

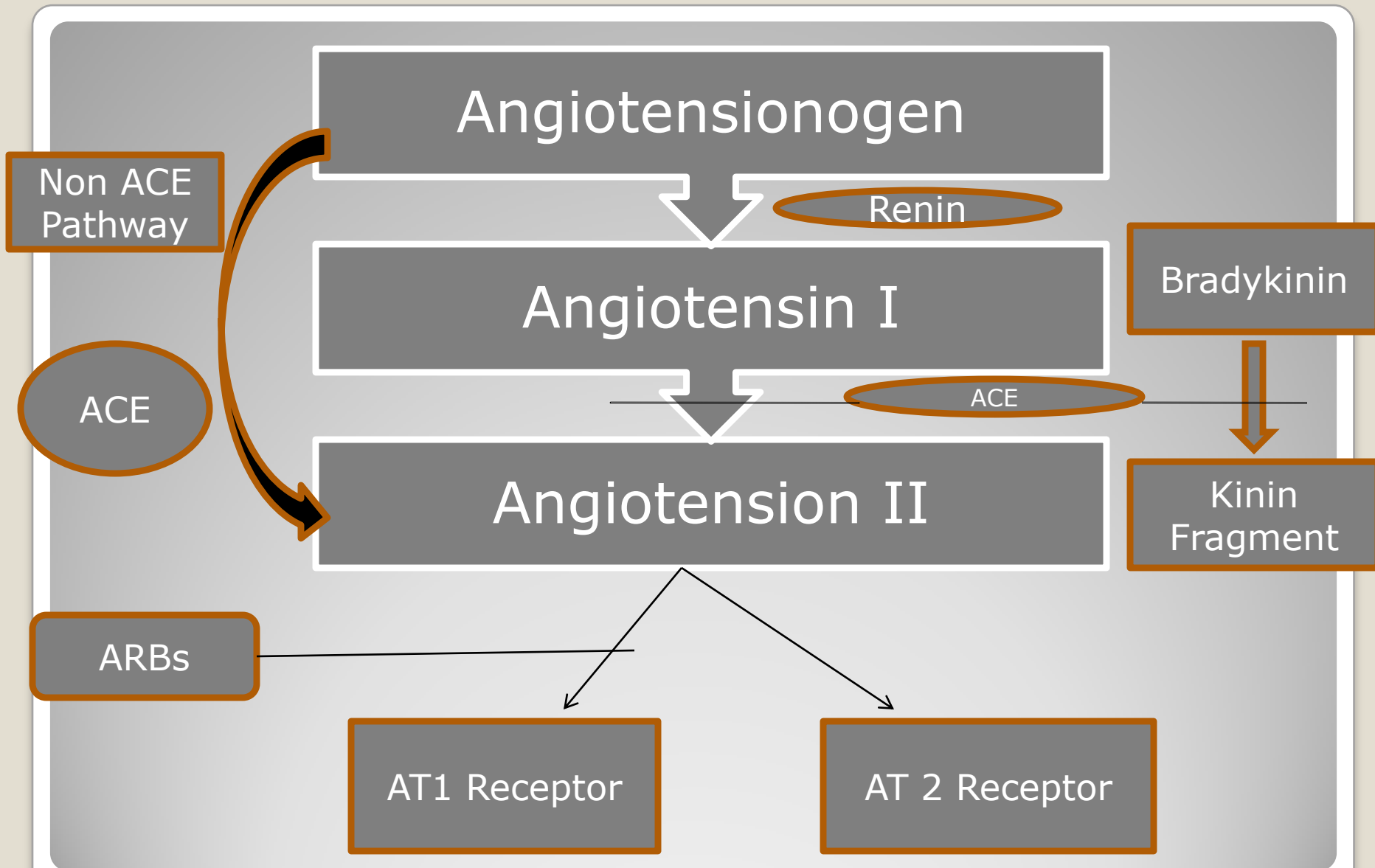
Hypertension

Roopa B.S
Lecturer, Department of Pharmacy Practice

- Persistent elevated arterial blood pressure.
- **Essential or Primary Hypertension** – Cause is unknown, cannot be cured but controlled.
- **Secondary Hypertension** - Cause is identifiable and potential to cure.

