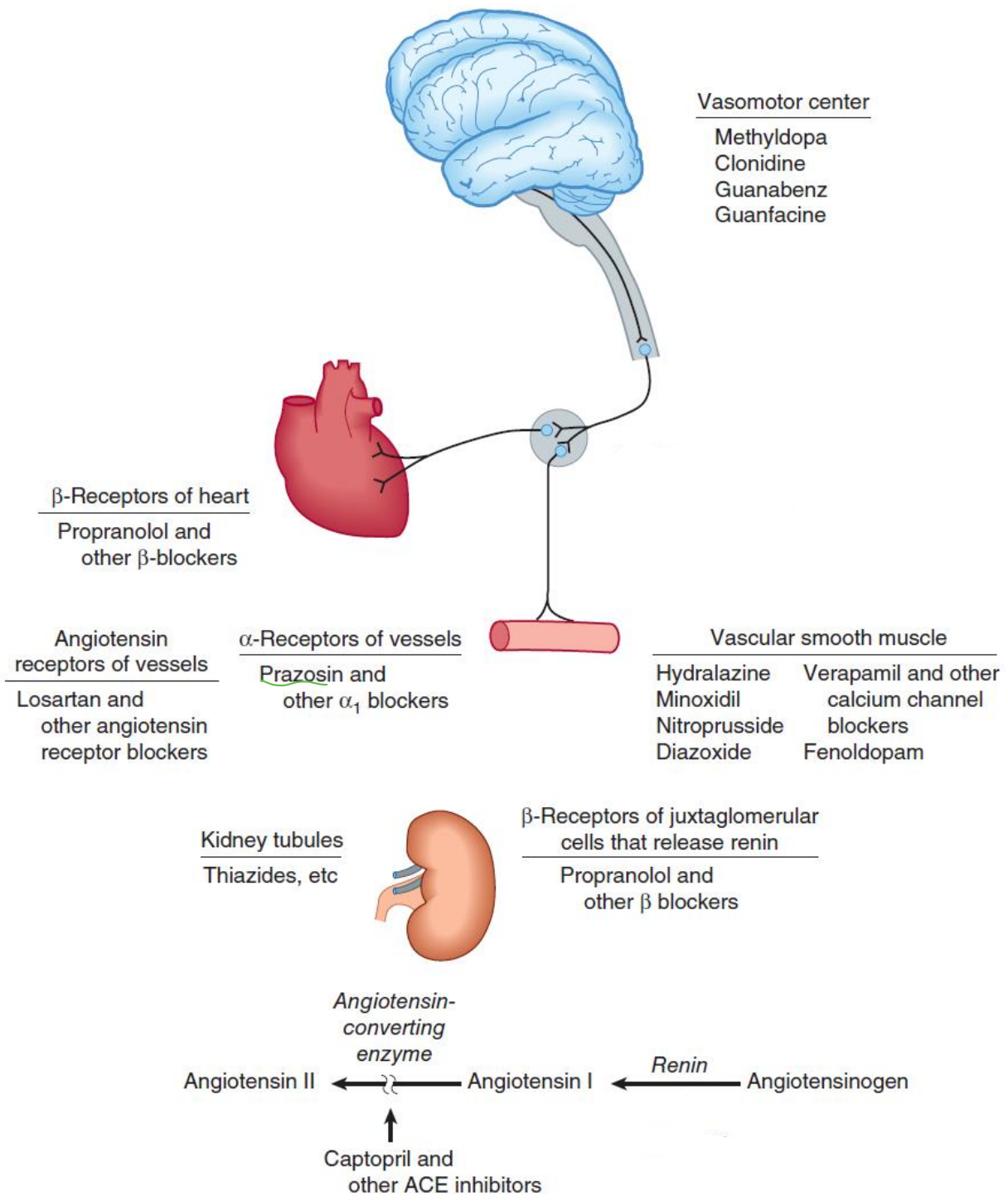


Sites of Action of the Major Classes of Antihypertensive Drugs



ANTIHYPERTENSIVE AGENTS

Match each antihypertensive agent with its corresponding side effects.

- Lisinopril (Zestril, Prinivil) Hyperkalemia, Cough, Angioedema
- Terazosin (Hytrin) Orthostatic Hypotension
- Propranolol (Inderal) Bronchconstriction in Asthma / COPD
- Nifedipine (Procardia) Reflex Tachycardia
- Furosemide (Lasix) Hypokalemia, Hypomagnesemia, Hypocalcemia
- Clonidine (Catapres) Sedation

Match each antihypertensive agent with its corresponding drug class / MOA.

