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Review

Unravelling the Complexity of Hypertension: Mechanism, Management and Beyond

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Abstract:

Hypertension, commonly known as high blood pressure, is a significant global health concern affecting millions worldwide. This review aims to provide a comprehensive understanding of hypertension, including its epidemiology, etiology, pathophysiology, diagnosis, and management strategies. Epidemiologically, hypertension is widespread, with prevalence rates varying across different demographic groups. It is a multifactorial condition influenced by genetic predisposition, lifestyle factors, and comorbidities such as diabetes and obesity. The pathophysiology of hypertension involves complex interplays between vascular, renal, neural, and hormonal mechanisms, leading to increased peripheral vascular resistance and cardiac workload. Diagnosis of hypertension relies on accurate blood pressure measurement and classification based on established guidelines. Lifestyle modifications, including dietary changes, regular exercise, and stress management, form the cornerstone of non-pharmacological management. However, pharmacotherapy becomes necessary for many individuals to achieve target blood pressure levels and reduce cardiovascular risks. Various classes of antihypertensive medications, including diuretics, beta-blockers, ACE inhibitors, angiotensin receptor blockers, calcium channel blockers, and others, are available, with selection guided by individual patient characteristics and comorbidities Additionally, hypertension management encompasses addressing associated risk factors such as dyslipidaemia and implementing strategies for secondary prevention of complications like stroke, myocardial infarction, and renal dysfunction.

Keywords: *Hypertension, Resistance Hypertension, Blood Pressure, Epidemiology, pathophysiology*

Introduction:

Hypertension is not a chronic disease, but it is independently associated with cardiovascular diseases in the elderly. Although it constitutes one of the most frequent factors for cerebrovascular diseases, it is an amendable to modifications factor. Hypertension, or elevated arterial blood pressure, is a substantial public health problem, affecting 25% of the adult population in industrialized societies. This disorder is a major risk factor for many common causes of morbidity and mortality including stroke, myocardial infarction, congestive heart failure, and end stage renal disease [1].

It is estimated that approximately 1% of patients with hypertension will at some point, develop a hypertensive crisis, and it has been estimated that hypertensive emergencies account for 25% of all patient visits to the medical section of an emergency department (ED), with hypertensive emergencies detected in one-third of these cases (3). Before the advent of antihypertensive therapy, this complication occurred in up to 7% of the hypertensive population (3). Men are affected twice as frequently as women. Among specific situations such as postoperative hypertensive crisis, the

incidence varies depending on the population being reported; however, such a crisis is reported more frequently with immediate postoperative bypass surgical graft patients. Also, preclampsia (pregnancy-induced hypertension with significant proteinuria 300 mg/l or 500 mg/24-h) occurs in approximately 7% of all pregnancies, with most of them being null-gravidas [2].

Today many different terms have been applied to defi ne acute severe elevations in BP, and the current terminology is somewhat confusing. The 2003 Joint National Committee (JNC) on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7) defi nes "hypertensive crisis" as a systolic BP (SBP) 179 mmHg or a diastolic BP (DBP) 109 mmHg with or without acute target organ involvement, while it is important to defi ne a true emergency from urgency [3].

Blood pressure must be tightly regulated to permit uninterrupted perfusion of all vital organs. For example, even transient interruption in blood flow to the brain will cause loss of consciousness, and longer interruptions will result in death of unperfused tissues. Conversely, higher pressures that deliver flow exceeding metabolic demand provide little or no metabolic gain but increase damage to blood vessels and organs. These consider actions dictate the normal ranges of blood pressure [4].

Epidemiology and Physiology

Substantial effort has been devoted to defining the pathogenesis of blood pressure variation. Epidemio logic studies have documented the impact of a variety of factors, including age, gender, and body mass index. Diet has also been implicated, with salt, potassium, and calcium suggested as important factors. How these factors influence physiology to alter blood pressure has been the subject of extensive investigation.

Both SBP and DBP increase with age. SBP rises progressively until the age of 70 or 80, whereas DBP increases until the age of 50 or 60 and then tends to level or even decline slightly. This combination of changes probably reflects stiffening of the blood vessels and reduced arterial compliance and leads to a large increase in pulse pressure with aging. Pulse pressure has been shown to be the best predictor of structural alterations in the arteries [4].

