THE CARDIOVASCULAR SYSTEM

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INTRODUCTION

This chapter is designed to be a review of the basic science and pathophysiology of the cardiovascular system written for general surgery residents. It is not intended to be a review for trainees in the disciplines of cardiology or cardiovascular surgical specialties.

Obviously, it is impossible to include every facet of the cardiovascular system in such a review. However, this chapter should allow surgical residents to review the basic scientific principles of the cardiovascular system as it applies to the care of the general surgical patient. This chapter also provides a concise introduction to the pathophysiology of various cardiovascular disorders. A list of selected references follows this chapter, and residents are urged to use these references because they are not only complete but also readable, in-depth sources of information.

BASIC SCIENCE OF THE PERIPHERAL VASCULAR SYSTEM

Arterial Anatomy

The arteries of the body are divided histologically into three layers. The intima is the layer that contains endothelial cells and, in some places, a single layer of subendothelial smooth muscle cells. Beneath the intima, dividing it from the media, is the internal elastic membrane. The media is the major structural component of the artery containing smooth muscle cells, elastin, proteoglycans, and collagen. The media is separated from the third layer, the adventitia, by the external elastic membrane. When a typical endarterectomy is performed, the cleavage plane is at the level of the external elastic membrane. The blood supply for the inner part of the media comes from direct diffusion from the lumen of the blood vessel wall, and the outer part of the media is supplied by smaller penetrating arteries known as vasovasorum. The third layer, the adventitia, contains elastic tissue, fibroblasts, and collagen, and provides about 60% of the strength of the blood vessel itself.

The Role of Endothelium in the Cardiovascular System

The vascular endothelium is a crucial mediator of vascular physiology. Endothelial cells are involved actively in angiogenesis, coagulation, platelet interaction, inflammation, immune response, synthesis of connective tissue components, metabolic functions and, most importantly, the regulation of vascular tone. The endothelium is, of course, normally non-thrombogenic; therefore, platelets do not adhere to an intact, quiescent endothelial lining. Platelets do, however, adhere to inflamed endothelium or to the basal lamina of vessels denuded of their endothelial coverings. Endothelial cells secrete prostacyclin (PGI2) and nitric oxide (NO), otherwise known as endothelium-derived relaxing factor (EDRF). Both of these compounds are active mediators of vasodilation and potent inhibitors of platelet adhesion and aggregation. Endothelial cells also contribute to anticoagulant properties of the intact vessel via the synthesis of thrombomodulin and protein S, both of which activate protein C, a substance synthesized in the liver that suppresses the actions of factor V and VIII of the coagulation cascade. Heparin sulfate, a component of intact endothelial cell membranes, accelerates the inactivation of thrombin and other coagulation factors by plasma antithrombin III. Furthermore, endothelial cells are involved in thrombolysis through the secretion of tissue plasminogen activators.

The vascular endothelium also operates as a critical modulator of vascular tone. EDRFs are synthesized and released
tachycardic episodes. Normal impulses travel through the A-V node and are then transmitted rapidly retrograde through these abnormal pathways, resulting in tachycardia. The pathways can be mapped and treated either surgically or with catheter ablation techniques in the electrophysiology laboratory. When the pathway is ablated, the delta wave should disappear.

Automatic supraventricular tachycardias can also occur; these are arrhythmias that are continuous and related to the firing of the conduction mechanism of a specialized area, usually in the atrium. Often, these constant tachycardias will ultimately cause ventricular dilation and heart failure. They too can be treated surgically by direct ablative techniques or by catheter ablation techniques.

**Ventricular Arrhythmias**

Ventricular arrhythmias are divided into two basic groups. The first group is ventricular fibrillation, which includes polymorphic ventricular tachycardia. Polymorphic ventricular tachycardia is an irregular-looking rhythm by electrocardiogram (ECG) that is a form of coarse ventricular fibrillation. The mechanisms for the ventricular fibrillation depends on the clinical situation. Ventricular fibrillation is a disorganized arrhythmia of the ventricle and most often occurs on the basis of a metabolic derangement. Less often it is the result of reentry. This derangement can also be caused by ischemia, most notably associated with an acute myocardial infarction. Automaticity in such a case would be related to dying Purkinje fibers or to metabolic changes in the myocardium. Treatment for these kinds of arrhythmias is related to correction of the metabolic abnormality and pharmacologic agents that decrease the sensitization to abnormal impulses. Common drugs used to treat the rate of depolarization are lidocaine hydrochloride and procainamide hydrochloride. Beta-blockers may also be useful in treating ventricular ectopy.

