Cystic Renal Disease, for USMLE Step One

Howard J. Sachs, MD
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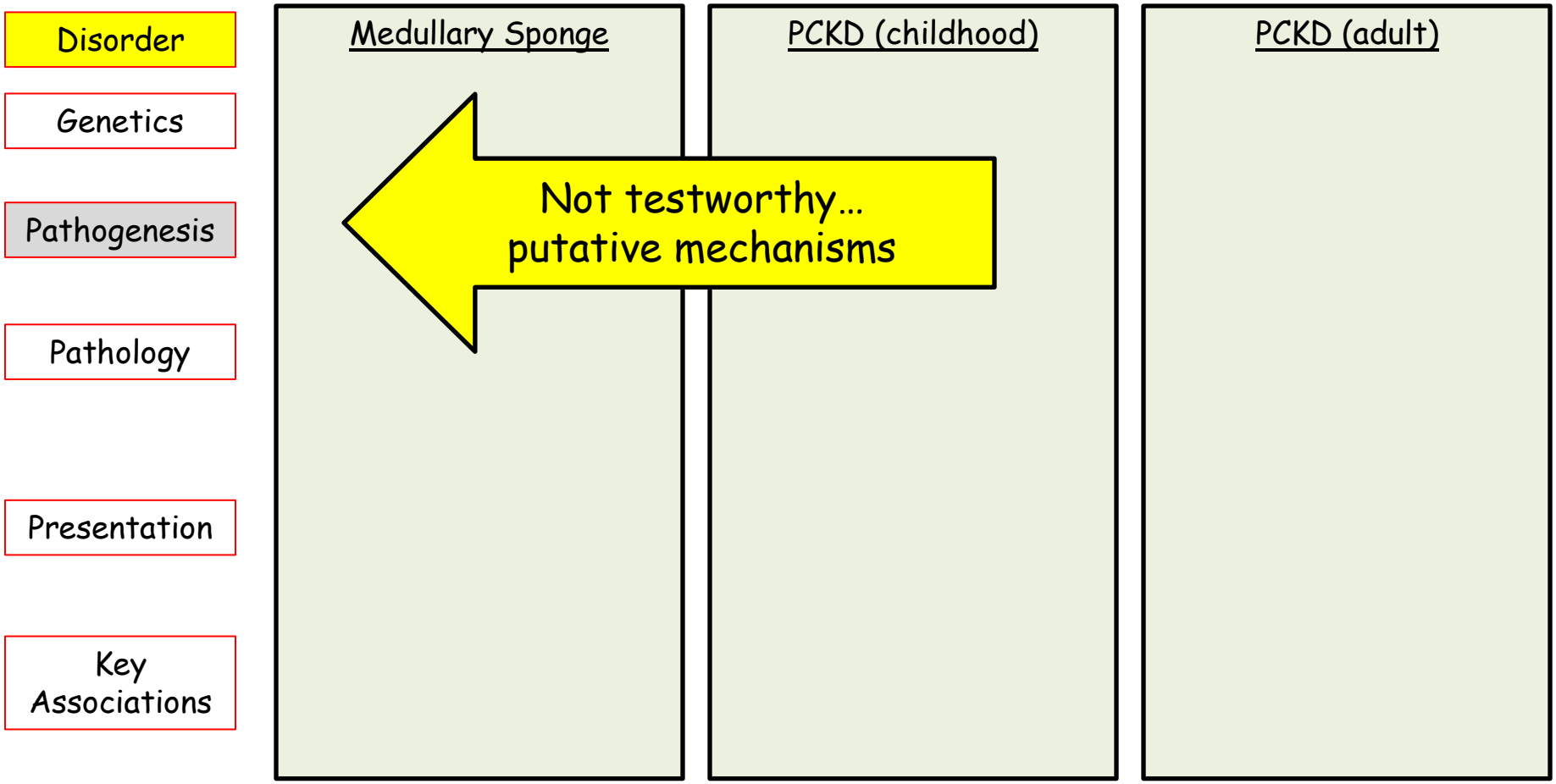
The Major Players

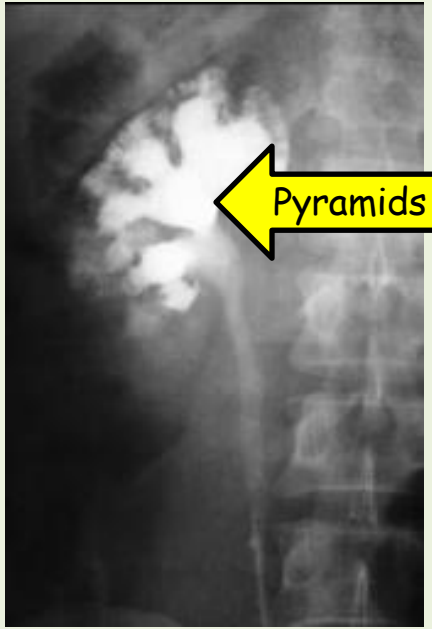
- Medullary Sponge Kidney (MSK)

- Polycystic Kidney Disease (PKD)
  - Autosomal Recessive: Childhood
  - Autosomal Dominant: ADult

Disorder	Medullary Sponge	PCKD (childhood)	PCKD (adult)
Genetics			
Pathogenesis			
Pathology			
Presentation			
Key Associations			


Disorder
Genetics
Pathogenesis
Pathology
Presentation
Key Associations
Medullary Sponge
PCKD (childhood)
PCKD (adult)
Not testworthy…
putative mechanisms

Disorder	Medullary Sponge
Genetics	Φ
Pathogenesis	Unknown (congenital)
Pathology	Cystic dilations of the terminal collecting ducts in the renal medulla
Presentation	Incidental finding on radiograph Normal renal function
Key Associations	1. Dilated (ectatic) 2. Collecting ducts 3. Medullary portion (not cortical)



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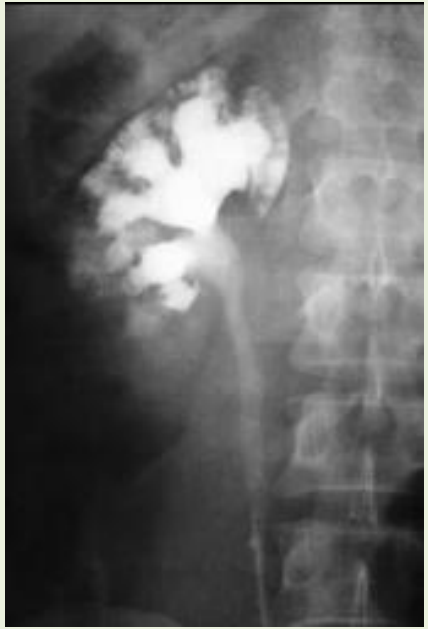
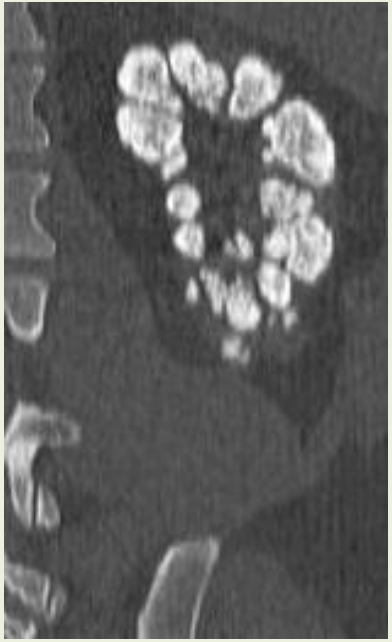
Key Associations	Nephrolithiasis





