

Hyalinosis and Sclerosis

Glomerular patterns of chronic injury

Plasma-protein insudation

Collagenous matrix scar

Why separate these two findings?

- Hyalinosis identifies plasma-protein insudation into damaged glomerular structures.
- Sclerosis identifies newly accumulated collagenous extracellular matrix.
- Both may narrow or obliterate capillary lumens, but are not synonymous.

Hyaline

Leaked plasma proteins

Sclerosis

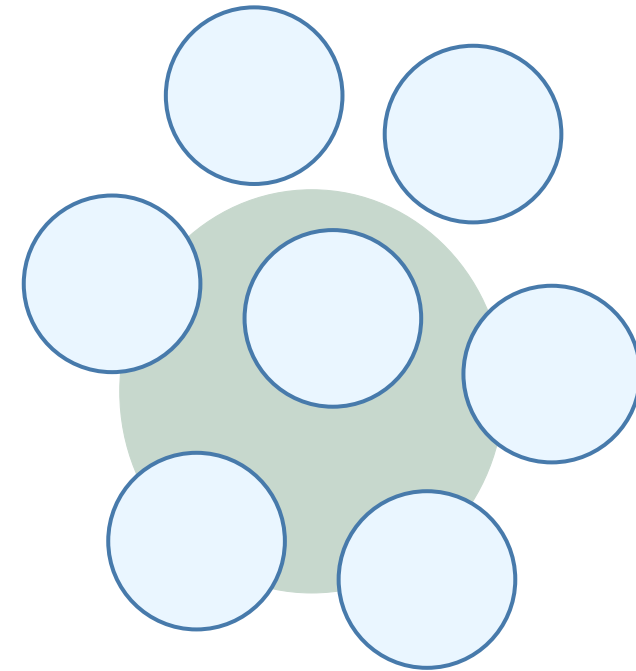
Collagen-rich matrix

Learning outcomes

- Identify hyalinosis and sclerosis by composition and light-microscopic appearance.
- Classify focal, diffuse, segmental, global, mesangial, and capillary-loop patterns.
- Connect podocyte loss, hyperfiltration, and diabetes to glomerular scarring.
- Interpret patterns without mistaking morphology for a unique etiology.

Glomerular tuft: The structural setting

- Anastomosing capillaries form a specialized filtration network.
- Capillary loops have a common barrier built from endothelium, GBM, and podocytes.
- Mesangial tissue supports the tuft and occupies intercapillary spaces.

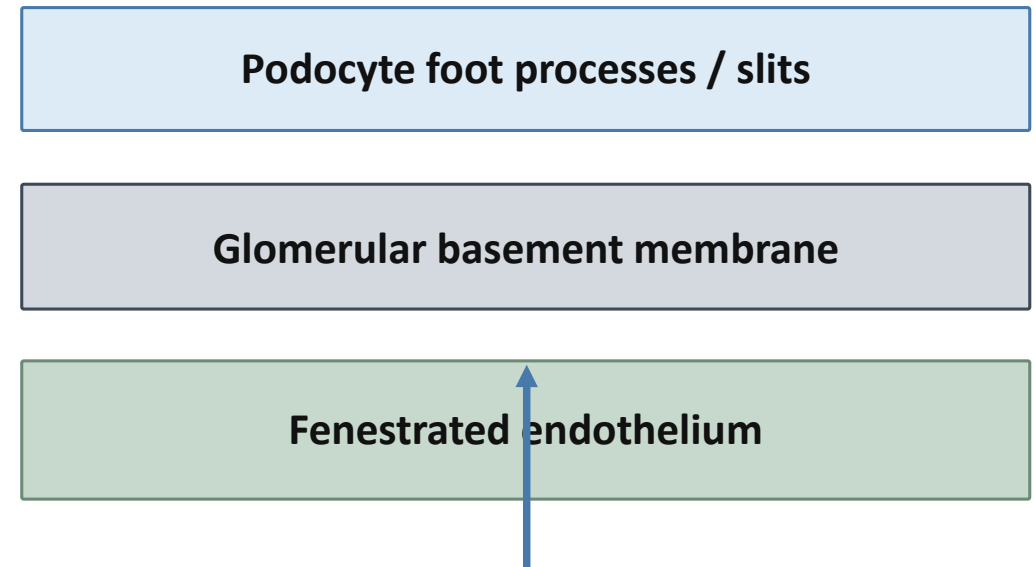


Schematic tuft

Three layers of the filtration barrier

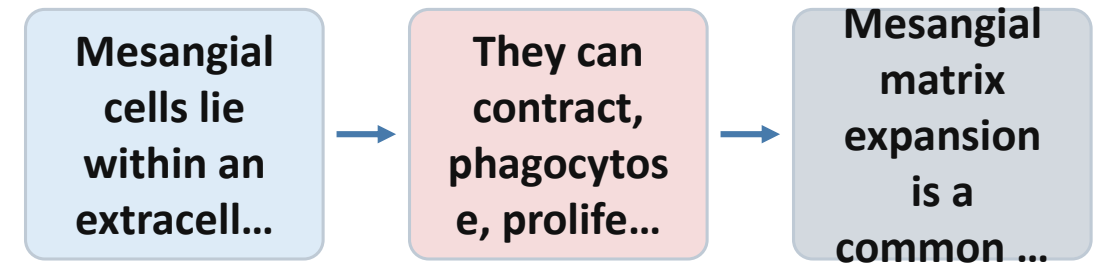
- Fenestrated capillary endothelium faces blood.
- The glomerular basement membrane (GBM) supplies a central matrix barrier.
- Interdigitating podocyte foot processes and slit diaphragms face urinary space.

Normal selective filtration



The mesangium is a matrix-producing compartment

- Mesangial cells lie within an extracellular meshwork between capillary loops.
- They can contract, phagocytose, proliferate, and synthesize matrix and collagen.
- Mesangial matrix expansion is a common anatomical substrate of sclerosis.



Normal protein restriction

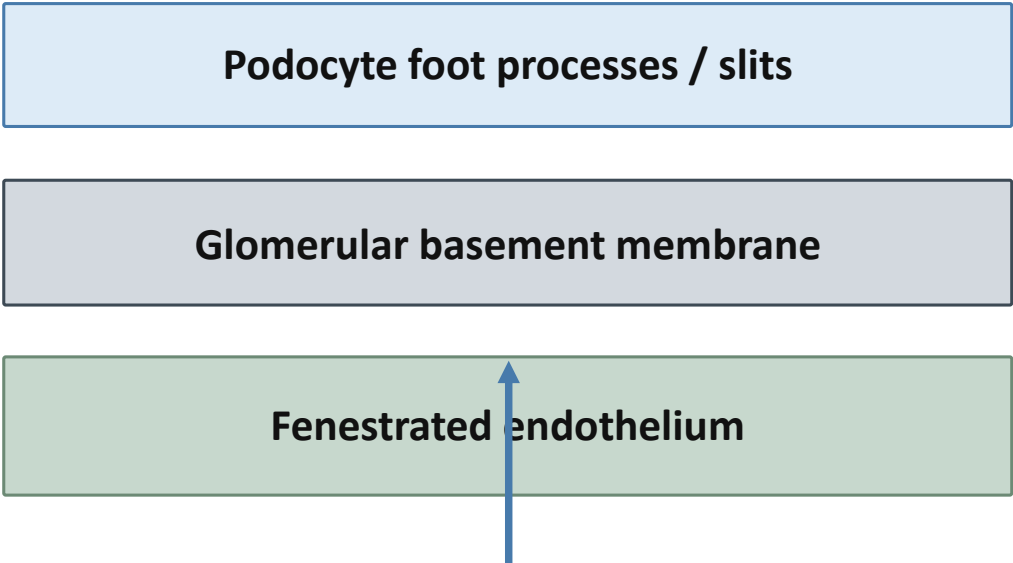
- Water and small solutes traverse the filtration barrier readily.
- Large proteins, including albumin, are normally retained in plasma.
- Size and charge selectivity depend on the integrated capillary wall.

Normal selective filtration

Podocyte foot processes / slits

Glomerular basement membrane

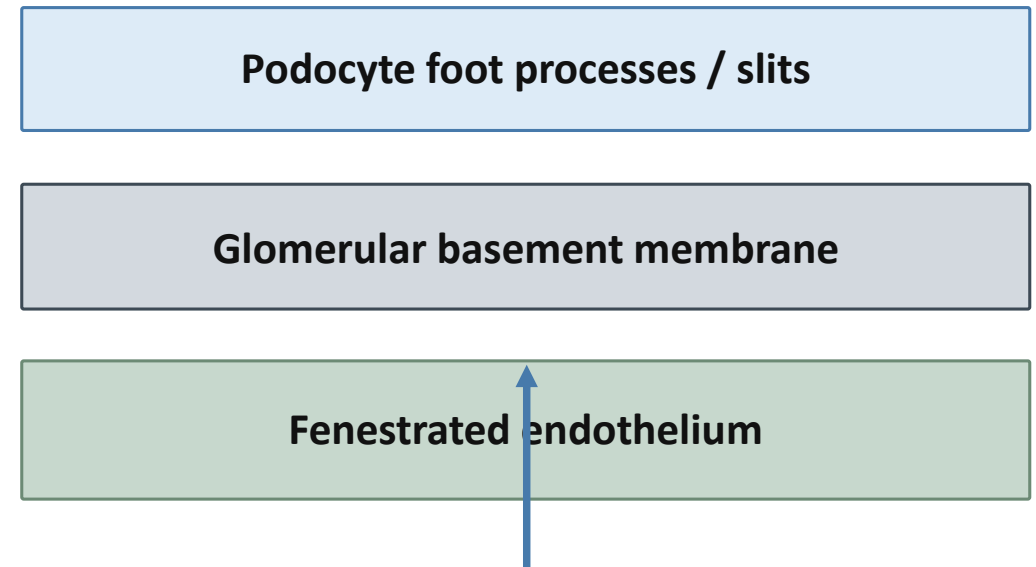
Fenestrated endothelium



Podocytes stabilize the filtration barrier

- Foot processes interdigitate around glomerular capillaries.
- Slit diaphragms contain nephrin and associated structural proteins.
- Podocyte maintenance of GBM and barrier integrity limits protein escape.

Normal selective filtration



Four general responses to glomerular injury

- Hypercellularity may reflect proliferation, leukocyte influx, or crescents.
- GBM thickening can arise through deposits, new matrix, or GBM remodeling.
- Hyalinosis is extracellular plasma-protein deposition.
- Sclerosis is collagenous matrix accumulation and scarring.

