Name: **Digoxin (Lanoxin)**

Class: CHF Rx (Cardiac Glycoside)

Mech.: Inhib. of Na^+/K^+ ATPase → ↑ release of Ca^{2+} from SR → ↑ myocardial contractility. Also ↑ sensitivity of AV node to vagal stimulation → ↓ ventricular rate in atrial flutter or fibrillation (i.e., anti-arrhythmic).

Absorption:

Dist.:

Metab.: Very little.

Excretion, **t_**: Urine. Short t_.

Toxicity/S.E.s: Low therapeutic index. Toxicity enhanced by hypokalemia. Arrhythmias (possibly life-threatening), anorexia, n/v/d, drowsiness, fatigue, visual disturbances. Verapamil or quinidine → ↑ toxicity.

Utility: Treat heart failure. DOC for atrial fibrillation/flutter.

Special Features: No active metabolites. Shorter t_, less GI absorption, and less protein binding than digitoxin. Only cardiac glycoside routinely used.

Name: **Digitoxin (Crystodigin)**

Class: CHF Rx (Cardiac Glycoside)

Mech.: Inhib. of Na^+/K^+ ATPase → ↑ release of Ca^{2+} from SR → ↑ myocardial contractility. Also ↑ sensitivity of AV node to vagal stimulation → ↓ ventricular rate in atrial flutter or fibrillation (i.e., anti-arrhythmic).

Absorption:

Dist.: Strong protein binding.

Metab.: Hepatic metab.

Excretion, **t_**: Feces. Longer t_ than digoxin.

Toxicity/S.E.s: Low therapeutic index. Toxicity enhanced by hypokalemia. Arrhythmias (possibly life-threatening), anorexia, n/v/d, drowsiness, fatigue, visual disturbances. Verapamil or quinidine → ↑ toxicity.

Utility: Treat heart failure.

Special Features: Active metabolites. Longer t_, more GI absorption, and more protein binding than digoxin.

Name: **Dobutamine (Dobutrex)**

Class: CHF Rx (Mixed (α-β) Agonist (Cardioselective))

Mech.: Stim. α and β receptors, but not DA. → ↑ CO w/o ↑ HR. ↑ stroke volume. No/little change in peripheral resistance. ↑ cAMP → ↑ contractility.

Absorption: IV → rapid onset (1-2 min). Peak effect ~ 10 min.

Dist.:

Metab.: Methylation by COMT. Conjugation

Excretion, **t_**: 2 min.

Toxicity/S.E.s: ↑ BP, ↑ HR, tachycardia, ventricular ectopic activity. ↑ myocard. O_2 consump. may cause ↑ size MI. Tachyphylaxis to β stim.

Utility: Short-term treatment of cardiac decompensation after cardiac surgery or w/CHF or acute MI. Often DOC after acute MI. Treatment of shock after correction of hypovolemia.

Name: **Dopamine**

Class: CHF Rx (β-Adrenergic Agonist)

Mech.: ↓ dose → D1 stim. ↑ dose → β1 stim. Also releases NE from symp. neur. Causes vasodilation in renal, mesenteric, and coronary beds → ↑ renal blood flow, glomerular filtration, and Na^+ excretion. Also causes ↓ Na^+ and H_20 resorption. High doses → ↑ HR. Usu. increases systolic BP and pulse pressure. Low-mod. doses → static or decreased vasc. resistance. High conc. → α1 activation → vasoconstriction → ↑ BP. ↑ cAMP → ↑ contractility.

Absorption: No oral. IV. Onset w/in 5 min.

Dist.:

Metab.: Catab. by COMT and MAO, esp. in liver and kidneys. Glucuronidation and sulfconjugation

Excretion, **t_**: Duration of action 10 min. t_: 2 min.

Toxicity/S.E.s: Nausea, vomiting, tachycardia, anginal pain, arrhythmia, headache, hypertension, vasoconstriction. Usu. due to excessive symp activity. Treat by stopping admin. or w/α blockers. Local ischemic necrosis. Contraind. w/pheochromocytomas, uncorrected tachyarrhythm. or vent. fibrillation, MAO inhibitors, furazolidone. Adjust dose w/tricyclics.

Utility: Some shock (e.g., oliguria and low-normal periph. resist, cardiogenic/septic shock). CHF.

Name: **Amrinone (Inocor)**

Class: CHF Rx (PDE Inhibitor)

Mech.: Inhib. of PDE III→ ↑ cAMP → ↑ contractility, ↑ stroke volume, ↑ ejection fraction, ↑ heart rate, ↑ exercise capacity. In smooth muscle, inhib. → vasodilation.

Absorption: IV only.

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: ↑ mortality from heart failure (possibly due to arrhythmogenesis).

Utility: Treat CHF.

Special Features:

Name: **Hydralazine**

Class: CHF Rx (Vasodilator)

Mech.: Acts directly on smooth muscle cells → vasodilation. Mech. unknown. ↓ BP → reflex tachycardia & ↑ CO. ↑ renin concentration. ↑ NE in heart failure.

Absorption:

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Reversible lupus-like synd. Headache, nausea, sweating, arrhythmia, angina, tachycardia.

Utility: Treat CHF. Chronic use → reduction in two year mortality by 34%. Almost always coadmin. w/β-blocker (to oppose tachycardia) and a diuretic (to decrease Na^+ retention). Treat resistant HTN and hypertensive emergencies.

Special Features:

Name: **Diazoxide (Hyperstat I.V.)**

Class: CHF Rx (Vasodilator) (Antihypertensive)

Mech.: Direct arteriolar vasodilation → ↓ TPR → reflex ↑ in HR & CO.

Absorption: IV.

Dist.:

Metab.:

Excretion, **t_**: Long duration of action.

Toxicity/S.E.s: Severe tachycardia, prolonged hypotension (possibly resulting in stroke or MI).

Utility: Treat hypertensive emergencies, hypertensive encephalopathy, and eclampsia.

Special Features:

Name: **Minoxidil (Loniten)**

Class: CHF Rx (Vasodilator) (Antihypertensive)

Mech.: Direct arteriolar vasodilation → ↓ TPR → reflex ↑ in HR & CO.

Absorption: Oral.

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Severe tachycardia. Serious Na^+ & H_2O retention → volume overload, edema, CHF. Hypertrichosis.

Utility: Treat severe-malignant HTN refractory to other drugs. Male pattern baldness.

Special Features: Reflex tachycardia may be severe, requiring concomitant use of a diuretic and a β-blocker.

Name: **Nitroprusside (Nipride)**

Class: Antihypertensive Agent

Mech.: Stim. membrane-assoc. guanylyl cyclase in vascular smooth muscle cells → ↑ intracellular cGMP → activation of cGMP-dependent protein → vasodilation of arterial and venous vessels→ reflex tachycardia. Reduces BP in all pts., regardless of etiology. Decreases afterload and preload.

Absorption: Continuous IV infusion. Oral → cyanide poisoning.

Dist.:

Metab.:

Excretion, **t_**: Minutes

Toxicity/S.E.s: Tachycardia, hypotension, cyanide toxicity (Rx w/sodium thiosulfate).

Utility: Hypertensive emergencies.

Special Features:

Name: **Verapamil (Calan)**

Class: Calcium-Entry Blocking Agent (Antidysrhythmic Agent Class IV)

Mech.: Binds to L-type Ca^{2+} channels → ↓ Ca^{2+} in arterial smooth muscle cells → vasodilation → ↓ cardiac afterload. Little/no effect on venous vessels. ↓ inotropy, chronotropy, & dromotropy. Net = ↓ HR, ↓ conduction, ↓ contractility, ↓ BP. May inhib. platelet aggreg.

Absorption: Oral → nearly complete absorption. 1st pass metab→↓ bioavail. IV.

Dist.: Significant protein binding.

Metab.: Hepatic. Inducible metab. Inhibits hepatic enzymes. Active metabolites.

Excretion, **t_**: 1.5-6 hr. Repeated oral dose → ↑ t_ due to hepatic saturation. Longer t_ in elderly or pts w/hepatic cirrhosis or renal insuff.

Toxicity/S.E.s: Dizziness, hypotension, headache, constipation, gingival hyperplasia, flushing, edema. Aggravation of myocardial ischemia (less than w/DHPs). Serious toxicities (bradycardia, transient asystole, exacerbation of heart failure) are rare, but may occur after IV admin; coadmin w/β-blocker (c/i); or in pts. w/ventricular dysfxn, conduction disturbances, or systolic BP < 90 mm Hg (c/i). ↑ digoxin levels. C/i w/CHF, quinidine.

Utility: Rx angina (stable, variant, unstable), arrhythmias, hypertension. More effective than propranolol for unstable angina. DOC (IV) for paroxysmal supraventricular tachycardias. Reentry arrhythmias.

Special Features: Blocking action is frequency and voltage dependent. ∴ more effective in rapidly depolarizing cells. At vasodilatory doses, greater negative chronotropic, dromotropic, and inotropic effects than the dihydropyridines. Greatest effect on heart of channel blockers.

