

Chronic Pyelonephritis and Reflux Nephropathy

Renal tubulointerstitial pathology: mechanisms, morphology and clinical
consequences

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Learning objectives: Recognize and explain renal scarring

LECTURE OUTCOMES

- Define chronic pyelonephritis by its tubulointerstitial and pelvocalyceal involvement.
- Explain how vesicoureteral and intrarenal reflux favor polar scars.
- Identify gross and microscopic hallmarks and interpret clinical consequences.
- Distinguish major mimics and explain secondary glomerulosclerosis.

Core diagnostic link: Renal cortical scar + underlying deformed calyx.

Chronic pyelonephritis: An anatomic definition

CORE CONCEPT

- Chronic tubulointerstitial inflammation produces irreversible renal scarring.
- The calyces and renal pelvis participate in the destructive process.
- Calyceal involvement separates this pattern from many other interstitial nephritides.

Pelvocalyceal abnormality is part of the lesion, not an incidental imaging finding.

Chronic pyelonephritis is not synonymous with all TIN

MORPHOLOGIC DISTINCTIONS

General chronic tubulointerstitial injury

- Tubular atrophy and interstitial fibrosis
- Can arise from numerous different etiologies
- May lack characteristic calyceal damage

Chronic pyelonephritis

- Tubular and interstitial injury
- Irregular renal scarring
- Overlying deformation of pelvis/calices

Diagnostic specificity comes from lesion distribution and collecting-system involvement.

Relationship to acute pyelonephritis

CORE CONCEPT

- Acute pyelonephritis is predominantly suppurative renal infection.
- Repair after acute inflammation can leave irregular cortical scars.
- Persistent reflux or obstruction makes recurrent injury and scarring more likely.

Chronic disease requires a recognized scar pattern; Recurrent acute symptoms are not mandatory.

The anatomic pathway: Lower tract to renal parenchyma

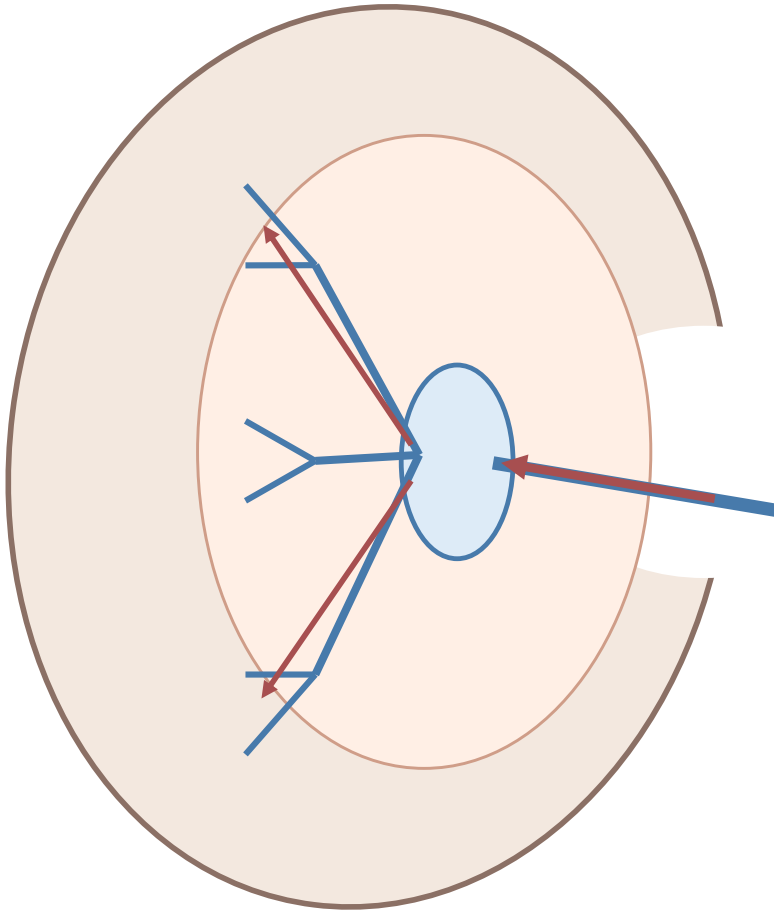
ANATOMIC CONTEXT

- Urine passes from the kidney through the pelvis and ureter into the bladder.
- The vesicoureteral junction normally limits retrograde urine flow.
- Reflux can move bladder contents toward the renal pelvis and, in susceptible papillae, parenchyma.

Two distinct retrograde steps matter: Vesicoureteral reflux and intrarenal reflux.

Where reflux-induced injury occurs

ANATOMIC SCHEMATIC



Vesicoureteral reflux

- Backward flow from bladder toward ureter and collecting system.

Intrarenal reflux

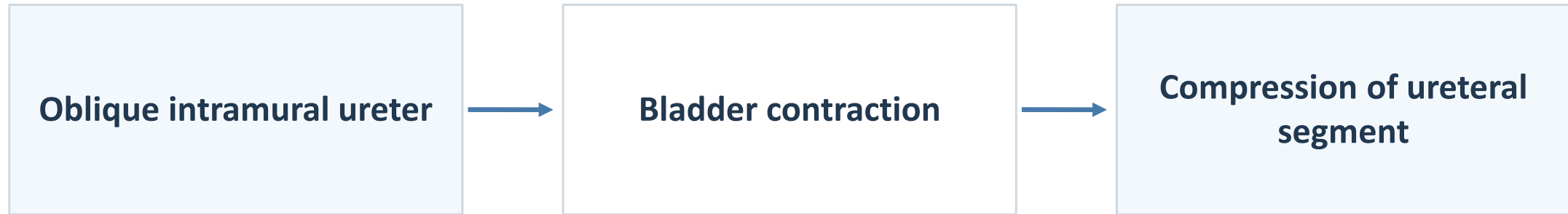
- Extension from the pelvis into papillary ducts and renal tissue.

Schematic — not a specimen or radiographic image

Schematic arrows indicate the direction of retrograde flow, not an incidence estimate.

