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Drugs for Cardiac Arrhythmias

The drugs of choice for treatment of common cardiac arrhythmias are listed in the table that begins on the next page; some drugs are recommended for indications for which they have not been approved by the US FDA. The dosages and adverse effects of each drug are listed in the table that begins on page 80. Antiarrhythmic drugs may themselves cause arrhythmias, which can be fatal. Some of these drugs may increase rather than decrease mortality, especially in patients with structural heart disease.

CLASSIFICATION OF ANTIARRHYTHMIC DRUGS — Classification of drugs used for treatment of cardiac arrhythmias is based on the premise that drugs with similar electrophysiologic effects are also similar in their therapeutic effects and cardiac toxicity. However, many of them are not. In this article, the choice of drugs is based mainly on the results of controlled trials and clinical experience.

AMIODARONE — Among available antiarrhythmics, amiodarone (*Cordarone*, and others) is the most effective in preventing recurrences of atrial fibrillation and of ventricular tachycardia or fibrillation. In 2 large studies, amiodarone was more effective than sotalol or other drugs in reducing recurrences of symptomatic atrial fibrillation (D Roy et al, N Engl J Med 2000; 342:913; AFFIRM Investigators, J Am Coll Cardiol 2003; 42:20). In patients more than 60 years old undergoing cardiothoracic surgery, amiodarone prophylaxis decreased the incidence of atrial fibrillation, ventricular tachycardia and stroke (J Kluger and CM White, Card Electrophysiol Rev 2003; 7:165). A meta-analysis of 13 trials evaluating use of amiodarone in a total of 6553 high-risk patients with congestive heart failure or a recent myocardial infarction reported a statistically significant 29% reduction in sudden death, and a 13% reduction in total mortality (Amiodarone Trials Meta-analysis Investigators, Lancet 1997; 350:1417). The Sudden Cardiac Death in Heart Failure Trial (SCD-HeFT) found, however, that the drug did not lower mortality in patients with an ejection fraction ≤35% and class II or III congestive heart failure (GH Bardy et al, presented at American College of Cardiology 53rd Annual Scientific Session, New Orleans, March 8, 2004).

Intravenous (IV) amiodarone is effective for treatment and prevention of ventricular fibrillation and recurrent, hemodynamically destabilizing ventricular tachycardia. In patients with out-of-hospital cardiac arrest, the incidence of survival to hospital admission (but not discharge) was higher with IV amiodarone than with lidocaine or placebo (PJ Kudenchuk et al, N Engl J Med 1999; 341:871; P Dorian et al, N Engl J Med 2002; 346:884). IV amiodarone has largely supplanted lidocaine as the drug of choice in cardiac arrest situations (Guidelines, Circulation 2000; 102 suppl I:I-86). IV amiodarone can (with a time delay) convert atrial fibrillation to sinus rhythm, and it slows

Drugs of Choice for Common Arrhythmias

Arrhythmia	Drug of choice	Alternatives	Remarks
Atrial fibrillation or flutter[1]			
Acute management[2]	Rate control: IV verapamil, diltiazem, a beta-blocker or digoxin		
	Conversion: DC cardioversion	IV procainamide or ibutilide; single large oral dose of propafenone or flecainide	Ibutilide infusion may increase the effectiveness of DC cardioversion[3]
Chronic treatment[2]	Rate control: verapamil, diltiazem, a beta-blocker or digoxin		Radiofrequency ablation may be effective in selected patients[4]
	Maintenance of sinus rhythm[5]: amiodarone, sotalol, flecainide or propafenone, dofetilide	Quinidine, procainamide, disopyramide	
Other supraventricular tachycardias[6]			
Acute management	IV adenosine, verapamil or diltiazem[7,8]	IV esmolol, another beta-blocker or digoxin for termination[7]	DC cardioversion or atrial pacing may be effective for some patients, but are only rarely required
Long-term suppression	Beta-blockers, verapamil, diltiazem, flecainide, propafenone, amiodarone, sotalol, or digoxin	Quinidine, procainamide or disopyramide	Radiofrequency ablation can cure most patients
Premature ventricular complexes (PVCs) or non-sustained ventricular tachycardia	No drug therapy indicated for asymptomatic patients without structural heart disease[9]	For symptomatic patients, a beta-blocker	There is no evidence that prolonged suppression with drugs improves survival. For post-MI patients, treatment with a beta-blocker has decreased mortality, and treatment with flecainide or moricizine has increased it.

