Diseases of Urinary System

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Learning objectives

By the end of this course; you should know:

- Common diseases involving kidney and urinary bladder
- Clinical presentation of renal diseases
- Morphology of common renal diseases
- Types of glomerulonephritis and their clinical impact
- Main features of nephritic and nephrotic syndromes
- Growth disordered and **TUMOURS** of the kidney, ureter and urinary bladder.

Talks outlines

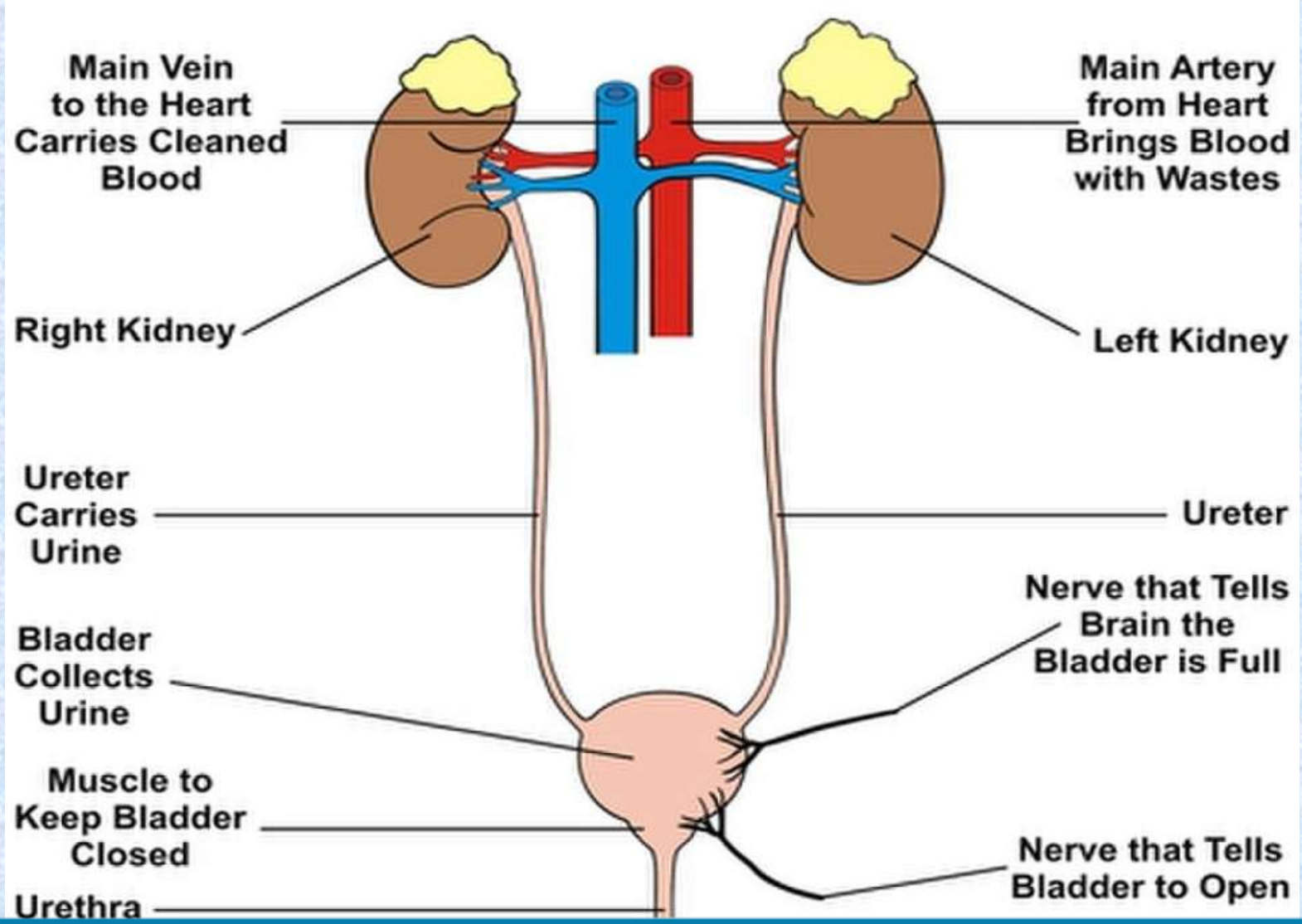
- **Diseases of the kidney:**
  - Renal anomalies
  - Golumerulonephritis
  - Tubulo-interstitial renal diseases
  - Renal stones
  - Renal tumors
  - Renal failure

- **Diseases of the ureter and urinary bladder**
  - Inflammatory diseases
  - Neoplastic lesions

Renal Diseases

Renal diseases

Urinary system



Renal diseases

Renal function

WATER. Ensures that there's not too much or too little water in the body.

BLOOD PRESSURE. Makes sure that pressure isn't too high or too low.

WASTES. Gets rid of urea, uric acid, toxins, and other wastes via urine.

BONES. Activates vitamin D, which helps the body absorb calcium.

ACID-BASE BALANCE. Makes sure that the body isn't too acidic or too alkaline.

HEART. Maintains a balance of electrolytes (like potassium, sodium, and calcium), which is critical for heart rhythm.

BLOOD. Releases erythropoietin, which tells bone marrow to make red blood cells.

Renal diseases

Manifestations of renal diseases

Renal colic

Chronic loin pain

Hematuria

Pyuria

Renal mass

and others

Microscopic proteinuria

Microscopic hematuria

Generalized edema

Hypertension

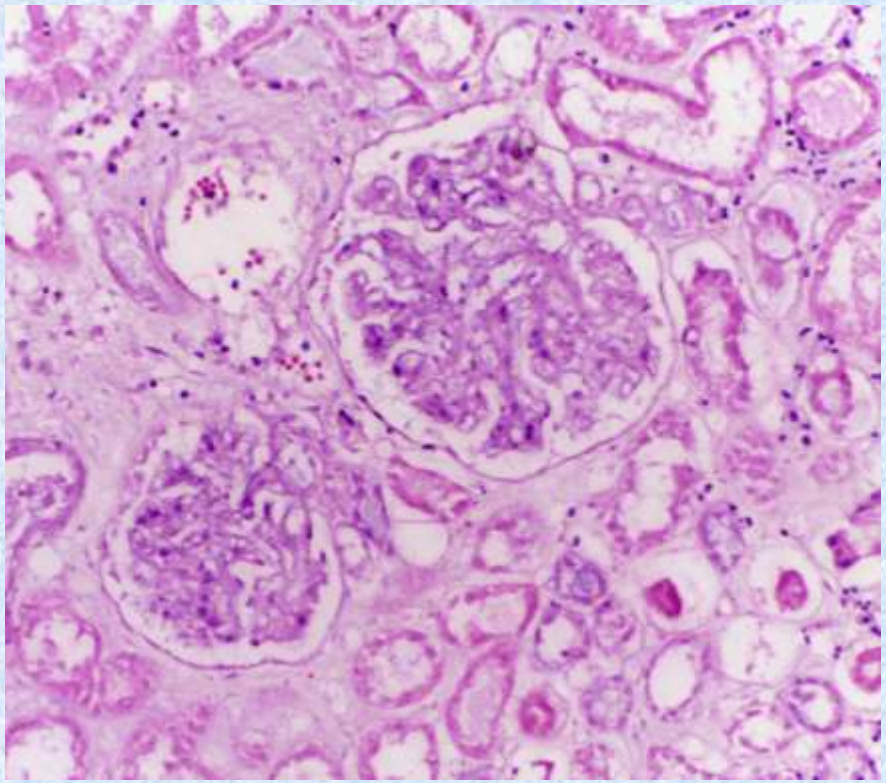
Anemia

Renal diseases

Main histological components of kidney

Diseases of kidney may involve:

- Renal glomeruli
- Renal tubules
- Renal interstitium
- Renal vessels



In chronic conditions; the four elements are involved

Renal diseases

Congenital kidney diseases

Renal diseases

Congenital kidney diseases

1. Unilateral agenesis
2. Hypoplasia
3. Horseshoe kidney
4. Ectopic kidney
5. Double ureter
6. Ureteric stricture
7. Aberrant renal artery
8. Polycystic kidney

Renal diseases

Congenital kidney diseases

Polycystic kidney

Infantile type

- A rare disease
- Autosomal recessive
- Incompatible with life
- Numerous cortical and medullary cysts
- Congenital hepatic cysts and fibrosis

