Congenital Anomalies of The Kidney & Glomerular Diseases I

By

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A Lecturer of Pathology

Aims of This Lecture

- Enumerate congenital anomalies of the kidney and discuss polycystic kidney.
- Define glomerulonephritis, pathogenitic mechanisms of underlying glomerular injury and tissue reaction of glomerular injury.
- Define nephrotic and acute nephritic syndromes and their causes.

Congenital Anomalies of The Kidney

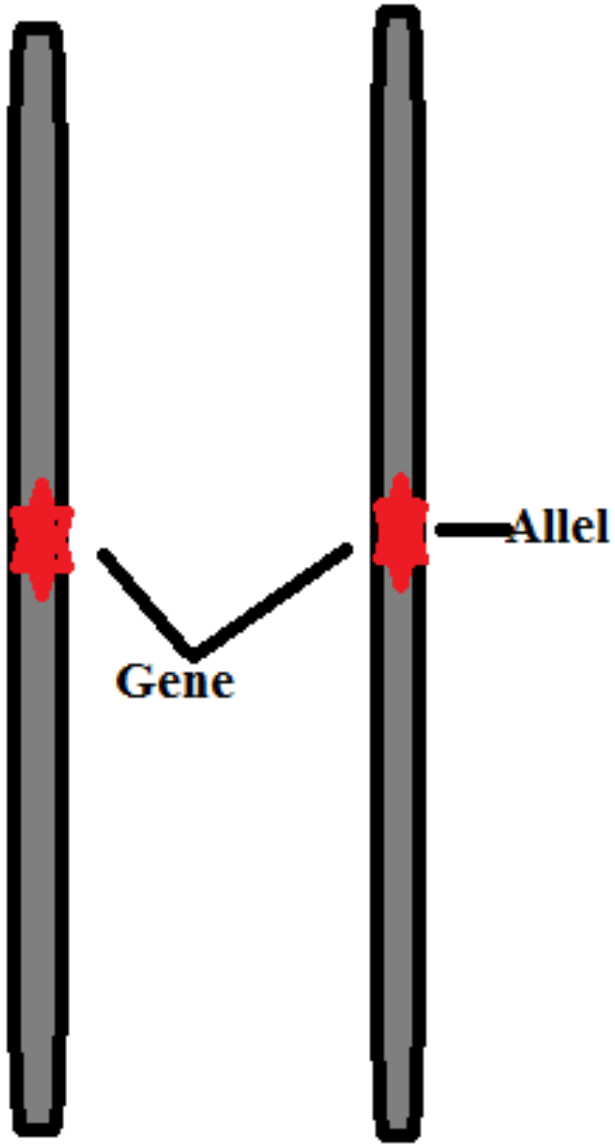
- **Agenesis:** Complete absence of one kidney. The other one shows compensatory hypertrophy.
- **Hypoplasia:** Failure of one kidney to develop to the normal size. It remains small in size. The other one shows compensatory hypertrophy.
- **Ectopic kidney:** The kidney fails to migrate up to the normal position and remains in the pelvis or at the pelvic brim.
- **Horse-shoe kidney:** Both kidneys are fused together usually along the lower poles by renal or fibrous tissue.
- **Congenital Double Ureters and Double Pelvis.**
- **Polycystic kidney disease:**
    A. Autosomal dominant polycystic kidney disease.
    B. Autosomal recessive polycystic kidney disease.

Autosomal Dominant Polycystic Kidney Disease (ADPKD).

ADPKD is a hereditary condition characterized by gradually-expanding cysts that progressively destroy the renal parenchema (cortex and medulla) of both kidneys, finally causing renal failure.

Incidence: It is one of the most common hereditary human disorders, occurring in about 1:2 per 1000 live birth and accounting for approximately 10% of cases requiring dialysis or renal transplantation. Males and females are equally affected. There is no racial predilection.

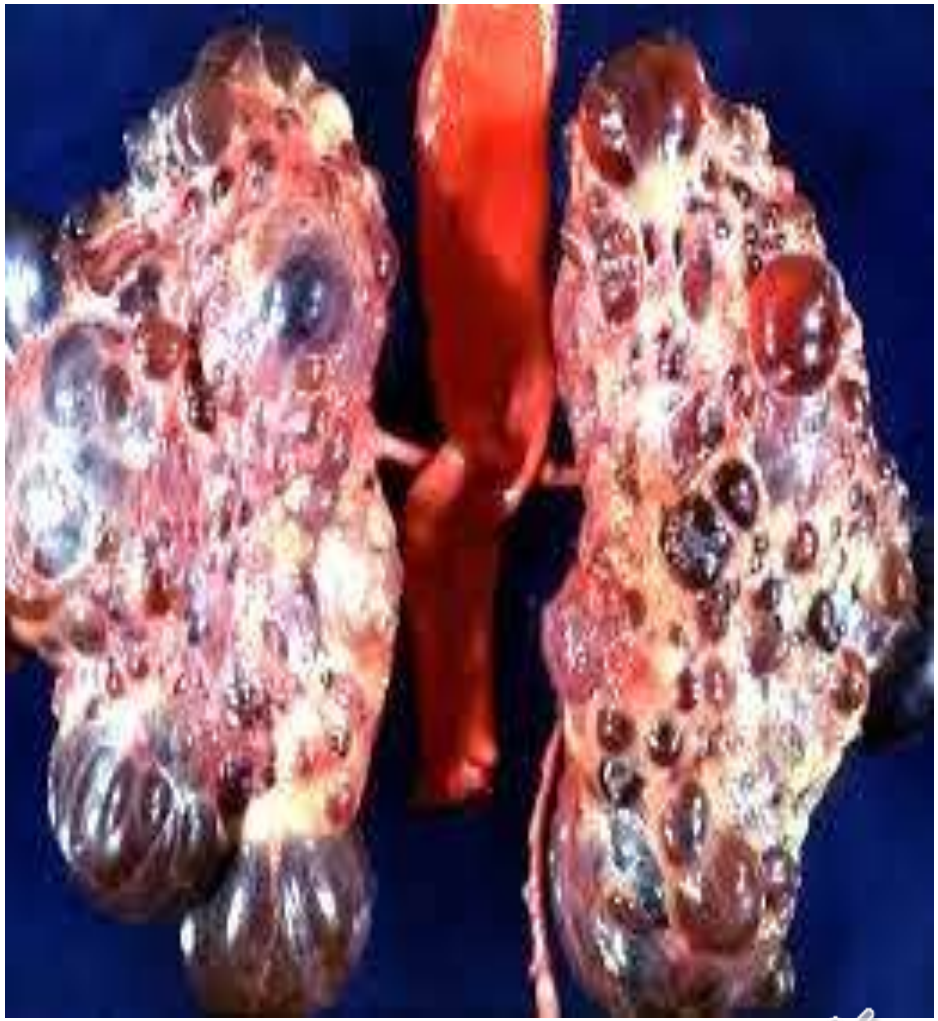
Mode of inheritance



Mode of inheritance: The pattern of inheritance is autosomal dominant; each offspring of an affecting individual has a 50% chance of inheriting the disease. The disease is caused by a mutation affecting any of two genes; ***PKD1 located on chromosome 16 or PKD2 located on chromosome 4.*** Mutation in PKD1 gene is responsible for 85-90% of all cases of ADPKD, while mutation in PKD2 gene is responsible for the remaining cases (10-15%). A small number of families with ADPKD don't show mutation of either PKD1 or PKD2 , raising the susceptibility of presence of an yet unidentified PKD3 gene.

