Diseases of the kidney

1) Congnital anomalies
2) Glomerular diseases

By

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Why we study renal diseases?

*Renal diseases are responsible for a great deal of **morbidity** but, fortunatly are not major causes of mortality.

*Million of persons are affected annually by non fatal renal diseases.

*The **cost** of dialysis and transplantation program exceeds several billion of dollars annually.

*Lastly, renal diseases has special importance to the clinician because, so many of the deaths occur in **young** people.

Normal Kidney

The human kidneys serve to convert over 1700 liters of blood/ day into about one liter of highly specialized concentrated fluid called urine. In so doing, the kidney **excretes** the wast products of metabolism, precisely **regulates** the body's concentration of water and salt, **maintains** the appropriate acid balance of the plasma and serves as an **endocrine** organ. The physiologic mechanisms that the kidney has evolved to carry out these functions recquire a high degree of structural complexity.

From the stand point of its diseases, the kidney can be divided into four components;

- Glomeruli.
- Tubules.
- Interstitium.
- Blood vessels.

The Glomerulus:

It is a vascular - epithelial organ designed for the ultrafiltration of the plasma.

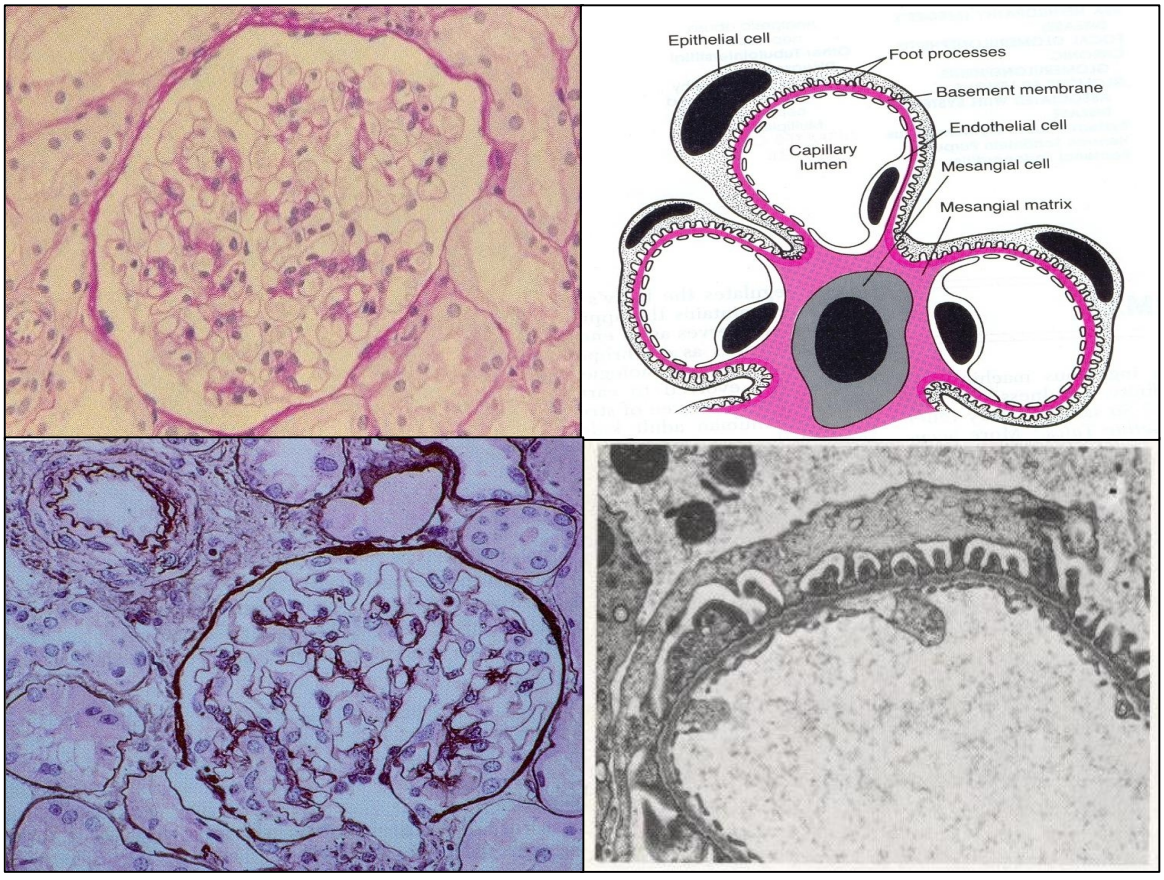


Fig.1: normal glomerulus.

A. Hematoxylin & Eosin stain. B. Sliver stain.

C. Diagramatic representation of the glomerulus.

D. Electron micrograph of the normal glomerulus showing podocytes and its foot processes.

Traditionally, diseases of the kidney have been divided into these that affect the four basic morphologic components.

