of these reflected waves has many clinical implications for treatment of the patient in shock, first, with respect to measurement and interpretation of pressures throughout the cardiovascular system [see *Sidebar Energy Propagation throughout the Arteries and Its Effect on Pressures in Those Arteries*], and second, with respect to understanding and treating some of the abnormalities underlying the shock state. (The behavior of the reflected waves has additional implications for treatment of patients with certain medical problems, such as isolated systolic hypertension, but those issues lie outside the scope of this chapter.)

With respect to understanding and treating shock, if a patient's arteries are abnormally stiff (e.g., as a result of age, calcification, distention, activation of vessel wall receptors, or external compression), the propagation velocity will be high, which means that the waves will return early, the systolic pressure at the aortic root will rise, and the diastolic pressure will fall. The elevated systolic pressure will increase ventricular oxygen requirements; the unaffected MAP will do nothing for tissue perfusion.

If the propagation velocity can be reduced, then the systolic pressure will come down, and the MAP will stay the same. This is usually a desirable result for a patient in shock, in that myocardial oxygen requirements will decrease while perfusion pressures are maintained. Accordingly, in the treatment of shock, there is often a clinical benefit to be gained from interventions aimed at reducing arterial stiffness.

Several options are available for decreasing arterial stiffness on the left side of the circulation, including diuresis or fluid restriction, ACE inhibition, and the use of agents that increase the production of nitric oxide near the arterial walls. The aortic counterpulsating balloon pump can be extremely effective in dealing with systemic arterial stiffness. (In fact, that is its only function.) Options for treating stiff arteries on the right side of the circulation include adjustment of the ventilator, diuresis to decrease the vascular volumes, and, in extreme cases, operative decompression of the pulmonary vasculature in patients with an abdominal compartment syndrome. (The elevated diaphragm can compress the pulmonary vasculature and the left atrium.) In addition, pharmacologic interventions may provide some benefit on occasion.

As mentioned (see above), the arterial impedance facing the ventricles can be determined in the catheterization laboratory by using catheters that can precisely measure pressures and flows at the roots of the arteries. To describe this complex interplay of wave propagation and reflection with a single number, to quantify responses to interventions, and to do both of these things with numbers available in the intensive care unit, one can calculate the hindrance facing the right ventricle as the RVESP (or, equivalently, the pulmonary arterial end-systolic pressure) divided by the stroke volume.^{2,81}

The resulting value—the effective pulmonary arterial elastance—will be high if a given stroke volume creates a high systolic pressure and low if the stroke volume creates a low pressure. (It is worth mentioning that although this value is an elastance and is expressed in the units used for elastance, it reflects not only the properties of the arteries but also those of the arterioles, as well as the hindrance imposed on the right ventricle by the left side of the heart during diastolic filling. After all, the amplitude of the reflected waves depends on the arterioles and on the hindrance imposed by the left side of the heart. The value for effective elastance takes into account all of the factors that may hinder ventricular empty-

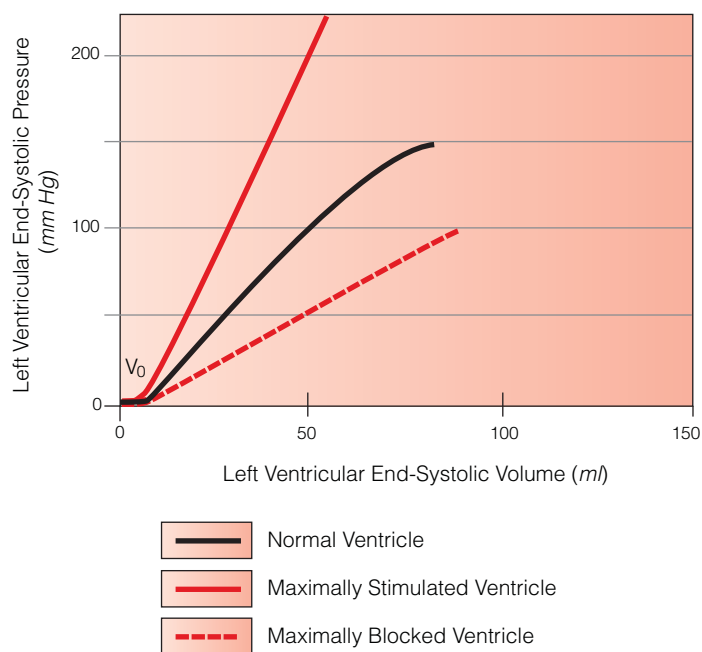


Figure 7 Shown is LVESP plotted against LVESV at end-systole, as seen in a normal ventricle, a maximally stimulated ventricle, and a maximally blocked ventricle. Once the LVESV exceeds the unstressed volume (V_0), the LVESP increases in a fairly linear way. The energy-generating potential of the three ventricles can be taken as the slopes of the relations: 2.0, 4.0, and 1.0 mm Hg/ml, respectively [see Figure 5].

ing.) A normal value for the effective elastance of the pulmonary artery in a 60 kg person is 0.2 mm Hg/ml. In severe pulmonary disease (as is seen with ARDS), the effective elastance can increase by as much as a factor of 8. The hindrance faced by the ventricle can be enormous.

It is difficult to measure the effective aortic root elastance in the ICU, but accurate measurements can be made in the catheterization laboratory.⁷ The problem is estimating the aortic root end-systolic pressure. In the ICU, however, one will know that the pressure in the aortic root at end-systole (and the LVESP) must be higher than the mean pressure. One can make an educated guess as to how much higher it will be, based on the patient's age, the presence or absence of underlying disease processes (e.g., diabetes), and whether the patient is receiving any agents (e.g., an alpha agonist) that would be expected to increase the elastance of the arteries in the systemic circulation. Once one has a reasonable estimate of the aortic root end-systolic pressure, one can use the stroke volume, obtained from measurements made by the Swan-Ganz catheter, to calculate the effective elastance of the aortic root. A normal value is 1.0 mm Hg/ml.² In a patient who is experiencing a severe hypertensive crisis or a patient who has been given pressors (perhaps without full consideration of the consequences), it might increase by a factor of 4. With inflammatory states, it might be as low as 0.5 mm Hg/ml.

VENTRICULAR-ARTERIAL COUPLING

In addressing the problem of ventricular-arterial coupling, it is useful to start by considering the pressure-volume relations in a ventricle and in the root of the artery receiving the energy from the ventricle. We will use the left side of the circulation for illustration, though we could just as well use the right side, which in some surgical patients is the critical side (and which is easier to analyze by

using data from a Swan-Ganz catheter). There is more information in the literature about the left side of the circulation, however, and more options are available for intervention on that side. Regardless of which side of the heart is considered, the concepts are the same.

The left ventricle is stiff at end-systole.³ If the intraventricular pressure is plotted as a function of the intraventricular volume at end-systole, a fairly straight line will be generated [see Figure 7]. The slope of this line is the end-systolic elastance, which, as noted (see above), can serve as a descriptor for the energy-producing capabilities of the ventricle.

The x-intercept of the relation is not 0 but a value slightly greater than 0. This is an example of an unstressed volume. A typical value for the end-systolic unstressed volume in a 60 kg person is quite low, on the order of 6 ml. In patients with severe congestive heart failure, the unstressed volume can be as high as 60 ml, as a manifestation of a globally flabby heart, but in most patients, it can be assumed to be close to 0 ml.

