Antiarrhythmics

20

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I. OVERVIEW

In contrast to skeletal muscle, which contracts only when it receives a stimulus, the heart contains specialized cells that exhibit automaticity. That is, they intrinsically generate rhythmic action potentials in the absence of external stimuli. These "pacemaker" cells differ from other myocardial cells in showing a slow, spontaneous depolarization during diastole (phase 4), caused by an inward positive current carried by sodium and calcium ions. This depolarization is fastest in the sinoatrial (SA) node (the normal initiation site of the action potential), and it decreases throughout the normal conduction pathway through the atrioventricular (AV) node to the bundle of His and the Purkinje system. Dysfunction of impulse generation or conduction at any of a number of sites in the heart can cause an abnormality in cardiac rhythm. Figure 20.1 summarizes the drugs used to treat cardiac arrhythmias.

CLASS I (Na^+-channel blockers)

Disopyramide (IA) NORPACE
Flecainide (IC) TAMBOCOR
Lidocaine (IB) XYLOCAINE
Mexiletine (IB) MEXITIL
Procainamide (IA) PRONESTYL
Propafenone (IC) RYTHMOL
Quinidine (IA) QUINIDEX, QUINAGLUTE

CLASS II (ß-adrenoreceptor blockers)

Atenolol TENORMIN
Esmolol BREVIBLOC
Metoprolol LOPRESSOR, TOPROL-XL

CLASS III (K^+ channel blockers)

Amiodarone CORDARONE, PACERONE
Dofetilide TIKOSYN
Dronedarone MULTAQ
Ibutilide CORVERT
Sotalol BETAPACE, SORINE

CLASS IV (Ca^{2+} channel blockers)

Diltiazem CARDIZEM, CARTIA XT
Verapamil CALAN, ISOPTIN SR, VERELAN

OTHER ANTIARRHYTHMIC DRUGS

Adenosine ADENOCARD
Digoxin LANOXIN
Magnesium sulfate

Figure 20.1
Summary of antiarrhythmic drugs.

II. INTRODUCTION TO THE ARRHYTHMIAS

The arrhythmias are conceptually simple. Dysfunctions cause abnormalities in impulse formation and conduction in the myocardium. However, in the clinical setting, arrhythmias present as a complex family of disorders with a variety of symptoms. To make sense of this large group of disorders, it is useful to organize the arrhythmias into groups according to the anatomic site of the abnormality: the atria, the AV node, or the ventricles. Figure 20.2 summarizes several commonly occurring arrhythmias. Although not shown, each of these abnormalities can be further divided into subgroups depending on the electrocardiogram findings.

A. Causes of arrhythmias

Most arrhythmias arise either from aberrations in impulse generation (abnormal automaticity) or from a defect in impulse conduction.

1. **Abnormal automaticity:** The SA node shows the fastest rate of phase 4 depolarization and, therefore, exhibits a higher rate of discharge than that occurring in other pacemaker cells exhibiting automaticity. Thus, the SA node normally sets the pace of contraction for the myocardium. If cardiac sites other than the SA node show enhanced automaticity, they may generate competing stimuli, and arrhythmias may arise.

