Diseases of Urinary System

(Part 2)

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Pathology of urinary tract diseases

Glomerulonephritis

Pathology of urinary tract diseases

Intended Learning objectives

By the end of this course; you should:

- Identify common causes of GN
- Describe pathological changes of main types of GN

Pathology of urinary tract diseases

Glomerulonephritis

Nephritic syndrome

- **Common causes**

➢ **Primary renal diseases**

1. Acute diffuse GN
2. Rapidly progressive GN
3. IgA nephropathy (Berger`s disease)

➢ **2ry to systemic diseases**

1. SLE
2. Purpura

Nephrotic syndrome

- **Common causes**

➢ **Primary renal diseases**

1. Membranous GN
2. Membranoproliferative GN
3. Minimal change GN
4. Focal segmental GN

➢ **2ry to systemic diseases**

1. Diabetic nephropathy
2. Renal amyloidosis
3. SLE

Pathology of urinary tract diseases

Glomerulonephritis

Common primary causes of nephritic syndrome

1. **Acute diffuse (post-infectious) GN**
2. **Rapidly progressive GN**
3. **IgA nephropathy (Berger`s disease)**

Pathology of urinary tract diseases

Acute post-infectious GN

Pathology of urinary tract diseases

Acute post-infectious GN

Incidence: Usually affects children and young adults

Pathogenesis:

(1) glomerular trapping of circulating immune complexes and

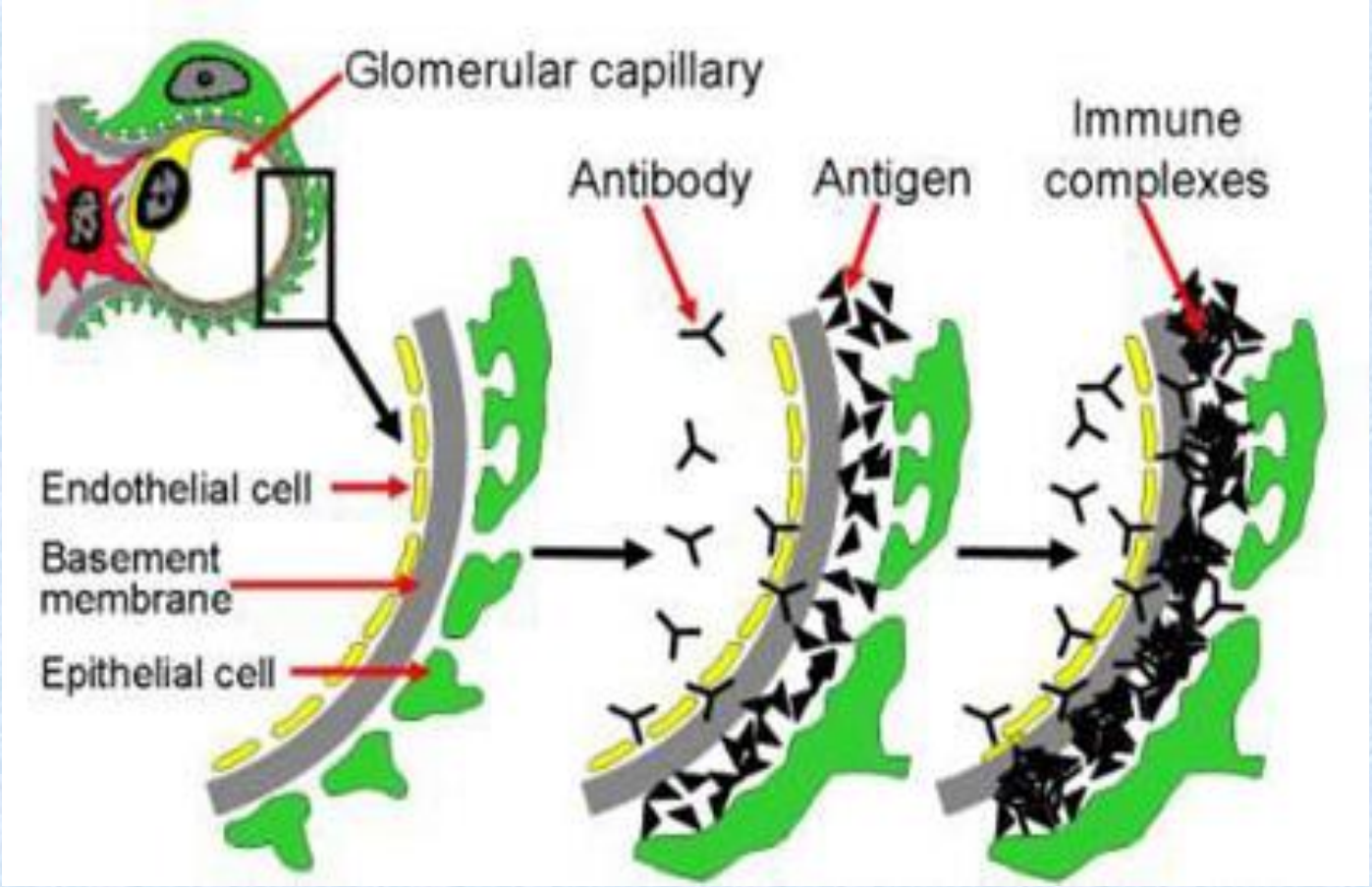
- (2) in situ immune antigen-antibody complex formation resulting from antibodies reacting with either streptococcal components deposited in the glomerulus

Pathology of urinary tract diseases

Acute post-infectious GN

Incidence: Usually affects children and young adults

Pathogenesis:

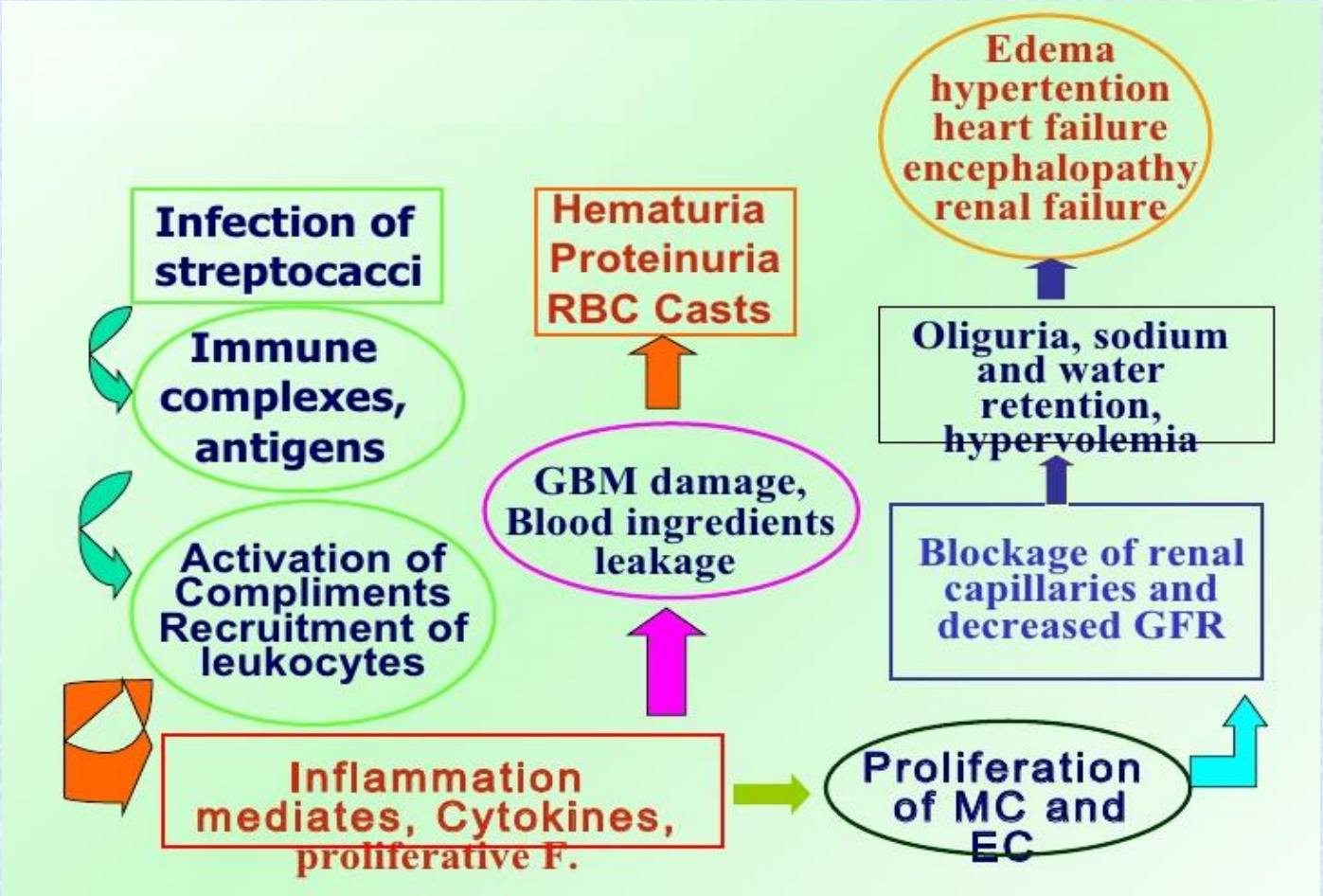


Pathology of urinary tract diseases

Acute post-infectious GN

Incidence: Usually affects children and young adults

Pathogenesis:



Pathology of urinary tract diseases

Acute post-infectious GN

Grossly: The kidneys are slightly enlarged & pale due to edema

MP:

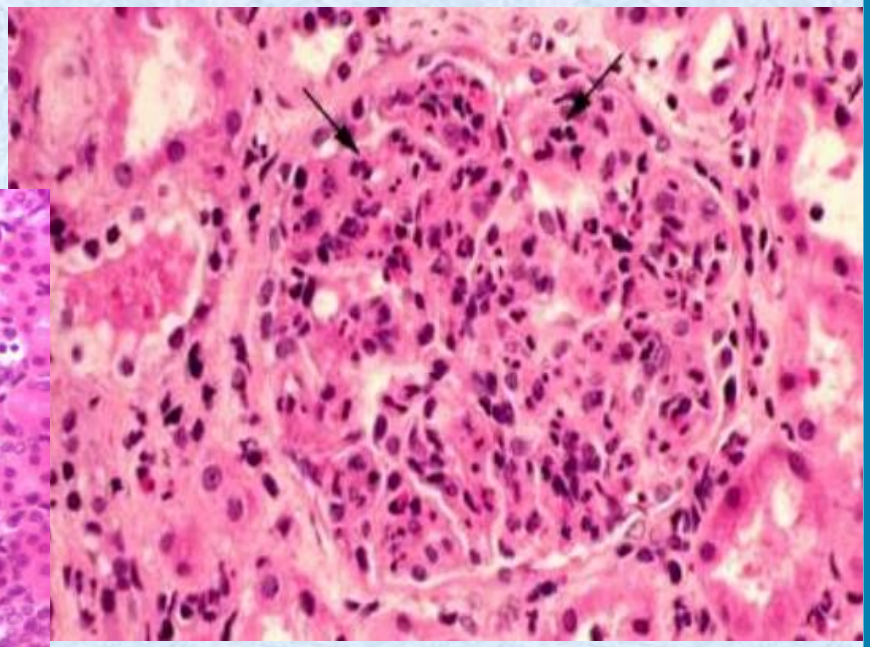
- **Glomeruli**: hyper-cellular due to proliferation of epithelial, endothelial and mesangial cells and infiltration by neutrophils
- **Tubules**: cloudy swelling of lining cells and RBCs cast of the lumen
- **Blood vessels**: **NO** significant changes
- **Interstitial tissue**: infiltration by neutrophils
- **EM**: sub-epithelial deposition of Humps of immune complex
- **Immunfluorescence**: demonstrate IgG and complement elements

