

Introduction

1-Hypertension is defined as **persistently elevated arterial blood pressure (BP)**. (See **Table -1** for the classification of BP in adults).

Table-1: Classification of Blood Pressure in Adults

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

2-**Isolated systolic hypertension** is diastolic blood pressure (DBP) <80 mm Hg and systolic blood pressure (SBP) ≥130 mm Hg.

3-**Hypertensive crisis** (BP >180/120 mm Hg) is categorized as **hypertensive emergency** (extreme BP elevation **with acute or progressing end-organ damage**. **End organ damage usually refers to damage occurring in major organs fed by the circulatory system (heart, kidneys, brain, eyes) which can sustain damage due to uncontrolled hypertension, hypotension, or hypovolemia**) or **hypertensive urgency** (extreme BP elevation **without acute or progressing end-organ injury**).

Pathophysiology

1-Hypertension may result from an unknown etiology (**primary or essential hypertension**) or from a specific cause (**secondary hypertension**).

2-Secondary hypertension (<10% of cases) is usually caused by **chronic kidney disease (CKD) or renovascular disease**.

3-**Examples of drugs that may increase BP include** corticosteroids, estrogens, NSAIDs, cyclosporine, erythropoietin, and venlafaxine.

4-Factors contributing to development of primary hypertension include: **Humoral abnormalities** [involving the renin–angiotensin–aldosterone system (RAAS)], **disturbances in the CNS**, **Abnormalities in renal system**, **Deficiency in synthesis of vasodilating substances** in vascular endothelium or **excess vasoconstricting substances**, and **high sodium intake or lack of dietary calcium**.

5-Major causes of death include cerebrovascular events, cardiovascular (CV) events, and renal failure. Probability of premature death correlates with the severity of BP elevation.

Clinical presentation

1-Patients with **uncomplicated primary hypertension are usually asymptomatic initially**.

2-Patients with **secondary hypertension** may have **symptoms of the underlying disorder**.

Diagnosis

1-Elevated BP may be the only sign of primary hypertension on physical examination.

2-Diagnosis should be based on the average of **two or more readings taken at each of two or more clinical encounters**.

3-**Signs of end-organ damage occur primarily in the eyes, brain, heart, kidneys, and peripheral vasculature**.

4-**Laboratory tests:** Blood urea nitrogen (BUN), serum creatinine with estimated glomerular filtration rate (eGFR), fasting lipid panel, fasting blood glucose, serum electrolytes (sodium, potassium, calcium), uric acid, hemoglobin and hematocrit (**the ratio of the volume of red blood cells to the total volume of blood.**), and spot urine albumin-to-creatinine ratio. A 12-lead electrocardiogram (ECG) should also be obtained.

Treatment

1-Goals of Treatment: The overall goal is to reduce morbidity and mortality from CV events. The 2017 ACC/AHA (**American College of Cardiology (ACC) and American Heart Association**) guideline recommends a goal BP of **<130/80 mm Hg for most patients**.

2-For older ambulatory, community-dwelling patients, the goal is SBP <130 mm Hg. For **institutionalized older patients and those with a high disease burden or limited life expectancy**, consider a relaxed SBP goal of **<150 mm Hg (or <140 mm Hg if tolerated)**.

Nonpharmacologic Therapy

A-Implement lifestyle modifications in all patients with elevated BP or stage 1 or 2 hypertension.

B-These measures alone are appropriate initial treatment for patients with elevated BP or stage 1 hypertension who are at low risk of ASCVD (**atherosclerotic cardiovascular disease**) (ie, primary prevention with a 10-year ASCVD risk <10%). Start drug therapy for these patients when BP is $\geq 140/90$ mm Hg.

C-For patients with stage 1 or 2 hypertension who already have ASCVD (secondary prevention) or an elevated 10-year ASCVD risk $\geq 10\%$, **the threshold for starting drug therapy is $\geq 130/80$ mm Hg with a goal BP of <130/80 mm Hg**.

D-Lifestyle modifications shown to lower BP include:

(1) **weight loss** if overweight or obese, (2) the Dietary Approaches to Stop Hypertension (**DASH**) eating plan, (3) **reduced salt intake**, ideally to 1.5 g/day sodium (3.8 g/day sodium chloride), (4) **physical activity** (90–150 min/week of aerobic or dynamic resistance training), and (5) **moderation of alcohol intake** (≤ 2 drinks/day in men and ≤ 1 drink/day in women). Although **smoking** cessation does not control BP, it reduces CV disease risk and **should be encouraged**.

Pharmacologic Therapy

General Approach to Treatment

1-Initial drug selection depends on the **degree of BP elevation** and presence of **compelling indications** for certain drugs.

2-Use a **single first-line drug** as initial therapy in most patients with newly diagnosed **stage 1 hypertension**.

3-Start **combination drug therapy** (preferably with two first-line drugs) as the initial regimen in patients with newly diagnosed **stage 2 hypertension**.

