Glomerular disease = kidney disease affecting the glomerular filtration membrane which compound from 3 layers

① endothelium ② Basement membrane ③ Podocyte foots (epithelium)

cause the protein and RBC to leakage cause proteinuria / hematuria / RBC cast / dysmorphic

the basement membrane ↓ albumin ↓ ↓ so keep albumin inside capillaries

1] Nephrotic Syndrome = impaired the barrier (mainly podocyte) cause massive proteinuria >3.5g/day

*general Diagnostic → ① urinalysis - proteinuria - just for albumin loss. Not detect Ig loss like multiple myeloma (+3 / +4)

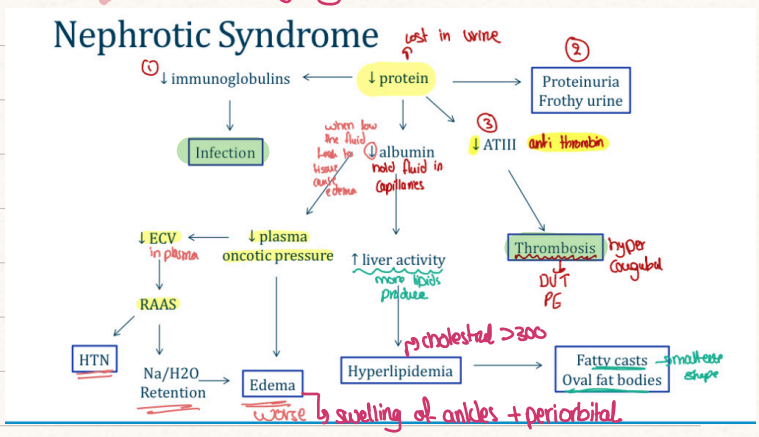
② renal biopsy → Definitive test

③ 24 hr urine collection >3.4g/day protein

④ Urine protein / Cr → 3.5:1

*general treatment =

- HTN + proteinuria → ACEI / ARBs
- Hyperlipidemia → statin
- edema → sodium restriction



* Major Causes =

1] Minimal Change disease / Lipoid nephrosis

*most common cause of nephrotic in children after URTI → caused by effacement of foot process (flattened) of podocyte cause lose -ve basement cause leakage of protein (albumin here Not IG) (not at risk of infection)

* Triggered by Cytokines

* Secondary to Hodgkin lymphoma (more cytokines) autoimmunological trigger → URTI / Allergic reaction (bee sting) / recent immunization

* mostly idiopathic

*Renal biopsy → LM normal / Negative IF / effacement of podocyte on EM

*Treatment = good prognosis to steroids

2] Focal Segmental glomerulosclerosis (FSGS)

<50% affected ↓ → only part of glomerulus affected → scarring of glomerulus by dense deposition of collagen

*cause effacement of podocytes by unknown cause (primary FSGS) *2nd to HIV / Sickle cell anemia / Heroin users / massive obesity and interferon treatment in HCV / HBV + loss of nephrons (single kidney or surgical kidney removal)

*most common cause in black people (African-American)

*Renal biopsy = LM pink material deposit / sclerosis } EM = effacement

*Treatment = Treat underlying cause - No response to steroid progressive to CKD within 10-20 y

3] Membranous nephropathy / membranous glomerulonephritis = Type V of lupus nephritis

→ immune complex deposition cause thick glomerular basement membrane

Renal biopsy → LM: capillary / BM thickening / IF: granular IgG / C_3 deposition / EM: subepithelial deposition (spike and dome)

*Idiopathic associated with antibody against phospholipase A2 receptor (PLA2R) to podocytes so +ve serum anti PLA2R antibody test

*2nd to SLE 10% + solid tumors (lung cancer / colon cancer / melanoma) + HBV / HCV + Drugs (penicillamine, gold, NSAIDs) caused to treat Rheumatoid Arthritis

*Most common cause of nephrotic in Caucasian Adults → poor prognosis → progress to ESRD + spontaneous remission

*Treatment :- rituximab / steroids / cyclophosphamide

4] Diabetic Nephropathy

Hyperglycemia → Non enzymatic glycosylation of tissue protein → mesengial expansion + BM thickening → leakage of protein to urine