With severe elevations of BP, endothelial injury and fibrinoid necrosis of the arterioles ensue. This process results in ischemia and the release of additional vasoactive mediators generating a vicious cycle of ongoing injury. The renin – angiotensin system is often activated, leading to further vasoconstriction and the production of pro inflammatory cytokines. The volume depletion that results from pressure natriuresis further stimulates the release of vasoconstrictor substances from the kidney. These collective mechanisms can culminate in end-organ hypo-perfusion, ischemia and dysfunction that manifests as a hyper tensive emergency.

BP Regulation

BP is regulated via several physiological mechanisms to ensure an adequate tissue blood flow. BP is determined by the rate of blood flow produced by the heart (cardiac output) and the resistance of the blood vessels to blood flow. The resistance is produced mainly in the arterioles and is known as the systemic vascular resistance. There are several physiological mechanisms that allow BP to maintain into normal range such as:

1. The autonomic nervous system is the most rapidly responding regulator of BP and receives continuous information from the baroreceptors situated in the carotid sinus and the aortic arch. This information is relayed to the vasomotor center. A decrease in BP causes activation of the sympathetic nervous system resulting in increased contractility of the heart (β receptors) and vasoconstriction of both arterial and venous side of the circulation (α receptors) [5].
2. The capillary fluid shift mechanism refers to the exchange of fluid that occurs across the capillary membrane between the blood and the interstitial fluid. The fluid movement is controlled by the capillary BP, the interstitial fluid pressure as well as the colloid osmotic pressure of the plasma. Low BP results in fluid moving from the interstitial space into circulation, helping to restore blood volume and BP.
3. Hormonal mechanisms exist both for lowering and raising BP. They act in various ways including vasoconstriction and vasodilation. The principal hormones raising BP are:
    1. Adrenaline and noradrenaline secreted from the adrenal medulla in response to sympathetic nervous system stimulation. They increase cardiac output and cause vasoconstriction.
    2. Renin-angiotensin-aldosterone production is increased in the kidney when stimulated by hypotension. Angiotensin is converted in the lung to Angiotensin II which is a potent vasoconstrictor. In addition, these hormones stimulate

the production of aldosterone from the adrenal cortex which decreases urinary fluid loss from the body (sodium retention-potassium loss). This system is responsible for the long-term maintenance of BP but is also activated very rapidly in the presence hypertension [6].

4. The kidneys help to regulate the BP by increasing the blood volume and also by the renin-angiotensin system (RAS) described above. They are the most important organs for the longterm control of the BP [7].

Table 1: Blood Pressure Categories

Blood Pressure Category	Systolic mm HG Upper Number	Diastolic mm HG Lower Number
Normal	Less than 120	Less than 80
Elevated	120-129	Less than 80
High Blood Pressure (Hypertension) Stage 1	130-139	80-89
High Blood Pressure (Hypertension) Stage 2	140 or Higher	90 or Higher
Hypertensive Crisis (See Your Doctor Immediately)	Higher than 180	Higher than 120

Causes and Risk Factors of Hypertension

High blood pressure has many risk factors, including:

- **Age.** The risk of high blood pressure increases with age. Until about age 64, high blood pressure is more common in men. Women are more likely to develop high blood pressure after age 65.
- **Race.** High blood pressure is particularly common among Black people. It develops at an earlier age in Black people than it does in white people.
- **Family history.** You're more likely to develop high blood pressure if you have a parent or sibling with the condition.
- **Obesity or being overweight.** Excess weight causes changes in the blood vessels, the kidneys and other parts of the body. These changes often increase blood pressure. Being overweight or having obesity also raises the risk of heart disease and its risk factors, such as high cholesterol.
- **Lack of exercise.** Not exercising can cause weight gain. Increased weight raises the risk of high blood pressure. People who are inactive also tend to have higher heart rates.
- **Tobacco use or vaping.** Smoking, chewing tobacco or vaping immediately raises blood pressure for a short while. Tobacco smoking injures blood vessel walls and speeds up the process of hardening of the arteries. If you smoke, ask your care provider for strategies to help you quit.
- **Too much salt.** A lot of salt — also called sodium — in the body can cause the body to retain fluid. This increases blood pressure.
- **Low potassium levels.** Potassium helps balance the amount of salt in the body's cells. A proper balance of potassium is important for good heart health. Low potassium levels may be due to a lack of potassium in the diet or certain health conditions, including dehydration.
- **Drinking too much alcohol.** Alcohol use has been linked with increased blood pressure, particularly in men.
- **Stress.** High levels of stress can lead to a temporary increase in blood pressure. Stress-related habits such as eating more, using tobacco or drinking alcohol can lead to further increases in blood pressure.
- **Certain chronic conditions.** Kidney disease, diabetes and sleep apnea are some of the conditions that can lead to high blood pressure.
- **Pregnancy.** Sometimes pregnancy causes high blood pressure [8].