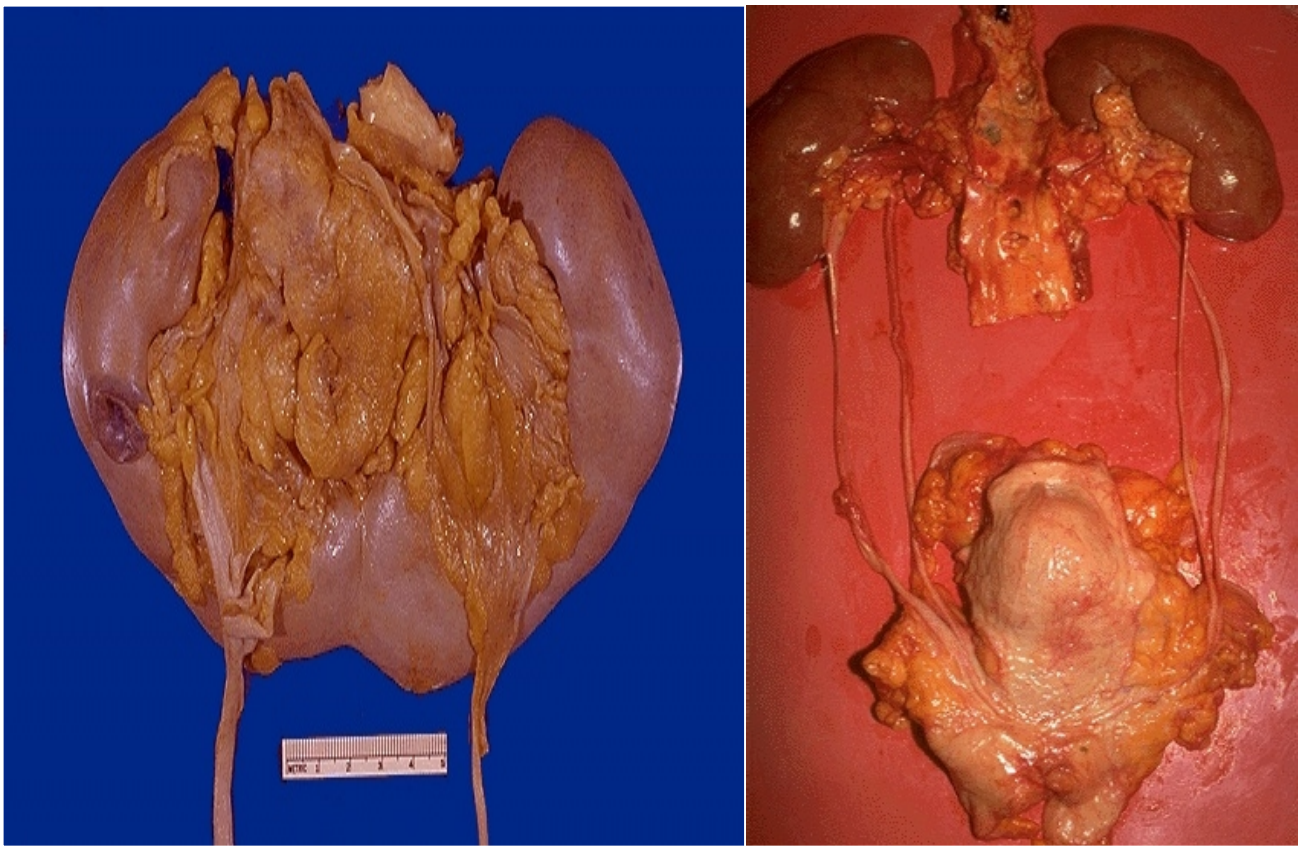
However, there is a tendency for all forms of chronic renal diseases ultimately to destroy all four components of the kidney.

Congenital Anomalies

About 10% of all persons are born with potentially significant malformation of the urinary system. Renal dysplasia and hypoplasia accounts for 20% of renal failure in children.

They include:

1) **Agenesis of the kidney**: complete absence of one kidney.
2) **Hypolpasia:** Failure of the kidney to develop to normal size.
3) **Horse shoe kidney**: Both kidneys are fused together, usually at lower poles.
4) **Ectopic kidney**: the kidney fails to migrate up to the normal position and remains in the pelvis.
5) **Miscellaneous anomalies**:
   - A- Double or extra renal pelvis.
   - B- Anomalies in renal arteries.
   - C- Double ureters.



A B

Fig 2 : Congenital anomalies of the kidney.
A. Horse shoe kidney
B. Double ureters.

Cystic Diseases of The Kidney

As a group, they are important for several reasons:

1) They are relatively common and often represent diagnostic problems for clinicians, radiologists and pathologists.
2) Some forms are major cause of CRF.
3) They can occasionally be confused with malignant tumors.

1) Adult polycystic disease

*It is relatively common, affecting 1/1000 persons and accounting for 10% of cases requiring transplantation.
It is autosomal dominant and usually manifested in 3rd-5th decades and associated with congenital cystic liver and congenital cerebral aneurysms

Pathogenesis: Due to failure of fusion of convoluted and collecting tubules.

Gross picture:

Both kidneys are enlarged and may reach enormous size, each one may weight up to 4 Kg with cystic outer and cut sections. The cysts are of variable sizes with clear or bluish content. The cysts may be communicated together but not with the renal pelvis.

Microscopic picture:

The cysts are lined by flat or cubical epithelium. Functioning nephrons are detected between the cysts.

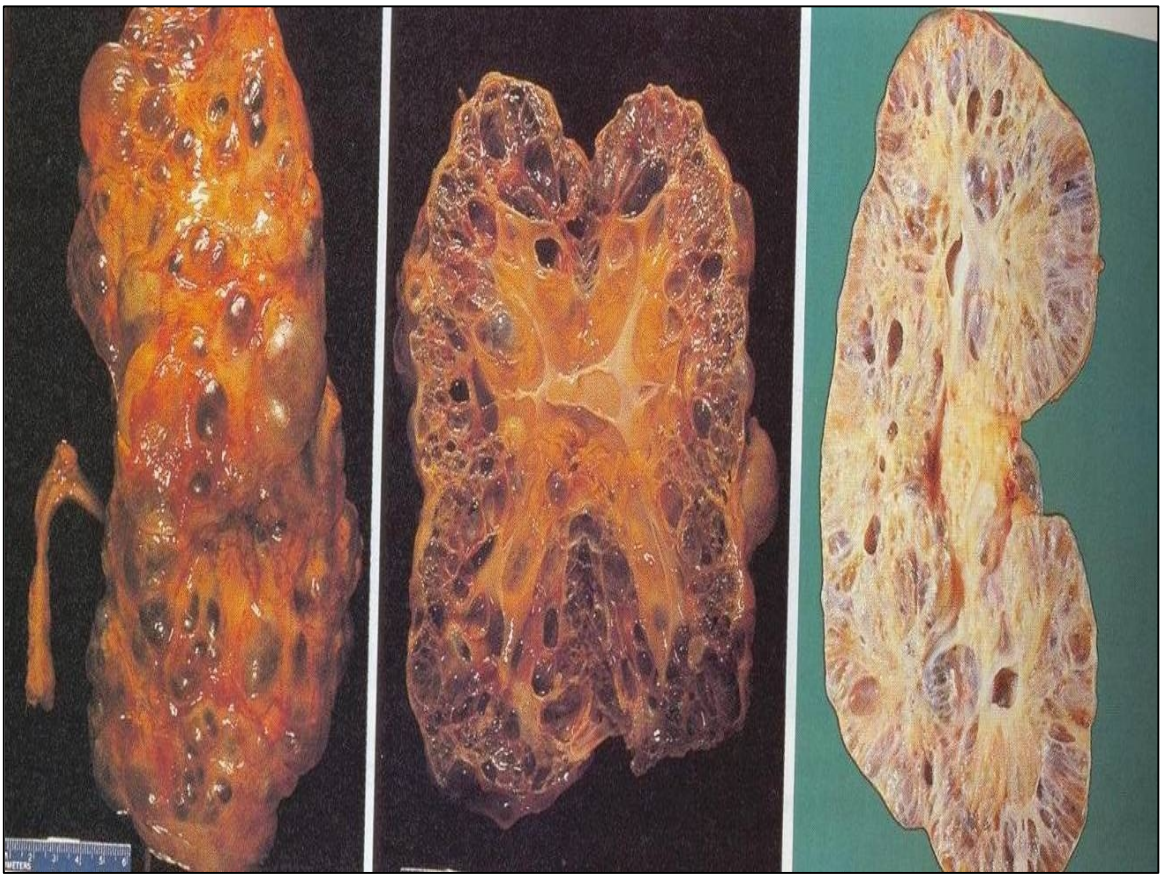
Complications: hematuria, secondary infections, hypertension and CRF.

