Cardiac Dysfunction in the Perioperative Period:
Pathophysiology, Diagnosis, and Treatment

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In the past decade, improved understanding of the hemodynamic and mechanical mechanisms of myocardial contraction and cardiac performance has contributed to the better care of patients who have heart disease and circulatory derangements. Advances in engineering and electronic technology have contributed to the development of methods routinely employed for monitoring cardiovascular function in severely ill cardiac patients. These methods have found widespread clinical application and have replaced clinical impressions with accurate measurements.

Prompt diagnosis and intervention are necessary to treat cardiac dysfunction. The appropriateness of treatment selected depends on an understanding of the pathophysiologic mechanism involved, identification of the cause of inadequate peripheral perfusion, and correction of extracardiac factors that may contribute to low cardiac output.

The mechanism of cardiac function and the electrophysiology of the heart are briefly reviewed here as a basis for subsequent discussion of the diagnosis and management of cardiac dysfunction in the perioperative period.

Cardiac Function

Cardiac Output

The performance of the heart is regulated by the integration of four major determinants: 1) preload (end-diastolic pressure or volume), 2) afterload (intramyocardial systolic tension), 3) contractile or inotropic state of the myocardium, and 4) heart rate.1-8 In certain cardiac disorders, it is important to add dyssnergy of ventricular contraction. Vascular factors also control the performance of the ventricle (table 1).

The preload, which establishes the initial muscle fiber length, is determined by the intraventricular pressure and volume. In general terms, preload may be described by the right and left end-diastolic ventricular filling pressures and is clinically assessed by measurements of right and left atrial (or pulmonary capillary wedge) pressures, respectively.

Starling demonstrated that the force of myocardial contraction and stroke volume depends directly on preload. Subsequently it was demonstrated that the relations between ventricular end-diastolic pressure and stroke work, called the ventricular function curve, could be altered by pharmacologic or neurohumoral influences (fig. 1).7

Changes of preload greatly alter cardiac output. In the perioperative period, reduction of preload leading to decreased cardiac output may occur with hypovolemia (hemorrhagic shock), displacement of blood from the thorax (positive-pressure ventilation), or cardiac compression (tamponade). In addition, severe impairment of right ventricular contractility (right heart failure) may lead to decreased left ventricular filling.

Although a reduction in stroke volume often results in arterial hypotension, arterial pressure can be maintained with increase in peripheral vascular resistance.

Afterload, which is defined as the ventricular wall tension during systole, is dependent on the end-diastolic radius of the ventricle, the aortic diastolic pressure, and wall thickness. The extent to which the intraventricular pressure will have to rise during systole depends on the aortic pressure. The radius of the ventricle is determined by the preload. It is obvious that all these myocardial and vascular factors are interdependent, and a simple change in one will affect the others. For example, in some patients who have heart disease, stroke volume declines when afterload is increased, i.e., ventricular ejection is reduced. Conversely, when afterload is reduced, the impedance to ventricular ejection decreases, and stroke volume increases. In the perioperative period, alterations of afterload may result from changes in vascular tone and resistance. In patients who have

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Arterial volume is affected by stroke volume. The distensibility of the vascular wall, which determines compliance and resistance of the vascular bed, is under the influence of the autonomic nervous system. Systolic arterial pressure depends more on arterial volume during ejection, while diastolic pressure depends more on vascular resistance. Thus, arterial pressure represents a complex interaction of cardiac and peripheral factors.\textsuperscript{10,11}

In the perioperative period, hypotension may result from impaired myocardial contractility or a decreased preload, and/or afterload. Hypertension may result from increased afterload (arterial vasoconstriction).

**Myocardial Oxygen Consumption (MV\textsubscript{O\textsubscript{2}})**

The three major determinants of oxygen consumption are intramyocardial wall tension, contractile state of the myocardium, and heart rate.\textsuperscript{12} In recent years it has become apparent that MV\textsubscript{O\textsubscript{2}} is far more dependent on the pressure generated by the ventricle than it is on the volume ejected. Therefore, an increase in stroke work, when associated with an increase in stroke volume, is less costly, in terms of MV\textsubscript{O\textsubscript{2}}, than when associated with an increase in intraventricular tension. In other words, a given systolic arterial pressure generated by a high stroke volume is associated with a lower MV\textsubscript{O\textsubscript{2}} than that generated by increased vascular resistance.

**Cardiac Dysfunction**

**Pathophysiology and Diagnosis**

Cardiac dysfunction results from a combination of abnormal loading (preload, afterload) and depressed contractility. The clinical and hemodynamic manifestations are not the same in all types of cardiac dysfunction, nor in all stages of heart failure. Dependent upon the ability of the diseased heart to maintain adequate blood flow to the tissues, cardiac dysfunction has been classified as compensated and noncompensated.

<table>
<thead>
<tr>
<th>Table 1. Determinants of Cardiac Performance</th>
</tr>
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<tbody>
<tr>
<td>1. Myocardial Factors</td>
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<tr>
<td>1. Preload (venous return)</td>
</tr>
<tr>
<td>2. Afterload (ventricular wall tension)</td>
</tr>
<tr>
<td>3. Contractility</td>
</tr>
<tr>
<td>4. Heart rate</td>
</tr>
<tr>
<td>2. Vascular Factors</td>
</tr>
<tr>
<td>1. Capacitance (venous)</td>
</tr>
<tr>
<td>2. Inertia</td>
</tr>
<tr>
<td>3. Blood viscosity</td>
</tr>
<tr>
<td>4. Arteriolar radius</td>
</tr>
<tr>
<td>5. Arterial compliance</td>
</tr>
<tr>
<td>6. Arteriovenous communication</td>
</tr>
</tbody>
</table>
PERIOPERATIVE CARDIAC DYSFUNCTION

With the onset of cardiac dysfunction, two major compensatory mechanisms are available: 1) the Frank-Starling principle, and 2) the sympathetic nervous system. A third mechanism is available in chronic heart failure: ventricular hypertrophy. The Frank-Starling mechanism of ventricular dilation operates with an increase of end-diastolic volume and pressure (preload) that permits more forceful contraction in the presence of a lowered and depressed function curve (fig. 1). This increased end-diastolic pressure increases myocardial oxygen demand and may be associated with pulmonary and/or systemic congestion. Augmented sympathetic activity has two major effects on the circulation. Sympathetic stimulation of the heart leads to increases in heart rate and in the force of contraction. Stimulation of the peripheral vasculature leads to an increase in vascular tone, increasing venous return and vascular resistance (afterload). Thus, normal systolic arterial pressure can be maintained by higher vascular resistance, and normal cardiac output by an increase in heart rate when stroke volume is diminished. These compensatory mechanisms increase preload, afterload, heart rate, and contractility, and thus increase myocardial oxygen consumption. However, should compensatory mechanisms become inoperative or inadequate, cardiac output must decrease. As a consequence, hypotension and impaired perfusion lead to organ dysfunction and failure. Hemodynamically, this condition is characterized by elevated ventricular filling pressures, hypotension, low cardiac output, and elevated vascular resistance (table 3). Clinical symptoms include cold and poorly perfused extremities, dyspnea, pulmonary and systemic congestion, poor oxygenation, metabolic acidosis, and reduction of urinary output.

Acute pulmonary edema may develop in the presence of left ventricular failure. An increase in the preload and/or afterload (venous return, peripheral resistance) may temporarily increase the workload of the already impaired left ventricle. There are two forms of pulmonary edema, interstitial and intra-alveolar. The former is more common. The diagnosis of pulmonary edema can be made from the chest x-ray, measurement of arterial blood gases (increased A-aD02), and auscultation of the lungs. In interstitial edema, the chest x-ray is characterized by generalized cloudiness or haziness of the lung fields extending to the periphery. Vascular markings lose their sharp outline and peribronchial cuffing may be seen. Intra-alveolar edema results in radiodensities that are essentially perihilar and bilaterally symmetrical (middle and inner zones of the lung).

