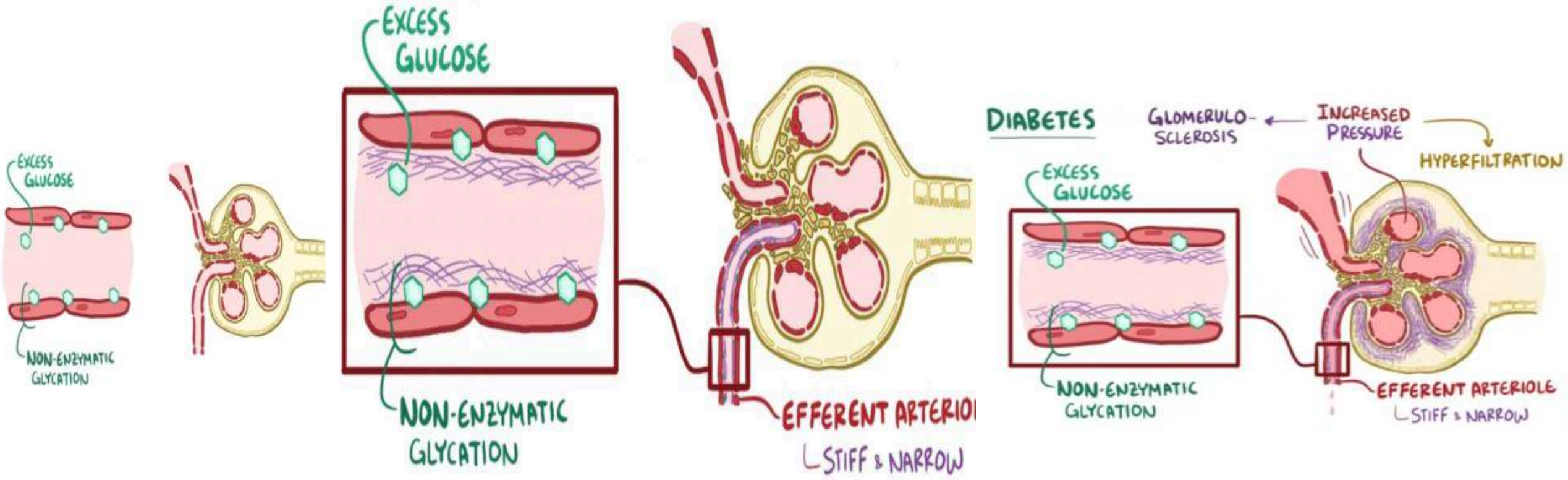
Lec 3 CKD LK

Diabetic nephropathy

- **(chronic uncontrolled dm) Hyperglycemi**
- → nonenzymatic glycation of proteins → varying degrees of damage to

all types of kidney cell.

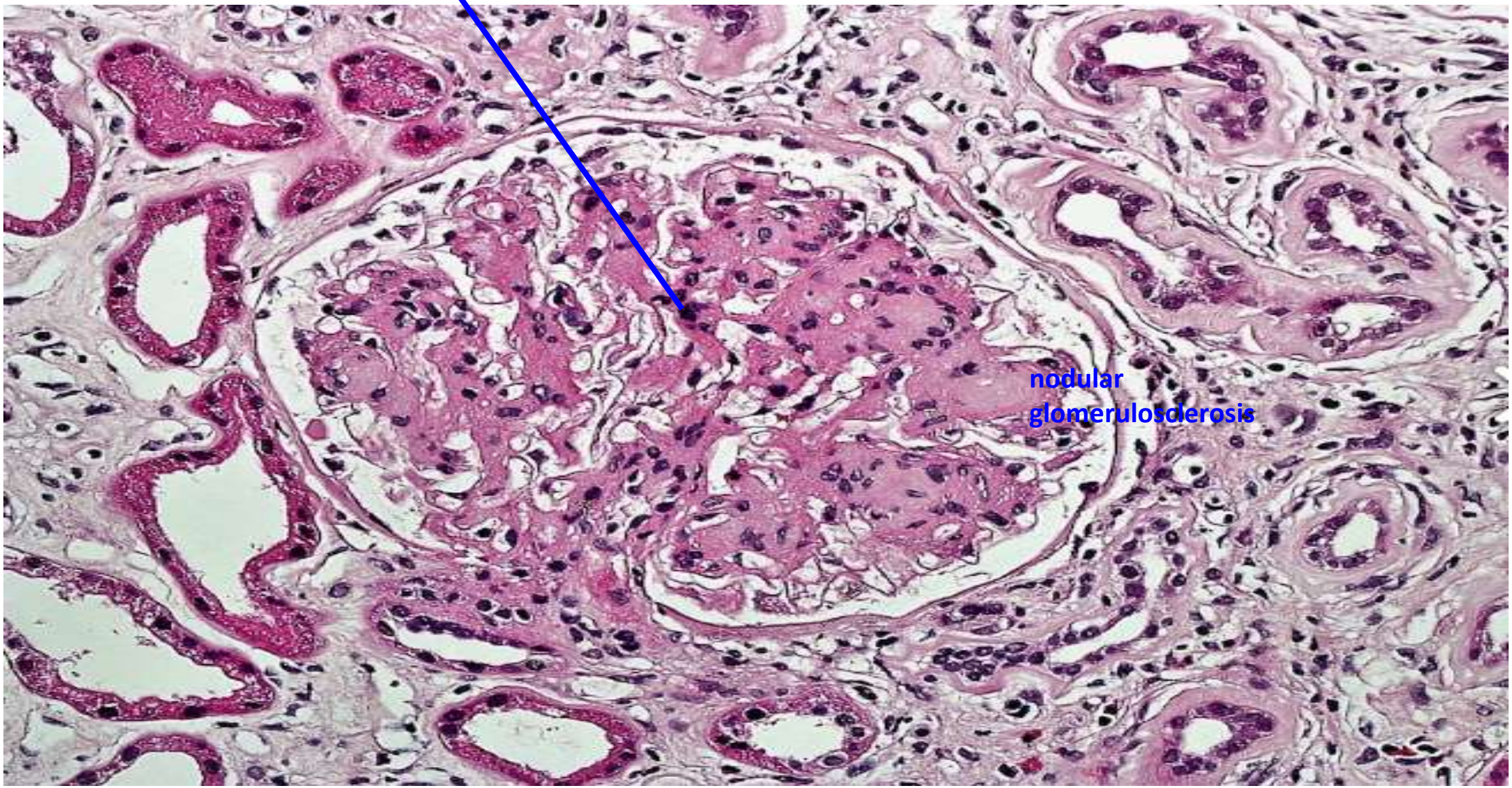
All components affected



H&E

Glomeruli

hypercellularity >proliferation of mesangial cells



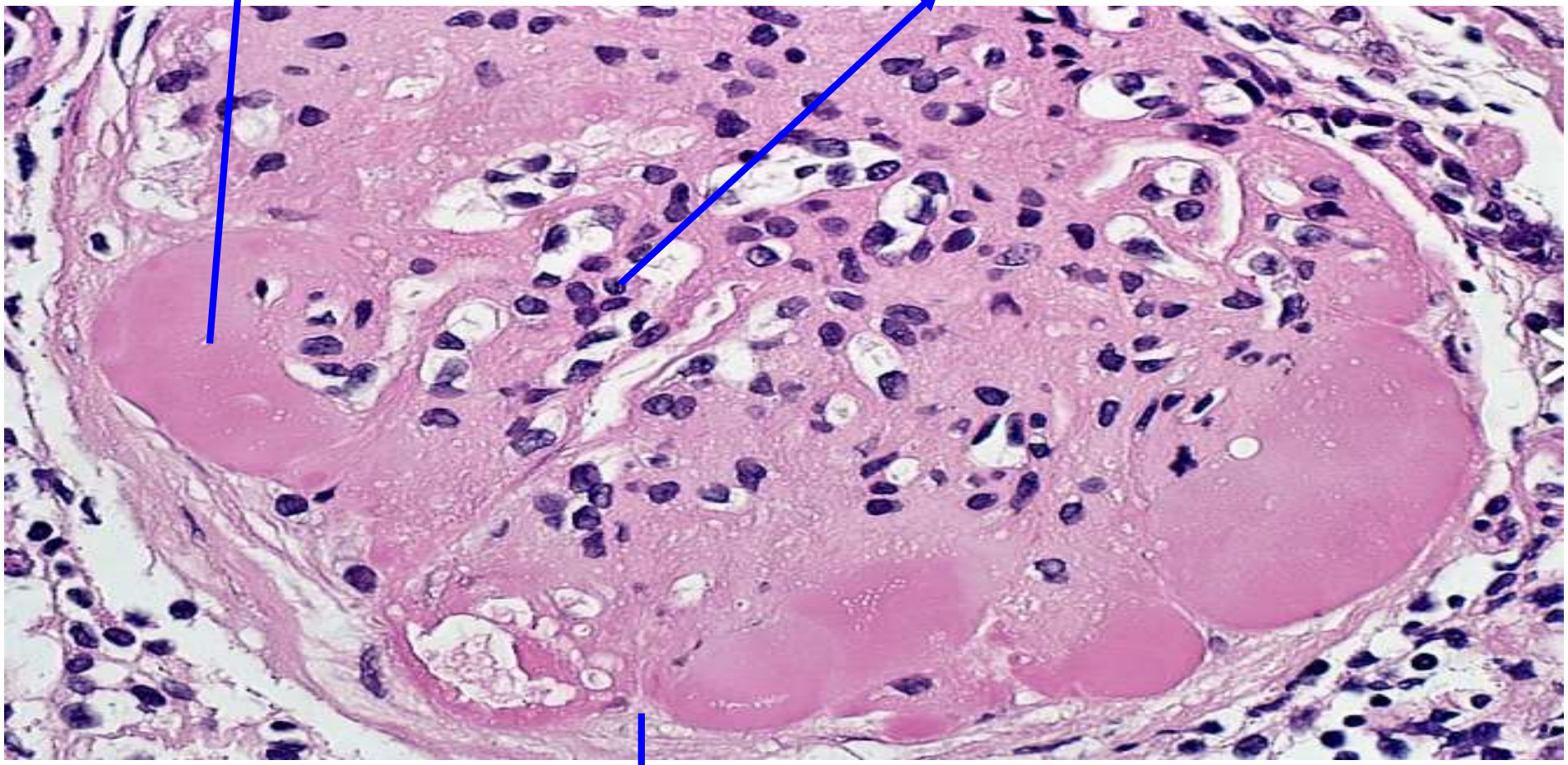
H&E

Glomeruli

Kimmelstiel Wilson nodules

Nodules of pink hyaline material form in regions of glomerular capillary loops in the glomerulus

Specific to **diabetic nephropathy** and amyloidosis

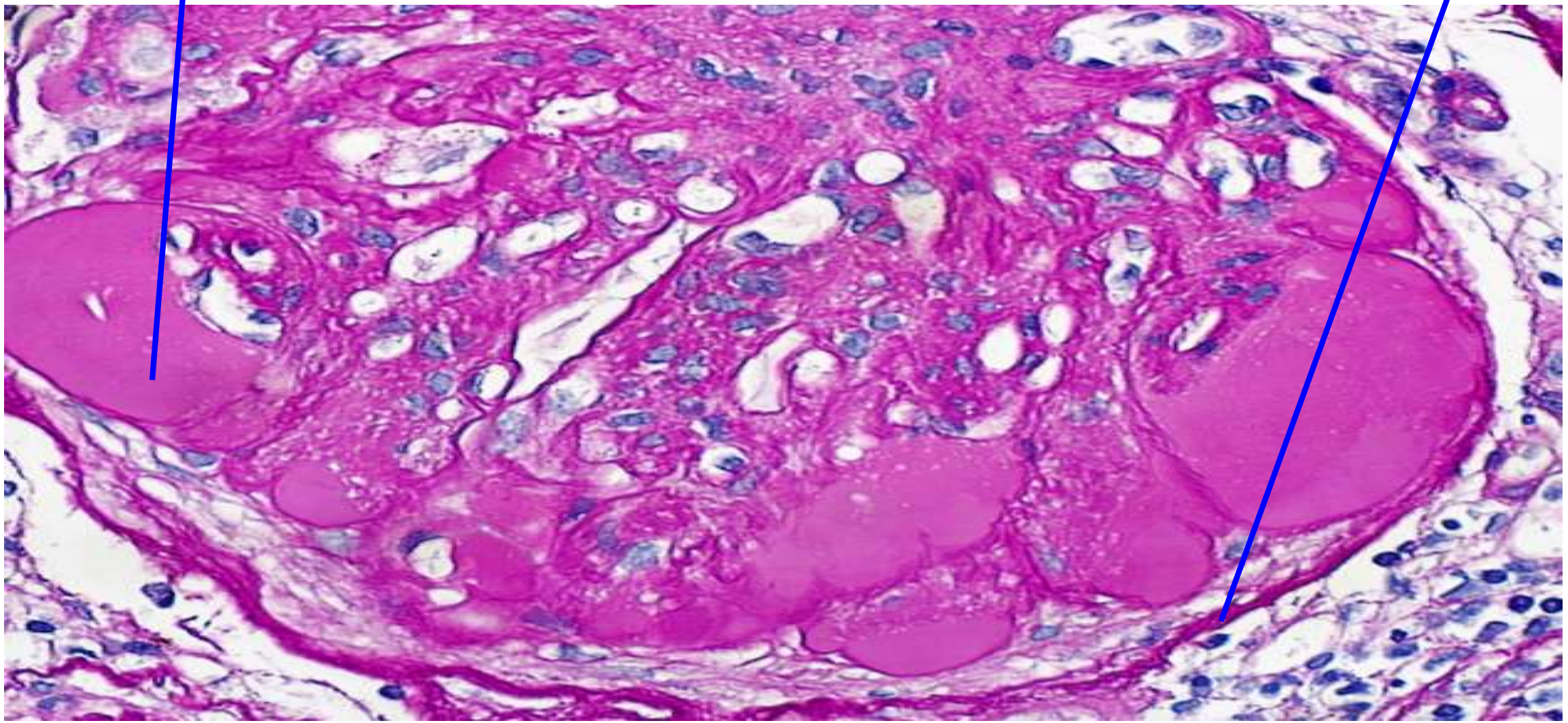


PAS stain

Glomeruli

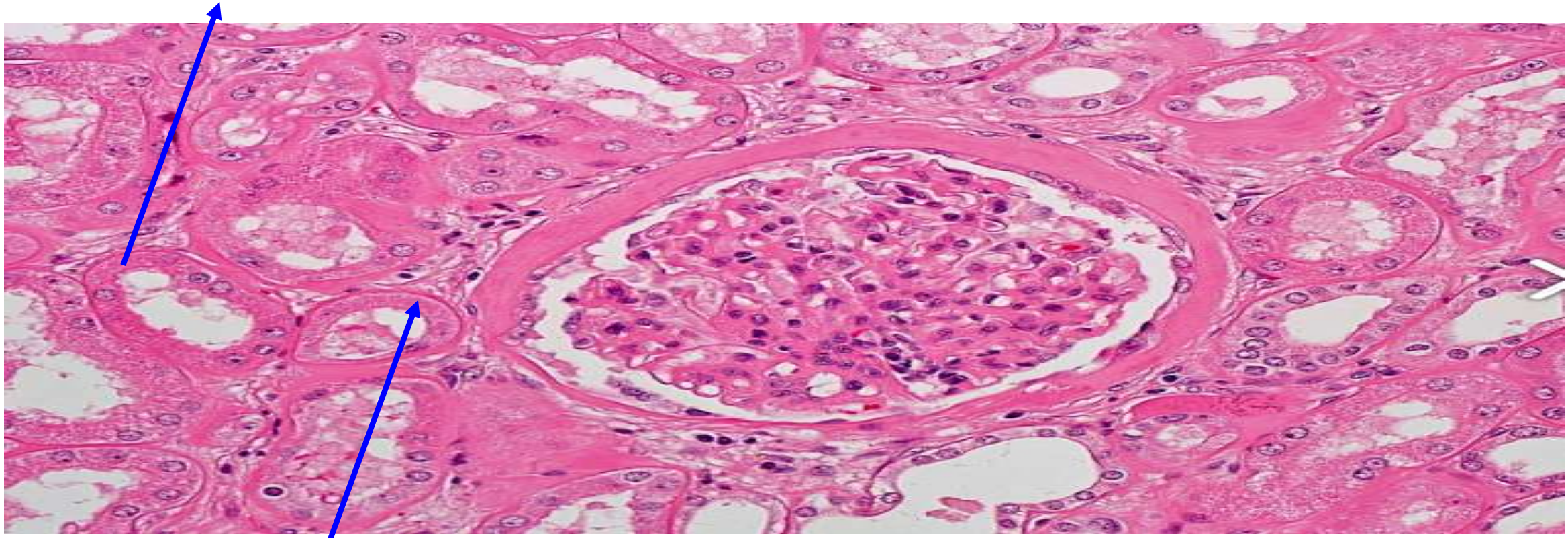
Kimmelstiel Wilson nodules hyalinization **nodular**