2)Infantile polycystic kidney disease

*It is a rare developmental, autosomal recessive anomaly.
*Perinatal, neonatal, infantile and juvenile subcategories have been identified.

Morphology:

Both kidneys are enlarged with smooth outer surface. Cut section reveals numerous small cysts distributed in the cortex and medulla giving the kidney spongy appearance.



A B C

Fig. 3: Polycystic kidney.
A&B. Adult type C. Infantile type

Glomerular Diseases

*They constitute some of the major problems encountered in nephrology. Indeed, chronic GN is the most common cause of CRF in man.

*There are two main types of GN:

1) **Primary GN**: The kidney is the primary target of the disease.
2) **Secondary GN**: The glomeruli are injured in the course of systemic diseases.

However' both the clinical manifestations and the glomerular histologic changes in primary and secondary forms can be similar.

Clinical manifestation of the glomerular diseases

The clinical manifestation of the glomerular diseases are grouped into five syndromes:

1) **Nephritic Syndrome;** It is dominated by acute onset of gross hematuria, hypertension, mild/ moderate proteinuria, edema and oliguria.
2) **ARF;** dominated by oliguria or anuria (no urine flow).
3) **Nephrotic Syndrome;** characterized by massive proteinuria (more than 3.5 gm/day), hypoalbuminemia, severe edema, hyperlipidemia and lipiduria (lipid in urine)
4) **Asymptomatic hematuria or proteinuria or** combination of both.
5) **CRF:** characterized by prolonged symptoms and sign of uremia

Pathogenesis of glomerular injury

Although we know little about etiologic agents or triggering events, it is clear that immune mechanisms underlie most cases of primary and many of secondary glomerulonephritis.

I- Immune mechanisms:

Antibody mediated injury are the most common type of glomerular injury as glomerular deposits of immunoglobulins and complements are detected in more than 70% of cases.

Two forms of antibody mediated injury have been established:

1) The antibodies react directly with intrinsic tissue antigens (Anti GBM nephritis) or planted antigens (IgA nephropathy).
2) Deposition of circulating antigen antibody complexes in the glomeruli

II- Non Immune Mechanisms:

1) loss of glomerular polyanion as in minimal change disease.
2) Hemodynamic changes (glomerular hyperfiltration) as in focal segmental glomerulosclerosis .

Diagnosis of glomerular diseases

Renal biopsy is the golden standard to diagnose renal diseases and the following methods are used to diagnose glomerular diseases.

1**) Light microscopic** examination and staining with H&E, PAS stain and Masson trichrome stain.

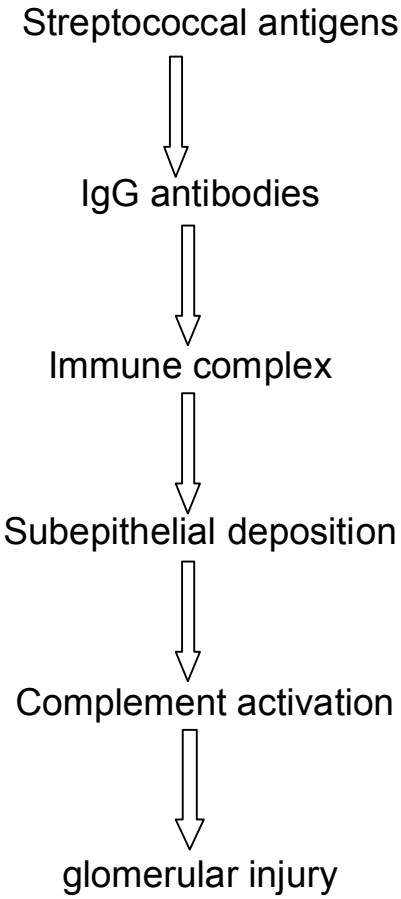
2)Immunostaining by using immunoperoxidase or immunoflourescent technique.

3)Electron microscope to detect the ultrastructural changes and it is essential to diagnose certain disease.

Acute Diffuse Proliferative GN (Post-streptococcal GN)

*It is a fairly common glomerular disease. Usually appears 1-4 weeks after sore throat or tonsillitis caused by group A beta haemolytic streptococci (nephrogenic strain). It occurs most commonly in children 6-10 years but the adult can be affected.

Etiology and pathogenesis:
During the latent period between infection and nephritis, antibodies are formed against streptococcal antigens. The reaction occurs in the serum and the immune complex deposit between the GBM and epithelial cells initiating the glomerular injury.



Microscopic picture

1) All the glomeruli are enlarged and hypercellular due to proliferation of endothelial, mesangial and epithelial cells as well as due to infiltration by neutrophils and monocytes. There may be crescent formation.
2) The tubules show hydropic degeneration and may contain red cell casts. The interstitium is edematous and may be infiltrated by neutrophils.
3) Immunoflourescent microscopy, there are granular deposits of IgG and C3 along GBM and in the mesangium.
4) By electron microscopy there is subepithelial electron dense deposits (humps)

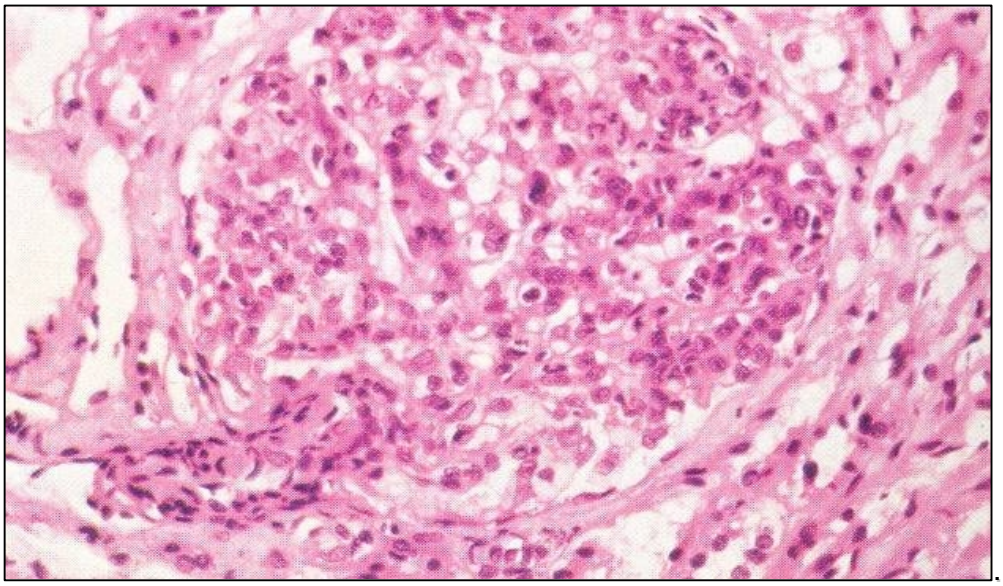


Fig. 4: Acute diffuse proliferative GN. The glomerulus is hypercellular due to proliferation of endothelial, mesangial and podocytes as well as leucocytic infiltration

General manifestations:

In the classic case, the child develops abrupt onset of fever, malaise, oliguria and hematuria 1-2 weeks after recovery from sore throat or tonsillitis. Then there is picture of nephritic syndrome.