Circulatory shock represents a state of severely impaired blood flow throughout the body sufficient to cause tissue damage. Shock may result from heart failure, diminished blood volume, decreased vasomotor tone, or greatly increased resistance to blood flow. The common denominator is a rapid, severe reduction in blood flow to the tissues, with consequent tissue anoxia. In the absence of hypovolemia, arrhythmia and drug-induced myocardial depression, circulatory shock is associated with left ventricular failure due to myocardial infarction or severe congestive heart failure due to valvular disease or intrinsic myocardial disease (cardiomyopathy). Cardiogenic shock is one of the major complications of acute myocardial infarction. It is estimated to occur in 15 per cent of hospitalized patients and, when not treated promptly, is associated with an 80 per cent mortality rate. The most significant physiologic defect in cardiogenic shock due to myocardial infarction is ventricular dysfunction consequent to loss of functional myocardial muscle.

In the early stages of cardiogenic shock, various circulatory reflexes (as well as pain and fear) cause intense activity of the sympathetic nervous tone, maintaining the arterial pressure. However, increased

### Table 3. Hemodynamic Alterations in Congestive Heart Failure*

<table>
<thead>
<tr>
<th></th>
<th>Left-sided Failure</th>
<th>Right-sided Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td>↑</td>
<td>↑</td>
</tr>
<tr>
<td>Ventricular filling pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left</td>
<td>↑↑</td>
<td>Normal or ↑</td>
</tr>
<tr>
<td>Right</td>
<td>Normal or ↓</td>
<td>↑ or ↑</td>
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<tr>
<td>Arterial pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td>Normal or ↓</td>
<td>↓ or ↑</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>↑↑</td>
<td>↑ or ↑</td>
</tr>
<tr>
<td>Vascular resistance</td>
<td>↑↑</td>
<td>↑ or ↑</td>
</tr>
<tr>
<td>Systemic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pulmonary</td>
<td>↑↑</td>
<td>↑ or ↑</td>
</tr>
<tr>
<td>Cardiac output</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Stroke volume</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Ventricular stroke work</td>
<td></td>
<td></td>
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<tr>
<td>Left</td>
<td>↓↓</td>
<td>↓ or ↑</td>
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<tr>
<td>Right</td>
<td>↑↑</td>
<td></td>
</tr>
</tbody>
</table>

*↑ = increase; ↓ = decrease.

### Table 2. Etiology of Cardiac Dysfunction in the Perioperative Period

1. Blood loss
2. Anesthetic drugs
3. Hypoxia
4. Hypercapnia
5. Acid–base imbalance
6. Electrolyte abnormalities
7. Surgical manipulations
8. Drugs (quinidine, digitalis, methyl dopa, antihypertensive, propranolol)
9. Pre-existing heart disease
10. Pre-existing disease (respiratory, metabolic, endocrine)
sympathetic tone also augments $MV_{te}$. As shock progresses, arterial pressure falls low enough to complicate the already inadequate cardiac output, thus leading to tissue damage, including that of the myocardium. Depression of myocardial contractility results in further decreases in stroke volume, cardiac output, and systemic blood pressure.\textsuperscript{20,21} Decreased coronary perfusion pressure further reduces myocardial oxygen delivery, which in turn results in further ischemia and necrosis of the myocardium. Progressively, vasomotor failure develops from accumulating cellular metabolites, and vascular dilation leads to further reduction of the arterial pressure and venous return (peripheral "pooling" due to venodilation).\textsuperscript{22,23}

Experimental\textsuperscript{24,25} and clinical\textsuperscript{26} studies have demonstrated impairment of sympathetic reflex vasoconstriction in cardiogenic shock due to myocardial infarction. This lack of vascular response to a fall in cardiac output has been attributed to inhibition of vasoconstriction\textsuperscript{25,26} and competitive vasodilation.\textsuperscript{27} It has been suggested that chemical and mechanical stimuli arising from the ischemic myocardium and mediated by vagal and sympathetic pathways activate receptors in the myocardium. Thus, compensatory vasoconstriction is incomplete and hypotension is accentuated.

During the course of shock, extreme ischemia occurring in the pancreas leads to degenerative processes, activated by pancreatic enzymes. One of the toxic factors released into the circulation from the pancreas is a peptide, the myocardial toxic factor (MTF), which may reduce myocardial contractility.\textsuperscript{28}

Impaired tissue perfusion results in generalized and local tissue acidosis. Failure of oxygen transport results in anaerobic metabolism and consequently, an increase in tissue and blood lactate. In addition, carbon dioxide that is not removed by the blood reacts locally, in the cells, with water and various tissue buffers to form intracellular acidic substances.

**Evaluation and Management**

Monitoring of patients who have cardiac dysfunction includes ECG, arterial blood pressure, central venous pressure, arterial blood gases and pH, electrolytes, and urinary output. Central venous pressure is not a reliable indicator of left ventricular filling pressure (LVFP). Conversely, LVFP does not reflect central venous pressure (fig. 2). Presently a flow-directed pulmonary-artery catheter is used to monitor pulmonary arterial and capillary wedge pressures, LVFP, and cardiac output by thermodilution.\textsuperscript{29,30} We insert the catheter, prior to anesthesia, when the patient has a history of recent myocardial infarction, severe myocardial ischemic disease, congestive heart failure, or pulmonary hypertension. It is also used in management of patients who have sustained major trauma and those who have multisystem disease who are undergoing major surgical procedures and need massive volume replacement. Complications from the insertion of the catheter are infrequent, but include premature ventricular beats, atrial arrhythmias.\textsuperscript{31} A-V block, pulmonary infarction, and hemorrhage.

Although determination of cardiac output can aid in evaluation of a patient’s cardiac condition, it must be interpreted in relation to other hemodynamic variables and clinical manifestations. Cardiac output depends on heart rate and stroke volume. These, in turn, depend on other factors, previously
mentioned. Cardiac output is influenced by the tissue metabolic needs. Indices derived from cardiac output (stroke volume, cardiac index, vascular resistance, stroke work) have been used for estimating prognosis. In general, patients who have low cardiac indices (less than 2.2 l/min/m²) or stroke volumes (less than 20 ml) and increased ventricular filling pressures have grave prognoses. An absolute requirement for the treatment of cardiac dysfunction is adequate intravascular volume, since hypovolemia is a frequent cause of impaired cardiac performance. Low cardiac output under these conditions may be explained solely on the basis of decreased preload when the myocardial contractile state is normal. In this event, adequate volume replacement may be the only therapeutic intervention needed. In patients who have ventricular dysfunction, volume expansion to achieve higher than normal ventricular filling pressures, in itself, may improve cardiac output. It will also provide optimal plasma volume prior to administration of inotropic drugs or initiation of other therapeutic interventions. Volume expansion in patients who have elevated filling pressures (above 15 mm Hg) should be undertaken with caution, because an excessive increase in filling pressure (to 25 mm Hg or more) may lead to pulmonary edema. The therapy should be guided by the left ventricular filling pressure on an individual basis. Fluid administration should not be continued when left ventricular filling pressure rises without improvement of cardiac function (unchanged blood pressure, low urinary output, persistent low cardiac output). Obviously, volume expansion is indicated for patients who have low or normal filling pressures (4 to 8 mm Hg) before instituting treatment with vasoactive drugs. Volume expansion is not indicated in management of patients who have pulmonary edema.

