Glomerulonephritis

Glomerulonephritis (GN) refers to a group of diseases characterized by inflammation of the glomeruli, the filtering units of the kidney, often leading to hematuria, proteinuria, hypertension, and renal dysfunction. This guide provides physician assistant (PA) students with a comprehensive framework to understand the differential diagnosis, diagnostic approach, causes, and hospital management of GN in adults, with case scenarios to apply the knowledge.

Clinical Presentation

Symptoms:

• Hematuria (gross or microscopic; cola-colored urine).

• Edema (periorbital, lower extremity) due to proteinuria and hypoalbuminemia.

• Hypertension (from sodium retention, renin-angiotensin activation).

• Oliguria or anuria (severe cases with acute kidney injury [AKI]).

• **Constitutional symptoms:** Fatigue, fever, weight loss (if systemic disease).

Physical Exam:

• Hypertension (e.g., BP >140/90 mmHg).

• Edema (periorbital, pitting in legs).

• Rash, arthralgias (systemic diseases like SLE, vasculitis).

• Crackles (pulmonary edema in severe AKI).

When to Suspect Glomerulonephritis

• **Rapidly Progressive Glomerulonephritis (RPGN):** Rapid decline in renal function (days to weeks), hematuria, proteinuria, often with systemic symptoms (e.g., fever, hemoptysis in vasculitis).

• **Nephritic Syndrome:** Hematuria (RBC casts), proteinuria (<3.5 g/day), hypertension, edema, oliguria.

• **Nephrotic Syndrome (Overlap):** Heavy proteinuria (>3.5 g/day), hypoalbuminemia, edema, hyperlipidemia (e.g., minimal change disease, membranous GN).

• **Systemic Symptoms:** Rash, arthritis, hemoptysis, sinusitis (e.g., SLE, vasculitis).

• **Post-Infectious:** Recent infection (e.g., streptococcal pharyngitis, endocarditis) with hematuria, edema.

Differential Diagnosis

• RPGN (Crescentic GN):

o Anti-GBM disease (Goodpasture's syndrome).

o ANCA-associated vasculitis (GPA, MPA).

o Immune complex GN (e.g., SLE, post-infectious GN).

• Nephritic Syndrome:

o Post-infectious GN (e.g., post-streptococcal).

o IgA nephropathy (Berger's disease).

o Lupus nephritis (SLE).

o Membranoproliferative GN (MPGN).

• Nephrotic Syndrome (Overlap):

o Minimal change disease (MCD).

o Focal segmental glomerulosclerosis (FSGS).

o Membranous nephropathy.

• Other:

o Acute interstitial nephritis (AIN): Drug-induced, infection-related.

o Acute tubular necrosis (ATN): Ischemia, nephrotoxins.

Labs and Diagnostic Studies

Initial Labs:

• **Urinalysis:** Hematuria, proteinuria, RBC casts (nephritic), granular casts (ATN), dysmorphic RBCs (glomerular origin).

• **CBC:** Anemia (chronic disease, hemolysis in SLE), leukocytosis/leukopenia (infection, vasculitis).

• **Renal Function:** Elevated BUN/Cr (AKI), low eGFR.

• **Electrolytes:** Hyperkalemia, metabolic acidosis (AKI).

• **Albumin:** Hypoalbuminemia (nephrotic syndrome).

• **Inflammatory Markers:** ESR, CRP elevated in vasculitis, SLE.

Specific Tests:

• **Complement (C3, C4):** Low in SLE, MPGN, post-infectious GN; normal in IgA nephropathy, ANCA vasculitis.

• **ANCA:** c-ANCA/PR3 (GPA), p-ANCA/MPO (MPA, EGPA).

• **ANA, Anti-dsDNA:** Positive in SLE; anti-dsDNA specific for lupus nephritis.

• **Anti-GBM Antibodies:** Positive in Goodpasture's syndrome.

• **ASO Titer, Anti-DNase B:** Elevated in post-streptococcal GN.

• **Hepatitis Serologies:** HBV, HCV (MPGN, cryoglobulinemia).

• **Cryoglobulins:** Positive in cryoglobulinemic GN.

• **Serum Protein Electrophoresis (SPEP):** Monoclonal gammopathy in amyloidosis (secondary GN).