1. Medullary Nephrocalcinosis
2. Nephrolithiasis

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Pathology	Cystic dilations of the terminal collecting ducts in the renal medulla
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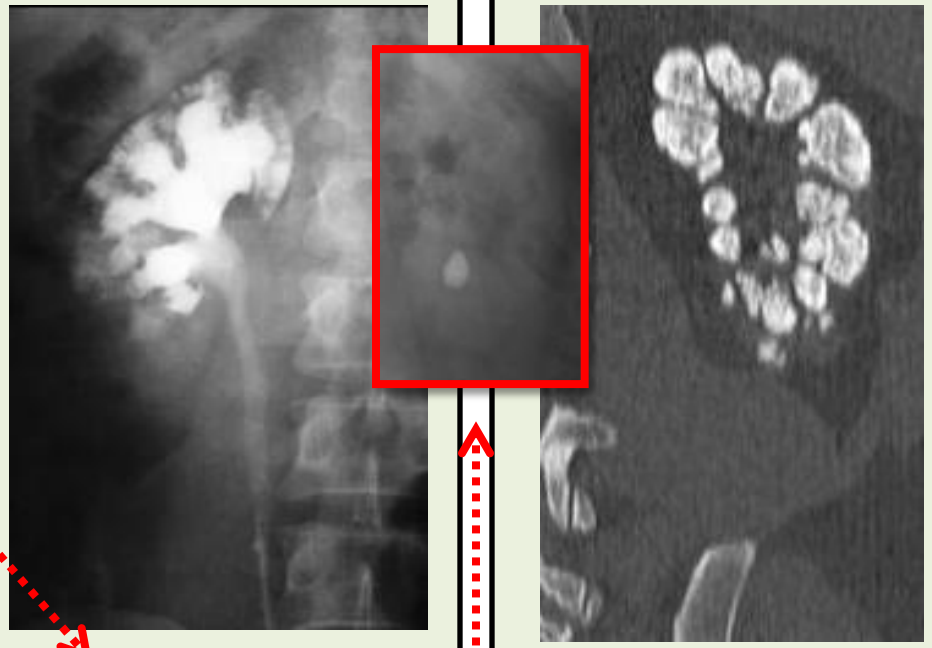
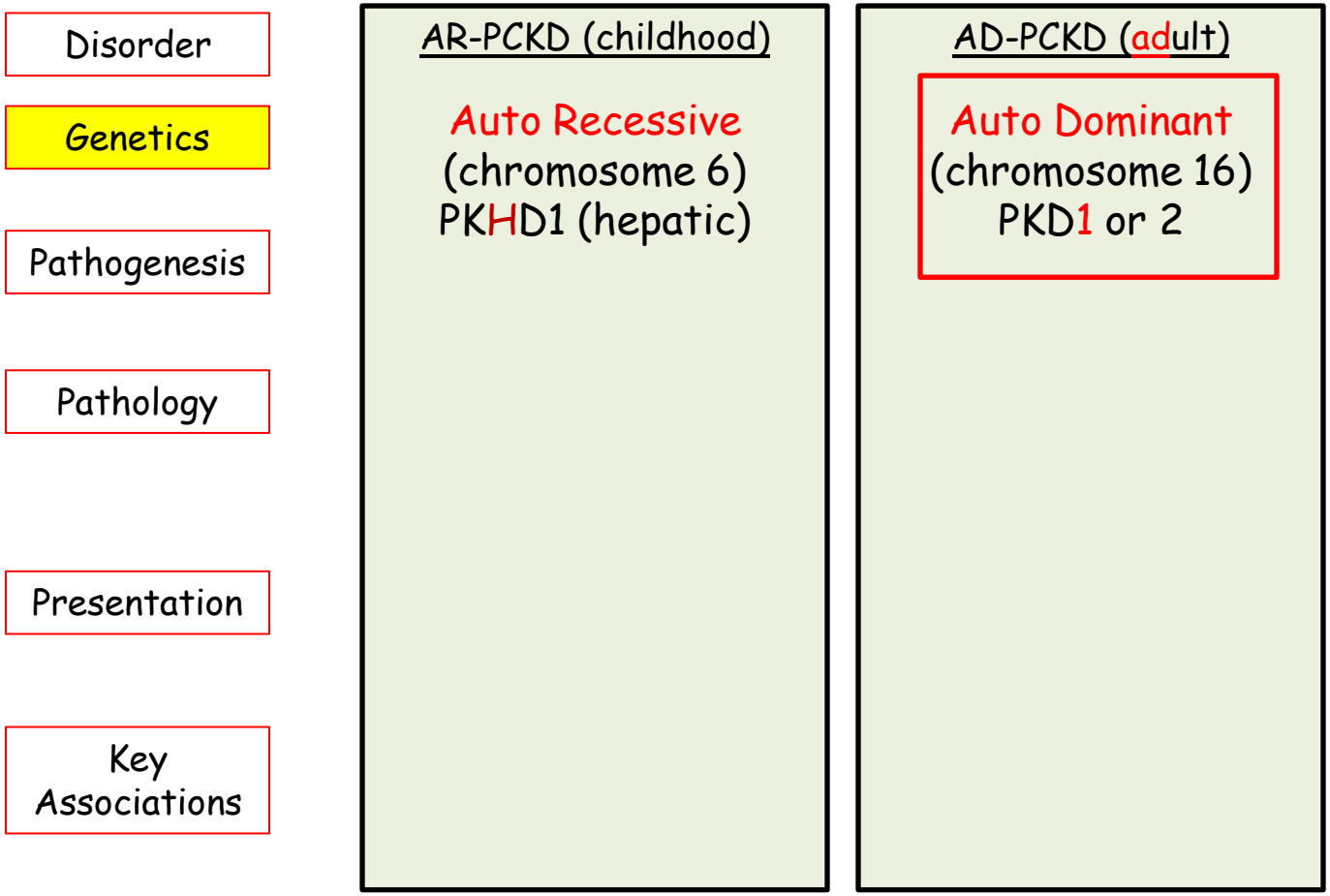