High blood pressure is most common in adults. But kids can have high blood pressure too. High blood pressure in children may be caused by problems with the kidneys or heart. But for a growing number of kids, high blood pressure is due to lifestyle habits such as an unhealthy diet and lack of exercise [9].

- **Body Fat**

  Excess body fat is the dominant factor predisposing to blood pressure elevation in cross-sectional and longitudinal population studies. The effect is apparent from infancy and childhood2 through to the elderly, with a continuum of effect throughout the entire distribution of body fat.3 Body fat excess, particularly central obesity, is associated with the so-called metabolic syndrome of impairment of insulin sensitivity, glucose intolerance, and dyslipidemia, which compounds with the effects of blood pressure elevation to increase the risk of cardiovascular disease.4 Hence lifestyle determinants of obesity, along with cigarette smoking, are critical targets for public health campaigns against heart attack and stroke [10].

Complications

The excessive pressure on the artery walls caused by high blood pressure can damage blood vessels and body organs. The higher the blood pressure and the longer it goes uncontrolled, the greater the damage.

Uncontrolled high blood pressure can lead to complications including:

- **Heart attack or stroke.** Hardening and thickening of the arteries due to high blood pressure or other factors can lead to a heart attack, stroke or other complications.
- **Aneurysm.** Increased blood pressure can cause a blood vessel to weaken and bulge, forming an aneurysm. If an aneurysm ruptures, it can be life-threatening.
- **Heart failure.** When you have high blood pressure, the heart must work harder to pump blood. The strain causes the walls of the heart's pumping chamber to thicken. This condition is called left ventricular hypertrophy. Eventually, the heart can't pump enough blood to meet the body's needs, causing heart failure.
- **Kidney problems.** High blood pressure can cause the blood vessels in the kidneys to become narrow or weak. This can lead to kidney damage.
- **Eye problems.** Increased blood pressure can cause thickened, narrowed or torn blood vessels in the eyes. This can result in vision loss.
- **Metabolic syndrome.** This syndrome is a group of disorders of the body's metabolism. It involves the irregular breakdown of sugar, also called glucose. The syndrome includes increased waist size, high triglycerides, decreased high-density lipoprotein (HDL or "good") cholesterol, high blood pressure and high blood sugar levels. These conditions make you more likely to develop diabetes, heart disease and stroke.
- **Changes with memory or understanding.** Uncontrolled high blood pressure may affect the ability to think, remember and learn.
- **Dementia.** Narrowed or blocked arteries can limit blood flow to the brain. This can cause a certain type of dementia called vascular dementia. A stroke that interrupts blood flow to the brain also can cause vascular dementia [11].

Diagnosis and Classification of Hypertension

The JNC-7 has defined criteria for normal BP, prehypertension and stage 1 and 2 of hypertension. Guidelines from the European Society of Hypertension/ European Society of Cardiology (ESH/ESC 2007 and 2009 update) stratify hypertension somewhat differently. As with the previous ESH/ESC guidelines, the authors have again omitted the “prehypertension” category, as defined in JNC-7, because they believe that it implies that a large part of the population is “sick” and that this raises anxiety and leads to unnecessary physician visits. The authors also felt that the population of people who would fall into a prehypertension category would be so diverse to allow treatment recommendations for the whole group. The diagnosis of hypertension should be based on at least 3 different BP measurements taken on ≥ 2 separate office visits. The majority of cases are due to essential hypertension. However, it is important to identify correctable causes of hypertension also known as secondary hypertension. History and examination may give clues to the presence of an underlying disease such as renal failure, renovascular disease, hyperaldosteronism, phaechromocytoma or Cushing syndrome. Other suggestive factors are lack of family history of hypertension, unusual course, early complications or resistance to therapy [12].