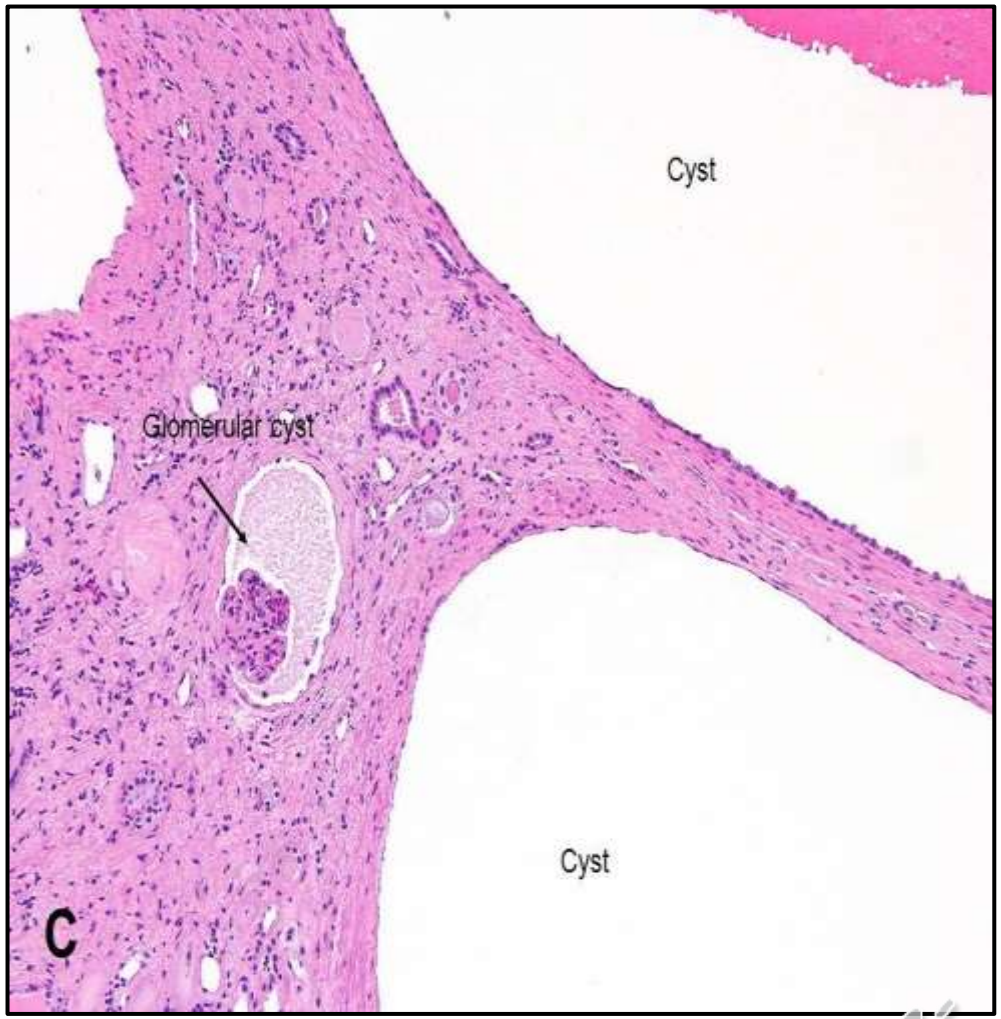
Gross picture

ADPKD is bilateral disease. Both kidneys are markedly enlarged by a large number of cysts which gradually enlarge throughout life. The cysts replace renal parenchyma which is in sever, advanced cases, can be detected only microscopically. Stones and haemorrhage inside the cysts may be seen.



Microscopically

The cysts develop in all segments of the renal tubules and glomerular capsule. In early stages; the fluid of the cysts is derived from the glomerular filtrate. But when the cysts enlarge; they lose their attachment to the renal tubules and their fluid is derived exclusively from their lining epithelial cells. the cysts are lined by cuboidal, flattened epithelium, focal areas of hyperplasia may be seen.



Clinical picture

- Most cases become symptomatic during fourth and fifth decades of life.
- Clinical manifestations include flank pain, flank masses, haematuria, hypertension and renal failure.
- About 20%of patients develop stones, most frequently uric acid stones.
- ADPKD caused by mutation in PKD2 gene has less sever disease course with later age at diagnosis. Late onset of hypertension and renal failure.
- Radiographic findings are usually diagnostic.

Complications

- Hypertension,
- Renal stones.
- Chronic renal failure.
- Renal adenoma in 20% of cases with **ADPKD.**
- **ADPKD** is considered a systemic disease as more than 50% of cases develop cysts in other organs as liver, pancrease, spleen, pineal gland, seminal vesicles and lungs.
- Other anomalies including cereberal and coronary artery aneurysms, mitral valve prolapse, skeletal anomalies.

Autosomal Recessive Polycystic Kidney Disease (AR-PKD)

Classic infantile AR-PKD:

AR-PKD is a rare developmental anomaly, having autosomal recessive pattern of inheritance.

- Newborns with severe form of the disease die shortly after birth usually because of respiratory insufficiency.
- In other cases, death from renal failure may occur in infancy or early childhood.
- AR-PKD is a rare condition, about 1/ 6000-14000 live births.
- **All cases of classic** AR-PKD have mutations in polycystic kidney and hepatic disease-1 (PKHD1) gene located on chromosome 6.

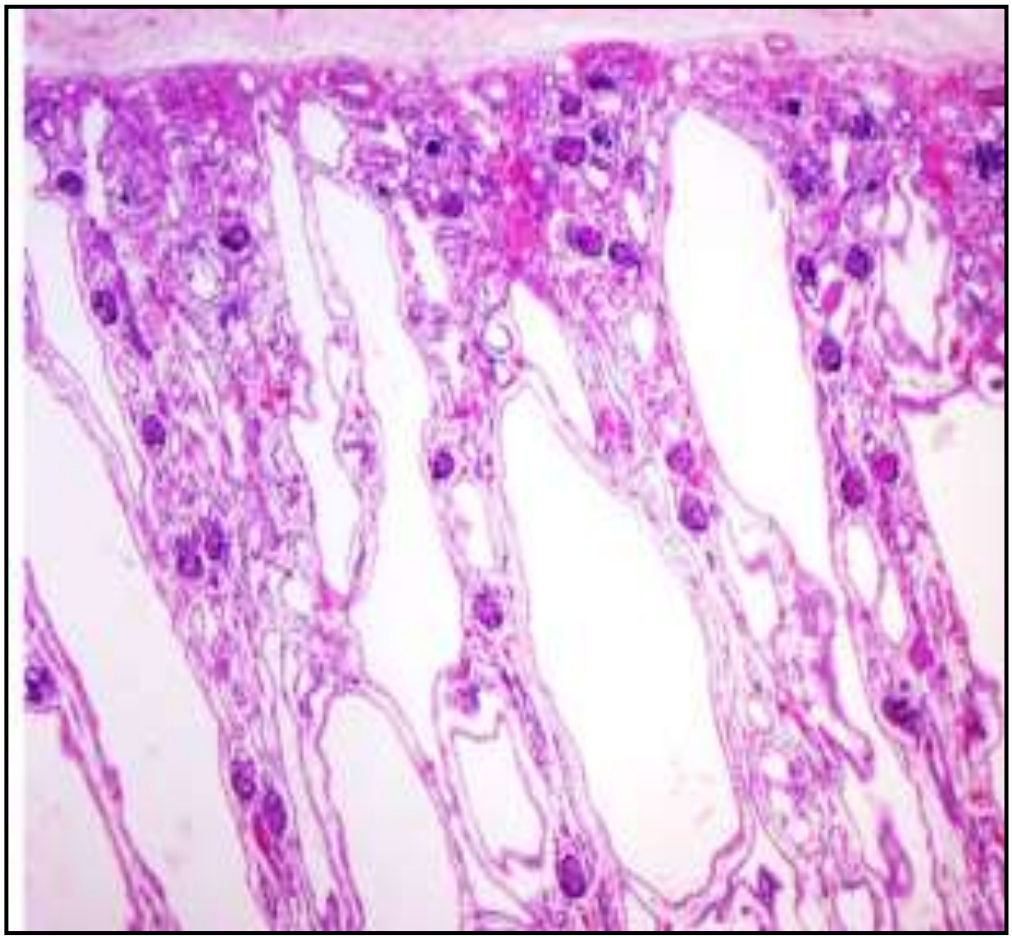
Pathological picture:

Grossly:

The kidneys are enlarged, have a smooth external surface, cut section revealed numerous small cysts in the cortex and medulla give the kidney a sponge appearance.

Microscopically:

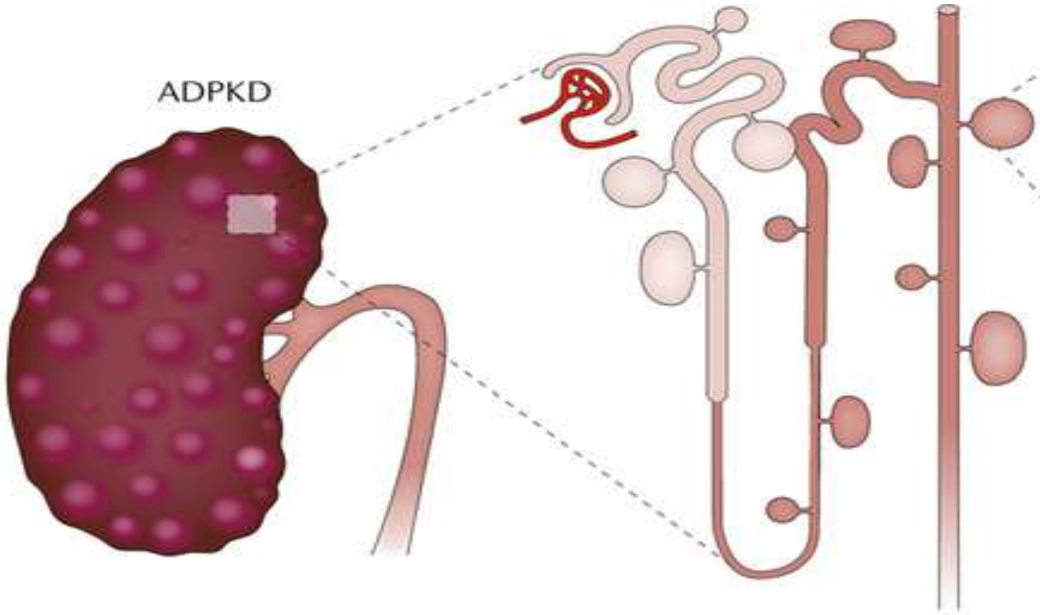
There is dilatation of all collecting tubules. The cysts have a uniform lining of cuboidal cells denoting their origin from collecting tubules.