Imaging:

• **Renal Ultrasound:** Assess kidney size (small in chronic disease), rule out obstruction, hydronephrosis.

• **Chest X-Ray/CT:** For systemic diseases (e.g., pulmonary hemorrhage in Goodpasture's, nodules in GPA).

Other Studies:

• **Urine Protein-to-Creatinine Ratio (UPCR):** Quantifies proteinuria (>3.5 g/day in nephrotic syndrome).

• **Renal Biopsy:** See below for indications.

When to Do a Renal Biopsy

Indications:

• **Unclear Diagnosis:** Atypical presentation, uncertain etiology (e.g., nephritic vs. nephrotic features).

• **RPGN:** Rapid decline in renal function with hematuria, proteinuria (to identify crescentic GN, e.g., anti-GBM, ANCA).

• **Systemic Disease with Renal Involvement:** SLE, vasculitis, suspected cryoglobulinemia.

• **Persistent Proteinuria/Hematuria:** Unexplained proteinuria >1 g/day or persistent hematuria after initial workup.

• **Failure to Respond:** No improvement with empirical treatment (e.g., post-infectious GN not resolving).

Contraindications:

• Uncontrolled hypertension, coagulopathy, solitary kidney, active infection at biopsy site.

• End-stage renal disease (ESRD) with small kidneys (<9 cm, unlikely to change management).

Findings:

• **Anti-GBM:** Linear IgG deposition along GBM.

• **ANCA Vasculitis:** Pauci-immune crescentic GN (minimal immune deposits).

• **Post-Infectious GN:** Subepithelial humps, granular IgG/C3.

• **IgA Nephropathy:** Mesangial IgA deposits.

• **Lupus Nephritis:** Full house staining (IgG, IgA, IgM, C3, C1q).

Different Causes of Glomerulonephritis

Primary GN:

• **IgA Nephropathy (Berger's Disease):** Most common; mesangial IgA deposits; presents with gross hematuria post-URI.

• **Membranous Nephropathy:** Subepithelial immune deposits; nephrotic syndrome, often PLA2R antibody positive.

• **Minimal Change Disease (MCD):** Nephrotic syndrome, podocyte effacement; common in children, also adults (e.g., NSAID-related).

• **Focal Segmental Glomerulosclerosis (FSGS):** Nephrotic syndrome, segmental scarring; primary or secondary (e.g., HIV, obesity).

• **Membranoproliferative GN (MPGN):** Nephritic/nephrotic overlap, immune complex (HCV, SLE) or complement-mediated (C3GN).

Secondary GN:

• **Post-Infectious GN:** Post-streptococcal (2-4 weeks after pharyngitis/skin infection), endocarditis; low C3, subepithelial humps.

• **Lupus Nephritis (SLE):** Class I-VI; nephritic/nephrotic features, low C3/C4, anti-dsDNA positive.

• **ANCA-Associated Vasculitis:** GPA, MPA; RPGN, hemoptysis, pauci-immune GN.

• **Anti-GBM Disease (Goodpasture's Syndrome):** RPGN, pulmonary hemorrhage, linear IgG on biopsy.

• **Cryoglobulinemic GN:** HCV-related, nephritic syndrome, purpura, low C4, cryoglobulins positive.

• **Henoch-Schönlein Purpura (HSP):** IgA vasculitis; purpura, arthralgias, nephritic syndrome.

• **Infectious Causes:** HBV, HIV (e.g., HIV-associated nephropathy, FSGS-like).

Hospital Management of Glomerulonephritis in Adults

Hospital management of GN focuses on stabilizing patients with acute presentations (e.g., RPGN, pulmonary hemorrhage, AKI), initiating treatment, and addressing complications.

• Initial Stabilization:

o Fluid Management: IV fluids for hypovolemia (e.g., NS 500 mL bolus); cautious in pulmonary edema (use diuretics, e.g., furosemide 40 mg IV).

o Blood Pressure Control: Target <130/80 mmHg; ACEi/ARB (e.g., lisinopril 10 mg PO daily) if proteinuria; IV agents (e.g., nicardipine 5-15 mg/h) for hypertensive emergency.

o Dialysis: Urgent if AKI with life-threatening complications (e.g., hyperkalemia, uremia, pulmonary edema); hemodialysis preferred.