hyalinization **capsule**



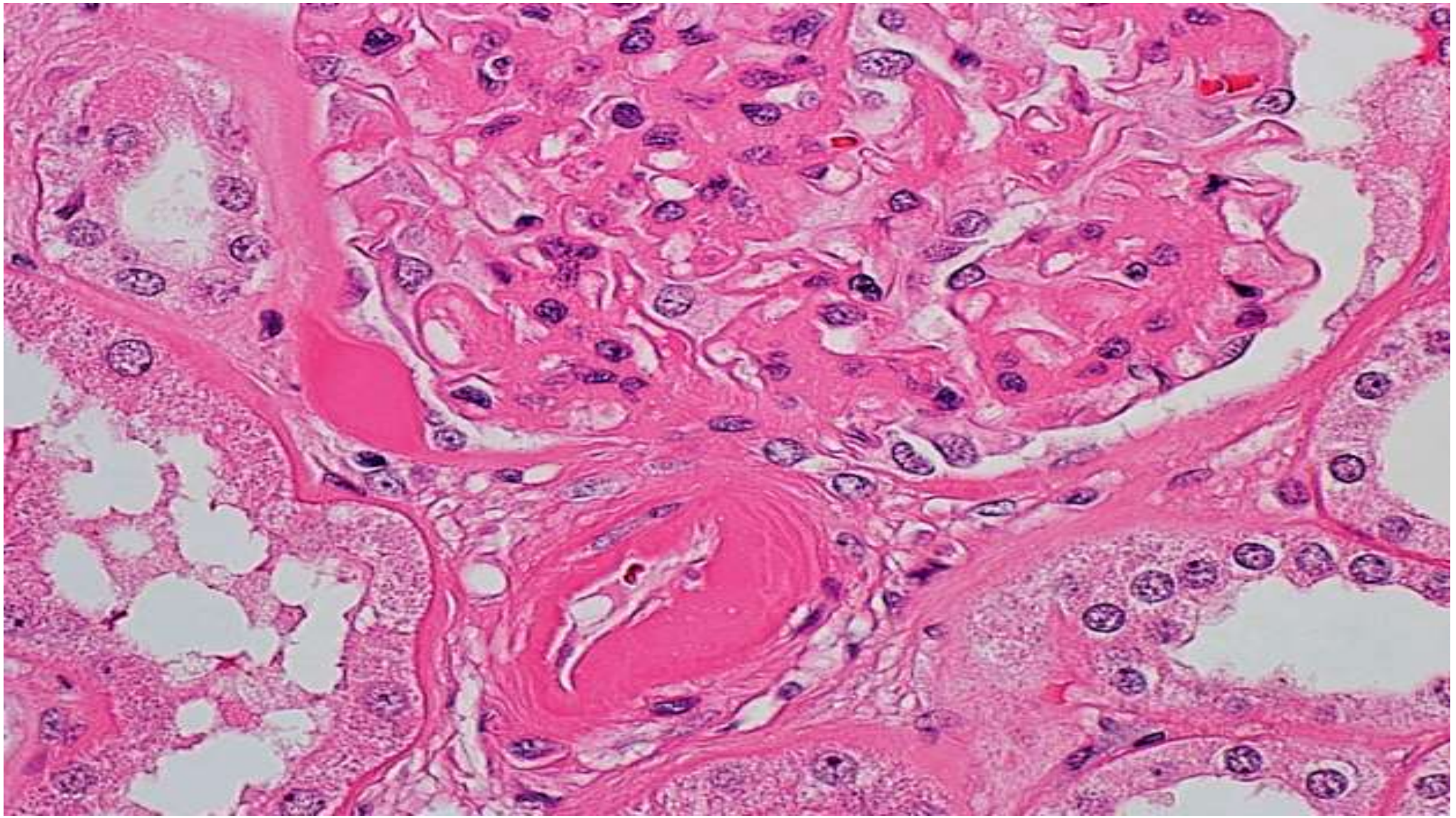
Tubules

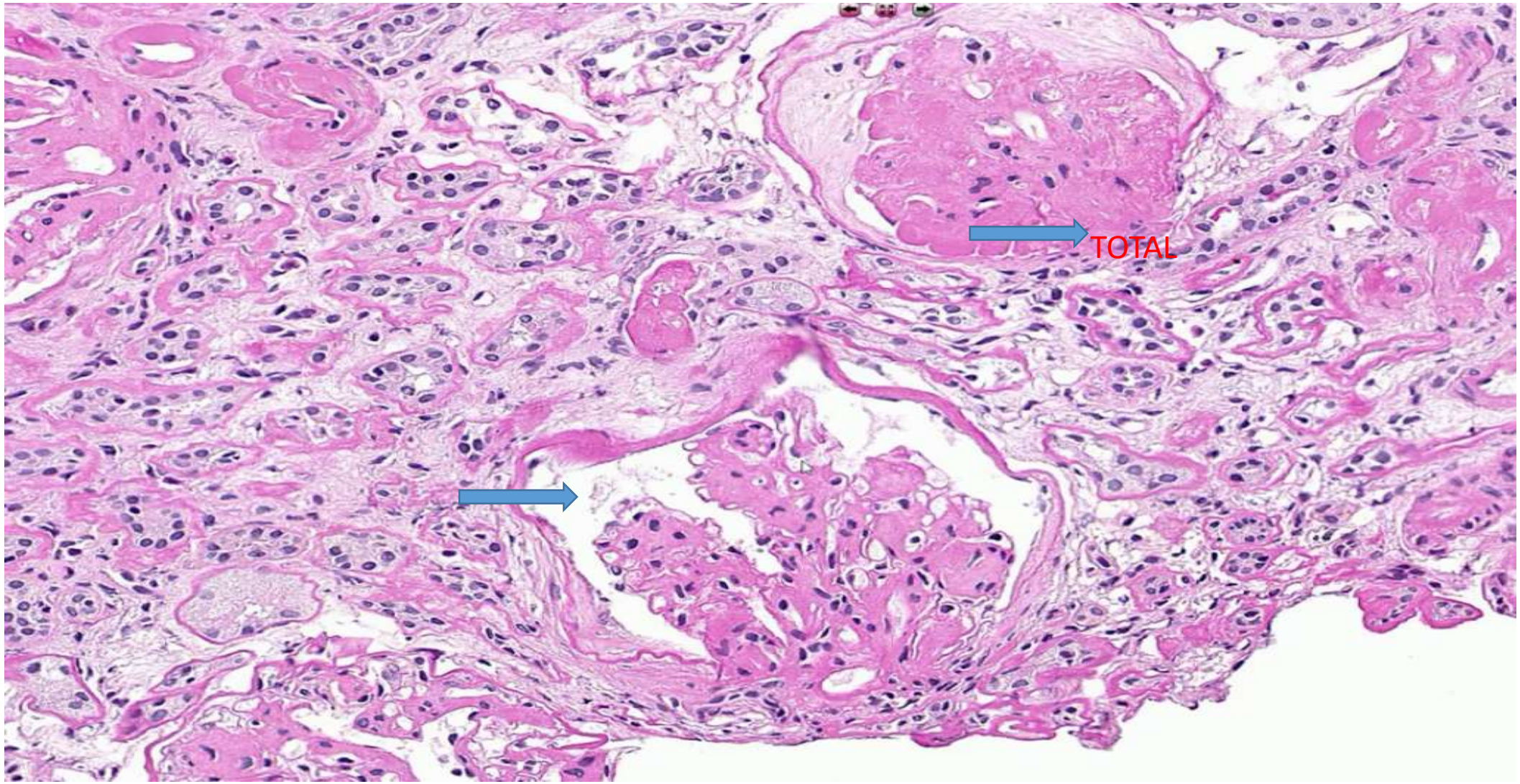
> TBM thickening, and tubular hypertrophy