Course:

1)Complete recovery in 95% of children and 65% of adult.
2)Severe hypertension AHF or ARF.
3)Progress Rapidly progressive GN.
Chronic GN.

Rapidly Progressive GN (Crescentic GN)

*It is a clinicopathologic syndrome characterized by :
1) Rapid & progressive decline in renal function.
2) Histologically; formation of crescents.

*Aetiology:

1) Post infectious; follow acute diffuse proliferative GN, especially in adults.
2) In association with systemic disease as PAN, SLE & Goodpasture's syndrome
3) Idiopathic

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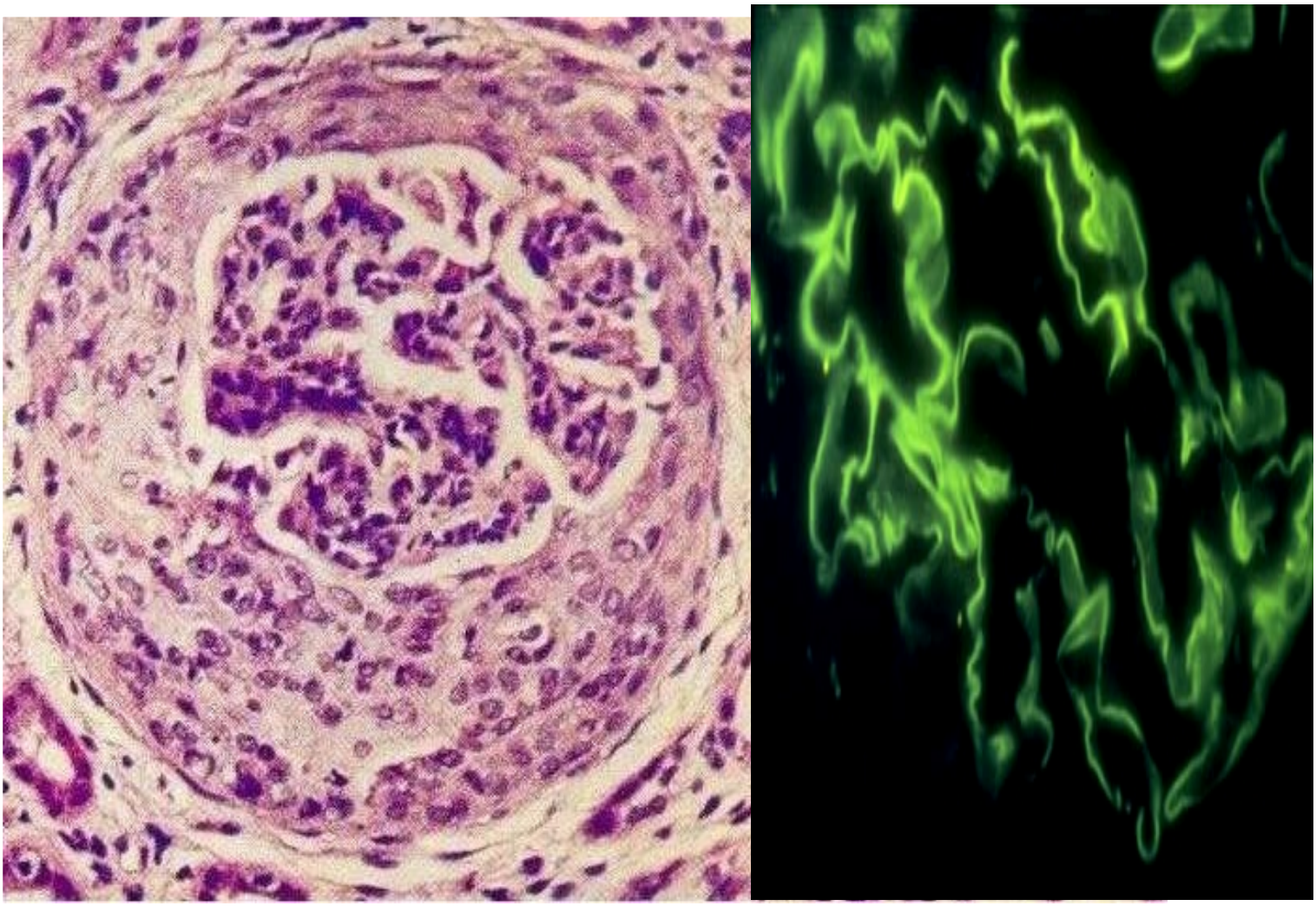
Morphology:

1) Grossly; the kidneys are pale, enlarged with petechial Hg. on the outer surface.
2)The glomeruli are enlarged, hypercellular showing proliferation of endothelial, mesangial and epithelial cells as well as leucocytic infiltration. Usually there is glomerular necrosis and may be glomerular capillary thrombosis.
3) Crescents are formed in the Bowman space and compressing the tufts. They are formed of proliferating parietal epithelial cells, fibrin and migrating monocytes and leucocytes.

5) By immunoflourescence microscopy, in Goodpasture syndrome there is linear deposition of IgG and C3 along GBM.



A **B**

Fig. 5: Crescentic glomerulonephritis.
A. crescent compresing the tuft
B. Linear deposition of IgG along GBM.

Clinical manifestations

Usually there is picture of nephritic syndrome with rapid decline in renal function which may proceed to renal failure. In Goodpasture syndrome there is hemoptysis.

Course:

Rapidly fatal from;

1)Acute renal failure. **2)**Hypertension

3)Pulmonary Hg. In Goodpature syndrome.

Nephrotic Syndrome (NS)

*The syndrome is fundamently the result of excessive glomerular permeability to plasma protein and thus heavy proteinuria is its prime characteristic.