1. Randomized trials have found no difference in outcome between rate control and rhythm control in patients who can tolerate either (AFFIRM Investigators, N Engl J Med 2002; 347:1825; I van Gelder et al, N Engl J Med 2002; 347:1834).
2. Anticoagulation may be required. Digoxin, verapamil, diltiazem and possibly beta-blockers may be dangerous for patients with Wolff-Parkinson-White syndrome. Patients with Wolff-Parkinson-White syndrome and atrial fibrillation should be treated with IV procainamide or IV amiodarone if hemodynamically stable and, if not, with DC cardioversion.
3. H Oral et al, N Engl J Med 1999; 340:1849.
4. Medical Letter 2004; 46:59.
5. Choice of drugs varies with the clinical setting (EN Prystowsky, Am J Cardiol 1998; 82 suppl 4A:3I). The incidence of atrial fibrillation following cardiac surgery can be reduced by preoperative sotalol (JA Gomes et al, J Am Coll Cardiol 1999; 34:334), amiodarone (E Daoud et al, N Engl J Med 1997; 337:1785) or a beta blocker.
6. These are mostly AV nodal reentry and AV reentry utilizing an accessory atrioventricular connection (bypass tract). Vagotonic maneuvers (such as carotid sinus massage, gagging, or the Valsalva maneuver) that impair AV nodal conduction may be tried first. For rarer forms of supraventricular tachycardia (e.g. atrial tachycardia), drugs are often less effective for suppression; AV nodal blockers (such as digoxin, beta-blockers or calcium-channel blockers) can be used to slow the rate. Radiofrequency ablation can also be used.
7. Verapamil, diltiazem, digoxin and possibly beta-blockers may be dangerous for patients with Wolff-Parkinson-White syndrome.
8. Verapamil and diltiazem should be used with caution in patients receiving intravenous beta-blockers, those with congestive heart failure and those taking oral quinidine.
9. One study in asymptomatic patients with non-sustained ventricular tachycardia, coronary disease, reduced ejection fraction and ventricular tachycardia inducible by programmed electrical stimulation found that treatment with an implantable cardioverter-defibrillator (ICD), but not antiarrhythmic drugs, reduced mortality (AE Buxton et al, [MUSTT] N Engl J Med 1999; 341:1882).

Drugs of Choice for Common Arrhythmias

Arrhythmia	Drug of choice	Alternatives	Remarks
Sustained ventricular tachycardia[10,11]	Amiodarone[10,11]	Procainamide, lidocaine[10,11]	Long-term therapy[12]: Implantable cardioverter-defibrillator (ICD), amiodarone
Ventricular fibrillation[13]	Amiodarone[13]	Procainamide,[13] lidocaine	Long-term therapy[12]: Implantable cardioverter-defibrillator (ICD), amiodarone
Cardiac glycoside induced ventricular tachyarrhythmias[11,14]	Digoxin-immune Fab (digoxin antibody fragments – *Digibind; Digifab*)	Lidocaine, phenytoin	Self-limited if digoxin is stopped. Phenytoin can also be effective. Avoid DC cardioversion except for ventricular fibrillation or sustained ventricular tachycardia. A beta-blocker or procainamide can make heart block worse.
Drug-induced torsades de pointes	IV magnesium sulfate	Cardiac pacing, isoproterenol	Causative agents (e.g., quinidine) should be discontinued. Magnesium sulfate may be effective even in absence of hypomagnesemia. Potassium should be used to raise serum K to between 4.5 and 5.0 mEq/L[14]

