

Nephritic Syndrome

From glomerular inflammation to clinical presentation

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Learning outcomes

- Recognize the clinical pattern of nephritic syndrome and explain each manifestation.
- Link glomerular inflammatory lesions to capillary-wall leakage and reduced GFR.
- Interpret LM, immunofluorescence and electron-microscopy patterns.
- Differentiate key etiologic mechanisms and identify rapidly progressive disease.

Clinical syndromes organize glomerular disease

- Glomerular diseases can be primary or manifestations of systemic disease.
- Nephritic and nephrotic presentations reflect different dominant injury patterns.
- A clinical syndrome narrows the differential but does not establish etiology.

From kidney injury to clinical phenotype

Site and mechanism of glomerular damage

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graph TD; A[Site and mechanism of glomerular damage] --> B[Inflammatory capillary injury → nephritic pattern]; A --> C[Podocyte/barrier injury → nephrotic pattern]; A --> D[Overlapping injury → mixed presentation];
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Inflammatory capillary injury
→ nephritic pattern

Podocyte/barrier injury →
nephrotic pattern

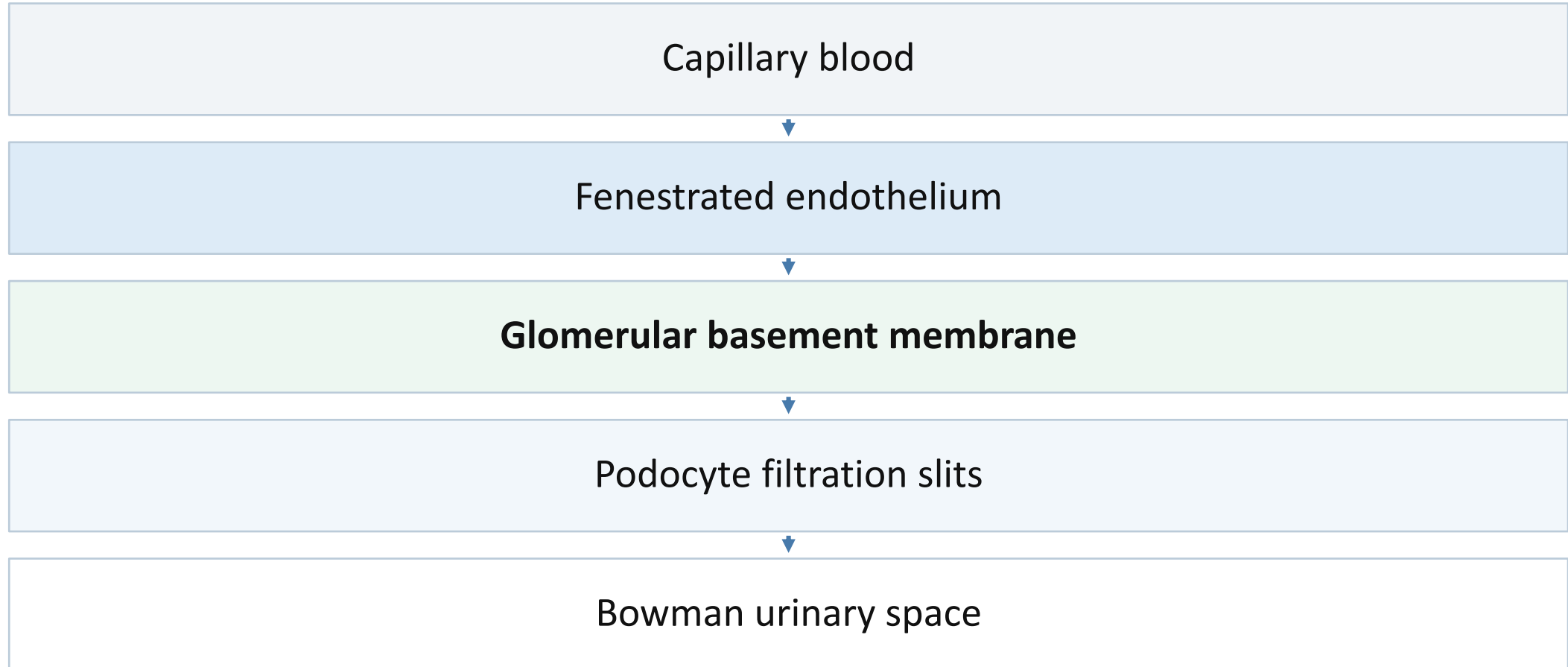
Overlapping injury → mixed
presentation

Original editable conceptual diagram — not a histological specimen

The nephritic syndrome is an inflammatory phenotype

- Glomerular inflammation defines the pathologic substrate.
