PATHOLOGY TEAM
439

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Hypertension

Objectives:

- Know the etiology, risk factors and complications of hypertension,
- Be Able identify patient risk factors amenable to treatment by lifestyle modification
- investigate patients appropriately for causes of secondary hypertension.

Index:
Important
NOTES
Extra Information

Hypertension

A sustained systolic pressure in excess of 140 mm Hg or a sustained diastolic pressure more than 90 mm Hg **(>140/90)**

Common problem

Asymptomatic until late
Silent Killer – painless

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

Hypertension is an important factor which contributes in development of:

- Coronary heart disease
- Cerebrovascular accidents (stroke)
- Cardiac hypertrophy
- Congestive heart failure
- Aortic dissection
- Renal failure
- Retinopathy

Risk Factors

Hereditary
Genetics-family history

Race.
African-Americans

Heavy alcohol consumption

Age and Gender
Men & postmenopausal women

Diabetes

Diet
particularly sodium intake

Obesity, stressful or inactive

Use of oral contraceptives

Classification of Hypertension cont..

Based on Etiology or cause

1-Primary/ Essential Hypertension (95%) :

Mechanisms largely unknown. It is idiopathic. 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.

Genetic Factors

There is a strong genetic component (family history) e.g. a genetic effect is involved in making people more susceptible or less susceptible to high salt diet etc.

1- Defect in renal sodium homeostasis

Reduced renal sodium excretion is a key initiating event in most forms of essential hypertension.
How? decreased sodium excretion lead to → increase in fluid volume 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.

2- Functional vasoconstriction

abnormality in vascular tone such as;
increased sympathetic stimulation leading to →
vasoconstriction leading to → increased peripheral resistance (high blood pressure).

3- Structural abnormality in vascular smooth muscle

leads to increased peripheral resistance.

4- Rare gene disorders

By increasing renal sodium reabsorption e.g. **Liddle syndrome:** 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 also correlates with potassium loss (hypokalemia)
Example of genetic disorder: young people have high blood pressure called Liddle syndrome and it caused by mutation of Sodium channel proteins that present in epithelial cells of tubular of the kidney.

Environmental Factors

- **Stress**
- **Obesity**
- **Smoking**
- **physical inactivity**
- **heavy consumption of salt**

2-Secondary Hypertension (5-10%)

it can be due to pathology in the renal, endocrine, vascular or neurogenic systems.

Renal	**1-Glomerulonephritis** **2-Renal artery stenosis** **3-Renal vasculitis** **4-Adult polycystic disease 5-Chronic renal disease** **6-Renin producing tumors**
Endocrine	**1-Adrenocortical hyperfunction** (Cushing syndrome, primary aldosteronism, congenital adrenal hyperplasia) **2-Hyperthyroidism/Thyrotoxicosis** **3-Hypothyroidism/Myxedema** **4-Pheochromocytoma** **5-Acromegaly** **6-Exogenous hormones** (glucocorticoids, estrogen e.g. oral contraceptives) Pregnancy-induced
Vascular	**1-Coarctation of aorta** **2-Vasculitis e.g.Polyarteritis nodosa 3-Increased intravascular volume** **4- Increased cardiac output** **5-Rigidity of the aorta**
Neurogenic	**1-Psychogenic** **2-Increased intracranial pressure** **3- Sleep apnea** **4-Acute stress, including surgery**

Skipped by doctor

Classification of Hypertension

Based on Clinical Features

Benign	Malignant
1- The BP is at modest level (not very high). . 2- It can be idiopathic HTN or secondary HTN. 3- Fairly stable over years to decades 4- Compatible with long life.	There is rapidly rising BP which often leads to end organ damage. 2-It can be a complication of any type of HTN (i.e. essential or secondary). 3-It is seen in 5% of HTN patients 4-The diastolic pressure is usually over 120 mmHg. 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