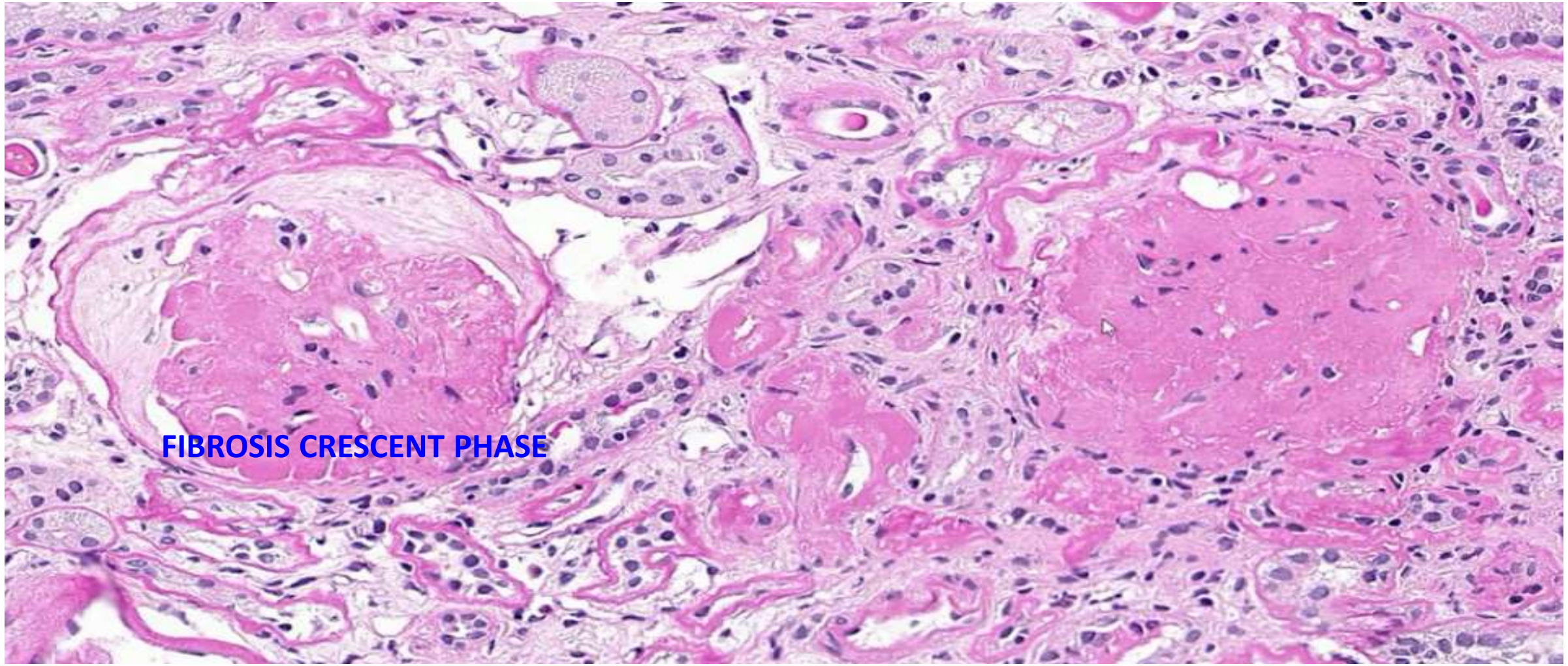
Drop of nuclear in tubular cell

hyalinization of afferent and efferent arterioles



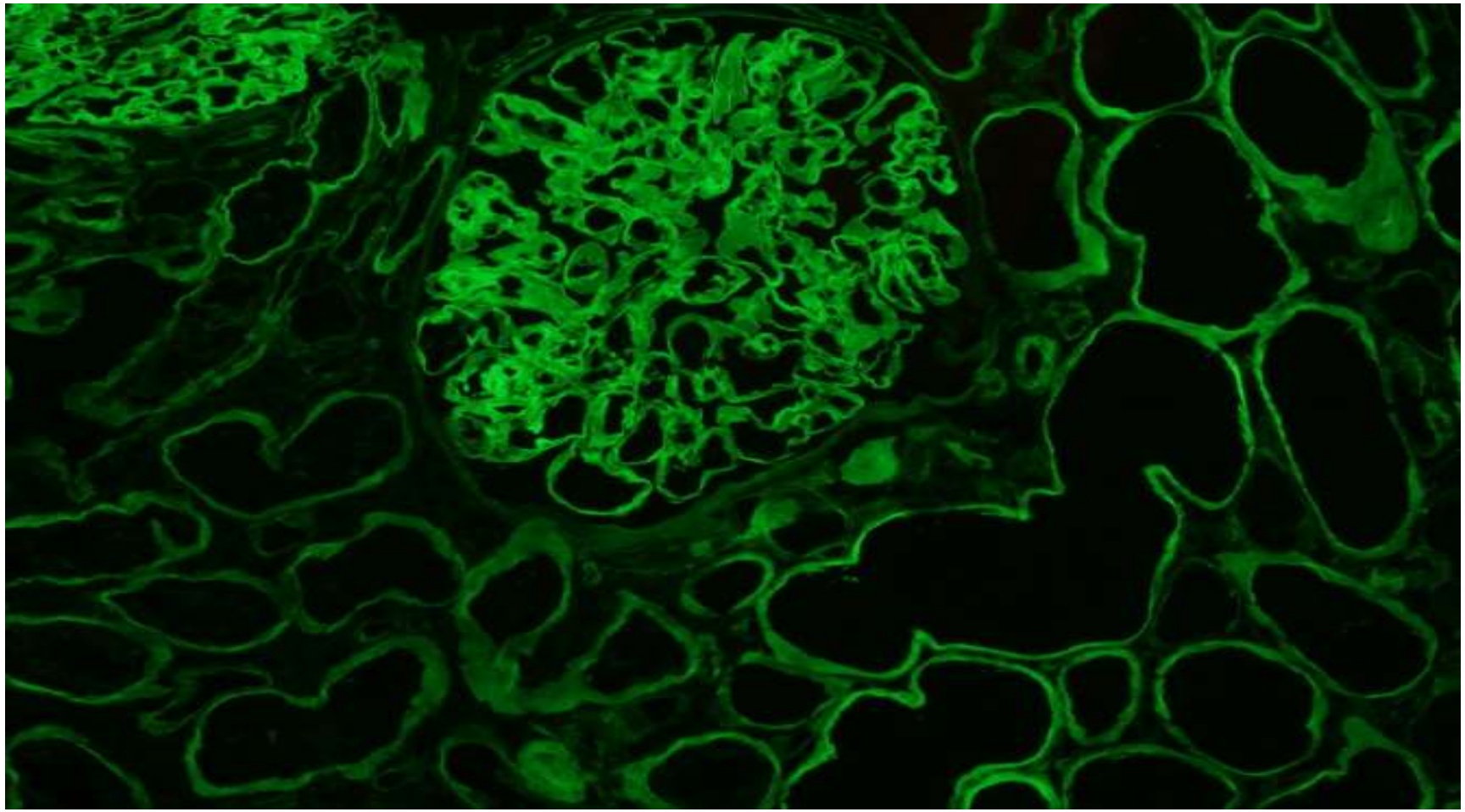

TOTAL

ADDVANCE STAGE



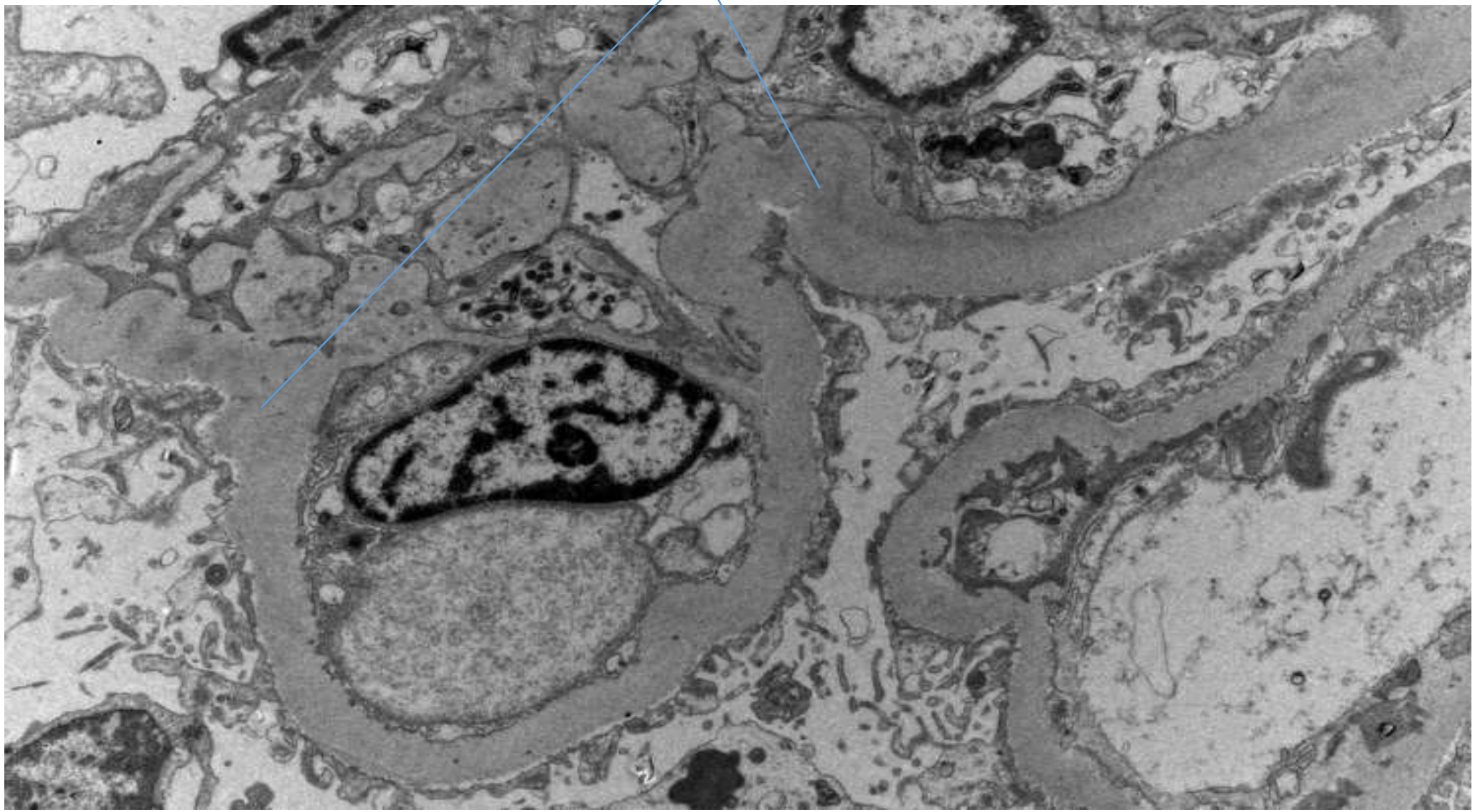
IF

Igg deposition (diffuse /linear)



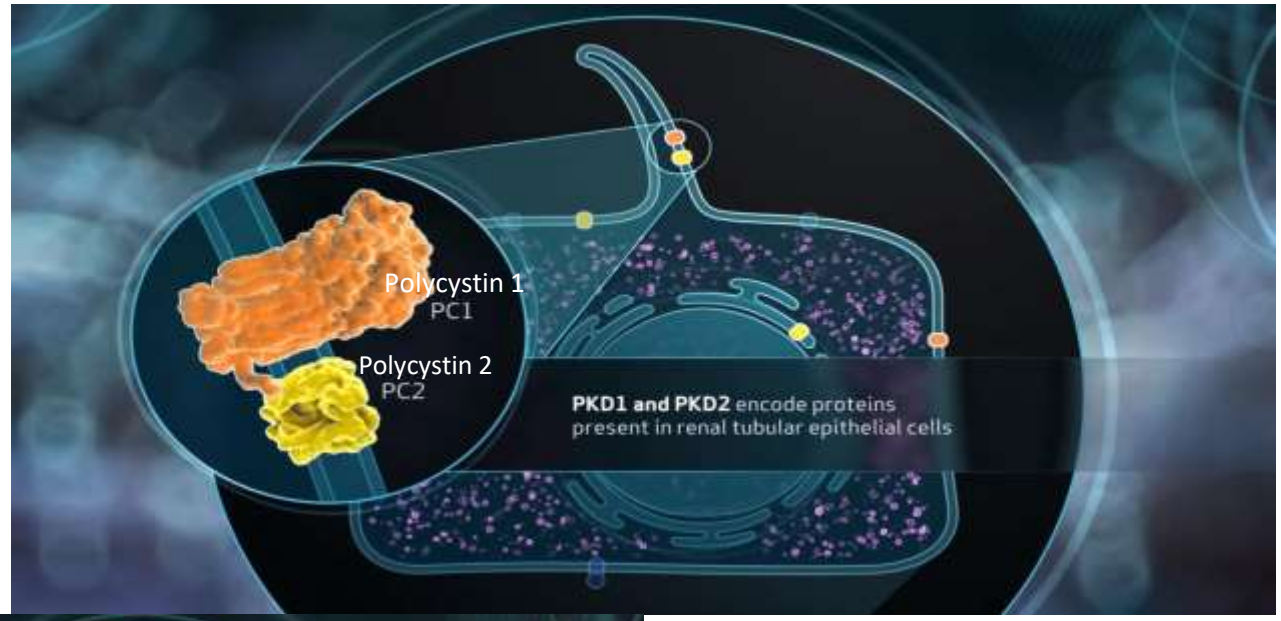
EM

thickening of basement membrane

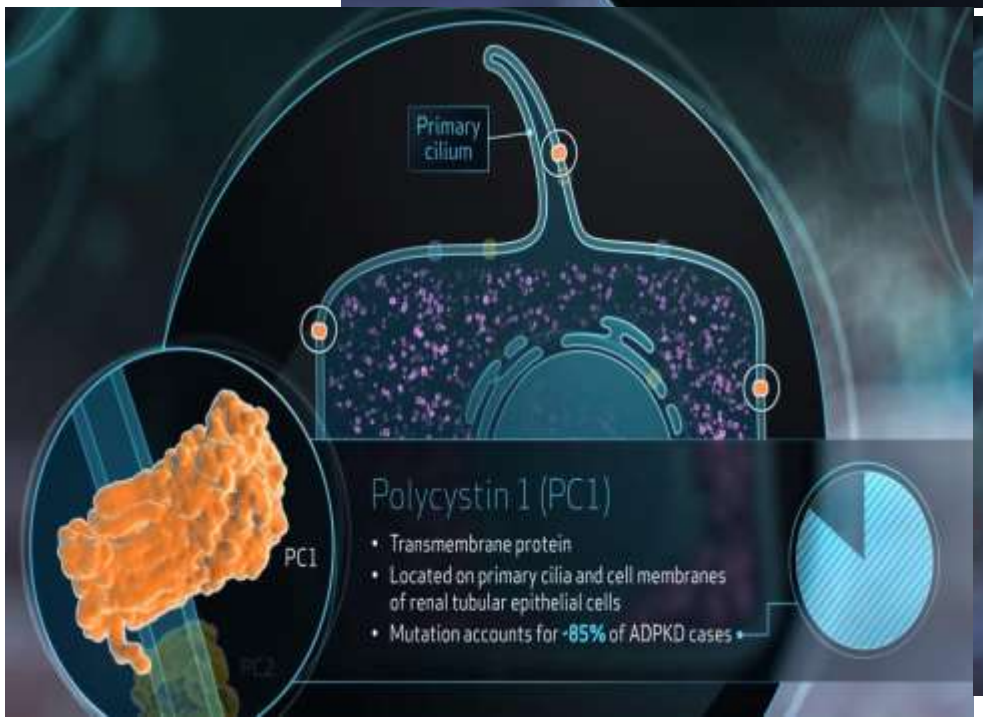


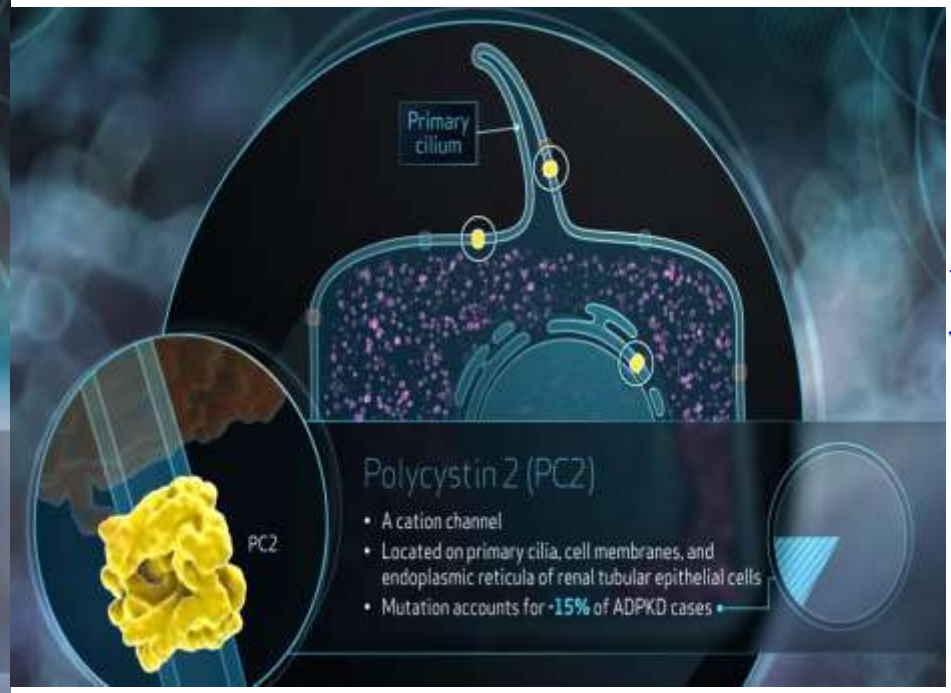
L11 Renal cysts and anomliesLK

polycystin 1 (PKD1,MC (85%)
polycystin 2 (PDK2,(15%)



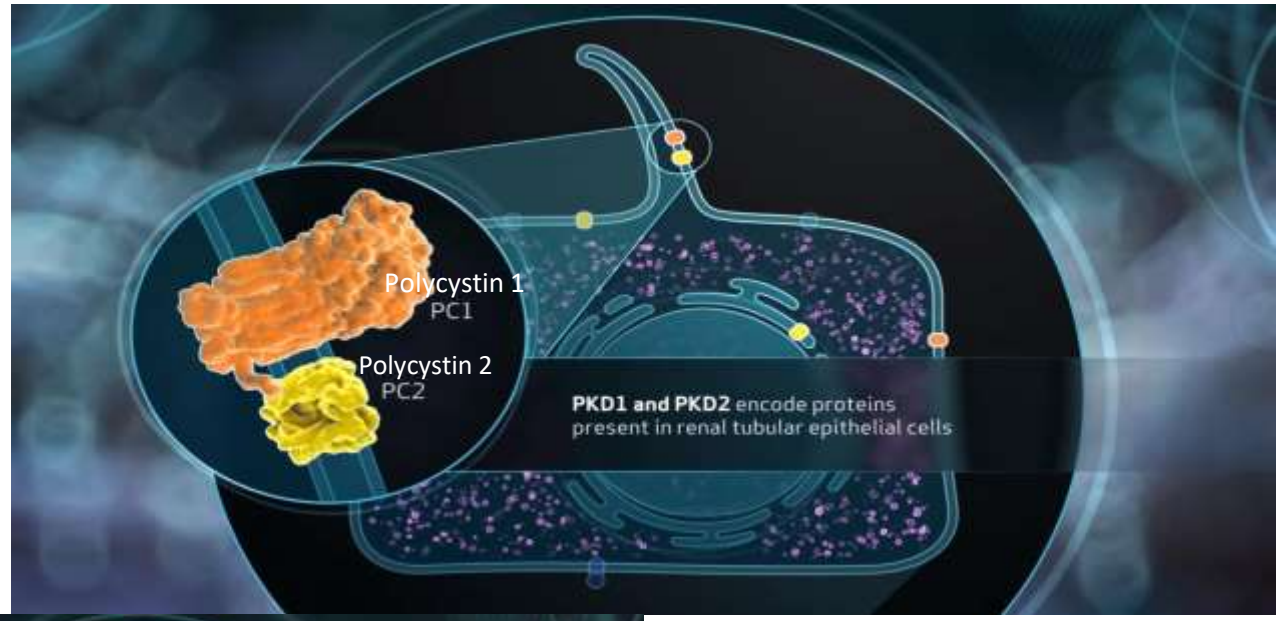
Polycystin 1
Primary cilia
Tubular epithelial cell



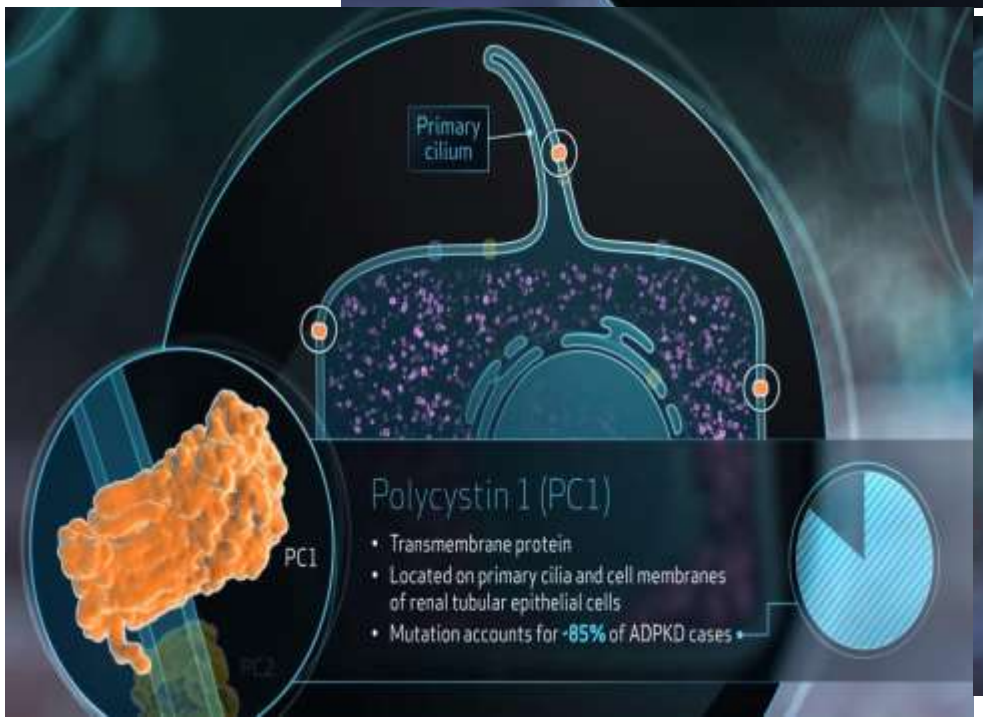


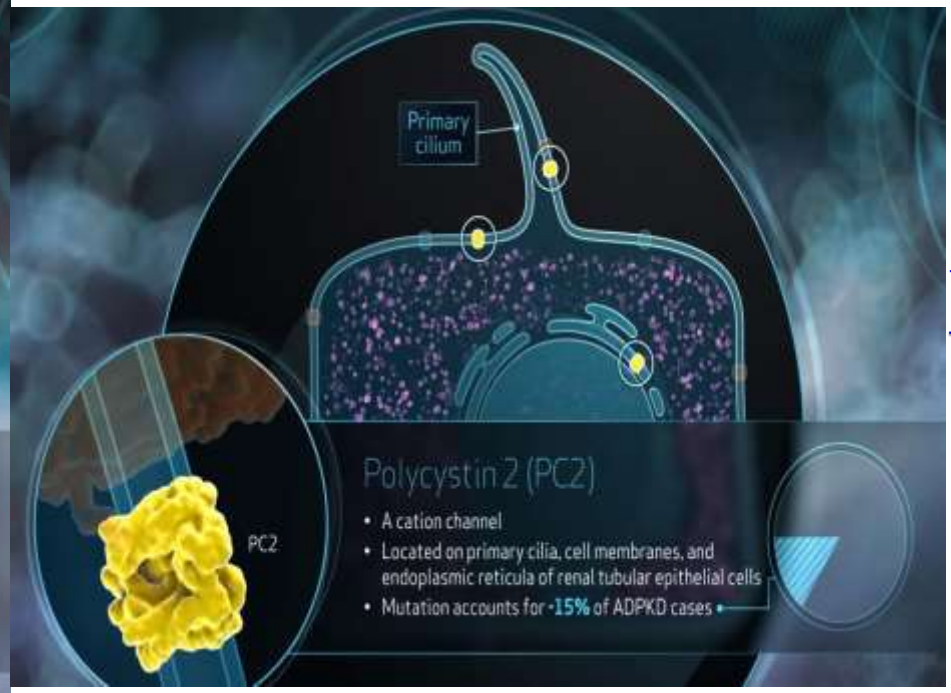
Polycystin 2
Primary cilia
Tubular epithelial cell
Endoplasmic reticulun

polycystin 1 (PKD1,MC (85%)
polycystin 2 (PDK2,(15%)

