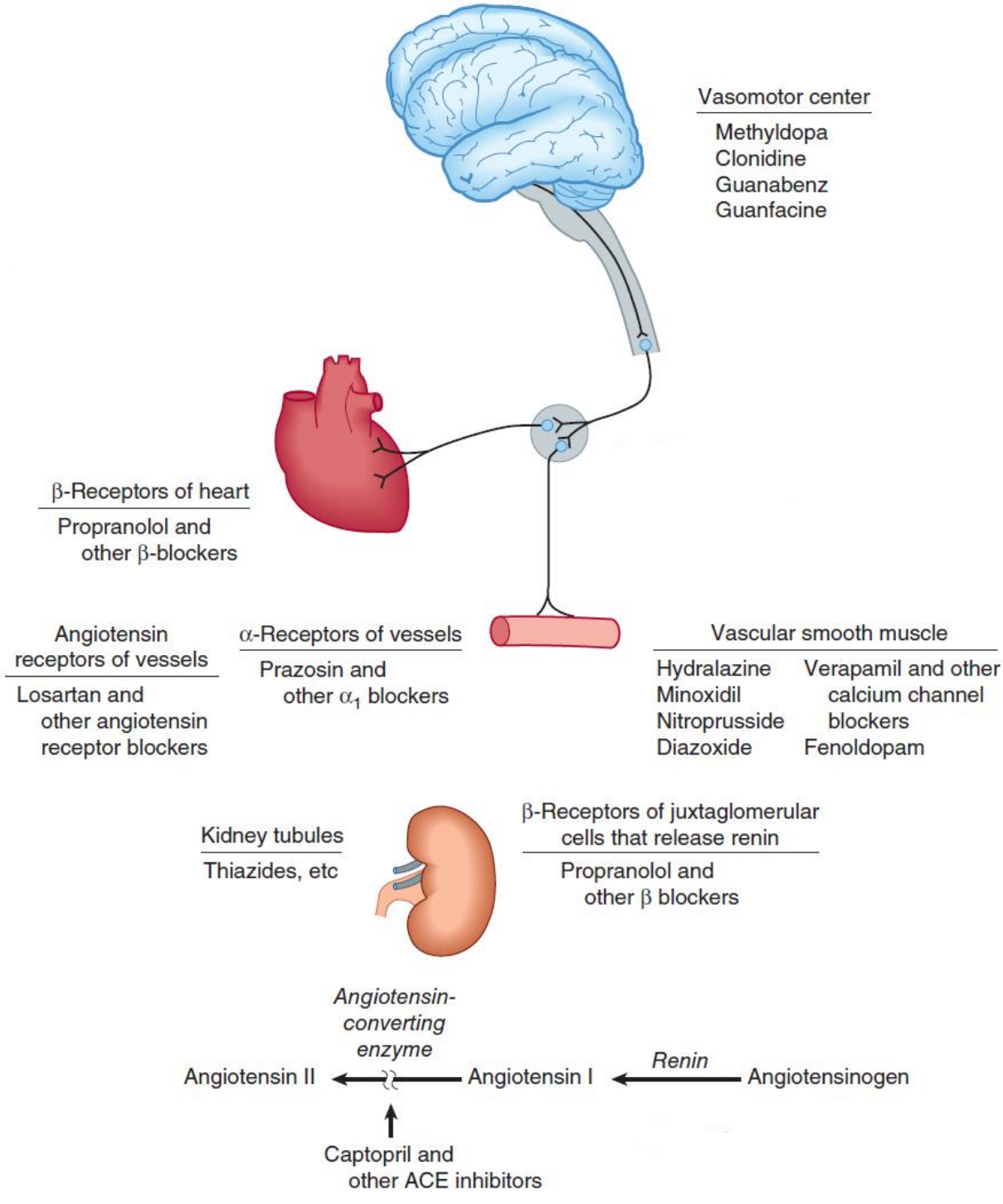
Sites of Action of the Major Classes of Antihypertensive Drugs



Antihypertensive Agents (Class Notes)

I. Diuretics • MOA: ↑ urine volume → ↓ blood volume → ↓ BP

A. Thiazides → block Na/H_2O reabsorption in distal tubule (5-10% Na/H_2O reabsorption)

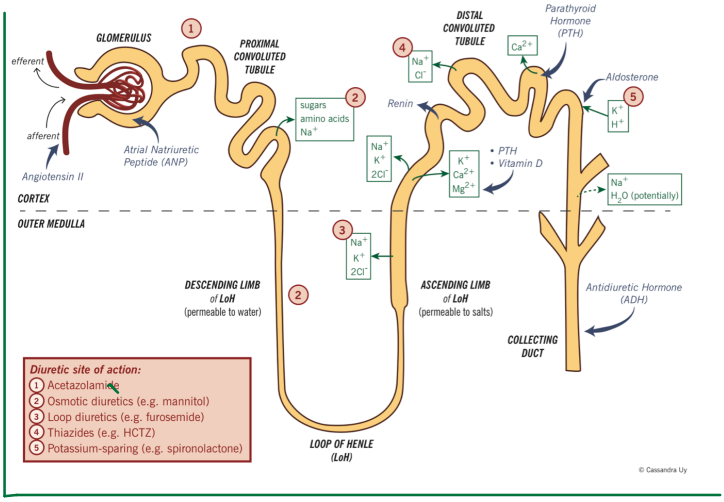
(1) HCTZ (Hydrodiuril) 12.5 – 50 mg caps/tabs

(2) Chlorthalidone (Diuril)

- longer DOA than HCTZ

(3) Metolazone (Zaroxolyn)

- works on the proximal tubule
- may be combined w/ Loop diuretic to enhance effects



B. Loop Diuretics

- block Na/H_2O reabsorption in the ascending Loop of Henle (20-25% Na/H_2O reabsorption)

(1) Furosemide (Lasix)

(2) Bumetanide (Bumex)

- when CrCl < 30 ml/min, Loop diuretics are indicated, since thiazide diuretics are not effective in renally impaired patients

C. K^+ Sparing Diuretics

(1) Spironolactone (Aldactone) – also an aldosterone antagonist

- may cause gynecomastia/impotence in men

(2) Triamterene (Dyrenium)