- Hematuria is prominent because injured capillary walls permit red cells to escape.
- Reduced filtration produces oliguria, azotemia, sodium and water retention.

Filtration barrier: Where nephritic injury acts



Schematic: Filtration passes from capillary lumen toward urinary space

The classic clinical constellation

- Hematuria: Microscopic or macroscopically visible, often with RBC casts.
- Proteinuria: Usually subnephrotic; Edema may accompany fluid retention.
- Reduced GFR: May produce oliguria and biochemical azotemia.
- Hypertension: Commonly related to retention of fluid and renal hemodynamics.

A single lesion produces two functional consequences

Glomerular cellular proliferation + inflammatory infiltration



Capillary-wall damage → red cells / protein enter urinary space



Capillary-flow impairment → reduced GFR

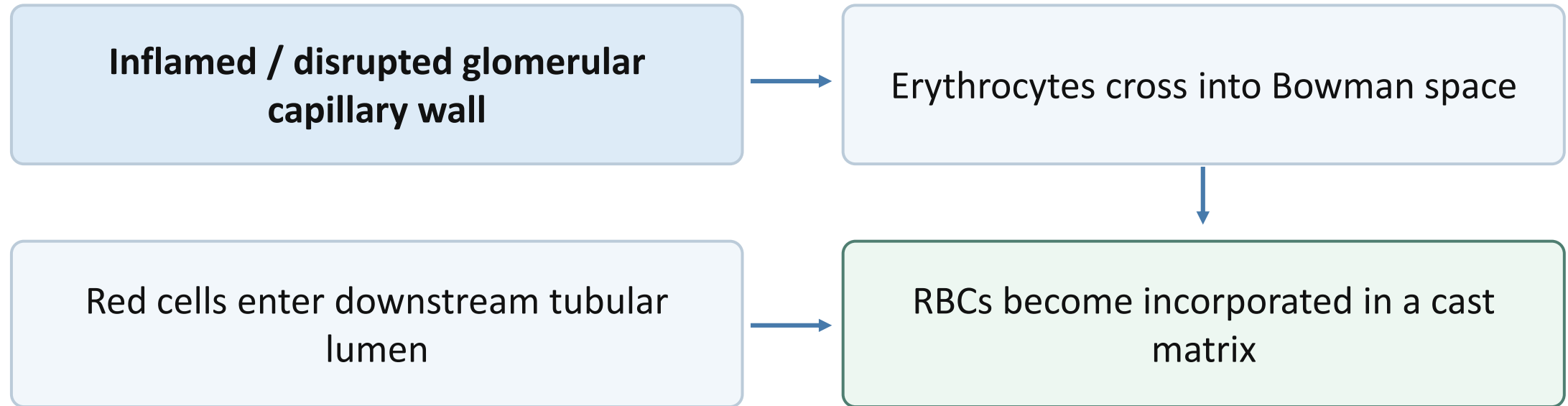


Urinary abnormalities + fluid retention + azotemia

Hematuria is the defining urinary clue

- Erythrocytes pass through inflamed, damaged glomerular capillary walls.
- Hematuria can be visible or detected only by microscopic examination.
- A glomerular source is supported by dysmorphic erythrocytes and RBC casts.

Why red cell casts localize bleeding to the nephron



Schematic explanation of the glomerular–tubular sequence; Not urine microscopy

Proteinuria is usually below nephrotic intensity

- Inflammatory glomerular capillary damage allows protein leakage.
- The usual degree is mild to moderate rather than massive.
- Subnephrotic proteinuria does not exclude severe loss of GFR.

