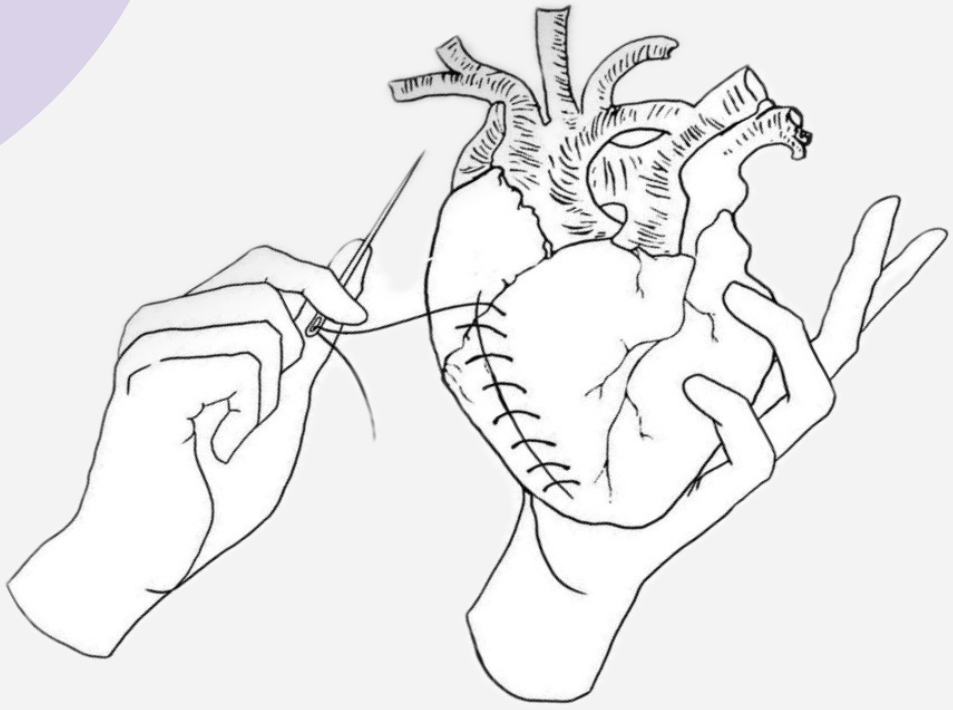
# Pathology & Pathogenesis of Hypertension



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COLOR INDEX:

MAIN TEXT (BLACK )

FEMALE SLIDES (PINK)

MALE SLIDES (BLUE)

IMPORTANT (RED)

DR'S NOTE (GREEN)

EXTRA INFO (GREY)

# Objectives

Know the etiology, risk factors and complications of hypertension, so as to be able to identify patient risk factors amenable to treatment by lifestyle modification, and to investigate patients appropriately for causes of secondary hypertension.

## Key principles to be discussed:

1. Raised systemic blood pressure is a major cause of morbidity and mortality.
2. Hypertension can cause or contribute to: atherosclerosis, left ventricular hypertrophy, chronic renal failure, cerebrovascular disease and retinopathy.
3. Normal values for blood pressure.
4. Causes of secondary hypertension.
5. Genetic and environmental factors contributing to the aetiology of essential hypertension.
6. Pathology of blood vessels (blood vessels changes) in both primary and secondary hypertension.

If you want to read the lecture from Robbins click here

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# Hypertension

## Definition

A sustained systolic pressure in excess of 140 mm Hg or a sustained diastolic pressure more than 90 mm Hg. (>140/90)in at least 3 different readings

*New Guidelines of ACC/AHA state a lower threshold of hypertension. As above 130/80 is considered the new threshold for stage 1 HTN.*

*This is because new studies show benefits in having a lower blood pressure than 140/90*

*A famous clinical trial is the SPRINT Trial 2015. you can read its results here:*

*A Randomized Trial of Intensive versus Standard Blood-Pressure Control | New England Journal of Medicine*

Common problem (25% of population)

Asymptomatic until late
-Silent Killer-
painless.

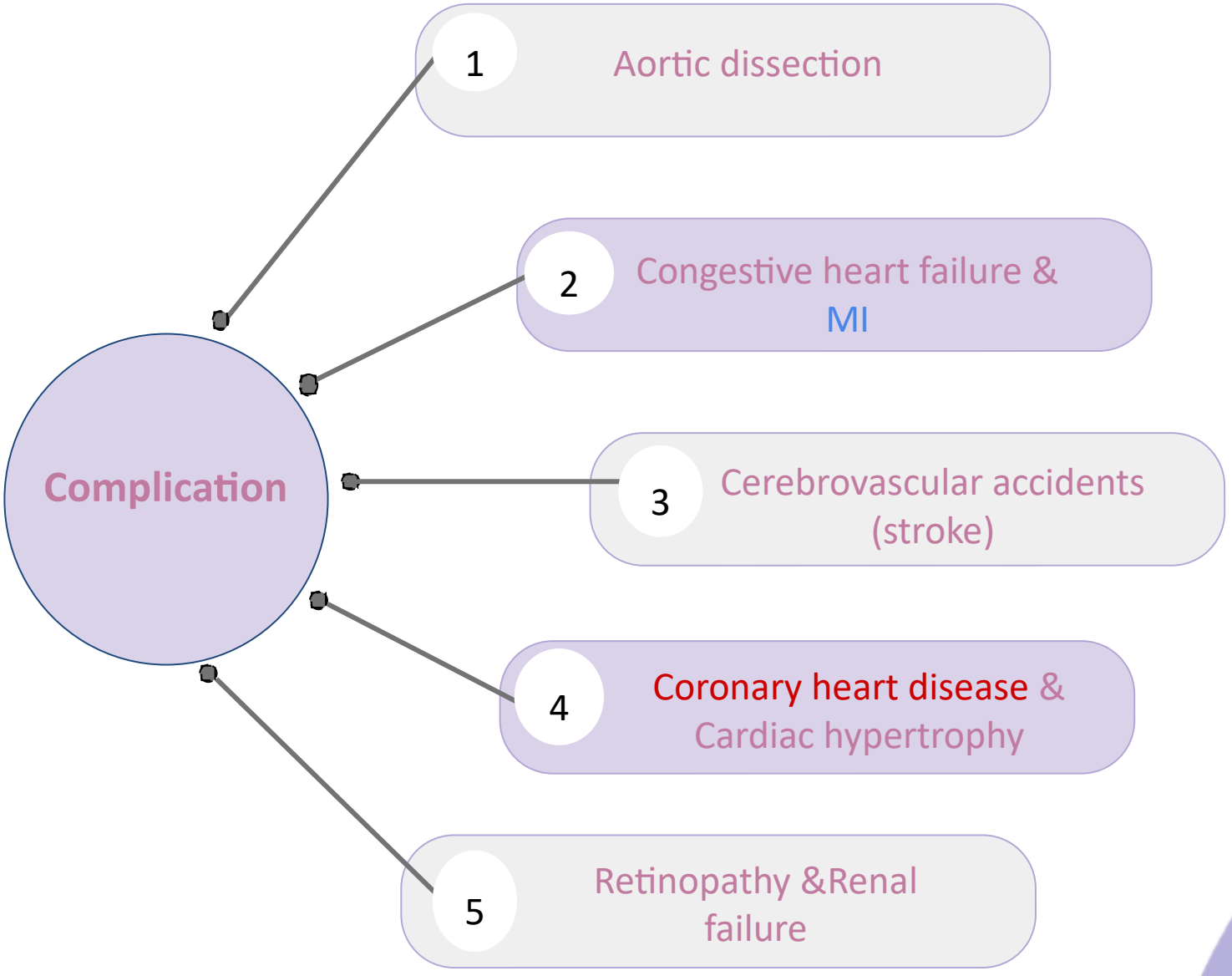
Complications alert to diagnosis but late.