D. Side Effects

(1) Hypokalemia — Prevent/Treat with the following:

ⓐ K-Sparing Diuretics w/ Thiazides

Examples: Dyazide & Maxzide (HCTZ + Triamterene)

(b) KCl Supplements

Examples: KDur 20mEq/40mEq SR tabs
KCl 10% Liquid (immediate absorption)

(c) KCl IV infusion (KCl riders)

Example: KCl 20mEq in NS 250ml IVPB
infuse over 2 hours

(2) Hypomagnesemia – Prevent/Treat w/ Mg supplements

Examples: Magnesium Oxide 400mg tabs } PO
Slo-Mg 84mg SR tabs }
Magnesium sulfate 1-2 GM IVPB } IV
infuse over 1-2 hours

(3) Hypocalcemia with Loop Diuretics
(Note: Thiazides are calcium-sparing)

- Prevent/Treat with calcium supplements

TUMS ($CaCO_3$) 800-1200 mg PO daily

Calcium Gluconate 1-2 GM IVPB over 1-2 hours

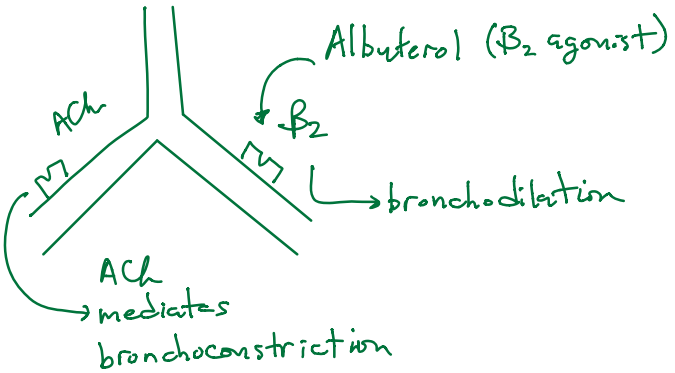
II. Beta-Blockers
- Non-selective beta-blockers block β_1, β_2
- Selective beta-blockers block β_1

A. Non-Selective Beta-Blockers

Propranolol (Inderal)

- use with caution in patients with COPD/asthma since propranol blocks β_2 receptors in the airways and competes with albuterol (β_2 agonist) for β_2 receptor sites.
- propranolol also blocks β_2 receptors in the liver in diabetics

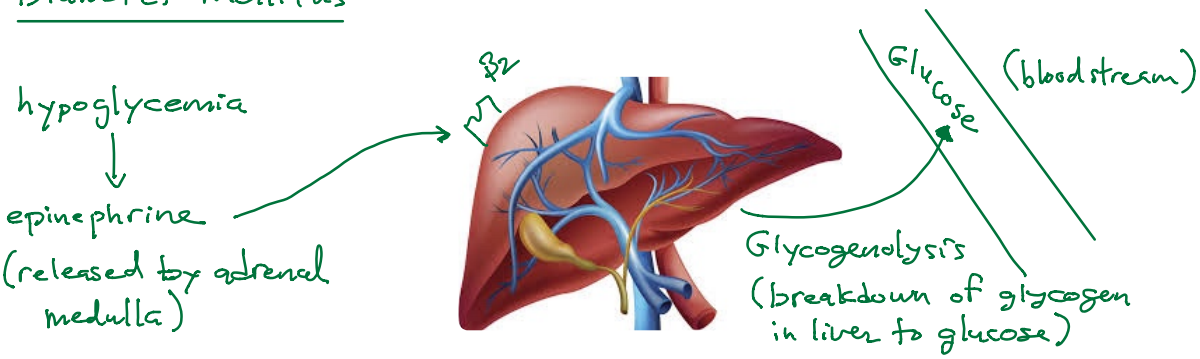
COPD/Asthma



Duoneb
= albuterol + ipratropium
(B_2 agonist) (ACh blocker)

inhalational bronchodilator which stimulates B_2 and block ACh receptors in bronchioles

Diabetes Mellitus



- During hypoglycemic episodes, Epi is released into the bloodstream by the adrenal medulla to stimulate B_2 receptors in the liver to initiate glycogenolysis. Non-selective beta-blockers block glycogenolysis and prevent glucose replacement during hypoglycemic episodes.
- Note: "ALL" beta-blockers (ie., selective and non-selective) will mask the sympathetic signs & symptoms (caused by Epi) during hypoglycemia in diabetics.

B. Selective B_1 - Blockers

(1) Metoprolol
- metoprolol tartrate (Lopressor) (BID dosing)
- metoprolol succinate (Toprol XL) (Once daily dosing)

(2) Atenolol (Tenormin)

III. Alpha-Beta Blockers (combined α_1 and β_1/β_2 blockers)

(1) Labetolol (Trandate)

(2) Carvedilol (Coreg)

Note: Nonselective beta blocking

- (blood vessels) → vasodilation → ↓ BP
- block β_1 (heart) → ↓ HR, ↓ conduction, ↓ contractility → ↓ BP

IV. Alpha-1 Blockers (block α-1 receptors → vasodilation → ↓ BP)

(1) Prazosin (Minipres)

(2) Doxazosin (Cardura)

(3) Terazosin (Hytrin)

→ also indicated for BPH (benign prostatic hypertrophy)

Side Effects

Orthostatic Hypotension → vertigo → syncope

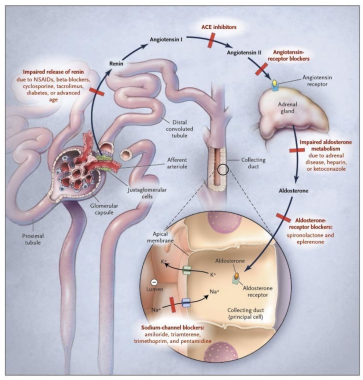
(therefore, terazosin is dosed once daily at bedtime (QHS))

V. ACE-Inhibitors

(1) Captopril (Capoten)

(2) Enalapril (Vasotec)

(3) Lisinopril (Prinivil, Zestril)