*Many glomerular diseases whether primary or secondary may evoke NS.

Membranous GN

It is the most common cause of syndrome in adult.

Aetiology:

*85% of patient is idiopathic.

*It may occur in association with systemic disease as carcinoma, SLE, Drugs, infections (Hepatitis B & C and Bilharziasis) and metabolic disorders.

Morphology

1) There is diffuse uniform thickening of the GBM without cellular proliferation.

2) By immunoflourescence microscopy there are granular deposition of IgG and complement between the GBM and epithelial cells.

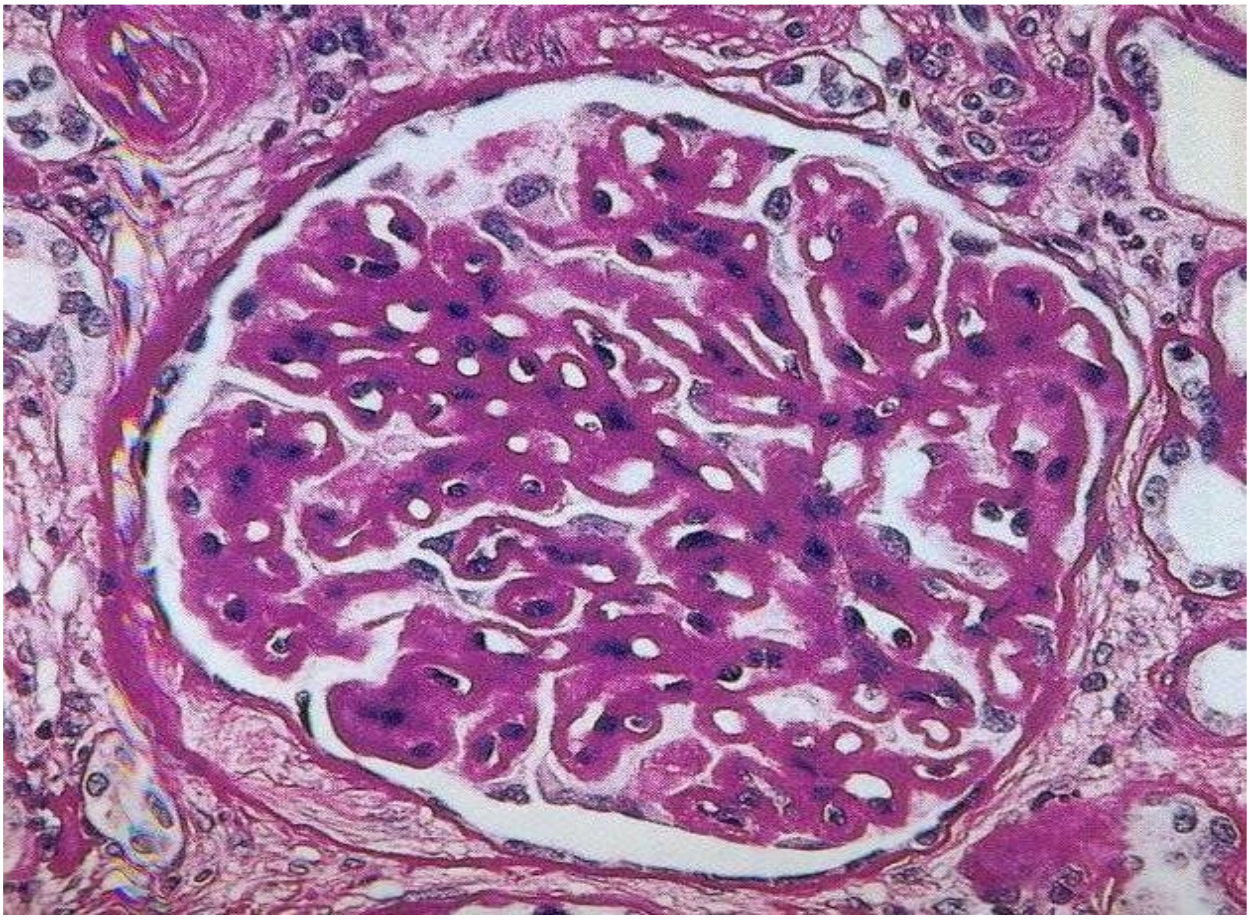


Fig.6: membranous GN showing diffuse thickening of the GBM

Minimal change GN
(No change under light microscopy)

*It is the most common cause of NS in children (2-6 years).
*The most characteristic features are normal appearance of the glomeruli by light microscopy and dramatic response to corticosteroid therapy.
*The etiology in unkown, but it may follow respiratory tract infections.
Morphologically; no pathological changes are detected by light or immunoflourescent microscopy. By **EM**, there are