4-The **four first-line options** are angiotensin-converting enzyme (**ACE**) inhibitors, angiotensin II receptor blockers (**ARBs**), calcium channel blockers (**CCBs**), and **thiazide diuretics**.

5- **β -Blockers** should be reserved to treat a **specific compelling indication** or in **combination** with a first-line antihypertensive agent for patients without a compelling indication.

6-**Other antihypertensive** drug classes (α 1-blockers, direct renin inhibitors, central α 2-agonists, and direct arterial vasodilators) may be used for select patients **after implementing first-line agents**.

Compelling Indications

Compelling indications are **specific comorbid conditions for which clinical trial data support using specific antihypertensive drug classes to treat both hypertension and the compelling indication**. Selection of drug therapy should follow an evidence-based order.

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A-Heart Failure with Reduced Ejection Fraction (HFrEF)

1-Guideline-directed medical therapy consists of three to four drugs: **ACE inhibitor or ARB plus diuretic**, followed by addition of an evidence-based **β -blocker** and **possibly a mineralocorticoid receptor antagonist**. (**Spironolactone and eplerenone**)

2-Start an **ACE inhibitor or ARB in low doses to avoid orthostatic hypotension** because of the high renin state in HF.

3-**Diuretics reduce edema**, and **loop diuretics** are often needed, especially in patients with advanced HF and/or CKD.

4- **β -Blockers are part of standard treatment**. Because of the risk of exacerbating HF, β -blockers must be **started in very low doses and titrated slowly to high doses based on tolerability**.

5-**Bisoprolol, carvedilol, and metoprolol succinate** are the only β -blockers **proven** to be beneficial in HFrEF.

6-After implementation of a standard three-drug regimen, other agents may be added to further reduce CV morbidity and mortality, and reduce BP if needed. **A mineralocorticoid receptor antagonist** (spironolactone or eplerenone) may be considered at this point.

B-Heart Failure with Preserved Ejection Fraction (HFpEF)

1-Unlike interventions in HFrEF that decrease morbidity and mortality, **trials using the same medications in HFpEF have not shown similar benefits.**

2-Therefore, treatment **should be targeted at signs and symptoms** (eg, dyspnea, fatigue, edema), appropriate management of underlying coronary artery disease, and attainment of goal BP to prevent HF progression.

3-Patients should use a **β -blocker or an ACE inhibitor (or ARB) for treatment of hypertension**, and they should receive a **diuretic if signs and symptoms of edema are present.**

C-Stable Ischemic Heart Disease (SIHD)

1- **β -Blockers (without ISA) (intrinsic sympathomimetic activity) (characterizes a group of beta blockers that are able to stimulate beta-adrenergic receptors (agonist effect) and to oppose the stimulating effects of catecholamines (antagonist effect) in a competitive way).** are first-line therapy in SIHD; they reduce BP and improve angina symptoms by decreasing myocardial oxygen consumption and demand.

2- **β -Blockers should be used for hypertension treatment in patients with SIHD.** An ACE inhibitor or ARB has been shown to reduce CV events as an add-on to a β -blocker.

3-**A long-acting nondihydropyridine CCB (calcium channel blockers, Diltazem) is an alternative to a β -blocker in SIHD**, but β -blockers are the therapy of choice. A dihydropyridine CCB (**amlodipine**) may be considered as **add-on therapy in SIHD patients who have ongoing ischemic symptoms** (but cardiac stimulation makes these agents less desirable).

4-**For acute coronary syndromes, first-line therapy includes a β -blocker and ACE inhibitor (or ARB).**

D-Diabetes Mellitus

1-**All four first-line antihypertensive classes** (ACE inhibitors, ARBs, CCBs, thiazides) reduce CV events in patients with diabetes, with no evidence of difference in all-cause mortality, CV mortality, HF, or stroke.

2-The risk of kidney disease progression is low in the absence of albuminuria (urine albumin-to-creatinine ratio ≥ 30 mg/g [3.4 mg/mmol creatinine]). **Therefore, any first-line agent can be used to control hypertension in patients with diabetes in the absence of albuminuria.**

3-Regardless of the initial agent selected, most patients require combination therapy, which **typically includes an ACE inhibitor (or ARB) with a CCB or thiazide.**

4-After first-line agents, a β -blocker is a useful add-on therapy for BP control in patients with diabetes. However, they **may mask symptoms of hypoglycemia** (tremor, tachycardia, and palpitations **but not sweating**) in tightly controlled patients, and delay recovery from hypoglycemia **Despite these potential problems, β -blockers can be used safely in patients with diabetes.**

E-Chronic Kidney Disease

1-In addition to lowering BP, **ACE inhibitors and ARBs reduce intraglomerular pressure, which may further slow CKD progression.**

2-**Start with low doses and evaluate the serum creatinine soon after starting therapy** to minimize the risk of rapid and profound BP drops that could precipitate acute kidney injury (AKI).

