



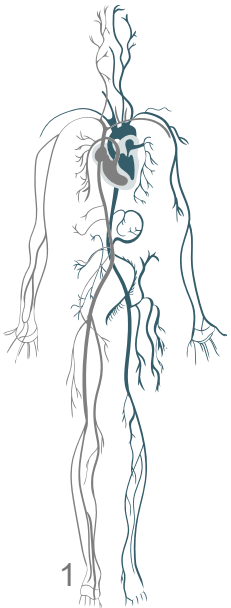
MID | Lecture 1

وَلَقَدْ خَلَقْنَا الْإِنْسَانَ وَنَعْلَمُ مَا تُوَسَّوَسُ بِهِ نَفْسُهُ وَنَحْنُ أَقْرَبُ إِلَيْهِ مِنْ حَبْلِ الْوَرِيدِ
اللهم إنا نعوذ بك من شرور أنفسنا ومن سيئات أعمالنا

Anti- hypertensives (pt.1)

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Anti-hypertensives

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Blood Pressure

- Blood pressure is the force that circulating blood exerts on walls of arteries.
- Two blood pressures are measured, systolic blood pressure and diastolic blood pressure.
- Systole occurs while the heart contracts.
Diastole occurs while the heart rests between beats.
- $\text{Blood pressure} = \text{Cardiac output} \times \text{Peripheral vascular resistance} (\text{CO} \times \text{PVR})$

Introduction into blood pressure

- Blood circulates in our vessels and applies force on them, and blood pressure is the measure used to describe this force.
- **The normal blood pressure is 120/80 mmHg.**
- The top number represents the systolic pressure (when the heart pumps blood out), and the bottom number represents the diastolic pressure (when the heart pauses between beats).
- The two determinants of BP are targeted in pharmacology:
- **Cardiac Output (CO)**, which generally refers to the amount of blood the heart pumps out per minute, is directly related to the amount of blood pumped, and the higher the amount, the higher the pressure.
- **Peripheral vascular resistance (PVR)** occurs when constriction of blood vessels increases pressure.

Definition: Hypertension

**Elevation of arterial blood pressure above
(130/80) mm Hg (boarder line)**

Some criteria must be considered to diagnose a patient with hypertension.
For example, a patient had visited the renal clinic and their blood pressure was 135/85 mmHg.

- A lot of reasons may have led to this reading, such as stress and climbing the stairs, but it doesn't mean that this person is hypertensive. Multiple readings must be **taken twice a day** using a household digital blood pressure monitoring device (**for at least 14 days**), taking into account the **circadian rhythm** and **hormonal regulation**. Cortisol and adrenaline levels rise in the morning and are associated with high blood pressure.

Classification of Hypertension

Blood Pressure Categories



BLOOD PRESSURE CATEGORY	SYSTOLIC mm Hg (upper number)		DIASTOLIC mm Hg (lower number)
NORMAL	LESS THAN 120	and	LESS THAN 80
ELEVATED	120 – 129	and	LESS THAN 80
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 1	130 – 139	or	80 – 89
HIGH BLOOD PRESSURE (HYPERTENSION) STAGE 2	140 OR HIGHER	or	90 OR HIGHER
HYPERTENSIVE CRISIS (consult your doctor immediately)	HIGHER THAN 180	and/or	HIGHER THAN 120

→ Pre-hypertensive people must be careful to not develop hypertension, taking certain measures to keep their blood pressure in the normal ranges.

Must Go to Emergency department

Primary (Essential) Hypertension

- **90% of cases have no specific cause (idiopathic)**
- **High blood pressure associated with increased peripheral vascular resistance**
- **Multifactorial abnormalities**
 - **Genetics**
 - **Stress**
 - **Environment and diet (Smoking/High salt diet)**
- ✓ **Secondary hypertension** is another type of hypertension that accounts for about 10% of cases, it's caused by identifiable underlying medical conditions, such as kidney, thyroid or adrenal disorders. These conditions can interfere with the normal regulatory mechanisms that control blood pressure causing hypertension.