10. DC cardioversion is the safest and most effective treatment. It is preferred by most cardiologists for sustained ventricular tachycardia causing hemodynamic compromise.
11. Some ventricular tachycardias can be caused or exacerbated by bradycardia or heart block. In the presence of high-grade heart block, antiarrhythmic drugs can cause cardiac standstill. When high-grade heart block is present, therefore, a temporary pacemaker should be inserted before using antiarrhythmic drugs; pacing may abolish the arrhythmia. When a drug must be used in the presence of heart block, lidocaine is least likely to increase the block.
12. Beta-blockers are often added. If ICD shocks are frequent, antiarrhythmic drugs (sotalol, amiodarone, mexiletine) are often added empirically and if shocks recur, radiofrequency catheter ablation is used.
13. Defibrillation is the treatment of choice; drugs are for prevention of recurrence.
14. KCl can be given carefully, 10-20 mEq/hr IV, to patients with low or normal serum potassium concentrations. Extreme care must be taken to keep serum potassium below 5.0 mEq/L. In the presence of heart block not associated with atrial tachycardia, potassium should be withheld if the serum concentration is greater than 4.5 mEq/L because high serum potassium may increase atrioventricular block.

the ventricular response (P Chevalier et al, J Am Coll Cardiol 2003; 41:255; LM Letelier et al, Arch Intern Med 2003; 163:777).

Adverse Effects – Severe adverse effects, particularly pulmonary toxicity, can occur with usual doses of amiodarone and may be irreversible or lethal. Pulmonary toxicity can persist for months after treatment is stopped. Gastrointestinal (GI) upset and increased hepatic enzyme activity are common; cirrhosis and fatal hepatic necrosis have been reported. Low doses of amiodarone appear to cause fewer GI and hepatic adverse effects (VR Vorperian et al, J Am Coll Cardiol 1997; 30:791). Thyroid dysfunction, including thyroiditis, can occur; thyroid function should be monitored before and during therapy (EN Pearce et al, N Engl J Med 2003; 348:2646). Blue-gray discoloration and other skin reactions are common, and rarely optic neuritis can occur and has led to permanent loss of vision. Peripheral neuropathy can also occur. The drug can cause bradyarrhythmias requiring implantation of a permanent pacemaker (V Essebag et al, J Am Coll Cardiol 2003; 41:249). Although amiodarone prolongs the QT interval, torsades de pointes is very uncommon (Medical Letter 1995; 37:114). Because of its adverse effects, other drugs are often used first, particularly in younger patients, unless the patient has severe structural heart disease. Phlebitis and hypotension are adverse effects of IV amiodarone.

Drug Interactions – Amiodarone can increase the serum concentrations, pharmacological effects and toxicity of digoxin, diltiazem, quinidine, pro-

cainamide, flecainide, beta-blockers, lidocaine, warfarin and other drugs (see *The Medical Letter Adverse Drug Interactions Program*). Used together with dofetilide, ibutilide and other drugs that prolong the QT interval, amiodarone can have an additive effect on QT prolongation.

BETA-ADRENERGIC BLOCKERS — Beta-blockers can control the ventricular rate in atrial fibrillation or flutter, and terminate and prevent recurrences of paroxysmal supraventricular tachycardias (B Olshansky et al, J Am Coll Cardiol 2004; 43:1201). They are safer, although somewhat less effective, than other drugs for suppression of symptomatic premature ventricular complexes (PVCs). Sudden withdrawal of a beta-blocker in a patient with angina pectoris may precipitate myocardial ischemia or a cardiac arrhythmia. Drugs in this class approved by the US FDA for treatment of various arrhythmias include **propranolol** (*Inderal,* and others), **acebutolol** (*Sectral,* and others) and **esmolol** *(Brevibloc)*. Esmolol is an intravenous cardioselective agent with an elimination half-life of about nine minutes; it is effective in controlling the ventricular response in atrial flutter or fibrillation, particularly after cardiac surgery. Both therapeutic and adverse effects (hypotension, bradycardia) usually disappear within 30 minutes after stopping an infusion. Beta-blockers, except those with intrinsic sympathomimetic activity, decrease both short- and long-term mortality after myocardial infarction. Bisoprolol *(Zebeta)*, carvedilol *(Coreg)* and metoprolol *(Lopressor, Toprol XL)* have been shown to reduce mortality in patients with heart failure (JM Foody et al, JAMA 2002; 287:883).