Hypercellularity

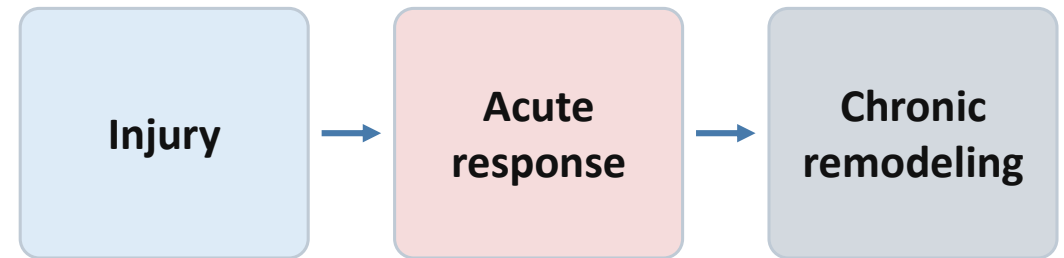
GBM thickening

Hyalinosis

Sclerosis

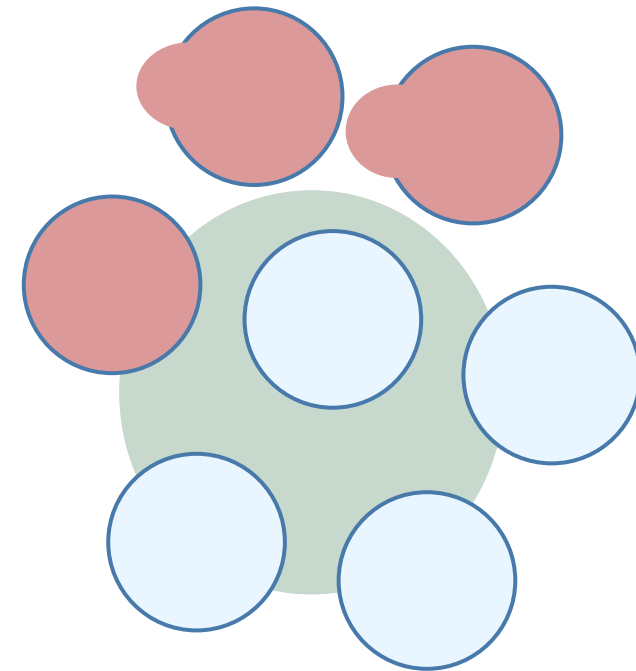
Acute reactions and chronic consequences

- Cellular proliferation and inflammatory infiltrates are prominent in active lesions.
- Hyalinosis and sclerosis are typical chronic structural responses.
- A biopsy may contain active damage and chronic injury simultaneously.



Hyalinosis: Morphologic definition

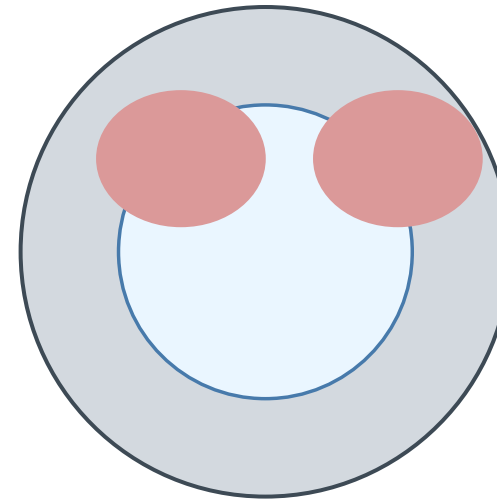
- Accumulation of homogeneous, eosinophilic material within glomerular structures.
- The material is extracellular and amorphous on light microscopy.
- The descriptor records an appearance, not a disease-specific diagnosis.



Schematic tuft

What is glomerular hyaline?

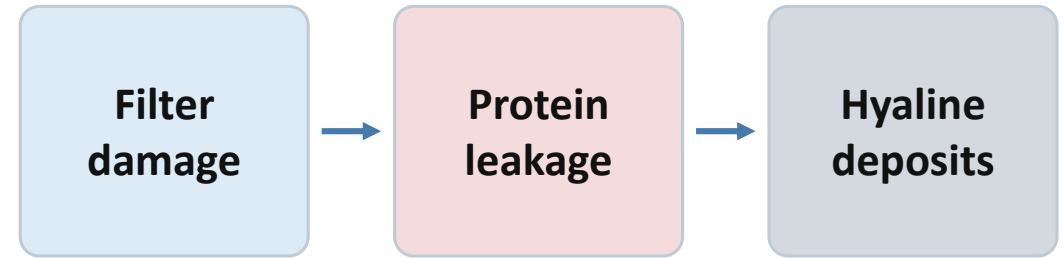
- Composed largely of high-molecular-weight plasma proteins.
- These proteins have escaped from the circulation across a damaged filter.
- Protein insudation differs fundamentally from collagen synthesis.



Capillary lumen

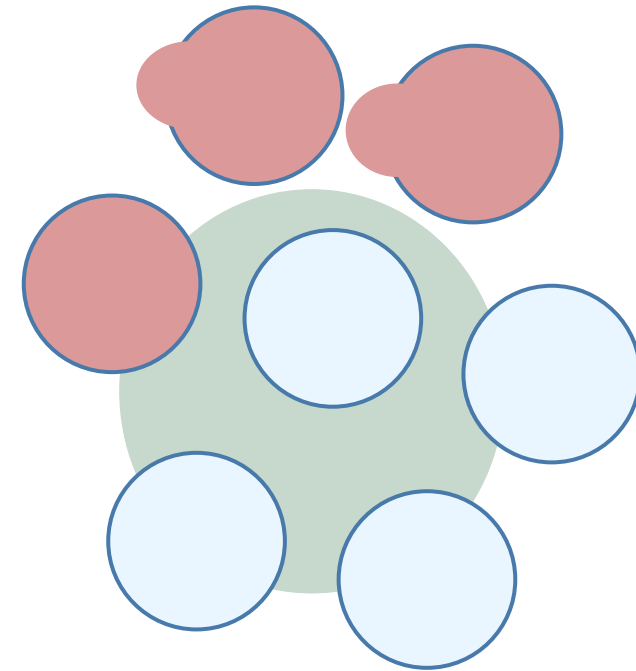
A causal sequence for hyalinosis

- Barrier injury increases local permeability to plasma proteins.
- High-molecular-weight proteins become trapped in glomerular structures.
- Extracellular protein-rich accumulations form recognizable hyaline deposits.



Homogeneous and eosinophilic: What this conveys

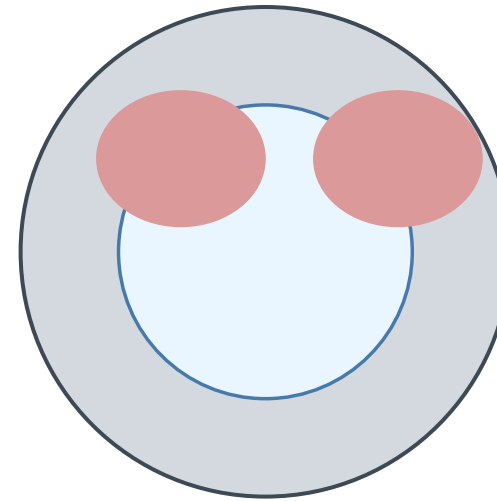
- “Homogeneous” refers to a relatively uniform light-microscopic texture.
- “Eosinophilic” refers to pink-red staining on hematoxylin–eosin sections.
- Neither adjective alone identifies the precise plasma protein composition.



Schematic tuft

Endothelial or capillary-wall injury permits insudation

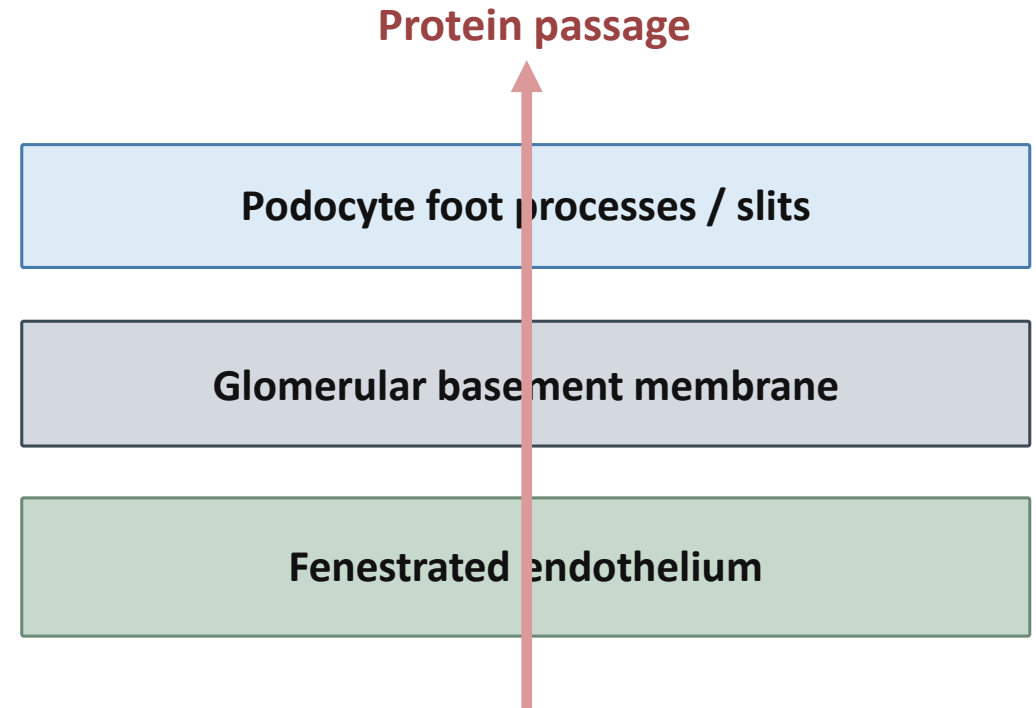
- Damage to endothelial cells or the capillary wall compromises filtration integrity.
- Plasma proteins can enter and accumulate within the injured tuft.
- The lesion is a response to barrier failure, not proof of one causal disease.



Capillary lumen

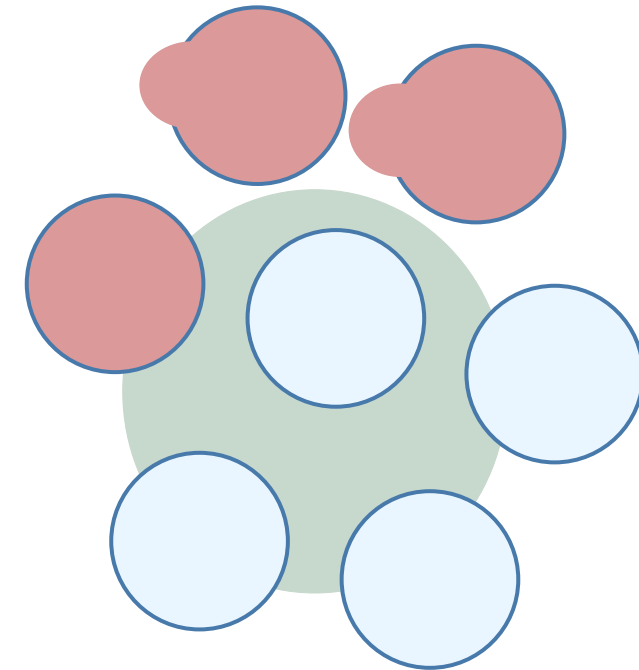
Podocyte depletion also promotes hyalinosis

- Extensive loss of podocytes leaves portions of GBM without epithelial coverage.
- The denuded surface becomes susceptible to increased protein permeability.
- Hyalinosis can follow podocyte loss in diabetes and collapsing glomerulosclerosis.