Special Definitions of Hypertension

- **White-coat Hypertension:** A term reserved for those not on antihypertensive medications but with persistently elevated office BP (≥ 140/90 mmHg) together with a normal daytime ambulatory BP (≤ 135/85 mmHg), is also more common in the elderly and is more frequent among centenarians.
- **Masked Hypertension:** It is defined as normal BP at office associated with high BP at home, has been shown to be associated with an increased risk of cardiovascular events. Masked hypertension is frequent in the elderly and is associated with a high vascular profile. These results should encourage a more widespread use of home BP monitoring in this age segment.
- **Pseudo Hypertension:** It is a falsely increased SBP caused by atherosclerotic and other vascular changes associated with age. The Osler maneuver (i.e. the presence of radial artery pulse that is still palpable after the cuff is inflated above the systolic pressure) should be performed if pseudo hypertension is suspected, though it has low sensitivity and specificity. Confirmation of pseudo hypertension requires direct intraarterial measurement of BP.
- **Resistant Hypertension:** It is defined as BP that remains above goal despite the concurrent use of 3 antihypertensive agents of different classes. Ideally, one of the three agents should be a diuretic and all agents should be prescribed at optimal dose amounts. Like the American Heart Association statement, the JNC 7 guidelines also include patients who are well controlled but require 4 or more medications as having resistant hypertension. Resistant hypertension is prevalent across all ages but is more prevalent in elderly patients. Several factors have been identified as contributors to resistant hypertension. Poor patient adherence, physical inertia, inadequate doses or inappropriate combinations of antihypertensive drugs, excess alcohol intake and sleep apnea are some of the most common causes of resistance. Secondary forms of hypertension represent another important contributor to drug resistance.
- **Dipper or Non-dipper Patient:** It is to say whether BP falls at night compared to daytime values. A nighttime fall is normal (nocturnal BP drop of 10%-20%, followed by an increase early in the morning). It correlates with variations in sympathetic activity but with other factors such as sleep quality, age, hypertensive status, marital status, and social network support. In addition, nocturnal hypertension is associated with end organ damage and is a much better indicator than the daytime BP reading. It should be noted that there is also a category of patients who, rather than non-dippers are extremely dippers (≥ 20% nocturnal BP fall) and this group may be at risk for silent and clinical cerebral ischemia through hypoperfusion during sleep. The frequency of non-dippers is higher in the elder [13].

High Blood Pressure Dangers: Hypertension's Effects on Your Body:

Damage to the Arteries

Healthy arteries are flexible, strong and elastic. Their inner lining is smooth so that blood flows freely, supplying vital organs and tissues with nutrients and oxygen.

Over time, high blood pressure increases the pressure of blood flowing through the arteries. This may cause:

- **Damaged and narrowed arteries.** High blood pressure can damage the cells of the arteries' inner lining. When fats from food enter the bloodstream, they can collect in the damaged arteries. In time, the artery walls become less elastic. This limits blood flow throughout the body.
- **Aneurysm.** Over time, the constant pressure of blood moving through a weakened artery can cause part of the artery wall to bulge. This is called an aneurysm. An aneurysm can burst open and cause life-threatening bleeding inside the body. Aneurysms can form in any artery. But they're most common in the body's largest artery, called the aorta [14].

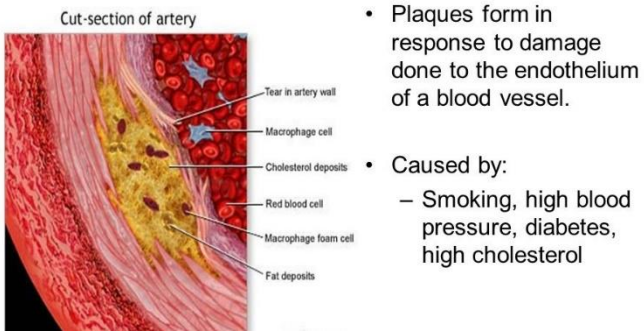

Fig.1 Damage to arteries

Damage to the Heart

High blood pressure can cause many heart conditions, including:

- **Coronary artery disease.** High blood pressure can narrow and damage the arteries that supply blood to the heart. This damage is known as coronary artery disease. Too little blood flow to the heart can lead to chest pain, called angina. It can lead to irregular heart rhythms, called arrhythmias. Or it can lead to a heart attack.
- **Heart failure.** High blood pressure strains the heart. Over time, this can cause the heart muscle to weaken or become stiff and not work as well as it should. The overwhelmed heart slowly starts to fail.
- **Enlarged left heart.** High blood pressure forces the heart to work harder to pump blood to the rest of the body. This causes the lower left heart chamber, called the left ventricle, to thicken and to enlarge. A thickened and enlarged left ventricle raises the risk of heart attack and heart failure. It also increases the risk of death when the heart suddenly stops beating, called sudden cardiac death.
- **Metabolic syndrome.** High blood pressure raises the risk of metabolic syndrome. This syndrome is a cluster of health conditions that can lead to can lead to heart disease, stroke and diabetes. The health conditions that make up metabolic syndrome are high blood pressure, high blood sugar, high levels of blood fats called triglycerides, low levels of HDL cholesterol, which is the "good" cholesterol, and too much body fat around the waist [15].