In the early stages of HTN there are few or no symptoms.

*By: Khalid Alohali 44*

# Hypertension

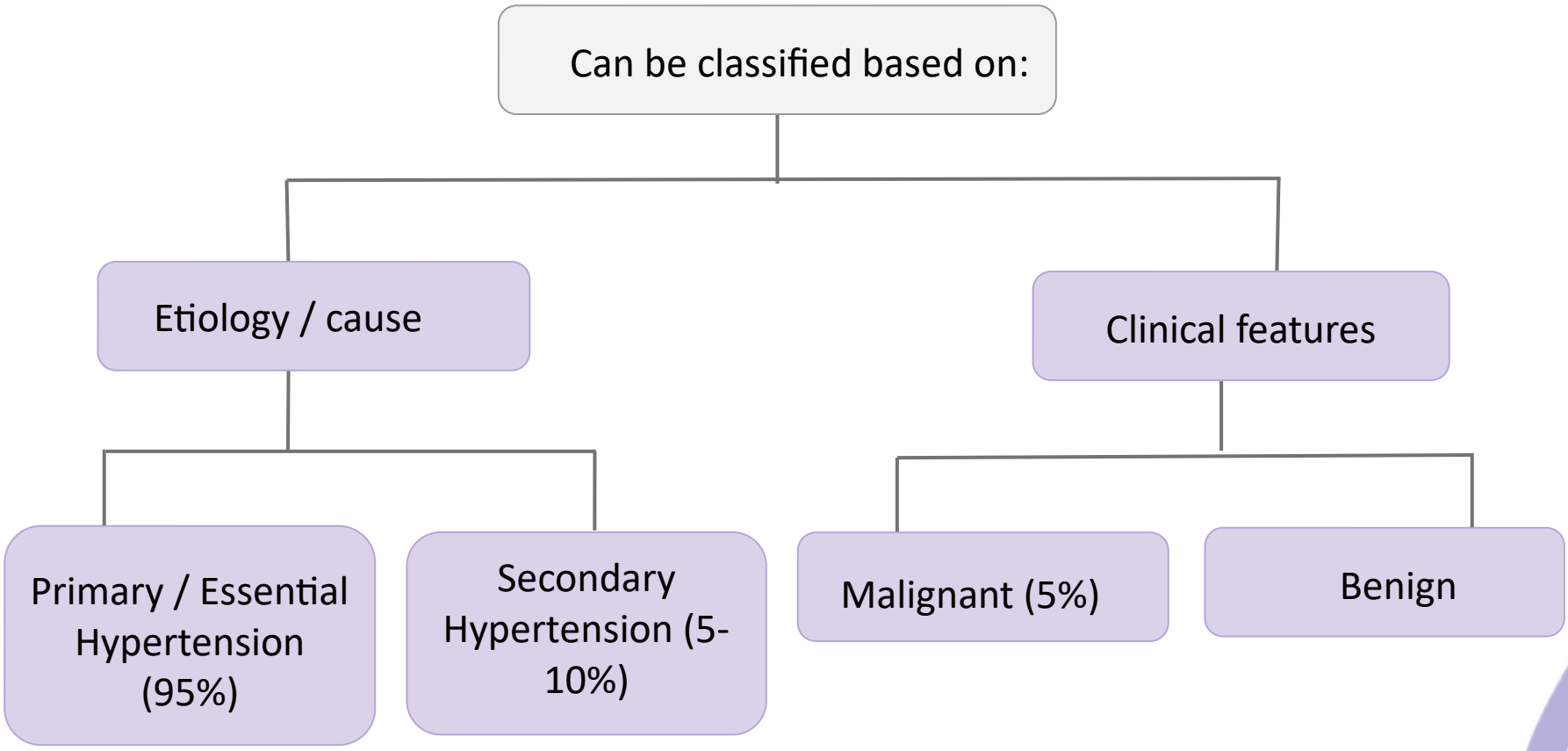
Hypertension is an important factor which contributes in development of:



# Risk factors for hypertension

- Hereditary: Genetics-family history
- Race: African-Americans
- Gender: Men & postmenopausal women
- Age
- Obesity & Sedentary or inactive lifestyle
- Diet, particularly sodium intake
- Lifestyle-stressful
- Heavy alcohol consumption
- Diabetes
- Use of oral contraceptives

