

# Congenital, developmental & cystic diseases of the kidney

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# Lecture outline

- Congenital and developmental diseases of the kidney
- Cystic diseases of the kidney

# Congenital and developmental diseases of the kidney

- Agenesis
- Hypoplasia
- Ectopic kidneys
- Horseshoe kidney

*See next slide*

## Agenesis

- \***If bilateral:** incompatible with life
  - ...usually seen in stillborn infants
  - ...often associated with other defects (hypoplastic lungs...etc.)
- \***If unilateral:** compatible with life
  - ...compensatory hypertrophy of the solitary kidney
  - ...some patients: progressive glomerulosclerosis & chronic kidney disease...this is due to ECM deposition and epithelial/endothelial injury which resulted from the adaptive hemodynamic changes that accompanied the hypertrophy

## Hypoplasia

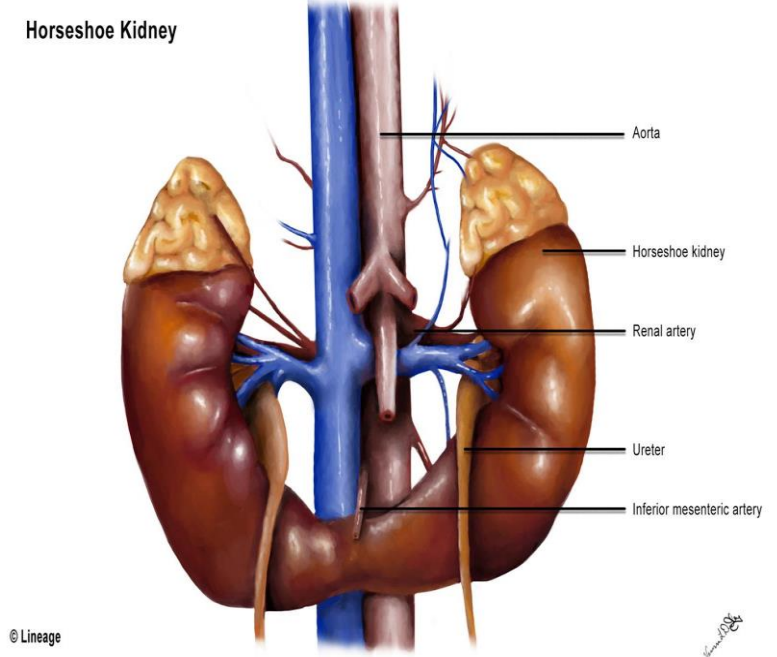
- = failure to develop to normal size
- ...more commonly unilateral
- ...if bilateral: renal failure in early childhood
- ...low birth weight infants are more at risk
- ...this is “true” hypoplasia

## Ectopic kidneys

- ...usually not remarkable
- ...but risk of kinking/tortuosity of ureters...obstruction & bacterial infection

## Horseshoe kidneys

- = fusion of:
  - \*upper poles...10%
  - or \*lower poles...90%
- ...continuous across the midline anterior to the great vessels
- \*This anomaly is found in 1 in 500 to 1000 autopsies



# Cystic diseases of the kidney

- Hereditary, developmental or acquired

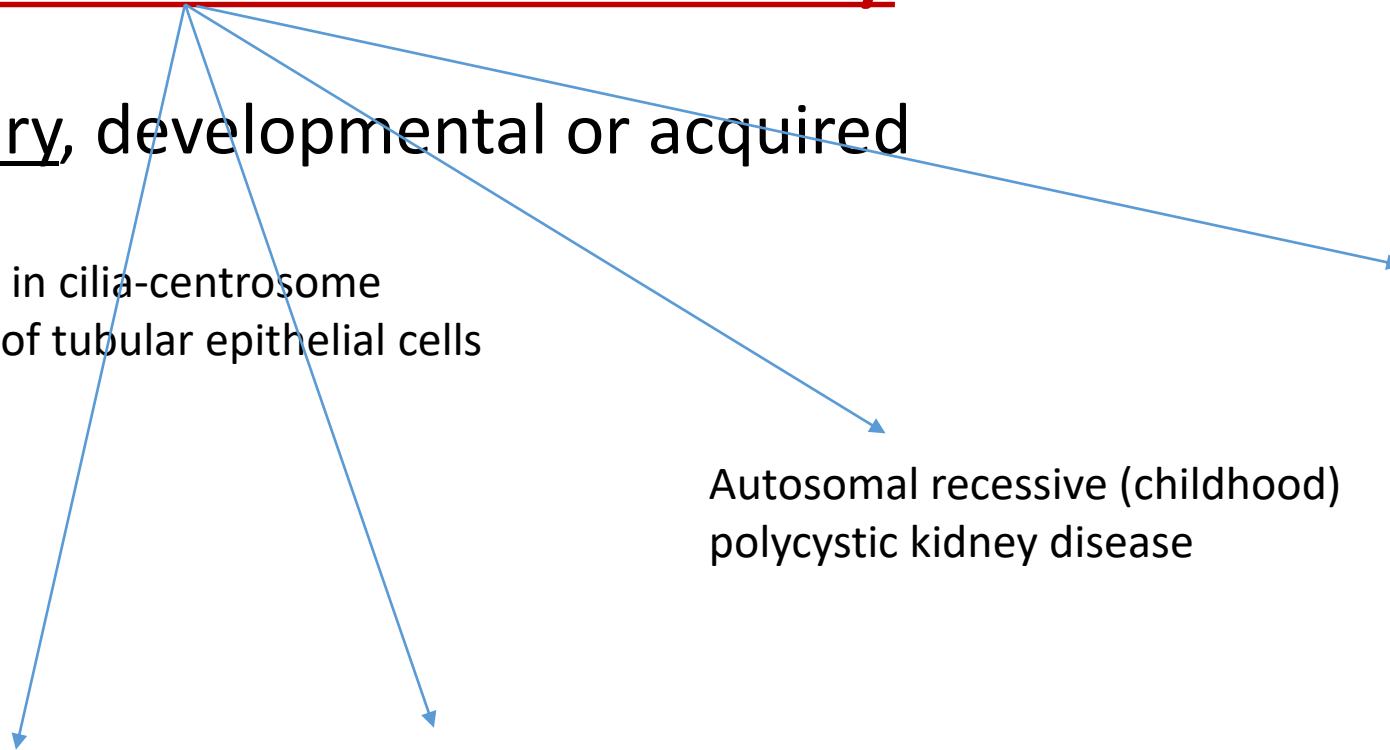
...defects in cilia-centrosome  
complex of tubular epithelial cells

