

Cystic Diseases of the Renal Medulla

Medullary sponge kidney | Nephronophthisis

Cortex

Corticomedullary junction

Medulla / papillary ducts

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Learning objectives

- Distinguish collecting-duct dilatation from progressive tubulointerstitial disease.
- Identify the characteristic renal distribution and morphology of both entities.
- Connect nephronophthisis-associated tubular damage with its clinical presentation.
- Use clinical context and renal morphology to formulate a focused differential diagnosis.

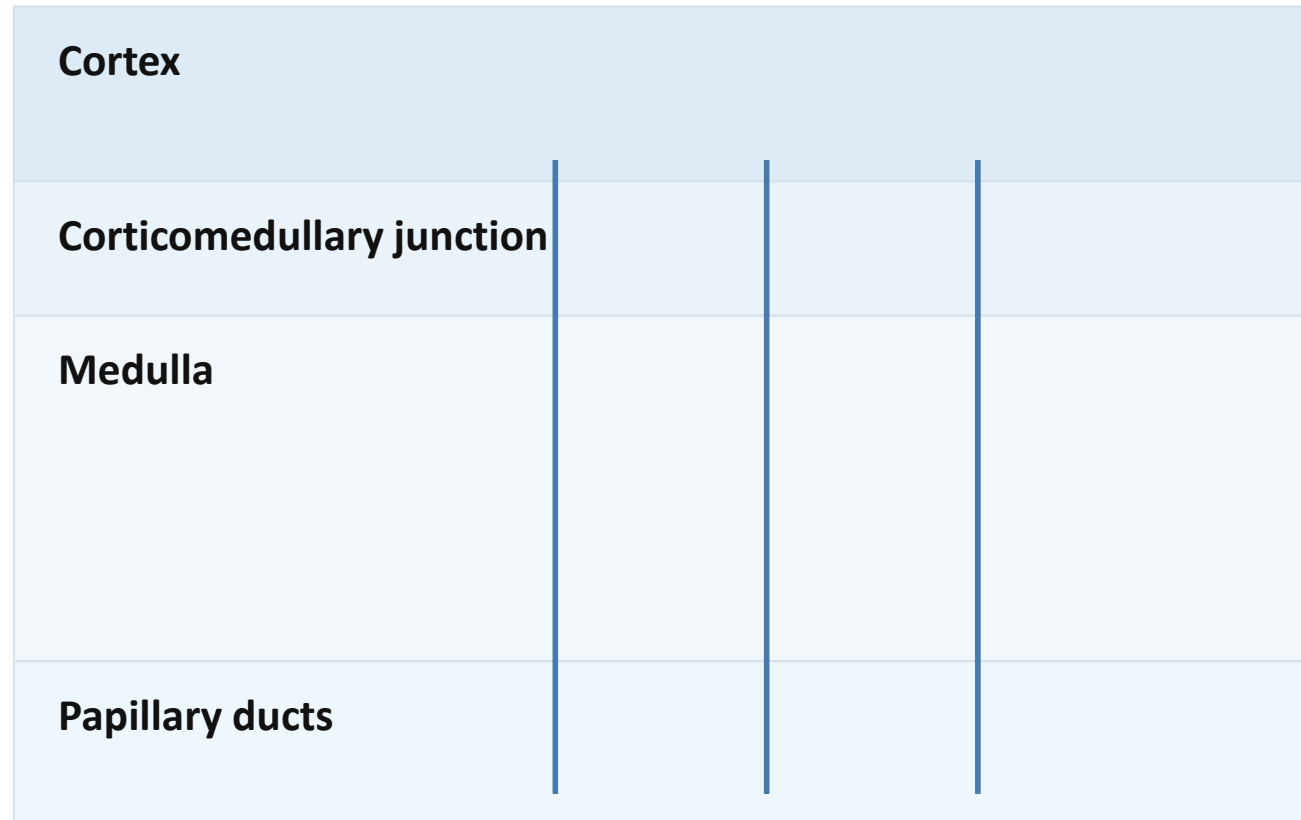
Two medullary cystic diseases, two very different courses

Feature	Medullary sponge kidney	Nephronophthisis
Underlying pattern	Collecting-duct dilatation	Progressive tubular injury and fibrosis
Usual setting	Adult; often radiographic discovery	Childhood or adolescence
Functional course	Renal function usually normal	Progressive renal insufficiency
Core pathology	Medullary papillary duct changes	Corticomedullary cysts + cortical injury

A medullary cyst does not establish the prognosis

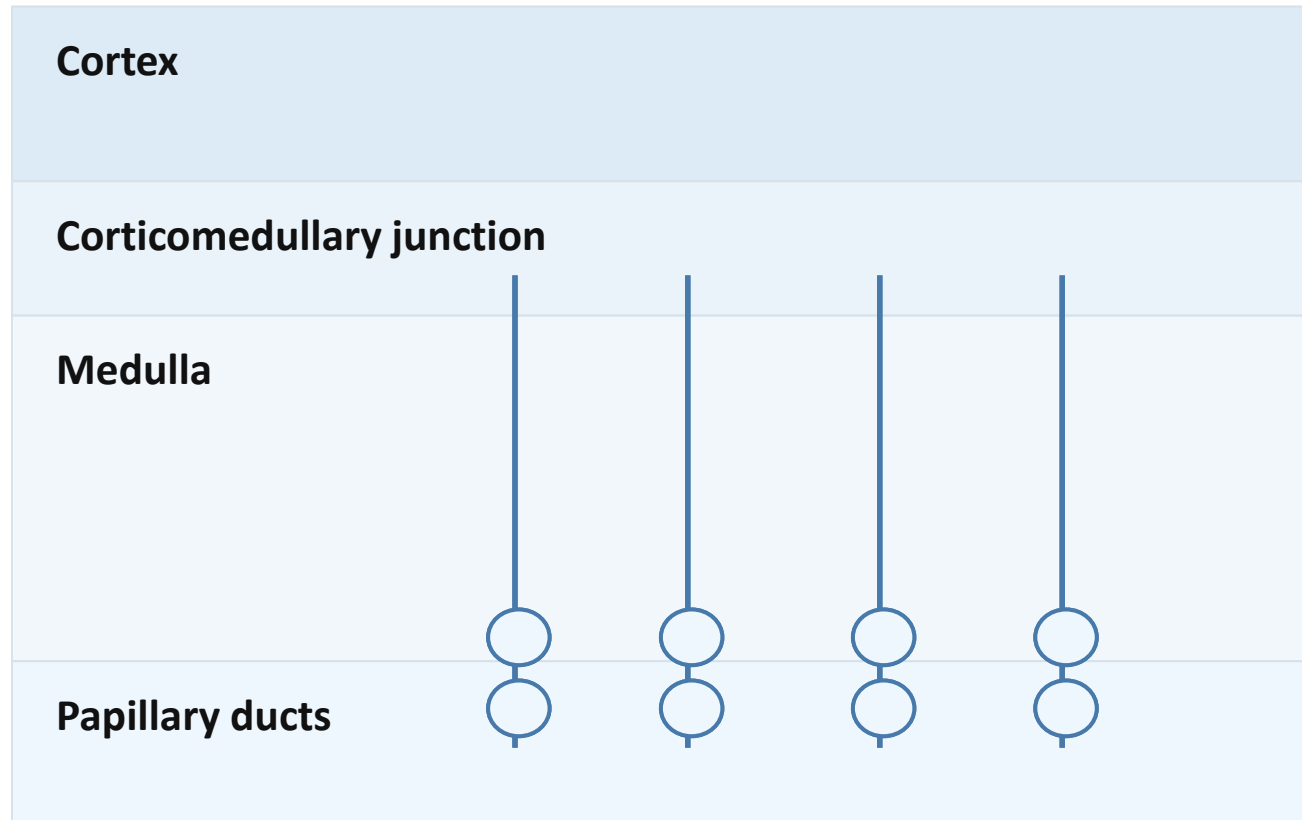
- Both entities can contain cysts within the renal medulla.
- In medullary sponge kidney, the characteristic finding is ductal dilatation.
- In nephronophthisis, progressive cortical tubulointerstitial damage explains loss of function.
- The tissue response around cysts and the clinical age pattern resolve the apparent similarity.