Hypoventilation should be corrected. Mechanical ventilation with PEEP may be used to improve blood oxygenation without having to administer an inspired oxygen concentration of more than 60 to 70 per cent. Respiratory hyperventilation leading to alkalemia should be corrected. Severe metabolic acidemia of perfusion failure is spontaneously reversed when effective circulation is restored. When possible, hypertonic sodium bicarbonate should be avoided because an excess of sodium increases the risks of heart failure and of a hyperosmolar state. Electrolyte abnormalities should be promptly treated.

Although volume expansion and correction of underlying abnormalities may enhance cardiac output temporarily, pharmacologic interventions may be necessary to improve cardiac function. The aim of drug therapy is: 1) to improve myocardial contractility, 2) to reduce resistance to ventricular ejection, 3) to relieve pulmonary congestion and improve oxygenation, and 4) to prevent serious cardiac arrhythmias. The selection of therapy for a patient who has cardiac dysfunction should be determined by right and left ventricular filling pressures (preload), systemic blood pressure and vascular resistance (afterload), and cardiac output. It is also important to consider whether the drug affects the viability of ischemic myocardium by altering the imbalance between myocardial oxygen demand and supply. Increases in contractility and heart rate produced by an inotropic drug definitely increase myocardial oxygen consumption. However, the increase in perfusion pressure that results from the improvement of ventricular function compensates for the increase in myocardial oxygen demand.

**Isoproterenol**

Isoproterenol is a pure beta-adrenergic agonist. It significantly increases heart rate and cardiac output, while arterial pressure may increase, decrease, or remain unchanged. Although cardiac output increases with isoproterenol, myocardial oxygen demand is also increased and anaerobic myocardial metabolism may result. The increased MV_{O_2} associated with the use of isoproterenol may lead to extension of ischemia and necrosis.

Isoproterenol has been shown to decrease pulmonary vascular resistance by direct stimulation of arteriolar beta-adrenergic receptors. Thus, isoproterenol may be useful for patients who have right ventricular dysfunction and pulmonary hypertension. Recently, it was reported that isoproterenol improved right ventricular performance in patients who had primary pulmonary hypertension.

Because of its electrophysiologic effects on the heart, isoproterenol may be used in patients with slow heart rates and low cardiac outputs. Therapy should be initiated at a low dose of 1 to 1.5 µg/min, administered as an infusion intravenously. The drug should be administered cautiously because of the tachycardia, ventricular arrhythmias, and hypotension it may cause.

**Epinephrine**

This drug is an endogenous sympathomimetic amine that acts on both alpha- and beta-adrenergic receptors. Epinephrine stimulates cardiac beta-adrenergic receptors, causing an increase of myocardial contractility and frequency of contraction. Because epinephrine enhances excitability, lowers the threshold for pacemaker tissue, and augments
rhythmicity, tachycardia and ventricular irritability may complicate therapy. The effect of epinephrine on the peripheral vasculature is mixed alpha- and beta-adrenergic agonistic. With small doses there is a transient fall in arterial blood pressure due to vaso-dilation (beta effect). At higher doses, peripheral vaso-constriction due to alpha stimulation causes an increase in arterial pressures. The net effect of epinephrine on total systemic vascular resistance is the result of its effects on the various regional vascular beds. Epinephrine is a useful drug, particularly when arterial hypotension and low cardiac output are due to impaired cardiac function rather than hypovolemia. The usual starting dose of epinephrine is 1 to 2 μg/min as an intravenous infusion. The doses range from 1 to 4 μg/min.

**Dopamine**

Dopamine, an endogenous catecholamine, is the immediate precursor of norepinephrine. Dopamine possesses both beta-adrenergic and alpha-adrenergic receptor properties. Stimulation of beta receptors in the heart by the drug increases myocardial contractility and heart rate. It also releases norepinephrine from myocardial catecholamine-storage sites. These effects of dopamine on the heart can be blocked by propranolol. During dopamine administration, there are increases in cardiac output, stroke volume, and, at higher doses, mean aortic pressure.

The effect of dopamine on vascular smooth muscle is due to stimulation of both beta- and alpha-adrenergic receptors. The predominant effect depends on its separate actions on the regional vascular beds. With small doses (2 to 4 μg/kg/min) vascular resistance does not change, or may even decrease. At higher doses (more than 6 μg/kg/min), peripheral alpha-receptor stimulation predominates, and an increase in peripheral and pulmonary vascular resistance occurs. Coronary arterial vasoconstriction may occur with large doses of dopamine.

In patients who have normal pulmonary vasculature, dopamine significantly reduces pulmonary vascular resistance. It exerts an unusual vasodilation in the renal, mesenteric, coronary, and cerebral arterial vascular beds. This effect is not blocked by atropine, propranolol, or other beta antagonists. Studies support the concept of a specific dopamine vascular receptor. Dopamine has been found to increase renal blood flow. This increase is usually accompanied by improvement in glomerular filtration and natriuresis.

Dopamine administration to a patient who has ischemic heart disease at a rate that augments cardiac output and decreases systemic vascular resistance (small dose) does not alter oxygen tension in the coronary sinus or myocardial extraction ratio of lactate. However, myocardial oxygen consumption increases when more rapid infusion increases systemic vascular resistance and heart rate. Dopamine is administered intravenously at an initial rate of 2–3 μg/kg/min. Doses range from 2 to 8 μg/kg/min.

**Norepinephrine**

Norepinephrine is the chemical neurotransmitter stored and liberated by postganglionic adrenergic nerves. Norepinephrine acts predominantly on alpha-adrenergic receptors and has lesser action on beta receptors except in the heart. Its beta-receptor inhibitory and metabolic actions are weak. Norepinephrine stimulates beta receptors in the heart, causing an increase in myocardial contractility. With small doses (1–2 μg/min), cardiac output increases while resistance remains unchanged. With large doses (more than 3 μg/min), cardiac output is unchanged or decreased and total peripheral vascular resistance is increased. The enhancement of vascular resistance significantly increases the workload of the left and right ventricles. Severe constriction reduces the blood flow to the kidney, skeletal muscle and liver. Aggravation of oliguria may result from treatment of low cardiac output with norepinephrine. The circulating plasma volume is reduced by fluid transudation to the extracellular space during prolonged therapy with this drug, this volume loss further exacerbating the low-cardiac-output state.

In patients who have pulmonary hypertension, norepinephrine may worsen the hemodynamic situation by increasing pulmonary vascular resistance. This increased right ventricular afterload may aggravate right ventricular dysfunction.

The use of pure alpha-adrenergic stimulating drugs without positive inotropic action has limited applicability in the treatment of cardiogenic shock, because the drugs increase afterload without a concomitant increase in contractility.

Although the use of one inotropic drug may improve the low-cardiac-output state, it is often necessary to use a combination of various catecholamines for an optimal balance among cardiac output, heart rate and rhythm, arterial pressure and peripheral blood flow. A combination of norepinephrine and phenolamine has been advocated for support of the circulation in low-cardiac-output states. The adverse effects of vasoconstriction caused by norepinephrine are negated by the alpha blockade of phenolamine while the beta-adrenergic stimulating effects of increased contractility and augmented cardiac output are preserved.
Vasodilators

In patients who have cardiac impairment, an increase in resistance may be so intense that additional specific pharmacologic intervention is necessary. In recent years various vasodilator drugs have been demonstrated to improve cardiac performance in patients who have chronic heart failure due to cardiopulmonary or coronary-artery disease. Pharmacologic unloading of the ventricle constitutes a new approach in the clinical treatment of congestive heart failure and cardiogenic shock. Properly administered, peripheral vasodilators lower myocardial oxygen consumption by reducing preload and afterload.