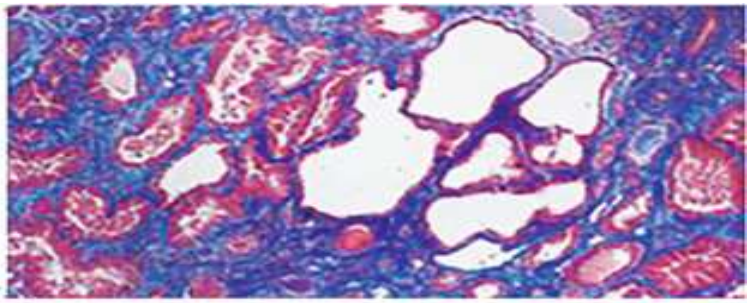


- In almost all cases, there are multiple biliary cysts in enlarged portal tracts.
- Some older children and adolescents with AR-PKD have asymptomatic, minor renal involvement (just few renal cysts) and progressive portal fibrosis, leading to portal hypertension.

a

ADPKD

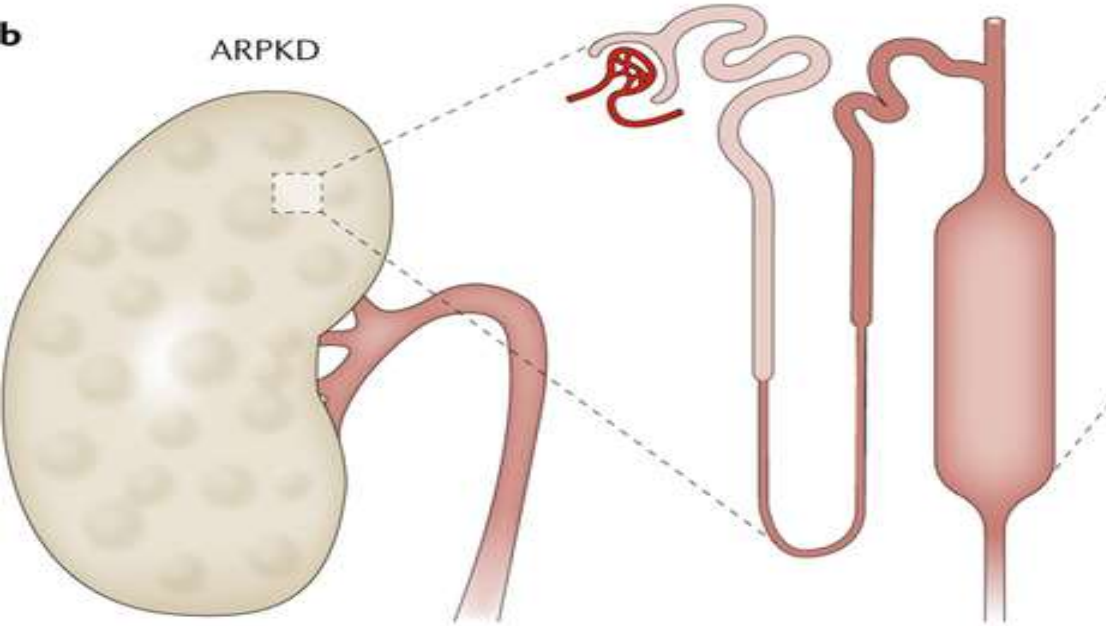


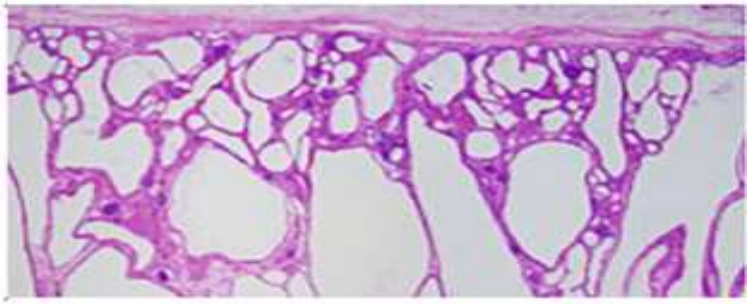


- Typically adult onset
- Mutations in *PKD1* (~80%) or *PKD2* (~15%)
- Cystic kidneys (all nephron levels but mainly distal regions), bile ducts and liver
- Hypertension in at least 20–40% of children and adolescents and in most adult patients (50–70% of patients before GFR decline)
- Intracranial aneurysms in ~8% of patients (increased three-fold in patients with a positive family history)
- ESRD in 50% of patients by 60 years of age