CALCIUM-CHANNEL BLOCKERS — Verapamil *(Calan,* and others) and **diltiazem** *(Cardizem,* and others) prolong AV nodal refractoriness and are effective in terminating and preventing recurrences of many supraventricular tachycardias and slowing the ventricular rate in atrial fibrillation or flutter. Their IV use can be complicated by hypotension or bradycardia, especially with concurrent use of other cardiodepressant drugs, in patients with underlying heart disease and in those with sustained ventricular tachycardia. Either diltiazem or verapamil can raise serum digoxin levels, and both interact with many other drugs, including beta-blockers (see *The Medical Letter Adverse Drug Interactions Program*). Usual doses of dihydropyridine calcium-channel blockers (all except verapamil and diltiazem) have no antiarrhythmic activity.

ADENOSINE — Given IV, the nucleoside adenosine *(Adenocard)* is highly effective in terminating many supraventricular arrhythmias, but generally not multifocal atrial tachycardia or atrial fibrillation or flutter (LI Ganz and PL Friedman, N Engl J Med 1995; 332:162). Although it can cause heart block, hypotension, transient atrial fibrillation, non-sustained ventricular tachycardia and chest discomfort, adenosine is preferred to verapamil or diltiazem because it disappears from the circulation within seconds. As with calcium-channel blockers or digoxin, patients with Wolff-Parkinson-White (WPW) syndrome who are in atrial fibrillation or flutter may develop extremely rapid ventricular rates when given standard doses of adenosine (DV Exner et al, Ann Intern Med 1995; 122:351).

SOTALOL AND DOFETILIDE — The major mechanism of action of both of these agents is prolongation of the QT interval.

Sotalol *(Betapace, Betapace AF,* and others) is a nonselective beta-blocker that is as effective as quinidine, and safer, for prevention of recurrences of atrial fibrillation (JL Anderson and EN Prystowsky, Am Heart J 1999; 137:388). In patients with implantable cardioverter-defibrillators, use of sotalol reduced the risk of death from any cause or delivery of a first shock for any reason (A Pacifico et al, N Engl J Med 1999; 340:1855). Major adverse effects are those related to beta-blockade and prolongation of the QT interval, with a risk of torsades de pointes.

Dofetilide *(Tikosyn)* is a selective blocker of one specific cardiac repolarizing current (JP Mounsey and JP DiMarco, Circulation 2000; 102:2665). It is used orally to convert atrial fibrillation and to maintain sinus rhythm after cardioversion, but not for treatment of ventricular arrhythmias or paroxysmal atrial fibrillation. In patients with advanced heart failure, dofetilide decreased the incidence of rehospitalization for worsening heart failure and did not increase mortality (C Torp-Pedersen et al, N Engl J Med 1999; 341:857). The major risk is torsades de pointes, which occurred in 0.5% to 3.3% of patients in controlled trials. The drug must be started in the hospital and patients must be closely monitored for renal function and QT interval. Because of its pharmacologic selectivity, other adverse effects are uncommon. Dofetilide interacts with many other drugs (see *The Medical Letter Adverse Drug Interactions Program*). Coadministration of verapamil, a CYP3A4 substrate, has increased plasma concentrations of dofetilide and is contraindicated. Dofetilide should also not be used with other drugs that prolong the QT interval, such as sotalol or amiodarone.