The responses to vasodilator therapy differ between patients who have elevated left ventricular filling pressures (LVFP) and those whose LVFP's are within normal limits. In the former, vasodilator drugs increase stroke volume and cardiac output, and decrease systemic vascular resistance, while arterial pressure does not change significantly. In the latter, decreased peripheral vascular resistance produces a marked reduction in venous return, thereby decreasing stroke volume, and systemic hypotension and tachycardia may occur (table 4).

Nitroprusside, nitroglycerin, and phentolamine are the drugs more often used for vasodilation. Their actions on the systemic, arterial and venous vascular systems, as well as on the pulmonary vasculature, differ.

Nitroprusside has a direct effect on the smooth muscle of the vascular bed that is independent of sympathetic innervation. The drug has no direct effect on myocardial contractility. Nitroprusside has been shown to increase coronary blood flow in experimental animals. The principal action of nitroprusside on left ventricular performance is mediated by mechanical unloading of the heart (fig. 9). It has been shown that nitroprusside decreases the work of the right ventricle by reducing pulmonary vascular resistance.

Nitroprusside also provides a rapid, convenient method for reversal of acute postoperative episodes of hypertension in patients who have coronary-artery disease. Because sudden decreases in blood pressure may occur with administration of nitroprusside, the drug should be used at low infusion rates of 10 to 15 μg/min, which may be increased gradually until the desired hemodynamic improvement is achieved. When a marked decrease in arterial pressure occurs without significant reduction in LVFP and increase in cardiac output, the drug should be discontinued. Arterial pressure promptly returns to previous levels following discontinuation of drug administration. Nitroprusside should not be used when hypovolemia is present. Volume expansion may be necessary to counteract hypotension.

Nitroglycerin has been shown to lower abruptly LVFP during acute angina pectoris with resolution of myocardial ischemia. It is used for patients who have acute myocardial infarction and heart failure. The major therapeutic effect of sublingual nitroglycerin is accomplished principally through decreased venous return since sublingual nitroglycerin diminishes ventricular preload relatively more than afterload. There is no direct effect on myocardial contractility. This results in decreased left ventricular end-diastolic volume and pressure, which reduces intraventricular wall tension and myocardial oxygen consumption.

With nitroglycerin, arterial pressure and LVFP decrease, and pulmonary edema is relieved. Cardiac output may or may not change, and systemic vascular resistance is not consistently reduced. The differences may be related to various degrees of failure present in different populations studied (fig. 4).

Nitroglycerin is administered sublingually (0.3–0.4 mg) or intravenously at an infusion rate of 0.2 to 1 μg/kg/min. Hypotension and tachycardia may occur during administration. The duration of the effect of sublingual nitroglycerin is between 15 and 20 minutes.

Phentolamine is an alpha-adrenergic blocking drug. Its vasodilating effects are due to both...

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**Table 4. Hemodynamic Effects of Vasodilation***

<table>
<thead>
<tr>
<th></th>
<th>Normal Ventricular Function</th>
<th>Ventricular Dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
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<td>Unchanged</td>
</tr>
<tr>
<td>Arterial pressure</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systemic</td>
<td>↓</td>
<td>Unchanged or ↓</td>
</tr>
<tr>
<td>Pulmonary</td>
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<td></td>
</tr>
<tr>
<td>Ventricular filling pressure</td>
<td></td>
<td>↓ or ↓ or ↓</td>
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<td>Left</td>
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<td>Right</td>
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<tr>
<td>Vascular resistance</td>
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</tr>
<tr>
<td>Stroke volume</td>
<td>↓</td>
<td>↑</td>
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* ↓ = decrease; ↑ = increase.
alpha blockade and direct vascular smooth muscle relaxation. Phentolamine has been shown to have positive inotropic action on the heart due to stimulation of beta-adrenergic sites (direct) and due to sympathetic discharge causing indirect stimulation of beta receptors in the heart (indirect). Vasodilation affects both arterial and venous beds. In general, the effects of phentolamine are similar to those of nitroprusside. Phentolamine is administered at an infusion rate of 1.5 to 2 μg/kg/min. Hypotension, tachycardia and hypoglycemia may complicate its administration.

**Diuretic Drugs**

Fluid and electrolyte abnormalities in congestive heart failure result from reduced glomerular filtration and increased reabsorption of sodium and water in the proximal renal tubules. In the chronic edematous state, activation of the renin–angiotensin–aldosterone humoral system contributes to augmented reabsorption of sodium in the distal tubules at the expense of potassium loss. In some patients, inappropriate secretion of antidiuretic hormone accentuates dilutional hyponatremia. All these fluid and electrolyte derangements are the result of decreased cardiac output and redistribution of renal flow to the inner cortex and medulla, leaving the outer cortex underperfused.

Ethacrynic acid and furosemide are the two most potent diuretic drugs available, with rapid onsets and relatively short durations of action. Ethacrynic acid and furosemide inhibit sodium reabsorption at the sites of isosmotic sodium reabsorption in the proximal tubule. They also inhibit sodium transport in the ascending limb of the loop of Henle and interfere with concentration of urine at the distal diluting sites, leading to formation of an isosmotic urine.

Furosemide appears to improve renal blood flow and redistribute renal flow from the medulla to the cortex. Therefore, it is particularly useful in con-
gestive heart failure associated with low urinary output. Ethacrynic acid does not inhibit carbonic anhydrase or increase renal bicarbonate excretion, and it is effective in promoting diuresis in systemic acidosis and alkalosis. It has been recently reported that furosemide reduces pulmonary capillary pressure, prior to its diuretic effect, with little change in cardiac output or heart rate in patients who have heart failure due to acute infarction.\textsuperscript{91–93}

Diuresis produced by these drugs is associated with a urinary loss of sodium, chloride, potassium, and ammonium ions. Hypochloremic alkalosis develops in response to these agents when they are given in high therapeutic doses. Potassium depletion may potentiate cardiac arrhythmias in patients being treated with digitalis. Therefore, proper replacement of these electrolytes, particularly potassium and chloride, is important. The usual intravenous dose of furosemide is 20–80 mg; the comparable dose of ethacrynic acid is 10–80 mg. Acute pulmonary edema and congestion are the main indications for use of diuretics in the perioperative period.

**Mechanical Support**

In recent years, invasive mechanical cardiac assist devices have been developed\textsuperscript{84} in an attempt to support the failing myocardium in cardiogenic shock. Among the several cardiac assist devices, intra-aortic balloon pumping (IABP) has emerged as the temporary mechanical treatment of choice for cardiogenic shock and refractory left ventricular failure.\textsuperscript{95} The improved hemodynamic state obtained by IABP often provides the damaged myocardium a critical interval in which to benefit from medical and surgical corrective measures and time to recover adequate, independent pumping ability.\textsuperscript{96} Full recovery from the shock state, however, remains limited by the extent of the original infarction.

Intra-aortic balloon pumping employs the principle of counterpulsation,\textsuperscript{97,98} a synchronized assist, with the heart’s own action, peaking during diastole and bottoming out during systole. Counterpulsation is instituted by a non-occlusive balloon supported by a catheter that is inserted into the descending aorta (below the origin of left subclavian artery) through the femoral artery and is triggered by the R-wave of the ECG. The balloon is inflated with helium during diastole and deflated during systole, thus alternately increasing and decreasing aortic volume. Removing volume from the aortic root during systole and returning it during diastole, counterpulsation decreases left ventricular work, lowers systolic arterial pressure and augments diastolic pressure, thus maintaining mean perfusion pressure (fig. 5). The reduction of cardiac work and systolic arterial pressure suggests that myocardial oxygen requirements are reduced. Enhancement of diastolic pressure augments coronary perfusion, since coronary blood flow occurs largely during diastole. On the other hand, the reduction in left ventricular filling pressure with consequent reduction in diastolic wall tension with IABP should also be beneficial for coronary perfusion. The hemodynamic improvement after institution of IABP is evidenced by the increase in stroke volume, decreases in left ventricular filling pressure and pulmonary arterial pressure, the lessening of ECG myocardial ischemic changes, and alleviation of angina pectoris.

