

Nephrosclerosis

Vascular remodeling, cortical scarring, and severe hypertensive injury

Renal pathology

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Learning objectives

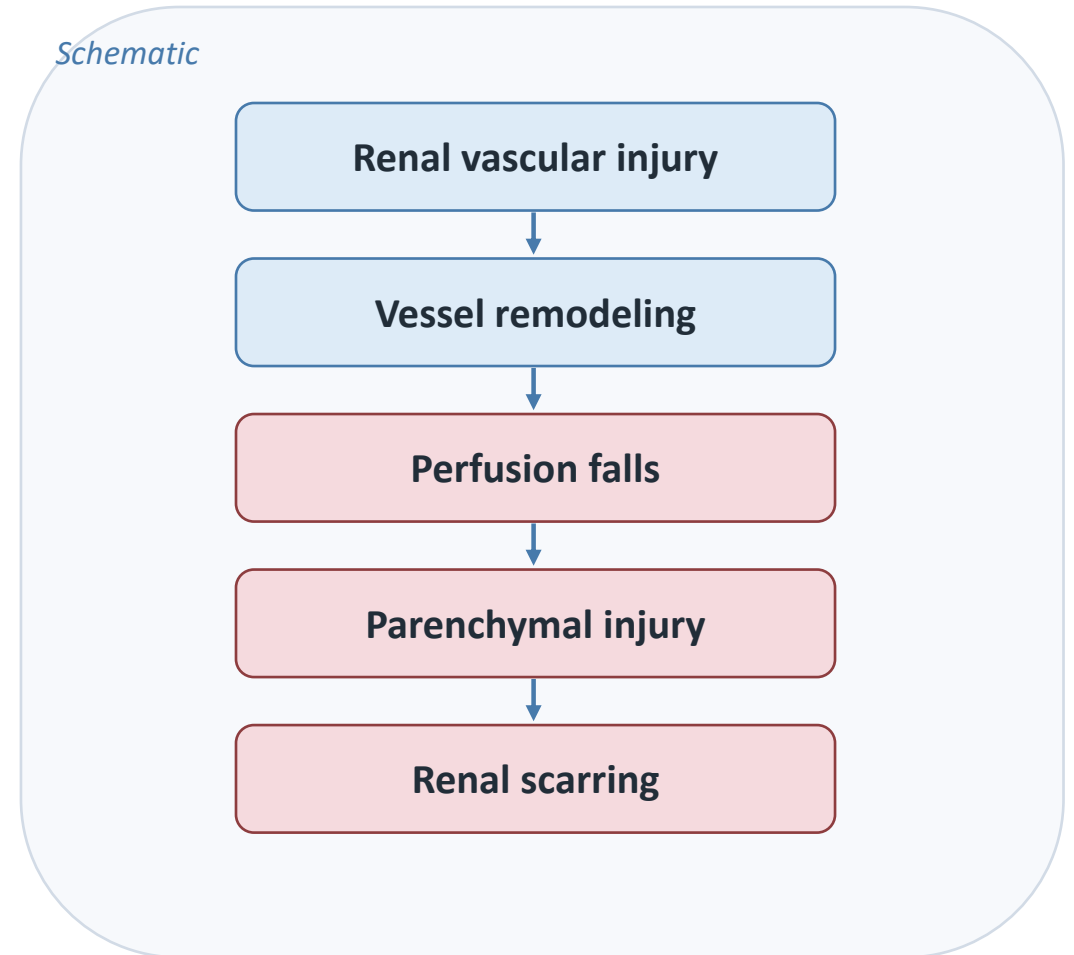
- Define nephrosclerosis by the compartments involved.
- Connect vascular wall injury to ischemic nephron loss.
- Recognize characteristic gross and microscopic alterations.
- Distinguish ordinary nephrosclerosis from severe hypertensive injury.

The kidney in systemic vascular disease

Mechanism

Renal vessels are involved secondarily in many kidney diseases.
Systemic vascular disorders can also produce primary renal injury.
Hypertension and renal disease have a bidirectional clinical relationship.

Schematic



Nephrosclerosis is a pattern, not one lesion

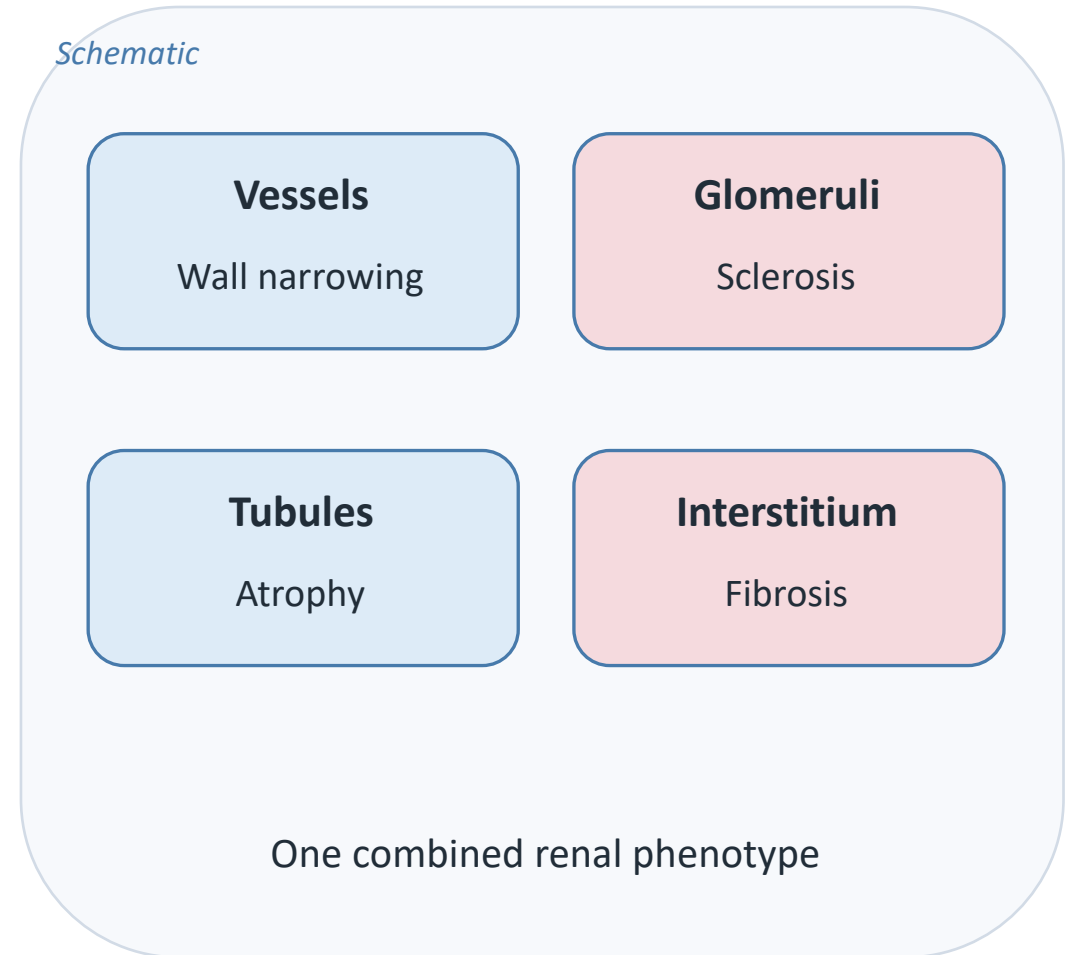
Core teaching points

It is a constellation of non-specific structural abnormalities.

Glomerular, tubular, interstitial, arterial, and arteriolar damage coexist.

No individual component alone defines the whole pattern.

Schematic



Four tissue components define the pattern

Core teaching points

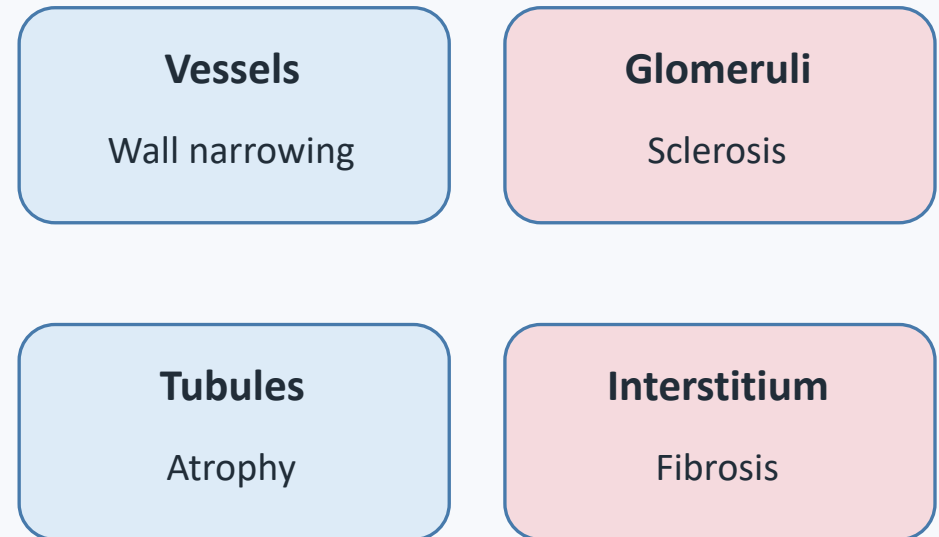
Glomerulosclerosis: Scarring of glomerular tufts.

Tubulointerstitial damage: Tubular atrophy and interstitial fibrosis.

Arteriosclerosis: Disease of small arterial walls.

Arteriolosclerosis: Disease of the arteriolar walls.

Schematic



One combined renal phenotype

Hypertension is an association, not a prerequisite

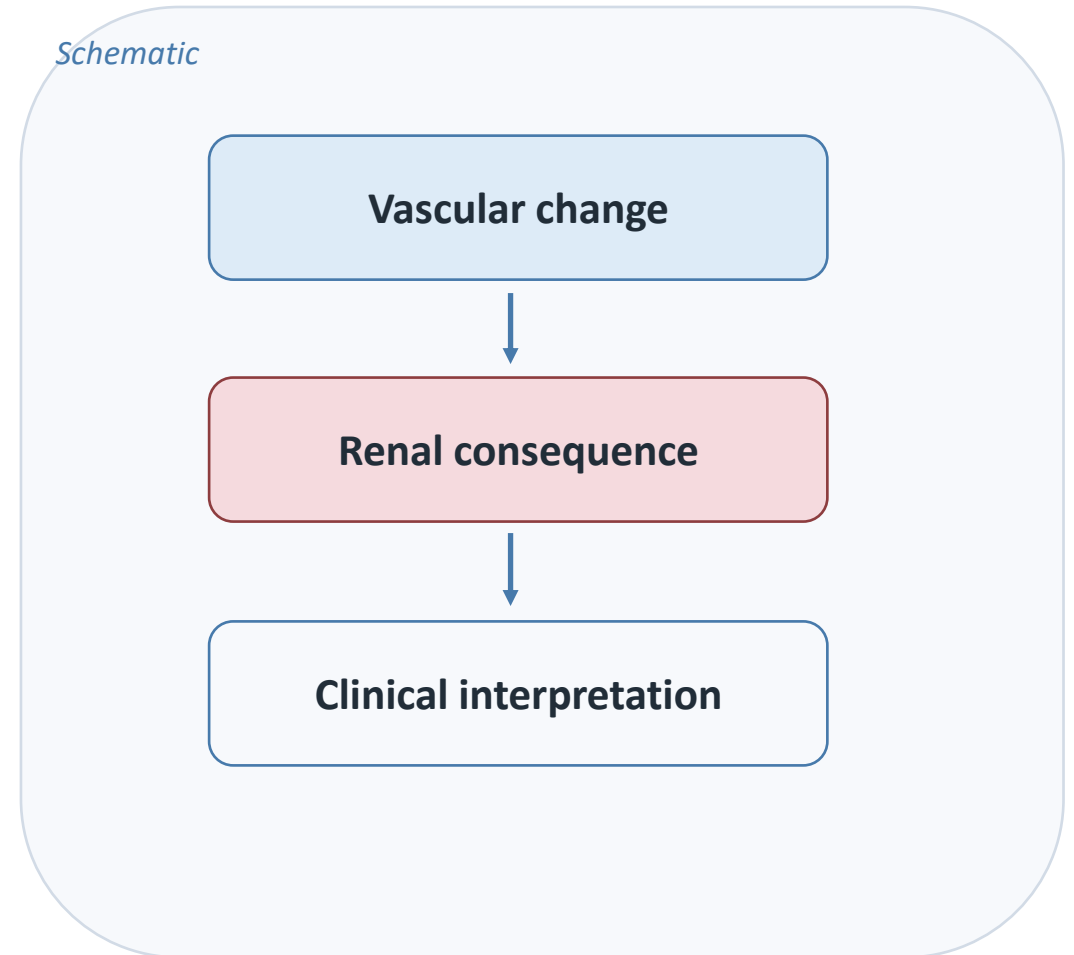
Core teaching points

Nephrosclerosis is strongly associated with elevated blood pressure.

A nephrosclerotic pattern can also occur without hypertension.

Interpret the histology within the patient's vascular context.

Schematic



Age contributes to nephrosclerotic change

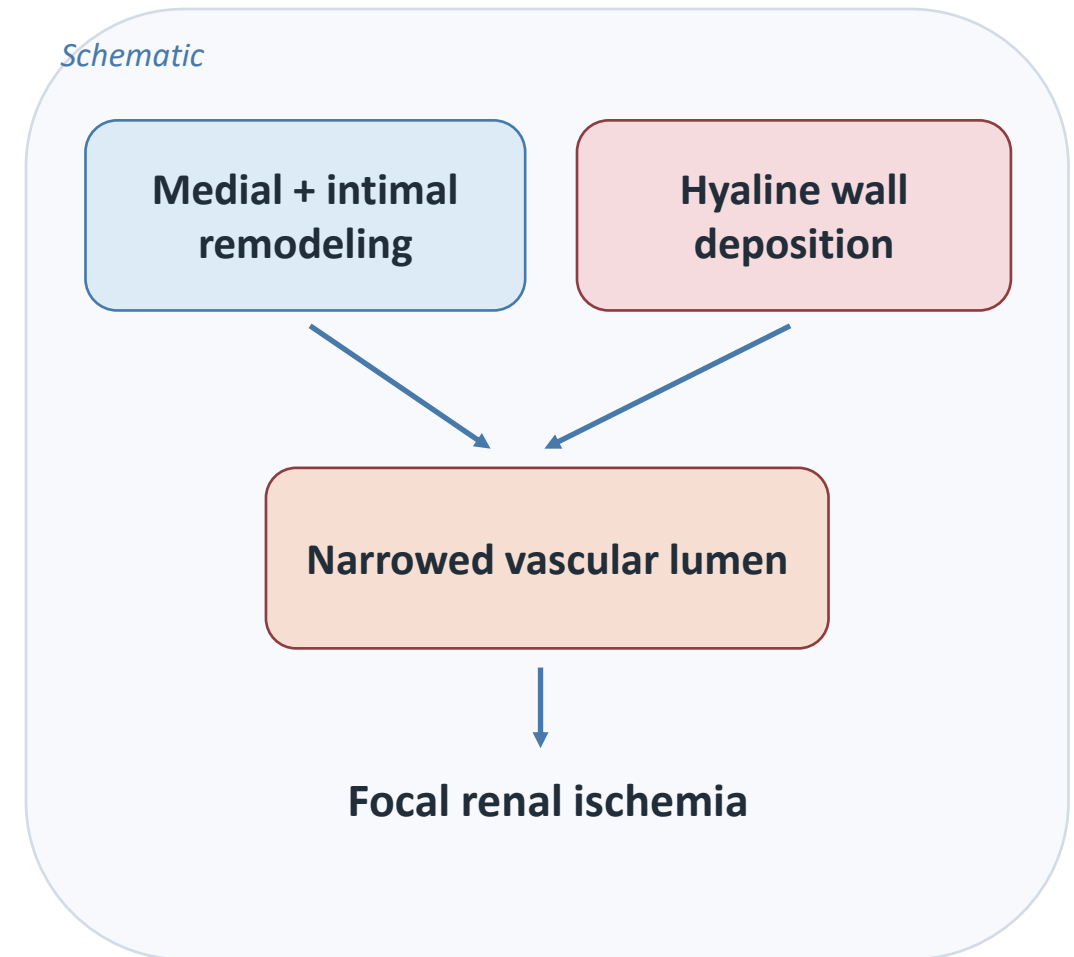
Mechanism

The frequency of nephrosclerosis rises with advanced age.

Aging contributes to remodeling of small renal arteries.

Age-associated vascular change may coexist with hypertension.

Schematic



Population observations require careful interpretation

Greater frequency in people of African descent than in people of Northern European descent.

This is a population-level observation, not a lesion-specific marker.

The biopsy pattern alone cannot identify ancestry or causation.