F-Secondary Stroke Prevention

1-A **thiazide diuretic, either alone or combined with an ACE inhibitor,** is recommended for patients with history of stroke or transient ischemic attack.

2-The threshold for starting antihypertensive drug therapy in patients **with a history of stroke is when BP is >140/90 mm Hg** (goal of <130/80 mm Hg).

FIRST-LINE ANTIHYPERTENSIVE AGENTS

Angiotensin-Converting Enzyme Inhibitors (captopril, enalapril, fosinopril, imidapril, lisinopril, perindopril, quinapril, ramipril, andtrandolapril)

1-ACE inhibitors block conversion of angiotensin I to angiotensin II, a potent vasoconstrictor and stimulator of aldosterone secretion.

2-**Starting doses should be low with slow dose titration.** Acute hypotension may occur at the onset of therapy.

3-ACE inhibitors decrease aldosterone and can increase serum potassium concentrations. **Hyperkalemia** occurs primarily in patients with CKD or those also taking potassium supplements, potassium-sparing diuretics, mineralocorticoid receptor antagonists, ARBs, or direct renin inhibitors.

4-**AKI is an uncommon but serious side effect;** preexisting kidney disease increases risk. Bilateral renal artery stenosis or unilateral stenosis renders patients dependent on the vasoconstrictive effect of angiotensin II on efferent arterioles, making them particularly susceptible to AKI.

5-Serum creatinine concentrations often increase, but modest elevations (eg, absolute increases <1 mg/dL) **do not warrant treatment changes.** Discontinue therapy or reduce dose if larger increases occur.

6-**Angioedema occurs in <1% of patients.** Drug withdrawal is necessary, and some patients may require drug treatment and/or emergent intubation to support respiration.

Angioedema is an area of swelling (edema) of the lower layer of skin and tissue just under the skin or mucous membranes. The swelling may occur in the face, tongue, larynx, abdomen, or arms and legs.

7-An **ARB can generally be used in patients with a history of ACE inhibitor-induced angioedema,** with careful monitoring.

8-A **persistent dry cough** occurs in up to 20% of patients and is thought to be due to inhibition of bradykinin breakdown.

10-ACE inhibitors (as well as ARBs and direct renin inhibitors) are contraindicated in pregnancy.

Angiotensin II Receptor Blockers (candesartan, eprosartan, irbesartan, losartan, olmesartan, telmisartan, and valsartan)

1-The ARBs directly block the angiotensin II type 1 receptor that mediates the effects of angiotensin II.

2-Unlike ACE inhibitors, **ARBs do not block bradykinin breakdown and this accounts for the lack of cough as a side effect.**

3-The combination of an ACE inhibitor and ARB has no additional benefit but is associated with a higher risk of side effects and should be avoided.

4-**All ARBs have similar antihypertensive efficacy.** Addition of a CCB or thiazide diuretic significantly increases antihypertensive efficacy.

5-ARBs have a low incidence of side effects. Like ACE inhibitors, they may cause renal **insufficiency, hyperkalemia, and orthostatic hypotension.**

Calcium Channel Blockers

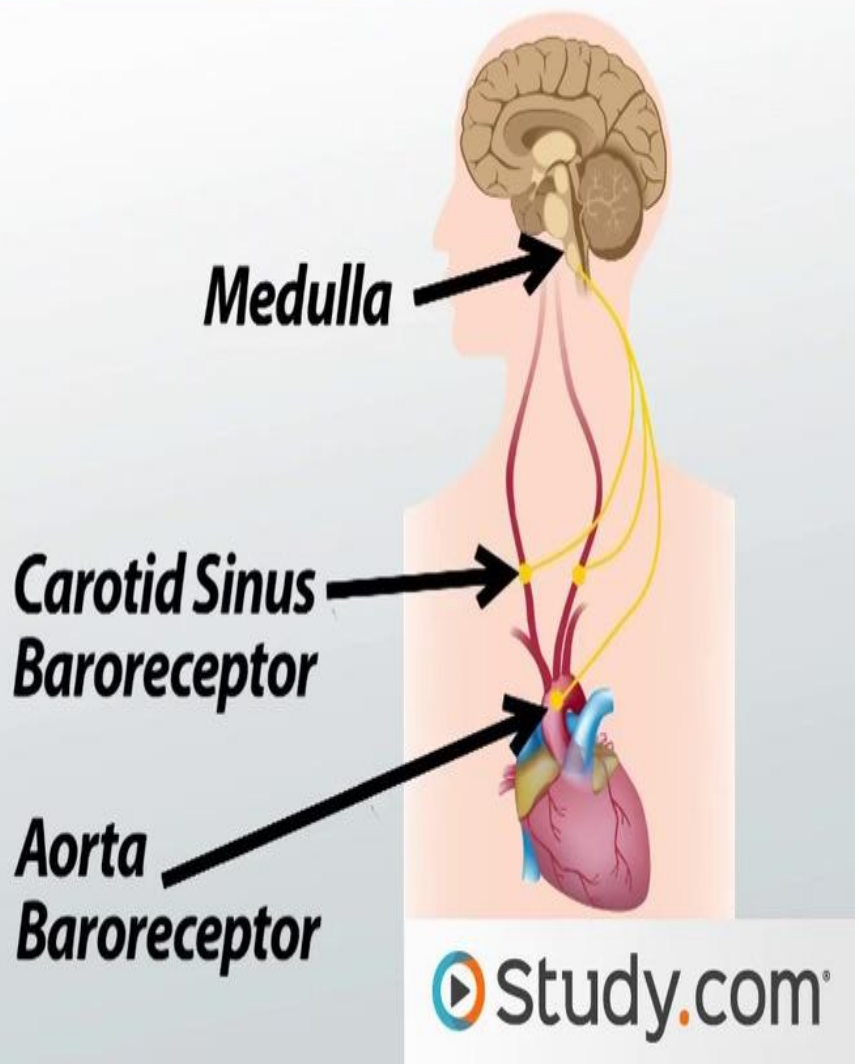
1-Dihydropyridine and nondihydropyridine CCBs are first-line antihypertensive therapies and are also used in addition to or instead of other first-line agents for the compelling indication of ischemic heart disease.