The slope of the line can then be approximated as the LVESP divided by the LVESV.⁸⁰ Other points on the line can also be used to make this calculation, but they will not be known unless one is in the catheterization laboratory and can make sophisticated measurements of both pressure and volume as end-diastolic volumes or vascular impedances are altered. Accordingly, the aforementioned approximation is the most clinically useful calculation. The plot will look quite different in a person with maximal beta-adrenergic stimulation or a person with maximal beta blockade [see Figure 7].

The pressure-volume relation for the aortic root can be plotted on a graph in a similar fashion [see Figure 8]. In this case, the LVESV is still plotted on the x-axis, whereas the end-systolic pressure in the aortic root is plotted on the y-axis. This relation depends on the LVEDV. The example of a normal, resting 60 kg

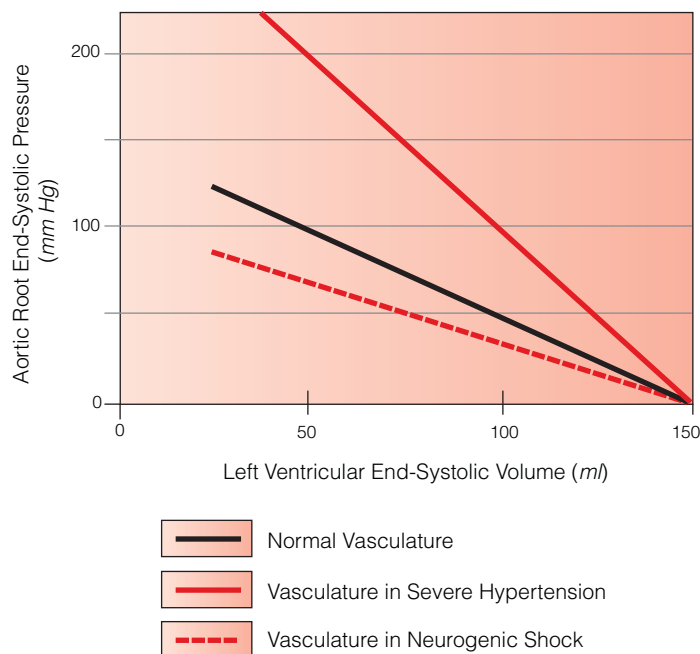


Figure 8 Shown is aortic root end-systolic pressure plotted against LVESV, as seen in a normal vasculature, the vasculature of a patient with severe hypertension, and the vasculature of a patient in neurogenic shock. The LVEDV is assumed to be 150 ml. The magnitudes of the slopes of the relations for the three vasculatures (1.0, 2.0, and 0.75 mm Hg/ml, respectively) can be taken to represent the hindrances facing the ventricles.

person with an LVEDV of 150 ml will illustrate this point. If the LVESV is 150 ml, the stroke volume will be 0 ml; if the stroke volume is 0 ml, the heart will generate no energy for filling the aortic root, and the end-systolic aortic root pressure will be 0 mm Hg. If, however, the LVESV is 50 ml (a normal value) and the LVEDV is held constant at 150 ml, the stroke volume will be 100 ml; a stroke volume of 100 ml in a normal, resting person will generate an aortic root end-systolic pressure of 100 mm Hg.

If points representing these two scenarios are plotted on the graph, a line can be drawn between them to represent the relation between the end-systolic pressure in the aortic root and the LVESV. The magnitude of the slope of this line is calculated by dividing the aortic root end-systolic pressure by the stroke volume. In this case, the calculation yields a value of 1.0 mm Hg/ml. This value can be taken as the effective elastance of the aortic root at end-systole, which, in turn, can be taken as a single-number representation of the hindrance (impedance) facing the left ventricle. Different values will be obtained in a patient with severe hypertension or a patient in neurogenic or warm septic shock [see Figure 8].

To deal with the problem of ventricular-arterial coupling, one then plots the two pressure-volume relations (for the left ventricle and the aortic root) at end-systole on the same graph [see Figure 9]. The LVESP must equal the end-systolic pressure in the aortic root. (In fact, the pressures throughout most of systole, with the exception of isovolumic contraction, are about the same.) The only point on the graph where the two pressures are equal is the point where the two lines intersect. This point defines the specific end-systolic volume and pressure for a patient with a specific unstressed ventricular end-systolic volume, a specific ventricular end-systolic elastance, a specific end-diastolic volume, and a specific effective aor-

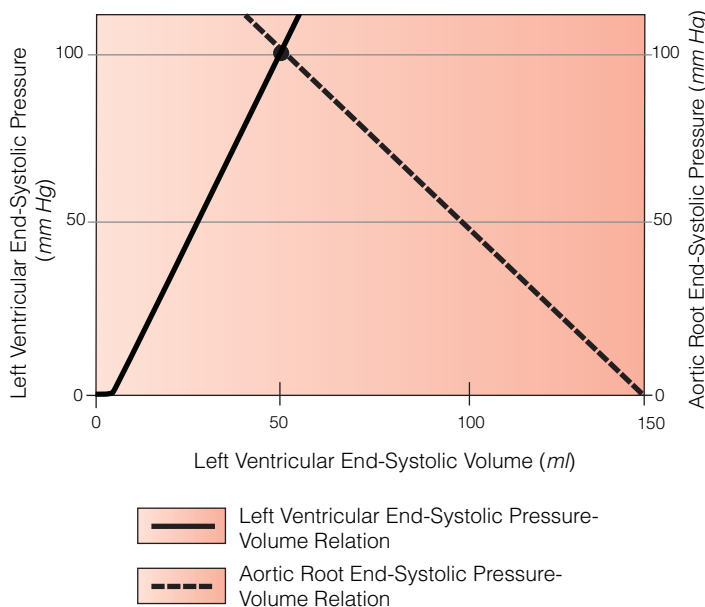


Figure 9 Illustrated is the superposition of the normal pressure-volume relation for the left ventricle at end-systole [see Figure 7] onto the normal pressure-volume relation for the aortic root at end-systole [see Figure 8]. The two pressures must be the same. Thus, in this case, the LVESV must be 50 ml, and both the LVESP and the aortic root end-systolic pressure must be 100 mm Hg (point C in Figures 5 and 10). That is, the end-systolic point is determined by the end-systolic unstressed volume, the ventricular end-systolic elastance, the ventricular end-diastolic volume, and the effective arterial elastance.