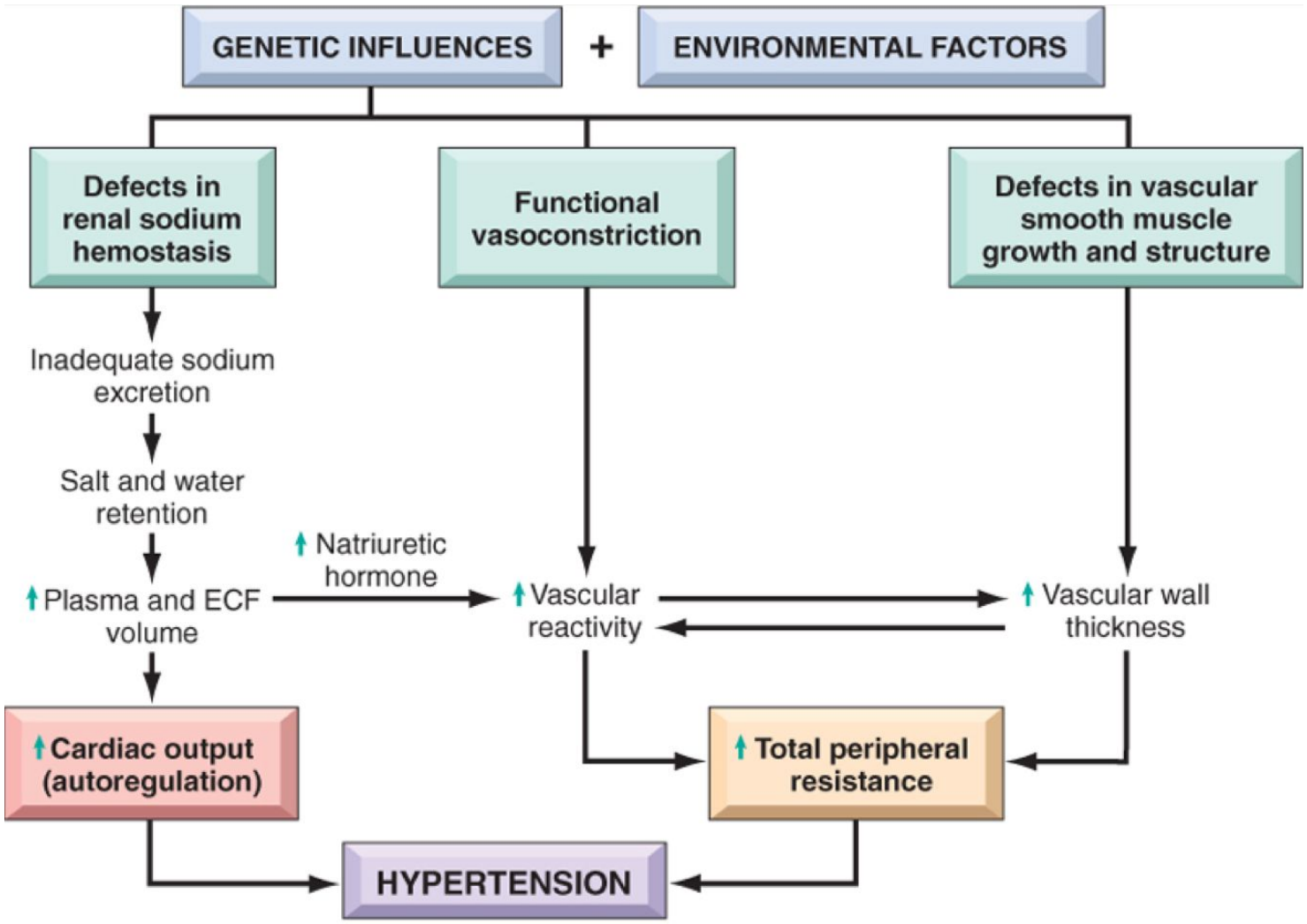
Regulation Of Blood Pressure

There are 2 hemodynamic variables that are involved in the regulation of BP. They are **Cardiac output** and **Peripheral vascular resistance.**

