TABLE 9-3 COMMON SIDE EFFECTS OF SELECT ANTIARRHYTHMIC DRUGS

DRUG	MAJOR SIDE EFFECTS
Quinidine	Nausea, diarrhea, abdominal cramping Cinchonism: decreased hearing, tinnitus, blurred vision, delirium Rash, thrombocytopenia, hemolytic anemia Hypotension, torsades de pointes (quinidine syncope)
Procainamide	Drug-induced lupus syndrome Nausea, vomiting Rash, fever, hypotension, psychosis, agranulocytosis Torsades de pointes
Disopyramide	Anticholinergic: dry mouth, blurred vision, constipation, urinary retention, closed angle glaucoma Hypotension, worsening heart failure
Lidocaine	CNS: dizziness, perioral numbness, paresthesias, altered consciousness, coma, seizures
Mexiletine	Nausea, vomiting CNS: dizziness, tremor, paresthesias, ataxia, confusion
Flecainide	CNS: blurred vision, headache, ataxia Congestive heart failure, ventricular proarrhythmia
Propafenone	Nausea, vomiting, constipation, metallic taste to food Dizziness, headache, exacerbation of asthma, ventricular proarrhythmia
β-Blockers	Bronchospasm, bradycardia, fatigue, depression, impotence Congestive heart failure
Calcium-channel blockers	Congestive heart failure, bradycardia, heart block, constipation
Amiodarone	Agranulocytosis, pulmonary fibrosis, hepatopathy, hyperthyroidism or hypothyroidism, corneal microdeposits, bluish discoloration of the skin, nausea, constipation, bradycardia
Sotalol	Same as β-blockers, torsades de pointes
Dronedarone	Diarrhea, QT prolongation and torsades de pointes, death, bradycardia, congestive heart failure, hepatocellular injury, interstitial lung disease
Ibutilide	Torsades de pointes
Dofetilide	Torsades de pointes, headache, dizziness, diarrhea

CNS, Central nervous system.

up to 20% of patients. Serious adverse effects include potentially irreversible pulmonary fibrosis, optic neuropathy producing visual impairment, hyperthyroidism, and severe hepatic toxicity. Less serious adverse effects include hypothyroidism, neurologic toxicity, sun sensitivity, QT prolongation, and bradycardia.

Sotalol blocks β-adrenoreceptors and delayed rectifier K^+ channels, decreasing sinoatrial node automaticity, slowing AV conduction velocity, and prolonging repolarization. It effectively treats a large number of ventricular and supraventricular arrhythmias.

Dofetilide, a selective class III agent used primarily to treat atrial arrhythmias, blocks delayed rectifier K^+ channels to prolong action potential duration and QT intervals. The risk of TdP is about 1% among patients without structural heart disease but as high as 4.8% among patients with congestive heart failure.

Ibutilide, an intravenous class III agent, is used for the acute termination of recent-onset AF and atrial flutter. The risk of polymorphic VT with administration of ibutilide is 8.3%.

Dronedarone is an orally available class III drug demonstrated to reduce the risk of first hospitalization due to cardiovascular events or death from any cause for patients in sinus rhythm with a history of paroxysmal or persistent AF. Dronedarone may not be used in the setting of permanent AF or in patients with New York Heart Association (NYHA) class IV heart failure or symptomatic heart failure with recent decompensation because the drug increases the risk of cardiovascular death in these populations. Other major side effects of dronedarone are severe hepatotoxicity, interstitial lung disease, bradycardia, and QT prolongation.

Other Antiarrhythmic Agents

The Singh–Vaughn Williams classification scheme does not describe several agents commonly used in cardiac arrhythmia management. *Adenosine* is a parental agent with an elimination half-life of 1 to 6 seconds. The drug binds to A1 receptors to activate K^+ channels, decreasing the action potential duration and hyperpolarizing membrane potentials in the atria, sinoatrial node, and AV node. Indirectly, adenosine blocks catecholamine-stimulated adenylate cyclase activation, decreasing cAMP and consequently decreasing Ca^{2+} influx. Used clinically for its ability to produce transient AV block, adenosine can terminate SVT when the AV node contributes to the reentrant circuit.

Digoxin inhibits Na^+, K^+-ATPase, increasing intracellular Na^+ concentrations and stimulating the Na^+-Ca^{2+} exchanger to increase intracellular Ca^{2+}, accounting for its positive inotropic effect. Digoxin also acts through the autonomic nervous system to enhance vagal tone, slowing sinus rates, shortening the atrial refractory period, and prolonging AV conduction. Digoxin is therefore used for rate control in patients with atrial arrhythmias.

Cardioversion and Defibrillation

Direct current cardioversion and defibrillation represent the cornerstone of acute therapy for unstable tachyarrhythmias and play an important role in the termination of medication-refractory stable tachyarrhythmias. Organized VTs and SVTs may be terminated by synchronized cardioversion—shock delivery synchronized to the QRS complex—to restore normal rhythm. Synchronization is critical to avoid induction of VF by delivering energy during the relative refractory period of the cardiac cycle. Defibrillation entails the asynchronous delivery of electrical current to depolarize a critical mass of myocardium and terminate VF. Successful defibrillation is time dependent, with the likelihood of success declining by approximately 10% per minute from the onset of VF.

Defibrillation may be delivered internally through an implantable cardioverter-defibrillator (ICD) or externally through an automatic external defibrillator (AED). Current-generation AEDs use biphasic waveforms, achieving greater first-shock efficacy compared with older devices delivering monophasic waveforms. ICDs, implanted in patients for primary and secondary prevention of sudden cardiac death (SCD), deliver defibrillation shocks directly to the endocardium through an RV lead. With direct delivery of energy, relatively lower energy levels (<40 J) are typically effective.

Ablation

Catheter ablation plays an important role in the therapy of a broad range of arrhythmias, such as SVT, atrial arrhythmias, and VT. The ascendance of catheter ablation derives in part from the