diffuse and uniform effacement of the foot processes of the podocytes

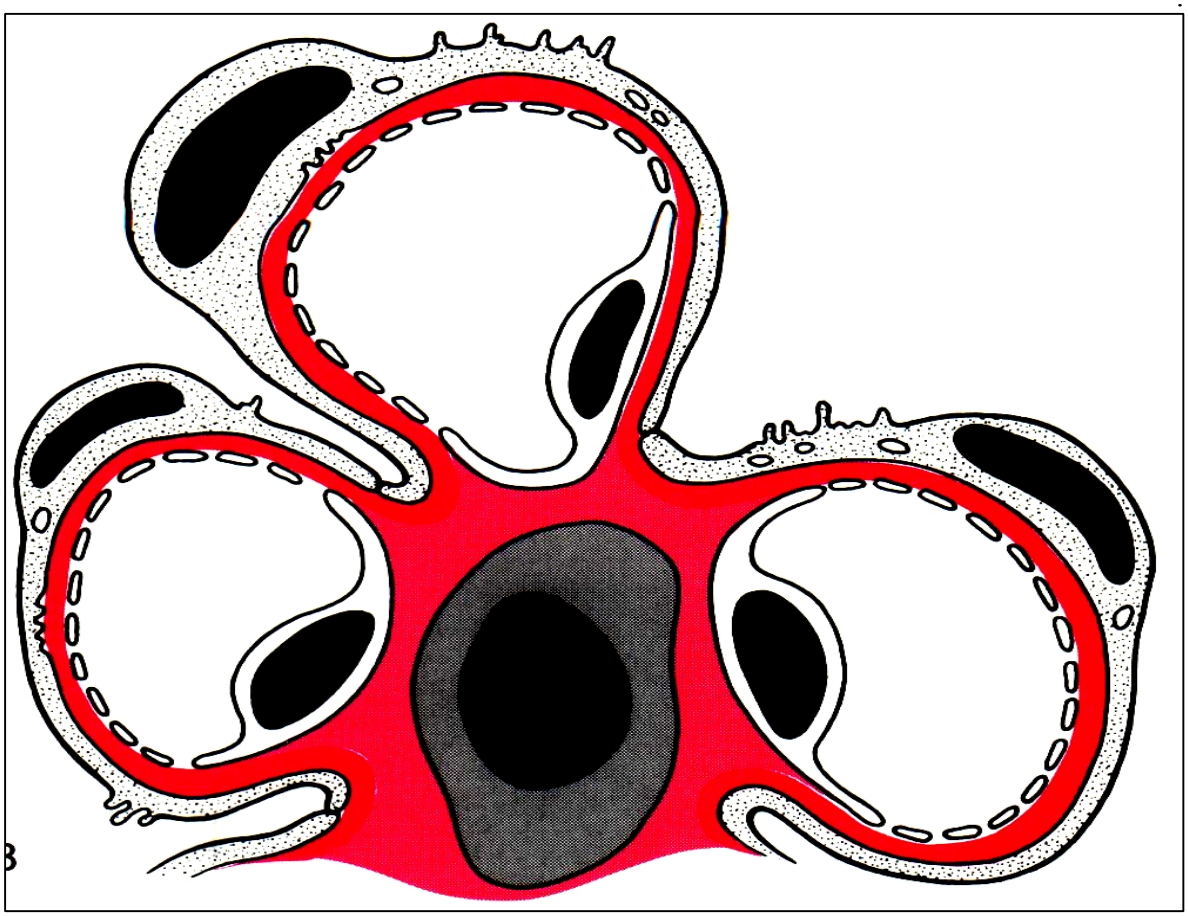


Fig .7: Diagrammatic representation of minimal change disease showing diffuse loss of foot processes.

Focal segmental glomerulosclerosis(FSGS)

*This lesion is characterized by sclerosis of only portion of the capillary tuft (segmental) in some glomeruli (focal).
*It is classified into:

1) Idiopathic: account for 10-15% of nephrotic syndrome. However, the patients may be presented by hematuria & protienuria.

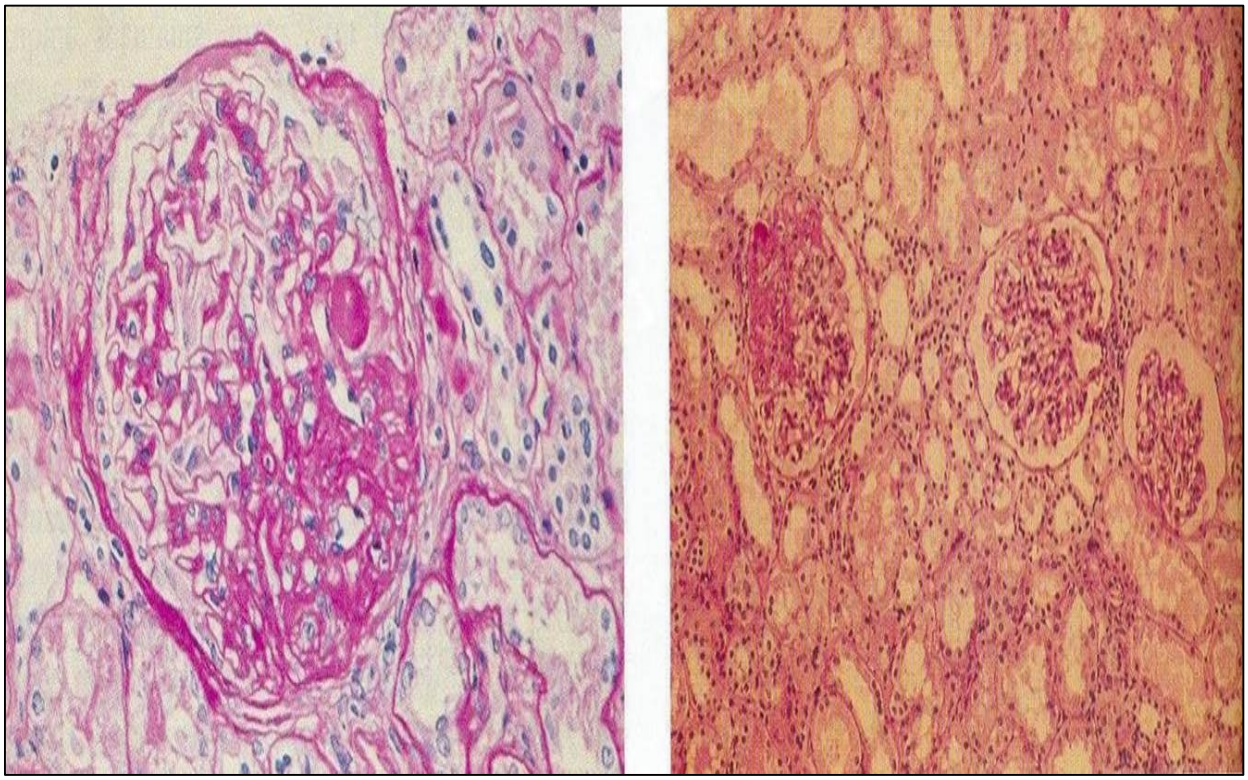
2) Secondary type;

*Other type of GN or systemic disease.

*Heroin abuse or Aids.

Morphology:

1) Segmental sclerosis and hyalinosis of some glomeruli, usually the juxtamedullary ones.
2) The rest of the glomeruli are normal or may show mesangial cell proliferation.
3) By immunoflourescent microscopy there may be deposition of IgM and C3.



B A

Fig. 8: Focal segmental glomerulosclerosis. Hyalinosis and sclerosis of portion (in A) of some glomeruli (A)

Membranoproliferative GN (Mesangiocapillary GN)

This group of disorders is characterized histologically by alterations of the GBM and proliferation of glomerular cells.
*The pateints present with NS but may presents with hematuria or proteinuria.
*50% of the cases progress to CRF.
*It may be primary (idiopathic) or secondary (associated with HCV).

*The idiopathic type is divided into two types I and II on the basis of distinct ultrastructural and immunoflourescent findings.

Morphology:

1)The glomeruli are enlarged, hypercellular with accentuation of the normal lobulations as well as thickening of the GBM.
2) The hypercellularity is mainly due to mesangial cell proliferation with interposition of the mesangial processes into the GBM creating double contour or tram track appearance (by PAS or silver stain).