Monomorphic ventricular tachycardia is an entirely different arrhythmia. This is a uniform kind of ventricular tachycardia that is often associated with cardiovascular collapse. This arrhythmia often occurs in the first 48 hours after acute myocardial infarction; in this circumstance, it is the result of automaticity. This arrhythmia more commonly occurs later after myocardial infarct and is caused by a reentry mechanism. When the myocardial infarction occurs, some of the tissue is clearly dead and some is absolutely normal. Neither of these kinds of tissue causes arrhythmias. Rather, the injured border-zone tissue between the normal and dead tissue provides a substrate for micro reentry. Many unidirectional blocks exist, and as a result, there is an anatomic focus for this arrhythmia. With an anatomic focus, the arrhythmia is less likely to be sensitive to drugs. Frequently, this arrhythmia needs to be treated surgically by endocardial resection of the border-zone tissue between the normal and dead endocardium.

The most common clinical arrhythmia is premature ventricular contractions (PVCs). In the face of an acute myocardial infarction or a metabolic derangement, PVCs can lead to ventricular fibrillation. As such, the metabolic derangement needs to be corrected, and PVCs may be suppressed by using lidocaine. However, in the absence of cardiac ischemia, PVCs are a benign arrhythmia. In fact, suppression with drugs often leads to a more malignant form of arrhythmia, ventricular tachycardia, or ventricular fibrillation. Although the frequency of the PVCs are often suppressed by treatment, the first PVC seen may lead to the malignant arrhythmia. Therefore, the goal of treating a patient with PVCs is to elucidate and treat the cause.

**Electrophysiologic Testing**

When a persistent ventricular arrhythmia is present, it should be tested to see if it is inducible or if the arrhythmia occurs in the absence of other precipitating factors. Electrophysiologic testing is performed in the laboratory, using catheters in the ventricle to stimulate the heart. If the arrhythmia can be stimulated by using multiple PVCs, then the arrhythmia is certainly of the reentry mechanism, and appropriate therapy can be instituted. In addition, electrophysiologic testing allows for serial drug testing to determine if the arrhythmia can be treated pharmacologically, without taking a chance on empiric drug choices (4). Other treatments for ventricular arrhythmias include endoventricular ablative techniques, which usually involve surgical resection of scar or the use of automatic implantable cardioverter defibrillators.

**CARDIAC FUNCTION**

**Determinants of Function and Therapeutic Manipulation of Performance**

To treat patients with reduced cardiac function appropriately, it is necessary to have an understanding of the physiologic determinants of cardiac function. Such an understanding will allow the appropriate surgical care of acutely ill and chronically debilitated patients who are undergoing surgical procedures.

There are five basic factors that interact to determine the ability of the heart to function as an effective pump. These factors are also interdependent, and manipulations in one may produce changes in another. They are preload, afterload, electrical state of the heart (rate, rhythm, conduction, etc.), contractility, and compliance.

