

Acute Proliferative Glomerulonephritis

Postinfectious and infection-associated forms

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Learning objectives

- Relate microbial antigens and immune complexes to glomerular inflammation.
- Recognize the defining light, immunofluorescence, and electron microscopic findings.
- Connect the pathology with nephritic manifestations and laboratory findings.
- Differentiate typical childhood disease from more variable adult presentations and outcomes.

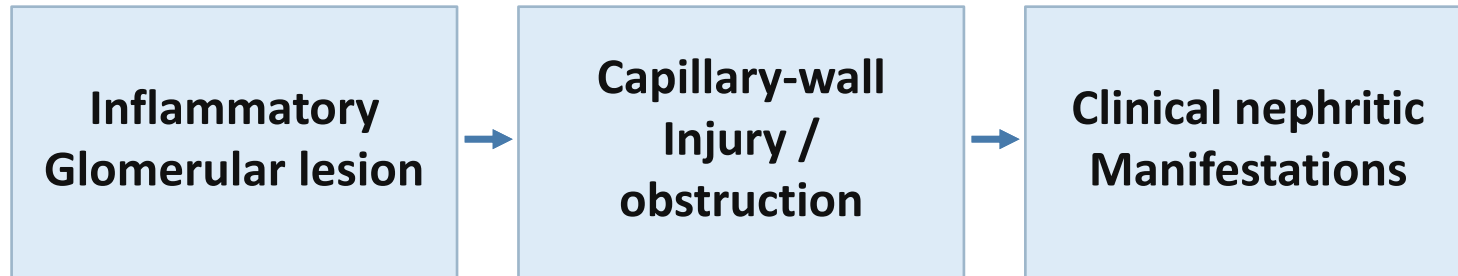
Clinical recognition: A nephritic presentation

Illustrative teaching vignette

- A school-aged child develops dark urine and periorbital puffiness after a sore throat.
- Urinalysis identifies dysmorphic erythrocytes and red-cell casts.
- The question is whether a delayed infection-triggered immune process explains the renal findings.

Which glomerular mechanisms link the infection to the urinary findings?

The lesion belongs to the nephritic spectrum



- Nephritic GN is defined by glomerular inflammation rather than isolated protein leakage.
- A proliferative response and leukocytic infiltration injure glomerular capillary walls.
- Hematuria with erythrocyte casts is the central urinary clue.
- A fall in glomerular filtration leads to oliguria, salt and water retention, and azotemia.

Core definition: Acute proliferative GN

- Immune complexes containing microbial antigens accumulate or form within glomeruli.
- Leukocytes are recruited; Glomerular endothelial and mesangial cells proliferate.
- Diffuse endocapillary hypercellularity produces the characteristic inflammatory lesion.
- The usual clinical expression is an acute nephritic syndrome.

Two related infection contexts

Postinfectious

- Glomerular inflammation follows a preceding microbial illness.
- Classic example: Nephritis after streptococcal pharyngitis or impetigo.
- An intervening latent period supports an adaptive immune response.

Infection-associated

- A comparable immune complex lesion accompanies several bacterial, viral, or parasitic infections.
- The pathogen and clinical context vary.
- Granular immune deposits and humps can occur in nonstreptococcal disease.

Why infections matter in this glomerulopathy



An immune-mediated renal lesion—not direct bacterial invasion of the glomerulus—is the textbook mechanism.

The streptococcal clinical setting

- Group A β -hemolytic streptococcal infection is the classical antecedent.
- Upper respiratory infection and cutaneous infection (impetigo) are recognized triggers.
- The source describes poststreptococcal GN as declining in the United States but remaining important worldwide.
- Not every streptococcal infection is followed by nephritis.

Poststreptococcal GN affects many ages

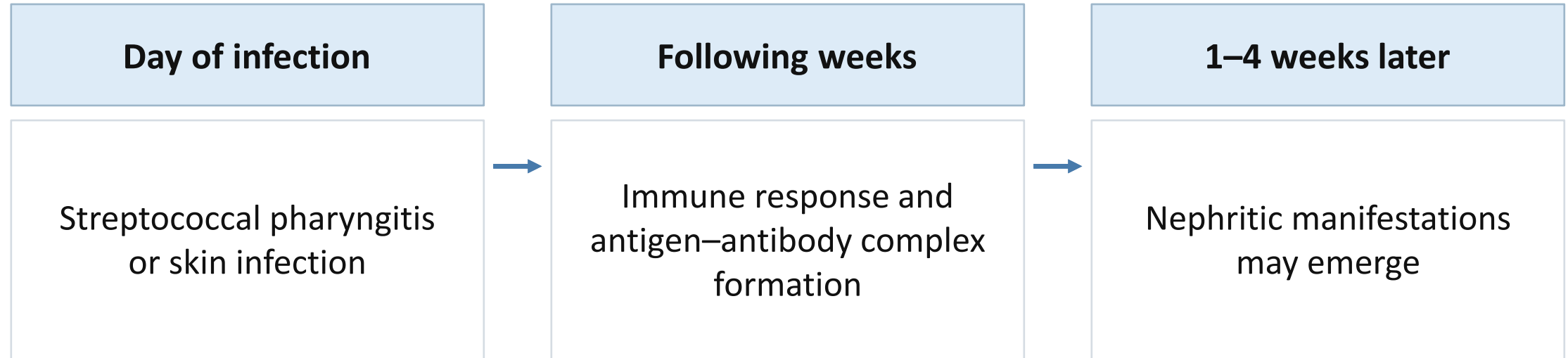
Children

- The source identifies ages 6–10 years as the peak period.
- Classical presentation is often clinically recognizable.
- Renal recovery is common in affected children.

Adults

- Adults of any age may develop the disease.
- Edema, newly recognized hypertension, or azotemia may predominate.
- The clinical and recovery course is less predictably benign.

Latency is part of the pathogenesis



The reported range is a source-based description, not an individually diagnostic time cutoff.

Pharyngitis and impetigo are antecedent sites

Pharyngeal infection

- Sore throat may resolve before edema or hematuria begins.
- A child can develop nephritis after apparent recovery.
- A postinfection interval separates the two illnesses.

Cutaneous infection

- Impetigo is another classical preceding infection.
- The textbook associates skin infection with crowding and limited hygiene.
- The renal syndrome is immune-mediated, not a direct skin-to-kidney spread.

Only some streptococcal strains are nephritogenic

- Susceptibility is linked to particular group A streptococcal strains.
- M-protein typing and classical nephritogenic M types 1, 4, and 12.
- The streptococcal strain acts as an antigenic trigger; It is not a renal pathology marker.
- The clinical diagnosis does not rest on demonstrating a specific M type.