Two processes produce the arterial lesions

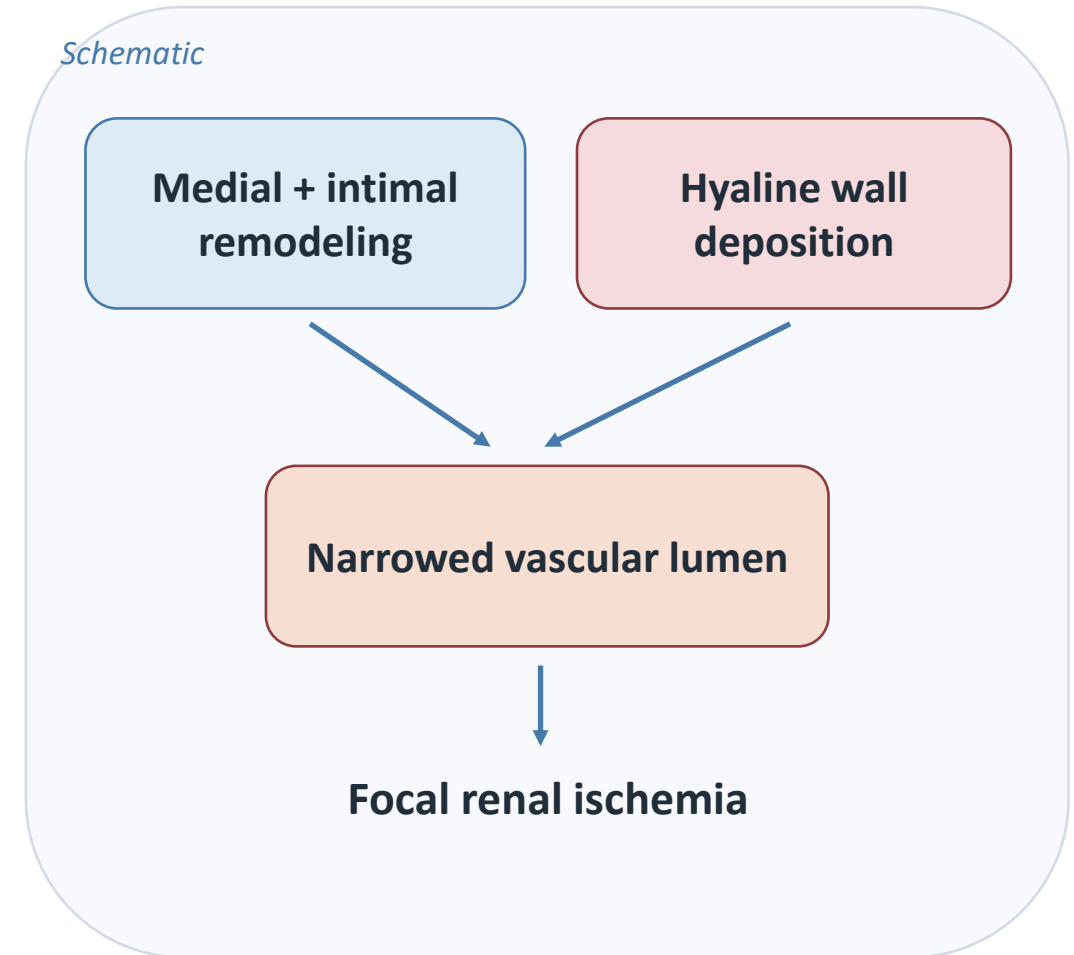
Mechanism

Medial and intimal thickening alter vessel geometry.

Arteriolar hyalinization increases wall thickness.

Both routes converge on luminal narrowing and ischemia.

Schematic

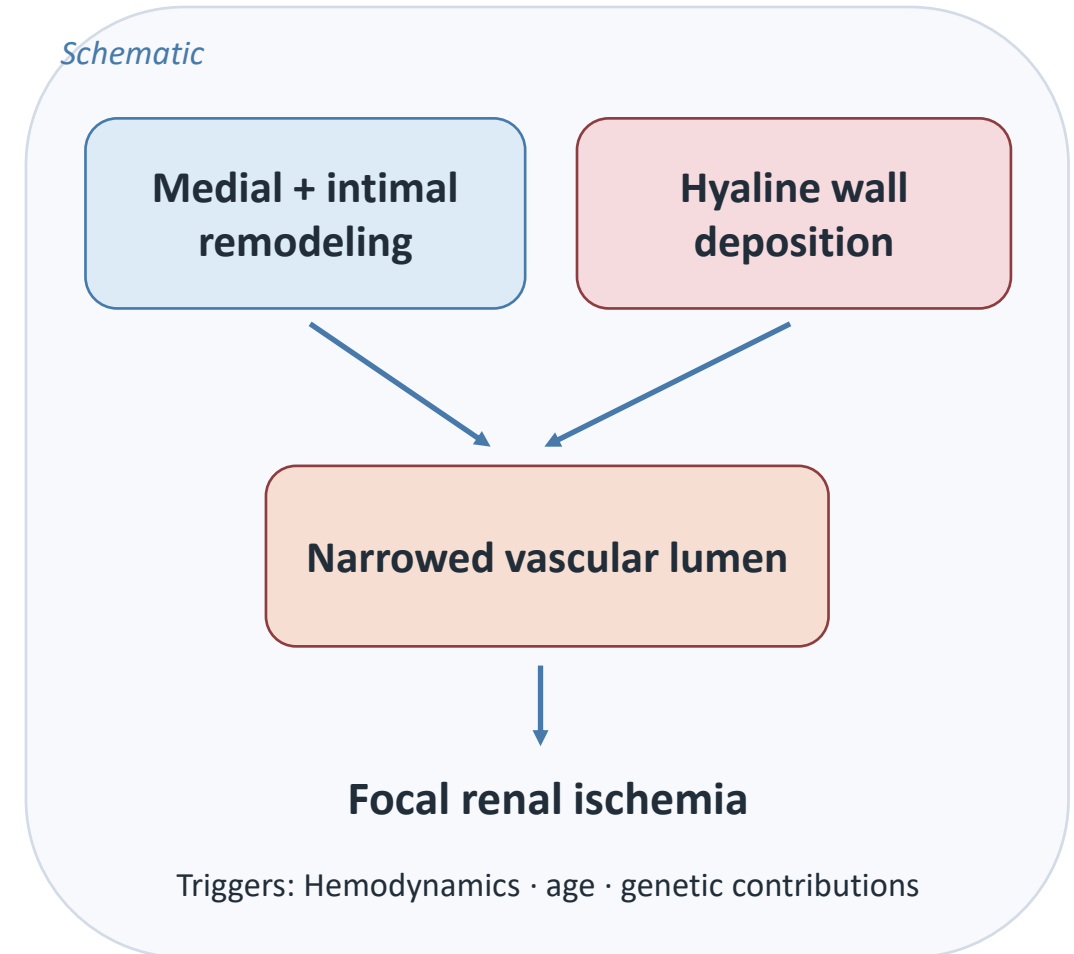


Drivers of medial and intimal thickening

Mechanism

Hemodynamic changes, including hypertension, remodel the wall. Aging also participates in wall thickening. Genetic defects can contribute in some individuals.

Schematic



Vascular remodeling reduces the lumen

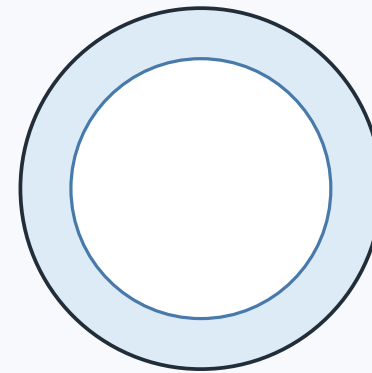
Morphologic interpretation

Medial and intimal layers occupy more of the vessel cross-section.

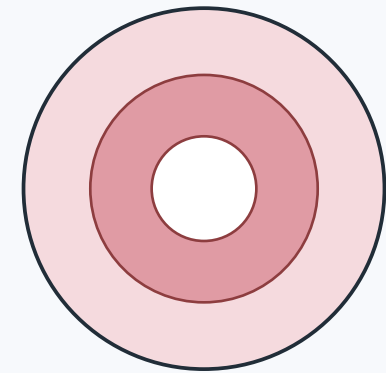
A narrower lumen restricts downstream tissue perfusion.

The pathologic impact is focal rather than uniformly distributed.

Schematic



Relatively open lumen



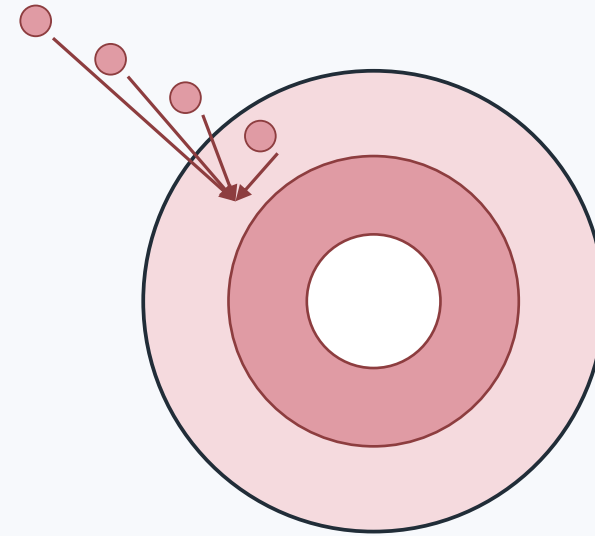
Thickened hyaline wall

Hyalinization begins with endothelial injury

Mechanism

Injured endothelium permits plasma proteins to enter the vessel wall.
Wall proteins accumulate as eosinophilic hyaline material.
Hypertension may contribute to the endothelial damage.

Schematic



Plasma proteins enter injured wall

Hyaline arteriosclerosis: Structural consequence

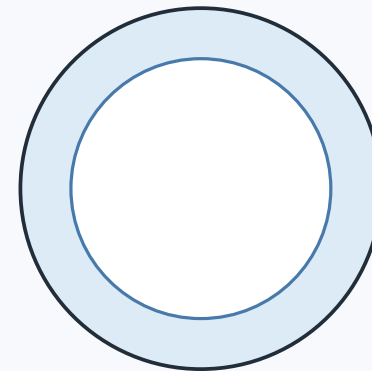
Morphologic interpretation

Homogeneous hyaline thickens the arteriolar wall.

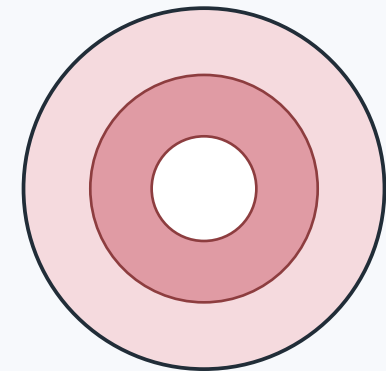
The residual lumen becomes narrow.

The lesion is a vascular substrate for ischemic renal injury.

Schematic



Relatively open lumen



Thickened hyaline wall

Wall thickness and lumen diameter are linked

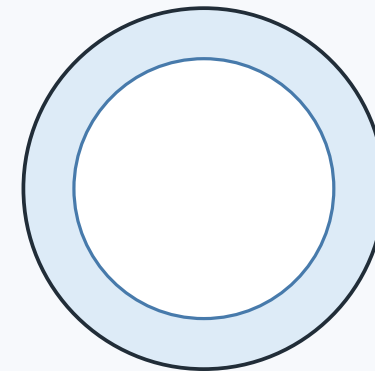
Morphologic interpretation

The disease process is not simply increased vessel caliber.

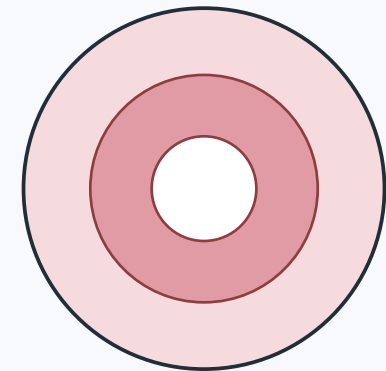
Intramural material and wall remodeling encroach on the lumen.

Downstream parenchyma experiences reduced blood supply.

Schematic



Relatively open lumen



Thickened hyaline wall

Arteriosclerosis and arteriolosclerosis are distinct terms

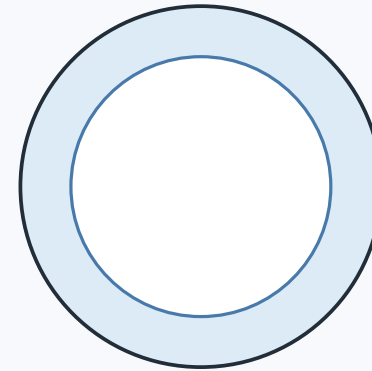
Morphologic interpretation

Small arteries exhibit intimal and medial structural remodeling.

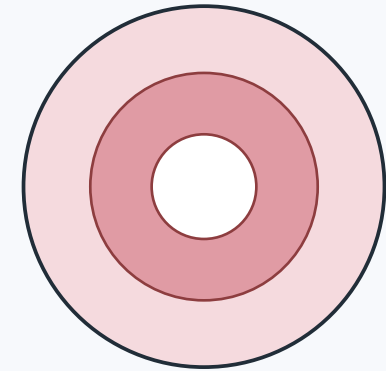
Arterioles commonly show hyaline wall thickening.

Both vessel classes contribute to nephrosclerosis.

Schematic



Relatively open lumen



Thickened hyaline wall

The vascular-to-parenchymal cascade

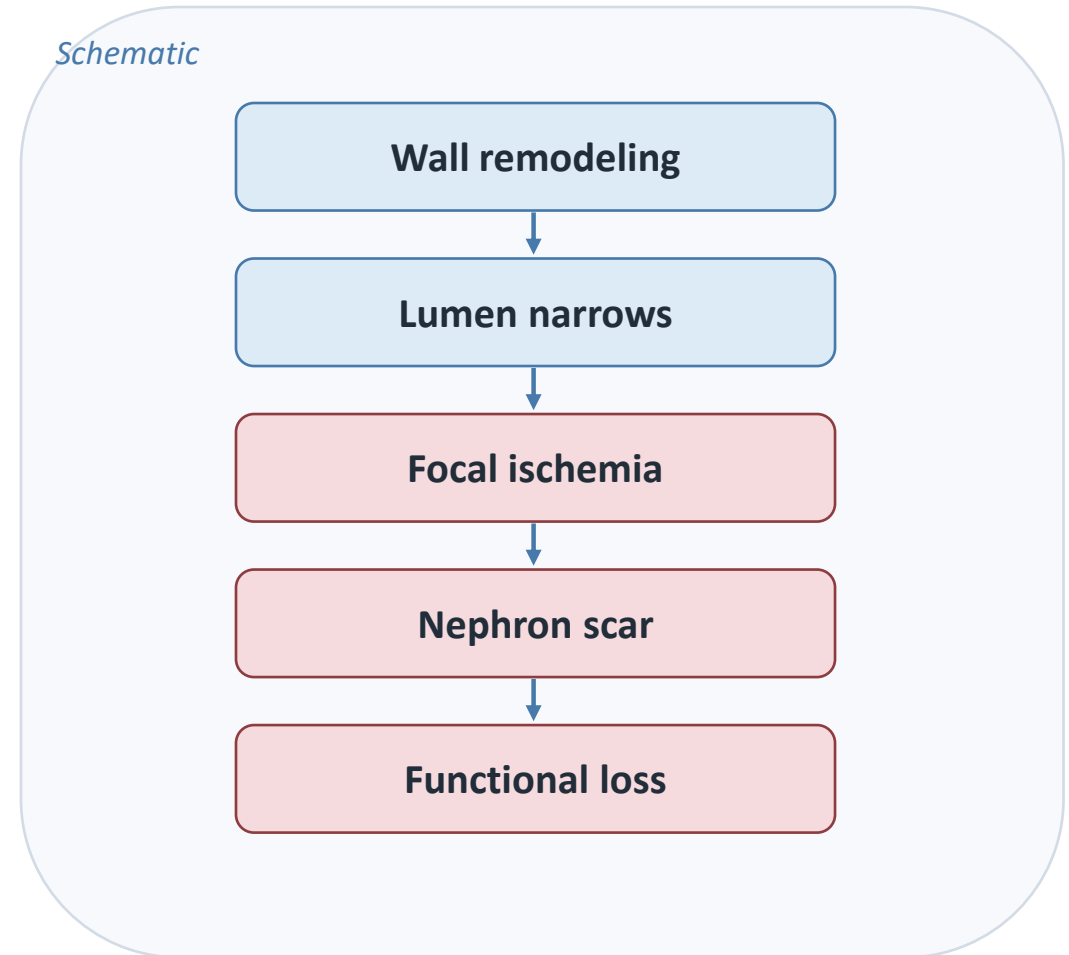
Mechanism

Wall thickening → luminal loss → reduced renal perfusion.

Persistent focal ischemia injures glomeruli and tubules.

Scarring ultimately decreases functional renal mass.

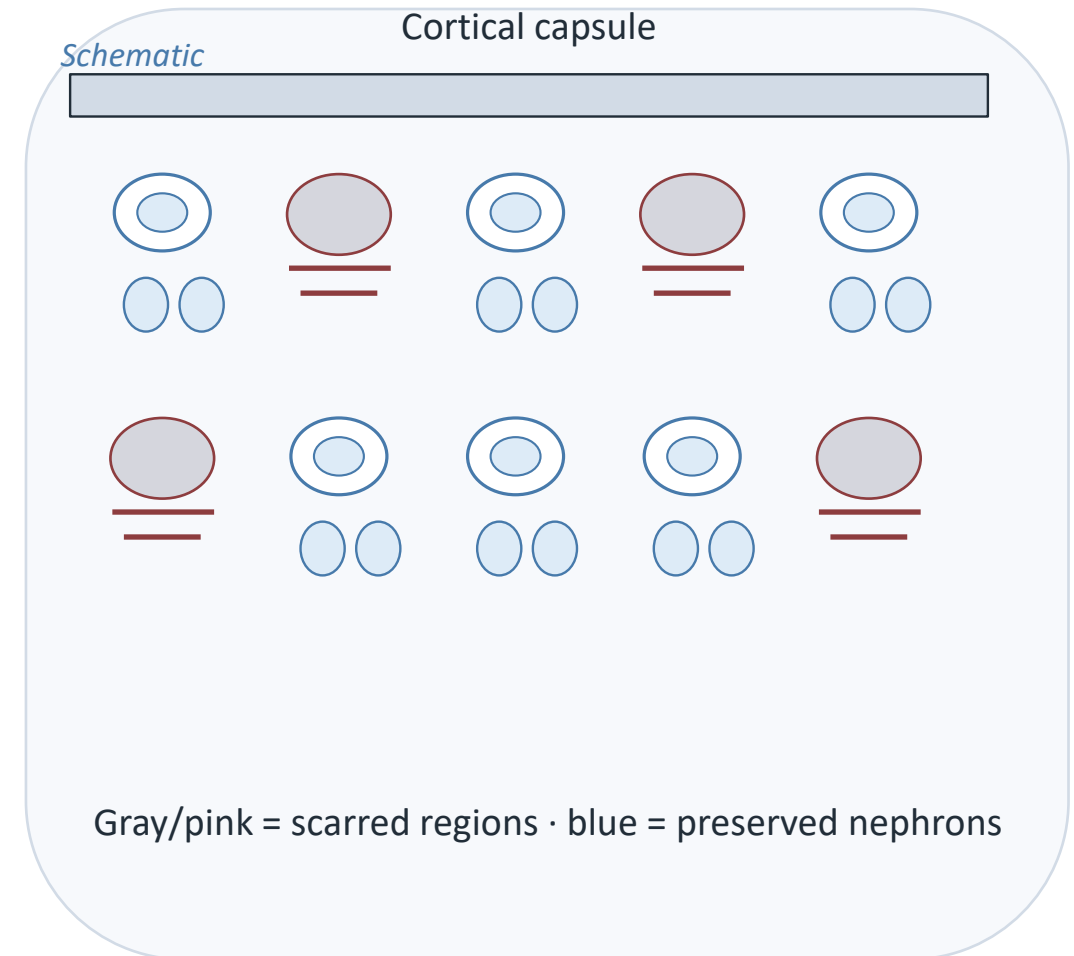
Schematic



Why ischemic injury is patchy

Morphologic interpretation

The degree of narrowing varies between small vascular territories.
Some nephron regions scar while adjacent regions remain preserved.
This heterogeneity explains the uneven cortical microscopic pattern.