BP = Cardiac Output x Peripheral Resistance

Cardiac Output	Peripheral resistance
is affected by **blood volume** and is dependent on **sodium concentrations.** Explanation: How Sodium affects my CO? because Sodium (salt) always attract water. "Remember that if you eat salty Fries you will get thirsty and will drink more water why? because salt attracts the water in your body and absorb it by kidney, so more water in your body means more blood volume this will result more CO in the body therefore Blood pressure will be High". Let's summarize it as steps: More salt (sodium) | Water will be absorbed (by Kidney) | More water in the body (by drinking water) | High blood volume | More CO | **High Blood Pressure**	it is the resistance of the arteries to blood flow. When the arteries constrict → the resistance increases. when they dilate → the resistance decreases. Peripheral resistance is regulated at the level of the **arterioles**. Arterioles also known as **resistance vessels.** **Peripheral resistance is determined by three factors:** **1.Autonomic activity:** sympathetic activity constricts peripheral arteries. And Parasympathetic activity dilates peripheral arteries. **2.Pharmacologic agents:** vasoconstrictor drugs increase resistance while vasodilator drugs decrease it. **3.Blood viscosity:** increased viscosity of blood will increases resistance. **Note**: An increased blood flow in the arterioles induces vasoconstriction to protect tissues against hyperperfusion. 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).

For Explanation



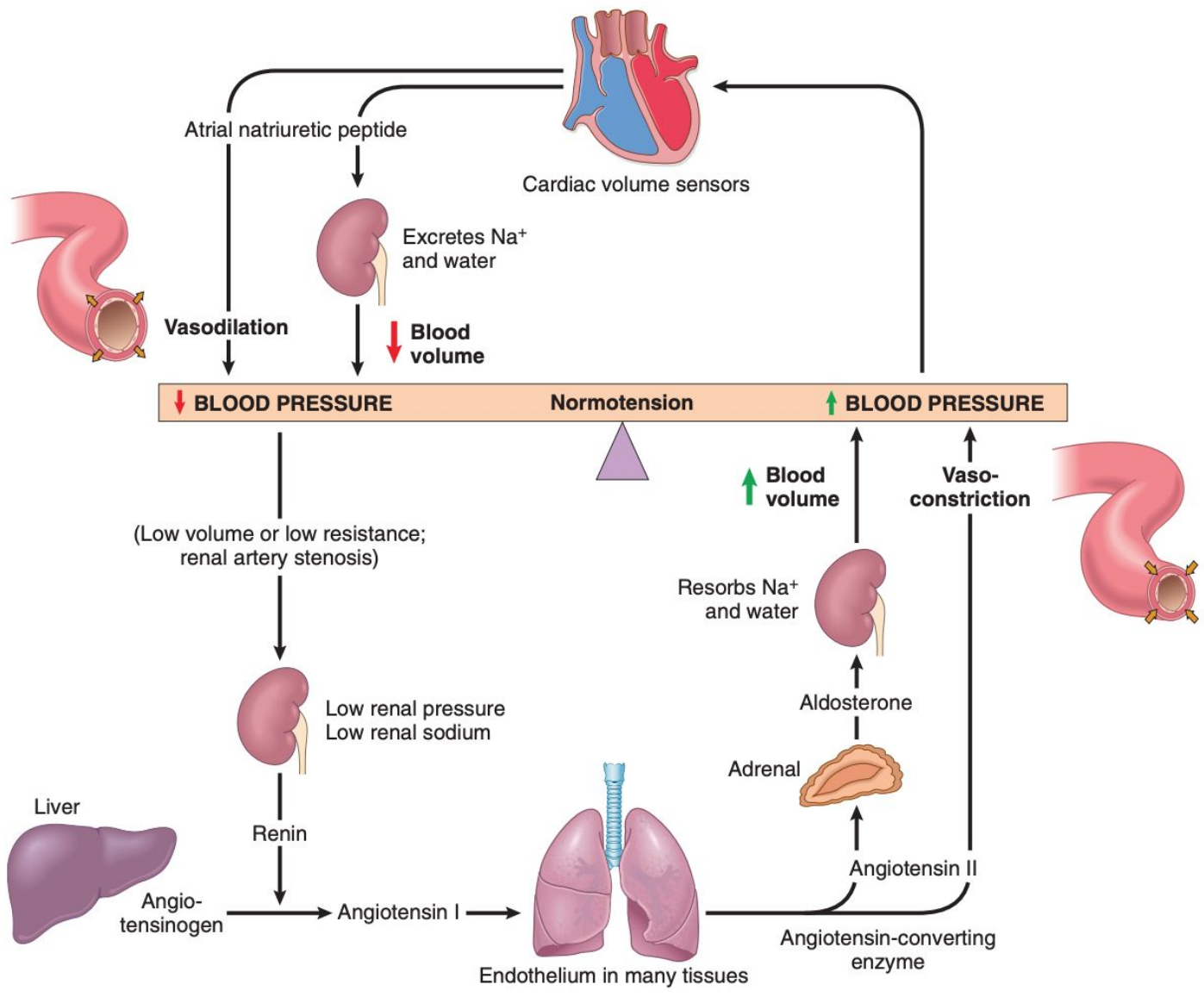
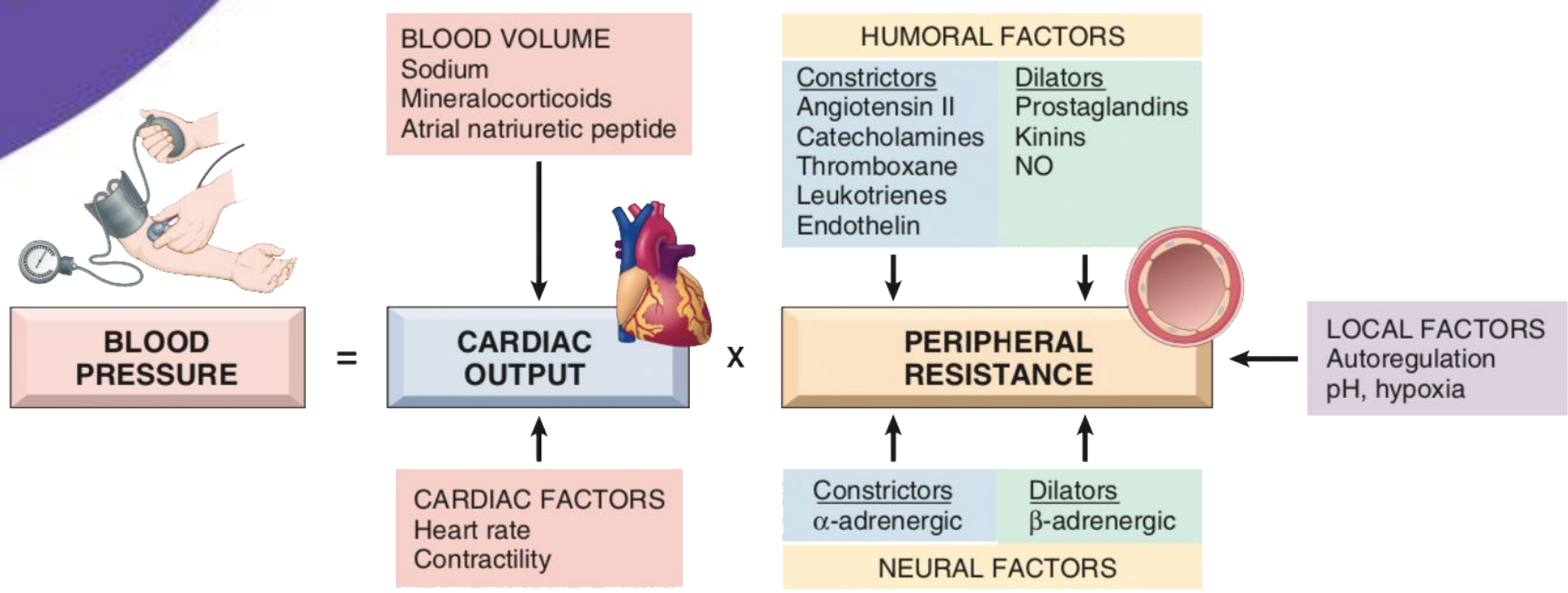