The antigenic candidate: SpeB

- Streptococcal pyogenic exotoxin B (SpeB) is implicated in many cases.
- The source considers SpeB the principal antigen in most—but not all—poststreptococcal cases.
- SpeB has been localized to characteristic hump-like deposits.
- The qualifier matters: No single antigen explains every case.

Four observations support immune complex injury

Latency

Time is needed for antibody formation.

Serology

Antibodies to streptococcal antigens are commonly elevated.

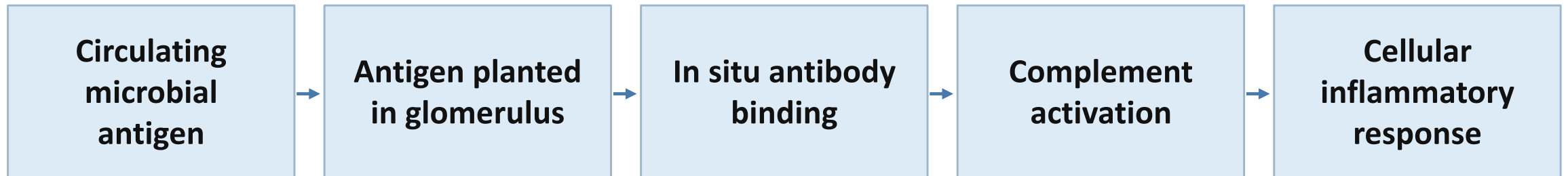
Complement

Serum complement is reduced during activation/consumption.

Deposits

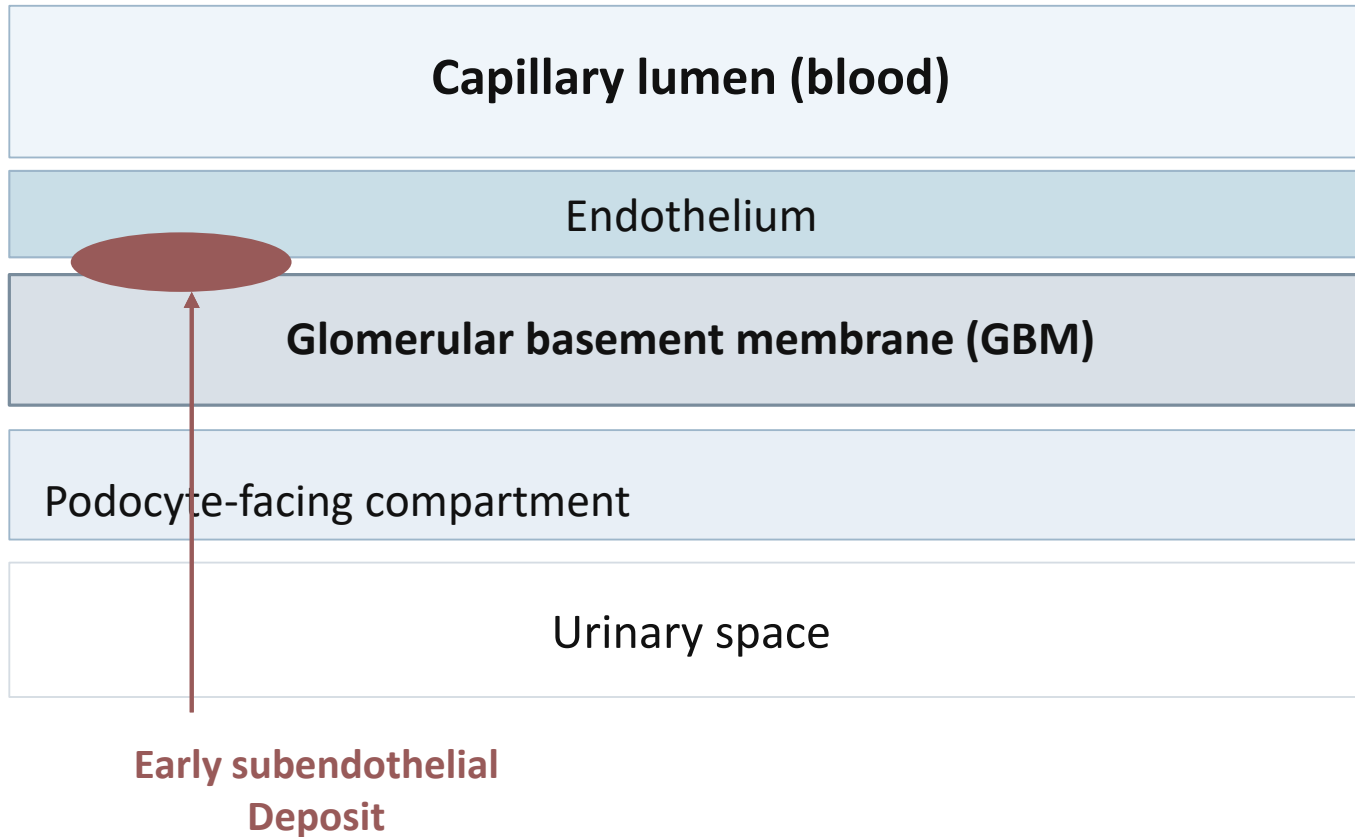
Glomeruli contain granular immune reactants.

Proposed sequence of immune complex formation



The precise intraglomerular sequence is incompletely understood.

