

# A Review on Hypertensive and Antihypertensive Drugs

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**Abstract:** One of the primary contributors to illness and premature death around the globe is hypertension, a complex, diverse, and multi-system illness. Major guidelines define it as having a systolic blood pressure exceeding 130 mmHg and/or a diastolic blood pressure surpassing 80 mmHg. Approximately 30% of individuals worldwide are affected by hypertension, rendering it a quite common condition. With the range of antihypertensive drug classes available, high blood pressure can be effectively managed with minimal side effects. This review focuses on two main aspects: the modes of action and the side effects of the different classes of antihypertensive medications. To enhance the understanding of which type of hypertension corresponds best to a specific pharmacological class of antihypertensive drugs, the mechanisms of action are examined through a pharmacological lens, including the molecular receptor targets, the various locations in the arterial system, and the sites of action outside the arteries. In addition, pharmacological mechanisms are utilized to define and clarify side effects, providing insights into their origins and identifying which patients should avoid particular medications.

**Keywords:** Definition of hypertension, its classification, epidemiological aspects, risk factors, symptoms, Anti-hypertensive medications, definition, classification, mechanism of action, indications, contraindications, side effects

## I. INTRODUCTION

Numerous classes of antihypertensive medications are currently accessible, enabling effective management of hypertension with minimal adverse effects. This research concentrates on two main subjects: the modes of action and the side effects associated with various pharmacological categories of antihypertensive drugs. A pharmacological perspective is employed to examine the mechanism of action, which encompasses the molecular receptor targets, various points along the arterial system, and the extra-arterial action sites, to gain deeper insights into the specific type of hypertension for which a particular pharmacological class of antihypertensive medication is most suitable. Additionally, in order to enhance the understanding of how side effects manifest and to identify individuals who should avoid specific drugs, pharmacological mechanisms are utilized to define and clarify these effects.<sup>1</sup>

### Objective:

- Outline the recommendations for administering antihypertensive drugs and assist in selecting options for initial treatment.
- Examine the various classes of anti-hypertensive medications, outlining the recommendations for initiating combination therapy when monotherapy is unsuccessful.
- Summarize the major adverse effects associated with each category of antihypertensive drugs.
- Determine the strategy utilized by the interprofessional team to establish a suitable care plan for a patient with hypertension.<sup>2</sup>

### Hypertension:

**Definition** - As per WHO, hypertension is a continuous elevation in blood pressure, specifically 140 mmHg for systolic and 90 mmHg for diastolic.<sup>3</sup>



### Classification of Hypertension:

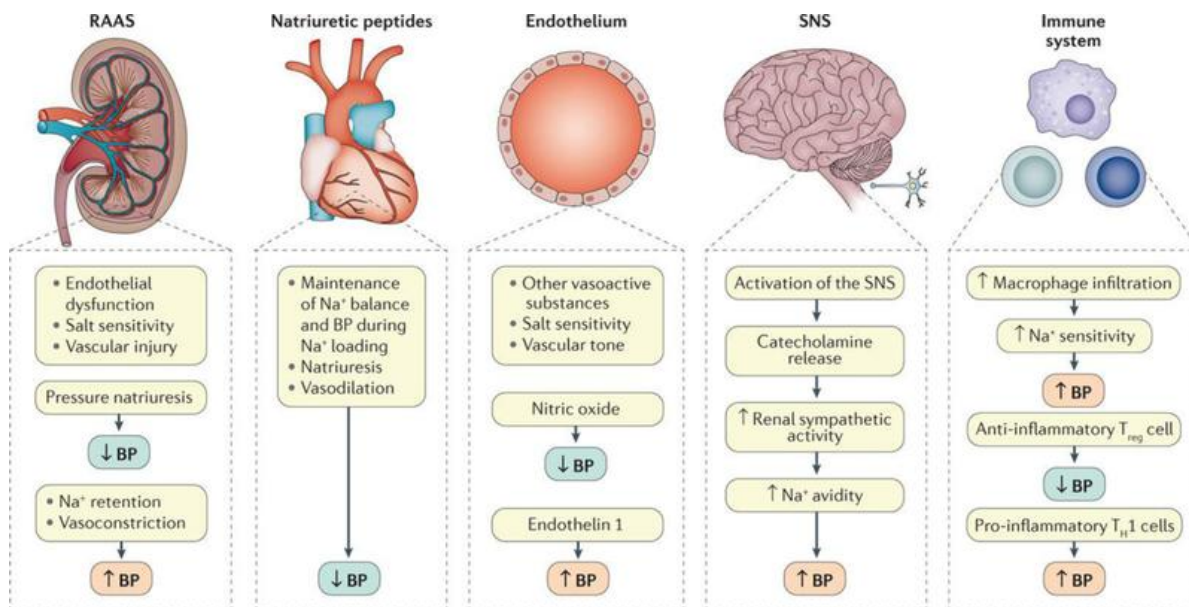
Category	Systolic (mmHg)	Diastolic (mmHg)
Normal	< 130	<85
Mild (Stage I)	140-159	90-99
Moderate (Stage II)	160-179	100-109
Severe (Stage III)	180-209	110-119
Very severe (Stage IV)	>210	>120