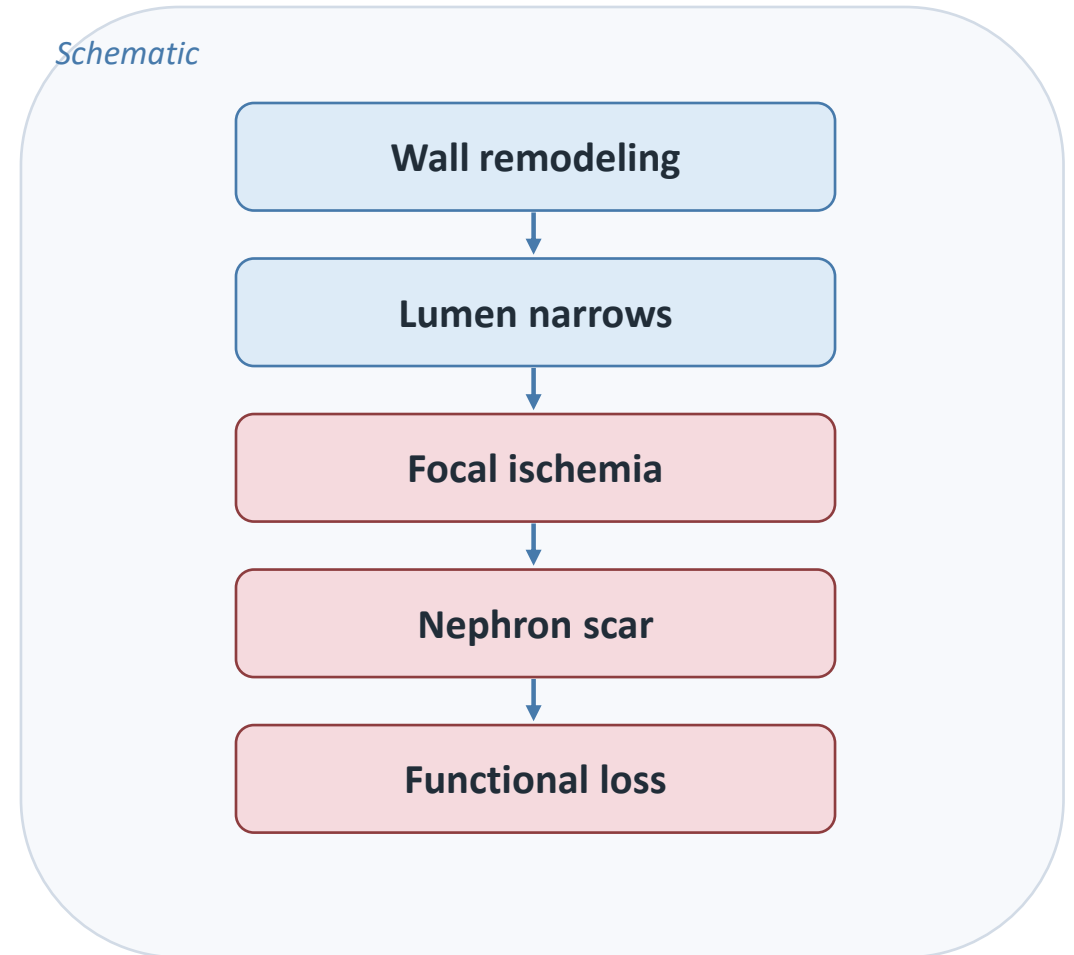


The ultimate outcome is nephron loss

Mechanism

Glomerular and tubulointerstitial damage
accumulate together.
Atrophic tubules no longer maintain normal
functional mass.
Scar replaces previously functioning cortex.

Schematic

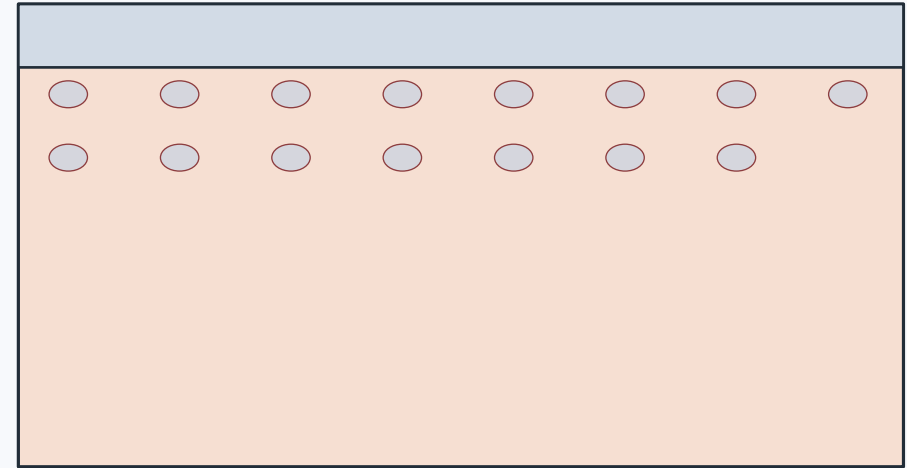


Gross kidney size is variable

Morphologic interpretation

Kidneys may remain near normal size.
Others are moderately reduced in size.
Average kidney weights of approximately
110–130 g.

Schematic



Fine, repeated cortical surface irregularities

Fine cortical granularity is characteristic

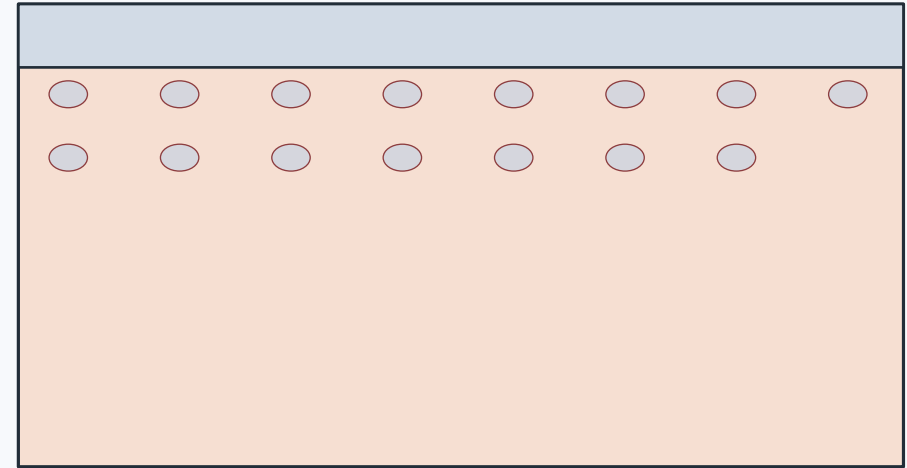
Morphologic interpretation

The cortical surface has a fine, even granular texture.

The texture to grain leather.

The finding reflects numerous small underlying scars.

Schematic



Fine, repeated cortical surface irregularities

Why the renal cortex shrinks

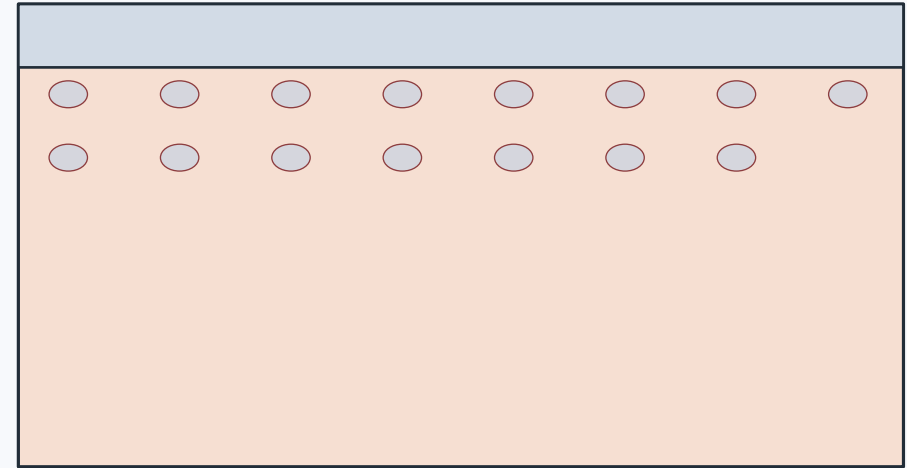
Morphologic interpretation

Cortical scar formation removes functioning parenchyma.

Loss of cortical volume accounts for most of the decreased mass.

Gross shrinkage therefore has a microscopic structural basis.

Schematic



Fine, repeated cortical surface irregularities

A granular surface reflects multiple small scars

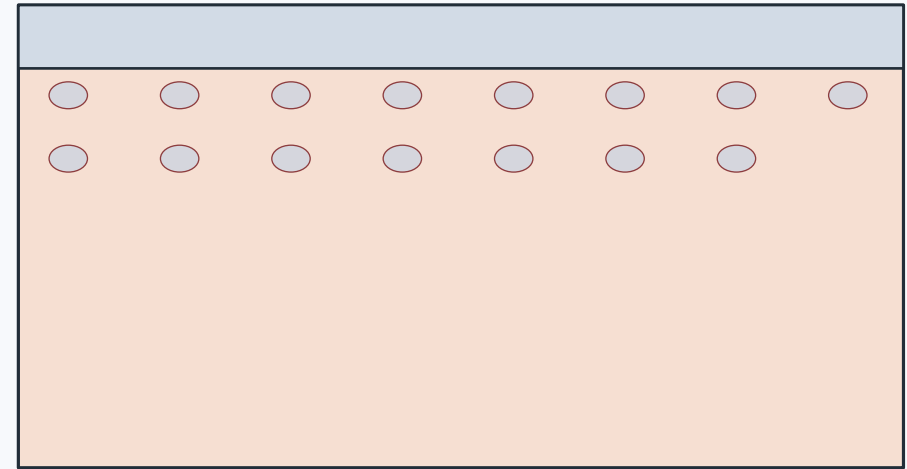
Morphologic interpretation

Many subcapsular scars subtly alter the renal contour.

Small regions of better-preserved cortex remain between them.

The aggregate produces diffuse fine granularity.

Schematic



Fine, repeated cortical surface irregularities

Arterioles show narrowed lumina

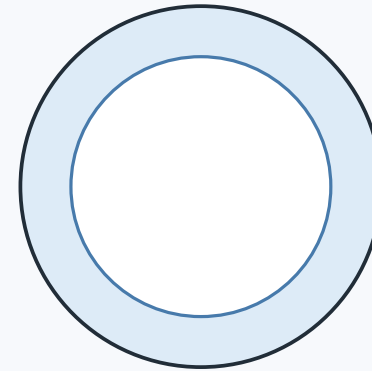
Morphologic interpretation

Microscopy demonstrates thickened arteriolar walls.

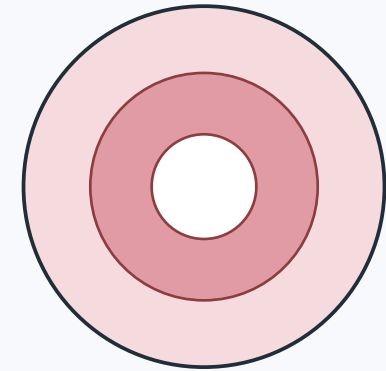
Hyalinization contributes to luminal encroachment.

The lesion is termed hyaline arteriosclerosis.

Schematic



Relatively open lumen



Thickened hyaline wall

How to read a hyaline arteriole schematic

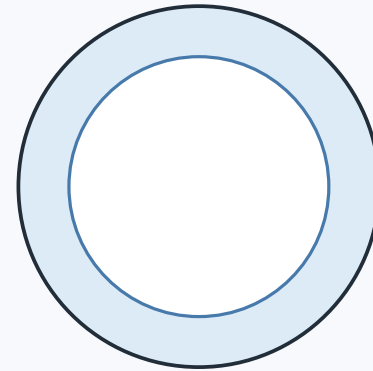
Morphologic interpretation

Locate the luminal space first.

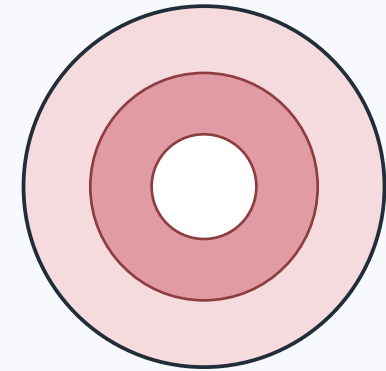
Identify broad homogeneous material in the surrounding wall.

Ask whether the lumen is narrowed relative to the wall.

Schematic



Relatively open lumen

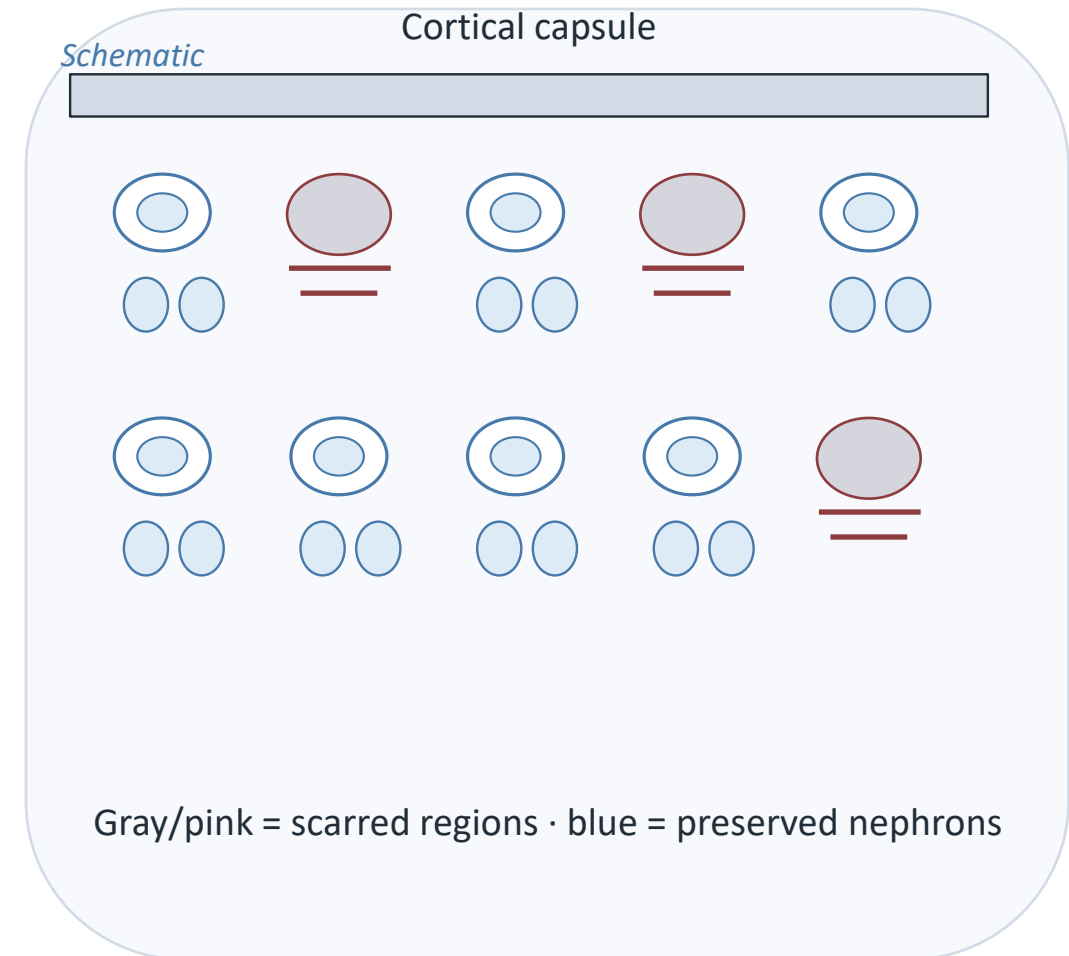


Thickened hyaline wall

Subcapsular scarring explains the surface change

Morphologic interpretation

Microscopic scars occur immediately beneath the capsule.
Sclerotic glomeruli and tubular dropout characterize these sites.
Their arrangement produces the fine cortical irregularity.