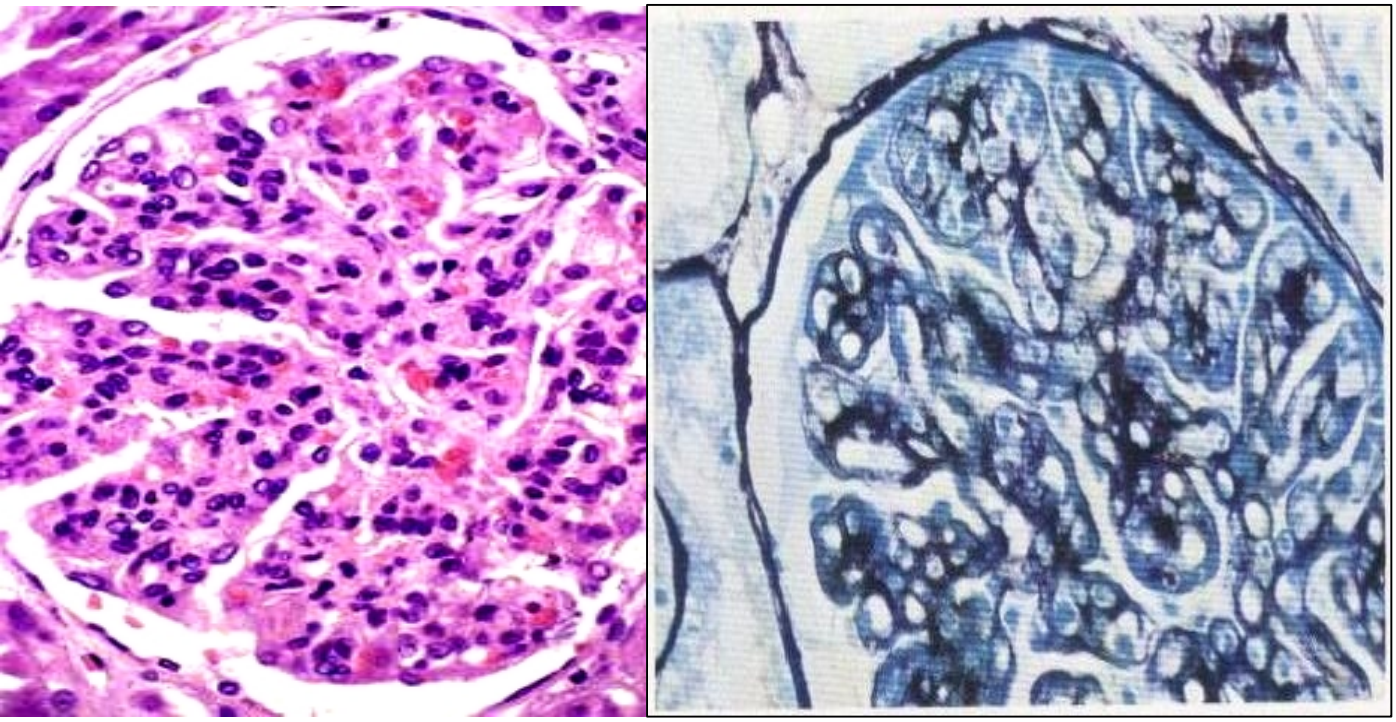


Fig.9: Mesangiocapillary glomerulonephritis.
A. showing accentuation of the normal lobulation and increased cellularity.
B. Showing double contour appearance

3)EM and IF:

A. Type I: there is subendothelial deposits of IgG and C3.
B. Type II (densec deposits disease) : there is irregular electron dense deposits in the GBM and C3 in the basement membrane and mesangium.

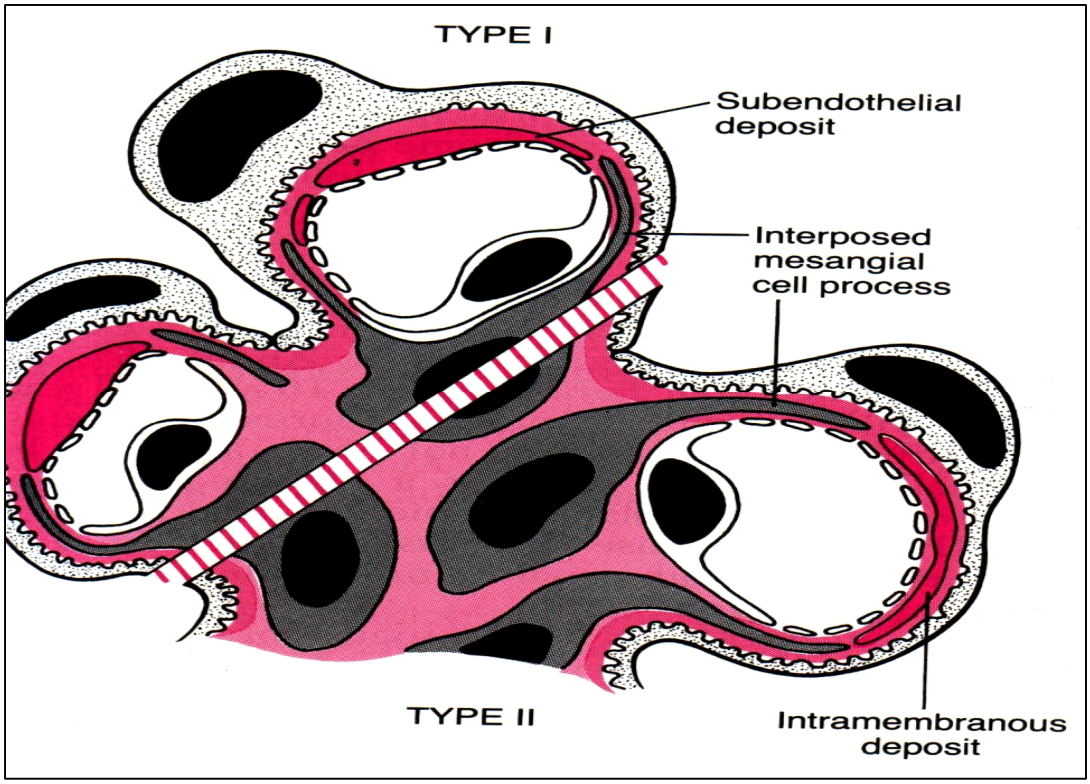


Fig.10: Diagrammatic presentation showing both type of the mesangiocapillary GN

Focal proliferative GN

Some glomeruli show segmental proliferations.
Aetiology:
1) Idiopathic.
2) Secondary to:
Upper respiratory tract infections, PAN, SLE and Henoch Shonlien purpura.
***Clinically**; hematuria, proteinuria or NS
***IF**; IgA or IgM and C3.

