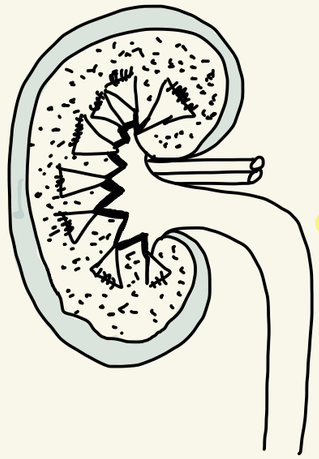


morphologic components of kidney:

carry out many functions that require a high degree of structural complexity.

1) Glomeruli
2) Tubules
3) Interstitium
4) Blood vessels.

Q: How to assess kidney function ?

Answer:
1- Kidney function test (KFT) —> BUN / creatinine
2- Basal metabolic panel —> KFT /electrolyte / blood glucose
3- Glomerular filtration rate (GFR)—> a measure of renal excretory function (>90 ml/min/m2)

Q: Important investigations !!

Answer:
1- urine-analysis (dipstick, microscopy)
2- Urine culture

Note

we choose creatinine to assess kidney function due to :

1- Constant production
2- Freely filtered by the kidney
3- Easy to measure
4- Used to estimate GFR in different equations

Renal diseases

Renal diseases are responsible for a great deal of morbidity & mortality

Azotemia

an elevation of blood urea nitrogen(BUN) and creatinine levels

usually reflects a decreased glomerular filtration rate (GFR)

Uremia

When azotemia gives rise to clinical manifestations & systemic biochemical abnormalities

1) Failure of renal function excretory function

2) Metabolic & endocrine alterations incident to renal damage.

Acute kidney injury

abrupt onset of renal dysfunction (an acute increase in serum creatinine)

associated with " oliguria or anuria " (decreased or no urine flow, respectively)

Chronic kidney disease

progressive scarring in the kidney of any cause

Causing Metabolic & electrolyte abnormalities as:
-hyperphosphatemia
-dyslipidemia
-metabolic acidosis

"asymptomatic until the most advanced stages"
when:
symptoms of uremia develop

End-stage renal disease (ESRD)

Irreversible loss of renal function requiring:

1- Dialysis
2-transplantation
** due to severe progressive scarring in the kidney from any cause

Urinary tract infection (UTI)

1- bacteriuria & pyuria (bacteria and leukocytes in the urine)

2- Symptomatic or asymptomatic

3- Affect the kidney (pyelonephritis) or the bladder (cystitis) only

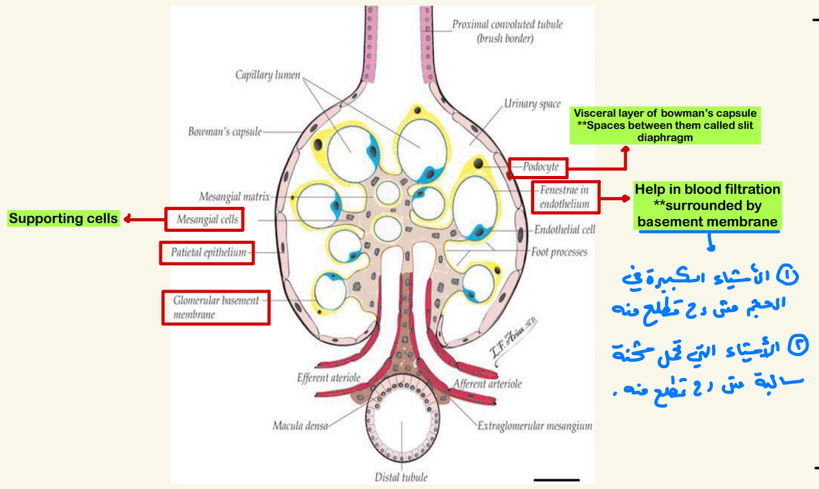
Nephrolithiasis

formation of stones in the collecting system

Manifested by renal colic & hematuria

Nephrons

GLOMERULAR DISEASES
A major problems in nephrology;
Chronic glomerulonephritis is one of the most common causes of chronic kidney disease



① الأشياء الكبيرة في الحجم مش رح تطلع منه
② الأشياء اللي تحمل شحنة سالبة مش رح تطلع منه.

