

Lupus Nephritis

Immune-complex mechanisms · renal morphology · clinical correlations

Renal pathology teaching lecture

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Learning outcomes

- Locate immune deposits within the glomerular filtration barrier and predict their injury patterns.
- Distinguish the defining renal morphology of lupus nephritis classes I–VI.
- Connect glomerular, tubulointerstitial, and vascular lesions with clinical syndromes.
- Interpret clinicopathologic vignettes without treating urine findings as a histologic class.

Why the kidney matters in systemic lupus

- Systemic lupus erythematosus (SLE) produces heterogeneous renal lesions.
- Glomerular immune-complex injury is a major mechanism.
- Tubulointerstitial and vascular injury may accompany glomerulonephritis.

Renal involvement is more than glomerulonephritis.

Anatomic compartments at risk

Within the glomerulus

- Mesangium
- Glomerular capillary walls
- Endothelial and epithelial compartments

Beyond the glomerulus

- Tubules and interstitium
- Tubular/peritubular capillary basement membranes
- Renal vessel intima and media

The glomerular filtration barrier

Capillary lumen

Endothelium

Subendothelial zone

Glomerular basement membrane



Subepithelial zone

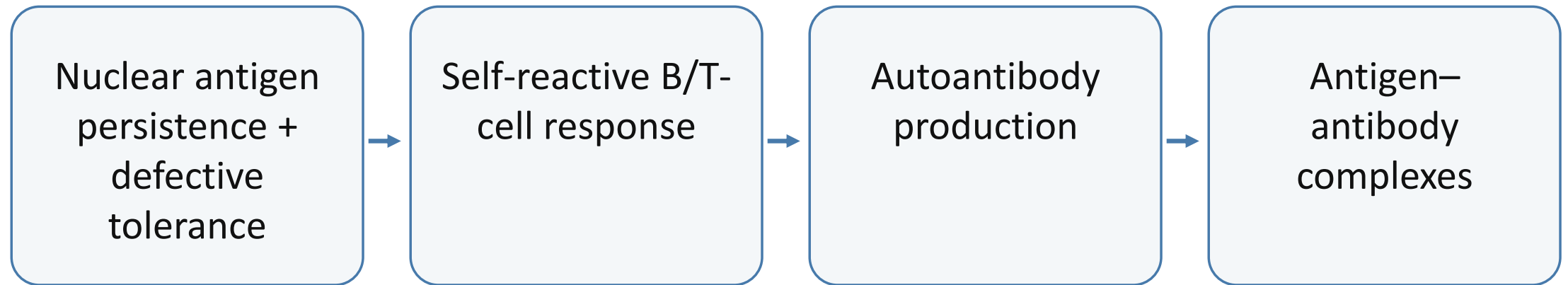
Podocyte / urinary space

Endothelium faces circulating immune reactants.

The basement membrane separates endothelium from podocytes.

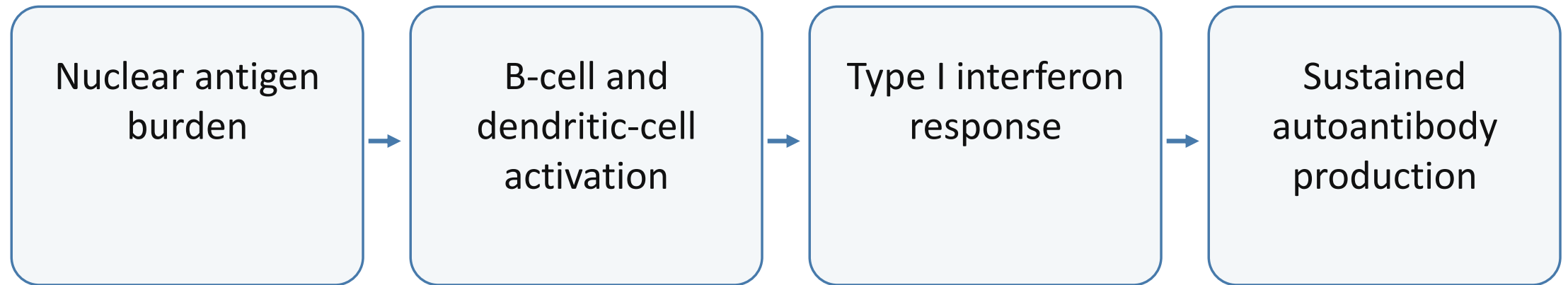
Deposit position helps determine the inflammatory response.

Systemic immune dysregulation precedes renal injury



Schematic — directional teaching model; Not a patient-specific pathway.

An amplifying lupus immunologic circuit



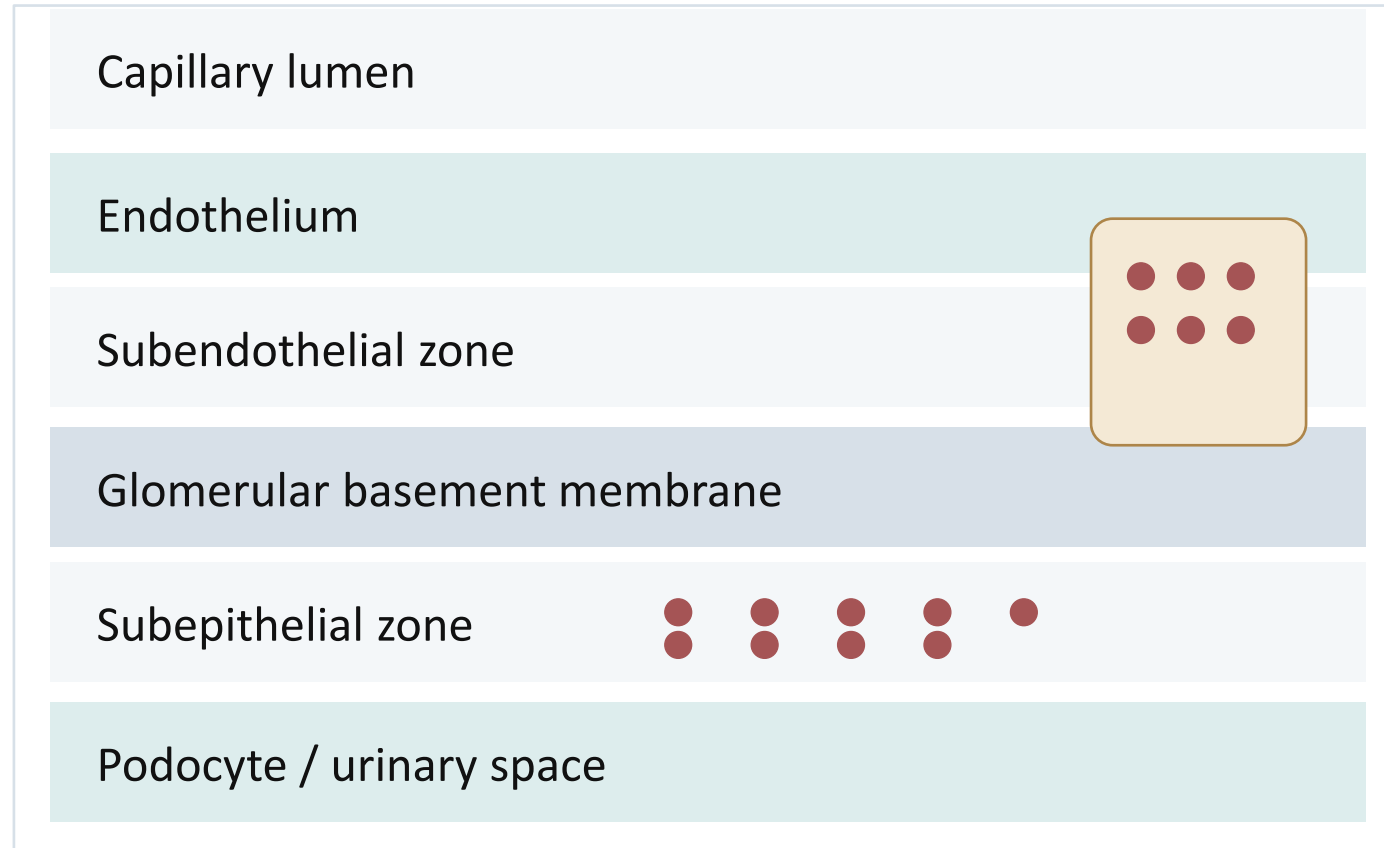
Schematic — directional teaching model; Not a patient-specific pathway.