FLECAINIDE AND PROPAFENONE — Flecainide *(Tambocor),* and **propafenone** *(Rythmol)* markedly decrease the speed of cardiac conduction. **Moricizine** *(Ethmozine)* also slows conduction but is uncommonly used. All three are effective in suppressing ventricular arrhythmias, but they can also aggra-

vate existing arrhythmias or precipitate new ones, especially in patients with underlying heart disease and sustained ventricular tachycardia. Use of flecainide or moricizine in post-myocardial infarction patients with asymptomatic ventricular arrhythmias was associated with an increase in mortality compared to placebo (AE Epstein et al, JAMA 1993; 270:2451). Whether propafenone, which also has beta-blocking activity in some patients, would have the same effect is unknown. Flecainide and propafenone are effective in preventing episodes of paroxysmal supraventricular tachycardia and atrial fibrillation in patients with otherwise healthy hearts. Single large oral doses of propafenone or flecainide have been used to terminate atrial fibrillation (A Capucci et al, Am J Cardiol 2003; 92:1345). An AV-nodal blocking agent such as digoxin, verapamil or a beta-blocker is almost always given first because these drugs, like quinidine, procainamide and disopyramide, can precipitate unusually slow atrial flutter leading to an increased ventricular response, occasionally up to 200-250/min. Propafenone can increase serum digoxin concentrations to toxic levels.

QUINIDINE, PROCAINAMIDE, DISOPYRAMIDE — Because of frequent toxicity, these older drugs are only used occasionally now, mainly in patients not tolerating other agents. The major adverse effects of **quinidine** include diarrhea, nausea, QT prolongation and torsades de pointes (even at low doses), and thrombocytopenia. Quinidine can increase digoxin concentrations to potentially toxic levels, and it also interacts with many other drugs (see *The Medical Letter Adverse Drug Interactions Program*).

Procainamide *(Pronestyl,* and others) can be given IV, but hypotension can occur with high or rapid loading doses. With long-term use, adverse extracardiac effects, such as fever or rash, are fairly common. Many patients develop antinuclear antibodies (ANA) after 3 to 6 months of therapy, and up to 30% develop a lupus-like syndrome, which usually disappears slowly when the drug is discontinued. Agranulocytosis unrelated to the lupus reaction occurs in 0.5% of patients. Torsades de pointes has been reported with high concentrations of either the drug or its active metabolite n-acetyl procainamide (NAPA). It should be used with great caution in patients with renal failure.

Disopyramide *(Norpace,* and others) can aggravate heart failure, and anticholinergic effects are often prominent; urinary retention frequently requires discontinuation of the drug. Torsades has been reported.

OTHER AGENTS — Digoxin *(Lanoxin,* and others) can control ventricular response in atrial fibrillation or flutter and may terminate some paroxysmal (reentrant) supraventricular arrhythmias, but other drugs are more effective. Digoxin, like verapamil and diltiazem, may accelerate conduction down the accessory pathway and therefore is contraindicated for use in atrial fibrillation in patients with the WPW syndrome. IV **magnesium** appears to be effective in preventing recurrent drug-induced torsades de pointes and in some arrhythmias related to digitalis toxicity. It has been used as an alternative to amiodarone for treatment of shock-refractory cardiac arrest, particularly for suspected torsades or hypomagnesemia.

Ibutilide *(Corvert)* is given IV for termination of atrial fibrillation or flutter (KT Murray, Circulation 1998; 97:493). It is effective in about 60% of patients with atrial flutter and 30% with atrial fibrillation. QT prolongation and torsades de pointes can occur; the incidence of torsades is about 3-4% (RM Gowda et al, Int J Cardiol 2004; 95:219).