• Immunosuppression:

- RPGN (Anti-GBM, ANCA, Lupus):
  - **Induction:** Methylprednisolone 500-1000 mg IV daily x 3 days, then prednisone 1 mg/kg/day PO (max 60 mg).
  - **Cyclophosphamide:** 15 mg/kg IV q2-3 weeks (ANCA, severe lupus nephritis) or rituximab 375 mg/m² IV weekly x 4 doses (ANCA).
  - **Plasma Exchange:** 7-10 sessions over 2 weeks for anti-GBM, ANCA with pulmonary hemorrhage, or severe lupus nephritis.
- Post-Infectious GN:
  - **Supportive:** Usually self-limiting; salt restriction, diuretics for edema (furosemide 40 mg IV), treat infection (e.g., penicillin for strep).
  - **Steroids:** Rarely needed unless RPGN (e.g., methylprednisolone 500 mg IV daily x 3 days).
- IgA Nephropathy:
  - **Supportive:** ACEi/ARB for proteinuria; salt restriction.
  - **Severe (RPGN):** Prednisone 1 mg/kg/day PO x 4-6 weeks; cyclophosphamide if crescents >50%.
- Lupus Nephritis (Class III/IV):
  - **Induction:** Methylprednisolone 500 mg IV daily x 3 days, then prednisone 1 mg/kg/day PO + mycophenolate mofetil (MMF) 2-3 g/day PO or cyclophosphamide.
  - **Maintenance:** MMF or azathioprine 2 mg/kg/day PO.

• Management of Complications:

- Pulmonary Hemorrhage (Goodpasture's, ANCA):
  - **Supportive:** Oxygen, intubation if respiratory failure (low tidal volumes 6 mL/kg).
  - **Immunosuppression:** Methylprednisolone 1 g IV daily x 3 days, cyclophosphamide 15 mg/kg IV.

- **Plasma Exchange:** 7-10 sessions for diffuse alveolar hemorrhage.
- **Monitoring:** Daily chest X-ray/CT, hemoglobin, ABG.

- AKI/Hyperkalemia:
  - **Dialysis:** For K+ >6.5 mEq/L, acidosis (pH <7.2), or uremia (e.g., pericarditis, encephalopathy).
  - **Medical:** Kayexalate 30 g PO, insulin/dextrose (10 units IV insulin + D50W 50 mL), calcium gluconate 1 g IV for cardiac protection.
- Infection (Steroid/Cyclophosphamide Risk):
  - **Antibiotics:** Broad-spectrum (e.g., cefepime 2 g IV q8h + vancomycin 15 mg/kg IV q12h) if infection suspected.
  - **Prophylaxis:** TMP-SMX 1 DS tab PO daily (PCP prophylaxis) during high-dose immunosuppression.

• Monitoring:

- Daily Cr, urine output, urinalysis (RBC casts resolution).
- **Serial labs:** K+, pH, albumin, complement (C3/C4 normalization in post-infectious GN).
- Blood pressure, weight (fluid status).

Complications

• Renal:

o ESRD: 20-30% of RPGN cases progress to dialysis within 1 year if untreated.

o Chronic Kidney Disease (CKD): Persistent proteinuria, hypertension (e.g., IgA nephropathy).

• Systemic:

o Pulmonary hemorrhage (Goodpasture's, ANCA): Respiratory failure, ARDS.

o Sepsis: Immunosuppression increases risk (mortality 10-20% in severe cases).

• Treatment-Related:

o Steroids: Osteoporosis, diabetes, infection risk.

o Cyclophosphamide: Hemorrhagic cystitis, infertility, malignancy (e.g., bladder cancer).

o Rituximab: Infusion reactions, infections (e.g., HBV reactivation).

Prognosis

• **Post-Infectious GN:** Excellent in children (>90% recover); adults 60-80% recover, 10-20% progress to CKD.

• **IgA Nephropathy:** 20-40% progress to ESRD over 20 years; worse with heavy proteinuria, hypertension.

• **Lupus Nephritis:** Class III/IV 5-year renal survival 70-80% with treatment; worse if untreated.

• **ANCA Vasculitis:** 5-year survival 70-80% with treatment; poor if untreated (90% mortality within 1 year).

• **Anti-GBM Disease:** Poor prognosis if untreated (80% ESRD); 5-year survival 60-70% with treatment.