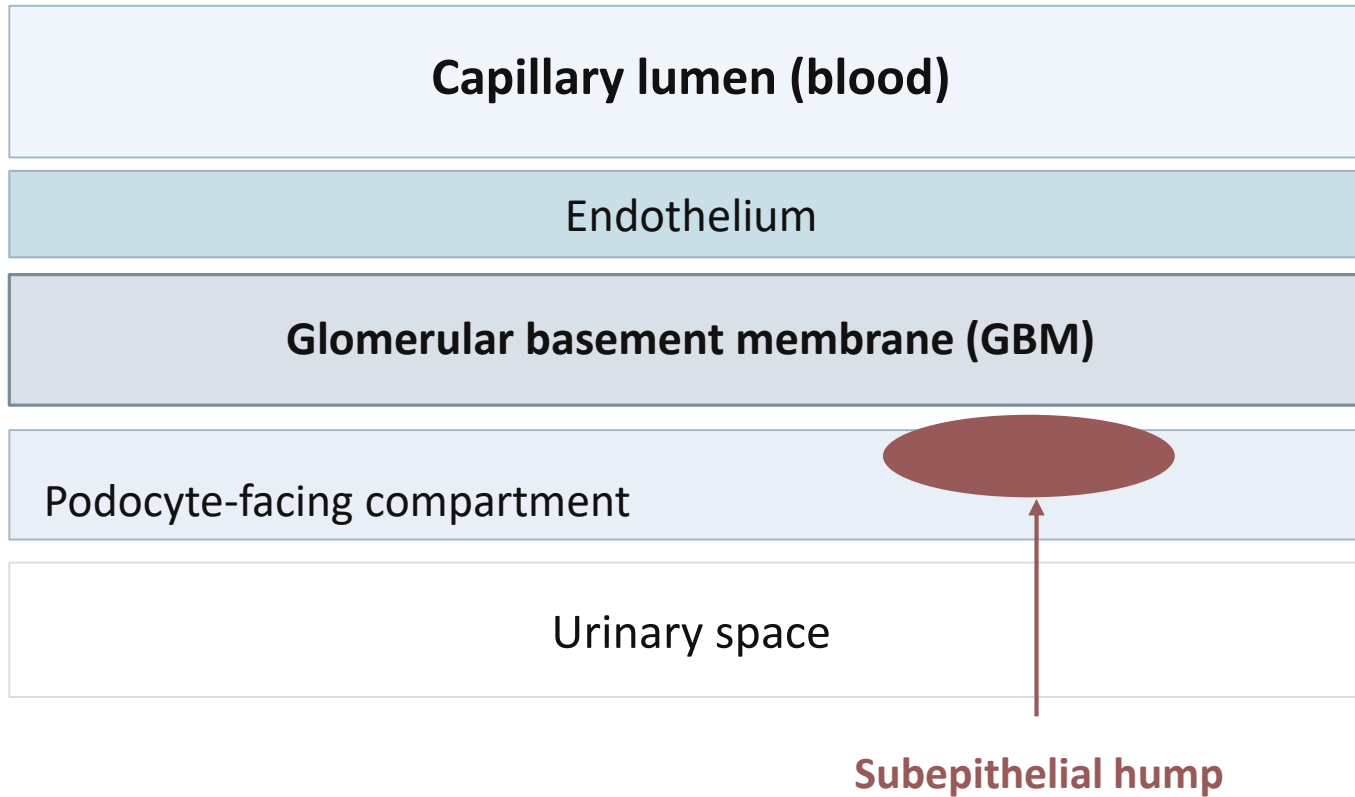
Planted antigens are initially subendothelial



- Circulating exogenous antigens can lodge near the endothelial aspect of capillary walls.
- Specific antibodies bind at these sites and form immune complexes in situ.
- Deposits can provoke inflammation before the characteristic subepithelial pattern develops.

Schematic of capillary-wall compartments — not electron microscopy

Subepithelial humps develop later



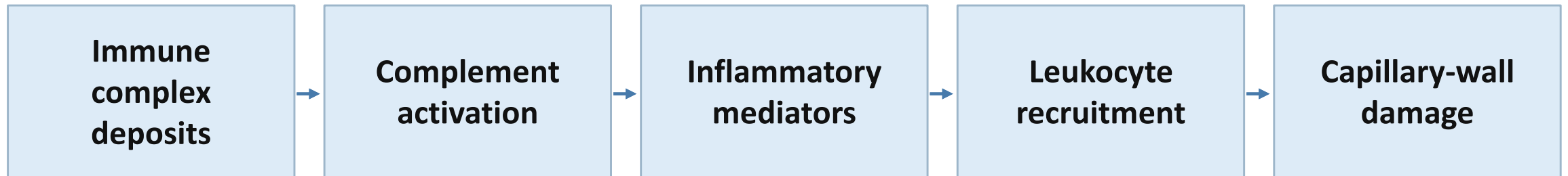
- Dissociation and re-formation of deposits across the GBM.
- The mechanism of this redistribution remains incompletely understood.
- Large subepithelial immune deposits produce the classical electron-microscopic humps.

Schematic of capillary-wall compartments — not electron microscopy

Circulating complexes may contribute

- Antigen–antibody complexes can form in the circulation as well as within glomerular capillary walls.
- The source allows a contribution from circulating immune complex deposition.
- A granular immunofluorescence pattern supports immune complex deposition, not a unique route of formation.
- Mechanistic interpretations should not be presented as proven movement of individual deposits.

Complement links deposition to inflammation



Complement consumption explains the frequently decreased serum C3.

What the low serum C3 signifies

- Complement activation accompanies microbial-antigen immune complex injury.
- Consumption can reduce circulating concentrations of C3 and other complement components.
- A low C3 level is supportive within the clinical context, not independently diagnostic.
- The tissue counterpart is granular C3 deposition in glomeruli.

Leukocytes participate in glomerular injury

- Neutrophils and monocytes infiltrate glomerular capillary loops.
- Infiltration produces an exudative component of the histologic pattern.
- The inflammatory infiltrate contributes to capillary obstruction and wall injury.
- The resulting leakage and filtration deficit explain the nephritic presentation.

Beyond streptococci: Bacterial associations

Bacterial examples

- Staphylococcal endocarditis
- Pneumococcal pneumonia
- Meningococemia

Teaching implication

- A similar immune-complex pattern is not specific to streptococci.
- The underlying infection must be considered in context.
- The renal biopsy must be interpreted alongside the infectious history.

Viral and parasitic associations

Viral examples

- Hepatitis B and hepatitis C
- Mumps, HIV, varicella
- Infectious mononucleosis

Parasitic examples

- Malaria
- Toxoplasmosis
- The listed pathogens are associations, not proof that every infection produces this lesion.

An infection-associated pattern is not organism-specific

- Multiple microbial infections can lead to a broadly similar inflammatory glomerular lesion.
- Granular immune staining and subepithelial humps occur beyond poststreptococcal GN.
- The histologic pattern establishes the type of injury; History and ancillary studies establish the likely association.
- An absent classic sore-throat history does not exclude infection-associated disease.

Morphologic overview: The three diagnostic modalities

Light microscopy

Diffuse endocapillary hypercellularity and leukocytic exudation.

Immunofluorescence

Granular immunoglobulin and C3 deposits in capillary walls/mesangium.

Electron microscopy

Predominantly subepithelial electron-dense humps; Other deposits can coexist.

Light microscopy: Enlarged hypercellular glomeruli

- Glomerular tufts are enlarged because capillary compartments are crowded by cells.
- The increase reflects both infiltrating inflammatory cells and intrinsic cell proliferation.
- The capillary loops become difficult to recognize as their lumina narrow.
- This is an active inflammatory pattern, not primarily sclerosis.