Anatomical placement of hyaline deposits

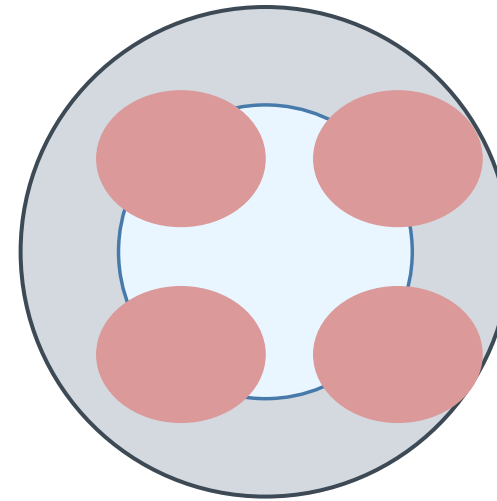
- Hyaline material accumulates within glomerular capillary-wall or tuft structures.
- Its distribution should be described in relation to capillary loops and mesangium.
- Location can aid pattern recognition but is not an etiologic test by itself.



Schematic tuft

Hyalinosis can occlude capillary lumens

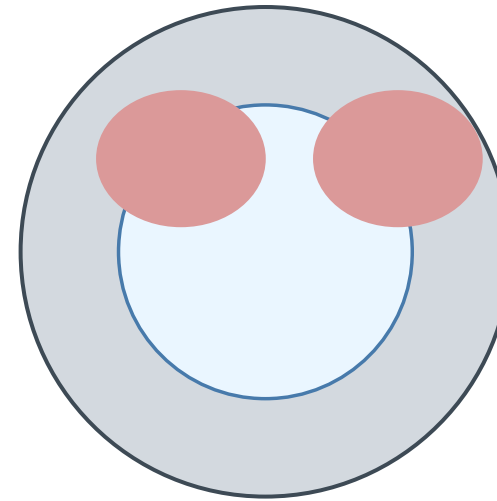
- Small insudative deposits need not close the filtration channel.
- Extensive protein-rich accumulation can fill portions of the tuft.
- Luminal obliteration converts a deposit into a structural barrier to perfusion.



Capillary lumen

Protein escape links injury and hyalinosis

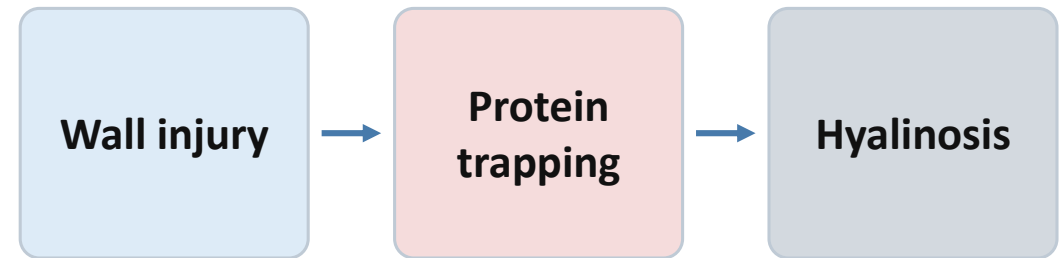
- Podocyte and barrier damage produces proteinuria by impairing filtration selectivity.
- Protein trapping inside the tuft underlies glomerular hyaline insudation.
- Urinary protein excretion and tissue hyaline deposition are related but distinct findings.



Capillary lumen

Hyalinosis is a shared injury response

- It can follow multiple mechanisms of glomerular filter damage.
- Endothelial injury and substantial podocyte loss are two recognized routes.
- Identical-looking hyaline material does not establish a unique underlying disease.



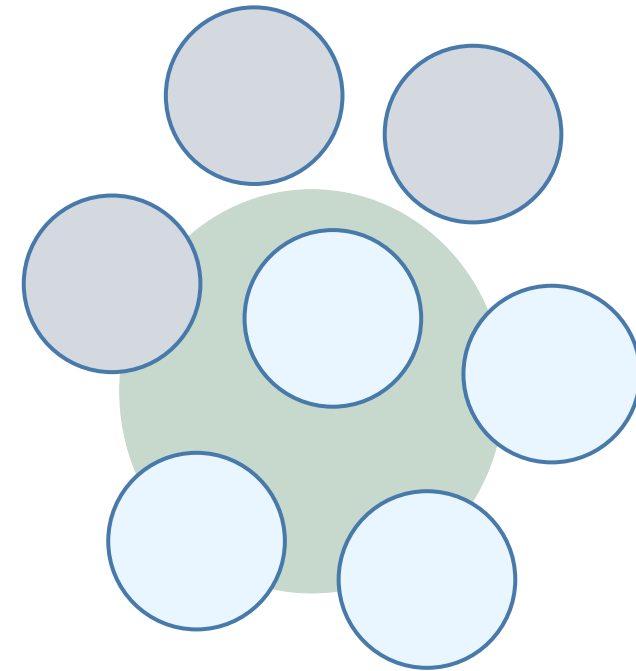
Hyalinosis versus sclerosis

- Hyalinosis: Leaked high-molecular-weight plasma proteins.
- Sclerosis: Deposition of collagenous extracellular matrix.
- Both can eventually diminish available capillary lumens.

Feature	Hyalinosis	Sclerosis
Main material	Plasma-derived proteins	Collagenous extracellular matrix
Process	Insudation / entrapment	Matrix accumulation / scarring
Functional result	Possible luminal occlusion	Partial or complete capillary obliteration

Sclerosis: Morphologic definition

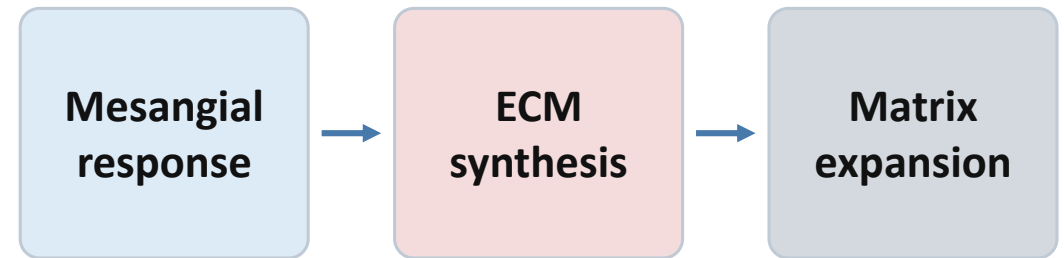
- Deposition of extracellular collagenous matrix within glomeruli.
- May occur in mesangial regions, capillary loops, or both.
- Advanced scarring progressively replaces functional capillary structures.



Schematic tuft

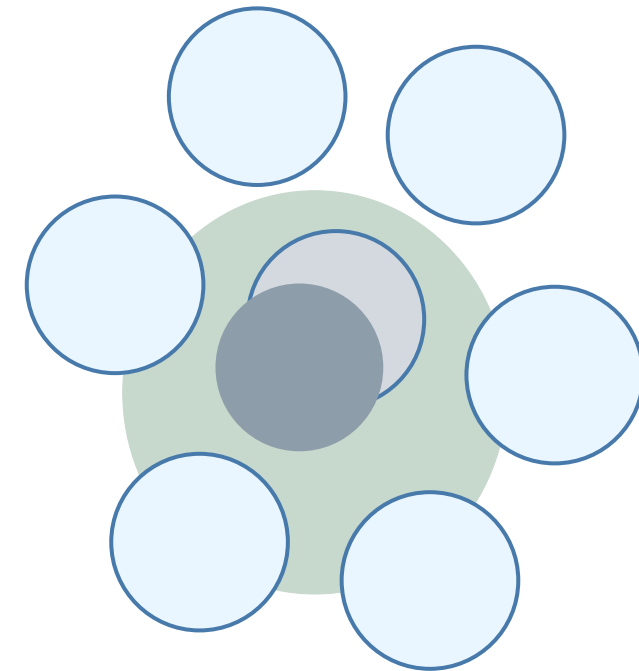
Matrix synthesis supplies the sclerotic lesion

- Mesangial cells possess the capacity to synthesize matrix and collagen.
- Persistent glomerular injury can be accompanied by extracellular matrix expansion.
- The defining product is matrix, not plasma-protein insudate.



Mesangial sclerosis

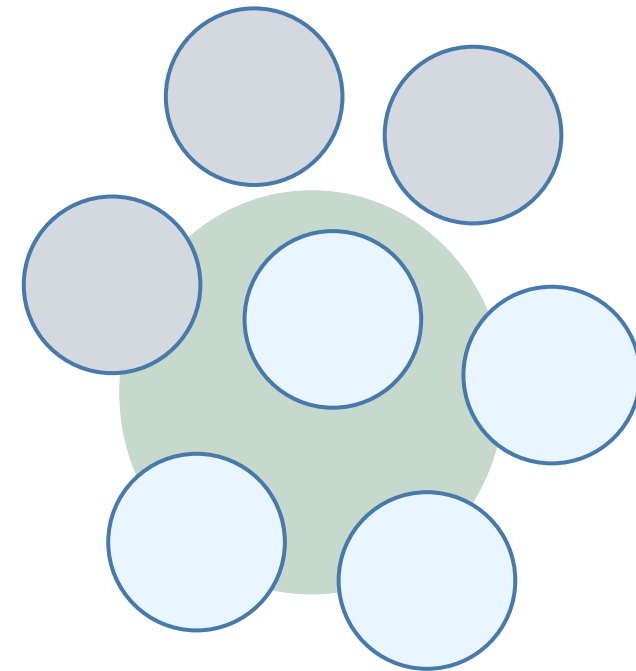
- Collagenous matrix accumulates principally in the mesangial compartment.
- Expanding mesangial regions alter the architecture between capillary loops.
- Diabetic glomerulosclerosis frequently has a substantial mesangial component.



