

Overview

Hypertension (elevated blood pressure (BP)) : is a common, chronic disorder that affects 65 million Americans and over 1 billion people worldwide. Left untreated, hypertension can lead to heart disease, kidney disease, and stroke. Conversely, a treatment program of lifestyle modifications and drug therapy can reduce both BP and the risk of long-term complications.

However, it is important to appreciate that we cannot cure hypertension; we can only reduce symptoms

Blood pressure categories

Defines four BP categories:

A-- normal

B- prehypertension

C- stage 1 hypertension, and hypertension (Table 46-1).

D- stage 2

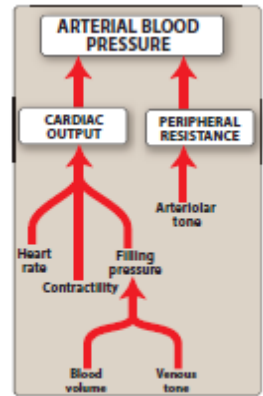


Figure 17.3 Major factors influencing blood pressure.

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

Data from The Seventh Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. JAMA 289:2560–2572, 2003.

A- Normal : normal BP is defined as systolic BP below 120 mm Hg and diastolic BP below 80 mm Hg,

B- Prehypertension: Prehypertension is defined as systolic BP of 120 to 139 mm Hg or diastolic BP of 80 to 89 mm Hg.

BP in this range carries an increased risk of cardiovascular disease,, those with BP in the prehypertension range have a 2- to 3-fold increased risk of cardiovascular events. To reduce risk, these people should adopt certain health-promoting lifestyle changes

C-Hypertension: Hypertension is defined as systolic BP above 140 mm Hg or diastolic BP above 90 mm Hg. If systolic BP is above 140 mm Hg and diastolic BP is below 90 mm Hg,

Hypertension categories

There are two broad categories of hypertension: primary hypertension and secondary hypertension.

As indicated in Table 46-2, primary hypertension is by far the most common form of hypertensive disease. Less than 10% of people with hypertension have a secondary form.

MANAGEMENT OF CHRONIC HYPERTENSION

Treatment Goals

1-For most patients with stage 1 or stage 2 hypertension, the goal is to maintain systolic BP below 140 mm Hg and diastolic BP below 90 mm Hg.

2- The ultimate goal in treating hypertension is to reduce cardiovascular and renal morbidity and mortality.

LIFESTYLE MODIFICATIONS

1-Lifestyle changes offer multiple cardiovascular benefits they do so with little cost and minimal risk.

2- they may actually prevent hypertension.

3- When implemented after hypertension has developed, they can lower BP, thereby decreasing or eliminating the need for drugs.

4- lifestyle modifications can decrease other cardiovascular risk factors. Accordingly, all patients should be strongly encouraged to adopt a healthy lifestyle.

Strategies of Life style modification

1- Weight Loss.

2- Sodium Restriction.

3- Alcohol Restriction.

4- Diet Restriction.

5- Aerobic Exercise.

6- Smoking Cessation.

7- Maintenance of Potassium and Calcium Intake.