1. Dilated (ectatic)
2. Collecting ducts
3. Medullary portion


Disorder
Genetics
Pathogenesis
Pathology
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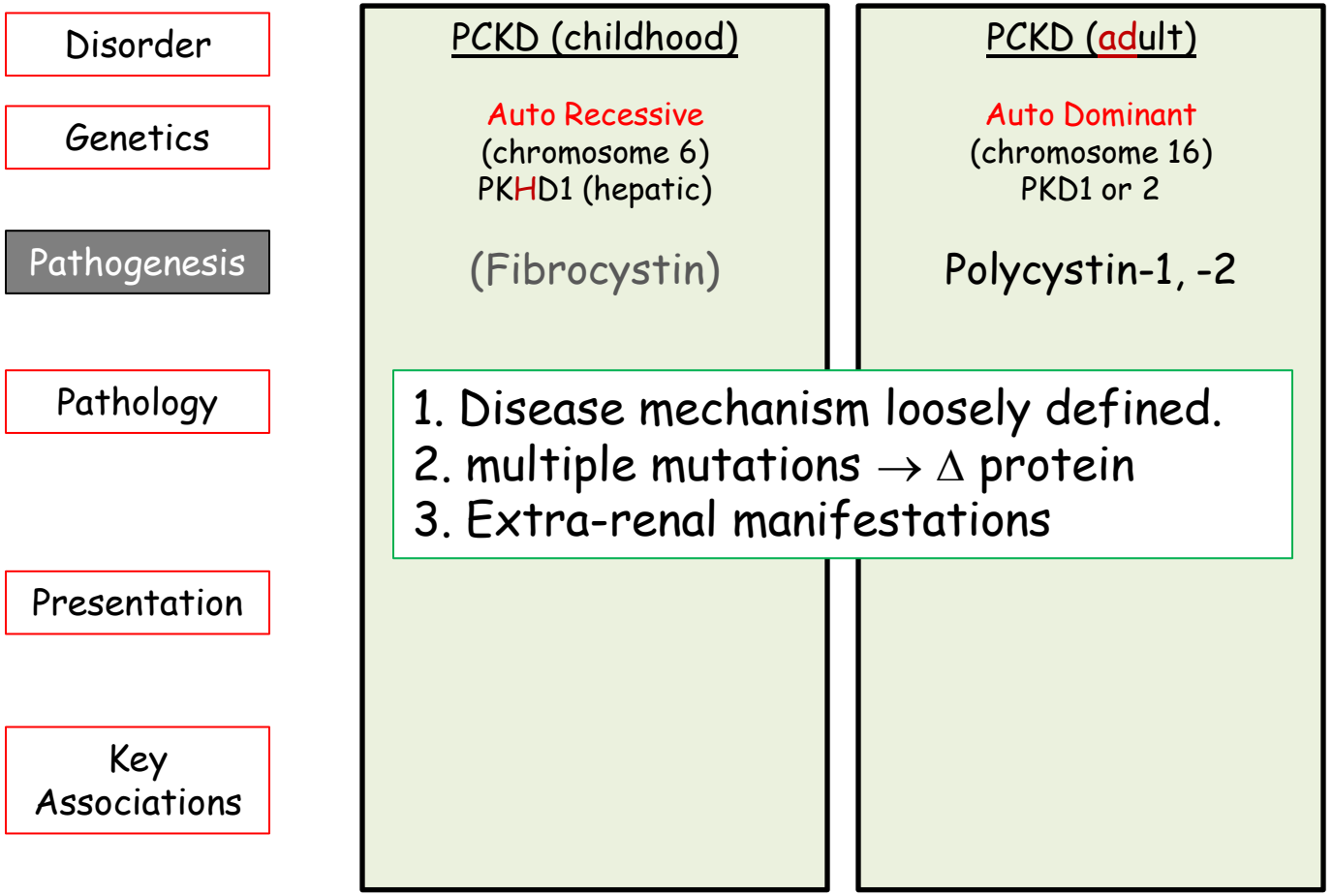
Key Associations
AR-PCKD (childhood)
Auto Recessive
(chromosome 6)
PKHD1 (hepatic)
AD-PCKD (adult)
Auto Dominant
(chromosome 16)
PKD1 or 2

	PCKD (childhood)	PCKD (adult)
Disorder		
Genetics	Auto Recessive (chromosome 6) PKHD1 (hepatic)	Auto Dominant (chromosome 16) PKD1 or 2
Pathogenesis	(Fibrocystin)	Polycystin-1, -2
Pathology		
Presentation		
Key Associations		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Polycystin-1, -2
1. Disease mechanism loosely defined.
2. multiple mutations → Δ protein
3. Extra-renal manifestations