Normal antireflux mechanism

PATHOGENESIS

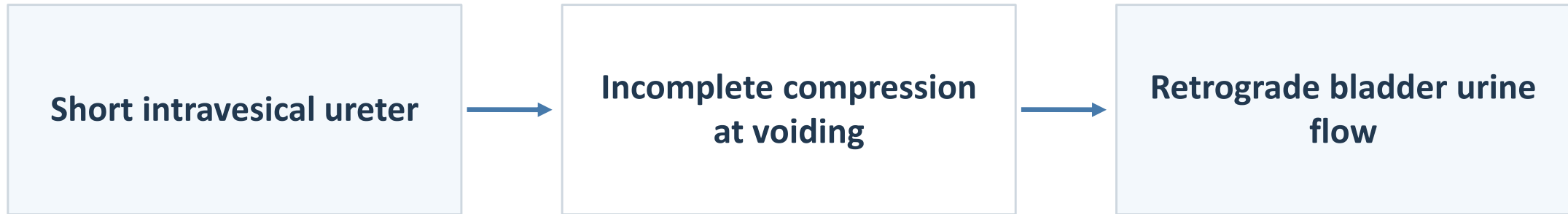


The usual ureteral insertion functions as a one-way valve during increased intravesical pressure.

Valve competence prevents urine from returning toward the kidney.

Congenital predisposition to vesicoureteral reflux

PATHOGENESIS



Congenital absence or shortening of the intravesical ureteral segment.

A structural valve defect allows reflux even without acquired obstruction.

Congenital versus acquired reflux

ETIOLOGIC MECHANISMS

Congenital

- Absent or short intravesical ureteral course
- Failure of normal antireflux closure
- Important in children

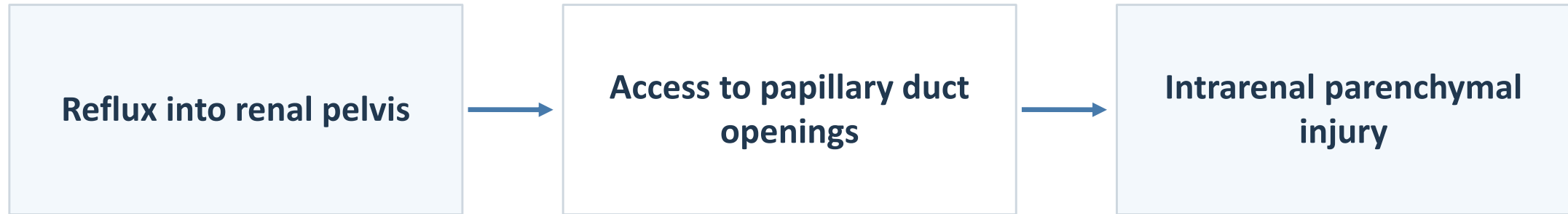
Acquired

- Inflammation can alter ureteral contractility
- Bladder dysfunction can increase residual urine
- Neurogenic bladder may favor reflux and stasis

These mechanisms are source-described; They need not occur in every patient.

Intrarenal reflux carries urine into the renal tissue

PATHOGENESIS



Open ducts at papillary tips provide an intrarenal route for infected urine.

This pathway links a lower urinary tract abnormality to focal cortical scarring.

Why reflux scars preferentially affect the poles

MORPHOLOGIC DISTINCTIONS

Upper and lower poles

- Flattened or concave papillary tips are more common
- Papillary ducts are more accessible to retrograde urine
- Scars frequently cluster in polar regions

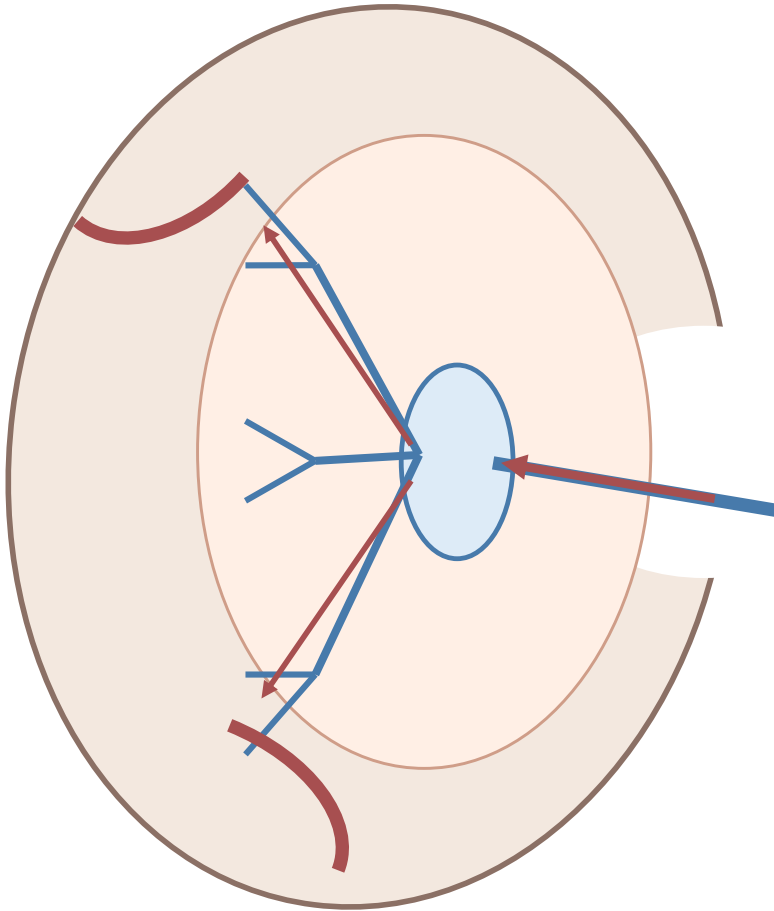
Mid-renal zones

- Pointed convex papillary tips are more common
- Anatomy is less favorable for intrarenal reflux
- This is a tendency, not an absolute boundary

Papillary geometry helps explain the distribution of reflux nephropathy.