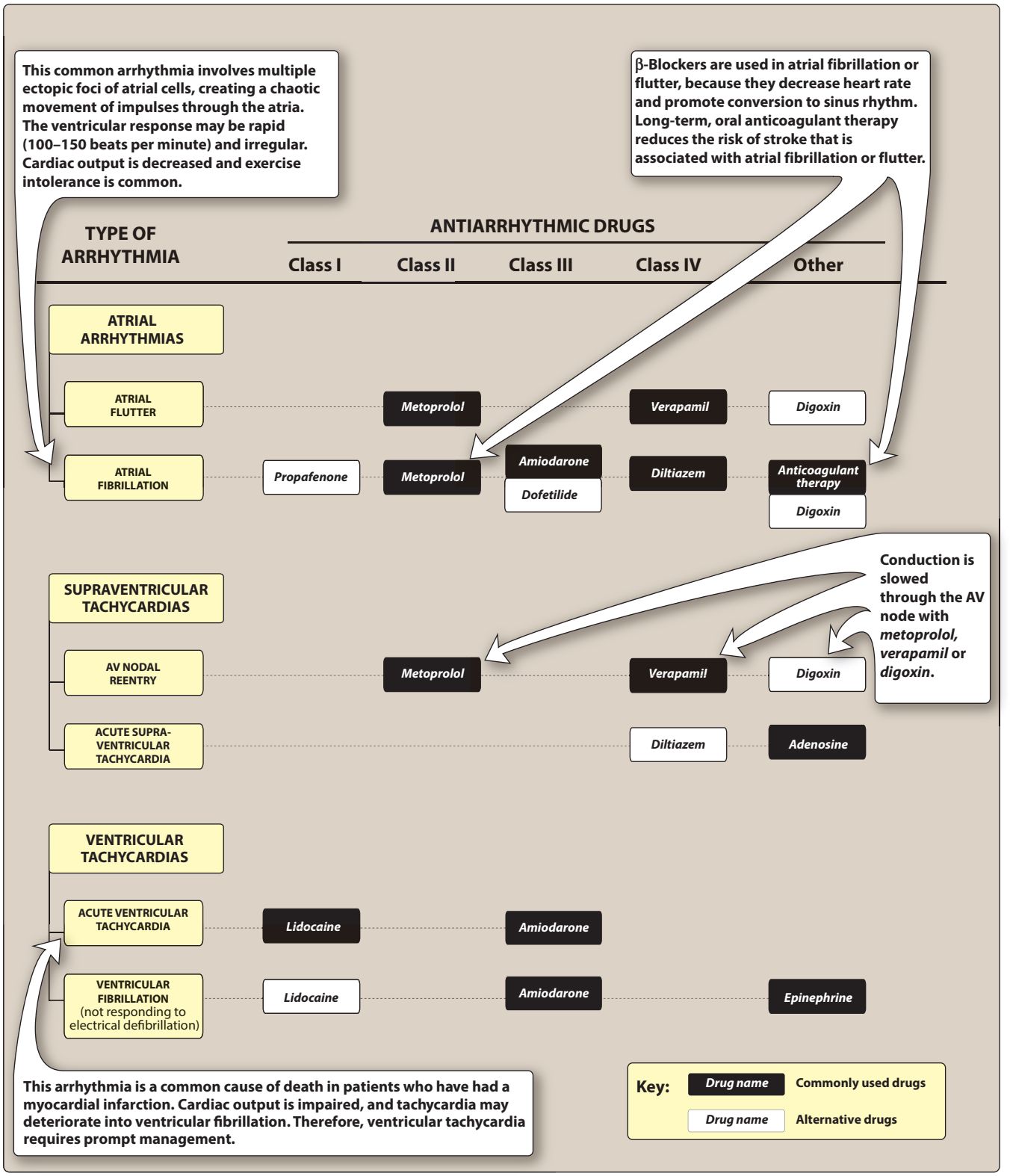

Figure 20.2
Therapeutic indications for some commonly encountered arrhythmias. AV = atrioventricular.

Most of the antiarrhythmic agents suppress automaticity by blocking either Na^+ or Ca^{2+} channels to reduce the ratio of these ions to K^+. This decreases the slope of phase 4 (diastolic) depolarization and/or raises the threshold of discharge to a less negative voltage. Antiarrhythmic drugs cause the frequency of discharge to decrease. This effect is more pronounced in cells with ectopic pacemaker activity than in normal cells.

2. **Abnormalities in impulse conduction:** Impulses from higher pacemaker centers are normally conducted down pathways that bifurcate to activate the entire ventricular surface (Figure 20.3). A phenomenon called reentry can occur if a unidirectional block caused by myocardial injury or a prolonged refractory period results in an abnormal conduction pathway. Reentry is the most common cause of arrhythmias, and it can occur at any level of the cardiac conduction system. This short-circuit pathway results in reexcitation of the ventricular muscle, causing premature contraction or sustained ventricular arrhythmia. Antiarrhythmic agents prevent reentry by slowing conduction (class I drugs) and/or increasing the refractory period (class III drugs), thereby converting a unidirectional block into a bidirectional block.

B. Antiarrhythmic drugs

As noted above, antiarrhythmic drugs can modify impulse generation and conduction to prevent arrhythmias from occurring or to reduce symptoms associated with arrhythmias. Unfortunately, many of the antiarrhythmic agents are known to have dangerous proarrhythmic actions—that is, to cause arrhythmias. Inhibition of potassium (K^+) channels (typically thought of as class III activity) widens the action potential and can, thus, prolong the QT interval. If prolongation is excessive, these drugs increase the risk of developing life-threatening ventricular tachyarrhythmias (torsades de pointes). The most common cause of QT prolongation is drug-induced, although other conditions (for example, ischemia and hypokalemia) and genetic profiles may contribute. QT prolongation is not only seen with class III antiarrhythmics. Drugs such as *cisapride* and *terfenadine* were withdrawn from the market because of severe and fatal arrhythmias. Many drugs are known to prolong the QT interval, such as macrolide antibiotics and antipsychotics. Caution should be employed when combining drugs with additive effects on the QT interval or when giving QT-prolonging antiarrhythmic drugs with drugs known to inhibit their metabolism. As such, the benefit of antiarrhythmic drugs must always be compared to the potential for serious adverse effects or drug interactions. [Note: Implantable cardioverter defibrillators are becoming more widely used to manage ventricular arrhythmias.]

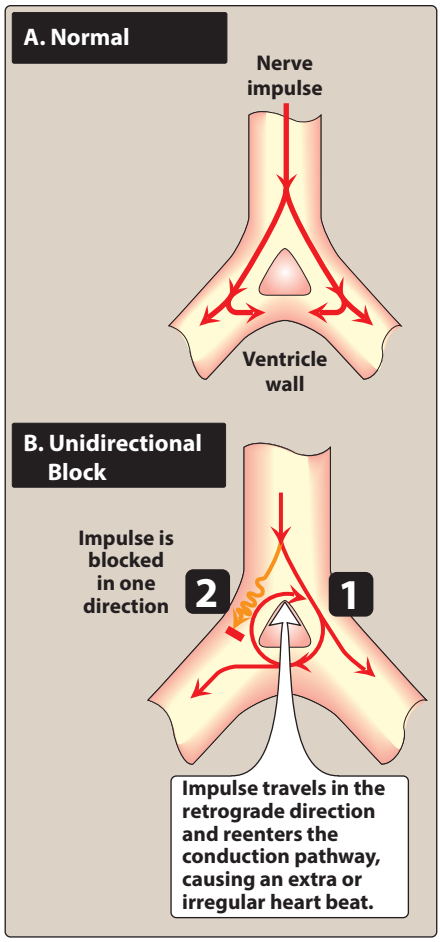

Figure 20.3
Schematic representation of reentry.