Medullary diseases with cysts

Autosomal recessive (childhood)  
polycystic kidney disease

Simple cysts

Autosomal dominant (adult)  
polycystic kidney disease



# Simple cysts

- Clinically insignificant, commonly found incidental/postmortem lesions
- Multiple or single
- 1-5 cm in diameter...rarely as large as 10 cm
- Translucent glistening smooth membrane
- Lined by a single layer of cuboidal or flattened cuboidal epithelium  
...may be atrophic
- Usually confined to the cortex
- May present with hemorrhage & pain

The importance is in differentiating them from tumors  
...simple cysts have: -smooth contours  
-avascular  
-fluid rather than solid tissue signal  
on ultrasonography

# Simple cysts, cont'd...acquired cystic kidney disease

- In patients with end-stage renal disease...dialysis for many years
- Multiple
- In the cortex & the medulla
- May bleed...causing hematuria
- Risk for renal neoplasms...especially cystic ones

# Autosomal dominant (adult) polycystic kidney disease (ADPKD)

- Multiple cysts
- In both kidneys
- Ultimately destroy the intervening parenchyma
- Accounts for 10% of cases of chronic kidney disease
- In 85-90%: *PKD1* gene on the short arm of chromosome 16 is defective  
...encodes large and complex cell membrane-associated protein called polycystin-1...see the next 2 slides



# ADPKD, pathogenesis

- Polycystin-1 normally localizes to the primary cilium of tubular cells
- Cilia serve as mechanosensors of fluid flow
- Polycystin mutations will cause defects in mechanosensing
- Abnormal signal transduction...calcium influx
- Dysregulation of cell polarity, proliferation, cell–cell and cell–matrix adhesion, & secretion from the tubular epithelial cells
- Cyst formation  
...the cysts progressively enlarge overtime

Also: inflammation & fibrosis

# ADPKD, pathogenesis...cont'd

- Germline mutations of the *PKD1* gene are present in all renal tubular cells of affected individuals...but: cysts develop in only some tubules  
  
...which means: a second “somatic hit” is required for cyst development

# ADPKD, pathogenesis...cont'd

- *PKD2* gene

- ...10-15% of the cases

- ...on chromosome 4, encodes polycystin-2



- ...a calcium-permeable membrane channel

- ...also localized to cilia

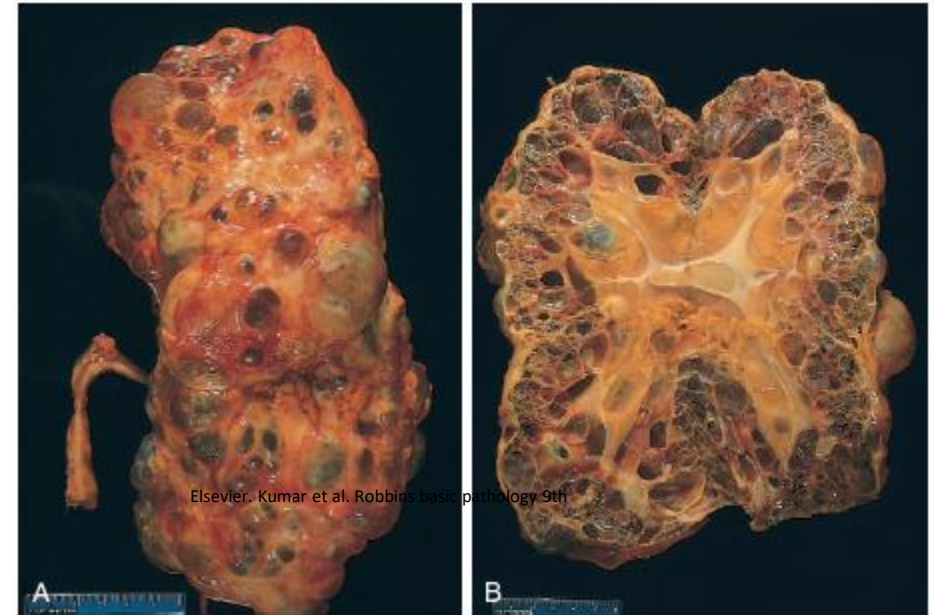
- ...acts together with polycystin-1 to form heterodimer