2-Dihydropyridine CCBs may cause reflex sympathetic activation, (leads to physiological arousal – increased vigilance, heart rate, and blood flow to the skeletal muscles, and decreased blood flow to the gastrointestinal system and skin (which is why arousal leads to cold hands and feet)) and all agents (**except amlodipine and felodipine**) may have negative inotropic effects. (vascular smooth muscle relaxation (vasodilation), decreased myocardial force generation (negative inotropy),

3-**Verapamil** decreases heart rate, slows atrioventricular (AV) nodal conduction, and produces a negative inotropic effect that may precipitate HF in patients with borderline cardiac reserve. **Diltiazem decreases AV conduction and heart rate to a lesser extent than verapamil.**

4-**Diltiazem and verapamil can cause cardiac conduction abnormalities** such as bradycardia, AV block, and HF. Both can cause peripheral edema and hypotension. Verapamil causes **constipation** in about 7% of patients.

5-Dihydropyridines cause a baroreceptor-mediated reflex increase in heart rate because of potent peripheral vasodilating effects. Dihydropyridines do not decrease AV node conduction and are not effective for treating supraventricular tachyarrhythmias.



6-Short-acting nifedipine may rarely increase *وتيرة* frequency, intensity *وشدة* , and duration of angina in association with acute hypotension. This effect may be obviated *تجنب* by using **sustained-release formulations of nifedipine or other dihydropyridines.**

7-Other side effects of dihydropyridines are dizziness, flushing, headache, gingival hyperplasia, and peripheral edema.



peripheral edema

Diuretics

1-**Thiazides are the preferred type of diuretic and are a first-line option for most patients with hypertension.** Chlorthalidone (thiazide-like) is preferred over hydrochlorothiazide, especially in resistant hypertension, because it is more potent on a milligram-per-milligram basis. **Potency refers to the amount (mg, g, moles, etc.) of drug needed to produce a level of effect. Relative potency is the ratio of the amounts of each needed to produce the specified effect. Thus, one drug, the standard (S), is assigned unit potency and the second drug (U) is compared to that of S**

2-**Loop diuretics (Furosemide, Bumetanide and Torsemide) are more potent for inducing diuresis but are not ideal antihypertensives unless edema treatment is also needed.** Loop diuretics are sometimes required over thiazides in patients with severe CKD when eGFR is $<30 \text{ mL/min/1.73 m}^2$, especially when edema is present.

3-**Potassium-sparing diuretics are weak antihypertensives when used alone** and provide minimal additive effect when combined with a thiazide or loop diuretic. Their primary use is in combination with another diuretic **to counteract potassium-wasting properties.**

4-Mineralocorticoid receptor antagonists (spironolactone and eplerenone) are also potassium-sparing diuretics that are usually **used to treat resistant hypertension because elevated aldosterone concentrations are prevalent in this setting.** They are also used as add-on agents in patients with **HFrEF** with or without concomitant hypertension.

5-Acutely, diuretics lower BP by causing diuresis. With chronic therapy, **reduced peripheral vascular resistance** is responsible for persistent hypotensive effects.

6-Combining diuretics with other antihypertensive agents usually results in an **additive hypotensive effect** because of independent mechanisms of action. Furthermore, many nondiuretic antihypertensive agents induce sodium and water retention, which is counteracted by concurrent diuretic use.

