Nephrotic syndrome = pOdocyte

Massive proteinuria, Hypoalbuminemia, Generalized edema, Hyperlipidemia & lipiduria.

	Minimal-Change Disease	Focal Segmental Glomerulosclerosis (FSGS)	MembranouS nephropathy
1ry cause			
Site	Podocyte (Visceral epithelium)	Podocyte	Subepithelial
Microscope	- LM → **normal** - EM → Diffuse effacement of podocyte foot process. IF → normal	- LM → Hyalinosis, no evident of prolife. - EM → Effacemnt of foot processes - IF → granular deposition of **IgM**, C3.	- LM → Diffuse thickening of the capillary wall. - EM → Subepithelial deposite, Spike & dome patteren. - IF → Granular deposite (in-situ cpx.) IgG & C3
Notes	- Most freq. cause of nephrotic. - Children. - No hypertension. - Selective proteinuria. (only albumin) - No fibrosis - History of bee sting (smtm) - T-cell derivative factor. - Lipid-laden → particularly in proximal tubule. - known as lipoid nephrosis.	- Affect some glomeruli → Focal. - Affect some glomerulus → Segmental. - 2ry to heroin or HIV nephropathy. - A sequence variant in the apolipoprotein L1 gene (APOL1) strongly associated with ↑ risk of FSGS & Renal failure in African descent → (autosomal dominant). - To differentiate bet. Minimal and FSGS (bc they are similar to each other): 1- The incident of hematuria & hypertension is higher in FSGS. 2- FSGS associated proteinuria is non-selective. - smtms caused by mutation in NPHS2 gene which code: Podocin protein.	- Spikes = basement membrane material. - Dome = immune complex deposits. - Most common in 30-60 yrs (Adults) - Associated with SLE V - Chronic. - non-selective proteinuria. - Heymann nephritis. - Absence of inflammatory cells. - Associated w\ **azotemia** - Autoimmune response against phospholipase A_2.
2ry	**Diabetic nephropathy**	**Amyloidosis**	**Lupus nephritis** (class V) (Lupus membranous glomerulopathy)
Microscope	- LM →Arteriolar hyalinization, mesengial matrix expansion & glomerular basement mem thickening. - EM → **Kimmelstiel-wilson nodule**.	- LM → Massive amyloid deposits in **mesengium** & glomeruli and arterioles, tubular involvement. - Stained w\ Congo-red stain. - Polarized light → Vertified by Apple-Green birefringence.	- LM → Diffuse thickening of peripheral capillary walls (string-popcorn) + ↑ **mesengial** matrix. - LM → [silver methenamine (jones)]: - Spike & dome patteren. - When cut tangentially→ moth-eaten. - (wire-loop) appearance = SLE IV.

NephrItis syndrome = Inflammation

Hematuria (red cell casts in urine), some oliguria and azotemia, Hypertension. + proliferation of cells.

Cause	Acute post-infectious GN	IgA nephropathy "berger disease"	Alport syndrome
Site	Subepithelial & mesengium	Mesengeium	GBM
Microscope	- LM → ↑ cellularity (PMNs) - EM → deposit immune cpx in subepithelial (Humb shape= large) - IF → Granular deposition of IgG and C3. "Lumpy bumpy"	- IF → Mesengial deposition of IgA & C3.	- LM → Foam cells. - EM → - Early: thin glomerular basement mem. - Late: thick laminated basement mem "Basketweave"
Notes	- Caused by complement activation of classical pathway. (immune cpx activate complement) & alternative. - Caused by streptococcal antigens which cross-react with glomeruli "Nephritic Strains" - streptococcal exotoxin B (Spe B) - streptococcal GAPDH. - Affect all glomeruli (Diffused) - Endocapillary proliferation. - 7-14 dys → after pharyngitis. - 14-21 dys → after skin infection. - Bact. Culture → -ve. - ASO → evidence in pharyngitis but not skin infection due to cholesterol & lipid in the skin. anti-DNAse B titre → for skin infection. - Hypocomplementemia.	- begins as gross hematuria. - Non-specific upper respiratory tract infection. - The most common disease revealed by biopsy worldwide. - Purely renal disorder (unlike Henoch-Scholein purpura) - Abnormal glycosylated IgA. - The absence of C1q & C4 = Activation of alternative pathway (= serum complement C2 and C4 will be normal) - It occurs w\ ↑ frequency in individual w\ Celiac disease & liver disease. - children & young adults. - It could be Asymptomatic hematuria and proteinuria.	- Mutation in genes encoding GBM protein "collagen type IV" - It could be Asymptomatic hematuria and proteinuria = proteinyria < 1g\24h, had a normal kidney function. - a clinical manifestation of good-pasture syndrome. - Hearing problems.