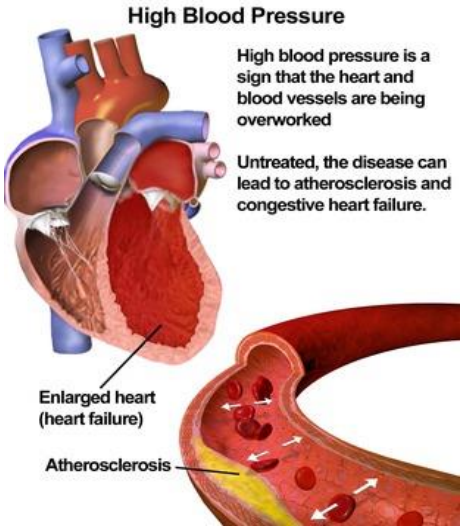

Fig.2 Damage of heart

Damage to the Brain

The brain depends on a nourishing blood supply to work right. High blood pressure may affect the brain in the following ways:

- **Transient ischemic attack (TIA).** Sometimes this is called a ministroke. A TIA happens when the blood supply to part of the brain is blocked for a short time. Hardened arteries or blood clots caused by high blood pressure can cause TIAs. A TIA is often a warning sign of a full-blown stroke.
- **Stroke.** A stroke happens when part of the brain doesn't get enough oxygen and nutrients. Or it can happen when there is bleeding inside or around the brain. These problems cause brain cells to die. Blood vessels damaged by high blood pressure can narrow, break or leak. High blood pressure also can cause blood clots to form in the arteries leading to the brain. The clots can block blood flow, raising the risk of a stroke.
- **Dementia.** Narrowed or blocked arteries can limit blood flow to the brain. This could lead to a certain type of dementia, called vascular dementia. A single stroke or multiple tiny strokes that interrupt blood flow to the brain also can cause vascular dementia.
- **Mild cognitive impairment.** This condition involves having slightly more troubles with memory, language or thinking than other adults your age have. But the changes aren't major enough to impact your daily life, as with dementia. High blood pressure may lead to mild cognitive impairment [16].

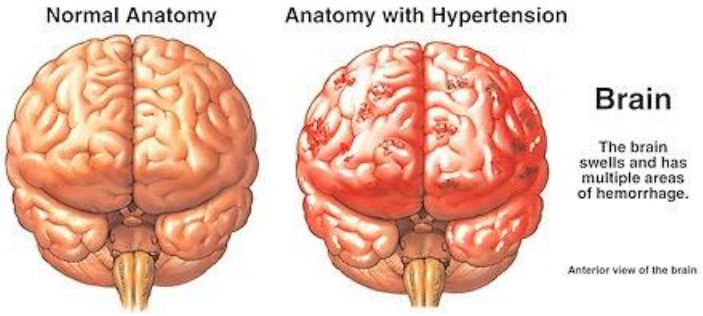

Fig.3 Damage of brain

Damage to the Kidneys

Kidney's filter extra fluid and waste from the blood — a process that requires healthy blood vessels. High blood pressure can damage the blood vessels in and leading to the kidneys. Having diabetes along with high blood pressure can worsen the damage.

Damaged blood vessels prevent the kidneys from being effective at filtering waste from the blood. This allows dangerous levels of fluid and waste to collect. When the kidneys don't work well enough on their own, it's a serious condition called kidney failure. Treatment may include dialysis or a kidney transplant. High blood pressure is one of the most common causes of kidney failure [17].