Side Effects

Hyperkalemia

Cough

Angioedema

Caution

ACE-I's & ARB's are contraindicated during pregnancy

Treatment of Angioedema

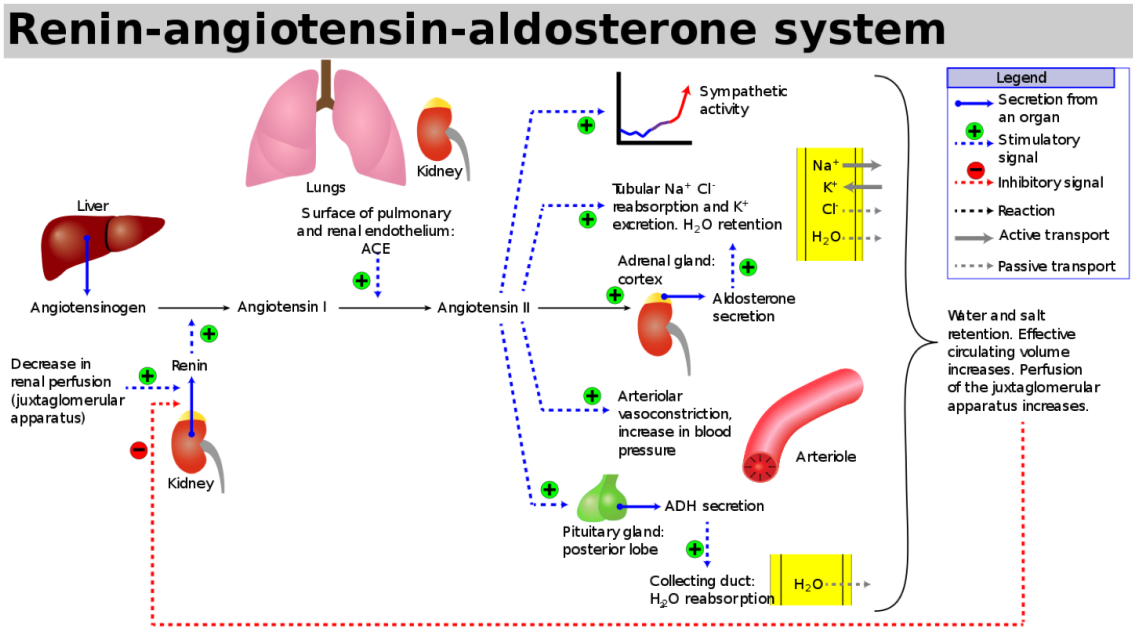
(1) Diphenhydramine (Benadryl) 50 mg IVP

(2) Famotidine (Pepcid) 20 mg IVP

(3) Methylprednisolone (Solu-Medrol) 125 mg IVP

(4) Epinephrine 0.3 mg IM every 5-15 mins PRN (angioedema associated with anaphylaxis)

Mechanisms of Action of ACE-I's and ARB's



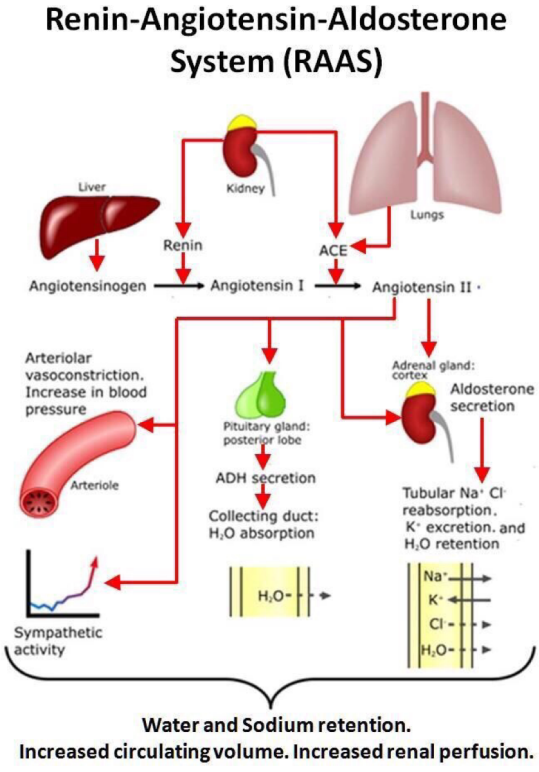
VI. Angiotensin II Receptor Blockers (ARB's)

(1) Losartan (Cozaar)

(2) Valsartan (Diovan)

Caution: ACE-I's & ARB's are contraindicated in pregnancy.

Note: If switching from ACE-I to ARB (due to cough or angioedema), allow a 6-week washout period before starting an ARB.



VII. Calcium Channel Blockers

A. Dihydropyridines
- Amlodipine (Norvasc)
- Nifedipine (Procardia)

↳ block calcium influx into vascular smooth muscle
↓
vasodilation → ↓BP

- may cause reflex tachycardia (+++) in response to baroreceptor stimulation (aortic bodies and carotid sinuses)

B. Nondihydropyridines
- Diltiazem (Cardizem)
- Verapamil (Calan, Isoptin)

↳ block calcium influx into cardiac muscle → ↓ myocardial contractility → ↓BP
and nodal tissue → { ↓ HR ; ↓ conduction velocity (AV node) } → ↓ BP

- verapamil & diltiazem may also be used to treat SVT (supraventricular tachycardia) and atrial fibrillation
- verapamil should be used with caution in patients with heart failure because it can reduce contractility (i.e., negative inotropic effect) in a "weak" heart.

Effects	Nifedipine (Procardia)	Diltiazem (Cardizem)	Verapamil (Calan, Isoptin)
vasodilation	(+++)	(+)	(+/-)
reflex tachycardia	(+++)	(+)	0
AV block (negative inotrope)	0	(+)	(+++)

Note: Nifedipine has the greatest potency (+++) for vasodilation and reflex tachycardia
Verapamil has the greatest potency (+++) for AV blocking effect and causing a negative inotropic effect (decreased contractility) on the heart.