Regional anatomy: Cortex to papillary ducts



- Cortex contains the parenchyma that can undergo tubulointerstitial atrophy.
- Corticomedullary junction is the favored cyst location in nephronophthisis.
- Medullary collecting/papillary ducts are dilated in medullary sponge kidney.

The location of cysts supports the diagnosis



Dilated medullary collecting ducts

- Medullary sponge kidney: Dilated papillary collecting ducts.
- Nephronophthisis: Cysts often cluster at the corticomedullary junction.
- Localization must be integrated with organ size, cortical injury and clinical context.

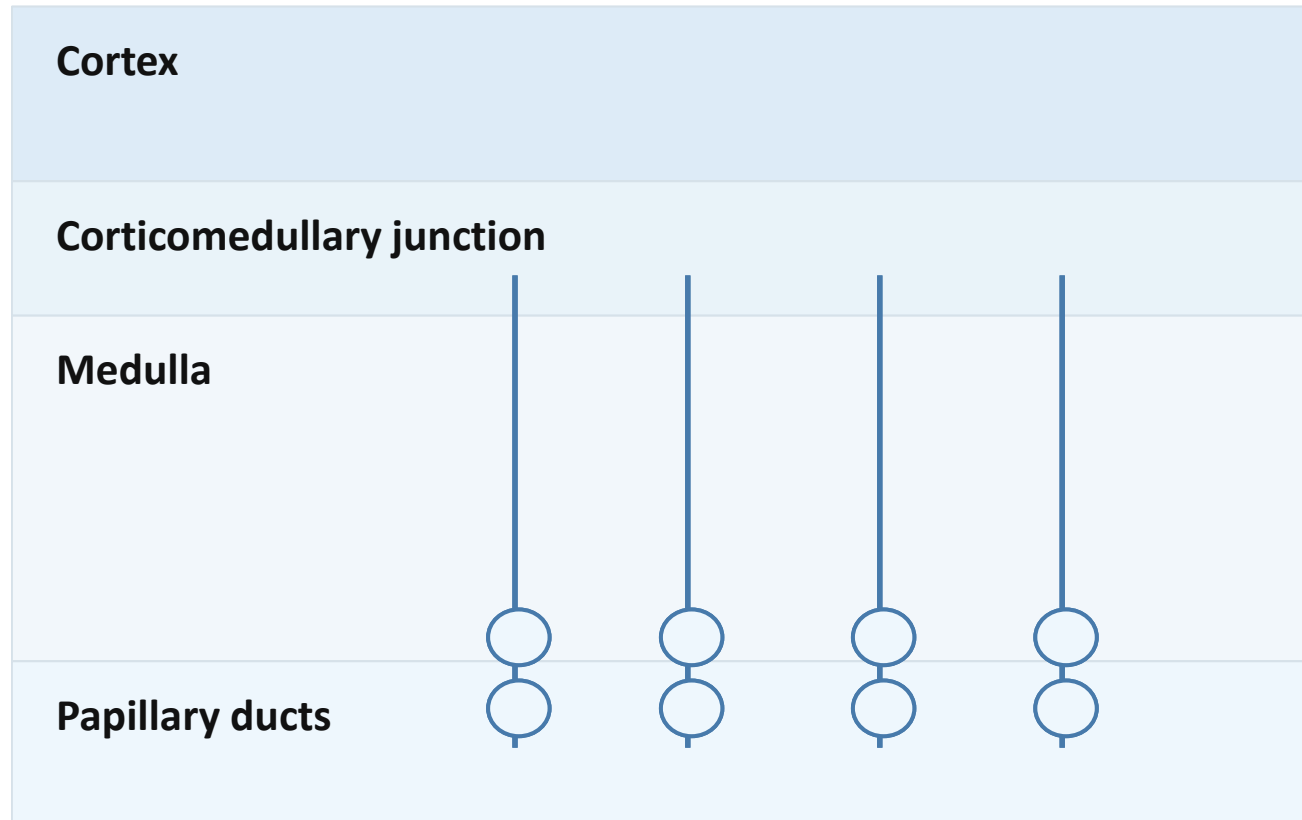
Pattern recognition begins with the surrounding kidney

Observation	Likely interpretation
Medullary dilatation + preserved cortex	Favours medullary sponge kidney
Small kidney + corticomedullary cysts	Favours nephronophthisis
Cortical atrophy + fibrosis	Explains progressive insufficiency in nephronophthisis
Cysts without characteristic clinical context	Insufficient for definitive classification

Medullary sponge kidney: Definition

- Multiple cystic dilatations of collecting ducts within the renal medulla.
- The terminology is restricted to this collecting-duct abnormality.
- The condition is a relatively common structural change.
- It is usually innocuous rather than a progressive parenchymal disorder.

Medullary sponge kidney is a duct-centred lesion

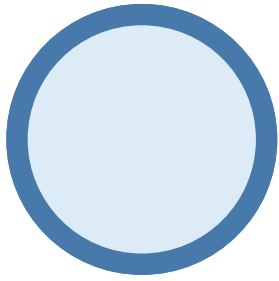


Dilated medullary collecting ducts

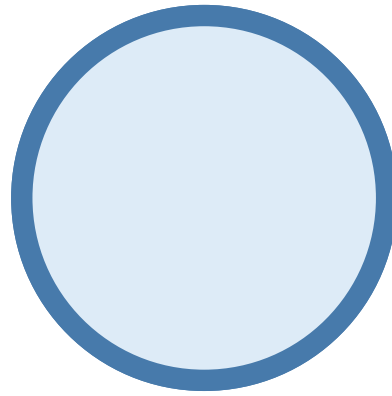
- Cystic structures arise from dilated collecting ducts.
- Papillary/medullary location is central to the definition.
- It is not synonymous with a kidney diffusely replaced by cysts.