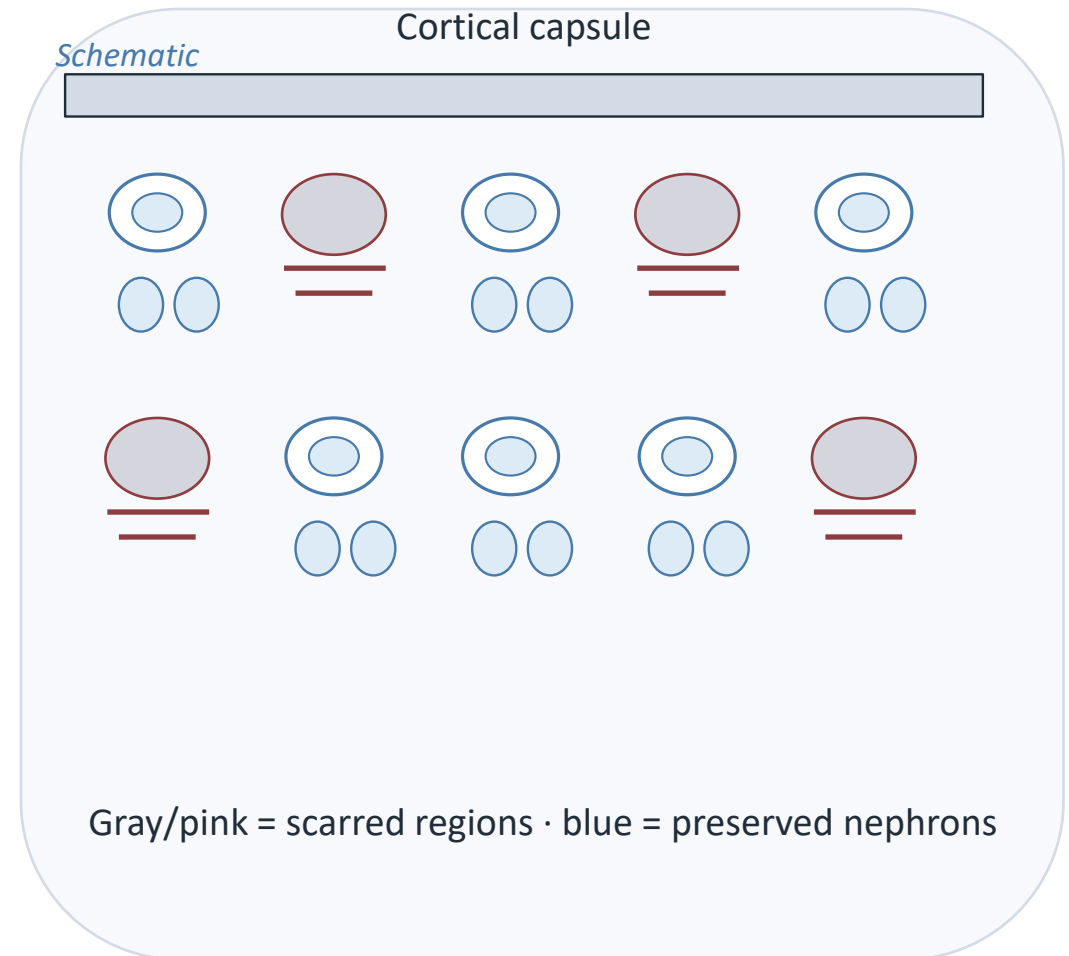
Scarring alternates with preserved tissue

Morphologic interpretation

Damaged cortical fields are not always confluent.

Sclerotic glomeruli and lost tubules occur beside viable nephrons.

This variability is expected with segmental vascular ischemia.



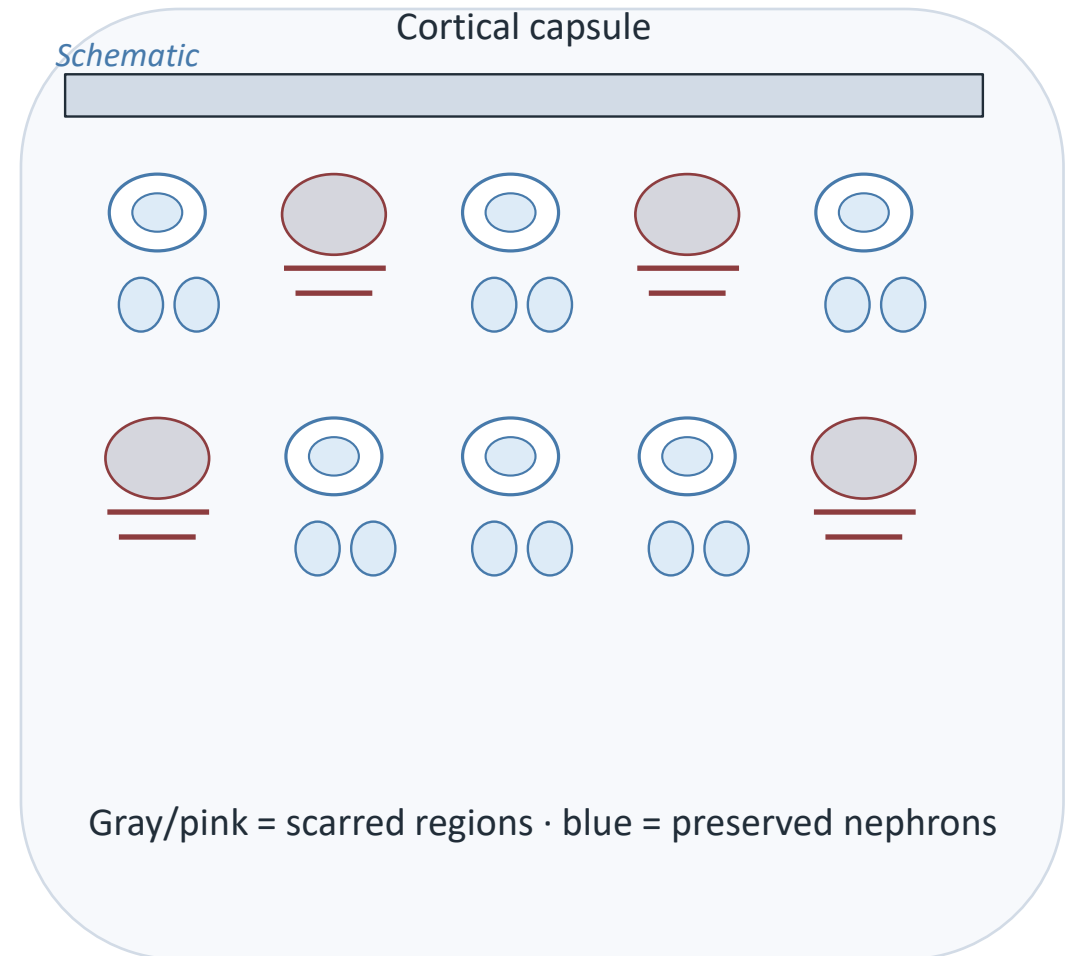
Tubular dropout identifies lost renal parenchyma

Morphologic interpretation

Scarring sites contain fewer recognizable tubules.

Tubular loss is coupled with adjacent interstitial fibrosis.

The pattern is a component of chronic tubulointerstitial injury.

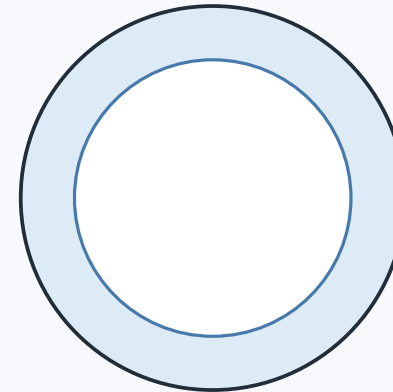


Interlobular and arcuate arteries are involved

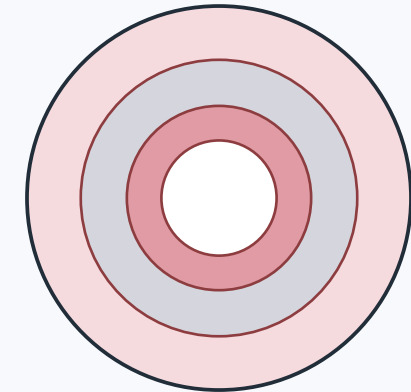
Morphologic interpretation

Disease extends beyond the smallest arterioles.
Both interlobular and arcuate arteries develop wall remodeling.
Their lesions add to downstream luminal narrowing.

Schematic



Baseline artery



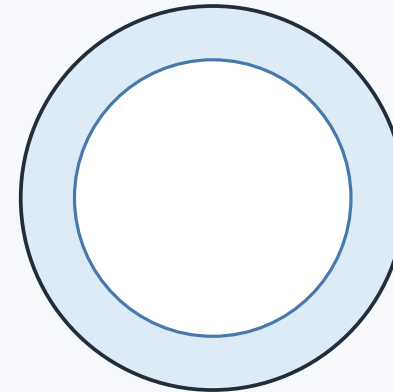
Intimal and medial growth

Fibroelastic hyperplasia: A layered arterial lesion

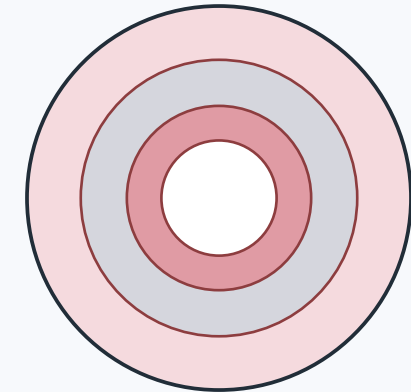
Morphologic interpretation

Medial hypertrophy increases wall mass.
The internal elastic lamina is replicated.
Myofibroblastic intimal tissue expands the wall inward.

Schematic



Baseline artery



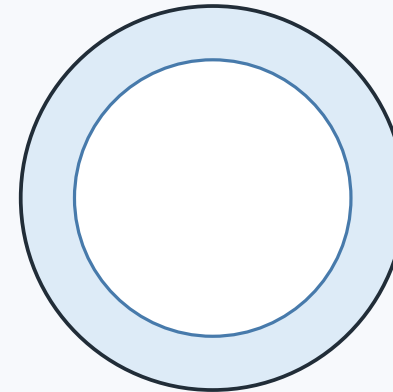
Intimal and medial growth

Internal elastic lamina replication

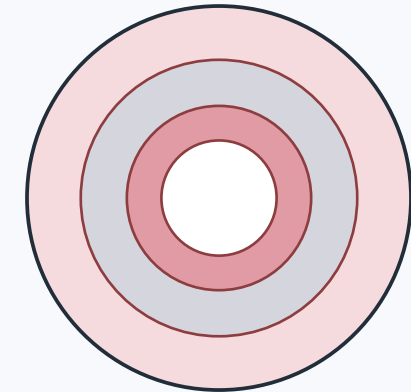
Morphologic interpretation

Multiple elastic layers appear within the remodeled arterial wall. This accompanies medial hypertrophy and intimal thickening. The combined lesion is designated fibroelastic hyperplasia.

Schematic



Baseline artery



Intimal and medial growth

Elastic-layer replication contributes to fibroelastic hyperplasia

Intimal myofibroblastic accumulation

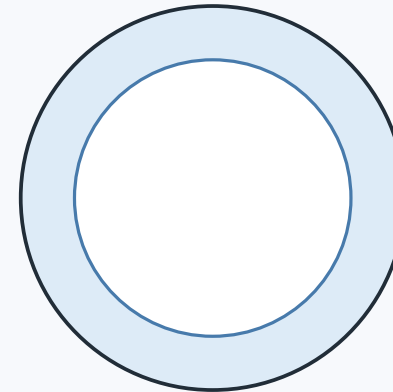
Morphologic interpretation

Myofibroblastic tissue contributes to intimal thickening.

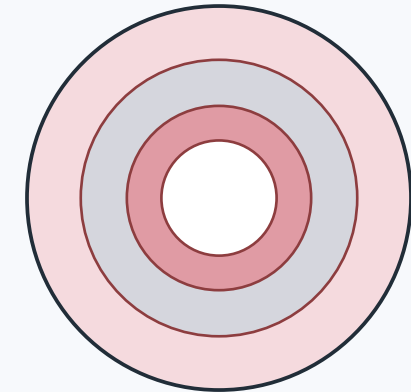
Expansion of the intima further restricts the lumen.

This process accompanies arteriolar hyalinization.

Schematic



Baseline artery



Intimal and medial growth

Age and blood pressure intensify arterial remodeling

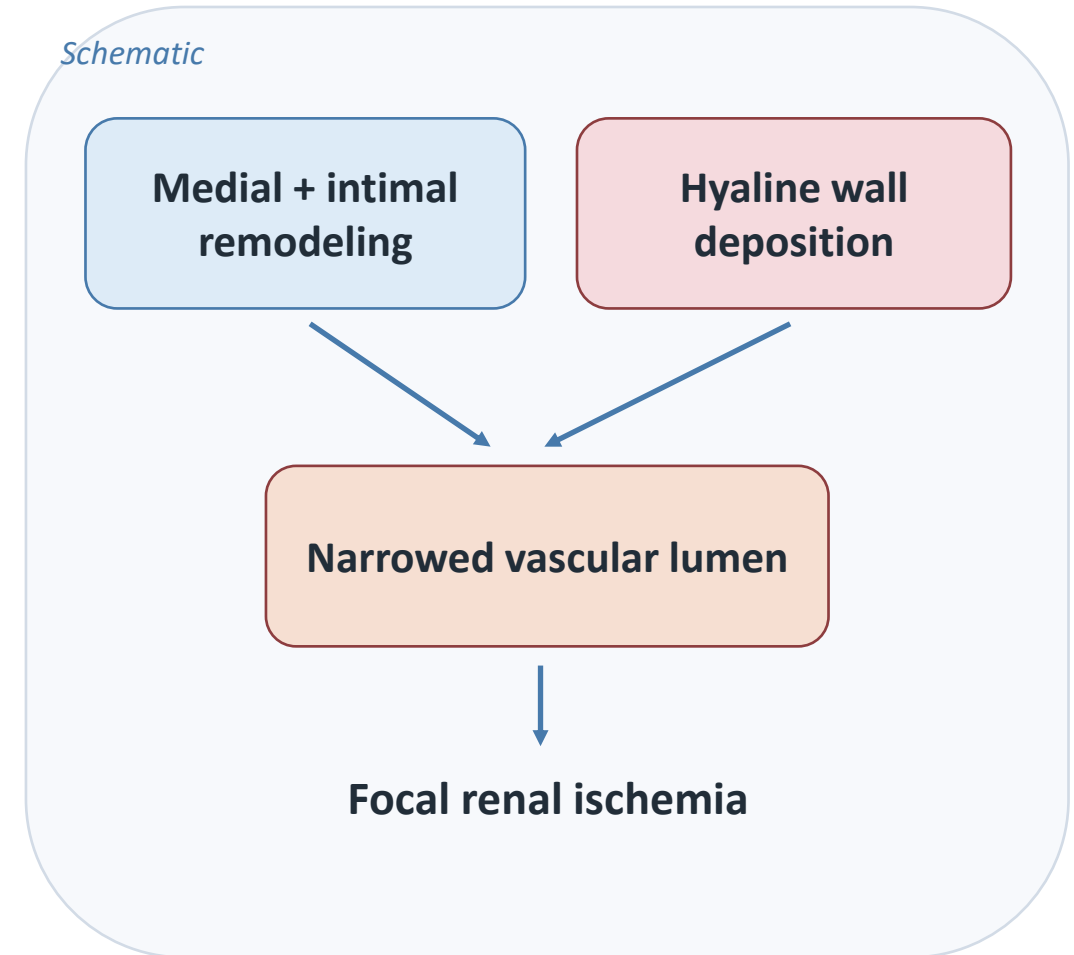
Mechanism

Fibroelastic hyperplasia increases in severity with age.

Hypertension is associated with greater severity.

It often coexists with hyaline arteriolosclerosis.

Schematic



Patchy ischemic atrophy has two tissue targets

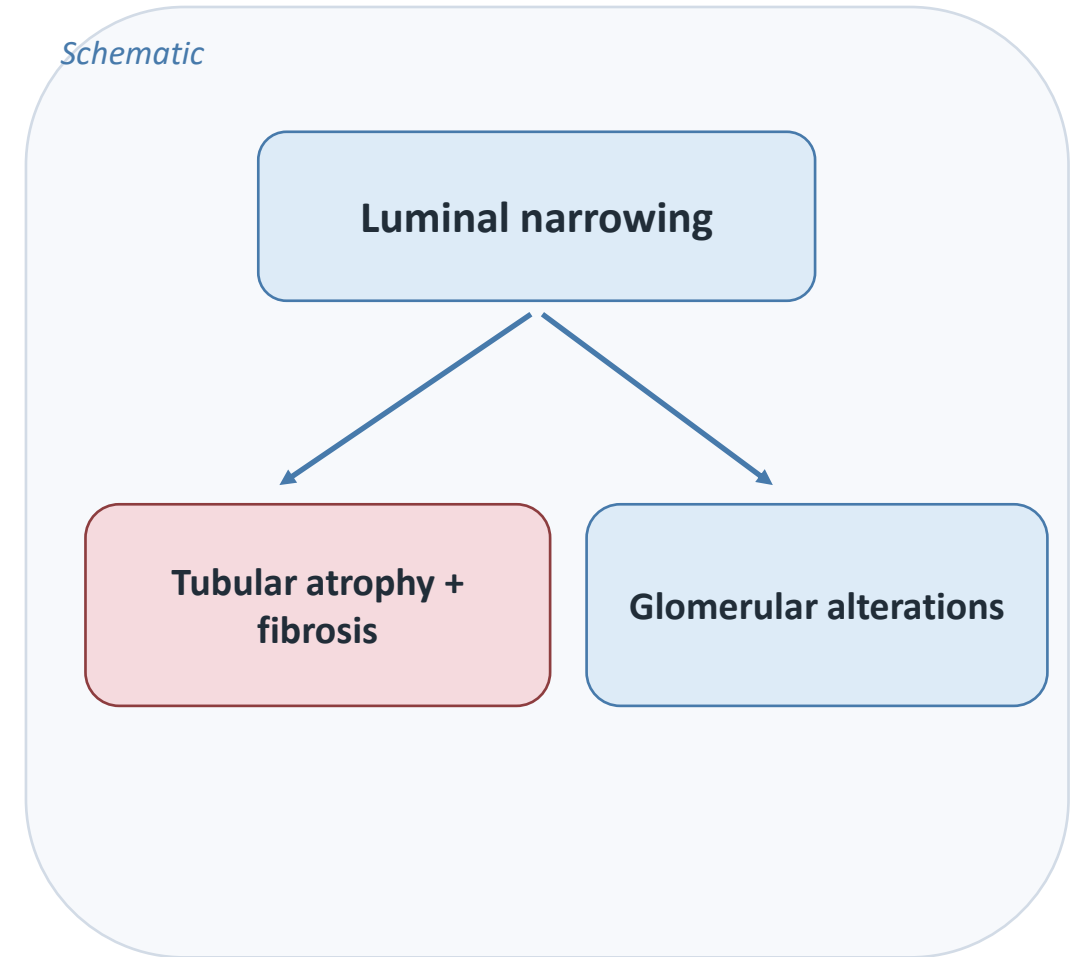
Mechanism

Tubules and interstitium develop atrophy and fibrosis.