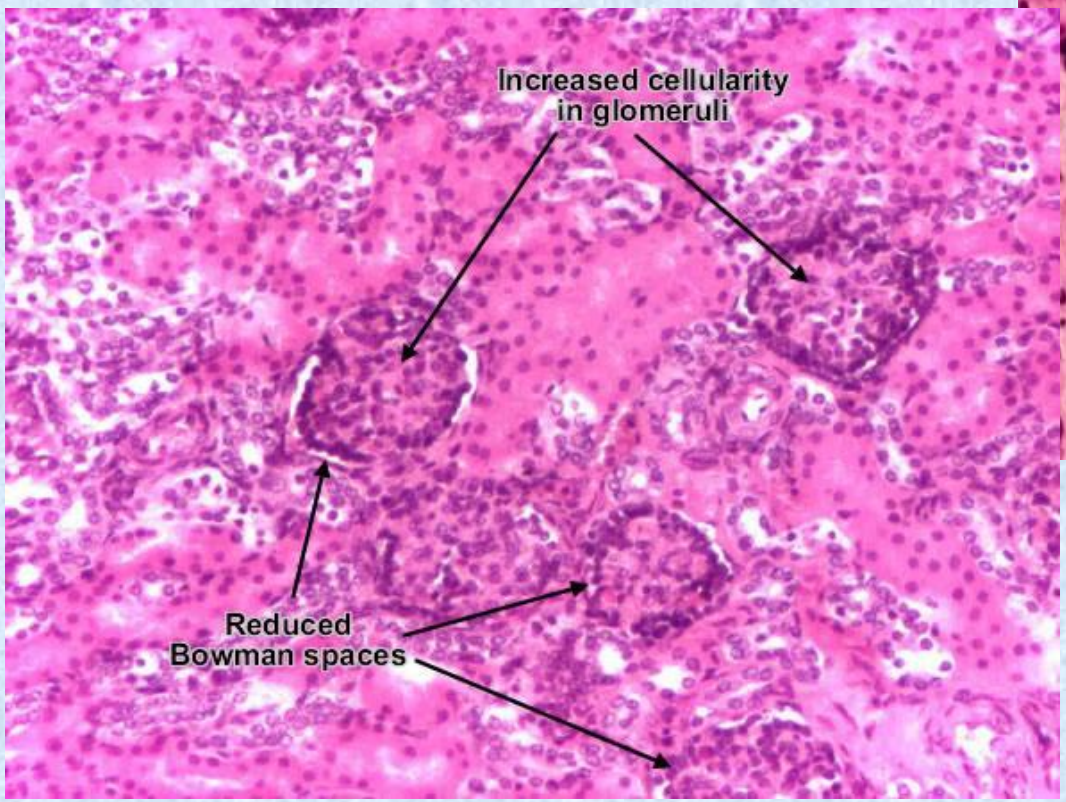
Pathology of urinary tract diseases

Acute post-infectious GN

Grossly: The kidneys are slightly enlarged & pale due to edema

MP:



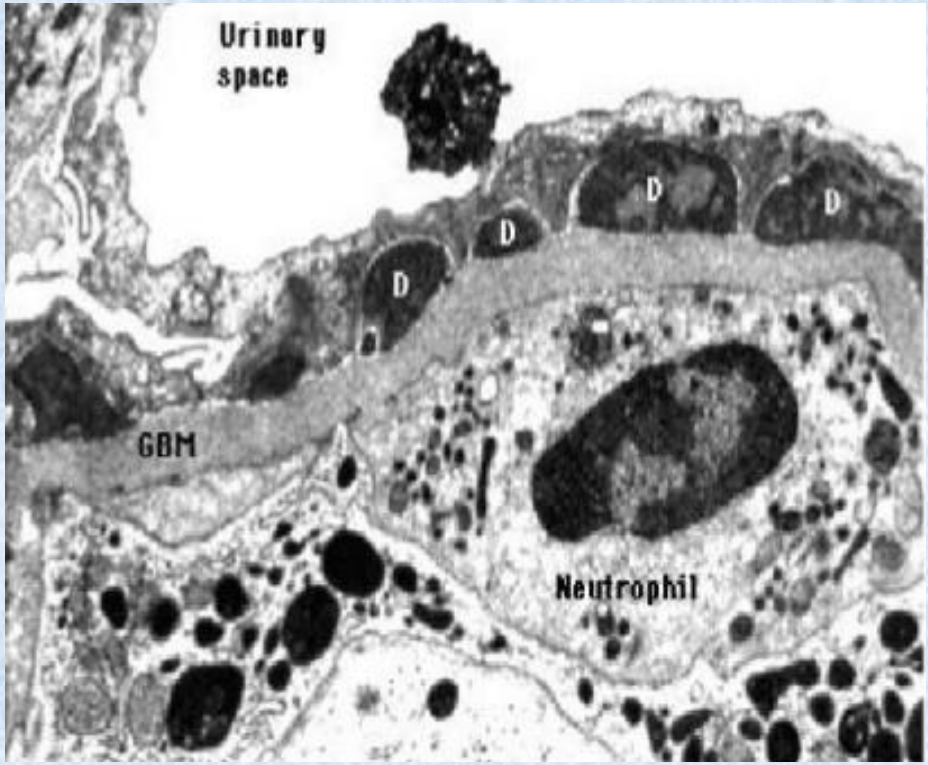


Pathology of urinary tract diseases

Acute post-infectious GN

Grossly: The kidneys are slightly enlarged & pale due to edema

EP:



Pathology of urinary tract diseases

Acute post-infectious GN

Clinical and biochemical changes:

- ***Fever and malaise***

- ***Nephritic syndrome:***
  - Gross hematuria (smoky urine)
  - Mild to moderate hypertension.
  - Oliguria
  - Mild nephritic edema

- ***Urine analysis:***
  - Hematuria
  - Mild proteinuria
  - High specific gravity
  - Hyaline and RBCs casts

- ***Blood picture:***
  - Mild anemia
  - High ASO titre
  - Low serum complement
  - Mild increased serum urea and creatinin

Pathology of urinary tract diseases

Acute post-infectious GN

Fate:

- **In children: (excellent prognosis):**
  - 95% of affected children resolve within 2-3 weeks
  - The remaining cases may progress to rapidly progressive form and may develop renal failure

- **In adults:** less favorable prognosis compared to children: about 60% resolve completely

Pathology of urinary tract diseases

Rapidly progressive (crescentic) GN

Pathology of urinary tract diseases

Rapidly progressive (crescentic) GN

Definition:

A serious condition characterized:

- Clinically by rapid deterioration of renal function with significant features of nephritic syndrome
- Pathologically by formation of cellular crescent

Etiology:

1. Develop on top of acute post-infectious GN
2. Good Pasteur syndrome or anti-glomerular membrane (anti-GBM) antibody.
3. As a part of systemic disease as SLE and henoch-shonlien purpura
4. Idiopathic