Name: **Nifedipine (Procardia)**

Class: Calcium-Entry Blocking Agent (Dihydropyridine)

Mech.: Binds to L-type Ca^{2+} channels → ↓ Ca^{2+} in arterial smooth muscle cells → vasodilation → ↓ TPR, ↑ coronary blood flow, ↓ cardiac afterload. Little/no effect on venous vessels. No direct effect on conduction or automaticity. Vasodilation → reflex ↑ sympathetic response → ↑ HR, ↑ contractility. Net = ↓ BP, ↑ HR, ↑ contractility, ↑ CO. May inhib. platelet aggreg.

Absorption: Oral → nearly complete absorption. 1st pass metab→↓ bioavail. IV.

Dist.: Significant protein binding.

Metab.: Hepatic. Inducible metab. Inactive metabolites.

Excretion, **t_**: 1.5-6 hr. Repeated oral dose → ↑ t_ due to hepatic saturation. Longer t_ in elderly or pts w/hepatic cirrhosis or renal insuff.

Toxicity/S.E.s: Dizziness, hypotension, headache, flushing, peripheral edema, gingival hyperplasia. Aggravation of myocardial ischemia, angina. C/i w/CHF.

Utility: Rx angina (stable, variant, unstable), arrhythmias, hypertension. DOC for stable angina w/persistent HTN, sinus bradycardia, or AV node dysfxn. W/β-blocker & nitrate → ↓ rest angina, ↓ risk of MI, ↓ risk of emergency revascularization.

Special Features:

Name: **Diltiazem (Cardizem)**

Class: Calcium-Entry Blocking Agent (Antidysrhythmic Agent Class IV)

Mech.: Binds L-type Ca^{2+} channels→ ↓ Ca^{2+} in arterial smooth muscle cells → vasodilation → ↓ TPR, ↑ coronary blood flow, ↓ cardiac afterload. Little/no effect on venous vessels. ↓ inotropy, chronotropy, & dromotropy. Net = ↓ HR, ↓ contractility, ↓ BP. May inhib. platelet aggreg.

Absorption: Oral → nearly complete absorption. 1st pass metab→↓ bioavail. IV.

Dist.: Significant protein binding.

Metab.: Hepatic. Inducible metab. Inhib. hepatic enzymes. Active metabolites.

Excretion, **t_**: 1.5-6 hr. Repeated oral dose → ↑ t_ due to hepatic saturation. Longer t_ in elderly or pts w/hepatic cirrhosis or renal insuff.

Toxicity/S.E.s: Dizziness, hypotension, headache, flushing, edema, constipation (less than verapamil), bradycardia, gingival hyperplasia. Aggravation of myocardial ischemia (less than w/DHPs). ↑ digoxin levels. C/i for pts. w/systolic BP<90 mm Hg or w/conduction disturbances. C/i w/CHF, β-blockers, quinidine.

Utility: Rx angina (stable, variant, unstable). Supraventricular tachycardia, reentry arrhyth..

Special Features: Blocking action is frequency and voltage dependent. ∴ more effective in rapidly depolarizing cells. Hemodynamic effects between those of dihydropyridines and verapamil.

Name: **Bepridil (Vascor)**
Class: Calcium-Entry Blocking Agent (Antidysrhythmic Agent Class IV)
Mech.: Binds to L-type Ca^{2+} channels → ↓ Ca^{2+} in arterial smooth muscle cells → vasodilation → ↓ TPR, ↑ coronary blood flow, ↓ cardiac afterload. Little/no effect on venous vessels. ↓ inotropy, chronotropy, & dromotropy. Blocks cardiac Na^+/K^+ channel. May inhib. platelet. aggreg.
Absorption: Oral → nearly complete absorption. 1st pass metab→↓ bioavail. IV.
Dist.: Significant protein binding.
Metab.: Hepatic.
Excretion, **t_**: Long (24-50 hr.). Repeated oral dose → ↑ t_ due to hepatic saturation. Longer t_ in elderly or pts w/hepatic cirrhosis or renal insuff.
Toxicity/S.E.s: 2° to vasodilation—dizziness, hypotension, headache, flushing, edema. Aggravation of myocardial ischemia. Drug-induced long QT syndrome (DILQT, "torsades de pointes"). C/i w/CHF, β-blockers.
Utility: Rx angina (stable, variant, unstable), supraventricular tachycardia, reentry arrhythmias, hypertension.

Name: **Nimodipine (Nimotop)**
Class: Calcium-Entry Blocking Agent (Dihydropyridine)
Mech.: Binds to L-type Ca^{2+} channels → ↓ Ca^{2+} in arterial smooth muscle cells → vasodilation → ↓ TPR, ↑ coronary blood flow, ↓ cardiac afterload. Little/no effect on venous vessels. No direct effect on conduction or automaticity. Vasodilation → reflex ↑ sympathetic response → ↑ HR, ↑ contractility. Net = ↓ BP, ↑ HR, ↑ contractility, ↑ CO. May inhib. platelet aggreg.
Absorption: Oral → nearly complete absorption. 1st pass metab→↓ bioavail. IV.
Dist.: Significant protein binding.
Metab.: Hepatic. Inactive metabolites.
Excretion, **t_**: 1.5-6 hr. Repeated oral dose → ↑ t_ due to hepatic saturation. Longer t_ in elderly or pts w/hepatic cirrhosis or renal insuff.
Toxicity/S.E.s: 2° to vasodilation—dizziness, hypotension, headache, flushing, edema. Aggravation of myocardial ischemia, angina. C/i w/CHF.
Utility: Rx angina (stable, variant, unstable). DOC for stable angina w/persistent HTN, sinus bradycardia, or AV node dysfxn.

Name: **Hydrochlorothiazide (Hydrodiuril)**
Class: Diuretic (Thiazide)
Mech.: Inhib. Na^+ & Cl^- transport in the cortical thick ascending limb and the early distal tubule → ↑ NaCl and water excretion & ↓ excretion of Ca^{2+} and uric acid.
Absorption: Oral → good absorption. Takes effect in 1 hr.
Dist.: **Metab**.: **Excretion**, **t_**: Short duration of action.
Toxicity/S.E.s: Hypokalemia, hyponatremia, hyperuricemia, weakness, hypercalcemia, metabolic alkalosis, postural hypotension, hypercholesterolemia, hypertriglyceridemia, hyperglycemia (in patients w/DM), and rare hypersensitivity rxns. C/i—pts susceptible to problems with hypokalemia (cirrhosis, pts on digitalis), hyperuricemia (gout), or hypercalcemia. Adverse rxns w/digitalis, lithium. Altered doses of anti-diabetic agents required. Long-term NSAID use may decrease anti-HTN effects.
Utility: Treat hypertension, CHF, nephrotic synd., other Na^+-retaining states. Reduce Ca^{2+} excretion (e.g., prevention of kidney stones).
Special Features: Most commonly prescribed class of diuretics. Most frequently used class of anti-HTN agents. Milder diuretic action than loop diuretics. Rel. ineffective in renal insuff.

Name: **Chlorthalidone (Hygroton)**
Class: Diuretic (Thiazide)
Mech.: Inhib. Na^+ & Cl^- transport in the cortical thick ascending limb and the early distal tubule → ↑ NaCl and water excretion & ↓ excretion of Ca^{2+} and uric acid.
Absorption: Oral → good absorption. Takes effect in 1 hr.
Dist.: **Metab**.: **Excretion**, **t_**: Long duration of action.
Toxicity/S.E.s: Hypokalemia, hyponatremia, hyperuricemia, weakness, hypercalcemia, metabolic alkalosis, postural hypotension, hypercholesterolemia, hypertriglyceridemia, hyperglycemia (in patients w/DM), and rare hypersensitivity rxns. C/i—pts susceptible to problems with hypokalemia (cirrhosis, pts on digitalis), hyperuricemia (gout), or hypercalcemia. Adverse rxns w/digitalis, lithium. Altered doses of anti-diabetic agents required. Long-term NSAID use may decrease anti-HTN effects.
Utility: Treat hypertension, CHF, nephrotic synd., other Na^+-retaining states. Reduce Ca^{2+} excretion (e.g., prevention of kidney stones).
Special Features: Most commonly prescribed class of diuretics. Most frequently used class of anti-HTN agents. Milder diuretic action than loop diuretics. Rel. ineffective in renal insuff.

Name: **Furosemide (Lasix)**
Class: Diuretic (Loop Diuretic)
Mech.: Blocks the $Na^+/K^+/Cl^-$ co-transporter in the apical membrane of the thick ascending limb of Henle's loop → ↑ excretion of urinary water, Na^+, K^+, Ca^{2+}, & Mg^{2+}. Also causes venous and renal vasodilation.
Absorption: Oral, IV. Takes effect in 20 min.
Dist.: **Metab**.:
Excretion, **t_**: 1-1.5 hr. Shorter duration than thiazides.
Toxicity/S.E.s: Hypokalemia (esp. dangerous if pt. is on digitalis), Ca^{2+} & Mg^{2+} depletion, metabolic alkalosis, volume contraction, mild hyperglycemia, thiazide-like lipid changes, sulfonamide allergy cross-rxn, ototoxicity. C/i—pts. susceptible to volume contraction from excessive diuresis (e.g., elderly), and pts. susceptible to problems w/hypokalemia (e.g., cirrhosis, digitalis). Adverse rxn w/lithium, aminoglycosides. Altered doses of anti-diabetic agents required.
Utility: Diuresis for hypertension when a short-acting diuretic is indicated. Treat HTN refractory to thiazides. Very useful in conditions refractory to less potent diuretics (e.g., CHF, renal insufficiency, nephrotic synd.). Treat hypercalcemia.
Special Features: Most potent diuretics available. Can cause excretion of up to 20% of filtered Na^+.