Fig. 10.4 Interplay of renin, angiotensin, aldosterone, and atrial natriuretic peptide in blood pressure regulation

Regulation Of Blood Pressure



Endocrine factors: Renin, Angiotensin, Aldosterone, ADH

Endocrine Factors:

Role of Renin-Angiotensin-Aldosterone in Regulating BP

Extra From Robbins:

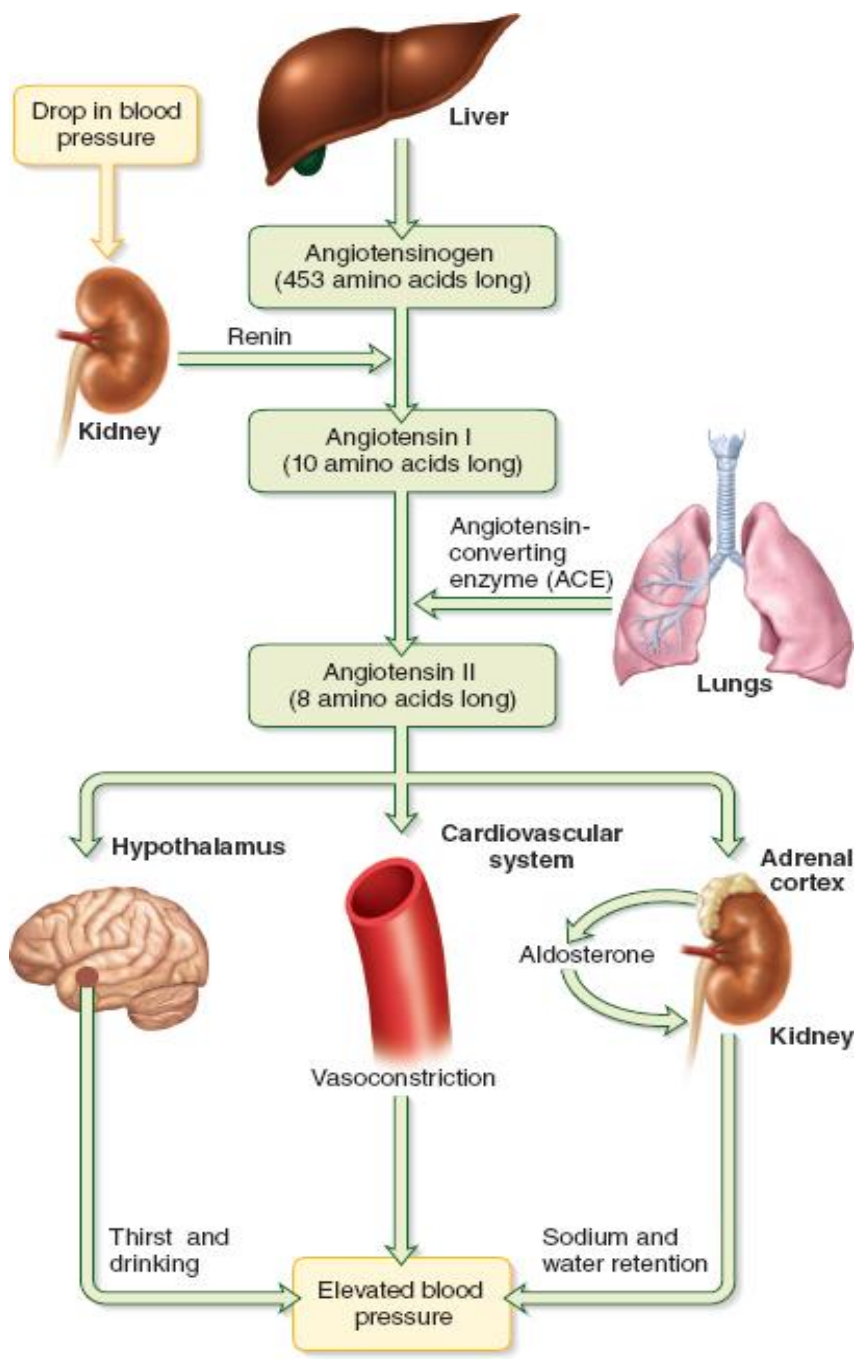
Renin is released in response to low blood pressure in afferent arterioles, elevated levels of circulating catecholamines, or low sodium levels in the distal convoluted renal tubules. The latter occurs when the *glomerular filtration rate* falls (e.g., when the cardiac output is low), leading to increased sodium reabsorption by the proximal tubules.

Renin cleaves *plasma angiotensinogen* to *angiotensin I*, which in turn is converted to *angiotensin II* by angiotensin-converting enzyme (ACE), mainly a product of vascular endothelium. Angiotensin II raises blood pressure by:

(1) inducing vascular contraction

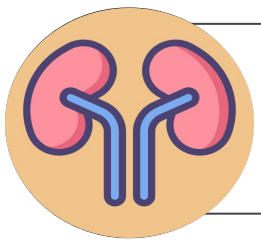
(2) stimulating aldosterone secretion by the adrenal gland (from Zona Glomerulosa)

(3) increasing tubular sodium reabsorption. *Adrenal aldosterone* increases blood pressure by increasing sodium reabsorption (and thus water) in the distal convoluted tubule, which increases blood volume.

