Pathology
HYPERTENSION

SUFIA HUSAIN

ASSOCIATE PROFESSOR

PATHOLOGY DEPARTMENT

COLLEGE OF MEDICINE

KSU, RIYADH

MARCH 2021

REFERENCE: ROBBINS & COTRAN PATHOLOGY AND RUBIN'S PATHOLOGY

Objectives:

At the end of the lecture, the student should:

- 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:

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

LECTURE OUTLINE

- Definition and risk factors
- Classification
  - Primary & secondary HTN
  - Causes of secondary HTN
  - Benign vs malignant HTN
- Pathogenesis
- Regulation of blood pressure
- Vascular morphology in HTN
- Heart in HTN
- Complications of HTN

Hypertension & Hypertensive Vascular Disease

- Common problem
- Asymptomatic until late - Silent Killer – painless.
- Complications alert to diagnosis but late.
- **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 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 for Hypertension

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

HTN can be classified in 2 ways:

1. Based on etiology or cause
2. Based on clinical features

Classification: based on etiology/cause

I. **Primary/Essential Hypertension (95%) :** Mechanisms largely unknown. It is idiopathic.

II. **Secondary Hypertension (5-10%):** it can be due to pathology in the renal, endocrine, vascular or neurogenic systems

Causes of Secondary Hypertension

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

Classification 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.

- **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 (BP)

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

Regulation of Blood Pressure (BP)

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:

- Autonomic activity: sympathetic activity constricts peripheral arteries.
- Pharmacologic agents: vasoconstrictor drugs increase resistance while vasodilator drugs decrease it.
- Blood viscosity: increased viscosity increases resistance.

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).

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

Pathogenesis of essential hypertension

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)

1. ***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.

   a) 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 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.

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

   c) Structural abnormality in vascular smooth muscle also leads to increased peripheral resistance.