- Diltiazem (Cardizem) Calcium Channel Blocker
- Losartan (Cozaar) Angiotensin II Blocker (ARB)
- Lisinopril (Zestril, Prinivil) ACE-Inhibitor
- Labetalol (Trandate) Alpha-Beta Blocker
- Metoprolol (Toprol, Lopressor) Beta-Blocker
- Terazosin (Hytrin) Alpha-1 Blocker
- Hydralazine (Apresoline) Direct-Acting Vasodilator

Antihypertensive Agents (Class Notes)

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

A. Thiazides → block $\text{Na}^+/\text{H}_2\text{O}$ reabsorption in distal tubule (5-10% $\text{Na}^+/\text{H}_2\text{O}$ reabsorption)

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

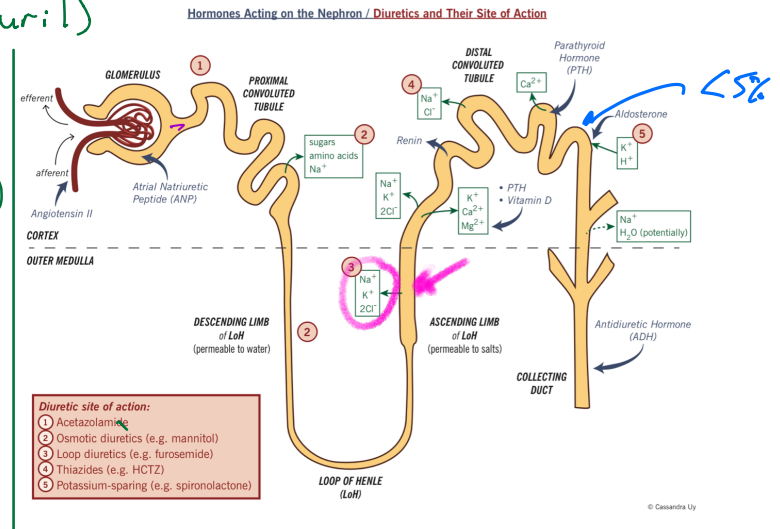
(2) Chlorthalidone (Diuril)

- longer DOA than HCTZ

(3) Metolazone (Zaroxolya)

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

Hydrochlorothiazide



B. Loop Diuretics

- block $\text{Na}^+/\text{H}_2\text{O}$ reabsorption in the ascending Loop of Henle (20-25% $\text{Na}^+/\text{H}_2\text{O}$ reabsorption)

(1) Furosemide (Lasix)

(2) Bumetanide (Bumex)

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

Furosemide > HCTZ > Triamterene

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: Dyszide & Maxzide (HCTZ + Triamterene)

Hypokalemia

SE

Furosemide → hypokalemia, hypomagnesemia

treated with

(M)

hypocalcemia

HCTZ

hypokalemia

hypomagnesemia

(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 (CaCO₃) 800-1200mg 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

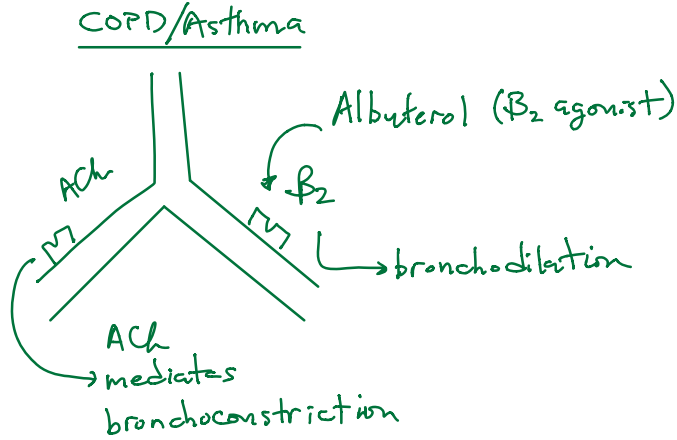
Propranolol (Inderal)

- use with caution in patients with COPD/asthma since propranolol 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

masks the signs and symptoms of hypoglycemia in diabetics

SE
(M)
bronchoconstriction in asthma and COPD

- Beta Blockers
- ① ↓ HR
 - ② ↓ conduction velocity
 - ③ ↓ myocardial contractility
- } → ↓ BP

