Post-Infectious Glomerulonephritis (PSGN vs IRGN): Diagnosis & Prognosis

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Post-Infectious Glomerulonephritis (PSGN vs IRGN): Diagnosis & Prognosis

Definition & Epidemiology

PSGN = Acute GN following streptococcal infection (usually throat; skin infection possible)

IRGN = Acute GN following ANY infection (broader term; includes non-streptococcal causes)

Key Distinction

- **PSGN:** Specifically Group A Streptococcus (GAS); classic "post-streptococcal"
- **IRGN:** Any infection → GN (Staph, Gram-negatives, fungi, viruses; more common now)

Epidemiology: - **Peak incidence:** Children 6–12 years old (PSGN most common) - **Rising incidence of IRGN in elderly** (associated with chronic infections, endocarditis) - **Cure rate:** 95% in children; 50–60% full recovery in adults (age-dependent)

Pathophysiology: Immune Complex Deposition

Mechanism: Complement-Mediated Glomerulonephritis

Classical pathway activation: 1. **Streptococcal antigen** (M protein, hyaluronic acid) deposited in glomerulus 2. **Anti-streptococcal antibodies** (anti-streptolysin O, ASO; anti-DNase B) bind → immune complexes form 3. **Complement C1q** binds to immune complex → **C1s** activates → **C3 cleaves** 4. **C3a, C5a** (anaphylatoxins) chemotact neutrophils → infiltration 5. **C5b-9** (MAC, membrane attack complex) forms → cell lysis

Result: Acute glomerular inflammation with **heavy C3 deposition**

> [!important] **C3-dominant IF pattern = hallmark of PSGN/IRGN** (vs. IgA GN which is IgA-dominant; vs. lupus which is IgG-dominant)

IRGN: Broader Antigenic Sources

Non-streptococcal causes now ↑ (esp. in elderly): - **Staph aureus** (especially MRSA; right heart endocarditis) - **Gram-negatives:** E. coli, Klebsiella - **Fungal:** Coccidioidomycosis, histoplasmosis - **Viral:** Parvovirus, EBV, HCV - **Parasitic:** Malaria, schistosomiasis

Mechanism often same: Immune complex deposition + C3 activation (Differs slightly: some IRGN = C3GN without C4 ↓; others have mixed patterns)

Clinical Presentation

Typical History (PSGN)

Timeline: - **Throat infection:** Strep pharyngitis 1–3 weeks prior to GN onset - **OR skin infection:** Impetigo (may precede by 3–6 weeks) - Asymptomatic period between infection resolution and GN

Presenting symptoms: - **Hematuria** (macroscopic or microscopic on UA) - **Edema** (periorbital, lower extremities; often morning-prominent) - **Hypertension** (acute onset; may be severe) - **Oliguria** (↓ urine output; mild AKI) - **Dark/cola-colored urine** (RBCs)

Atypical Features (May indicate IRGN or alternate diagnosis)

- **Absence of preceding infection** (consider IgA GN, FSGS, other primary GN)
- **Presentation >3 months post-infection** (PSGN rare if >3 mo; IRGN may persist longer)
- **Absence of hematuria** (atypical; PSGN classically has hematuria)
- **Nephrotic-range proteinuria** (>3.5 g/day; suggests FSGS or membranous, not PSGN)

Diagnostic Workup

1. Clinical & Laboratory Assessment

Test	Finding	Significance
Urinalysis	RBC, RBC casts, dysmorphic RBCs	Confirms glomerulonephritis
Urine culture	Sterile	Rules out infection in urinary tract
Serum Cr	↑ (usually <2–3 mg/dL; rarely >4)	Mild-to-moderate AKI
BMP	↑ K, ↓ HCO_3 (acidosis)	Secondary to oliguria
CBC	Normal (may ↓ Hgb if hematuria chronic)	—

2. Serologic Tests (Essential for PSGN)

Test	Result	Timing	Significance
ASO titer	↑ (>200 Todd units)	Peak 2–4 weeks post-infection	Gold standard for strep confirmation
Anti-DNase B	↑ (>200 units)	Similar timeline	Confirms streptococcal infection
C3	↓ (typically <50 mg/dL)	Returns to normal 6–8 weeks	Complement consumption marker
C4	Normal	—	(↓ in other immune complex GN)
ANCA	Negative	—	Excludes vasculitis
ANA, anti-dsDNA	Negative	—	Excludes lupus
Cryoglobulins	May be positive (IRGN)	—	Suggests chronic infection (HCV?)

