Drug Tables of CVS Pharmacology

DRUG SUMMARY TABLE: Drugs Used in Hypertension

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Diuretics (see also Chapter 15)				
Hydrochlorothiazide, chlorthalidone	Block Na/Cl transporter in distal convoluted tubule	Hypertension, mild edema	Oral Duration: 8–12 h	Hypokalemia, hyperglycemia, hyperuricemia, hyperlipidemia
Furosemide	Block Na/K/2Cl transporter in thick ascending limb	Hypertension, heart failure, edema, hypercalcemia	Oral, parenteral Duration: 2–3 h	Hypokalemia, hypovolemia, ototoxicity
Sympathoplegics				
Centrally acting				
Clonidine	Agonist at α_2 receptors • in CNS this results in *decreased* SANS outflow	Hypertension	Oral and transdermal Oral duration: 2–3 days • transdermal 1 wk	Sedation, danger of severe rebound hypertension if suddenly stopped
Methyldopa	Prodrug converted to methylnorepinephrine in CNS, with effects like clonidine	Hypertension	Oral Duration: 12–24 h	Sedation, induces hemolytic antibodies
Ganglion blockers				
Hexamethonium	Obsolete prototype nicotinic acetylcholine (ACh) receptor blocker in ganglia • blocks all ANS transmission	None	Oral, parenteral; no CNS effect	Severe orthostatic hypotension, constipation, blurred vision, sexual dysfunction
Trimethaphan: IV, obsolete short-acting ganglion blocker for hypertensive emergencies, controlled hypotension *Mecamylamine:* oral ganglion blocker, several hours' duration, enters CNS				
Postganglionic neuron blockers				
Reserpine	Blocks vesicular pump (VMAT) in adrenergic neurons	Obsolete in hypertension, Huntington's disease	Oral Duration: 5 days	Sedation • severe psychiatric depression (high doses)
Guanadrel: blocks release of norepinephrine, depletes stores; oral, long duration; severe orthostatic hypotension (*guanethidine*, a similar drug, was withdrawn in the United States)				
Alpha blockers				
Prazosin	Selective α_1 blocker • reduces peripheral vascular resistance • prostatic smooth muscle tone	Mild hypertension, benign prostatic hyperplasia	Oral Duration: 6–8 h	First dose orthostatic hypotension
Doxazosin, terazosin: similar to prazosin but longer duration of action				
Beta blockers				
Propranolol	Prototype nonselective β blocker • reduces cardiac output • possible secondary reduction in renin release	Hypertension • many other applications (see Chapter 10)	Oral, parenteral Duration: 6–8 h (extended release forms available)	Bronchospasm in asthmatics • excessive cardiac depression, sexual dysfunction, sedation, sleep disturbances
Atenolol, metoprolol: like propranolol but β_1-selective; fewer adverse effects *Labetalol, carvedilol:* combined α and β blockade; oral and parenteral				

(*Continued*)

DRUG SUMMARY TABLE: Drugs Used in Hypertension (*Continued*)