7-**Side effects of thiazides** include hypokalemia, hypomagnesemia, hypercalcemia, hyperuricemia, hyperglycemia, dyslipidemia, and sexual dysfunction.

8-Loop diuretics have less effect on serum lipids and glucose, but hypokalemia is more pronounced, and **hypocalcemia may occur.**

9-Hypokalemia and hypomagnesemia may cause muscle fatigue or cramps, and severe electrolyte abnormalities may result in serious cardiac arrhythmias. Low-dose therapy causes less electrolyte disturbances than higher doses.

10-**Potassium-sparing diuretics may cause hyperkalemia,** especially in patients with CKD or diabetes and in patients receiving concurrent treatment with a mineralocorticoid receptor antagonist, ACE inhibitor, ARB, direct renin inhibitor, or potassium supplement.

11-**Spironolactone may cause gynecomastia** in up to 10% of patients; this effect occurs rarely with eplerenone.

ALTERNATIVE ANTIHYPERTENSIVE AGENTS

β -Blockers

1-Evidence suggests وتشير الأدلة that β -blockers may not reduce CV events as well as ACE inhibitors, ARBs, CCBs, or thiazides when used as the initial drug in patients who do not have a compelling indication for a β -blocker.

2- β -Blockers are appropriate **first-line agents when used to treat specific compelling indications** or when an ACE inhibitor, ARB, CCB, or thiazide cannot be used.

3- β -Blockers also have an important role as add-on therapy to first-line agents in patients with hypertension but no compelling indications.

4-Atenolol, betaxolol, bisoprolol, metoprolol, and nebivolol are β_1 -cardioselective at low. As a result, they are **less likely to provoke bronchospasm and vasoconstriction** and are safer than nonselective β -blockers in patients with asthma or diabetes who have a compelling indication for a β -blocker. Cardioselectivity is a dose-dependent phenomenon, and the effect is lost at higher doses.

5-Acebutolol, carteolol, and **pindolol** possess **intrinsic sympathomimetic activity (ISA)** or partial β -receptor agonist activity. Theoretically, these drugs may have advantages in select patients with HF or sinus bradycardia. Unfortunately, **they do not reduce CV events as well as other β -blockers and may increase CV risk in patients with SIHD. Thus, agents with ISA are rarely needed and have no role in hypertension management.**

6-Atenolol and nadolol have **relatively long half-lives and are excreted renally**; the dosage may need to be reduced in patients with renal insufficiency.

7-Even though the half-lives of other β -blockers are shorter, once-daily administration still may be effective.

8-Cardiac side effects include bradycardia, AV conduction abnormalities, and acute HF. Blocking β_2 -receptors in arteriolar smooth muscle may cause cold extremities and aggravate intermittent claudication or Raynaud phenomenon because of decreased peripheral blood flow. **Raynaud's Phenomenon is a process in which the fingers (and less commonly, the toes) turn different colors (white, blue, and red) in response to certain triggers such as cold or stress.** It can be associated with discomfort or a “pins and needles” sensation



9-Increases in serum lipids and glucose appear to be transient and of little clinical significance.

10-**Abrupt cessation of β -blocker therapy can produce cardiac ischemia** (angina, chest pain), a CV event, or even death in patients with coronary artery disease. In patients without heart disease, abrupt discontinuation of β -blockers may be associated with tachycardia, sweating, and generalized malaise in addition to increased BP. **For these reasons, the dose should always be tapered gradually over 1–2 weeks before discontinuation.**

α 1-Receptor Blockers

1-Prazosin, terazosin, and doxazosin are selective α 1-receptor blockers that inhibit catecholamine uptake in smooth muscle cells of peripheral vasculature, resulting in vasodilation and BP lowering.

2-A **first-dose phenomenon characterized by orthostatic hypotension** accompanied by transient dizziness or faintness, palpitations, and even syncope **الاغماء** may occur within 1–3 hours of the first dose or after later dosage increases.

3-The patient should take the first dose (and subsequent first increased doses) at **bedtime**. Occasionally, orthostatic hypotension and dizziness persist with chronic administration.

4-Sodium and water retention can occur; these agents are most effective when given with a thiazide to maintain antihypertensive efficacy and minimize edema.

5-These agents block postsynaptic α 1-adrenergic receptors on the prostate capsule, causing relaxation and decreased resistance to urinary outflow. Although they can provide symptomatic benefit in men with benign prostatic hyperplasia, **they should be used to lower BP only in combination with first-line antihypertensive agents.**

Direct Renin Inhibitor

Aliskiren blocks the RAAS (The **Renin-Angiotensin-Aldosterone System**) at its point of activation, resulting in reduced plasma renin activity and BP. It is approved for monotherapy or in combination therapy. **Its role in the management of hypertension is limited.**

Central α 2-Agonists

1-**Clonidine, guanfacine, and methyldopa** lower BP primarily by stimulating α 2-adrenergic receptors in the brain, which reduces sympathetic outflow from the vasomotor center. **(it stimulates the sympathetic system to constrict vessels).**