Risk factors of primary hypertension

- **Genetics** and family history: If one or both parents have hypertension, you are more susceptible of developing the disease.
- **Stressful working environments.**
- **High salt diet:** Excess sodium raises sodium concentration in the blood, causing the kidneys to retain more water. This increases blood volume and elevates blood pressure.
 - Diuretics work by increasing the excretion of sodium and water from the kidneys.
- **Smoking**
 - a) Directly: when you smoke, nicotine stimulates nicotinic acetylcholine receptors in **autonomic ganglia** and the **adrenal medulla**, leading to the release of epinephrine and norepinephrine. These catecholamines activate **α_1 -adrenergic receptors**, causing **vasoconstriction** and a rise in blood pressure. Note that blood vessels **lack parasympathetic** innervation.
 - b) Indirectly: Smoking causes tissue hypoxia, and the heart compensates by **increasing the heart rate**, which in turn **raises the cardiac output and the blood pressure**.

Furthermore about genetics :

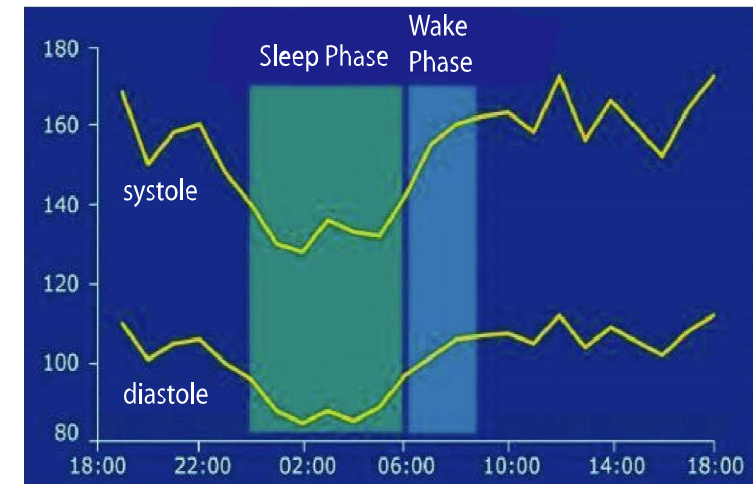
- Certain ethnic groups have genetic polymorphisms that increase their risk of hypertension. A study conducted in the USA found that African Americans are more likely to develop hypertension than White Americans, and men have a higher risk than women. The results of the study showed the following order of risk:

1. African American men
2. White men
3. African American women
4. White women

- **Role of Estrogen and Age:** The study included participants aged **30 to 45** years. Women are generally protected from hypertension due to **estrogen**, which has a cardioprotective effect by reducing the risk of cardiovascular diseases. This explains their lower risk compared to men. However, after the age of 45 to 50 years or after menopause, when estrogen levels **decrease**, women's risk of hypertension rises and becomes equal to that of men.

Clinical Presentation

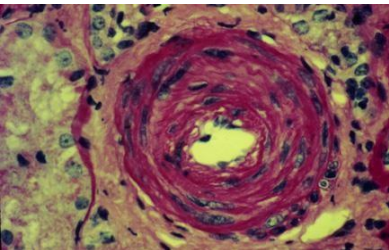
- Most times asymptomatic (a ‘silent’ disease) or “Silent Killer”; since it’s a very serious disease if left untreated, it can damage vital organs leading to death (go to slide 11)
- One of its symptoms is a Headache which is not specific and can be caused by many factors for example, it
 - Coincides with the morning surge in BP which is normal
 - Circadian variation of blood pressure —a natural daily rhythm in which blood pressure rises in the morning and decreases during sleep.
- People usually do not associate this headache with hypertension, which often leads to a delay in diagnosis. However, this is no longer the case with the widespread use of digital home blood pressure monitoring devices



Uncomplicated to Complicated/Malignant Hypertension Leads to End-Organ Damage

- Chronic hypertension (chronic pressure on BVs wall) alters blood vessel/cardiac muscle structure that leads to :
 - Decrease blood vessel diameter. ¹
 - Diminishes distribution of oxygenated blood to tissue targets
 - Cardiac hypertrophy; Any increase in pressure within the aorta or other blood vessels that follow it causes the heart to work & to pump the blood harder for it to overcome that high pressure. Over time, this compensatory response leads to cardiac **enlargement** and other structural changes, which eventually progress to **heart failure**.
 - High blood pressure ultimately leads to major end-organ damage i.e., heart attack, stroke, renal failure
- That's why we Need to diagnose and treat hypertension early

vascular hyperplasia¹



Structural changes that lead to *decreased* blood flow to organs:
1. **Thickening** of the smooth muscle layer due to **hypertrophy**, and in severe cases, **hyperplasia**, which **narrows** the BVs.