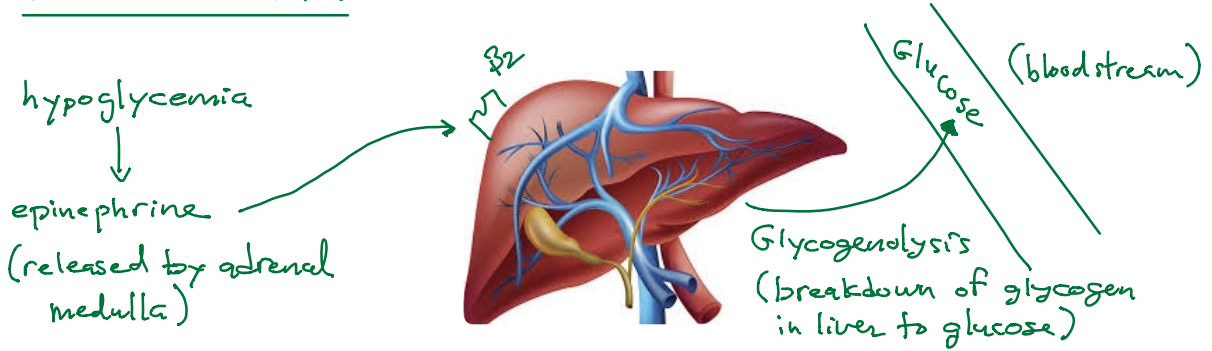


Duoneb

= albuterol + ipratropium
(β_2 agonist) (ACh blocker)

inhalational bronchodilator which stimulates β_2 and block ACh receptors in bronchioles

Diabetes Mellitus



- During hypoglycemic episodes, Epi is released into the bloodstream by the adrenal medulla to stimulate β_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 (i.e., selective and non-selective) will mask the sympathetic signs & symptoms (caused by Epi) during hypoglycemia in diabetics.

B. Selective β_1 -Blockers

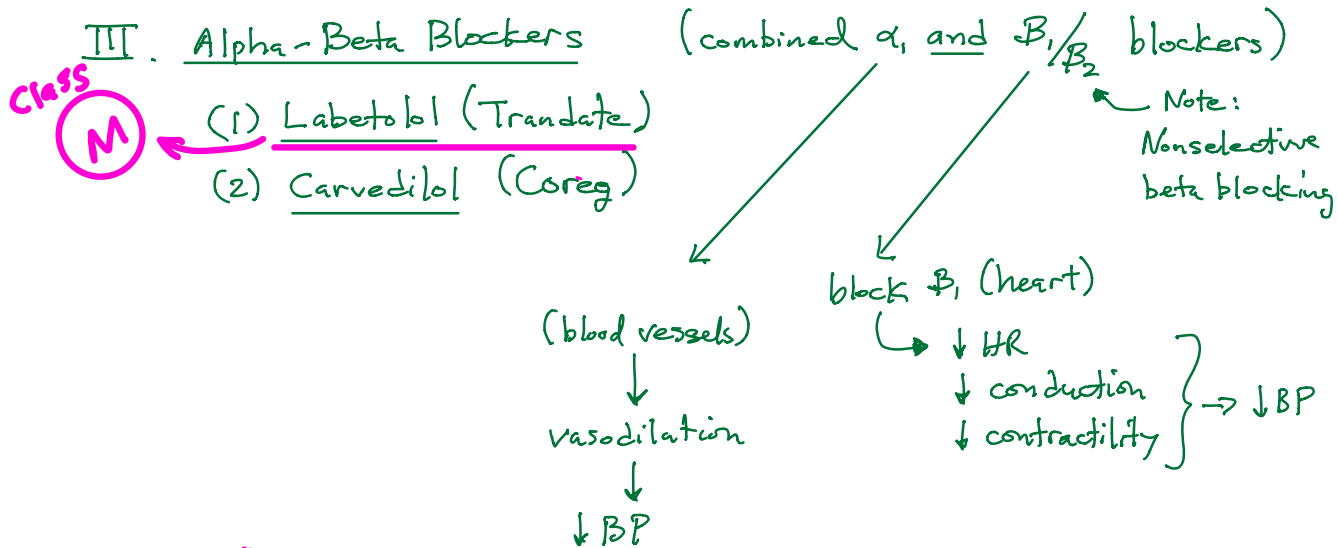
✓ preferred in asthma & COPD patients

(1) Metoprolol
(M) class

metoprolol tartrate (Lopressor)
(BID dosing)

metoprolol succinate (Toprol XL)
(Once daily dosing)