2-Clonidine is often used in resistant hypertension, and **methyldopa is frequently used for pregnancy-induced hypertension.**

3-Chronic use results in sodium and fluid retention. Other side effects include depression, orthostatic hypotension, dizziness, and anticholinergic effects (eg, dry mouth, sedation). **Abrupt cessation may lead to rebound hypertension**

4-Methyldopa rarely causes hepatitis or hemolytic anemia. A transient elevation in hepatic transaminases occasionally occurs. Discontinue therapy if persistent increases in liver function tests occur, because this may herald onset of fulminant **الخاطف**, life-threatening hepatitis. **Coombs-positive hemolytic anemia occurs rarely**, and 20% of patients exhibit a

positive direct Coombs test without anemia. **For these reasons, methyldopa has limited usefulness except in pregnancy.**

Direct Arterial Vasodilators

1-**Hydralazine** and **minoxidil** directly relax arteriolar smooth muscle, resulting in vasodilation and BP lowering. Compensatory activation of baroreceptor reflexes increases sympathetic outflow, thereby increasing heart rate, cardiac output, and renin release. **Consequently, hypotensive effectiveness of direct vasodilators diminishes over time unless the patient is also taking a diuretic and a β -blocker.**

2-Direct vasodilators can precipitate angina in patients with underlying SIHD unless the baroreceptor reflex mechanism is blocked with a β -blocker. Nondihydropyridine CCBs can be used as an alternative to β -blockers in patients with contraindications to β -blockers.

3-**Hydralazine may cause a dose-related, reversible lupus-like syndrome**, which is more common in slow acetylators (**association hydralazine-induced lupus in slow acetylators. Presumably, this is because acetylation of the aromatic amine or hydrazine functional group leads to a non-toxic product**) . Lupus-like reactions

Lupus Symptoms

- Muscle and joint pain.
- Fatigue.
- Blurred vision.
- Fever.
- General ill feeling (malaise)
- Joint swelling.
- Loss of appetite.
- Pleuritic chest pain

can usually be avoided by limiting the maximum total daily dose to 200 mg. Because of side effects, hydralazine has limited usefulness for chronic hypertension management.

4-**Minoxidil cause reversible hypertrichosis** فرط الشعر on the face, arms, back, and chest may be troublesome. Minoxidil is reserved for resistant hypertension and for patients requiring hydralazine who experience drug-induced lupus.

SPECIAL POPULATIONS

Older Persons

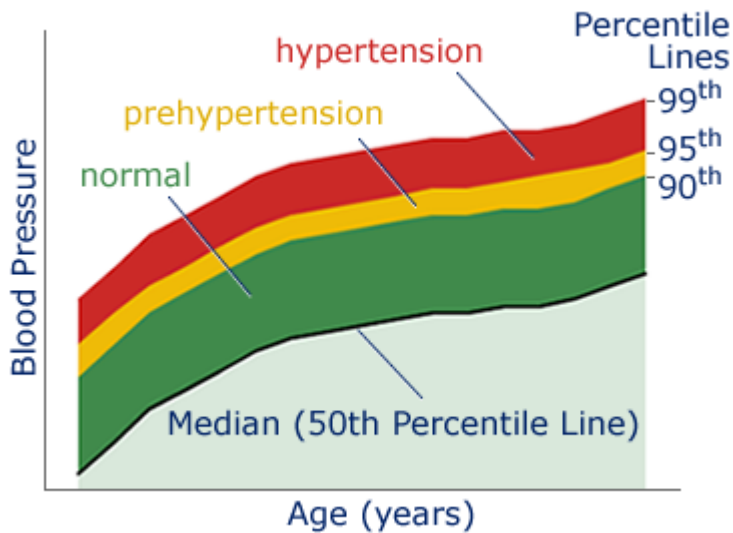
1-Older patients may present with either isolated systolic hypertension or elevation in both SBP and DBP. **CV morbidity and mortality are more directly correlated to SBP than to DBP in patients aged 50 and older.**

2-First-line antihypertensives provide significant benefits and can be used safely in older patients, **but smaller-than-usual initial doses must be used for initial therapy.**

Children and Adolescents

1-In children, hypertension is defined as **SBP or DBP that is >95th percentile** for sex, age, and height on at least three occasions. For adolescents, BP values between the 90th and

95th percentile, or $>120/80$ mm Hg, is considered elevated BP.



2-Because **secondary hypertension is more common in children and adolescents** than in adults, an appropriate workup is required if elevated BP is identified.

3-**Nonpharmacologic treatment is the cornerstone of therapy for primary hypertension.**

4-ACE inhibitors, ARBs, β -blockers, CCBs, and thiazide diuretics are all acceptable drug therapy choices.