VIII. Centrally-Acting Alpha-2 Agonists

(1) Clonidine (Catapres)

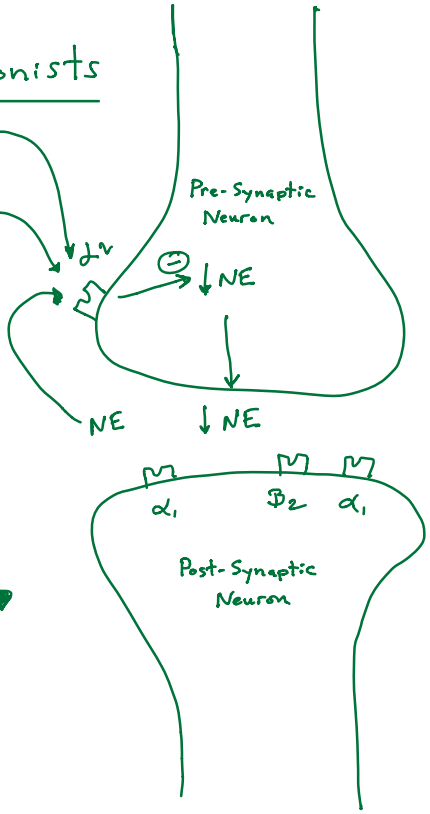
(2) Methyldopa (Aldomet)

stimulating presynaptic α_2 receptors in vasomotor and cardiac centers decreases norepinephrine (NE) release and decreases sympathetic outflow to the heart and blood vessels

↳ ↓ HR

↳ vasodilation

↓ BP



Medulla Oblongata

ARAS (consciousness)	Cardiac Center
Respiratory Center	Vasomotor Center

Note: #1 side effect of centrally-acting α_2 agonists is: sedation/drowsiness

IX. Direct-Acting Vasodilators

(1) Hydralazine (Apresoline)

(2) Minoxidil (Loniten)

} Potent Vasodilators

- Direct-acting diuretics are 3rd-4th line agents in the stepped-care treatment of HTN

↓↓ BP → ↓ renal blood flow → ↑ renin → Na/H_2O retention (treat with diuretic)

↓↓ BP → ↓↓ BP

↓↓ BP → baroreceptors → reflex tachycardia (treat with β-blocker)

Antihypertensive Agents Used for Hypertensive Urgencies/Emergencies

① Labetolol (Normodyne, Trandate) (IV)

α_1, β_1, β_2 blocks

Typical order:
Labetolol 10-20 mg IV Q6H prn SBP > 160-170

② Enalapril (Vasotec) (IV)

ACE-Inhibitor

Typical order: Enalapril 0.625-1.25 mg IV Q6H prn SBP > 160-170

③ Clonidine (Catapres) (PO)

Centrally-Acting α_2 Agonist

Typical order: Clonidine 0.1 mg PO Q6-8H prn SBP > 160-170

④ Hydralazine (IV)

Direct-Acting Vasodilator

Typical Order: Hydralazine 10-20 mg IV Q4-6H prn SBP > 160-170

⑤ Nicardipine (Cardene) (IV)

Calcium Channel Blocker (Dihydropyridine)