Diffuse and global are different descriptors

Diffuse

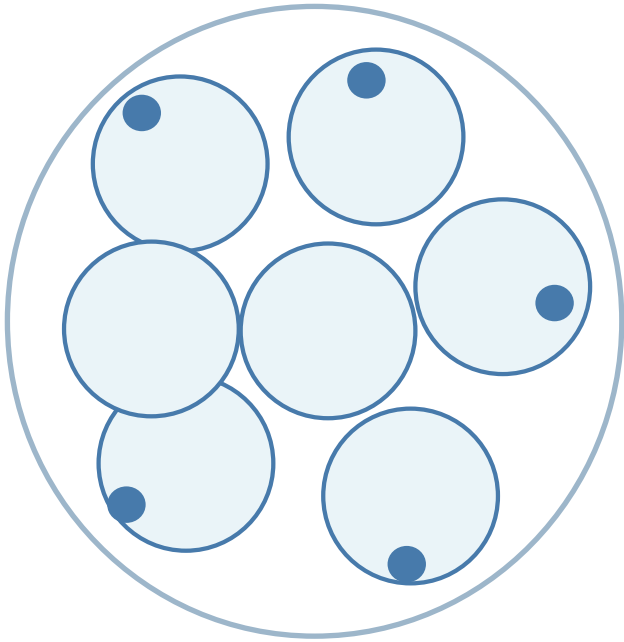
- The process affects most or all glomeruli sampled.
- Describes distribution across the biopsy.
- In the classic lesion, glomeruli are widely involved.

Global

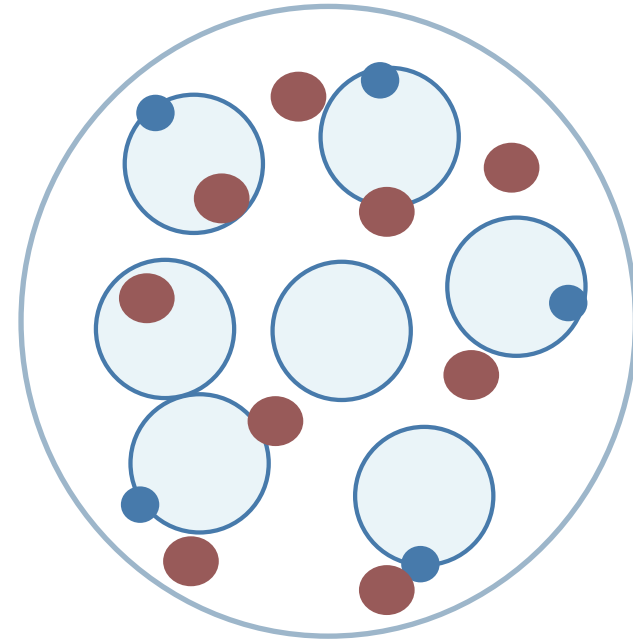
- Involvement extends through most or all of a given glomerular tuft.
- Describes extent within one glomerulus.
- The classical proliferative response is both diffuse and global.

Normal versus hypercellular tuft — schematic

Relatively open capillary loops



Inflamed, hypercellular tuft



Schematic of capillary-loop hypercellularity — not a histologic micrograph

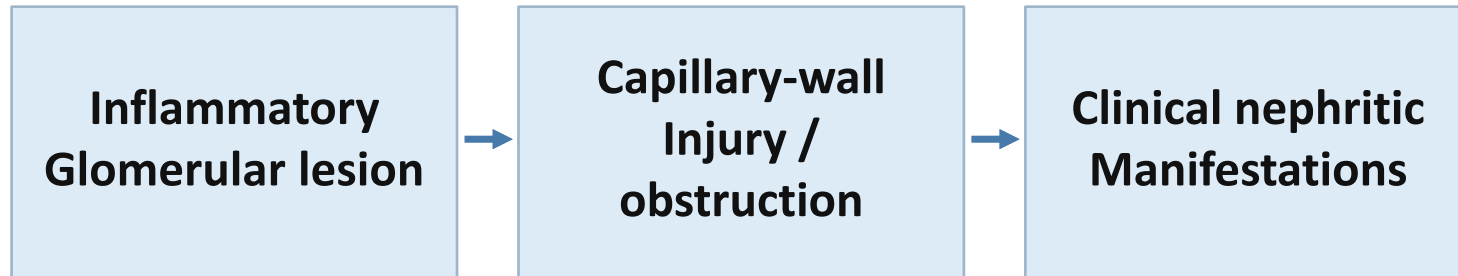
Exudative component: Neutrophils and monocytes

- The glomerular lesion has a prominent leukocytic inflammatory component.
- Neutrophils and monocytes contribute to the increased intracapillary cellularity.
- Distinguish recruited inflammatory cells from proliferation of mesangial or endothelial cells.
- A capillary lumen may contain leukocytes even when the surrounding tuft is hypercellular.

Intrinsic proliferation: Mesangial and endothelial cells

- Mesangial-cell proliferation adds cells in central tuft regions.
- Endothelial-cell proliferation expands the capillary-wall compartment.
- Together with leukocytic influx, these changes create endocapillary hypercellularity.
- The resulting morphology is proliferative and exudative.

Endothelial swelling compounds luminal narrowing



- Endothelial swelling adds to proliferation and inflammatory cell recruitment.
- Capillary channels become constricted or obliterated.
- The aggregate effect is impaired glomerular filtration.

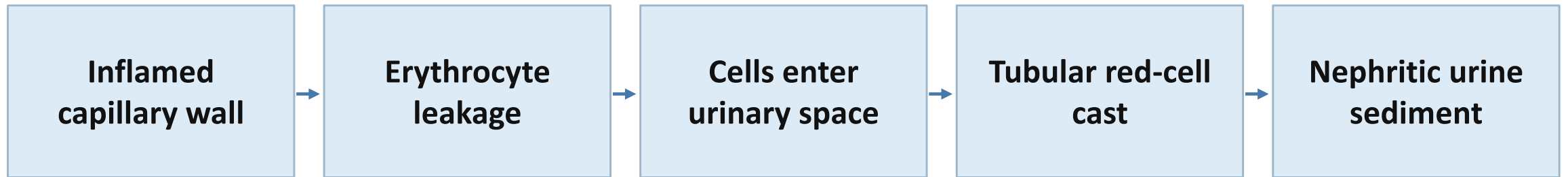
Severe cases may form crescents

- Crescent formation is described in the severe end of the morphologic spectrum.
- Crescents represent an extracapillary proliferative response in Bowman space.
- Their presence signals greater injury than uncomplicated endocapillary proliferation.
- A rapidly progressive syndrome is an uncommon but serious potential evolution.