III. CLASS I ANTIARRHYTHMIC DRUGS

Antiarrhythmic drugs can be classified according to their predominant effects on the action potential (Figure 20.4). Although this classification is convenient, it is not entirely clear-cut, because many drugs have actions relating to more than one class or may have active metabolites with a different class of action. Class I antiarrhythmic drugs act by blocking

CLASSIFICATION OF DRUG	MECHANISM OF ACTION	COMMENT
IA	Na^+ channel blocker	Slows Phase 0 depolarization in ventricular muscle fibers
IB	Na^+ channel blocker	Shortens Phase 3 repolarization in ventricular muscle fibers
IC	Na^+ channel blocker	Markedly slows Phase 0 depolarization in ventricular muscle fibers
II	β-Adrenoreceptor blocker	Inhibits Phase 4 depolarization in SA and AV nodes
III	K^+ channel blocker	Prolongs Phase 3 repolarization in ventricular muscle fibers
IV	Ca^{2+} channel blocker	Inhibits action potential in SA and AV nodes

Figure 20.4
Actions of antiarrhythmic drugs. SA = sinoatrial; AV = atrioventricular.

voltage-sensitive sodium (Na^+) channels. The use of sodium channel blockers has declined due to their proarrhythmic effects, particularly in patients with reduced left ventricular function and ischemic heart disease.

A. Use dependence

Class I drugs bind more rapidly to open or inactivated sodium channels than to channels that are fully repolarized following recovery from the previous depolarization cycle. Therefore, these drugs show a greater degree of blockade in tissues that are frequently depolarizing. This property is called use dependence (or state dependence), and it enables these drugs to block cells that are discharging at an abnormally high frequency, without interfering with the normal, low-frequency beating of the heart. The class I drugs have been subdivided into three groups according to their effect on the duration of the ventricular action potential (Figure 20.4).

B. Class IA antiarrhythmic drugs: Quinidine, procainamide, and disopyramide

Quinidine [KWIN-i-deen] is the prototype class IA drug. Other agents in this class include *procainamide* [proe-KANE-a-mide] and *disopyramide* [dye-soe-PEER-a-mide]. Because of their concomitant class III activity, they can precipitate arrhythmias that can progress to ventricular fibrillation.

1. **Mechanism of action:** *Quinidine* binds to open and inactivated sodium channels and prevents sodium influx, thus slowing the rapid upstroke during phase 0 (Figure 20.5). It decreases the slope of phase 4 spontaneous depolarization, inhibits potassium channels, and blocks calcium channels. Because of these actions, it slows conduction velocity and increases refractoriness. *Quinidine* also has mild α-adrenergic blocking and anticholinergic actions. *Procainamide* and *disopyramide* have actions similar to those of *quinidine*. However, there is less anticholinergic activity associated with *procainamide* and more with *disopyramide*. Neither *procainamide* nor *disopyramide* has α-blocking activity.

Disopyramide produces a negative inotropic effect that is greater than the weak effect exerted by *quinidine* and *procainamide*, and unlike the other drugs, it causes peripheral vasoconstriction. The drug may produce a clinically important decrease in myocardial contractility in patients with systolic heart failure.

2. **Therapeutic uses:** *Quinidine* is used in the treatment of a wide variety of arrhythmias, including atrial, AV junctional, and ventricular tachyarrhythmias. *Procainamide* is available in an intravenous formulation only and may be used to treat acute atrial and ventricular arrhythmias. However, electrical cardioversion or defibrillation and *amiodarone* have mostly replaced *procainamide* in clinical use. *Disopyramide* is used in the treatment of ventricular arrhythmias as an alternative to *procainamide* or *quinidine* and may also be used for maintenance of sinus rhythm in atrial fibrillation or flutter.

3. **Pharmacokinetics:** *Quinidine sulfate or gluconate* is rapidly and almost completely absorbed after oral administration. It undergoes extensive metabolism primarily by the hepatic cytochrome P450 3A4 (CYP3A4) isoenzyme, forming active metabolites. *Procainamide* has a relatively short duration of action of 2 to 3 hours. A portion of *procainamide* is acetylated in the liver to *N*-acetylprocainamide (NAPA), which prolongs the duration of the action potential. Thus, NAPA has properties and side effects of a class III drug. NAPA is eliminated via the kidney, and dosages of *procainamide* may need to be adjusted in patients with renal failure. *Disopyramide* is well absorbed after oral administration. It is metabolized in the liver to a less active metabolite and several inactive metabolites. *Disopyramide* is a substrate of CYP3A4. About half of the drug is excreted unchanged by the kidneys.

4. **Adverse effects:** Large doses of *quinidine* may induce the symptoms of cinchonism (for example, blurred vision, tinnitus, headache, disorientation, and psychosis). Drug interactions are common with *quinidine* since it is an inhibitor of both CYP2D6 and P-glycoprotein. Intravenous administration of *procainamide* may cause hypotension. *Disopyramide* has the most anticholinergic adverse effects of the class IA drugs (for example, dry mouth, urinary retention, blurred vision, and constipation). Both *quinidine* and *disopyramide* should be used with caution with potent inhibitors of CYP3A4.

C. Class IB antiarrhythmic drugs: Lidocaine and mexiletine

The class IB agents rapidly associate and dissociate from sodium channels. Thus, the actions of class IB agents are manifested when the cardiac cell is depolarized or firing rapidly. The class IB drugs *lidocaine* [LYE-doe-kane] and *mexiletine* [MEX-i-le-teen] are useful in treating ventricular arrhythmias.

1. **Mechanism of action:** In addition to sodium channel blockade, *lidocaine* and *mexiletine* shorten phase 3 repolarization and decrease the duration of the action potential (Figure 20.6).