- The percentage of men having BP is higher when compared to women (before the age of 45 yrs)

1. RAAS
2. Natriuretic Hormone
3. Insulin Resistance and Hyperinsulinemia
4. Neuronal regulation.
5. Peripheral autoregulatory Components.
6. Vascular endothelial mechanisms
7. Electrolytes and other chemicals



AT1	AT2
Vasoconstriction	Action is less defined
Aldosterone	Effects is masked by AT1 mediated effects.
Vasopressin	
Sodium Retention	
Decrease renal perfusion	

- ANH is released in response to atrial stretch and a variety of other signals induced by hypervolemia and exercise.

Atrial Natriuretic Hormone

- Increased insulin concentrations lead to hypertension
- Insulin induce hypertrophy of vascular smooth muscle cells.
- Exact Mechanism is unknown

Insulin Resistance and Hyperinsulinemia

- When β_1 -receptors stimulated in the heart results in increase in heart rate and contractility.
- When β_2 -receptors stimulated in the arterioles and venules causes vasodilation.
- Stimulation of postsynaptic
- α -receptors (α_1) on arterioles and venules results in vasoconstriction.

NEURONAL REGULATION

- Renal defect in excretion of sodium.

PERIPHERAL AUTOREGULATORY COMPONENTS

- When there is deficiency in synthesis of vasodilating substances (prostacyclin and bradykinin)
- When excess vasoconstricting substances (angiotensin II and endothelin I) .
- Nitric oxide is produced in the endothelium, relaxes the vascular epithelium, and is a very potent vasodilator.

Lead to hypertension, atherosclerosis, and other CV diseases.

VASCULAR ENDOTHELIAL MECHANISMS

- Role of Sodium
- Calcium Increase- Vascular Resistance
- and Potassium depletion- Increase in vascular resistance.

ELECTROLYTES AND OTHER CHEMICALS

- Tachycardia
- Palpitation
- Headache
- Drowsiness
- Visual abnormalities
- Pain and edema in legs
- Sweating