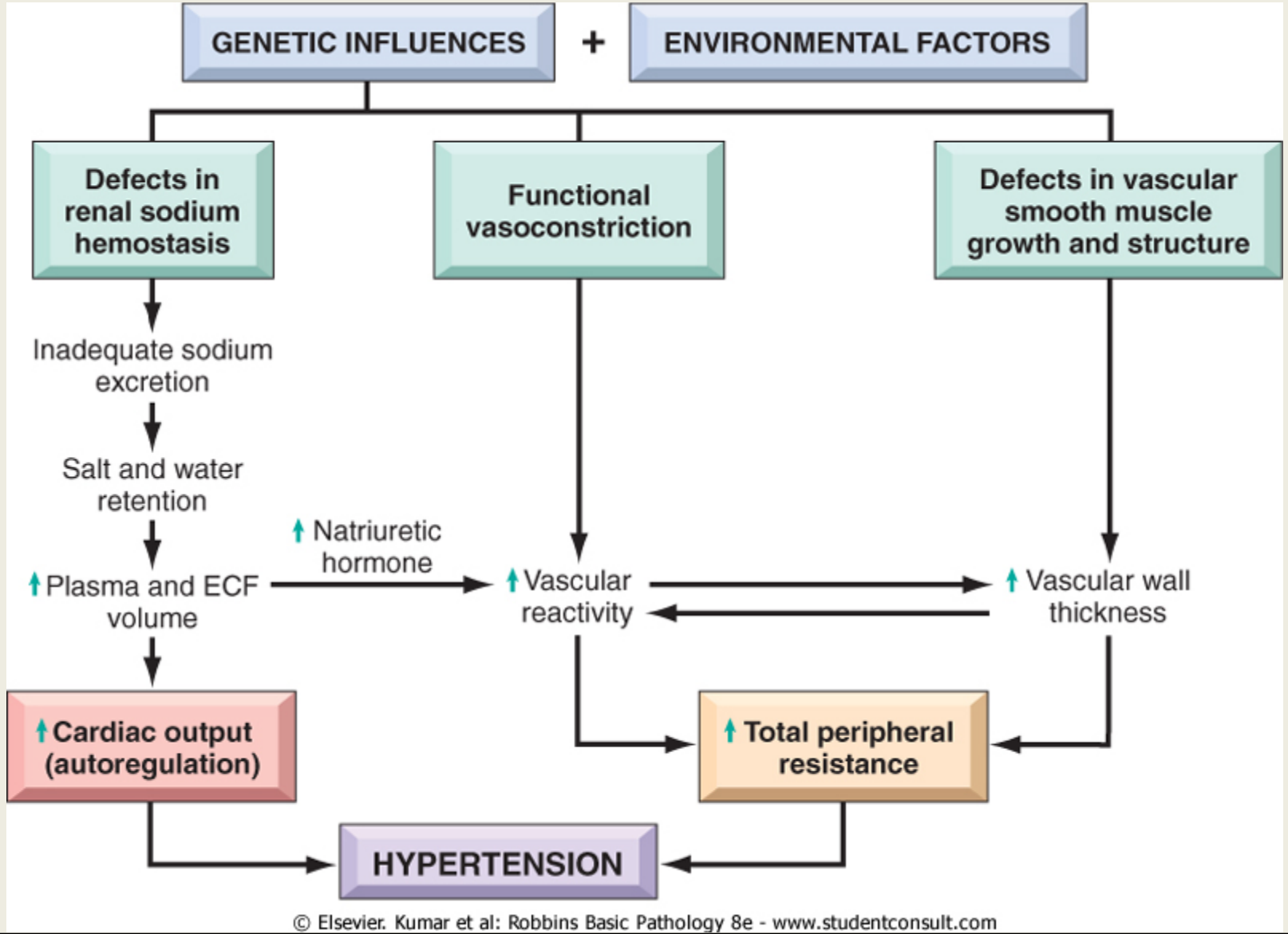
Pathogenesis of essential hypertension

d) 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).

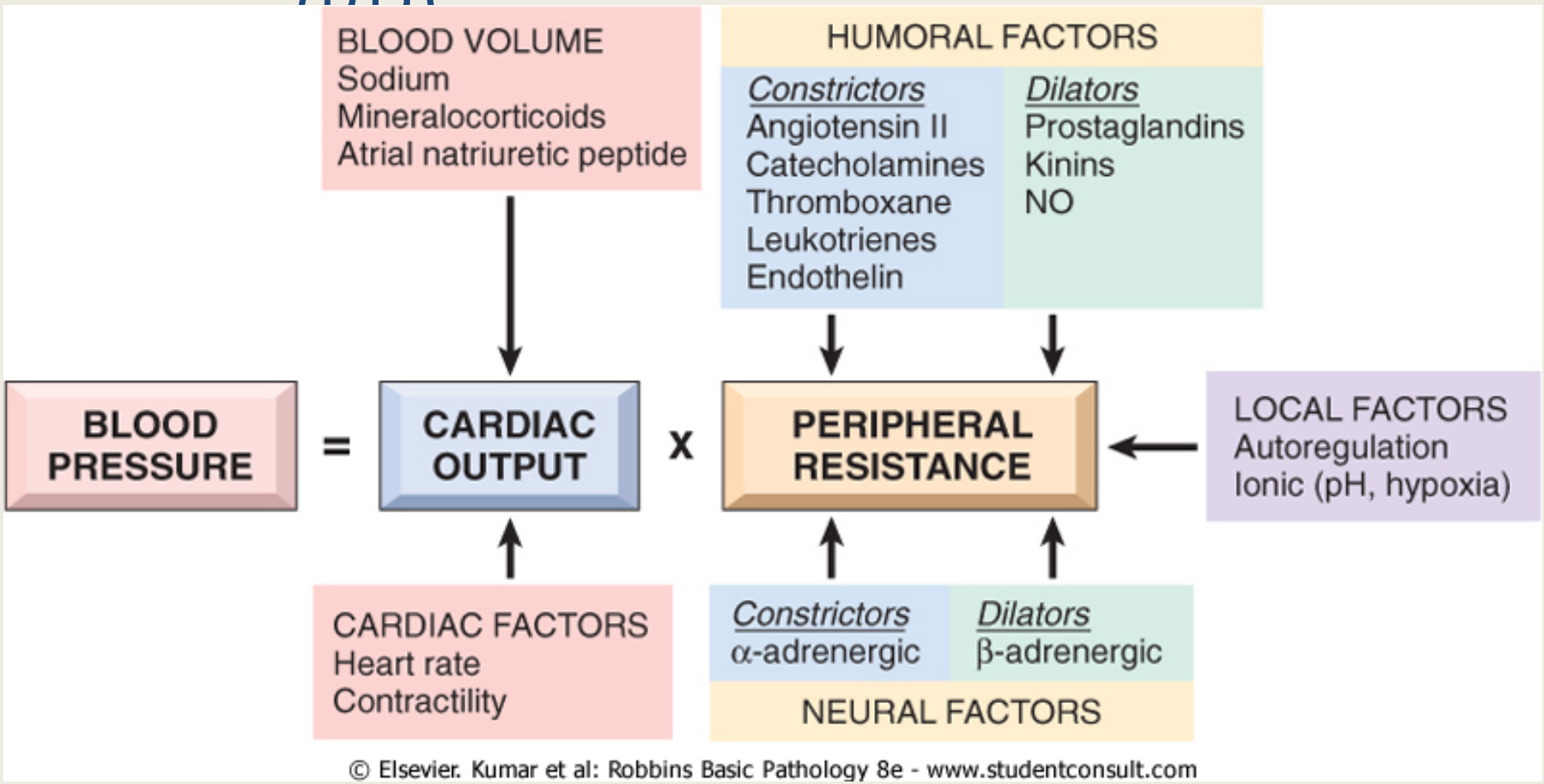
2. ***Environmental factors:*** stress, obesity, smoking, physical inactivity and heavy consumption of salt also play a role.