Major Classes of Antihypertensive Drugs

1- Diuretics

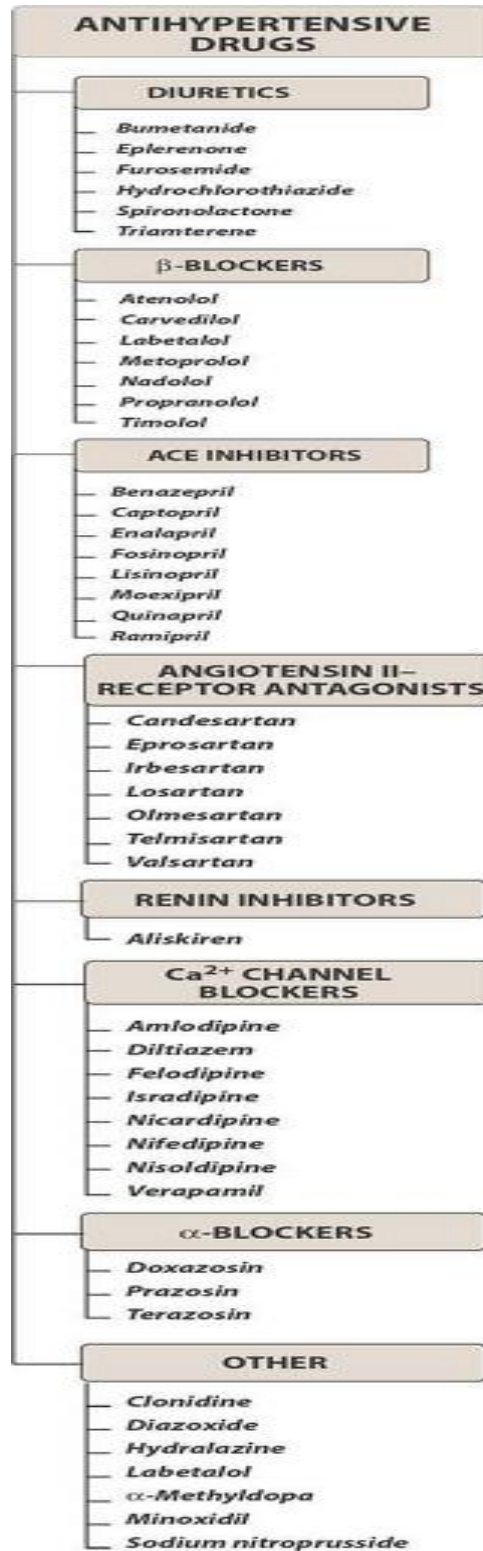
2- Sympatholytic (Antiadrenergic Drugs)

3- Centrally acting antihypertensive

4- Adrenergic neuronal blockers

5- Direct vasodilators

6- Calcium channel blockers



الشكل للاطلاع وملاحظة تقسيم الادوية

Diuretics

Diuretics are drugs that increase the volume of urine excreted.

Most diuretic agents are inhibitors of renal ion transporters that decrease the reabsorption of Na^+ at different sites in the nephron. As a result, Na^+ and other ions, such as Cl^- , enter the urine in greater than normal amounts along with water, which is carried passively to maintain osmotic equilibrium.

Diuretics, thus, increase the volume of urine and often change its pH, as well as the ionic composition of the urine and blood.

Diuretics subclass :

A- Thiazide diuretics

B- High-ceiling diuretics (Loop diuretics)

C- Potassium-Sparing Diuretics

D- Drugs that Suppress the Renin-Angiotensin –Aldosterone system (RAAS)

Thiazide-like Diuretics

These compounds lack the thiazide structure, but, like the thiazides, they have the unsubstituted sulfonamide group and, therefore, **share their mechanism of action**. The therapeutic uses and adverse effect profiles are similar to those of the thiazides.

- **Chlorthalidone:** Chlorthalidone [klor-THAL-i-done] is a **non-thiazide derivative** that behaves pharmacologically like hydrochlorothiazide. It has a long duration of action and, therefore, is often used once daily to treat hypertension.
- **Metolazone:** Metolazone [me-TOL-ah-zone] is more potent than the thiazides and, unlike the thiazides, causes Na^+ excretion even in advanced renal failure.

High-ceiling diuretics (Loop diuretics)

The loop diuretics (furosemide, torsemide, bumetanide, and ethacrynic acid) act promptly by blocking sodium and chloride reabsorption in the kidneys, even in patients with poor renal function or those who have not responded to thiazide diuretics. Loop diuretics cause decreased renal vascular resistance and increased renal blood flow.

❖ Furosemide & Torsemide

Adverse Effects

Most adverse effects are like those of the thiazides:

- ✓ Hypokalemia
- ✓ Dehydration
- ✓ Hyperglycemia
- ✓ hyperuricemia
- ✓ **disruption of lipid metabolism** (ie, reduction of HDL cholesterol and elevation of LDL cholesterol and triglycerides).
- ✓ **Ototoxicity:** Reversible or permanent hearing loss may occur with loop diuretics, particularly when used in conjunction with other ototoxic drugs (for example, aminoglycoside antibiotics).