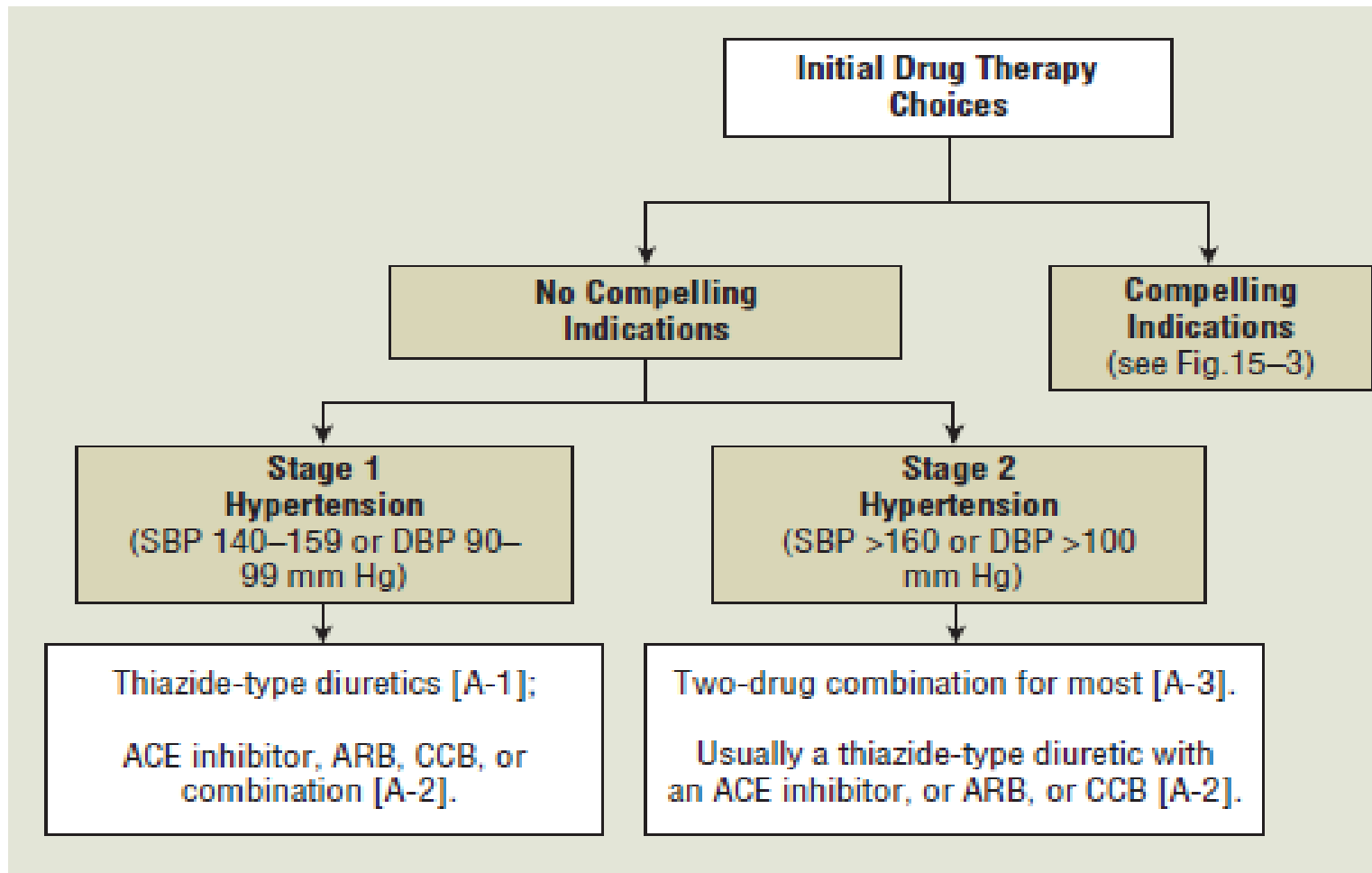
Clinical Presentation

TABLE 15-3**Classification of Blood Pressure in Adults
(Age ≥ 18 Years)^a**

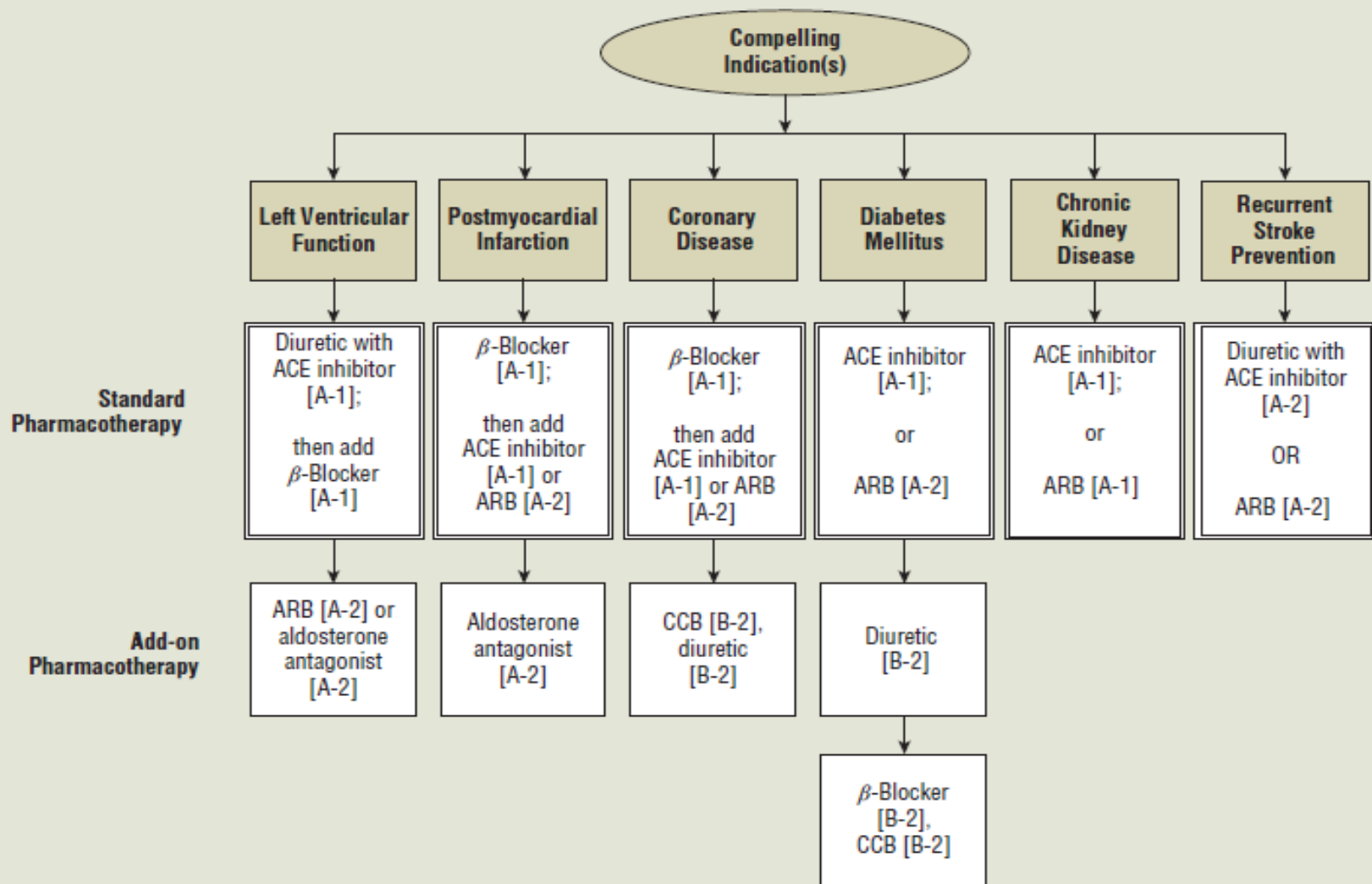
Classification	Systolic Blood Pressure (mm Hg)		Diastolic Blood Pressure (mm Hg)
Normal	<120	and	<80
Prehypertension ^b	120–139	or	80–89
Stage 1 hypertension	140–159	or	90–99
Stage 2 hypertension	≥ 160	or	≥ 100

TABLE 15-4 Lifestyle Modifications to Prevent and Manage Hypertension

Modification	Recommendation	Approximate Systolic Blood Pressure Reduction (mm Hg) ^a
Weight loss	Maintain normal body weight (body mass index 18.5–24.9 kg/m ²)	5–20 per 10-kg weight loss
DASH-type dietary patterns	Consume a diet rich in fruits, vegetables, and low-fat dairy products with a reduced content of saturated and total fat	8–14
Reduced salt intake	Reduce daily dietary sodium intake as much as possible, ideally to ≈ 65 mmol/day (1.5 g/day sodium, or 3.8 g/day sodium chloride)	2–8
Physical activity	Regular aerobic physical activity (at least 30 min/day, most days of the week)	4–9
Moderation of alcohol intake	Limit consumption to ≤ 2 drinks/day in men and ≤ 1 drink/day in women and lighter-weight persons	2–4



Treatment



- 3 visits, unless BP > 180/110
- Proper cuff size, arm supported at the level of the heart
 - Use the higher of two arms
 - Repeat after several minutes
 - **False positives**
 - Cigarettes, caffeine, pain, anxiety
 - Drugs: amphetamines, cocaine, cold remedies, NSAIDs, estrogen, glucocorticoids, TCAs, cyclosporine.
 - Consider “white coat” hypertension in patients with office-home mismatch (about 25% of patients with mild office HTN)

Diagnosis

- ☐ **Diuretics**
- ☐ **ACE inhibitors**
- ☐ **ARBs**
- ☐ **Calcium channel blockers**
- ☐ **β -Blockers**