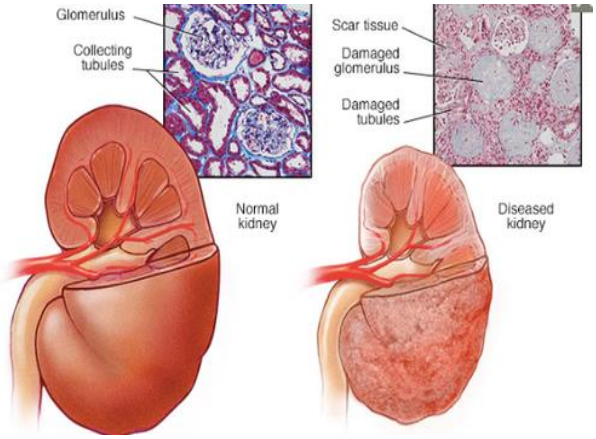

Fig.4 Damage of kidney

Hypertensive Crisis:

A hypertensive crisis is a sudden, severe increase in blood pressure. The blood pressure reading is 180/120 millimeters of mercury (mm Hg) or greater. A hypertensive crisis is a medical emergency. It can lead to a heart attack, stroke or other life-threatening health problems.

Severely high blood pressure can damage blood vessels and body organs, including the heart, brain, kidneys and eyes. During a hypertensive crisis, the heart may not be able to pump blood effectively.

Hypertensive crises are grouped into two categories.

- **Urgent hypertensive crisis.** Blood pressure is 180/120 mm Hg or greater. There are no signs of organ damage.
- **Emergency hypertensive crisis:** Blood pressure is 180/120 mm Hg or greater. There is life-threatening damage to the body's organs.

Causes of a hypertensive crisis include:

- Forgetting to take blood pressure medication
- Suddenly stopping certain heart medications, such as beta blockers
- Medication interactions

- Tumor of the adrenal gland (pheochromocytoma)

Symptoms of a hypertensive crisis may include:

- Anxiety
- Blurred vision
- Chest pain
- Confusion
- Nausea and vomiting
- Not responding to stimulation (unresponsiveness)
- Seizures
- Severe headache
- Shortness of breath

If you get a very high blood pressure reading at home and don't have any symptoms, relax for a few minutes. Then check your blood pressure again. If it's still very high, seek medical care.

Call 911 or emergency medical services if your blood pressure is 180/120 mm Hg or greater and you have chest pain, shortness of breath, or symptoms of stroke. Stroke symptoms include numbness or tingling, trouble speaking, or changes in vision.

Treatment for a hypertensive crisis may include a hospital stay to monitor for organ damage. Medications to lower blood pressure are given by mouth or IV [18].

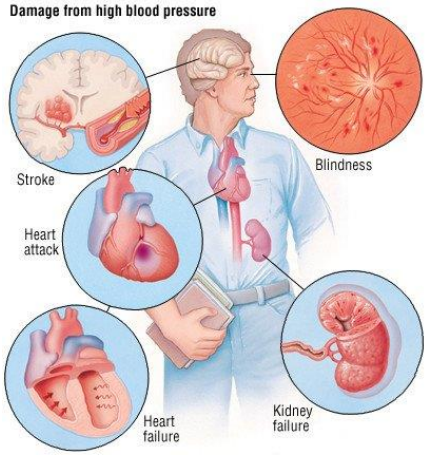

Fig.5 Damage from high blood pressure

Treatment and Mangaement of Hypertension:

Lifestyle changes

A healthy lifestyle is the first line of defense against high blood pressure. Habits that help control blood pressure include:

- eating a healthy diet
- staying physically active
- maintaining a healthy weight
- avoiding excessive alcohol consumption
- quitting smoking and avoiding second hand smoke
- managing stress
- eating less salt
- limiting caffeine
- monitoring blood pressure at home
- getting support from family and friends

High blood pressure drugs

Some people find that lifestyle changes alone are enough to control their high blood pressure. But many also take medication to treat their condition. There are many different types of blood pressure medications with different modes of action.

If one drug doesn't lower your blood pressure enough, another might do the job. For some people, a combination of two or more drugs may be needed to keep their blood pressure under control.

Hypertension medications can be divided into the categories listed below, based on how they work. The drugs in each section are just a sampling of what's available.

- **Diuretics**

Diuretics, sometimes called water pills, help the kidneys get rid of excess water and salt (sodium). This reduces the volume of blood that needs to pass through the blood vessels. As a result, blood pressure goes down.

There are three major types of diuretics defined by how they work. They include:

- thiazide diuretics (chlorthalidone, Microzide, Diuril)
- potassium-sparing diuretics (amiloride, Aldactone, Dyrenium)
- loop diuretics (bumetanide, furosemide)
- combination diuretics, which include more than one variety used together

Diuretics in the thiazide group generally have fewer side effects than the others, particularly when taken at the low doses commonly used in treating early high blood pressure.