Typical Order:
5-15 mg/hr infusion for SBP > 185/DBP > 110 indicated for Stroke

Tx of Atrial Fibrillation/Flutter & SVT

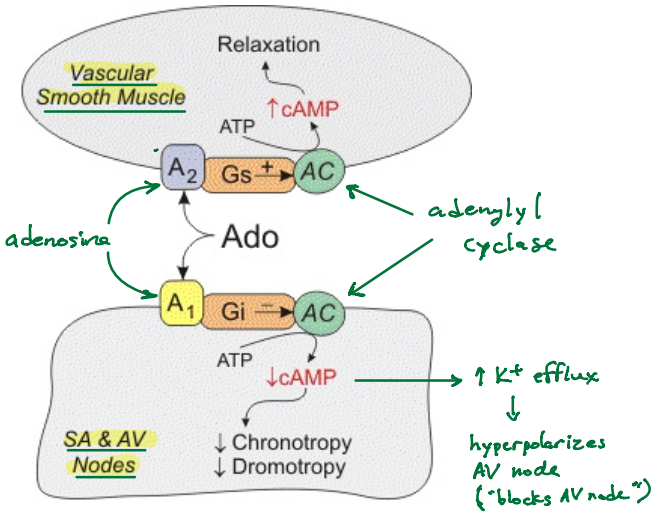
Diltiazem 10 mg IV Q4H prn HR > 120

Metoprolol 5 mg IV Q4-6H prn HR > 120

Digoxin 8-12 mcg/kg IV loading dose, then 125-250 mcg IV/PO daily

Verapamil 2.5-5 mg IVP, May repeat x 1 dose in 15-30 mins

Adenosine (SVT) 6 mg IVP over 1-3 seconds, May repeat with 12 mg IVP in 1-2 mins



Oral Antihypertensive Drugs *(1 of 3)*

Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
Primary Agents				
Thiazide or thiazide-type diuretics	**Chlorthalidone**	12.5–25	1	• Chlorthalidone preferred based on prolonged half-life and proven trial reduction of CVD • Monitor for hyponatremia and hypokalemia, uric acid and calcium levels. • Use with caution in patients with history of acute gout unless patient is on uric acid-lowering therapy.
	Hydrochlorothiazide	25–50	1	
	Indapamide	1.25–2.5	1	
	Metolazone	2.5–10	1	
ACE Inhibitors	**Benazepril**	10–40	1 or 2	• Do not use in combination with ARBs or direct renin inhibitor • Increased risk of hyperkalemia, especially in patients with CKD or in those on K+ supplements or K+-sparing drugs • May cause acute renal failure in patients with severe bilateral renal artery stenosis • Do not use if history of angioedema with ACE inhibitors. • Avoid in pregnancy
	Captopril	12.5–150	2 or 3	
	Enalapril	5–40	1 or 2	
	Fosinopril	10–40	1	
	Lisinopril	10–40	1	
	Moexipril	7.5–30	1 or 2	
	Perindopril	4–16	1	
	Quinapril	10–80	1 or 2	
	Ramipril	2.5–10	1 or 2	
	Trandolapril	1–4	1	
ARBs	**Azilsartan**	40–80	1	• Do not use in combination with ACE inhibitors or direct renin inhibitor • Increased risk of hyperkalemia in CKD or in those on K+ supplements or K+-sparing drugs • May cause acute renal failure in patients with severe bilateral renal artery stenosis • Do not use if history of angioedema with ARBs. Patients with a history of angioedema with an ACEI can receive an ARB beginning 6 weeks after ACEI discontinued. • Avoid in pregnancy
	Candesartan	8–32	1	
	Eprosartan	600–800	1 or 2	
	Irbesartan	150–300	1	
	Losartan	50–100	1 or 2	
	Olmesartan	20–40	1	
	Telmisartan	20–80	1	
	Valsartan	80–320	1	
CCB—dihydropyridines	**Amlodipine**	2.5–10	1	• Avoid use in patients with HFrEF; amlodipine or felodipine may be used if required • Associated with dose-related pedal edema, which is more common in women than men
	Felodipine	5–10	1	
	Isradipine	5–10	2	
	Nicardipine SR	5–20	1	
	Nifedipine LA	60–120	1	
	Nisoldipine	30–90	1	
CCB—nondihydropyridines	**Diltiazem SR**	180–360	2	• Avoid routine use with beta blockers due to increased risk of bradycardia and heart block • Do not use in patients with HFrEF • Drug interactions with diltiazem and verapamil (CYP3A4 major substrate and moderate inhibitor)
	Diltiazem ER	120–480	1	
	Verapamil IR	40-80	3	
	Verapamil SR	120–480	1 or 2	
	Verapamil-delayed onset ER (various forms)	100–480	1 (in the evening)	

Table is continued in the next two pages

Oral Antihypertensive Drugs *(2 of 3)*

Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
Secondary Agents				
Diuretics—loop	**Bumetanide**	0.5–4	2	• Preferred diuretics in patients with symptomatic HF. Preferred over thiazides in patients with moderate-to-severe CKD (e.g., GFR <30 mL/min)
	Furosemide	20–80	2	
	Torsemide	5–10	1	
Diuretics—potassium sparing	**Amiloride**	5–10	1 or 2	• Monotherapy agents minimally effective antihypertensives • Combination therapy of potassium sparing diuretic with a thiazide can be considered in patients with hypokalemia on thiazide monotherapy • Avoid in patients with significant CKD (e.g., GFR <45 mL/min)
	Triamterene	50–100	1 or 2	
Diuretics—aldosterone antagonists	**Eplerenone**	50–100	12	• Preferred agents in primary aldosteronism and resistant hypertension • Spironolactone associated with greater risk of gynecomastia and impotence compared to eplerenone • Common add-on therapy in resistant hypertension • Avoid use with K+ supplements, other K+-sparing diuretics or significant renal dysfunction • Eplerenone often requires twice daily dosing for adequate BP lowering
	Spironolactone	25–100	1	
Beta blockers—cardioselective	**Atenolol**	25–100	12	• Beta blockers are not recommended as first-line agents unless the patient has IHD or HF • Preferred in patients with bronchospastic airway disease requiring a beta blocker • Bisoprolol and metoprolol succinate preferred in patients with HFrEF • Avoid abrupt cessation
	Betaxolol	5–20	1	
	Bisorolol	2.5–10	1	
	Metoprolol tartrate	100–400	2	
	Metoprolol succinate	50–200	1	
Beta blockers—cardioselective and vasodilatory	**Nebivolol**	5–40	1	• Induces nitric oxide-induced vasodilation • Avoid abrupt cessation
Beta blockers—noncardioselective	**Nadolol**	40–120	1	• Avoid in patients with reactive airways disease • Avoid abrupt cessation
	Propranolol IR	160–480	2	
	Propranolol LA	80–320	1	
Beta blockers—intrinsic sympathomimetic activity	**Acebutolol**	200–800	2	• Generally avoid, especially in patients with IHD or HF • Avoid abrupt cessation
	Carteolol	2.5–10	1	
	Penbutolol	10–40	1	
	Pindolol	10–60	2	

Table is continued in the next page

Oral Antihypertensive Drugs *(3 of 3)*

Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
Secondary Agents *(continued from previous page)*				
Beta blockers—combined alpha- and beta-receptor	**Carvedilol**	12.5–50	2	• Carvedilol preferred in patients with HFrEF • Avoid abrupt cessation
	Carvedilol phosphate	20–80	1	
	Labetalol	200–800	2	
Direct renin inhibitor	**Aliskiren**	150–300	1	• Do not use in combination with ACE inhibitors or ARBs • Aliskiren is very long acting • Increased risk of hyperkalemia in CKD or in those on K+ supplements or K+ sparing drugs • May cause acute renal failure in patients with severe bilateral renal artery stenosis • Avoid in pregnancy
Alpha-1 blockers	**Doxazosin**	1–8	1	• Associated with orthostatic hypotension, especially in older adults • May consider as second-line agent in patients with concomitant BPH
	Prazosin	2–20	2 or 3	
	Terazosin	1–20	1 or 2	
Central alpha1-agonist and other centrally acting drugs	**Clonidine oral**	0.1–0.8	2	• Generally reserved as last-line due to significant CNS adverse effects, especially in older adults • Avoid abrupt discontinuation of clonidine, which may induce hypertensive crisis; clonidine must be tapered to avoid rebound hypertension
	Clonidine patch	0.1–0.3	1 weekly	
	Methyldopa	250–1000	2	
	Guanfacine	0.5–2	1	
Direct vasodilators	**Hydralazine**	250-200	2 or 3	• Associated with sodium and water retention and reflex tachycardia; use with a diuretic and bet a blocker • Hydralazine associated with drug-induced lupus-like syndrome at higher doses • Minoxidil associated with hirsutism and requires a loop diuretic. Can induce pericardial effusion
	Minoxidil	5–100	1 -3	

*Dosages may vary from those listed in the FDA approved labeling (available at http://dailymed.nlm.nih.gov/dailymed/index.cfm).