**Preload**

Preload is the degree of tension on a muscle when it begins to contract. Thus, the initial filling volume or pressure of the left ventricle before contraction determines the sar-
comere length and, hence, the muscle performance of individual fibers. True preload is the end-diastolic volume of the left ventricle. Ignoring compliance of the heart, end-diastolic pressure of the left ventricle is usually considered to be the preload. The physiologic correlate of the sarcomere length-tension relationship is the Frank-Starling curve. This curve shows that progressive increases in left ventricular filling volume cause progressive increases in ventricular-developed pressure until a peak level of function is reached. Additional increases in volume beyond this maximum level do not produce improvements in performance. The greater the stretch of the heart muscle during filling, the greater the force of contraction and the quantity of blood that will be pumped into the aorta. Simply put, within physiologic limits the heart pumps what it can get. The anatomic cellular correlate of this physiologic phenomenon describes the stretching of myofibers or muscle cells within the walls of the ventricular chamber such that individual sarcomeres within myocytes increase in length from a resting level of 1.9 µm to a maximum level of 2.2 µm. At 2.2 µm, the overlap of actin and myosin filaments allows the maximum number of cross-bridges to be formed between these elements. This produces the maximum degree of force generation by each cell. Because of the elastic properties of myocardial cells, it is extremely difficult to stretch sarcomeres significantly beyond 2.2 µm under physiologic conditions. In fact, any elongation of sarcomeres beyond 2.2 µm would reduce the overlap of actin and myosin filaments, thereby reducing performance. Thus, the anatomic correlate of the Frank-Starling curve is the ability of the muscle cell to increase force generation as sarcomere length and ventricular filling volumes increase. Increases in volume beyond that which causes optimum sarcomere length will not improve ventricular performance and may be detrimental. Therefore, the preload, filling volume, or pressure in the left ventricle determines the position of the ventricle on the Frank-Starling curve and predicts cardiac performance. Clinically, patients with poor left ventricular function may need higher filling pressures to pump adequate cardiac output volumes.

Preload itself depends on the capacitance of the vascular system and the blood volume. Preload can be influenced by volume expansion or contraction and by changes in the capacitance of the venous and arterial circulations. Factors that may reduce venous return to the heart, such as gravitational effects, venodilators, positive pressure ventilation, and PEEP ventilation, may change preload and, therefore, myocardial performance.

Afterload

Afterload is the pressure in the artery leading from the ventricle. We think of afterload as the arterial resistance against which the heart must overcome to eject blood into the systemic circulation. Loosely, it is defined as the systemic vascular resistance. The capacitance of the arterial system and the volume of blood contained within the system are the components that contribute to peripheral vascular resistance. Thus, change in either arterial capacitance or blood volume will affect afterload. As myocardial functional reserve is reduced by disease, manipulation of afterload may be an important method of improving ventricular performance.

\[
SVR = \frac{MAP - RA}{CO \times 80}
\]

Where: \(SVR\) = systemic vascular resistance, \(MAP\) = mean arterial pressure, \(RA\) = mean right atrial pressure, and \(CO\) = cardiac output.

Because this resistance is the force against which the heart must eject to create forward flow, when the resistance is lowered, the cardiac output should increase.

Two special cases of mechanical afterload manipulation deserve mention: intraaortic balloon pumps (IABPs) and military antishock trousers (MAST). The former mechanically decreases afterload while preserving diastolic coronary perfusion pressure by deflating just before systolic cardiac ejection and inflating when the aortic valve has closed. This device is useful for unstable cardiac patients. The latter, MAST, elevate central blood pressure primarily by increasing afterload. Unfortunately, the afterload increase is often peripheral to large, leaking arterial defects in the setting of central penetrating trauma or ruptured aneurysms. This peripheral increase in afterload is the physiologic equivalent of cross-clamping the aorta at the level of its bifurcation. Thus, one must be aware of the effects of this increased afterload on the heart and the aorta or its major branches above this “clamp.”

Electrical State of the Heart

Cardiac output is defined by the following equation:

\[
CO = HR \times SV
\]

\(HR\) = heart rate; \(SV\) = stroke volume

Thus, increases in heart rate are directly related to increases in cardiac output. However, as heart rate increases beyond 90 beats/min, the total cardiac output may actually begin to decrease. Stroke volume decreases at faster heart rates because the heart cannot fill as completely. Therefore, as heart rate increases beyond 90 beats/min, the total cardiac output may actually decrease as stroke volume begins to decrease at a faster rate than heart rate increases. Thus, tachycardia occurs at the expense of diastole, robbing the heart of the time it needs to refill the ventricle. This highlights the importance of rate-control therapy in patients with atrial fibrillation.

It is also important to consider the effect of cardiac rhythm on ventricular performance. Sinus rhythm itself, with the coordinated initial depolarization of the atrium fol-
headed by depolarization of the ventricle, has an important influence on myocardial performance. In fact, as ventricular compliance decreases, the "atrial kick" provided in normal sinus rhythm has an even more important contribution to cardiac output, approaching a 25% increase. Thus, not only is heart rate a determinant of cardiac performance, but the coordinated depolarization of the cardiac chambers achieved in sinus rhythm also produces a substantial contribution.