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

PATHOGENESIS of Essential Hypertension

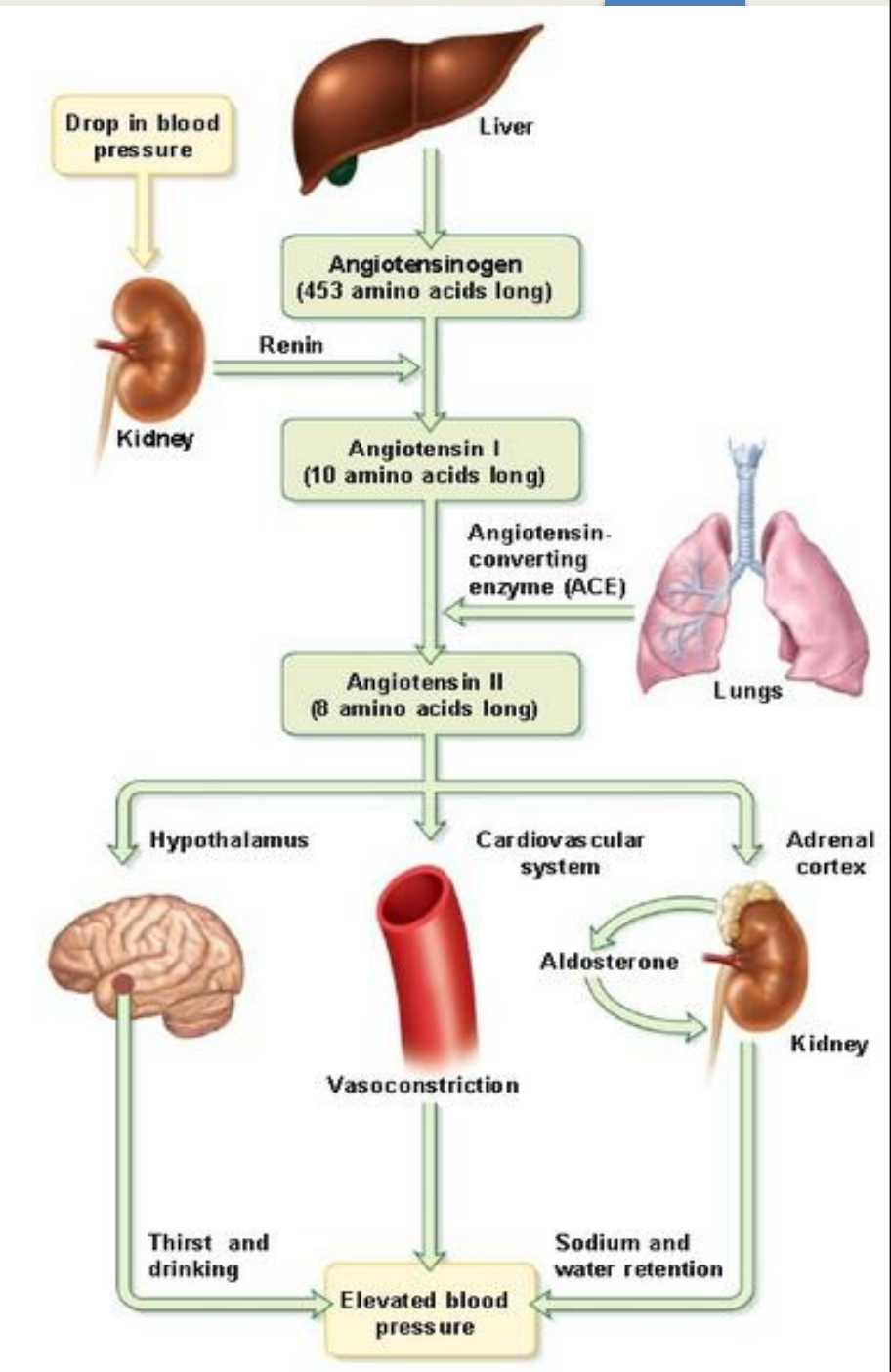


Regulation of Blood Pressure (BP)



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

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



http://pblh2012.wikispaces.com/Week+23+-+Starting+Work

Atrial natriuretic peptide / factor / hormone (Cardionatrine / Cardiodilatine / atriopeptin)

- 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
- **In the kidney:**
  - It decreases sodium reabsorption and increases water loss.
  - It inhibits renin secretion, thereby inhibiting the renin–angiotensin–aldosterone system
- **In adrenal gland:**
  - It reduces aldosterone secretion by the zona glomerulosa of the adrenal cortex.
- **In arterioles:**
  - It promotes vasodilatation
- **In adipose tissue**
  - It increases the release of free fatty acids from adipose tissue.