Name: **Triamterene (Dyrenium)**
Class: Diuretic (Potassium Sparing Diuretic)
Mech.: Inhib. Na^+ channel in the apical membrane of the late distal tubule and collecting duct → block of electrochemical gradient that drives K^+ & H^+ secretion → diuresis & ↓ excretion of K^+ & H^+. Weak anti-HTN activity.
Absorption: Oral
Dist.:
Metab.:
Excretion, **t_**: 1° = kidney. 3 hr.
Toxicity/S.E.s: Hyperkalemia (most severe), n/v (most common), metabolic acidosis. Hyponatremia may occur in old folks. Absolutely contraindicated with hyperkalemia. Adverse rxns w/lithium, ACE inhibitors. Rare renal failure w/NSAIDs.
Utility: Usu. given w/another diuretic (often thiazide or loop). Combination usu. → normal K^+ excretion. Used to prevent or correct hypokalemia, and to avoid K^+ depletion in pts. on digitalis.
Special Features: Rel. weak diuretic.

Name: **Amiloride (Midamor)**
Class: Diuretic (Potassium Sparing Diuretic)
Mech.: Inhib. Na^+ channel in the apical membrane of the late distal tubule and collecting duct → block of electrochemical gradient that drives K^+ & H^+ secretion → diuresis & ↓ excretion of K^+ & H^+.
Absorption: Oral
Dist.:
Metab.:
Excretion, **t_**: 1° = kidney. 6 hr.
Toxicity/S.E.s: Hyperkalemia (most severe), n/v (most common), metabolic acidosis. Hyponatremia may occur in old folks. Absolutely contraindicated with hyperkalemia.
Utility: Usu. given w/another diuretic (often thiazide or loop). Combination usu. → normal K^+ excretion.
Special Features: Rel. weak diuretic.

Name: **Spironolactone (Aldactone)**
Class: Diuretic (Potassium Sparing Diuretic) (Aldosterone Antagonist)
Mech.: Competitive inhib. of aldosterone → block of aldost.-stim. Na^+ reabsorption and K^+/H^+ excretion in late distal tubule and collecting duct. Also reduces aldost.-stim. ammoniagenesis throughout the nephron.
Absorption: Oral. Takes up to 2 days to be effective.
Dist.:
Metab.: Hepatic.
Excretion, **t_**: 20 hr.
Toxicity/S.E.s: Hyperkalemia, gynecomastia, amenorrhea. Absolutely contraindicated w/hyperkalemia.
Utility: Most efficacious in pts. w/high plasma levels of aldosterone (e.g., 1° hyperaldosteronism due to an adrenal tumor or hyperplasia; 2° hyperaldost. due to cirrhosis, etc.).
Special Features: Only diuretic that acts through the blood side of the tubule. Rel. weak diuretic.

Name: **Clonidine (Catapres)**
Class: Centrally Acting Antiadrenergic Agent/Opioid Withdrawal Suppressant
Mech.: Stimulates inhibitory α2 receptors in central cardiovasc pathways involving EPI or NE. α2 are G-protein coupled to inhibit adenylyl cyclase →
↓ cAMP → ↓ central symp. activity.
Absorption: Oral, transdermal.
Dist.: Acts at medullary and spinal sites.
Metab.:
Excretion, **t_**:
Toxicity/S.E.s: Prominent sedation, dry mouth, depression in those so inclined, constipation. S.E.s may be reduced by transdermal admin. May potentiate actions of other CNS depressants. Rebound hypertension, nervousness, insomnia if w/drawn too quickly.
Utility: Treat hypertension. DOC for treating opioid w/drawal. No abstinence synd. when withdrawn.
Special Features: Direct α2 activation. Very potent (<0.5 mg/day). CV reflexes remain intact; normal homeostatic responses to exercise are maintained.

Name: **Guanabenz (Wytensin)**
Class: Centrally Acting Antiadrenergic Agent
Mech.: Stimulates inhibitory α2 receptors in central cardiovasc pathways involving EPI or NE. α2 are G-protein coupled to inhibit adenylyl cyclase →
↓ cAMP → ↓ central symp. activity.
Absorption: Oral.
Dist.: Acts at medullary and spinal sites.
Metab.:
Excretion, **t_**:
Toxicity/S.E.s: Prominent sedation, dry mouth, depression in those so inclined, constipation. May potentiate actions of other CNS depressants. Rebound hypertension, nervousness, insomnia if w/drawn too quickly.
Utility: Treat hypertension.
Special Features: Direct α2 activation. CV reflexes remain intact; normal homeostatic responses to exercise are maintained.

Name: **Methyldopa (Aldomet)**
Class: Centrally Acting Antiadrenergic Agent
Mech.: Stimulates inhibitory α2 receptors in central cardiovasc pathways involving EPI or NE. α2 are G-protein coupled to inhibit adenylyl cyclase →
↓ cAMP → ↓ central symp. activity.
Absorption:
Dist.: Act at medullary and spinal sites.
Metab.:
Excretion, **t_**:
Toxicity/S.E.s: Prominent sedation, dry mouth, nightmares, depression, movement disorders, endocrine disturbances (lactation), anemia, rare hypersensitivity of skin and liver. Possible toxic psychosis if given w/levodopa.
Utility: Treat hypertension.
Special Features: Activates α2 via metabolite methylnorepinephrine (false transmitter). Probably the most used hypotensive agent in mgt. of pregnant E

Name: **Reserpine**
Class: Adrenergic Neuron Blocking Agent
Mech.: Depletes NE, 5-HT, DA from nerve terminals in periph. and CNS. Also depletes some EPI from adrenal medulla. 1° = impairs storage of NE in terminals → ↓ NE available for release. Cause slow fall in BP, some bradycardia, slight inhib. of cardiovasc reflexes, inhib of catechol. release actions of indirect sympathomimetics, ↓ CO, ↓ TPR.
Absorption: Oral
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s: Sedation, nightmares, psychic depression (suicide). In GI, parasymp tone predominates (cramps, diarrhea, exacerbated peptic ulcer). Nasal congestion, bradycardia. May potentiate effects of CNS depressants. Adverse interactions w/MAOIs.
Utility: Treat mild-mod. hypertension (concurrent diuretic therapy). Periph. vasc. disease (Raynaud's Synd.). Antipsychotic (seldom used; higher doses).
Special Features: No longer considered very useful

Name: **Guanethidine (Ismelin)**
Class: Adrenergic Neuron Blocking Agent
Mech.: Taken up at NE nerve terminal by NE transport system. Blocks release of NE by action potential or indirect agents. Eventually depletes NE. Causes ↓ BP, some bradycardia. No adrenal effect.
Absorption: Poor oral.
Dist.: No CNS.
Metab.:
Excretion, **t_**: 5 days.
Toxicity/S.E.s: Marked postural & exercise hypotension, bradycardia, fluid retention, asthma aggravation, diarrhea, inhib. of ejaculation. But no CNS effects. C/I for pheochromocytoma (supersens), impending CHF or partial heart block, bronchial asthma. Not to be used in comb. w/MAO inhibitors or sympathomimetics. TCAs block uptake into nerve terminals.
Utility: Mod.-severe hypertension (very effective, but last resort due to severe side effects).
Special Features: Supersensitivity develops (↑ effect of direct acting, but ↓ effect of indirect). Onset 1-3 wks. No longer considered very useful.

Name: **Prazosin (Minipress)**
Class: α-Blocking Agent
Mech.: Blocks α1 receptors in vasculature → ↓ phospholipase C activation, ↓ IP_3 formation, ↓ Ca^{2+} released from intracellular stores → arteriolar & venous vasodilation.
Absorption: Oral. 50% bioavailability
Dist.:
Metab.:
Excretion, **t_**: 3 hr.
Toxicity/S.E.s: 1st dose syncope (1%), dizziness, headaches, weakness.
Utility: Treat periph. vasc. disease (Raynaud's Disease), hypertension (lowers BP w/o producing sig. tachycardia), pheochromocytoma (phenoxybenz. is best), benign prostatic hyperplasia (relieves obstruction symptoms).
Special Features: Prazosin-type α blockers are the only clinically useful anti-hypertensive α-receptor antagonists. Produce less tachycardia than do direct vasodilators. Readily combined w/other drugs.