Contractility

The inherent ability of the myocardium to generate force independent of loading conditions is characterized by contractility. The inotropic state of the myocardium can be influenced by endogenous and exogenous catecholamines. An assessment of contractility forces can be obtained by measuring the maximum rate of rise of ventricular pressure over time (dp/dt_max). This measurement is a basic reflection of contractility as long as preload conditions are held constant.

Ejection fraction (EF) is the ratio of the stroke volume (SV), defined as the volume ejected by the ventricle in systole, to the end-diastolic volume (EDV).

\[ EF = \frac{SV}{EDV} \]

Ejection fraction is a useful indicator of ventricular function. Normal ejection fraction is greater than 65%. Although it depends on preload and afterload conditions, ejection fraction can be used to evaluate and compare contractility at baseline.

Compliance

Left ventricular compliance (C), or the relationship between the filling pressure (P) and chamber volume (V), is an indicator of the ease of ventricular distensibility.

\[ C = \frac{\Delta V}{\Delta P} \]

Myocardial ischemia, edema, hypertrophy, amyloidosis, restrictive cardiomyopathies, pericardial disease, and pericardial tamponade decrease ventricular compliance. As compliance decreases, the ventricle becomes stiffer and less distensible. This may produce less diastolic filling and decreased cardiac performance.

Measurement of Cardiac Performance

Cardiac index is the most frequently used parameter of myocardial performance in surgical patients. Normal cardiac index ranges between 2.5 and 4.5 L/min/m². Two clinically applicable methods of determining cardiac output are based on principals of metabolite transport and indicator dilution.

Clinically one can grossly evaluate the adequacy of the cardiac output by several readily available, noninvasive parameters such as blood pressure, urine output, extremity perfusion, and level of consciousness. Blood pressure itself is not always a good indicator of cardiac output. Recall that \[ BP = CO \times SVR \]. So blood pressure may be maintained in the face of a low cardiac output by a high systemic vascular resistance. Urine output is usually a reliable parameter. In the absence of diuretics, a urine output in adults of greater than 30 ml/hour implies an adequate output by virtue of adequately perfused kidneys. Extremity perfusion is very worthwhile to evaluate, given that warm extremities indicate an adequate cardiac output. However, extremity assessment is confounded in patients with peripheral vascular disease who will have cool extremities even with an adequate cardiac output. Finally, level of consciousness is useful information. A patient who is alert and awake is obviously receiving adequate brain perfusion and likely has an adequate cardiac output.

Pharmacologic Interventions

Sympathomimetic Amines

The primary cardiac effects of the sympathomimetic amines (catecholamines) are mediated by way of \( \beta \)-adrenergic receptors. These agents produce an increase in myocardial contractility, an increase in the frequency of pacemaker discharge in the S-A and A-V nodes, and an increase in A-V node conduction velocity. These agents also produce effects on the vascular system through \( \alpha \)- and \( \beta \)-adrenergic receptors. The vasoconstrictor response is mediated by \( \alpha \)-adrenergic receptors, and the vasodilator response is mediated by \( \beta \)-adrenergic receptors. The \( \beta_1 \) receptor types are primarily on the heart, and stimulation leads to an increase in heart rate and contractility. \( \beta_2 \) receptor types are predominantly on the smooth muscles of blood vessels and bronchi. Stimulation of the \( \beta_2 \)-adrenergic receptors leads to vasodilation and bronchodilation. The relative potencies of the various sympathomimetic amines on adrenergic receptors are shown in Table 15.1.