Polar distribution of cortical injury

ANATOMIC SCHEMATIC



Upper-pole lesion

- Discrete scar above a distorted calyx.

Lower-pole lesion

- A second potential site for reflux-associated scarring.

Schematic — not a specimen or radiographic image

Source hallmark: Preferential upper- and lower-pole scarring with calyceal deformation.

Urinary tract infection and reflux act together

CAUSAL FRAMEWORK

- Ascending renal infection is more common than hematogenous spread.
- Reflux provides a route for infected urine to reach the renal pelvis.
- Repeated episodes of injury and healing can produce chronic scarring.

Reflux increases access; Infection supplies an inflammatory insult.

Chronic scars may develop without recognized acute attacks

CORE CONCEPT

- The key-concepts summary allows repeated injury with or without clinically apparent acute pyelonephritis.
- A child with reflux may first be evaluated for hypertension rather than infection.
- Absence of a documented febrile urinary infection does not exclude old reflux-associated scarring.

Clinical history and renal morphology may diverge.

Urine outflow obstruction amplifies infection risk

PATHOGENESIS



Examples in the source include calculi, tumors, outlet obstruction and neurogenic bladder.

Identify the underlying abnormality rather than viewing infection in isolation.

Two pathways to chronic pyelonephritic damage

MORPHOLOGIC DISTINCTIONS

Reflux-associated pathway

- Incompetent vesicoureteral junction
- Intrarenal reflux, especially at poles
- Focal polar scarring with calyceal deformation

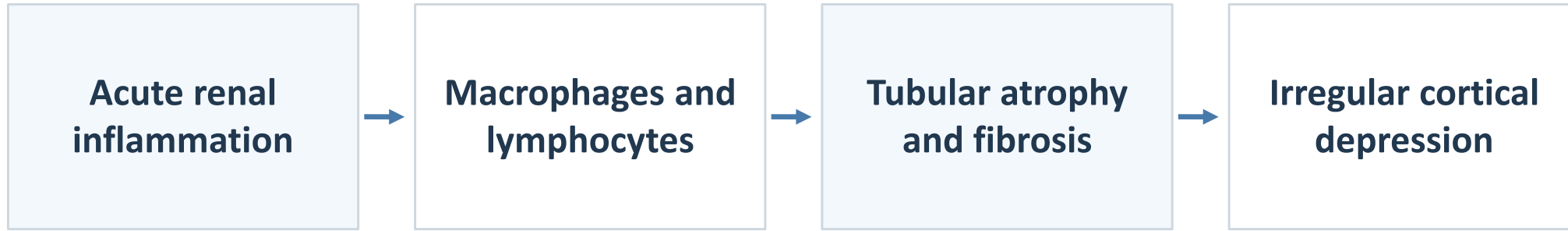
Obstruction-associated pathway

- Impaired drainage and urinary stasis
- Persistent or recurrent ascending infection
- Progressive cortical and collecting-system damage

Different predisposing anatomy can converge on the chronic scar pattern.

From acute inflammation to a mature scar

PATHOGENESIS



The source describes replacement of neutrophils by mononuclear inflammatory cells during healing.

Reparative fibrosis produces persistent architectural distortion.

Why isolated cystitis often remains below the kidney

LOCALIZATION

- Bladder colonization does not automatically mean renal parenchymal infection.
- In the absence of vesicoureteral reflux, infection usually remains in the bladder.
- Additional susceptibility arises from obstruction, stasis or impaired host defense.

A route of spread is needed to explain progression from lower-tract infection to renal scar.

Reflux nephropathy is important in children

CLINICAL CONTEXT

- Children may have congenital abnormalities of the vesicoureteral junction or lower urinary tract.
- Severe urinary tract abnormalities can cause lasting renal parenchymal destruction.
- Hypertension evaluation may uncover renal scarring before symptomatic renal failure.

Preventable or treatable urinary tract abnormalities can precede an irreversible renal scar.

Ascending infection: Source-described microbiology

ETIOLOGIC CONTEXT

- Enteric gram-negative bacilli cause most urinary tract infections in the source discussion.
- *Escherichia coli* predominates; *Proteus*, *Klebsiella* and *Enterobacter* are additional examples.
- These organisms explain infection risk, not a unique microbial signature of chronic scars.

Histologic scarring alone does not establish the species responsible for earlier infection.

Chronic pyelonephritis: Predominant tissue compartments

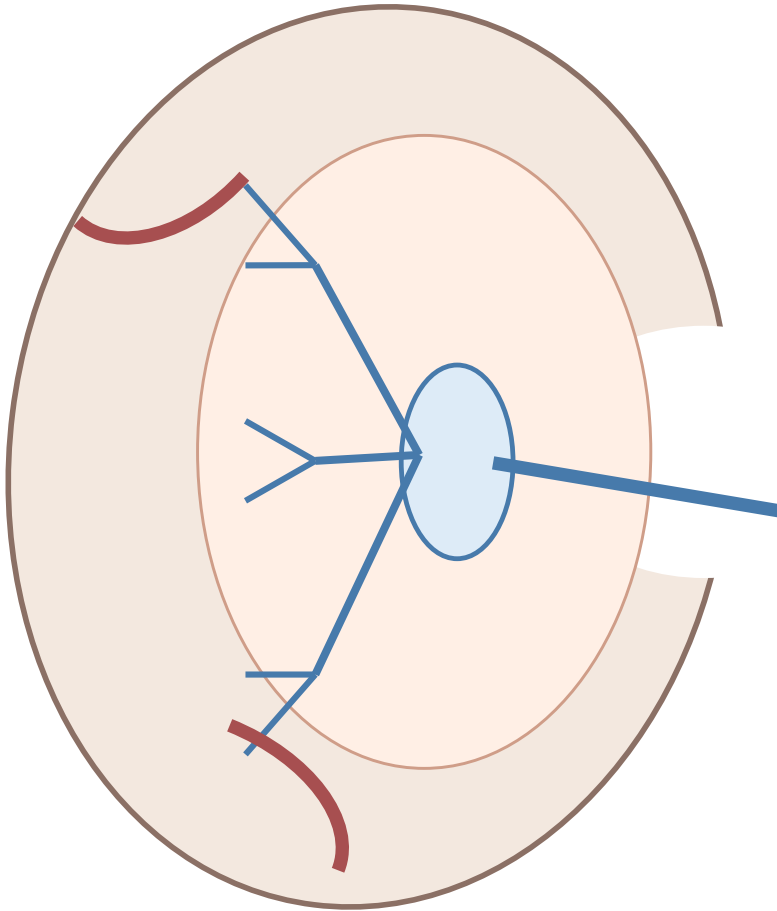
CORE CONCEPT

- Tubules and interstitium are the principal sites of microscopic chronic injury.
- Pelvocalyceal structures show accompanying inflammation, distortion or fibrosis.
- Glomeruli are initially relatively preserved but may develop secondary changes.