Name: **Propranolol (Inderal)**
Class: Nonselective β-Blocking Agent
Mech.: Competitive blockade of β1 and β2 receptors. No α effect. Decreases conversion of T_4 to T_3 by inhibiting hepatic monodeiodinase.
Absorp.: Good oral (>90%). Low bioavail.: ~30%. Plasma levels vary 20x btwn. patients.
Dist.:93% bound to protein. Enters CNS. **Metab**.: Hepatic **Excret.**, **t_**: Short t_ (3.5-6 hr).
Toxicity/S.E.s: **CV**—hypotension, bradycardia. C/i for AV. May exacerbate angina (unopposed α receptor action). **Resp**—c/i in asthmatics, COPD, bronchitis, allergic rhinitis. **Metab**—caution w/diabetics (masks sign of hypoglycemia: tachycardia). **CNS**—weakness, fatigue, nightmares, depression. **GI**—n/v (uncommon). **Hypersens**—rash, hematologic disorders (rare).
Utility: Mild-mod HTN (↓ CO → ↓ BP; blocks renin release). Adjunct to direct vasodilators for severe HTN (prevents reflex tachycardia). Angina pectoris (prophylactic → ↑ exercise tolerance 2° to ↓ O_2 demand). Cardiac arrhythmias (esp. supravent. tachyarrhyths). Acute MI (prophylaxis & reduction of infarct size and failure). Modifies risk factors assoc. w/atherosclerosis. Increases O_2 delivery to ischemic cardiac tissue.
Special Features: Abrupt w/drawal may trigger MI. Not as effective against variant angina as channel blockers and nitrates. Long-term antiarrhythmic β-blocker Rx → ↓ mortality.

Name: **Nadolol (Corgard)**
Class: Nonselective β-Blocking Agent
Mech.: Competitive blockade of β1 and β2 receptors. No α effect.
Absorp.: Poor oral (>30%). Low bioavail: ~30%. Plasma levels vary 7x btwn. pts.
Dist.: 30% bound to protein.
Metab.: **Excretion**, **t_**: Renal. Long t_ (14-24 hr). Unchanged in urine.
Toxicity/S.E.s: **CV**—hypotension, bradycardia, c/i for AV block. May exacerbate angina (unopposed α receptor action). **Resp**—c/i in asthmatics, COPD, bronchitis, allergic rhinitis. **Metab**—caution w/diabetics (masks sign of hypoglycemia: tachycardia). **CNS**—weakness, fatigue, nightmares, depression. **GI**—n/v (uncommon). **Hypersens**—rash, hematologic disorders (rare).
Utility: Hypertension (↓ CO → ↓ BP; blocks renin release). Angina pectoris (prophylactic → ↑ exercise tolerance due to ↓ O_2 demand). Cardiac arrhythmias (esp. supravent. tachyarrhyths). Acute MI (prophylaxis and reduction of infarct size and failure). Pheochromocytoma (in comb. w/alpha blocker). Essential tremor. Migraine headache (prophylaxis). Performance anxiety

Name: **Timolol (Blocadren)**

Class: Nonselective β-Blocking Agent

Mech.: Competitive blockade of β1 and β2 receptors. No α effect.

Absorption: Good oral (>90%). High bioavailability ~75%. Plasma levels vary 7x btwn. patients. β-blocking plasma conc. 5-10 ng/mL (low). Eye drops.

Dist.: 10% bound to protein. **Excretion, t_**: Hepatic, renal. Short t_ (3-4 hr).

Toxicity/S.E.s: **CV**—hypotension, bradycardia, c/i for AV block. **Resp**—c/i in asthmatics, COPD, bronchitis, allergic rhinitis. **Metab**—caution w/diabetics (masks sign of hypoglycemia: tachycardia). **CNS**—weakness, fatigue, nightmares, depression. **GI**—n/v (uncommon). **Hypersens**—rash, hematologic disorders (rare).

Utility: Hypertension (↓ CO → ↓ BP; blocks renin release). Angina pectoris (prophylactic → ↑ exercise tolerance due to ↓ O_2 demand). Cardiac arrhythmias (esp. supravent. tachyarrhyths). Acute MI (prophylaxis and reduction of infarct size and failure). Pheochromocytoma (in comb. w/alpha blocker). Essential tremor. Migraine headache (prophylaxis). Performance anxiety. Eyedrops for open-angle glaucoma (↓ production of aqueous humor).

Special Features: Abrupt w/drawal may trigger MI. Cardioselectivity not great.

Name: **Pindolol (Visken)**

Class: Nonselective β-Blocking Agent (Partial Agonist)

Mech.: Partial agonists of β1 and β2 receptors. No α effect. Some intrinsic sympathomimetic activity.

Absorption:

Dist.:

Excretion, t_:

Toxicity/S.E.s: Mild chronic fatigue, low exercise tolerance, sedation, nightmares, depression, ↑ airway resistance (β2 effect).

Utility: Hypertension (esp. HTN w/moderate bradycardia).

Special Features: Much less effect on HR and CO compared to other β-blockers. Less disturbance of lipid and carbohydrate metab. compared to other β-blockers.

Name: **Metoprolol (Lopressor)**

Class: Cardioselective β1-Blocking Agent

Mech.: Selective blockade of β1 (heart, kidney) w/rel. sparing of β2. No α effect.

Absorption: Good oral (>95%). Bioavailability ~50%. Plasma levels vary 10x btwn. patients.

Dist.: 12% bound to protein. **Metab**.: Hepatic **Excretion**, **t_**: Short t_ (3-4 hr).

Toxicity/S.E.s: **CV**—hypotension, bradycardia, c/i for AV block. **Resp**—c/i in asthmatics, COPD, bronchitis, allergic rhinitis. **Metab**—caution w/diabetics (masks sign of hypoglycemia: tachycardia). **CNS**—weakness, fatigue, nightmares, depression. **GI**—n/v (uncommon). **Hypersens**—rash, hematologic disorders (rare).

Utility: Hypertension (↓ CO → ↓ BP; blocks renin release). Angina pectoris (prophylactic → ↑ exercise tolerance due to ↓ O_2 demand). Cardiac arrhythmias (esp. supravent. tachyarrhyths). Acute MI (prophylaxis and reduction of infarct size and failure). Pheochromocytoma (in comb. w/alpha blocker). Essential tremor. Migraine headache (prophylaxis). Performance anxiety.

Special Features: Abrupt w/drawal may trigger MI. Cardioselectivity not great.

Name: **Labetalol (Trandate)**

Class: Nonselective β and α1 Blocking Agent

Mech.: Competitive blockade of β1, β2, and α receptors.

Absorption:

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: **CV**—orthostatic hypotension, sexual dysfxn, bradycardia, c/i for AV block. **Resp**—c/i in asthmatics, COPD, bronchitis, allergic rhinitis. **Metab**—caution w/diabetics (masks sign of hypoglycemia: tachycardia). **CNS**—weakness, fatigue, nightmares, depression. **GI**—n/v (uncommon). **Hypersens**—rash, hematologic disorders (rare). Also α effects.

Utility: Hypertension (↓ CO → ↓ BP; blocks renin release). Angina pectoris (prophylactic → ↑ exercise tolerance due to ↓ O_2 demand). Cardiac arrhythmias (esp. supravent. tachyarrhyths). Acute MI (prophylaxis and reduction of infarct size and failure). Pheochromocytoma (in comb. w/alpha blocker). Essential tremor. Migraine headache (prophylaxis). Performance anxiety.

Features: Abrupt w/drawal may trigger MI. More ↓ side effects. Widely used

Name: **Captopril (Capoten)**

Class: ACE Inhibitor

Mech.: Inhib. production of angiotensin II → block of vasoconstriction and aldosterone stim. → ↓ TPR, ↓ Na^+/H_20 retention → ↓ BP. Also blocks inactivation of bradykinin → vasodilation. Diminishes normal ↑ in epinephrine and aldosterone seen in CHF.

Absorption:

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Postural hypotension, renal insufficiency, hyperkalemia, persistent dry cough, rash, angioneurotic edema. C/i in 2nd & 3rd trimesters of pregnancy. Prob. not a great idea for 1st trimester either.

Utility: Treat HTN, CHF, MI.

Special Features:

Name: **Enalapril (Vasotec)**

Class: ACE Inhibitor

Mech.: Inhib. production of angiotensin II → block of vasoconstriction and aldosterone stim. → ↓ TPR, ↓ Na^+/H_20 retention → ↓ BP. Also blocks inactivation of bradykinin → vasodilation. Diminishes normal ↑ in epinephrine and aldosterone seen in CHF.

Absorption:

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Postural hypotension, renal insufficiency, hyperkalemia, persistent dry cough, rash, angioneurotic edema. C/i in 2nd & 3rd trimesters of pregnancy. Prob. not a great idea for 1st trimester either.

Utility: Treat HTN, CHF, MI.

Special Features: Inactive prodrug. Converted to enalaprilat (acts like captopril).

Name: **Lisinopril (Zestril, Prinivol)**

Class: ACE Inhibitor

Mech.: Inhib. production of angiotensin II → block of vasoconstriction and aldosterone stim. → ↓ TPR, ↓ Na^+/H_20 retention → ↓ BP. Also blocks inactivation of bradykinin → vasodilation. Diminishes normal ↑ in epinephrine and aldosterone seen in CHF.

Absorption:

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Postural hypotension, renal insufficiency, hyperkalemia, persistent dry cough, rash, angioneurotic edema. C/i in 2nd & 3rd trimesters of pregnancy. Prob. not a great idea for 1st trimester either.

Utility: Treat HTN, CHF, MI.

Special Features: Lysine derivative of enalaprilat.

Name: **Losartan (Cozaar)**

Class: Angiotensin II Antagonist

Mech.: Competitive inhib. of angiotensin II → smooth muscle relaxation (vasodilation), ↓ Na^+ & H_20, ↓ plasma volume → ↓ BP.