Both Nephrotic & Nephritic (more nephritic)

Membranoproliferative GN (Mesangiocapillary GN)→ Chronic, Hypercellular

	Type I	Type II (Dense Deposit Disease)
Site	Subendothelial	intramembranous dense deposits
Microscope	- LM → **Lobular**, Proliferation of mesengial & endothelial cells, Splitting of GBM. (**Tram-track**) double contour. - EM → Subendothelial electrone dense deposit - IF → granular deposits of IgG, C3.	- LM → Ribbon-like (in intramembranous; within basement mem) - IF → granular deposits of C3 only
Notes	- caused by circulating immune cpx. - associated w\ **Hepatitis B and C**, & SLE. - C1q and C4 (classical pathway) & IgG are present. = activation of both classical and alternative pathways	- Excessive complement activation = Hypocomplementemia. - Ab against C3 convertase → C3 nephritic factor - C1q and C4 (classical pathway) & IgG are absent. = activation of alternative pathway only. - ↓ serum level of factor B. – mutation of factor H

Rapidly progressive GN = Crescents

RPGN is a clinical entity w\ features of nephrItic syndrome and rapid loss of renal function.

	Type I → Anti-GBM	Type II → Immune cpx	Type III → Pauci immune
Pathological disease	Goodpasture syndrome	- Postinfectious GN - SLE - IgA nephropathy - Henoch-Schonlein purpura (IgA) - Membraonoproliferative GN	- **ANCA** disease (vasculitis) e.g.: - Wegener's granulomatosis - Microscopic polyangiitis - Churg-strauss syndrome.
Microscope	- LM → Segmental necrosis, proliferation of parietal epithelial, PMNs = **Crescent** - EM → Ag-Ab cpx is not high enough to be seen. - IF → **Linear IgG & C3**.	- LM → Segmental necrosis, **Cresent.** - EM → direct deposits. - IF → **Granular** patteren	- LM → Segmental necrosis, PMNs and mononuclear cells & **Crescent**. - EM → No deposits. - IF → Nothing
Notes	- Crescent formed by: 1- Proliferation of parietal cells. 2- Migration of monocyte\macrophage into Bowman's space. - The Abs recognize type IV collagen.	- Granular (lumpy bumpy) pattern staining of GBM and\or mesengium. - May occur as a **complication** of any of the immune complex nephritides.	- Characterized by lack of Anti-GBM. - Oliguria & azotemia are more pronounced.

CHRONIC RENAL FAILURE

	Chronic nephrItic syndrome	End stage renal disease
Characteristics	- **Azotemia**. - Active urine sediment (variable) - Proteinuria (variable) - Past history of RPGN, nephrotic syndrome, or nephritic syndrome. - **Hypertension**.	Uremic syndrome - Skin manifestation – pruritus, uremic "frost", skin. - Cardiac manifestations – Uremic pericarditis, left ventricular hypertrophy. - Neurological manifestation – peripheral neuropathy. - Pulmonary complications – pneumonitis & hemorrhage. - Hematopoietic manifestations – Anamia, bleeding diathesis. - Skeletal abnormalities – renal osteodystrophy (2ry hyperparathyroidism) - metabolic imbalances. * Pathogenesis: Uremic "toxins" → Middle molecules → The "trade off" hypothesis. * Treatment: 1-Supporative therapy. 2-Dialysis. 3-Renal transplantation.
	Signs of uremia 1- Loss of appetite. 2- Lethargy 3- ↑ BUN (blood urea nitrogen)	

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