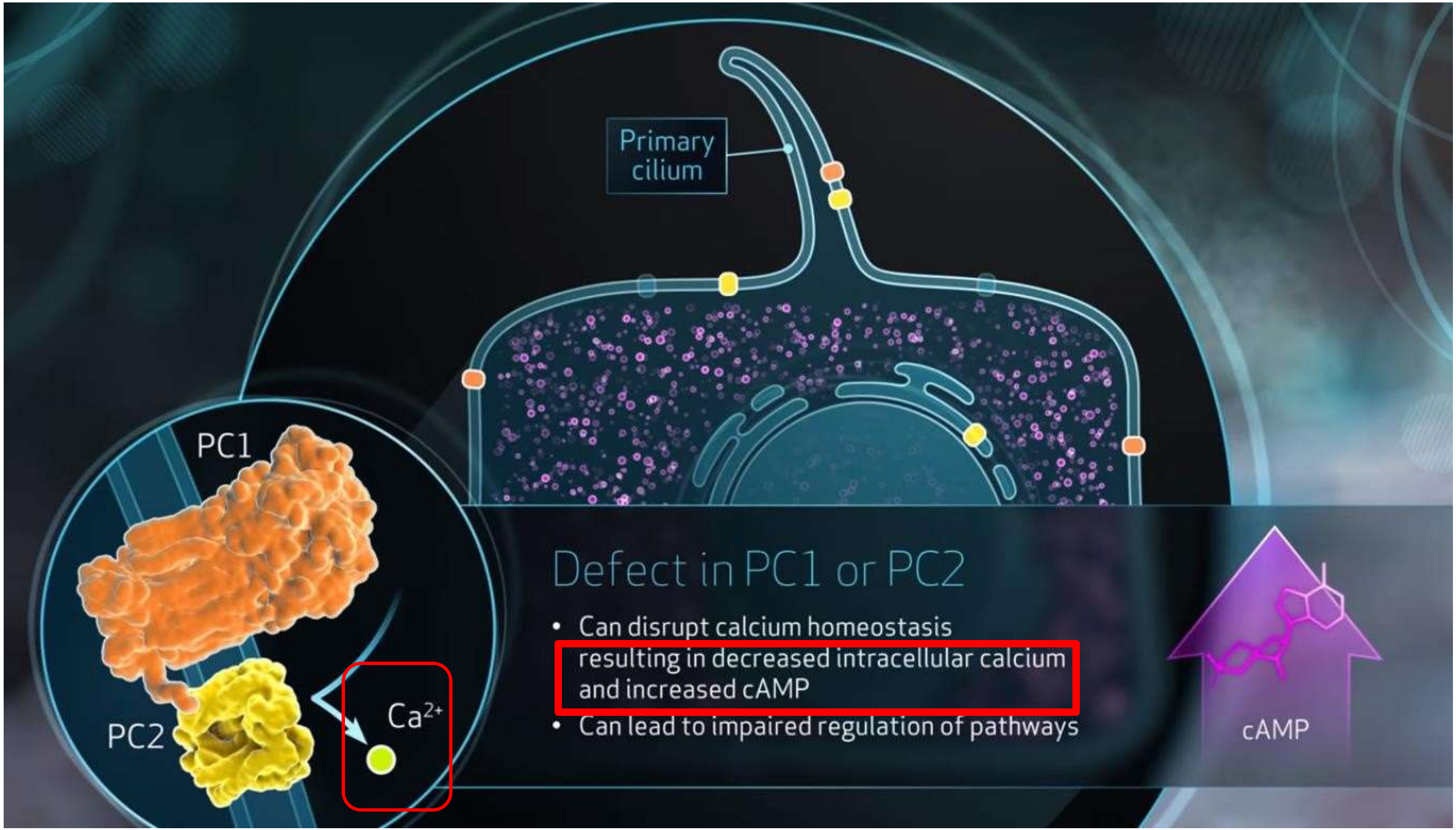


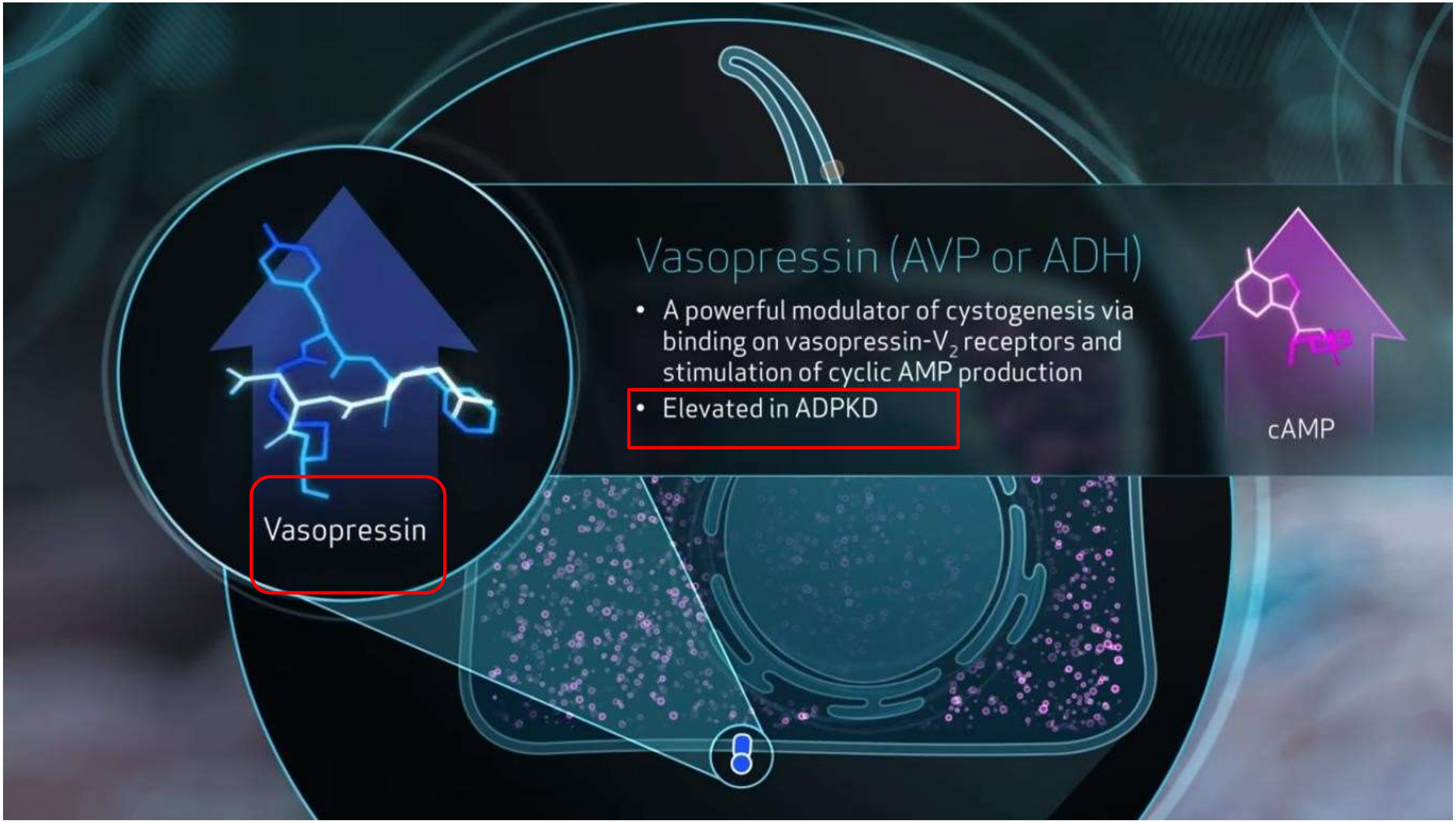
Polycystin 1
Primary cilia
Tubular epithelial cell

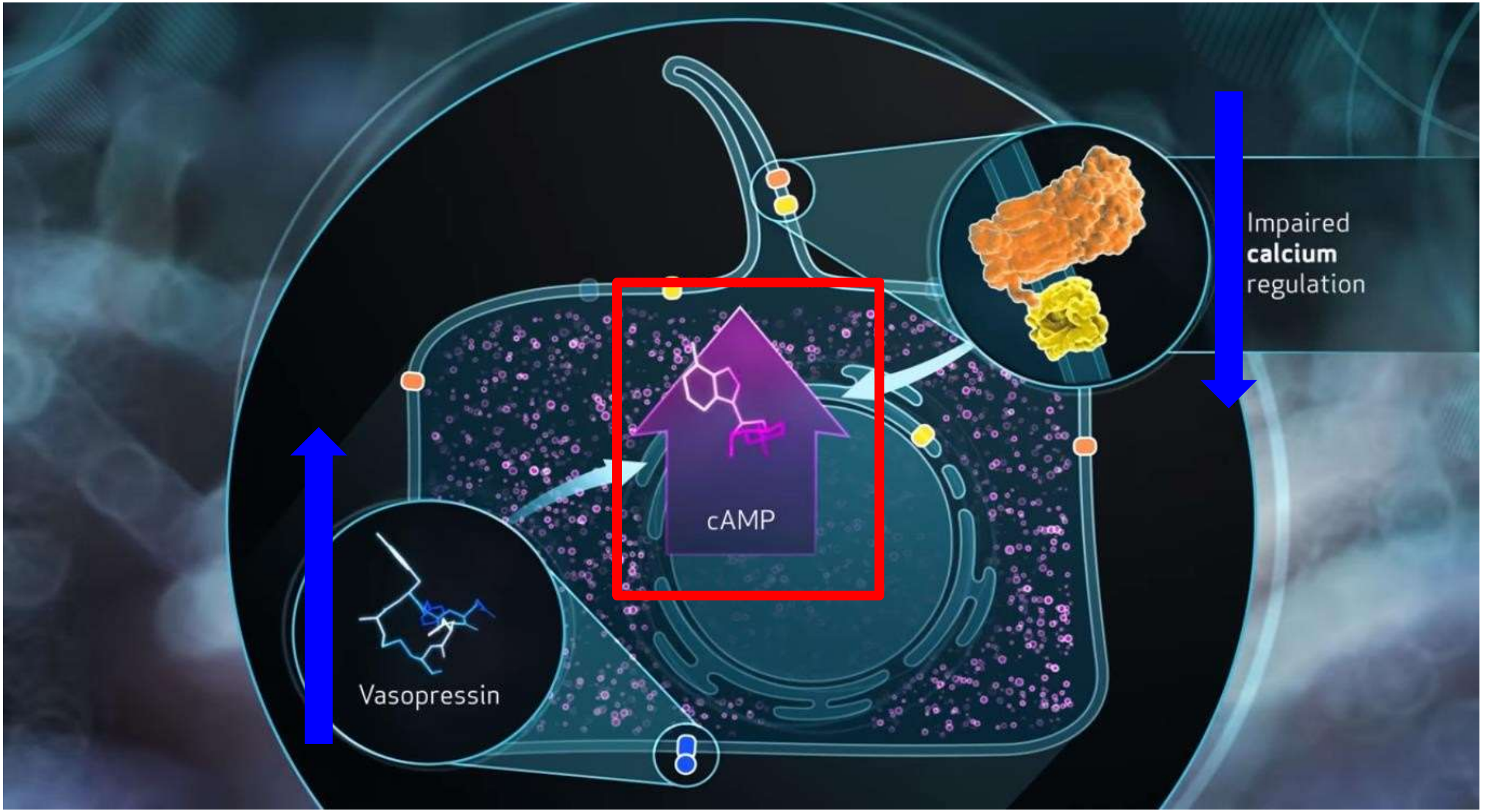


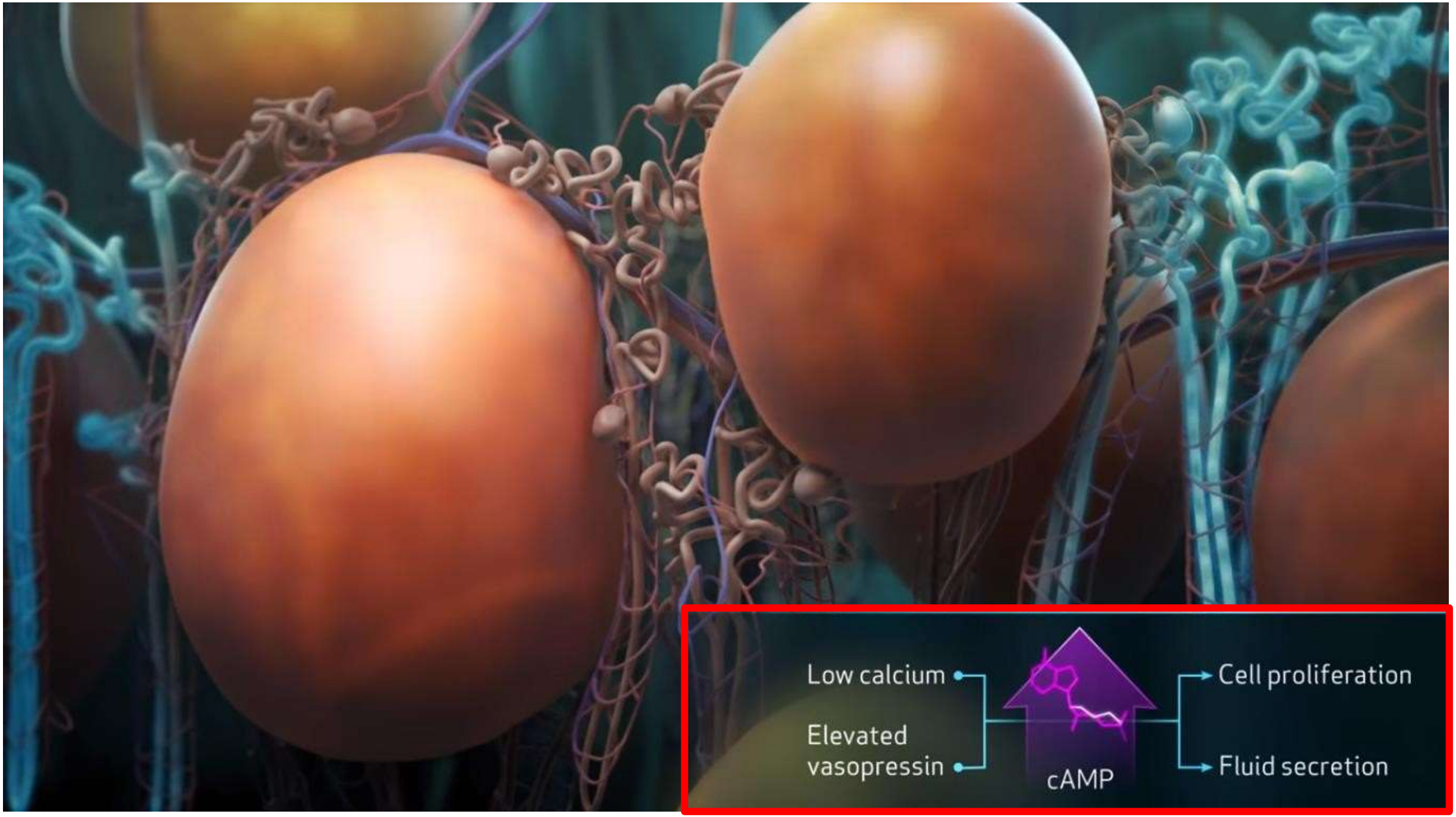


Polycystin 2
Primary cilia
Tubular epithelial cell
Endoplasmic reticulun


Primary cilium
PC1
PC2
Ca^{2+}
Defect in PC1 or PC2
• Can disrupt calcium homeostasis resulting in decreased intracellular calcium and increased cAMP
• Can lead to impaired regulation of pathways
cAMP