Nephritic versus nephrotic: Dominant injury

Nephritic

- Inflammatory glomerular injury
- Hematuria and RBC casts
- Azotemia, oliguria, hypertension

Nephrotic

- Severe filtration-barrier dysfunction
- Heavy protein loss and hypoalbuminemia
- Generalized edema and lipid abnormalities

Why glomerular inflammation decreases GFR

Endothelial / mesangial proliferation and leukocyte accumulation



Capillary lumina become narrowed or obliterated



Effective glomerular filtration falls



Oliguria and retention of nitrogenous solutes

Oliguria: A functional consequence

- Urine output can fall because inflamed glomeruli filter less plasma.
- Severe oliguria suggests important loss of filtration and may signal RPGN.
- Oliguria should be interpreted together with renal function and urinary sediment.

Edema follows impaired excretion

Inflammatory glomerular disease → reduced GFR



Reduced renal sodium and water excretion



Extracellular fluid retention



Edema; Sometimes conspicuous around the eyes

Mechanisms of hypertension in nephritic syndrome

Glomerular inflammation and reduced perfusion



Sodium / water retention + renin release from ischemic kidneys



Expansion of circulating volume and vasoconstrictor influence



Elevated systemic blood pressure

Azotemia reflects diminished filtration

- Elevated blood urea nitrogen and serum creatinine define azotemia.
- Reduced GFR limits elimination of nitrogenous metabolic products.
- Azotemia denotes impaired excretory function; Uremia includes systemic manifestations.

Mechanistic correspondence at the bedside

Finding	Underlying pathophysiology
RBCs / RBC casts	Capillary-wall inflammatory damage with glomerular bleeding
Subnephrotic proteinuria	Increased permeability of injured capillary wall
Oliguria and azotemia	Reduced filtration as capillary lumina narrow
Edema / hypertension	Sodium–water retention; renin release may contribute

Inflammation, not simply permeability, is central

- Nephritic lesions typically show proliferative glomerular injury.
- Intrinsic glomerular cells multiply or swell while leukocytes enter.
- Severe reactions may disrupt capillary walls and culminate in crescents.

Components of glomerular hypercellularity

Inflammatory glomerular hypercellularity

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graph TD; A[Inflammatory glomerular hypercellularity] --> B[Endothelial cell proliferation / swelling]; A --> C[Mesangial cell proliferation]; A --> D[Neutrophil / monocyte infiltration];
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Endothelial cell proliferation /
swelling

Mesangial cell proliferation

Neutrophil / monocyte
infiltration

Original editable conceptual diagram — not a histological specimen

Endocapillary proliferation compromises blood flow

- Enlarged glomeruli become hypercellular in acute proliferative GN.
- Intracapillary cell accumulation and endothelial swelling narrow capillary lumina.
- These changes account for reduced filtration and acute functional impairment.

Mesangial proliferation is part of the response

- Mesangial cells can proliferate in many immune-mediated glomerular injuries.
- Some diseases show predominantly mesangial rather than diffuse endocapillary changes.
- The location and distribution of proliferation help refine the differential.

Leukocyte influx amplifies capillary injury

- Neutrophils and monocytes may enter inflamed glomerular tufts.
- Inflammatory mediators contribute to endothelial and GBM damage.
- The combined injury enables escape of blood into the urinary space.