Immune complexes are central to renal SLE

- Many SLE lesions represent immune-complex (type III) hypersensitivity.
- DNA–anti-DNA complexes can be detected in glomeruli and small vessels.
- Granular immunoglobulin/complement deposition supports the mechanism.

**Complex formation →
localization →
inflammatory injury**

Where immune complexes accumulate

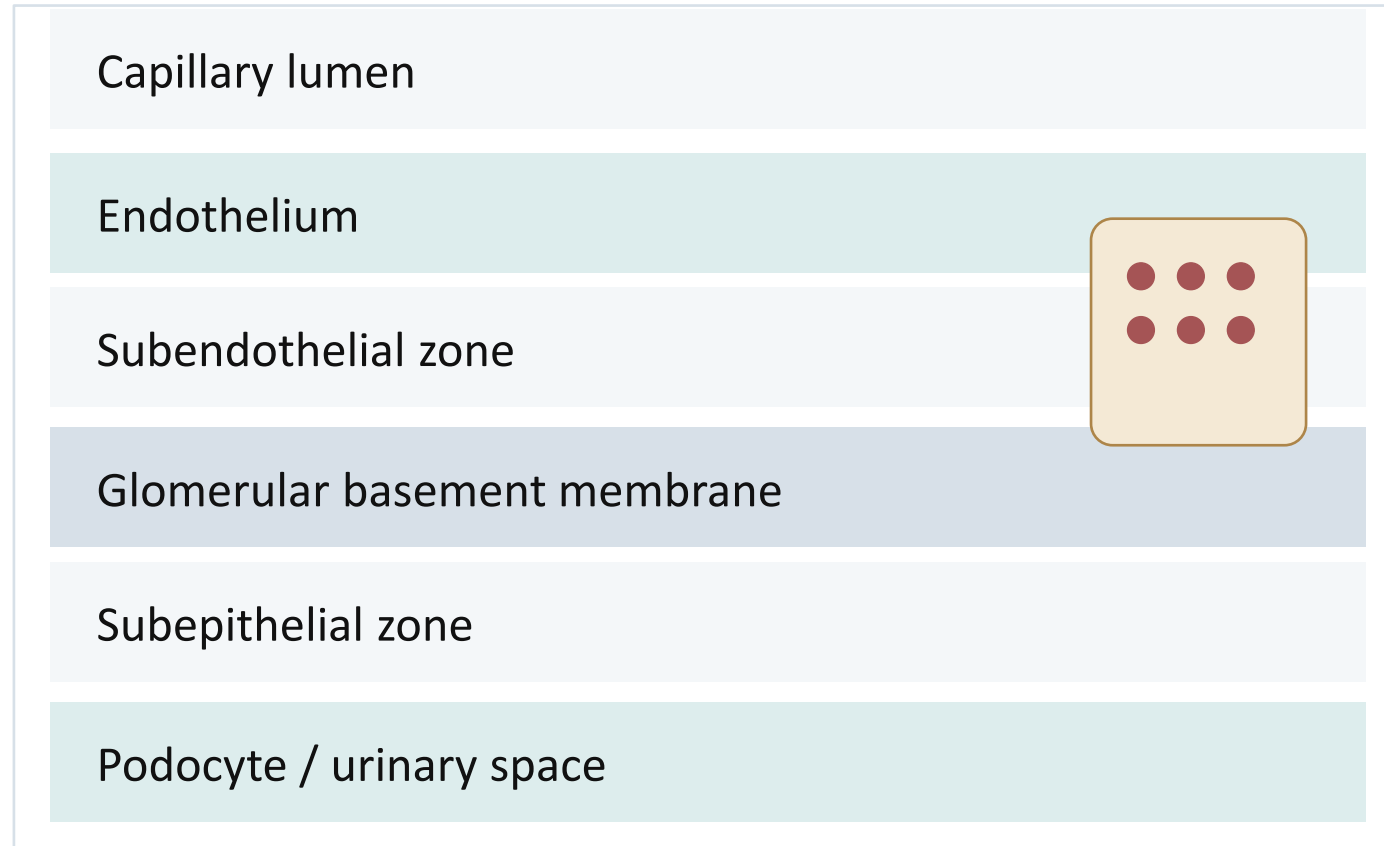


Mesangial deposits

Subendothelial capillary-wall deposits

Subepithelial capillary-wall deposits

Mesangial deposits: The earliest patterns



Immune complexes occupy the mesangial compartment.

Mesangial proliferation may occur.

Light microscopy can remain normal when deposits are sparse.

Subendothelial deposits: Inflammatory access

Capillary lumen

Endothelium

Subendothelial zone



Glomerular basement membrane

Subepithelial zone

Podocyte / urinary space

Deposits lie between endothelium and GBM.

Circulating inflammatory cells can respond readily.

Endocapillary proliferation, necrosis, and crescents may follow.

Subepithelial deposits: Capillary-wall injury

Capillary lumen

Endothelium

Subendothelial zone

Glomerular basement membrane

Subepithelial zone



Podocyte / urinary space

Deposits lie between GBM and podocytes.

The GBM separates deposits from the circulation.

Membranous remodeling and heavy proteinuria are characteristic.

Deposit localization predicts dominant injury

Compartment	Predominant pathologic response	Typical lupus association
Mesangium	Mesangial immune deposition ± proliferation	Classes I–II
Subendothelial	Endocapillary inflammation and proliferative injury	Classes III–IV
Subepithelial	Capillary-wall thickening and proteinuria	Class V

Immunoreactants in lupus nephritis

- Immunoglobulin G is commonly present in deposited immune complexes.
- IgA and IgM frequently accompany IgG.
- Complement components C3 and C1q are also often detected.

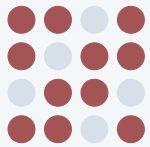
Multiple immune reactants can coexist.

The meaning of granular immunofluorescence

Discrete immune-complex deposits yield a granular distribution.