Table.1- Classification of Hypertension

### Epidemiology

In pre-industrial cultures, blood pressure levels exhibited narrow variances with average figures remaining relatively stable throughout the aging process, typically around 115/75 mmHg—a figure that likely reflects the standard (or optimal) blood pressure for humans. Conversely, in most modern societies, systolic blood pressure consistently increases with age in both men and women. This widespread observation may be accounted for by the fact that age serves as an indicator for the likelihood and duration of exposure to various environmental influences that elevate blood pressure incrementally over time, such as high sodium intake, low dietary potassium consumption, being overweight or obese, alcohol consumption, and lack of physical activity. Additional elements, such as genetic factors or negative intrauterine conditions like gestational hypertension or pre-eclampsia, show minor yet significant correlations with elevated blood pressure levels in adulthood. Even slight increases in the average blood pressure of a population result in substantial rises in the total number of individuals experiencing hypertension.

As economic growth advances, hypertension first impacts individuals with a higher socioeconomic standing, but during later phases of economic progress, the occurrence of hypertension and its effects are most significant among those with lower socioeconomic status; this trend is observed both nationally and internationally.<sup>4</sup>



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Figure.1. The main neuroendocrine systems involved in the regulation of blood pressure

**Risk factors:** Changeable risk factors comprise poor dietary habits (high salt intake, diets rich in saturated and trans fats, insufficient consumption of fruits and vegetables), lack of physical activity, use of tobacco and alcohol, and being



overweight or obese. Furthermore, environmental factors contribute to hypertension and related conditions, with air pollution being the most critical. Unchangeable risk factors consist of a familial history of hypertension, being older than 65 years, and the presence of other illnesses like diabetes or kidney disease.

**Symptoms:** Many individuals with high blood pressure do not experience any symptoms. Extremely elevated blood pressures can lead to headaches, visual disturbances, chest discomfort, and other signs. Monitoring your blood pressure is the most effective method to determine if you have high blood pressure. If high blood pressure goes untreated, it can lead to additional health issues such as kidney disease, heart disease, and stroke. Individuals with severely elevated blood pressure (typically 180/120 or above) may encounter symptoms such as:

- severe headaches
- chest pain
- dizziness
- difficulty breathing
- nausea
- vomiting
- hazy eyesight or other alterations in vision
- Anxiety
- Confusion
- buzzing in the ears
- nosebleeds
- abnormal heart rhythm,

If you are facing any of these symptoms along with high blood pressure, get medical attention right away. The sole method for identifying hypertension is through a measurement of blood pressure by a healthcare provider. The process of measuring blood pressure is fast and without discomfort. While it is possible for individuals to use automated devices to check their own blood pressure, it is crucial to have a healthcare professional conduct an evaluation for assessing risks and related health issues.<sup>5</sup>

**Prevention:** Adjustments in lifestyle can contribute to reducing elevated blood pressure and can assist those with hypertension. Numerous individuals who implement these modifications may still require medication. Implementing these lifestyle adjustments may assist in preventing and reducing high blood pressure.

**Do:**

- Eat more vegetables and fruits.
- Sit less.
- Engage in more physical activities, such as walking, jogging, swimming, dancing, or exercises that enhance strength, such as weightlifting.
- Achieve a minimum of 150 minutes of moderate-intensity aerobic exercise each week, or 75 minutes of vigorous aerobic exercise weekly.
- Engage in strength training activities two or more times weekly.
- Reduce weight if you are overweight or obese.
- Follow the medication instructions provided by your healthcare provider.
- Maintain scheduled meetings with your health care provider.

**Don't:**

- consume excessive amounts of salty foods (aim to keep below 2 grams daily)
- consume foods rich in saturated or trans fats
- smoke or use tobacco
- consume excessive amounts of alcohol (1 drink per day maximum for women, 2 for men)
- Miss or share medication.



- Lowering blood pressure helps avert heart attacks, strokes, and kidney injury, along with various other health issues.