> [!tip] **Serologic patterns distinguish PSGN from other GN:** - **PSGN:** ↓C3, normal C4, ↑ASO/anti-DNase B - **Lupus:** ↓C3 and C4 (both), ↑ANA, ↑anti-dsDNA - **ANCA-GN:** Normal C3/C4, ↑ANCA - **IgA GN:** Normal C3/C4, negative serology

3. Renal Biopsy (For Definitive Diagnosis)

Indications: - Atypical presentation (rapid GFR decline, nephrotic proteinuria, delayed recovery) - Diagnostic uncertainty - Severe AKI requiring urgent treatment decision

LM (Light Microscopy) — PSGN: - **Acute proliferative GN:** Hypercellular glomeruli with endocapillary proliferation - **Crescent formation:** Minimal (0–5%); more suggests other diagnosis - **Interstitium:** Mild inflammation

IF (Immunofluorescence) — GOLD STANDARD: - **C3-dominant:** Bright granular C3 deposition (**hallmark**) - **IgG, IgM:** Often present but LESS intense than C3 (vs. lupus which is IgG-dominant) - **C1q:** Often present - **IgA:** Absent (if present, suggests IgA GN instead)

EM (Electron Microscopy): - **"Subepithelial humps"** — large subepithelial immune deposits (pathognomonic for PSGN) - Endothelial proliferation - No "wire-loop" (that's lupus)

PSGN vs IRGN: Key Differences

Feature	PSGN	IRGN
Preceding infection	Strep pharyngitis (1–3 weeks)	Variable (days–months); less acute
Common organisms	GAS (ONLY)	Staph, gram-negatives, fungi, others
C3 pattern	↓ C3 (most); normalizes by 6–8 weeks	Variable; may persist longer if chronic infection
C4	Normal	Normal
ASO/anti-DNase B	Elevated	Negative

Feature	PSGN	IRGN
Proteinuria	Mild-to-moderate (<3 g/day)	Variable; may be heavy (3–10 g/day) in some
Prognosis (children)	>95% recover fully	50–70% recover; 30–50% CKD/ESRD
Prognosis (adults)	50–60% recover fully; 20–30% CKD	30–40% recover; 40–50% CKD/ESRD
Duration to recovery	6–12 weeks (median)	Months–years; may be chronic
Crescent formation	Rare (<5%)	More common (may indicate worse prognosis)

> [!warning] **IRGN has WORSE prognosis than PSGN, especially in adults.** Modern practice: Most "post-infectious GN" are actually IRGN (not streptococcal). Always seek underlying infection source in adults.

Management Strategy

Step 1: Identify & Treat Underlying Infection

CRITICAL: Must treat streptococcal infection even if diagnosed late

Antibiotics for confirmed PSGN: - **Penicillin V:** 250 mg QID × 10 days (oral; typical) - **OR Intramuscular penicillin:** 1.2 MU IM × 1 dose - **If allergic:** Cephalexin 500 mg QID × 10 days (or erythromycin/azithromycin if beta-lactam allergy)

IRGN: Treat underlying infection source - **Endocarditis:** Long-term IV antibiotics (4–6 weeks) - **UTI/bacteremia:** 2–4 weeks IV antibiotics (repeat cultures to confirm eradication) - **Skin infection:** 10–14 days appropriate coverage

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Step 2: Supportive Management

Fluid & electrolyte: - **Fluid restriction** if oliguria + edema/pulmonary edema (restrict to 800 mL/day + UO) - **Na restriction:** <2 g/day (reduces HTN, edema) - **K restriction:** <2 g/day if K >5.5 mmol/L - **Monitor closely:** Daily weights, I&Os, BP trends

Blood pressure control: - **Goal:** Reduce edema; prevent pulmonary edema; protect GFR - **First-line:** Diuretics (furosemide if volume overload) - **Antihypertensives:** ACE-I/ARB (also reduce proteinuria; use cautiously if Cr ↑ >20% post-start) - **Target BP:** <120 mmHg systolic (age-adjusted; avoid hypotension)