b

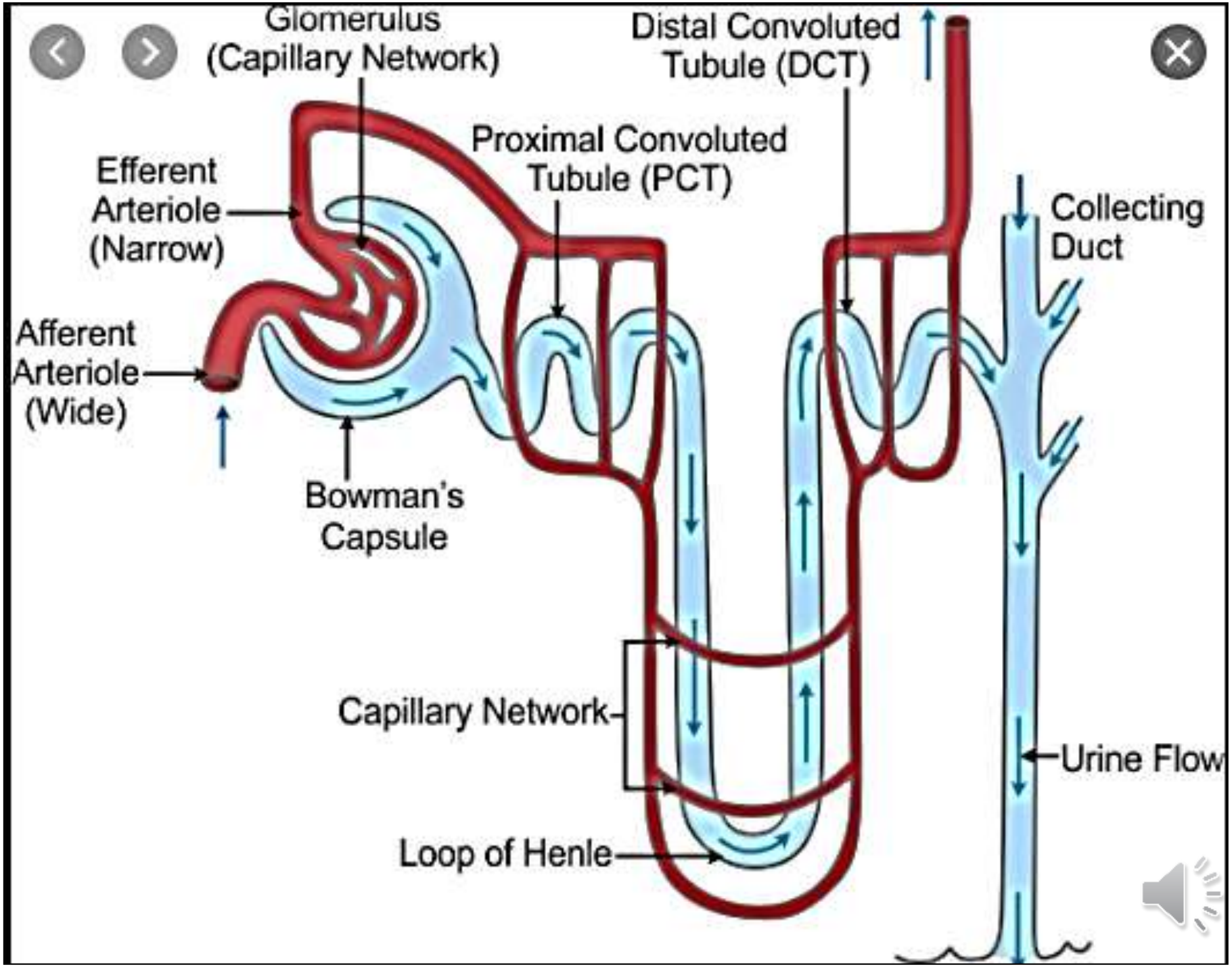
ARPKD





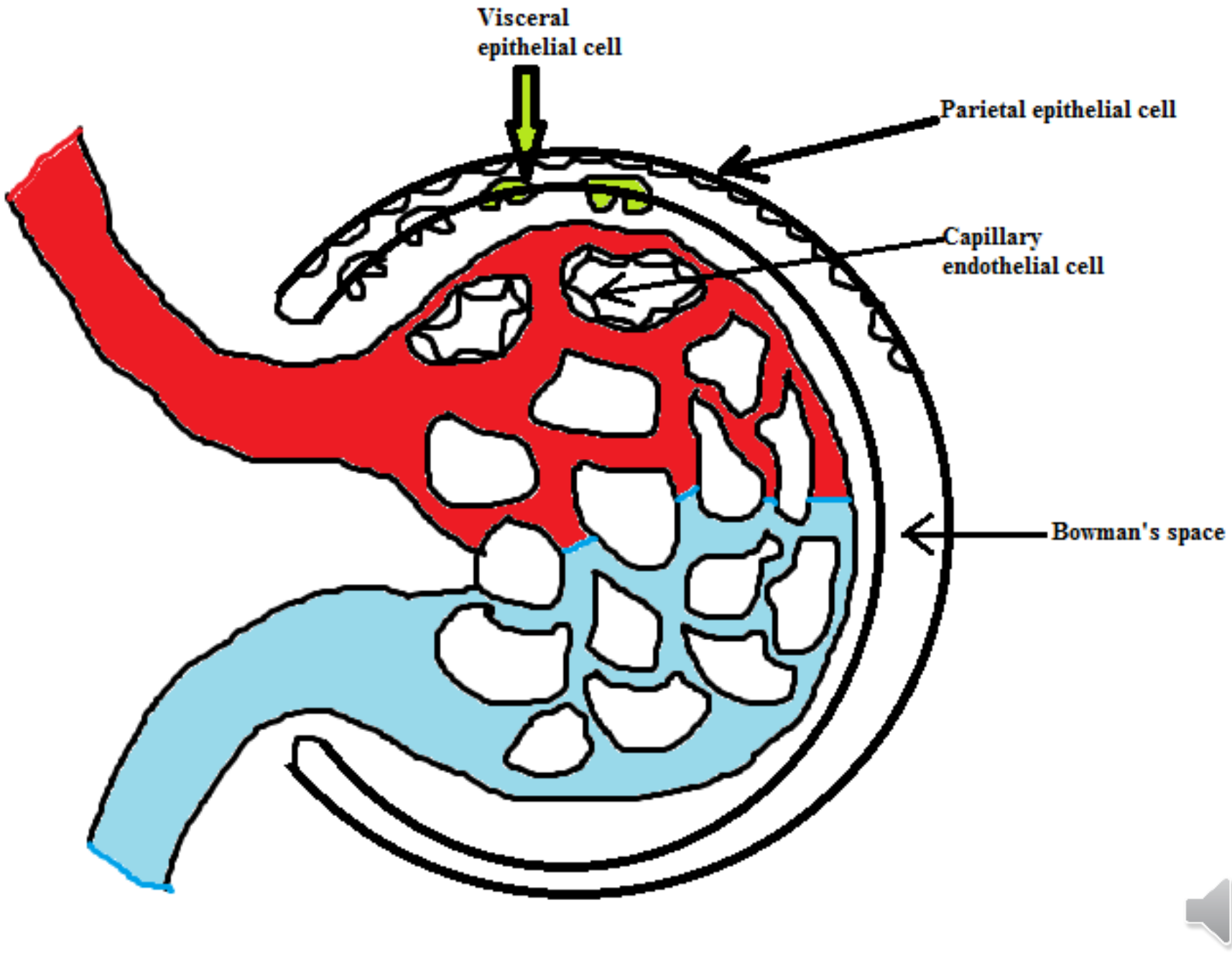
- Typically paediatric onset
- Mutations in *PKHD1* and *DZIP1L*
- Cystic kidneys (collecting ducts and distal tubules) and bile ducts
- Hepatic fibrosis
- Hypertension in up to 75% of children (often during the first few months of life)
- Intracranial aneurysms only described in case reports
- ESRD in 60% of patients by 20 years of age