Severe injury can progress beyond endocapillary GN

Intense immunologic and inflammatory capillary injury



Focal necrosis and breaks in glomerular basement membrane

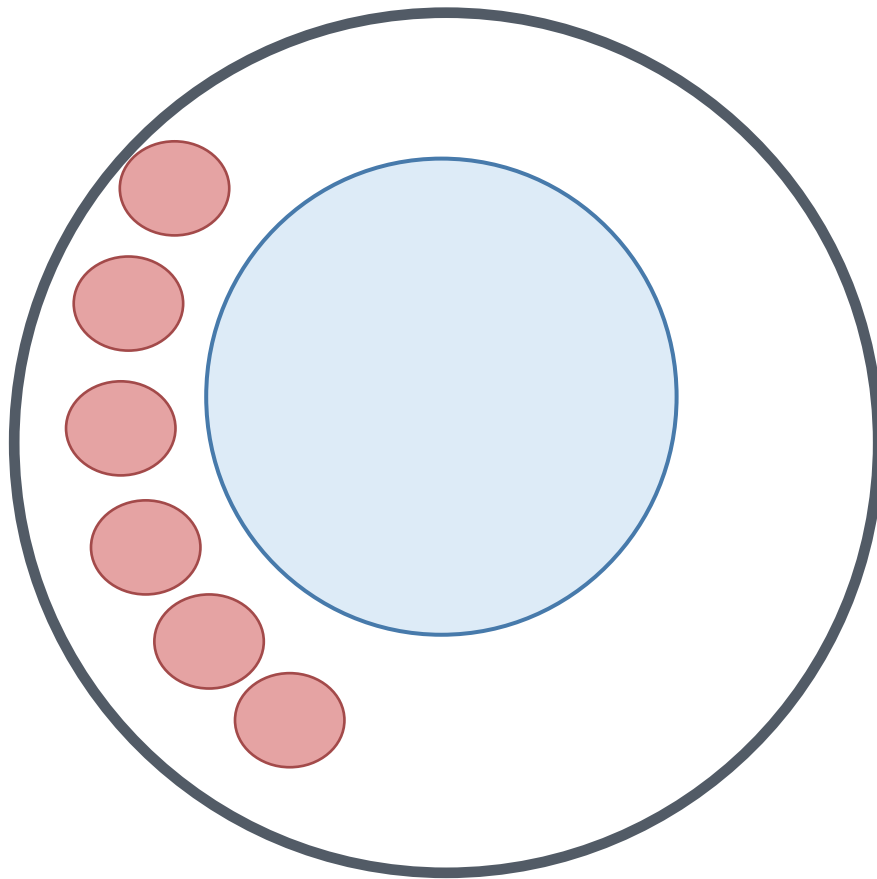


Fibrin and inflammatory mediators enter Bowman space



Extracapillary cellular proliferation produces crescents

Crescent formation: Breach of the filtration barrier



Tuft necrosis + GBM rupture

Inflammatory mediators and fibrin enter urinary space

Extracapillary proliferation

Parietal epithelial cells and macrophages form a crescent

Simplified schematic — not a light-microscopy image

Acute inflammatory lesions versus chronic damage

Active injury

- Cellular hypercellularity and leukocytes
- Segmental necrosis or cellular crescents
- Potential reversibility depends on mechanism and timing

Chronic injury

- Organized fibrous crescents
- Glomerulosclerosis and tubular fibrosis
- Persistent loss of filtering nephron mass

Most causes arise from immune-mediated injury

- Antibody-mediated glomerular damage can activate complement and recruit leukocytes.
- Immune complexes are common; Other injury involves anti-GBM autoantibodies.
- ANCA-associated pauci-immune disease causes necrotizing inflammation without conspicuous deposits.

Three major immune patterns

Inflammatory glomerular injury

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graph TD; A[Inflammatory glomerular injury] --> B[Immune-complex mediated: Granular deposits]; A --> C[Anti-GBM antibody mediated: Linear IgG]; A --> D[Pauci-immune / ANCA related: Sparse deposits];
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Immune-complex mediated:
Granular deposits

Anti-GBM antibody mediated:
Linear IgG

Pauci-immune / ANCA related:
Sparse deposits

Original editable conceptual diagram — not a histological specimen

Immune-complex glomerulonephritis

Circulating complexes or in-situ complexes involving glomerular antigens



Complexes lodge / form in defined glomerular compartments



Complement and leukocyte responses damage capillary walls



Proliferative GN and nephritic urinary changes

Why immune complexes appear granular

- Deposited complexes occur as discontinuous foci along the capillary wall or mesangium.
- Immunofluorescence reveals punctate deposits of immunoglobulin and/or complement.
- The pattern supports immune-complex deposition; It is not a disease-specific diagnosis.