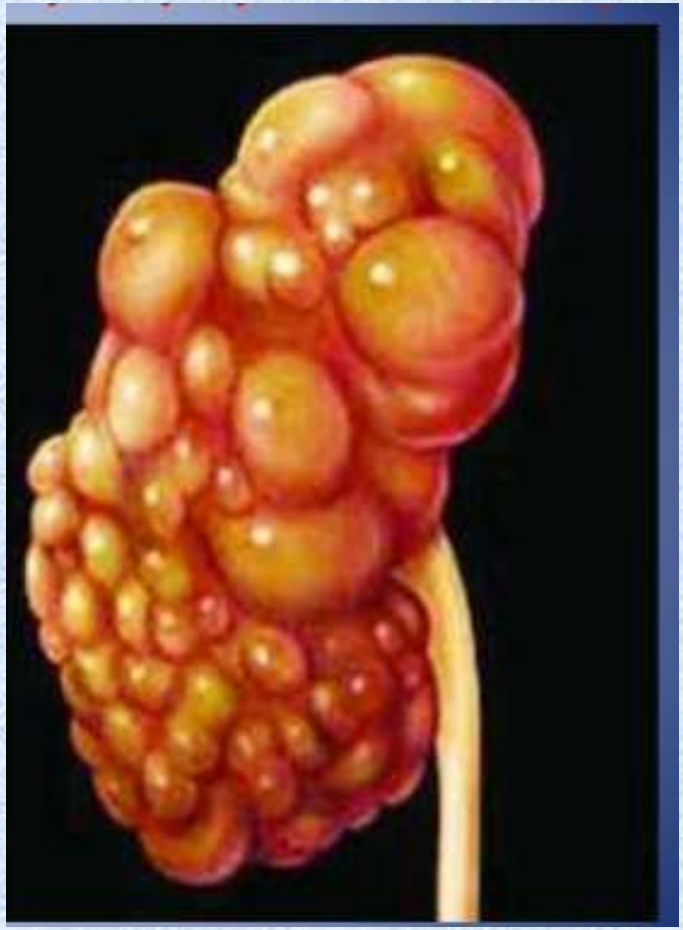
Adult type

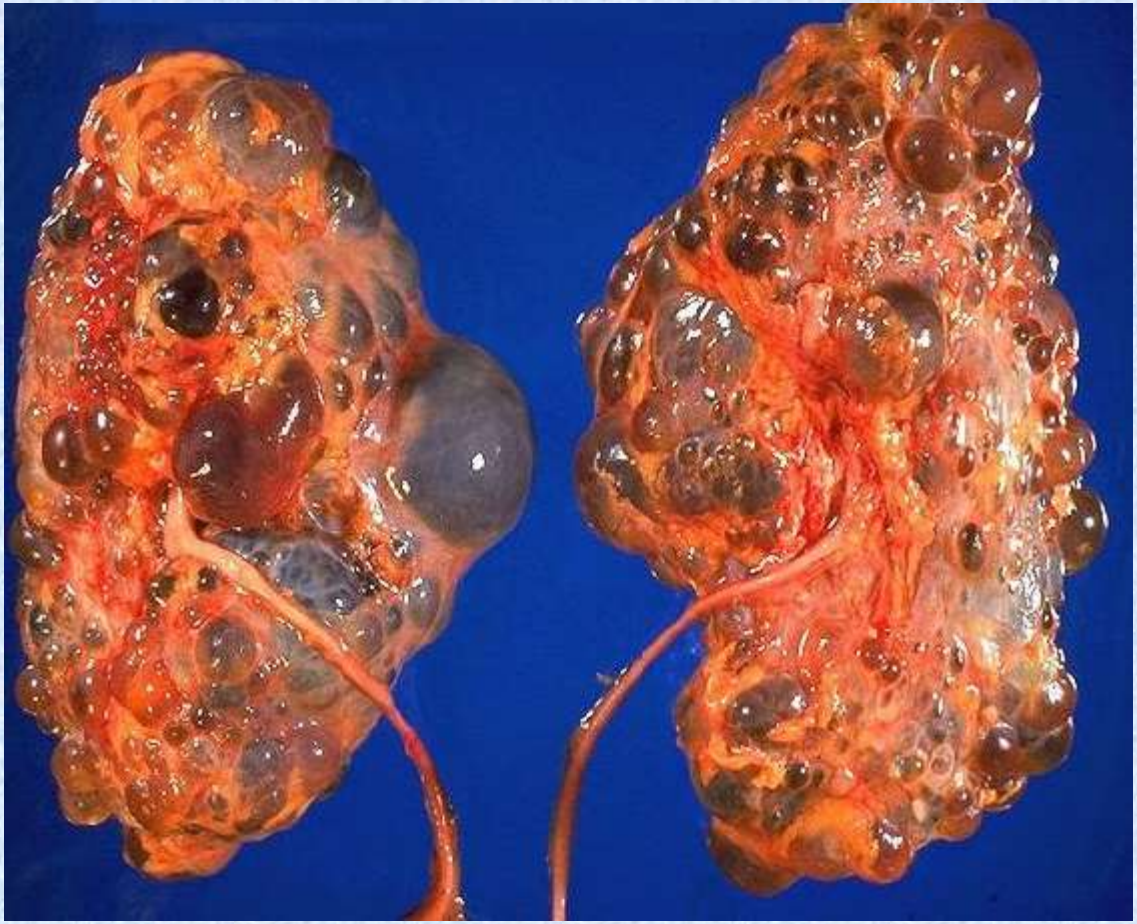
- Autosomal dominant.
- Failure of communication of convoluted/collecting ducts
- Numerous large cysts with smooth lining
- Interstitial compression/fibrosis
- May present with:
  - Renal mass
  - Hematuria
  - Hypertension
  - Seconder infection