2. **Therapeutic uses:** Although *amiodarone* has supplanted *lidocaine* for use in ventricular fibrillation or pulseless ventricular tachycardia (VT), *lidocaine* may be useful as an alternative. *Lidocaine* may also be used in polymorphic VT or in combination

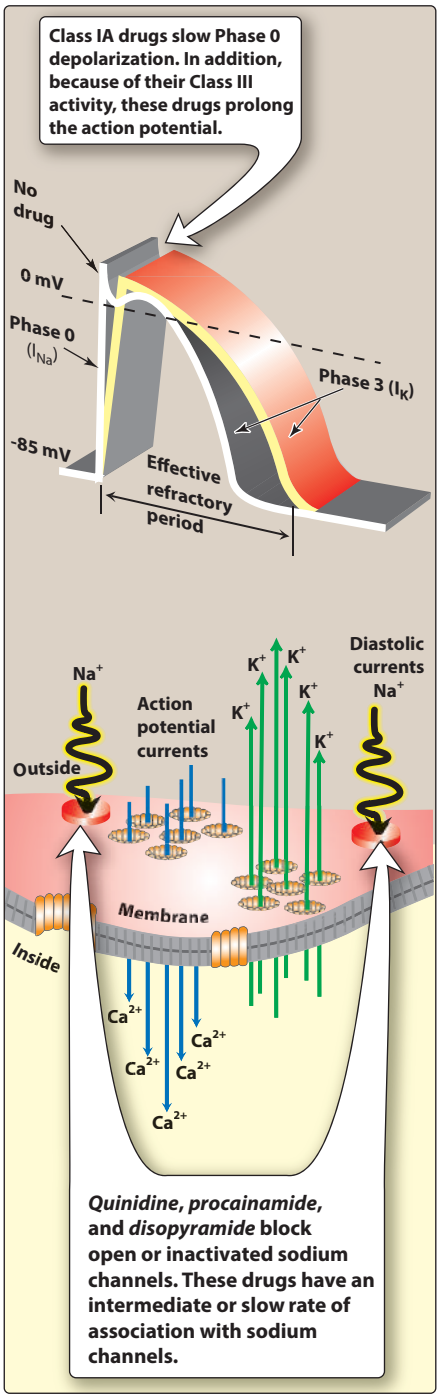

Figure 20.5
Schematic diagram of the effects of class IA agents. I_{Na} and I_K are transmembrane currents due to the movement of Na^+ and K^+, respectively.

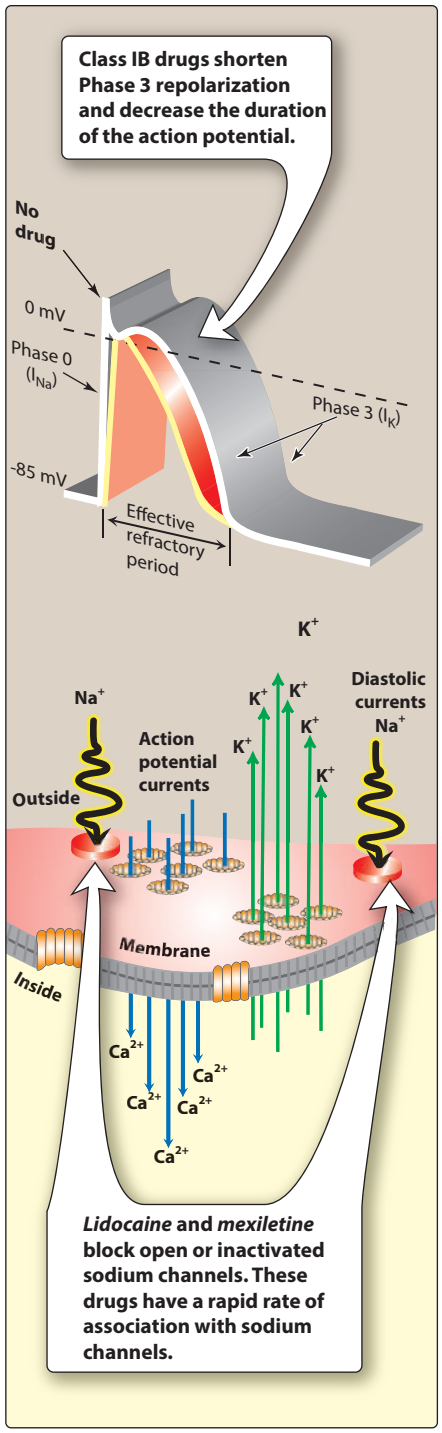

Figure 20.6
Schematic diagram of the effects of class IB agents. I_{Na} and I_K are transmembrane currents due to the movement of Na^+ and K^+, respectively.

with *amiodarone* for VT storm. The drug does not markedly slow conduction and, thus, has little effect on atrial or AV junction arrhythmias. *Mexiletine* is used for chronic treatment of ventricular arrhythmias, often in combination with *amiodarone*.

3. **Pharmacokinetics:** *Lidocaine* is given intravenously because of extensive first-pass transformation by the liver, which precludes oral administration. The drug is dealkylated to two less active metabolites, primarily by CYP1A2 with a minor role by CYP3A4. *Lidocaine* should be monitored closely when given in combination with drugs affecting these CYP isoenzymes. As *lidocaine* is a high extraction drug, drugs that lower hepatic blood flow (β-blockers) may require *lidocaine* dose adjustment. *Mexiletine* is well absorbed after oral administration. It is metabolized in the liver primarily by CYP2D6 to inactive metabolites and excreted mainly via the biliary route.

4. **Adverse effects:** *Lidocaine* has a fairly wide therapeutic index. It shows little impairment of left ventricular function and has no negative inotropic effect. Central nervous system (CNS) effects include nystagmus (early indicator of toxicity), drowsiness, slurred speech, paresthesia, agitation, confusion, and convulsions, which often limit the duration of continuous infusions. *Mexiletine* has a narrow therapeutic index and caution should be used when administering the drug with inhibitors of CYP2D6. Nausea, vomiting, and dyspepsia are the most common adverse effects.

D. Class IC antiarrhythmic drugs: Flecainide and propafenone

These drugs slowly dissociate from resting sodium channels and show prominent effects even at normal heart rates. Several studies have cast serious doubts on the safety of the class IC drugs, particularly in patients with structural heart disease.