The site and sequence of injury explain later functional findings.

Characteristic gross appearance

ANATOMIC SCHEMATIC



Cortical surface

- Coarse, discrete depressions and irregular contours.

Underlying collecting system

- Corresponding calyceal dilatation, blunting or deformation.

Schematic — not a specimen or radiographic image

The surface scar and the distorted calyx should be interpreted together.

A cortical scar is a three-dimensional lesion

GROSS MORPHOLOGY

- Coarse cortical depression reflects loss of functioning renal tissue.
- A discrete lesion extends through cortex toward the corticomedullary region.
- The underlying calyx is dilated, blunted or distorted.

The scar–calyx relationship is more discriminating than surface irregularity alone.

Calyceal blunting and papillary flattening

CORE CONCEPT

- Scarred parenchyma overlies a dilated or deformed calyx.
- The corresponding papilla can appear flattened.
- Scarring of tissue around the calyceal epithelium contributes to structural distortion.

Papillary flattening and calyceal deformity are established morphologic hallmarks.

Patchy rather than uniform renal involvement

CORE CONCEPT

- Scars vary from one to several in an affected kidney.
- When bilateral, scarring tends to be asymmetric.
- Preserved parenchyma may separate areas of chronic injury.

Focality and asymmetry help distinguish reflux-associated scarring from diffuse processes.

Chronic pyelonephritis versus chronic glomerulonephritis

MORPHOLOGIC DISTINCTIONS

Chronic pyelonephritis

- Coarse, irregular, discrete surface scars
- Often asymmetric bilateral involvement
- Underlying calyceal dilatation or blunting

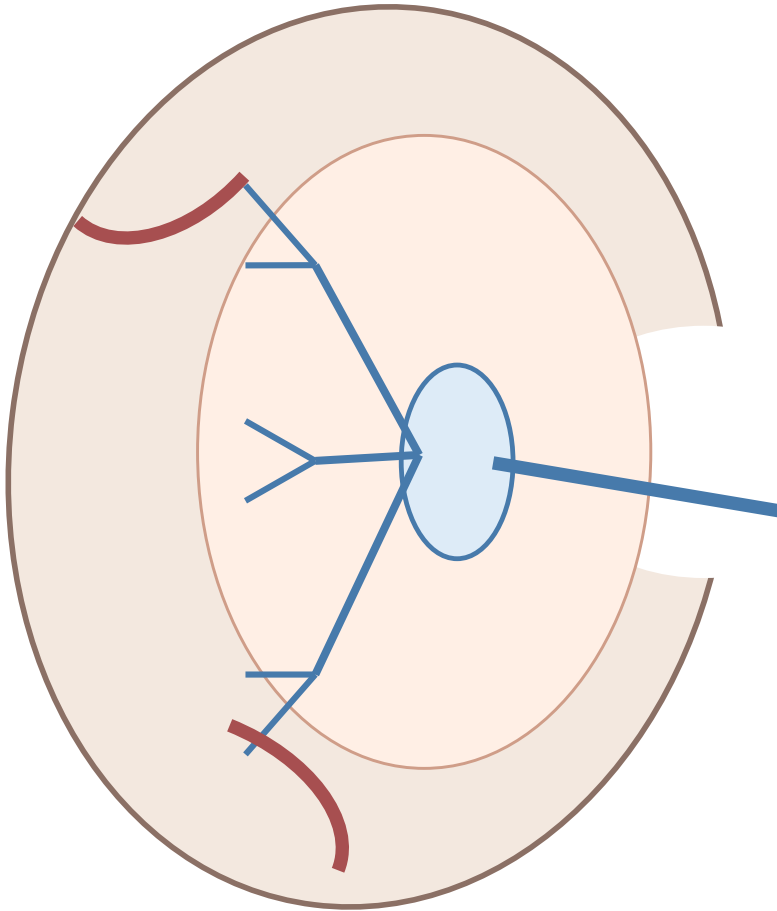
Chronic glomerulonephritis

- Diffuse, relatively symmetric contracted kidneys
- Scarring is not organized around deformed calyces
- Glomerular disease dominates the injury pattern

Gross pattern directs the differential; Correlation with histology remains necessary.

The scar–calyx correlation: A pattern-based approach

ANATOMIC SCHEMATIC



Observation

- Coarse corticomedullary cortical scar.

Anatomic counterpart

- Blunted/deformed calyx directly beneath.