# HTN classification



# Classification of Hypertension based on etiology/cause

| | | |
|---|---|---|
| **Primary / Essential Hypertension (95%)** | Mechanisms largely unknown. It is **idiopathic**. | |
| **Secondary Hypertension Endocrine (5-10%)**<br><br>it can be due to pathology in: | **Renal** | ‣ Acute glomerulonephritis<br>‣ Renal artery stenosis<br>‣ Renal vasculitis<br>‣ Adult polycystic disease<br>‣ Chronic renal disease<br>‣ Renin producing tumors |
| | **Endocrine** | ‣ Adrenocortical hyperfunction (Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia which is an example of gene defect affecting aldosterone metabolism)<br>‣ Hyperthyroidism / Thyrotoxicosis<br>‣ Hypothyroidism / Myxedema<br>‣ Pheochromocytoma<br>‣ Acromegaly<br>‣ Exogenous hormones (glucocorticoids, estrogen [including pregnancy-induced and oral contraceptives] and sympathomimetics)<br>‣ Pregnancy-induced |
| | **Vascular** | ‣ Coarctation of aorta<br>‣ Vasculitis e.g.Polyarteritis nodosa<br>‣ Increased intravascular volume<br>‣ Increased cardiac output<br>‣ Rigidity of the aorta |
| | **Neurogenic** | ‣ Psychogenic<br>‣ Increased intracranial pressure<br>‣ Sleep apnea<br>‣ Acute stress, including surgery |
| | **Pulmonary** | Pulmonary diseases |

# Classification of Hypertension based on Clinical features

**Benign:**

- The BP is at modest level (not very high)
- It can be idiopathic HTN or secondary HTN
- Fairly stable over years to decades.
- Compatible with long life.

Females slides

**Malignant 5% :**

- there is rapidly rising BP which often leads to end organ damage
- It can be a complication of any type of HTN (i.e. essential or secondary)
- It is seen in 5% of HTNsive patients.
- **The diastolic pressure is usually over 120mmHg**
- It is associated with:
  - Widespread arterial necrosis and thrombosis
  - Rapid development of renal failure
  - Retinal hemorrhage and exudate, with/without papilledema
  - Hypertensive encephalopathy
  - Left ventricular failure
  - Leads to death in 1 or 2 years if untreated.

# Regulation Of Blood Pressure

Females slides

Definition of Blood pressure:
is a function of cardiac output and peripheral vascular resistance

**There are 2 hemodynamic variables that are involved in the regulation of BP :**

1- Cardiac output and 2-Peripheral vascular resistance

BP = Cardiac Output x Peripheral Resistance

## Cardiac Output

is affected by blood volume and is dependent on sodium concentrations.

## Peripheral resistance

it is the resistance of the arteries to blood flow. When the arteries constrict the resistance increases and when they dilate the resistance decreases. Peripheral resistance is regulated at the level of the arterioles. Arterioles are also known as resistance vessels. Peripheral resistance is determined by three factors:

Note: An increased blood flow in the arterioles induces vasoconstriction to protect tissues against hyperperfusion.

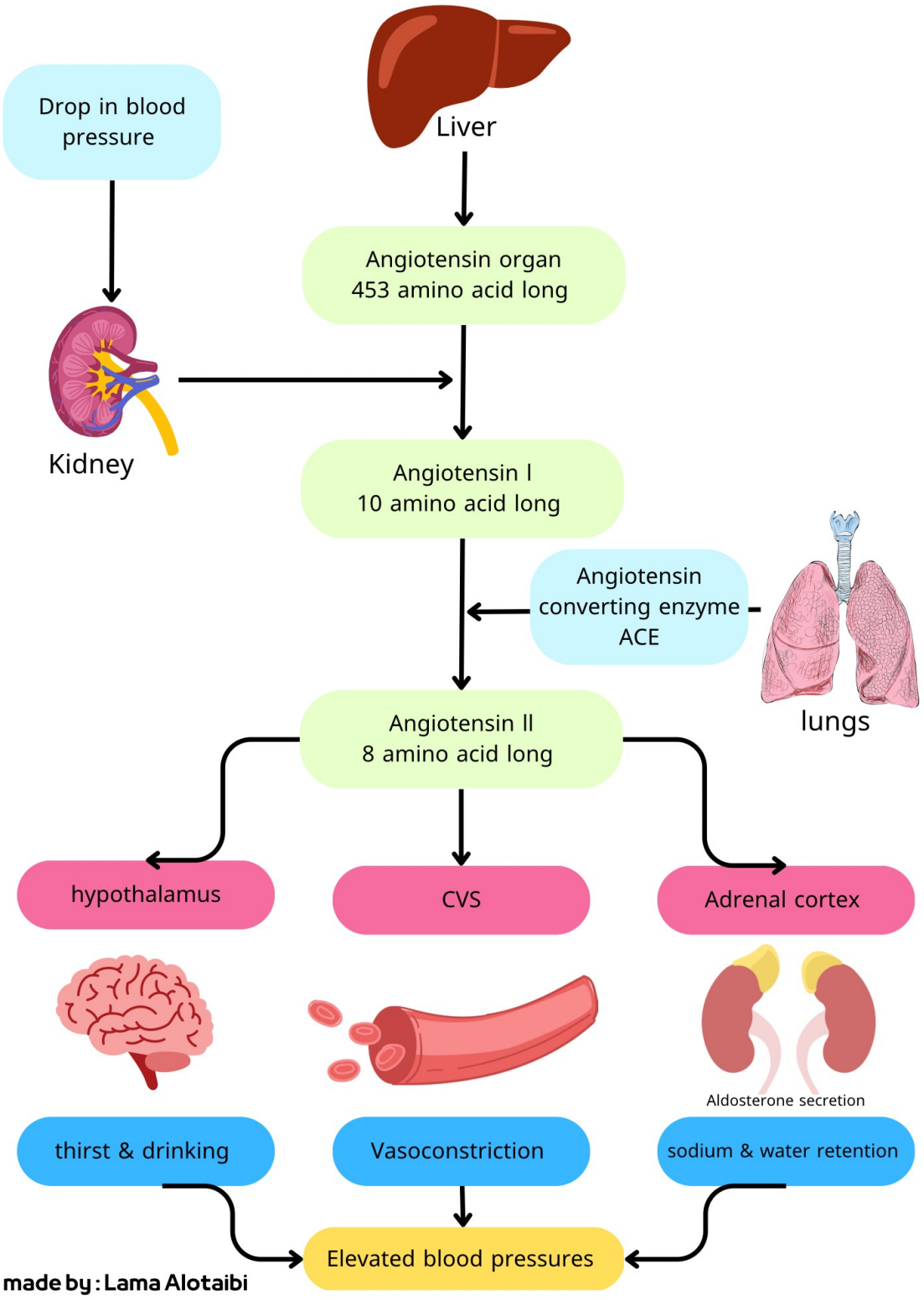
**Autonomic activity:** sympathetic activity constricts peripheral arteries. (Sympathetic stimulation: arteries constrict. Parasympathetic stimulation: arteries dilate.)