Anti-GBM antibody disease

Autoantibodies recognize intrinsic GBM antigen



Antibody binding occurs along the continuous basement membrane



Inflammatory injury can become necrotizing and crescentic



RPGN; Some patients also have pulmonary hemorrhage

Linear immunofluorescence indicates anti-GBM binding

- Anti-GBM autoantibodies bind antigens distributed along the GBM.
- This produces diffuse linear staining for immunoglobulin on IF.
- The linear pattern differs mechanistically from granular immune-complex deposition.

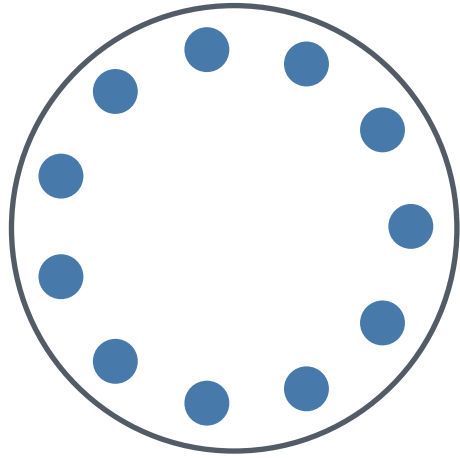
Pauci-immune GN: Destructive injury with few deposits

- Immunofluorescence and EM show little or no immune-complex deposition.
- Many patients have circulating PR3-ANCA or MPO-ANCA.
- The associated lesion often includes segmental fibrinoid necrosis and crescents.

C3-dominant disease points to complement dysregulation

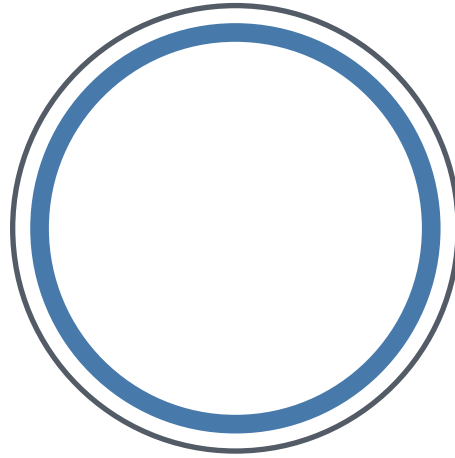
- Predominant C3 with limited immunoglobulin may indicate abnormal alternative-pathway regulation.
- Most C3-related glomerular disease has noncrescentic patterns; Rarely it is crescentic.
- C3-dominant staining requires integration with microscopy and complement studies.

Immunofluorescence patterns: Conceptual comparison



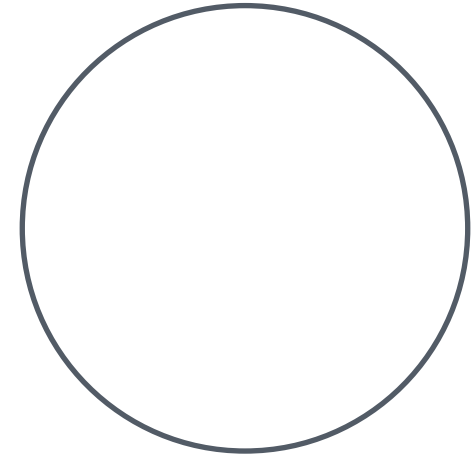
Granular deposits

Discrete immune-complex foci



Linear staining

Antibody to continuous GBM
antigen



Pauci-immune

Little or no immune deposition

Schematic patterns only — not clinical immunofluorescence micrographs

Three microscopy modalities answer different questions

Modality	What it establishes
Light microscopy	Site, activity and distribution of proliferation, necrosis, crescents, scarring
Immunofluorescence	Type and spatial pattern of Ig / complement deposits
Electron microscopy	Ultrastructural localization of deposits and GBM disruption

Electron microscopy localizes immune deposits

- Subepithelial deposits lie on the podocyte-facing side of the GBM.
- Subendothelial deposits lie nearer the capillary lumen; Mesangial deposits occupy the mesangium.
- Site and morphology of deposits provide etiologic clues in context.