Collecting-duct dilatation: Structural concept

Usual duct



Dilated duct



Cuboidal epithelial lining around lumen

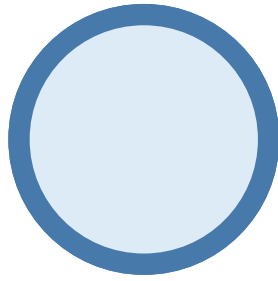
- Dilation expands the ductal lumen while retaining an epithelial lining.
- The lesion primarily reflects an anatomic alteration in medullary duct calibre.
- Robbins does not establish a specific initiating molecular mechanism.

Medullary sponge kidney: Gross morphology

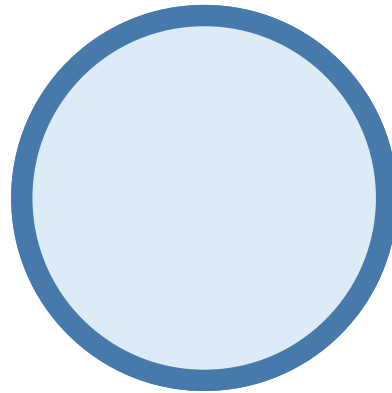
- Medullary papillary ducts are visibly dilated on gross examination.
- Small cysts can be present within the medulla.
- The diagnostic pattern is centred on the papillary collecting system.
- The passage does not describe characteristic destructive cortical lesions.

Cystic spaces retain an epithelial lining

Usual duct



Dilated duct



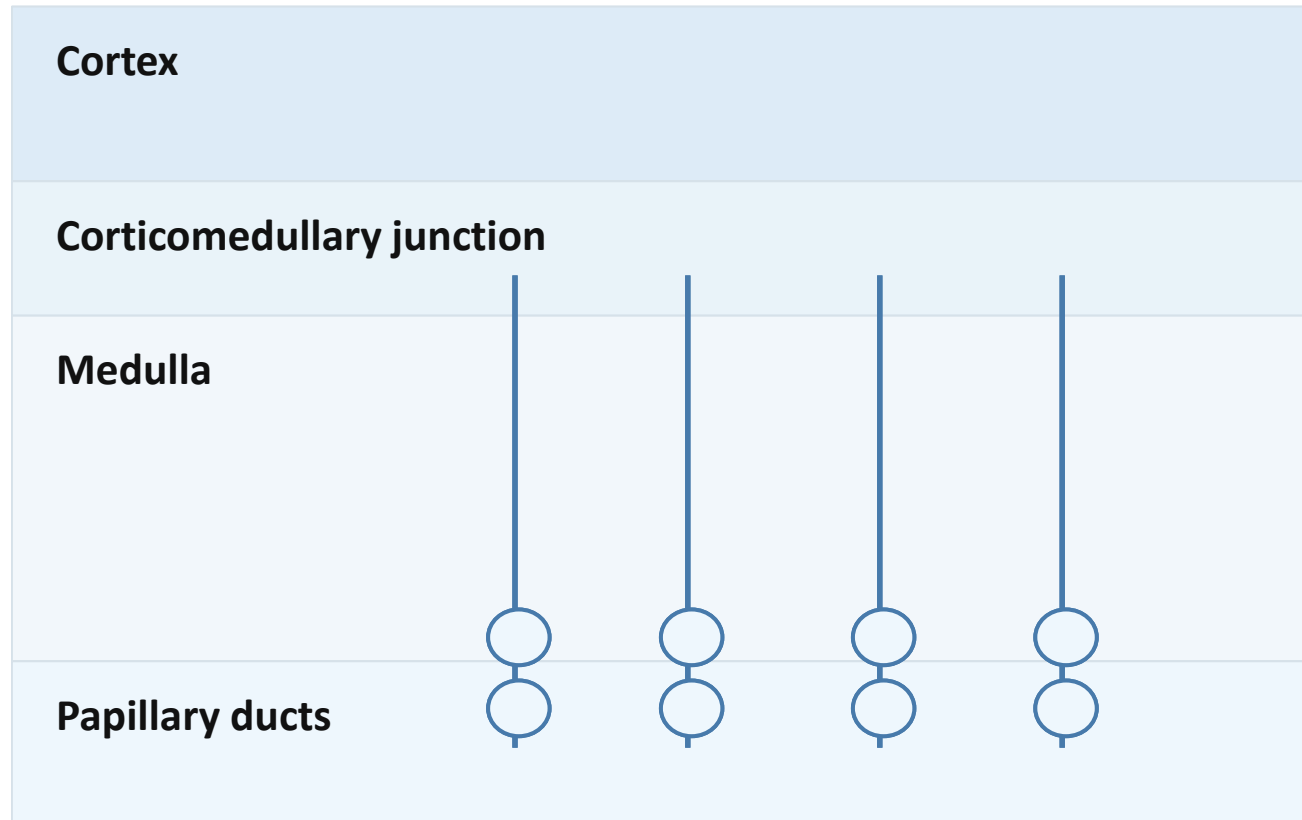
Cuboidal epithelial lining around lumen

- Cuboidal epithelium is the usual cyst lining.
- Transitional epithelium may occasionally line cysts.
- Histologic identification requires attention to the dilated duct and its epithelial boundary.

An epithelial lining does not imply malignancy

- The term “cyst” here refers to dilatation of a pre-existing epithelial duct.
- Cuboidal or occasional transitional epithelial lining is a described morphologic feature.
- Medullary sponge kidney as benign, not as a neoplastic cystic process.
- Do not interpret lining morphology alone without distribution and renal context.

Medullary sponge kidney: Cortical sparing



Dilated medullary collecting ducts

- Cortical scarring is absent in uncomplicated medullary sponge kidney.
- A preserved cortex is compatible with usually normal renal function.
- Cortical scars prompt consideration of superimposed pathology.

Cortical scarring suggests a superimposed process

- Robbins explicitly qualifies cortical sparing when pyelonephritis is present.
- An accompanying infection can change the pathology of an otherwise benign lesion.
- Do not attribute cortical scars to uncomplicated medullary sponge kidney.
- Recognize concurrent disease before inferring intrinsic progression.

Medullary sponge kidney: Typical clinical setting

- Usually encountered in adults.
- Often discovered during radiographic evaluation rather than through progressive kidney failure.
- Renal function is typically normal.
- The radiographic presentation must be linked back to medullary collecting-duct anatomy.

Imaging can reveal a medullary duct abnormality

IMAGING PRINCIPLE



Excretory urography as a method showing medullary cysts. Imaging shows the pattern; Clinical assessment determines its significance.

Preserved renal function is a discriminator

- Renal function is usually normal in medullary sponge kidney.
- Medullary ductal cysts therefore do not imply inevitable progression to ESKD.
- Declining kidney function should not be attributed automatically to this finding.
- Assess superimposed or alternative renal disease when cortical injury is present.