Vasopressin (AVP or ADH)
• A powerful modulator of cystogenesis via binding on vasopressin-V_2 receptors and stimulation of cyclic AMP production
• Elevated in ADPKD
cAMP
Vasopressin

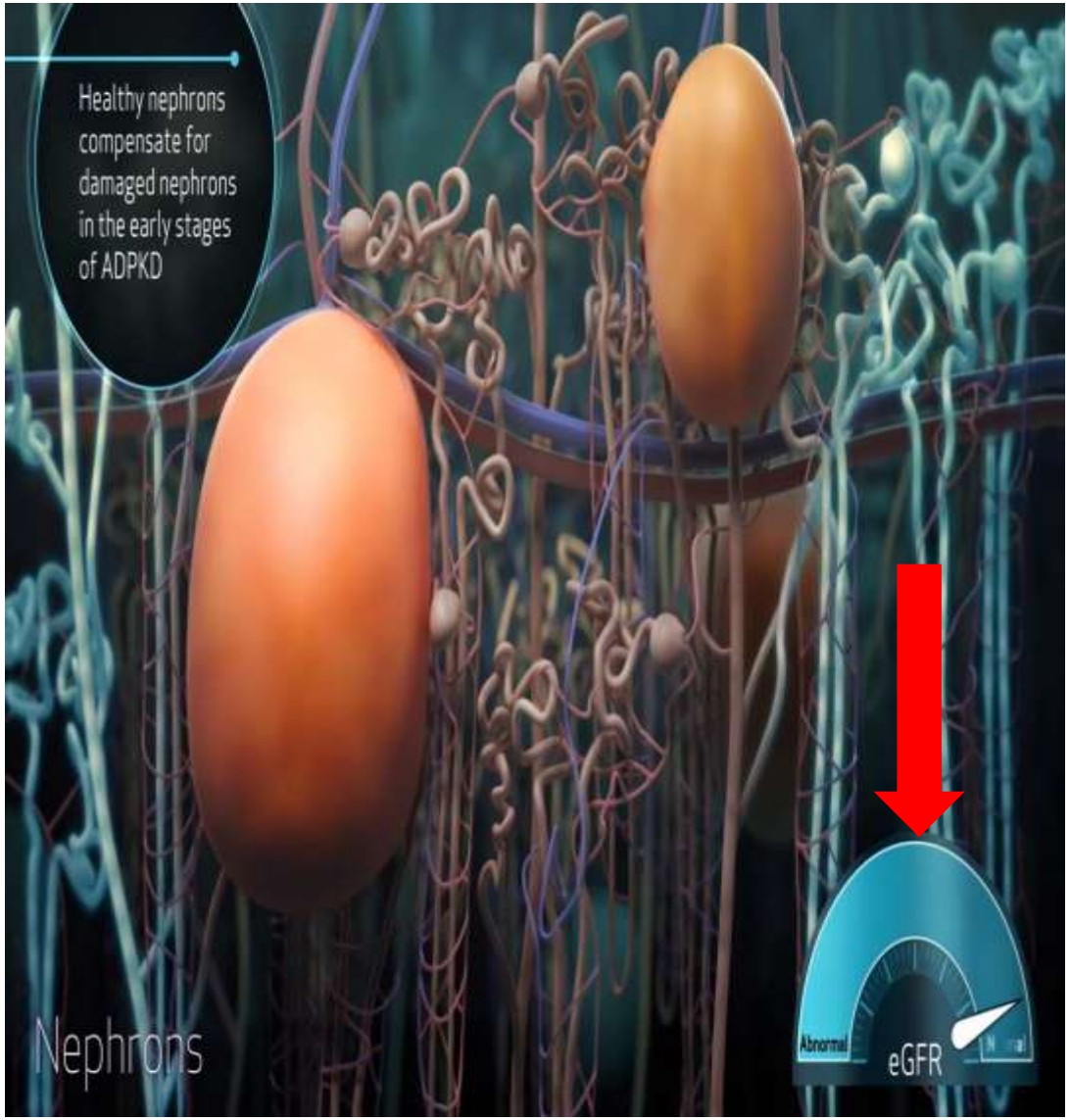

Impaired
calcium
regulation
cAMP
Vasopressin

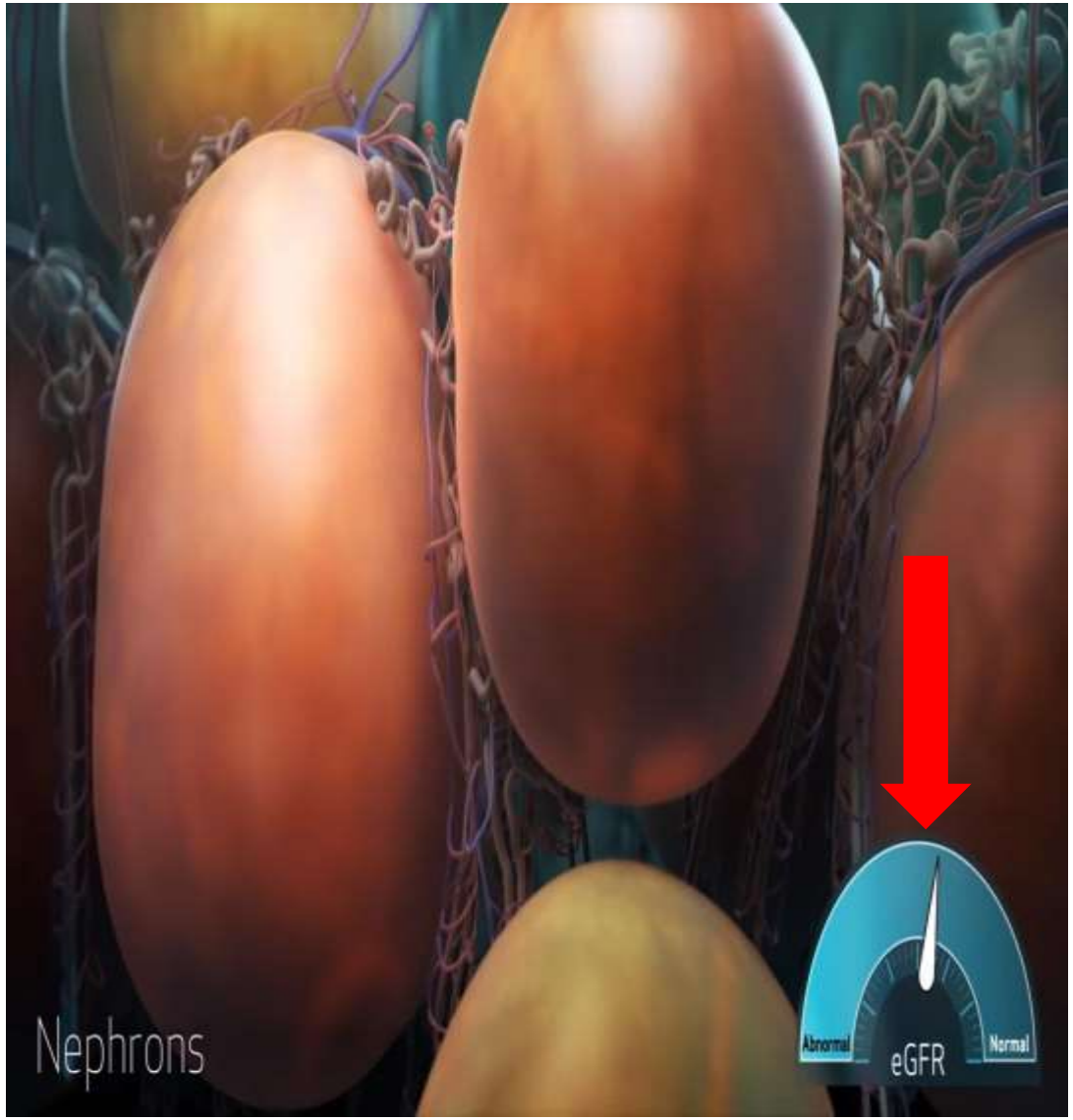

Low calcium
Elevated vasopressin
cAMP
Cell proliferation
Fluid secretion

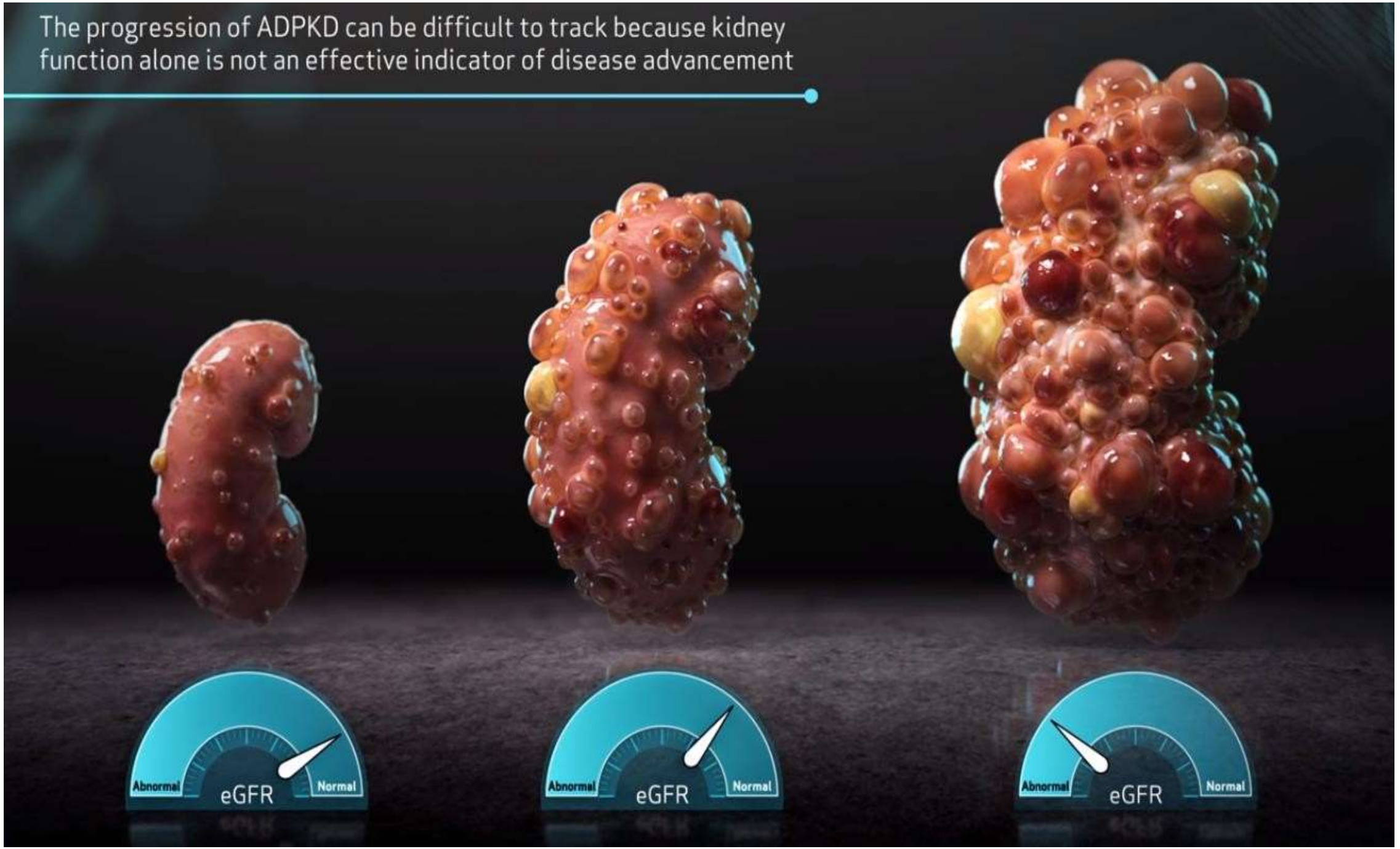

cAMP*
*cAMP = Cyclic AMP
Main mechanisms leading to cyst formation and expansion in ADPKD:
• Fluid secretion
• Cell proliferation

Cysts form in **all regions of the nephron**, **enlarging and** **<u>expanding throughout life</u>**

Normal renal function is maintained **until** mid **adulthood** in most patients





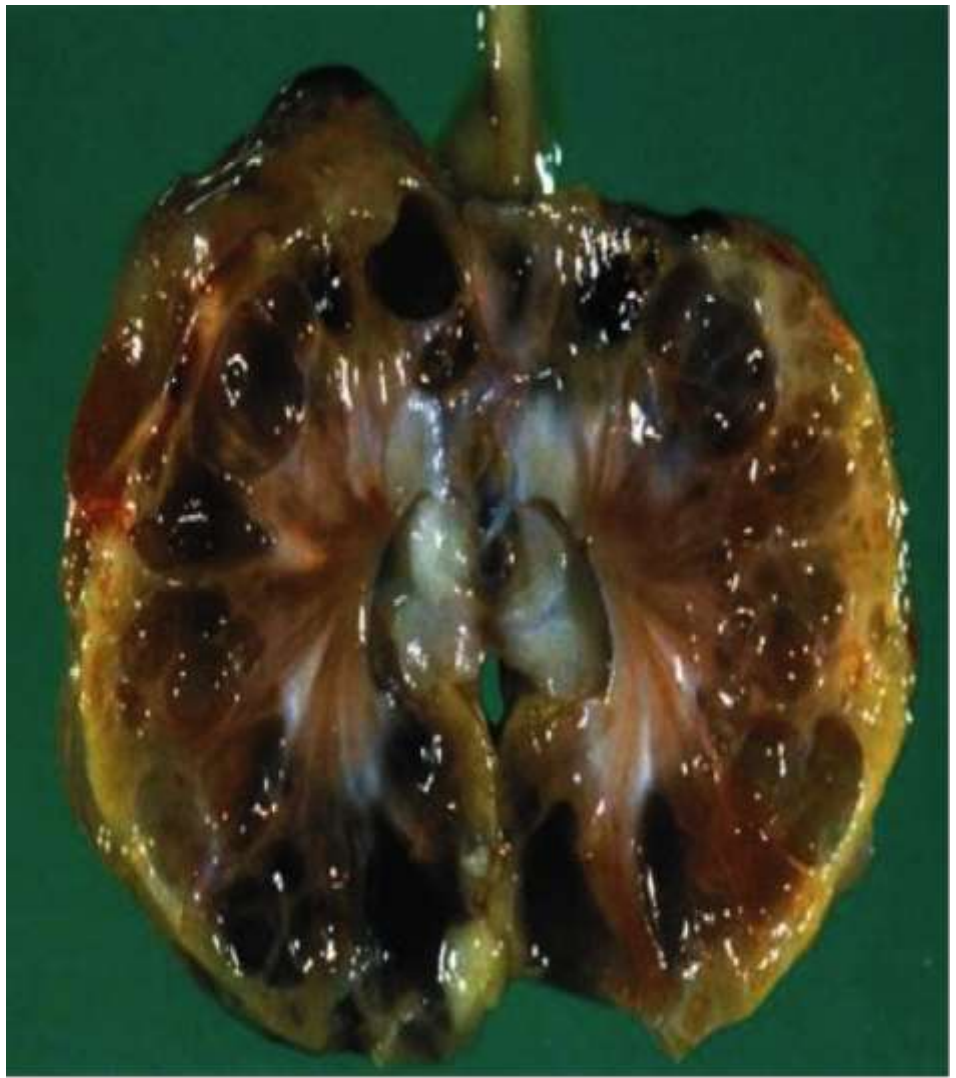

The progression of ADPKD can be difficult to track because kidney function alone is not an effective indicator of disease advancement
Abnormal
eGFR
Normal
Abnormal
eGFR
Normal
Abnormal
eGFR
Normal

