Glomerulonephritis: Early Identification, Management, and Treatment Updates

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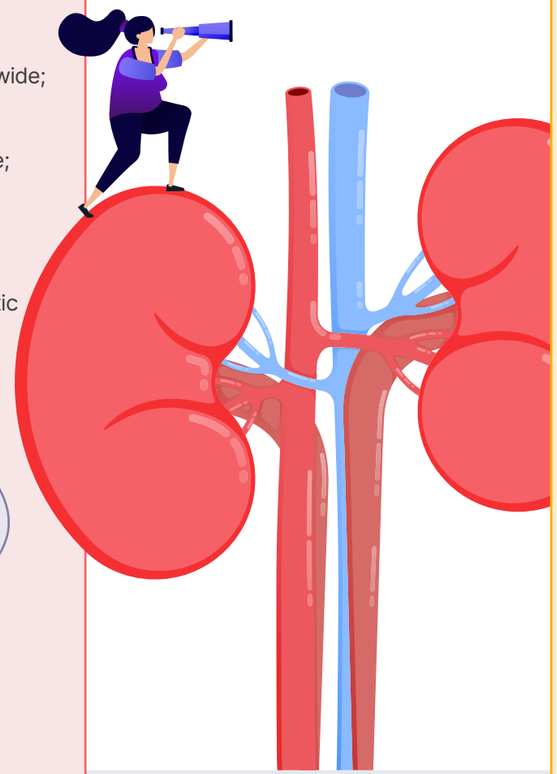
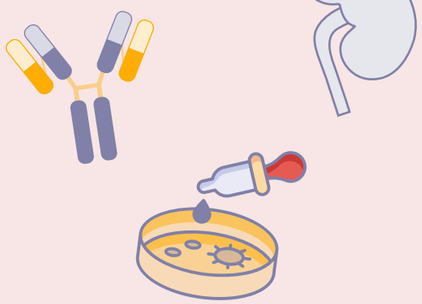
Overview, Epidemiology, and Progression

GN is a group of immune-mediated disorders affecting the glomeruli and is a leading cause of CKD and ESRD worldwide. GN is broadly classified as either primary, originating within the kidney (such as IgAN or membranous nephropathy), or secondary, occurring as part of a systemic condition (such as lupus or vasculitis).

Primary:

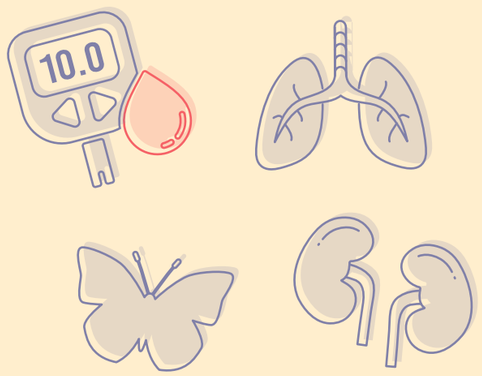
- PSGN: immune complex GN after streptococcal infection; usually self-limiting in children.
- IgAN: most common primary GN worldwide; may be secondary to liver disease, infections, or autoimmune disease.[1]
- MN: common adult nephrotic syndrome; often PLA2R antibody-mediated.
- FSGS: segmental glomerular scarring; primary or secondary (e.g., viral/adaptive causes).
- MCD: most common childhood nephrotic syndrome; steroid responsive.
- MPGN: immune complex- or complement-mediated glomerular injury pattern.





Secondary:

- LN: immune complex GN secondary to systemic lupus erythematosus; biopsy classification guides treatment.[2]
- AAV: pauci-immune crescentic GN with systemic vasculitis features.
- Anti-GBM disease: autoantibody-mediated rapidly progressive GN, often with pulmonary haemorrhage.[3]
- Diabetic and hypertensive glomerulopathy: major non-inflammatory causes of chronic kidney disease.[4]
- Infection-associated GN: immune complex GN triggered by infections.
- Monoclonal gammopathy-associated GN: GN linked to plasma cell or B cell disorders.



Progression

Early diagnosis and intervention are crucial to prevent GN progression to CKD. Renal biopsy is the gold standard for subtype classification; however, it is typically performed in specialist centres, making timely referral essential.[5,6]

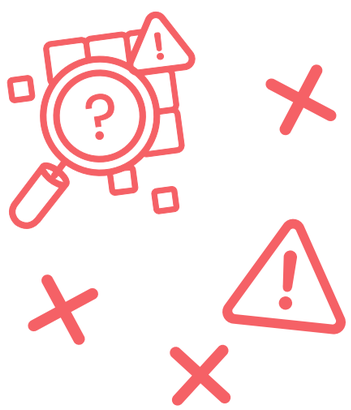
Major Complications and Risk Factors

Complications:

- AKI: rapid loss of kidney function, especially in crescentic/RPGN forms (e.g., ANCA, anti-GBM).[7]
- CKD and ESRD: progressive kidney function decline can occur across all GN types.[3]
- Cardiovascular disease: Increased long-term risk linked to chronic inflammation and hypertension.[3]

Risk factors for GN progression:

- Proteinuria (>1 g/day): strong predictor of ESRD risk; reducing proteinuria improves outcomes.[7]
- Hypertension: key modifiable risk factor; RAAS inhibition slows CKD progression.
- Histological severity: crescents, fibrosis, and sclerosis predict poorer prognosis.
- Delayed immunosuppression: worse renal outcomes in immune-mediated GN (e.g., LN, AAV).



Treatment Updates in Specific Subtypes

IgAN:

- First-line: blood pressure control and RAAS inhibition.
- Immunosuppression guided by proteinuria and progression risk.
- Sparsentan reduced proteinuria in the PROTECT trial and gained FDA approval in 2023.[8]

AAV:

- Induction: rituximab or cyclophosphamide plus corticosteroids.
- Avacopan achieved steroid-sparing remission with improved safety in the ADVOCATE trial.
- Maintenance therapy is typically rituximab.[9]

MN:

- First-line: RAAS blockade and risk stratification using proteinuria and anti-PLA2R titres.
- Rituximab is increasingly preferred for moderate/high-risk or refractory disease.
- Emerging therapies include obinutuzumab and belimumab.

LN:

- Induction: mycophenolate or cyclophosphamide, followed by maintenance immunosuppression.
- Belimumab improved renal outcomes in the BLISS-LN trial.
- Voclosporin is approved with mycophenolate and low-dose steroids.[8]

Anti-GBM disease:

- Standard therapy: plasma exchange, high-dose corticosteroids, and cyclophosphamide.
- Emerging: antigen-specific Treg therapies under investigation for targeted immune suppression.

Abbreviations

AAV: ANCA-associated vasculitis; AKI: acute kidney injury; CKD: chronic kidney disease; ESRD: end-stage renal disease; FSGS: focal segmental glomerulosclerosis; GBM: glomerular basement membrane; GN: glomerulonephritis; GPA: granulomatosis with polyangiitis; IgAN: IgA nephropathy; LN: lupus nephritis; MCD: minimal change disease; MN: membranous nephropathy; MPA: microscopic polyangiitis; MPGN: membranoproliferative GN; PLA2R: phospholipase A2 Receptor; PSGN: post-streptococcal glomerulonephritis; RAAS: renin-angiotensin-aldosterone system; Treg: regulatory T cell.

References

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