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Vasodilators, oral				
Calcium channel blockers				
Nifedipine, other dihydropyridines	Prototype L-type calcium channel blockers • combine moderate vascular effect with weak cardiac effect	Hypertension, angina	Oral Duration: 6–24 h	Constipation
Verapamil, diltiazem oral and parenteral; also used in arrhythmias; greater cardiodepressant effects than dihydropyridines; verapamil blocks P-glycoprotein transporter (see Chapter 5)				
Older oral vasodilators				
Hydralazine	Probably causes release of nitric acid (NO) by endothelial cells • causes arteriolar dilation	Hypertension (also used in heart failure in combination with isosorbide dinitrate)	Oral Duration: 6–8 h	Tachycardia, salt and water retention, lupus-like syndrome
Minoxidil	Prodrug, sulfate metabolite opens K^+ channels, causes arteriolar smooth muscle hyperpolarization and vasodilation	Severe hypertension • male-pattern baldness	Oral, topical Duration: 6–8 h	Marked tachycardia, salt and water retention • hirsutism
Vasodilators, parenteral				
Nitroprusside	Releases NO from drug molecule	Hypertensive emergencies • cardiac decompensation	Parenteral only Duration: minutes • requires constant infusion	Excessive hypotension • prolonged infusion may cause thiocyanate and cyanide toxicity
Diazoxide	K^+ channel opener in smooth muscle, secretory cells	Hypertensive emergencies • hypoglycemia due to insulin-secreting tumors	Parenteral for hypertension, oral for insulinoma	Hyperglycemia • edema, excessive hypotension
Fenoldopam	D_1 agonist • causes arteriolar dilation	Hypertensive emergencies	Parenteral only, very short duration	Excessive hypotension
Renin antagonist				
Aliskiren	Renin inhibitor • reduces angiotensin I synthesis	Hypertension	Oral Duration: 12 h	Angioedema, renal impairment
Angiotensin antagonists				
ACE inhibitors				
Captopril	ACE inhibitor • reduces angiotensin II synthesis	Hypertension, diabetic renal disease, heart failure	Oral Half-life: 2.2 h but large doses provide duration of 12 h	Cough • hyperkalemia • teratogen
Benazepril, enalapril, lisinopril, others: like captopril but longer half-lives				
Angiotensin II receptor blockers (ARBs)				
Losartan	Blocks AT_1 receptors	Hypertension	Oral Duration: 6–8 h	Hyperkalemia • teratogen
Candesartan, irbesartan, others: like losartan				

ACE, angiotensin-converting enzyme; ANS, autonomic nervous system; CNS, central nervous system; SANS, sympathetic autonomic nervous system.

DRUG SUMMARY TABLE: Drugs Used in Angina

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Short-acting nitrate				
Nitroglycerin, sublingual (SL)	Releases nitric oxide (NO), increases cGMP (cyclic guanosine monophosphate), and relaxes vascular smooth muscle	Acute angina pectoris • acute coronary syndrome	Rapid onset (1 min) • short duration (15 min)	Tachycardia, orthostatic hypotension, headache
Isosorbide dinitrate (SL): like nitroglycerin SL but slightly longer acting (20–30 min)				
Intermediate-acting nitrate				
Nitroglycerin, oral	Like nitroglycerin SL • active metabolite dinitroglycerin	Prophylaxis of angina	Slow onset • Duration: 2–4 h	Same as nitroglycerin SL
Isosorbide dinitrate and mononitrate, oral: like nitroglycerin oral				
Pentaerythritol tetranitrate and other oral nitrates: like nitroglycerin oral				
Long-acting nitrate				
Transdermal nitroglycerin	Like nitroglycerin oral	Prophylaxis of angina	Slow onset • long duration of absorption: 24 h • duration of effect: 10 h (tachyphylaxis)	Same as nitroglycerin SL • loss of response is common after 10–12 h exposure to drug
Ultrashort-acting nitrite				
Amyl nitrite	Same as nitroglycerin SL	Obsolete for angina • some recreational use	Volatile liquid, vapors are inhaled • onset seconds Duration: 1–5 min	Same as nitroglycerine SL
Calcium channel blockers				
Verapamil	Blocks L-type Ca^{2+} channels in smooth muscle and heart • decreases intracellular Ca^{2+}	Angina (both atherosclerotic and vasospastic), hypertension • AV-nodal arrhythmias; migraine	Oral, parenteral Duration: 6–8 h	Constipation, pretibial edema, flushing, dizziness • Higher doses: cardiac depression, hypotension
Diltiazem: like verapamil; shorter half-life				
Nifedipine	Dihydropyridine Ca^{2+} channel blocker; vascular > cardiac effect	Angina, hypertension	Oral • slow-release form Duration: 6–8 h	Like verapamil • less constipation, cardiac effect
Amlodipine, felodipine, nicardipine, nisoldipine: like nifedipine but longer acting				
Beta blockers				
Propranolol	Blocks sympathetic effects on heart and blood pressure • reduces renin release	Angina, hypertension, arrhythmias, migraine, performance anxiety	Oral, parenteral Duration: 6 h	See Chapter 10
Atenolol, metoprolol, other β *blockers:* like propranolol; most have longer duration of action				
Other antianginal drugs				
Ranolazine	Blocks late Na^+ current in myocardium, reduces cardiac work	Angina	Oral Duration: 10–12 h	QT prolongation on ECG • inhibits CYP3A and 2D6
Ivabradine	Blocks pacemaker Na^+ current (I_f) in sinoatrial node, reduces heart rate	Investigational: angina, heart failure	Oral, administered twice daily	Unknown
Drugs for erectile dysfunction				
Sildenafil, tadalafil, vardenafil	Block phosphodiesterase 5 • increase cGMP	Erectile dysfunction in men	Oral Duration: hours	Interaction with nitrates • priapism