Absorption: Oral.

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Hyperkalemia, fetal toxicity (c/i in 2nd & 3rd trimesters).

Utility: Treat hypertension.

Special Features: Angioneurotic edema and dry cough of ACE inhibitors not manifested.

Name: **Lovastatin (Mevacor)**
Class: Blood Lipid-Lowering Agent (HMG CoA Reductase Inhibitor)
Mech.: Inhib. of HMG CoA reductase → ↓ cholesterol pool, ↑ apoB/E receptor activity, ↑ LDL clearance. Large reduction of cholesterol and LDL. Little/no ↓ in TGs, little/no ↑ in HDL, no change in VLDL.
Absorption: **Dist**.: **Metab**.: **Excretion**, **t_**:
Toxicity/S.E.s: Common mild GI disturbances. Reversible elevations of liver enzymes in 4-7% (if AST or ALT > 3x normal, discontinue). Possible muscle damage—much more likely w/concurrent cyclosporine, gemfibrozil, niacin, or erythromycin; or if pt has hepatic disease, a severe infxn, or renal insufficiency. Continued use w/myopathy may → severe myositis, rhabdomyolysis, or acute renal failure. Can shorten sleep period by up to 18%. C/i in kids & preg. E.
Utility: Treat pts. w/type IIA/IIB hyperlipidemia refractory to diet and other drugs. May not be useful for pts. w/homozygous familial hypercholesterolemia.
Special Features: Most effective drug class for lowering LDL. Probably better tolerated than other cholesterol lowering drugs. Synergistic effects w/resins and niacin. If taken once/day, take at night (peak cholesterol synth. occurs between 12:00-3:00 a.m.).

Name: **Pravastatin (Pravochol)**
Class: Blood Lipid-Lowering Agent (HMG CoA Reductase Inhibitor)
Mech.: Inhib. of HMG CoA reductase → ↓ cholesterol pool, ↑ apoB/E receptor activity, ↑ LDL clearance. Large reduction of cholesterol and LDL. Little/no ↓ in TGs, little/no ↑ in HDL, no change in VLDL.
Absorption: **Dist**.: **Metab**.: **Excretion**, **t_**:
Toxicity/S.E.s: Common mild GI disturbances. Reversible elevations of liver enzymes in 4-7% (if AST or ALT > 3x normal, discontinue). Possible muscle damage—much more likely w/concurrent cyclosporine, gemfibrozil, niacin, or erythromycin; or if pt has hepatic disease, a severe infxn, or renal insufficiency. Continued use w/myopathy may → severe myositis, rhabdomyolysis, or acute renal failure. C/i in kids & preg. E.
Utility: Treat pts. w/type IIA/IIB hyperlipidemia refractory to diet and other drugs. May not be useful for pts. w/homozygous familial hypercholesterolemia.
Special Features: Most effective drug class for lowering LDL. Probably better tolerated than other cholesterol lowering drugs. Synergistic effects w/resins and niacin. If taken once/day, take at night (peak cholesterol synth. occurs between 12:00-3:00 a.m.).

Name: **Simvastatin (Zocor)**
Class: Blood Lipid-Lowering Agent (HMG CoA Reductase Inhibitor)
Mech.: Inhib. of HMG CoA reductase → ↓ cholesterol pool, ↑ apoB/E receptor activity, ↑ LDL clearance. Large reduction of cholesterol and LDL. Little/no ↓ in TGs, little/no ↑ in HDL, no change in VLDL.
Absorption: **Dist**.: **Metab**.: **Excretion**, **t_**:
Toxicity/S.E.s: Common mild GI disturbances. Reversible elevations of liver enzymes in 4-7% (if AST or ALT > 3x normal, discontinue). Possible muscle damage—much more likely w/concurrent cyclosporine, gemfibrozil, niacin, or erythromycin; or if pt has hepatic disease, a severe infxn, or renal insufficiency. Continued use w/myopathy may → severe myositis, rhabdomyolysis, or acute renal failure. Can shorten sleep period by up to 18%. C/i in kids & preg. E.
Utility: Treat hyperlipidemia IIA/IIB refractory to diet and other drugs. May not be useful for pts. w/homozygous familial hypercholesterolemia.
Special Features: Most effective drug class for lowering LDL. Probably better tolerated than other cholesterol lowering drugs. Synergistic effects w/resins and niacin. If taken once/day, take at night (peak cholesterol synth. occurs between 12:00-3:00 a.m.).

Name: **Cholestyramine (Cholybar)**
Class: Blood Lipid-Lowering Agent (Resin)
Mech.: Binds bile acids in intestine → ↑ defecation of bile acids, ↑ conversion of cholesterol to bile acids, ↓ pool of hepatic cholesterol, ↑ activity of apoB/E receptor, ↑ LDL clearance, ↓ plasma cholesterol. Moderate ↓ in cholesterol & LDL. Mild ↑ in HDL. Zero-moderate ↑ in TG & VLDL.
Absorption: Oral. No absorption.
Dist.: **Metab**.: **Excretion**, **t_**:
Toxicity/S.E.s: Up to 50% refuse to continue Rx. Flatulence, constipation, gas, n/v, steatorrhea. Supersaturation of cholesterol in bile → gallstones, need for cholecystectomy. ↓ bile → ↓ absorption of lipid-soluble drugs/vitamins. Binds acidic drugs. Weak stim. of VLDL synth. Do not use in pts. w/hyperTG w/o concurrent TG-lowering agent.
Utility: Treat hyperlipidemia IIA/IIB. Use alone or w/niacin, probucol, or HMG CoA reductase inhib.
Special Features: GI S.E.s reduced if taken immediately prior to meals. _ dose + Metamucil™ → ↓ constipation & bloating, but sim. efficacy.

Name: **Colestipol (Colestid)**
Class: Blood Lipid-Lowering Agent (Resin)
Mech.: Binds bile acids in intestine → ↑ defecation of bile acids, ↑ conversion of cholesterol to bile acids, ↓ pool of hepatic cholesterol, ↑ activity of apoB/E receptor, ↑ LDL clearance, ↓ plasma cholesterol. Moderate ↓ in cholesterol & LDL. Mild ↑ in HDL. Zero-moderate ↑ in TG & VLDL.
Absorption: Oral. No absorption.
Dist.: **Metab**.: **Excretion**, **t_**:
Toxicity/S.E.s: Flatulence, constipation, gas, n/v, steatorrhea. Supersaturation of cholesterol in bile → gallstones, need for cholecystectomy. ↓ bile → ↓ absorption of lipid-soluble drugs/vitamins. Binds acidic drugs. Weak stim. of VLDL synth. Do not use in pts. w/hyperTG w/o concurrent TG-lowering agent.
Utility: Treat hyperlipidemia IIA/IIB. Use alone or w/niacin, probucol, or HMG CoA reductase inhib.
Special Features: GI S.E.s reduced if taken immediately prior to meals. _ dose + Metamucil™ → ↓ constipation & bloating, but sim. efficacy.

Name: **Nicotinic Acid (Niacin)**
Class: Blood Lipid-Lowering Agent
Mech.: Reduces synth. rate of VLDL. Inhib. lipolysis of TG in adipocytes. Large ↓ in TG. Moderate ↓ in cholesterol & VLDL. Mild ↓ in LDL. Zero-moderate ↑ in HDL.
Absorption:
Dist.: **Metab**.:
Excretion, **t_**:
Toxicity/S.E.s: Cutaneous flushing (92%), itching (49%), rashes (20%). Reduce w/aspirin pretreatment, admin. after meals, small init. dose gradually increased in size. Pruritis, dry skin, ↑ pigmentation, hepatotoxicity, n/v, dyspepsia, peptic ulceration, ↑ urinary frequency, dysuria, gout. High doses → hepatic/pancreatic dysfxn. Coadmin. anti-hypertensives → dizziness, syncope. Sustained-release preparations more commonly assoc. w/hepatotoxicity, dry eyes, ↑ pigmentation, hyperglycemia.
Utility: Prob. DOC for hyperlipidemias IV and V. Very useful for III. Can be used for II. Synergy w/resins.
Special Features:

Name: **Gemfibrozil (Lopid)**
Class: Blood Lipid-Lowering Agent (Fibric Acid Derivative)
Mech.: ↑ catabolism of VLDL, in part 2° to ↑ activity of lipoprotein lipase in adipose tissue. Moderate ↓ in TG & VLDL. Mild ↓ in LDL and cholesterol. Moderate ↑ in HDL.
Absorption:
Dist.:
Metab.: Glucuronide conjugation.
Excretion, **t_**: Renal excretion.
Toxicity/S.E.s: Generally well tolerated. GI distress, rash, musculoskeletal pain, blurred vision, anemia, leukopenia, gallstones. Adjust dose in pts. w/renal insufficiency.
Utility: DOC for hyperlipidemia III. Better tolerated than niacin for type IV, although less effective. Decreases frequency of CHD-related incidents.
Special Features:

Name: **Clofibrate (Atromid-S)**
Class: Blood Lipid-Lowering Agent (Fibric Acid Derivative)
Mech.: ↑ catabolism of VLDL, in part 2° to ↑ activity of lipoprotein lipase in adipose tissue. Moderate ↓ in TG & VLDL. Zero-mild ↓ in cholesterol. Zero-mild ↑ in HDL. Mild ↑ or ↓ in LDL.
Absorption:
Dist.:
Metab.: Glucuronide conjugation.
Excretion, **t_**: Renal excretion.
Toxicity/S.E.s: Generally well tolerated. Gallstones, nausea, diarrhea, abdominal discomfort. Displaces weakly acidic drugs (T3, T4, warfarin, phenytoin) from plasma proteins. Binds cholestyramine.
Utility: Treat severe hyperlipidemia IV refractory to gemfibrozil or niacin.
Special Features: Does not appear to decrease frequency of CHD-related incidents.