Adapted with permission from Chobanian AV, Bakris GL, Black HR, et al. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. JAMA. 2003; 289:2560-72

Table 18

Intravenous Antihypertensive Drugs for Treatment of Hypertensive Emergencies *(1 of 2)*

Agent	Drugs	Usual Dose Range	Comments
CCB-dihydropyridines	**Nicardipine**	Initial 5 mg/h, increasing every 5 min by 2.5 mg/h to maximum 15 mg/h.	Contraindicated in advanced aortic stenosis; no dose adjustment needed for elderly.
	Clevidipine	Initial 1–2 mg/h, doubling every 90 s until BP approaches target, then increasing by < double every 5–10 min; maximum dose 32 mg/h; maximum duration 72 h.	Contraindicated in pts with soybean, soy product, egg, and egg product allergy and in pts with defective lipid metabolism (e.g., pathological hyperlipidemia, lipoid nephrosis or acute pancreatitis). Use low-end dose range for elderly pts.
Vasodilators-nitric oxide dependent	**Sodium nitroprusside**	Initial 0.3–0.5 mcg/kg/min; increase in increments of 0.5 mcg/kg/min to achieve BP target; maximum dose 10 mcg/kg/min; duration of treatment as short as possible. For infusion rates ≥4–10 mcg/kg/min or duration >30 min, thiosulfate can be coadministered to prevent cyanide toxicity.	Intra-arterial BP monitoring recommended to prevent "overshoot". Lower dosing adjustment required for elderly. Tachyphylaxis common with extended use. Cyanide toxicity with prolonged use can result in irreversible neurologic changes and cardiac arrest.
	Nitroglycerin	Initial 5 mcg/min; increase in increments of 5 mcg/min every 3–5 min to a maximum of 20 mcg/min.	Use only in pts with acute coronary syndrome and/or acute pulmonary edema. Do not use in volume-depleted pts.
Vasodilators-direct	**Hydralazine**	Initial 10 mg via slow IV infusion (maximum initial dose 20 mg); repeat every 4–6 h as needed.	BP begins to decrease within 10–30 min and the fall lasts 2–4 h. Unpredictability of response and prolonged duration of action do not make hydralazine a desirable first-line agent for acute treatment in most pts.
Adrenergic blockers beta1 receptor selective antagonist	**Esmolol**	Loading dose 500–1,000 mcg/kg/min over 1 min followed by a 50 mcg/kg/min infusion. For additional dosing, the bolus dose is repeated and the infusion increased in 50 mcg/kg/min increments as needed to a maximum of 200 mcg/kg/ min.	Contraindicated in pts with concurrent beta-blocker therapy, bradycardia and/or decompensated HF Monitor for bradycardia. May worsen HF. Higher doses may block beta2 receptors and impact lung function in reactive airway disease.

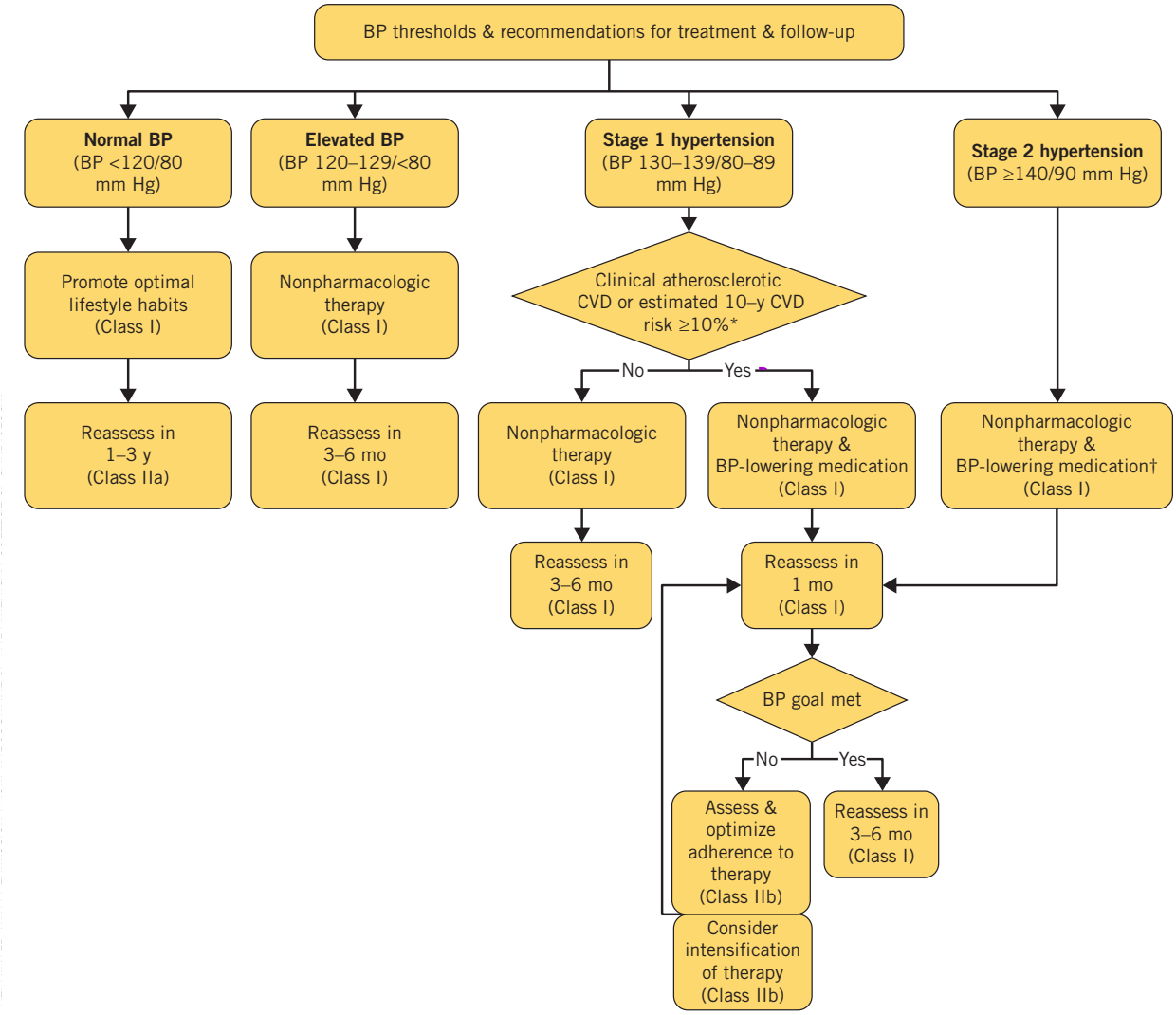
Table will be continued in the next page

ACC/AHA: Clinical Practice Guidelines (2017)

TABLE 1. Comparing BP classifications[4,7]

If the patient's systolic and diastolic BPs fall into different categories, classify the patient's hypertension according to the highest category.