Capillary-
wall deposits



Mesangial
deposits



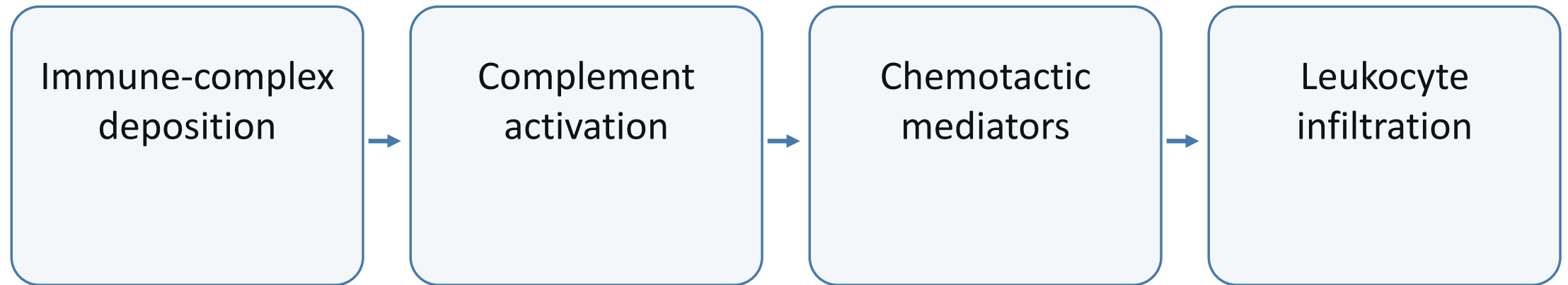
Mixed
distribution

Schematic fluorescence clusters; Not a real immunofluorescence photomicrograph.

Light microscopy, IF, and EM answer different questions

Technique	Primary question	Example in lupus nephritis
Light microscopy	What architectural injury is present?	Proliferation, necrosis, sclerosis
Immunofluorescence	Which immune reactants and distribution?	Granular immunoglobulin/complement
Electron microscopy	Exactly where are deposits?	Mesangial, subendothelial, subepithelial

Complement recruits inflammatory effectors



Schematic — directional teaching model; Not a patient-specific pathway.

Cells amplify glomerular injury

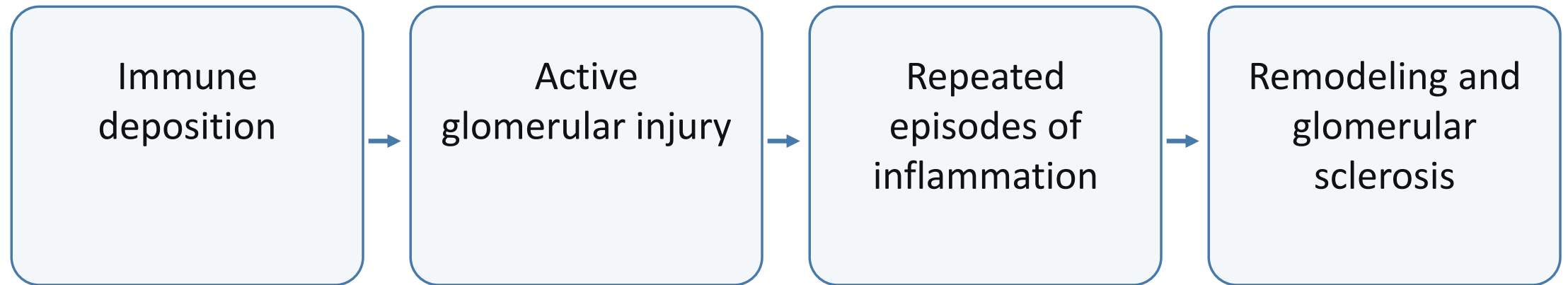
Recruited leukocytes

- Neutrophils release proteases and reactive oxygen species
- Monocytes/macrophages release inflammatory mediators
- Inflammation can damage capillary walls

Intrinsic glomerular cells

- Mesangial cells produce cytokines and growth factors
- Endothelial/mesangial proliferation narrows capillary lumina
- Persisting stimulation promotes remodeling

Acute inflammation versus persistent injury



Schematic — directional teaching model; Not a patient-specific pathway.

Clinical presentations form a spectrum

Urinary findings

- Microscopic or gross hematuria
- Proteinuria of varying degree
- Red cell casts with active nephritic injury

Renal/vascular effects

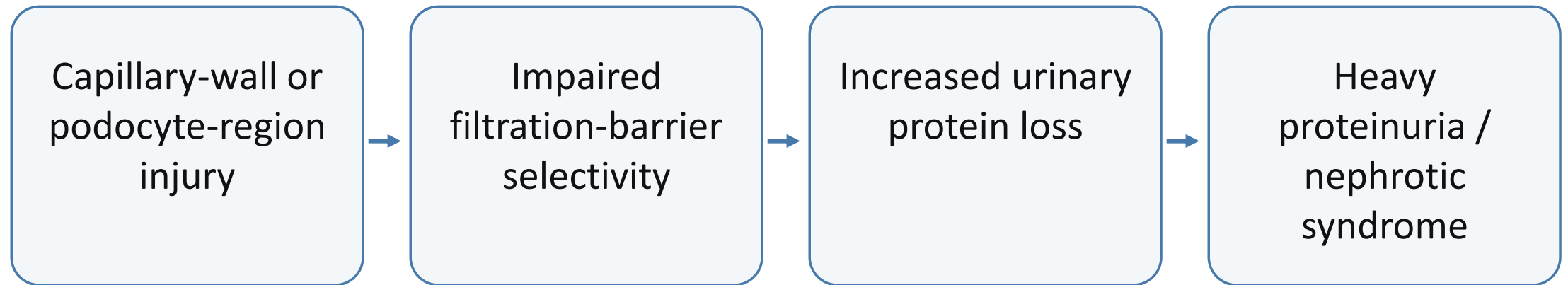
- Nephritic or nephrotic syndrome
- Rapidly progressive glomerulonephritis
- Reduced renal function and hypertension

Hematuria reflects glomerular capillary injury

- Active capillary-wall damage permits erythrocytes to enter the urine.
- Hematuria may be microscopic or macroscopically visible.
- Red cell casts support an intrarenal nephritic sediment.

**Urine findings identify
a syndrome, not a
class.**

Proteinuria: Link morphology to permeability



Schematic — directional teaching model; Not a patient-specific pathway.

Reduced renal function has structural correlates

- Inflammation, capillary narrowing, and necrosis can impair filtration.
- Rapidly progressive forms may feature extensive crescents.
- Chronic glomerular scarring reduces the surviving filtration surface.

Active injury and chronic scarring must be distinguished.

Interpreting a kidney biopsy

Light microscopy: Map inflammation, necrosis, proliferative lesions, sclerosis



Immunofluorescence: Document immune-reactant distribution



Electron microscopy: Localize electron-dense deposits



Integrate glomerular, tubulointerstitial, and vascular findings

The six morphologic patterns

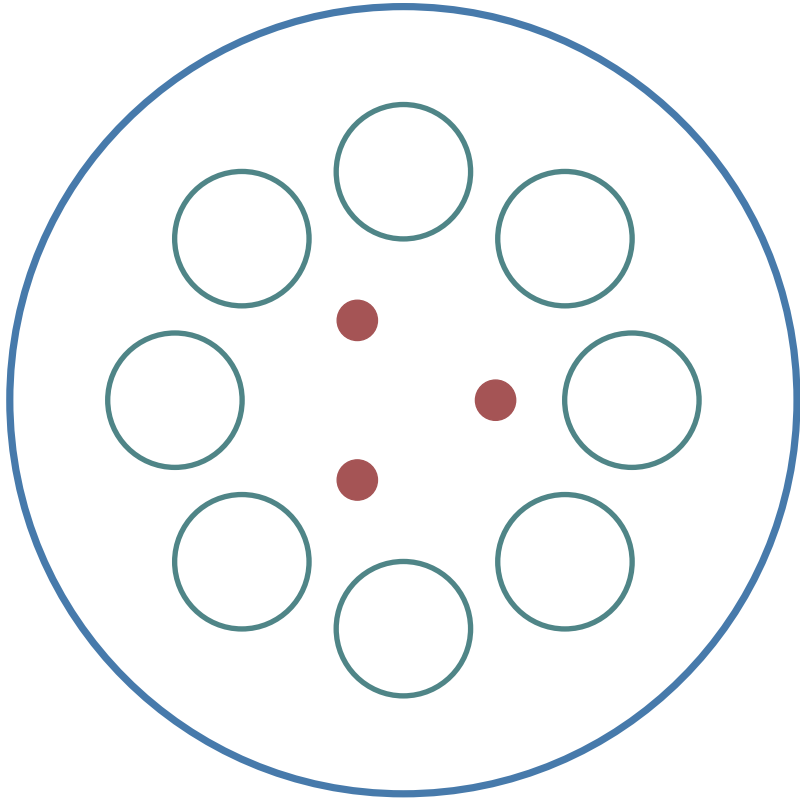
Class	Name	Dominant defining feature
I	Minimal mesangial	Deposits; normal light microscopy
II	Mesangial proliferative	Mesangial cellular/matrix increase
III	Focal	<50% glomeruli affected
IV	Diffuse	>50% glomeruli affected
V	Membranous	Subepithelial deposits; capillary thickening
VI	Advanced sclerosing	≥90% globally sclerosed glomeruli