Morphology of blood vessels in HTN:

In large Blood Vessels (Macroangiopathy)

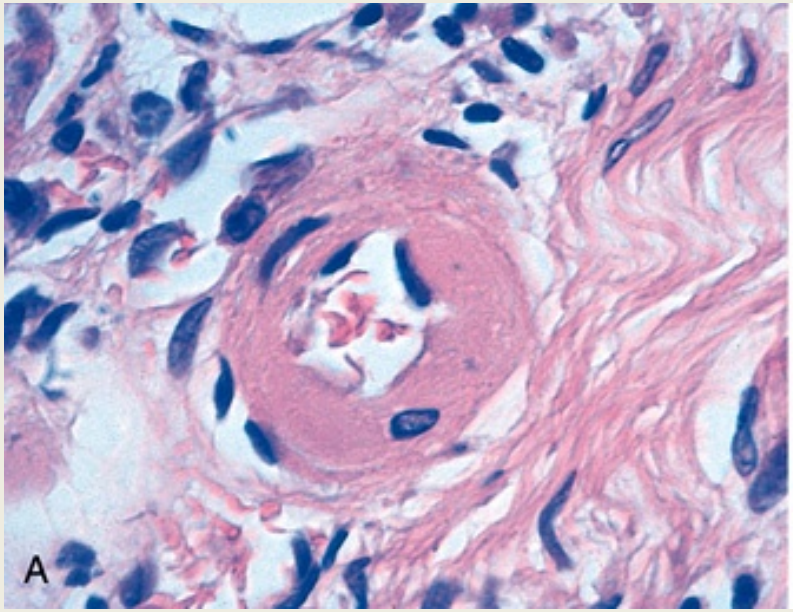
- Atherosclerosis. HTN is a major risk factor in AS.

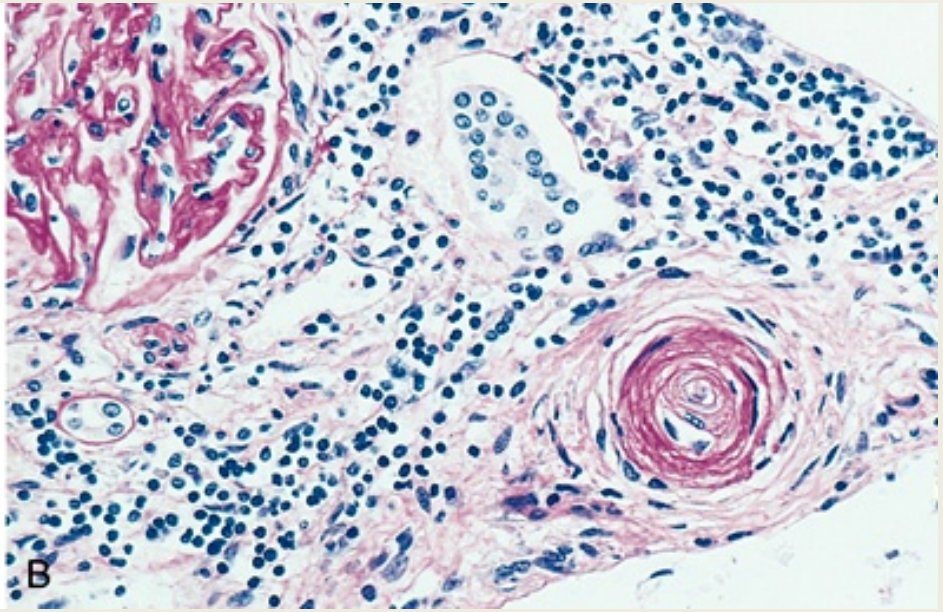
In small Blood Vessels (Microangiopathy)

- Arteriolosclerosis

1. Hyaline arteriolosclerosis:
   - 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
2. Hyperplastic arteriolosclerosis:
   - Characteristic of malignant hypertension.
   - Can show onion-skinning on histology causing luminal obliteration of vascular lumen
   - May be associated with necrotizing arteriolitis and fibrinoid necrosis of the blood vessel.