↑GFR → glomerular HTN → glomerulosclerosis → Nephrotic Syndrome

*Renal biopsy → LM: mesengial expansion + GBM thickening + sclerosis Kimmelstiel wilson lesion

5] Amyloidosis

deposition of amyloid protein to (kidney) - most commonly organ involved

Renal biopsy → LM : Congo red stain show apple green birefringence

6] Membranoproliferative Glomerulonephritis

↳ thick ↳ increased No. of mesengial Cells

* cause nephritic or nephrotic / Rare disease

*appear as renal failur PBUN/Cr + Hematuria + proteinuria *Treated by steroids and immunosuppressants

1] Type I *common → immunocomplex deposition IgG + C3 cause split basement membrane (subendothelial)

LM :- Tram track IF :- granular *Idiopathic or 2nd to Hep B/C

2] Type II rare (dense deposit)

Children (5-15) associated with C3 nephritic factor IgG autoantibody that stabilize C3 convertase which activate alternative pathway → ↓C3 on serum and deposit on BM with absent of IgG

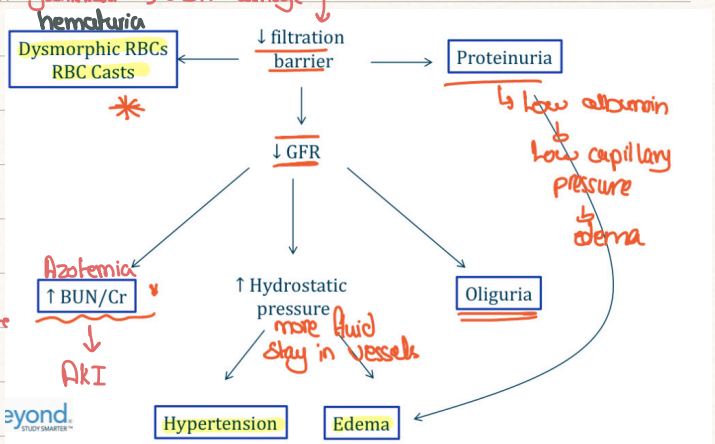
LM: tram track EM: dense deposit *Leak to ESRD

{Hypocomplmetemia}

	Type I	Type II
Pathology	Immune Complex	Complement (C3)
Microscopy	LM: Tram Tracks	EM: Dense Deposits
Associations	Hepatitis	Children

2] Nephritic Syndrom → inflammation of glomerular → GBM damage

* protein uria < 3.5g/day
* present with fatigue (uremia)
* Diagnosis :- ① urinalysis (cast+protein) ② BUN/Cr
③ Renal biopsy
* Treatment :- HTN + proteinuria → ACEI / ARBs
immunosuppresion → glucocorticoid / Cyclophosphamide / Mycophenolate



* Major Cause :-

1] Post Infectious GN

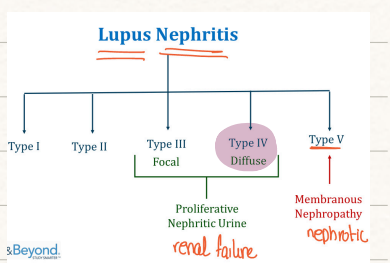
* Type III hypersensitivity
* Children follows group A-B hemolytic strep infection 2-4 weeks after URTI pharyngitis / impetigo (skin infection)
cause immunocomplex deposition + hypercellular in glomerular → No specific therapy → spontaneous resolution → recover completly
* Can occure with adult → poor prognosis → renal insufficiency after 10-40 y → RPGN <not URTI
Staph + Strep
Diagnosis :- biopsy (adult) / serology ASOA (child) / Hypocomplementemia
LM :- enlarged / hypercellular glomerular EM :- subendothelial Antibodies IF :- granular (starry sky lumpy dumpy)
IgG + C3

2] IgA Nephropathy (Berger's disease)

* most common form of glomerulonephritis * repeated episodes of hematuria after days RS infection or GI infection cause ↑ IgA Synthesis → IgA immune complex → glomerular injury → over times can lead to ESRD (20-25y) + Henoch Schonlein purpura
Diagnosis → serum IgA ↑ + Renal biopsy → LM: mesengial polifration / IF: IgA granular / EM: mesengial IC deposition
Treatment → glucocorticoids