(2) Atenolol (Tenormin)



IV. Alpha-1 Blockers (block α_1 receptors → vasodilation → ↓ BP)

- (1) Prazosin (Minipres)
 (2) Doxazosin (Cardura)
 (3) Terazosin (Hytrin)
- Class M**
- Side Effects**
Orthostatic Hypotension
 ↓ vertigo
 ↓ syncope
- (therefore, terazosin is dosed once daily at bedtime (QHS))
- SE M**
-

V. ACE-Inhibitors

- (1) Captopril (Capoten)
 (2) Enalapril (Vasotec)
 (3) Lisinopril (Prinivil, Zestril)
- Class M**

- Side Effects**
 { Hyperkalemia
 Cough
 Angioedema
- SE M**
-

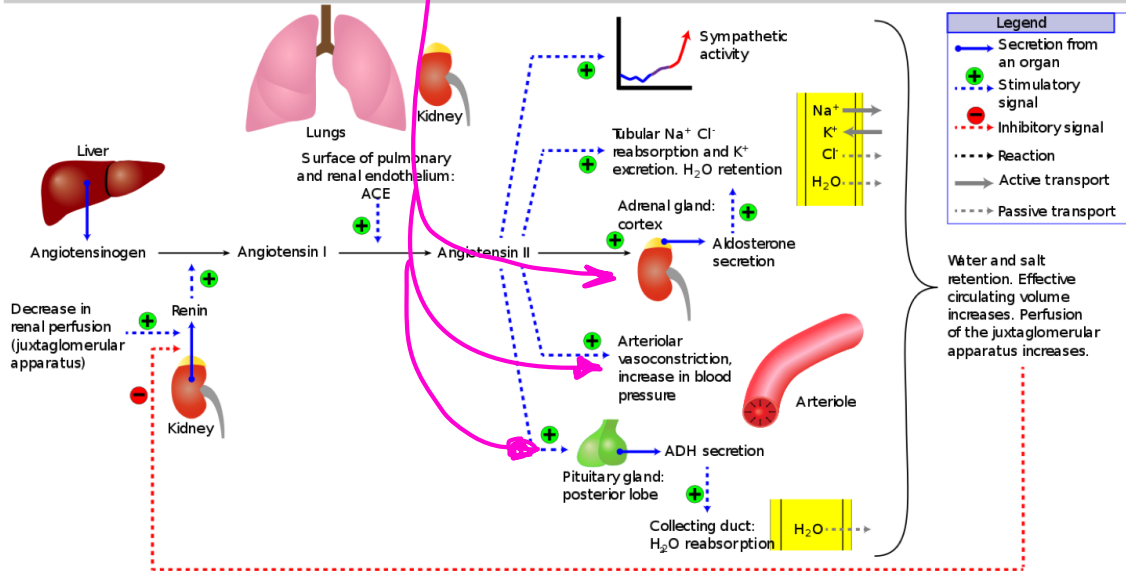
✓ A hypertensive patient who has high serum renin levels is best treated with _____.

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

✓ ACE-I block ACE to decrease production of angiotensin II, resulting in _____.

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

Renin-angiotensin-aldosterone system



VI. Angiotensin II Receptor Blockers (ARB's)

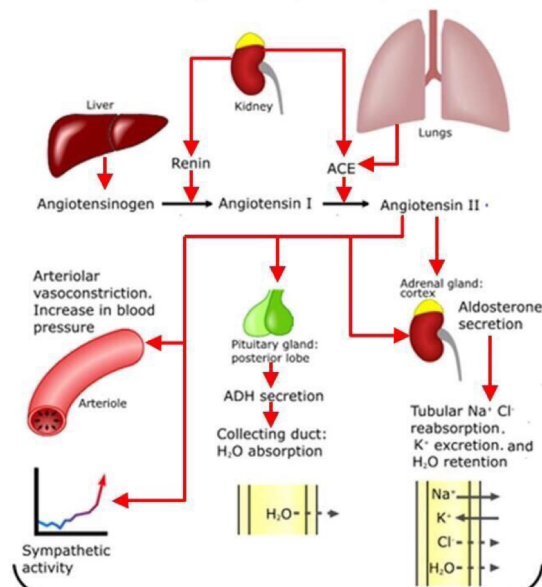
Class M

- ← (1) Losartan (Cozaar)
- (2) Valsartan (Diovan)