- **Beta-blockers**

Beta-blockers help the heart to beat with less speed and force. The heart pumps less blood through the blood vessels with each beat, so blood pressure decreases. There are many drugs within this classification, including:

  - atenolol (Tenorim)
  - propranolol (Inderal)
  - metoprolol tartrate (Lopressor)
  - metoprolol succinate (Toprol-XL)
  - carvedilol (Coreg)

- **Alpha-beta-blockers**

Alpha-beta-blockers have a combined effect. They're a subclass of beta-blockers that block the binding of catecholamine hormones to both alpha and beta receptors. They can decrease the constriction of blood vessels like alpha-1 blockers, and slow down the rate and force of the heartbeat like beta-blockers.

Carvedilol (Coreg) and labetalol hydrochloride (Normodyne) are common alpha-beta-blockers.

- **Angiotensin converting enzyme (ACE) inhibitors**

ACE inhibitors help the body produce less of a hormone called angiotensin II, which causes blood vessels to narrow. These medications decrease blood pressure by helping blood vessels expand and let more blood through.

Some ACE inhibitors include:

  - benazepril hydrochloride (Lotensin)
  - captopril (Capoten)
  - enalapril maleate (Vasotec)
  - fosinopril sodium (Monopril)

- **Angiotensin II receptor blockers (ARBs)**

ARBs block the action of angiotensin II directly on the blood vessels. It attaches at the receptor site on the blood vessels and keeps them from narrowing. This causes blood pressure to fall.

ARBs include:

  - candesartan (Atacand)
  - eprosartan mesylate (Teveten)
  - irbesartan (Avapro)
  - losartan potassium (Cozaar)
  - telmisartan (Micardis)

- **Calcium channel blockers**

Movement of calcium into and out of muscle cells is necessary for all muscle contractions. Calcium channel blockers limit calcium from entering the smooth muscle cells of the heart and blood vessels. This makes the heart beat less forcefully with each beat and helps blood vessels relax. As a result, blood pressure decreases.

Examples of these medications include:

- amlodipine besylate (Norvasc, Lotrel)
- felodipine (Plendil)
- diltiazem (Cardizem)
- isradipine (DynaCirc, DynaCirc CR)
- verapamil hydrochloride (Calan SR, Covera-HS, Isoptin SR, Verelan)

- **Alpha-1 blockers**

Your body produces types of hormones called catecholamines when under stress, or chronically in some disease states. Catecholamines, such as norepinephrine and epinephrine, cause the heart to beat faster and with more force. They also constrict blood vessels. These effects raise blood pressure when the hormones attach to a receptor.

The muscles around some blood vessels have what are known as alpha-1 or alpha adrenergic receptors. When a catecholamine binds to an alpha-1 receptor, the muscle contracts, the blood vessel narrows, and blood pressure rises.

Alpha-1 blockers bind to alpha-1 receptors, blocking catecholamines from attaching. This keeps them from narrowing blood vessels so blood is able to flow through the blood vessels more freely, and blood pressure falls.

Alpha-1 blockers are primarily used to treat benign prostatic hyperplasia (BPH) in men, but are also used to treat high blood pressure.These drugs include:

- doxazosin mesylate (Cardura)
- prazosin hydrochloride (Minipress)
- terazosin hydrochloride (Hytrin)

- **Alpha-2 receptor agonists (central agonists)**

Alpha-2 receptors are different from alpha-1 receptors. When an alpha-2 receptor is activated, the production of norepinephrine is blocked. This decreases the amount of norepinephrine produced. Less norepinephrine means less constriction of blood vessels and a lower blood pressure.

Methyldopa (Aldomet) is an example of this type of drug. It's a common choice for high blood pressure treatment during pregnancy because it generally poses few risks to the mother and fetus.

Other examples include:

- clonidine hydrochloride (Catapres)
- guanabenz acetate (Wytensin)
- guanfacine hydrochloride (Tenex)

Since alpha-2 receptor agonists can work in the brain and central nervous system, they're also known as "central agonists." This makes these medications useful for treating a large range of medical conditions beyond high blood pressure.

- **Vasodilators**

Vasodilators relax the muscles in the walls of blood vessels, especially small arteries (arterioles). This widens the blood vessels and allows blood to flow through them more easily. Blood pressure falls as a result.