Morphologic classes can overlap or evolve

- Distinct patterns are not immutable disease stages.
- Classes may overlap, and a patient's lesion can change over time.
- Membranous lesions can coexist with proliferative classes.
- Biopsy findings describe the sampled kidney at a particular time.

**Avoid a rigid I → II →
III → IV → V → VI
progression.**

Class I: Minimal mesangial lupus nephritis



Schematic — not diagnostic histology.

Mesangial immune-complex deposits detected by IF or EM.

No structural abnormality on routine light microscopy.

Described as very uncommon.

Why class I can escape light microscopy

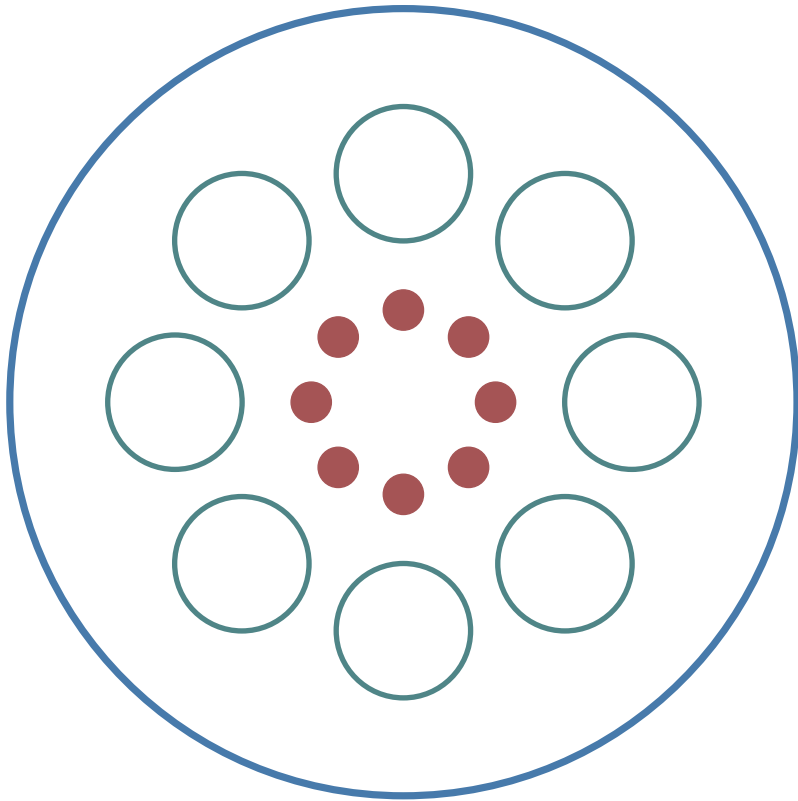
Light microscopy

- Glomerular architecture remains unremarkable
- No required hypercellularity or capillary-wall thickening

IF and electron microscopy

- Reveal mesangial immune deposits
- Establish an immune-complex lesion despite normal LM

Class II: Mesangial proliferative nephritis



Schematic — not diagnostic histology.

Mesangial cell proliferation is the defining change.

Mesangial matrix may also increase.

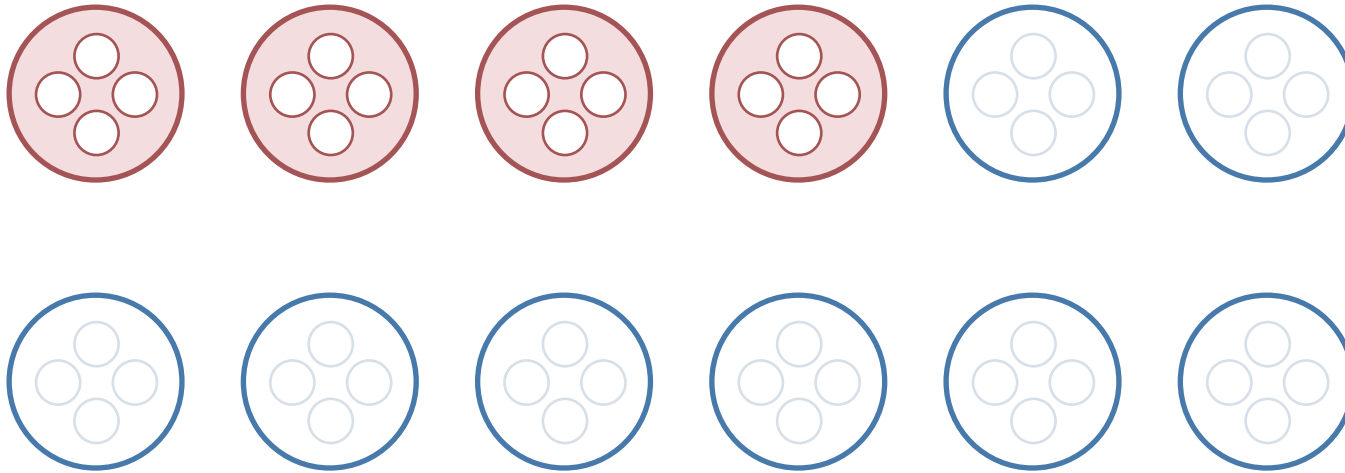
Granular mesangial Ig/complement deposition without active endocapillary inflammation.

Class I versus class II

Feature	Class I	Class II
Mesangial deposits	Present on IF/EM	Present on IF/EM
Light microscopy	No structural change	Mesangial proliferation ± matrix
Capillary inflammation	Not defining	Absent as class-defining lesion

Class III: Focal lupus nephritis

Illustrative 12-glomerulus sampling grid



Fewer than 50% of glomeruli are involved.

Injured glomeruli may have segmental or global lesions.

Active lesions and scars may coexist.

4 / 12 schematic glomeruli affected

Schematic — drawn glomeruli are not biopsy specimens.