Glomeruli develop several ischemic structural alterations.

Both components reflect restricted local perfusion.

Schematic



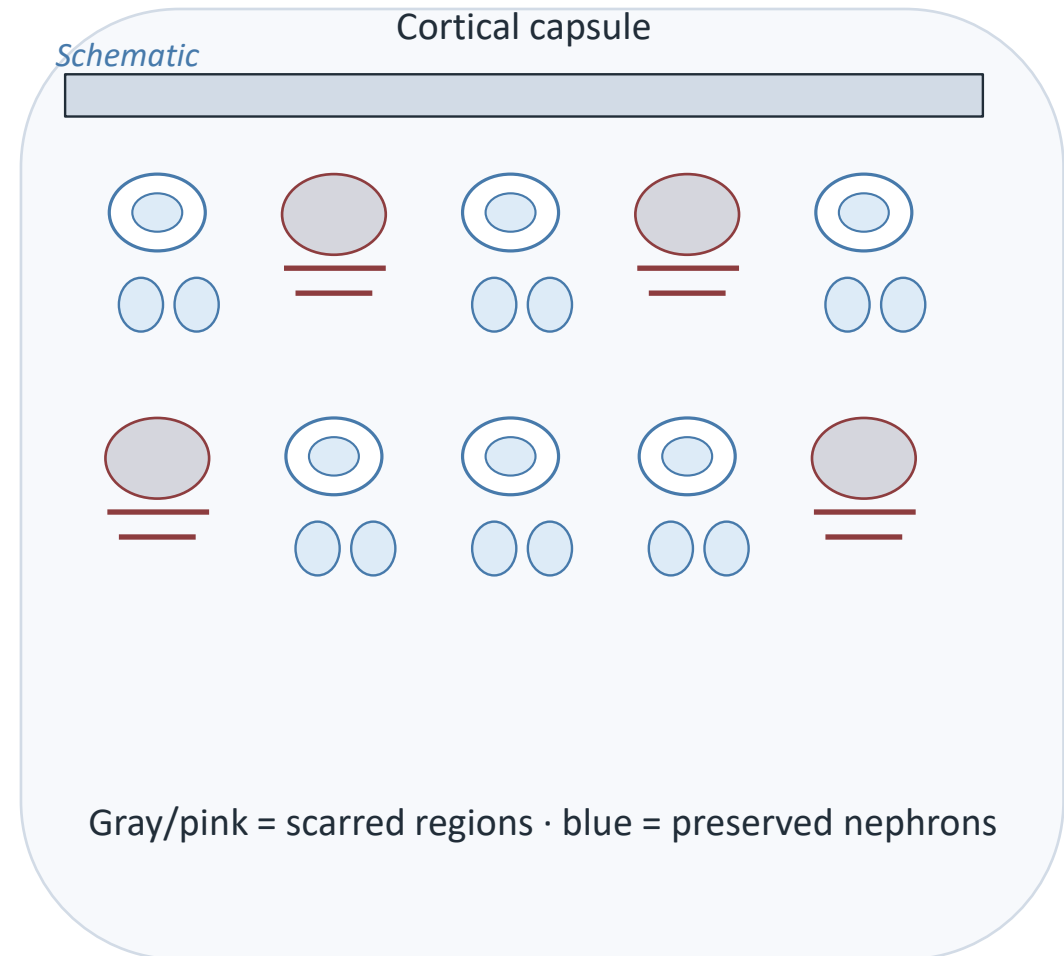
Tubular atrophy and interstitial fibrosis

Morphologic interpretation

Atrophic tubules occur within ischemic cortical territories.

Interstitial fibrosis occupies part of the damaged tissue.

Together these lesions signify established chronic scarring.



Glomerular basement membrane collapse

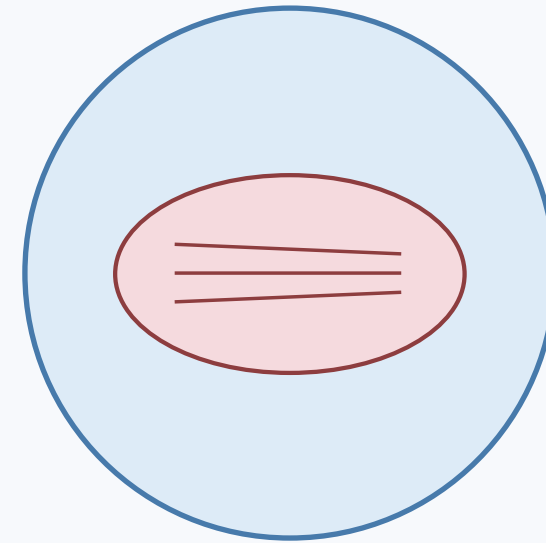
Morphologic interpretation

Ischemic glomeruli may have collapsed capillary loops.

The glomerular basement membrane becomes folded or collapsed.

This is one of several routes toward a sclerotic glomerulus.

Schematic



Collapsed tuft

Collagen deposition in Bowman space

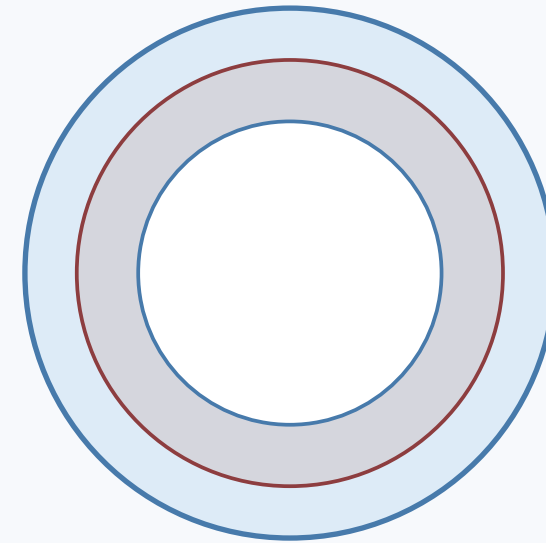
Morphologic interpretation

Ischemic glomeruli can accumulate collagen in Bowman space.

This adds extracellular scar material around the tuft.

The change accompanies other chronic glomerular alterations.

Schematic



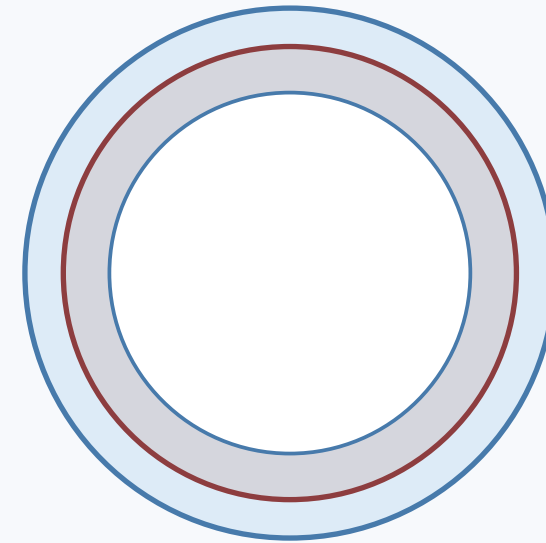
Collagen in Bowman space

Periglomerular fibrosis

Morphologic interpretation

Fibrous tissue may expand around the glomerular capsule.
Scarring is therefore not restricted to the glomerular tuft.
Periglomerular fibrosis links the glomerulus with interstitial injury.

Schematic



Periglomerular scar

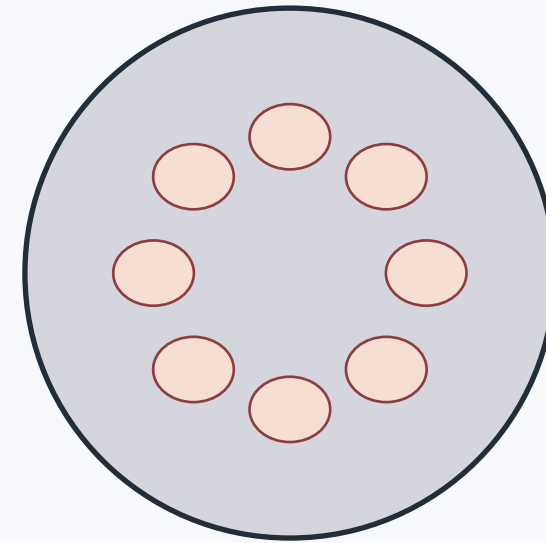
Global glomerulosclerosis is an endpoint

Morphologic interpretation

The entire glomerular tuft may become sclerosed.

The former filtration unit is replaced by scar.
Numerous affected glomeruli contribute to lost functional mass.

Schematic



Sclerosed tuft

Global and segmental sclerosis can coexist

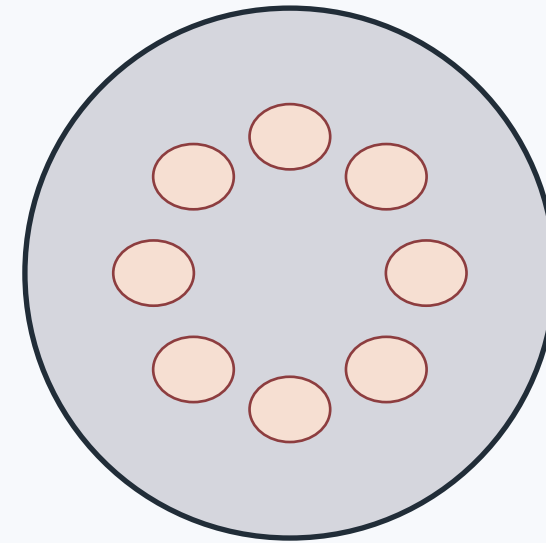
Morphologic interpretation

Both global and segmental glomerulosclerosis.

Vascular narrowing can be part of the sequence leading to either.

Neither pattern is exclusive to nephrosclerosis.

Schematic



Sclerosed tuft

Larger ischemic territories produce regional scars

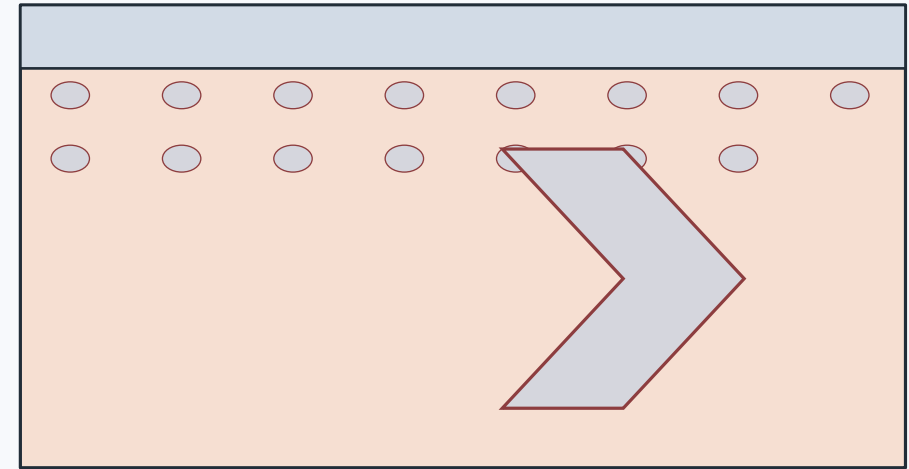
Morphologic interpretation

Pronounced ischemia may involve a large parenchymal region.

Wedge-shaped infarcts or regional scars can result.

The macroscopic pattern differs from fine diffuse granularity.

Schematic



Regional scar

Severe ischemic scarring can resemble renal ablation injury

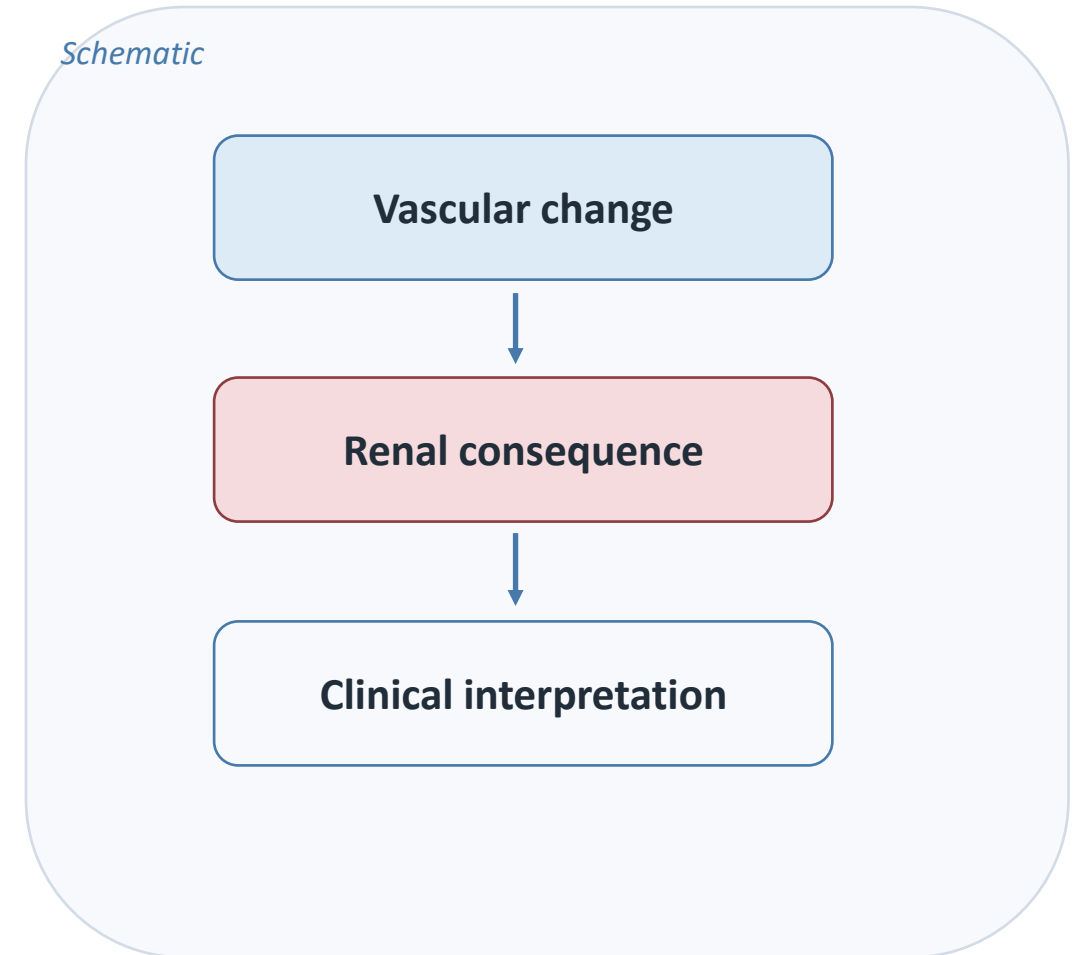
Core teaching points

Marked regional nephron loss may induce similar histologic changes.

Morphologic resemblance does not establish the same cause.

Source context and distribution are essential to interpretation.

Schematic



Integrating the vascular and tissue findings

Core teaching points

Identify arterial or arteriolar luminal narrowing.

Look for neighboring glomerular and tubulointerstitial scarring.

Correlate the microscopic pattern with a granular cortical surface.

Schematic

Wall injury

Hyalinization

Ischemia

Reduced perfusion

Nephrons

Scarring

Kidney

Cortical loss

One combined renal phenotype

Typical clinical course is not rapidly uremic

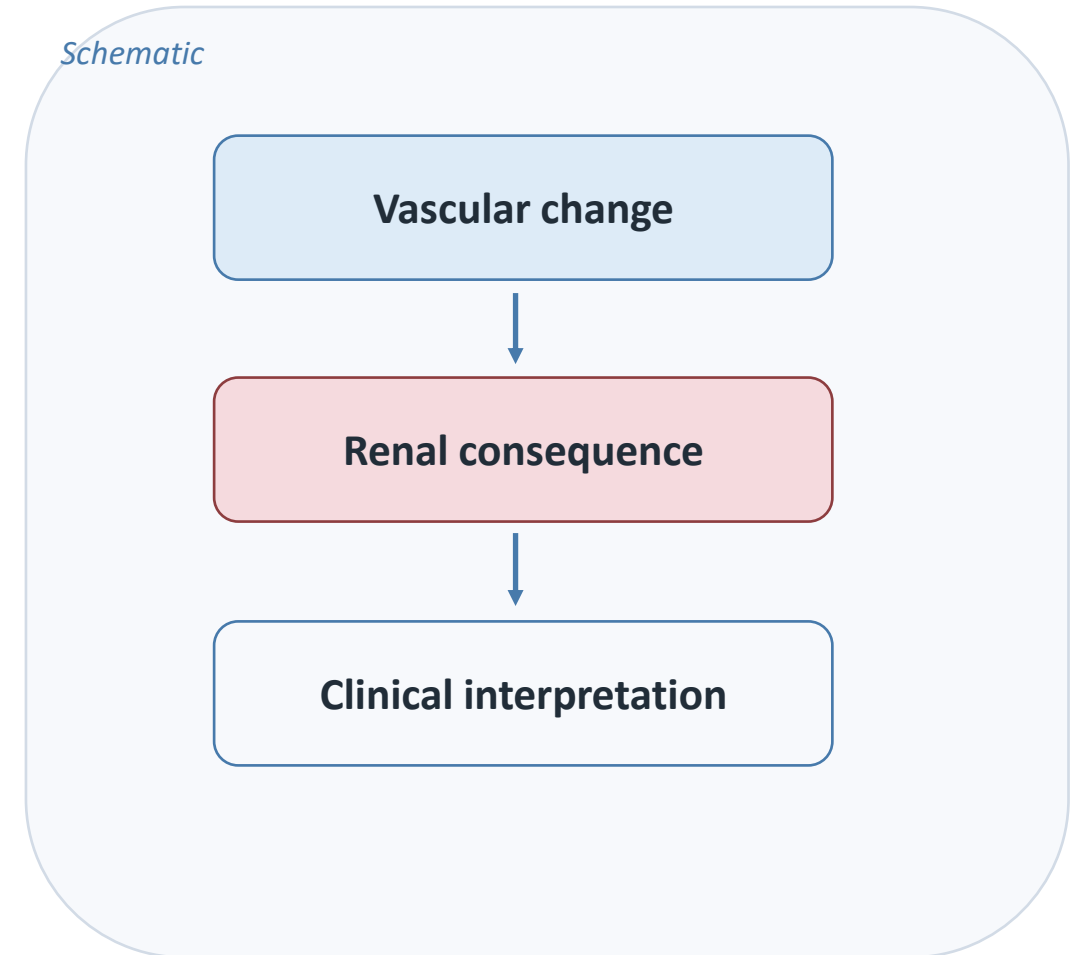
Clinical interpretation

Uncomplicated nephrosclerosis usually does not cause uremia.