Name: **Probucol (Lorelco)**
Class: Blood Lipid-Lowering Agent (Fibric Acid Derivative)
Mech.: Stim. LDL clearance by non-receptor pathways. May reduce risk of atherogenesis w/o altering serum cholesterol levels. May block oxidation of LDL. Moderate ↓ in cholesterol, LDL, & HDL. No effect on TG or VLDL.
Absorption:
Dist.: Stored in fat.
Metab.:
Excretion, **t_**:
Toxicity/S.E.s: Generally very well tolerated (2-6% incidence). Flatulence, n/v/d, abd. pain, headache, rash. C/i in monkeys (cardiac arrhythmias). Stored in fat. ∴ E advised to wait 6 mo. after last dose before becoming pregnant.
Utility: Treat hyperlipidemia IIA/IIB, but prob. not drug o' first choice. May be useful for homozygous familial hypercholesterolemia (IIA). May cause regression of xanthomas.
Special Features: ↓ in LDL takes 1-3 mo., but some pts. don't respond. Does

Name: **Nitroglycerin (Nitro-Bid)**
Class: Antianginal Agent (Organonitrate)
Mech.: Converted to NO → activation of cytosolic guanylate cyclase → ↑ cGMP → activation of cGMP-dependent protein kinase → smooth muscle relaxation → vasodilation. Greater effect in veins & large arteries than in resistance vessels → ↓↓ preload, ↓ afterload → ↓ work → ↓ O_2 demand. Inhib. of platelet fxn.
Absorption: Sublingual preferred. IV. Oral → ↑ 1st pass metab, low bioavail. Buccal/transdermal → slow absorption.
Dist.:
Metab.: Hepatic (glutathione-organic nitrate reductase), extra-hepatic. Plasma clearance >> C.O.
Excretion, **t_**: Renal. 3 min. Short duration of action (20-30 min.).
Toxicity/S.E.s: Orthostatic hypotension, tachycardia, severe throbbing headache, dizziness, flushing, syncope. C/i w/elevated ICP.
Utility: Treat angina. Subling. not suitable for maintenance therapy. IV for severe recurrent unstable angina. Oral/buccal/transdermal for prophylaxis, but may → tolerance.

Name: **Isosorbide Dinitrate (Isordil)**
Class: Antianginal Agent (Organonitrate)
Mech.: Converted to NO → activation of cytosolic guanylate cyclase → ↑ cGMP → activation of cGMP-dependent protein kinase → smooth muscle relaxation → vasodilation. Greater effect in veins & large arteries than in resistance vessels → ↓↓ preload, ↓ afterload → ↓ work → ↓ O_2 demand. Inhib. of platelet fxn.
Absorption: Sublingual preferred → complete absorption. Oral → ↑ 1st pass metab, low bioavail. Buccal/transdermal → slow absorption.
Dist.:
Metab.: 80% converted to active metabolite 5-ISMN before entering systemic circulation. Hepatic inactivation via glutathione-organic nitrate reductase.
Excretion, **t_**: Renal. 10 min. Short duration of action (20-30 min.).
Toxicity/S.E.s: Orthostatic hypotension, tachycardia, severe throbbing headache, dizziness, flushing, syncope. C/i w/elevated ICP.
Utility: Treat angina. Subling. not suitable for maintenance therapy. Oral/buccal/transdermal for prophylaxis, but may → tolerance

Name: **Amyl Nitrate**
Class: Antianginal Agent (Organonitrate)
Mech.: Converted to NO → activation of cytosolic guanylate cyclase → ↑ cGMP → activation of cGMP-dependent protein kinase → smooth muscle relaxation → vasodilation. Greater effect in veins & large arteries than in resistance vessels → ↓↓ preload, ↓ afterload → ↓ work → ↓ O_2 demand. Inhib. of platelet fxn.
Absorption: Inhalation → rapid onset.
Dist.:
Metab.: Hepatic inactivation via glutathione-organic nitrate reductase.
Excretion, **t_**: Renal. Short duration of action (3-5 min.).
Toxicity/S.E.s: Orthostatic hypotension, tachycardia, severe throbbing headache, dizziness, flushing, syncope. C/i w/elevated ICP.
Utility: Treat angina. Not suitable for maintenance therapy.
Special Features:

Name: **Acetylsalicylic Acid (Aspirin)**
Class: Antithrombotic Agent (Antiplatelet Agent)
Mech.: Irrevers. acetylation of cyclooxygenase → ↓ platelet thromboxane synth.
Absorption: Oral → rapid absorption.
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s: GI hemorrhage, hemorrhagic stroke. Use w/caution in pts on long-term oral anticoagulants. Hypersensitivity rxns—generalized urticaria, bronchial asthma, laryngeal edema, bronchoconstriction, hypotension, shock—may occur in 20-25% of pts w/asthma, nasal polyps, or chronic urticaria.
Utility: Acute MI, stable/unstable angina, 2° prevention in MI survivors. TIA. 2° prevention in nondisabling ischemic stroke. Prevention of saphenous vein bypass graft occlusion. Post-coronary angioplasty. 1° MI prophylaxis (325 mg/d) adjunctive to risk factor management. Headache.
Special Features: Low dose Rx optimal—75-325 mg/d. Antithrombotic use is

Name: **Dipyridamole (Persantine)**
Class: Antithrombotic Agent (Antiplatelet Agent)
Mech.: Inhib. PDE in platelets → ↑ cAMP → inhib. of platelet activation.
Absorption:
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s:
Utility: Prevention of systemic embolism in pts. w/prosthetic heart valves. Admin. in combination w/warfarin.
Special Features: When used alone, ineffective for Rx of cerebral or CV thrombotic events. Not proven to be of additional benefit when admin. w/aspirin. Antithrombotic use is primarily for arterial thromboses.

Name: **Ticlopidine (Ticlid)**
Class: Antithrombotic Agent (Antiplatelet Agent)
Mech.: Unknown. Through some effect on platelet membranes, blocks ADP-induced aggregation. Interacts w/membrane glycoprotein IIb/IIIa.
Absorption:
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s: Diarrhea, GI cramping, rash, ↑ LDL & VLDL, leukopenia, agranulocytosis, pancytopenia.
Utility: Treat thromboses in patients unable to take aspirin. May be more effective than aspirin in 2° prevention of stroke in pts w/previous TIA.
Special Features: Several days required for effects to develop. Effects persist for several days after cessation of treatment. As effective in E as in G. Antithrombotic use is primarily for arterial thromboses.

Name: **Abciximab (Reo-Pro)**
Class: Antithrombotic Agent (Antiplatelet Agent)
Mech.: Monoclonal antibody to GPIIb/IIIa. Interferes w/platelet-adhesive protein interactions.
Absorption:
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s:
Utility: Treat high risk angioplasty pts.
Special Features:

Name: **Heparin**
Class: Antithrombotic Agent (Anticoagulant)
Mech.: Catalyzes complex formation btwn. plasma antithrombin III and various serine proteases of the coagulation pathway, including thrombin and activated factors IX, X, XI, & XII. Effect primarily due to thrombin inhib. Prevents further clot formation and thrombus propagation. Does not alter organized clots.
Absorp.: IV, continuous IV→immed. onset. SC→1-2 hr onset w/variable bioavail.
Dist.: **Metab**.: Hepatic.
Excretion, **t_**: Rel. short t_. ↓ t_ w/pulm. embolism. ↑ t_ w/hepatic cirrhosis or end-stage renal disease.
Toxicity/S.E.s: 1° = bleeding. Thrombocytopenia (bovine > porcine)—mild, severe (delayed onset; can occur w/heparin resistance → thromboembolism & DIC). Long-term use → osteoporosis. Non-teratogenic, but discontinue prior to delivery.
Utility: Symptomatic calf vein thrombi or thrombi extending above the popliteal vein, pulm. embolus, atrial fibrillation, valvular heart disease, CAD, adjunct to post-MI thrombolytic therapy. Use in general surgery for E on oral contraceptives.
Special Features: Primarily used for venous thromboses. Most widely used antithromb. agent. Monitor PTT to achieve desired dose—1.5-2.5x normal PTT is therapeutic. ↑ recurrence rate if PTT < 1.5 x normal or if therapeutic levels aren't achieved w/in 24 hr. Few drug interactions.