Other high-ceiling agents

In addition to furosemide, three other high-ceiling agents are available:

❖ Ethacrynic acid & Bumetanide

Potassium-Sparing Diuretics

A-Aldosterone Antagonists (eg, Spironolactone)

B- Non-Aldosterone Antagonists (eg, Triamterene & Amiloride).

❖ Spironolactone

❖ Triamterene

Drugs that Suppress the RAAS

Because the RAAS plays an important role in controlling BP, drugs that suppress the system—especially the ACE inhibitors—have a significant role in controlling hypertension.

ACE Inhibitors

The ACE inhibitors, such as enalapril [e-NAL-ah-pril] and lisinopril [lye- SIN-oh-pril], are recommended as first-line treatment of hypertension in patients with a variety of compelling indications, including high coronary disease risk or history of diabetes, stroke, heart failure, myocardial infarction, or chronic kidney disease

❖ **Captopril, Enalapril , Lisinopril**

Angiotensin II Receptors Blockers.(Sartans group)

These drugs are alternatives to the ACE inhibitors. block the AT1 receptors, decreasing the activation of AT1 receptors by angiotensin II.

Their pharmacologic effects are similar to those of ACE inhibitors in that they produce arteriolar and venous dilation and block aldosterone secretion, thus lowering blood pressure and decreasing salt and water retention

❖ **Valsartan, Telmisartan, Losartan and irbesartan**

Direct Renin Inhibitors (DRIs)

❖ **Aliskiren**

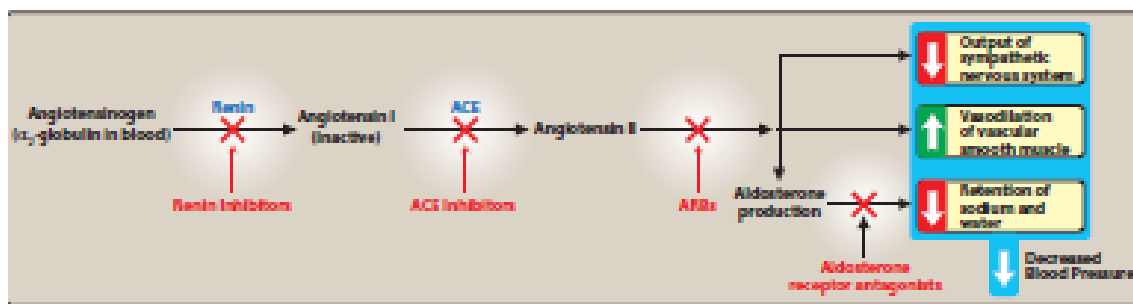
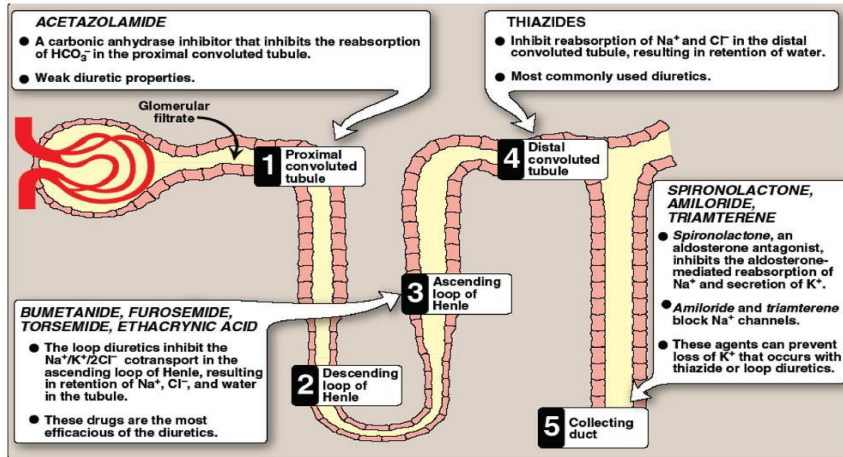