**Pharmacologic agents**: vasoconstrictor drugs increase resistance, while vasodilator drugs e.g. nitroglycerin decrease It.

**Blood viscosity:** increased viscosity increases resistance.

# Regulation Of Blood Pressure

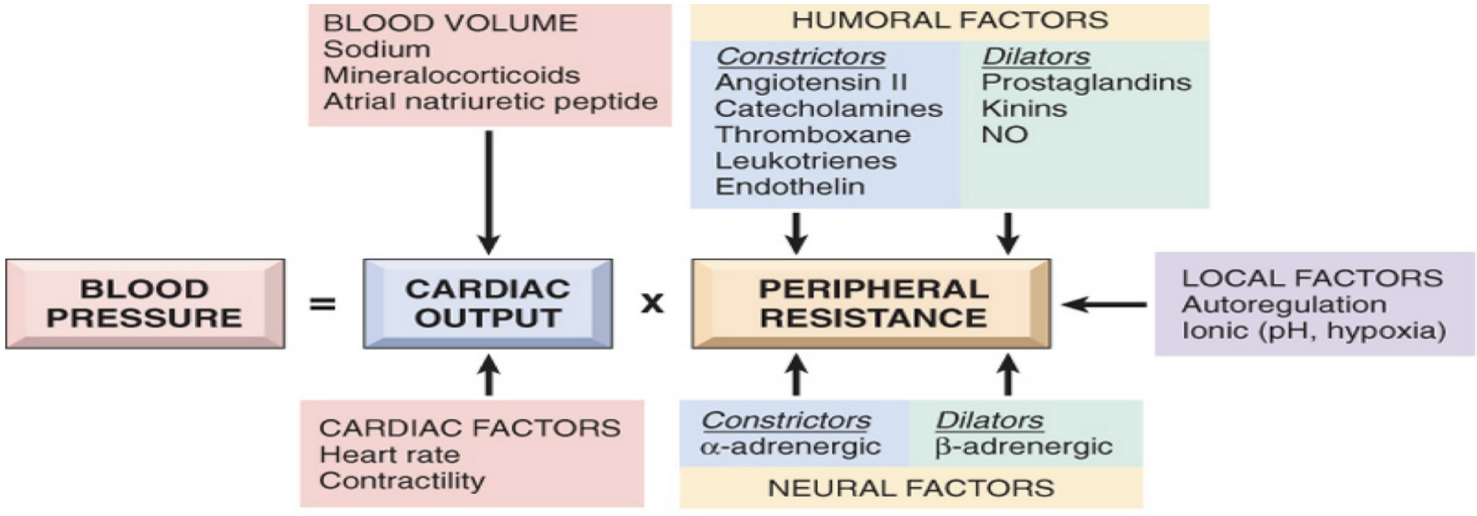
Females slides



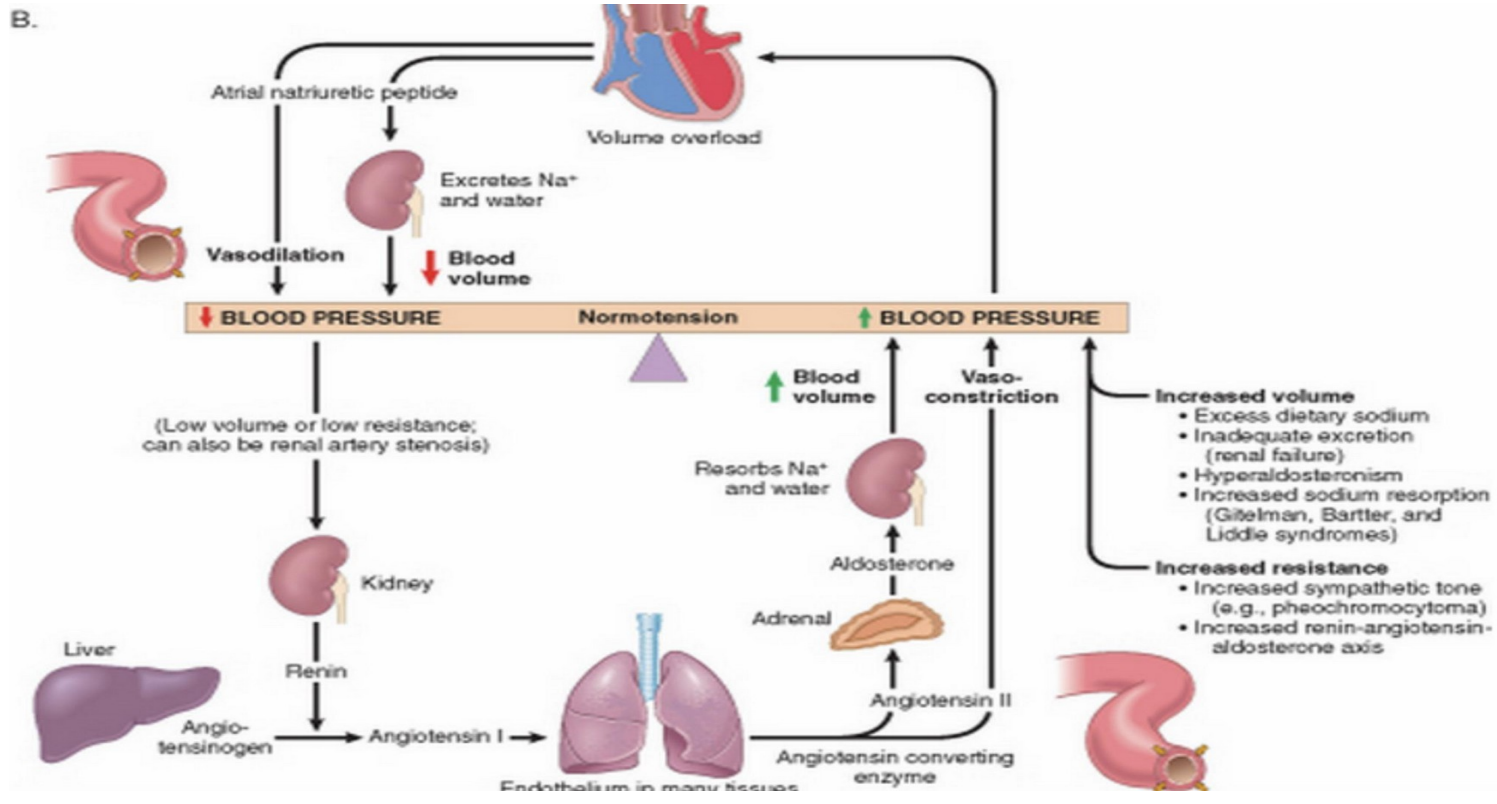

ENDOCRINE FACTORS:
role of renin- angiotensin-aldosterone in regulating BP

# Regulation Of Blood Pressure

Normal BP is maintained by a balance between factors that induce vasoconstriction (e.g. angiotensin II and catecholamines) and factors that induce vasodilation (e.g. kinins, prostaglandins and nitric oxide).




**ENDOCRINE FACTORS:** **Renin, Angiotensin, ADH, Aldosterone**




Renin-angiotensin-aldosterone and atrial natriuretic peptide rule

# Pathogenesis of essential hypertension

Specific Mechanism were only in females slides

## Kidney

**Defect in renal sodium homeostasis:**

- reduced renal sodium excretion is a key initiating event in most forms of essential hypertension.
- Decreased sodium excretion -> leads to increase in fluid volume (feel thirst -> drink water) and therefore -> increase in cardiac output and therefore -> elevated BP.
- This is usually due to defect in cell membrane function affecting the Na/Ca transport.