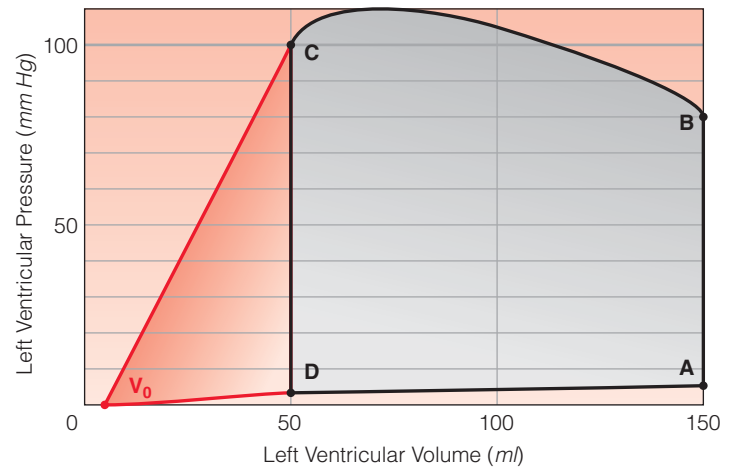


Figure 10 Illustrated is the pressure-volume relation for the left ventricle over an entire cardiac cycle. The work done on the left ventricle during diastole (or, equivalently, the energy added to the ventricle during systole) is the area under the curve DA. The energy added to the aortic root by virtue of ventricular contraction is the area contained within the loop ABCD. The total energy added to the aortic root during a single heartbeat is the sum of these two areas. The heat dissipated in the ventricular wall during isovolumic relaxation is equal to the area contained within the triangle CV_0D .

tic elastance. That is, this graphic analysis allows one to predict how a particular ventricle with particular characteristics will interact with an arterial system with a particular impedance.¹⁻³

PRESSURE-VOLUME LOOPS AND THERMODYNAMICS OF VENTRICULAR CONTRACTION

The next step is to draw a pressure-volume loop for the ventricle, working on the assumption that the unstressed end-systolic volume, the ventricular end-systolic elastance, the end-diastolic volume, and the effective aortic elastance are known. Typical values would be 6 ml, 2 mm Hg/ml, 150 ml, and 1 mm Hg/ml, respectively. From the analysis previously described (see above), it follows that the end-systolic volume will be 50 ml and the end-systolic pressure will be 100 mm Hg [see Figure 10].

At the beginning of systole (point A), the ventricle has a volume of 150 ml and an end-diastolic pressure of 8 mm Hg (if the patient is breathing spontaneously). The ventricle then contracts until the pressure in the chamber exceeds the pressure in the aortic root and the aortic valve opens (point B).

As the blood contained in the ventricle is pushed into the aortic root, ventricular volume decreases until end-systole (point C) is reached. It should be kept in mind that the pressure inside the ventricle at any time during ventricular emptying is determined by the balance between the volume and the stiffness of the chamber at that time. The pressure increases from the beginning of ventricular emptying to, roughly, the midportion of systole. That is, the effect of the rapidly increasing stiffness of the ventricle [see Figure 5] overcomes the effect of the decreasing volume as the ventricle empties. From the midportion of systole to end-systole, the effect of the decreasing volume starts to dominate as it overcomes the still-increasing stiffness, and the pressure gradually falls.

No work is done on the aortic root during isovolumic contraction, from point A to point B. (The volume of the ventricle is unchanged.) Work is, however, done on the aortic root from the opening of the aortic valve to end-systole, from point B to point C. (In fact, this is the only time during the cardiac cycle when work is being done on the aortic root.)

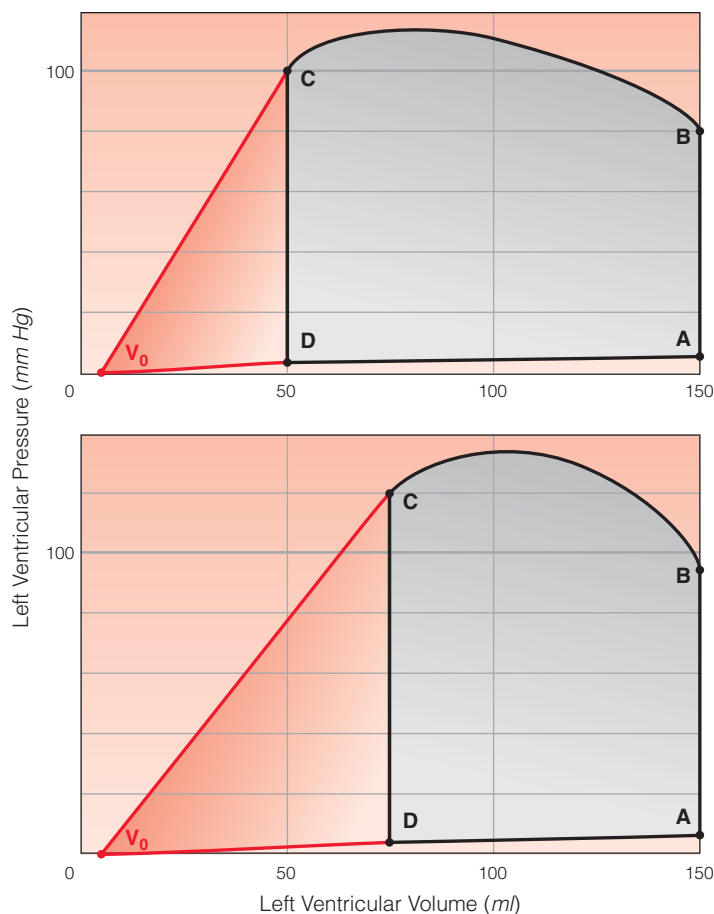


Figure 11 Shown are two pressure-volume loops generated by different ratios of effective aortic elastance to left ventricular end-systolic elastance. If the aortic root elastance is approximately half the ventricular end-systolic elastance (a), as in a normal resting subject, the ventricle will produce its work with optimal efficiency. If the aortic elastance equals the ventricular elastance (b), as when the same subject is given a vasoconstrictor, the pressure will increase and the ventricle will produce slightly more work, but substantially more energy will be wasted in the form of heat dissipation during isovolumic relaxation. If the vasoconstrictor is given to produce a higher pressure that is even higher, the work will begin to fall off, and the energy wasted as heat dissipated in the ventricular wall will increase even more.

The actin and myosin myofilaments then suddenly disengage at end-systole (point C), and the ventricle switches from its maximally contracted state to an increasingly compliant one. The result is another isovolumic phase as the ventricular pressure drops to its lowest value during the cardiac cycle at the beginning of diastolic filling (point D).

Although no work is done during isovolumic relaxation (the phase involves no change in volume), the ventricle loses energy: it started out, at end-systole (point C), with a high pressure and a set volume, but it ended up, at the beginning of diastole (point D), with a low pressure and the same volume. This energy was not used for work, did not generate any appreciable sound, and did not produce any kinetic energy; therefore, it must have been lost in the form of heat, as the actin and myosin filaments lost the chemical energy that was binding them together.

Finally, the chamber fills again and returns to its initial state, from point D to point A. During this time, work is being done on the ventricle by the energy produced from contraction of the left

atrium and by the residual energy pushed into the left side of the heart from contraction of the right ventricle.

The work done on the ventricle during diastole is represented by the area under the diastolic pressure-volume curve and the x-axis, which is approximately equal to the mean diastolic pressure multiplied by the stroke volume. The work done on the aortic root by the contraction of the ventricle is represented by the area contained within the curve, or the difference between the end-systolic and mean diastolic pressures multiplied by the stroke volume. The total work done on the aortic root with each cardiac cycle is represented by the entire area under the curve, down to the x-axis. It can be approximated as the end-systolic pressure multiplied by the stroke volume.

Also illustrated is the wasted energy associated with the loop (i.e., the energy lost in the form of heat dissipated in the ventricular wall during isovolumic relaxation). This variable is represented by the area contained within a triangle whose apices are the points V₀, D, and C (i.e., the unstressed volume, the beginning of diastolic filling, and end-systole).