Deposit location changes interpretation

EM: Glomerular immune-complex location

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graph TD; A[EM: Glomerular immune-complex location] --> B[Subepithelial: Classic postinfectious humps]; A --> C[Mesangial: Prominent in IgA nephropathy]; A --> D[Subendothelial: Inflammatory immune GN];
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Subepithelial: Classic
postinfectious humps

Mesangial: Prominent in IgA
nephropathy

Subendothelial: Inflammatory
immune GN

Original editable conceptual diagram — not a histological specimen

Postinfectious GN: A prototype nephritic disease

- Immune complexes involving microbial antigens drive cellular proliferation and leukocyte influx.
- Streptococcal infection is classic, but other bacterial, viral and parasitic infections occur.
- The clinical pattern combines hematuria, reduced filtration and hypertension or edema.

Poststreptococcal GN: A latent immune response

Pharyngeal or skin infection by nephritogenic streptococci



Delay while antigen-specific immune response develops



Immune-complex formation with complement activation



Acute nephritic syndrome after infection

Postinfectious GN: Pathogenesis from antigen to tuft

- Circulating or planted microbial antigens interact with antibodies.
- Complement activation recruits inflammatory cells and stimulates hypercellularity.
- Streptococcal pyogenic exotoxin B is implicated in many poststreptococcal cases.

Postinfectious GN: Light-microscopy phenotype

- Typical lesions show diffuse, global endocapillary proliferation.
- Neutrophils and monocytes contribute to marked hypercellularity.
- Capillary lumina narrow; Severe cases can show crescents and tubular RBC casts.

Postinfectious GN: Characteristic immune deposits

- Immunofluorescence commonly shows granular IgG and C3 in GBM and mesangium.
- Electron microscopy classically shows subepithelial electron-dense humps.
- Early subendothelial and other deposits also may be found.

Complement consumption supports the mechanism

- Activation of complement can reduce circulating C3 in postinfectious GN.
- Antistreptococcal antibody titers may support a recent streptococcal trigger.
- Neither laboratory result should be treated as a substitute for clinicopathologic correlation.

Postinfectious GN: Children and adults

Typical pediatric presentation

- Acute illness after recent infection
- Smoky urine, edema, oliguria
- Many children recover renal function

Adult presentation

- May be less typical or overt
- New hypertension, edema or azotemia
- Outcome may be less favorable

Rapidly progressive GN is a clinical urgency

- RPGN is defined by rapid decline in glomerular filtration with a nephritic picture.
- Severe oliguria and azotemia can develop over a short interval.
- Crescents often dominate the biopsy, but RPGN is a clinical syndrome rather than one cause.

RPGN: Why filtration may deteriorate rapidly

Necrotizing capillary-wall inflammation



GBM rupture and fibrin leakage



Cellular crescents compress glomerular tufts



Abrupt decline in functioning capillary surface and GFR

RPGN morphology: Crescents and necrosis

- Cellular crescents occupy Bowman space and may compress the tuft.
- Pauci-immune lesions characteristically show segmental fibrinoid necrosis.
- Fibrous crescents indicate organization or longer-standing injury.

RPGN immunopathologic classification

Mechanism	IF signature	Examples / clue
Anti-GBM	Linear IgG $\pm$ C3	Renal-limited disease or pulmonary–renal syndrome
Immune complex	Granular Ig / complement	Postinfectious GN; lupus; IgA-associated disease
Pauci-immune	Sparse / absent deposits	ANCA-associated vasculitis; renal-limited forms

Anti-GBM disease may involve lung and kidney

- Target antigen lies in the noncollagenous region of type IV collagen $\alpha 3$ chain.
- The shared basement-membrane antigen explains pulmonary and renal injury in some patients.
- Pulmonary hemorrhage together with nephritic renal failure is a major diagnostic clue.

Systemic immune disease can present nephritically

- Proliferative lupus nephritis is an important example of systemic immune-complex GN.
- IgA-related glomerular disease and IgA vasculitis can produce nephritic injury.
- Clinical assessment must look beyond the kidney when immune GN is suspected.

ANCA-related injury may be renal-limited or systemic

- Pauci-immune crescentic GN can accompany granulomatosis with polyangiitis.
- Microscopic polyangiitis is another associated systemic vasculitis.
- Some patients have kidney-limited pauci-immune glomerulonephritis.