Structural injury may nevertheless reduce functional renal mass.

Clinical severity therefore differs from morphologic presence.

Schematic

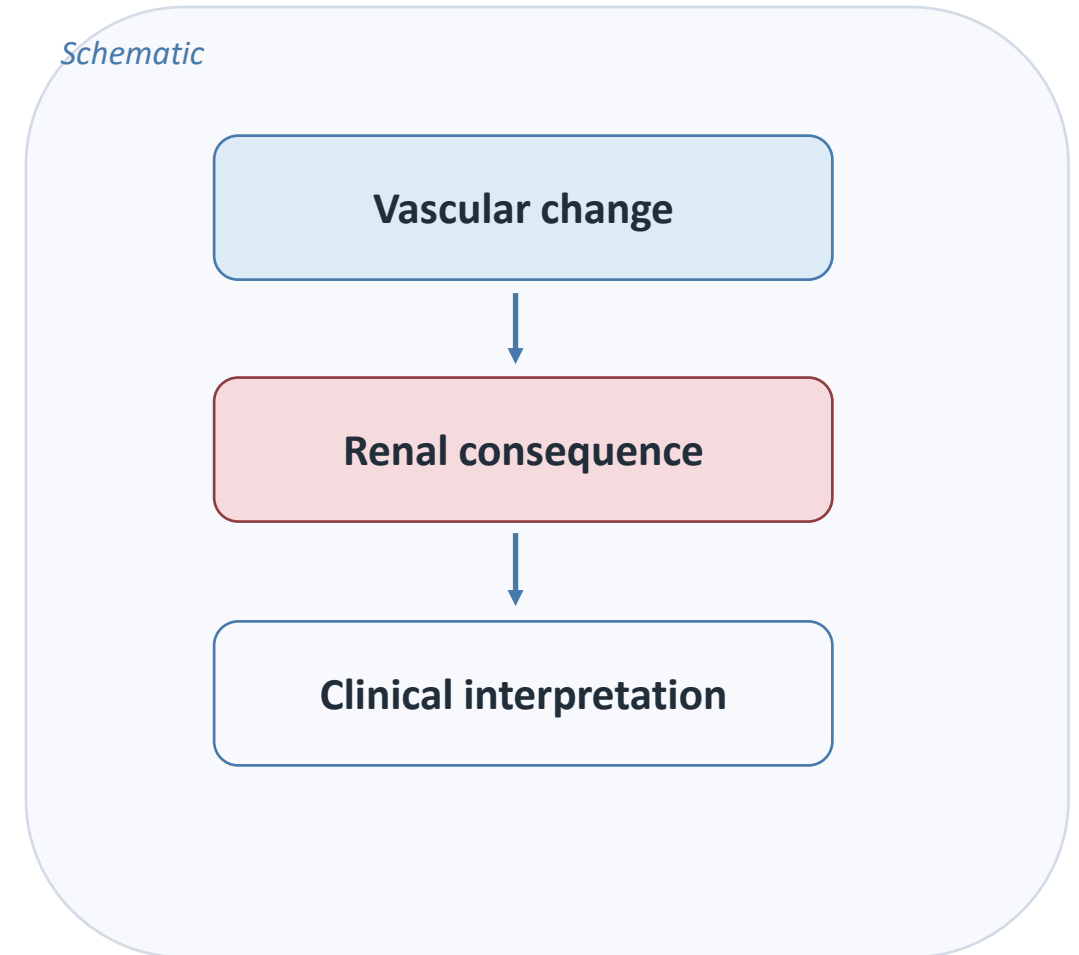


Two groups at increased risk of renal failure

Clinical interpretation

Hypertensive people of African descent.
Patients with severe blood pressure elevation are also at risk.
These groups are described epidemiologically, not as a biopsy rule.

Schematic

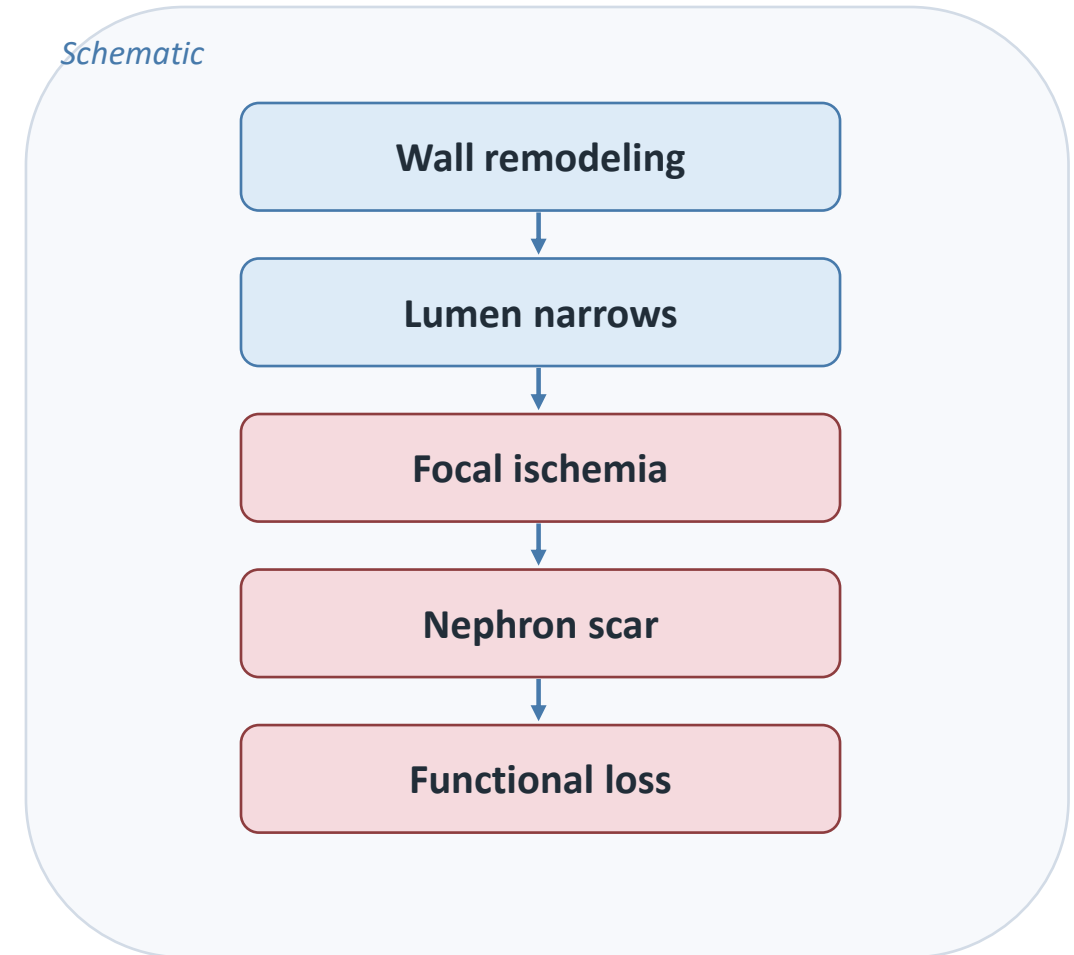


Accelerated hypertension changes the clinical trajectory

Mechanism

Severe blood pressure escalation may coincide with rapid renal decline. The accelerated or malignant phase is linked to rapid renal failure. This differs from the usual slow, patchy nephrosclerotic pattern.

Schematic



Severe (malignant) hypertension is a systemic syndrome

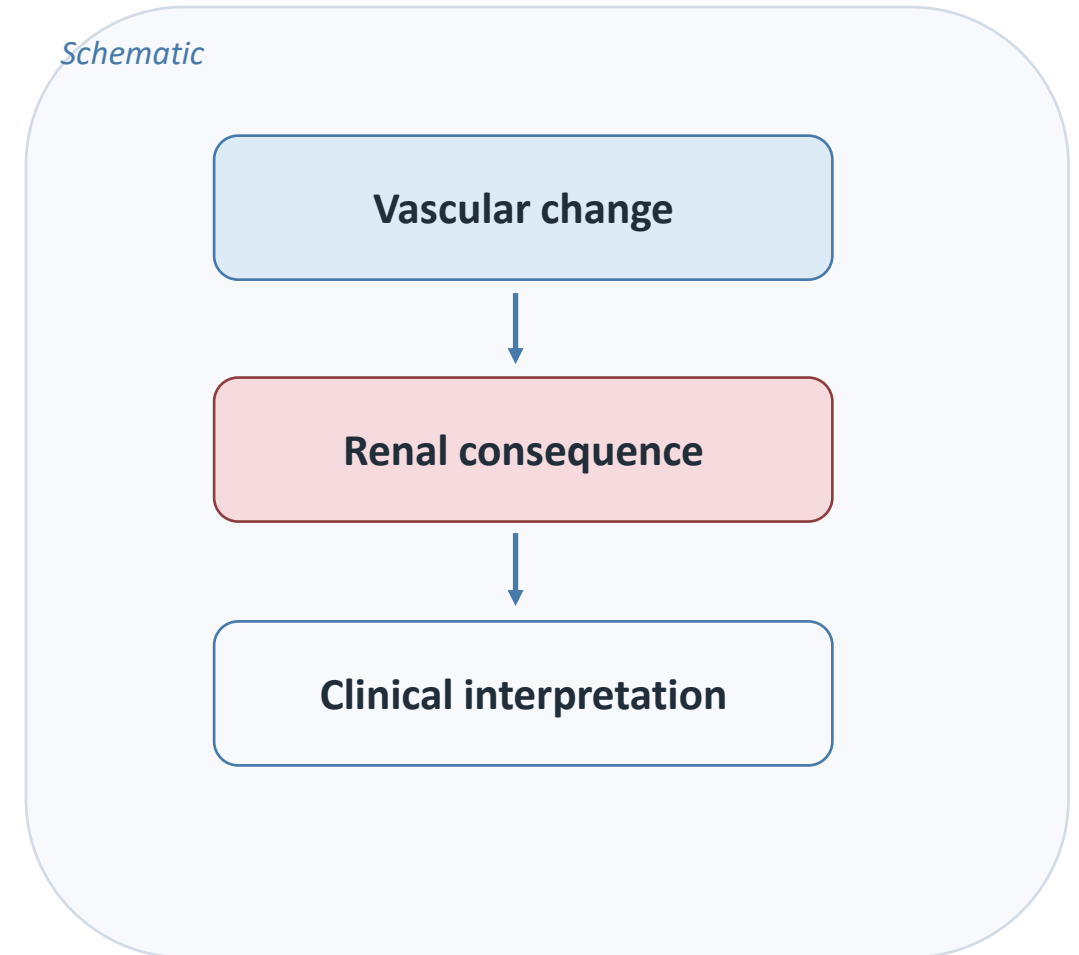
Clinical interpretation

Very high blood pressure accompanied by organ injury.

Renal failure and retinal vascular changes are central features.

It is more than the presence of hyaline arteriolosclerosis.

Schematic



The blood-pressure description

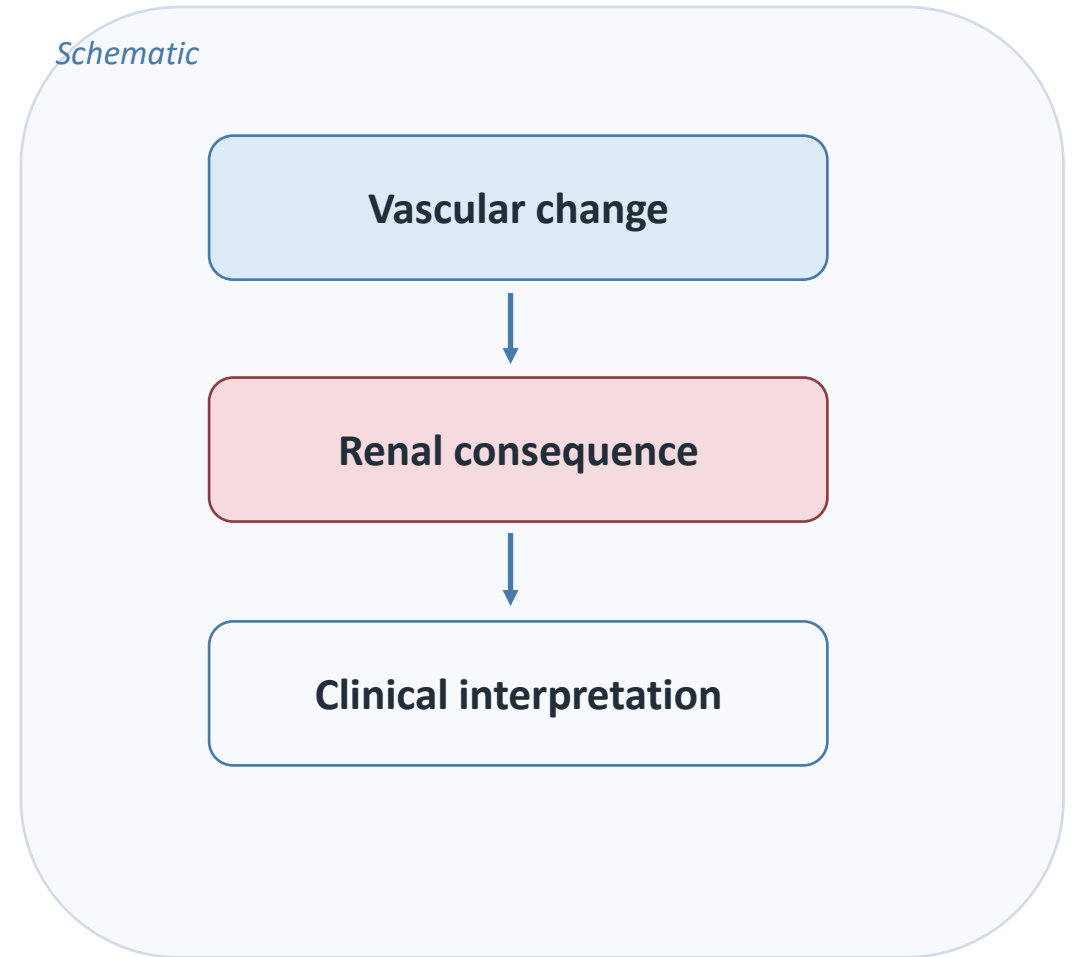
Clinical interpretation

The text describes systolic pressure above 180 mm Hg.

It also describes diastolic pressure above 120 mm Hg.

Interpret these numbers as this textbook description, not a stand-alone current diagnostic algorithm.

Schematic



Retinal findings point to severe vascular injury

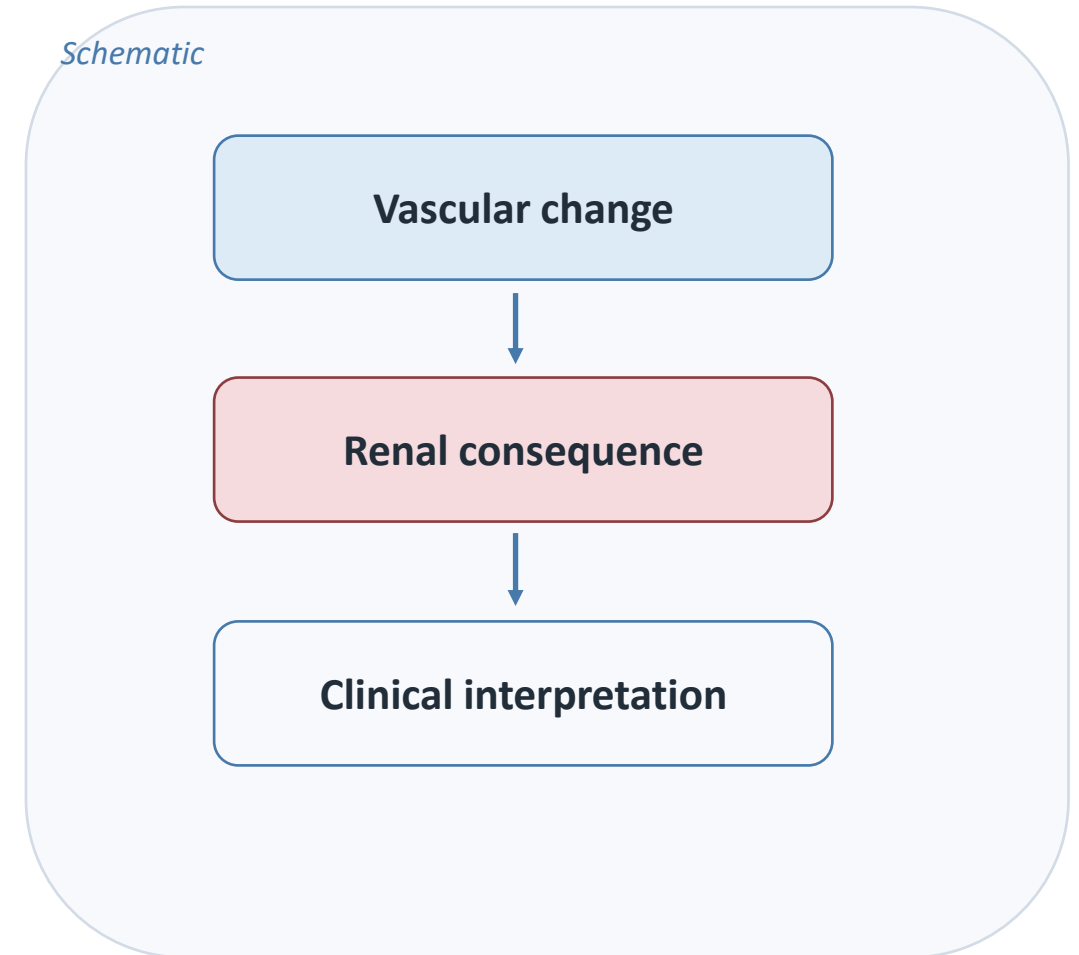
Clinical interpretation

Retinal hemorrhages and exudates may be present.