Hydralazine hydrochloride (Apresoline) and minoxidil (Loniten) are examples of these [16].

Conclusion

Hypertension is an important risk factor for cardiovascular morbidity and mortality, especially in the elderly. Multiple trials have been shown that not only is it safe to treat hypertension in the elderly, but also that will decrease stroke, HF, myocardial infarction and all-cause mortality. Hypertension treatment also reduces the incidence of cognitive impairment and dementia in the elderly. The adoption of a healthy lifestyle is one of the cornerstones of hypertension management. Evidence indicates that several classes of antihypertensive drugs are effective in preventing cardiovascular events, but usually no single drug is adequate to control BP in most elderly with hypertension. Individualization of the treatment should be guided by the presence of concomitant cardiovascular risk factors. The

assessment of subclinical cardiovascular organ damage resulting to an earlier onset of antihypertensive therapy leads to a reduction of the total cardiovascular risk. For all those reasons, physicians should treat hypertension in their patients regardless of their age.

References:

1. Laurent S, Boutouyrie P. Arterial stiffness and hypertension in the elderly. Frontiers in cardiovascular medicine. 2020 Oct 29;544302.
2. Aronow WS. Managing Hypertension in the elderly: What's new? American Journal of Preventive Cardiology. 2020 Mar 1;100001.
3. Oliveros E, Patel H, Kyung S, Fugar S, Goldberg A, Madan N, Williams KA. Hypertension in older adults: Assessment, management, and challenges. Clinical cardiology. 2020 Feb; 43:99-107.
4. Komilovich EB, Jamshidovich AS. Hypertension etiology. 2024 Feb 4; 38:32.
5. Griendling KK, Camargo LL, Rios FJ, Alves-Lopes R, Montezano AC, Touyz RM. Oxidative stress and hypertension. Circulation research. 2021 Apr 2;993-1020.
6. Hamilton GA. Measuring adherence in a hypertension clinical trial. European Journal of Cardiovascular Nurse 2019; 219-228.
7. Levy D, Larson MG, Vasan RS, Kannel WB, Ho KK. The progression from hypertension to congestive heart failure. JAMA 1996; 1557-1562.
8. Lloyd-Jones DM, Evans JC, Levy D. Hypertension in adults across the age spectrum: current outcomes and control in the community. 2005; 466-472.
9. Ong KL, Tso AW, Lam KS, Cheung BM. Gender difference in blood pressure control and cardiovascular risk factors in Americans with diagnosed hypertension. Hypertension 2008; 1142-1148.
10. 3 Hertz RP, Unger AN, Cornell JA, Saunders E. Racial disparities in hypertension prevalence, awareness, and management. Arch Intern Med 2023; 2098-2104.
11. Millar JA, Lever AF. Implications of pulse pressure as a predictor of cardiac risk in patients with hypertension. Hypertension 2019;907-911.
12. 2 Wallace SM, Yasmin CM, Mäki-Petäjä KM, Booth AD, Cockcroft JR, Wilkinson IB. Isolated systolic hypertension is characterized by increased aortic stiffness and endothelial dysfunction. Hypertension 2013; 228-233.
13. Davis BR, Langford HG, Blaufox MD, Curb JD, Polk BF, Shulman NB. The association of postural changes in systolic blood pressure and mortality in persons with hypertension: the Hypertension Detection and Follow-up Program experience. Circulation 2013;340-346.
14. 7 Kario K, Eguchi K, Nakagawa Y, Motai K, Shimada K. Relationship between extreme dippers and orthostatic hypertension in elderly hypertensive patients. Hypertension 2018; 77-82.
15. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL, Jones DW, Materson BJ, Oparil S, Wright JT, Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension 2014;1206-1252.
16. Angeli F, Reboldi G, Verdecchia P. Masked hypertension: evaluation, prognosis, and treatment. Am J Hypertens 2010; 941-948.
17. 2 Perry HM, Davis BR, Price TR, Applegate WB, Fields WS, Guralnik JM, Kuller L, Pressel S, Stamler J, Probstfield JL. Effect of treating isolated systolic hypertension on the risk of developing various types and subtypes of stroke: the Systolic Hypertension in the Elderly Program (SHEP). JAMA 2000; 465-471.
18. Lawes CM, Bennett DA, Feigin VL, Rodgers A. Blood pressure and stroke: an overview of published reviews. Stroke 2004;776-785.

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