The major problem in managing the patient in shock is to balance cardiac energy production against edema formation and myocardial oxygen requirements. The total amount of energy transmitted into the aortic root per minute is the total work done on the root per heartbeat multiplied by the heart rate. The total amount of heat dissipated in the ventricular wall during isovolumic relaxation is the area of the aforementioned triangle multiplied by the heart rate. The left-side oxygen requirements for the myocardium are directly proportional to the sum of the total amount of power produced and the total amount of heat dissipated in the ventricular wall. Thus, in considering cardiac energy production in the context of edema formation and myocardial oxygen requirements, the pressure-volume loop, along with the heart rate, tells one everything that one needs to know.

Construction of the pressure-volume loop for a ventricle requires knowledge of the ventricular end-systolic unstressed volume, the ventricular end-systolic elastance, the end-diastolic volume, and the effective arterial elastance. Even if exact values for these variables are not available, one will generally have some feeling for them, both on clinical grounds and from measurements made with invasive monitoring. One can then predict how these variables will affect the loop [see Figures 7, 8, 9, 10, and 11], as well as envision how intervention will affect the loop, for better or worse [see Figure 11].

The analysis can be done either graphically [see Figure 11] or mathematically [see Table 5]. In either case, it will allow one to predict how an intervention will affect the abnormality (given the uncertainty of some of the measurements that will be available) and the costs of correcting the abnormality by a particular intervention. Once the analysis is complete, the remaining task is to decide what the goals of resuscitation should be and how they should be achieved.

Goals for Cardiovascular Resuscitation in Treatment of Shock

Efforts have been made to avoid using any invasive cardiovascular measurements in resuscitation from severe shock (e.g., by using gastric mucosal pH as an end point for resuscitation), but to date, such efforts have not proved helpful outside carefully controlled research environments. There is wide agreement that invasive monitoring is still needed in the treatment of severe shock; however, there is no consensus on what to do with the values obtained from monitoring.

Table 6 Effects of Position and Strenuous Exercise on Cardiovascular Volumes and Pressures in a Young, Well-Conditioned 60 kg Woman

Variables	Supine (Resting)	Upright (Resting)	Upright (Exercising)
Lower-body venular volume (ml)	1,920	> 1,920	< 1,920
Lower-body venular pressure (mm Hg)	20	> 20	< 20
Upper-body venular volume (ml)	960	< 960	> 960
Upper-body venular pressure (mm Hg)	10	< 10	> 10
Right ventricular end-diastolic volume (ml)	150	133	145
Right ventricular end-diastolic pressure (mm Hg)	5	5	5
Right ventricular and pulmonary arterial end-systolic pressure (mm Hg)	22.5	22.5	35
Mean pulmonary arterial pressure (mm Hg)	15	15	20
Left ventricular end-diastolic volume (ml)	150	133	145
Left ventricular end-diastolic pressure (mm Hg)	8	8	8
Left ventricular and aortic root end-systolic pressure (mm Hg)	100	100	145
Mean aortic pressure (mm Hg)	90	90	110

One approach is to try to find a single parameter that can serve as the goal of resuscitation. The best candidate parameter is probably the $S_{mv}O_2$, measured with a pulmonary arterial catheter. This value can be quite helpful in minute-to-minute management during resuscitation from hemorrhagic shock. It is considerably less helpful, however, for resuscitation of patients in inflammatory shock, who often have quite high $S_{mv}O_2$ values, partly because of peripheral shunting through the cutaneous vasculature and partly because of functional shunting by cells that cannot metabolize the oxygen presented to them. In the setting of inflammatory shock, a high $S_{mv}O_2$ may even indicate a severe metabolic derangement rather than resolution of shock.

Another approach is to attempt to determine whether the patient's oxygen consumption (measured with a pulmonary arterial catheter and based in part on measurements of cardiac output) depends on oxygen delivery (the product of cardiac output, hemoglobin concentration, and arterial oxygen saturation). Unquestionably, at very low levels of oxygen delivery, oxygen consumption must decrease. At excessively high levels, however, oxygen consumption may continue to rise if oxygen delivery is increased by the administration of inotropes. These agents usually have beta-adrenergic effects and can increase peripheral oxygen metabolism; they also increase myocardial oxygen requirements. Thus, the act of increasing delivery can increase overall consumption.

Yet another approach is to maintain all patients at very high levels of oxygen delivery without making any attempt to ascertain whether there is a correlation between delivery and peripheral consumption. Two randomized trials evaluated this approach; neither found any evidence of benefit.^{87,88}

Our approach is to start, as any clinician would, by attempting to resolve the clinical abnormalities observed without subjecting the patient to invasive monitoring. If this attempt is unsuccessful, we insert monitoring catheters and use the information obtained from them to try to achieve reasonable ventricular power production with acceptable efficiency while minimizing the formation of edema. This approach is supported by a compelling study that underscored the value of taking a thermodynamic approach to resuscitation and indicated that the goal for resuscitation of the typical shock patient need be little more than a reasonable blood pressure and a reasonable cardiac output.

We do, however, set different treatment goals for different patients, depending on individual patient requirements and capabilities (see above). In general, the hearts of well-conditioned per-

sons can do more than those of poorly conditioned persons, and young hearts are more capable than old ones. Measurements of organ blood flows from the exercise physiology literature can help put this observation in perspective [see Tables 6 and 7].^{4,5,74,89-106} As

Table 7 Effects of Position and Exercise on Organ Blood Flow and Oxygen Consumption in a Young, Well-Conditioned 60 kg Woman

Variables	Supine (Resting)	Upright (Resting)	Upright (Exercising)
Whole body			
Blood flow (L/min)	6.0	5.0	22.0
Venous O ₂ saturation	76%	71.6%	11%
O ₂ consumption (ml/min)	210	210	3,180
Splanchnic viscera			
Blood flow (L/min) (% of total)	1.50 (25%)	1.25 (25%)	0.30 (1%)
Venous O ₂ saturation	77%	73%	18%
O ₂ consumption (ml/min)	50	50	40
Kidneys			
Blood flow (L/min) (% of total)	1.20 (20%)	1.00 (20%)	0.25 (1%)
Venous O ₂ saturation	91%	90%	65%
O ₂ consumption (ml/min)	12	12	12
Brain			
Blood flow (L/min) (% of total)	0.90 (15%)	0.75 (15%)	0.75 (3%)
Venous O ₂ saturation	67%	60%	59%
O ₂ consumption (ml/min)	45	45	45
Heart			
Blood flow (L/min) (% of total)	0.24 (4%)	0.20 (4%)	0.80 (4%)
Venous O ₂ saturation	46%	35%	1%
O ₂ consumption (ml/min)	20	20	130
Skeletal muscle			
Blood flow (L/min) (% of total)	1.20 (20%)	1.00 (20%)	19.5 (89%)
Venous O ₂ saturation	61%	54%	8%
O ₂ consumption (ml/min)	70	70	2,940
Skin			
Blood flow (L/min) (% of total)	0.30 (5%)	0.25 (5%)	0.30 (1%)
Venous O ₂ saturation	93%	91%	88%
O ₂ consumption (ml/min)	2	2	2
Other organs			
Blood flow (L/min) (% of total)	0.66 (11%)	0.55 (11%)	0.10 (0%)
Venous O ₂ saturation	87%	85%	31%
O ₂ consumption (ml/min)	11	11	11

an example, in strenuous exercise, cardiac output can increase by a factor of 3 to 4. Blood flow to the splanchnic viscera and the kidneys can fall to levels as low as 20% of normal, with no long-term ill effects. (The organs survive by extracting a higher percentage of the oxygen delivered to them.) During strenuous but not exhausting exercise in a warm environment, blood flow to the skin can increase from a baseline of 300 ml/min to levels as high as 6 L/min in an effort to offload heat and keep body temperature within acceptable limits. (We are not aware of any studies that have measured blood flow to the skin of patients in inflammatory shock, but we suspect that it may be as high as 3 L/min for a 60 kg person.)