The current role of intra-aortic balloon counterpulsation is to provide temporary support in selected cases of cardiogenic shock secondary to myocardial infarction, in hemodynamically unstable patients during emergency coronary arteriography and ventriculography in patients with refractory angina pectoris, and in conjunction with open-heart surgery (pre-, intra- and postoperatively).
Cardiac Arrhythmias

Arrhythmias occur often during anesthesia and operation, as well as in the early postoperative period. Electrolyte imbalance (particularly low serum potassium), hypoxemia, hypercapnia, acid–base abnormalities, anesthetic and other drugs, surgical trauma, and pre-existing cardiac disease are among the factors that predispose to the development of arrhythmias during the perioperative period. Arrhythmias may effect cardiac performance to different extents, depending on the type of arrhythmia, the presence of cardiac disease, and the patient's overall clinical condition.100

An understanding of the mechanism of action of the drugs used to treat cardiac arrhythmias is dependent on comprehension of the electrophysiologic abnormalities responsible for, or contributing to, the electrical disturbance. Thus, this discussion begins with basic considerations of the electrophysiologic properties of cardiac tissue and the abnormal mechanism underlying the genesis and perpetuation of arrhythmias. Within the framework provided by this review, the pharmacology and therapeutic applications of the antiarrhythmic drugs are discussed.

Normal Electrophysiology

Cardiac cells have the ability to maintain an electrical potential across their cell membrane. The various phases of the cardiac action potential are associated with alterations in the permeability of the cell membrane, mainly to Na⁺, K⁺, and Ca²++. The action potentials and ionic changes during the cardiac cycle are illustrated schematically in figure 5.

In resting cardiac cells during electrical diastole, a negative transmembrane potential of approximately −90 mV is maintained. This action potential is designated the resting potential. During the resting period (phase 4) the concentration of K⁺ is higher inside the cell, whereas the concentrations of Na⁺ and Ca²⁺ are higher in the extracellular space. The resting cell membrane is relatively permeable to K⁺ but much less so to Na⁺ and Ca²⁺. Furthermore, an active transport pump mechanism supported by adenosine triphosphate continuously extrudes Na⁺ from the cell interior and pumps in K⁺.

On excitation (at point E), the resting membrane potential is abruptly changed to the threshold level of about −60 to −70 mV, and the cell membrane suddenly becomes permeable to Na⁺. During this period of depolarization (phase 0), intense Na⁺ influx carries positive charges into the cell and the transmembrane voltage quickly becomes positive. At the end of phase 0, the cell is polarized with the inside positive by about +25 mV with respect to the outside (fig. 6). This represents the spike action potential. The rate of rise of this spike action potential determines the velocity of conduction, which in the sinoatrial (S-A) node, the atria, the atrioventricular (A-V) node and the ventricles is represented collectively on the ECG as the P wave duration, P-R interval and QRS duration (phase 0).

As the influx of Na⁺ subsides, the negative intracellular action potential is re-established, and repolarization occurs. This period of repolarization is divided into three stages, phases 1, 2 and 3 (fig. 6). Phase 1 constitutes an early brief period of limited repolarization. The principal ionic influx responsible for phase 1 is attributed to a transient inward Cl⁻ current. During phase 2, or the plateau of the action potential, there is a weak inflow of Ca²⁺ and Na⁺. This slow inward current of Ca²⁺ is involved in excitation–contraction coupling, and probably contributes to activating the contractile proteins during contraction. Catecholamines have been shown to enhance this
inward flow of Ca++, a phenomenon probably related to their positive inotropic action.

During phase 2 there is an outward current of positively charged K ions that tend to make the interior of the cell membrane more negative. This outward flow of K+ promotes rapid repolarization and phase 3, rapid repolarization, starts (fig. 6). The efflux of K+ during this period is associated with inactivation of the slow inward currents of Na+ and Ca++. The inside of the cell membrane becomes progressively more negative, and the transmembrane potential returns to its resting value. Cardiac fibers regain their ability to develop a normal response only when membrane voltage reaches its maximal value of about −90 mV, at which time the sodium pump is again activated for ionic transport. Thus, the excess Na+ that had entered the cell is eliminated in exchange for K+. The process of repolarization determines the duration of the action potential, and is represented electrocardiographically by the QT interval. The duration of the action potential is directly related to the refractory period of cardiac muscle, during which an electrical stimulus cannot evoke depolarization.

In the heart two types of action potential, fast and slow responses, have been observed. The resting membrane potential of the fast response is considerably more negative than that of the slow response. In addition, the slope of the upstroke (phase 0) is steeper, and the amplitude of the action potential and the extent of the overshoot of the fast response are greater than those associated with the slow response. The fast response action potential is observed in the myocardial fibers, the atria and ventricles, and the Purkinje fibers. The slow response is characteristic of fibers of the S-A and A-V nodes. The fast response may be altered to slow conduction either spontaneously or following pharmacologic interventions. Because the rate of rise of the upstroke and the amplitude of the action potential are important determinants of propagation velocity, in the slow-response cardiac tissue the conduction velocity is much slower and the tendency for the impulse to be blocked is greater than in tissues with the fast response.

For cardiac muscle fibers that do the contractile work of the heart, depolarization current is generated by potential differences that result from arrival of a propagated action potential. Certain cardiac fibers, however, are capable of undergoing self-excitation by generating impulses spontaneously, thus possessing the property of automaticity. Fibers that have this capability can, under appropriate circumstances, function as a pacemaker. In these fibers, transmem-

**Fig. 6.** Diagram of transmembrane electrical potential, the electrocardiogram (ECG) and cation movements across the cell membrane (CM). 4 = resting period (diastolic depolarization); 0 = rapid depolarization; 1, 2, and 3 = repolarization. The horizontal line at the bottom of the diagram represents the cell membrane (CM), and the arrows the movements of cations to intracellular (INTRA) and to extracellular (EXTRA) spaces. The electrical potential of a spontaneously depolarizing automatic cardiac cell (solid line) and after quinidine (broken line) are shown here. E = excitation.

brane voltage is not maintained at a steady value during the resting phase, as in other cardiac cells; rather, there is a slow spontaneous decrease in membrane potential (phase 4 depolarization). When the membrane potential reaches the threshold voltage (activating), the cell will excite itself. The occurrence of spontaneous diastolic depolarization in specialized automatic fibers is considered to be the normal mechanism for automaticity. Automaticity is a property of cardiac fibers normally controlling heart rhythm (S-A node, atrial fibers, A-V node, His–Purkinje system).

**Clinical Aspects and Mechanism of Arrhythmias**

Arrhythmias may be due to alterations in a formation of the cardiac impulse related to automaticity, to alterations in impulse propagation affecting conduction, or to a combination of altered automaticity and altered conduction (table 5).