**Table 15.1. The Relative Potencies and Sites of Influence of the Sympathomimetic Amines**

<table>
<thead>
<tr>
<th>Sympathomimetic Amines</th>
<th>Vascular</th>
<th>Cardiac</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( \alpha )</td>
<td>( \beta )</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Dopamine(^a)</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>Epinephrine</td>
<td>++</td>
<td>+</td>
</tr>
<tr>
<td>Norepinephrine</td>
<td>++</td>
<td>+</td>
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<tr>
<td>Isoproterenol</td>
<td>-</td>
<td>+</td>
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\(^a\) Dopamine produces mesenteric and renal vascular dilation by activating dopaminergic receptors. It also acts on \( \alpha \)- and \( \beta \)-receptors directly and can cause the release of endogenous norepinephrine.
The β-receptor activity of dobutamine is much more important than its α-adrenergic effects. At infusion rates of 5 µg/kg/min, dobutamine acts primarily as a positive inotropic agent by increasing myocardial contractility. Dobutamine has more of a chronotropic effect than does dopamine and is often limited by tachycardia. Dobutamine also reduces peripheral vascular resistance by stimulating the β receptors in the peripheral vasculature. After an initial dose of dobutamine, increases in doses are titrated to hemodynamic and clinical improvement.

The effects of dopamine are mediated by three different receptors at low-, intermediate-, and high-dose levels of drug treatment. Thus, a dose-dependent action of this drug occurs on the renal vasculature, heart, and peripheral vasculature. At low “renal” doses (1 to 5 µg/kg/min), dopamine has a primary effect on stimulating dopaminergic (D₁) receptors in the renal and mesenteric vasculature. This effect is predominantly vasodilation, resulting in augmentation of renal blood flow.

As intermediate “cardiac” levels of dopamine dosage are achieved in the range of 5 to 10 µg/kg/min, the effect is primarily on increasing cardiac contractility and heart rate through the β₁-receptors.

As high “pressor” levels of dopamine infusion are reached (10 µg/kg/min), a significant degree of peripheral vasoconstriction results as α-adrenergic receptors are activated. This activation causes a significant elevation of systemic vascular resistance. Maintenance of renal vasodilation is lost at these high infusion rates. This drug also has an arrhythmogenic effect, especially at these high doses.

Epinephrine is a potent α- and β-adrenergic agent with a significant inotropic effect on myocardial contractility. It is also associated with significant α-agonist activity and can increase peripheral arterial vascular tone with all of the potentially negative effects seen with decreased peripheral perfusion. Epinephrine is started at a dose of 1 µg/min and can be increased as high as 5 to 10 µg/min, although these higher doses are rarely used.

Norepinephrine is an extremely potent α-agonist and can be used as a potent pressor agent. Dosage frequently begins in the range of 1 µg/min and can be titrated to increase systemic blood pressure. This agent causes increased activity of all α-receptors with significant elevations in arterial resistance. It may produce marked decreases in coronary, renal, and peripheral perfusion. Peripheral vasoconstriction usually overshadows positive inotropism. However, norepinephrine is specifically indicated in patients with hypotension because of a low systemic vascular resistance and preserved cardiac output such as seen with sepsis and neurogenic shock.

Isoproterenol has a pure β-adrenergic effect. Its clinical use is usually restricted to situations such as bradycardias or for which enhancement of heart rate and condition are desirable, such as the denervated heart after transplantation. It is also a potent pulmonary vasodilator.

Digitalis Glycosides

Digoxin is the most widely used clinical digitalis glycoside. It has a positive inotropic effect on myocardial performance. The effects of digoxin are related to its ability to increase the intracellular calcium available to the contractile apparatus. This effect is achieved by binding with sarcoplasmic reticulum calcium ATPase and thus blocking the active transport of sodium in exchange for potassium. The increased accumulation of sodium within the cell leads to an increased concentration of calcium through the sodium–calcium ion-exchange mechanism. Digitalis-containing compounds also slow conduction through the A-V node and can be of therapeutic value in treating supraventricular tachycardias.

Digoxin has significant interactions with quinidine, verapamil, and amiodarone, which cause its concentration in the blood to be increased. Remember that the pharmacokinetics of digoxin are such that the equilibration is not achieved until 6 to 8 hours after the administration of an oral or intravenous dose. Thus, serum levels should be measured after equilibration has occurred.