2. **Sclerosis** (hardening) of the blood vessels, resulting in **loss of elasticity** and **impaired dilation**, thereby further decreasing organ perfusion.

Additional explanation regarding figure:

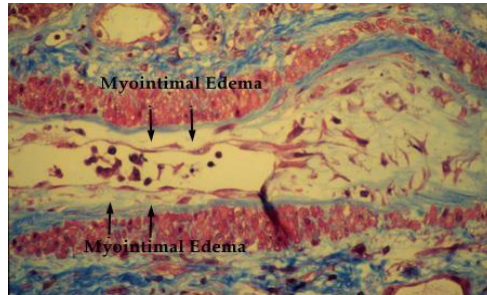
- **Eyes:**

High BP can also lead to **papilledema** = edema in the eye that affects vision, possibly causing blindness.

papilledema



edema



- **Sexual dysfunction:**

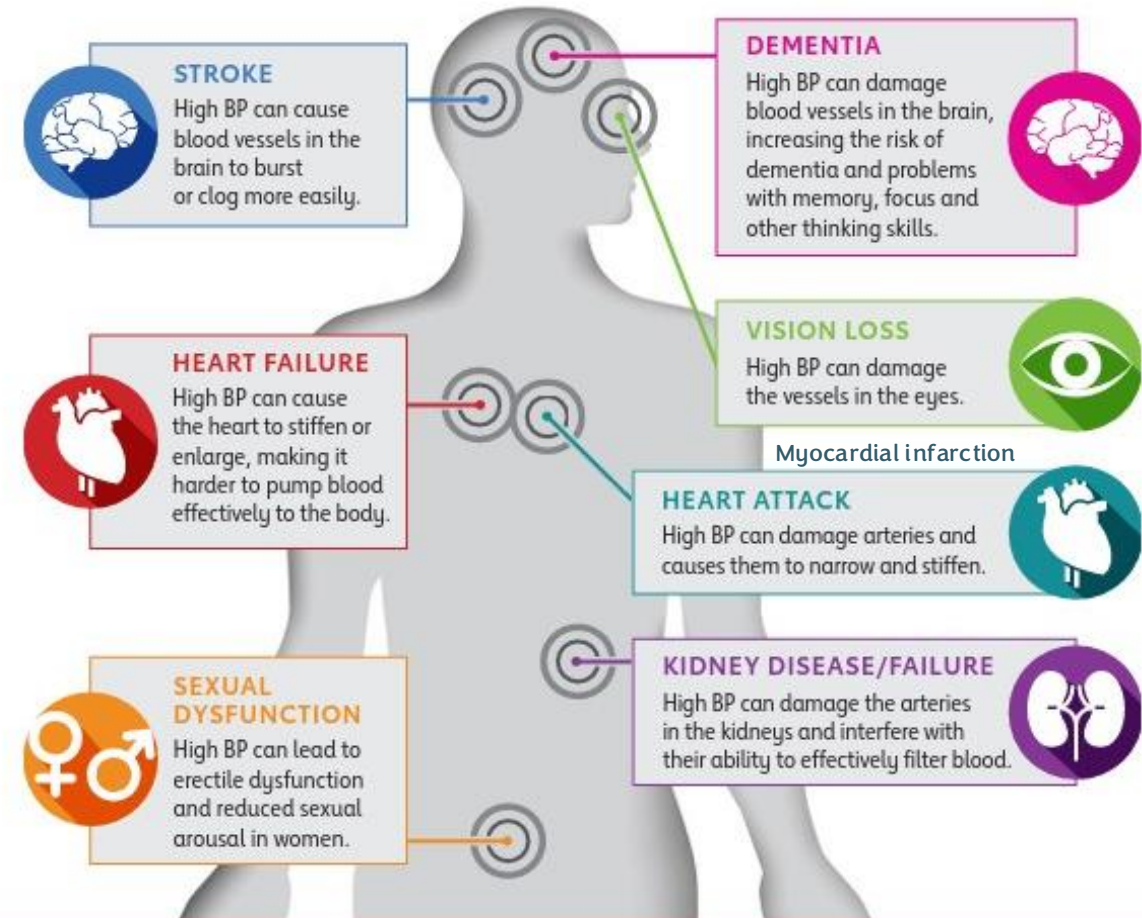
The corpus cavernosum in penile tissue can be affected, impairing its relaxation and leading to erectile dysfunction in males.