Papilledema may occur, but is not required in the description.

Papilledema represents optic-disc swelling linked to elevated intracranial pressure.

Schematic



Severe hypertension primarily injures microvessels

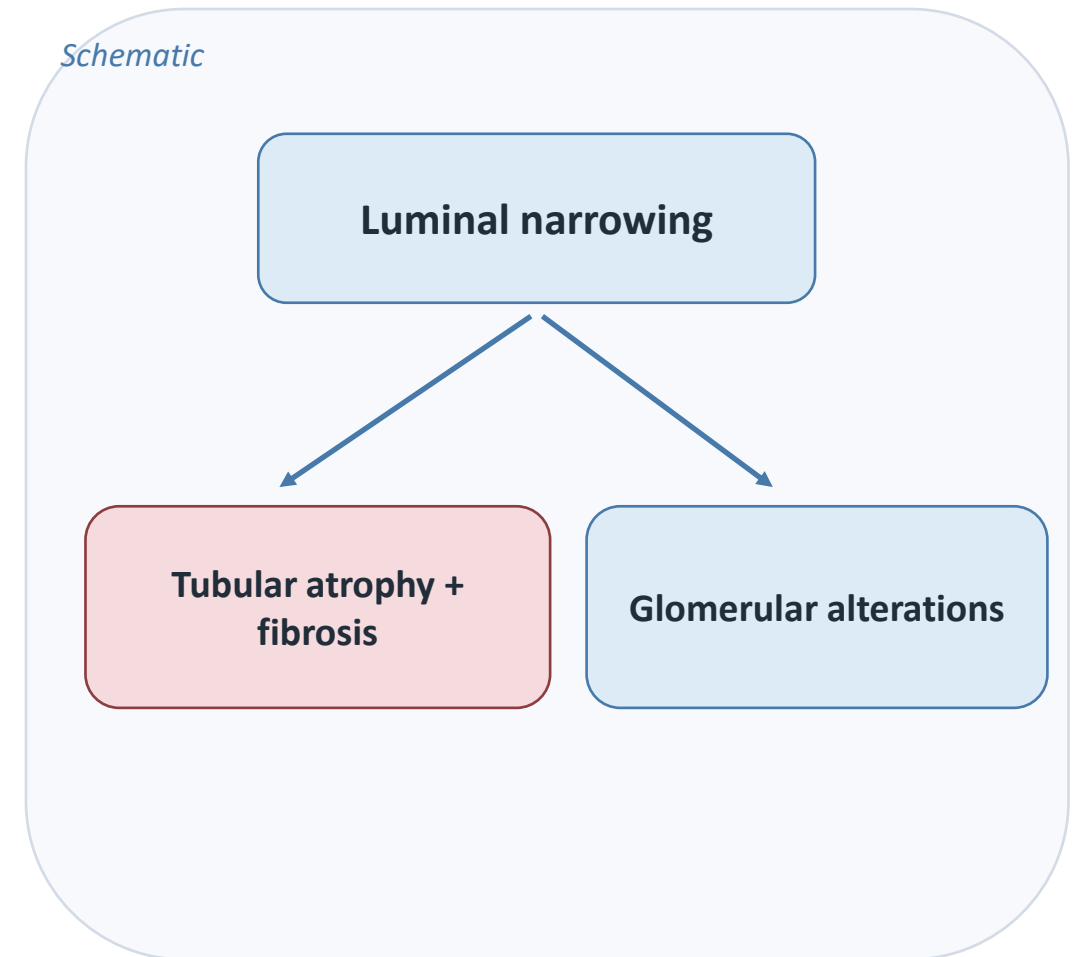
Mechanism

Endothelial injury and microvascular damage become prominent.

Intimal cellular proliferation can rapidly narrow small vessels.

Fibrinoid necrosis may accompany proliferative arteriolar lesions.

Schematic



Hyperplastic arteriolosclerosis forms onion-skin layers

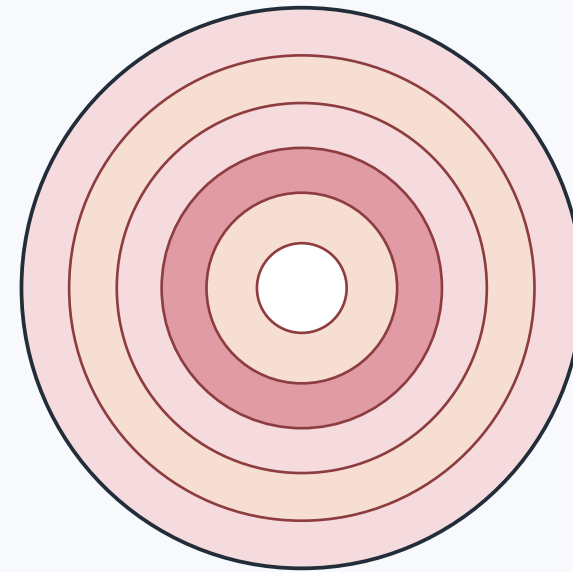
Morphologic interpretation

Concentric intimal proliferation surrounds the vascular lumen.

The arrangement has an onion-skin appearance.

Interlobular arteries and larger arterioles are typical sites.

Schematic



Concentric intimal cell proliferation

Onion-skin proliferation may obliterate a vessel

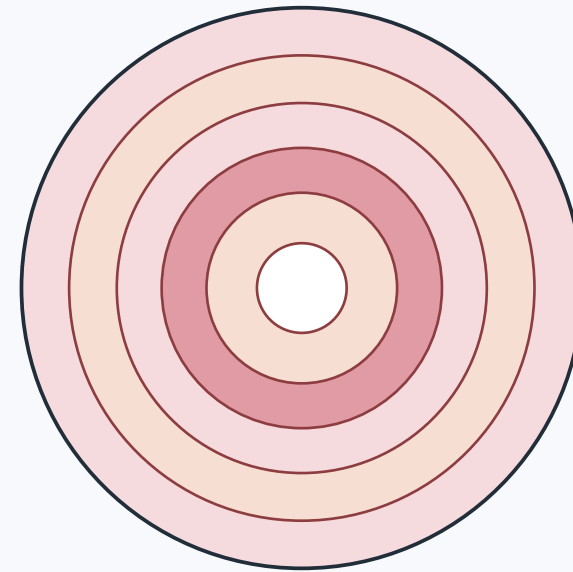
Morphologic interpretation

Multiple cellular layers markedly expand the intima.

The residual lumen may become critically narrow or obliterated.

This is the proliferative arteriolar lesion of severe hypertension.

Schematic



Concentric intimal cell proliferation

Fibrinoid necrosis is a separate severe lesion

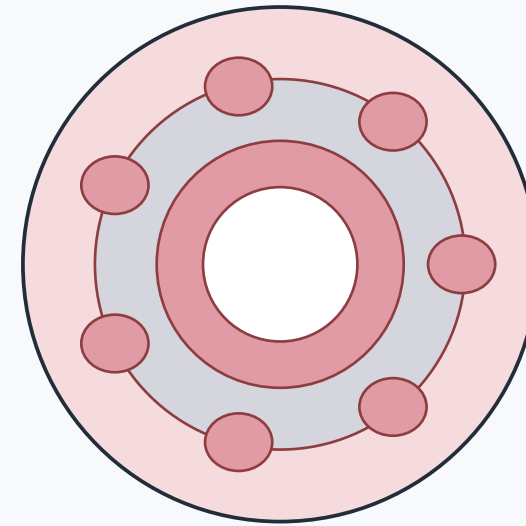
Morphologic interpretation

Arterioles may show destructive fibrinoid change.

This is different from bland hyaline arteriosclerosis.

Severe hypertension can involve both proliferative and necrotizing injury.

Schematic



Destructive wall change (conceptual)

Glomerular injury may include microthrombi

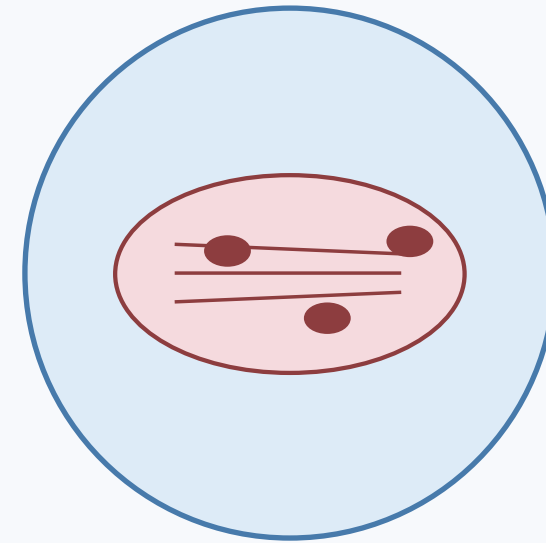
Morphologic interpretation

Fibrinoid injury can affect glomerular structures.

Microthrombi may be present inside glomeruli.

This helps explain overlap with thrombotic microangiopathic patterns.

Schematic



Collapsed tuft

Small luminal thrombi (conceptual)

Microangiopathic hemolysis may accompany vascular injury

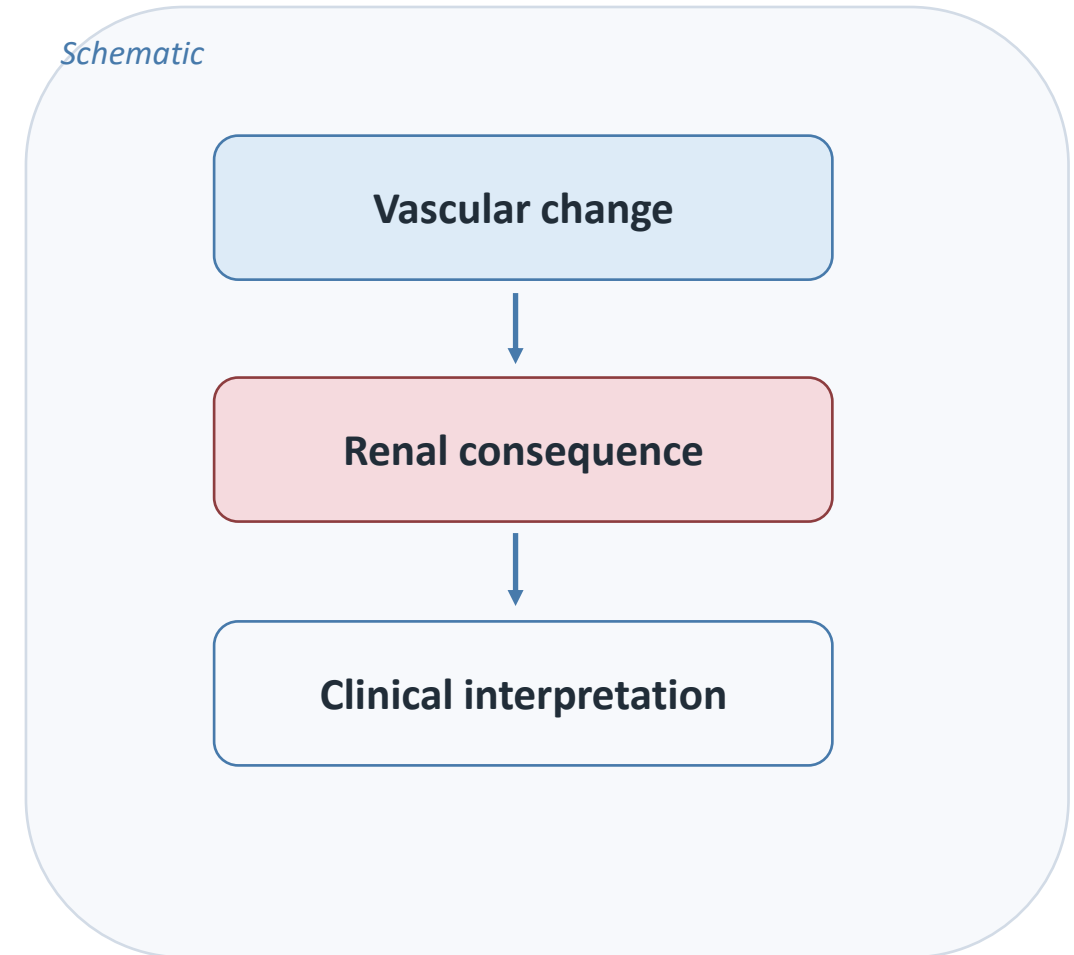
Clinical interpretation

Severe microvascular endothelial injury may damage red cells.

A microangiopathic hemolytic anemia can result.

This laboratory phenotype is not unique to a single underlying disease.

Schematic



Severe hypertension and TMA overlap morphologically

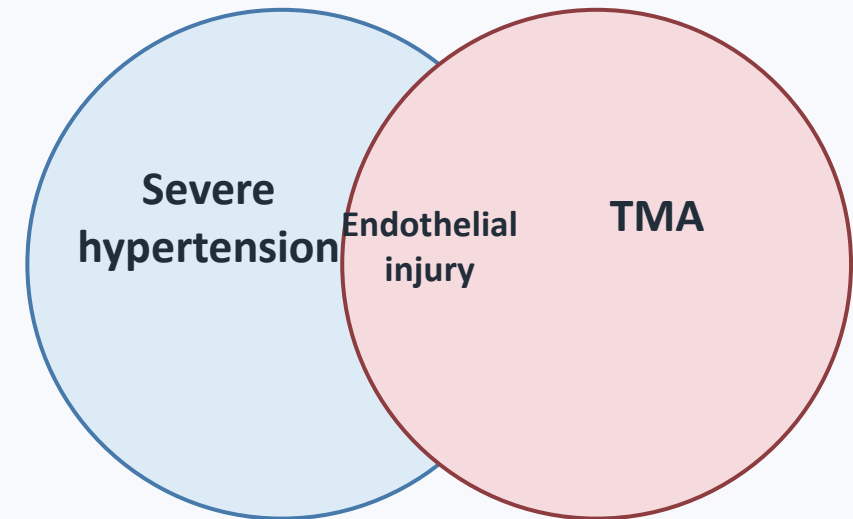
Core teaching points

Both may show endothelial injury and microvascular disease.

Both can produce glomerular microthrombi and hemolysis.

Overlapping tissue injury does not establish identical pathogenesis.

Schematic



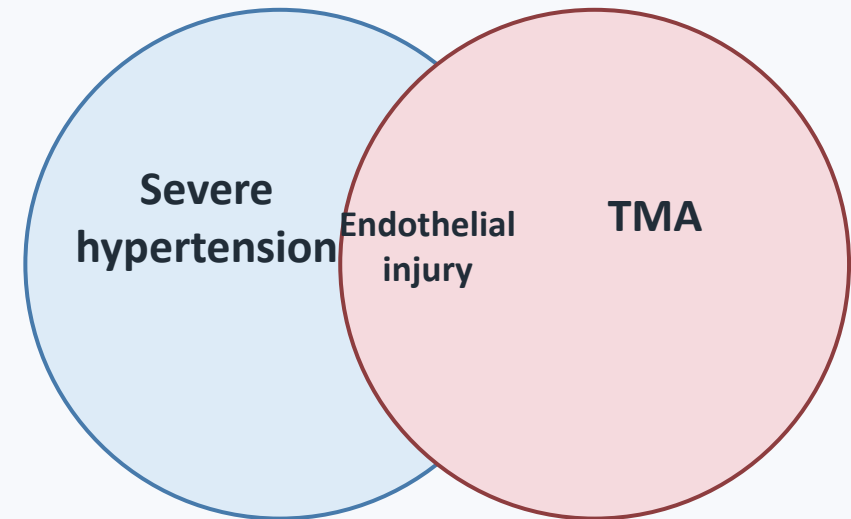
Overlap $\neq$ identical cause

TMA and hypertension remain pathogenetically distinct

Core teaching points

Robbins explicitly separates their pathogenetic origins.
Characteristic TMA molecular defects are not present in hypertension.
Differential diagnosis requires clinical and etiologic integration.