## CNS

**Functional vasoconstriction:** abnormality in vascular tone such as increased sympathetic stimulation will cause vasoconstriction leading to increased peripheral resistance.

## Blood vessel muscle

**Structural abnormality** in vascular smooth muscle also leads to increased peripheral resistance. (Born with abnormal blood vessels with low capacity)

## Genetic Mutations

**Also rare gene disorders** can cause HTN by increasing renal sodium reabsorption e.g. Liddle syndrome.

- Liddle syndrome is an inherited autosomal dominant type of HTN, that begins in childhood. It is caused by mutations of the epithelial sodium channel protein (ENaC) which leads to increased sodium reabsorption in the renal tubules (followed by water), which leads to hypertension.
- Reabsorption of sodium is also correlates with potassium loss (hypokalemia).

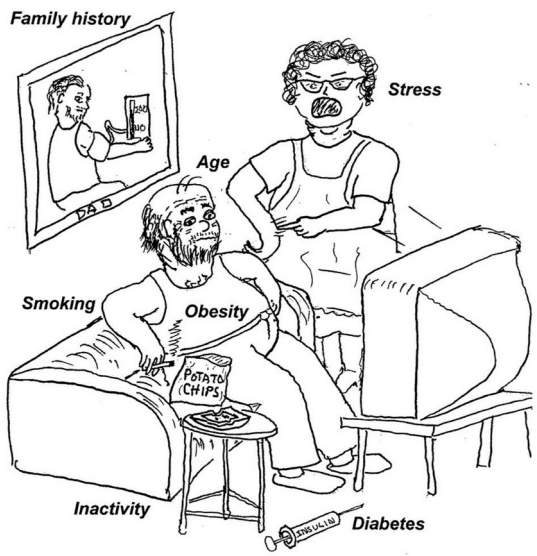
The difference between Defect in renal sodium homeostasis -> manifested at late age, >40s
Liddell syndrome -> early during childhood

# Environmental factors

Females slides

Environmental factors

1. smoking , Alcohol
2. Stress , Physical inactivity
3. obesity , Fat Consumption
4. Oral contraceptives
5. Heavy Salt Consumption