Pathology of urinary tract diseases

Rapidly progressive (crescentic) GN

Grossly: The kidneys are slightly enlarged & pale due to edema

MP:

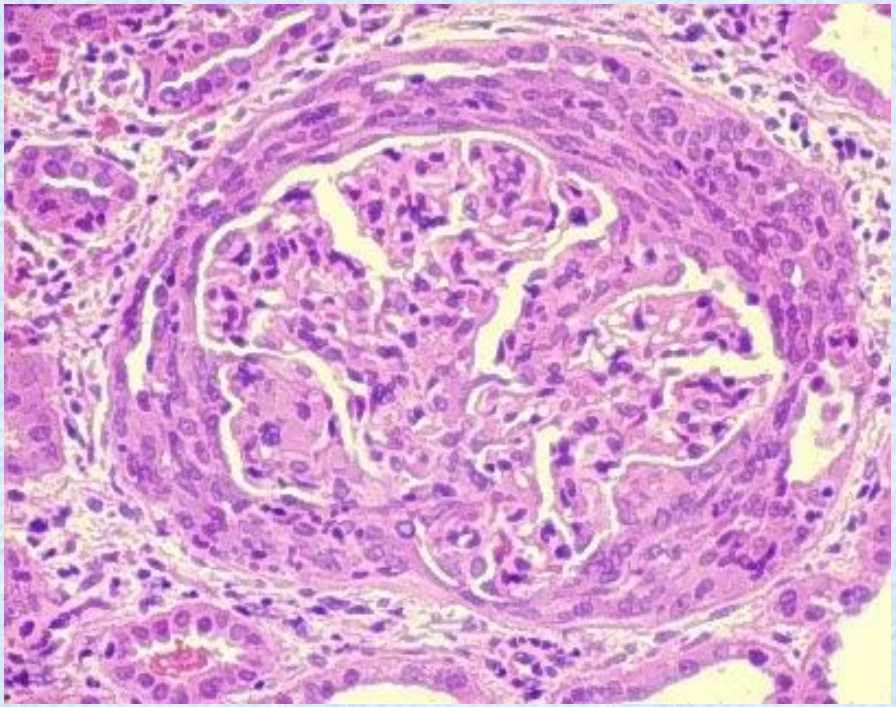
- **Glomeruli**:
  - Hyper-cellular (proliferation of epithelial, endothelial and mesangial cells and infiltration by neutrophils).
  - Crescent formation: proliferation of parietal epithelium leads to obliteration of Bowman`s space
  - Glomerular tufts: focal thrombosis and necrosis
- **Tubules**: focal necrosis and RBCs cast in the lumen
- **Blood vessels**: may show thrombosis
- **Interstitial tissue**: infiltration by neutrophils and focal necrosis and subsequent development of fibrosis.

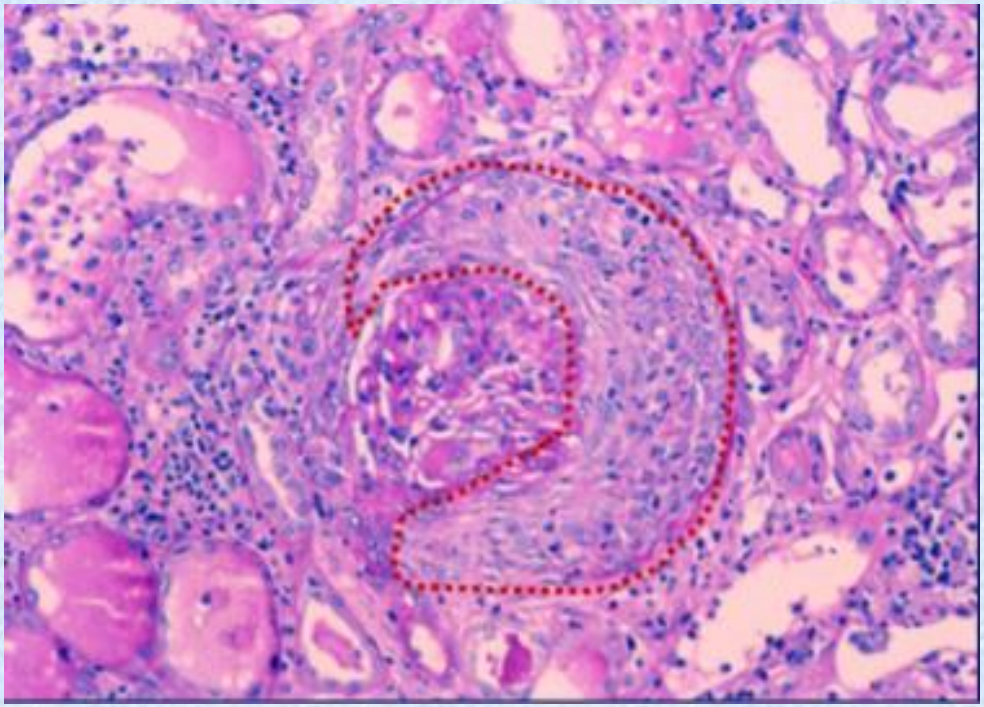
Pathology of urinary tract diseases

Rapidly progressive (crescentic) GN

Grossly: The kidneys are slightly enlarged & pale due to edema

MP:





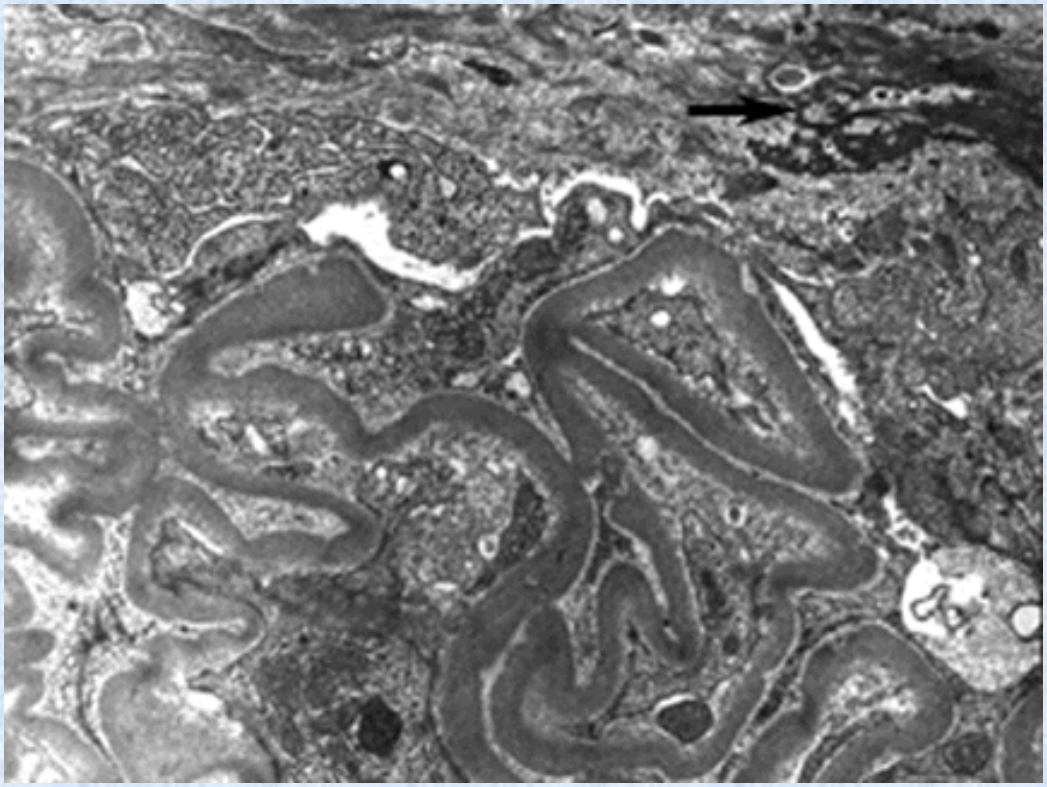
Pathology of urinary tract diseases

Rapidly progressive (crescentic) GN

Grossly: The kidneys are slightly enlarged & pale due to edema

MP:

- **EM:** linear deposition of immune complex
- **Immunofluorescence:** demonstrate IgG and complement elements



Pathology of urinary tract diseases

Rapidly progressive (crescentic) GN

Clinical presentation and fate:

- Sever form of nephritic syndrome
- Acute renal failure
- Chronic cases progress to chronic GN

Pathology of urinary tract diseases

Immunoglobulin A nephropathy

General features

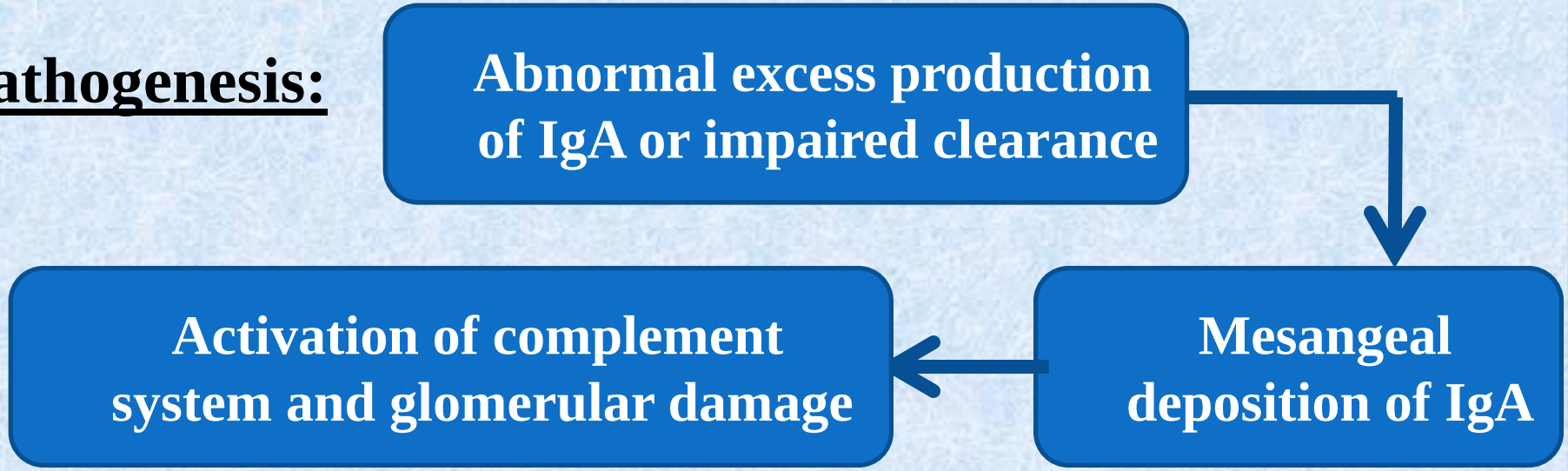
-Affect children and young adults (10-30 years)

-Occurs within 1-2 days after non specific respiratory infections

-The commonest cause of recurrent microscopic or gross hematuria

-Hematuria usually lasts several days then subsides and recurs again

Pathogenesis:



Pathology of urinary tract diseases

Immunoglobulin A nephropathy

MP:

-Variable histological features.

-The glomeruli may appear normal (no change under light microscope).

-May show mesangial proliferation and hyper-cellularity

-May showed crescentic GN features.

EM: Mesangial deposition of immune complex

Immunofluorescence: demonstrate IgA and complement elements in the mesangium

Fate: good prognosis compared to RPGN

Pathology of urinary tract diseases

Glomerulonephritis

Common primary causes of nephrotic syndrome

1. ***Minimal change GN***
2. ***Membranous GN***
3. ***Membranoproliferative GN***
4. ***Focal segmental GN***

Pathology of urinary tract diseases

Minimal change GN

General features

-Most common of GN in ***children***

-Exact etiology is unknown

-Immune mediated

-Characterized clinically by ***heavy proteinuria***

Grossly: Normal appearing kidney

MP: No significant changes under light microscope

EM: Fusion or effacement of foot processes (*foot process disease*)