1. **Mechanism of action:** *Flecainide* [FLEK-a-nide] suppresses phase 0 upstroke in Purkinje and myocardial fibers (Figure 20.7). This causes marked slowing of conduction in all cardiac tissue, with a minor effect on the duration of the action potential and refractoriness. Automaticity is reduced by an increase in the threshold potential, rather than a decrease in slope of phase 4 depolarization. *Flecainide* also blocks potassium channels leading to increased action potential duration, even more so than *propafenone*. *Propafenone* [proe-PA-fen-one], like *flecainide*, slows conduction in all cardiac tissues but does not block potassium channels.

2. **Therapeutic uses:** *Flecainide* is useful in the maintenance of sinus rhythm in atrial flutter or fibrillation in patients without structural heart disease (left ventricular hypertrophy, heart failure, atherosclerotic heart disease) and in treating refractory ventricular arrhythmias. *Flecainide* has a negative inotropic effect and can aggravate chronic heart failure. Use of *propafenone* is restricted mostly to atrial arrhythmias: rhythm control of atrial fibrillation or flutter and paroxysmal supraventricular tachycardia prophylaxis in patients with AV reentrant tachycardias. The latter indication takes advantage of the β-blocking properties of *propafenone*.

3. **Pharmacokinetics:** *Flecainide* is absorbed orally and is metabolized by CYP2D6 to multiple metabolites. The parent drug and metabolites are mostly eliminated renally, and dosage adjustment may be required in renal disease. *Propafenone* is metabolized to active metabolites primarily via CYP2D6, and also by CYP1A2 and CYP3A4. The metabolites are excreted in the urine and the feces.

4. **Adverse effects:** *Flecainide* is generally well tolerated, with blurred vision, dizziness, and nausea occurring most frequently. *Propafenone* has a similar side effect profile, but it may also cause bronchospasm due to its β-blocking effects. It should be avoided in patients with asthma. *Propafenone* is also an inhibitor of P-glycoprotein. Both drugs should be used with caution with potent inhibitors of CYP2D6.

IV. CLASS II ANTIARRHYTHMIC DRUGS

Class II agents are β-adrenergic antagonists, or β-blockers. These drugs diminish phase 4 depolarization and, thus, depress automaticity, prolong AV conduction, and decrease heart rate and contractility. Class II agents are useful in treating tachyarrhythmias caused by increased sympathetic activity. They are also used for atrial flutter and fibrillation and for AV nodal reentrant tachycardia. In addition, β-blockers prevent life-threatening ventricular arrhythmias following a myocardial infarction. [Note: In contrast to the sodium channel blockers, β-blockers and class III compounds, such as *sotalol* and *amiodarone*, are increasing in use.]

Metoprolol [me-TOE-pro-lol] is the β-blocker most widely used in the treatment of cardiac arrhythmias. Compared to nonselective β-blockers, such as *propranolol* [pro-PRAN-oh-lol], it reduces the risk of bronchospasm. It is extensively metabolized in the liver primarily by CYP2D6 and has CNS penetration (less than *propranolol*, but more than *atenolol* [a-TEN-oh-lol]). *Esmolol* [ESS-moe-lol] is a very-short-acting β-blocker used for intravenous administration in acute arrhythmias that occur during surgery or emergency situations. It has a fast onset of action and a short half-life, making it ideal for acute situations and also limiting its adverse effect profile. *Esmolol* is rapidly metabolized by esterases in red blood cells. As such, there are no pharmacokinetic drug interactions.

V. CLASS III ANTIARRHYTHMIC DRUGS

Class III agents block potassium channels and, thus, diminish the outward potassium current during repolarization of cardiac cells. These agents prolong the duration of the action potential without altering phase 0 of depolarization or the resting membrane potential (Figure 20.8). Instead, they prolong the effective refractory period, increasing refractoriness. All class III drugs have the potential to induce arrhythmias.

A. Amiodarone

1. **Mechanism of action:** *Amiodarone* [a-MEE-oh-da-rone] contains iodine and is related structurally to thyroxine. It has complex

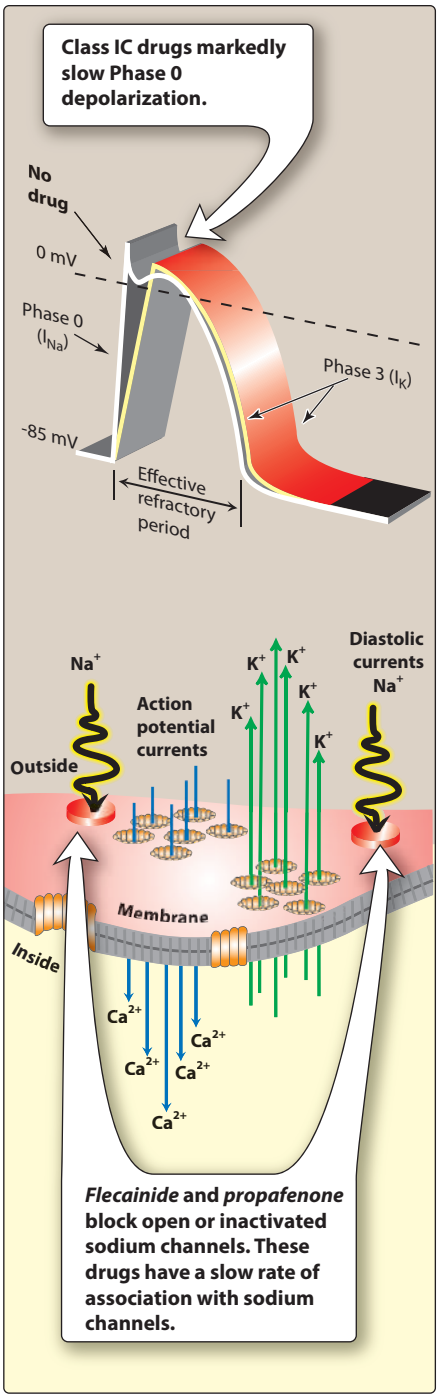

Figure 20.7
Schematic diagram of the effects of class IC agents. I_{Na} and I_K are transmembrane currents due to the movement of Na^+ and K^+, respectively.