RISK FACTORS FOR ESSENTIAL HYPERTENSION

# Pathogenesis Of Essential Hypertension

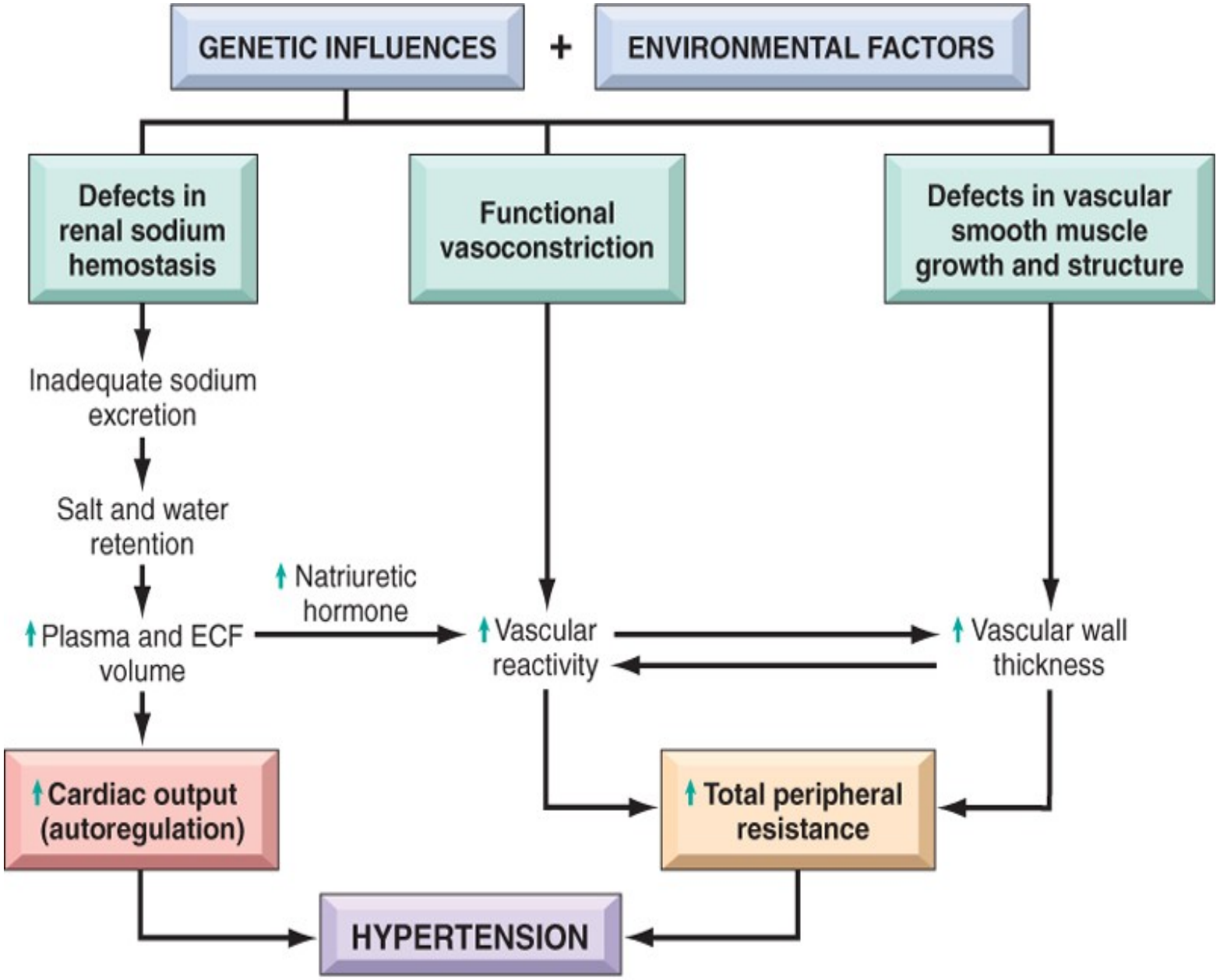
## Essential Hypertension

### Event

in hypertension, both increased blood volume and increased peripheral resistance contribute to the increased pressure. Essential HTN However reduced renal sodium excretion in the presence of normal arterial pressure (initially) is probably a key initiating event.

### When does it occur ?

Essential HTN occurs when the relationship between cardiac output and peripheral resistance is altered. Multiple genetic and environmental factors ultimately increase the cardiac output and/or peripheral resistance (BP = Cardiac Output x Peripheral Resistance)



# Atrial Natriuretic peptide/factor/hormone (cardiomatrine/cardiodilatine/atriopeptin)

Females slides

It is a protein/ polypeptide/ hormone secreted by the heart muscle cells in the atria of heart (atrial myocytes).

It is a powerful vasodilator and is involved in the homeostatic balance of body water, sodium, potassium and fat.

It is released in response to high blood volume. It acts to reduce the water, sodium and adipose loads on the circulatory system, thereby reducing blood pressure.

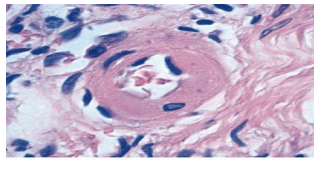
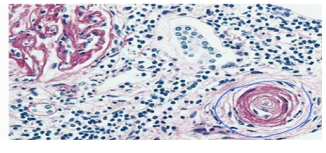
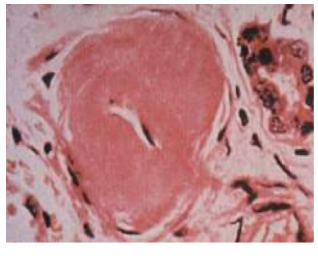
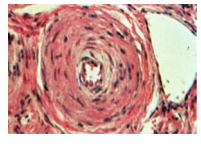
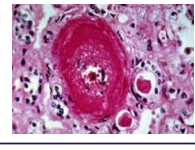
It has exactly the opposite function of the aldosterone secreted by the zona glomerulosa. (Opposite of RAAS effects)

## Effects of ANP :

| in the kidney | in adrenal gland | in Arterioles | in Adipose tissue |
|---|---|---|---|
| •Decreases sodium reabsorption and increases water loss.<br>• Inhibits renin secretion, thereby inhibiting the the kidney renin–angiotensin–aldosterone system. | • Reduces aldosterone secretion by the zona glomerulosa In of the adrenal the adrenal glands cortex. | • Promotes vasodilation. | • Increases the release of free fatty acids from adipose tissue. |