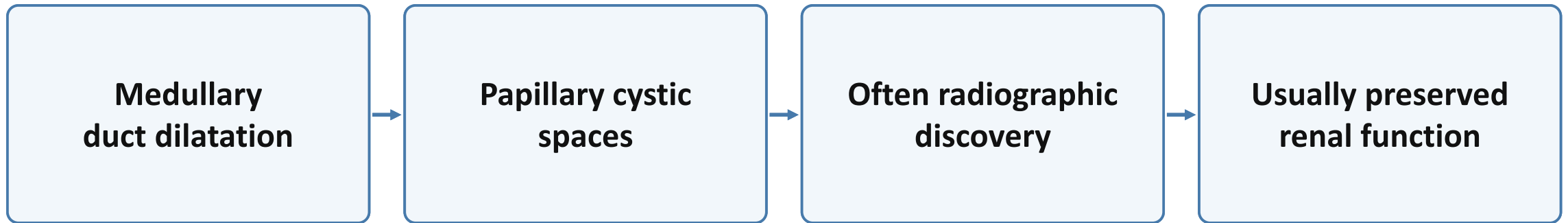
Medullary sponge kidney: Reported clinical associations

Finding	Interpretive teaching point
Hematuria	A possible clinical clue; not specific to the lesion
Urinary tract infection	Consider an associated or superimposed process
Recurrent renal stones	Recognized association in the Robbins cystic disease table
Usually normal kidney function	Separates this disorder from progressive nephronophthisis

Mechanistic uncertainty must be preserved

- The pathogenesis of medullary sponge kidney is unknown.
- The structural phenotype does not establish a molecular cause.
- No specific genetic locus or obligate pathogenic pathway should be assigned on this source.
- Its generally benign behaviour is an observation, not an explanation of origin.

Medullary sponge kidney: The clinicopathologic pattern

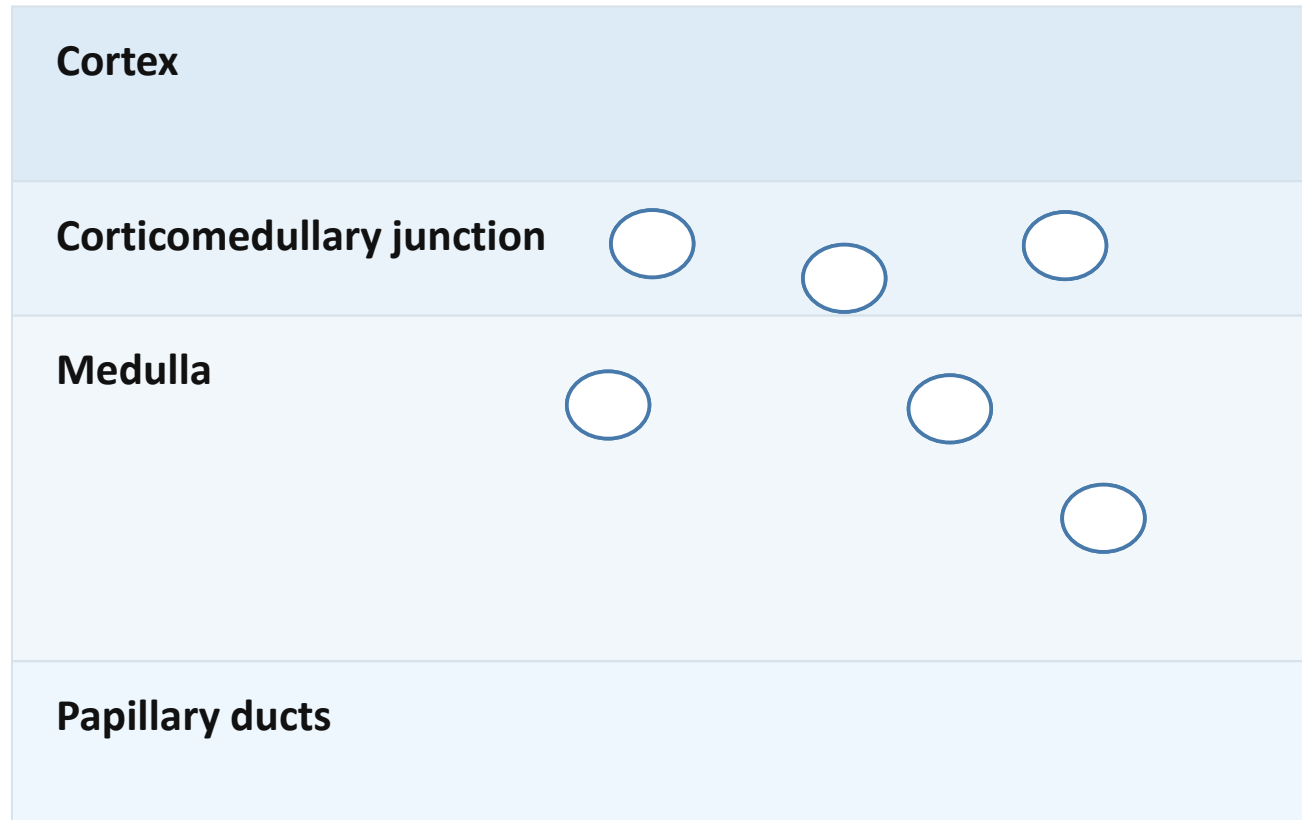


Hematuria, urinary tract infection or stones may be associated; They do not change the central benign structural classification by themselves.

Nephronophthisis: Definition and defining injury

- A group of progressive renal disorders with cysts in the medulla.
- Cysts are often most prominent at the corticomedullary junction.
- Tubular atrophy and interstitial fibrosis involve both medulla and cortex.
- Cortical tubulointerstitial injury ultimately underlies renal insufficiency.

Nephronophthisis: Cysts favour the junction



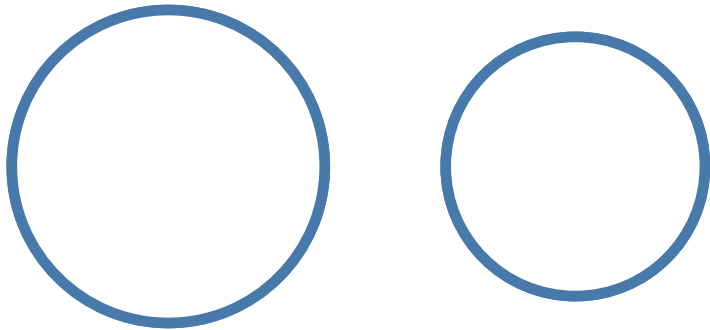
- Variable numbers of medullary cysts occur.
- The corticomedullary junction is a characteristic concentration site.
- The cortex may also contain small cysts.
- Distribution differs from papillary duct dilatation in medullary sponge kidney.

Cyst concentration near junction

Nephronophthisis: Small, contracted kidneys

- The kidneys are small rather than massively enlarged.
- The external surfaces appear contracted and granular.
- Medullary cysts are present, often concentrated near the corticomedullary junction.
- Gross configuration reflects chronic parenchymal injury, not cyst volume alone.