**Altered Sinoatrial Rhythms**

The frequency of pacemaker firing is controlled by the activity of the sympathetic and vagal nervous system. Increased sympathetic activity enhances heart rate by decreasing the threshold or the magnitude of resting potential. Increased vagal activity diminishes heart rate by reducing the slope of the diastolic potential. Cardiac rate changes gradually under
Table 5. Cardiac Arrhythmias

<table>
<thead>
<tr>
<th>Arrhythmia</th>
<th>Rhythm</th>
<th>ECG Changes</th>
<th>Electrophysiologic Mechanism</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sinus bradycardia</td>
<td>Regular</td>
<td>P, QRS, T normal</td>
<td>Reduction in the slope of the pacemaker potential</td>
<td>Usually no treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P-P long</td>
<td></td>
<td>Atropine (0.5–1.0 mg, iv)</td>
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<td></td>
<td></td>
<td></td>
<td>Removal of cause</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pacing</td>
</tr>
<tr>
<td>Sinus tachycardia</td>
<td>Regular</td>
<td>P, QRS, T normal</td>
<td>Increase in the slope of pacemaker potential</td>
<td>Removal of cause</td>
</tr>
<tr>
<td></td>
<td></td>
<td>P-P short</td>
<td></td>
<td>Sedation</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Propranolol</td>
</tr>
<tr>
<td>Paroxysmal atrial</td>
<td>Regular</td>
<td>No P wave</td>
<td>Increase in the slope of atrial ectopic pacemaker</td>
<td>Sedation</td>
</tr>
<tr>
<td>tachycardia</td>
<td></td>
<td>QRS normal</td>
<td></td>
<td>Vagal stimulation (carotid massage, Valsalva)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Neostigmine (0.5–1.0 mg, iv)</td>
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<td></td>
<td></td>
<td></td>
<td>Edrophonium (5–10 mg, iv)</td>
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<td>Digitalis</td>
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<td></td>
<td></td>
<td></td>
<td>DC electric shock</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td>Alpha agonist (phenylephrine)</td>
</tr>
<tr>
<td>Premature atrial beats</td>
<td>Irregular</td>
<td>P abnormal</td>
<td>Enhanced atrial ectopic autamoticity</td>
<td>No treatment</td>
</tr>
<tr>
<td></td>
<td></td>
<td>QRS usually normal</td>
<td>Re-entry phenomenon</td>
<td>Atropine</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Pacing</td>
</tr>
<tr>
<td>Premature ventricular</td>
<td>Irregular</td>
<td>Absent P wave</td>
<td>Enhanced ventricular ectopic autamoticity</td>
<td>Removal of cause</td>
</tr>
<tr>
<td>beats</td>
<td></td>
<td>Abnormal QRS and T</td>
<td>Compensatory pause</td>
<td>Lidocaine (50–100 mg, iv)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Propranolol</td>
</tr>
<tr>
<td>Atrial flutter</td>
<td>Regular</td>
<td>f waves</td>
<td>Repetitive ectopic firing</td>
<td>Digitalis</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>Regular</td>
<td>No p waves</td>
<td>Irregular fluctuation of potential</td>
<td>DC countershock</td>
</tr>
<tr>
<td></td>
<td>Irregular</td>
<td>QRS normal</td>
<td></td>
<td>Pacing override</td>
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<tr>
<td></td>
<td></td>
<td>A-V block</td>
<td></td>
<td>Propranolol</td>
</tr>
<tr>
<td>Ventricular tachycardia</td>
<td>Regular</td>
<td>Aberrant QRS</td>
<td>Rhythmic repetitive ventricular ectopic firing</td>
<td>DC countershock</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Independent P waves</td>
<td></td>
<td>Lidocaine</td>
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<td></td>
<td></td>
<td>Procainamide</td>
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<tr>
<td></td>
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<td></td>
<td></td>
<td>Propranolol</td>
</tr>
<tr>
<td>Ventricular fibrillation</td>
<td>Irregular</td>
<td>No P, QRS, T waves</td>
<td>Repetitive ventricular firing</td>
<td>DC countershock</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Irregular waves</td>
<td></td>
<td>Lidocaine iv</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Cardiopulmonary resuscitation</td>
</tr>
</tbody>
</table>

natural conditions, and several beats are necessary to attain a new steady state.

Sinus tachycardia is not infrequent during anesthesia, operation, and the postoperative period. In most instances, when the rate is not excessive and the myocardium is normal, it is well tolerated. Tachycardia (120 to 160 beats/min) in the presence of coronary heart disease may lead to myocardial ischemia and damage due to the reduction of coronary blood flow during diastole\textsuperscript{180} and the increase in myocardial oxygen consumption. The treatment of sinus tachycardia is usually directed at the underlying cause, which may be hypovolemia, fever, pain, anxiety, light anesthesia, congestive heart failure, or a hypermetabolic state, such as hyperthyroidism or sepsis. When sinus tachycardia causes myocardial ischemia or impaired cardiac performance, propranolol, administered intravenously in increments (0.25 to 0.5 mg) during careful monitoring of the ECG and arterial pressure, is indicated. A total of 1 mg can be given over a 20–25-minute period.

Sinus bradycardia may be asymptomatic and require no treatment. Marked slowing, however, may produce inadequate perfusion of vital organs (heart, brain, kidneys). Atrial and ventricular ectopic rhythms are more apt to occur with bradycardia. Under these circumstances attempts should be made to enhance heart rate (atropine, atrial pacing).

Sinus arrhythmia is a normal sinus rhythm in which periodic variations in the heart rate occur in relation to respiration. The heart rate accelerates during inspiration and slows again on expiration. It is due to alterations in vagal tone and can be abolished by atropine.

Premature Systoles

Atrial Extrasystoles. Two principal mechanisms are responsible for these extrasystoles: premature beat
coupled to a normally conducted beat, which probably reflects a re-entry phenomenon, and premature beat as the result of enhanced automaticity in an atrial ectopic focus.

In the ECG, the atrial extrasystole is characterized by a premature P wave that differs in appearance from the configuration of the normal P wave. The QRS complex of the premature beat is usually normal in configuration because the spread of ventricular excitation occurs via the usual pathways. With very premature contractions, however, the QRS complex is different (aberrant conduction). The interval between the premature beat and the next normal beat is almost equal to the normal cardiac cycle duration, when the ectopic focus is near the S-A node.

Occasional atrial premature beats generally require no treatment. When extrasystoles occur with excessive frequency they are more likely to lead to paroxysmal atrial arrhythmias or atrial fibrillation. Speeding of the heart rate (atropine, atrial electrical pacing) abolishes premature beats. Quinidine or propranolol may be needed to suppress extrasystoles in the symptomatic individual.

Ventricular Extrasystoles. Ventricular extrasystole or premature beat is a cardiac contraction of ectopic impulse arising from a ventricular focus. Premature ventricular contractions (PVC's) are the commonest of the cardiac arrhythmias. Premature ventricular beats often occur during cardiac and thoracic surgical procedures. Other potential causes include digitalis toxicity, systemic hypoxia, regional myocardial ischemia and injury, hypokalemia, hypocalcemia, acidosis, and hypercapnia. The QRS and T waves differ strikingly from the normal because the ectopic impulse takes an abnormal and longer course through the ventricle (aberrant conduction). The ventricular extrasystole is followed by an abnormally long pause preceding the subsequent normal sinus beat. This compensatory pause occurs because the ventricle is still refractory from the preceding ectopic beat when the next sinus impulse arrives (long R-R interval).

In some instances, PVC's are asymptomatic and require no treatment. PVC's, however, are of greater importance after myocardial ischemia or infarction because of their potential for producing life-threatening ventricular tachycardia or fibrillation. The risk is greater when PVC's fall within the "vulnerable" period. Treatment is indicated when more than three or four extrasystoles occur per minute, when they are multifocal in origin, when they occur in salvos of three or more, and when they occur near the peak of the T waves of the preceding QRS complexes (vulnerable period). The last type is likely to initiate ventricular tachycardia. In addition, PVC's in the early postoperative period should be treated unless the patient has been known to have long-standing, singly-occurring extrasystoles. Treatment or correction of the underlying disorders may lead to disappearance of the PVC's. Potassium should be given to correct hypokalemia when digitalis toxicity is suspected. Correction of metabolic acidosis, respiratory disorders, hypotension, and electrolyte abnormalities should be prompt. Meanwhile, lidocaine may be given intravenously, particularly when the patient has heart disease, in a 50–100-mg bolus. Lidocaine infusion at a rate of 1–2 mg/min may also be used. Procainamide (250–400 mg, orally or im) may be used to complement lidocaine therapy. In management of patients who have severe, threatening ventricular irritability, propranolol (0.5–1.0 mg, iv) may be administered. Diphenhydantoin, 50–100 mg, iv, very slowly, can be used with success, especially when the PVC's are due to digitalis. When PVC's are associated with marked bradycardia, the above-mentioned antiarrhythmic drugs are contraindicated unless a pacemaker is inserted. Atrial pacing or atropine can be used to increase heart rate and suppress ventricular ectopic activity.