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

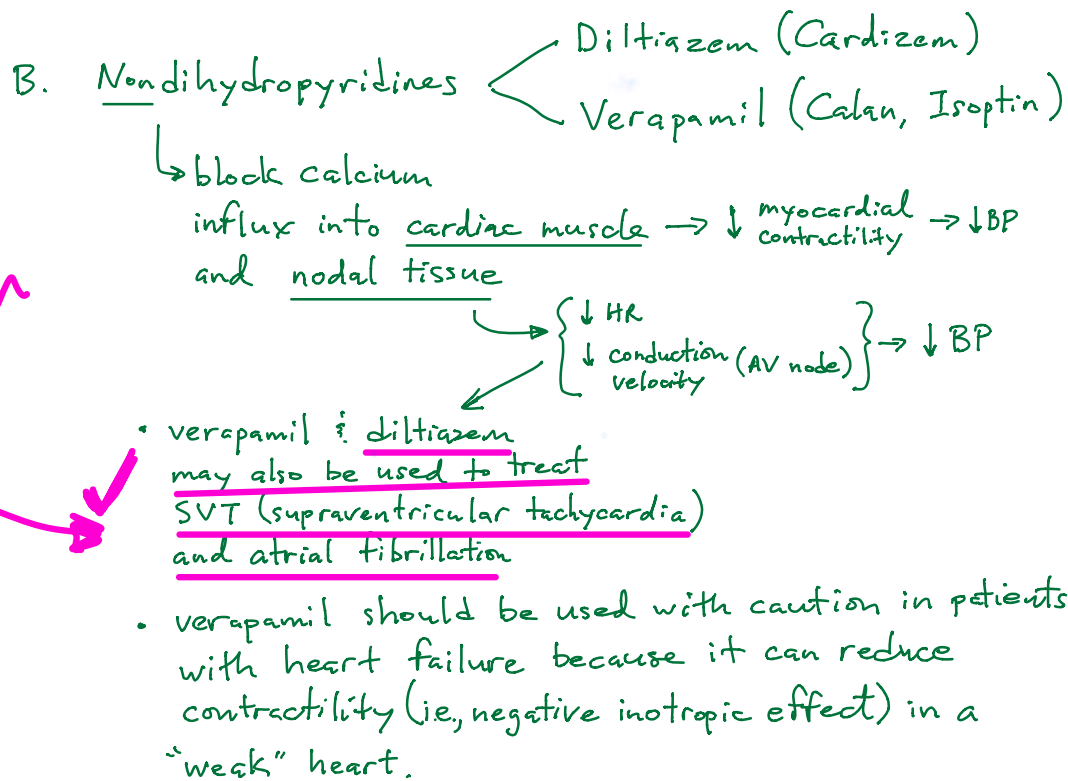
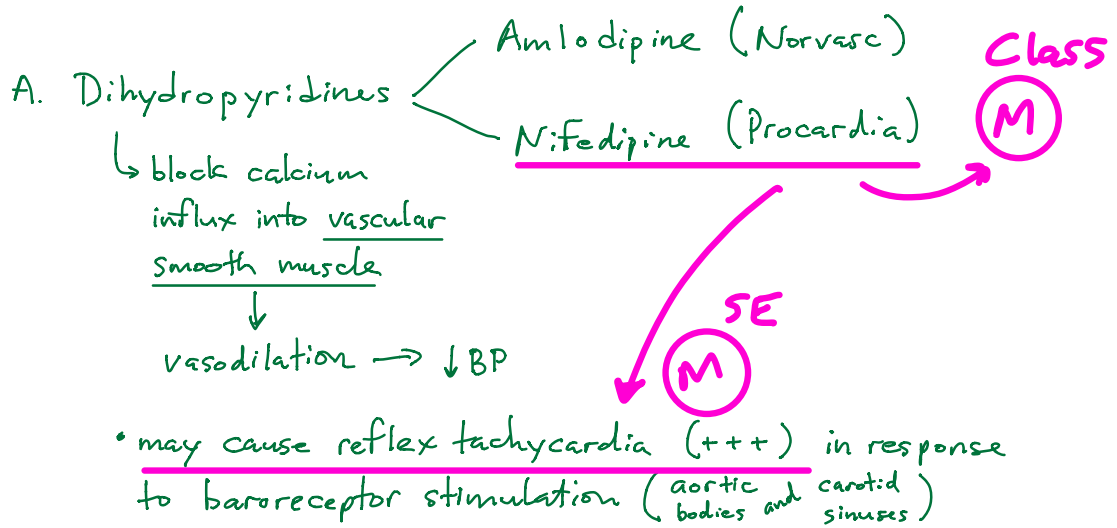
Note: IF switching from ACE-I to ARB (due to cough or angioedema), allow a 6-week washout period before starting an ARB.