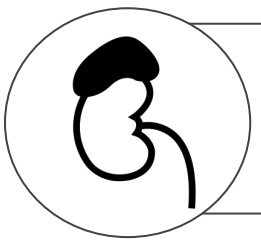


Atrial Natriuretic Peptide/Factor/Hormone (Cardionatrine/Cardiodilatine/Atriopeptin)

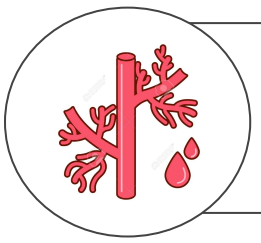
- Protein/polypeptide/hormone secreted by the heart muscle cells in the atria of heart (atrial myocytes).
- Powerful vasodilator and is involved in the homeostatic balance of body water, sodium, potassium and fat.
- Released in response to high blood volume. It acts to reduce the water, sodium and adipose loads on the circulatory system, thereby reducing blood pressure.
- Has exactly the opposite function of the aldosterone secreted by the zona glomerulosa.



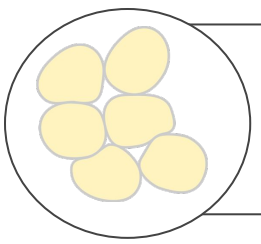
In Kidney:
· decreases sodium reabsorption and increases water loss.
· Inhibits renin secretion, thereby inhibiting the renin–angiotensin–aldosterone system.



In Adrenal Gland: Reduces aldosterone secretion by the zona glomerulosa of the adrenal cortex.



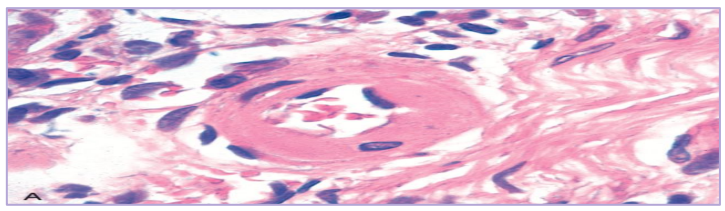
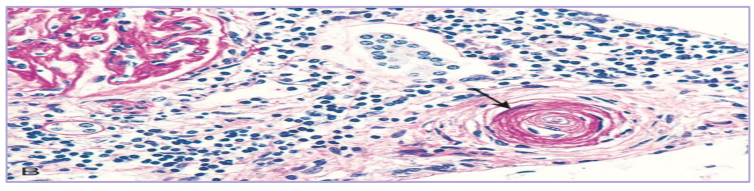
In Arterioles: Promotes vasodilation.

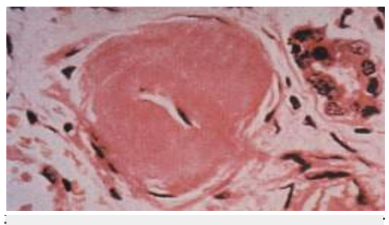


In Adipose tissue: Increases the release of free fatty acids from adipose tissue.

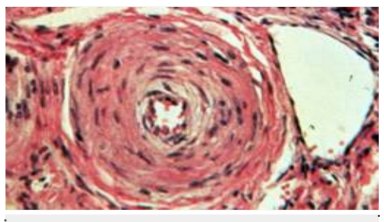
Morphology Of Blood Vessels In HTN

Based on Etiology or cause

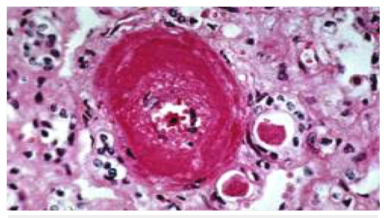
In large Blood Vessels (Macroangiopathy)	In small Blood Vessels (Microangiopathy) *Arteriolo*sclerosis
*Athero*sclerosis. HTN is a major risk factor in AS.	**A-Hyaline arteriolosclerosis:** **Differentiating between them is important** • Seen in benign hypertension. • Can also be seen in elderly and diabetic patients even without hypertension. • Can cause diffuse renal ischemia which ultimately leads to benign nephrosclerosis.  A. Hyaline arteriolosclerosis: hyalinosis of arteriolar wall with narrowing of lumen **B-Hyperplastic arteriolosclerosis:** • Characteristic of malignant hypertension. • Can show onion-skinning on histology causing luminal obliteration of vascular lumen. (Narrowed Lumen) • May be associated with necrotizing arteriolitis and fibrinoid necrosis of the blood vessel.  B. Hyperplastic arteriolosclerosis (onion-skinning) causing luminal obliteration of vascular lumen



Hyaline/Benign hypertension



Hyperplastic/Malignant hypertension showing onion skinning



Hyperplastic/malignant hypertension showing fibrinoid necrosis.