Segmental and global describe area within a tuft

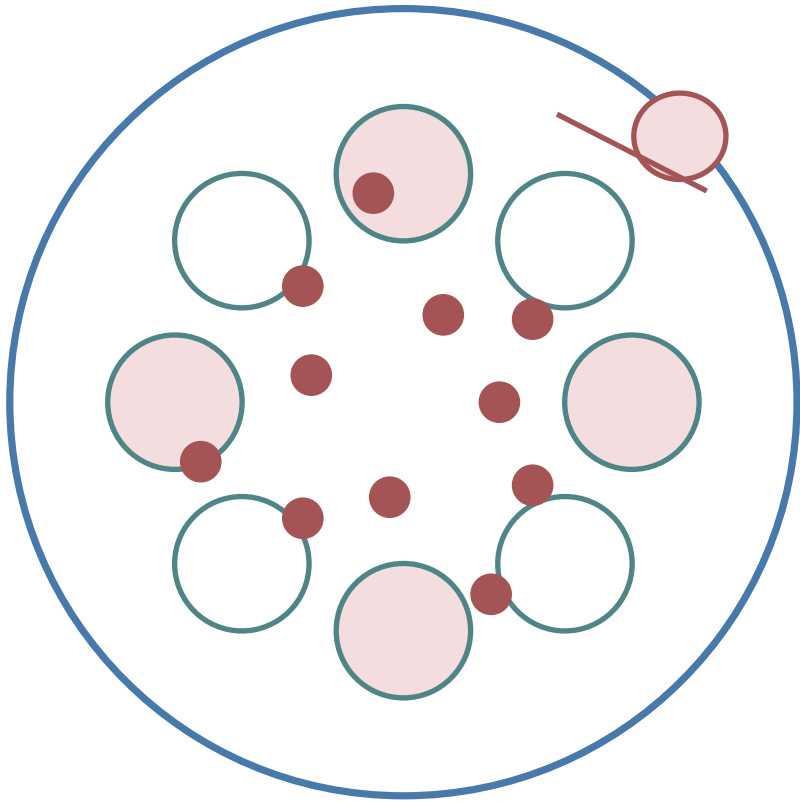
Segmental lesion

- Only a portion of one glomerulus is affected
- Necrosis or scarring need not involve the whole tuft

Global lesion

- An entire glomerular tuft is affected
- The focal/diffuse distinction concerns how many glomeruli are involved

Class III: Active cellular and capillary lesions



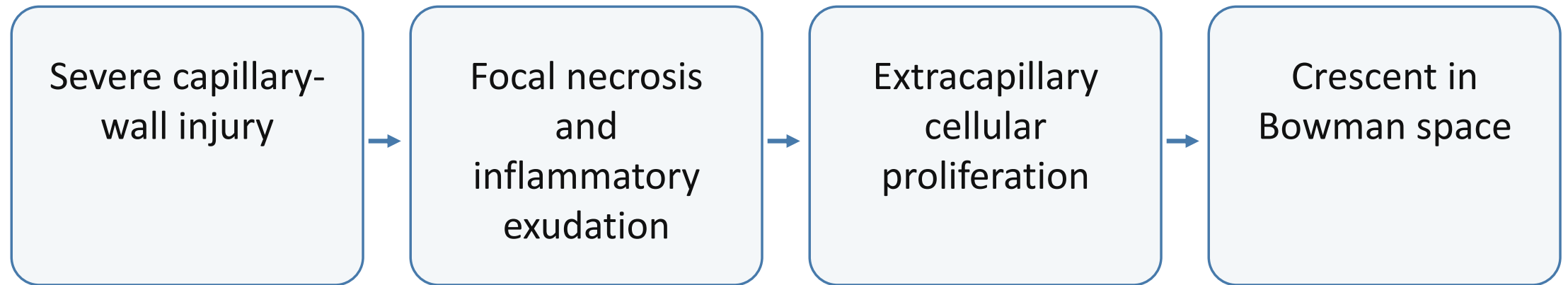
Schematic — not diagnostic histology.

Endothelial and mesangial cell swelling/proliferation.

Leukocyte accumulation and capillary necrosis.

Hyaline thrombi may be encountered.

Necrosis can trigger crescent formation



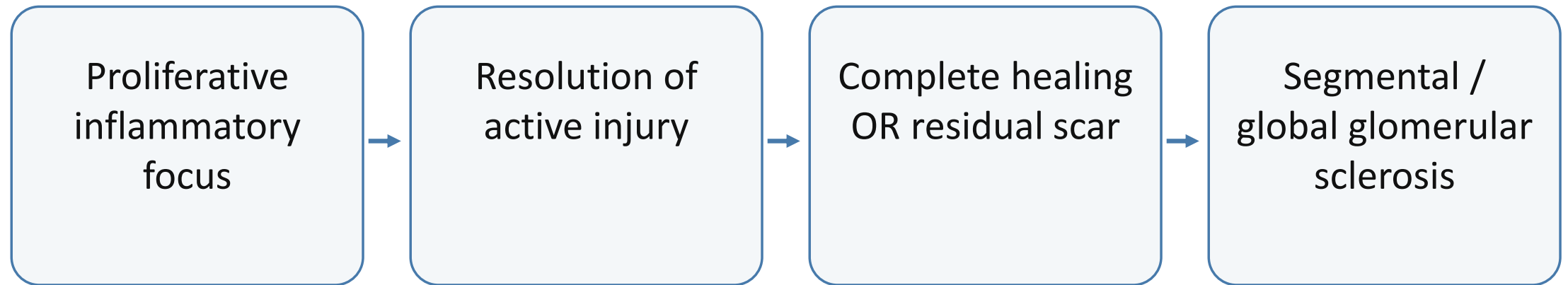
Schematic — directional teaching model; Not a patient-specific pathway.

Class III: Active nephritic sediment

- Active focal lesions can manifest with hematuria and proteinuria.
- Red cell casts are often present during active nephritis.
- Presentation may extend to acute renal insufficiency.

**Focal in distribution
does not mean
clinically trivial.**

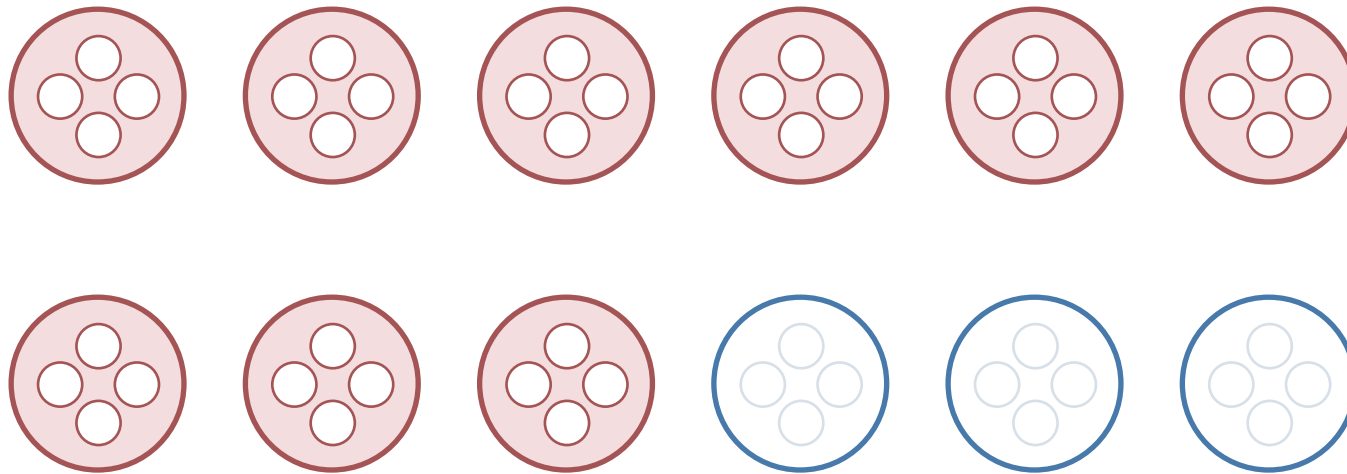
Healing after focal proliferative injury



Schematic — directional teaching model; Not a patient-specific pathway.