Schematic tuft

Sclerosis of capillary loops

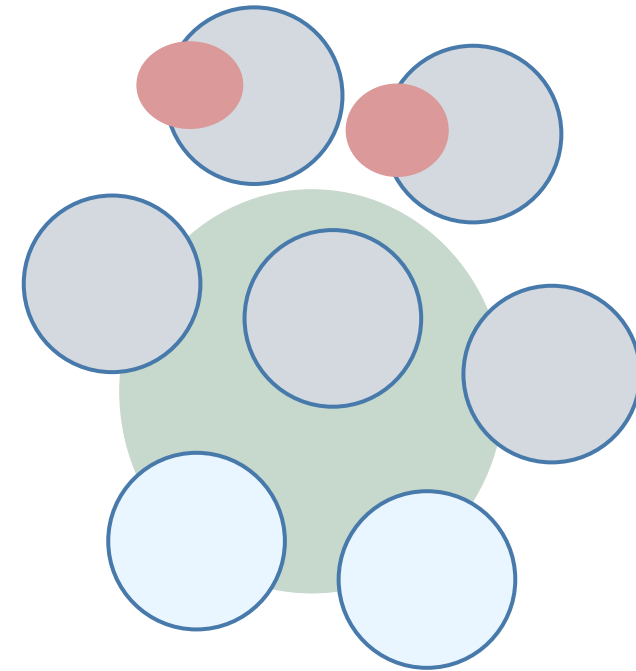
- Scar formation can involve filtration capillary walls or loops.
- Capillary lumens may become progressively narrowed or obliterated.
- The distribution differs from sclerosis limited to the mesangial core.



Schematic tuft

Combined mesangial and capillary sclerosis

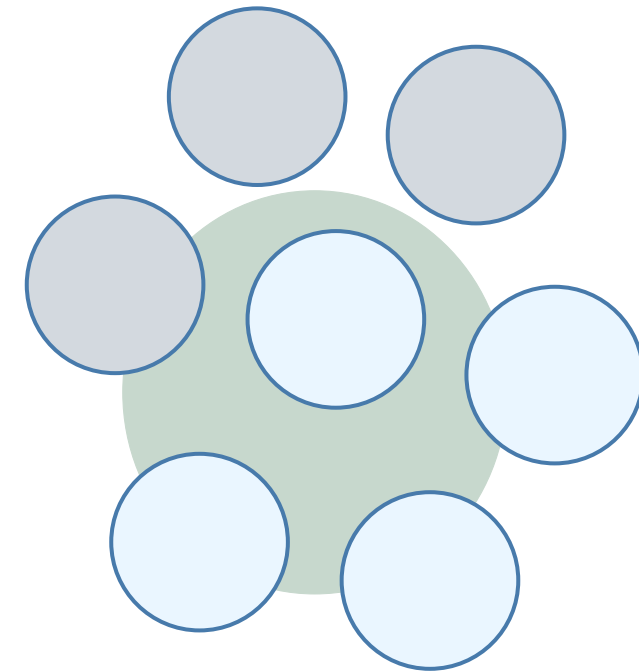
- Matrix accumulation may span both anatomical compartments.
- Patterns are best described rather than reduced to a single generic label.
- Widespread involvement can markedly reduce remaining open filtration surface.



Schematic tuft

Segmental sclerosis affects part of a glomerulus

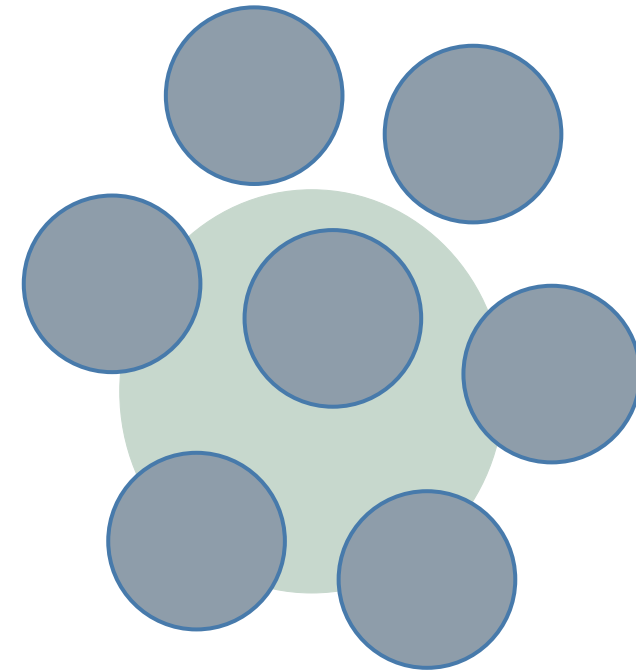
- Only a portion of the individual glomerular tuft is scarred.
- Remaining capillary loops may retain patent lumens.
- Segmental describes intraglomerular extent, not the percentage of glomeruli affected.



Schematic tuft

Global sclerosis affects an entire glomerulus

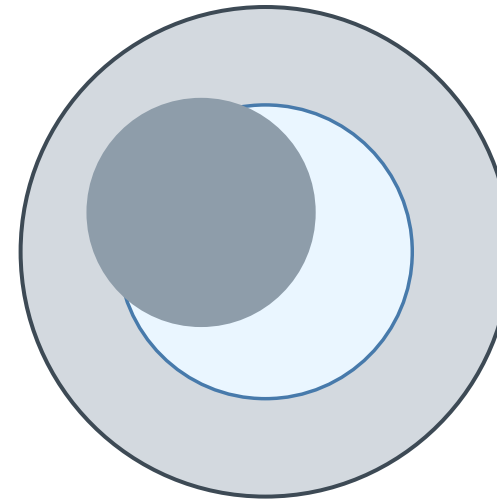
- The entire individual tuft is replaced or occupied by sclerosis.
- All glomerular capillary lumens in that tuft are effectively lost.
- Global refers to the glomerulus, not necessarily every glomerulus in the biopsy.



Schematic tuft

From matrix expansion to filtration loss

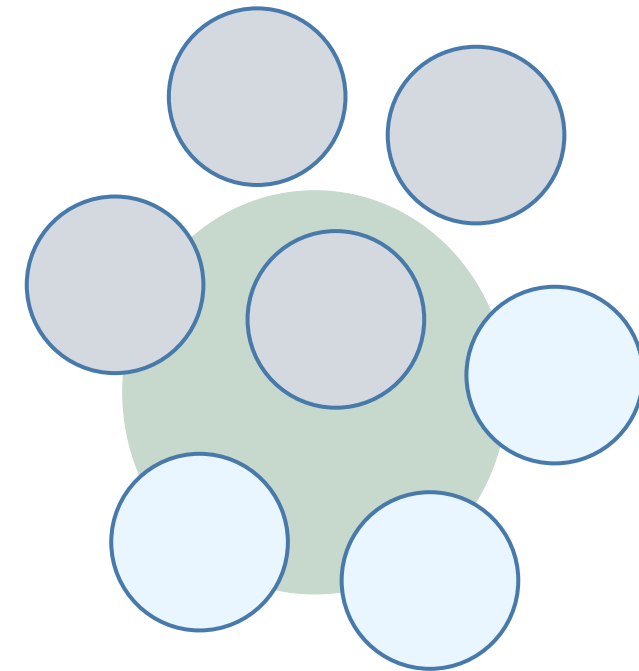
- ECM progressively encroaches upon capillary spaces.
- Some or all tuft lumens may ultimately be obliterated.
- Loss of patent glomerular capillaries reduces the effective filtration apparatus.



Capillary lumen

Capillary collapse is not the same as matrix deposition

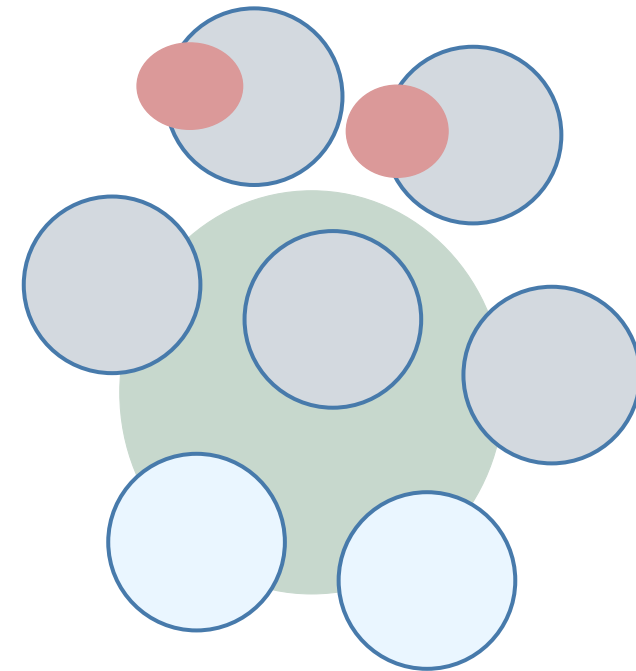
- Collapse is a geometric event: Capillary loops retract or lose their lumens.
- Sclerosis is a compositional event: Excess collagenous matrix accumulates.
- Both occur together in focal segmental glomerulosclerosis.



Schematic tuft

Hyalinosis and sclerosis often coexist

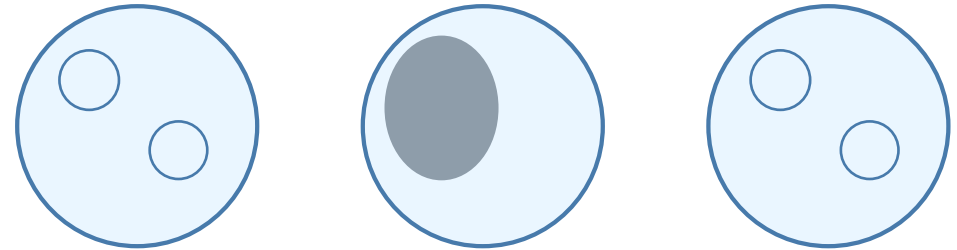
- Protein trapping can develop in areas where capillary walls are hyperpermeable.
- Concurrent collapse and matrix accumulation produce a sclerosing lesion.
- FSGS exemplifies combined hyalinosis, capillary collapse, and sclerosis.



Schematic tuft

Distribution at the kidney level: Focal or diffuse

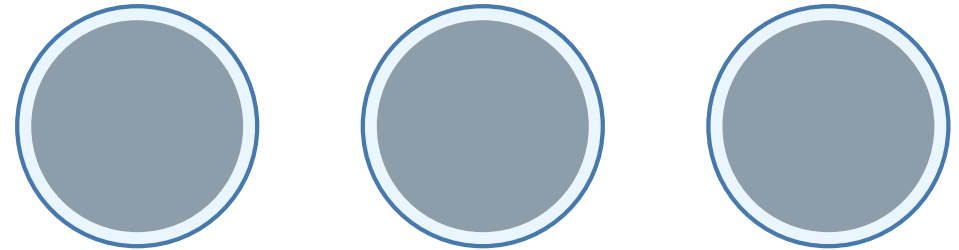
- Focal means only a fraction of glomeruli in the kidney are involved.
- Diffuse means glomeruli throughout the kidney are involved.
- This axis describes the number of glomeruli affected, not intratuft extent.