IgA nephropathy (Berger disease)

*It is characterized by the presence of prominant IgA deposits in the mesangial region.
*The patient presents with recurrent gross or microscopic hematuria and mild protienuria.
*The course is slowly progressive.
*It may be primary secondary (liver or intestinal disease).

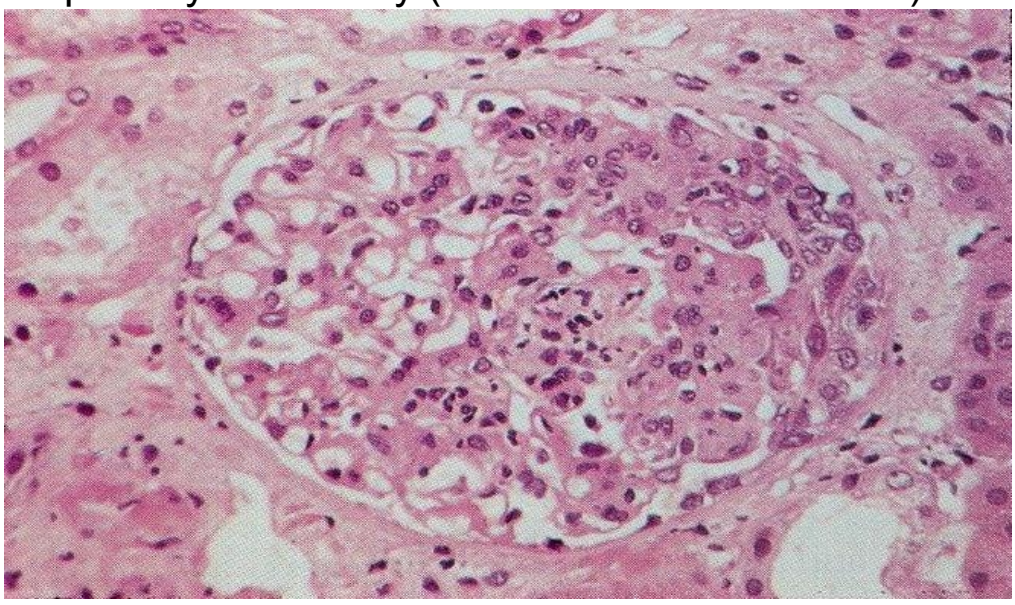


Fig. 11: Focal proliferative GN showing segmental proliferation of the tuft

Chronic GN

It is the end stage of most glomerular disease
*Clinically; The patient presented by CRF

Gross picture:

-bilateral symmetrically Shrunken kidneys with capsular adhesions.
-Granular outer surface with tiny bluish cysts
-Cut section: atrophic renal parenchyma, indistinct cortex and medulla and thickened blood vessels.

Microscopic picture:

1)Most of the glomeruli are fibrosed, and the viable one may show the original disease.
2) the tubules show atrophy with dilatation.
3) The interstitium shows fibrosis and lymphocytic infiltrations.
4) The blood vessels have thick wall.

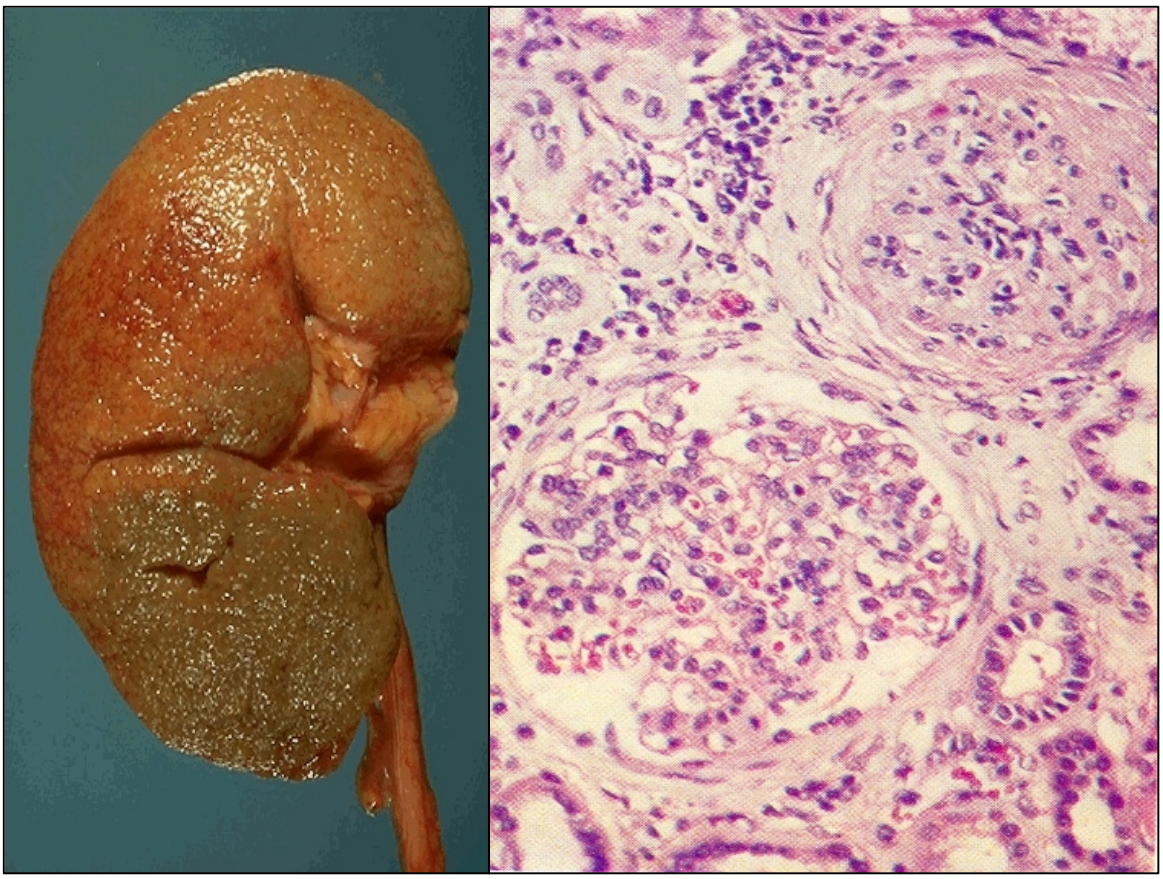


Fig. 12: Chronic GN.
A. gross picture with granular outer surface.
B. microscopic picture with fibrosed glomeruli.

Glomerular lesions associated with systemic diseases

1) SLE.
2) Henoch-Schonlein Purpura.
3) Bacterial endocarditis.
4) Diabetic GS.
5) Amyloidosis.
6) Vasculitis.
7) Plasma cell dyscrasias.