**Minimize the dangers of high blood pressure by:**

- reducing and managing stress
- regularly checking blood pressure
- treating high blood pressure
- managing other medical conditions
- reducing exposure to polluted air.<sup>5</sup>

**Antihypertensive Drugs:**

**Definition** - These are the pharmaceutical agents that lower high blood pressure (BP) and bring it back to a normal level.<sup>6</sup>

**Classification:**

Class	Examples
<b>Targeting renin–angiotensin system</b>	
Angiotensin-converting enzyme inhibitors	Captopril, lisinopril, ramipril
Angiotensin receptor antagonists	Candesartan, losartan, valsartan
Direct renin antagonists	Aliskiren
<b>Adrenoceptor antagonists</b>	
$\beta$ -Blockers	Atenolol, metoprolol, propranolol
$\alpha$ -Blockers	Doxazosin, labetalol (also a $\beta$ -blocker), phentolamine, phenoxybenzamine
<b>Calcium channel blockers</b>	
Phenylalkamines	Verapamil
Dihydropyridines	Amlodipine, nifedipine, nimodipine
Benzothiazepines	Diltiazem
<b>Diuretics</b>	
Thiazides	Bendroflumethiazide, hydrochlorothiazide
Loop	Furosemide, bumetanide

**Table.1- Classification of Antihypertension**

**Mechanism of Action-**

**1. ACE inhibitors-** reduce blood pressure by obstructing the angiotensin-converting enzyme, resulting in a reduction in the generation of angiotensin II and an elevation in bradykinin levels by preventing its breakdown, which brings about vasodilation.

**2. Beta-blockers-** function by preventing catecholamines from attaching to the Beta 1, 2, and 3 receptors. Beta-1 receptors are predominantly found in cardiac muscle, while beta-2 receptors are situated in the bronchial and peripheral vascular smooth muscles, and beta-3 receptors are present in the adipose tissue of the heart. Cardio-selective beta-blockers (such as metoprolol succinate, metoprolol tartrate, atenolol, betaxolol, and acebutolol) target only beta-1 receptors, leading to fewer bronchospastic episodes. By obstructing the binding of catecholamines to the beta receptors, beta-blockers exert a negative inotropic effect, which results in a reduced heart rate, consequently aiding in the decrease of oxygen demand.

**3. Alpha-blockers-** function by blocking alpha-1 receptors, which reduces contractions of vascular smooth muscle, resulting in vasodilation.<sup>7</sup>



**4. Calcium channel blockers-** The action mechanism of CCBs is associated with the blockage of  $\text{Ca}^{2+}$  influx into cells; this happens through the interaction with L-type voltage-dependent calcium channels found in the cardiac muscle. This phenomenon can result in peripheral vasodilation, particularly observed in dihydropyridines, or a negative inotropic effect on the heart muscle in non-dihydropyridines, which inhibits the sinoatrial and atrioventricular nodes, resulting in decreased cardiac contractility and conduction.

**5. Thiazide and Thiazide like diuretics-** The precise mechanism by which thiazide-type diuretics function remains partially unknown. Thiazides obstruct sodium transport in the distal tubule by inhibiting the  $\text{Na}/\text{Cl}$  channels. They can have a minor influence on the proximal tubule by disrupting sodium transport, yet their primary effect is in the distal tubule. Thiazides lead to initial fluid depletion that is linked to reduced cardiac output, which tends to stabilize within 6 to 8 weeks after initiating treatment through a reverse auto regulation mechanism while maintaining blood pressure control; thiazide diuretics may temporarily stimulate the renin-angiotensin system and increase systemic vascular resistance, which can hinder an effective response to the diuretic therapy. This heightened renin-angiotensin activity may diminish with prolonged thiazide usage, and the addition of an ACE inhibitor or ARB may improve blood pressure regulation. Furthermore, thiazide-type diuretics exhibit a slight vasodilator effect, although the underlying mechanism remains unclear.

**6. Loop diuretics-** Function by enhancing sodium elimination at the medullary and cortical regions of the thick ascending limb. This process results in a reduction in volume, subsequently causing a drop in blood pressure.<sup>8</sup>

**Indication:**

- 1) Hypertension
- 2) CHF
- 3) MI
- 4) Angina pectoris
- 5) edema
- 6) Asthma
- 7) Liver disease
- 8) Kidney disease
- 9) Scleroderma crisis
- 10) Heart failure
- 11) Peripheral vascular disease
- 12) Bradyarrhythmias
- 13) Diabetic nephropathy
- 14) Hypertrophic cardiomyopathy
- 15) Cardiac arrhythmias.<sup>9</sup>

**Contraindication:**

- 1) Anuria
- 2) Liver disease
- 3) Renal failure
- 4) Pregnancy
- 5) Hyperkalaemia
- 6) Potassium sparing diuretics
- 7) Diabetics
- 8) lactation
- 9) liver cirrhosis
- 10) asthma



- 11) acute heart failure
- 12) bronchitis
- 13) kidney disease
- 14) hepatic failure
- 15) anemia.<sup>10</sup>

**Adverse effects:**

- 1) dizziness
- 2) fatigue
- 3) electrolyte imbalance
- 4) vomiting
- 5) hypotension
- 6) Hyperkalaemia
- 7) Dry cough
- 8) Nausea<sup>11</sup>
- 9) Urticaria
- 10) Bowel upset
- 11) Headache
- 12) Diarrhea
- 13) Angioedema
- 14) Bradycardia
- 15) Palpitation <sup>12</sup>

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