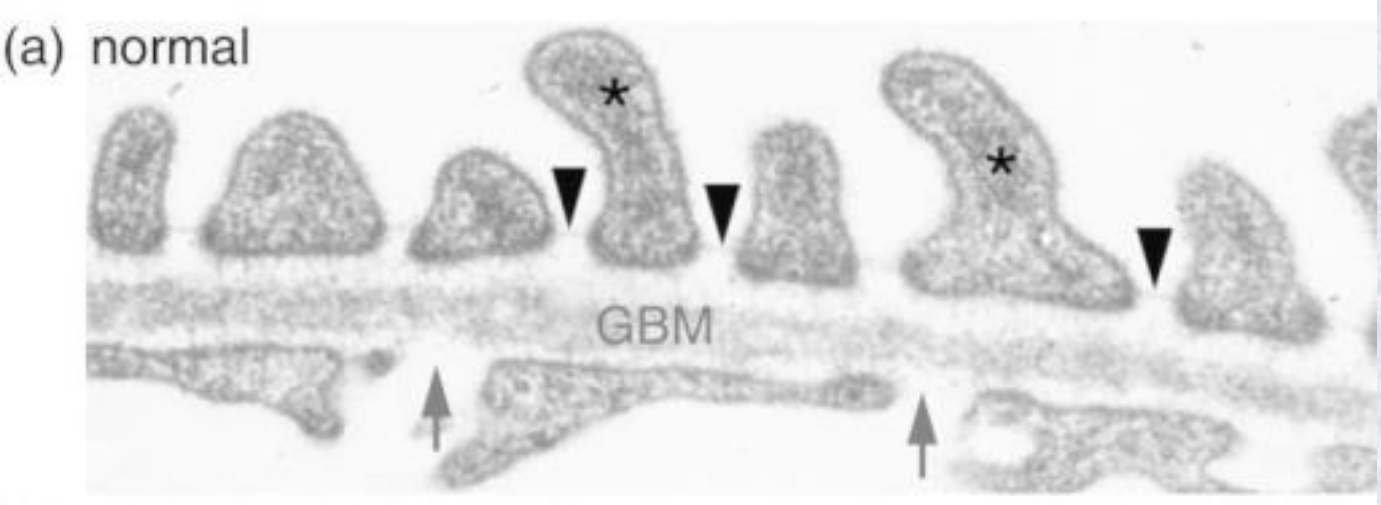
Fate: - Excellent response to steroid particularly in children

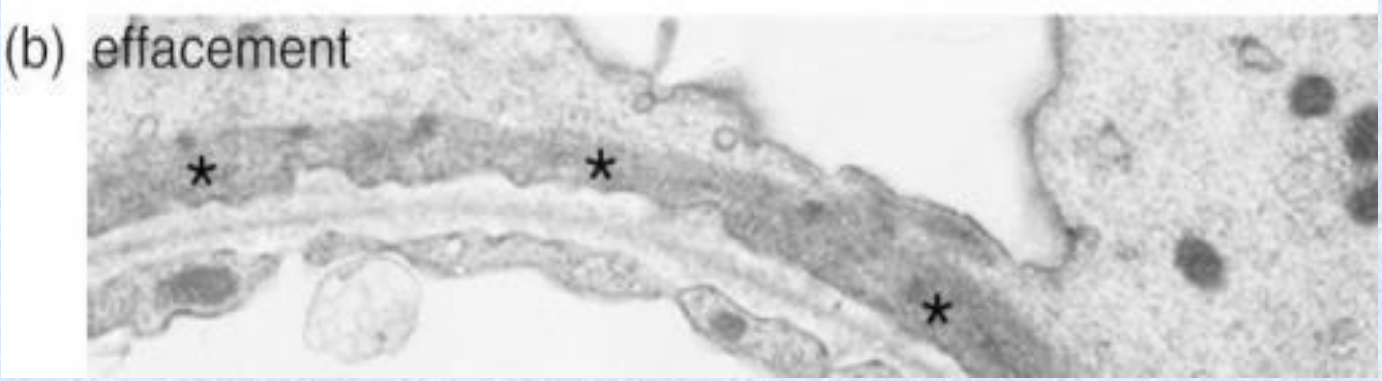
- Rarely, the disease may progress to chronic renal failure

Pathology of urinary tract diseases

Minimal change GN

EM: Fusion or effacement of foot processes (*foot process disease*)





Pathology of urinary tract diseases

Membranous GN

General features

-A slowly progressive pattern of GN.

-More commonly in adults but may involve children

Etiology/pathogenesis:

-***Primary:*** Ag implantation on glomerular BM → Ag/Ab reaction and sub-epithelial formation of immune complex with complement activation.

-***Secondary*** in other diseases: SLE, viral hepatitis, malaria, tumors, diabetes and secondary to some drugs as NSAI

Clinically: usually presents with nephrotic syndrome

Pathology of urinary tract diseases

Membranous GN

Grossly: NO significant changes

MP: Diffuse thickening of glomerular BM

EM: Sub-epithelial deposition of dense immune complexes

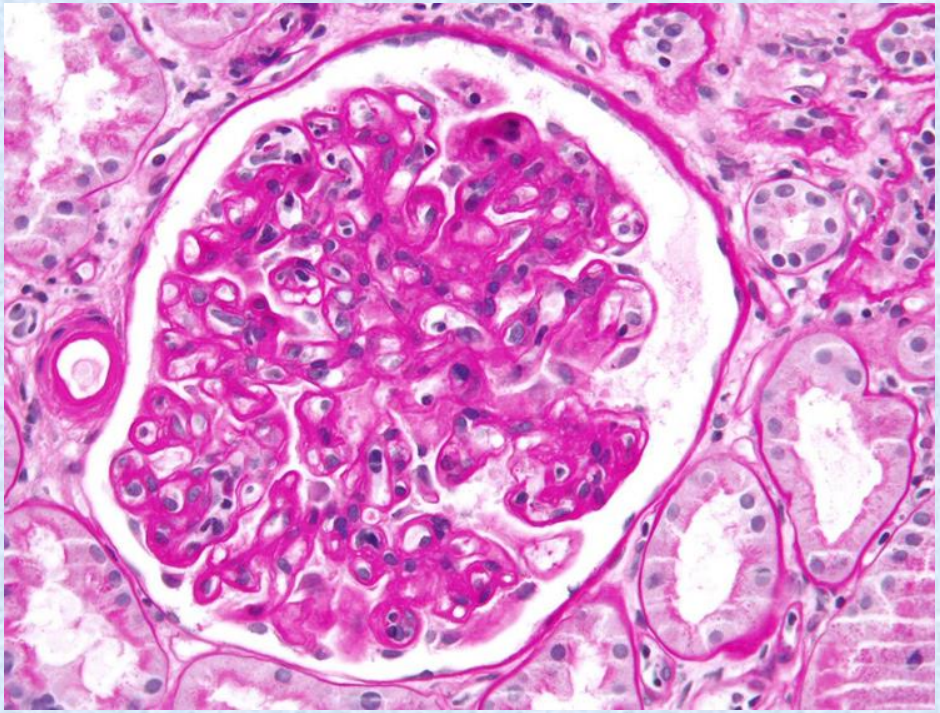
Immunofluorescence: Deposition of IgG immune complexes and complement components along glomerular BM