Lidocaine *(Xylocaine,* and others), which is only given IV, is mainly metabolized by the liver. Patients with heart failure or with decreased hepatic function and those more than 70 years old should receive lower maintenance doses. Clearance of the drug often decreases during therapy; monitoring plasma concentrations can decrease toxicity. Drugs that inhibit CYP3A4 can decrease the clearance of lidocaine, and concurrent use of mexiletine can cause additive CNS toxicity, including seizures. The practice of giving lidocaine prophylactically to patients with suspected acute myocardial infarction has been abandoned because clinical trials failed to show a reduction in mortality. Current CPR guidelines recommend lidocaine only as an alternative to amiodarone as first-line therapy for ventricular arrhythmias causing cardiac arrest (Guidelines, Circulation 2000; 102 suppl I:I-86). **Mexiletine** *(Mexitil)* is an orally effective congener of lidocaine. Nausea and tremor are common, but may be reduced when the drug is given with food.

RISK OF TORSADES — Hypokalemia, hypomagnesemia, bradycardia and high drug doses (except with quinidine) increase the risk of torsades de pointes with all QT-prolonging drugs (DM Roden, N Engl J Med 2004; 350:1013).

NONPHARMACOLOGIC APPROACHES — Radiofrequency (RF) catheter ablation is a technique in which small areas of tissue responsible for the genesis or maintenance of some arrhythmias can be identified and destroyed (F Morady, N Engl J Med 1999; 340:534). RF catheter ablation is especially effective for AV nodal reentry, atrioventricular reentry due to an accessory pathway, atrial flutter, and idio-

Dosage and Adverse Effects of Some Antiarrhythmic Drugs

Drug	Usual dosage[1] and interval	Effect on ECG	Adverse effects
BETA-ADRENERGIC BLOCKERS			
Propranolol (*Inderal*, and others)	PO: 10-80 mg q6h (long-acting formulation available) IV: 1-5 mg total (1 mg/min)	Bradycardia Prolongs PR No change QRS	Heart block, hypotension, heart failure, bronchospasm, depression
Metoprolol (*Lopressor*, and others)	PO: 25-100 mg bid or 50-200 mg once/d (long-acting formulation) IV: 2.5-5 mg q2-5 min (up to 15 mg)	Bradycardia Prolongs PR No change QRS	Heart block, hypotension, heart failure, bronchospasm, depression
Acebutolol (*Sectral*, and others)	PO: 200 mg bid, increase gradually to 600-1200 mg/day	Bradycardia Prolongs PR No change QRS	Hypotension, bradycardia, bronchospasm, antinuclear antibodies, arthritis, myalgia, arthralgia, lupus-ike syndrome, pulmonary complications
Esmolol *(Brevibloc)*	IV loading: 500 mcg/kg over one minute, followed by 50 mcg/kg/min; titrate to desired effect Usual maintenance: 100 mcg/kg/min; maximum 300 mcg/kg/min	Bradycardia Prolongs PR No change QRS	Hypotension, heart block, heart failure, bronchospasm, pain at infusion site
CALCIUM-CHANNEL BLOCKERS			
Verapamil (*Calan*, and others)	IV initial: 5-10 mg over 2-3 min; repeat in 15-30 min, if necessary (max 20 mg) IV maintenance: 5-10 mg/hr PO: 40-120 mg tid or qid (long-acting formulation available)	Bradycardia Prolongs PR No change QRS	Heart block, heart failure, hypotension, asystole, dizziness, headache, fatigue, edema, nausea, constipation
Diltiazem (*Cardizem*, and others)	IV initial dose: 0.15-0.35 mg/kg (10-25 mg) over 2 min, may be repeated in 15 min IV infusion: 5-15 mg/hr PO: 60-180 mg bid (long-acting formulation)	Bradycardia Prolongs PR No change QRS	Hypotension, heart block, asystole, heart failure
AMIODARONE			**Oral Amiodarone:**
(*Cordarone*, and others)	PO loading: 800-1200 mg/day for 1-2 weeks then 600-800 mg/day for 4 weeks PO maintenance: 100-200 mg/day IV loading: 150 mg over 10 minutes, which can be repeated once if needed, followed by 360 mg over 6 hours IV maintenance: 0.5-1 mg/min Cardiac arrest: 300 mg IV push	Bradycardia Prolongs PR, QRS and QT	Pulmonary fibrosis, bradycardia, heart block, torsades de pointes (unusual), hyper- or hypothyroidism, GI upset, alcoholic-like hepatitis, peripheral neuropathy, ataxia, tremor, dizziness, photosensitivity, blue-gray skin, corneal microdeposits, optic neuritis **IV Amiodarone:** Hypotension, bradycardia, phlebitis at site of administration
SOTALOL AND DOFETILIDE			
Sotalol (*Betapace*, and others)	PO: 80-160 mg twice daily (higher doses may be associated with increased adverse effects including torsades de pointes)	Bradycardia Prolongs PR, QT	Heart block, hypotension, bronchospasm, bradycardia,
Dofetilide *(Tikosyn)*	PO: 500 mcg bid	Prolongs QT	Torsades de pointes