Ectopic Tachycardias. Ectopic or paroxysmal tachycardias originate from some ectopic site in the heart, and are characterized by sudden appearance and abrupt reversion to normal. Episodes of paroxysmal tachycardias may persist for only a few beats, or for many hours or days, and the episodes often recur.

Paroxysmal supraventricular tachycardias originate in the atria or in the A-V junctional tissues. The tachycardias occur as the result of rapid firing of an ectopic pacemaker cell or as the result of an impulse circling a re-entry loop repetitively.

In paroxysmal atrial tachycardia (150 to 250 beats/min) that originates from an ectopic focus, each atrial complex is usually conducted to the ventricle. The QRS complexes are normal since activation of the ventricles proceeds through the normal pathway. Frequently, no treatment is required. Cessation of this arrhythmia is often achieved by maneuvers that increase vagal tone. Carotid sinus pressure (unilateral) for 5 to 10 seconds with continuous ECG monitoring will often abruptly convert the arrhythmia to normal sinus rhythm. Neostigmine in small doses (0.5–1.0 mg) or edrophonium chloride (5–10 mg) intravenously may be successful in slowing the heart rate. Alpha agonists (phenylephrine, methoxamine) given intravenously to raise the systolic arterial
pressure to 130–160 mm Hg may be helpful. Rapid digitalization with intravenous digoxin may convert the arrhythmia to sinus rhythm by slowing the rate of the ectopic pacemaker and prolonging atrioventricular conduction. When atrial pacing wires are available, atrial pacing at a rate faster than the spontaneous rate of paroxysmal atrial tachycardia may “capture” the atria, suppress the ectopic focus, and restore sinus rhythm. Electrical cardioversion may be necessary when these techniques fail to convert the arrhythmia, particularly in a patient who is hypotensive (figs. 7 and 8).

Atrial flutter is a rapid ectopic atrial tachyarrhythmia that results in an atrial rate between 250 and 350 beats/min and a regular ventricular response of 2:1 or 3:1, depending on the extent of atrioventricular block. Atrial flutter is common following cardiac surgery. This arrhythmia can be resistant to digitalis therapy, and larger than usual doses of digitalis may be necessary either to convert flutter to sinus rhythm or to induce an acceptable stable atrioventricular block. Atrial pacing at a faster rate than the atrial flutter may often convert the flutter to atrial fibrillation, a rhythm relatively easy to control with digitalis.\textsuperscript{133,134} Consideration must be given to the need for cardioversion because of the risk of ventricular fibrillation, particularly when digitalis has been already administered.\textsuperscript{135}

Atrial fibrillation is characterized by extremely rapid, irregular atrial impulses, faster than 350 beats/min, and by irregular rapid ventricular beats. This arrhythmia may occur as paroxysms of an irregular tachycardia or, more often, it may become established as a permanent condition. Severe hemodynamic derangement usually results when atrial fibrillation occurs suddenly, and cardioversion with direct-current countershock is the treatment of choice in this situation (fig. 9). When the patient has chronic longstanding atrial fibrillation, attempts to convert the rhythm may not be successful or even hemodynamically useful. As with atrial flutter, forethought is advisable concerning the need for cardioversion in patients who have been receiving digitalis therapy. In such patients, increments of digoxin (0.25 mg) car
FIG. 8. Hemodynamic alterations in response to atrial pacing, recorded in a patient in whom nodal rhythm developed during coronary-artery operation. Note, in the left panel, arterial (AP), left atrial (LAP) and pulmonary arterial pressures are within normal limits (sinus rhythm). Immediately upon the occurrence of nodal arrhythmia, AP decreased abruptly, while large "v" waves appeared in LAP. Following the institution of atrial ("A") pacing at faster rate than the nodal rate, arterial pressure was restored and the "v" waves in LAP were abolished. These "v" waves that appeared during nodal rhythm result from untimed contraction of the atrium and ventricle. Deformation of arterial pressure is due to the intra-aortic balloon pump.

be used to control ventricular rate and re-establish satisfactory hemodynamics. Digitalization should be continued until the ventricular rate is decreased to an acceptable range. In the non-digitalized patient 0.5–0.75 mg digoxin, iv, can be given initially at increments of 0.25 mg over a period of 20 to 30 minutes; thereafter, 0.25 mg, iv, at three- to four-hour intervals to a total of 1.0 to 1.5 mg. When digitalization does not produce adequate rate control, propranolol in small doses (0.25–0.5 mg, iv) may be used.

Ventricular tachycardia: A premature impulse reaching the ventricles in their "vulnerable" period can initiate a repetitive response in the form of ventricular tachycardia or fibrillation. During the vulnerable period (which coincides with the downslope of the T wave) there is considerable variability in the excitability of the cardiac cells. Some fibers are still in the refractory period, others have fully recovered their excitability, and still others are able to conduct impulses at very slow conduction velocity. Thus, the action potentials are propagated over the ventricles in multiple wavelets at varying conduction velocity.

Ventricular tachycardia is almost always the result of heart disease, particularly ischemic heart disease. Numerous drugs, including digitalis, quinidine, cyclopropane, chloroform, and potassium, and metabolic and electrolyte abnormalities have been incriminated also.

Hypotension, shock, congestive heart failure, and pulmonary edema are often associated with ventricular tachycardia. Ventricular fibrillation may also develop. The electrocardiographic diagnosis is made from the rapid (more than 120 beats/min), repeated, abnormal QRS complexes, reflecting aberrant intraventricular impulse conduction. Independent P waves or retrograde P waves may be found also.

Sustained ventricular tachycardia in the cardiac patient necessitates emergency treatment. Direct-current countershock is the treatment of choice (100–150 joules initially). When countershock is not available, or when the situation is less urgent, lidocaine in a bolus of 50–100 mg may be given intravenously. If not effective, it may be repeated in 2 or 3 minutes. A lidocaine drip should be started.
and continued until the danger of recurrence of the tachycardia has passed.

Procainamide may be given intravenously (50–100 mg). The dose may be repeated at 2–3-minute intervals to a total of 0.5–1 g. Propranolol, 0.5–1.0 mg, iv, may also be used to suppress the arrhythmia. Correction of any underlying cause is very important. Electrical pacing to overdrive the arrhythmia may be useful when the tachycardia is recurrent.

Ventricular fibrillation is the common mechanism of cardiac arrest and death from any cause. This is an emergency. The irregular, continuous, uncoordinated twitchings of the ventricular muscle fibers result in no output of blood. Unless active treatment is instituted immediately, irreversible damage to the brain and other organs results. Precordial electroshock is administered immediately. Cardiopulmonary resuscitation measures of closed-chest cardiac massage, intubation, and ventilatory support are necessary when direct-current cardioversion is not immediately successful.

Lidocaine, procainamide, propranolol, and sodium bicarbonate are also used.