Manage AKI if present: - Avoid nephrotoxins (NSAIDs, contrast) - Monitor Cr trend - RRT if needed (hyperkalemia, pulmonary edema, uremia refractory to diuretics)

Step 3: Immunosuppression (RARELY Needed in PSGN)

Indication: ONLY if: - Rapidly progressive GN (RPGN) with crescent formation (>50% glomeruli) - Serum Cr >4 mg/dL with rapid decline - Clinical deterioration despite conservative Rx

Agent: - **Pulse methylprednisolone:** 1 g IV daily × 3 days - **Followed by prednisone:** 1 mg/kg/day × 4 weeks, then taper - ± **Cyclophosphamide:** If severe RPGN

> [!tip] **Steroids NOT routine in PSGN** — most children resolve spontaneously without immunosuppression. Reserve for severe RPGN (rare).

IRGN may benefit from steroids if severe/progressive (especially non-streptococcal)

Step 4: Monitor for Complications

Complication	Mechanism	Management
Hypertensive crisis	Acute HTN from GN inflammation	Nitroglycerin IV, labetalol if encephalopathy
Acute pulmonary edema	Volume overload + HTN	Furosemide IV, diuresis, intubation if severe
Acute kidney injury → ESRD	Severe glomerular necrosis, crescent formation	RRT if needed; monitor trend closely
Persistent hematuria	Ongoing glomerular inflammation	Normal; may persist 6–12 months
Nephrotic syndrome	Proteinuria >3.5 g/day (less common in PSGN)	Diuretics, consider ACEI/ARB if proteinuria heavy

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Prognosis & Long-Term Follow-Up

Children (PSGN)

- **>95% full recovery** of renal function
- **<5% progress to ESRD**
- **Timeline:** Hematuria resolves in months; proteinuria within 6 months
- **Follow-up:** Urine dipstick monthly × 6 months, then 6-monthly × 2 years

Adults (PSGN)

- **50–60% full recovery**
- **20–30% develop CKD** (may progress to ESRD over 10–20 years)
- **10% rapidly progressive** (crescentic disease)
- **Predictors of poor outcome:** Age >50, delayed presentation, severe AKI (Cr >3), heavy proteinuria (>1 g/day)

IRGN (Any Age)

- **30–40% full recovery**
- **40–50% progress to CKD/ESRD**
- **Poor prognosis if:**
  - Underlying infection not eradicated (endocarditis persistence)
  - Heavy proteinuria (>3.5 g/day)
  - Crescent formation on biopsy
  - Delayed diagnosis (serology may be negative)

Related Resources

- Comprehensive PSGN/IRGN Pathophysiology
- AKI Staging & Management
- GN Differential Diagnosis

Self-Test Questions

1. **9-year-old with throat infection 2 weeks ago; now hematuria + edema; Cr 1.2; ↓C3, ↑ASO titer**
   - Diagnosis: PSGN (post-streptococcal GN)
   - Management: Penicillin (if not given); diuretics for edema; BP control; expect spontaneous recovery
   - Prognosis: >95% will recover fully
2. **72-year-old with chronic osteomyelitis, persistent bacteremia, now hematuria + RBC casts, Cr 2.8; ↓C3, negative ASO, positive blood cultures (Staph)**
   - Diagnosis: IRGN (infection-related GN, not PSGN)
   - Management: Aggressive antibiotic therapy (4–6 weeks IV); consider biopsy if RPGN suspected
   - Prognosis: 40–50% will progress to CKD; depends on infection eradication
3. **35-year-old, C3 normalizes at 6 weeks but proteinuria 2 g/day persists, Cr rising to 1.5**
   - Assessment: Recovery from PSGN incomplete; developing CKD component
   - Action: Biopsy? (May show FSGS superimposed or other disease)
   - Management: ACE-I/ARB for proteinuria; continue monitoring Cr

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References: KDIGO Glomerulonephritis Classification & Management. Nasr SH, Fidler ME. PSGN vs IRGN: Current Perspectives. Semin Nephrol. 2021;41(4).