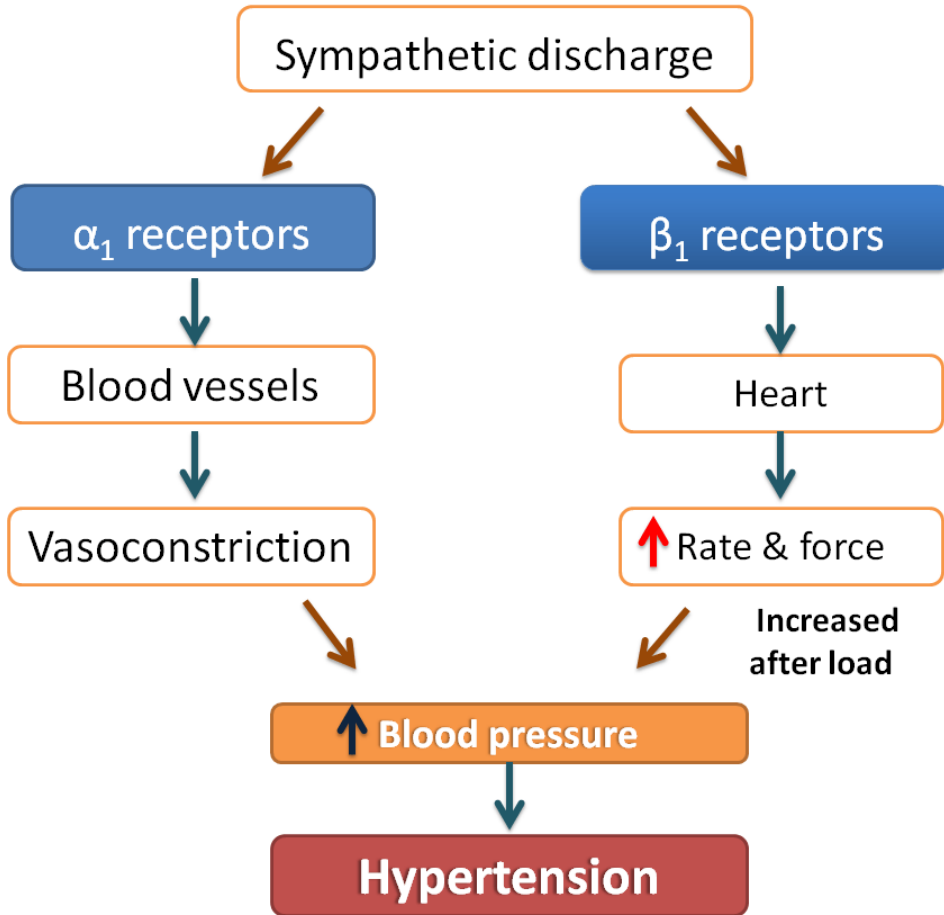
Figure 17.10
Effects of various drug classes on the renin–angiotensin–aldosterone system. Blue = drug target enzymes; red = drug class.

Scheme diagram for Effects of drugs on Renin-Angiotensin –Aldosteron system **الشكل للحفظ**

Thiazides



الشكل للحفظ مع اسماء الادوية Site of different diuretics action with examples drugs



Scheme diagram for The effects of sympathetic system activation on blood pressure control
 الشكل مطلوب

للرسم

Sympatholytics (Antiadrenergic Drugs)

Sympatholytic drugs suppress the influence of the sympathetic nervous system on the heart, blood vessels, and other structures. These drugs are used widely for hypertension.