Class IV: Diffuse lupus nephritis

Illustrative 12-glomerulus sampling grid



Greater than 50% of glomeruli are involved.

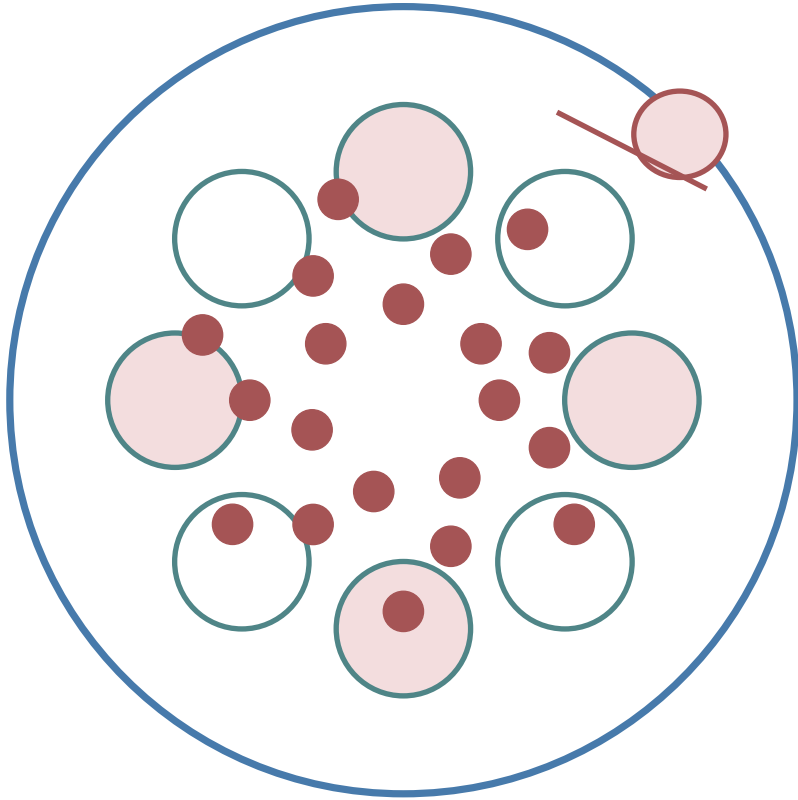
Lesions resemble those of class III but are more extensive.

Described as the commonest and most severe form.

9 / 12 schematic glomeruli affected

Schematic — drawn glomeruli are not biopsy specimens.

Class IV: Pronounced proliferative injury



Schematic — not diagnostic histology.

Endothelial, mesangial and epithelial cell proliferation.

Numerous glomeruli exhibit capillary inflammation.

Glomerular damage may progress toward sclerosis.

Class IV: Crescentic disease can be extensive

- Cellular crescents occupy Bowman space.
- Crescents reflect a severe response to capillary injury.
- Marked extracapillary proliferation may impair glomerular filtration.

**A crescent is a lesion,
not a separate lupus
class.**

Wire loops are subendothelial immune deposits

Capillary lumen

Endothelium

Subendothelial zone



Glomerular basement membrane

Subepithelial zone

Podocyte / urinary space

Extensive subendothelial complexes thicken the capillary-wall profile.

Light microscopy may show a circumferential “wire-loop” appearance.

EM demonstrates corresponding electron-dense deposits.

Correlating the wire-loop lesion across modalities

Observation	Interpretation	Technique
Circumferential capillary thickening	Wire-loop appearance	Light microscopy / PAS
Dense deposits beneath endothelium	Subendothelial immune complexes	Electron microscopy
Granular capillary immune reaction	Deposited immunoglobulin/complement	Immunofluorescence

Class IV: Clinical expectations

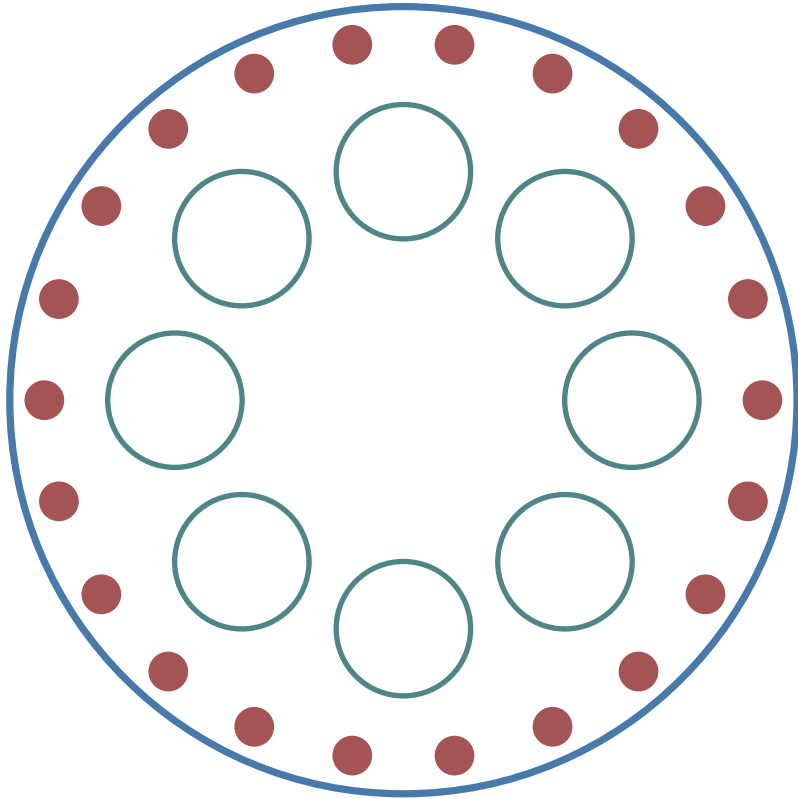
- Hematuria and proteinuria are usually present.
- Hypertension is common in diffuse proliferative disease.
- Renal dysfunction varies from mild to severe.

**Extent and activity
jointly influence the
phenotype.**

Focal versus diffuse proliferative lupus nephritis

Feature	Class III	Class IV
Glomeruli involved	<50% in source	>50% in source
Type of active lesion	Proliferation, necrosis $\pm$ crescents	Similar lesions, more extensive
Clinical range	Mild urine changes to insufficiency	Often symptomatic; dysfunction common
Potential outcome	Healing or scarring	Scarring may develop

Class V: Membranous lupus nephritis



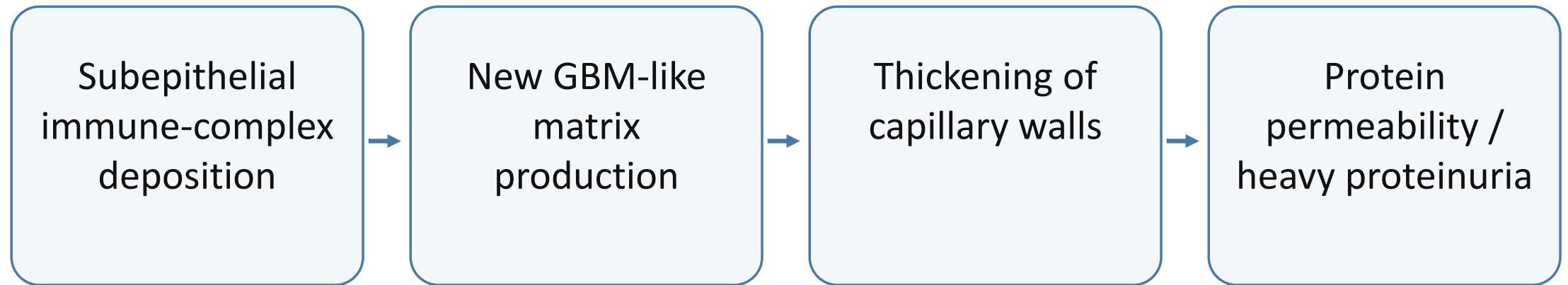
Schematic — not diagnostic histology.