Interpretation

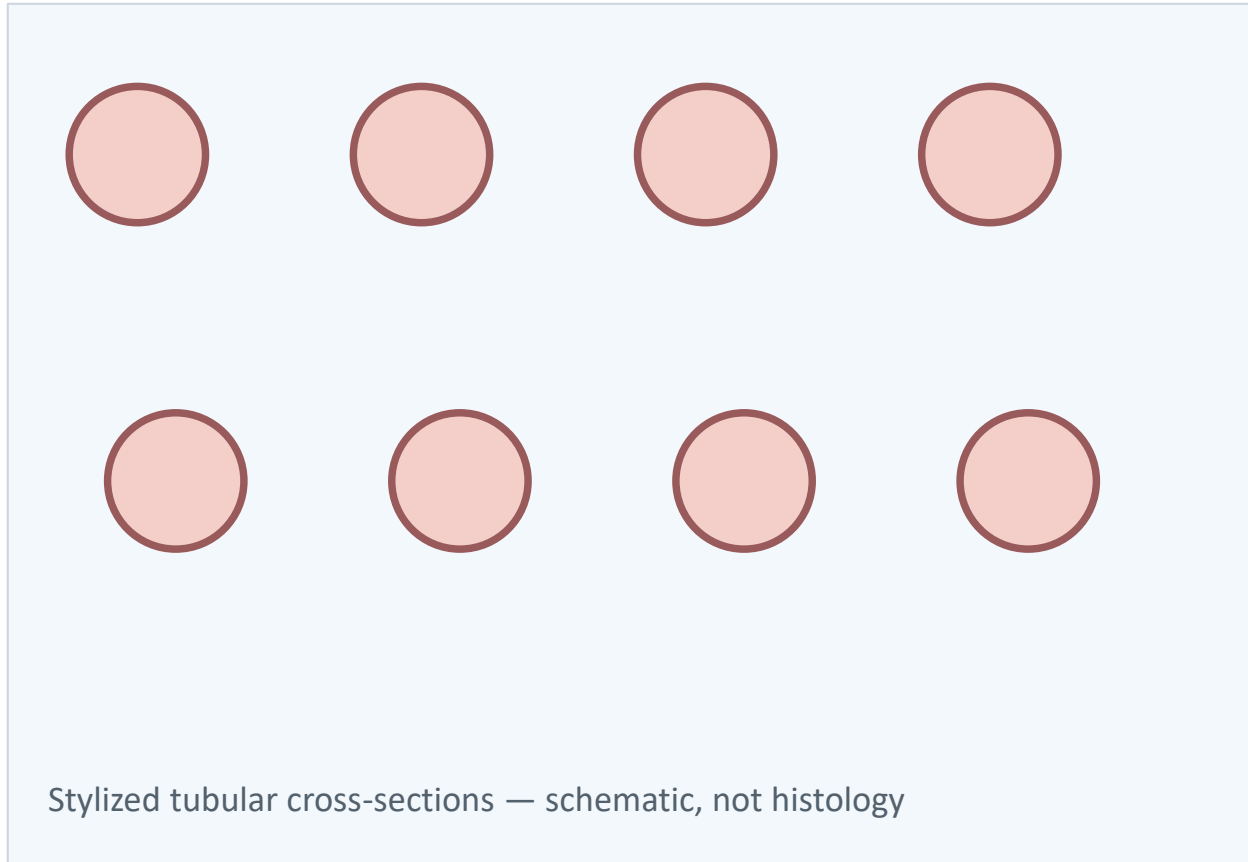
- Pattern supports chronic pyelonephritis/reflux-associated injury.

Schematic — not a specimen or radiographic image

Isolated interstitial fibrosis does not have the same diagnostic specificity.

Tubular atrophy within scarred cortex

HISTOMORPHOLOGY — SCHEMATIC

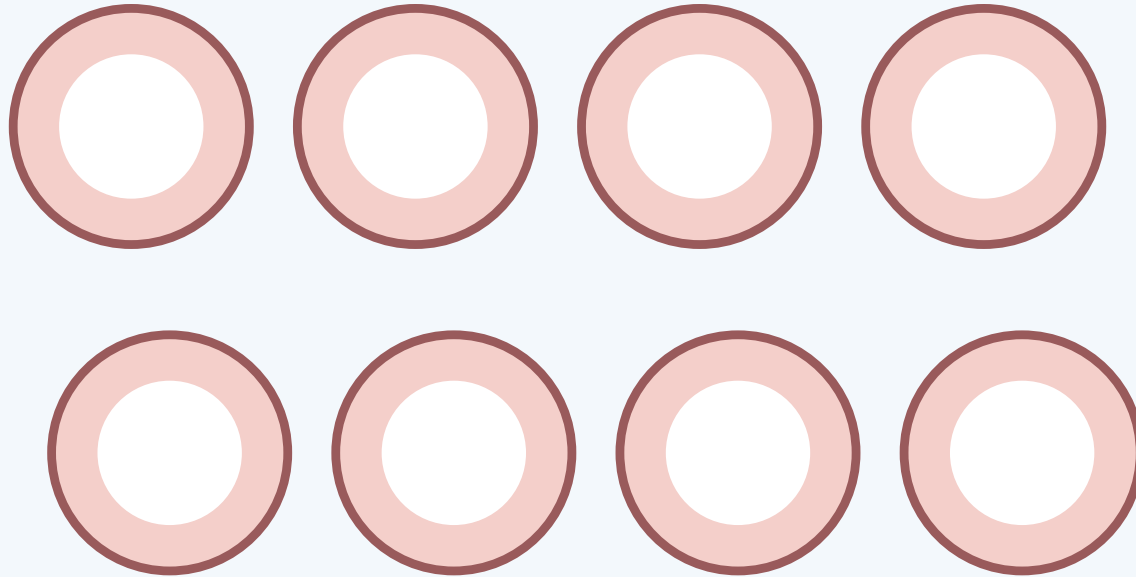


- Chronic injury causes shrinkage and loss of normal tubules.
- Atrophic tubular profiles coexist with interstitial collagen deposition.
- The process is often patchy, with less-affected intervening cortex.

Tubular loss contributes directly to nephron mass reduction.