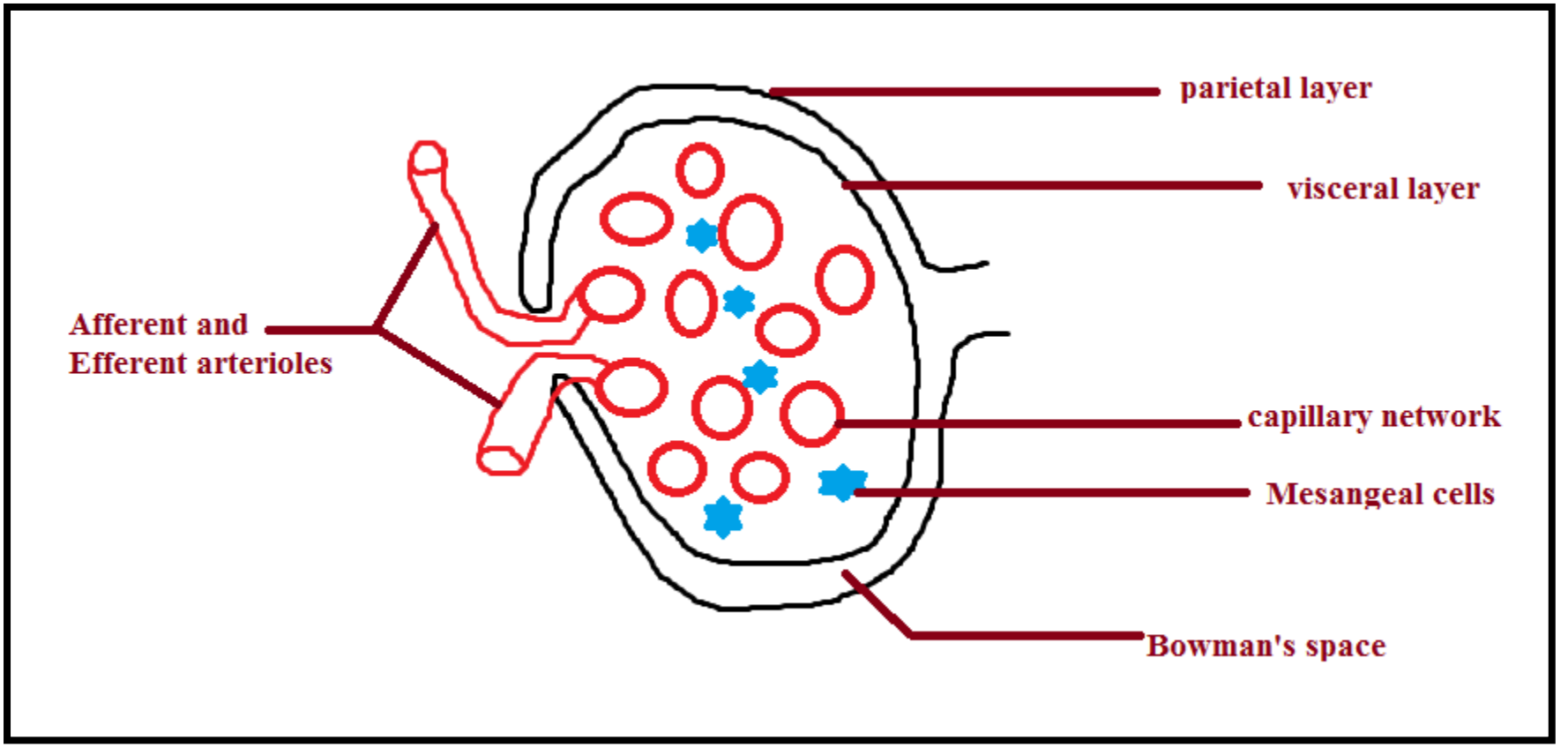
Glomerular diseases

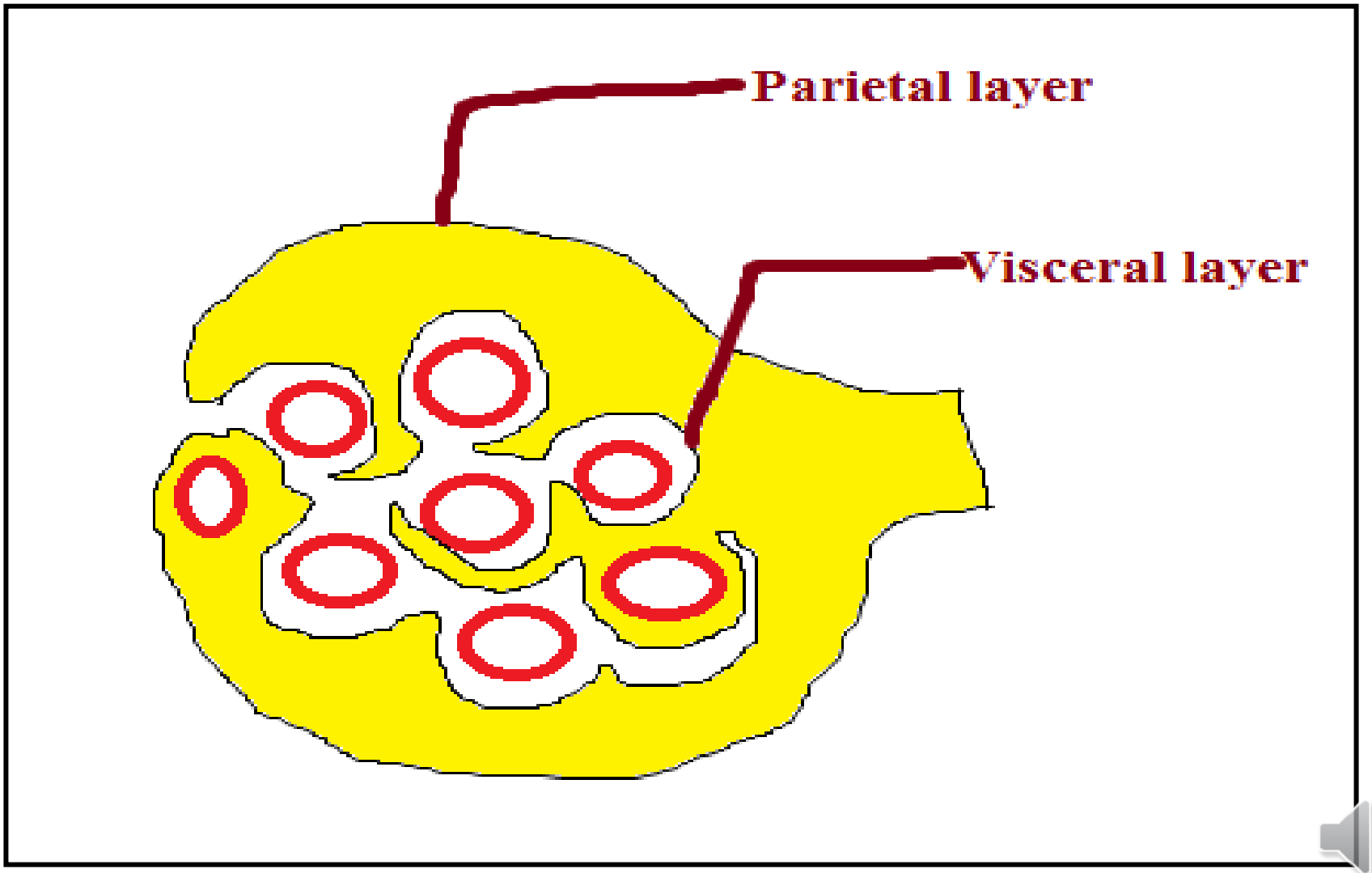

Glomerulus
(Capillary Network)
Distal Convoluted
Tubule (DCT)
Proximal Convoluted
Tubule (PCT)
Efferent
Arteriole
(Narrow)
Collecting
Duct
Afferent
Arteriole
(Wide)
Bowman's
Capsule
Capillary Network
Urine Flow
Loop of Henle

Important Items

I- The glomerulus is composed of an anastomosing network of capillaries incorporated in Bowman’s capsule. It is lined by two layers of epithelial cells; the visceral epithelial cells that are incorporated into and become an intrinsic part of the capillary wall and separated from the endothelial cells by a basement membrane. The parietal epithelial cells line the Bowman's space.


Visceral
epithelial cell
Parietal epithelial cell
Capillary
endothelial cell
Bowman's space


parietal layer
visceral layer
Afferent and
Efferent arterioles
capillary network
Mesangeal cells
Bowman's space

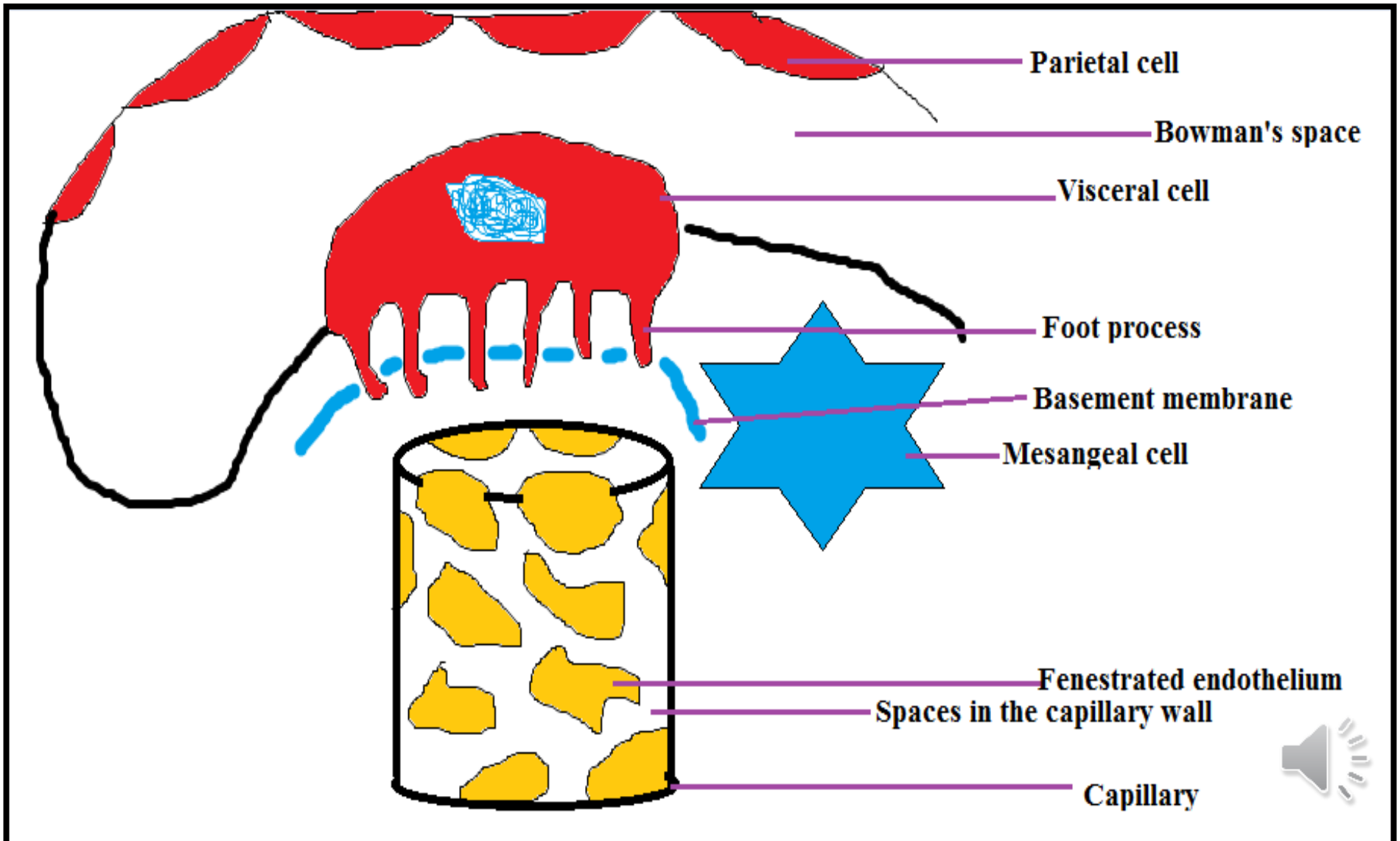

Parietal layer
Visceral layer

II- Glomerular Capillary Wall

The glomerular capillary wall is the filtring membrane and consists of the following structures:

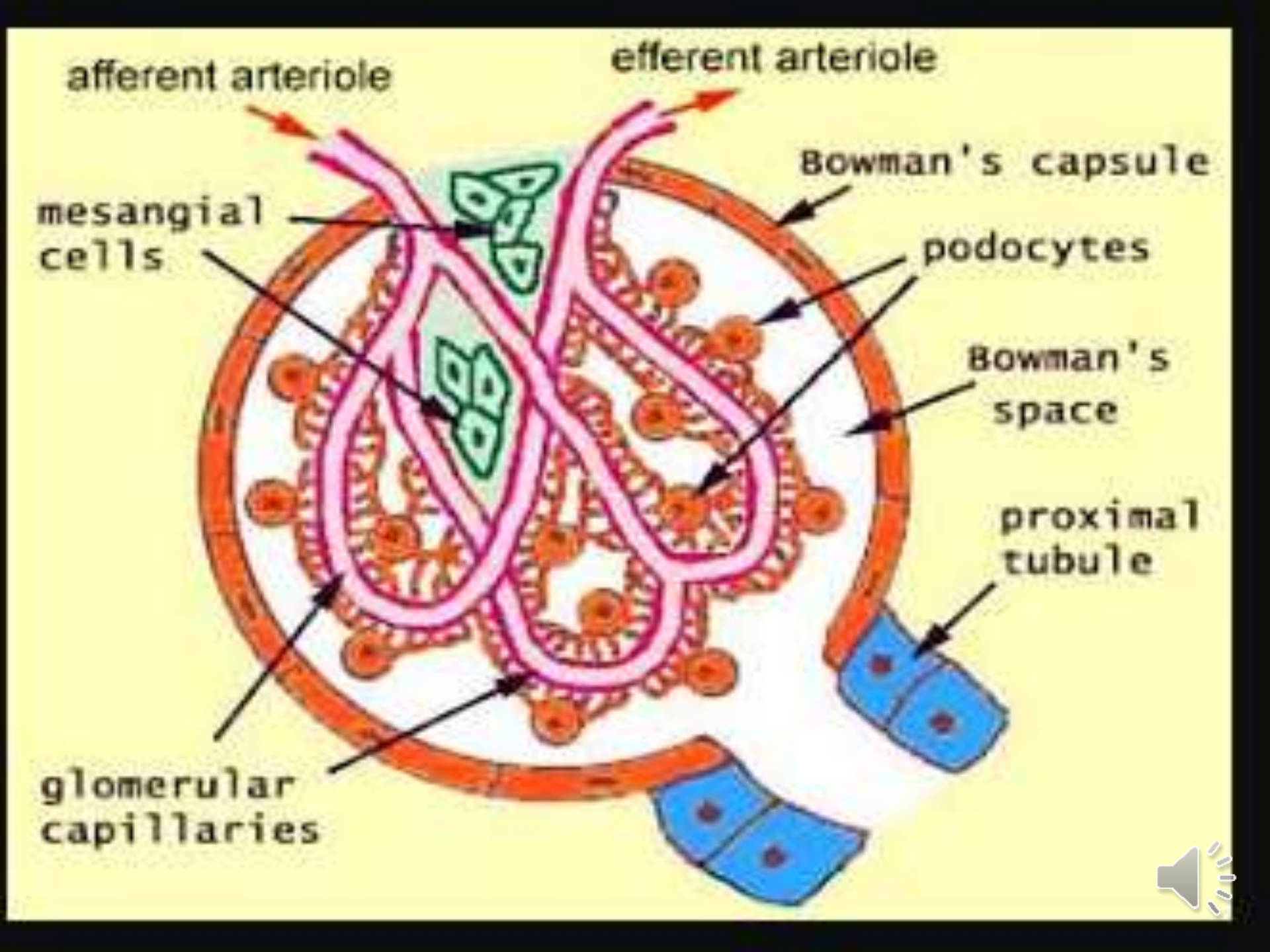
- A thin layer of fenestrated endothelial cells.
- A glomerular basement membrane.
- Visceral epithelial cells (podocytes).