Antiarrhythmic Drugs

Although various drugs are capable of controlling cardiac arrhythmias, the clinical pharmacology and electro-physiology of certain commonly used antiarrhythmic drugs is discussed here.101–109

Quinidine

Quinidine is concentrated in the cell membrane and modifies cation flux during both action and resting phases of the membrane potential.110,111 During diastolic depolarization (phase 4), as quinidine reduces Na⁺ influx into the cell, automaticity is depressed. This direct effect on automaticity is usually counteracted by the vagolytic effect of quinidine; therefore, no change or even slight acceleration of the sinus rate occurs at therapeutic blood levels of the drug.112

Quinidine diminishes conduction velocity by decreasing passive influx of Na⁺ during rapid depolarization (phase 0), thus prolonging the action potential. Furthermore, quinidine, by reducing membrane permeability to passive K⁺ efflux during rapid repolarization (phase 3), prolongs the action potential and the refractory period. Thus, quinidine reduces membrane responsiveness by decreasing conduction velocity, automaticity, excitability, and the amplitude of the propagated action potential (table 6).

Indications for quinidine administration include atrial fibrillation, premature beats, and supraventricular tachycardia in the late postoperative period.

Procainamide

Procainamide appears to possess all the electrophysiologic properties of quinidine.113 They both
depress spontaneous diastolic depolarization or automaticity, slow conduction velocity, and prolong the refractory period. The toxic effects of quinidine and procainamide are similar. Of special note is the syndrome resembling systemic lupus erythematosus that has been reported to occur in patients receiving procainamide therapy.

The indications and contraindications for procainamide are similar to those for quinidine. It can be administered intravenously in 100-mg increments slowly at 5-minute intervals until the desired effect is achieved or a total dose of 700–1,000 mg is reached. Severe hypotension may occur during iv administration. This drug, unlike quinidine, is only minimally bound to plasma proteins.

**Lidocaine**

Lidocaine is effective in the treatment of premature ventricular beats and ventricular tachycardia. Although lidocaine resembles procainamide in chemical structure, it differs markedly in electrophysiologic properties (table 6). From the few data available on the electrical action of lidocaine, it appears that the drug does not alter cation exchange in the S-A and A-V nodes. Conduction is not altered in the ventricles with lidocaine, indicating that the drug does not influence Na+ influx during excitation. During repolarization in the ventricles, lidocaine enhances K+ exit from the cell, thus shortening the duration of the action potential. As the action potential is shortened, the duration of the functional refractory period, relative to the duration of the action potential, is increased. Finally, lidocaine appears to depress Na+ influx during diastolic depolarization, thereby reducing automaticity.

The initial dose of lidocaine is 1 mg/kg as a single intravenous injection. The dose can be repeated once every 3 to 5 minutes to a total of 3–4 mg/kg. Lidocaine can be used as an infusion at a rate of 1–4 mg/min to prevent recurrence of PVC's. In recommended dosage, the drug is free of cardiac toxicity. Lidocaine toxicity is essentially limited to central nervous system aberrations, including fasciculation, disorientation, drowsiness, and convulsions.

**Diphenhydantoin**

Diphenhydantoin (DPH) is effective in the treatment of digitalis-induced arrhythmias. Like lidocaine, DPH depresses digitalis-enhanced ventricular automaticity without adversely affecting intraventricular conduction, while it tends to reverse digitalis-induced prolonged atrioventricular conduction. DPH may or may not increase conduction velocity. Therefore, increased ventricular response in supraventricular tachycardias may occur due to the ability of DPH to enhance A-V nodal conduction. DPH also decreases automaticity by decreasing diastolic depolarization.

Diphenhydantoin is administered orally or parenterally. In the perioperative period intravenous administration is preferred. The usual dose of DPH is 100 mg, given as a bolus slowly and repeated after 5 minutes as needed.

Toxicity is uncommon when DPH is administered carefully in small incremental doses. However, severe hypotension, bradycardia and atrioventricular block have been reported to occur with DPH—apparently due to marked depression of diastolic depolarization and automaticity.

**Digitalis**

Digitalis preparations are most effective in reducing ventricular rate in the setting of supraventricular tachycardias. The effects of digitalis on the electrophysiologic properties of the cardiac muscle are complex and vary considerably with dose, type of cardiac tissue involved, and automatic activities. The electrophysiologic effects of the drug on conduction tissue are due to increased automaticity, reduced conduction velocity, and decreased refractoriness (table 6). Indirect effects mediated through the vagus may lead to slowing of the heart rate also. Digitalis depresses the activity of the sodium–potassium exchange systems across the cardiac muscle membrane, with consequent increase in intracellular sodium and loss of potassium from the cardiac cell. The loss of intracellular potassium is related to the electrical toxic effects of digitalis. The actions of digitalis on conduction velocity and refractoriness in the myocardial conductive tissue are responsible for the occurrence of re-entry arrhythmias with the drug.

Digitalis reduces the ventricular rate in supraventricular tachycardias, by prolonging the functional refractory period of the A-V node. Thus, in atrial flutter with 2:1 A-V block, prolongation of the refractory period may reduce the ventricular rate by leading to a higher degree of block. Similarly, in patients who have paroxysmal atrial tachycardia,

<table>
<thead>
<tr>
<th>Table 6. Electrophysiology of Antiarrhythmic Drugs*</th>
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<tbody>
<tr>
<td>Drug</td>
</tr>
<tr>
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</tr>
<tr>
<td>Procainamide</td>
</tr>
<tr>
<td>Quinidine</td>
</tr>
<tr>
<td>Lidocaine</td>
</tr>
<tr>
<td>Diphenhydantoin</td>
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<tr>
<td>Digitalis</td>
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<tr>
<td>Propranolol</td>
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</tbody>
</table>

* = no change; ↑ = increase; ↓ = decrease.
prolongation of the refractory period with digitalis may lead to slowing of the heart rate. In atrial fibrillation the frequency of atrial impulses converging on the A-V node can be affected by digitalis, which shortens the refractory period of atrial muscle. Thus, atrial impulses that enter the A-V node when it is unable to propagate the impulses to the ventricle will be concealed within the node, and thereby the impulses that successfully traverse the node are reduced. Because digitalis diminishes conduction velocity at the A-V node and decreases refractoriness in myocardial conductive tissue, it may provoke re-entrant tachyarrhythmias.

**Propranolol**

Propranolol, a beta-adrenergic receptor-blocking drug, has been used in the management of supraventricular and ventricular arrhythmias (tachycardias or extrasystoles) resulting from digitalis toxicity and ischemic heart disease. The antiarrhythmic action of propranolol results mainly from inhibition of beta-adrenergic stimulation of the heart. Although propranolol has a direct membrane-mediated action, this appears to be relatively less important with the usual therapeutic concentrations of the drug. The increased automaticity, enhanced conduction velocity and shortening of refractory period resulting from sympathetic stimulation can be reversed by beta blockade with propranolol. In addition, the direct membrane effects of propranolol result in decreased influx of Na+ during depolarization and enhanced K+ efflux from the cell during repolarization. These beta-blocking and direct effects of propranolol result in diminished automaticity and conduction velocity, and refractoriness is increased.

Propranolol is used in the perioperative period for the treatment of sinus tachycardias, paroxysmal supraventricular tachycardias, premature beats, arrhythmias due to digitalis toxicity, and atrial fibrillation with fast ventricular response. In the perioperative period, propranolol is given intravenously as a single injection of 0.25–0.5 mg. This dose can be repeated at 5-minute intervals until the desired effect is achieved or to a total of 1–2 mg. Severe hypotension due to myocardial depression, bradycardia, and A-V block may complicate the use of propranolol. Bronchial asthma and heart block are contraindications to its use. In cases of heart block, when pacing is available, small doses of propranolol may be administered.

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