Dilated and hypertrophied tubules coexist with atrophy

HISTOMORPHOLOGY — SCHEMATIC



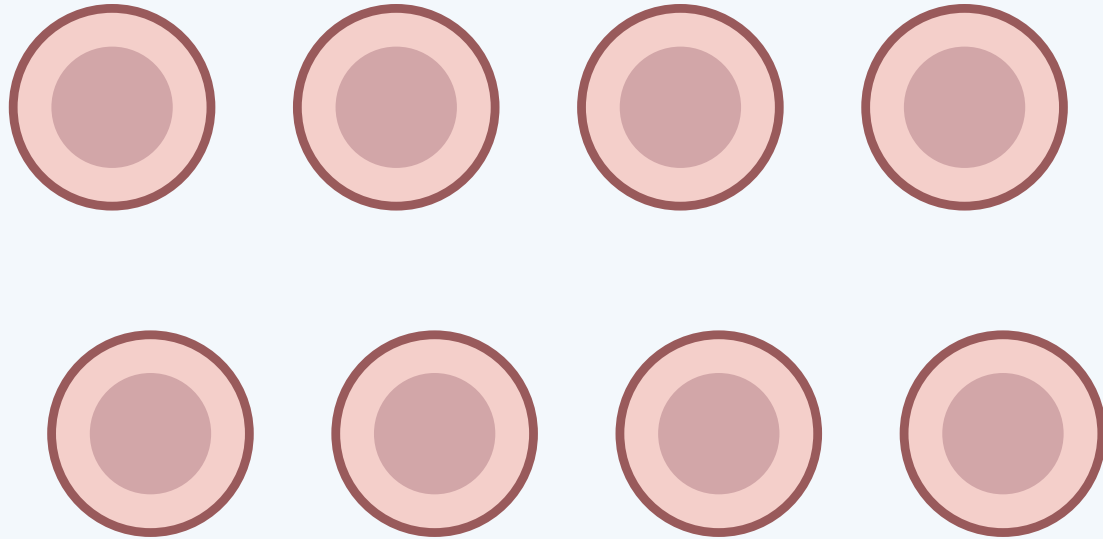
Stylized tubular cross-sections — schematic, not histology

- Remaining tubules may be enlarged or dilated.
- Flattened epithelium can line distended tubular lumina.
- Heterogeneous tubular calibers reflect remodeling of damaged parenchyma.

A mixed atrophic–dilated tubular pattern is typical of chronic damage.

Thyroidization: A characteristic microscopic pattern

HISTOMORPHOLOGY — SCHEMATIC



Stylized tubular cross-sections — schematic, not histology

- Dilated tubules may contain rounded, homogeneous proteinaceous casts.
- The appearance resembles thyroid follicles filled with colloid.
- Thyroidization is useful but not pathognomonic without the anatomic context.

A resemblance to thyroid tissue describes morphology, not thyroid differentiation.

Interstitial fibrosis records cumulative injury

MICROSCOPIC MORPHOLOGY

- Fibrous replacement extends through both cortex and medulla.
- Fibrosis often surrounds atrophic or distorted tubules.
- Collagenous scars accompany loss of functioning nephron segments.

Chronicity is demonstrated by fibrosis and tubular atrophy, not just inflammatory cells.

Mononuclear inflammatory infiltrates

CORE CONCEPT

- Chronic interstitial infiltrates accompany renal parenchymal scarring.
- Lymphocytes and plasma cells are prominent after resolution of acute neutrophilic inflammation.
- Inflammation may remain conspicuous even in fibrotic areas.

Inflammation and scarring frequently coexist in chronic pyelonephritis.

Inflammation and fibrosis near the calyces

CORE CONCEPT

- Fibrosis can involve the tissues around the calyceal epithelium.
- A marked chronic inflammatory infiltrate may accompany the lesion.
- This collecting-system component supports the diagnosis in the correct setting.

Calyceal alterations are not a separate, unrelated disease process.

Glomeruli: Relative early preservation

CORE CONCEPT

- Tubulointerstitial lesions dominate the primary injury.
- Glomeruli may appear normal in relatively early or less advanced areas.
- Later glomerular alterations often reflect ischemia and systemic hypertension.

Preserved glomeruli do not contradict severe adjacent tubular scarring.

Ischemic glomerular alterations in advanced disease

CORE CONCEPT

- Periglomerular fibrosis may develop in chronically scarred cortex.
- Some glomeruli undergo fibrous obliteration.
- Chronic hypertension can compound secondary glomerular injury.

Distinguish secondary glomerular lesions from a primary glomerulonephritis.

How loss of renal mass leads to secondary FSGS

PATHOGENESIS



The source attributes secondary FSGS to adaptive changes after substantial parenchymal loss.

Proteinuria can emerge years after the initiating renal injury.

Secondary FSGS may occur after reflux has ceased

CORE CONCEPT

- Significant proteinuria can arise several years after scar formation.
- Continued bacterial infection or persistent reflux is not required at that late stage.
- Adaptive stress on remaining glomeruli is implicated in the secondary lesion.

Current urine sterility does not negate old scarring as the origin of glomerulosclerosis.

Histomorphologic reading sequence

DIAGNOSTIC COMPARISON

Compartment	Expected features	Interpretation
Tubules	Atrophy; Dilation; Thyroidization	Chronic tubular remodeling
Interstitialium	Inflammation and fibrosis	Chronic scarring
Calyces	Inflammation; Pericalyceal fibrosis	Characteristic anatomic context
Glomeruli	Often spared; Later ischemia/FSGS	Usually secondary change

Report the pattern and its distribution; Do not diagnose from a single nonspecific feature.

Xanthogranulomatous pyelonephritis: Distinctive variant

SPECIAL MORPHOLOGIC PATTERN

- A rare form of chronic pyelonephritis.
- Marked by accumulations of lipid-laden foamy macrophages.
- Inflammatory admixture can include lymphocytes, plasma cells, neutrophils and giant cells.

Foamy macrophage-rich inflammation creates a striking mass-forming appearance.

Associations of xanthogranulomatous inflammation

CORE CONCEPT

- Frequent association with Proteus infection.
- Urinary obstruction is another important accompanying condition.
- Gross lesions can form large yellow–orange nodules.

The combination of obstruction, infection and macrophage-rich tissue injury is characteristic.

Xanthogranulomatous lesion versus renal carcinoma

MORPHOLOGIC DISTINCTIONS

Xanthogranulomatous pyelonephritis

- Yellow–orange mass-like lesion possible
- Foamy macrophages with inflammatory cells
- Often associated with obstruction/infection

Renal cell carcinoma

- Can also present as a renal mass
- Gross yellow coloration can overlap
- Requires independent morphologic evaluation

A mass-like gross appearance alone cannot establish neoplasia.