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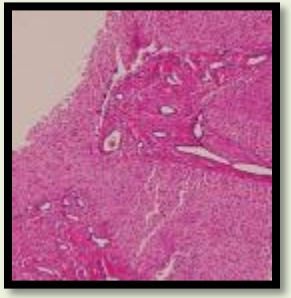
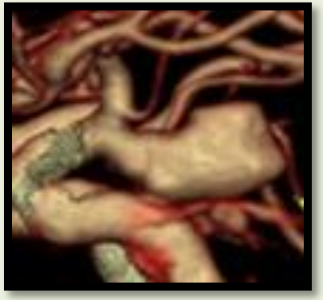
Presentation		
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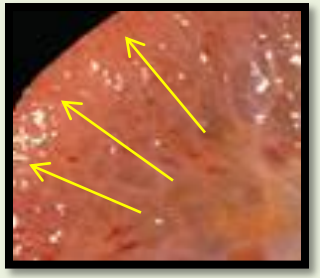
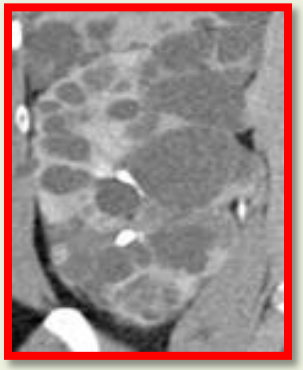
Presentation		
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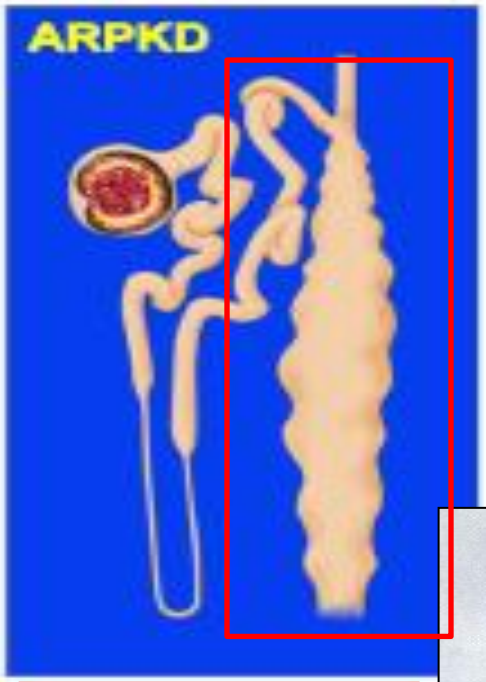
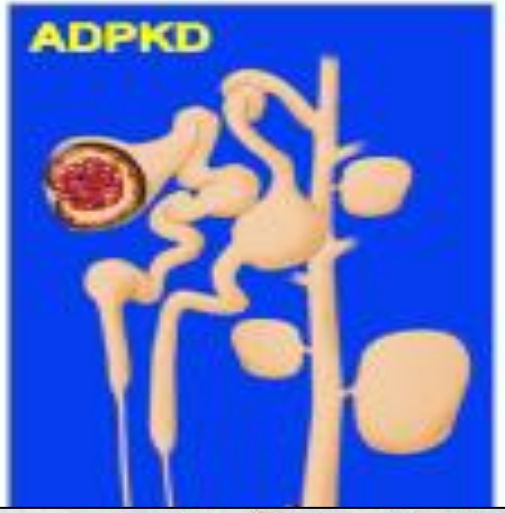
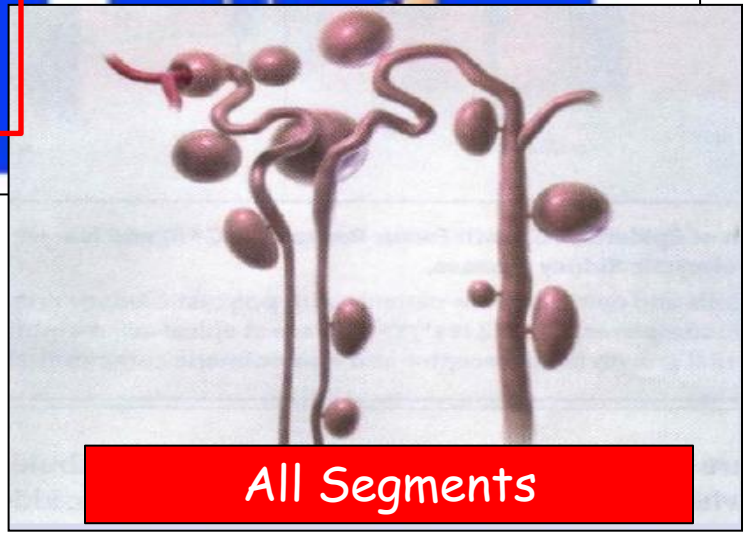
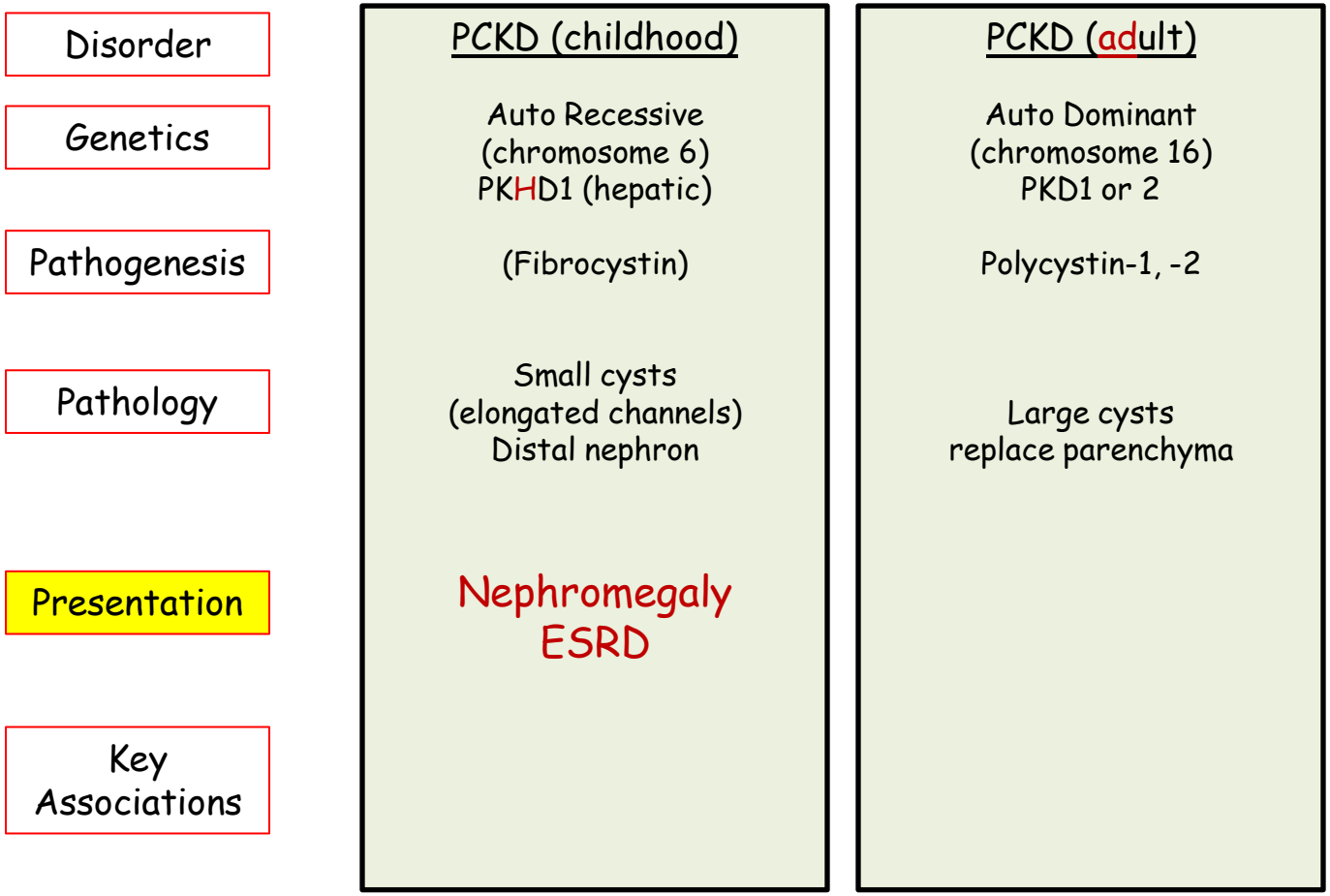




Distal Nephron



All Segments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ESRD
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Polycystin-1, -2
Large cysts
replace parenchyma