As indicated in Table there are four subcategories of sympatholytic drugs:

- (1) Beta blockers,
- (2) Alpha1 blockers,
- (3) alpha/beta blockers,
- (4) Centrally acting alpha2 agonists,

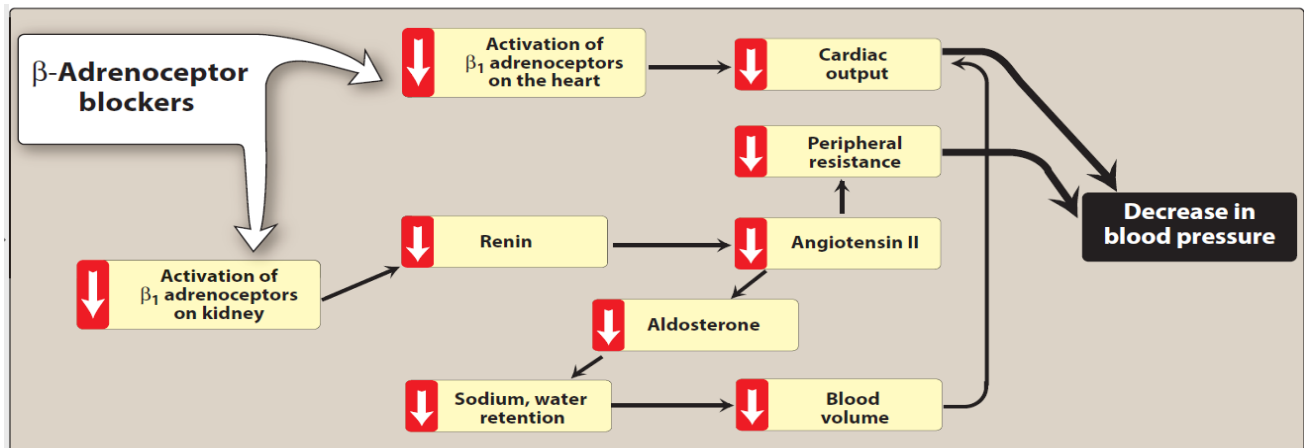
Beta-Adrenergic Blockers

β -Blockers are a treatment option for hypertensive patients with concomitant heart disease or heart failure .

- **Non selective β -blocker** : propranolol [proe PRAN-oh-lol], which acts at both β_1 and β_2 receptors.
- **Selective blockers of β_1 receptors**, such as **Metoprolol , Atenolol & Nebivolol** are among the most commonly prescribed β -blockers.

❖ **Propranolol & Metoprolol** are among the most widely used antihypertensive drugs

المعلومات التالية تخص اي من الدوائين اعلاه



Scheme diagram for Actions of B-receptor blockers in hypertension therapy الشكل مطلوب للرسم

Alpha/Beta Blockers:

❖ **Carvedilol and Labetalol.**

المعلومات التالية تخص اي من الدوائين اعلاه

- **Class & subclass** : Alpha/Beta Blockers , Sympatholytics Antihypertensive
- **mechanism of action** : Carvedilol and labetalol are unusual in that they can block alpha 1 receptors as well as beta receptors. Blood pressure reduction results from a combination of actions:

- (1) alpha1 blockade promotes dilation of arterioles and veins
- (2) blockade of cardiac beta1 receptors reduces heart rate and contractility
- (3) blockade of beta1 receptors on juxtaglomerular cells suppresses release of renin.

Alpha1 Blockers

❖ Doxazosin & Terazosin

المعلومات التالية تخص اي من الدوائين اعلاه

Centrally Acting Alpha2 Agonists

❖ Clonidine & Methyldopa

Calcium Channel Blockers

CALCIUM CHANNEL BLOCKERS

Mode of action:

- Interference with Ca^{++} uptake in smooth muscles & cardiac muscle
- Dilation of peripheral arterioles



Reduction in PVR



Reduction in Afterload

No effect on preload

Negative inotropic effect

Scheme diagram for action of Ca^{++} channel blockers in hypertension الرسم مطلوب
للحفظ

The calcium channel blockers (CCBs) fall into two groups:

A- Dihydropyridines: This rapidly expanding class of calcium-channel blockers includes :

- The first-generation agents : Nifedipine
- second-generation agents: Amlodipine, Felodipine

B- Non-dihydropyridines :

- ❖ Verapamil
- ❖ Diltiazem

Direct-Acting Vasodilators

- Hydralazine and Minoxidil