DRUG SUMMARY TABLE: Drugs Used in Heart Failure

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Diuretics				
Furosemide, other loop diuretics	Reduces preload, edema by powerful diuretic action on thick ascending limb in nephron • vasodilating effect on pulmonary vessels	Acute and chronic heart failure, especially acute pulmonary edema • other edematous conditions, hypercalcemia (see Chapter 15)	Oral, parenteral Duration: 2–4 h	Ototoxicity • hypovolemia, hypokalemia
Spironolactone	Antagonist of aldosterone in kidney plus poorly understood reduction in mortality	Chronic heart failure, aldosteronism	Oral Duration: 24–48 h	Hyperkalemia • gynecomastia
Eplerenone: similar to spironolactone but lacks gynecomastia effect				
Angiotensin-converting enzyme (ACE) inhibitors and receptor blockers				
Captopril	Blocks angiotensin-converting enzyme, reduces All levels, decreases vascular tone and aldosterone secretion. Reduces mortality	Heart failure, hypertension, diabetes	Oral; short half-life but large doses used Duration: 12–24 h	Cough, renal damage, hyperkalemia, contraindicated in pregnancy
Benazepril, enalapril, others: like captopril				
Losartan, candesartan, others: angiotensin receptor blockers (see Chapter 11); benefits not documented as well as those of ACE inhibitors				
Positive inotropic drugs				
Cardiac glycosides: digoxin	Inhibits Na^+/K^+ ATPase sodium pump and increases intracellular Na^+, decreasing Ca^{2+} expulsion and increasing cardiac contractility	Chronic heart failure, nodal arrhythmias	Oral, parenteral Duration: 40 h	Arrhythmogenic! Nausea, vomiting, diarrhea, visual and endocrine changes (rare)
Sympathomimetics: dobutamine	$Beta_1$-selective sympathomimetic, increases cAMP and force of contraction	Acute heart failure	Parenteral Duration: a few minutes	Arrhythmias
Beta blockers				
Carvedilol, metoprolol, bisoprolol	Poorly understood reduction of mortality, possibly by decreasing remodeling	Chronic heart failure	Oral Duration varies (see Chapter 10)	Cardiac depression (see Chapter 10)
Vasodilators				
Nitroprusside	Rapid, powerful vasodilation reduces preload and afterload	Acute severe decompensated failure	IV infusion Duration: a few minutes	Excessive hypotension • thiocyanate and cyanide toxicity
Hydralazine + isosorbide dinitrate	Poorly understood reduction in mortality	Chronic failure in African Americans	Oral	Headache, tachycardia
Nesiritide	Atrial peptide vasodilator, diuretic	Acute severe decompensated failure	Parenteral Duration: a few minutes	Renal damage, hypotension

cAMP, cyclic adenosine monophosphate.

CHECKLIST

When you complete this chapter, you should be able to:

- ☐ Describe the distinguishing electrophysiologic action potential and ECG effects of the 4 major groups of antiarrhythmic drugs and adenosine.
- ☐ List 2 or 3 of the most important drugs in each of the 4 groups.
- ☐ List the major toxicities of those drugs.
- ☐ Describe the mechanism of selective depression by local anesthetic antiarrhythmic agents.
- ☐ Explain how hyperkalemia, hypokalemia, or an antiarrhythmic drug can cause an arrhythmia.