Only selected glomeruli affected

Distribution within a glomerulus: Segmental or global

- Segmental indicates involvement of only part of an individual glomerulus.
- Global indicates involvement of the entire individual glomerulus.
- This axis is independent of focal versus diffuse distribution.



Global within each tuft

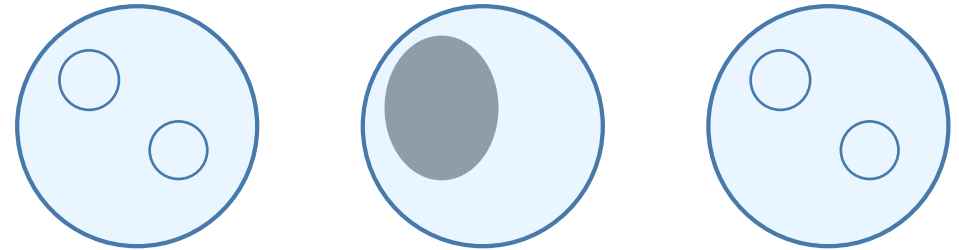
A two-axis vocabulary prevents confusion

- Focal/diffuse describes between-glomerulus distribution.
- Segmental/global describes within-glomerulus extent.
- Both axes may be combined in a complete morphological description.



Focal segmental: How to read the phrase

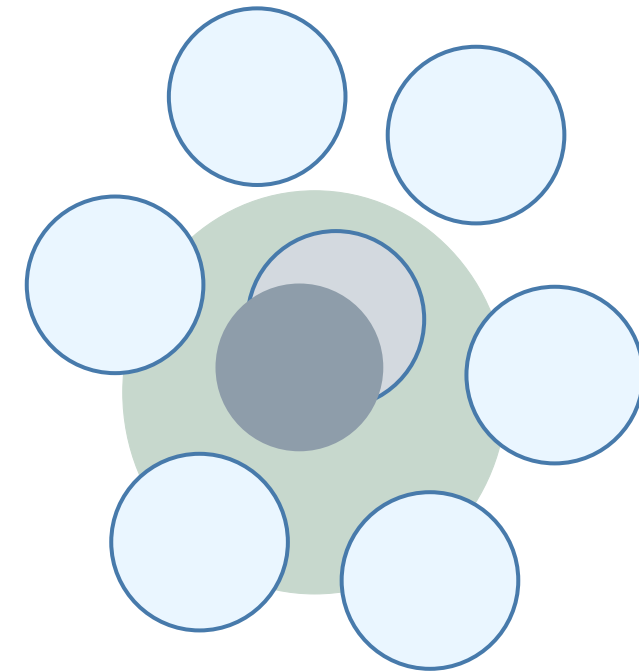
- Focal: Some glomeruli have lesions while others remain uninvolved.
- Segmental: Affected glomeruli show sclerosis of only part of the tuft.
- A lesion can be missed when the biopsy samples too few glomeruli.



Only selected glomeruli affected

Mesangial versus capillary-loop dominance

- A mesangial pattern is centered between capillary loops.
- A capillary-loop pattern is centered on filtration capillaries.
- Report dominant location independently of focal/diffuse or segmental/global extent.



Schematic tuft

A disciplined glomerular morphology report

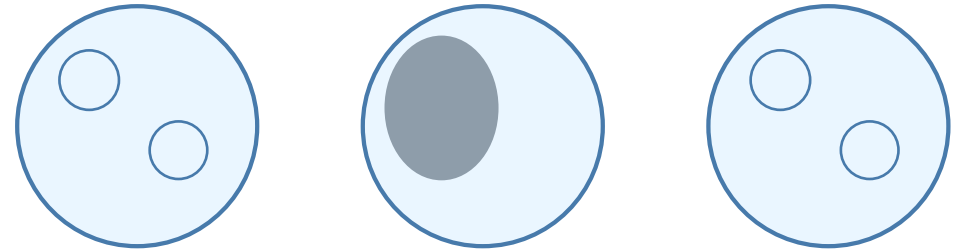
- First state material: Hyaline deposits, collagenous matrix, or both.
- Then report compartment: Mesangial, capillary loop, or combined.
- Finally record the number of glomeruli and intratuft extent affected.



Integrated morphological description

Sampling matters for focal lesions

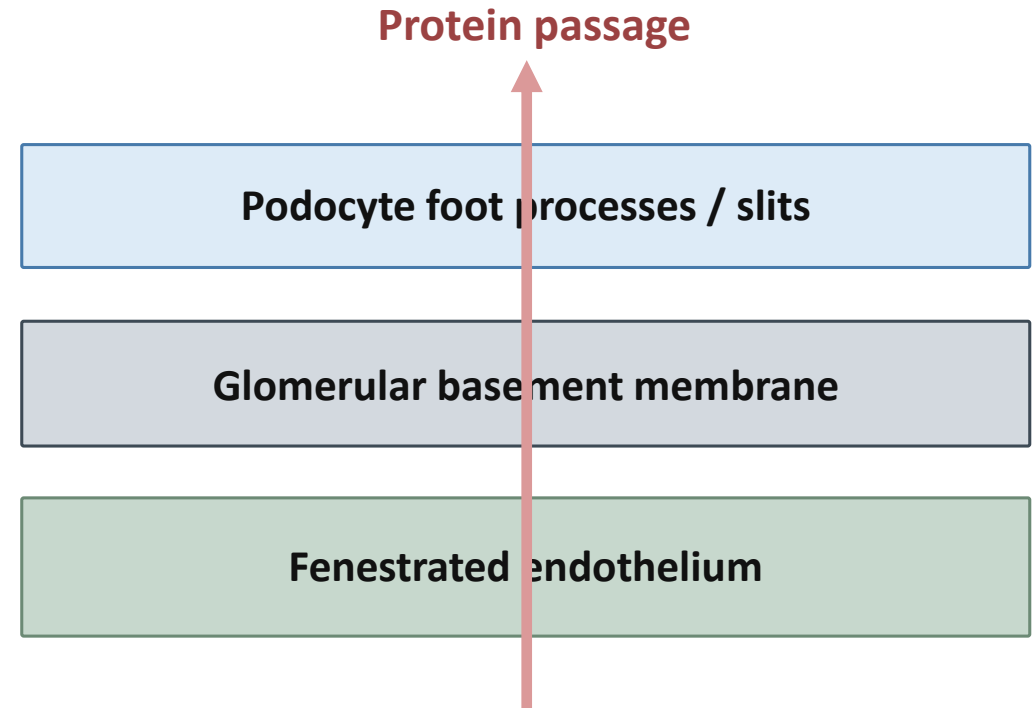
- FSGS lesions may initially affect only a minority of glomeruli.
- A small biopsy can miss a focal segmental lesion.
- An apparently uninvolved glomerulus does not exclude widespread podocyte injury.



Only selected glomeruli affected

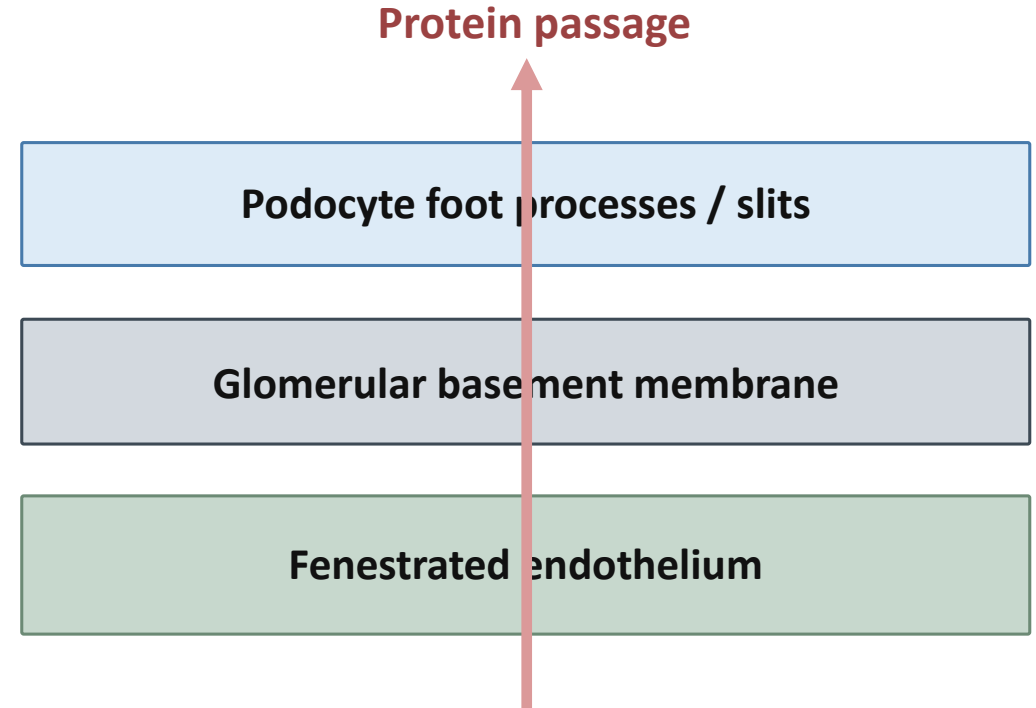
Podocytopathy: Injury begins at the filter

- Podocyte injury can occur with immune and nonimmune insults.
- Morphologic changes include foot-process effacement and loss of slit diaphragms.
- Severe injury can progress to detachment and podocyte depletion.



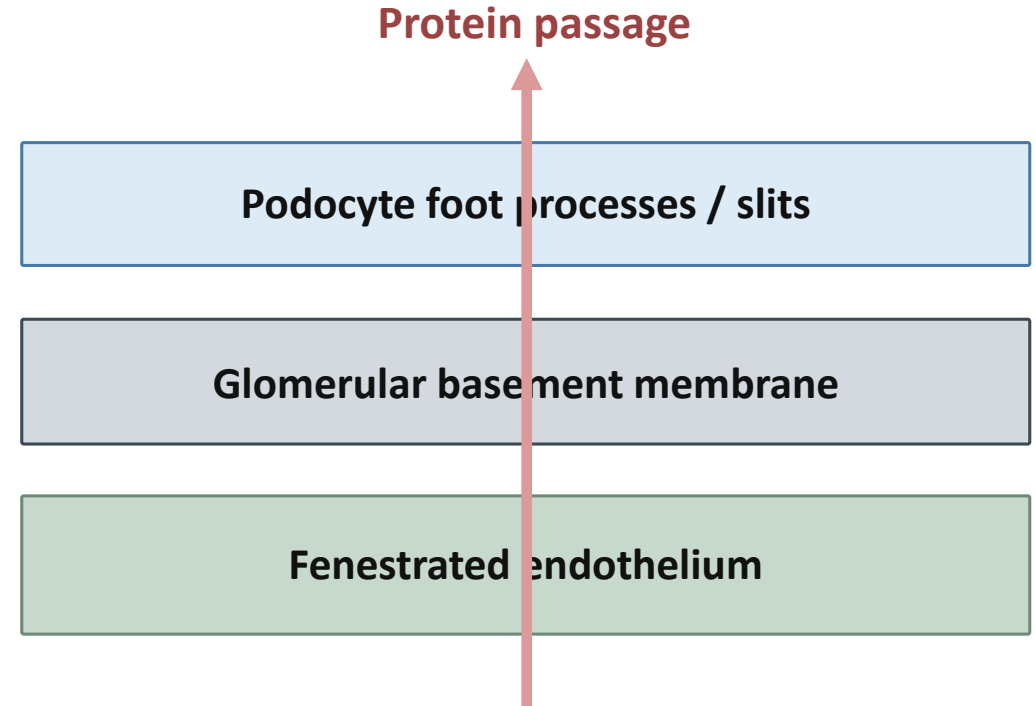
Foot-process effacement precedes visible scar

- Foot processes become flattened and the slit-diaphragm apparatus is disrupted.
- Increased permeability and proteinuria can occur before segmental sclerosis is evident.
- Electron-microscopic injury and light-microscopic scarring occupy different stages.