# Morphology of blood vessels in HTN:

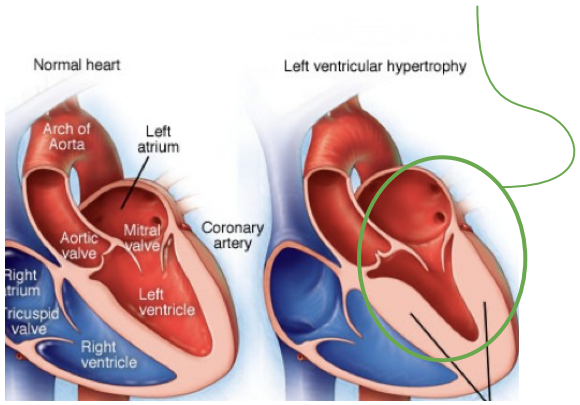
Females slides

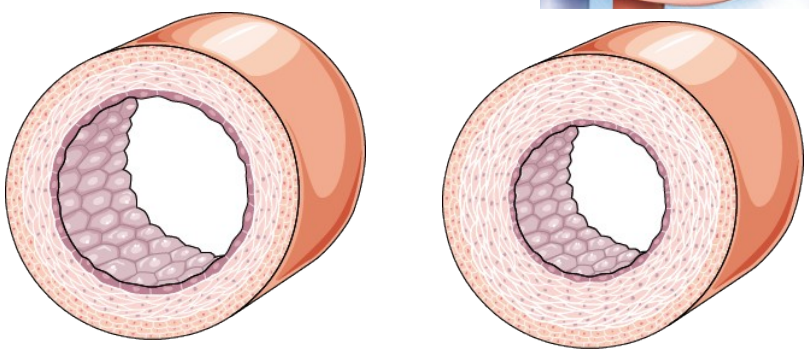
<table>
<tr><td>In large Blood Vessels (Macroangiopathy)</td><td colspan="2">Atherosclerosis. HTN is a major risk factor in AS.<br>• Accelerate atherogenesis<br>• Arteriosclerosis (particularly in the kidney), lead to thick wall and narrow lumen</td></tr>
<tr><td rowspan="3">In small Blood Vessels (Microangiopathy)</td><td>Hyaline arteriolosclerosis</td><td>Hyperplastic arteriolosclerosis</td></tr>
<tr><td>• Seen in benign hypertension<br>• Can also be seen in elderly and diabetic patients even without hypertension.<br>• Can cause diffuse renal ischemia which ultimately leads to benign nephrosclerosis</td><td>• Characteristic of malignant hypertension.<br>• Can show onion-skinning on histology causing luminal obliteration of vascular lumen<br>• May be associated with necrotizing arteriolitis and fibrinoid necrosis of the blood vessel.</td></tr>
<tr><td colspan="2"></td></tr>
<tr><td rowspan="3">Morphology</td><td>Lumen become small and thick Hyaline arteriosclerosis: hyalinosis of arteriolar wall with narrowing of lumen. Irreversibly<br>  </td><td>Hyperplastic arteriolosclerosis hyalinosis of arteriolar wall with (onion skinning) causing obliteration loose if space of vascular lumen<br>  </td></tr>
<tr><td>Hyaline/ Benign hypertension<br>  </td><td>hyperplastic/malignant hypertension showing onion skinning<br>  </td></tr>
<tr><td></td><td>hyperplastic/malignant hypertension showing fibrinoid necrosis.<br>  </td></tr>
</table>

# Left ventricular cardiac hypertrophy

Females slides

1. also known as left sided hypertensive cardiomyopathy/ hypertensive heart disease)
2. Longstanding poorly treated HTN can a left sided hypertensive heart disease.
3. Left ventricular hypertrophy is an adaptive response to pressure overload due to HTN.
4. HTN induces left ventricular pressure overload which leads to hypertrophy of the left ventricle with increase in the weight of the heart and the thickness of the LV wall



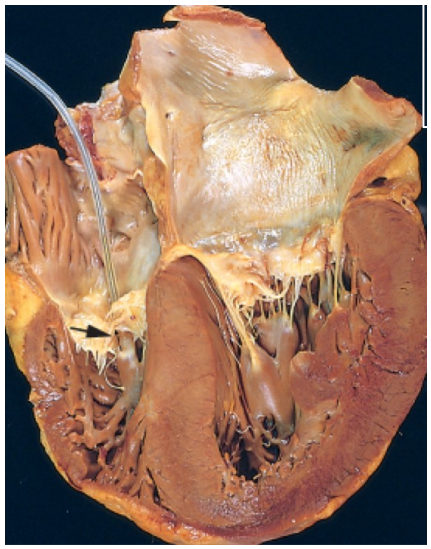
Normal

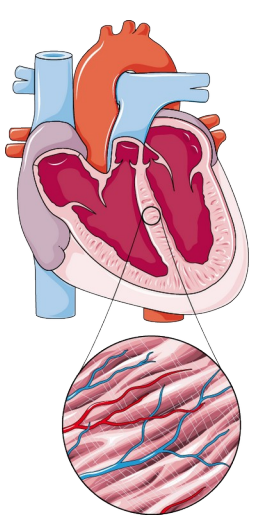
Hypertrophy

# Systemic hypertensive cardiac disease

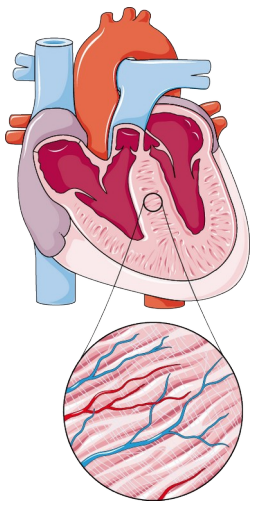
males slides

- History of hypertension or extracardiac anatomical evidence of HTN
- LVH:concentric with absence of other cause of LVH
- The free LV wall is > 2cm and the weight of the heart is > 500 grams (M: may ask on numbers)
- Long-term: dilatation and wall thinning
- Treatment of HTN helps recovery





Normal



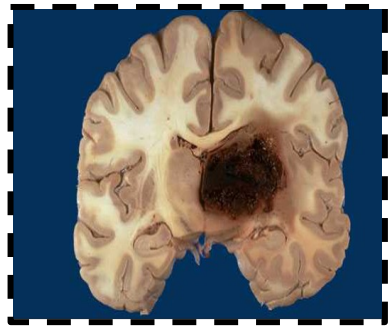
Hypertrophy

# Complications in HTN

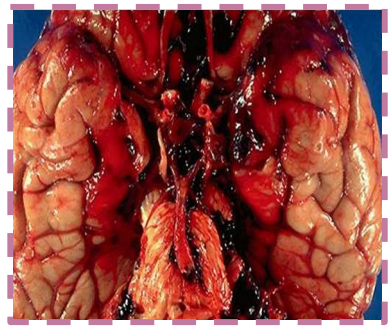
The organs damaged in HTN are:

| Cardiovascular | Kidney | Eyes | Brain |
|---|---|---|---|
| 1- Left ventricular cardiac hypertrophy (left sided hypertensive cardiomyopathy/ hypertensive heart disease)<br>2- Coronary heart disease<br>3- Aortic dissection<br>4-heart failure (hypertensive heart disease) | 1-Benign nephrosclerosis<br>2- Renal failure in untreated or in malignant hypertension | Hypertensive retinopathy is especially seen in malignant hypertension. | Hemorrhage, infarction leading to Cerebrovascular accidents |