Renal diseases

Congenital kidney diseases

Polycystic kidney



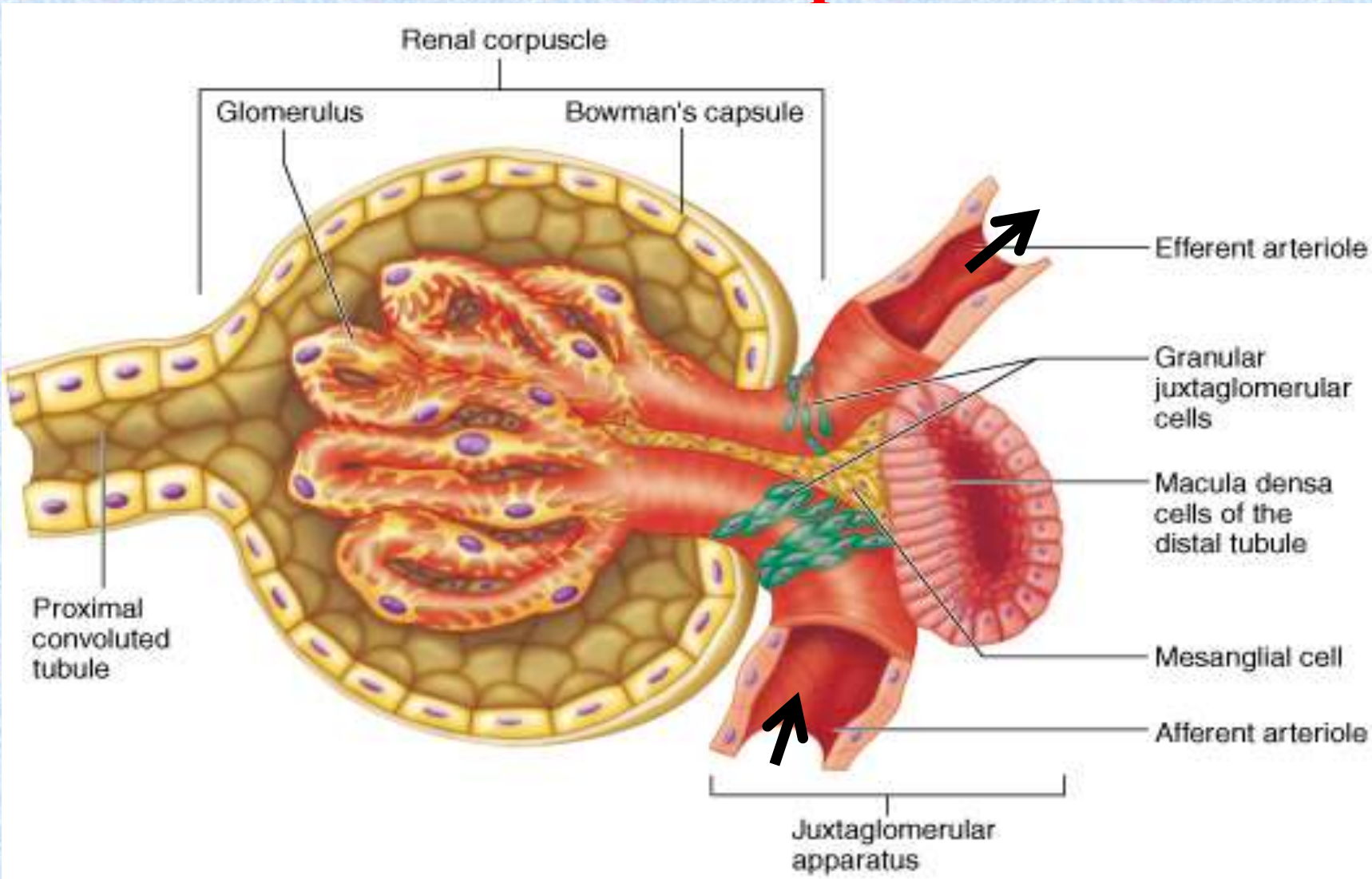


Renal diseases

Glomerulonephritis

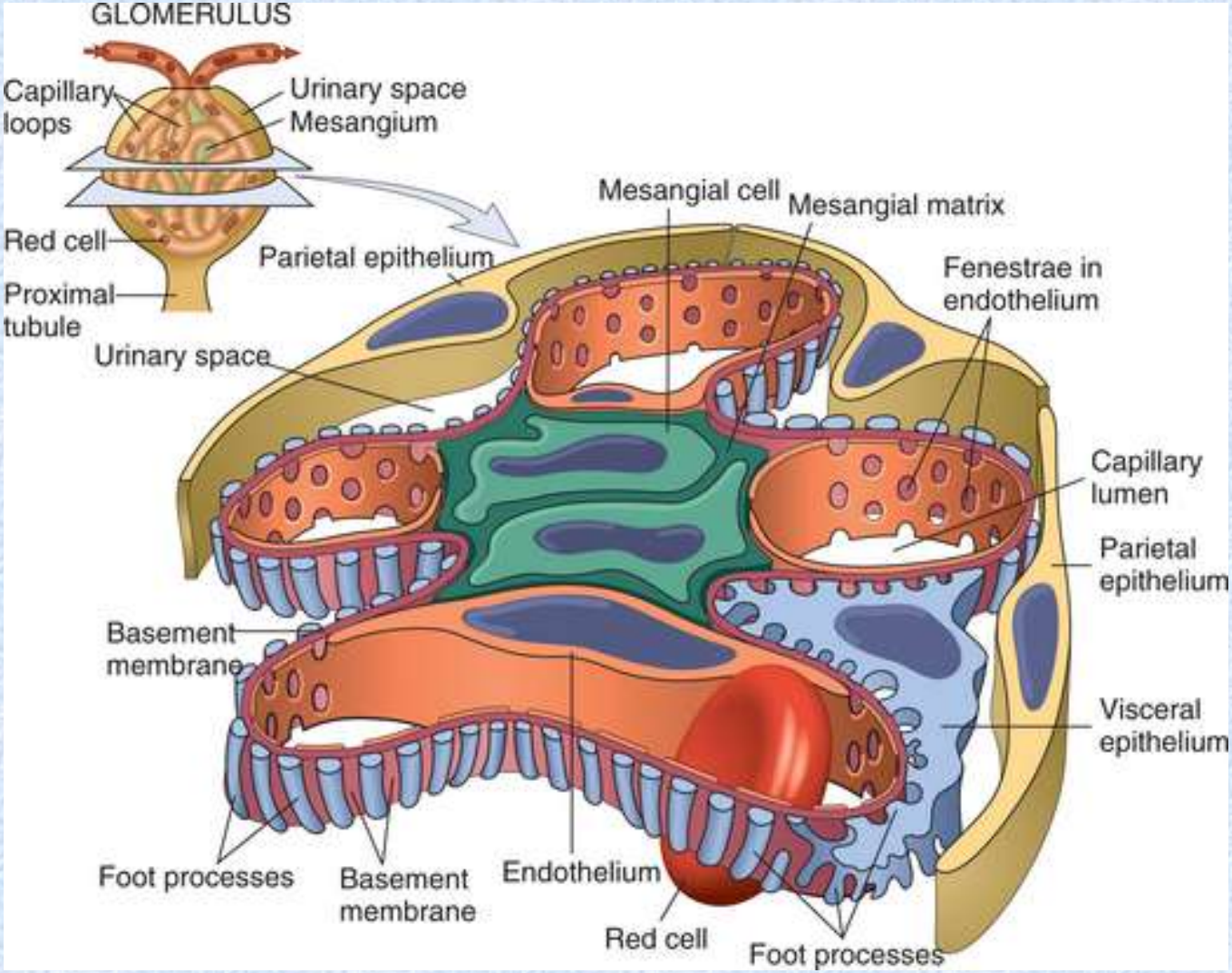
Renal diseases

Glomerulonephritis



Renal diseases

Glomerulonephritis



Renal diseases

Glomerulonephritis

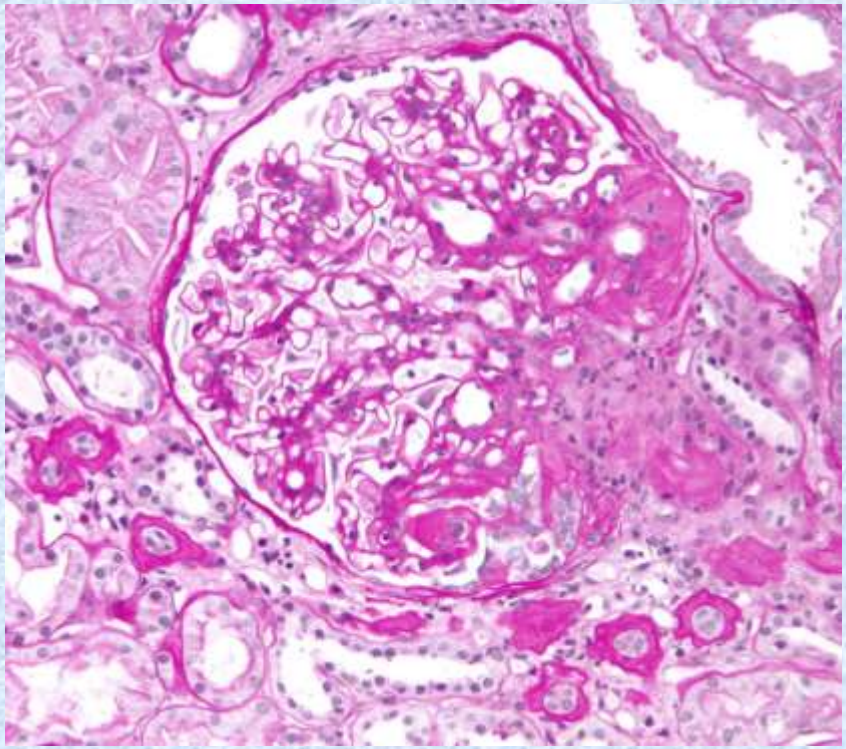
Pattern of glomerular involvement:

- **<u>Diffuse</u>**: All glomeruli are involved by the disease process. It could be:
  - *Global*: involve all glomerular tuft
  - *Segmental*: involve segment of the tuft

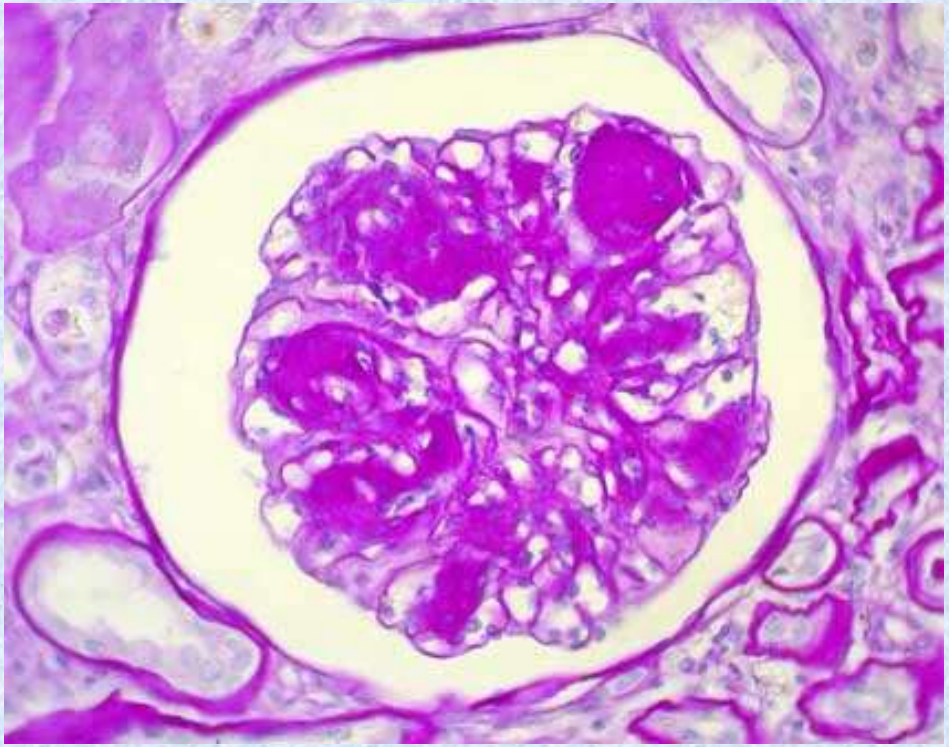
- **<u>Focal</u>**: Some glomeruli are involved by the diseases and others are normal; it could be
  - *Global*: involve all glomerular tufts
  - *Segmental*: involve segment of the tuft

Renal diseases

Glomerulonephritis



Segmental



Global

Renal diseases

Glomerulonephritis

Pathogenesis of GN: *usually immune complex mediated*

1. Deposition of circulating immune complexes in glomerular BM: occurs in SLE, post bacterial or post viral infections
2. In situ formation of immune complexes: antibody react with antigen fixed to the glomerular BM: occurs in post-bacterial GN
3. Anti-glomerular basement membrane antibody: formation of antibodies against structure of glomerular BM; occurs in Good pasture syndrome

The immune complex induces injury of glomerular BM by activation of complement system with release of chemical mediators

Renal diseases

Glomerulonephritis

Main clinical patterns of GN:

Nephritic syndrome

- **Def:** A clinical complex usually with acute onset.
- **Characterized by:**
  1. Hematuria
  2. Oliguria
  3. Hypertension
  4. Nephritic edema

Nephrotic syndrome

- **Def:** A clinical complex usually with insidious onset.
- **Characterized by:**
  1. Heavy proteinuria
  2. Hypoproteinemia
  3. Hyperlipidemia
  4. Nephrotic edema

Renal diseases

Glomerulonephritis

Main clinical patterns of GN:

Nephritic syndrome

- **Def:** A clinical complex usually with acute onset.
- **Characterized by:**
  4. **Nephritic edema**: mild morning starts around the eyes and resolve along the day

Nephrotic syndrome

- **Def:** A clinical complex usually with insidious onset.
- **Characterized by:**
  4. **Nephrotic edema**: prominent, generalized edema starts at the lower limbs and progress gradually

Renal 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

Renal diseases

Glomerulonephritis

Common primary causes of nephritic syndrome

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

Renal diseases

Acute post-infectious GN

Incidence: Usually affects children and young adults

Pathogenesis:

(1) glomerular trapping of circulating immune complexes and

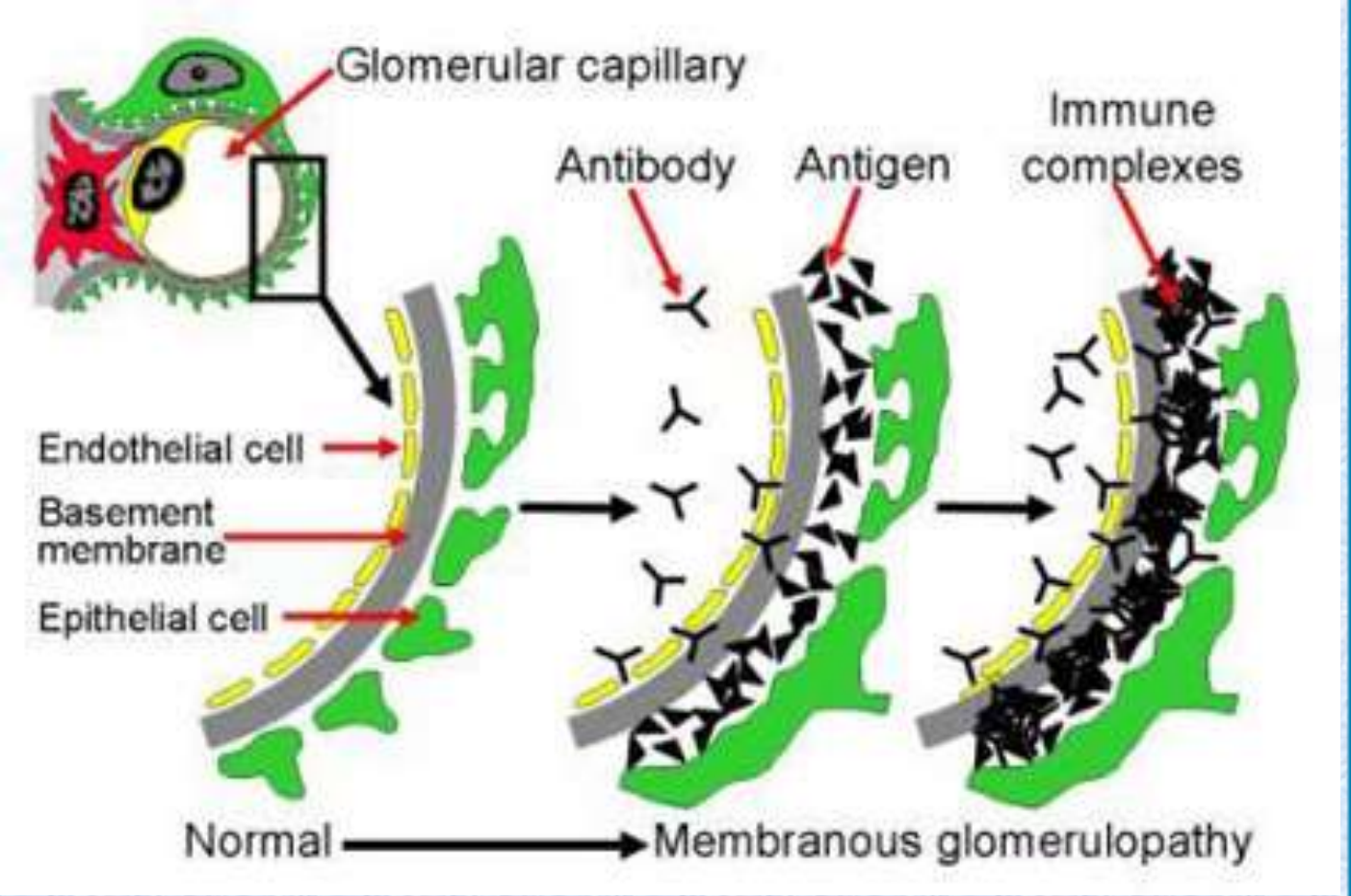
- (2) in situ immune antigen-antibody complex formation resulting from antibodies reacting with either streptococcal components deposited in the glomerulus

Renal diseases

Acute post-infectious GN

Incidence: Usually affects children and young adults

Pathogenesis:

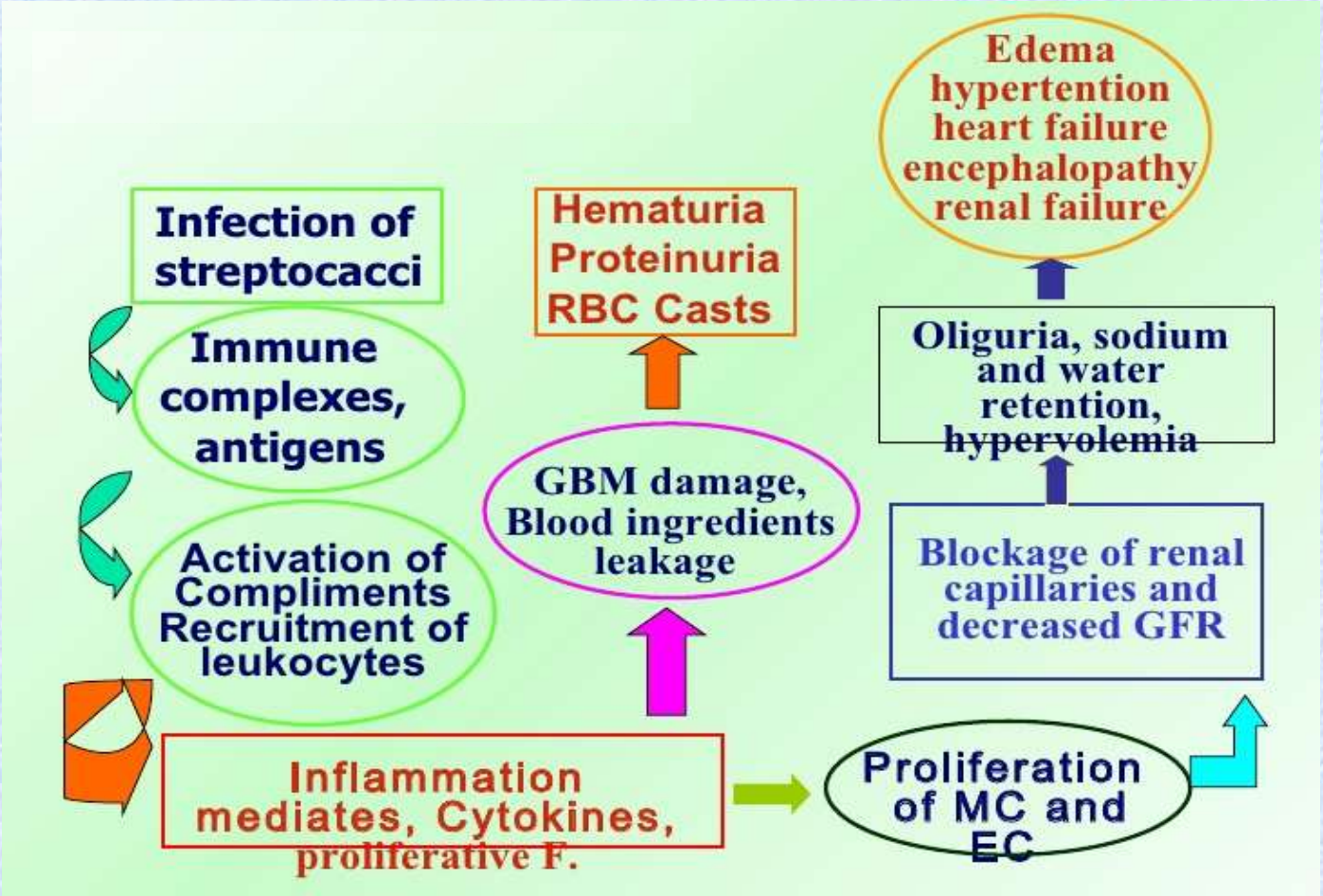


Renal diseases

Acute post-infectious GN

Incidence: Usually affects children and young adults

Pathogenesis:



Renal diseases

Acute post-infectious GN

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

MP:

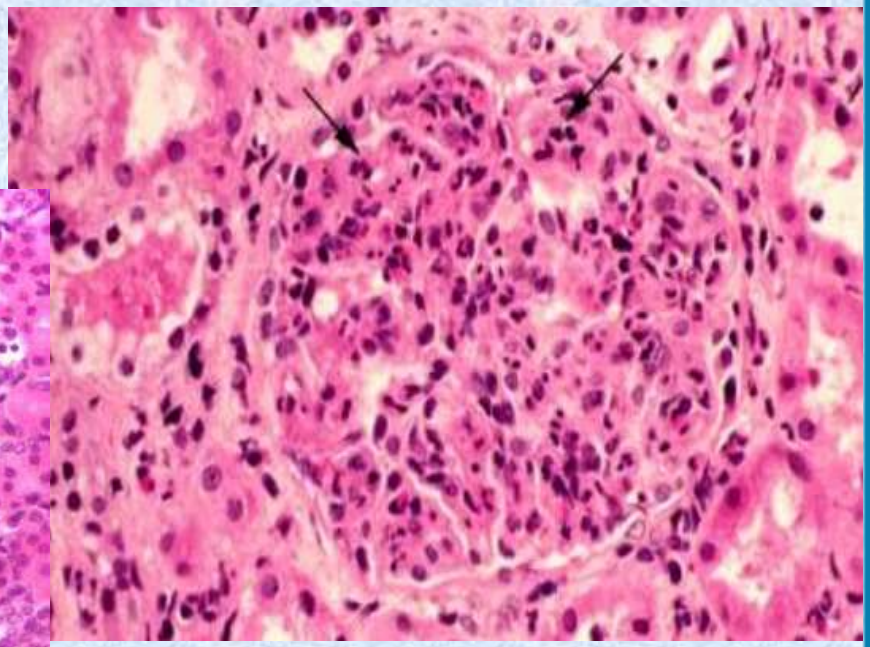
- **Glomeruli**: hyper-cellular due to proliferation of epithelial, endothelial and mesangial cells and infiltration by neutrophils
- **Tubules**: cloudy swelling of lining cells and RBCs cast of the lumen
- **Blood vessels**: NO significant changes
- **Interstitial tissue**: infiltration by neutrophils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