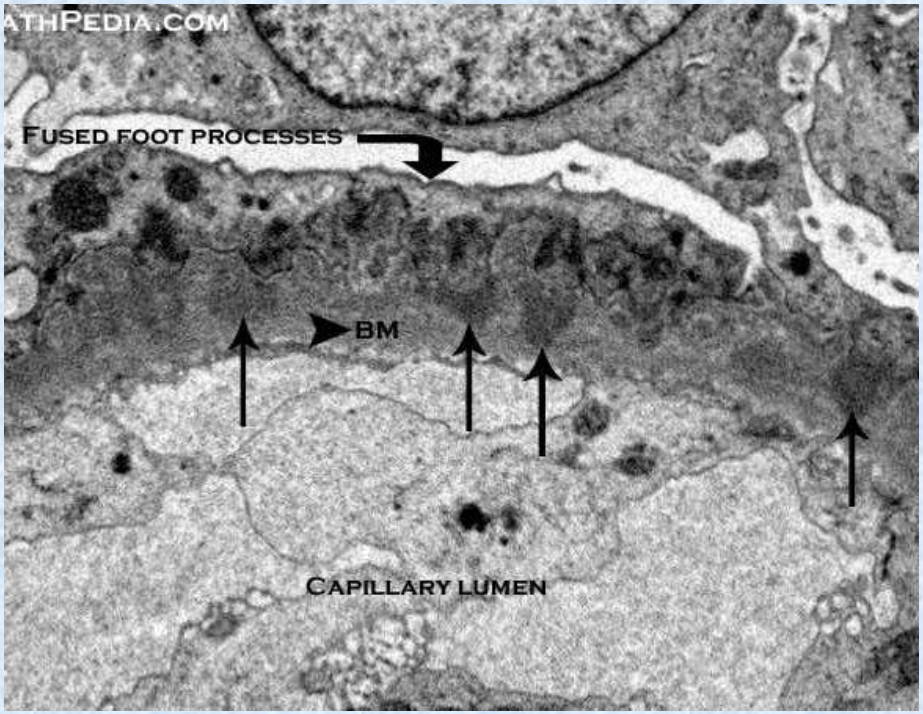
Fate:

- Usually does not respond to steroid particularly.
- 50% of cases progress to chronic renal failure within 2-20 years

Pathology of urinary tract diseases

Membranous GN





Pathology of urinary tract diseases

Membrano-proliferative GN

General features

-A slowly progressive form of GN.

-May occur in adults or children

Etiology/pathogenesis: **Two types**

- ***Type I MPGN (***secondary***):***

  The antigen is unknown and is commonly associated with HBV, SLE, and post-infection antigen

-***Type II MPGN (***dense deposits disease***):***

  due to excessive activation of C3 and its deposition in glomerular BM

Pathology of urinary tract diseases

Membrano-proliferative GN

Clinically:

- Most cases present with nephrotic syndrome.
- Few cases present as a symptomatic proteinuria
- Few cases may present as nephritic syndrome

Grossly: NO significant changes

MP:

-Glomeruli are slightly enlarged

-Glomerular hypercellularity due to proliferated mesangial cells

-Thick glomerular BM with splitting (double contour or tram-track appearance)

Pathology of urinary tract diseases

Membrano-proliferative GN

EM:

-Type I: sub-endothelial deposition of dense immune complexes.
-Type II: Dense deposits within the glomerular BM

Immunofluorescence:

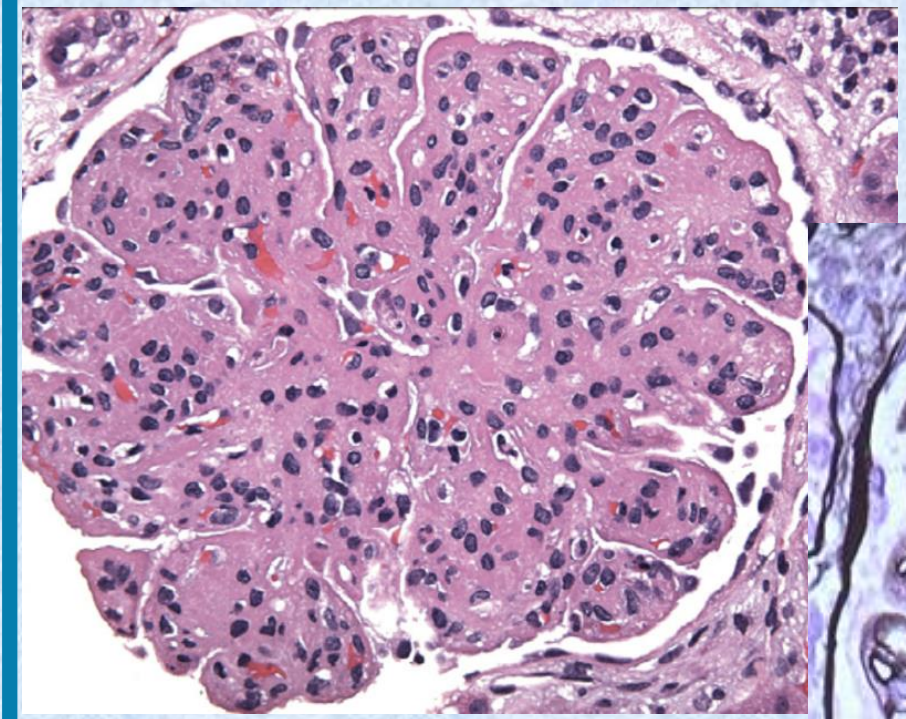
-Type I: sub-endothelial deposition of IgG complexes and C3
-Type II: Granular deposits of C3 deposits within glomerular BM