DRUG SUMMARY TABLE: Antiarrhythmic Drugs

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Group 1A				
Procainamide	Use- and state-dependent block of I_{Na} channels • some block of I_K channels. Slowed conduction velocity and pacemaker activity • prolonged action potential duration and refractory period	Atrial and ventricular arrhythmias, especially after myocardial infarction	Oral and parenteral • oral slow-release forms available • Duration: 2–3 h	Increased arrhythmias including torsades, hypotension, lupus-like syndrome
Disopyramide: similar to procainamide but longer duration of action; toxicity includes antimuscarinic effects and heart failure				
Quinidine: similar to procainamide but greater toxicity, including cinchonism (tinnitus, vertigo, headache), gastrointestinal disturbance, and thrombocytopenia				
Group 1B				
Lidocaine	Highly selective use- and state-dependent I_{Na} block; minimal effect in normal tissue; no effect on I_K	Ventricular arrhythmias post-myocardial infarction and digitalis-induced arrhythmias	IV and IM Duration: 1–2 h	Central nervous system (CNS) sedation or excitation
Mexiletine: similar to lidocaine but oral activity and longer duration of action; also used in neuropathic pain				
Group 1C				
Flecainide	Selective use- and state-dependent block of I_{Na}; slowed conduction velocity and pacemaker activity	Refractory arrhythmias	Oral	Increased arrhythmias • CNS excitation
Group 2				
Propranolol	Block of β receptors; slowed pacemaker activity	Postmyocardial infarction as prophylaxis against sudden death ventricular fibrillation; thyrotoxicosis	Oral, parenteral Duration: 4–6 h	Bronchospasm • cardiac depression, atrioventricular (AV) block, hypotension (see Chapter 10)
Metoprolol: similar to propranolol but β_1-selective				
Esmolol: selective β_1-receptor blockade; IV only, 10-min duration. Used in perioperative and thyrotoxicosis arrhythmias				

(*Continued*)

DRUG SUMMARY TABLE: Antiarrhythmic Drugs (*Continued*)

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Group 3				
Amiodarone	Strong I_K block produces marked prolongation of action potential and refractory period. Group 1 activity slows conduction velocity • groups 2 and 4 activity confer additional antiarrhythmic activity	Refractory arrhythmias • used off-label in many arrhythmias (broad spectrum antiarrhythmic action)	Oral, parenteral Half-life and duration of action: 1–10 wk	Thyroid abnormalities, deposits in skin and cornea, pulmonary fibrosis, optic neuritis • torsades is rare with amiodarone
Sotalol	I_K block and β-adrenoceptor block	Ventricular arrhythmias and atrial fibrillation	Oral Duration: 7 h	Dose-related torsades de pointes • cardiac depression
Ibutilide	Selective I_K block • prolonged action potential and QT interval	Treatment of acute atrial fibrillation	Ibutilide is IV only Duration: 6 h	Torsades de pointes
Dofetilide	Like ibutilide	Treatment and prophylaxis of atrial fibrillation	Oral Duration: 7 h	Torsades de pointes
Group 4				
Verapamil	State- and use-dependent I_{Ca} block slows conduction in AV node and pacemaker activity • PR interval prolongation	AV nodal arrhythmias, especially in prophylaxis	Oral, parenteral Duration: 7 h	Cardiac depression, constipation, hypotension
Diltiazem	Like verapamil	Rate control in atrial fibrillation	Oral, parenteral Duration: 6 h	Like verapamil
Dihydropyridines: calcium channel blockers but not useful in arrhythmias; sometimes precipitate them				
Miscellaneous				
Adenosine	Increase in diastolic I_K of AV node that causes marked hyperpolarization and conduction block • reduced I_{Ca}	Acute nodal tachycardias	IV only Duration: 10–15 s	Flushing, bronchospasm, chest pain, headache
Potassium ion	Increase in all K currents, decreased automaticity, decreased digitalis toxicity	Digitalis toxicity and other arrhythmias if serum K is low	Oral or IV	Both hypokalemia and hyperkalemia are associated with arrhythmogenesis. Severe hyperkalemia causes cardiac arrest
Magnesium ion	Poorly understood, possible increase in Na^+/K^+ ATPase activity	Digitalis arrhythmias and other arrhythmias if serum Mg is low	IV	Muscle weakness • severe hypermagnesemia can cause respiratory paralysis