Vascular pathology in hypertension

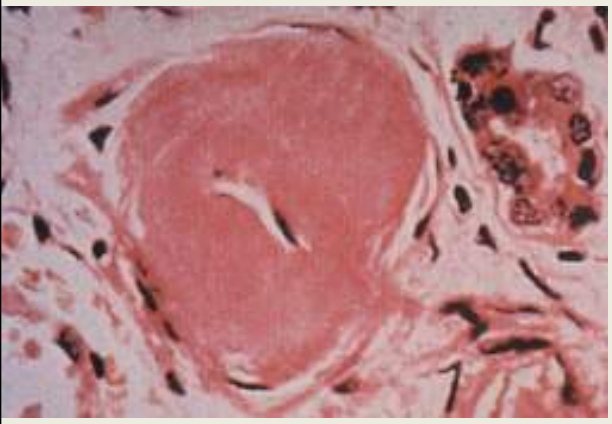




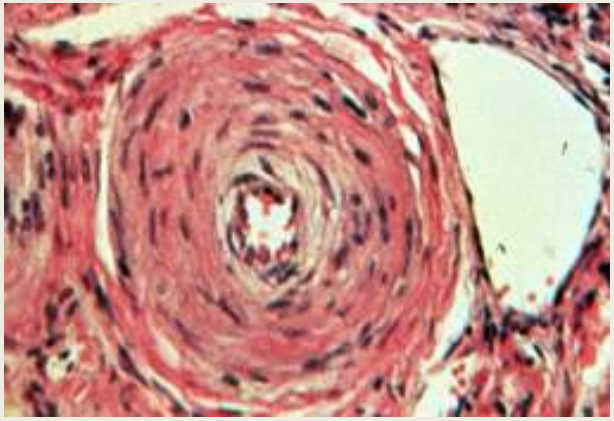
A. Hyaline arteriolosclerosis: hyalinosis of arteriolar wall with narrowing of lumen.

B. Hyperplastic arteriolosclerosis (onionskinning) causing luminal obliteration of vascular lumen

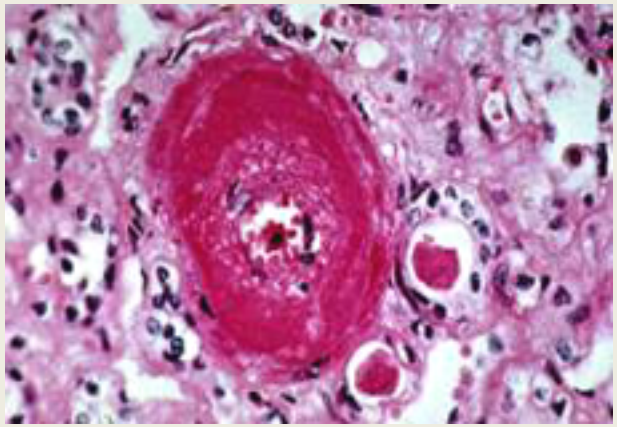
Vascular Pathology in Hypertension



Hyaline/ Benign hypertension



Hyperplastic/ Malignant hypertension showing onion skinning



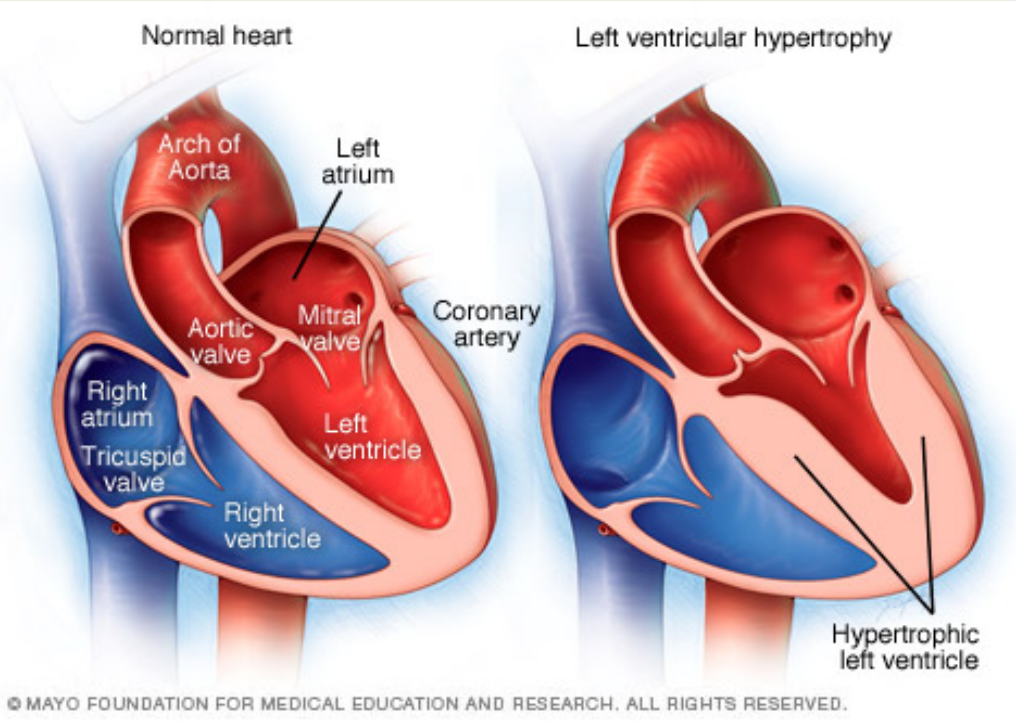
Hyperplastic/ Malignant hypertension showing fibrinoid necrosis.