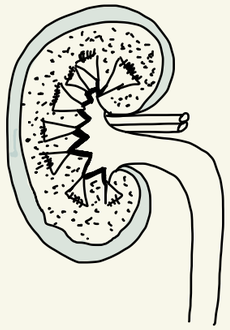
This structure is (glomerulus)
Which is:

"anastomosing network of capillaries invested by two layers of epithelium:

visceral → (composed of podocytes) is part of the capillary wall

&

parietal epithelium → encircles Bowman space (urinary space), the cavity in which filtrate of plasma collects



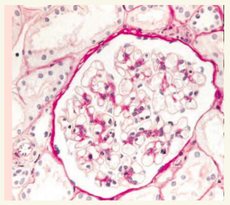
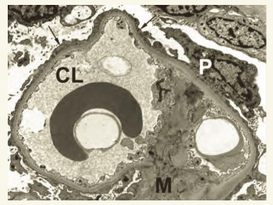
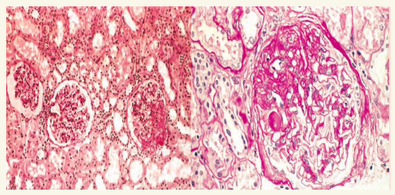
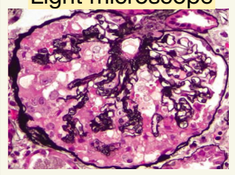
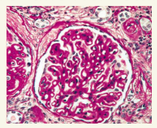
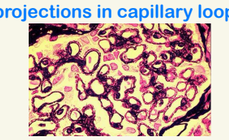
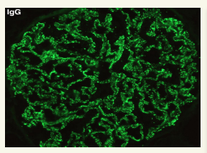
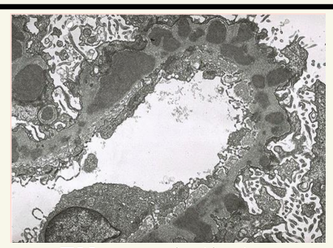
Glomerular diseases and injuries

- **Glomerular diseases**
  - Primary: kidney is the only or predominant organ involved
  - Secondary: Injured in the course of a systemic diseases
- **Immune mechanisms**
  - most types of primary diseases & many of the secondary
  - Deposition of circulating antigen-antibody complexes in :
    - Glomerular capillary wall
    - Mesangium
  - Antibodies reacting in situ within the glomerulus, either with :
    - (intrinsic) glomerular antigens
    - (extrinsic molecules) ⟶ that are planted in the glomerulus

---

common syndromes associated with glomerular diseases

- **Nephrotic syndrome**
  - Primary disease (in children) As
    - Minimal change disease (Most common in children)
    - Focal segmental glomerulosclerosis (most common in adults)
    - Membranous nephropathy (most common in older adults)
  - Secondary "systemic disease" (in adults) As
    - SLE
    - Diabetes
    - Amyldosis
  - Massive Proteinuria (Tested by 24 urine test) ⟶ daily protein loss in the urine of = > 3.5 g
  - Hypoalbuminemia ⟶ with plasmaalbumin < 3 g/dL
  - Generalized edema ⟶ the most obvious clinical manifestation (Due to loss of proteins)
  - Hyperlipidemia and lipiduria
- **Nephritic syndrome** ⟶ inflammation in the glomeruli, leading to:
  - ↓
  - proliferation of the cells in glomeruli & leukocytic infiltrate
  - Hematuria (red cells & red cell casts in urine) ⟶ Inflammation causes injury in capillaries →increase permeable to RBCs & other contents
  - Proteinuria (subnephrotic range) with or without edema
  - Azotemia ⟶ ↓ GFR (that will in increase level of BUM and creatinine) elevation of : blood urea nitrogen & creatinine levels
  - Hypertension ⟶ ↓ GFR + augmented Renin/aldosterone leads to: (fluid retention & ↑ plasma volume)