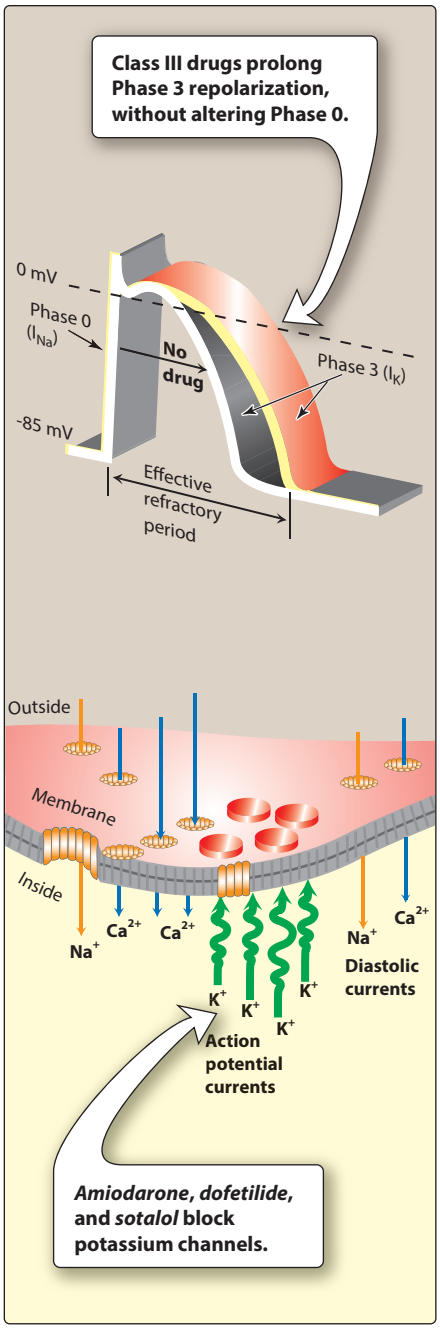

Figure 20.8
Schematic diagram of the effects of class III agents. I_{Na} and I_K are transmembrane currents due to the movement of Na^+ and K^+, respectively.

effects, showing class I, II, III, and IV actions, as well as α-blocking activity. Its dominant effect is prolongation of the action potential duration and the refractory period by blocking K^+ channels.

2. **Therapeutic uses:** *Amiodarone* is effective in the treatment of severe refractory supraventricular and ventricular tachyarrhythmias. *Amiodarone* has been a mainstay of therapy for the rhythm management of atrial fibrillation or flutter. Despite its adverse effect profile, *amiodarone* is the most commonly employed antiarrhythmic and thought to be the least proarrhythmic of the class I and III antiarrhythmic drugs.

3. **Pharmacokinetics:** *Amiodarone* is incompletely absorbed after oral administration. The drug is unusual in having a prolonged half-life of several weeks, and it distributes extensively in adipose tissue. Full clinical effects may not be achieved until months after initiation of treatment, unless loading doses are employed.

4. **Adverse effects:** *Amiodarone* shows a variety of toxic effects, including pulmonary fibrosis, neuropathy, hepatotoxicity, corneal deposits, optic neuritis, blue-gray skin discoloration, and hypo- or hyperthyroidism. However, use of low doses and close monitoring reduce toxicity, while retaining clinical efficacy. *Amiodarone* is subject to numerous drug interactions, since it is metabolized by CYP3A4 and serves as an inhibitor of CYP1A2, CYP2C9, CYP2D6, and P-glycoprotein.

B. Dronedarone

Dronedarone [droe-NE-da-rone] is a benzofuran *amiodarone* derivative, which is less lipophilic, has lower tissue accumulation, and has a shorter serum half-life than *amiodarone*. It does not have the iodine moieties that are responsible for thyroid dysfunction associated with *amiodarone*. Like *amiodarone*, it has class I, II, III, and IV actions. *Dronedarone* has a better adverse effect profile than *amiodarone* but may still cause liver failure. The drug is contraindicated in those with symptomatic heart failure or permanent atrial fibrillation due to an increased risk of death. Currently, *dronedarone* is used to maintain sinus rhythm in atrial fibrillation or flutter, but it is less effective than *amiodarone*.

C. Sotalol

Sotalol [SOE-ta-lol], although a class III antiarrhythmic agent, also has potent nonselective β-blocker activity. The levorotatory isomer (*l-sotalol*) has β-blocking activity, and *d-sotalol* has class III antiarrhythmic action. *Sotalol* blocks a rapid outward potassium current, known as the delayed rectifier. This blockade prolongs both repolarization and duration of the action potential, thus lengthening the effective refractory period. *Sotalol* is used for maintenance of normal sinus rhythm in patients with atrial fibrillation, atrial flutter, or refractory paroxysmal supraventricular tachycardia and in the treatment of ventricular arrhythmias. Since *sotalol* has β-blocking properties, it is commonly used for these indications in patients with left ventricular hypertrophy or atherosclerotic heart disease. This drug can cause the typical adverse effects associated with β-blockers but has a low rate of adverse effects when compared to other antiarrhythmic agents. The dosing interval should

be extended in patients with renal disease, since the drug is renally eliminated. To reduce the risk of proarrhythmic effects, *sotalol* is most often initiated in the hospital to monitor QT interval.