Renin-Angiotensin-Aldosterone System (RAAS)



Water and Sodium retention. Increased circulating volume. Increased renal perfusion.

VII. Calcium Channel Blockers



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

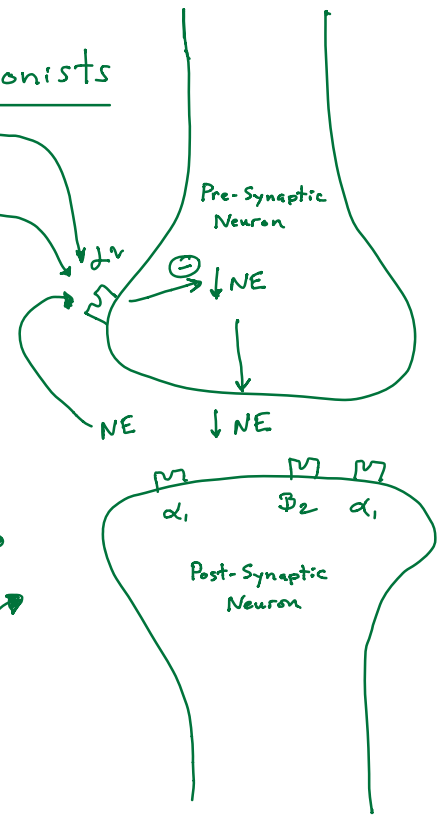
- (1) Clonidine (Catapres)
- (2) Methyldopa (Aldomet)

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

↳ vasodilation

↳ \downarrow HR

↳ \downarrow BP



Medulla Oblongata

ARAS (consciousness)	Cardiac Center
Respiratory Center	Vasomotor Center

Clonidine

(M) SE

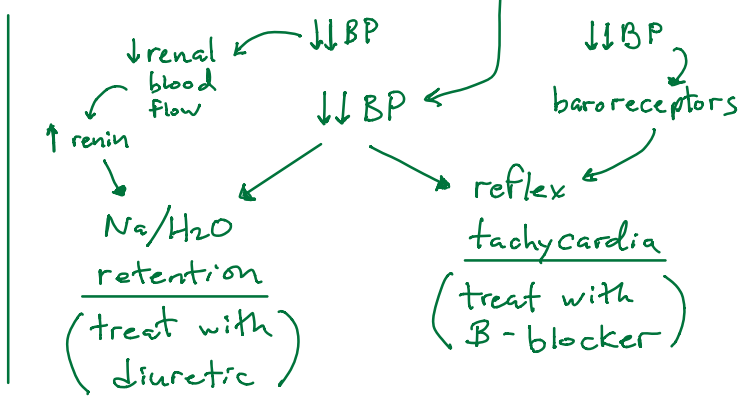
Note: #1 side effect of centrally-acting α_2 agonists is: sedation/drowsiness

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



(M) class

Antihypertensive Agents Used
for Hypertensive Urgencies/Emergencies

① Labetolol (Normadyne, Trandate) (IV)