Tubular and interstitial reactions

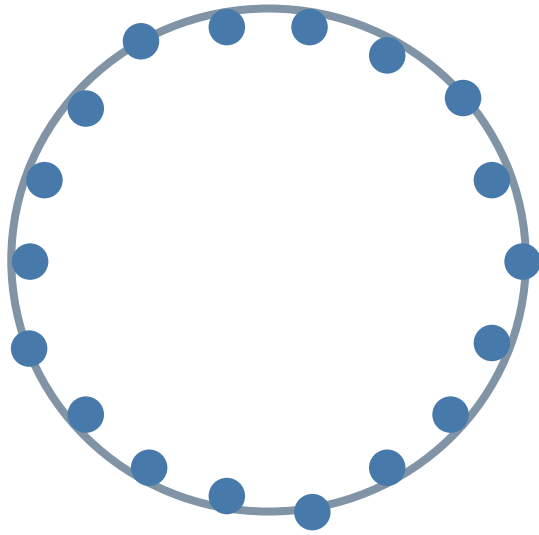
- Renal interstitium may show edema and inflammatory cells.
- Tubular lumina may contain red-cell casts originating from glomerular bleeding.
- These features help relate the glomerular lesion to urine sediment findings.
- They accompany, rather than replace, the characteristic glomerular lesion.

From glomerular capillary injury to a red-cell cast



The location of red-cell casts indicates bleeding within the nephron rather than a distal urinary tract source.

Immunofluorescence: A granular pattern



Discrete deposits

- Immune reactants deposit in discrete granules rather than as a smooth linear ribbon.
- IgG and complement C3 are characteristic.
- The pattern fits immune complex-mediated glomerular injury.

Schematic of granular reactivity — not an observed immunofluorescence specimen

Where immune deposits are detected by IF

- Granular IgG and C3 occur in the mesangium and along glomerular basement membranes.
- IgM can also be present in some biopsies.
- The quantity/distribution can be focal or sparse, despite the typical inflammatory light-microscopic pattern.
- No single fluorescence image should be overinterpreted as an etiologic diagnosis.

Granular IgG and C3 are the central IF pairing

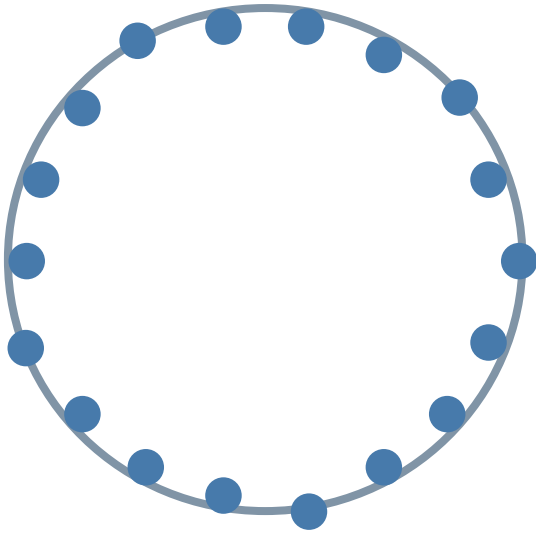
Immunoglobulins

- IgG is a classical component of the deposits.
- IgM may accompany the pattern.
- Some infection-associated forms can show granular IgA.

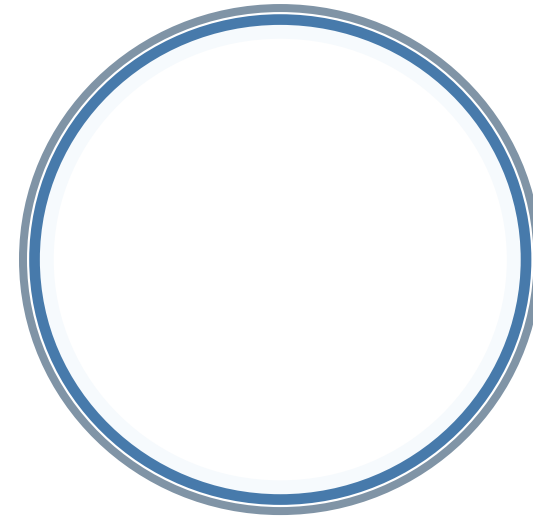
Complement

- C3 accompanies deposits in the glomeruli.
- The tissue staining aligns with systemic complement consumption.
- C3 alone is not sufficient to identify a particular infection.