Primary Antihypertensive drugs

- ❑ α 1-Blockers**
- ❑ Direct renin inhibitor**
- ❑ Central α 2-agonists**
- ❑ Peripheral adrenergic antagonist**
- ❑ Direct arterial vasodilators**

Alternative Antihypertensive agents

- **Four sub-class :**
- Thiazides, loops, potassium-sparing agents, and aldosterone antagonists.
- Diuretics act by diminishing sodium reabsorption at different sites in the nephron, thus increasing urinary sodium and water losses.
- Thiazide Diuretic- First line of Treatment.
- Potassium Sparing is weak Anti-Hypertensive, can be used to provide additive effect.

Diuretics

- Loop diuretics act in the thick ascending limb of the loop of Henle.
- Thiazide-type diuretics in the distal tubule and connecting segment (and perhaps the early cortical collecting tubule)
- Potassium-sparing diuretics in the aldosterone-sensitive principal cells in the cortical collecting tubule.
- Acetazolamide and mannitol act at least in part in the proximal tubule

Diuretics MOA

- Side effects :

Hypokalemia, hypomagnesemia,
hypercalcemia, hyperuricemia,
hyperglycemia.

- ACE inhibitors slows (inhibit) the activity of the enzyme ACE, which decreases the production of angiotensin II.
- Result, blood vessels enlarge or dilate, and blood pressure is reduced.

ACE Inhibitors

- **For high blood pressure:**
Benazepril, Enalapril, and Lisinopril
- **For heart failure:** Captopril, and Enalapril, Ramipril, and Trandolapril
- **After a heart attack:** Lisinopril
captopril, ramipril, and trandolapril
- **For diabetics:** Ramipril
- **For people with kidney disease:**
Benazepril, and Ramipril and
captopril,,

Drug (Generic Name)	People With Heart Failure		People Who Have Had a Heart Attack	People Who Have Diabetes and Other Heart Risk Factors		People with Kidney Disease	
	Reduce d Death	Improve Quality of Life	Reduce Death	Reduce Risk of hear attack or stroke	Reduce deaths	Reduce risk of Heart attack and stroke	Prevent decline in kidney function, kidney failure/ Reduce death
Benazepril	+						++
Captopril	++	++	++	++			++
Enalapril	++	++		+		++	
Fosinopril		++					
Lisinopril	+	++	++	++			
Moexipril							
Perindopril			0	++	0		
Quinapril					0		++
Ramipril	++	++	++	++	++	++	++
Trandolapril	++	++	++	++	++		

- ARBs do not block the breakdown of bradykinin. Therefore, some of the beneficial effects of bradykinin, such as vasodilation will not be seen with ARBs

ARB's

- Calcium channel blockers work by blocking voltage gated calcium channels in cardiac muscle and blood vessels. This decreases intracellular calcium leading to a reduction in muscle contraction.

Calcium Channel Blockers

- β -Blockers have negative chronotropic and inotropic cardiac effects that reduce cardiac output.
- Cardioselective β -blockers (e.g., atenolol, metoprolol).
- Propranolol and metoprolol undergo extensive first-pass metabolism, so the dose needed to attain β -blockade with either drug varies from patient to patient.
- Atenolol and Nadolol have are renally excreted. The dose of these agents may need to be reduced in patients with moderate to severe chronic kidney disease

Beta Blockers

- Prazosin, terazosin, and doxazosin are selective α_1 -receptor blockers.
- Inhibit the uptake of catecholamines in smooth muscle cells resulting in vasodilation and BP lowering

α_1 -Blockers

- ***Aliskiren***
- Directly Inhibits Renin at the point of activation and results in reduced plasma renin activity and BP lowering.

24 hour half life.

Direct Renin Inhibitor

- Clonidine, guanabenz, guanfacine, and methyldopa.
- Lower BP by stimulating α_2 -adrenergic receptors in the brain and reducing the sympathetic tone.

Central α_2 -Agonists.

- Hydralazine and minoxidil.
- Relax arteriolar smooth muscle resulting in vasodilation and BP lowering.