Systolic BP (mm Hg)	Diastolic BP (mm Hg)	2017 guideline	JNC 7
<120	<80	Normal	Normal
120-129	<80	Elevated	Prehypertension
130-139	80-89	Stage 1 hypertension	
140-159	90-99	Stage 2 hypertension	Stage 1 hypertension
≥160	≥100		Stage 2 hypertension



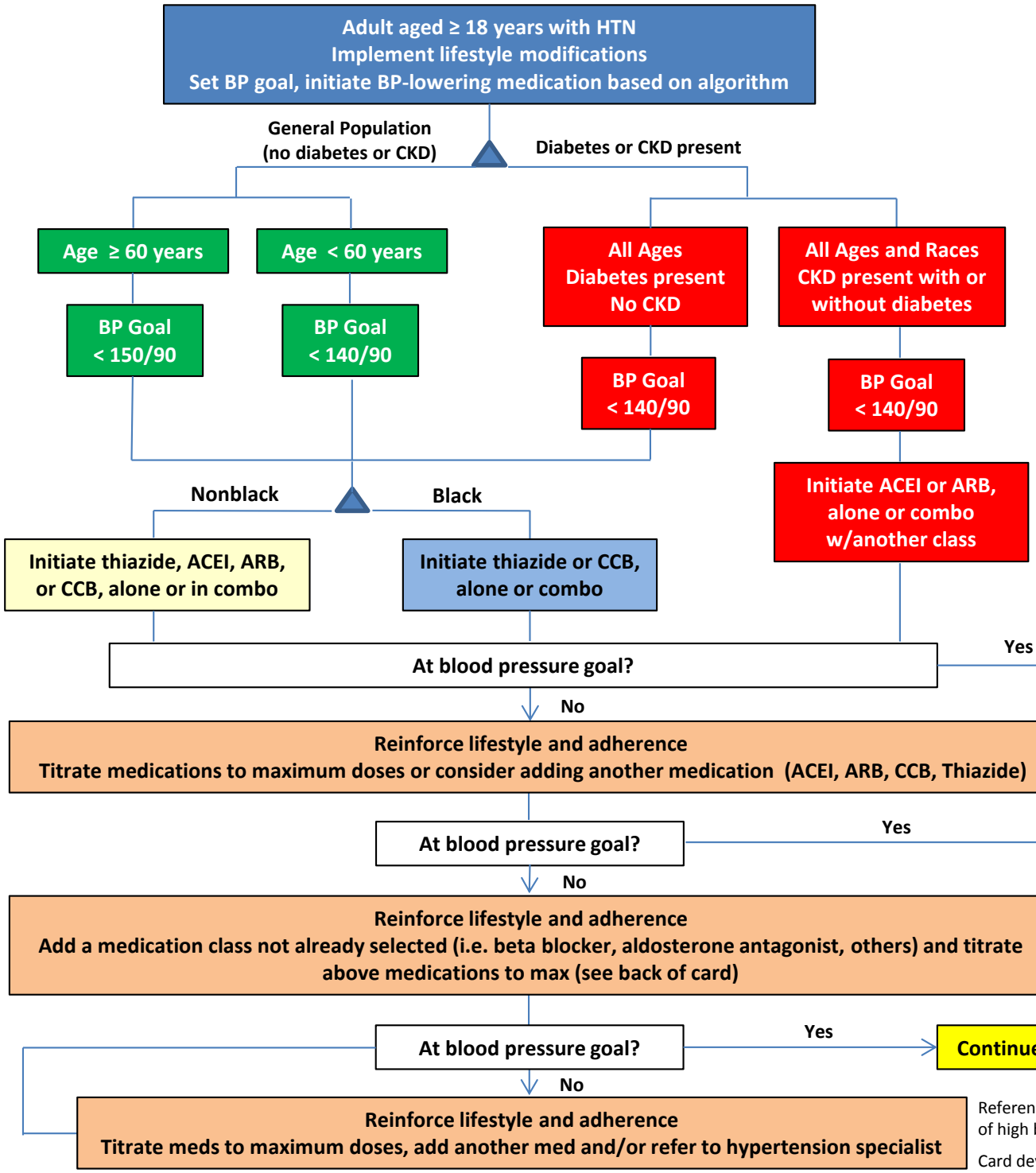
INITIAL TREATMENT RECOMMENDATIONS

- In the absence of specific compelling indications: ACE-I or ARB, CCB, and thiazide diuretic.
- General non-black population, including those with diabetes, initial pharm treatment should include: ACE-I or ARB, CCB, and thiazide diuretic.
- General black population, initial treatment should include: CCB and thiazide diuretic.
- All patients with CKD and HTN, initial tx should include: ACE-I or ARB → improve kidney outcomes
- In all hypertensive patients, if goal BP is not reached within a month of initiating treatment, increase the dose of the initial drug OR add a 2nd drug from a different class.