Nephronophthisis: Cyst epithelial lining



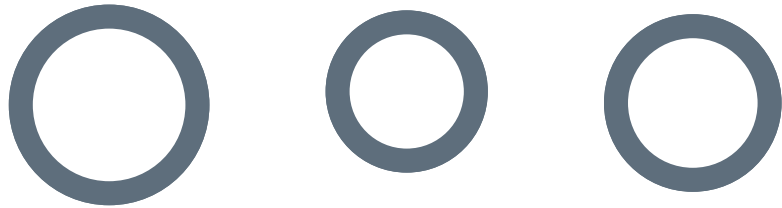
Flattened or cuboidal lining; Pericystic response

- Medullary cysts are lined by flattened or cuboidal epithelium.
- The cyst boundary may be accompanied by inflammatory cells or fibrous tissue.
- The pericystic reaction is an important distinction from a simple anatomic dilatation.

Pericystic inflammation and fibrosis

- Inflammatory cells may surround cystic tubular structures.
- Fibrous tissue may also surround cysts.
- The surrounding interstitium therefore provides diagnostic information beyond the lumen.
- A cyst should be interpreted within the broader tubulointerstitial pattern.

Cortical tubules show chronic damage



Thickened tubular basement membranes with atrophy

- Widespread tubular atrophy develops in the cortex.
- Tubular basement membranes become thickened.
- Interstitial fibrosis accompanies the tubular loss.
- Together these changes account for substantial functional decline.

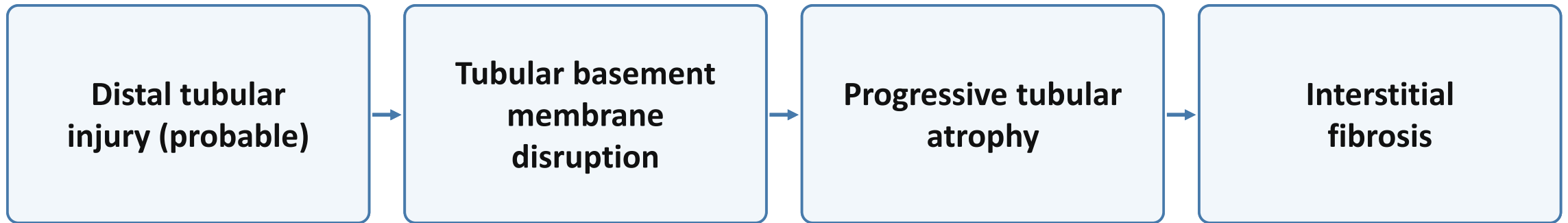
Glomeruli can be relatively preserved

- Generally preserved glomerular structure.
- The dominant morphologic lesion is tubulointerstitial, not primarily glomerular.
- Renal failure can occur even when glomerular architecture appears relatively intact.
- Primary glomerular destruction should not be assumed from advanced renal dysfunction alone.

Proposed initial lesion: Distal tubules

- Robbins suggests that injury probably begins in distal tubules.
- Tubular basement membrane disruption is an early proposed event.
- The word “probably” is important: The initial lesion is not presented as proven in every case.
- Later disease involves both medullary and cortical tubulointerstitium.

Proposed injury sequence in nephronophthisis



Progressive cortical involvement causes the renal insufficiency. This is a source-derived working sequence, not a complete molecular causal model.

Why cortical fibrosis matters more than cyst count

- Medullary cysts are a conspicuous feature but are not the only lesion.
- Cortical tubular atrophy removes functioning renal parenchyma.
- Interstitial fibrosis accompanies progressive tissue loss.
- Cortical tubulointerstitial damage as the cause of eventual insufficiency.

Recognized nephronophthisis clinical forms

Form	Characteristic context
Sporadic, nonfamilial	Disease without an established familial pattern
Familial juvenile	Most common recognized variant
Renal–retinal dysplasia	Renal disease accompanied by ocular lesions; ~15% in Robbins

Familial juvenile nephronophthisis

- The most common of the three clinical variants listed.
- Familial forms are inherited as autosomal recessive traits.
- They typically manifest during childhood or adolescence.
- The resulting course is progressive, unlike uncomplicated medullary sponge kidney.

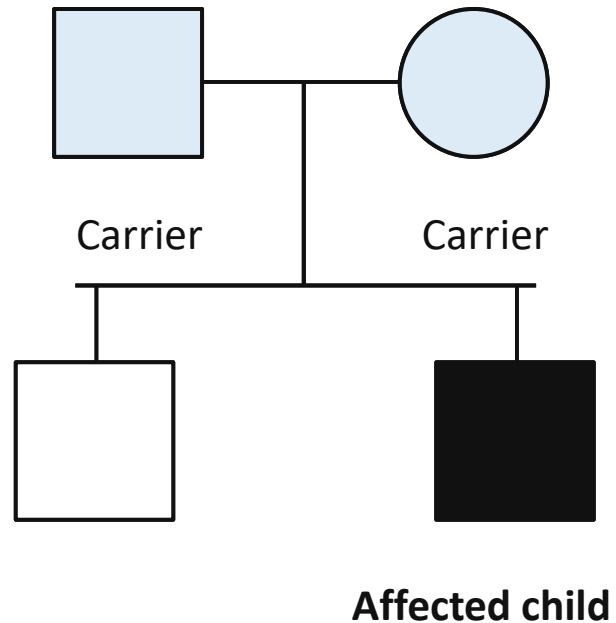
Renal–retinal dysplasia: Systemic involvement

- The renal disorder can coexist with ocular lesions.
- Renal–retinal dysplasia as a distinct clinical variant.
- The book quotes approximately 15% for this associated phenotype.
- Extrarenal findings are diagnostically informative in a child with unexplained chronic kidney disease.

Childhood or adolescent onset

- Familial nephronophthisis commonly becomes manifest early in life.
- The initial presentation may be tubular rather than a visible renal mass.
- Polydipsia and polyuria may precede the recognition of advanced renal insufficiency.
- Age at presentation distinguishes it from typical medullary sponge kidney.

Autosomal recessive transmission



Illustrative pedigree: Recessive transmission

- The familial forms follow an autosomal recessive pattern.
- An affected child need not have an affected parent.
- A positive family history in a sibling can support clinical suspicion.
- Inheritance helps distinguish this group from autosomal dominant tubulointerstitial disease.

Nephronophthisis is genetically heterogeneous

- Multiple associated NPHP and JBTS loci.
- The named NPHP products include a protein family called nephrocystins.
- Additional loci continue to be identified.
- Gene lists must not be treated as a fixed or exhaustive 2026 diagnostic panel.