Reno-hepatic

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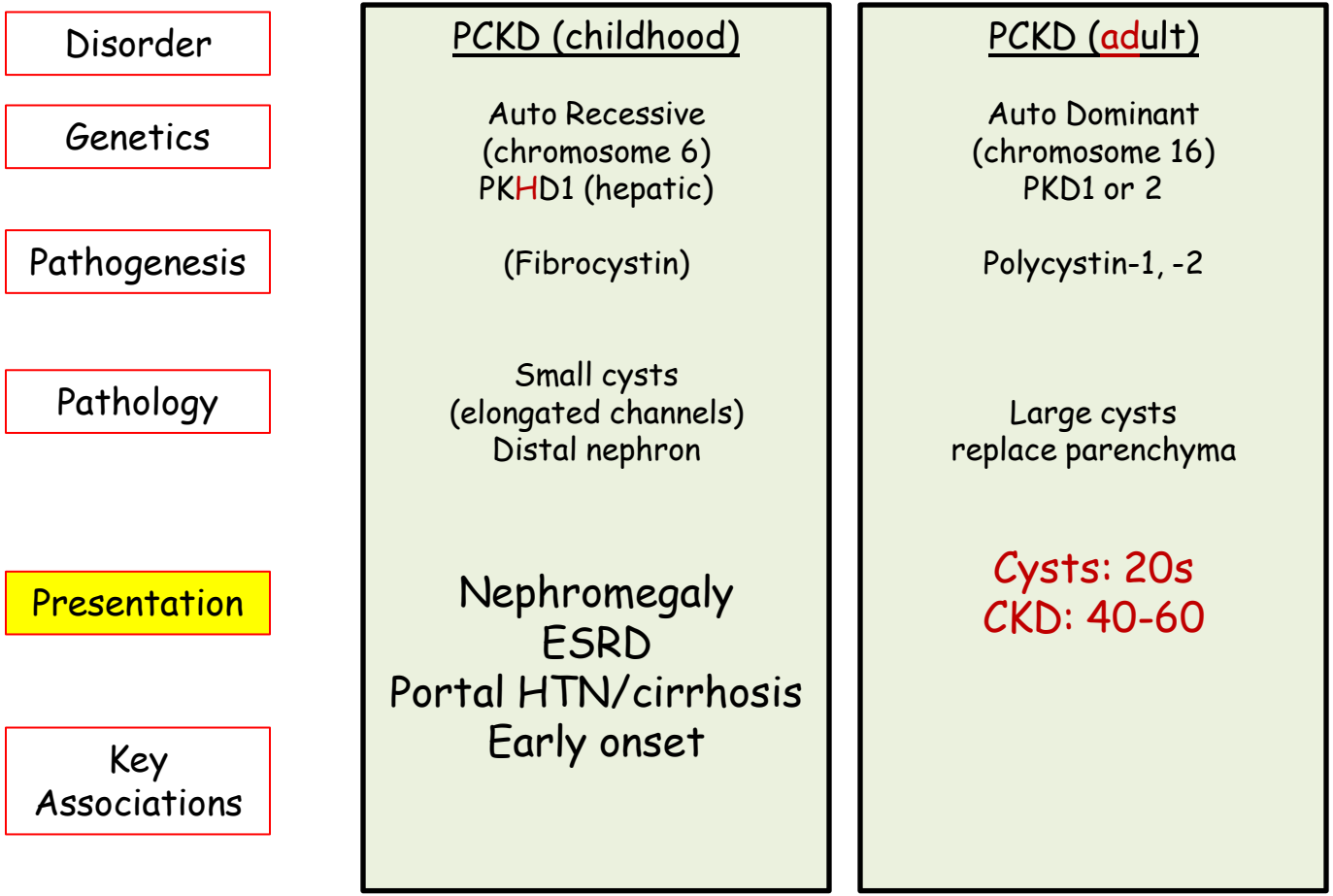
Key Associations		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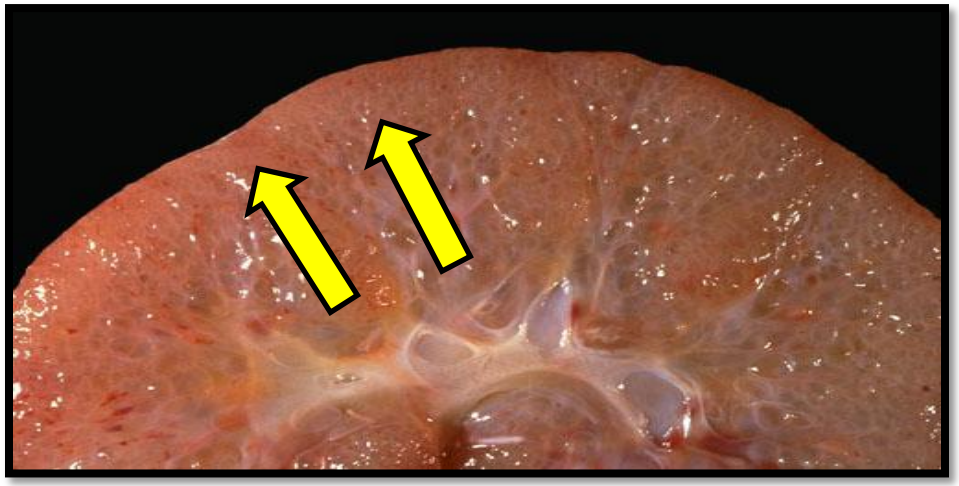
Key Associations	Hepatic fibrosis Oligohydramnios (Pulmonary hypoplasia)	Polycystic liver Berry Aneurysms

ARPKD: 'Reno-hepatic'

- Background
  - Cystic dilations of the renal collecting ducts with associated congenital defects of the hepatobiliary ducts → congenital hepatic fibrosis
- Pathogenesis
  - Mutation(s) of the PKHD1 gene (chromosome 6).
    - Different mutations → varied phenotypic expression (renal > = < biliary)
  - Encodes fibrocystin (an integral membrane protein) found in the renal collecting ducts AND hepatic bile duct epithelial cells
- Pathology
  - Enlarged kidneys with small (<2 mm) cysts radiating from medulla to the cortex → interstial fibrosis.
  - Biliary dysgenesis → dilated intrahepatic ducts and congenital hepatic fibrosis.

Elongated channels

ARPKD



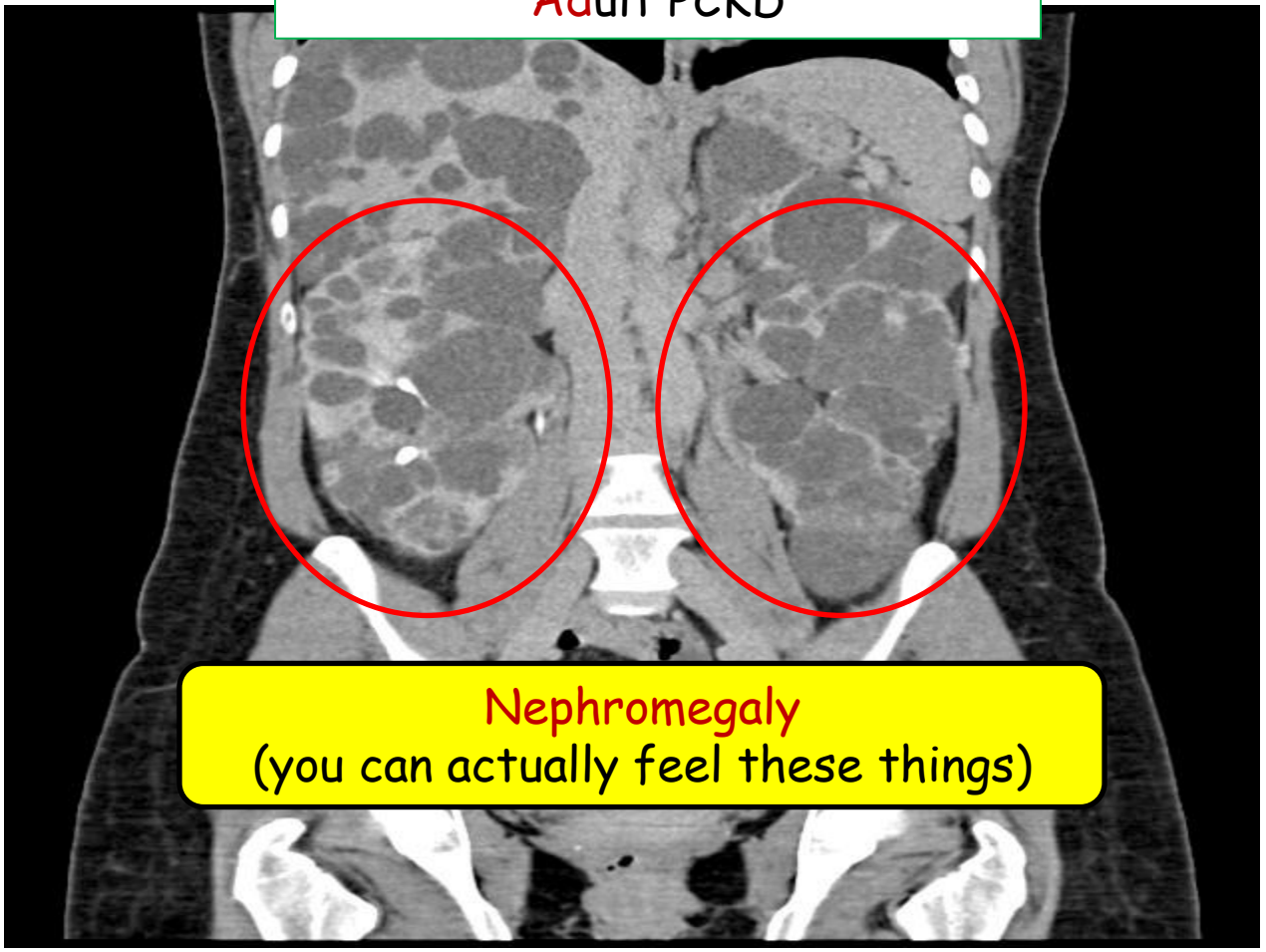
Number of ducts involved determine the severity of renal involvement