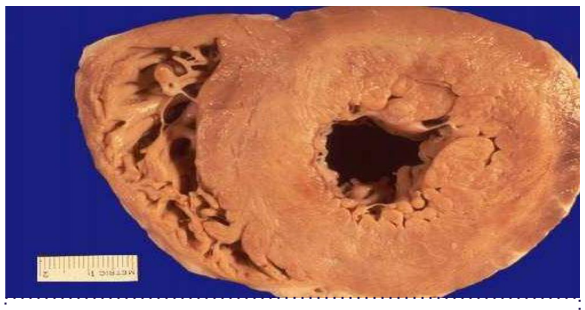
Left ventricular cardiac hypertrophy

Also known as left sided hypertensive cardiomyopathy/hypertensive heart disease

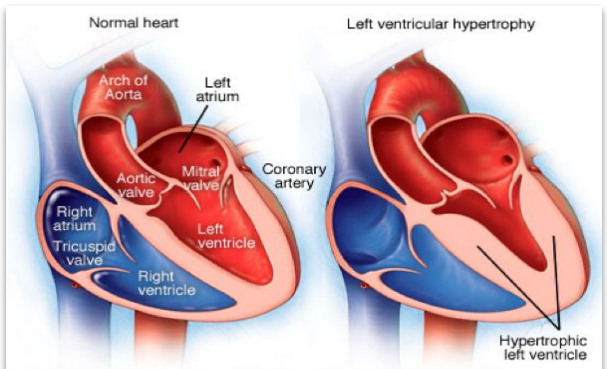
Pathogenesis

- Longstanding poorly treated HTN leads to left sided hypertensive heart disease.
- Hypertrophy of the heart is an adaptive response to pressure overload due to HTN

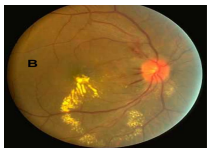
Hypertension → Left ventricular pressure overload → **hypertrophy of the left ventricle** with increase in the weight of the heart and the thickness of the LV wall



Left ventricular hypertrophy

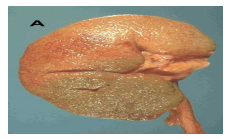


Complications



Eyes

Hypertensive retinopathy (Fig. B) is especially seen in malignant hypertension.

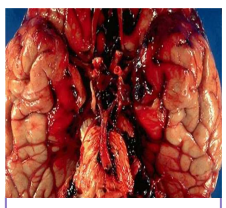


Kidney

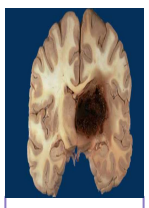
- Benign nephrosclerosis (Fig. A).
- Renal failure in untreated or in malignant hypertension.

Brain

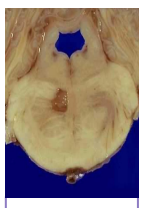
Hemorrhage, infarction leading to Cerebrovascular accidents.



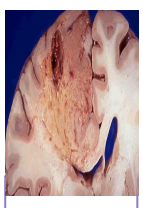
Subarachnoid hemorrhage



Cerebral hemorrhage



Lacunar infarct



Cerebral infarct

Cardiovascular

- Left ventricular cardiac hypertrophy
- Coronary heart disease
- Aortic dissection

Quiz

1- Which of the following is a sign of Hypertension

A- 85 mmHg Sustained Diastolic pressure	B- 95 mmHg Sustained Diastolic pressure	C- 130 mmHg Sustained Systolic pressure	D- 90 mmHg Sustained Systolic pressure

2- A 45-year-old man undergoes renal biopsy for evaluation of chronic renal failure. The patient is obese (BMI = 37 kg/m2) and admits to smoking two packs per day for 30 years. Physical examination reveals a blood pressure of 190/110 mm Hg. An echocardiogram shows conspicuous left ventricular hypertrophy. A renal biopsy discloses pathologic changes in small renal arteries, including "onion-skinning" and fibrinoid necrosis. The Congo red stain is negative. Laboratory studies show hematocrit of 40%, hemoglobin of 18.7 g/dL, serum cholesterol of 250 mg/dL, BUN of 45 mg/dL, and serum creatinine of 5.5 mg/dL. Which of the following is the most likely underlying cause of chronic renal failure in this patient?