Direct Arterial Vasodilators

TABLE 15-5 Primary Antihypertensive Agents

Class	Subclass	Drug (Brand Name)	Usual Dose Range (mg/day)	Daily Frequency	Comments
Diuretics	Thiazides	Chlorthalidone (Hygroton)	12.5–25	1	Dose in the morning to avoid nocturnal diuresis; thiazides are more effective antihypertensives than loop diuretics in most patients; use usual doses to minimize adverse metabolic effects; ideally maintain potassium concentration between 4.0–5.0 mEq/L to minimize metabolic effects; hydrochlorothiazide and chlorthalidone are generally preferred, with 25 mg/day generally considered the maximum effective dose; chlorthalidone is nearly twice as potent as hydrochlorothiazide; have additional benefits in osteoporosis; may require additional monitoring in patients with a history of gout or hyperglycemia
		Hydrochlorothiazide (Microzide)	12.5–25	1	
		Indapamide (Lozol)	1.25–2.5	1	
		Metolazone (Zaroxolyn)	2.5–5	1	
	Loops	Bumetanide (Bumex)	0.5–4	2	Dose in the morning and afternoon to avoid nocturnal diuresis; higher doses may be needed for patients with severely decreased glomerular filtration rate or left ventricular dysfunction
		Furosemide (Lasix)	20–80	2	
		Torsemide (Demadex)	5–10	1	
	Potassium sparing	Amiloride (Midamor)	5–10	1 or 2	Dose in the morning or afternoon to avoid nocturnal diuresis; weak diuretics that are generally used in combination with thiazide-type diuretics to minimize hypokalemia; avoid in patients with severe chronic kidney disease (estimated glomerular filtration rate <30 mL/min/1.73 m ²); may cause hyperkalemia, especially in combination with an ACE inhibitor, ARB, direct renin inhibitor or potassium supplements
		Amiloride/hydrochlorothiazide (Moduretic)	5–10/50–100	1	
		Triamterene (Dyrenium)	50–100	1 or 2	
		Triamterene/hydrochlorothiazide (Dyazide)	37.5–75/25–50	1	
	Aldosterone antagonists	Eplerenone (Inspra)	50–100	1 or 2	Dose in the morning or afternoon to avoid nocturnal diuresis; eplerenone contraindicated in patients with an estimated creatinine clearance <50 mL/min, elevated serum creatinine (>1.8 mg/dL in women, >2 mg/dL in men), and type 2 diabetes with microalbuminuria; avoid spironolactone in patients with chronic kidney disease (estimated glomerular filtration rate <30 mL/min/1.73 m ²); may cause hyperkalemia, especially in combination with an ACE inhibitor, ARB, direct renin inhibitor or potassium supplements
		Spironolactone (Aldactone)	25–50	1 or 2	
		Spironolactone/hydrochlorothiazide (Aldactazide)	25–50/25–50	1	