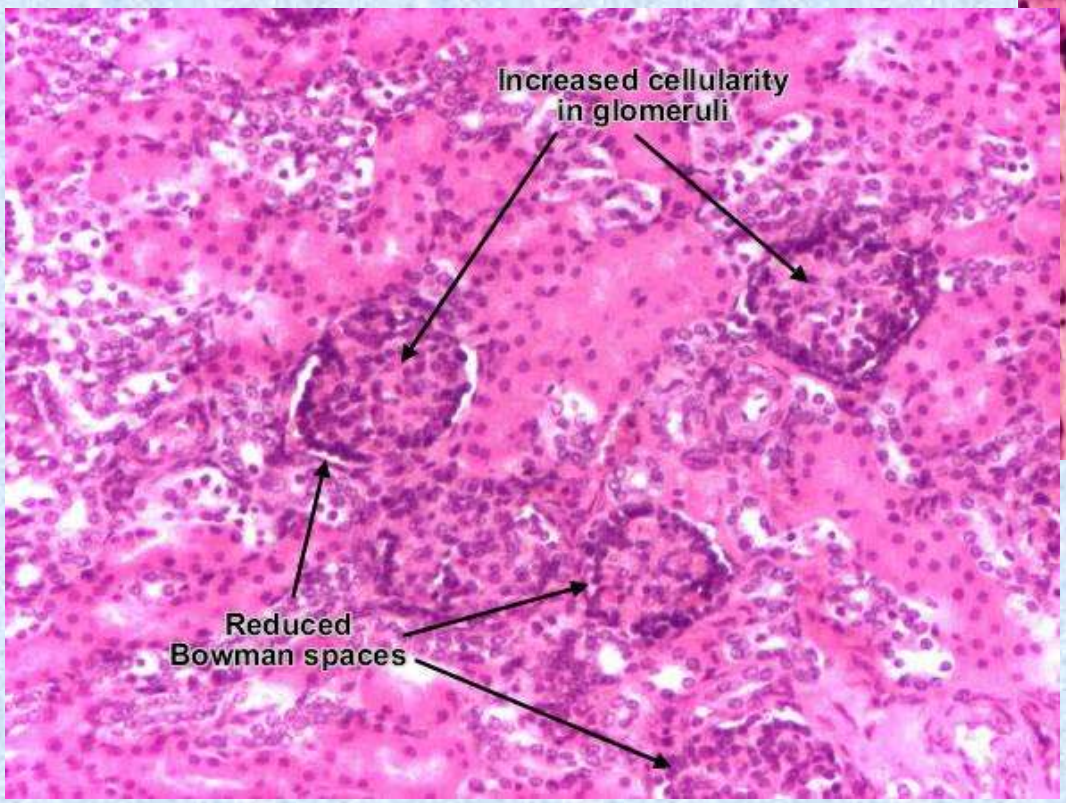
Renal diseases

Acute post-infectious GN

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

MP:



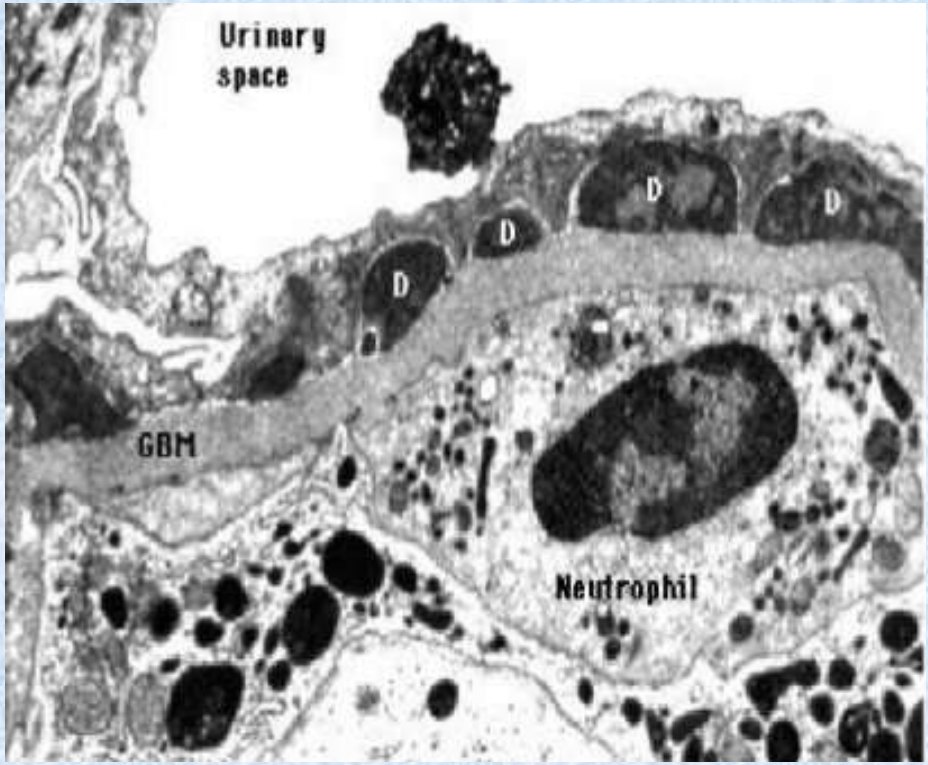


Renal diseases

Acute post-infectious GN

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

EP:



Renal 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

Renal 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

Renal 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

Renal diseases

Rapidly progressive (crescentic) GN

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

MP:

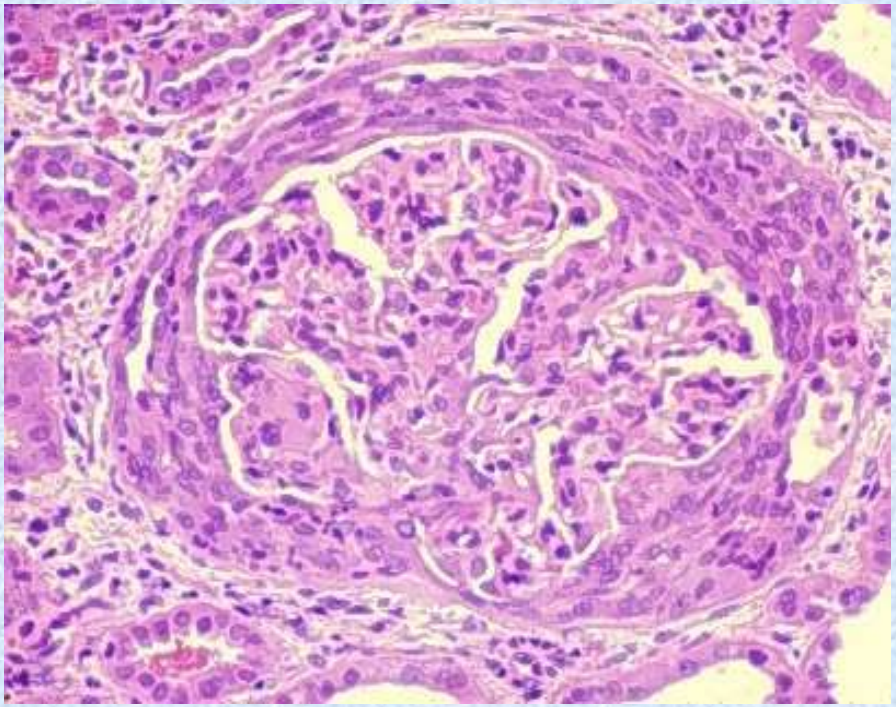
- **Glomeruli**:
  - Hyper-cellular (proliferation of epithelial, endothelial and mesangial cells and infiltration by neutrophils).
  - Crescent formation: proliferation of parietal epithelium leads to obliteration of Bowman`s space
  - Glomerular tufts: focal thrombosis and necrosis
- **Tubules**: focal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

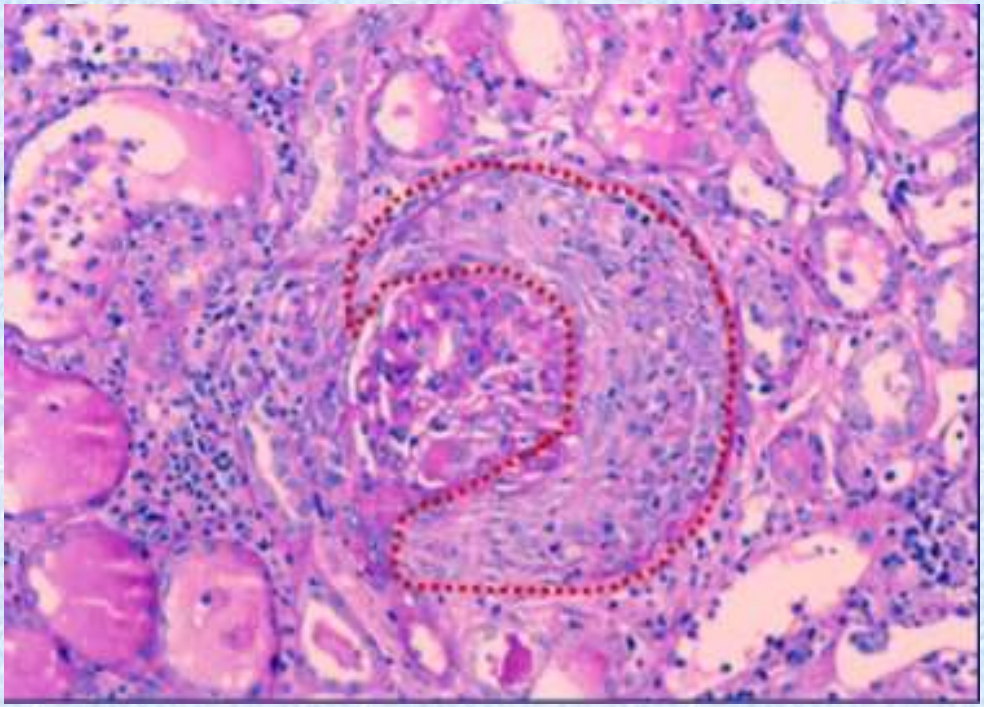
Renal diseases

Rapidly progressive (crescentic) GN

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

MP:





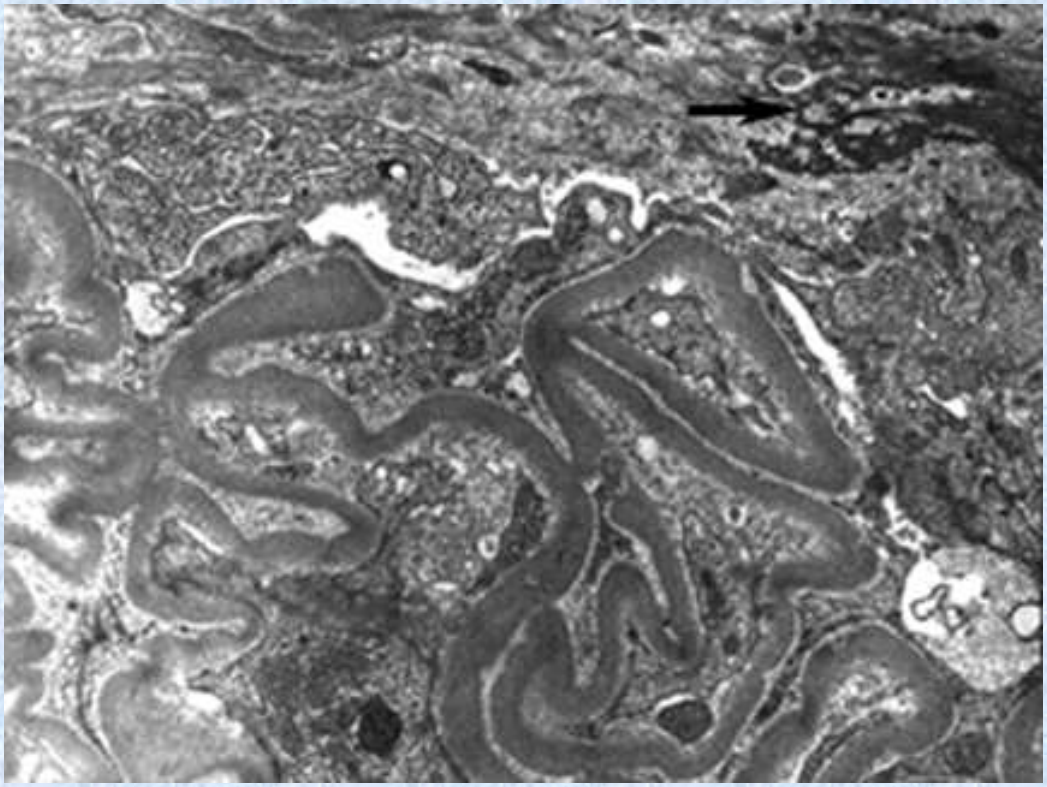
Renal diseases

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



Renal diseases

Rapidly progressive (crescentic) GN

Clinical presentation and fate:

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

Renal diseases

Immunoglobulin A nephropathy

General features

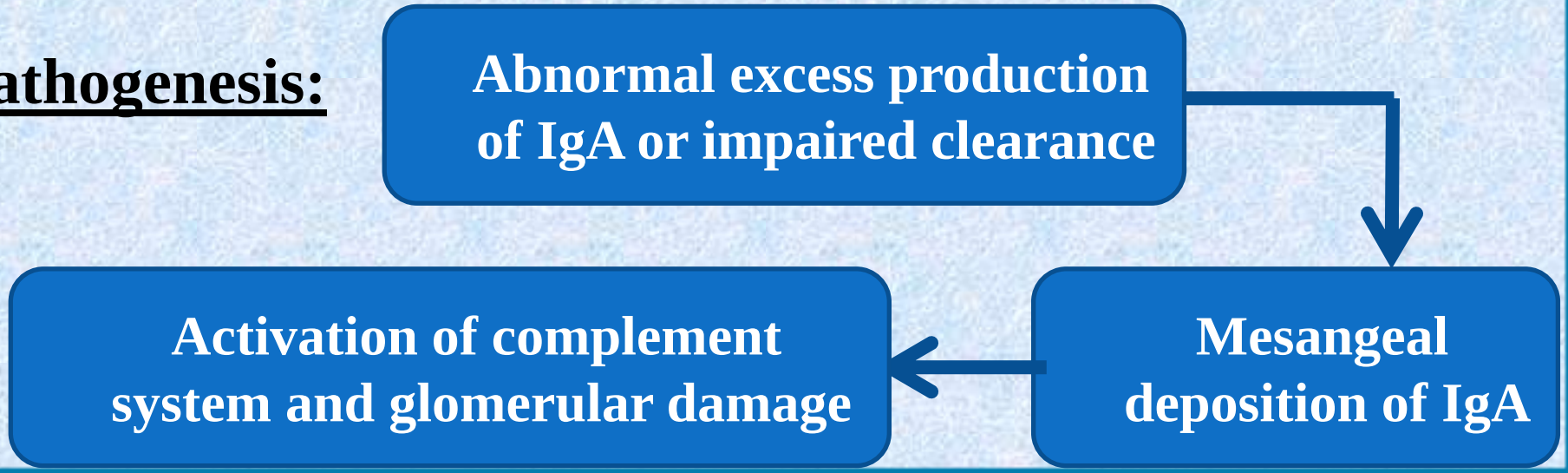
-Affect children and young adults (10-30 years)

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

-It is the most common cause of recurrent microscopic or gross hematuria

-Hematuria usually lasts several days then subside and recur again

Pathogenesis:



Renal diseases

Immunoglobulin A nephropathy

MP:

-Variable histological features.

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

-May show mesangial proliferation and hyper-cellularity

-May showed crescentic GN features.

EM: Mesangial deposition of immune complex

IF: demonstrate IgA and complement elements in the mesangium

Fate: good prognosis compared to RPGN

Renal diseases

Glomerulonephritis

Common primary causes of nephrotic syndrome

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

Renal 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*)

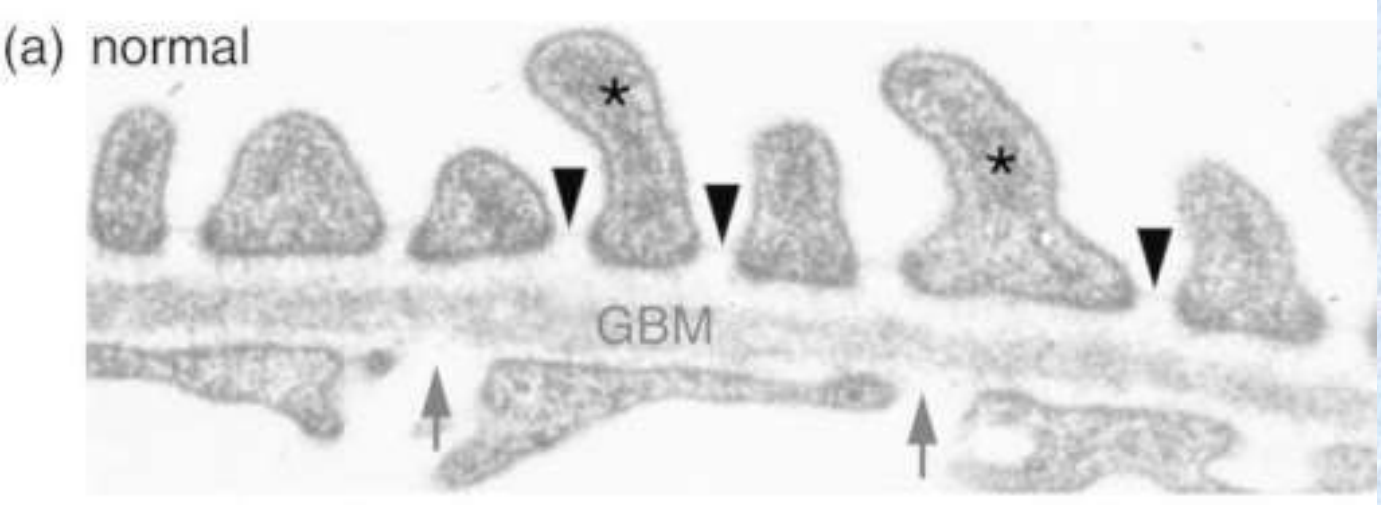
Fate: - Excellent response to steroid particularly in children

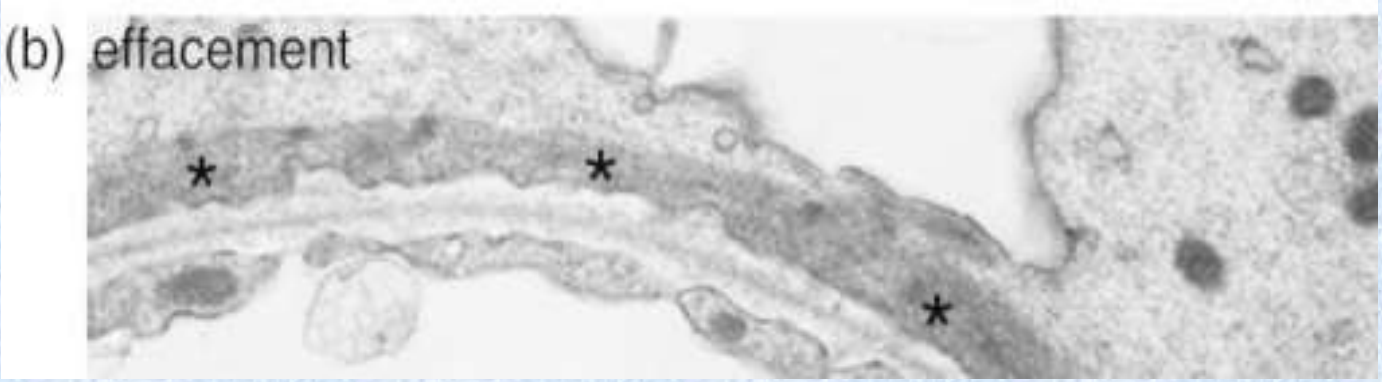
- Rarely, the disease may progress to chronic renal failure

Renal diseases

Minimal change GN

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





Renal diseases

Membranous GN

General features

-A slowly progressive form of GN.