Diffuse capillary-wall thickening is characteristic.

Subepithelial immune complexes are central.

Mesangial deposits frequently accompany the lesion.

How membranous remodeling forms



Schematic — directional teaching model; Not a patient-specific pathway.

Class V: Nephrotic presentation

- Severe proteinuria or nephrotic syndrome is characteristic.
- The lesion resembles membranous nephropathy morphologically.
- The context of SLE and immune deposition establishes the lupus setting.

**Membranous pattern
≠ absence of systemic
autoimmunity.**

Membranous and proliferative patterns may coexist

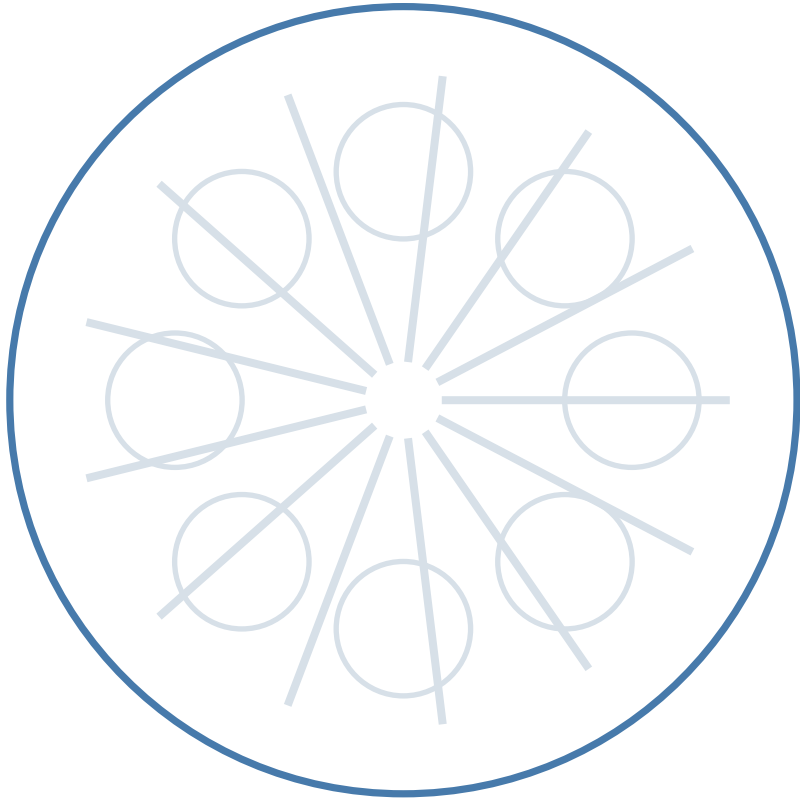
Membranous component

- Subepithelial deposits
- Capillary-wall thickening
- Often heavy proteinuria

Associated proliferative component

- Focal or diffuse glomerular inflammation
- Necrosis / crescents may coexist
- Can add hematuria or functional decline

Class VI: Advanced sclerosing nephritis



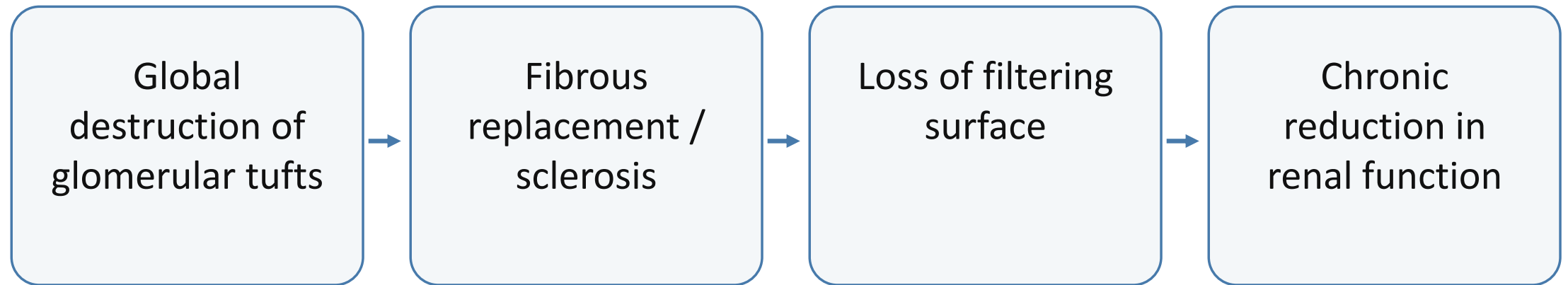
Schematic — not diagnostic histology.

At least 90% of glomeruli are globally sclerosed.

The definition describes extensive irreversible glomerular scarring.

Active deposits elsewhere do not replace the sclerosis criterion.

Why global sclerosis reduces kidney function



Schematic — directional teaching model; Not a patient-specific pathway.

Classes I, II and VI: Contrasting disease states

Feature	I	II	VI
Core identity	Silent mesangial deposits	Mesangial proliferation	Advanced global sclerosis
Diagnostic strength	IF/EM	LM + IF	LM assessment of scarring
Scope of injury	Minimal structural change	Mesangial expansion	≥90% globally scarred

Classes III, IV and V: The crucial discrimination

Feature	III	IV	V
Dominant pattern	Focal proliferative	Diffuse proliferative	Membranous
Deposit association	Subendothelial may occur	Prominent subendothelial	Subepithelial
Clinical cue	Hematuria ± renal decline	Nephritic + renal decline	Heavy proteinuria
Coexistence	May accompany V	May accompany V	May accompany III/IV

Renal lesions extend beyond glomeruli

Tubulointerstitial disease

- Interstitial inflammatory changes
- Tubular/peritubular immune deposits
- Occasionally predominant lesion

Vascular involvement

- Intimal/media immune-complex deposition
- Less frequent active vasculitis
- Occasional thrombotic microangiopathy

Lupus-associated podocytopathy is a distinct feature

- Podocytopathy in association with class I–II patterns.
- The morphology may resemble minimal change disease.
- Do not force all marked proteinuria into class V without examining additional lesions.

**A concurrent lesion
may explain
discordant
manifestations.**

Thrombotic microangiopathy requires separate recognition

- Thrombotic microangiopathy may accompany lupus-related renal injury.
- It is not defined solely by the glomerular immune-deposit class.
- A complete biopsy interpretation should record vascular injury independently.