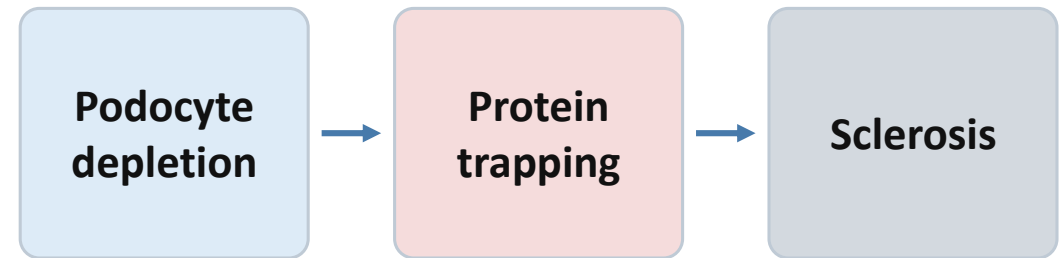
Podocyte detachment creates an unprotected GBM

- Podocytes have limited regenerative capacity.
- Persistent loss exposes segments of GBM and promotes abnormal permeability.
- The uncovered tuft becomes vulnerable to protein entrapment and collapse.



Primary FSGS: Protein trapping and matrix

- Podocyte loss may exceed compensation by surviving podocytes.
- Protein-rich material becomes trapped in hyperpermeable, denuded segments.
- Capillary collapse and increased ECM deposition culminate in hyalinosis and sclerosis.



FSGS names a lesion pattern, not one etiology

- The pattern can be primary, adaptive, inherited, or associated with direct podocyte injury.
- High-risk APOL1 alleles are associated with some podocyte-loss phenotypes.
- Morphology must be interpreted with the clinical and etiologic context.

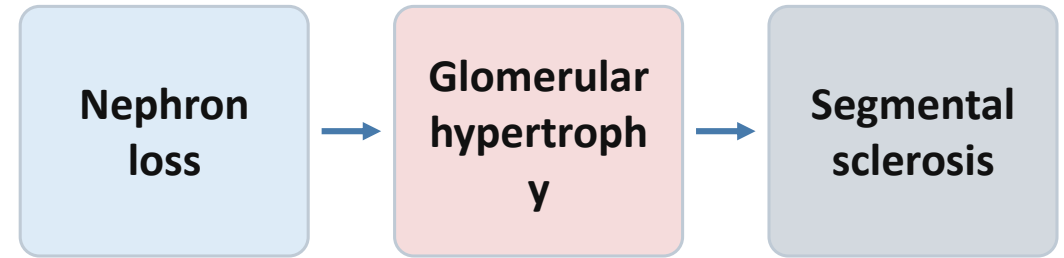
Primary FSGS

Adaptive or inherited

**Other podocyte
insults**

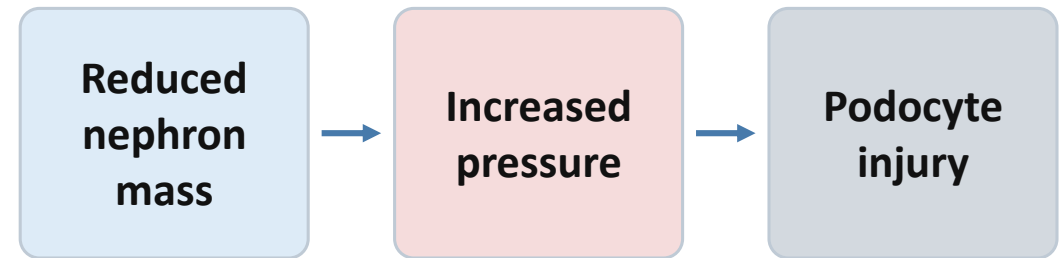
Adaptive glomerulosclerosis after nephron loss

- Reduction in functioning renal mass shifts workload onto remaining nephrons.
- Compensatory glomerular enlargement and high intracapillary pressure follow.
- These adaptive responses may contribute to podocyte injury and secondary scarring.



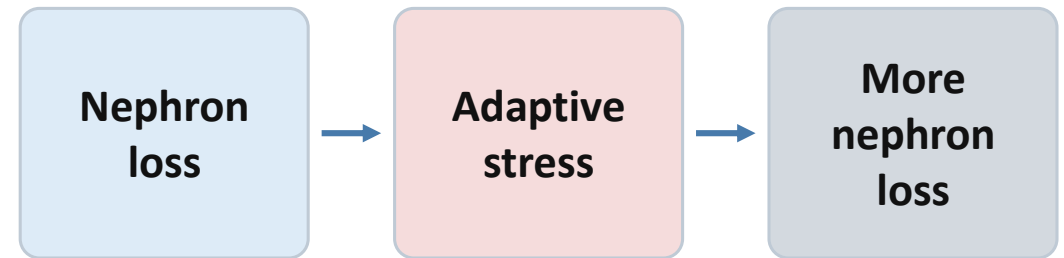
Hyperfiltration is initially compensatory

- Increased glomerular blood flow and filtration can maintain renal function initially.
- Sustained transcapillary pressure exposes the filter to mechanical stress.
- Long-term adaptation may become a driver of segmental sclerosis.



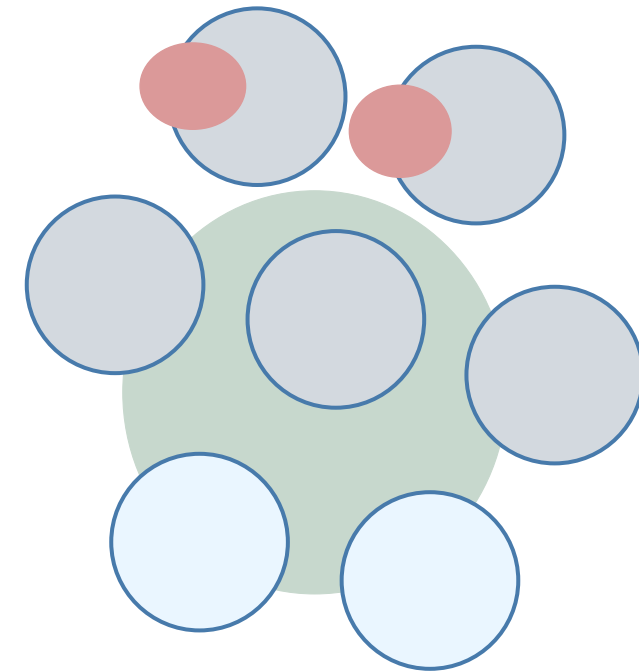
An amplification loop drives adaptive FSGS

- Glomerular hypertension injures podocytes and endothelium.
- Protein leakage, mesangial matrix accumulation, and sclerosis cause nephron loss.
- Further nephron loss magnifies hyperfiltration in the surviving glomeruli.



FSGS: The segmental lesion under light microscopy

- Collapse of capillary loops accompanies expanded matrix in scarred segments.
- Hyaline material may be trapped along capillary walls and occlude lumens.
- Lipid droplets and foamy macrophages may be present in the lesions.



Schematic tuft

FSGS: Ancillary pathology is contextual

- Electron microscopy can reveal widespread podocyte foot-process effacement.
- IgM and C3 may be present in sclerotic or mesangial areas on immunofluorescence.
- These findings are interpreted alongside lesion pattern and clinical presentation.

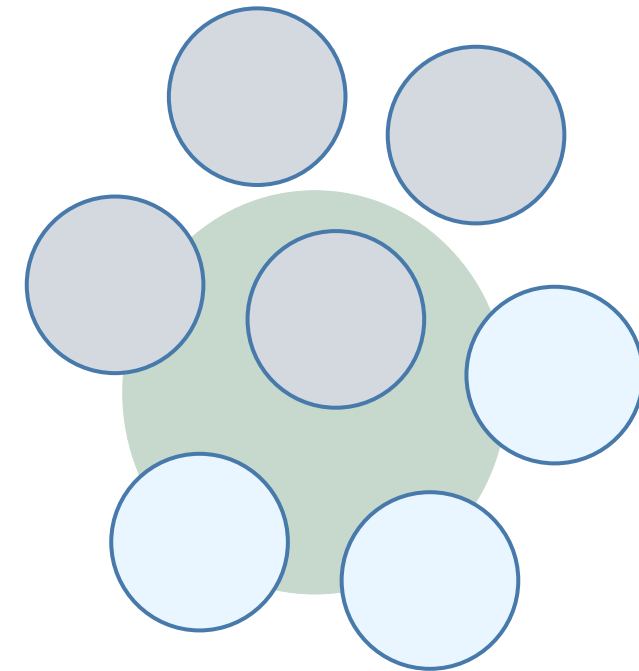
Light microscopy

Electron microscopy

Immunofluorescence

Collapsing glomerulopathy: Architectural loss

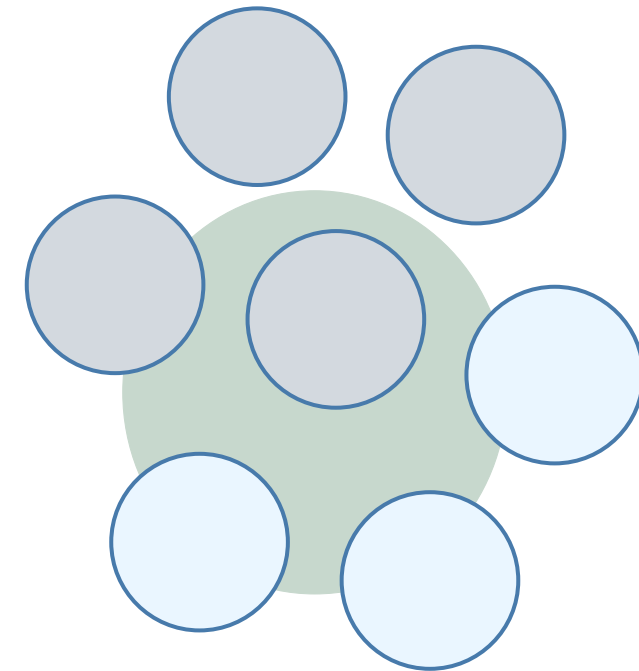
- The tuft shows retraction or collapse, sometimes with other FSGS-type lesions.
- Marked podocyte loss accompanies injury to the capillary architecture.
- Parietal epithelial-cell activation/proliferation may follow denudation.