Comparison of Hypertension Guidelines, 2011-2014

Blood Pressure (mm Hg)	NICE 2011	ESH/ESC 2013	AHA/ACC/CDC 2013	ASH/ISH 2014	JNC 8 2014	ACC/AHA/ASH IHD 2014
Definition of hypertension	≥140/90 and daytime ABPM or home BP ≥135/85	≥140/90	≥140/90	≥140/90	Not addressed	Not addressed
Drug therapy	≥160/100 or daytime ABPM ≥150/95	≥140/90	≥140/90	≥140/90	<60 yr ≥140/90 ≥60 yr ≥150/90	≥140/90
ß-Blockers as first-line drug	No (Step 4)	Yes	No (Step 3)	No (Step 4)	No	No Yes if CAD
Diuretic	Chlorthalidone Indapamide	Thiazides, Chlorthalidone, Indapamide	Thiazides	Thiazides, Chlorthalidone, Indapamide	Thiazides, Chlorthalidone, Indapamide	Thiazides, Chlorthalidone, Indapamide
Initiate therapy with two drugs	Not mentioned	In patients with markedly elevated BP	≥160/100	≥160/100	≥160/100	≥160/100
BP targets	<140/90 ≥80 yr <150/90	<140/90 elderly <80 yr; SBP 140-150; SBP <140 in fit patients; Elderly ≥80 yr; SBP 140-150	<140/90 Lower targets may be appropriate in some patients, including the elderly	<140/90 ≥80 yr <150/90	<60 yr <140/90 ≥60 yr <150/90	<140/90 <130/80 if CAD, CAD risk equivalent, stroke, TIA, Framingham risk score ≥20%
BP target in patients with diabetes mellitus	Not addressed	<140/85	<140/90 Lower targets may be considered	<140/90	<140/90	<140/90 Lower targets may be considered

JNC 8 Hypertension Guideline Algorithm



Initial Drugs of Choice for Hypertension

- ACE inhibitor (ACEI)
- Angiotensin receptor blocker (ARB)
- Thiazide diuretic
- Calcium channel blocker (CCB)

Strategy	Description
A	Start one drug, titrate to maximum dose, and then add a second drug.
B	Start one drug, then add a second drug before achieving max dose of first
C	Begin 2 drugs at same time, as separate pills or combination pill. **Initial combination therapy is recommended if BP is greater than 20/10mm Hg above goal**

Lifestyle changes:

- Smoking Cessation
- Control blood glucose and lipids
- Diet
  - ✓Eat healthy (i.e., DASH diet)
  - ✓Moderate alcohol consumption
  - ✓Reduce sodium intake to no more than 2,400 mg/day
- Physical activity
  - ✓Moderate-to-vigorous activity 3-4 days a week averaging 40 min per session.

Reference: James PA, Ortiz E, et al. 2014 evidence-based guideline for the management of high blood pressure in adults: (JNC8). JAMA. 2014 Feb 5;311(5):507-20

Card developed by Cole Glenn, Pharm.D. & James L Taylor, Pharm.D.

Considerations for individualizing antihypertensive therapy

Indication or contraindication	Antihypertensive drugs
Compelling indications (major improvement in outcome independent of blood pressure)	
Heart failure with reduced ejection fraction	ACE inhibitor or ARB, beta blocker, diuretic, aldosterone antagonist*
Postmyocardial infarction	ACE inhibitor or ARB, beta blocker, aldosterone antagonist
Proteinuric chronic kidney disease	ACE inhibitor or ARB
Angina pectoris	Beta blocker, calcium channel blocker
Atrial fibrillation rate control	Beta blocker, nondihydropyridine calcium channel blocker
Atrial flutter rate control	Beta blocker, nondihydropyridine calcium channel blocker
Likely to have a favorable effect on symptoms in comorbid conditions	
Benign prostatic hyperplasia	Alpha blocker
Essential tremor	Beta blocker (noncardioselective)
Hyperthyroidism	Beta blocker
Migraine	Beta blocker, calcium channel blocker
Osteoporosis	Thiazide diuretic
Raynaud phenomenon	Dihydropyridine calcium channel blocker
Contraindications	
Angioedema	Do not use an ACE inhibitor
Bronchospastic disease	Do not use a non-selective beta blocker
Liver disease	Do not use methyldopa
Pregnancy (or at risk for)	Do not use an ACE inhibitor, ARB, or renin inhibitor (eg, aliskiren)
Second- or third-degree heart block	Do not use a beta blocker, nondihydropyridine calcium channel blocker unless a functioning ventricular pacemaker
Drug classes that may have adverse effects on comorbid conditions	
Depression	Generally avoid beta blocker, central alpha-2 agonist
Gout	Generally avoid loop or thiazide diuretic
Hyperkalemia	Generally avoid aldosterone antagonist, ACE inhibitor, ARB, renin inhibitor
Hyponatremia	Generally avoid thiazide diuretic
Renovascular disease	Generally avoid ACE inhibitor, ARB, or renin inhibitor

Antihypertensives in Pregnancy (UpToDate)

Drug	Class	Initial dose	Usual effective dose range	Maximum suggested total daily dose	Comments
Labetalol	Combined alpha and beta blocker	100 mg 2 times daily, increase by 100 mg twice daily every 2 to 3 days as needed	200 to 800 mg in 2 divided doses	2400 mg	Can cause bronchoconstriction. Avoid in patients with asthma, chronic obstructive lung disease, heart failure, bradycardia (heart rate <60 beats per minute), or greater than first-degree heart block. The dosing interval can be increased to 3 times daily if blood pressure is increased prior to the next prescribed dose.
Hydralazine **NOTE:** Due to reflex tachycardia, monotherapy with oral hydralazine is not recommended; hydralazine may be combined with methyldopa or labetalol if needed as add-on therapy	Peripheral vasodilator	Begin with 10 mg 4 times per day, increase by 10 to 25 mg/dose every 2 to 5 days	50 to 100 mg in 2 to 4 divided doses	200 mg*	
Nifedipine extended release (ER)[¶]	Calcium channel blocker	30 to 60 mg once daily as an extended release tablet, increase at 7 to 14 day intervals	30 to 90 mg once daily	120 mg	Do not administer sublingually. Based upon clinical experience of UpToDate contributors, some patients better tolerate nifedipine ER administered in 2 divided doses, which may serve to minimize its peak to trough effects (eg, instead of increasing the dose to 60 mg once daily, it may be desirable in some patients to increase to 30 mg 2 times daily).
Methyldopa	Centrally acting alpha agonist	250 mg 2 to 3 times daily, increase every 2 days as needed[Δ]	250 to 1000 mg in 2 to 3 divided doses	3000 mg	Sedation is a common side effect.

Interdependent and Interacting Factors in Blood Pressure Regulation