-More commonly in adults but may involve children

Etiology/pathogenesis:

-***Primary:*** antigen implanted on glomerular BM with Ag/Ab reaction and 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

Renal diseases

Membranous GN

MP: Diffuse thickening of glomerular BM

EM: Sub-epithelial deposition of dense immune complexes

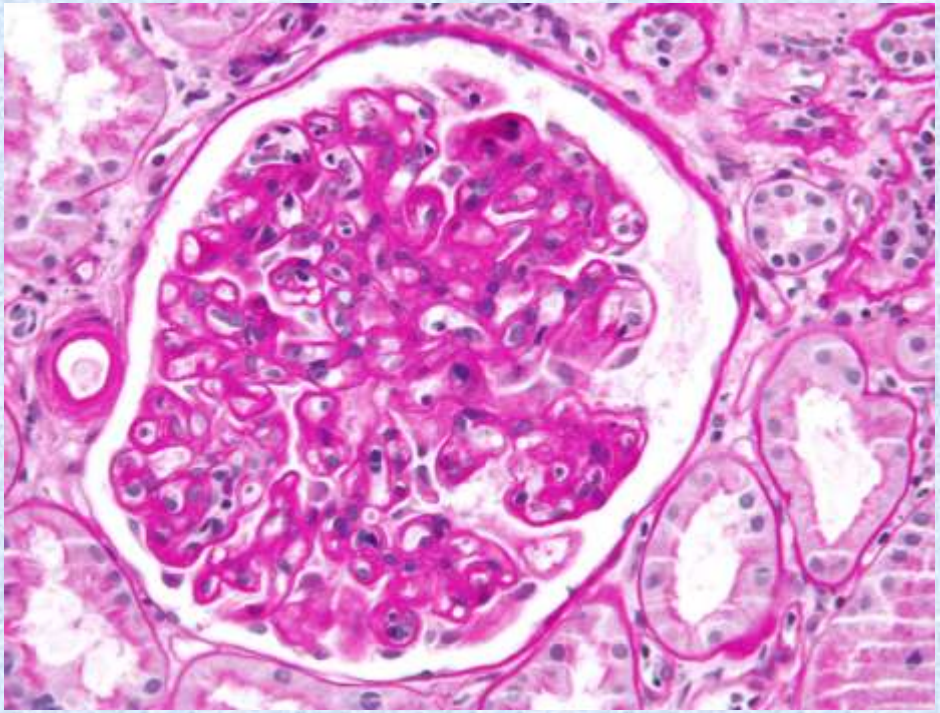
IF: Deposition of immune complexes (IgG) and complement along glomerular BM

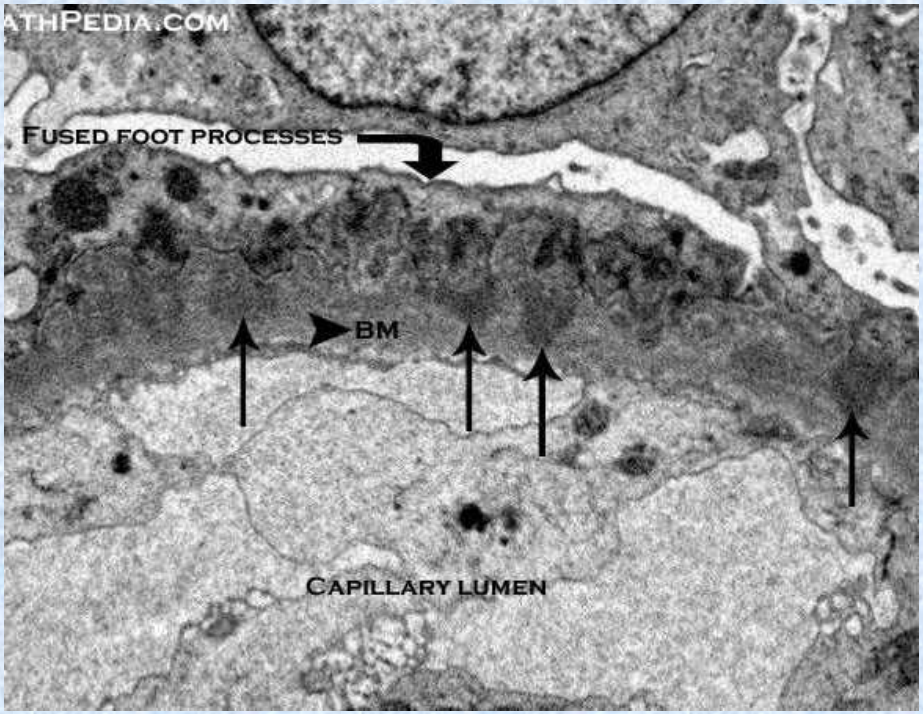
Fate:

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

Renal diseases

Membranous GN





Renal 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 with deposition in glomerular BM

Clinically:

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

Renal diseases

Membrano-proliferative GN

MP:

-Glomeruli are slightly enlarged

-Glomerular hypercellularity due to proliferated mesangial cells

-Thick GBM with splitting (double contour or tram-track)

EM:

-Type I: sub-endothelial deposition of dense immune complexes.

-Type II: Dense deposits within the GBM

IF:

-Type I: sub-endothelial deposition of IgG complexes and C3

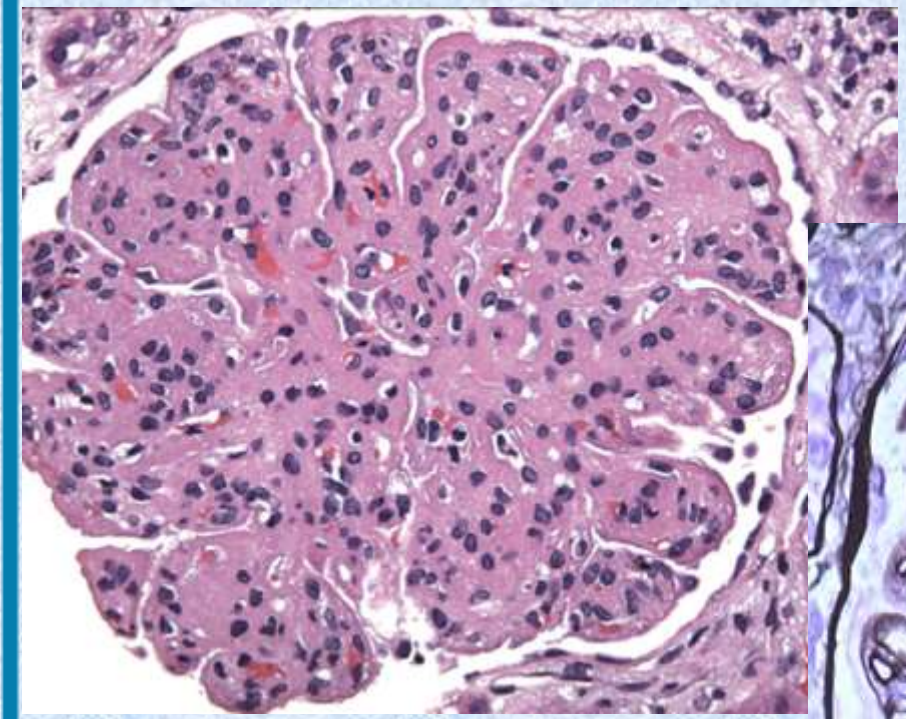
-Type II: Granular deposits of C3 deposits within GBM

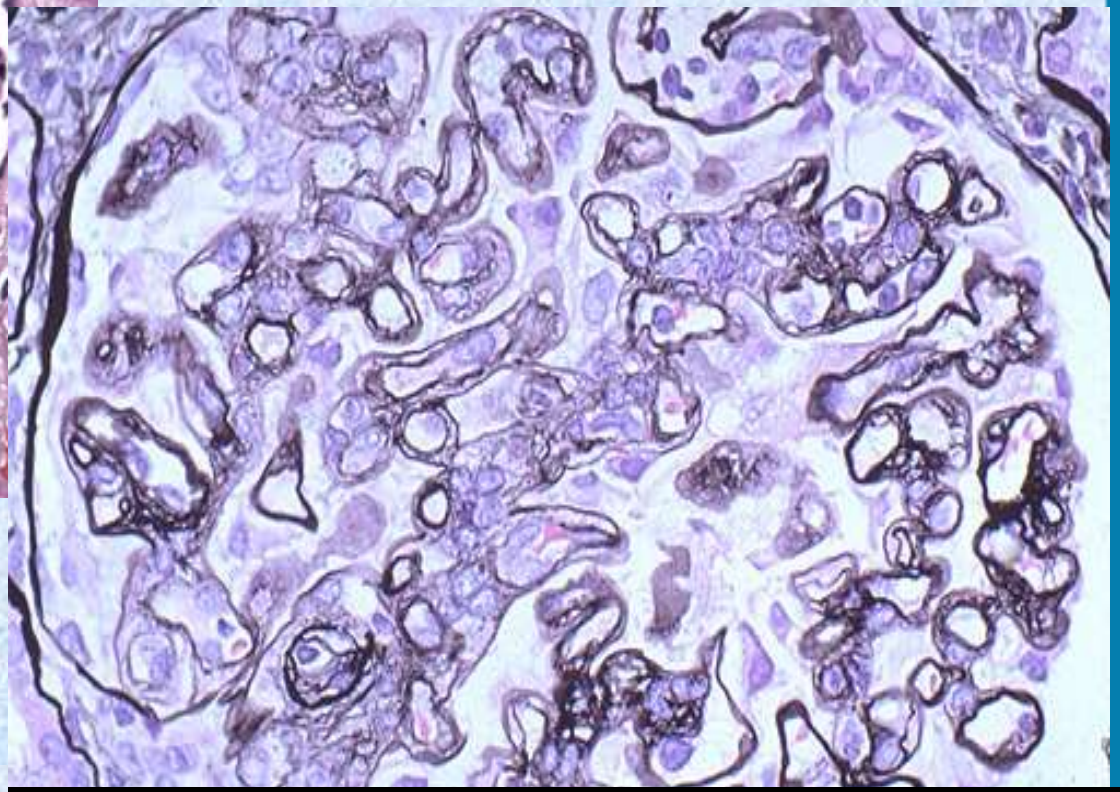
Fate:

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

Renal diseases

Membrano-proliferative GN





Double contour of BM (tram-track)

Renal diseases

Common secondary forms of GN

Include:

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

Renal 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.

Renal 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

IF: Deposition of several immunoglobulins and all types of complement components

Renal 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)

Renal 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.

Renal 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

Renal diseases

Tubulo-interstitial renal diseases

Renal diseases

Tubulo-interstitial renal diseases

Include:

- Renal tubular injury
- Pyelonephritis
- Drug induced interstitial renal diseases
- Renal vascular diseases including hypertensive nephrosclerosis (*see hypertension*)

Renal diseases

Acute tubular injury

- **Definition:**
  - Acute damage of renal tubules
  - Usually associated with high serum creatinine and acute renal failure
- **Etiology:**
  1. Toxic: caused by poisons, phosphorus, tetrachloride, drugs as ampicillin, thiazides, and NSAI.
  2. Anoxic (ischemic): caused by crush injuries, mismatched blood transfusion, severe burn and shock
- **Microscopically**: necrosis of tubular epithelium, RBCs and hyaline casts in tubular lumen, interstitial tissue edema
- **Clinically**: hypertension, oliguria and raised serum creatinine

Renal diseases

Pyelonephritis

- **Definition:**

  Inflammation of renal interstitial tissue and pelvi-calyceal system

- **Etiology:**

  Predisposing factors:

  1. Females are more susceptible due to short urethra.
  2. Pregnancy: due to compression of ureters by gravid uterus
  3. Decreased immunity: DM, steroids or immuno-suppressive therapy and AIDS
  4. Urinary tract obstruction: renal calculi, tumors and stricture as in bilharziasis
  5. Urinary instrumentation
  6. Vesico-ureteric reflux

Renal diseases

Pyelonephritis

- **Etiology:**

Routs of infection:

- Ascending infection through ureters
- Hematogenous spread

Causative organism

- Commonly E coli
- Other organisms: Bacillous proteus, klebsiella, staph aureus, streptococci and others

- **Pathological features:**
  - Main two forms: **acute** and **chronic**

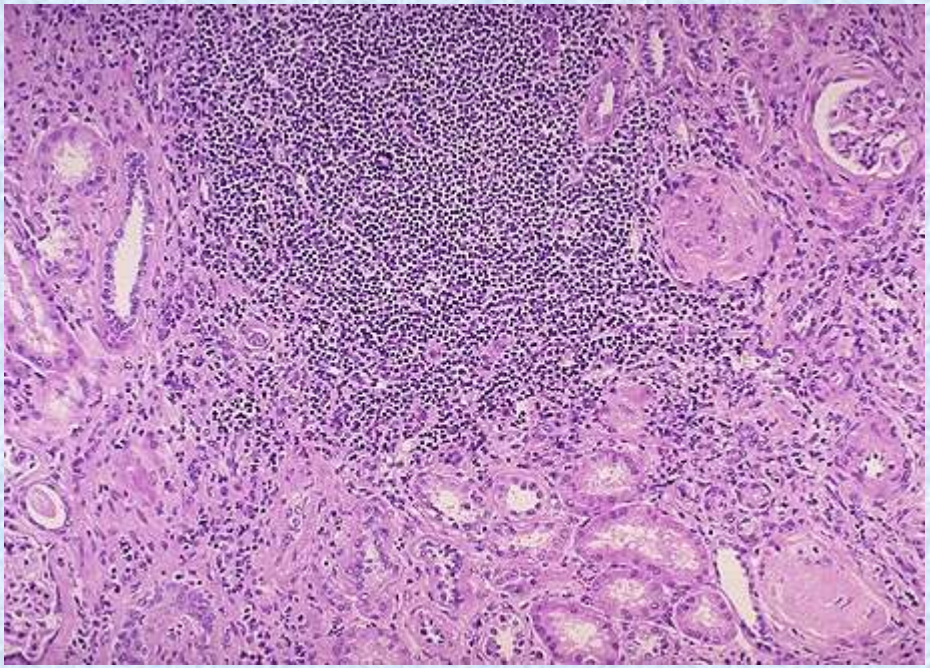
Renal diseases

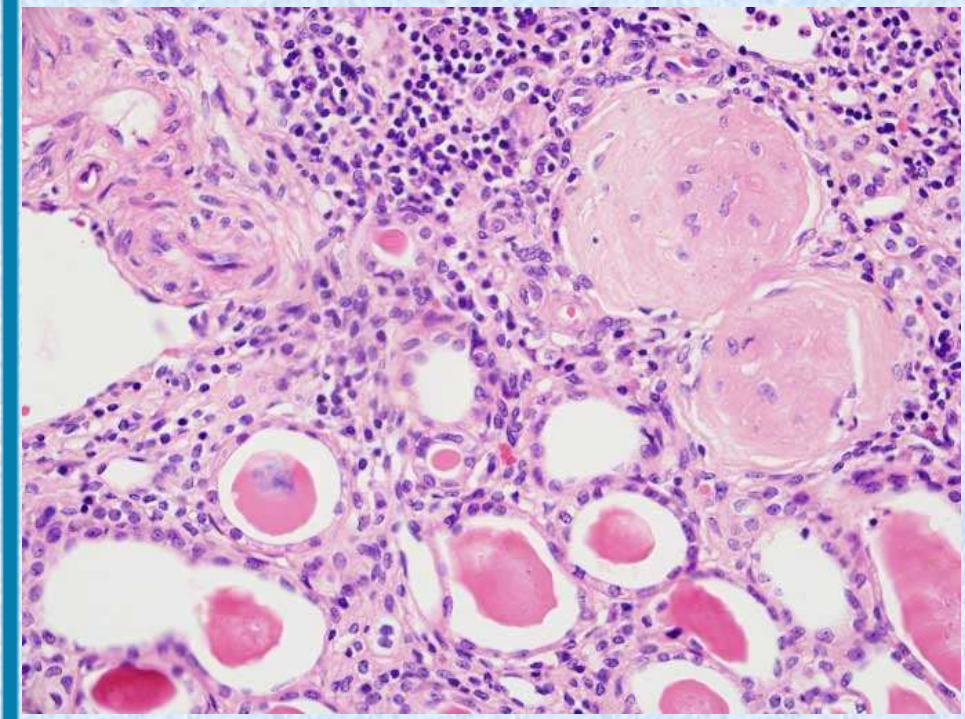
Types of pyelonephritis		
	Acute	**Chronic**
Clinically	-Frequency and dysuria -High grade fever & rigors -Acute loin pain -Urine analysis: pus cells, RBCs, proteins and cellular casts	-Chronic mild loin pain -Hypertension -Repeated acute attacks. -Urine analysis and kidney functions: raised serum createnin, pus cells and RBCs
Grossly: • Size: • Surface • Capsule • Cut section	 -Enlarged -Smooth -Strips easily -Cortex is differentiated -Small cortical abscesses	 -Asymmetrically contracted -Irregular -Adherent -Cortex is not differentiated -Fibrotic

Renal diseases

	Acute	Chronic
MP: • Glomeruli • Tubules: - *Lining:* - *Lumen* • Vessels • Interstitium	-No significant changes -Degenerated or damaged -RBCs cast -Congested capillaries -Infiltration by PNLs, pus cells & macrophages	-May be fibrotic or atrophic -Atrophic lining or fibrosis -Hyaline cast (thyroidization) -End-arteritis oblitrans -Infiltration by plasma cells, lymphocytes (lymphoid follicles) and fibroblasts
Fate and effects:	-If mild: recovery -If severe: acute renal failure -May lead to chronic form	-Hypertension -Renal calculi -End by chronic renal failure

Renal diseases





Chronic pyelonephritis

Renal diseases

Drug induced interstitial nephritis

- Antibiotics, analgesics, chemotherapy and different drugs have deleterious effect on renal tubules and interstitium.
- The injury is either:
  - ***Acute*** (see acute tubular injury)
  - ***Chronic:***
    - Also called analgesic nephropathy
    - *Pathogenesis*: Induction of chronic papillary degeneration, necrosis and interstitial inflammation or glomerular lesions.
    - *Grossly*: NO specific picture.
    - *MP*: coagulative necrosis of renal papillae, interstitial infiltration by lymphocytes followed by patchy fibrosis on long standing cases.
    - *Clinically*: hypertension, anemia and chronic renal failure

Thank you