Granular versus linear fluorescence



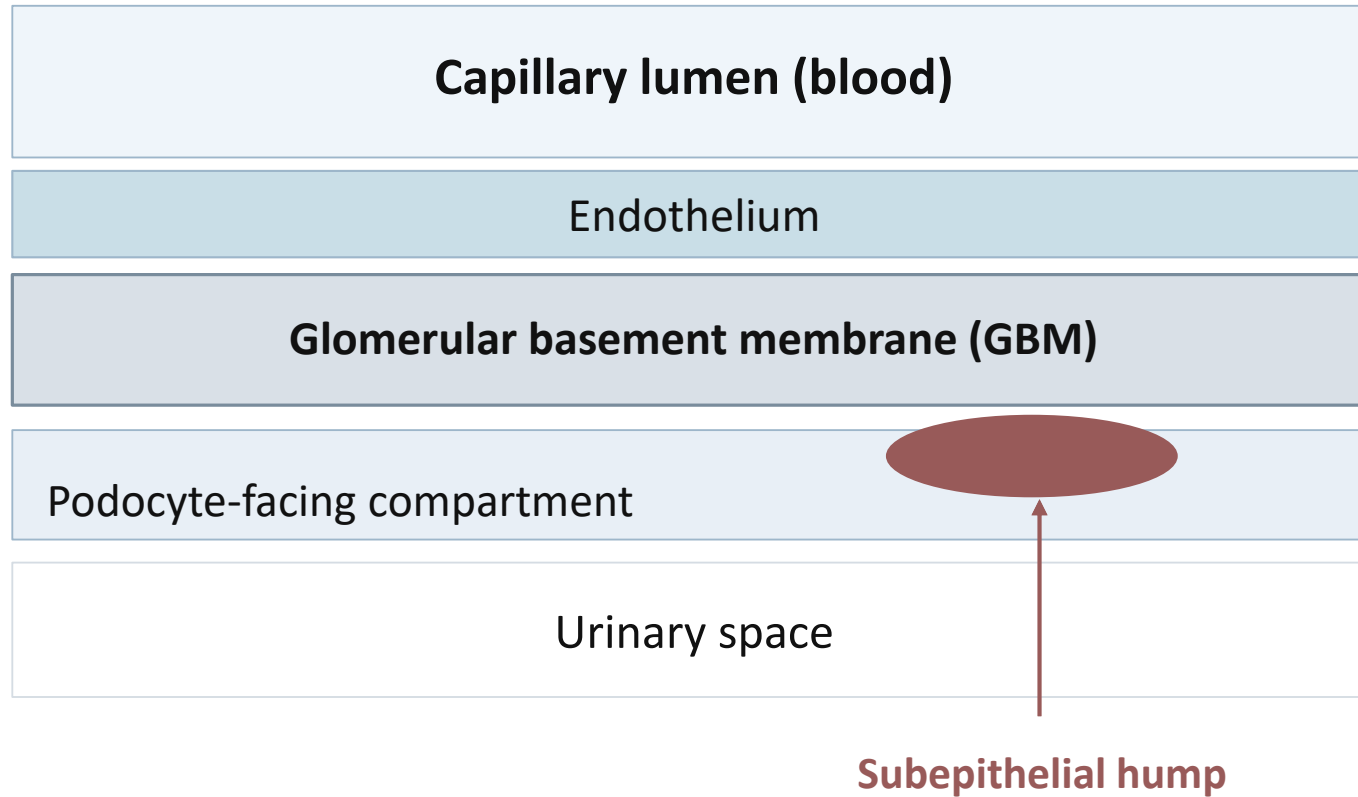
Granular immune deposits



Linear anti-GBM staining

Schematic comparison of deposition patterns — not fluorescence micrographs

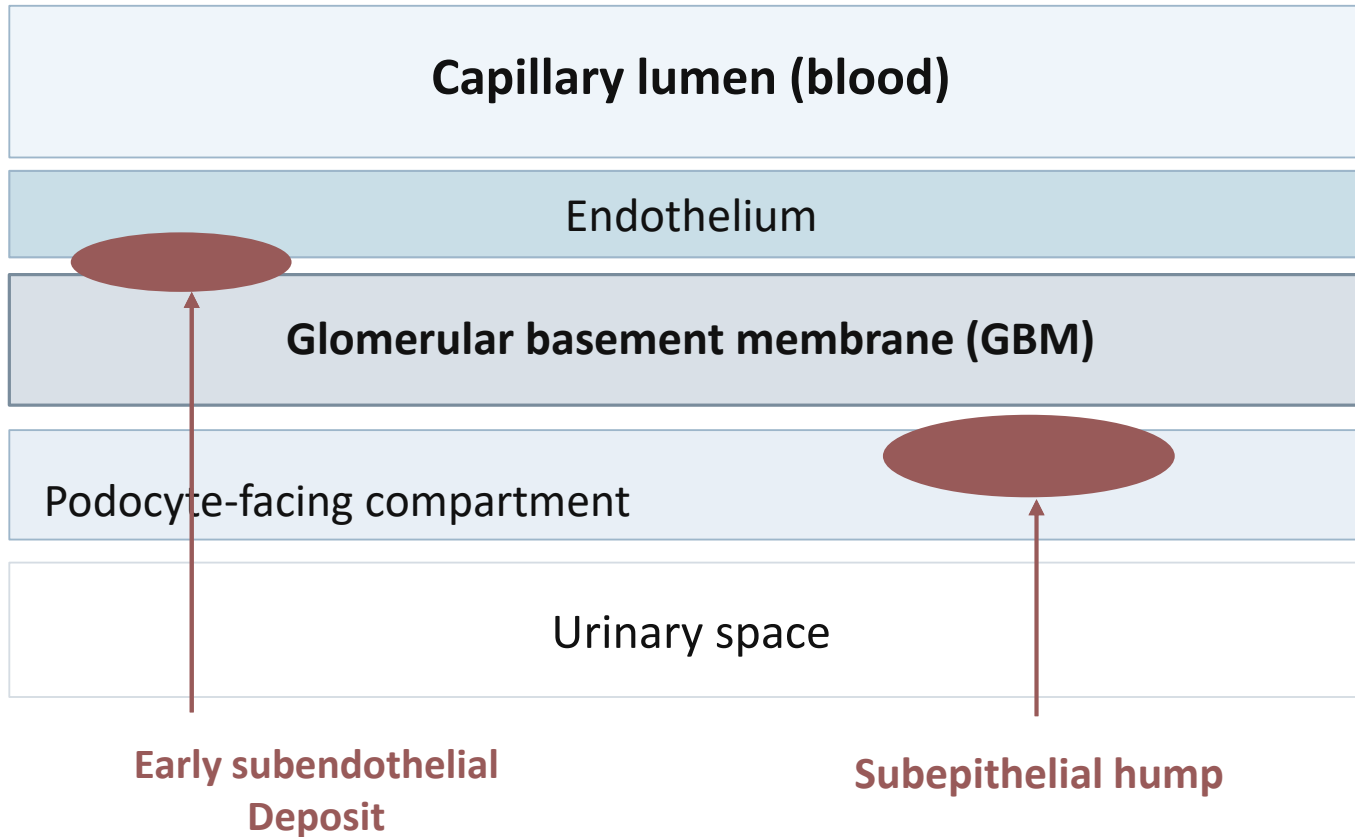
Electron microscopy: Subepithelial humps



- Discrete, amorphous electron-dense deposits lie on the epithelial side of the GBM.
- Their protruding contour gives the descriptive term “humps.”
- These deposits are a characteristic ultrastructural clue, not an exclusive marker of one organism.

Schematic of capillary-wall compartments — not electron microscopy

Early deposits may be subendothelial



- Subendothelial immune deposits are especially described early in the course.
- Mesangial and intramembranous deposits may coexist.
- Deposit location varies over time and between samples.

Schematic of capillary-wall compartments — not electron microscopy

Why deposit location matters

Subendothelial

- Directly adjacent to the vascular-side capillary compartment.
- Associated with early disease in the source narrative.
- Can accompany endothelial injury and inflammation.

Subepithelial

- External to the GBM, adjacent to podocytes.
- Characteristic large hump-like deposits.
- Forms the textbook ultrastructural signature.

A diagnostic triad, not three independent diseases

LM

Proliferative, exudative,
often diffuse and global

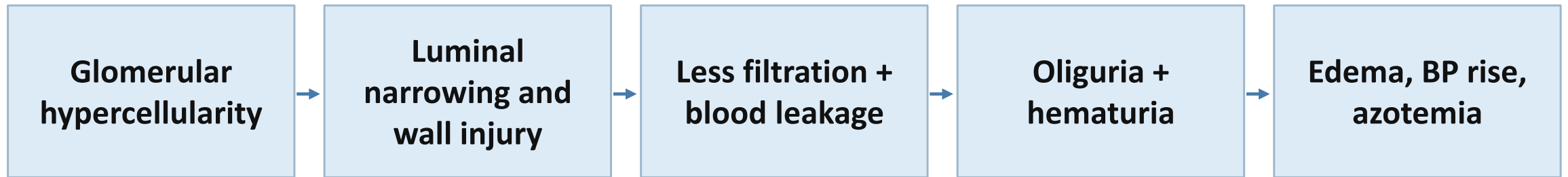
IF

Granular IgG/C3 $\pm$ other
immunoglobulins

EM

Subepithelial humps $\pm$
other deposit locations

Clinicopathologic chain: Injury to syndrome



Every clinical sign has a structural basis in the inflammatory glomerulus.