α_1 }
 β_1 } blocks
 β_2 }

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

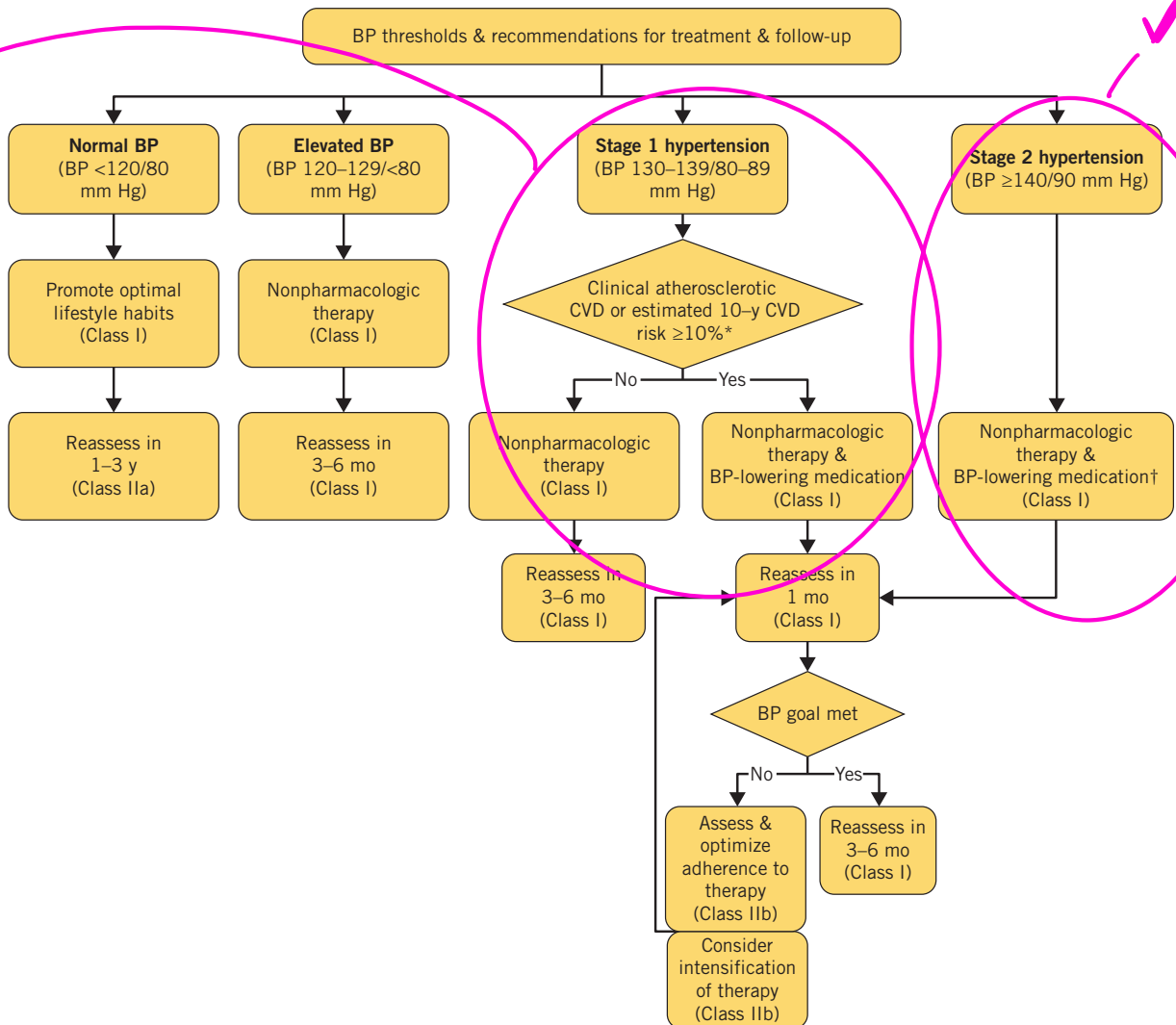
for SBP > 185/DBP > 110
indicated for Stroke

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	Stage 1 hypertension
140-159	90-99	Stage 2 hypertension	Stage 2 hypertension
≥160	≥100	Stage 2 hypertension	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.

① increase dose of initial drug ② add drug from different class ③ replace the initial drug with drug from a different class.

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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	
ARBs	Azilsartan	40-80	1	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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	
	Bisoprolol	2.5–10	1	
	Metoprolol tartrate	100–400	2	
	Metoprolol succinate	50–200	1	
Beta blockers—cardioselective and vasodilatory	Nebivolol	5–40	1	<ul style="list-style-type: none"> Induces nitric oxide-induced vasodilation Avoid abrupt cessation
Beta blockers—noncardioselective	Nadolol	40–120	1	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> 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)