DRUG SUMMARY TABLE: Diuretic Agents

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
Carbonic anhydrase inhibitors				
Acetazolamide	Inhibits carbonic anhydrase. In proximal tubule, bicarbonate reabsorption is blocked and Na^+ is excreted with HCO_3^-. In glaucoma, secretion of aqueous humor is reduced, and in mountain sickness, metabolic acidosis increases respiration	Glaucoma, mountain sickness • edema with alkalosis	Oral, parenteral Diuresis is self-limiting but effects in glaucoma and mountain sickness persist	Metabolic acidosis; sedation, paresthesias. Hyperammonemia in cirrhosis
Dorzolamide, brinzolamide: topical carbonic anhydrase inhibitors for glaucoma only				
Loop diuretics				
Furosemide, also bumetanide, torsemide	Inhibit $Na^+/K^+/2Cl^-$ transporter in thick ascending limb of loop of Henle. Cause powerful diuresis and increased Ca^{2+} excretion	Heart failure, pulmonary edema, severe hypertension; other forms of edema; hypercalcemia	Oral, parenteral	Metabolic hypokalemic alkalosis • ototoxicity • hypovolemia • efficacy reduced by nonsteroidal anti-inflammatory drugs. Sulfonamide allergy (rare).
Ethacrynic acid: like furosemide but not a sulfonamide and has some uricosuric effect				
Thiazide diuretics				
Hydrochlorothiazide, chlorthalidone (thiazide-like); many other thiazides	Inhibit Na^+/Cl^- transporter in distal convoluted tubule. Cause moderate diuresis and reduced excretion of calcium	Hypertension, mild heart failure, hypercalciuria with stones • nephrogenic diabetes insipidus	Oral	Metabolic hypokalemic alkalosis • early hyponatremia • increased serum glucose, lipids, uric acid • efficacy reduced by nonsteroidal anti-inflammatory drugs. Sulfonamide allergy (rare)
K^+-sparing diuretics				
Spironolactone, eplerenone	Steroid inhibitors of cytoplasmic aldosterone receptor in cortical collecting ducts • reduce K^+ excretion	Excessive K^+ loss when using other diuretics • heart failure • aldosteronism	Oral	Hyperkalemia • gynecomastia (spironolactone only)
Amiloride	Inhibitor of ENaC epithelial sodium channels in cortical collecting duct, reduces Na^+ reabsorption and K^+ excretion	Excessive K^+ loss when using other diuretics • usually in combination with thiazides	Oral	Hyperkalemia
Triamterene: like amiloride but much less potent				
SGLT2 inhibitors				
Canagliflozin, dapagliflozin	Inhibitors of sodium-glucose cotransporter in the proximal tubule, markedly increase glucose excretion	Diabetes	Oral	Urinary tract infections
Osmotic diuretics				
Mannitol	Osmotically retains water in tubule by reducing reabsorption in proximal tubule, descending limb of Henle's loop, and collecting ducts • in the periphery, mannitol extracts water from cells	Solute overload in rhabdomyolysis, hemolysis, tumor lysis syndrome • brain edema with coma • acute glaucoma	Intravenous; short duration	Hyponatremia followed by hypernatremia • headache, nausea, vomiting

(*Continued*)

DRUG SUMMARY TABLE: Diuretic Agents (*Continued*)

Subclass	Mechanism of Action	Clinical Applications	Pharmacokinetics	Toxicities, Interactions
ADH agonists				
Desmopressin, vasopressin	Agonists at V_1 and V_2 ADH receptors, activate insertion of aquaporin water channels in collecting tubule, reduce water excretion • vasoconstriction	Pituitary diabetes insipidus	Subcutaneous, nasal	Hyponatremia • hypertension
ADH antagonists				
Conivaptan	Antagonist at V_{1a}, V_2 receptors	SIADH, hyponatremia	Parenteral	Infusion site reactions
Tolvaptan: like conivaptan, more selective for V_2 receptors *Demeclocycline:* used in SIADH, mechanism unclear				

ADH, antidiuretic hormone; SIADH, syndrome of inappropriate antidiuretic hormone.