The typical child: Acute constitutional symptoms

- Malaise, fever, and nausea may accompany the onset of nephritis.
- Presentation is often abrupt following recovery from the infectious illness.
- Dark urine, edema, and decreased urine output direct attention to the kidneys.
- The time relationship is suggestive when combined with nephritic urine findings.

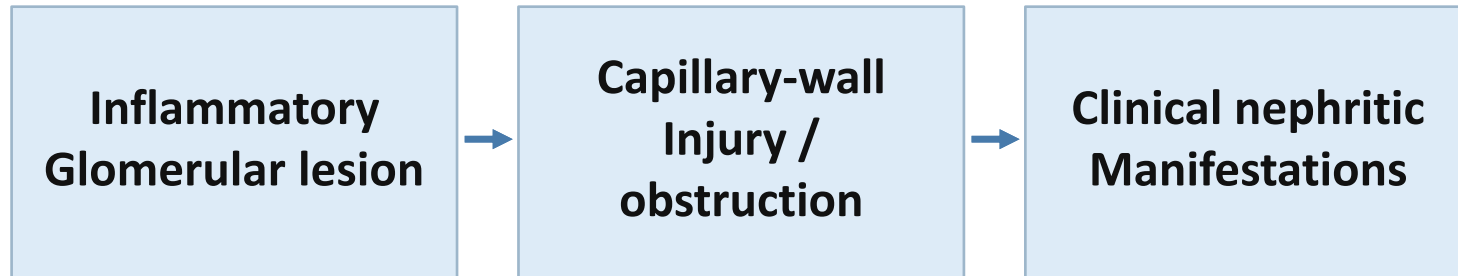
Hematuria may be visibly dark

- Urine is often described as smoky or cola-colored.
- Dysmorphic erythrocytes provide microscopic evidence of glomerular bleeding.
- Erythrocyte casts further localize bleeding to the nephron.
- Urine appearance alone cannot establish a postinfectious cause.

Proteinuria is usually non-nephrotic

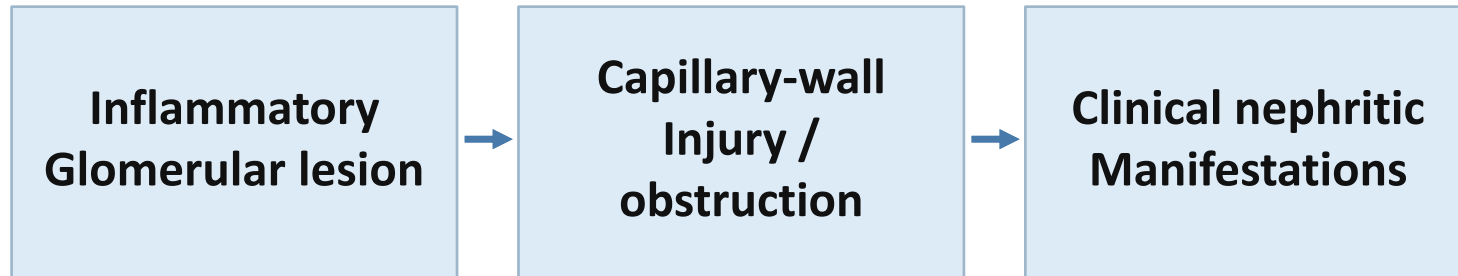
- Protein can cross the injured glomerular filtration barrier.
- The classical nephritic presentation has mild or subnephrotic proteinuria.
- Typical pediatric cases as usually having protein loss below 1 g/day.
- Persistent heavy proteinuria is an unfavorable prognostic marker in the source.

Periorbital edema reflects salt and water retention



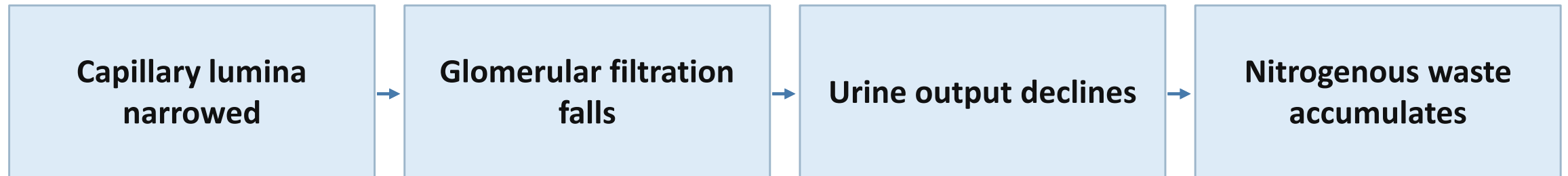
- Declining GFR reduces renal water and sodium excretion.
- Accumulated fluid expands the extracellular volume.
- Periorbital edema is a common visible manifestation in children.

Hypertension: Volume and renal hemodynamics



- Sodium and fluid retention contribute to increased blood pressure.
- Renin release from ischemic kidneys may also contribute.
- Hypertension can be the dominant initial adult clinical clue.

Oliguria and azotemia follow a reduction in GFR



The nephritic mechanism explains low urine output and elevation in blood urea nitrogen.

Adults may not present like the classical child

Classical pediatric picture

- Prior throat/skin infection
- Hematuria and periorbital edema
- Nephritic sediment and complement reduction

Atypical adult onset

- Sudden hypertension or edema
- Elevation in BUN may draw attention
- Potentially prolonged urine and renal abnormalities

Some disease is subclinical

- Not every infected individual develops overt edema or visibly dark urine.
- Microscopic hematuria may be detected by screening during outbreaks.
- This silent form reinforces that glomerular inflammation is a spectrum.
- A negative overt symptom history does not demonstrate absence of nephritis.

Antistreptococcal antibodies provide etiologic support

- Antibody titers to streptococcal antigens are increased in many affected patients.
- Such serology supports a preceding infection when clinical timing is compatible.
- An antibody result does not independently specify the renal lesion.
- Biopsy morphology and the nephritic syndrome address different parts of the diagnosis.

Complement and serology answer different questions

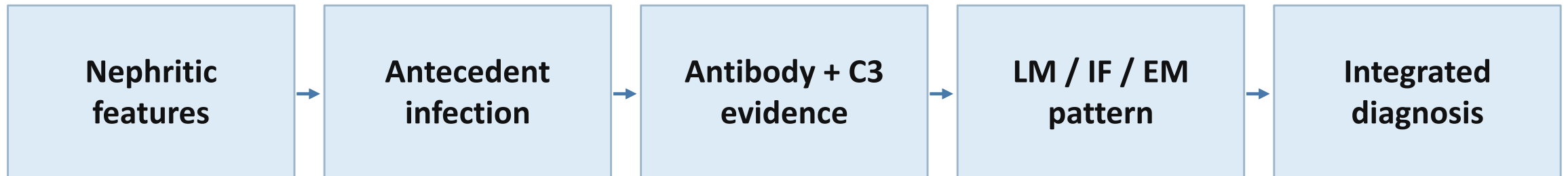
Low complement

- Reflects complement activation/consumption.
- Correlates with granular C3 in the glomerular deposits.
- Supports immune-complex pathophysiology.