Disease	General features	Pathogenesis	LM and IF	EM	Clinical features
Minimal change disease (MCD) abrupt nephrotic syndrome in an otherwise healthy child	1) relatively benign disorder 2) The most frequent cause of nephrotic syndrome in children -common age 1-7 years old- **but it can develop at any age	Pathogenesis: Unknown T- cell dysfunction ↓ release factors that damage podocytes & efface foot processes	1) Characterized by: glomeruli that have a normal appearance by light microscopy (minimal) 2) Negative IF 	**diffuse effacement (مسح) of the foot processes **The only obvious glomerular abnormality and it's seen on EM 	1) No hypertension and renal function is often preserved 2) Protein loss chiefly albumin →selective proteinuria (that will decrease plasma colloid osmotic pressure leading to leakage of from blood into EVS) 3) Prognosis for children is favorable **respond to a short course of corticosteroid therapy 4) Adults also respond to steroid therapy, but slower & relapses are more common 5) Less than 5% develop chronic kidney disease after 25 years
Focal segmental glomerulosclero-sis (FSGS)	May be primary (idiopathic) or secondary 1) Characterized by sclerosis of some (but not all) glomeruli (focal) that involves only a part of each affected glomerulus (segmental) Secondary causes: • HIV infection (5-10% of HIV patients) • Heroin abuse • other forms of GN 1) (IgA nephropathy) 2) Nephron loss •	Pathogenesis: not fully understood ↓ Injury to podocytes is thought to represent the initiating event of primary FSGS Collapsing glomerulopathy- FSGS morphologic variant 1) Collapse glomerular tuft and epithelial cell hyperplasia 2) severe form with worse prognosis 3) Can be: idiopathic, ass/with HIV infection, or drug-induced toxicities	LM Sclerosis in some glomeruli not all of them and in a segment not all of the affected glomerulus IF In affected glomeruli negative or nonspecific trapping of immunoglobulins 	Podocytes exhibit effacement of foot processes as in minimal change disease Light microscope 	1) 50% develop renal failure in 10years 2) Hematuria : present 3) Hypertension: present 4) Proteinuria: non-selective 5) Response to corticosteroids: Poor response
Membranous nephropathy	Chronic immune complex glomerulonephritis, either: 1) Antibodies reacting in situ to endogenous antigens 2) Antibodies reacting in situ to planted glomerular antigens	Primary (called idiopathic) "75% of cases" Antibodies against the podocyte antigen phospholipase A2 receptor (PLA2R) Secondary 1) Infections: chronic HBV, malaria , syphilis 2) Malignancies: Cancer of lung & colon & melanoma 3) Autoimmune diseases: particularly SLE 4) Exposure to inorganic salts (gold, mercury) 5) Drugs (penicillamine, captopril, NSAIDs)	LM diffuse thickening of the capillary wall (GBM glomerular basement membrane) on routine H&E stains  A silver stain (black) of the GBM ↓ appears with characteristics spikes (projections in capillary loops)   IF microscopy demonstrates that the granular deposits contain both immunoglobulins & complement	 EM reveals that: thickening is caused by subepithelial deposits, which nestle against the GBM and are separated from each other by small, spike-like protrusions of GBM matrix that form in reaction to the deposits (spike & dome pattern)	**Sudden onset full-blown nephrotic syndrome 1) Proteinuria is nonselective 2) Usually fails to respond to corticosteroid therapy 3) Secondary causes should always be ruled out 4) Variable prognosis: - Proteinuria persists in > 60% of patients - nearly 40% progress to renal failure over 2 to 20 years - (10-30%) benign course → partial or complete remission of proteinuria

Nephritic syndrome

may be caused by primary glomerular diseases:
1) postinfectious glomerulonephritis (GN) 2) various forms of crescentic GN
3) diffuse proliferative GN, IgA nephropathy
4) result of systemic disorders such as SLE

Membrano-proliferative Glomerulonephritis (MPGN)

Best considered as a pattern of immune mediated injury rather than a specific disease
Alterations in the GBM, mesangium and proliferation of glomerular cells

50% of cases → nephrotic syndrome

it may begin as acute nephritis or as mild proteinuria → هذا المرض يبدأ acute و إذا تحوّل إلى nephrotic رح يصير chronic

MPGN type I

(80% of cases)

Immune complex activate both classical (C1) & alternative (C3) complement pathways

Pathogenesis

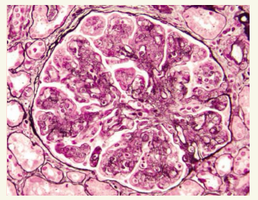
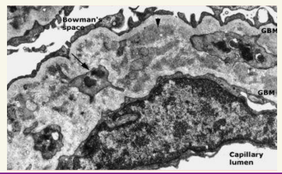
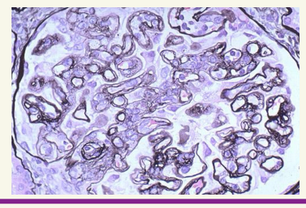
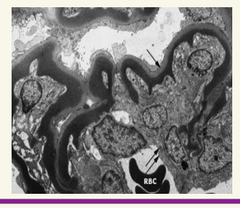
The antigens Mostly are proteins derived from infectious agents e.g: hepatitis C & B viruses

1) "planted" antigens:
after first binding to or becoming trapped within glomerular structures

2) Contained in preformed immune complexes deposited from the circulation

In type 1, these complexes deposit in subendothelium causing separation of basement membrane that will lead to:

1) proliferation of BM (thickening)
2) proliferation of mesengial cells (that will divide BM from half forming TRAM-TRICK appearance

Disease	Light microscope	Electron microscope	Immunoflorescence
MPGN I	Glomeruli are large have an accentuated lobular appearance; proliferation of mesangial & endothelial cells as well as infiltrating leukocytes 	Marked thickening of the glomerular capillary wall by immune deposits (short arrow) & by interposition of mesangial cell processes (long arrow) 	C3 is deposited in an irregular granular pattern, IgG and early complement components (C1q & C4)
MPGN 2	1) The GBM is thickened 2) glomerular capillary wall often shows a double contour, or "tram track" appearance evident with use of silver 	dense homogeneous deposits within the basement membrane Ribbon-like appearance of subendothelial & intramembranous material 	Only C3 is present in irregular foci in the GBM on either side but not within the dense deposits

MPGN type 2
Dense Deposit Disease

deposits will be in the "glomerular basement membrane"

Excessive complement activation

there will be C3 nephritic factor that lead to excessive activation of alternative pathway by cleavage of C3

Pathogenesis

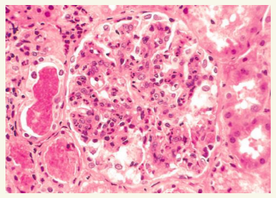
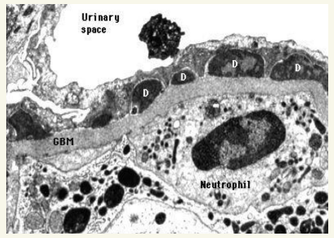
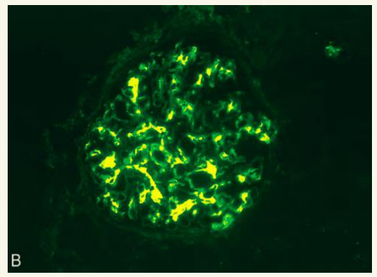
Complement dysregulation

** Autoantibody against C3 convertase (called C3 nephritic factor)

** Ab It stabilizes the enzyme
→ uncontrolled cleavage of C3 & activation of the alternative complement pathway

MPGN
Clinical manifestations

- The prognosis generally is poor
- No complete remission
- 40% progressed to renal failure
- 30% had variable degrees of renal insufficiency
- 30% had persistent nephrotic syndrome without renal failure

Disease	General features	Pathogenesis	. LM	EM and IF	Clinical features
Acute Postinfectious (Poststreptococcal) Glomerulonephritis	Glomerular deposition of immune complexes resulting in: (1) proliferation of & damage to glomerular cells (2) infiltration of leukocytes (esp. neutrophils) develops in a child 1-4 weeks after he/she recovers from: group A streptococcal infection	*Initial infection in pharynx or skin Classic pattern/most common →poststreptococcal GN but it may be associated with other organisms: (viral or bacterial) Immune complexes containing streptococcal antigens & specific antibodies formed in situ ↓ activate complement system Depositions will be sub-epithelial	increased cellularity of all glomeruli (nearly all glomeruli) caused by: 1) proliferation and swelling of endothelial and mesangial cells (2) infiltrating neutrophils and monocytes 	**EM** shows deposited immune complexes as subepithelial "humps" (on the epithelial side of GBM)  **IF** scattered granular deposits of IgG & complement within the capillary walls	• Most commonly present as acute nephritic syndrome • Fever, nausea, gross hematuria and mild proteinuria • Serum complement levels are low during the active phase of the disease • Serum anti–streptolysin O antibody titers are elevated in poststreptococcal cases • Recovery occurs in most children with poststreptococcal disease
IgA Nephropathy (Berger Disease) Chronic disease	** One of the most common causes of recurrent microscopic or gross hematuria ** Usually affects: children & young adults **An episode of gross hematuria (within 1-2 days of a nonspecific URTI) hematuria lasts days & subsides but it recurs periodically	Similar IgA deposits are present in a systemic disorder of children Henoch - Schonlein purpura Renal manifestations occur in one third of patients (same deposition pattern as IgA nephropathy) A genetically susceptible individual + URTI or GIT exposure to microbial ↓ ↑ ↑ ↑ IgA synthesis ↓ deposition of IgA & immune complexes in the mesangium	Different LM findings	**IF** deposition of IgA and C3, in the mesangial region (diagnostic) 	