Digitalis preparations can cause toxicity. The most important effects are ventricular arrhythmias. The most typical digitalis-induced rhythm is junctional tachycardia. This rhythm is a wide-complex rhythm originating high in the conduction system (near the “junction” of the A-V node and the His bundle). Ordinarily, a rhythm originating at this level would have a rate of about 40 beats/min. In digitalis toxicity, this rate is usually 80 to 120 beats/min. Digitalis toxicity may also be manifested by systemic signs and symptoms (i.e., gastrointestinal distress) and visual changes (i.e., seeing greens and yellows). Digitalis toxicity is more likely to be seen when the patient’s levels of potassium or magnesium are low.

Vasodilators

Nitroprusside is a pure smooth-muscle vasodilator that affects all vascular beds, including the arterial, venous, and coronary circulations. Treatment is usually initiated at a dose of 0.5 µg/kg/min and is titrated upward for an appropriate response in arterial pressure. Nitroprusside is an extremely effective agent when afterload reduction is required. Its effects are transient and can be reversed rapidly by reducing dosage or stopping the drug.

Despite its apparent beneficial effect, some evidence suggests that nitroprusside infusion in patients with significant myocardial ischemia can produce a steal phenomenon in which coronary blood flow is directed away from the areas of ischemia. Thus, this agent may not be desirable in such patients.

Nitroprusside is metabolized to cyanide. The cyanide can be metabolized into thiocyanate by the liver and excreted by the kidneys. With normal kidneys, its t₁/₂ is 4 days. However, patients with renal failure may develop thiocyanate
toxicity, manifested by tremors, hypoxia, nausea, disorientation, and hypothyroidism. This complication rarely occurs when the drug is used for less than 48 hours. The toxicity can be reversed by infusion of hydroxocobalamin, which converts thiocyanate into cyanocobalamin (vitamin B₁₂).

Nitroglycerin is also a smooth muscle vasodilator, with effects on the coronary and peripheral circulation. Nitroglycerin has a dose-dependent differential action. It acts primarily on veins at low-to-moderate dosages. At higher dosages, dilation of the systemic arterial vasculature occurs.

The therapeutic usefulness of nitroglycerin in patients with ischemic coronary artery disease occurs as a result of coronary arterial vasodilation. In addition, a reduction in preload occurs, which produces a decrease in myocardial oxygen consumption. Nitroglycerin is given intravenously with a dose beginning at 50 μg/min and can be titrated upward as required. Oral, sublingual, and dermal forms of this medication are available. Tachyphylaxis to nitroglycerin may develop over time. Options for re-establishing vascular effects include terminating use of the drug for a period of time and treatment with N-acetylcysteine.

Hydralazine is an excellent arterial vasodilator that can be given in bolus doses such as 10 to 50 mg intravenously every 6 hours. It is very potent and doses should be started low. Often it is used as an adjunctive drug to transition patients from the infusion vasodilators, like nitroprusside, over to oral agents for hypertension management.

Amrinone and milrinone are phosphodiesterase inhibitors. They appear to inhibit myocardial cyclic adenosine monophosphate (cAMP) phosphodiesterase activity, producing an increase in the cellular concentrations of cAMP. Amrinone and milrinone thus have positive inotropic effects: they increase ventricular performance and also appear to act on vascular smooth muscle to produce vasodilation. Thus both amrinone and milrinone increase cardiac output and decrease systemic and pulmonary vascular resistance. This lowering of pulmonary vascular resistance in patients with pulmonary hypertension gives these drugs unique value in treating right heart failure. Thrombocytopenia has been a problem with amrinone, but not with milrinone.

The calcium channel blockers can be used for the treatment of angina pectoris, supraventricular tachycardia, and hypertension. By inhibiting the flux of calcium through myocardial channels, calcium channel blockers produce a negative inotropic effect. Furthermore, calcium-dependent activity at the pacemaker cells of the sinus and A-V nodes is reduced and causes sinus bradycardia and prolonged A-V conduction. These agents produce a vasodilatory action on the coronary and peripheral arterial vasculature by directly interfering with calcium-induced smooth muscle contraction. They also appear to have an antivasospastic activity on the coronary vasculature. Many calcium channel blockers are currently available, and they vary in the relative degree of cardiac effect and peripheral vascular effect.