Left ventricular cardiac hypertrophy

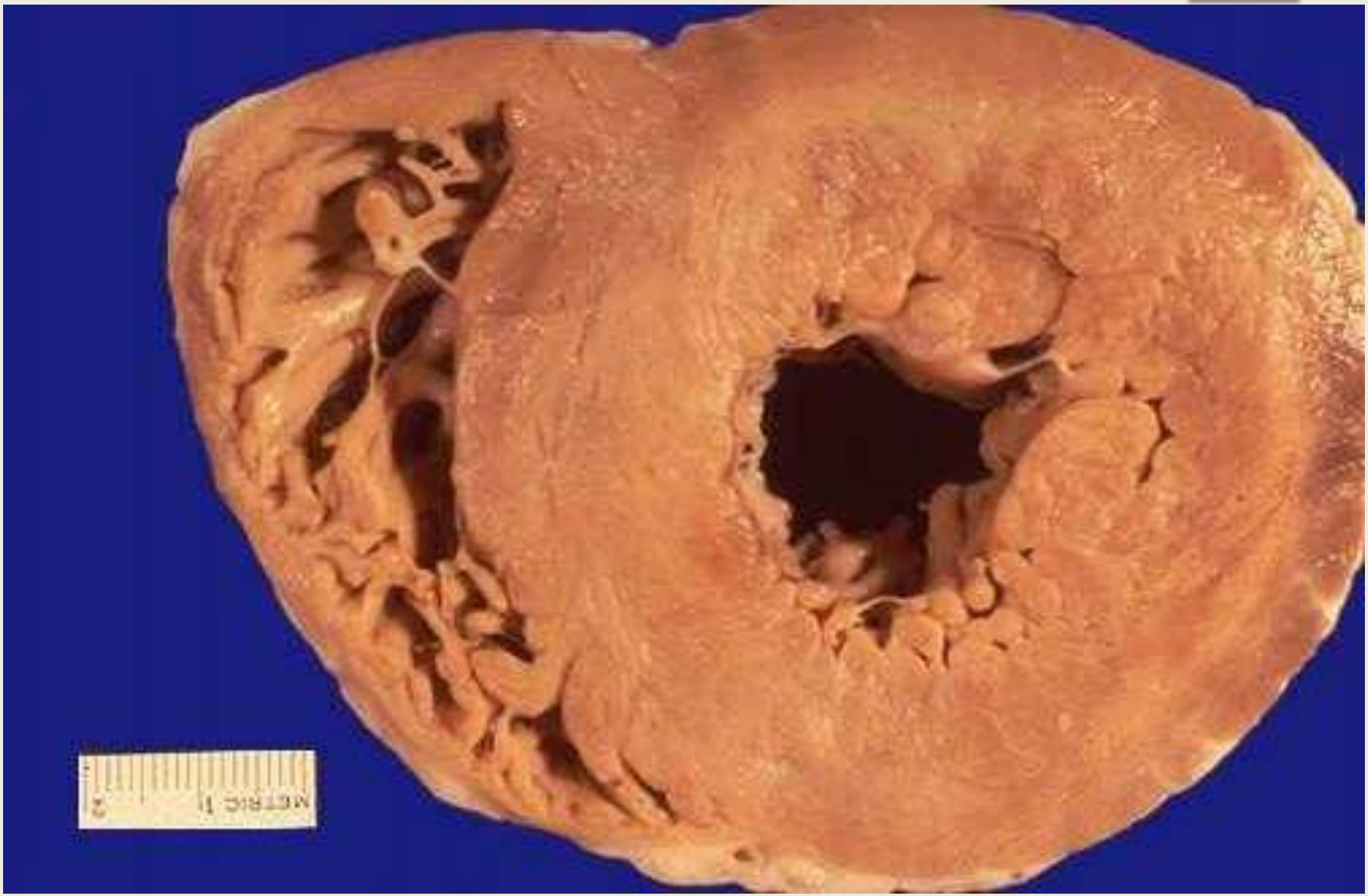
(also known as left sided hypertensive cardiomyopathy/ hypertensive heart disease)

- Longstanding poorly treated HTN can → left sided hypertensive heart disease.
- Left ventricular hypertrophy is an adaptive response to pressure overload due to HTN.