3] Diffuse proliferative glomerulonephritis

>50% of glomeruli affected ↳ increase cellularity (mesengial, endothelium, neutrophil)
accosiated with SLE - most common subtype - Type IV lupus nephritis → cause immune complex deposition in glomeruli → inflammatory response
Hypocomplementemia + Anti dsDNA
LM: wire looping "capillary loops thickened" EM: subendothelial deposition
IF: full house "granular" IgG, IgA, IgM, C3, C1q
* may associated with nephrotic
* may lead to ESRD + HD (hemodialysis)
* Treated with steroids + Cyclophosphamide



4] Alport Syndrome

Hereditary nephritis → type IV collagen defect mutation in alpha 3/4/5 (X-linked)

found in kidney → hematuria eye → ocular disturbances ear → Hearing Loss

child + family history

EM:- basket weave due to irregular thickining of Glomerular → No treatment → progress to ESRD / transplant

5] MPGN

6] Rapidly progressive glomerulonephritis (RPGN) / Crescentric GN

clinical Syndrome - rapid loss of renal function over days / weeks / months - inflammation of glomerulus

disrup filtration rate Renal biopsy → LM → accumulate macrophage / fibrin as crescent

Case scenarios- 1] Uremic Symptoms → fatigue / Anorexia

2] AKI → urinalysis ↑ BUN/Cr

3] Nephritic Syndrome → RBC cast / proteinuria

Causes- distinguished by IF

1] Type I : Linear IF (Ig deposition)

due to antiglomerular basement membrane antibodies {Anti GBM antibodies}

Unknown stimulus - type II hypersensitivity - Lineur IF of IgG

example- Goodpastures Syndrome

Antibody to collagen type IV to alpha 3 chain found on glomerular and alveoli basement membrane

Young male hemoptysis hematouria nephritic Syndrome

2] Type II : Granular IF (deposited Ig)

immune complex deposition in kidney - Type III hypersensitivity

example → Post Strep GN - RPGN (most common cause)

SLE - Diffuse - RPGN

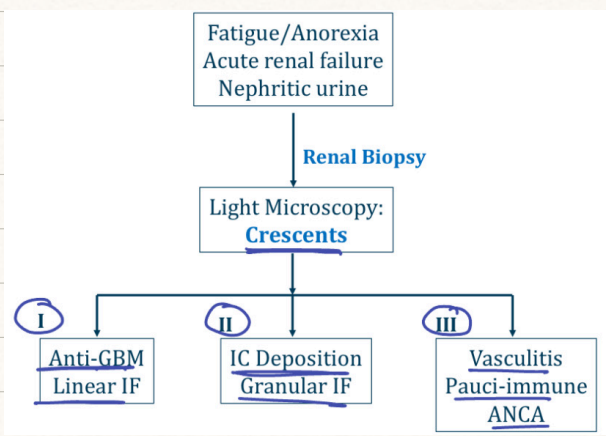
3] Type III : Negative IF

Pauci immune - No Ig deposition

ANCA positive → vasculitis Syndrome

wegeners - C-ANCA

microscopic polyangiitis + churg - P-ANCA



Disease	Presentation	Age	LM	IF	EM	Prognosis
MCD	nephrotic	Children	none	negative	Effaced foot processes	good
FSGS	nephrotic	adults	Segmental sclerosis	negative	Effaced foot processes	Poor?
MNP	nephrotic	adults	Thickened GBM	IgG+ C3+	Sub-epithelial spikes and domes	Poor?
MPGN-type1	Nephritic/ nephrotic	adults	Tram track	Ig s	Subendothelial deposits	poor
MPGN-type2	Nephritic/ nephrotic	adults	Tram track	C3+	Dense deposits	poor
IgA nephropth	nephritic	Children, young adults	variable	IgA+	Mesangial deposits	variable
PSGN	nephritic	children	hypercellularity	IgG+ C3+	Subepithelial deposits (humps)	good
Alport syndrome	hematuria, hearing loss	children	variable	negative	Basket weave GBM	poor