- ...so: a defect in any of the two will cause the same result

- ...However, *PKD2* mutations: slower disease progression

# ADPKD, morphology

- very large...may reach 4 kg for each kidney
- palpable
- may be formed solely of cysts...each 3-4 cm
- turbid, clear or hemorrhagic fluid
- cysts may arise at any level from tubules to collecting ducts
- variable, often atrophic lining
- occasionally, Bowman's capsules are involved in the cyst formation, and in these cases glomerular tufts may be seen within the cystic space
- some normal parenchyma may be dispersed among the cysts
- evidence of superimposed hypertension or infection is common
- asymptomatic liver cysts also occur in one-third of patients



# ADPKD, clinical features

- Usually does not produce symptoms until the fourth decade of life
- The most common presenting complaint is flank pain or a heavy, dragging sensation
- Acute distention of a cyst, either by intracystic hemorrhage or by obstruction, may cause excruciating pain
- Sometimes attention is first drawn to the lesion on palpation of an abdominal mass
- Intermittent gross hematuria commonly occurs
- The most important: hypertension (75% of patients) & infection

# ADPKD, clinical features...cont'd

- Saccular aneurysms of the circle of Willis...10-30% of patients
- More favorable than with most chronic kidney diseases...although it is ultimately fatal
- Slow progression
  - ...end-stage renal disease occurs at about 50 years of age
  - ...even nearly normal life spans are reported
- Treatment: renal transplantation
- Death: usually due to uremia or HTN

# Autosomal recessive (childhood) polycystic kidney disease (ARPKD)

- Rare
- Subcategories:
  - Perinatal
  - Neonatal
  - Infantile
  - Juvenile

→ most common
- The defect is in *PKHD1* gene, coding for a membrane receptor protein called fibrocystin
- Fibrocystin is found in cilia in tubular epithelial cells...unknown function

# ARPKD, morphology

- Numerous small cysts in the cortex and medulla...sponge-like appearance
- Uniform lining of cuboidal cells, reflecting their origin from the collecting tubules
- Invariably bilateral
- Multiple epithelium-lined liver cysts and proliferation of portal bile ducts  
...in almost all cases



Check <https://library.med.utah.edu/WebPath/TUTORIAL/RENCYST/RCYST027.html> for references



# ARPKD, clinical features

- Serious manifestations usually are present at birth
- Young infants may die quickly from hepatic or renal failure
- Patients who survive infancy develop liver cirrhosis  
...congenital hepatic fibrosis

# Medullary diseases with cysts

- **2 major types** of cystic disease affecting the medulla:
  - medullary sponge kidney
    - ...relatively common
    - ...usually innocuous
    - ...occasionally associated with nephrolithiasis
  - nephronophthisis-medullary cystic disease complex
    - ...almost always associated with renal dysfunction

# Nephronophthisis-medullary cystic disease complex

- Usually begins in childhood
- 4 variants:
  - Infantile
  - Juvenile...the most common
  - Adolescent nephronophthisis
  - Medullary cystic disease developing later in adult life

The most common genetic cause of end-stage renal disease in children and young adults

# Nephronophthisis-medullary cystic disease complex ...juvenile form

- 15-20% have extrarenal manifestations:
  - ...retinal abnormalities: retinitis pigmentosa and even early onset blindness
  - ...oculomotor apraxia
  - ...mental retardation
  - ...cerebellar malformations
  - ...liver fibrosis

## Nephronophthisis-medullary cystic disease complex, pathogenesis

- At least nine gene loci (NHP1 to NHP9) have been identified for the autosomal recessive forms of the nephronophthisis complex
- The majority of these genes encode proteins that are components of epithelial cilia

## Nephronophthisis-medullary cystic disease complex, morphology

- Small contracted kidneys
- Numerous small cysts lined by flattened or cuboidal epithelium are present...typically at the corticomedullary junction
- Chronic tubulointerstitial nephritis with tubular atrophy and thickened tubular basement membranes and progressive interstitial fibrosis...nonspecific

# Nephronophthisis-medullary cystic disease complex, clinical features

## Clinical Features

The initial manifestations are usually polyuria and polydipsia, a consequence of diminished tubular function. Progression to end-stage renal disease ensues over a 5- to 10-year period. The disease is difficult to diagnose because there are no serologic markers, and the cysts may be too small to be seen with radiologic imaging. Adding to this difficulty, cysts may not be apparent on renal biopsy if the corticomedullary junction is not well sampled. A positive family history and unexplained chronic renal failure in young patients should lead to suspicion of nephronophthisis.

Thank You