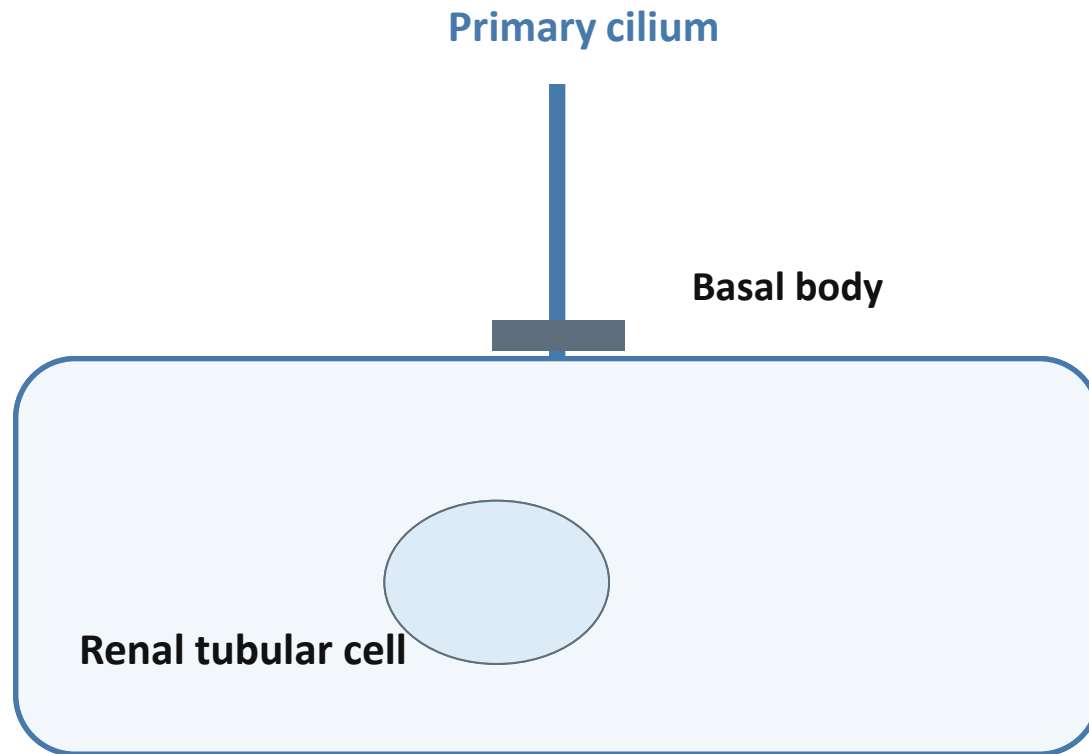
Genes named in the source

- The source enumerates NPHP1–NPHP11 among the nephronophthisis-associated loci.
- It additionally lists JBTS2, JBTS3, JBTS9 and JBTS11.
- This is the terminology reproduced in the supplied Robbins extract.
- The enumeration reflects the textbook passage rather than independently verified current gene nomenclature.

Nephrocystins: Cellular localization

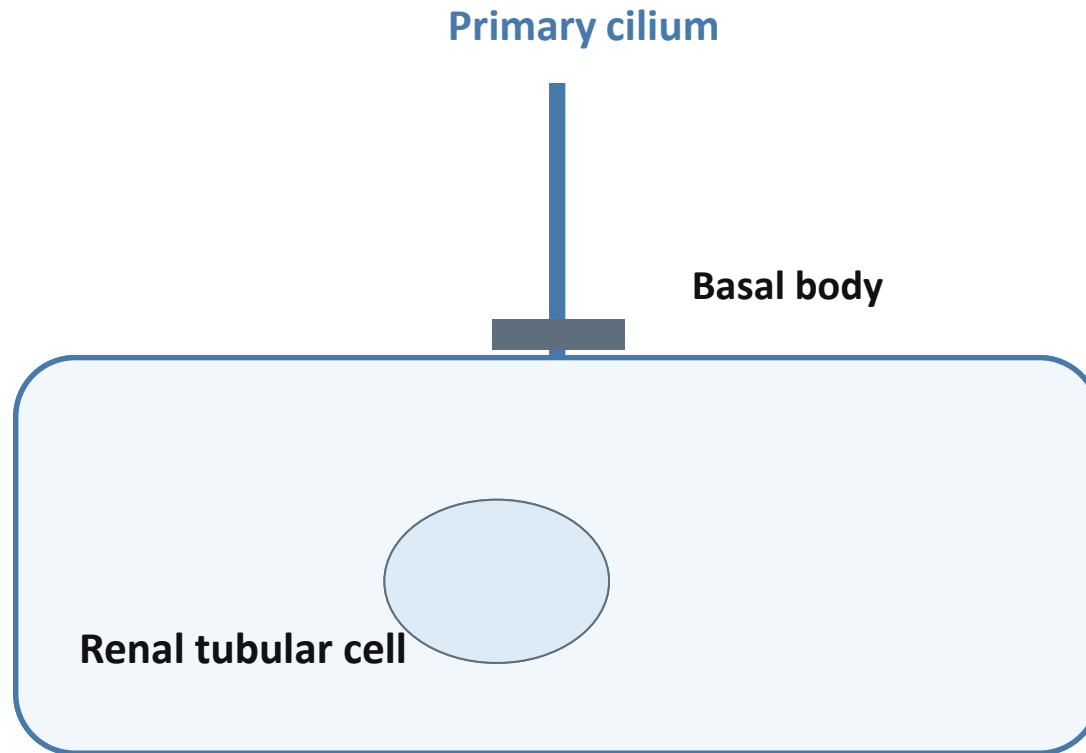
- The NPHP gene products are described as nephrocystins.
- The implicated proteins localize to primary cilia, basal bodies or centrosomes.
- These shared cellular compartments support the ciliopathy classification.
- The passage does not specify a unique downstream pathway for each gene.

Primary cilia and tubular epithelial biology



- The primary cilium is a cellular compartment implicated in these disorders.
- Associated proteins occupy the cilium itself and related anchoring structures.
- The structural localization helps explain the term ciliopathy.
- This drawing is a compartment map, not proof of a specific signal-transduction defect.

Basal body and centrosome: Linked compartments

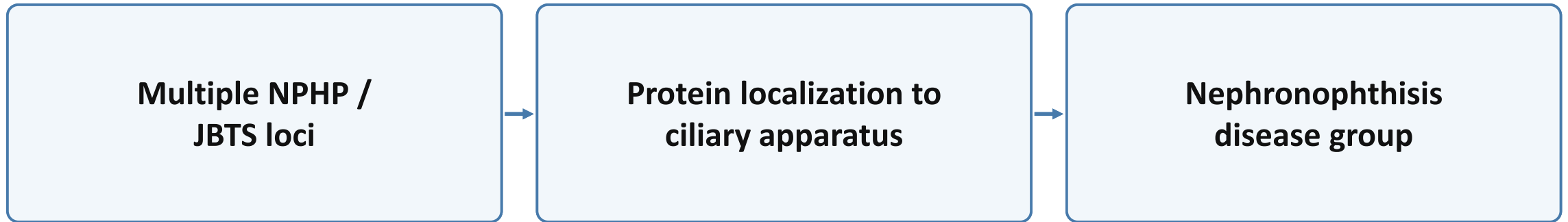


- The basal body is associated with the base of the primary cilium.
- The centrosome as the organelle from which basal bodies originate.
- Nephronophthisis proteins may be found in each of these sites.
- The localization is relevant to classification, not a stand-alone histologic test.