(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)



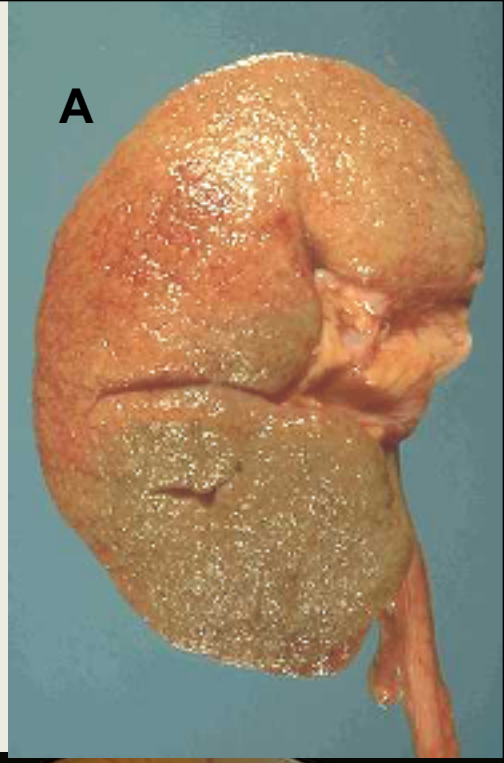
Left Ventricular Hypertrophy

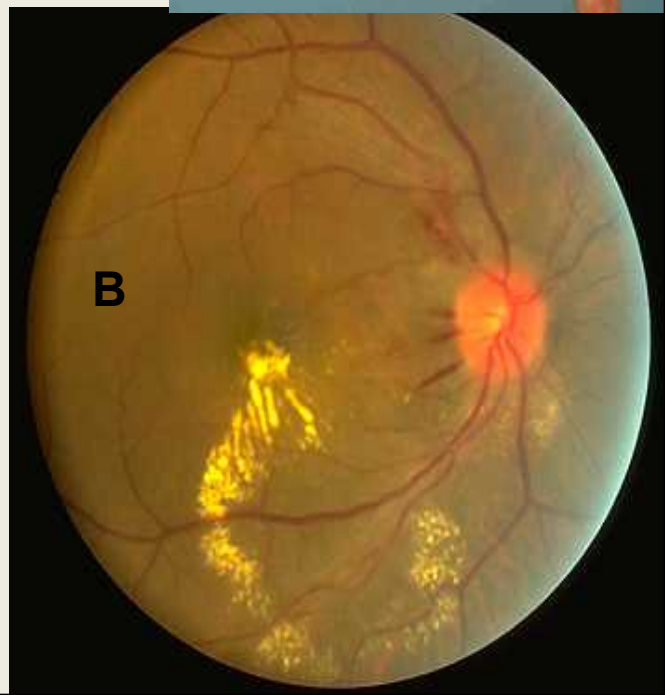


Complications in HTN:

The organs damaged in HTN are:

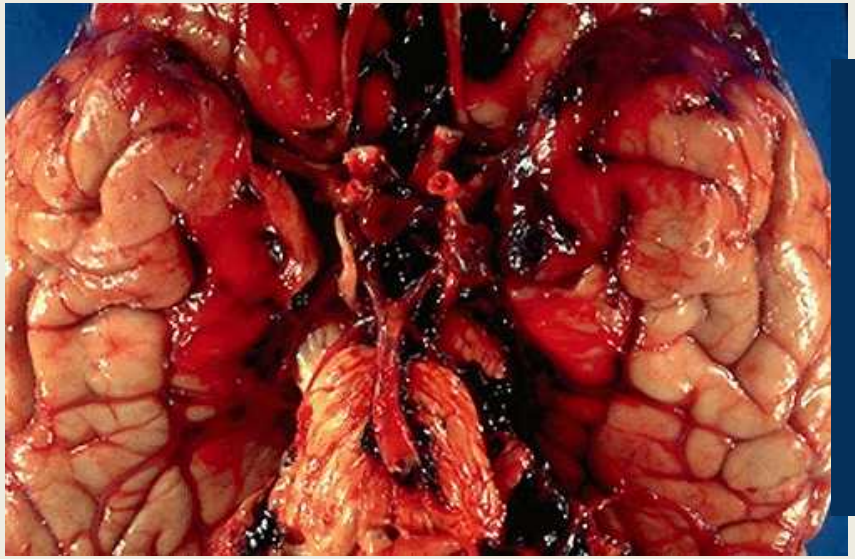
- Cardiovascular
  - Left ventricular cardiac hypertrophy (left sided hypertensive cardiomyopathy/ hypertensive heart disease)
  - Coronary heart disease
  - Aortic dissection
- Kidney
  - Benign nephrosclerosis (photo A)
  - Renal failure in untreated or in malignant hypertension
- Eyes
  - Hypertensive retinopathy (photo B) is especially seen in malignant hypertension.
- Brain
  - Hemorrhage, infarction leading to Cerebrovascular accidents