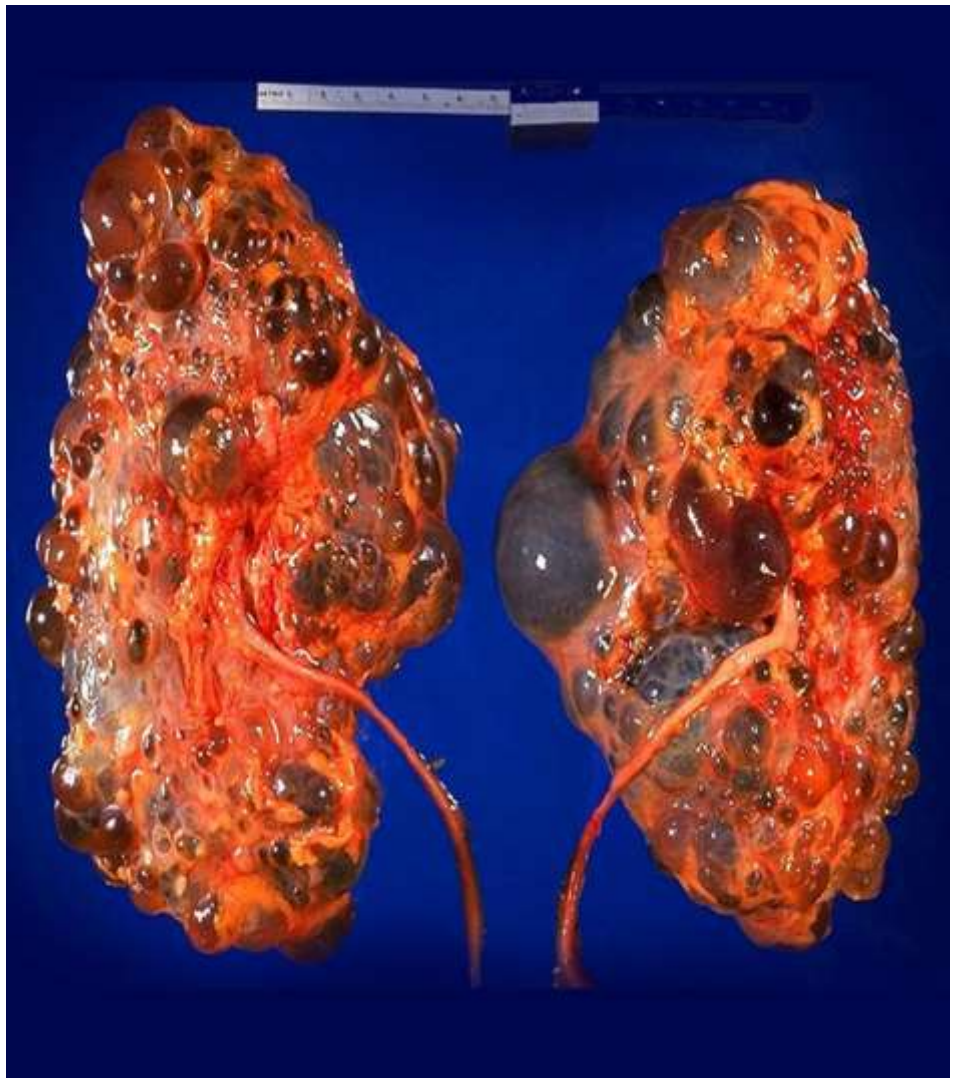
Gross description

Markedly enlarged kidneys (up to 8 kg)
composed of **sub- capsular cysts** up to 4 cm

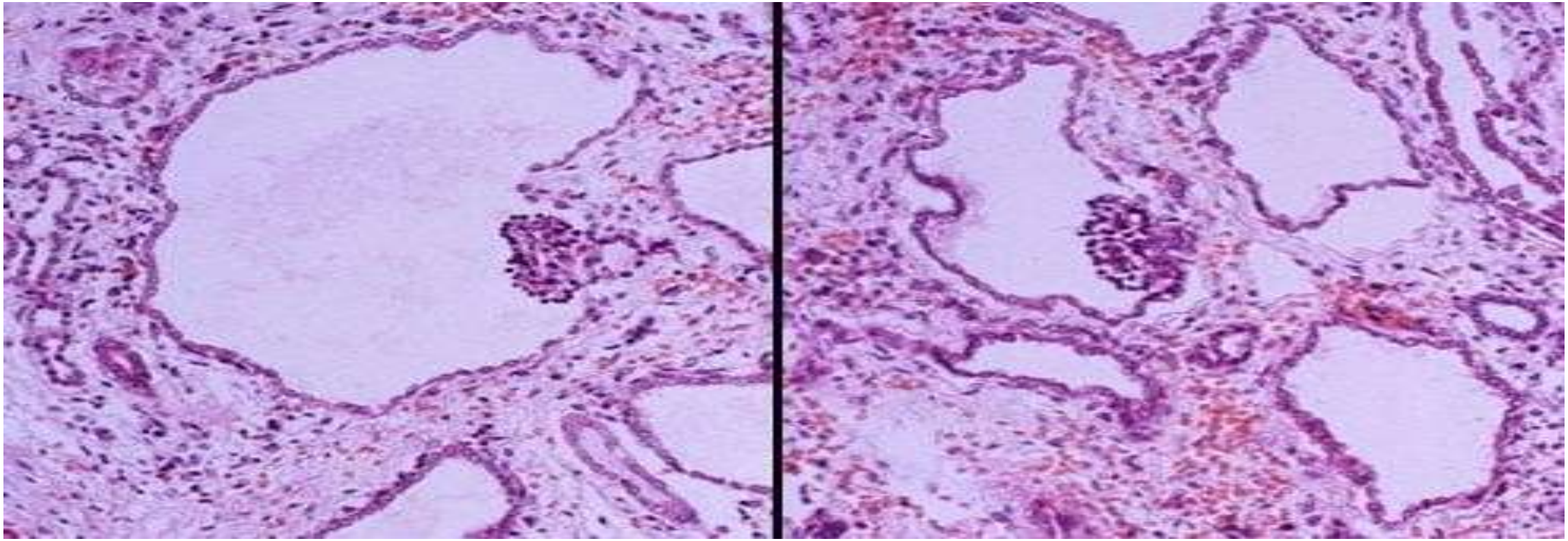
Cysts contain **clear to brown fluid**

Autosomal Dominant (Adult) Polycystic Kidney Disease

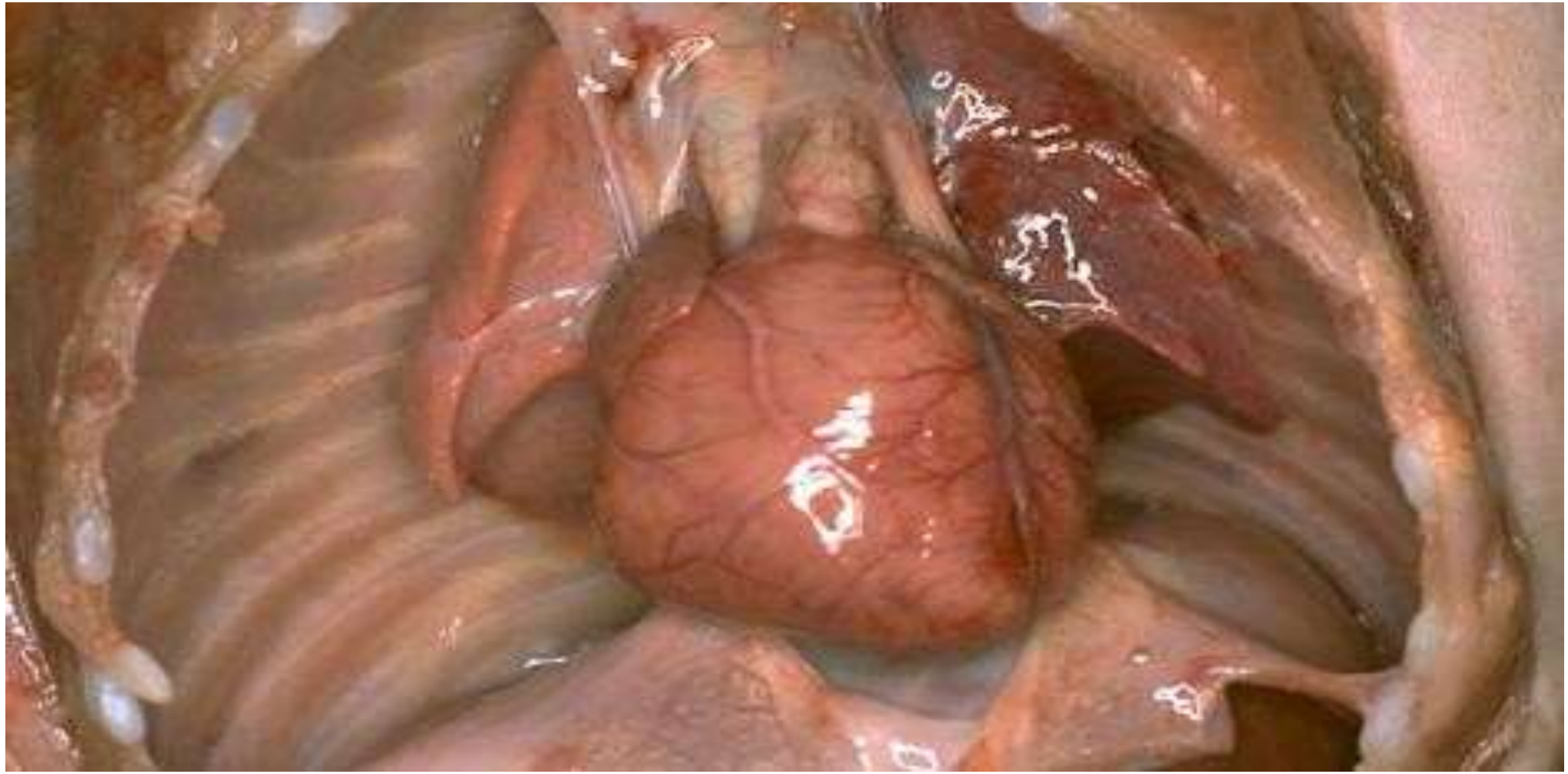




Cysts are lined by **cuboidal or flattened epithelium**



Pulmonary hypoplasia

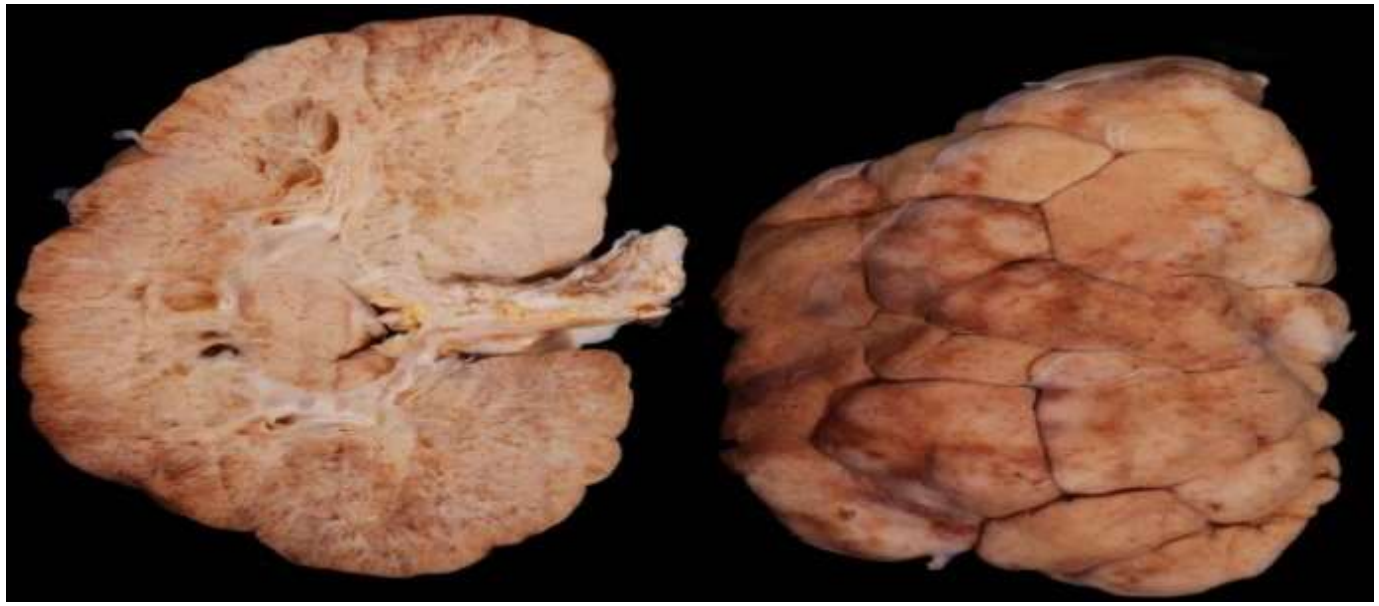


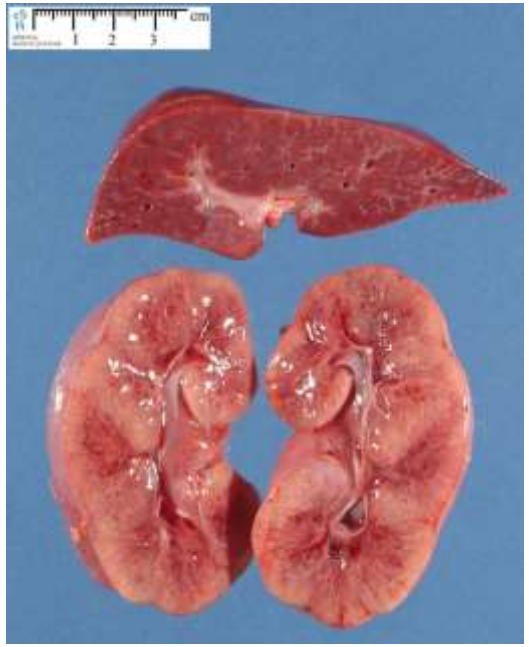
Gross description

Markedly enlarged kidneys with **smooth surface**

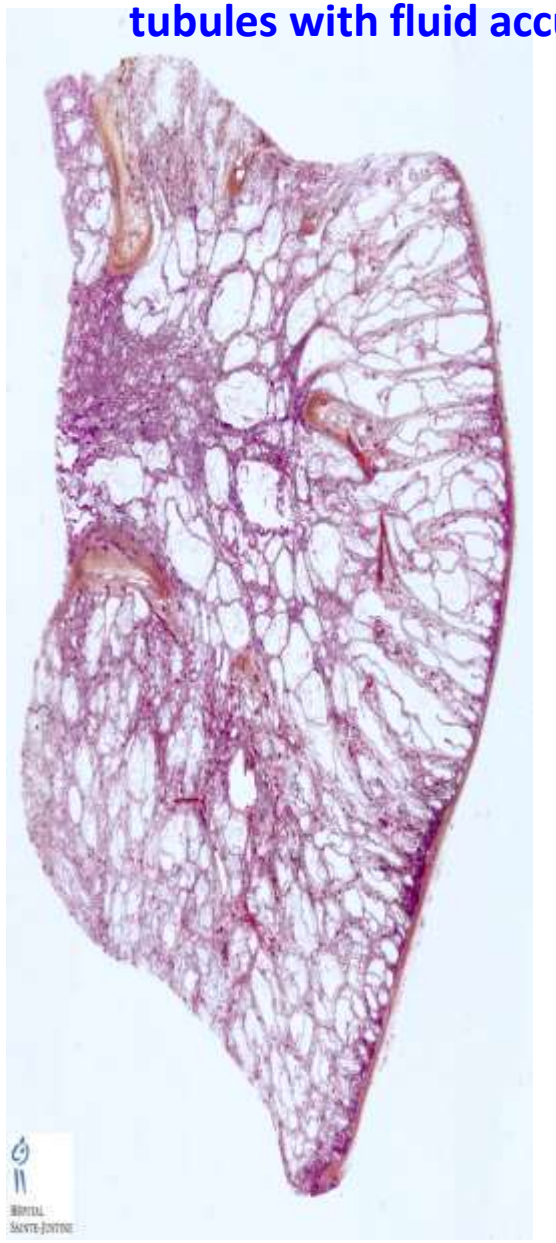
Small cysts in cortex and medulla (collecting ducts)