A-Primary HTN	B- CHF	C- Benign HTN	D- Malignant HTN

3- A 58-year-old man with a history of hyperlipidemia and high blood pressure presents to the emergency room for evaluation of headaches and blurred vision. His blood pressure is 200/115 mm Hg, and pulse is 95 per minute. Funduscopic examination reveals several small retinal microaneurysms and cotton-like zones of retinal edema and necrosis. Intravenous pyelography discloses small kidneys bilaterally. Renal arteriography shows stenoses of both renal arteries. Hypertension in this patient is caused by the renal release of which of the following hormones?

A- Angiotensin	B- aldosterone	C- renin	D- plasminogen

4- A 58-year-old obese woman (BMI = 32 kg/m2) complains of declining visual acuity of 6 months in duration. Physical examination reveals a pulse of 82 per minute, respirations 20 per minute, and blood pressure 195/110 mm Hg. Funduscopic examination shows "cotton-wool spots," retinal hemorrhage, "macular star," edema of the optic nerve, and arteriovenious nicking of retinal arterioles. A photograph of the ocular fundus is shown. These findings are best explained by which of the following mechanisms?

A- Hypertensive retinopathy	B- Central retinal vein occlusion	C- Central retinal artery occlusion	D- None

5- ANP released from the cardiac muscle n response to increased blood volume and high pressure , which one of the following its action to decrease BP?

A- Increase release of cholesterol	B- Increase release of fatty acids	C- Decrease release of fatty acids	D- Decrease release of cholesterol

6- Ahmed, a 78 year old obese male with hypertension (BMI = 40Kg/m2), was taking 2 classes of drugs showing poor response to the treatment. He died a month later and a cardiact biopsy was taken. What findings may be seen from the biopsy?

A-Left ventricular hypertrophy	B-Left ventricular pressure underload	C-Right ventricular pressure overload	D-Right ventricular pressure underload

SAQ

1-B , 2-D , 3-A , 5-B , 6-A

1- What are the clinical features of benign hypertension?
2- peripheral resistance is determined by three factors?
3- What type of Blood vessel morphology generally associated with HTN can be seen in some patients even without HTN
4- What are the complications caused of HTN towards the cardiovascular system

Answers

1-The BP is at modest level (not very high), Fairly stable over years to decades., It can be idiopathic HTN or secondary HTN, Compatible with long life.
2- Autonomic activity, Pharmacologic agents, Blood viscosity
3- Hyaline Arteriosclerosis
4- Left ventricular cardiac hypertrophy, Coronary heart disease, Aortic dissection

Risk factors: hereditary, race, gender, age, obesity, diet, stress, alcohol intake, diabetes, oral contraceptives, inactive lifestyle

Hypertension (HTN)
classified based on:

Etiology or Cause

95% — Primary/Essential Hypertension → idiopathic

5-10% — Secondary Hypertension → due to pathology in the renal, endocrine, vascular or neurogenic systems

Clinical Features

Benign
- BP at modest level.
- can be primary or secondary HTN.
- fairly stable.
- compatible with long life.

5% — **Malignant**
- rapidly rising BP.
- can be a complication of primary or secondary HTN.
- diastolic pressure is over 120 mmHg.
- associated with widespread necrosis, renal failure, retinal hemorrhage, encephalopathy & LV failure.
- death in 1 or 2 years if untreated.

Pathogenesis of Primary Hypertension

Genetic factors + Environmental factors

- Defect in renal sodium homeostasis → inadequate sodium excretion → salt and water retention → ↑ plasma and ECF volume → ↑ cardiac output
- Functional vasoconstriction → ↑ vascular reactivity
- Defects in vascular smooth muscle growth & structure → ↑ vascular wall thickness

↑ peripheral resistance

↑ cardiac output + ↑ peripheral resistance → **Hypertension**

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