D. Dofetilide

Dofetilide [doh-FET-il-ide] is a pure potassium channel blocker. It can be used as a first-line antiarrhythmic agent in patients with persistent atrial fibrillation and heart failure or in those with coronary artery disease. Because of the risk of proarrhythmia, *dofetilide* initiation is limited to the inpatient setting. The half-life of this oral drug is 10 hours. The drug is mainly excreted unchanged in the urine. Drugs that inhibit active tubular secretion are contraindicated.

E. Ibutilide

Ibutilide [eye-BYOO-tih-lide] is a potassium channel blocker that also activates the inward sodium current (mixed class III and IA action). *Ibutilide* is the drug of choice for chemical conversion of atrial flutter, but electrical cardioversion has supplanted its use. *Ibutilide* undergoes extensive first-pass metabolism and is not used orally. Because of the risk of QT prolongation and proarrhythmia, *ibutilide* initiation is limited to the inpatient setting.

VI. CLASS IV ANTIARRHYTHMIC DRUGS

Class IV drugs are the nondihydropyridine calcium channel blockers *verapamil* [ver-AP-a-mil] and *diltiazem* [dil-TYE-a-zem]. Although voltage-sensitive calcium channels occur in many different tissues, the major effect of calcium channel blockers is on vascular smooth muscle and the heart. *Verapamil* shows greater action on the heart than on vascular smooth muscle, and *diltiazem* is intermediate in its actions. In the heart, *verapamil* and *diltiazem* bind only to open depolarized voltage-sensitive channels, thus decreasing the inward current carried by calcium. They prevent repolarization until the drug dissociates from the channel, resulting in a decreased rate of phase 4 spontaneous depolarization. These drugs are therefore use-dependent. They also slow conduction in tissues that are dependent on calcium currents, such as the AV and SA nodes (Figure 20.9). These agents are more effective against atrial than against ventricular arrhythmias. They are useful in treating reentrant supraventricular tachycardia and in reducing the ventricular rate in atrial flutter and fibrillation. Both drugs are metabolized in the liver by CYP3A4. Dosage adjustments may be needed in patients with hepatic dysfunction. Both agents are also inhibitors of CYP3A4, as well as substrates and inhibitors of P-glycoprotein. As such, they are subject to many drug interactions.

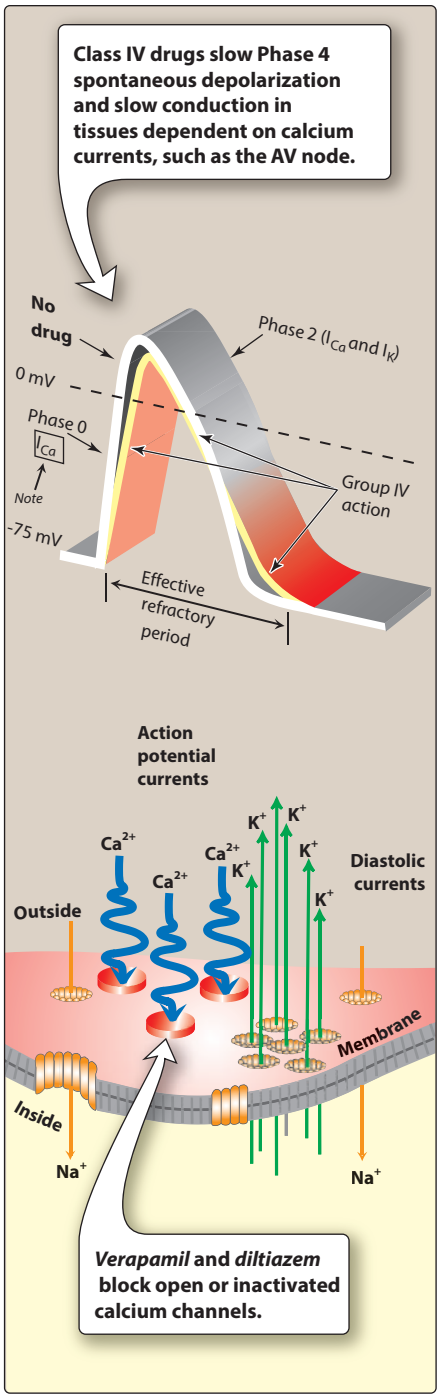

Figure 20.9
Schematic diagram of the effects of class IV agents. I_{Ca} and I_K are transmembrane currents due to the movement of Ca^{2+} and K^+, respectively.

VII. OTHER ANTIARRHYTHMIC DRUGS

A. Digoxin

Digoxin [di-JOX-in] inhibits the Na^+/K^+-ATPase pump, ultimately shortening the refractory period in atrial and ventricular myocardial cells while prolonging the effective refractory period and diminishing conduction

velocity in the AV node. *Digoxin* is used to control ventricular response rate in atrial fibrillation and flutter; however, sympathetic stimulation easily overcomes the inhibitory effects of *digoxin*. At toxic concentrations, *digoxin* causes ectopic ventricular beats that may result in VT and fibrillation. [Note: Serum trough concentrations of 1.0 to 2.0 ng/mL are desirable for atrial fibrillation or flutter, whereas lower concentrations of 0.5 to 0.8 ng/mL are targeted for systolic heart failure.]

B. Adenosine

Adenosine [ah-DEN-oh-zeen] is a naturally occurring nucleoside, but at high doses, the drug decreases conduction velocity, prolongs the refractory period, and decreases automaticity in the AV node. Intravenous *adenosine* is the drug of choice for abolishing acute supraventricular tachycardia. It has low toxicity but causes flushing, chest pain, and hypotension. *Adenosine* has an extremely short duration of action (approximately 10 to 15 seconds) due to rapid uptake by erythrocytes and endothelial cells.