Name: Enoxaparin (Lovenox)
Class: Antithrombotic Agent (Anticoagulant) (Low Molecular Weight Heparin)
Mech.: Catalyzes complex formation btwn. plasma antithrombin III and various serine proteases of the coagulation pathway, including thrombin and activated factors IX, X, XI, & XII. Effect primarily due to thrombin inhib. Less effect on thrombin than heparin. Prevents further clot formation and thrombus propagation. Does not alter organized clots.
Absorp.: SC → better bioavail. than heparin. Daily SC injxn has sim. efficacy to 2-3 injxns/d of heparin.
Dist.: **Metab**.: Hepatic.
Excretion, **t_**: Longer t_ than heparin. ↓ t_ w/pulm. embolism. ↑ t_ w/hepatic cirrhosis or end-stage renal disease.
Toxicity/S.E.s: 1° = bleeding. Thrombocytopenia (bovine > porcine)—mild, severe (delayed onset; can occur w/heparin resistance → thromboembolism & DIC). Long-term use → osteoporosis. Non-teratogenic, but discontinue prior to delivery.
Utility: 1° prevention of DVT after hip replacement surgery.
Special Features: Primarily used for venous thromboses. Monitor PTT to achieve desired dose—1.5-2.5x normal PTT is therapeutic. ↑ recurrence rate if PTT < 1.5 x normal or if therapeutic levels aren't achieved w/in 24 hr. Few drug interactions. Lower rate of bleeding than w/heparin.

Name: **Protamine Sulfate**
Class: Anticoagulant Antagonist
Mech.: Binds tightly to heparin and rapidly reverses its effects. Also interacts w/platelets, fibrinogen, and other plasma proteins → anticoagulant effect.
Absorption: IV infusion—slow rate.
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s:
Utility: Treat life-threatening hemorrhage 2° to heparin use.
Special Features: Use minimal effective dose.

Name: **Antithrombin III (ATnativ)**
Class: Antithrombotic Agent (Coagulation Inhibitor)
Mech.: Prepared from pooled human plasma. Inhibits coagulation factors (thrombin, IXa, Xa, XIIa).
Absorption:
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s:
Utility: Treat pts w/hereditary AT-III deficiency and neonates w/a family history of AT-III deficiency. Prophylaxis for deficient pts who are undergoing surgery or delivery at term.
Special Features:

Name: **Warfarin (Coumadin)**

Class: Antithrombotic Agent (Oral Anticoagulant)

Mech.: Vitamin K antagonist → ↓ γ-carboxylation of thrombin, factors, VII, IX, & X, and proteins C & S → inhib. of synth. of active coagulation factors. Does not alter organized clots.

Absorption: Oral.

Dist.: Almost completely bound (99%) to plasma proteins (mainly albumin).

Metab.: Microsomal enzymes in liver and kidneys.

Excretion, **t_**: Urine and stool.

Toxicity/S.E.s: Hemorrhage, hypersensitivity rxns., fetal toxicity. "Purple Toe" synd. (necrosis) assoc. w/protein C deficiency. During pregnancy, can cause birth defects and abortion. Many drug interactions.

Utility: Prevention of recurrent thrombotic events following acute Rx w/heparin. Valvular heart disease, prosthetic cardiac valves, AMI, atrial fibrillation.

Special Features: Max. effects require 2-7 days. Init. response may be procoagulant due to inhib. of protein C. Should have 6 day overlap w/heparin. Monitor PT.

Name: **Vitamin K_1 (Phytonadione)**

Class: Anticoagulant Antagonist

Mech.: Vit. K is necessary for γ-carboxylation of thrombin, factors VII, IX, & X, and proteins C & S. The γ-carboxylated residues are required for binding Ca^{2+}, which is essential for their activity.

Absorption: Oral or SC preferred. IV admin. may cause shock or anaphylaxis.

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: IV admin. may cause shock or anaphylaxis.

Utility: Reverse excessive bleeding due to warfarin—indicated for severe or continued bleeding if warfarin dosage adjustment is unsuccessful.

Special Features: Significant improvement in hemostasis may require as long as 24 hr. If immediate hemostasis is necessary, fresh frozen plasma should be infused.

Name: **Streptokinase (Streptase)**

Class: Antithrombotic Agent (Thrombolytic Agent)

Mech.: Derived from β-hemolytic streptococci. Forms a complex w/plasminogen, exposing its active site. Poor thrombus specificity—catalyzes conversion of circulating and fibrin-bound plasminogen—results in a systemic lytic state.

Absorption: IV. Admin. w/large loading dose to overcome plasma antibodies.

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Hemorrhage. Allergic rxns—pruritis, flushing, urticaria. Higher incidence of allergic rxns. w/readministration. Pronounced hypotension (usu. transient). Delayed fever and arthralgia.

Utility: Treat acute MI (w/in 6 hr. of symptoms), massive PE, acute proximal vein thromboses, occlusion of dialysis access sites and indwelling catheters, occlusion of prosthetic heart valves.

Special Features: Best results in pts. that receive therapy < 1 hr. after onset of symptoms and that achieve successful reperfusion. Pts. w/antibodies can develop therapeutic resistance.

Name: **Anistreplase/APSAC (Eminase)**

Class: Antithrombotic Agent (Thrombolytic Agent)

Mech.: Acylated plasminogen-streptokinase activator complex. Plasminogen active site is protected from inactivation. Poor thrombus specificity—catalyzes conversion of circulating & fibrin-bound plasminogen—results in a systemic lytic state.

Absorption: IV. Admin. w/large loading dose to overcome plasma antibodies.

Dist.: **Metab**.:

Excretion, **t_**: Longer t_ than streptokinase → sustained fibrinolytic effect.

Toxicity/S.E.s: Hemorrhage. Allergic rxns—pruritis, flushing, urticaria. Higher incidence of allergic rxns. w/readministration. Pronounced hypotension (usu. transient). Delayed fever and arthralgia.

Utility: Treat acute MI (w/in 6 hr. of symptoms), massive PE, acute proximal vein thromboses, occlusion of dialysis access sites and indwelling catheters, occlusion of prosthetic heart valves.

Special Features: Best results in pts. that receive therapy < 1 hr. after onset of symptoms and that achieve successful reperfusion. Pts. w/antibodies can develop therapeutic resistance.

Name: **Tissue Plasminogen Activator, tPA (Activase)**

Class: Antithrombotic Agent (Thrombolytic Agent)

Mech.: Recombinant product identical to endothelial tPA. Preferentially activates plasminogen that is bound to fibrin → greater clot specificity and potentially less systemic fibrinolysis than w/streptokinase.

Absorption: IV. Prolonged admin. necessary (generally given over 3 hr.). "Accelerated" regimen admin. over 90 min. (2/3 given w/in 1st 30 min.)

Dist.:

Metab.:

Excretion, **t_**: Short t_.

Toxicity/S.E.s: Hemorrhage.

Utility: Treat acute MI (w/in 6 hr. of symptoms), massive PE, acute proximal vein thromboses, occlusion of dialysis access sites and indwelling catheters, occlusion of prosthetic heart valves.

Special Features: Best results in pts. that receive therapy < 1 hr. after onset of symptoms and that achieve successful reperfusion. Expensive—several times more costly than streptokinase.

Name: **Urokinase (Abbokinase)**

Class: Antithrombotic Agent (Thrombolytic Agent)

Mech.: Urinary-type single chain plasminogen activator. Isolated from cultured human kidney cells.

Absorption:

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Hemorrhage.

Utility: Treat acute MI (w/in 6 hr. of symptoms), massive PE, acute proximal vein thromboses, occlusion of dialysis access sites and indwelling catheters, occlusion of prosthetic heart valves.

Special Features: Best results in pts. that receive therapy < 1 hr. after onset of symptoms and that achieve successful reperfusion. Generally non-antigenic. Does not cause allergic rxns.

Name: **Aminocaproic Acid (Amicar)**

Class: Thrombolytic Agent Antagonist

Mech.: Lysine analog. Binds to lysine sites on plasminogen and plasmin → blocks binding of plasmin to fibrin.

Absorption: IV (slow injxn).

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Thrombi that form during treatment are not lysed. Thrombosis may become a problem.

Utility: Treat bleeding from fibrinolytic therapy.

Special Features:

Name: **Tranexamic Acid (Amstat)**

Class: Thrombolytic Agent Antagonist

Mech.: Competitive inhib. of plasminogen activation.

Absorption: Oral.

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s:

Utility: Used for hemostasis in pts. undergoing oral surgery who are being treated w/oral anticoagulants.