To achieve the treatment goals, we begin by establishing adequate ventricular end-diastolic volumes. An inadequate end-diastolic volume cannot be compensated for, no matter what is done with the ventricular end-systolic elastance or effective aortic elastance. Inadequate ventricular end-systolic elastances can be compensated for with volume administration, up to a point, and low arterial impedances often do not require any compensation at all—the low hindrances may represent a compensatory response aimed at optimizing the efficiency with which energy is transmitted from the ventricle into the aortic root.

Surgeons are ideally suited to managing the problems associated with inadequate ventricular end-diastolic volumes. They know how to control bleeding; their technical training allows them to gain vascular access safely; they can decompress compartments subjected to excessively high pressures; and they appreciate the adverse consequences of not promptly addressing inadequate ventricular end-diastolic volumes. No surgeon likes dealing with an anastomotic breakdown, and no surgeon enjoys having to treat an overwhelming infection.

At the same time, it is important to remember that one must be judicious when administering fluid in an attempt to ensure adequate ventricular end-diastolic volumes. There is no thermodynamic free lunch. Unnecessary administration of fluid creates edema; excessively large end-ventricular volumes increase myocardial oxygen requirements unnecessarily. If one is unsure how best to balance the competing requirements of treatment, one should employ invasive monitoring to obtain additional information.

Invasive monitoring will allow one to adjust the RVEDV and LVEDV more precisely and to proceed with the next step—namely, adjusting the effective arterial elastances so that they are appropriately matched to the ventricular end-systolic elastances. The goal is to achieve adequate production of useful power while minimizing myocardial oxygen requirements. If the effective arterial elastance is adjusted so that it equals the estimated ventricular end-systolic elastance, maximum work per heartbeat will be achieved, but a substantial amount of heat will be dissipated in the ventricular wall during isovolumic relaxation [see *Figure 11 and Table 5*]. If the effective aortic elastance is adjusted so that it is approximately half the ventricular end-systolic elastance, less work will be done, but substantially less heat will be dissipated; thus, useful power will be produced much more efficiently. If the effective aortic elastance is allowed to exceed the ventricular end-systolic elastance, the pressure will increase, but the work produced will fall off and the myocardial oxygen requirements will increase—a situation that is rarely good for the patient.

For cases of hypovolemic and inflammatory shock, we start with the effective pulmonary arterial elastance. In these settings, this value frequently is excessively high: it is not unusual to see pulmonary arterial elastances that exceed the maximal right ventricular end-systolic elastance, which typically is on the order of 0.8 mm Hg/ml. There is no benefit to such a mismatch. Accordingly, we try to decrease the pulmonary arterial elastance through adjustment of

the ventilator, diuresis (if feasible), and, possibly, surgical decompression of the abdomen. We do not try to work on the effective aortic root elastance at this juncture; we do that later, if at all.

For cases of cardiogenic shock, we generally start with the effective aortic root elastance instead. In this setting, this value frequently is greater than the left ventricular end-systolic elastance. If the myocardium is badly compromised, the ventricular end-systolic elastance may be as low as 1.0 mm Hg/ml. If the effective aortic root elastance exceeds this value, the heart will be working inefficiently. Accordingly, we try to decrease the effective aortic elastance if possible, either with diuretics or with vasodilators. In some cases, this cannot be done. For example, a high systemic arterial pressure may be required for perfusion of the myocardium, especially in a patient who has coronary disease or a hypertrophied ventricle. It is important to remember, however, that a high aortic elastance comes at a price. One can always maintain a high arterial pressure, either by not trying to reduce it or by giving vasoconstrictors, but if the high pressure results in excessive myocardial oxygen requirements, one may be doing more harm than good.

After dealing with the end-diastolic volumes and the effective arterial elastances on both sides of the circulation, we turn to the ventricular end-systolic elastances. We find inotrope therapy to be advantageous at this stage. Increasing the ventricular end-systolic elastances will increase the stroke volume, the blood pressure, and the work done per heartbeat by the ventricle on the vasculature. If the inotrope increases the heart rate, it will increase the power generated by the ventricle (by increasing the cardiac output—the stroke volume multiplied by the heart rate).

In the case of hypovolemic and inflammatory shock, inotrope therapy usually does not have much of a downside. Most patients' ventricles will be able to deal with the increased oxygen requirements. In the case of cardiogenic shock, however, one might be willing to sacrifice some of the ventricular end-systolic elastance in order to reduce the elevated oxygen requirements induced by high intracellular calcium concentrations and to bring down the heart rate. The heart rate can be an extremely important consideration in this setting, for several reasons. To begin with, myocardial oxygen requirements are a linear function of the heart rate: doubling the heart rate doubles the oxygen requirements. Furthermore, increasing the heart rate may increase the impedance of the vasculature; the heart may beat so rapidly that the energy wave created by the previous ventricular contraction returns during the systole of the current contraction. In addition, a rapid heart rate may limit the time available for ventricular filling during diastole.

As a final measure, we increase the effective aortic root end-systolic elastance. It should be clear from the preceding discussion, however, that we prefer not to do this if it can be avoided. Most surgical patients have intact autonomic nervous systems and are not anesthetized. Furthermore, most surgical patients have good hearts. In the case of trauma or an emergency, any patient with a hopelessly failing heart would never have survived the injury or the initial insult imposed by the illness. In the case of elective surgery, a failing heart would usually have been noticed by the surgeon, who then would probably have attempted to modify the surgical approach to the problem or, perhaps, declined to operate on the patient in the first place. The low blood pressure in the upper extremity might be a manifestation of adjustments to a physiologic state that has complex undercurrents. It might reflect the need to offload heat to the environment; it might reflect the need to optimize the efficiency with which the heart interacts with the vasculature; or it might reflect a peculiarity of the measurement of the pressure (e.g., the pressure in the root of the aorta might be adequate even though the pressure in the arm might suggest other-

wise). One must pay attention to the blood pressure when managing a patient in shock, but not to the exclusion of other critical considerations. A balanced perspective is needed.

Vasoconstrictors will increase the blood pressure, but they may do so at the cost of reducing the amount of useful energy delivered into the arterial system if the effective arterial elastance already exceeds the ventricular end-systolic elastance. They will always increase the amount of oxygen required by the ventricle. Moreover, on the assumption that the effective aortic elastance ends up being greater than one half of the left ventricular end-systolic elastance, vasoconstrictors will always reduce the efficiency of energy production.

Conclusion

We thank those readers who have followed us thus far. We admit that none of this material is easy going, and we acknowledge that not everyone has the same love for the topic that we do. Moreover, we concede that the practical utility of some of the concepts we have discussed may not always be immediately obvious. At the same time, however, we maintain that these concepts, correctly understood and properly applied, can be of great value in the treatment of shock, and we hope we have given some indication as to why we believe this to be so.