C. Magnesium sulfate

Magnesium is necessary for the transport of sodium, calcium, and potassium across cell membranes. It slows the rate of SA node impulse formation and prolongs conduction time along the myocardial tissue. Intravenous *magnesium sulfate* is the salt used to treat arrhythmias, as oral *magnesium* is not effective in the setting of arrhythmia. Most notably, *magnesium* is the drug of choice for treating the potentially fatal arrhythmia torsades de pointes and *digoxin*-induced arrhythmias.

Study Questions

Choose the ONE best answer.

20.1 A 60-year-old woman had a myocardial infarction. Which of the following should be used to prevent life-threatening arrhythmias that can occur post–myocardial infarction in this patient?

A. Digoxin.
B. Flecainide.
C. Metoprolol.
D. Procainamide.
E. Quinidine.

Correct answer = C. β-Blockers such as metoprolol prevent arrhythmias that occur subsequent to a myocardial infarction. None of the other drugs has been shown to be effective in preventing postinfarct arrhythmias. Flecainide should be avoided in patients with structural heart disease.

20.2 Suppression of arrhythmias resulting from a reentry focus is most likely to occur if the drug:

A. Has vagomimetic effects on the AV node.
B. Is a β-blocker.
C. Converts a unidirectional block to a bidirectional block.
D. Slows conduction through the atria.
E. Has atropine-like effects on the AV node.

Correct answer = C. Current theory holds that a reentrant arrhythmia is caused by damaged heart muscle, so that conduction is slowed through the damaged area in only one direction. A drug that prevents conduction in either direction through the damaged area interrupts the reentrant arrhythmia. Class I antiarrhythmics, such as lidocaine, are capable of producing bidirectional block. The other choices do not have any direct effects on the direction of blockade of conduction through damaged cardiac muscle.

20.3 A 57-year-old man is being treated for an atrial arrhythmia. He complains of dry mouth, blurred vision, and urinary hesitancy. Which antiarrhythmic drug is he mostly like taking?

A. Metoprolol.
B. Disopyramide.
C. Dronedarone.
D. Sotalol.

Correct answer = B. The clustered symptoms of dry mouth, blurred vision, and urinary hesitancy are characteristic of anticholinergic adverse effects which are caused by class IA agents (in this case, disopyramide). The other drugs do not cause anticholinergic effects.

20.4 A 58-year-old woman is being treated for chronic suppression of a ventricular arrhythmia. After 1 week of therapy, she complains about feeling severe upset stomach and heartburn. Which antiarrhythmic drug is the likely cause of these symptoms?

A. Amiodarone.
B. Digoxin.
C. Mexiletine.
D. Propranolol.
E. Quinidine.

Correct answer = C. The patient is exhibiting a classic adverse effect of mexiletine. None of the other agents listed are likely to cause dyspepsia.

20.5 A 78-year-old woman has been newly diagnosed with atrial fibrillation. She is not currently having symptoms of palpitations or fatigue. Which is appropriate to initiate for rate control as an outpatient?

A. Amiodarone.
B. Dronedarone.
C. Esmolol.
D. Flecainide.
E. Metoprolol.

Correct answer = E. Only C and E are options to control rate. The other options are used for rhythm control in patients with atrial fibrillation. Since esmolol is IV only, the only option to start as an outpatient is metoprolol.

20.6 Which of the following is correct regarding digoxin when used for atrial fibrillation?

A. Digoxin works by blocking voltage-sensitive calcium channels.
B. Digoxin is used for rhythm control in patients with atrial fibrillation.
C. Digoxin increases conduction velocity through the AV node.
D. Digoxin levels of 1 to 2 ng/mL are desirable in the treatment of atrial fibrillation.

Correct answer = D. Digoxin works by inhibiting the Na^+/K^+-ATPase pump. It decreases conduction velocity through the AV node and is used for rate control in atrial fibrillation (not rhythm control). Digoxin levels between 1 and 2 ng/mL are more likely to exhibit negative chronotropic effects desired in atrial fibrillation or flutter. A serum drug concentration between 0.5 and 0.8 ng/mL is for symptomatic management of heart failure.

20.7 All of the following are adverse effects of amiodarone except:

A. Cinchonism.
B. Hypothyroidism.
C. Hyperthyroidism.
D. Pulmonary fibrosis.
E. Blue skin discoloration.

Correct answer = A. Cinchonism is a constellation of symptoms (blurred vision, tinnitus, headache, psychosis) that is known to occur with quinidine. All other options are adverse effects with amiodarone that require close monitoring.

20.8 Which arrhythmia can be treated with lidocaine?

A. Paroxysmal supraventricular ventricular tachycardia.
B. Atrial fibrillation.
C. Atrial flutter.
D. Ventricular tachycardia.

Correct answer = D. Lidocaine has little effect on atrial or AV nodal tissue; thus, it used for ventricular arrhythmias such as ventricular tachycardia.

20.9 A clinician would like to initiate a drug for rhythm control of atrial fibrillation. Which of the following coexisting conditions would allow for initiation of flecainide?

A. Hypertension.
B. Left ventricular hypertrophy.
C. Coronary artery disease.
D. Heart failure.

Correct answer = A. Since flecainide can increase the risk of sudden cardiac death in those with a history of structural heart disease, only A will allow for flecainide initiation. Structural heart disease includes left ventricular hypertrophy, heart failure, and atherosclerotic heart disease.

20.10 Which statement regarding dronedarone is correct?

A. Dronedarone is more effective than amiodarone.
B. QT interval prolongation is not a risk with dronedarone.
C. Dronedarone increases the risk of death in patients with permanent atrial fibrillation or symptomatic heart failure.
D. There is no need to monitor liver function with dronedarone.

Correct answer = C. Dronedarone is not as effective as amiodarone, QT prolongation is a risk with this drug, and liver function should be monitored when taking dronedarone since it increases the risk of liver failure. The drug is contraindicated in those with symptomatic heart failure or permanent atrial fibrillation due to an increased risk of death.