The doctor has covered **all** the details in this figure, so make sure to review it carefully and understand which organs are affected by hypertension

Consequences of High Blood Pressure

High blood pressure (BP) can cause other health problems, like:



A healthy blood pressure helps protect your kidneys, heart and your body's ability to use energy (metabolic health). Check your blood pressure today. Learn more at heart.org/BP.

Treating Hypertension

If we have a patient with **elevated** BP or **stage 1** hypertension, we don't have to go directly to drugs. We try to control BP by

Lifestyle Modification: Alterations in diet (ex, Lower salt intake⁽¹⁾), a plan to quit smoking, managing stress (high cortisol) and exercise⁽²⁾ may reduce blood pressure in some patients.

Drug Treatments: There are many antihypertensive drugs, commonly used in combination therapy. (Sometimes we use only 1 drug, but most of the time we use 2-3 drugs)

A Question from students but it's good to know:

Why don't we treat ***hypotension***?

- Hypotension is **not** considered a disease, but it is risky. We don't want the patient's diastolic BP to fall below 60, because this activates the sympathetic nervous system (baroreceptor reflex), increasing heart rate, which is problematic for patients with heart disease.
- Hypotension is a symptom, probably due to hypovolemia (bleeding, dehydration, kidney disease), and should be managed.

Relevant studies regarding previous slide

- (1) A study called **DASH** (Dietary Approaches to Stop Hypertension) looked at two populations: those who consumed a high-Na diet versus those who consumed less than 1600 mg of Na. The ones who took **less** sodium had a **lower** tendency to develop hypertension.
- (2) Studies have shown that **obesity** is linked to hypertension through multiple mechanisms, including high blood glucose (diabetes), endothelial dysfunction, and activation of the sympathetic nervous system and RAAS. These changes impair blood vessel wall function and increase blood pressure. Therefore, patients are advised to reduce weight through regular exercise and a balanced, healthy diet.

How to choose a suitable drug for a patient ?

- **Tailor treatment according diagnostic exam**

1. Underlying conditions (comorbidities): The cause of hypertension should be taken into account. For example, having renal disease.
2. Uncomplicated vs. complicated disease: Patients with heart failure can receive a drug that treats both conditions.
3. Ethnicity: For example, African Americans respond better to diuretics compared to White Americans. This is because their type of hypertension is often associated with low renin levels, making them more responsive to diuretics.
4. Severity of hypertension (stage): Stage 1 hypertension might require only one mild drug, while Stage 2 may need two stronger medications.
5. Pregnancy: Some women develop hypertension during pregnancy. Certain drugs are contraindicated during pregnancy (categories B, C, D, etc.).
6. Drug interactions: In a patient with diabetes who develops hypertension, some drugs can affect insulin levels. Also, in patients with high lipids, certain medications can increase lipid levels.
7. Patient compliance: Many patients take multiple medications for comorbidities like diabetes. Adding more drugs may overwhelm the patient, a situation called **polypharmacy**. The drug of choice should ideally cover the effects of two medications, reducing pill burden and improving compliance. Sometimes, drugs are substituted instead of added.

Antihypertensive drugs may be divided into the following classes: 10 categories

- Diuretics work on the Kidneys (مدرات البول)
- Calcium channel blockers
- Beta blockers ¹
- Angiotensin converting enzyme (ACE) inhibitors (ACEI) act on RAAS
- Angiotensin Receptor Blockers (ARBs) act on RAAS
- Central α 2-adrenergic receptor agonists²
- Adrenergic neuron blocking agents³
- Peripheral α -adrenergic antagonists⁴
- Vasodilators
- New drugs in the treatment of HT

4 drugs (numbered above¹⁻⁴) are related to sympathetic nervous system.



PHARMACOLOGY QUIZ LECTURE 1

Additional sources:

1. [DASH study link](#)
2. [Epidemiology of Hypertension and Cardiovascular Disease in African Americans study link](#)



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Scan the QR code or click it for FEEDBACK



Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			