A nephritic phenotype does not specify one disease

Syndrome-level diagnosis

- Hematuria $\pm$ RBC casts
- Subnephrotic proteinuria
- GFR decrease with variable edema and BP rise

Etiology-level diagnosis

- Clinical tempo and systemic features
- Serologic / complement investigations
- Biopsy LM, IF and EM correlation

Clinical tempo helps prioritize differential

Pattern	Example etiologies	Most informative clue
Acute after infection	Postinfectious immune-complex GN	Infection history; complement; granular IF
Rapid functional decline	Crescentic GN of several mechanisms	Crescents / necrosis; anti-GBM, ANCA, IF
Recurrent or systemic	IgA-associated or lupus-related GN	Mesangial IgA or systemic immune features

Urinalysis: Use the sediment, not just dipstick

- Document whether urinary blood is microscopic or visible.
- Examine for dysmorphic erythrocytes and red cell casts.
- Interpret the degree of proteinuria as part of the nephritic versus nephrotic pattern.

A practical diagnostic synthesis

Recognize nephritic urine sediment and altered kidney function



Assess tempo, preceding infection and systemic manifestations



Use serology and complement to narrow candidate mechanisms



Integrate LM + IF + EM if renal biopsy is indicated

Renal biopsy connects syndrome to mechanism

- Light microscopy distinguishes proliferative, necrotizing and crescentic patterns.
- Immunofluorescence separates linear, granular, C3-dominant and pauci-immune patterns.
- Electron microscopy identifies deposits and capillary-wall changes.

Nephritic and nephrotic features can overlap

- Proteinuria is usually subnephrotic but may be heavy in some crescentic cases.
- Some proliferative lupus lesions may generate both nephritic and nephrotic manifestations.
- Syndrome names summarize dominant findings; They are not mutually exclusive categories.

Case 1 — an acute postinfectious pattern

Illustrative clinical vignette

A school-aged child develops dark urine, periorbital edema and reduced urine volume after recovery from a throat infection.

Interpret the pattern

- Which findings establish the nephritic clinical pattern?
- Which LM, IF and EM features would support postinfectious GN?

Case 1 — integrated interpretation

- Dark urine, edema and oliguria point to glomerular inflammation with reduced GFR.
- Postinfectious GN predicts diffuse endocapillary hypercellularity with leukocytes.
- Granular IgG / C3 and subepithelial humps would support the immune-complex mechanism.

Case 2 — a rapidly progressive pattern

Illustrative clinical vignette

An adult develops new hematuria, marked azotemia and quickly falling urine output. Biopsy shows necrosis and numerous cellular crescents.

Interpret the pattern

- Why does the rate of functional decline alter urgency?
- What IF patterns divide the principal mechanistic categories?

Case 2 — classification by IF and serology

- Linear GBM staining suggests anti-GBM antibody disease.
- Granular deposits support immune-complex GN.
- Little or no deposition raises pauci-immune, often ANCA-associated GN.

Why persistent glomerular injury leaves permanent damage

Active glomerular damage with nephron loss



Compensatory stress on remaining nephrons



Glomerulosclerosis and secondary tubular / interstitial injury



Progressive loss of kidney function

Diagnostic pitfalls to avoid

- Do not equate every episode of hematuria with nephritic syndrome without evaluating GFR, sediment and BP.
- Do not assign a specific immune mechanism from light microscopy alone.
- Do not assume absence of heavy proteinuria implies mild renal injury.
- Do not equate the presence of crescents with a single etiology.

Core pathologic reasoning: Four propositions

- Nephritic syndrome reflects inflammation within the glomeruli.
- Capillary-wall damage explains red cells and protein in the urine.
- Cellular proliferation and inflammation impair filtration and cause systemic consequences.
- Immunopathology identifies the process; Severe necrotizing lesions may cause RPGN.

Primary reference and source limitations

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th edition (2026), renal pathology chapter.
- The lecture uses the nephritic syndrome discussion and adjacent glomerular-disease mechanisms.
- Conceptual diagrams are editable educational schematics, not diagnostic photomicrographs.
- Original chapter PDF / figure plates were not supplied for direct visual verification.