Schematic tuft

Why collapsing lesions fit this topic

- Severe podocyte depletion exposes the tuft to abnormal protein leakage.
- Capillary collapse reduces open glomerular lumen space.
- Hyalinosis and matrix remodeling are relevant consequences of severe injury.



Schematic tuft

Diabetes produces more than one matrix lesion

- Glomerular basement membranes thicken in diabetic microangiopathy.
- Mesangial matrix may expand diffusely or form nodules.
- Protein-rich hyalinosis is separate from collagenous mesangial sclerosis.

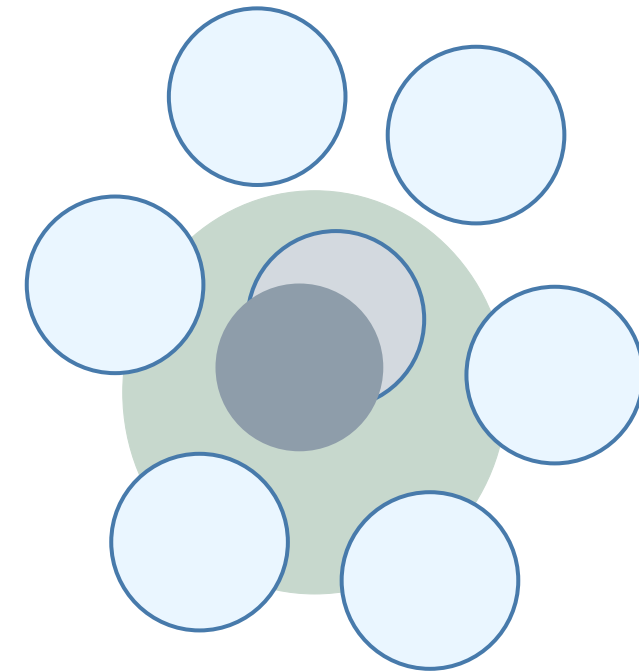
GBM thickening

Matrix sclerosis

Hyalinosis

Diffuse diabetic mesangial sclerosis

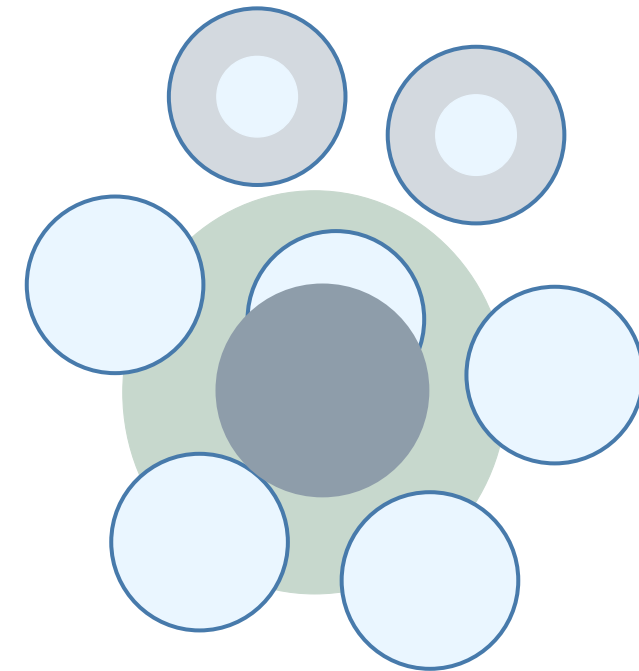
- Mesangial extracellular matrix increases throughout affected glomeruli.
- The excess matrix is PAS-positive on histologic sections.
- Increasing mesangial expansion correlates with worsening proteinuria and renal function.



Schematic tuft

Nodular diabetic glomerulosclerosis

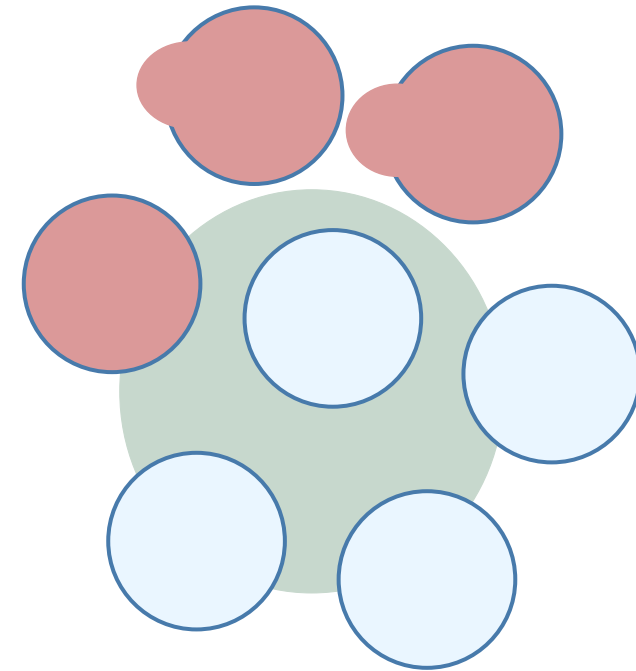
- Kimmelstiel–Wilson nodules are rounded PAS-positive mesangial matrix accumulations.
- They lie within glomerular lobules; Adjacent peripheral capillary loops may remain open.
- Nodules occur against a background of diffuse mesangial sclerosis.



Schematic tuft

Hyaline lesions accompanying diabetic sclerosis

- Hyaline material can accumulate in capillary loops as “fibrin caps.”
- Hyaline deposits may also adhere to Bowman capsule as “capsular drops.”
- The terms denote anatomical patterns of proteinaceous material, not collagen nodules.



Schematic tuft

Diabetic arteriolar hyalinosis is a distinct site

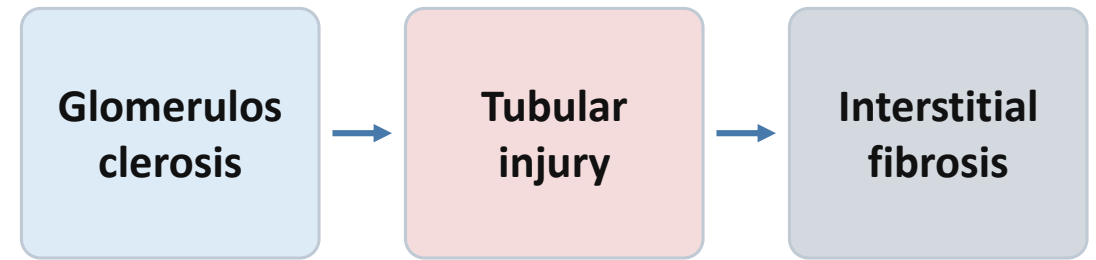
- Hyaline arteriosclerosis in diabetes can affect afferent and efferent arterioles.
- This is vascular hyalinosis, anatomically different from glomerular tuft deposits.
- Arteriolar injury contributes to renal ischemia and chronic damage.

Afferent arteriole

Efferent arteriole

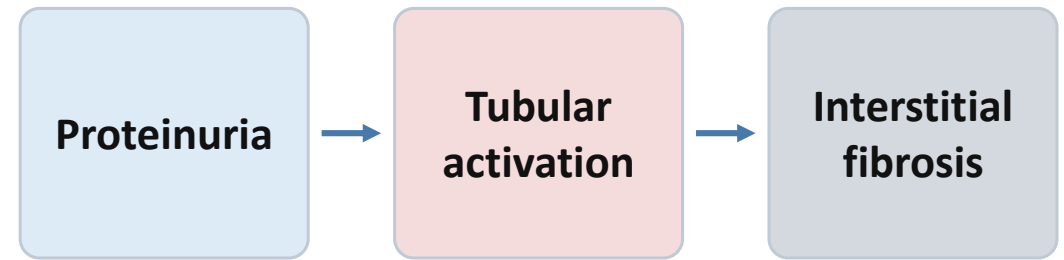
Glomerulosclerosis predicts wider renal damage

- Progressive kidney damage involves both glomerulosclerosis and tubulointerstitial fibrosis.
- Scarred glomeruli can compromise perfusion of downstream tubular segments.
- The fibrotic interstitium is clinically important beyond the glomerular lesion alone.



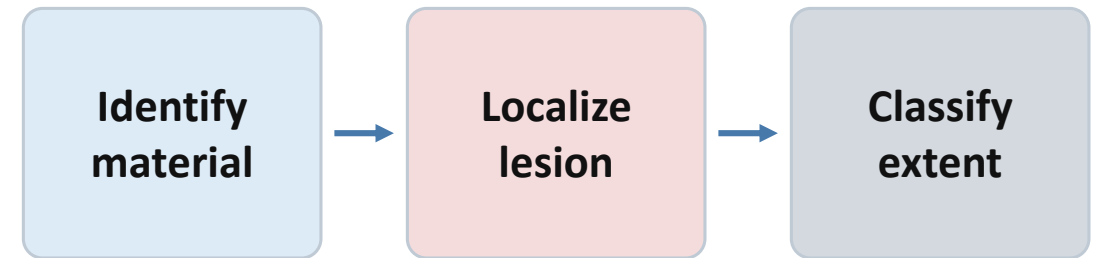
Proteinuria can reinforce tubulointerstitial injury

- Filtered proteins may injure and activate tubular epithelial cells.
- Activated tubules produce inflammatory and fibrogenic mediators.
- Tubulointerstitial fibrosis contributes to further functional decline.