ACE inhibitors		Benazepril (Lotensin)	10–40	1 or 2	Starting dose may be reduced 50% in patients who are on a diuretic, are volume depleted, or are very elderly because of risks of hypotension; may cause hyperkalemia in patients with chronic kidney disease or in those receiving potassium-sparing diuretics, aldosterone antagonists, ARB, or direct renin inhibitors; can cause acute kidney failure in patients with severe bilateral renal artery stenosis or severe stenosis in artery to solitary kidney; do not use in pregnancy or in patients with a history of angioedema
		Captopril (Capoten)	25–150	2 or 3	
		Enalapril (Vasotec)	5–40	1 or 2	
		Fosinopril (Monopril)	10–40	1	
		Lisinopril (Prinivil, Zestril)	10–40	1	
		Moexipril (Univasc)	7.5–30	1 or 2	
		Perindopril (Aceon)	4–16	1	
		Quinapril (Accupril)	10–80	1 or 2	
		Ramipril (Altace)	2.5–10	1 or 2	
ARBs		Trandolapril (Mavik)	1–4	1	Starting dose may be reduced 50% in patients who are on a diuretic, are volume depleted, or are very elderly because of risks of hypotension; may cause hyperkalemia in patients with chronic kidney disease or in those receiving potassium-sparing diuretics, aldosterone antagonists, ACE inhibitors, or direct renin inhibitor; can cause acute kidney failure in patients with severe bilateral renal artery stenosis or severe stenosis in artery to solitary kidney; do not cause a dry cough like ACE inhibitors may; do not use in pregnancy
		Candesartan (Atacand)	8–32	1 or 2	
		Eprosartan (Teveten)	600–800	1 or 2	
		Irbesartan (Avapro)	150–300	1	
		Losartan (Cozaar)	50–100	1 or 2	
		Olmесartan (Benicar)	20–40	1	
		Telmisartan (Micardis)	20–80	1	
Calcium channel blockers	Dihydropyridines	Valsartan (Diovan)	80–320	1	Short-acting dihydropyridines should be avoided, especially immediate-release nifedipine and nocardipine; dihydropyridines are more potent peripheral vasodilators than nondihydropyridines and may cause more reflex sympathetic discharge (tachycardia), dizziness, headache, flushing, and peripheral edema; have additional benefits in Raynaud's syndrome
		Amlodipine (Norvasc)	2.5–10	1	
		Felodipine (Plendil)	5–20	1	
		Isradipine (DynaCirc)	5–10	2	
		Isradipine SR (DynaCirc SR)	5–20	1	
		Nicardipine SR (Cardene SR)	60–120	2	
		Nifedipine long-acting (Adalat CC, Procardia XL)	30–90	1	
		Nisoldipine (Sular)	10–40	1	

TABLE 15-5 Primary Antihypertensive Agents (continued)

Class	Subclass	Drug (Brand Name)	Usual Dose Range (mg/day)	Daily Frequency	Comments	
β -Blockers	Nondihydropyridines	Diltiazem SR (Cardizem SR)	180–360	2	Extended-release and sustained-release products are preferred for hypertension; these agents block slow channels in the heart and reduce heart rate; may produce heart block, especially in combination with β -blockers; these products are not AB rated as interchangeable on a equipotent mg-per-mg basis because of different release mechanisms and different bioavailability parameters; Cardizem LA, Covera HS, and Verelan PM have delayed drug release for several hours after dosing; when dosed in the evening can provide chronotherapeutic drug delivery starting shortly before patients awake from sleep; have additional benefits in patients with atrial tachyarrhythmia	
		Diltiazem SR (Cardizem CD, Cartia XT, Dilacor XR, Diltia XT, Tiazac, Taztia XT)	120–480	1		
		Diltiazem ER (Cardizem LA)	120–540	1 (morning or evening)		
		Verapamil SR (Calan SR, Isoptin SR, Verelan)	180–480	1 or 2		
		Verapamil ER (Covera HS)	180–420	1 (in the evening)		
		Verapamil oral drug absorption system ER (Verelan PM)	100–400	1 (in the evening)		
	Cardioselective	Atenolol (Tenormin)	25–100	1	Abrupt discontinuation may cause re-bound hypertension; inhibit β_1 -receptors at low to moderate dose, higher doses also block β_2 -receptors; may exacerbate asthma when selectivity is lost; have additional benefits in patients with atrial tachyarrhythmia or preoperative hypertension	
		Betaxolol (Kerlone)	5–20	1		
		Bisoprolol (Zebeta)	2.5–10	1		
		Metoprolol tartrate (Lopressor)	100–400	2		
		Metoprolol succinate (Toprol XL)	50–200	1		
		Nonselective	Nadolol (Corgard)	40–120		1
			Propranolol (Inderal)	160–480	2	
			Propranolol long-acting (Inderal LA, InnoPran XL)	80–320	1	
			Timolol (Blocadren)	10–40	1	
		Intrinsic sympathomimetic activity	Acebutolol (Sectral)	200–800	2	Abrupt discontinuation may cause rebound hypertension; partially stimulate β -receptors while blocking against additional stimulation; no clear advantage for these agents; contraindicated in patients with coronary disease or post-myocardial infarction
			Carteolol (Cartrol)	2.5–10	1	
			Penbutolol (Levatol)	10–40	1	
			Pindolol (Visken)	10–60	2	
		Mixed α - and β -blockers	Carvedilol (Coreg)	12.5–50	2	Abrupt discontinuation may cause rebound hypertension; additional α -blockade produces more orthostatic hypotension
			Carvedilol phosphate (Coreg CR)	20–80	1	
			Labetalol (Normodyne, Trandate)	200–800	2	

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blocker; ER, extended-release; SR, sustained-release.