Glomerular capillary wall



III- Mesangeal cells:

The entire glomerular tuft is supported by mesangeal cells. they are lying between capillaries. Mesangeal cells produce mesangeal matrix that form a meshwork through which mesangeal cells are scattered. Mesangeal cells are contractile, phagocytic and capable of proliferation and lying down both matrix and collagen.


afferent arteriole
efferent arteriole
Bowman's capsule
mesangial cells
podocytes
Bowman's space
proximal tubule
glomerular capillaries

Glomerular diseases

Glomerular diseases constitute some of major problems in nephrology. Chronic glomerulonephritis is one of the most common causes of chronic renal failure. Glomeruli may be injured by a variety of factors and in the course of number of systemic diseases. Here, the glomerular injury is called secondary glomerulonephritis. In other conditions, the kidney is the only or the main organ involved. The latter constitutes various types of primary glomerulonephritis.

Glomerulopathy is a glomerular disease that don't have a cellular inflammatory component.

Glomerular diseases (Glomerulonephritis/ G.N.)

I- Primary glomerulonephritis:

- Acute diffuse proliferative G.N.
- Rapidly progressive G.N.
- Membranous G.N.
- Membrano-proliferative G.N.
- Minimal change G.N.
- Chronic G.N.

II- Secondary glomerulonephritis

- Immunological as SLE.
- Vascular as hypertension.
- Metabolic as D.M.

Clinical Manifestations of Glomerulonephritis

- Asymptomatic proteinuria, asymptomatic haematuria.
- Nephrotic syndrome.
- Nephritic syndrome.
- Rapidly progressive glomerulonephritis causing acute renal failure.
- Chronic renal failure.

Pathogenesis of glomerular injury

Most cases of G.N. are due to immune mechanisms:

1) ***In-situ immune complex deposition:*** Circulating antibodies react directly with antigens placed in the glomeruli either intrinsic or implanted as bacterial products or large protein particles. The antibody and the antigen form immune complex in the glomeruli that initiate inflammation and glomerular injury.
2) ***Deposition of circulating immune-complexes within the glomeruli:*** In this type , glomerular injury caused by trapping of circulating Ag/Ab complexes within the glomeruli.
3) ***Cell- mediated immunity.***

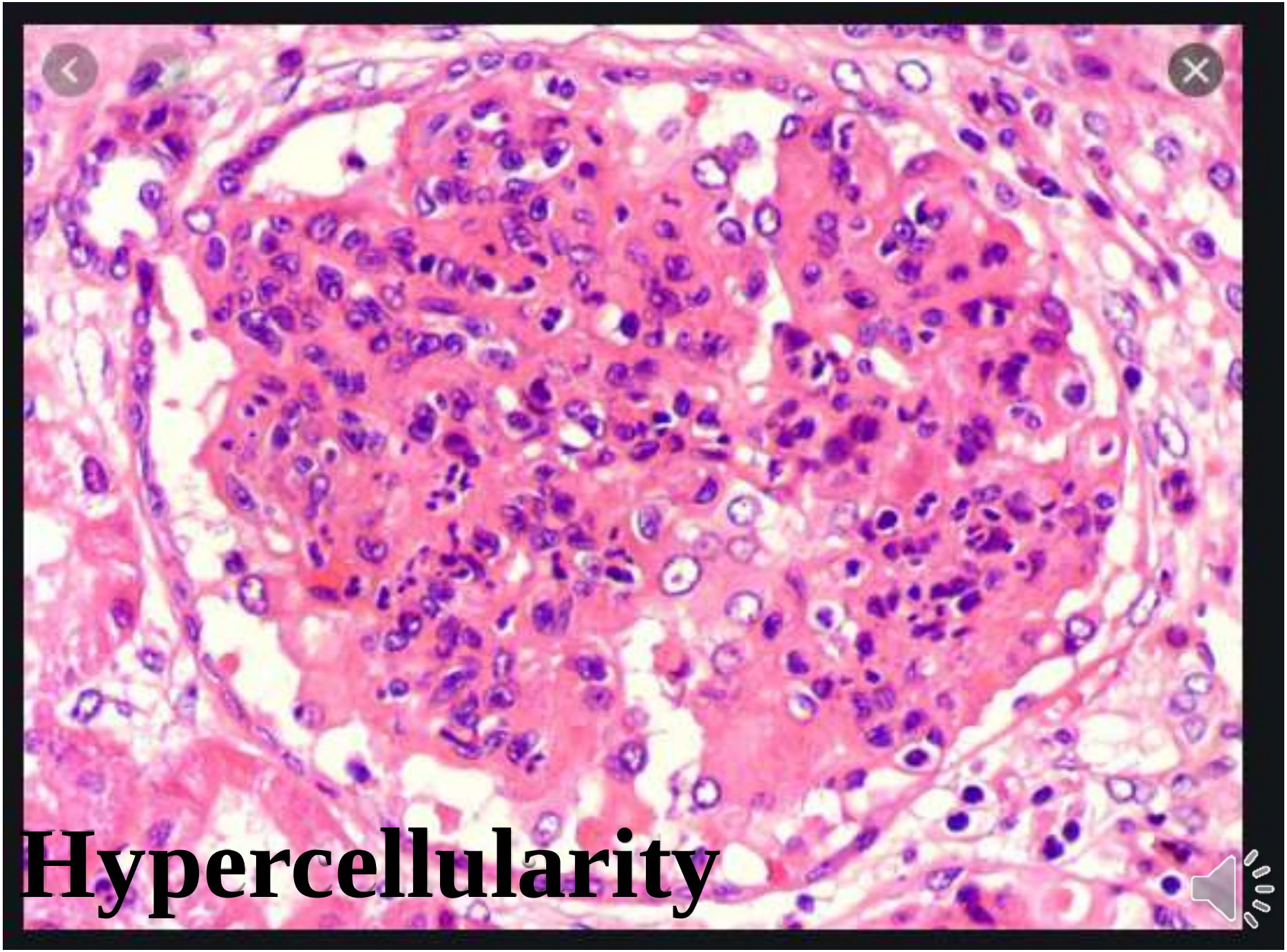
Histological Alteration of G.N.

Various types of G.N. are characterized by one or more four basic tissue reaction;

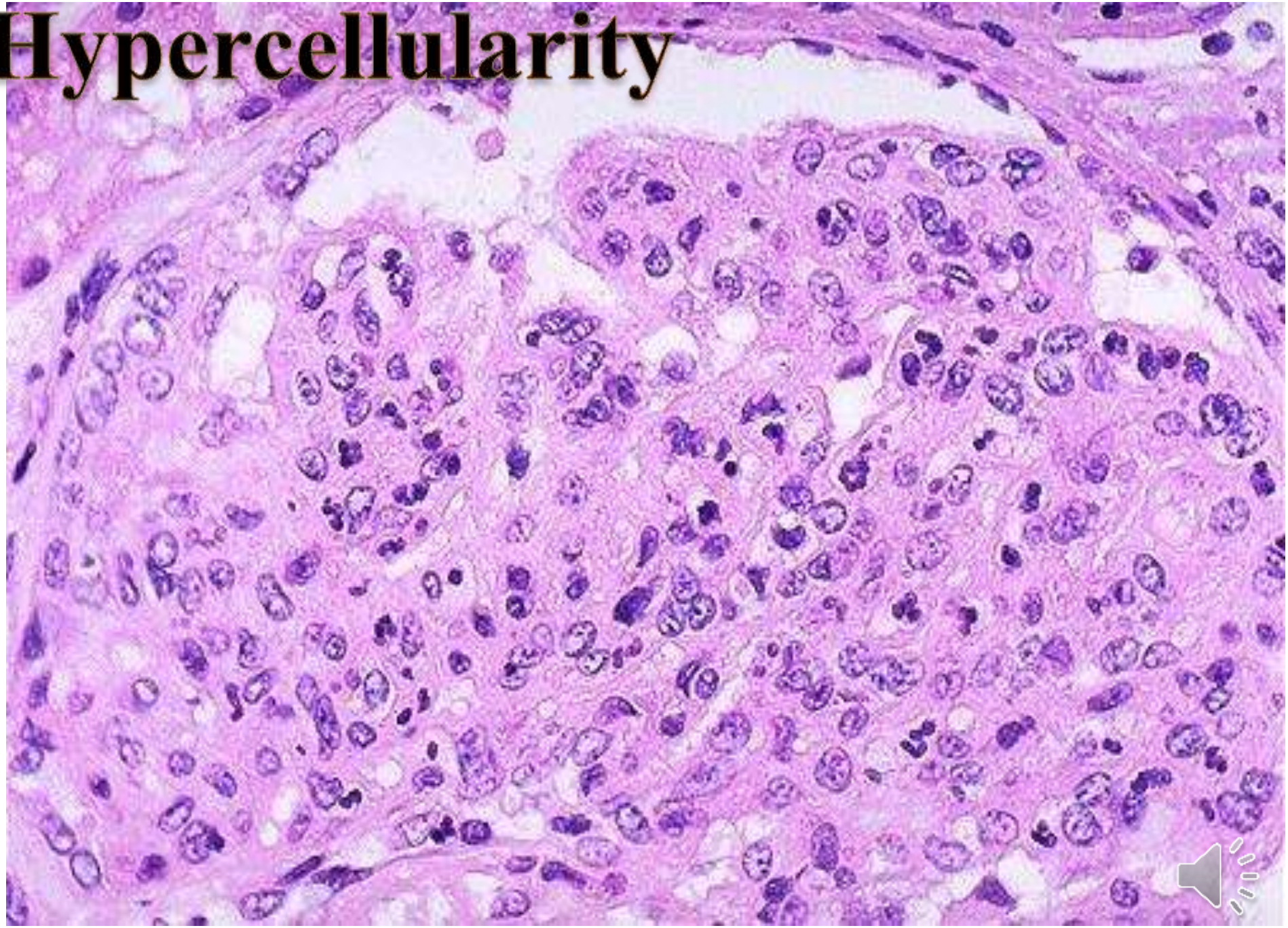
- ***Hypercellularity;*** increase number of cells in the glomerular capillary tufts due to proliferation of Mesangeal cells, endothelial cells or parietal epithelial cells. in addition to leucocytic infiltration (neutrophils, monocytes and lymphocytes in some cases).
- ***Thickening of the glomerular basement membrane.***
- ***Crescent formation:*** a crescent-shaped mass of cells may result from proliferation of parietal cells.
- ***Hyalinization and sclerosis.***