Benign nephrosclerosis

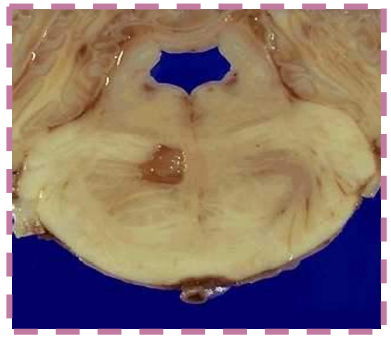


CEREBRAL HEMORRHAGE



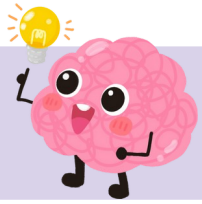
Subarachnoid Haemorrhage

Hypertensive retinopathy



Lacunar Infarct

CEREBRAL INFARCTION



# KEYWORDS

| | |
|---|---|
| Hypertension | • systolic pressure > 140 mmHg<br>• diastolic pressure > 90 mmHg |
| Primary/Essential Hypertension | • Most common<br>• Idiopathic<br>• Defect in renal sodium homeostasis<br>• Functional vasoconstriction<br>• Structural abnormality in vascular smooth muscle<br>• Gene disorder : Liddle syndrome |
| Secondary hypertension | • Due to renal , endocrine , vascular , neurological problems<br>• Renovascular disease is the most common |
| Benign hypertension | • Modest level<br>• Hyaline arteriosclerosis (pink)<br>• renal ischemia |
| Malignant hypertension | • Very high ( over 120 mmhg)<br>• Hyperplastic arteriolosclerosis (onion skin)<br>• Fibrinoid Necrosis |

Answers:
1- C 2-A 3-A 4-C 5-D

# MCQ

| 1- Which of the following best defines hypertension? | | | |
|---|---|---|---|
| A)Elevated systolic and diastolic blood pressure on at least 3 separate occasion | B)Elevated systolic blood pressure on at least 3 separate occasions | C)Elevated systolic and/or diastolic blood pressure on at least 3 separate occasions | D)Elevated diastolic blood pressure on at least 3 separate occasions |
| 2- Peripheral resistance is regulated predominantly at the level of: | | | |
| A)Arterioles | B) Arteries | C)Veins | D) Capillaries |
| 3- A sustained blood pressure in excess of how much is considered hypertension? *(according to these slides)* | | | |
| A)140/90 | B)128/79 | C)120/80 | D)115/65 |
| 4- The etiology of primary hypertension is usually: | | | |
| A)Cardiogenic | B)Neurogenic | C)Unknown | D)Renal |
| 5- Malignant HTN have diastolic pressure over: | | | |
| A) 75 | B)110 | C)100 | D)120 |

Answers:
6- C 7-A 8-D 9-C 10-D

# MCQ

| | | | |
|---|---|---|---|
| 6- Which of these can be seen in elderly and diabetic patients even without hypertension? | | | |
| A- Hyperplastic arteriolosclerosis | B) Left-Sided cardiomyopathy | C) Hyaline arteriolosclerosis | D- Atherosclerosis |
| 7-Liddle syndrome is caused by a mutation of which gene? | | | |
| A)ENaC | B) TGFBI | C)ABL1 | D) MTHFR |
| 8-All the following are complications of hypertension except? | | | |
| A)Kidney failure | B)Stroke | C)Retinopathy | D) Raynaud's phenomenon |
| 9- A patient living with hypertension for 10 years ( 160 / 100 ). In the last 3 months, his blood pressure was ( 200/120) and creatinine level was elevated. A biopsy of renal artery represents one of the following? | | | |
| A)Fibrin arteriolosclerosis | b)Polyarteritis nodosa | C)Hyperplastic arteriosclerosis | D) None of the above |
| 10- Hyperplastic arteriolosclerosis and fibrinoid necrosis are characteristics of which of the following diseases? | | | |
| A)Benign hypertension | B)Diabetes mellitus | C)Hyperlipidemia | D)Malignant hypertension |

Answers:
1-C 2- A 3- D

# Cases (EXTRA)

1-.A 40-year-old woman comes to the clinic due to 2 months of headaches and an irritating sound in her left ear. The patient states the sound is similar to a 'whooshing,' and she has noticed that it matches the timing of her own heartbeat. Past medical history is significant for asthma. Current medications include albuterol and inhaled corticosteroids as needed. Temperature is 37.0 °C (98.6 °F), pulse is 80/min, and blood pressure is 170/95 mmHg. Body mass index (BMI) is 32 kg/m2. On physical exam, cardiac and lung examination is within normal limits. A systolic bruit is heard below the left ear. Abdomen is soft and nontender, and bowel sounds are present. There is a bruit present over the abdomen on auscultation. Further evaluation of this patient is most likely to reveal which of the following?

| | | | |
|---|---|---|---|
| A.Elevated free cortisol on 24-hour urinalysis | B.Elevated CO2 on pulse oximetry | C. Elevated renin levels | D. None |

2- A 76-year-old man presents with difficulty breathing. He says that he becomes short of breath at night unless he uses three pillows to prop himself up. Measurements of vital signs reveal normal temperature, mild tachypnea, and a blood pressure of 180/100 mm Hg. Physical examination discloses obesity, bilateral 2+ pitting leg edema, hepatosplenomegaly, and rales at the bases of both lungs. An X-ray fi lm of the chest shows mild enlargement of the heart and a mild pleural effusion. Echocardiography reveals left ventricular hypertrophy without valvular heart

| | | | |
|---|---|---|---|
| A. Hypertensive heart disease | B. Renal failure | C.Dilated cardiomyopathy | D. Acute cor pulmonale |

3- A 19-year-old girl is brought to the emergency room with heart palpitations and dyspnea. Her past medical history is significant for an unrepaired atrial septal defect (ASD). Physical examination reveals cyanosis, distended jugular veins, hepatosplenomegaly, and a systolic ejection murmur. This patient has most likely developed which of the following complications of congenital heart disease?

| | | | |
|---|---|---|---|
| A) Aortic aneurysm | B) Myocardial infarction | C)Pneumonia | D)Pulmonary hypertension |

# Pathology team

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