Pregnancy

1-Preeclampsia (a condition in pregnancy characterized by high blood pressure, sometimes with fluid retention and proteinuria.) is defined as hypertension (elevated BP $\geq 140/90$ mm Hg on more than 2 occasions at least 4 hours apart after 20 weeks' gestation or $\geq 160/110$ mm Hg confirmed within a short interval) in association with **thrombocytopenia**, (deficiency of platelets in the blood. This causes bleeding into the tissues, bruising, and slow blood clotting after injury.) **impaired liver function, new-onset renal insufficiency, pulmonary edema, or new-onset cerebral or visual disturbances.** It can lead to life-threatening complications for both mother and fetus.

2-Eclampsia is the onset of convulsions in preeclampsia and is a medical emergency.

3-Definitive treatment of preeclampsia is **delivery**, and labor induction is indicated if eclampsia is imminent وشيك or حاضر. Otherwise, management consists of restricting activity, bed rest, and close monitoring. Salt restriction or other measures that contract blood volume should be avoided.

4-**Antihypertensives are used before induction of labor** if DBP is >105 mm Hg, with a target DBP of 95–105 mm Hg. Intravenous (IV) hydralazine is most commonly used; IV labetalol is also effective.

5-**Chronic hypertension** is hypertension that predates يسبق pregnancy. **Labetalol, long-acting nifedipine, or methyldopa is recommended as first-line therapy** due to favorable safety profiles. β -Blockers (except atenolol) and CCBs are also reasonable alternatives.

African Americans

1-Hypertension is more common and more difficult to control in African Americans than in those of other races; **treatment usually requires two or more antihypertensives** to reach a BP goal of <130/80 mm Hg.

2-**CCBs and thiazides are most effective in African Americans** and should be first-line in the absence of a compelling indication.

Pulmonary Disease and Peripheral Arterial Disease (PAD)

1-Although β -blockers (especially nonselective agents) have generally been avoided in hypertensive patients with asthma and COPD because of fear of inducing bronchospasm, **cardioselective β -blockers can be used safely.**

2- β -Blockers can theoretically be problematic in patients with PAD because of possible decreased peripheral blood flow secondary to unopposed **دون معارضة** stimulation of α 1-receptors that results in vasoconstriction. However, **available data indicate that β -blockers do not worsen claudication symptoms or cause functional impairment.** Therefore, **antihypertensive treatment for patients with PAD should follow the same general principles as patients without PAD.**

HYPERTENSIVE URGENCIES AND EMERGENCIES

1-Hypertensive urgencies are ideally managed by adjusting maintenance therapy, adding a new antihypertensive, increasing the dose of a current medication, or treating anxiety as applicable.

2-Acute administration of a **short-acting oral drug (captopril, clonidine, or labetalol)** followed by careful observation for several hours to ensure a gradual BP reduction is an option.

3-**Hypertensive emergencies require immediate BP reduction with a parenteral agent to limit new or progressing end-organ damage.** Nitroprusside is the agent of choice for minute-to-minute control in most cases.

Evaluation of therapeutic outcomes

1-Encourage patients to obtain a home BP monitor, record the results, and bring them to follow-up clinic visits.

2-Evaluate **BP response in the clinic 4 weeks after initiating or making changes in therapy** and compare the results to home BP readings.

3-**Once goal BP is obtained, monitor BP every 3–6 months**, assuming no signs or symptoms of acute end-organ damage. **Evaluate more frequently** in patients with a history of poor control, nonadherence, progressive end-organ damage, or symptoms of adverse drug effects.

4-Automated BP monitoring can be useful to establish effective 24-hour control and confirm white coat or masked uncontrolled hypertension.

5-**Monitor patients routinely for adverse drug events**, which may require dosage reduction or substitution with an alternative antihypertensive agent.

A-Perform laboratory monitoring **4 weeks after starting a new agent or dose increase, and then every 6–12 months in stable patients.**

B-For patients treated with eplerenone or spironolactone **monitor potassium concentrations and kidney function** within 3 days of initiation and again at 1 week to detect potential hyperkalemia.

6-Monitor patients for signs and symptoms of hypertension-associated complications.

A-Take a careful history for ischemic chest pain (or pressure), palpitationsالخفقان , dizziness, dyspnea, orthopneaاضطجاعي ضيق النفس , headache, sudden change in vision, one-sided weakness, slurred speech, and loss of balance.

B-Monitor fundoscopic changes on eye examination, LV hypertrophy on ECG, albuminuria, and changes in kidney function periodically.

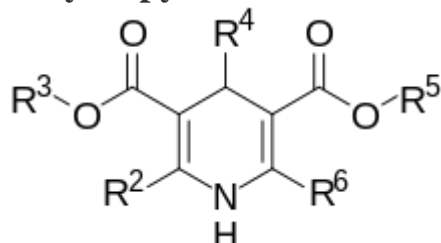
7-Assess patient adherence with the regimen regularly. Ask patients about changes in their general health perception, physical functioning, and overall satisfaction with treatment.