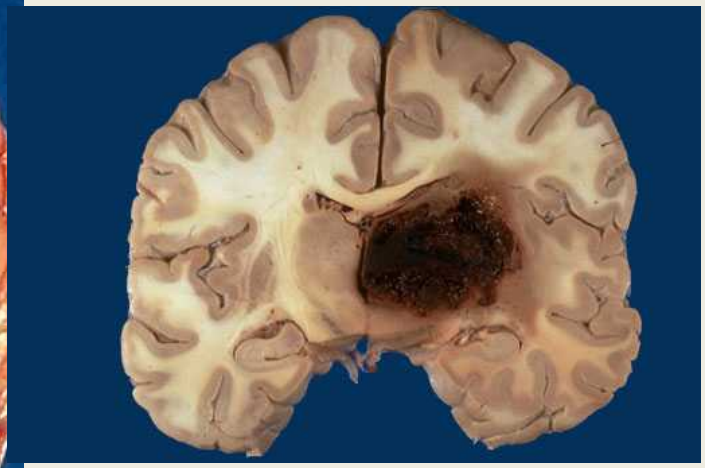




Subarachnoid Haemorrhage

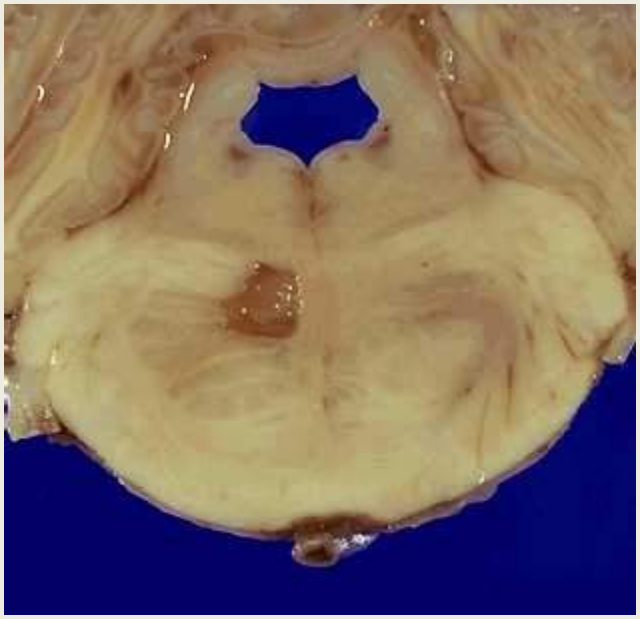
Cerebral Hemorrhage

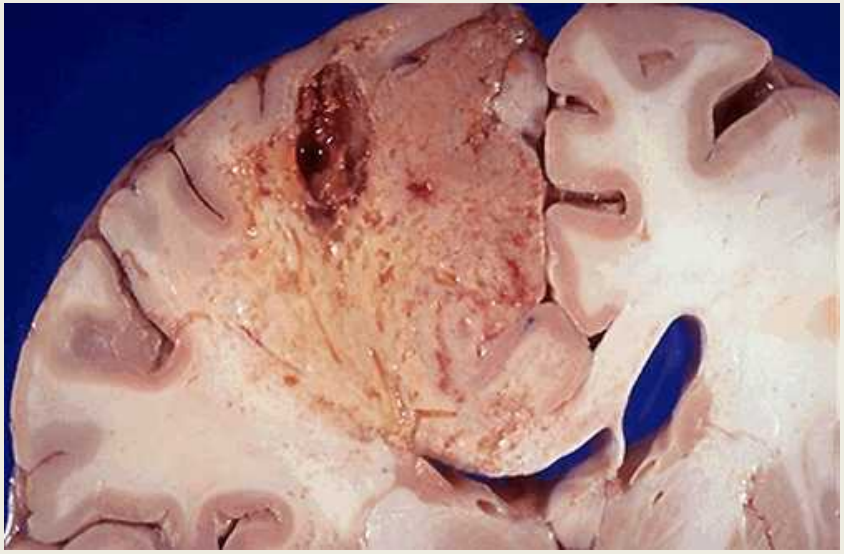




Lacunar Infarct

Cerebral Infarction





END