Key Pearls

• **Presentation:** Hematuria, proteinuria, edema, hypertension; systemic symptoms (rash, hemoptysis) suggest vasculitis/SLE.

• **Differential:** RPGN (anti-GBM, ANCA, lupus), nephritic (post-infectious, IgA), nephrotic (MCD, FSGS).

• **Labs:** Urinalysis (RBC casts), ANCA, ANA, complement, anti-GBM, ASO.

• **Renal Biopsy:** For unclear diagnosis, RPGN, systemic disease, persistent proteinuria/hematuria.

• **Causes:** Primary (IgA, membranous), secondary (post-infectious, lupus, vasculitis, anti-GBM).

• **Hospital Management:** Fluids, BP control, dialysis if needed; immunosuppression (steroids, cyclophosphamide, plasma exchange); treat complications (pulmonary hemorrhage, sepsis).

• **Prognosis:** Variable; best for post-infectious, worst for anti-GBM if untreated.

References

• **UpToDate:** “Glomerulonephritis: Diagnosis and Management” (2025). UpToDate GN

• **KDIGO:** “Guidelines for Glomerulonephritis” (2024). KDIGO Guidelines

• **ASN:** “Management of Rapidly Progressive Glomerulonephritis” (2023). ASN Guidelines

• **NEJM:** “Advances in the Treatment of Lupus Nephritis” (2024). NEJM Lupus

Case Scenarios

Case 1: A 38-Year-Old Male with Hematuria and Dyspnea

- Presentation: A 38-year-old male presents with 1 week of hematuria, cough, and dyspnea. Exam shows T 38°C, BP 150/95 mmHg, RR 24/min, SpO2 90% on room air, crackles in lungs, 2+ edema.
- Labs/Imaging: **Cr 3.0 mg/dL (baseline 1.0), urinalysis:** RBC casts, hematuria. Anti-GBM antibodies positive. CT chest: Diffuse alveolar hemorrhage.
- Diagnosis: Anti-GBM Disease (Goodpasture’s Syndrome) → Hematuria, dyspnea, anti-GBM positive, hemorrhage.
- Management: Admit to ICU. Start methylprednisolone 1 g IV daily x 3 days, then prednisone 1 mg/kg/day PO. Cyclophosphamide 15 mg/kg IV. Initiate plasma exchange (7 sessions). Oxygen via high-flow nasal cannula (SpO2 >90%). Monitor Cr (improves to 2.0 mg/dL), chest X-ray (hemorrhage resolving). Discharge with nephrology follow-up.

Case 2: A 45-Year-Old Female with Rash and AKI

- Presentation: A 45-year-old female with SLE presents with rash, arthralgias, and decreased urine output for 2 weeks. Exam shows T 37.5°C, BP 160/100 mmHg, malar rash, 2+ edema.
- Labs/Imaging: **Cr 2.5 mg/dL (baseline 0.8), urinalysis:** Proteinuria, hematuria, RBC casts. ANA positive, anti-dsDNA positive, C3/C4 low. Renal biopsy: Class IV lupus nephritis.
- Diagnosis: Lupus Nephritis (Class IV) → Rash, AKI, SLE, biopsy findings.
- Management: Admit for treatment. Start methylprednisolone 500 mg IV daily x 3 days, then prednisone 1 mg/kg/day PO. Mycophenolate mofetil 2 g/day PO. Lisinopril 10 mg PO daily (BP, proteinuria). Monitor Cr (improves to 1.5 mg/dL), UPCR (decreases). Discharge with rheumatology follow-up.

Case 3: A 30-Year-Old Male with Hematuria Post-URI

- Presentation: A 30-year-old male presents with gross hematuria and edema 3 weeks after a sore throat. Exam shows T 37°C, BP 145/90 mmHg, periorbital edema, 1+ pitting edema.

- Labs/Imaging: **Cr 1.2 mg/dL, urinalysis:** Hematuria, RBC casts. ASO titer elevated, C3 low. Renal ultrasound: Normal kidneys.
- Diagnosis: Post-Streptococcal GN → Hematuria, edema, post-URI, low C3.
- Management: Admit for supportive care. Start furosemide 40 mg IV BID (edema). Lisinopril 10 mg PO daily (BP control). Salt restriction, monitor urine output (improves). C3 normalizes at 2 weeks. No steroids (self-limiting). Discharge with nephrology follow-up.