Interpretation sequence for a renal biopsy

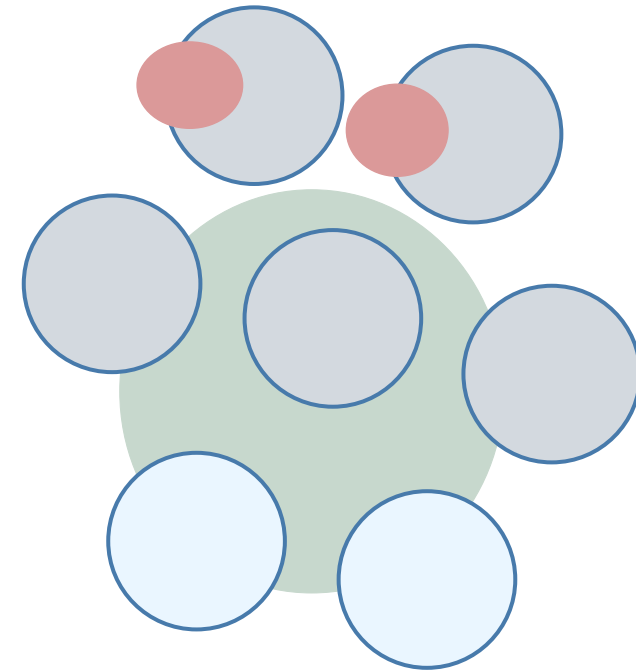
- Identify the principal morphologic abnormality: Hyaline, matrix, collapse, or mixed.
- Determine where it lies and how it is distributed across glomeruli.
- Integrate podocyte findings, vascular/tubular changes, and the clinical setting.



Case 1: Proteinuria and a segmental scar

- A biopsy shows a minority of glomeruli with a scarred segment of the tuft.
- The affected segment contains matrix, collapsed capillary loops, and hyaline material.
- Question: Which morphological terms are justified?

Hypothetical teaching vignette · schematic

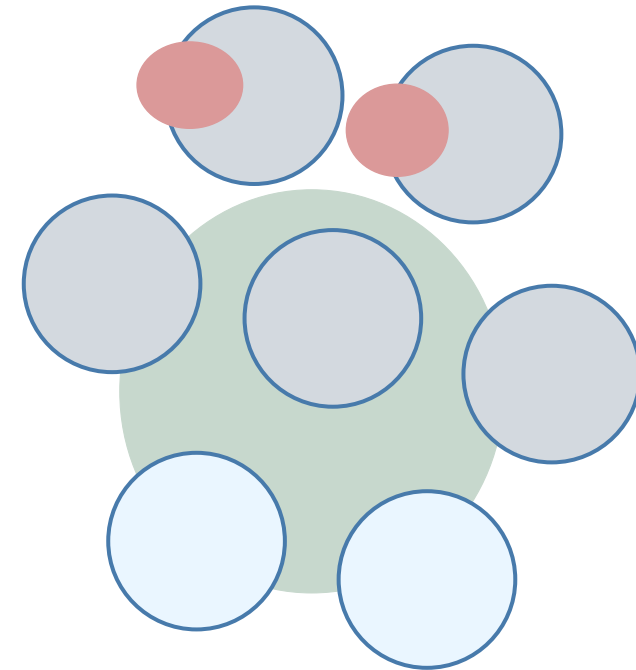


Schematic tuft

Case 1: Lesion-level interpretation

- Focal: Only some glomeruli are affected.
- Segmental: Only part of each affected tuft is scarred.
- Hyalinosis plus sclerosis: Protein insudation accompanies collagenous matrix.
- The pattern is compatible with FSGS; Its cause needs separate assessment.

Hypothetical teaching vignette · schematic

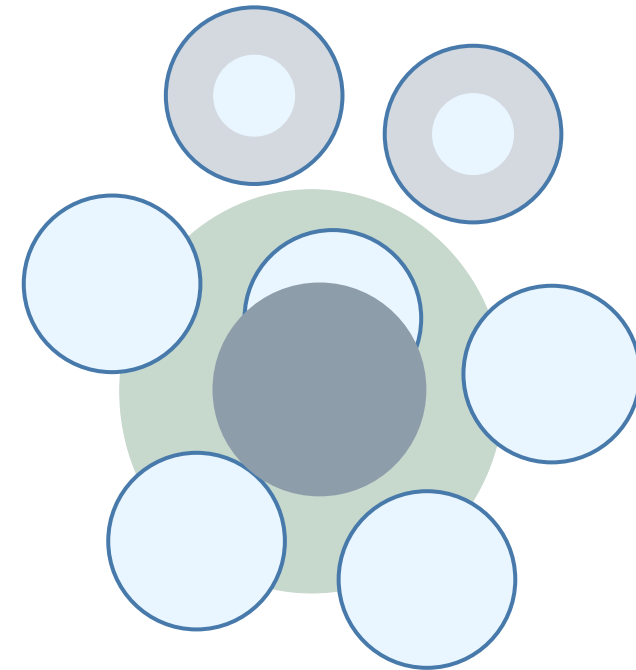


Schematic tuft

Case 2: Diabetic renal morphology

- A patient with established diabetes has diffuse PAS-positive mesangial expansion.
- Rounded mesangial nodules coexist with protein-rich capillary deposits.
- Question: Which components represent sclerosis and which represent hyalinosis?

Hypothetical teaching vignette · schematic

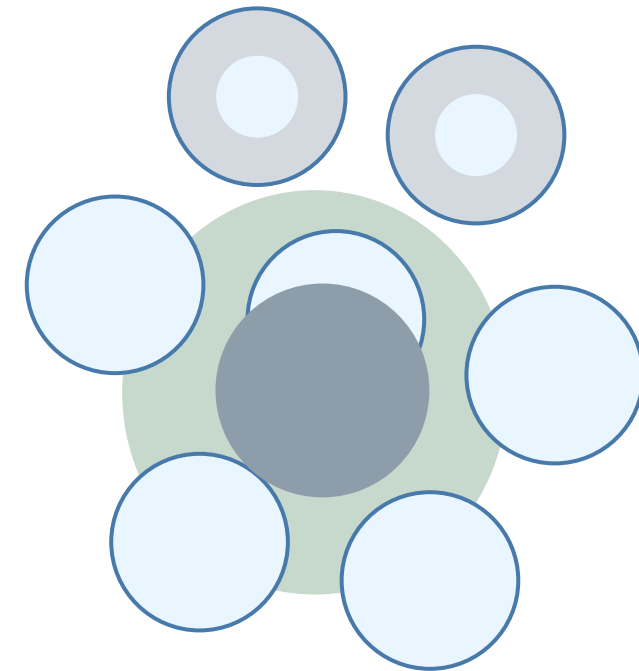


Schematic tuft

Case 2: Separating deposits from scar

- Diffuse/nodular mesangial matrix corresponds to diabetic glomerulosclerosis.
- Protein-rich capillary deposits correspond to hyalinosis (“fibrin caps”).
- Both may coexist, but they identify different extracellular materials.

Hypothetical teaching vignette · schematic

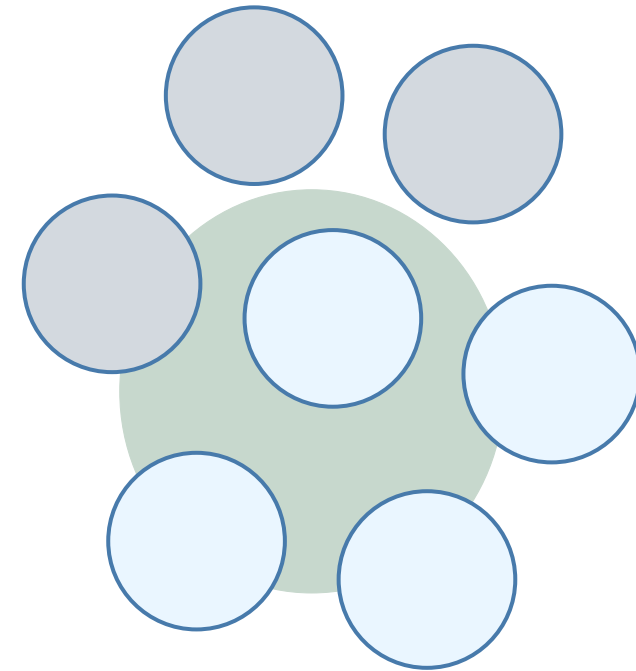


Schematic tuft

Case 3: Classify the distribution precisely

- Nearly every sampled glomerulus contains sclerosis confined to a segment.
- Only some loops in each affected glomerulus are obliterated.
- Question: Is the distribution focal, diffuse, segmental, or global?

Hypothetical teaching vignette · schematic

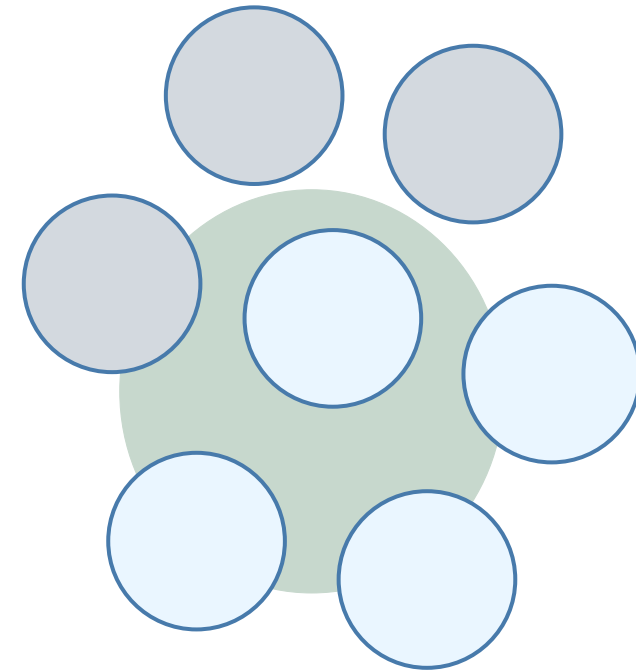


Schematic tuft

Case 3: Two descriptors are required

- Diffuse: Nearly all glomeruli in the sampled tissue are affected.
- Segmental: Only a portion of each involved glomerular tuft is scarred.
- “Diffuse segmental sclerosis” is morphologically meaningful; Axes are independent.

Hypothetical teaching vignette · schematic



Schematic tuft

Integrated differential: Three appearances

- Hyalinosis: Extracellular uniform eosinophilic plasma-protein material.
- Sclerosis: Expanded collagenous matrix in mesangium and/or loops.
- GBM thickening: A separate structural reaction that may accompany either finding.

Pattern	Defining structural change	Typical context in the source
Hyalinosis	Insudated high-molecular-weight proteins	Capillary-wall injury / podocyte loss
Sclerosis	Collagenous ECM accumulation	FSGS / diabetic glomerulosclerosis
GBM thickening	Expanded or remodeled basement membrane	Diabetes and multiple glomerulopathies

Five points to retain

- Hyaline is plasma-derived; Sclerosis is matrix-derived.
- Hyalinosis and sclerosis can coexist in an injured glomerulus.
- Focal/diffuse and segmental/global describe different spatial axes.
- Podocyte loss and maladaptive hyperfiltration can drive progressive sclerosis.
- A morphological pattern must not be mistaken for one exclusive etiology.

Primary textbook references

- Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026).
- Chapter 20: The Kidney — glomerular structure, injury responses, progression, and FSGS.
- Chapter 24: The Endocrine System — diabetic nephropathy and glomerulosclerosis.
- Conceptual illustrations in this lecture are original editable schematics, not photomicrographs.