- **Preeclampsia:** $>140/90$ mmHg after 20 weeks' gestation with proteinuria
 - restricted activity, bed rest, close monitoring beneficial
 - definitive treatment: delivery.

Eclampsia : Convulsions + Preeclampsia.

- **Gestational HTN** : new-onset hypertension arising after mid pregnancy in the absence of proteinuria

Hypertension in Pregnancy

Chronic HTN in Pregnancy

Drug/Class	Comments
Methyldopa	Preferred based on long-term follow-up data supporting safety
β -Blockers	Generally safe, but intrauterine growth retardation reported
Labetolol	Increasingly preferred over methyldopa because of fewer side effects
Clonidine	Limited data
Calcium channel blockers	Limited data; no increase in major teratogenicity with exposure
Diuretics	Not first-line, probably safe in low doses
ACE inhibitors, ARBs	Major teratogenicity has been reported with exposure (fetal toxicity, death)

- Beta Blockers are avoided.
- ACEI's OR CCB

Pulmonary Disease and Peripheral Arterial Disease

- Adjust Maintenance therapy and adding new antihypertensive drug.
- Oral captopril is one of the agents of choice and can be used in doses of 25 to 50 mg at 1- to 2-hour intervals.
- The onset of action of oral captopril is 15 to 30 minutes

Hypertensive Urgency

- Parenteral therapy

Hypertensive Emergency

- Failure to achieve goal BP in patients who are adhering to full doses of an appropriate three-drug regimen that includes a diuretic.

RESISTANT HYPERTENSION

TABLE 15-8 Parenteral Antihypertensive Agents for Hypertensive Emergency

Drug	Dose	Onset (min)	Duration (min)	Adverse Effects	Special Indications
Sodium nitroprusside	0.25–10 mcg/kg/min intravenous infusion (requires special delivery system)	Immediate	1–2	Nausea, vomiting, muscle twitching, sweating, thiocyanate and cyanide intoxication	Most hypertensive emergencies; caution with high intracranial pressure, azotemia, or in chronic kidney disease
Nicardipine hydrochloride	5–15 mg/h intravenous	5–10	15–30; may exceed 240	Tachycardia, headache, flushing, local phlebitis	Most hypertensive emergencies except acute heart failure; caution with coronary ischemia
Fenoldopam mesylate	0.1–0.3 mcg/kg/min intravenous infusion	<5	30	Tachycardia, headache, nausea, flushing	Most hypertensive emergencies; caution with glaucoma
Nitroglycerin	5–100 mcg/min intravenous infusion	2–5	5–10	Headache, vomiting, methemoglobinemia, tolerance with prolonged use	Coronary ischemia
Hydralazine hydrochloride	12–20 mg intravenous 10–50 mg intramuscular	10–20 20–30	60–240 240–360	Tachycardia, flushing, headache, vomiting, aggravation of angina	Eclampsia
Labetalol hydrochloride	20–80 mg intravenous bolus every 10 min; 0.5–2.0 mg/min intravenous infusion	5–10	180–360	Vomiting, scalp tingling, bronchoconstriction, dizziness, nausea, heart block, orthostatic hypotension	Most hypertensive emergencies except acute heart failure
Esmolol hydrochloride	250–500 mcg/kg/min intravenous bolus, then 50–100 mcg/kg/min intravenous infusion; may repeat bolus after 5 minutes or increase infusion to 300 mcg/min	1–2	10–20	Hypotension, nausea, asthma, first-degree heart block, heart failure	Aortic dissection; perioperative