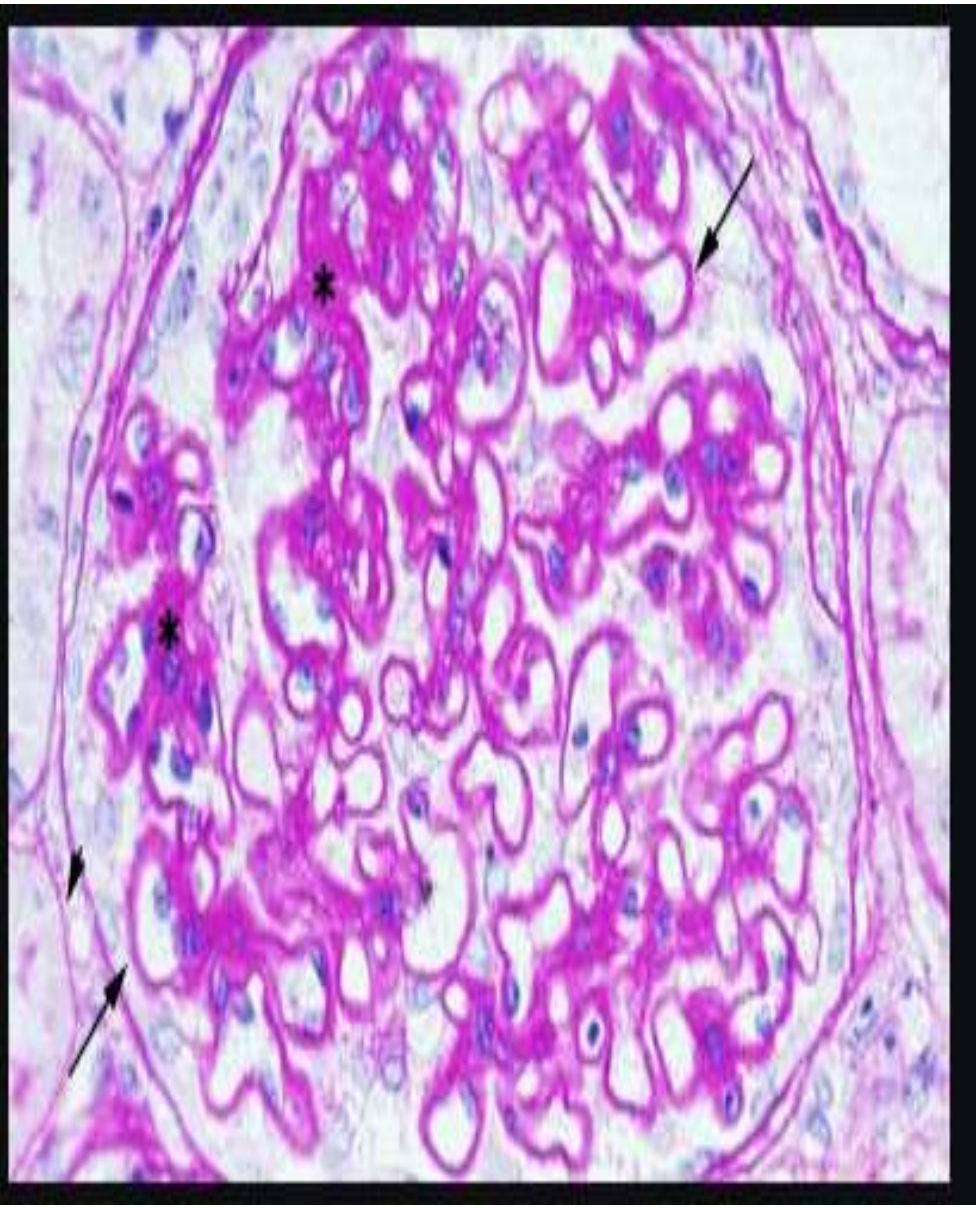
Other alterations:

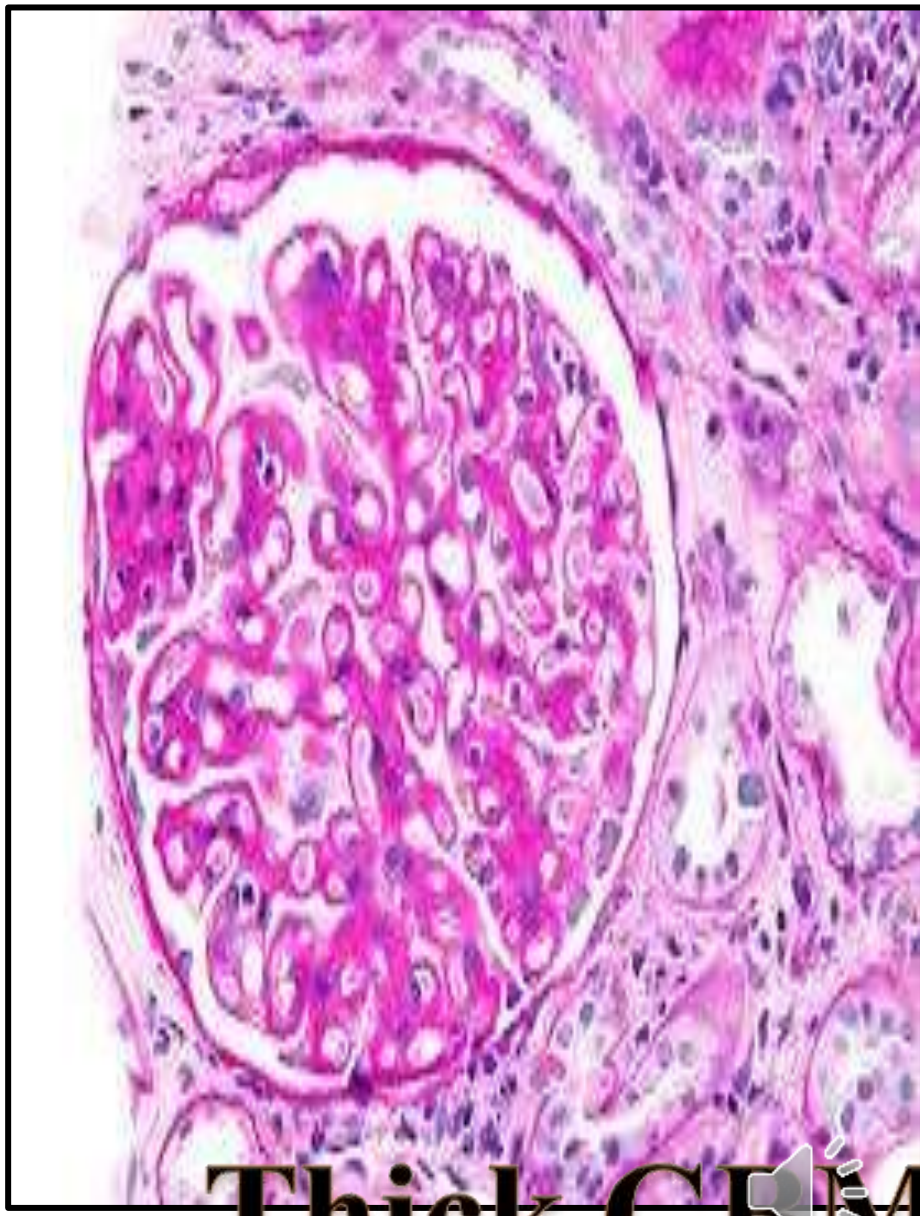
- Intra-capillary thrombosis.
- Fibrin deposition.
- Accumulation of lipids.