Chronic pyelonephritis may be clinically silent

CLINICAL PRESENTATION

- Onset is often insidious rather than abrupt.
- The kidney can accumulate scars before significant clinical attention.
- Renal insufficiency or hypertension may be the presenting problem.

The clinical severity at detection may exceed the recent symptomatic history.

Recurrent infection-type presentations

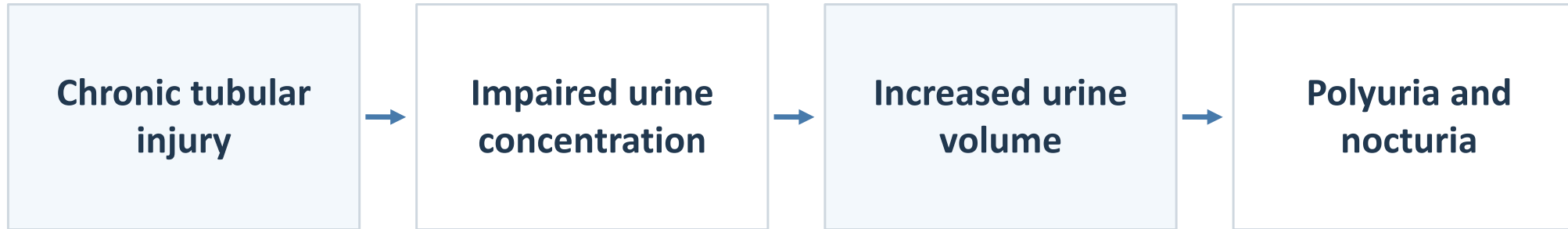
CORE CONCEPT

- Some patients experience recurring episodes of fever and back pain.
- Pyuria and bacteriuria may accompany active infection.
- These findings alone do not quantify pre-existing chronic scarring.

Clinical activity and accumulated structural injury are different dimensions of disease.

Tubular dysfunction causes polyuria and nocturia

PATHOGENESIS



Loss of concentrating capacity is especially characteristic of tubulointerstitial disease.

Tubular functional symptoms may precede prominent glomerular syndromes.

Hypertension can reveal childhood reflux nephropathy

CORE CONCEPT

- Children with renal scars may be investigated because of elevated blood pressure.
- Hypertension is a major clinical manifestation of chronic renal damage.
- Secondary glomerular lesions may coexist as disease progresses.

Consider renal parenchymal scarring in the clinical evaluation of hypertension.

Renal insufficiency emerges gradually

CORE CONCEPT

- Progressive loss of functional parenchyma reduces renal reserve.
- Azotemia or overt renal insufficiency may develop late.
- Bilateral disease and reduced remaining renal mass are clinically important.

Extent of established fibrosis helps explain chronic loss of function.

Urine findings: Active infection versus old scar

MORPHOLOGIC DISTINCTIONS

Current/recurrent infection

- Significant bacteriuria may be present
- Pyuria supports urinary inflammation
- Clinical symptoms may recur

Late scarred kidney

- Bacteriuria can be absent
- Tubular concentrating defects may persist
- Proteinuria may signal secondary glomerular injury

A negative culture does not reverse an established renal scar.

Proteinuria: A change in significance over time

CORE CONCEPT

- Proteinuria is usually mild in uncomplicated chronic pyelonephritic scarring.
- Some patients later develop substantial proteinuria due to secondary FSGS.
- Proteinuria may reach the nephrotic range in this subgroup.

Heavy proteinuria should prompt assessment for superimposed adaptive glomerular injury.

Why new proteinuria is prognostically important

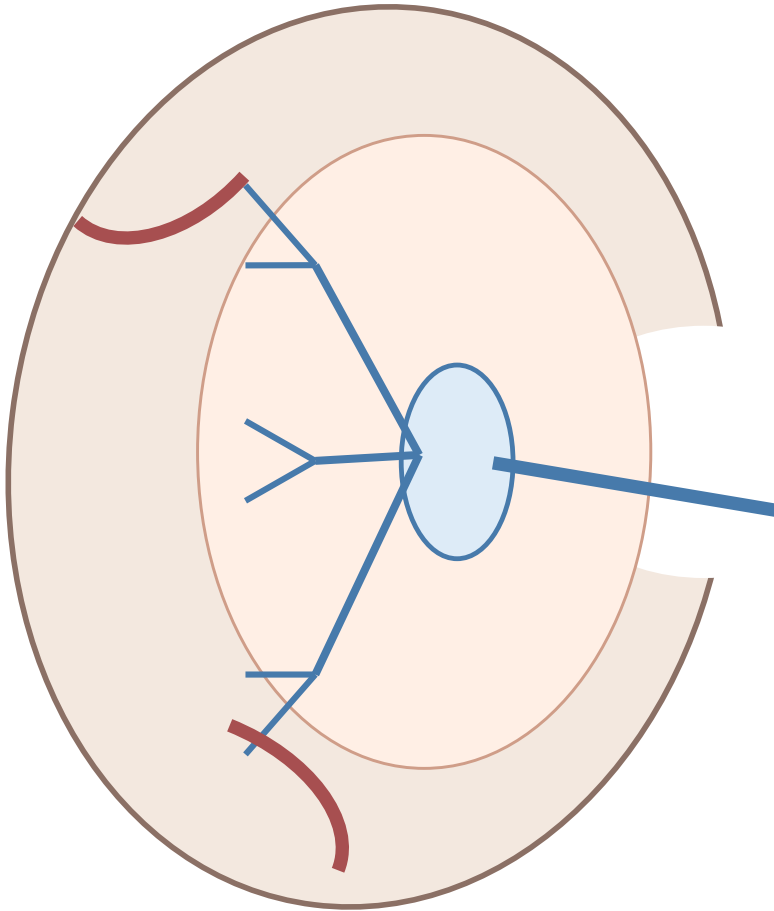
CORE CONCEPT

- Onset of significant proteinuria can indicate secondary FSGS.
- This change to an increased likelihood of progression to end-stage kidney disease.
- The prognostic inference comes from glomerular damage superimposed on pre-existing scarring.