Angiotensin-converting enzyme (ACE) inhibitors interfere with the pulmonary conversion of angiotensin I to angiotensin II. Angiotensin II is an extremely potent vasoconstrictor and also promotes adrenal gland release of aldosterone. This, in turn, produces systemic vasculature volume expansion through increased renal reabsorption of sodium. The ACE inhibitors play an important role in modifying the renin-angiotensin-aldosterone system. ACE inhibitors produce a significant reduction in systemic vasculature resistance by producing vasodilation and diminishing plasma volume. Treatment with these agents may produce hyponatremia and hyperkalemia. Captopril and enalapril are two commonly used ACE inhibitors.

Captopril is effective in the treatment of congestive heart failure and hypertension. The advantage of this agent is that it has less of the quality-of-life side effects produced by other antihypertensive agents that work on the central nervous system. Captopril reduces blood pressure by reducing preload and afterload, and it tends preferentially to maintain flow to the kidneys. Adverse effects associated with this drug include neutropenia, agranulocytosis, rise in serum creatinine, metallic taste, skin rash, proteinuria, angioedema, a persistent cough, and dysgeusia. Captopril is excreted by the kidneys, and increases in creatinine associated with initiation of captopril treatment may suggest a preexistent renal artery stenosis.

Enalapril is an ACE inhibitor with a prolonged duration of action because it requires metabolic conversion in the liver for activation. Enalapril may have a reduced number of side effects relative to captopril because enalapril is a non-sulphydryl-containing molecule. The sulphydryl moiety is thought to be a source of many of captopril's side effects. However, enalapril does retain some of the side effects of captopril such as neutropenia, angioedema, and cough. Many other ACE inhibitors are available.

**Mechanical Assist Devices**

Although the vast majority of patients who require supportive measures for decreased ventricular function respond to conservative medical measures, a small percentage of patients do require more aggressive treatment for survival. A number of mechanical devices are now available for use in such patients. The IABP was the first widely used device for support of the failing heart and is still a mainstay of mechanical ventricular support. However, new left ventricular assist devices (LVADs) are becoming available, and technology in this area is progressing rapidly. The ultimate form of ventricular assistance may be some form of total artificial heart.

The IABP supports the circulation by implementing the concept of counterpulsation. This theory suggests that the rapid expansion of vascular volume during diastole and the rapid reduction of vascular volume during systole can augment ventricular function significantly. This mechanism
provides increased diastolic blood pressure, which causes improved coronary flow and myocardial oxygen supply as well as peripheral perfusion during diastole. It also decreases afterload during systole, which causes improved cardiac performance and reduced myocardial work and oxygen demand. The initial attempts at implementing this theory were unsuccessful because of technical difficulties associated with the rapid infusion and removal of blood. However, the idea of an intravascular balloon that inflates during diastole and deflates during systole was found to be technically easier to implement than blood manipulation. The IABP works by two actions. First, the rapid inflation of a balloon in the descending aorta early in diastole (firing on the T wave) causes improved diastolic pressure and increased coronary and peripheral perfusion. This mechanism depends on a competent aortic valve, which makes aortic insufficiency an obvious contraindication. Second, just before systole (deflating on the R wave), the IABP rapidly deflates and lowers afterload, thereby producing improved myocardial performance by reducing peripheral resistance. Basically, the IABP provides systolic unloading and diastolic augmentation, thereby allowing the heart to increase performance at a lower energy demand.

The IABP remains the mainstay of mechanical support for the failing myocardium. Although the IABP is an effective means of mechanically augmenting ventricular performance, it depends on at least some remaining left ventricular function. In end stage of left ventricular failure, the IABP is of little value. The criteria for LVAD are blood pressure less than 90 mm Hg systolic and cardiac index less than 1.8 L/min/m², despite left atrial pressure of 25 mm Hg on maximal inotropic and IABP support.

The LVAD is capable of supporting the entire systemic and/or pulmonary circulation when ventricular performance is severely compromised. A variety of devices have been developed as LVAD pumps. These include roller pumps, centrifugal (vortex) pumps, and pneumatic pulsatile pumps. Each system has its inherent advantages and disadvantages and represents the development of newer technologies.