Schematic



Overlap $\neq$ identical cause

Ordinary nephrosclerosis versus severe hypertension

Feature	Ordinary nephrosclerosis	Severe hypertensive injury
Vascular wall	Hyaline arteriolosclerosis; Fibroelastic change	Hyperplastic arteriolosclerosis; Fibrinoid necrosis
Parenchyma	Patchy atrophy, sclerosis, fibrosis	May include necrosis and microthrombi
Clinical pattern	Uremia unusual if uncomplicated	Rapid renal failure may occur

Editable comparison derived descriptions

Three arteriolar patterns to discriminate

Lesion	Hallmark	Implication
Hyaline	Homogeneous wall material	Narrowed arteriole
Hyperplastic	Concentric cellular “onion skin”	Marked lumen reduction
Fibrinoid necrosis	Destructive fibrinoid wall change	Severe vascular injury

Editable comparison derived descriptions

Morphology exercise: A small narrowed arteriole

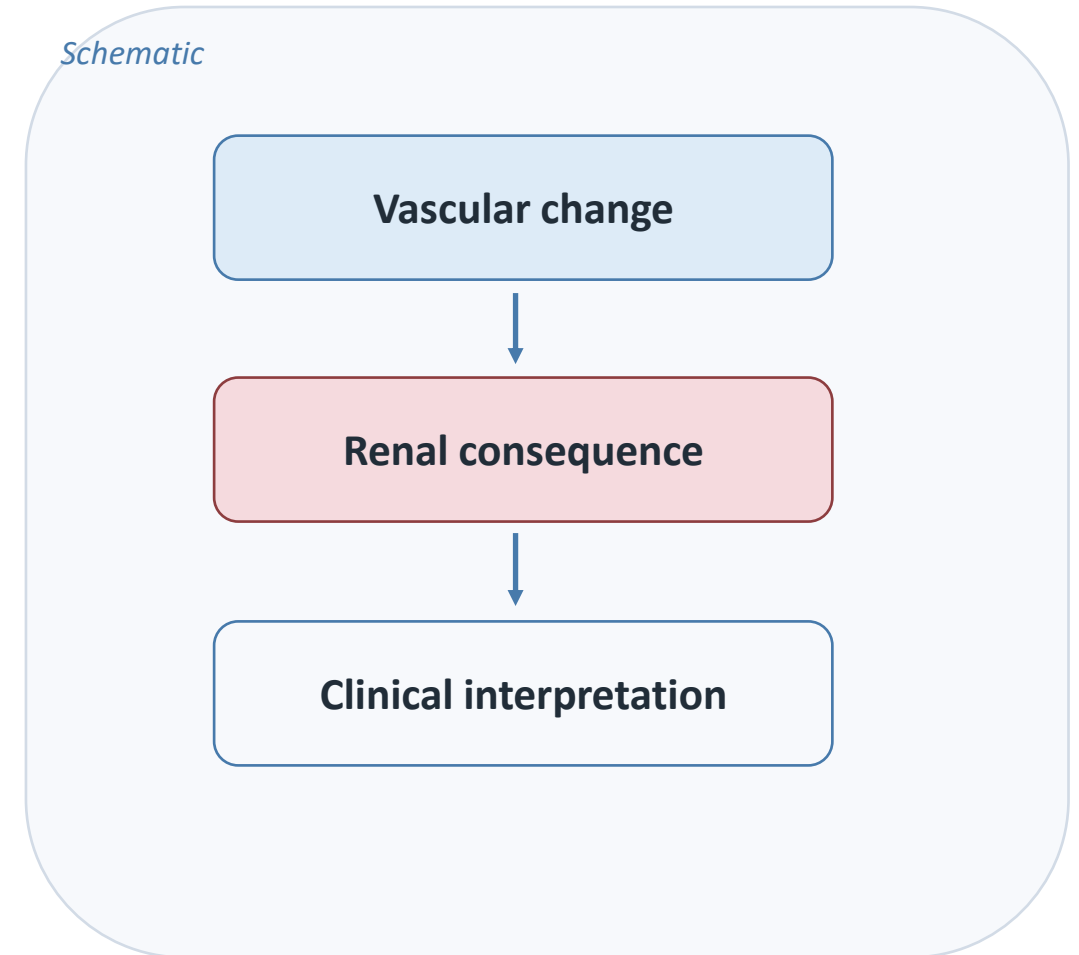
Problem to solve

A thickened, homogeneous, eosinophilic wall encroaches on the lumen.

There is no stated concentric cellular onion-skin proliferation.

Which named arteriolar process best fits this description?

Schematic



Morphology exercise: Reasoning

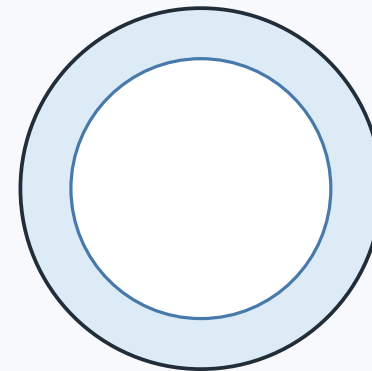
Morphologic interpretation

Homogeneous proteinaceous wall thickening favors hyaline arteriosclerosis.

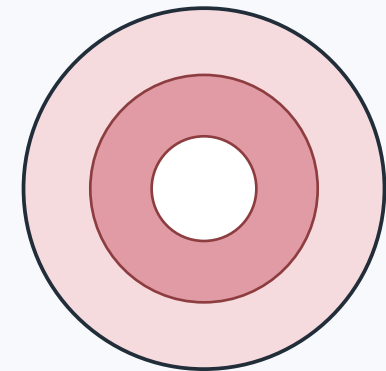
The narrowing predicts focal downstream ischemia.

Search the surrounding cortex for glomerular and tubular scars.

Schematic



Relatively open lumen



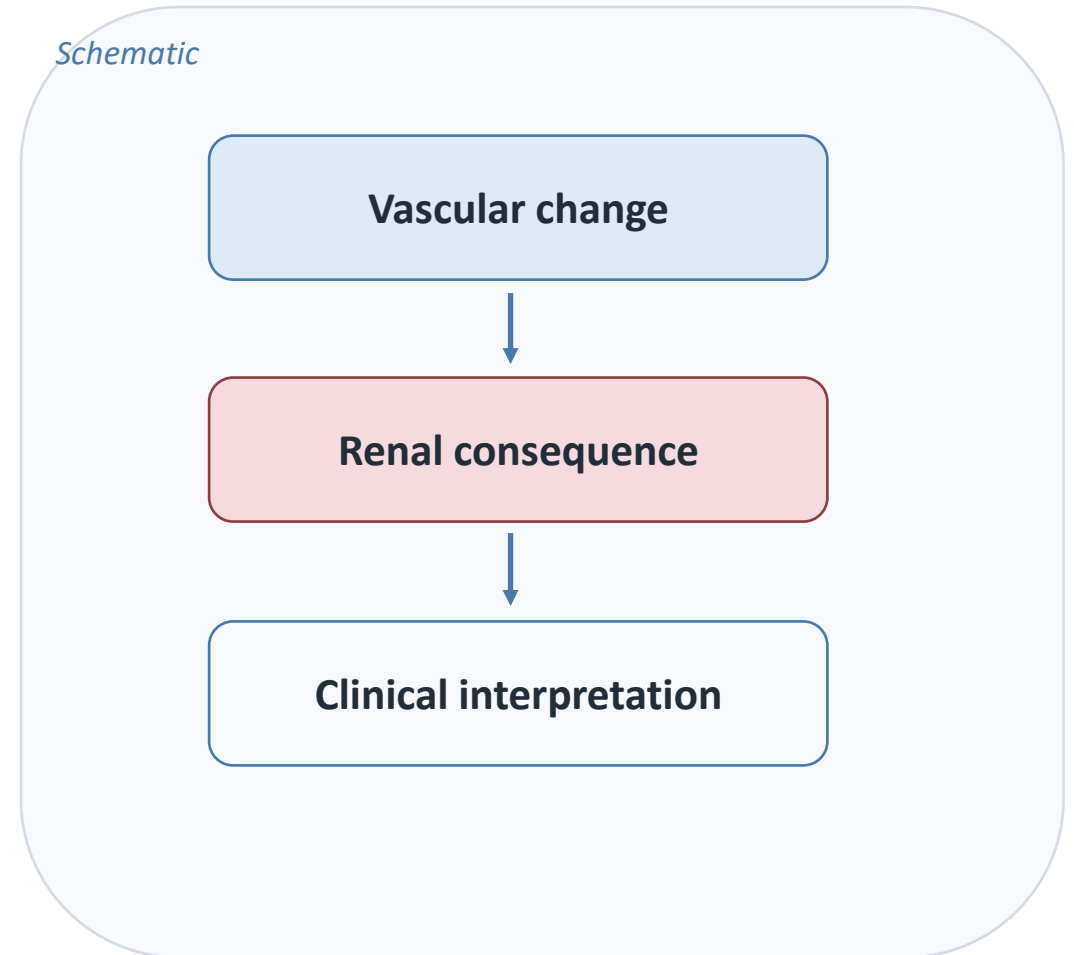
Thickened hyaline wall

Case exercise: A finely granular kidney

Problem to solve

The kidney is mildly reduced in size and finely granular.
Subcapsular scars contain sclerotic glomeruli and tubular dropout.
What vascular lesion would integrate these findings?

Schematic



Case reasoning: Connect cortex to vessels

Core teaching points

Small-vessel hyalinization and luminal narrowing are expected.
Focal ischemia links vascular changes to subcapsular scars.
The ensemble is compatible with nephrosclerosis.

Schematic

Wall injury

Hyalinization

Ischemia

Reduced perfusion

Nephrons

Scarring

Kidney

Cortical loss

One combined renal phenotype

Case exercise: Rapidly progressive vascular injury

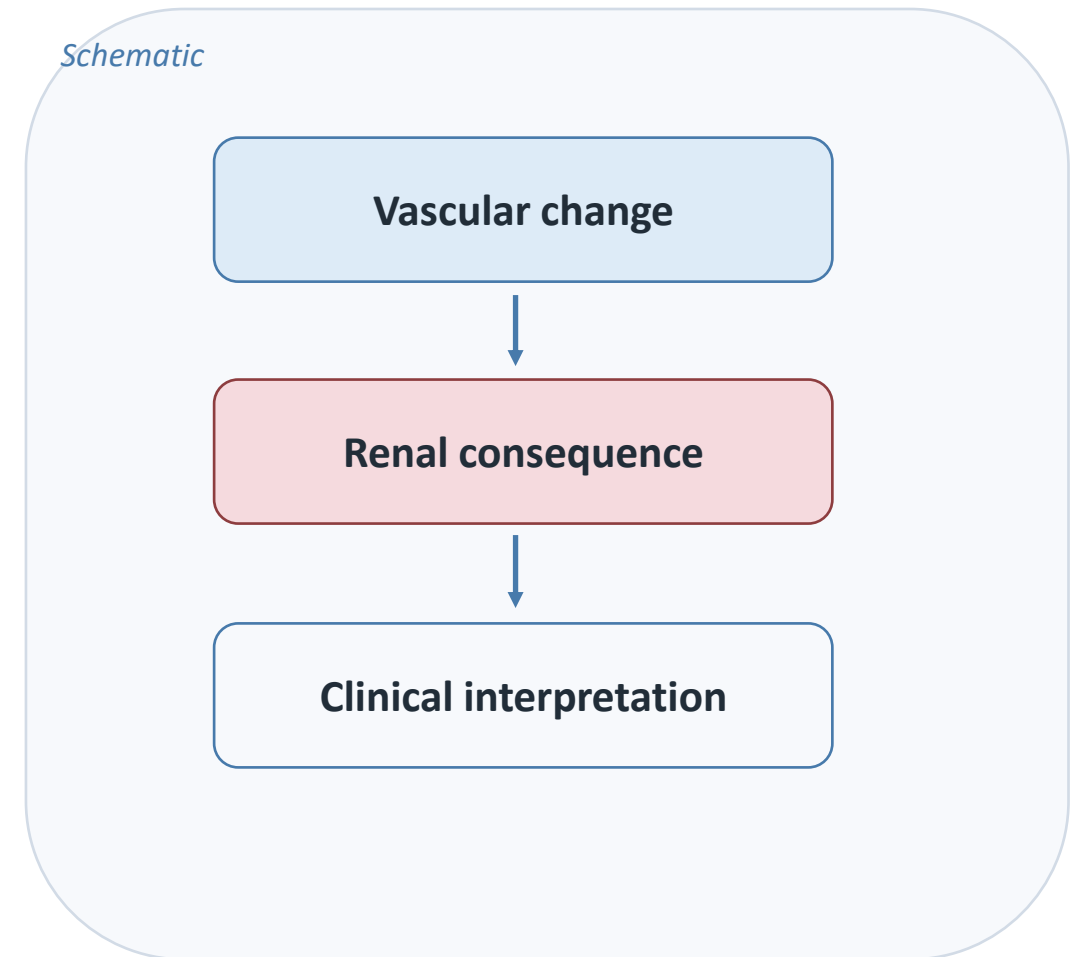
Problem to solve

Severe hypertension coincides with renal failure and retinal hemorrhages.

Biopsy shows concentric intimal cellular proliferation.

What further vascular lesion may accompany this pattern?

Schematic

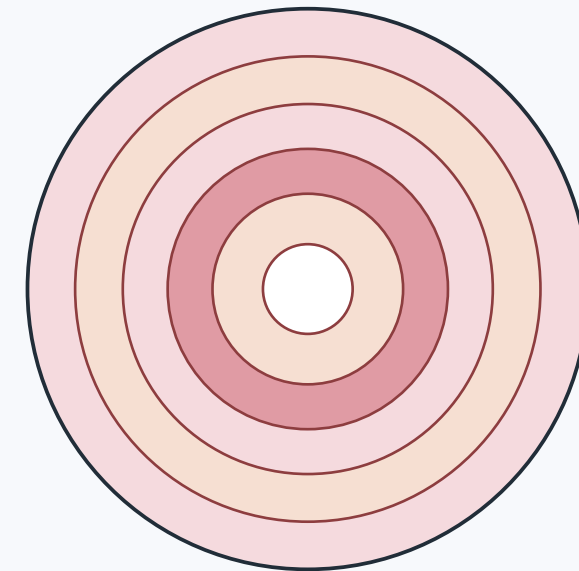


Case reasoning: Severe hypertensive injury

Morphologic interpretation

Onion-skin intimal proliferation is hyperplastic arteriolosclerosis. Arteriolar or glomerular fibrinoid necrosis may coexist. Glomerular microthrombi and hemolysis can complicate the picture.

Schematic



Concentric intimal cell proliferation

Diagnostic interpretation should be multilevel

Core teaching points

Vessel changes identify the ischemic substrate.

Glomerular and tubulointerstitial scars measure tissue consequences.

Clinical history distinguishes chronic from rapidly progressive injury.

Schematic

Wall injury

Hyalinization

Ischemia

Reduced perfusion

Nephrons

Scarring

Kidney

Cortical loss

One combined renal phenotype

Mechanism and morphology: Final synthesis

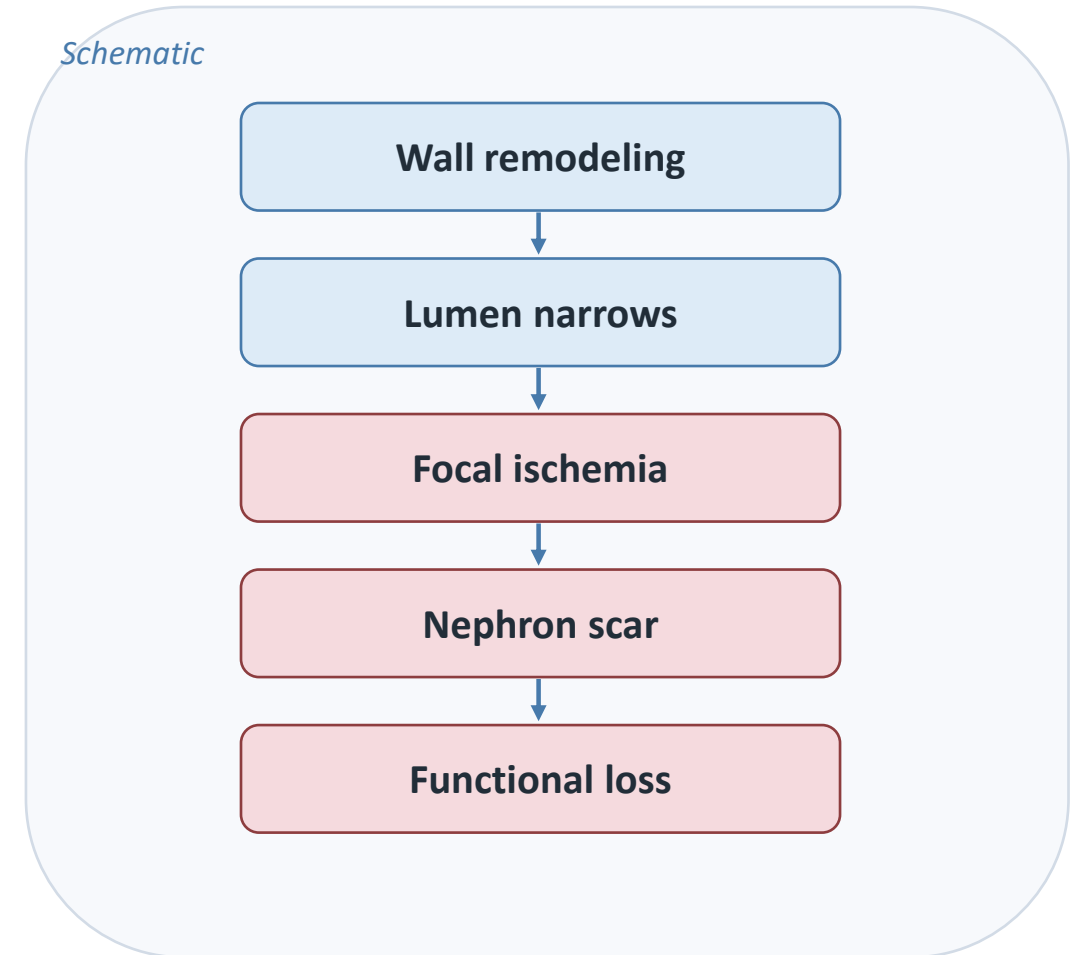
Mechanism

Wall remodeling and hyalinization reduce vascular lumina.

Ischemia produces patchy nephron scars and cortical shrinkage.

Severe hypertensive injury adds cellular proliferation and necrosis.

Schematic



Key distinctions for pathology review

Level	Principal clue	Tissue consequence
Vessels	Hyalinization and intimal thickening	Reduced perfusion
Parenchyma	Glomerular sclerosis and tubular atrophy	Cortical scars
Severe injury	Onion skin and fibrinoid necrosis	Rapid failure may occur

Editable comparison derived descriptions

Source and scope

Robbins, Cotran & Kumar: Pathologic Basis of Disease, 11th ed. (2026).
Chapter 20, The Kidney: “Vascular Diseases” and “Nephrosclerosis,” pp. 850–852.
Illustrations: original editable conceptual schematics; not histologic specimens.