1. Patients with decreased hepatic or renal function may require lower dosage.

Dosage and Adverse Effects of Some Antiarrhythmic Drugs

Drug	Usual dosage[1] and interval	Effect on ECG	Adverse effects
QUINIDINE, PROCAINAMIDE, DISOPYRAMIDE			
Quinidine (many manufacturers)	PO: 200-400 mg q6h (sulfate) 324-648 mg q8-12h (gluconate)	Prolongs QRS, QT and (±) PR	Diarrhea and other GI symptoms, cinchonism, hepatic granulomas and necrosis, thrombocytopenia, rash, hypotension, heart block, ventricular tachyarrhythmias, torsades de pointes, fever, lupus-like syndrome
Procainamide (*Pronestyl, Procanbid,* and others)	PO: 50 mg/kg/day in divided doses, q3-4h or q6h (sustained-released) or q12h (extended-release) IV loading: 20 mg/min (up to 17 mg/kg) IV maintenance: 2-4 mg/min	Prolongs QRS, QT and (±) PR	Lupus-like syndrome, confusion, disorientation, GI symptoms, rash, hypotension, ventricular arrhythmias, torsades de pointes, blood dyscrasias, fever, rare muscular weakness IV: hypotension, heart block
Disopyramide (*Norpace*, and others)	PO: 100-200 mg q6-8h or 150-300 mg q12h (long-acting formulation)	Prolongs QRS, QT and (±) PR	Anticholinergic effects (urinary retention, aggravation of glaucoma, constipation), hypotension, heart failure, ventricular tachyarrhythmias, torsades de pointes, heart block, nausea, vomiting, diarrhea, hypoglycemia, nervousness
FLECAINIDE, PROPAFENONE			
Flecainide[2] *(Tambocor)*	PO initial dose: 50-100 mg q12h, increase q4 days if required, by 50 mg q12h PO maintenance: ≤400 mg/day Cardioversion: 300 mg single dose PO[3]	Prolongs PR and QRS	Bradycardia, heart block, new ventricular fibrillation, sustained ventricular tachycardia, heart failure, dizziness, blurred vision, nervousness, headache, GI upset, neutropenia
Propafenone[2] *(Rythmol)*	PO initial dose: 150 mg q8h, increase q3-4 days if required or 225 mg q12h, increase q5 days if needed *(Rythmol SR)* PO maintenance: 225-425 mg q12h *(Rythmol SR)* Cardioversion: 600 mg single dose PO[3]	Prolongs PR and QRS	Bradycardia, heart block, new ventricular fibrillation, sustained ventricular tachycardia, heart failure, dizziness, lightheadedness, metallic taste, GI upset, bronchospasm, hepatic toxicity
ADENOSINE			
(Adenocard)	IV: 6 mg by rapid IV push followed by a saline flush; may use 12 mg for repeat rapid bolus injection	Prolongs PR Heart block (transient)	Facial flushing, transient dyspnea, chest discomfort (non-coronary), hypotension; may cause bronchoconstriction in patients with asthma
LIDOCAINE AND SIMILAR AGENTS			
Lidocaine (*Xylocaine*, and others)	IV loading: 1 mg/kg given over 2 min, then 0.5 mg/kg over 2 min every 8-10 min x 3 or 20 mg/min infused over 10 min IV maintenance: 1-4 mg/min	No significant change	Drowsiness or agitation, slurred speech, tinnitus, disorientation, coma, seizures, paresthesias, cardiac depression, especially with excessive accumulation in heart failure or liver failure or infusions for more than 24 hours, bradycardia/asystole
Mexiletine *(Mexitil)*	PO initial dose: 150-200 mg q8h taken with food PO maintenance: 150-300 mg q6-12h, maximum 1200 mg/day	No significant change	GI upset, fatigue, nervousness, dizziness, tremor, sleep upset, seizures, visual disturbances, psychosis, fever, blood dyscrasias, hepatitis