Cardiovascular physiology is close to unique among the biologic sciences, in that it is one of the few biologic disciplines that are based on the physical sciences (the others might be membrane physiology and pulmonary physiology), as well as one of the few

that can be described mathematically. The cardiovascular system has an elegance all its own. One can readily think about it in theoretical, even mathematical, terms and then apply that thinking to understanding and treating abnormalities. This is not to say that one's theoretical analysis will always be on target. Currently available measurements in the ICU still do not provide all of the information that one would like to have, as is illustrated by the problems associated with not knowing the ventricular unstressed volumes and the difficulties associated with making reliable measurements on the left side of the heart.

To us, the uncertainties surrounding cardiovascular physiology are a large part of what makes cardiovascular problems interesting. There are some problems that can only be addressed through trial and evaluation. If the patient is being monitored, it is relatively easy to determine the correctness of an intervention. In general, all one need do is try the intervention and then see what happens to the cardiac output and the vascular pressures. If the intervention fails, one can then try something else. If the intervention is successful, one knows that the hypothesis that led to the intervention was probably correct. (We say "probably" because there is still a possibility that the favorable response was a coincidence; one may just have been lucky.)

In any case, the response, whether favorable or not, will usually be evident within a short time. Sometimes, one will know in a matter of minutes that the chosen intervention was the right thing for the patient. The satisfaction to be gained from quick and definitive management of a complicated and serious cardiovascular problem can be enormous.

References

1. Nichols WW, O'Rourke MF, Hartley C, et al: McDonald's Blood Flow in Arteries: Theoretic, Experimental, and Clinical Principles. Arnold-Oxford University Press, London-New York, 1998
2. Asanoi H, Sasayama S, Kameyama T: Ventriculoarterial coupling in normal and failing heart in humans. *Circ Res* 65:483, 1989
3. Suga H: Ventricular energetics. *Physiol Rev* 70:247, 1990
4. Roddie IC: Circulation to skin and adipose tissue. *Handbook of Physiology*, vol III, section 2. Geiger SR, Shepherd JT, Abboud FM, Eds. Waverly Press, Baltimore, 1983, p 285
5. Rowell LB: Cardiovascular adjustments to thermal stress. *Handbook of Physiology*, vol III, section 2. Geiger SR, Shepherd JT, Abboud FM, Eds. Waverly Press, Baltimore, 1983, p 967
6. Kraut EJ, Chen S, Hubbard NE, et al: Tumor necrosis factor depresses myocardial contractility in endotoxemic swine. *J Trauma* 46:900, 1999
7. Kelly RP, Ting CT, Yang TM, et al: Effective arterial elastance as index of arterial vascular load in humans. *Circulation* 86:513, 1992
8. Suga H: Total mechanical energy of a ventricle model and cardiac oxygen consumption. *Am J Physiol* 236:H498, 1979
9. Jones DW, Appel LJ, Sheps SG, et al: Measuring blood pressure accurately: new and persistent challenges. *JAMA* 289:1027, 2003
10. Victorino GP, Battistella FD, Wisner DH: Does tachycardia correlate with hypotension after trauma? *J Am Coll Surg* 196:679, 2003
11. Demetriades D, Chan LS, Bhasin P, et al: Relative bradycardia in patients with traumatic hypotension. *J Trauma* 45:534, 1998
12. Brasel KJ, Guse C, Gentilello LM, et al: Heart rate: is it truly a vital sign? *J Trauma* 62:812, 2007
13. Aubier M, Trippenbach T, Roussos C: Respiratory muscle fatigue during cardiogenic shock. *J Appl Physiol* 51:499, 1981
14. Davis JO, Freeman RH: Mechanisms regulating renin release. *Physiol Rev* 56:1, 1976
15. Share L: Role of vasopressin in cardiovascular regulation. *Physiol Rev* 68:1248, 1988
16. Gore JM, Goldberg RJ, Spodick DH, et al: A community-wide assessment of the use of pulmonary artery catheters in patients with acute myocardial infarction. *Chest* 92:721, 1987
17. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. The Acute Respiratory Distress Syndrome Network. *N Engl J Med* 342:1301, 2000
18. Rankin JS, Olsen CO, Arentzen CE, et al: The effects of airway pressure on cardiac function in intact dogs and man. *Circulation* 66:108, 1982
19. Mayberry JC, Welker KJ, Goldman RK, et al: Mechanism of acute ascites formation after trauma resuscitation. *Arch Surg* 138:773, 2003
20. Jones RM, Moulton CE, Hardy KJ: Central venous pressure and its effect on blood loss during liver resection. *Br J Surg* 85:1058, 1998
21. Balogh Z, McKinley BA, Cocanour CS, et al: Supranormal trauma resuscitation causes more cases of abdominal compartment syndrome. *Arch Surg* 138:637, 2003
22. Derouin M, Couture P, Boudreault D, et al: Detection of gas embolism by transesophageal echocardiography during laparoscopic cholecystectomy. *Anesth Analg* 82:119, 1996
23. Sawyer RW, Bodai BI, Blaisdell FW, et al: The current status of intraosseous infusion. *J Am Coll Surg* 179:353, 1994
24. McGee DC, Gould MK: Preventing complications of central venous catheterization. *N Engl J Med* 348:1123, 2003
25. Deshpande KS, Hatem C, Ulrich HL, et al: The incidence of infectious complications of central venous catheters at the subclavian, internal jugular, and femoral sites in an intensive care unit population. *Crit Care Med* 33:13, 2005
26. Goetz AM, Wagener MM, Miller JM, et al: Risk of infection due to central venous catheters: effect of site of placement and catheter type. *Infect Control Hosp Epidemiol* 19:842, 1998
27. Trotter SJ, Veremakis C, O'Brien J, et al: Femoral deep vein thrombosis associated with central venous catheterization: results from a prospective, randomized trial. *Crit Care Med* 23:52, 1995
28. Macnab A, Christenson J, Findlay J, et al: A new system for sternal intraosseous infusion in adults. *Prehosp Emerg Care* 4:173, 2000
29. Calkins MD, Fitzgerald G, Bentley TB, et al: Intraosseous infusion devices: a comparison for potential use in special operations. *J Trauma* 48:1068, 2000
30. Wilmore DW: Metabolic response to severe surgical illness: overview. *World J Surg* 24:705, 2000
31. Finfer S, Bellomo R, Boyce N, et al: A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 350:2247, 2004
32. Moon PF, Hollyfield-Gilbert MA, Myers TL, et al: Fluid compartments in hemorrhaged rats after hyperosmotic crystalloid and hyperoncotic colloid resuscitation. *Am J Physiol* 270:F1, 1996
33. Myburgh J, Cooper J, Finfer S, et al: Saline or