A late glomerular phenotype changes the risk profile of a primarily tubulointerstitial disease.

Imaging correlates of established scarring

ANATOMIC SCHEMATIC



Renal size and contour

- Asymmetric contracted kidneys; Coarse cortical scars.

Collecting system

- Calyceal blunting and deformation beneath the scars.

Schematic — not a specimen or radiographic image

Radiologic identification relies on the combined parenchymal and calyceal pattern.

Demonstrating reflux is not the same as detecting scars

DIAGNOSTIC REASONING

- Voiding cystourethrography can demonstrate retrograde passage of contrast.
- Renal imaging may instead show old cortical scars and calyceal deformation.
- Current reflux may have resolved when chronic parenchymal consequences are discovered.

Tests answer different questions: Active reflux versus residual damage.

Diagnostic pattern recognition at a glance

DIAGNOSTIC COMPARISON

Finding	Supports	Important qualification
Polar cortical scars	Reflux-associated chronic injury	Not exclusive to reflux
Blunted/deformed calyces	Chronic pyelonephritic pattern	Also seen with analgesic nephropathy
Tubular thyroidization	Chronic tubulointerstitial damage	Not independently specific
Late heavy proteinuria	Secondary FSGS possible	Other glomerular causes need evaluation

Integrate imaging, anatomy, history, and tissue findings rather than using one feature.

Calyceal injury: Chronic pyelonephritis and analgesic nephropathy

MORPHOLOGIC DISTINCTIONS

Chronic pyelonephritis

- Reflux/obstruction often present
- Coarse polar corticomedullary scars
- Blunting of underlying calyces

Analgesic nephropathy

- Drug-related tubulointerstitial damage
- May also damage papillae and calyces
- Requires separate exposure and morphologic context

Both entities as important causes of calyceal involvement.

Distinguish primary interstitial disease from chronic GN

MORPHOLOGIC DISTINCTIONS

Tubulointerstitial-predominant injury

- Concentrating defects; Nocturia/polyuria
- Tubular atrophy, interstitial fibrosis
- Characteristic calyceal changes if pyelonephritic

Primary glomerular disease

- Dominant glomerular syndrome may be present
- Glomerular lesion drives initial kidney injury
- May secondarily cause tubulointerstitial scarring

Advanced renal disease can blur the clinical distinction.

Anatomic and etiologic differential diagnosis

DIAGNOSTIC PITFALLS

- Tubulointerstitial fibrosis by itself is not specific for reflux nephropathy.
- Drug or toxin injury can also cause chronic interstitial disease.
- Calyceal deformity plus reflux/obstruction history strengthens the attribution.

Avoid inferring a single past cause from a nonspecific microscopic scar.

Case: A child investigated for hypertension

CLINICOPATHOLOGIC APPLICATION

Clinical vignette

- School-age child with hypertension and an asymmetrically small kidney.
- Imaging identifies a polar cortical scar above a blunted calyx.

Interpret the findings

- Which renal disorder is favored?
- What urinary tract abnormality may explain the distribution?

Teaching interpretation

- Pattern supports reflux-associated chronic pyelonephritic scarring.
- Vesicoureteral and intrarenal reflux provide the anatomic mechanism.

Case: Thyroidization on a renal biopsy

CLINICOPATHOLOGIC APPLICATION

Clinical vignette

- Renal cortex shows tubular atrophy, dilated tubules with proteinaceous casts, and fibrosis.
- The biopsy lacks evidence about the collecting system.

Interpret the findings

- Does thyroidization alone prove reflux nephropathy?
- What other correlation is needed?

Teaching interpretation

- No; Thyroidization indicates chronic tubular damage.
- Seek radiologic calyceal deformity and relevant urinary tract history.

Case: Proteinuria long after childhood infection

CLINICOPATHOLOGIC APPLICATION

Clinical vignette

- Adult with a previously scarred kidney; Now substantial proteinuria.
- Current urine culture is negative and reflux is no longer documented.

Interpret the findings

- Why might proteinuria have increased?
- Does absence of present infection exclude the mechanism?

Teaching interpretation

- Secondary adaptive FSGS can follow loss of renal mass.
- It may occur without ongoing reflux or infection.

Mechanistic synthesis: From reflux to renal scarring

INTEGRATION

- Vesicoureteral reflux makes retrograde urine flow possible.
- Intrarenal reflux preferentially exposes papillary ducts at the upper and lower poles.
- Recurring injury and repair leave irregular cortical and calyceal scars.
- Chronic tubular and glomerular dysfunction then shape later manifestations.

Mechanism → distribution → morphology → clinical phenotype.

Morphologic synthesis: The decisive pattern

INTEGRATION

- Gross: Irregular coarse corticomedullary scars, often polar and asymmetric.
- Collecting system: Underlying calyceal blunting/deformity and papillary flattening.
- Microscopy: Tubular atrophy/dilatation, thyroidization, fibrosis and chronic inflammation.
- Glomeruli: Early relative preservation with later ischemia or secondary FSGS.

Read anatomy and histology as one connected lesion.

Clinical synthesis: What the renal scar predicts

INTEGRATION

- The onset may be silent or involve recurrent infection-like episodes.
- Tubular dysfunction causes impaired concentrating ability, polyuria and nocturia.
- Hypertension and renal insufficiency may bring patients to medical attention.
- New substantial proteinuria suggests secondary glomerular involvement and worse prognosis.

Clinical decline can continue after reflux or bacteriuria is no longer demonstrable.

Primary source and reading context

REFERENCE

Robbins, Cotran & Kumar: Pathologic Basis of Disease

11th edition (2026), Chapter 20: The Kidney

- “Chronic Pyelonephritis and Reflux Nephropathy,” pp. 844–845.
- Related section: “Pyelonephritis and Urinary Tract Infection,” pp. 840–844.
- Relevant original textbook figures: 20.25–20.26 (not reproduced in this deck).

Conceptual anatomical and microscopic drawings in this lecture are original schematics, not clinical images.