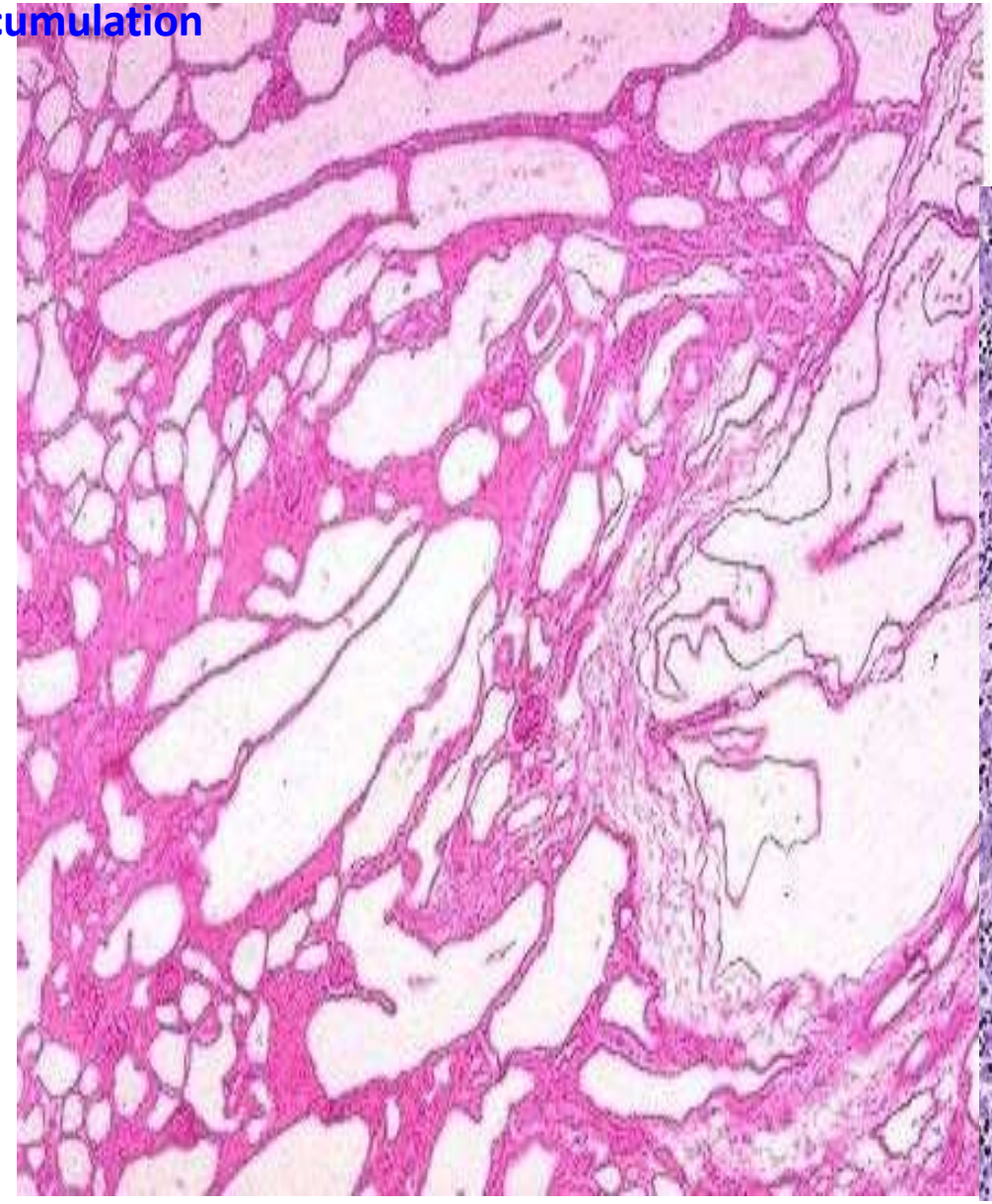
Dilated channels are perpendicular to cortical surface



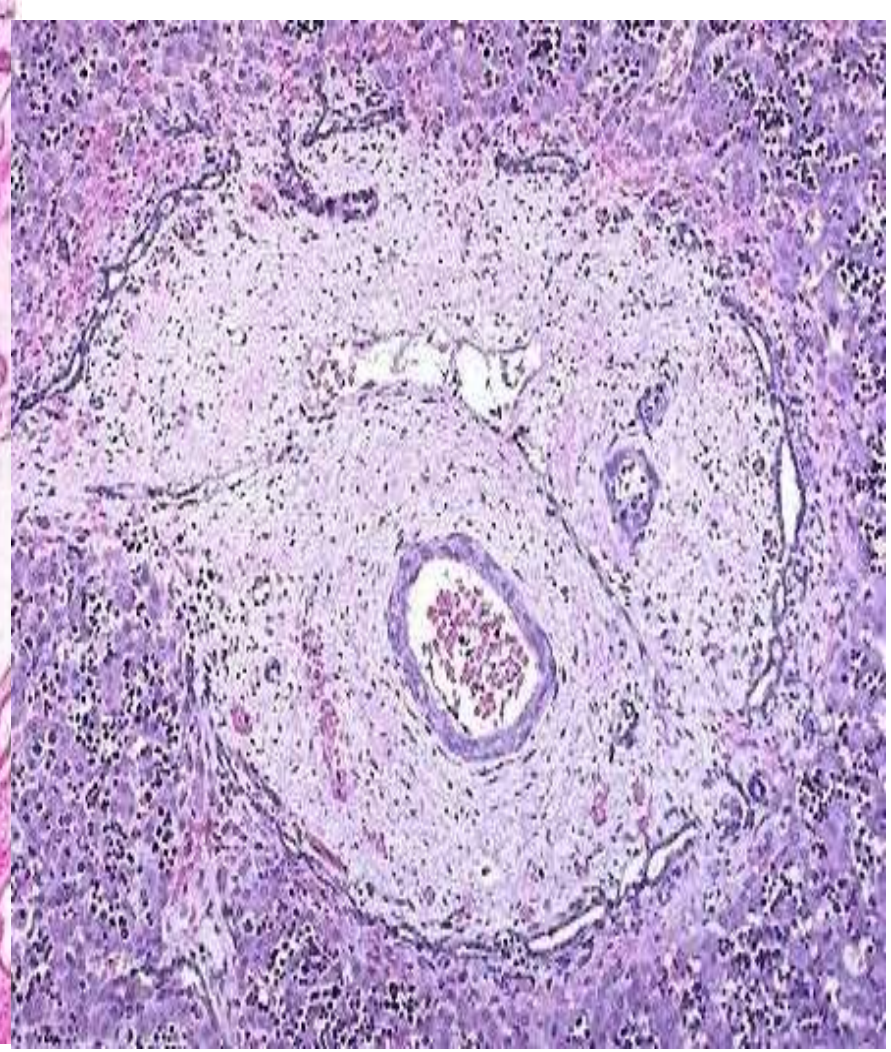


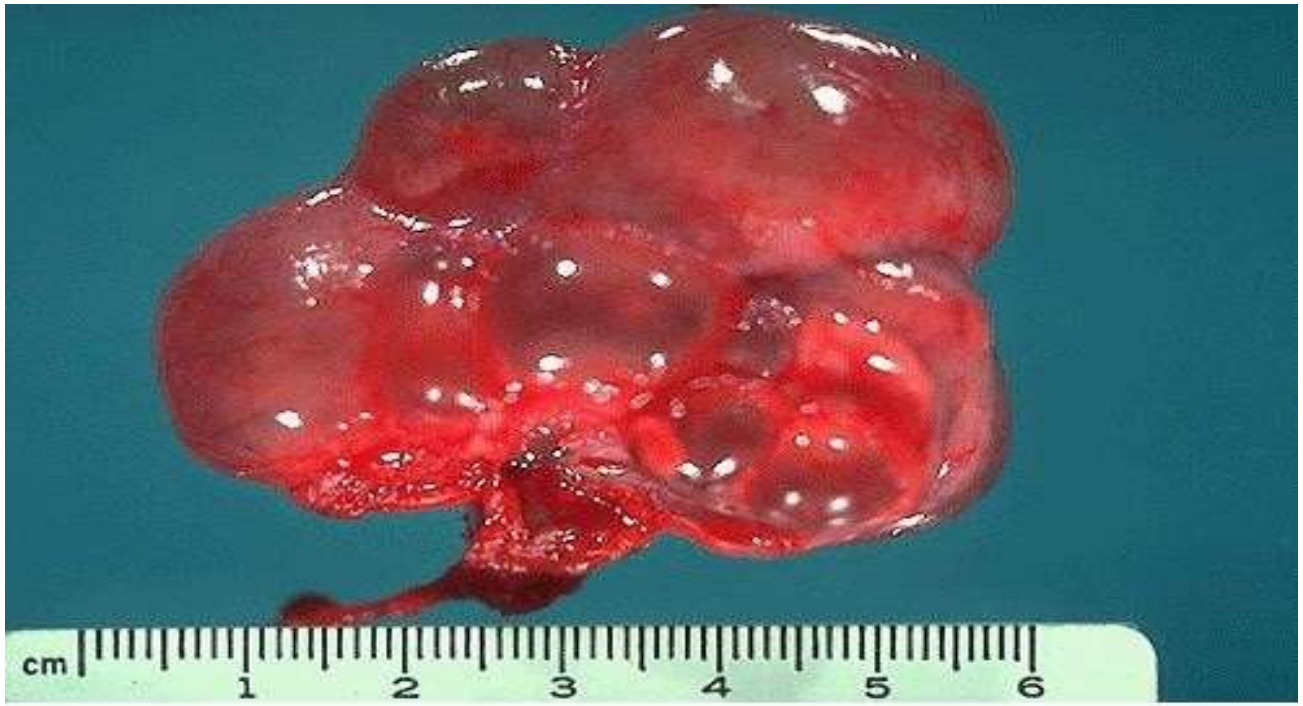
elongated cysts that form as dilations of all collecting tubules with fluid accumulation





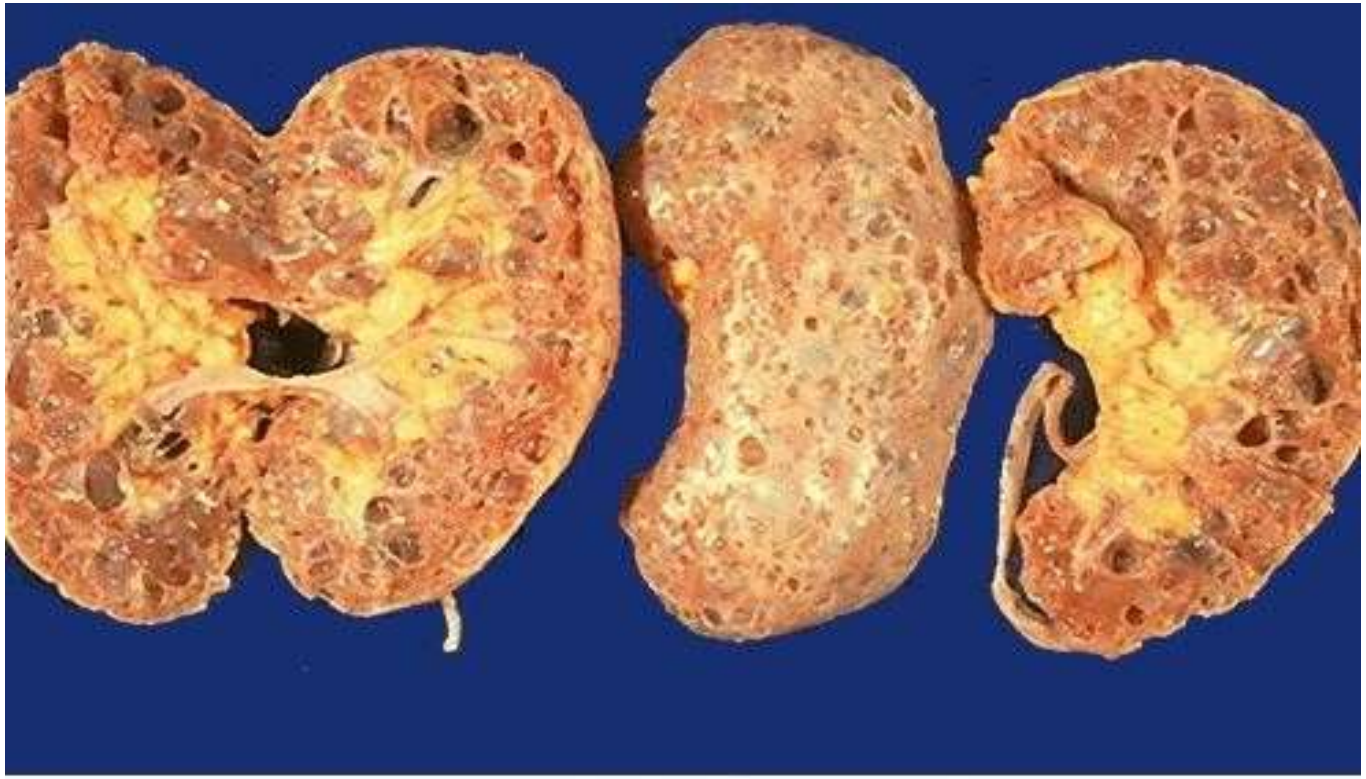
Portal fibrosis



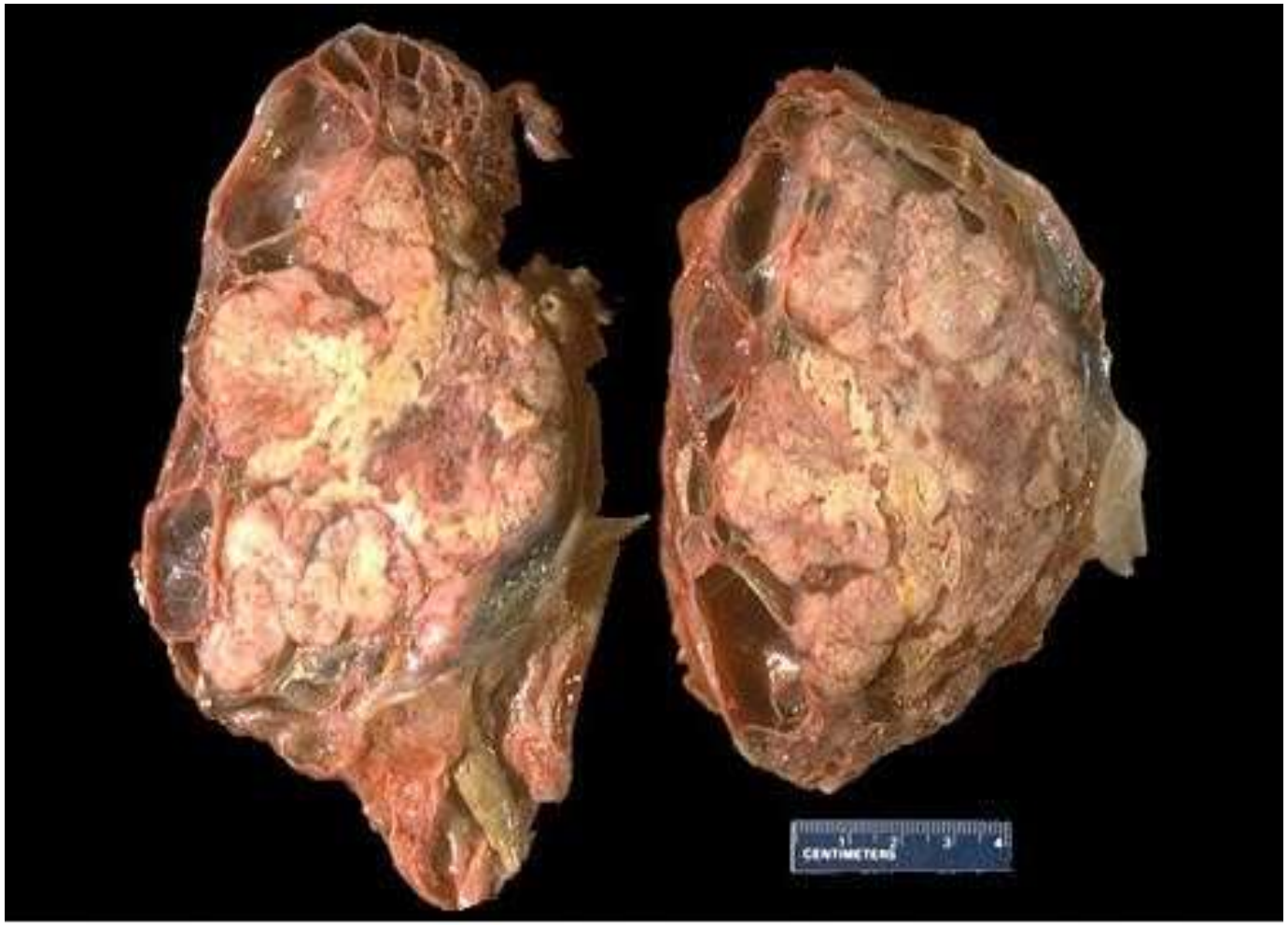


This is a multicystic dysplastic kidney. This condition must be distinguished from ARPKD because it occurs only sporadically and not with a defined inheritance pattern, though it is more common than ARPKD. The cysts of multicystic renal dysplasia are larger and more variably sized than those of ARPKD. Often, multicystic renal dysplasia is unilateral. If bilateral, it is often asymmetric. If bilateral, oligohydramnios and its complications can ensue, just as with ARPKD.