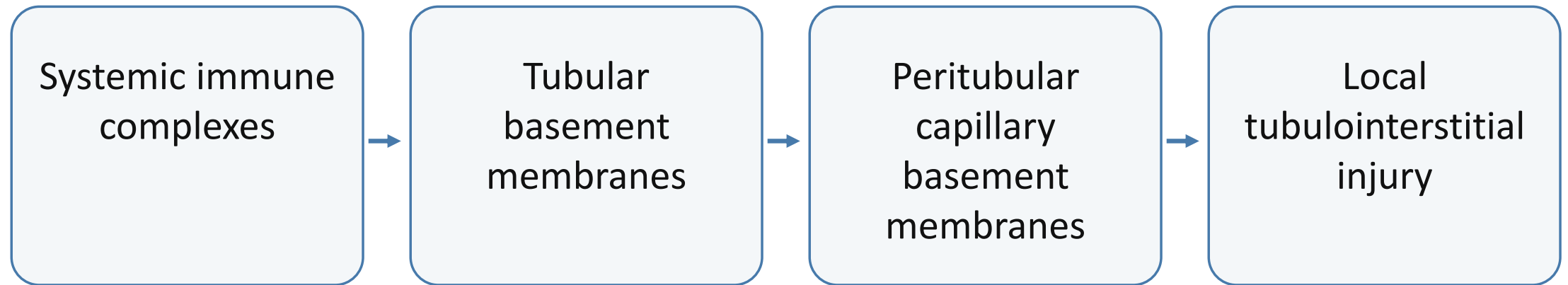
**Vascular pathology
adds information
beyond class I–VI.**

Tubular and interstitial lupus injury

- Tubulointerstitial abnormalities are frequent in lupus nephritis.
- Rare cases have predominantly tubulointerstitial lesions.
- Renal dysfunction therefore cannot be attributed only to glomerular tufts.

**Inspect tubules,
interstitium, and
vessels.**

Immune deposits occur outside glomeruli



Schematic — directional teaching model; Not a patient-specific pathway.

B-cell aggregates in the renal interstitium

- Well-organized interstitial B-cell follicles are occasionally present.
- Associated plasma cells may serve as local autoantibody sources.
- This finding emphasizes the immune activity of the renal interstitium.

**The interstitium can
be immunologically
active.**

Renal vascular involvement

More frequent observation

- Immune-complex deposition in arterial intima/media
- May coexist with glomerular or interstitial involvement

Less common severe pattern

- Active vasculitis with vessel-wall necrosis
- Lesions may accompany thrombotic microangiopathy

A whole-biopsy reporting framework

Glomerular class and extent: Mesangial, proliferative, membranous, or sclerosing



Active lesions: Inflammation, necrosis, crescents, immune deposits



Chronic lesions: Segmental/global sclerosis and fibrotic remodeling



Extraglomerular findings: Interstitial inflammation, deposits, vascular lesions

Clinical manifestations follow lesion anatomy

Dominant lesion	Mechanistic consequence	Clinical expression
Necrotizing capillary injury	Erythrocyte passage into filtrate	Hematuria; red cell casts
Barrier / podocyte-region damage	Increased protein permeability	Heavy proteinuria
Diffuse capillary injury	Reduced effective filtration	Impaired kidney function
Extensive sclerosis	Loss of functional glomeruli	Chronic renal failure

Activity and chronicity are different dimensions

Features of active injury

- Endocapillary leukocytes / proliferation
- Capillary necrosis
- Cellular crescents

Features of established damage

- Global or segmental sclerosis
- Residual fibrotic remodeling
- Reduced surviving filtration surface

Biopsy morphology and phenotype may diverge

- Classes overlap and may evolve over time.
- Glomerular lesions can coexist with podocytopathy or vascular injury.
- Urine abnormalities and renal function indicate impact; LM/IF/EM resolve anatomy.

**Avoid assigning a class
from symptoms
alone.**

Case: Normal glomeruli on light microscopy

HYPOTHETICAL TEACHING CASE

Patient with established SLE.

LM: Glomeruli have no structural change.

IF/EM: Mesangial immune-complex deposits.

PATTERN AND EXPLANATION

Class I — minimal mesangial lupus nephritis.

The immune deposition is real, but routine light microscopy lacks defining structural change.

Case: Mesangial proliferation without capillary injury

HYPOTHETICAL TEACHING CASE

Patient with established SLE.

LM: Increased mesangial cellularity and matrix.

IF: Granular mesangial immune deposits.
No active endocapillary inflammation.

PATTERN AND EXPLANATION

Class II — mesangial proliferative lupus nephritis.

The class is distinguished from class I by mesangial structural proliferation.

Case: Necrotizing glomerulonephritis in a minority of glomeruli

HYPOTHETICAL TEACHING CASE

SLE with hematuria and red cell casts.

Biopsy: Segmental necrosis and crescents in 4 of 12 glomeruli.

PATTERN AND EXPLANATION

Class III — focal lupus nephritis.

Only a minority of glomeruli is affected; Necrosis and crescents indicate active proliferative injury.

Case: Diffuse proliferation and wire loops

HYPOTHETICAL TEACHING CASE

SLE with hematuria, proteinuria, and impaired kidney function.

Biopsy: Extensive proliferative injury in 9 of 12 glomeruli; Subendothelial deposits.

PATTERN AND EXPLANATION

Class IV — diffuse lupus nephritis.

The extent exceeds half of sampled glomeruli; Wire loops reflect prominent subendothelial deposits.

Case: Severe proteinuria with capillary thickening

HYPOTHETICAL TEACHING CASE

SLE with nephrotic-range urinary protein loss.

Biopsy: Diffuse capillary-wall thickening and subepithelial deposits.

PATTERN AND EXPLANATION

Class V — membranous lupus nephritis.

Subepithelial immune deposition and basement-membrane remodeling account for the membranous morphology.

Case: Extensive global sclerosis

HYPOTHETICAL TEACHING CASE

SLE with longstanding reduction in renal function.

Biopsy: 10 of 11 glomeruli entirely globally sclerosed.

PATTERN AND EXPLANATION

Class VI — advanced sclerosing lupus nephritis.

More than 90% of glomeruli are globally scarred; The dominant lesion is chronic destruction.

A disciplined classification sequence

Are $\geq 90\%$ of glomeruli globally sclerosed? $\rightarrow$ consider class VI



Is there membranous subepithelial capillary-wall disease? $\rightarrow$ identify class V component



If active proliferation is present: Determine focal versus diffuse glomerular involvement



If mesangial only: Normal LM suggests I; Mesangial proliferation suggests II

What an immunofluorescence panel does not do

- Multiple immune-reactant deposits support immune-complex disease.
- Granular distribution helps localize deposits.
- The panel alone cannot quantify necrosis, crescents, or sclerosis.
- LM and EM remain essential for structural classification.

**Diagnostic integration
is stronger than any
one technique.**

Avoid confusion with other immune glomerulopathies

Consideration	Lupus nephritis	Other immune-complex disease
Systemic context	Established SLE / systemic autoimmunity	Alternative clinical context
Deposits	Frequently IgG $\pm$ IgA, IgM, C3, C1q	Composition/distribution vary
Interpretation	Class determined by morphology	Different disease-specific classification

Morphology-based recall: One feature per class

I	II	III	IV	V	VI
Mesangial deposits; normal LM	Mesangial proliferation	Focal proliferative	Diffuse proliferative	Membranous thickening	Global sclerosis $\geq 90\%$

Five pathology principles to retain

- Lupus nephritis is a systemic immune-complex disorder with several renal targets.
- Mesangial, subendothelial, and subepithelial deposits lead to different patterns of injury.
- Classes III and IV differ primarily in the extent of proliferative glomerular disease.
- Class V causes membranous remodeling; Class VI denotes extensive global sclerosis.
- Classify the biopsy with LM, IF, and EM while recording extraglomerular pathology.

Primary reference and scope

- Robbins, Cotran & Kumar: Pathologic Basis of Disease. 11th edition (2026).
- Lupus nephritis, glomerular immune injury, and systemic lupus pathogenesis sections.
- All figures in this lecture are original PowerPoint schematics, not diagnostic specimen images.
- Classification is interpreted alongside the full biopsy and clinical findings.