Reference

Joseph T. DiPiro, Robert L. Pharmacotherapy: A Pathophysiologic Approach, 11th Edition. 2021.

توضيح

Dihydropyridine



General chemical structure of dihydropyridine calcium channel blockers (dipines)
Dihydropyridine (DHP) calcium channel blockers are derived from the molecule [dihydropyridine](#) and often used to reduce systemic vascular resistance and arterial pressure. Sometimes when they are used to treat [angina](#), the vasodilation and hypotension can lead to reflex [tachycardia](#), which can be detrimental for patients with [ischemic](#) symptoms because of the resulting increase in [myocardial](#) oxygen demand. Dihydropyridine calcium channel blockers can worsen [proteinuria](#) in patients with [nephropathy](#).^[9]

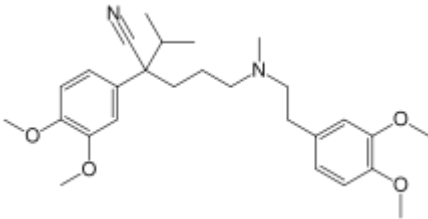
This CCB class is easily identified by the suffix "-dipine".

- [Amlodipine](#) (Norvasc)
- [Aranidipine](#) (Sapresta)
- [Azelnidipine](#) (Calblock)
- [Barnidipine](#) (HypoCa)
- [Benidipine](#) (Coniel)
- [Cilnidipine](#) (Atelec, Cinalong, Siscard) Not available in US

- [Clevudipine](#) (Cleviprex)
- [Efonidipine](#) (Landel)
- [Felodipine](#) (Plendil)
- [Isradipine](#) (DynaCirc, Prescal)
- [Lacidipine](#) (Motens, Lacipil)
- [Lercanidipine](#) (Zanidip)
- [Manidipine](#) (Calslot, Madipine)
- [Nicardipine](#) (Cardene, Carden SR)
- [Nifedipine](#) (Procardia, Adalat)
- [Nilvadipine](#) (Nivadil)
- [Nimodipine](#) (Nimotop) This substance can pass the [blood-brain barrier](#) and is used to prevent [cerebral vasospasm](#).
- [Nisoldipine](#) (Baymycard, Sular, Syscor)
- [Nitrendipine](#) (Cardif, Nitrepin, Baylotensin)
- [Pranidipine](#) (Acalas)

Non-dihydropyridine[[edit](#)]

Phenylalkylamine[[edit](#)]

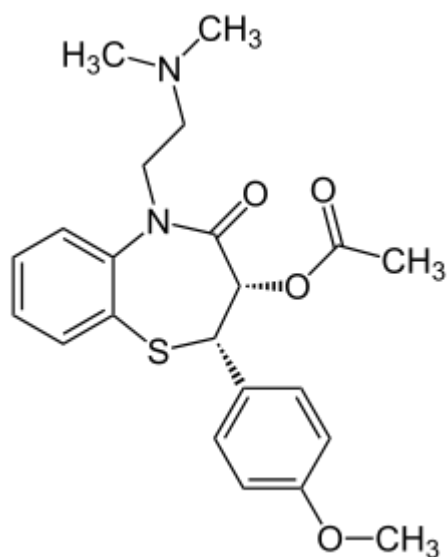


[Skeletal formula](#) of [verapamil](#)

Phenylalkylamine calcium channel blockers are relatively selective for myocardium, reduce myocardial oxygen demand and reverse coronary vasospasm, and are often used to treat angina. They have minimal vasodilatory effects compared with dihydropyridines and therefore cause less reflex tachycardia, making it appealing for treatment of angina, where tachycardia can be the most significant contributor to the heart's need for oxygen. Therefore, as vasodilation is minimal with the phenylalkylamines, the major mechanism of action is causing negative inotropy. Phenylalkylamines are thought to access calcium channels from the intracellular side, although the evidence is somewhat mixed.^[10]

- [Fendiline](#)
- [Gallopamil](#)
- [Verapamil](#) (Calan, Isoptin)

Benzothiazepine[[edit](#)]



Structural formula of diltiazem

Benzothiazepine calcium channel blockers belong to the benzothiazepine class of compounds and are an intermediate class between phenylalkylamine and dihydropyridines in their selectivity for vascular calcium channels. By having both cardiac depressant and vasodilator actions, benzothiazepines are able to reduce arterial pressure without producing the same degree of reflex cardiac stimulation caused by dihydropyridines.

- Diltiazem (Cardizem) (also used experimentally to prevent migraine)^[citation needed]

Nonselective^[edit]

While most of the agents listed above are relatively selective, there are additional agents that are considered nonselective. These include mibefradil, bepidil, flunarizine (BBB crossing), fluspirilene (BBB crossing),^[11] and fendiline.^[12]