Inversin is the NPHP2 gene product

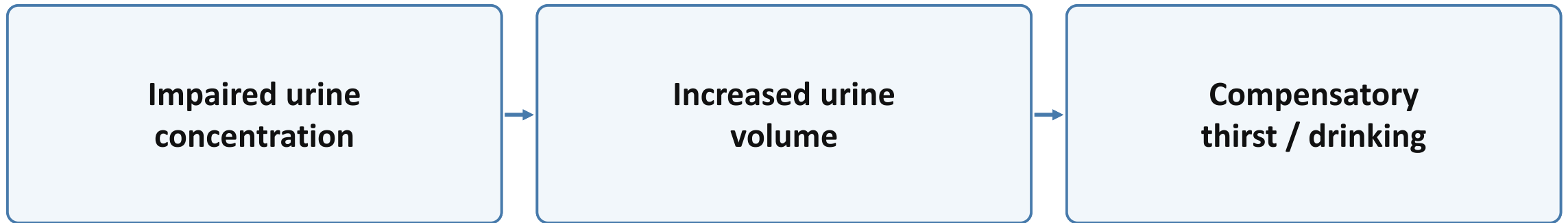
- NPHP2 as encoding inversin, also termed nephrocystin-2.
- Inversin participates in embryonic left–right patterning.
- This links at least one associated protein with development-related cellular biology.
- The source does not justify assigning the same developmental role to all nephrocystins.

Ciliopathy classification: What is established?



The association and subcellular localization are supported by Robbins. A complete gene-by-gene mechanism of tubular injury is not supplied in this passage.

Tubular concentrating defect explains early symptoms



The textbook explicitly links polyuria and polydipsia to a marked renal tubular concentrating defect.

Polyuria and polydipsia may be early clues

- Children commonly first present with increased urine output.
- Excessive thirst accompanies impaired renal concentrating ability.
- The symptoms point toward a tubular defect rather than a cyst-related compressive syndrome.
- Early symptoms can be more informative than the cyst burden seen on imaging.

Sodium wasting is a major tubular manifestation

- Sodium wasting as prominent.
- This is consistent with the wider tubular functional injury in nephronophthisis.
- Salt wasting supports a tubulointerstitial rather than purely structural diagnosis.
- The supplied passage does not specify serum sodium thresholds or testing cutoffs.

Tubular acidosis adds evidence of functional injury

- Tubular acidosis is described as a prominent manifestation.
- It coexists with an impaired concentrating mechanism and sodium wasting.
- These findings show that dysfunction can be evident before cysts are demonstrable.
- The passage does not define a specific renal tubular acidosis subtype.

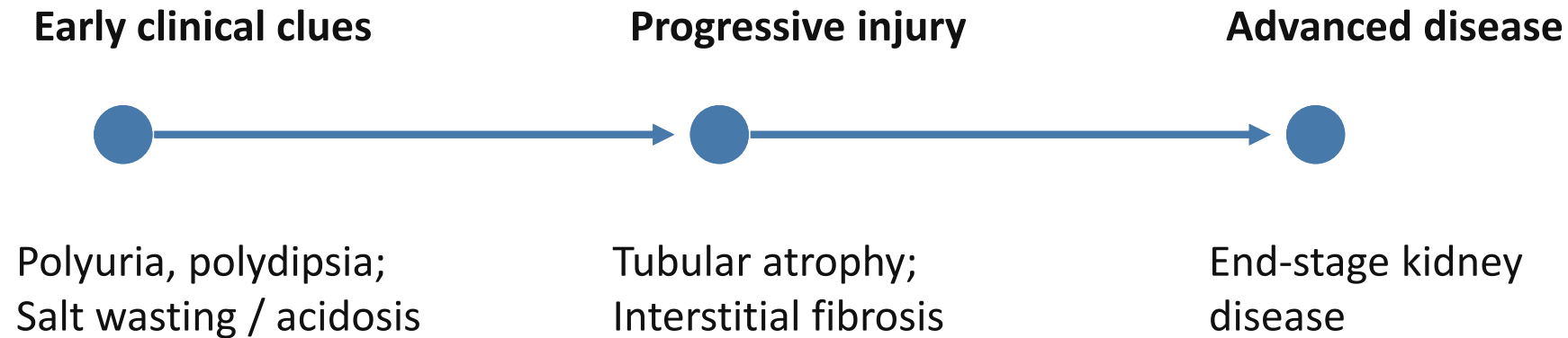
Nephronophthisis: Clinical features and pathology link

Clinical feature	Pathologic or functional connection
Polyuria and polydipsia	Severe renal concentrating defect
Sodium wasting	Associated tubular functional abnormality
Tubular acidosis	Associated defect of tubular handling
Growth retardation / anemia	Reported in Robbins comparative summary
Progressive kidney failure	Cortical tubular atrophy and interstitial fibrosis

Nephronophthisis is a major genetic cause of pediatric ESKD

- Robbins characterizes the nephronophthisis complex as the most common genetic cause of ESKD in children and young adults.
- This statement pertains to the disease group, not to any one clinical variant.
- The characteristic loss of renal function is driven by progressive tubulointerstitial injury.
- Consider this category when early-onset chronic kidney disease remains unexplained.

Nephronophthisis: Progressive clinical course



A progression to ESKD over approximately 5–10 years; This is not a fixed outcome for every individual.

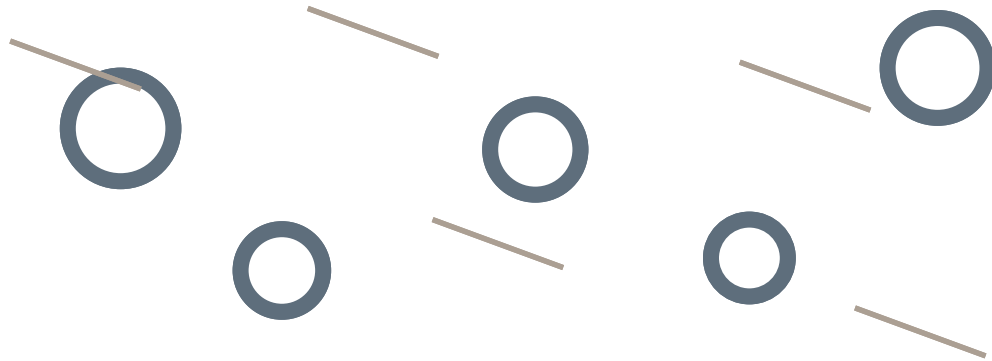
Imaging may underestimate nephronophthisis

- Medullary cysts can be too small to be recognized radiographically.
- An apparently nondiagnostic scan does not exclude the disease.
- Small kidneys and functional abnormalities may guide suspicion even without a convincing cyst pattern.
- Histologic and familial evidence should be weighed with clinical findings.

A clinical constellation supports consideration

- Child or adolescent with otherwise unexplained chronic kidney failure.
- Positive family history, where present.
- Chronic tubulointerstitial nephritis on renal biopsy.
- Robbins urges strong consideration of nephronophthisis when these features converge.

Biopsy pattern: Chronic tubulointerstitial disease



Tubular loss + expanded fibrotic interstitium

- Tubular atrophy and tubular basement membrane thickening in cortex.
- Interstitial fibrosis with possible pericyclic inflammatory cells.
- Glomerular structure is generally preserved.
- A biopsy pattern is not sufficient alone without age, inheritance and clinical correlation.