- albumin for fluid resuscitation in patients with traumatic brain injury. *N Engl J Med* 357:874, 2007
34. Collis RE, Collins PW, Gutteridge CN, et al: The effect of hydroxyethyl starch and other plasma volume substitutes on endothelial cell activation; an in vitro study. *Intensive Care Med* 20:37, 1994
 35. Treib J, Haass A, Pindur G: Coagulation disorders caused by hydroxyethyl starch. *Thromb Haemost* 78:974, 1997
 36. Boldt J, Dücke M, Kumle B, et al: Influence of different volume replacement strategies on inflammation and endothelial activation in the elderly undergoing major abdominal surgery. *Intensive Care Med* 30:416, 2004
 37. Huttner I, Boldt J, Haisch G, et al: Influence of different colloids on molecular markers of haemostasis and platelet function in patients undergoing major abdominal surgery. *Br J Anaesth* 85:417, 2000
 38. Roberts I, Alderson P, Bunn F, et al: Colloids versus crystalloids for fluid resuscitation in critically ill patients. *Cochrane Database Syst Rev* (4):CD000567, 2004
 39. Vassar MJ, Fischer RP, O'Brien PE, et al: A multicenter trial for resuscitation of injured patients with 7.5% sodium chloride: the effect of added dextran 70. The Multicenter Group for the Study of Hypertonic Saline in Trauma Patients. *Arch Surg* 128:1003, 1993
 40. Alam HB, Koustova E, Rhee P: Combat casualty care research: from bench to the battlefield. *World J Surg* 29(suppl 1):S7, 2005
 41. Rotstein OD: Novel strategies for immunomodulation after trauma: revisiting hypertonic saline as a resuscitation strategy for hemorrhagic shock. *J Trauma* 49:580, 2000
 42. Horton JW, Maass DL, White DJ: Hypertonic saline dextran after burn injury decreases inflammatory cytokine responses to subsequent pneumonia-related sepsis. *Am J Physiol Heart Circ Physiol* 290:H1642, 2006
 43. Rizoli SB, Rhind SG, Shek PN, et al: The immunomodulatory effects of hypertonic saline resuscitation in patients sustaining traumatic hemorrhagic shock: a randomized, controlled, double-blinded trial. *Ann Surg* 243:47, 2006
 44. Deitch EA, Shi HP, Feketeova E, et al: Hypertonic saline resuscitation limits neutrophil activation after trauma-hemorrhagic shock. *Shock* 19:328, 2003
 45. Mazzoni MC, Borgstrom P, Intaglietta M, et al: Capillary narrowing in hemorrhagic shock is rectified by hyperosmotic saline-dextran reinfusion. *Circ Shock* 31:407, 1990
 46. Angle N, Hoyt DB, Coimbra R, et al: Hypertonic saline resuscitation diminishes lung injury by suppressing neutrophil activation after hemorrhagic shock. *Shock* 9:164, 1998
 47. Holcomb JB: The 2004 Fitts Lecture: current perspective on combat casualty care. *J Trauma* 59:990, 2005
 48. Marik PE, Sibbald WJ: Effect of stored-blood transfusion on oxygen delivery in patients with sepsis. *JAMA* 269:3024, 1993
 49. Raghavan M, Marik PE: Anemia, allogenic blood transfusion, and immunomodulation in the critically ill. *Chest* 127:295, 2005
 50. Zallen G, Offner PJ, Moore EE, et al: Age of transfused blood is an independent risk factor for postinjury multiple organ failure. *Am J Surg* 178:570, 1999
 51. Agarwal N, Murphy JG, Cayten CG, et al: Blood transfusion increases the risk of infection after trauma. *Arch Surg* 128:171; discussion 176-7, 1993
 52. Moore FA, Moore EE, Sauaia A: Blood transfusion: an independent risk factor for postinjury multiple organ failure. *Arch Surg* 132:620, 1997
 53. Vincent JL, Baron JF, Reinhart K, et al: Anemia and blood transfusion in critically ill patients. *JAMA* 288:1499, 2002
 54. Hebert JR, Peterson KE, Hurley TG, et al: The effect of social desirability trait on self-reported dietary measures among multi-ethnic female health center employees. *Ann Epidemiol* 11:417, 2001
 55. Adrogue HJ, Madias NE: Management of life-threatening acid-base disorders: first of two parts. *N Engl J Med* 338:26, 1998
 56. Bernard GR, Vincent JL, Laterre PF, et al: Efficacy and safety of recombinant human activated protein C for severe sepsis. *N Engl J Med* 344:699, 2001
 57. Barie PS, Williams MD, McCollam JS, et al: Benefit/risk profile of drotrecogin alfa (activated) in surgical patients with severe sepsis. *Am J Surg* 188:212, 2004
 58. Vincent JL, Bernard GR, Beale R, et al: Drotrecogin alfa (activated) treatment in severe sepsis from the global open-label trial ENHANCE: further evidence for survival and safety and implications for early treatment. *Crit Care Med* 33:2266, 2005
 59. Dellinger RP: Recombinant activated protein C: decisions for administration. *Crit Care Med* 34:530, 2006
 60. Cronin L, Cook DJ, Carlet J, et al: Corticosteroid treatment for sepsis: a critical appraisal and meta-analysis of the literature. *Crit Care Med* 23:1430, 1995
 61. Annane D, Sebille V, Charpentier C, et al: Effect of treatment with low doses of hydrocortisone and fludrocortisone on mortality in patients with septic shock. *JAMA* 288:862, 2002
 62. Sibbald WJ, Paterson NA, Holliday RL, et al: The Trendelenburg position: hemodynamic effects in hypotensive and normotensive patients. *Crit Care Med* 7:218, 1979
 63. Mandel MA, Dauchot PJ: Radial artery cannulation in 1,000 patients: precautions and complications. *J Hand Surg [Am]* 2:482, 1977
 64. Slogoff S, Keats AS, Arlund C: On the safety of radial artery cannulation. *Anesthesiology* 59:42, 1983
 65. Bur A, Herkner H, Vlcek M, et al: Factors influencing the accuracy of oscillometric blood pressure measurement in critically ill patients. *Crit Care Med* 31:793, 2003
 66. Geddes LA, Voelz M, Combs C, et al: Characterization of the oscillometric method for measuring indirect blood pressure. *Ann Biomed Eng* 10:271, 1982
 67. Karamanoglu M, O'Rourke MF, Avolio AP, et al: An analysis of the relationship between central aortic and peripheral upper limb pressure waves in man. *Eur Heart J* 14:160, 1993
 68. Gardner RM: Direct blood pressure measurement—dynamic response requirements. *Anesthesiology* 54:227, 1981
 69. Kleinman B, Powell S, Kumar P, et al: The fast flush test measures the dynamic response of the entire blood pressure monitoring system. *Anesthesiology* 77:1215, 1992
 70. Komadina KH, Schenk DA, LaVeau P, et al: Interobserver variability in the interpretation of pulmonary artery catheter pressure tracings. *Chest* 100:1647, 1991
 71. Morris AH, Chapman RH, Gardner RM: Frequency of wedge pressure errors in the ICU. *Crit Care Med* 13:705, 1985
 72. Merrer J, De Jonghe B, Golliot F, et al: Complications of femoral and subclavian venous catheterization in critically ill patients: a randomized controlled trial. *JAMA* 286:700, 2001
 73. Kraut EJ, Owings JT, Anderson JT, et al: Right ventricular volumes overestimate left ventricular preload in critically ill patients. *J Trauma* 42:839; discussion 845-6, 1997
 74. Astrand P, Cuddy TE, Saltin B, et al: Cardiac output during submaximal and maximal work. *J Appl Physiol* 19:268, 1964
 75. Raja SG, Danton MD, MacArthur KJ, et al: Treatment of pulmonary arterial hypertension with sildenafil: from pathophysiology to clinical evidence. *J Cardiothorac Vasc Anesth* 20:722, 2006
 76. van den Horn GJ, Westerhof N, Elzinga G: Optimal power generation by the left ventricle: a study in the anesthetized open thorax cat. *Circ Res* 56:252, 1985
 77. Sunagawa K, Maughan WL, Burkhead D, et al: Left ventricular interaction with arterial load studied in isolated canine ventricle. *Am J Physiol* 245:H773, 1983
 78. Sunagawa K, Maughan WL, Sagawa K: Optimal arterial resistance for the maximal stroke work studied in isolated canine left ventricle. *Circ Res* 56:586, 1985
 79. Chang MC, Meredith JW, Kincaid EH, et al: Maintaining survivors' values of left ventricular power output during shock resuscitation: a prospective pilot study. *J Trauma* 49:26, 2000
 80. Sagawa K: The end-systolic pressure-volume relation of the ventricle: definition, modifications and clinical use. *Circulation* 63:1223, 1981
 81. Piene H: Pulmonary arterial impedance and right ventricular function. *Physiol Rev* 66:606, 1986
 82. O'Rourke MF, Kelly RP: Wave reflection in the systemic circulation and its implications in ventricular function. *J Hypertens* 11:327, 1993
 83. O'Rourke MF, Kelly RP, Avolio AP: *The Arterial Pulse*. Lea & Febiger, Philadelphia, 1992
 84. Kelly R, Hayward C, Avolio A, et al: Noninvasive determination of age-related changes in the human arterial pulse. *Circulation* 80:1652, 1989
 85. Avolio AP, Deng FQ, Li WQ, et al: Effects of aging on arterial distensibility in populations with high and low prevalence of hypertension: comparison between urban and rural communities in China. *Circulation* 71:202, 1985
 86. Avolio AP, Chen SG, Wang RP, et al: Effects of aging on changing arterial compliance and left ventricular load in a northern Chinese urban community. *Circulation* 68:50, 1983
 87. Gattinoni L, Brazzi L, Pelosi P, et al: A trial of goal-oriented hemodynamic therapy in critically ill patients. SvO₂ Collaborative Group. *N Engl J Med* 333:1025, 1995
 88. Hayes MA, Timmins AC, Yau EH, et al: Elevation of systemic oxygen delivery in the treatment of critically ill patients. *N Engl J Med* 330:1717, 1994
 89. Åstrand P-O, Rodahl K: *Textbook of Work Physiology: Physiological Bases of Exercise*. McGraw-Hill, New York, 1986
 90. Bevegård S, Holmgren A, Jonsson B: Circulatory studies in well trained athletes at rest and during heavy exercise, with special reference to stroke volume and the influence of body position. *Acta Physiol Scand* 57:26, 1963
 91. Donald DE: Splanchnic circulation. *Handbook of Physiology*, vol III, section 2. Geiger SR, Shepherd JT, Abboud FM, Eds. Waverly Press, Baltimore, 1983, p 219
 92. Ekblom B, Hermansen L: Cardiac output in athletes. *J Appl Physiol* 25:619, 1968
 93. Heath GW, Hagberg JM, Ehsani AA, et al: A physiological comparison of young and older endurance athletes. *J Appl Physiol* 51:634, 1981
 94. Heistad DD, Kontos HA: Cerebral circulation. *Handbook of Physiology*, vol III, section 2. Geiger SR, Shepard JT, Abboud FM, Eds. Waverly Press, 1983, p 137
 95. Holmberg S, Serzysko W, Varnauskas E: Coronary circulation during heavy exercise in control subjects and patients with coronary heart disease. *Acta Med Scand* 190:465, 1971