Special Features:

Name: **Quinidine (Quinidex)**
Class: Antidysrhythmic Agent (Class IA)
Mech.: Binds to open and inactivated Na^+ channels and prevents Na^+ influx → slowing of the rapid upstroke during phase 0. Also decreases the slope of phase 4 spontaneous depolarization. Prolongs repolarization. Inhibits arrhythmias due to ↑ normal automaticity. Intermed. speed of dissociation from Na^+ channels.
Absorption: Oral → rapid, nearly complete absorption.
Dist.: **Metab**.: **Excretion**, **t_**:
Toxicity/S.E.s: Proarrhythmic effects, negative inotropy, infranodal conduction block, DILQT. Cinchonism—n/v/d, tinnitus, headache, vertigo, auditory/visual disturbances. Hypotension (α-blocking activity). ↑ digoxin levels. Hypersensitivity rxns—rash, fever, angioneurotic edema, hepatitis. Reversible thrombocytopenia.
Utility: Treat atrial, AV junctional, & ventricular tachyarrhythmias. Maintain sinus rhythm after direct current cardioversion of atrial flutter or fibrillation. Prevent frequent ventricular tachycardia.
Special Features:

Name: **Procainamide (Pronestyl)**
Class: Antidysrhythmic Agent (Class IA)
Mech.: Binds to open and inactivated Na^+ channels and prevents Na^+ influx → slowing of the rapid upstroke during phase 0. Also decreases the slope of phase 4 spontaneous depolarization. Prolongs repolarization. Inhibits arrhythmias due to ↑ normal automaticity. Intermed. speed of dissociation from Na^+ channels.
Absorption: Oral. IV rarely used, as hypotension occurs w/too rapid infusion.
Dist.: **Excretion**, **t_**: Urine. 2-3 hr.
Metab.: Hepatic → active metabolite NAPA (↑ duration of action potential).
Toxicity/S.E.s: Proarrhythmic effects, negative inotropy, infranodal conduction block, DILQT. Hypotension (ganglion-blocking activity). Chronic use → reversible SLE-like synd. Depression, hallucination, psychosis, giddiness. Less GI intolerance than quinidine. Hypersensitivity rxns—fever, agranulocytosis, Raynaud's synd., myalgias, rashes, digital vasculitis.
Utility: Treat atrial, AV junctional, & ventricular tachyarrhythmias. Maintain sinus rhythm after direct current cardioversion of atrial flutter or fibrillation. Prevent frequent ventricular tachycardia.
Special Features:

Name: **Disopyramide (Norpace)**
Class: Antidysrhythmic Agent (Class IA)
Mech.: Binds to open and inactivated Na^+ channels and prevents Na^+ influx → slowing of the rapid upstroke during phase 0. Also decreases the slope of phase 4 spontaneous depolarization. Prolongs repolarization. Inhibits arrhythmias due to ↑ normal automaticity. Intermed. speed of dissociation from Na^+ channels. Peripheral vasoconstriction. The stereoisomers have opposite effects on repolarization.
Absorption:
Dist.:
Metab.: Hepatic.
Excretion, **t_**: Urine.
Toxicity/S.E.s: Proarrhythmic effects, negative inotropy, infranodal conduction block, DILQT. Anticholinergic effects—dry mouth, urinary retention, blurred vision, constipation. N/v/d, abd. pain. Less GI intolerance than quinidine.
Utility: Alt. to procainamide or quinidine for treatment of ventricular arrhythmia.
Special Features:

Name: **Lidocaine (Zylocaine)**
Class: Antidysrhythmic Agent (Class IB)
Mech.: Shortens phase 3 repolarization. Little change in action potential duration. Inhibits arrhythmias caused by abnormal automaticity. Rapid speed of dissociation from Na^+ channels.
Absorption: IV
Dist.:
Metab.: Hepatic.
Excretion, **t_**:
Toxicity/S.E.s: Fairly wide therapeutic index. Proarrhythmic effects, negative inotropy, infranodal conduction block. Drowsiness, slurred speech, paresthesia, agitation, confusion, convulsions, resp. depression, tinnitus, muscle twitching, psychosis, seizures. ↑ CNS toxicity if used w/tocainide or mexiletine (e.g., seizures).
Utility: DOC for sustained ventricular tachycardia. Treat ventricular arrhythmias arising during myocardial ischemia or digitalis-induced VA.
Special Features: Class IB drugs have the lowest potency as Na^+ channel blockers.

Name: **Tocainide (Tonocard)**

Class: Antidysrhythmic Agent (Class IB)

Mech.: Shortens phase 3 repolarization. Little change in action potential duration. Inhibits arrhythmias caused by abnormal automaticity. Rapid speed of dissociation from Na^+ channels.

Absorption: Oral

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Proarrhythmic effects, negative inotropy, infranodal conduction block. N/v, dizziness, disorientation, tremor. Hematologic effects (agranulocytosis, bone marrow suppression, thrombocytopenia) can be fatal.

Utility: Treat ventricular tachyarrhythmias (only as a last resort).

Special Features: Concurrent use w/quinidine may be effective at lower doses than either alone → ↓ adverse effects of each.

Name: **Mexiletine (Mexitil)**

Class: Antidysrhythmic Agent (Class IB)

Mech.: Shortens phase 3 repolarization. Decreases action potential duration. Inhibits arrhythmias caused by abnormal automaticity. Rapid speed of dissociation from Na^+ channels.

Absorption: Oral

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Proarrhythmic effects, negative inotropy, infranodal conduction block. N/v, dizziness, disorientation, tremor.

Utility: Chronic treatment of ventricular arrhythmias assoc. w/previous myocardial infarction.

Special Features: Concurrent use w/quinidine may be effective at lower doses than either alone → ↓ adverse effects of each.

Name: **Flecainide (Tambocor)**

Class: Antidysrhythmic Agent (Class IC)

Mech.: Slow dissociation from Na^+ channels → marked suppression of phase 0 upstroke → marked slowing of conduction. ↑ threshold potential → ↓ automaticity.

Absorption: Oral.

Dist.:

Metab.: Minimal.

Excretion, **t_**: 16-20 hr.

Toxicity/S.E.s: Long-term Rx → ↑ mortality. Dizziness, blurred vision, tremor, agitation, headache, nausea. Aggravation of preexisting arrhythmias, negative inotropy, induction of life-threatening ventricular tachycardia (CAST proarrhythmia), aggravation of CHF, infranodal conduction block.

Utility: Treat refractory ventricular arrhythmias. Suppress premature ventricular contraction. Treat AV nodal reentry, WPW-related arrhythmia.

Special Features: Class IC drugs have the highest potency as Na^+ channel blockers

Name: **Sotalol (Betapace)**

Class: Antidysrhythmic Agent (Class III)

Mech.: Blocks rapid outward K^+ current (delayed rectifier) → prolonged repolarization and action potential → ↑ effective refractory period. Little effect on rate of depolarization. L-isomer is a potent β-blocker.

Absorption:

Dist.:

Metab.:

Excretion, **t_**:

Toxicity/S.E.s: Rel. low rate of adverse effects. DILQT synd., sinus bradycardia.

Utility: Long-term therapy to decrease the rate of sudden death following acute MI. Modest ability to suppress ectopic beats and ↓ O_2 demand. Strong antifibrillary effect. Prevents arrhythmia and decreases mortality in pts. w/sustained ventricular tachycardia.

Special Features:

Name: **Amiodarone (Cordarone)**
Class: Antidysrhythmic Agent (Class III)
Mech.: Structurally related to thyroxine. 1° effect is prolongation of action potential and refractory period. Antiarrhythmic activity and antianginal activity.
Absorption: Oral.
Dist.:
Metab.:
Excretion, **t_**: 25-110 days.
Toxicity/S.E.s: Common (>75% of pts). Interstitial pulmonary fibrosis, GI intolerance, tremor, ataxia, dizziness, depression, nightmares, hallucinations, hyper/hypothyroidism, liver toxicity, photosensitivity, periph. neuropathy, muscle weakness, blue skin (I_2), possibly irreversible hepatic dysfxn. DILQT synd., sinus bradycardia. Asympt. corneal deposits in all pts. Substantial ↑ in LDL. Phospholipidosis. Enhances effect of warfarin. ↑ conc. of digoxin, quinidine, procainamide, et. al.
Utility: Treat severe refractory supraventricular and ventricular tachyarrhythmia.
Special Features: Usefulness limited by toxicity. Full effects may take up to 6

Name: **Adenosine (Adrenocard)**
Class: Antidysrhythmic Agent
Mech.: High doses → ↓ conduction velocity, ↑ refractory period, ↓ automaticity in the AV node.
Absorption: IV
Dist.:
Metab.:
Excretion, **t_**: Extremely short duration of action (15 sec.).
Toxicity/S.E.s: Low toxicity. Flushing, chest pain, hypotension, transient dyspnea, non-myocardial chest discomfort, metallic taste.
Utility: DOC for acute supraventricular tachycardia. Treat AV nodal reentry, orthodromic tachycardia.
Special Features:

Name: **Magnesium**
Class: Antidysrhythmic Agent
Mech.:
Absorption:
Dist.:
Metab.:
Excretion, **t_**:
Toxicity/S.E.s:
Utility: DOC for torsades de pointes (DILQT synd). Treat pts w/digitalis-induced arrhythmia if hypomagnesemia is present.
Special Features:

Hope. Pandora brought the box containing the evils and opened it. It was the gift of the gods to mankind, outwardly a fair, seductive gift and named the 'box of good fortune'. Then all the evils, living winged creatures, flew out; since then they have been hovering about doing harm to men by day and night. A single evil had not yet slipped out of the box; then, by the will of Zeus, Pandora shut the lid, and thus it remained within. Now man has the box of good fortune forever in the house and is amazed at the treasure he possesses in it; it stands at his service, he reaches for it when he desires to do so; for he does not know that the box Pandora brought was the box of evil and regards the evil that has remained behind as the greatest piece of good fortune - it is hope. For what Zeus wanted was that man, though never so tormented by the other evils, should nonetheless not throw life away but continue to let himself be tormented. To that end he gives men hope: it is in truth the worst of all evils, because it protracts the torment of men.

- Nietzsche