ARPKD: 'Reno-hepatic'

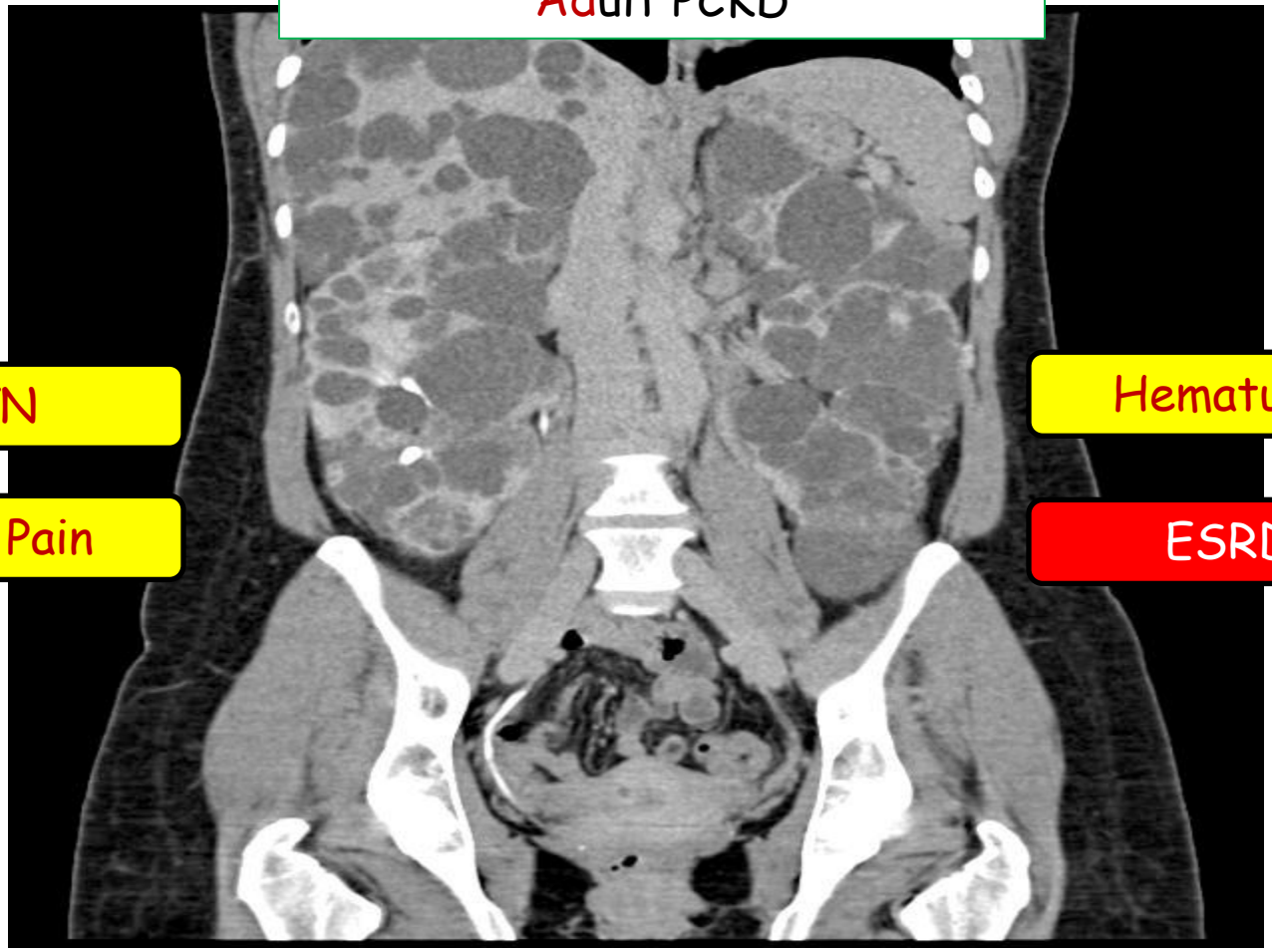
- Clinical Presentation: depends on the mutation
  - Prenatal:
    - Seen on U/S with poor corticomedullary differentiation and oligohydramnios
  - Neonatal:
    - If renal disease was severe → respiratory distress
  - Adolescent:
    - If renal disease less severe, may present with hepatic manifestation including s/s of portal HTN

- Special Notes
  - Pulmonary hypoplasia is secondary to renal failure (oligohydramnios)
    - Secondary manifestion ; may include Potter syndrome w/ associated limb and facial features