96. Janicki JS, Sheriff DD, Robotham JL, et al: Cardiac output during exercise: contribution of the cardiac, circulatory and respiratory systems. *Handbook of Physiology*, section 12. Rowell LB, Shephard JT, Eds. Oxford University Press, New York, 1996, p 649
97. Kitamura K, Jorgensen CR, Gobel FL, et al: Hemodynamic correlates of myocardial oxygen consumption during upright exercise. *J Appl Physiol* 32:516, 1972
98. Knox FG, Spielman WS: Renal circulation. *Handbook of Physiology*, vol III, section 2. Geiger SR, Shephard JT, Abboud FM, Eds. Waverly Press, Baltimore, 1983, p 183
99. Laughlin MH, Korthuis RJ, Duncker DJ, et al: Control of blood flow to cardiac and skeletal muscle during exercise. *Handbook of Physiology*, section 12. Rowell LB, Shephard JT, Eds. Oxford University Press, New York, 1996, p 705
100. Messer JV, Wagman RJ, Levine HJ: Patterns of human myocardial oxygen extraction during rest and exercise. *J Clin Invest* 41:725, 1962
101. Milnor WR: *Cardiovascular Physiology*. Oxford University Press, New York, 1990
102. Pollock ML, Foster C, Knapp D, et al: Effect of age and training on aerobic capacity and body composition of master athletes. *J Appl Physiol* 62:725, 1987
103. Shepherd JT: Circulation to skeletal muscle. *Handbook of Physiology*, vol III, section 2. Geiger SR, Shephard JT, Abboud FM, Eds. Waverly Press, Baltimore, 1983, p 319
104. Rowell LB, O'Leary DS, Kellogg DLJ: Integration of cardiovascular control systems in dynamic exercise. *Handbook of Physiology*, section 12. Rowell LB, Shephard JT, Eds. Oxford University Press, New York, 1996, p 770
105. Wade OL, Bishop JM: *Cardiac Output and Regional Blood Flow*. Blackwell Scientific Publications, Oxford, 1962
106. Wade OL, Bishop JM: The distribution of the cardiac output in normal subjects during exercise. *Cardiac Output and Regional Blood Flow*. Blackwell Scientific Publications, Oxford, 1962, p 95
107. Schmidt-Nielsen K: *Scaling: Why Is Animal Size So Important?* Cambridge University Press, Cambridge, 1994
108. Gephart FC, Dubois AB, Dubois EF: Clinical calorimetry: the basal metabolism of normal adults with special reference to surface area. *Arch Int Med* 17:902, 1916
109. Grollman A: Physiologic variations in the cardiac output of man. *Am J Physiol* 90:210, 1929
110. Kleiber M: Body size and metabolic rate. *Physiologic Reviews* 27:511, 1947
111. West GB, Brown JH, Enquist BJ: The fourth dimension of life: fractal geometry and allometric scaling of organisms. *Science* 284:1677, 1999
112. Brandfonbrener M, Landowne M, Shock NW: Changes in cardiac output with age. *Circulation* 12:557, 1955
113. Willett WC, Dietz WH, Colditz GA: Guidelines for healthy weight. *N Engl J Med* 341:427, 1999
114. Hosie KF: Thermal dilution technics. *Circ Res* 10:491, 1962
115. Swan HJ, Ganz W, Forrester J, et al: Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. *N Engl J Med* 283:447, 1970
116. Dhainaut JF, Brunet F, Monsallier JF, et al: Bedside evaluation of right ventricular performance using a rapid computerized thermodilution method. *Crit Care Med* 15:148, 1987