1. Patients with decreased hepatic or renal function may require lower dosage.
2. Should not be used in patients with congestive heart failure or ischemic heart disease.
3. Patients should also receive an AV nodal blocking agent such as verapamil, diltiazem or a beta-blocker.

Dosage and Adverse Effects of Some Antiarrhythmic Drugs

Drug	Usual dosage[1] and interval	Effect on ECG	Adverse effects
OTHER AGENTS			
Digoxin (*Lanoxin,* and others)	IV or PO loading: 1-1.5 mg over 24 hours in 3-4 divided doses Maintenance: 0.125-0.5 mg/day	Prolongs PR Depresses ST segment Flattens T wave	Bradycardia, AV block, arrhythmias, anorexia, nausea, vomiting, diarrhea, abdominal pain, headache, confusion, abnormal vision
Ibutilide *(Corvert)*	IV: 1 mg over 10 minutes; may repeat once after 10 minutes	Prolongs QT	Torsades de pointes
Magnesium sulfate	IV: 1-2 g over 5-60 minutes		Areflexia, respiratory depression, bradycardia, AV block, asystole with high doses

1. Patients with decreased hepatic or renal function may require lower dosage.

pathic ventricular tachycardia. It also has been used for treatment of atrial fibrillation (Medical Letter 2004; 46:59).

Implantable cardioverter/defibrillators (ICDs) — These devices are increasingly used for prophylaxis against sudden death due to arrhythmias. ICDs improve survival compared to antiarrhythmic drugs (mainly amiodarone) in patients resuscitated from cardiac arrest or treated for sustained ventricular tachycardia (JP DiMarco, N Engl J Med 2003; 349:1836; F Bokhari et al, Circulation 2004; 110:112). In asymptomatic patients with coronary artery disease judged to be at high risk for sudden death because of low ejection fraction and/or arrhythmias inducible by programmed electrical stimulation of the heart, 3 trials have now shown lower mortality in those with ICDs compared to those receiving conventional medical therapy with or without antiarrhythmic drugs (AJ Moss et al, [MADIT] N Engl J Med 1996; 335:1933; AE Buxton et al, [MUSTT] N Engl J Med 1999; 341:1882; AJ Moss et al, [MADIT II] N Engl J Med 2002; 346:877). Similar results have been reported in patients with nonischemic dilated cardiomyopathy and others with heart failure (A Kadish et al, N Engl J Med 2004; 350:2151; GH Bardy et al, Sudden Cardiac Death in Heart Failure Trial [SCD-HeFT], presented at American College of Cardiology 53rd Annual Scientific Session, New Orleans, March 8, 2004). Biventricular stimulation of the left and right ventricles simultaneously with a pacemaker, combined with a defibrillator, improved symptoms and survival in patients with heart failure and an intraventricular conduction delay (MR Bristow et al, N Engl J Med 2004; 350:2140). Adverse effects from ICDs include infection and painful discharges, which may be appropriate (due to ventricular arrhythmias) or inappropriate (due to supraventricular arrhythmias or electrical noise).

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