Adult PCKD



Adult PCKD



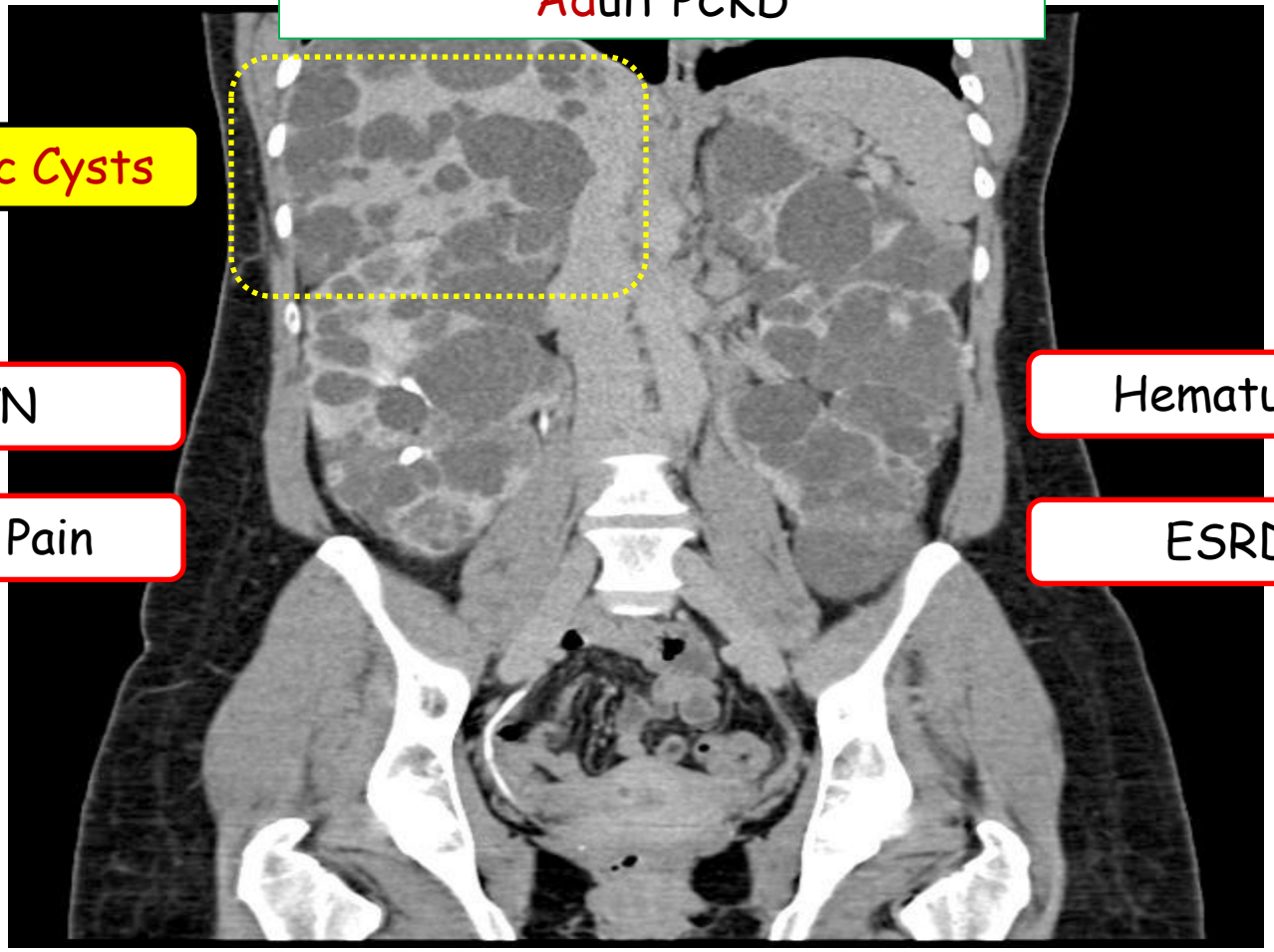
HTN

Flank Pain

Hematuria

ESRD

Adult PCKD



Hepatic Cysts

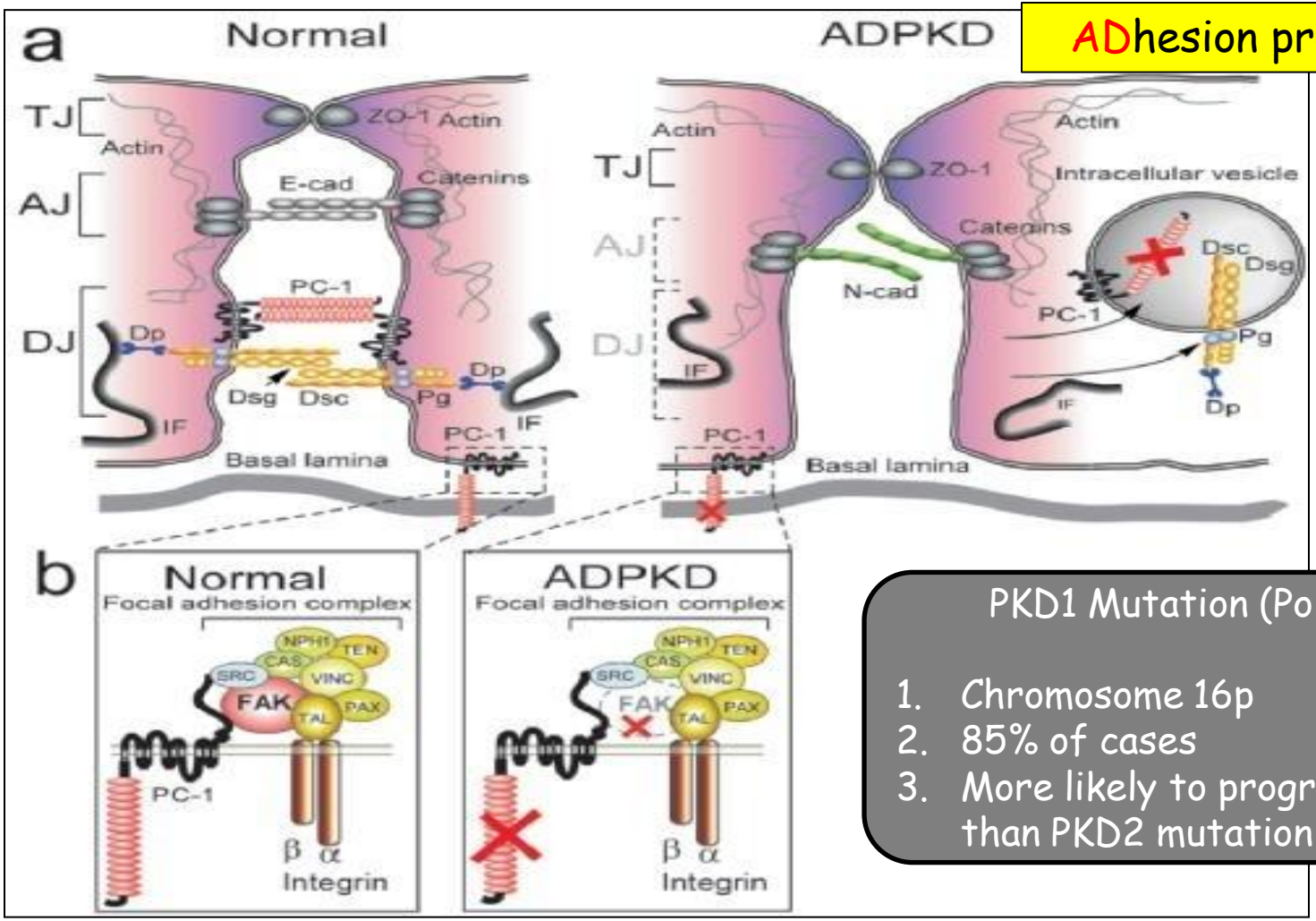
HTN

Flank Pain

Hematuria

ESRD

ADhesion problem

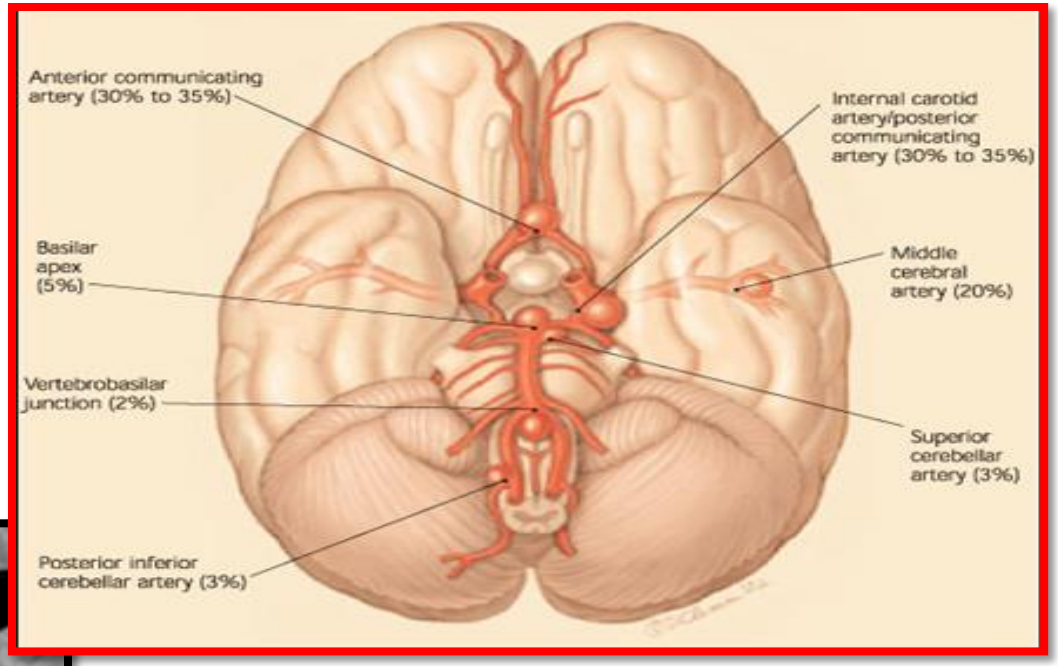


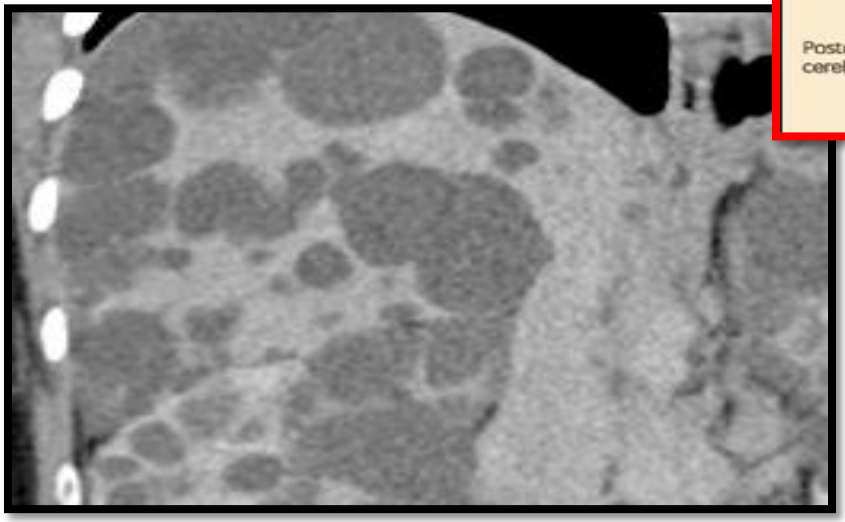
PKD1 Mutation (Polycystin-1)

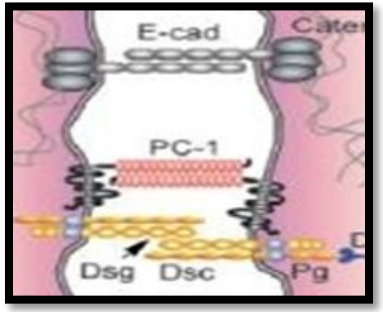
1. Chromosome 16p
2. 85% of cases
3. More likely to progress to ESRD than PKD2 mutation

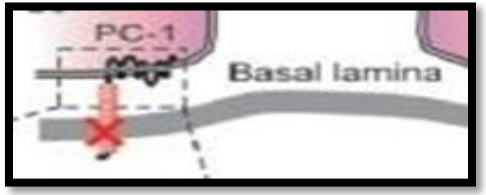
Extrarenal manifestations

Presumably share same polycystin defect affecting biliary epithelium and vascular sm mm?



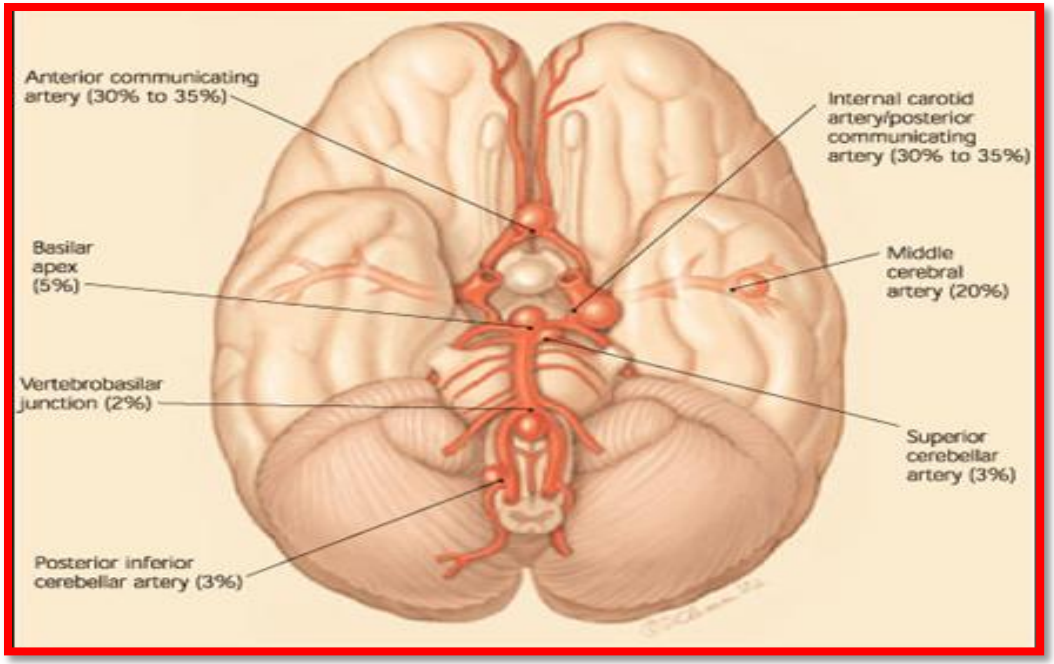






Risk Factors:

FH aneurysm
Poorly Controlled HTN
(Majority rupture <50 y.o.)



ADPKD → ESRD plus

- Background
  - Autosomal dominant cystic renal disorder characterized by progressive renal failure and extrarenal manifestations.
- Pathogenesis
  - PKD1 (gene) → polycystin-1 (protein); PKD2 → polycystin-2
    - Membrane protein: cell-cell; cell-matrix interaction; ↑ cell proliferation
    - Mechanism of cyst formation is uncertain (albeit interesting)
- Pathology – large cyts

ADPKD → ESRD plus

- Clinical
  - Renal: Flank pain, (cysts, stones, infection), hematuria, CKD (progressive)
  - Extrarenal: cerebral aneurysms (~10%), hepatic cysts
- Data
  - Ultrasound: number of cysts that vary by age
  - Genetic testing
- Special Notes
  - Aneurysms: ↑ risk with FH, HTN, larger size; majority rupture < 50 y.o.
    - Uncertain recommendation on screening although need to consider serial assessment (not a one and done)
  - Age (40+): GFR ↓ 5 ml/min/yr
  - ACE/ARB benefits beyond BP lowering (esp if proteinuria)

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Key Associations	Nephrolithiasis	Hepatic fibrosis Oligohydramnios (can't make hydramnios if you can't pee!)	Polycystic liver Berry Aneurysms
	Stones	Liver (lung)	ICH 2° Aneurysm

Cystic Renal Disease, for USMLE Step One

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