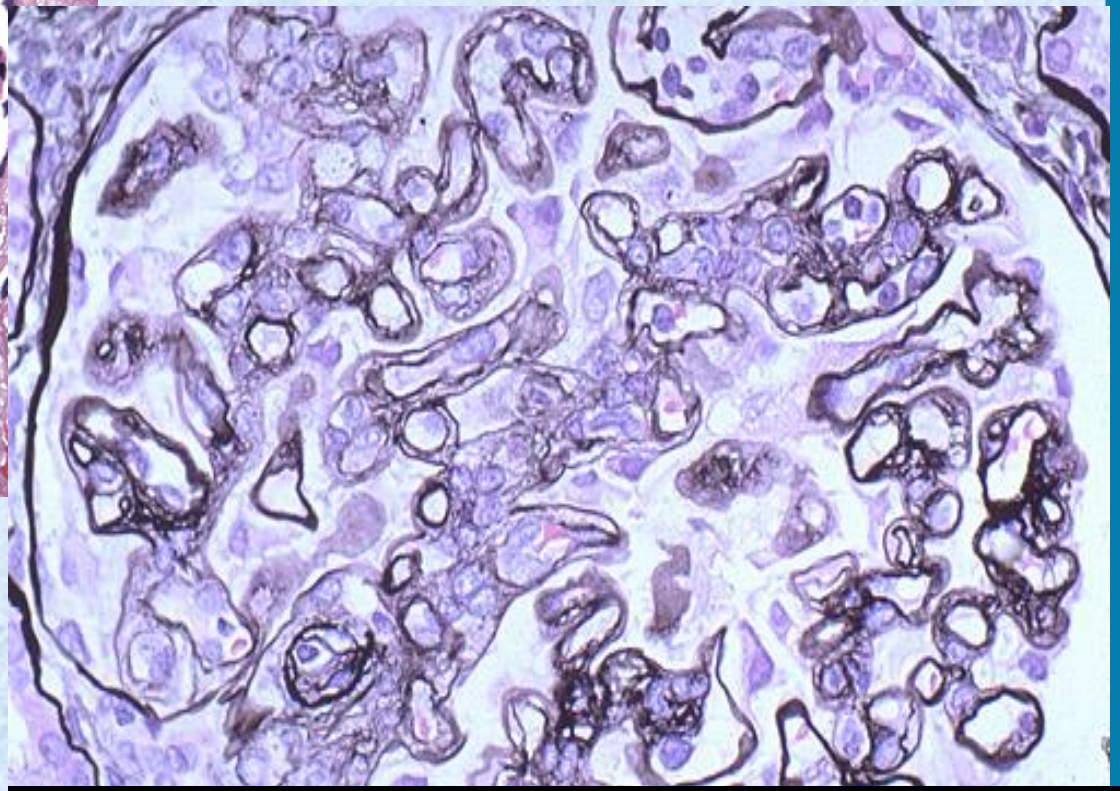
Fate:

- Usually poor prognosis; as 40% of the disease may progress to chronic renal failure with +/- 10 years

Pathology of urinary tract diseases

Membrano-proliferative GN





Double contour of BM (tram-track)

Pathology of urinary tract diseases

Common secondary forms of GN

Include:

1. **SLE nephropathy**
2. **Diabetic glomerulosclerosis**
3. **Renal amyloidosis**

Pathology of urinary tract diseases

Common secondary forms of GN

1- SLE nephropathy

General features

-Renal involvement is common in SLE.

-SLE induces heterogeneous clinical presentation and different glomerular lesions

Pathogenesis:

-Glomerular deposition of immune complexes that stimulate proliferation of endothelial, epithelial and mesangial cells.

Clinically:

-Commonly nephrotic syndrome

-Microscopic proteinuria

-May present with nephritic syndrome

-Chronic renal failure.

Pathology of urinary tract diseases

Common secondary forms of GN

1- SLE nephropathy

MP:

-Expanded hyper-cellular glomeruli.

-Features vary according to site of immune complex deposits

EM:

-Sub-endothelial, mesangial or sub-epithelial deposits of immune complexes

Immunofluorescence:

Deposition of several immunoglobulins and all types of complement components

Pathology of urinary tract diseases

Common secondary forms of GN

1- SLE nephropathy

Classification of lupus nephritis

ISN/RPS::Classification of Lupus Nephritis International society of nephropathy/renal pathology society	
Class I	Minimal mesangial LN
Class II	Mesangial proliferative LN
Class III	Focal LN* (<50% of glomeruli)
Class IV	Diffuse LN* (≥50% of glomeruli)
Class V	Membranous LN
Class VI	Advanced sclerosing LN (≥90% globally sclerosed glomeruli without residual activity)

Pathology of urinary tract diseases

Common secondary forms of GN

2. Diabetic glomerulosclerosis

General features

-DM is a major cause of renal glomerular injury

-It can lead to:

1. Diabetic glomerulosclerosis
2. Renal arterial sclerosis
3. Chronic repeated pyelonephritis
4. Renal papillary necrosis

Diabetic glomerulosclerosis could be:

-***Diffuse***: thickening of glomerular BM & mesangial proliferation

-***Nodular*** (Kimmelstiel Wilson`s disease): one or more hyaline nodule in glomerular mesangial matrix.

Pathology of urinary tract diseases

Chronic GN

General features

-Results from progressive sclerosis or scarring of renal glomeruli and ends by **renal failure**

-It is the end stage of different types of GN

Grossly

-Small sized kidneys

-Irregular shape

-Asymmetrical shape

-Thick adherent capsule

-Cortex could not be differentiated from medulla

MP:

-Scleroses of the glomeruli

-Interstitial tissue inflammation

-Atrophy of renal tubules.

-Thick renal arterioles

Pathology of urinary tract diseases

Self assessment:

Deposition of sub-epithelial humps of immune complex is commonly seen in:

a. Acute post-infectious glomerulonephritis
b. Rapidly progressive glomerulonephritis
c. Membranous glomerulonephritis
d. Membrano-proliferative glomerulonephritis
e. Minimal change glomerulonephritis

Double contour or tram-track appearance of glomerular BM could be seen in:

a. Acute post-infectious glomerulonephritis
b. Rapidly progressive glomerulonephritis
c. Membranous glomerulonephritis
d. Membrano-proliferative glomerulonephritis
e. Minimal change glomerulonephritis

Pathology of urinary tract diseases

Thank you