Streptococcal serology

- Documents a recent immune response to a specific class of microbial antigens.
- Supports the preceding streptococcal association.
- Does not directly establish GBM deposit location.

Integrating the diagnostic evidence



Interpret the evidence together; No single feature is exclusive to poststreptococcal GN.

Renal outcome in childhood is often favorable

- Recovery of renal function in more than 95% of affected children.
- Conservative management emphasizes appropriate sodium and water balance.
- This is a textbook epidemiologic estimate, not a guarantee for an individual child.
- A small subset follows a persistent or severe course.

A rare severe evolution: Rapidly progressive GN

- A very small minority of children with severe persistent oliguria.
- These patients can evolve into a rapidly progressive, crescentic pattern.
- This is distinct from the usual self-limited pediatric disease.
- Severe clinical deterioration calls for reassessment of renal pathology and course.

Persistent abnormalities identify greater risk

Features of a typical favorable course

- Resolution of renal functional impairment
- Diminishing nephritic clinical activity
- Improving urine abnormalities

Unfavorable markers

- Persistent heavy proteinuria
- Persistently abnormal GFR
- Prolonged active or chronic glomerular injury

Adult prognosis is more guarded

- A lower rate of prompt recovery in sporadic adult cases.
- Approximately 60% are described as recovering promptly; The estimate is cohort-dependent.
- Others have persistent hematuria, proteinuria, hypertension, or unresolved lesions.
- A subset develops chronic GN or rapidly progressive GN.

Different trajectories after acute inflammation

Infection-associated proliferative GN

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graph TD; A[Infection-associated proliferative GN] --> B[Resolution]; A --> C[Persistence]; A --> D[Severe progression]; B --> B1[Clinical and functional recovery]; C --> C1[Ongoing urine/renal abnormalities]; D --> D1[Crescentic injury or chronic GN];
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Resolution

Clinical and functional recovery

Persistence

Ongoing urine/renal abnormalities

Severe progression

Crescentic injury or chronic GN

Differential: Postinfectious versus IgA nephropathy

Postinfectious GN

- Immune-complex lesion after microbial infection
- Diffuse endocapillary exudative response
- Granular IgG/C3; Subepithelial humps are characteristic

IgA nephropathy (parent context)

- Recurrent hematuria is a common presentation
- Focal mesangial proliferative changes may occur
- Mesangial IgA predominance is a diagnostic clue

Differential: Postinfectious versus anti-GBM injury

Immune complex-mediated

- Granular immunofluorescence
- Microbial antigens and antibodies form deposits
- Subepithelial humps support an infection-related pattern

Anti-GBM injury

- Linear IgG staining along the GBM
- Antibody binds intrinsic basement-membrane targets
- May present with severe crescentic nephritis

Differential: The role of complement-dominant GN

- Persistent alternative-pathway dysregulation is central to C3-dominant glomerulopathies.
- Both infection-related GN and C3 glomerulopathy can involve complement and humps.
- A C3-dominant pattern must be assessed in the full pathologic and clinical context.
- Do not assign a specific complement-mediated diagnosis from a hump alone.

Interpretation pitfall: A hump is supportive, not specific

- Large subepithelial deposits are characteristic of the classical disease.
- Similar deposits can appear with other infections and some complement-mediated lesions.
- Correlate deposit distribution with IF, endocapillary activity, and clinical timing.
- Avoid reducing a multimodal renal biopsy diagnosis to one ultrastructural sign.

Interpretation pitfall: Infection does not equal causation

- A recent infection raises suspicion, but infectious illnesses are common.
- Nephritic sediment, complement results, and morphology strengthen the causal inference.
- Conversely, a compatible biopsy can prompt investigation of a less obvious infection.
- The source does not establish a one-to-one mapping between a specific microbe and the renal lesion.

Case exercise: The delayed pediatric syndrome

Illustrative teaching vignette

- Child with resolved pharyngitis followed by dark urine, eyelid swelling, and oliguria.
- Dysmorphic erythrocytes and red-cell casts are present.
- Serum C3 is reduced, and streptococcal antibody titers are increased.

Predict one finding each on LM, IF, and EM.

Case resolution: Predict the renal biopsy

LM prediction

Diffuse endocapillary hypercellularity with inflammatory leukocytes

IF prediction

Granular deposits including IgG and C3

EM prediction

Characteristic subepithelial hump-like deposits

Case exercise: Adult with ongoing infection

Illustrative teaching vignette

- Adult with a bacterial infection develops hypertension, edema, and renal dysfunction.
- Urinary findings support a nephritic lesion.
- The biopsy reveals endocapillary hypercellularity and granular immune deposits.

Why should the diagnosis not be restricted to classic poststreptococcal GN?

Case resolution: Broaden the infectious context

- A comparable immune complex pattern occurs in several nonstreptococcal infections.
- The classic postinfection latency need not describe every infection-associated presentation.
- The organism and kidney findings require joint clinical-pathologic interpretation.
- The renal pattern cannot, by itself, identify a specific pathogen.

Morphology-to-clinical correlation map

Capillary-wall injury

Hematuria, dysmorphic red cells, red-cell casts

Endocapillary obstruction

Reduced GFR, oliguria, azotemia

Sodium and water retention

Edema, hypertension

High-yield recognition pattern

Context

Recent or associated microbial infection

Syndrome

Acute nephritic findings

LM / IF

Diffuse proliferative exudative GN; Granular IgG/C3

EM

Subepithelial humps, with possible other deposits

What must remain uncertain

- The precise steps by which deposits relocate toward the epithelial side of the GBM are unresolved.
- SpeB is implicated in most—but not all—classical streptococcal cases.
- The same glomerular reaction pattern can arise with distinct pathogens.
- Population outcome estimates do not establish prognosis for a particular patient.

Clinical and morphologic summary

- Microbial antigen-containing immune complexes initiate a complement-linked, leukocyte-rich inflammatory reaction.
- The classic lesion is diffuse endocapillary proliferative GN with granular IgG/C3 and subepithelial humps.
- Capillary inflammation explains nephritic hematuria, oliguria, edema, and hypertension.
- Children usually recover; Persistent abnormalities and adult disease warrant greater caution.

Reference

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th edition (2026).
- Section: Acute Proliferative (Postinfectious and Infection-Associated) Glomerulonephritis.
- Related textbook material: Nephritic Syndrome and immune-complex mechanisms of glomerular injury.