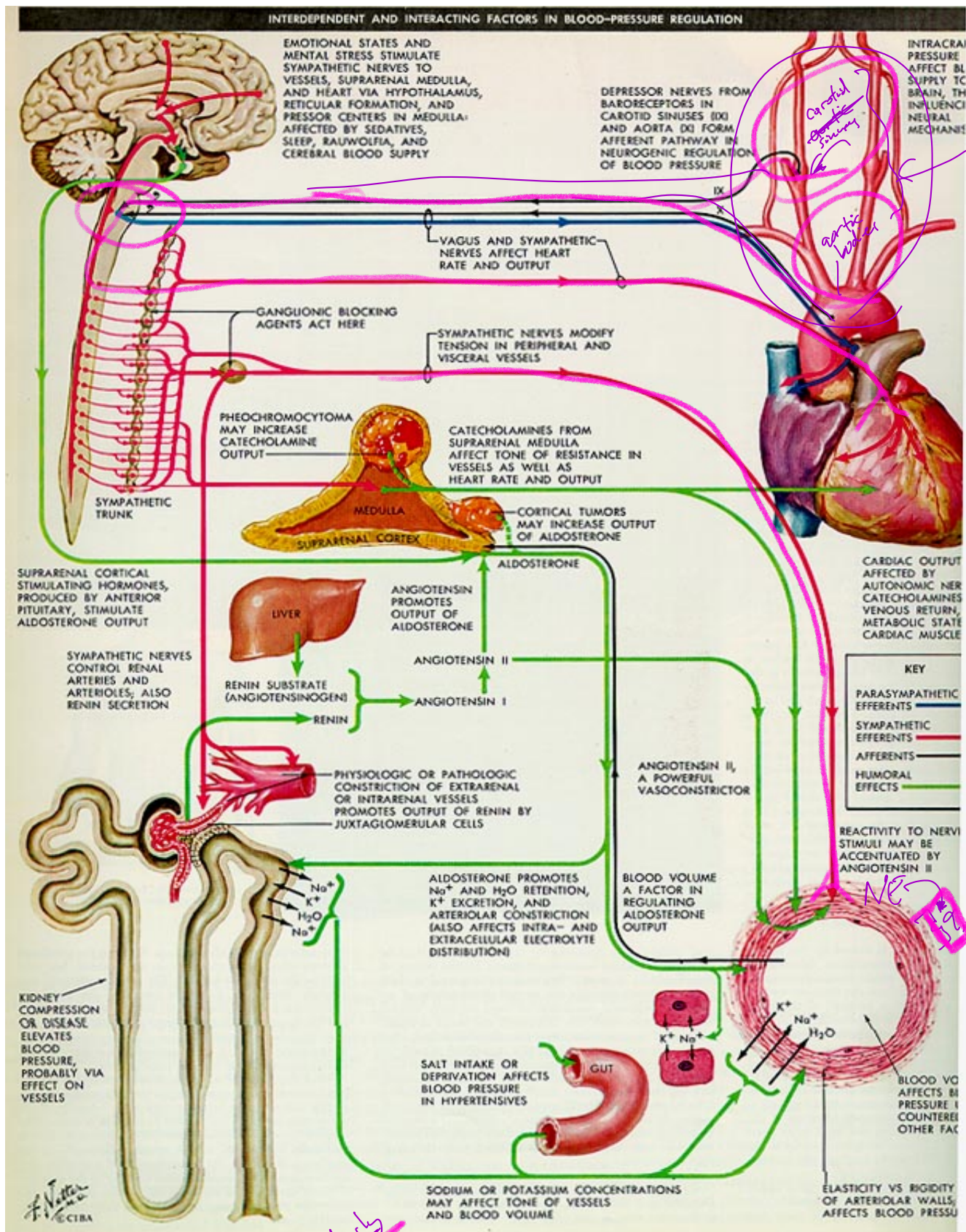
Class	Drug	Usual Dose, Range (mg per day)*	Daily Frequency	Comments
Secondary Agents (continued from previous page)				
Beta blockers—combined alpha- and beta-receptor	Carvedilol	12.5-50	2	<ul style="list-style-type: none"> • Carvedilol preferred in patients with HFrEF • Avoid abrupt cessation
	Carvedilol phosphate	20-80	1	
	Labetalol	200-800	2	
Direct renin inhibitor	Aliskiren	150-300	1	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • 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

Interdependent and Interacting Factors in Blood Pressure Regulation



Handwritten notes:
 ↑ Syncope ← ← ↑ vertigo ← ← ↑ dizziness