Integrating gross and microscopic morphology

Compartment	Nephronophthisis finding
Kidney surface / size	Small kidney; contracted granular external surface
Medulla	Cysts, often centred at corticomedullary junction
Cortex	Small cysts; tubular atrophy; thickened basement membranes; fibrosis
Glomeruli	Generally preserved architecture
Cyst environs	Inflammatory cells or fibrous tissue

Medullary sponge kidney versus nephronophthisis

Feature	Medullary sponge kidney	Nephronophthisis
Location	Medullary collecting ducts	Medulla, especially junction
Gross kidney	Dilated papillary ducts	Small, contracted, granular
Cortex	No scarring unless pyelonephritis	Atrophy and interstitial fibrosis
Usual age	Adult	Childhood / adolescence
Course	Usually benign	Progression to ESKD

Nephronophthisis versus ADTKD: Nomenclature matters

Feature	Nephronophthisis	ADTKD
Inheritance	Familial forms autosomal recessive	Autosomal dominant
Usual presentation	Childhood / adolescence	Progressive renal failure in adult life
Term “medullary cystic”	Cysts often at corticomedullary junction	Formerly called medullary cystic kidney disease
Cysts	Characteristic but may be tiny	Variable; often not medullary

ADTKD is a separate autosomal dominant disorder

- Robbins reclassifies former “medullary cystic kidney disease” as ADTKD.
- Listed genes include MUC1, UMOD, REN and HNF1B.
- Its progressive adult-onset renal failure and dominant inheritance distinguish it from familial juvenile nephronophthisis.
- Cysts in ADTKD may be absent or outside the medulla.

Nephronophthisis versus childhood polycystic kidney disease

Feature	Nephronophthisis	Autosomal recessive PKD
Typical organ size	Small, contracted kidneys	Enlarged cystic kidneys at birth
Principal pattern	Tubulointerstitial injury; junctional cysts	Collecting tubule dilatation
Extrarenal association	Ocular lesions in renal–retinal form	Hepatic fibrosis
Clinical framing	Progressive juvenile tubular disease	Neonatal / childhood cystic disease

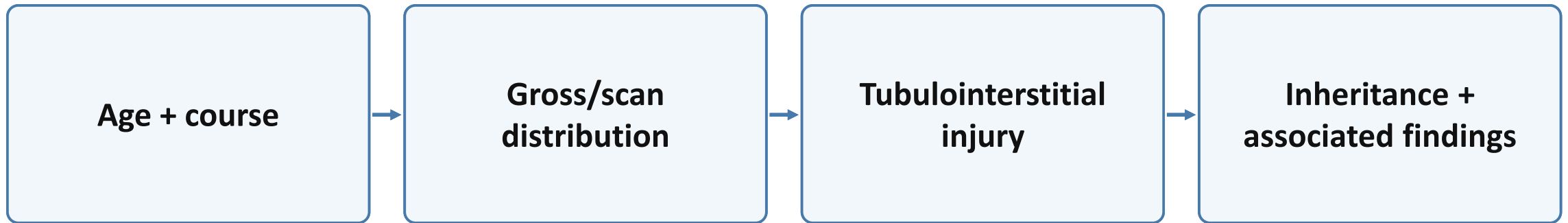
Nephronophthisis versus multicystic renal dysplasia

Feature	Nephronophthisis	Multicystic renal dysplasia
Typical architecture	Small shrunken kidney with junctional cysts	Enlarged, highly irregular multicystic kidney
Microscopic clue	Cortical atrophy, fibrosis, thickened TBM	Primitive mesenchyme ± cartilage; immature ducts
Clinical context	Childhood progressive tubular disorder	Often associated urinary tract malformations
Pathologic category	Tubulointerstitial disease	Renal developmental dysplasia

Nephronophthisis versus acquired cystic disease

Feature	Nephronophthisis	Acquired cystic disease
Context	Inherited/juvenile or sporadic complex	Long-standing ESKD with dialysis
Interpretation of cysts	Cysts accompany a disease causing failure	Cysts develop in an already failed kidney
Distribution	Especially corticomedullary junction	Cortical and medullary cysts
Additional concern	Progressive tubulointerstitial failure	Renal-cell carcinoma association in Robbins

A phenotype-first diagnostic decision



Juvenile polyuria, tubular dysfunction, small scarred kidneys and familial recessive history favour nephronophthisis; Adult radiographic medullary duct dilatation with preserved function favours medullary sponge kidney.

Case 1: Incidental medullary cystic finding

APPLICATION — ILLUSTRATIVE CLINICAL VIGNETTE

An adult undergoing urinary tract imaging has medullary papillary duct dilatations. Renal function is preserved. No cortical scarring is described.

Which diagnosis best fits this combination, and what would alter the interpretation?

Case 1: Interpretation

- Medullary sponge kidney best matches adult discovery with papillary duct dilatation.
- Usual preservation of renal function and absent cortical scarring support the diagnosis.
- Concurrent pyelonephritis may produce cortical scarring and modify the clinical picture.
- Associated stones, urinary infection or hematuria may be present without redefining the core lesion.

Case 2: Unexplained progressive juvenile disease

APPLICATION — ILLUSTRATIVE CLINICAL VIGNETTE

An adolescent develops persistent polyuria, polydipsia and progressive renal impairment. Imaging identifies few convincing cysts. A sibling has a similar illness.

What diagnosis should be considered despite nondiagnostic imaging?

Case 2: Interpretation

- Nephronophthisis should be strongly considered.
- Tubular concentrating failure explains the early polyuria and polydipsia.
- An affected sibling is consistent with a familial autosomal recessive disorder.
- Cysts may be too small to image; Chronic tubulointerstitial injury is more decisive than visible cyst count.

Diagnostic pitfall: A “normal” cyst search does not exclude disease

- Nephronophthisis may be radiographically subtle because cysts are small.
- Diagnosis requires attention to renal function, tubular manifestations and family history.
- Cortical atrophy/fibrosis can be informative even when cysts are sparse.
- A radiographic cyst burden must never be used as a stand-alone severity surrogate.

Final synthesis: Recognize the lesion, then the consequence

Question	Medullary sponge kidney	Nephronophthisis
What changes?	Medullary collecting-duct calibre	Tubules and interstitium progressively degenerate
Where is the clue?	Papillary medulla	Corticomedullary cysts + injured cortex
What happens to function?	Usually maintained	Progressive loss, ESKD
Who presents?	Usually adult	Often child / adolescent
What prevents error?	Check for associated infection / stones	Do not rely on visible cysts alone

Reference and image provenance

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026), Chapter 20, pp. 850, 858–860.
- Primary focus: “Cystic Diseases of the Renal Medulla,” including “Medullary Sponge Kidney” and “Nephronophthisis.”
- All anatomical, cellular, pedigree and morphology diagrams in this presentation are original editable schematics.
- No textbook photomicrographs, gross specimens or diagnostic imaging were reproduced.