Hypercellularity

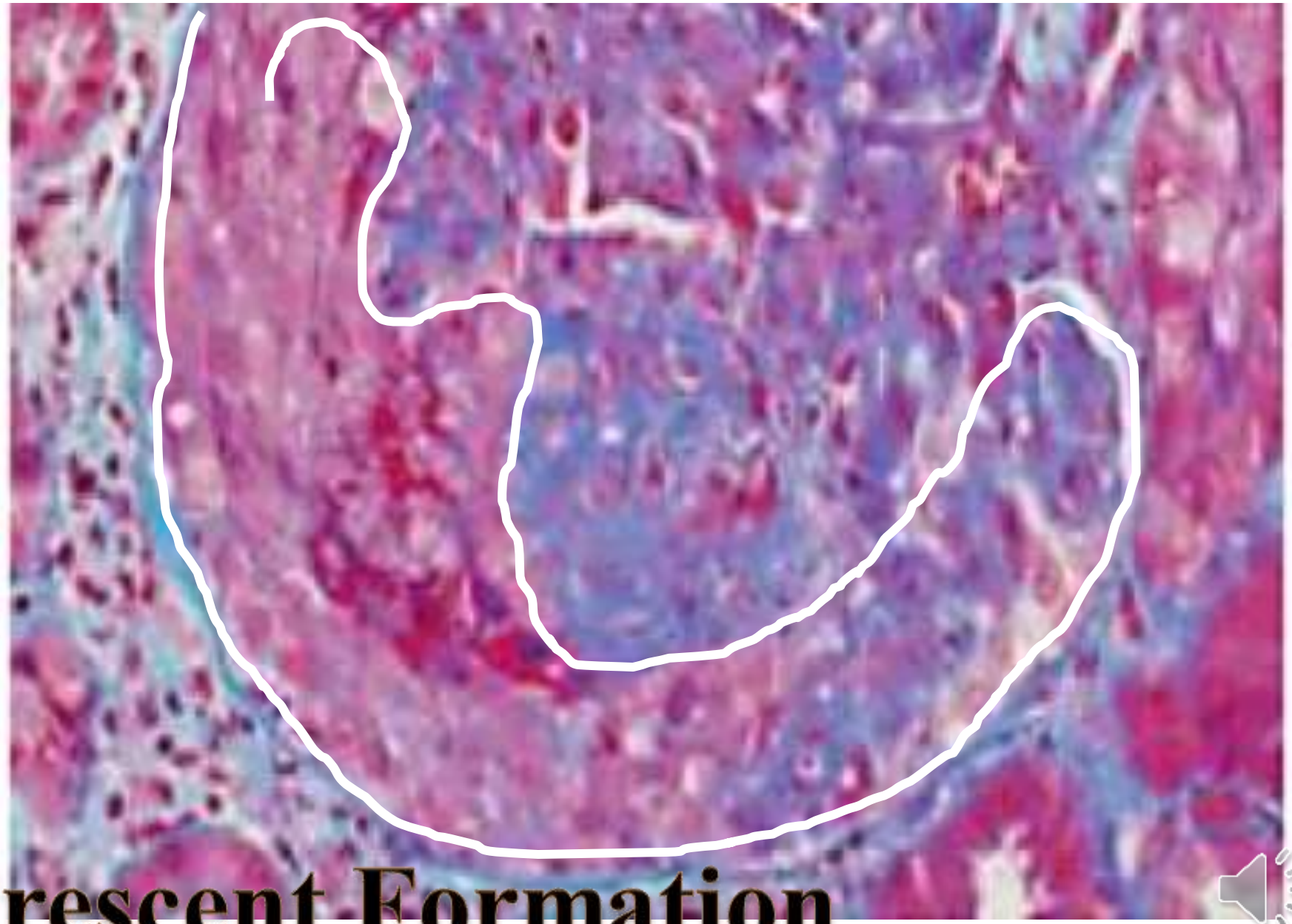
Hypercellularity



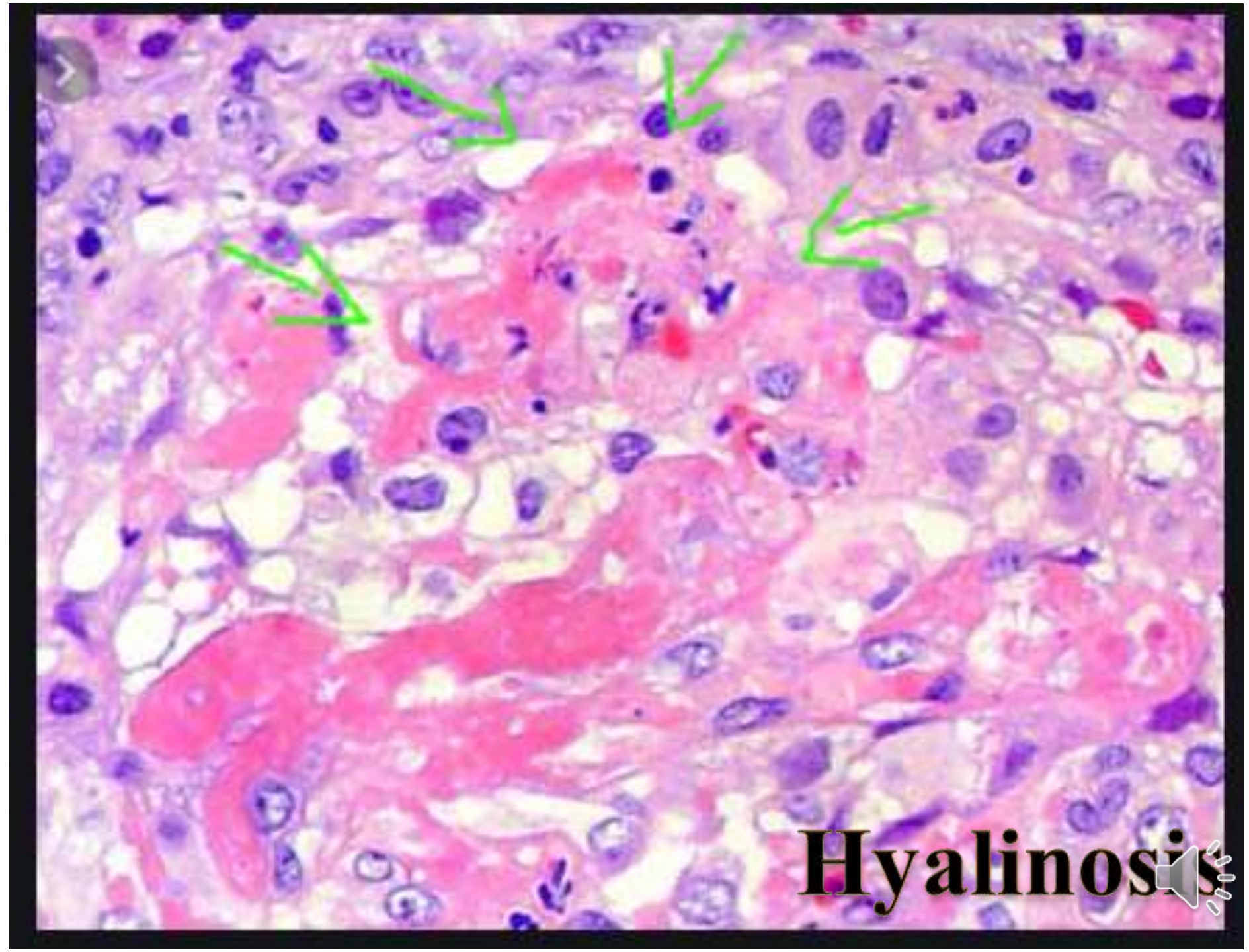




Thick GBM



Crescent Formation


Hyalinosis

Nephrotic syndrome

Definition: A group of renal glomerular diseases ; all are characterized by massive proteinuria, hypoalbuminaemia, generalized oedema and hyperlipidaemia.

- **Massive proteinuria:** daily loss of 3-5 gm/24 hours caused by increased permeability of the glomerular capillary tufts to protein.
- **Hypoalbuminaemia:** plasma albumin levels are less than 3 gm/ dl.
- **Generalized oedema:** is caused by 1) hypoproteinaemia with decrease in plasma osmotic pressure. 2) hypoalbuminaemia causing decrease in plasma volume due to loss of osmotic effect. This results in increased aldosterone release leading to sodium and water retention.
- **Hyperlipidaemia:** the exact cause is not compeletly understood, it may be due to protein loss.

Causes of Nephrotic Syndrome

1- Primary glomerular diseases:

- Membranous glomerulonephritis.
- Minimal change glomerulonephritis.
- Membrano-proliferative glomerulonephritis.
- Focal proliferative glomerulonephritis.
- Focal segmental glomerulosclerosis.

2- Systemic diseases:

- Diabetes mellitus.
- Amyloidosis.
- Systemic lupus erythematosis.
- Infections as HBV, Malaria.
- Malignancy.

Acute Nephritic Syndrome

- It is a glomerular syndrome characterized by acute onset of usually grossly visible haematuria (RBCs in urine). Mild to moderate proteinuria and hypertension.
- It is the classic presentation of acute post-streptococcal glomerulonephritis.


Thank You