Rapidly Progressive (Crescentic) Glomerulonephritis

هذا المرض ليس **syndrome** منفصل و إنّما عبارة عن مضاعفات لباقي الأنواع

It is a clinical syndrome
(not a specific etiologic form of GN)
↓
Rapid loss of renal function if untreated
(nephritic syndrome)
↓
oliguria
↓
(renal failure)
in weeks to months

Characterized by the presence of crescents
(crescentic GN)
↓
Formed by:
(1) proliferation of epithelial cells

(2) migration of monocytes macrophages into Bowman's space in response to injury

Associated with number of disease

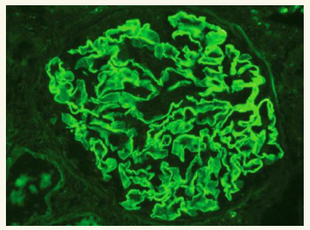
1) Anti-GBM antibody–mediated crescentic GN (Goodpasture disease)

2) Any of the immune complex nephritides

3) Pauci-immune RPGN Serum ANCA

Anti-GBM antibody–mediated crescentic GN (Goodpasture disease)

Characterized by linear deposits of IgG in GBM



In some patients: anti-GBM antibodies bind to pulmonary alveolar capillary BM to produce the clinical picture of pulmonary hemorrhages

→ Associated with renal failure Goodpasture syndrome

Anti-GBM Abs are in the serum (Diagnosis)

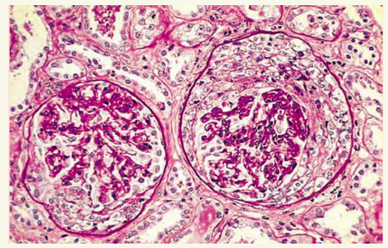
It is important to recognize Goodpasture disease benefit from plasmapheresis

→removes pathogenic antibodies from the circulation

1) Collapsed glomerular tufts

2) crescent-shaped mass of proliferating parietal epithelial cells

3) leukocytes internal to Bowman capsule



Hereditary Nephritis - Alport Syndrome

Hereditary nephritis
a group of heterogeneous familial renal diseases associated with mutations in collagen genes & manifest primarily with glomerular injury

Alport syndrome manifest by :
1) nephritis

2) sensorineural deafness

3) various eye disorders (lens dislocation, posterior cataracts and corneal dystrophy)

Inherited as an X-linked trait in ~ 85% of cases

GBM is composed of type IV collagen heterotrimers of α3, α4, & α5 type IV collagen

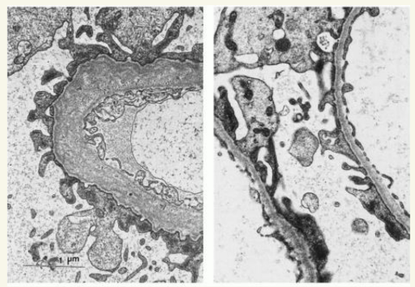
This form of type IV collagen is crucial for function of the lens, cochlea and glomerulus

→ Mutation of any one of the α chains results in defective heterotrimer assembly

→ manifestations of Alport syndrome

Early
GBM is thin & attenuated

Later
develops irregular foci of thickening, splitting and lamination yielding a " basket-weave appearance "



UGS-Pathology Lecture 1+2

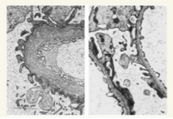
Focal segmental glomerulosclero-sis (FSGS)	May be primary (idiopathic) or secondary 1) Characterized by sclerosis of some (but not all) glomeruli (focal) that involves only a part of each affected glomerulus (segmental) Secondary causes: • HIV infection (5-10% of HIV patients) • Heroin abuse • other forms of GN 1) (IgA nephropathy) 2) Nephron loss

1. What of the following glomerular disease associated with HIV, Heroin addiction, sickle cell disease :

Answer : FSGS

Early
GBM is thin & attenuated

Later
develops irregular foci of thickening, splitting and lamination yielding a
" basket-weave appearance "



2. Patient come with neurodiffness, in EM has basket appearance, which disease :

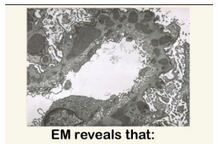
Answer : Alport

.3. False about membranous :

A. Proliferation and thickening of all glomeruli in IF ✗

B. EM: subendothelial & intermembranous depositions

Answer : B



EM reveals that:
thickening is caused by subepithelial deposits, which nestle against the GBM and are

غالبًا سؤال للمحاضرة الخامسة حتى الآن.

4. One of the following develop end stage renal disease:

A. Polycystic

~~B~~. **Horseshoe kidney**

C. Floating kidney

~~D~~. **Ectopic kidney**

Answer: A