HISTORY OF dialysis



These adult kidneys are about normal in size but have a few scattered **small cysts**, none of which is over 2 cm in size. This is cystic change associated with chronic renal dialysis.

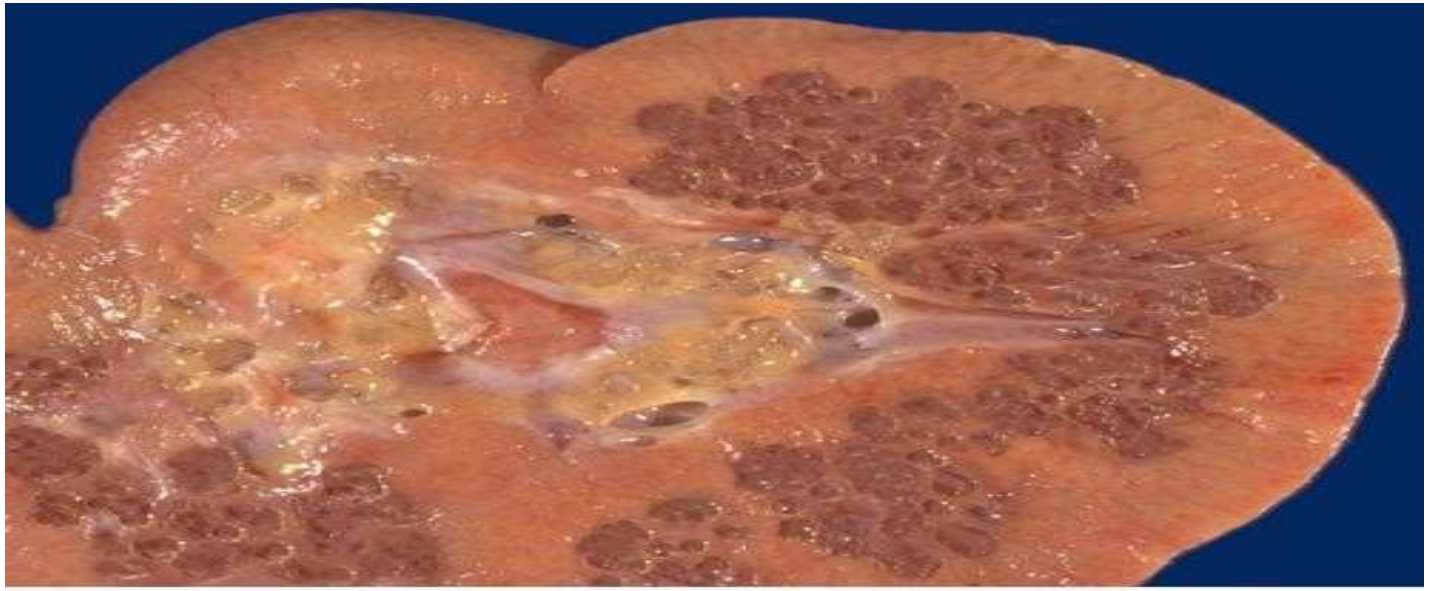


Cystic change resulting from long-term renal dialysis may rarely give rise to renal cell carcinoma. A large irregular tan variegated **mass** is seen here on sectioning of a kidney that has large **cysts** arranged around the mass.

Gross description

Normal sized kidneys with **multiple, small cysts** in **medullary** pyramids and papillae, giving medulla a **sponge-like appearance**

Most often **bilateral**



Note the **0.1 to 0.5 cm cysts** involving the inner medullary and papillary regions in this kidney. Note that the cortex appears normal. This is medullary sponge kidney (MSK), which is congenital, but most often occurs sporadically without a defined inheritance pattern. It is often bilateral, but incidental and found only on radiologic imaging studies, with an incidence of 0.5 to 1% in adults. MSK may become symptomatic in young adults, with onset of recurrent hematuria and/or urinary tract infection as a consequence of formation of calculi, which develop in 60% of cases. Renal failure is unlikely to occur, but may result from severe pyelonephritis.

normal cortex

Simple cyst •

Simple renal cysts, as seen here, have thin walls and are fluid filled. They can be multiple, but they are never as numerous as with polycystic change, and they do not predispose to chronic renal failure or to neoplasia. Such simple cysts become more common as persons become older.

1-Agenesis

Complete absence of renal tissue; unilateral or bilateral

Bilateral agenesis: incompatible with life; associated with large adrenal glands; leads to Potter (oligohydramnios) sequence;

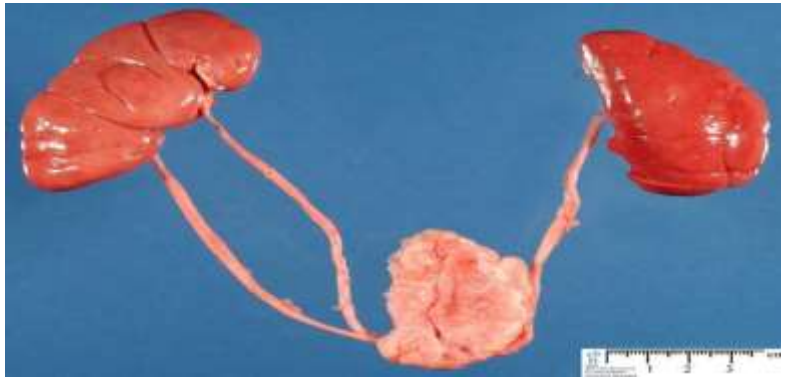
possible causes include maternal insulin dependent diabetes mellitus and male sex of fetus but usually no specific etiology

Unilateral agenesis: not fatal

2-Duplication of ureters

Usually asymptomatic;

may be associated with obstruction



3-Ectopic (displaced) kidneys

Usually **at pelvic brim**,
may have kinking of ureters

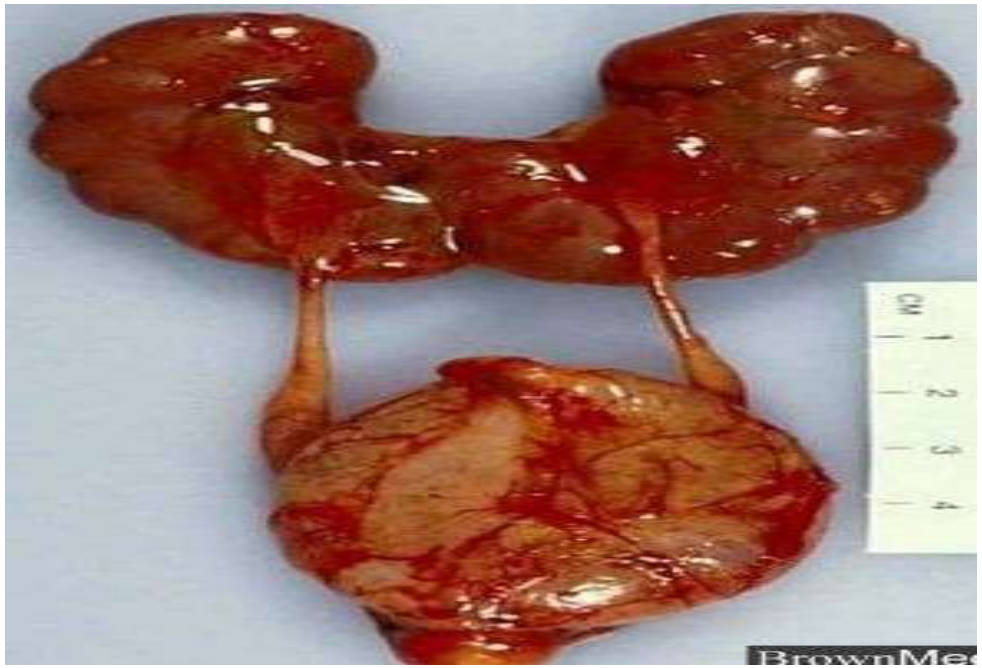
4-Horseshoe kidney

Most common congenital kidney anomaly

90% are fused at **lower** pole

Associated with obstruction, anomalous superior vena cava

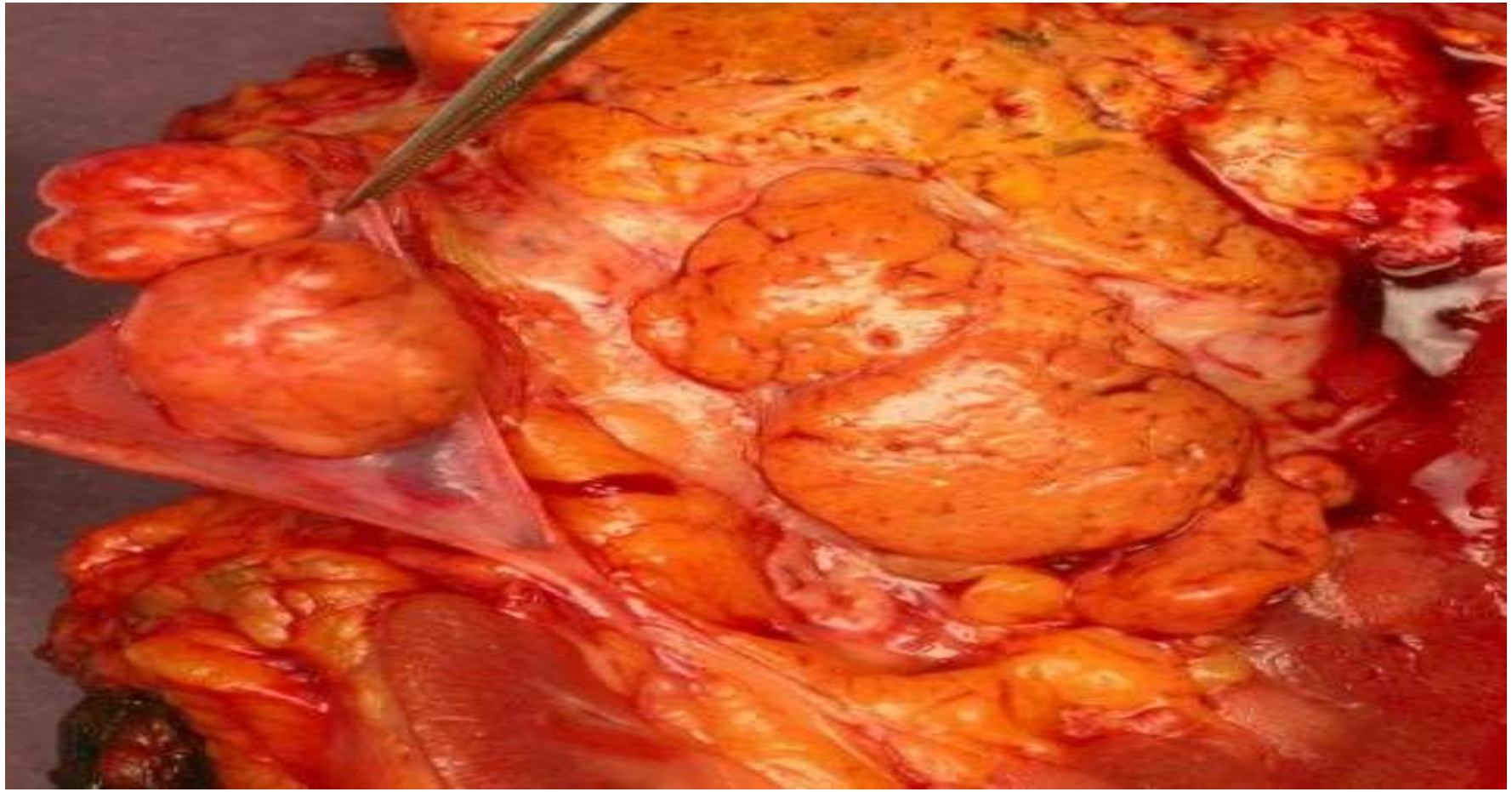
Complete fusion of the kidneys produces a formless mass in the pelvis (**pancake kidney**)



L12 Tumor-of-the-kidney-and-urinary-tractslk

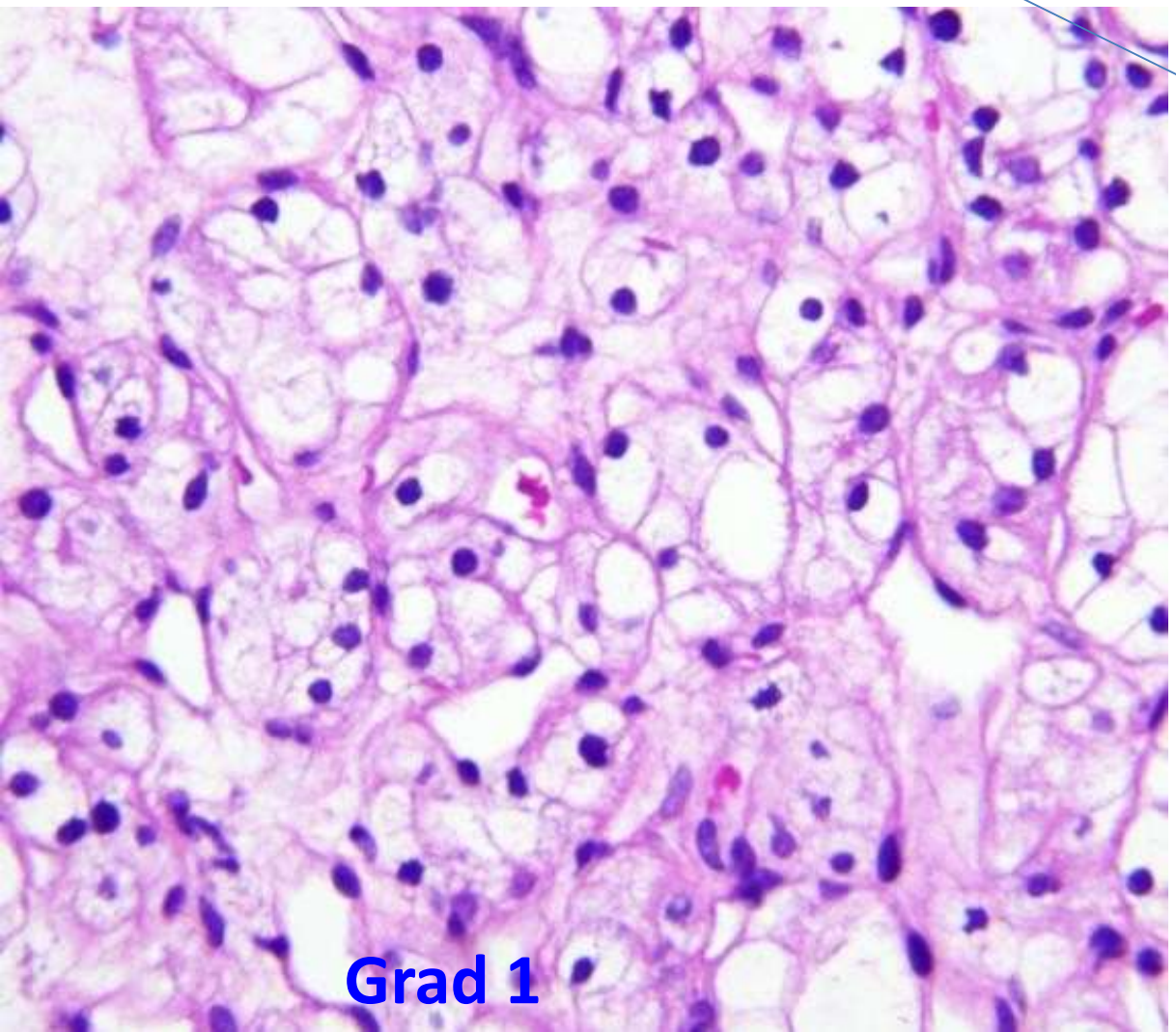
1-Clear Cell Carcinomas

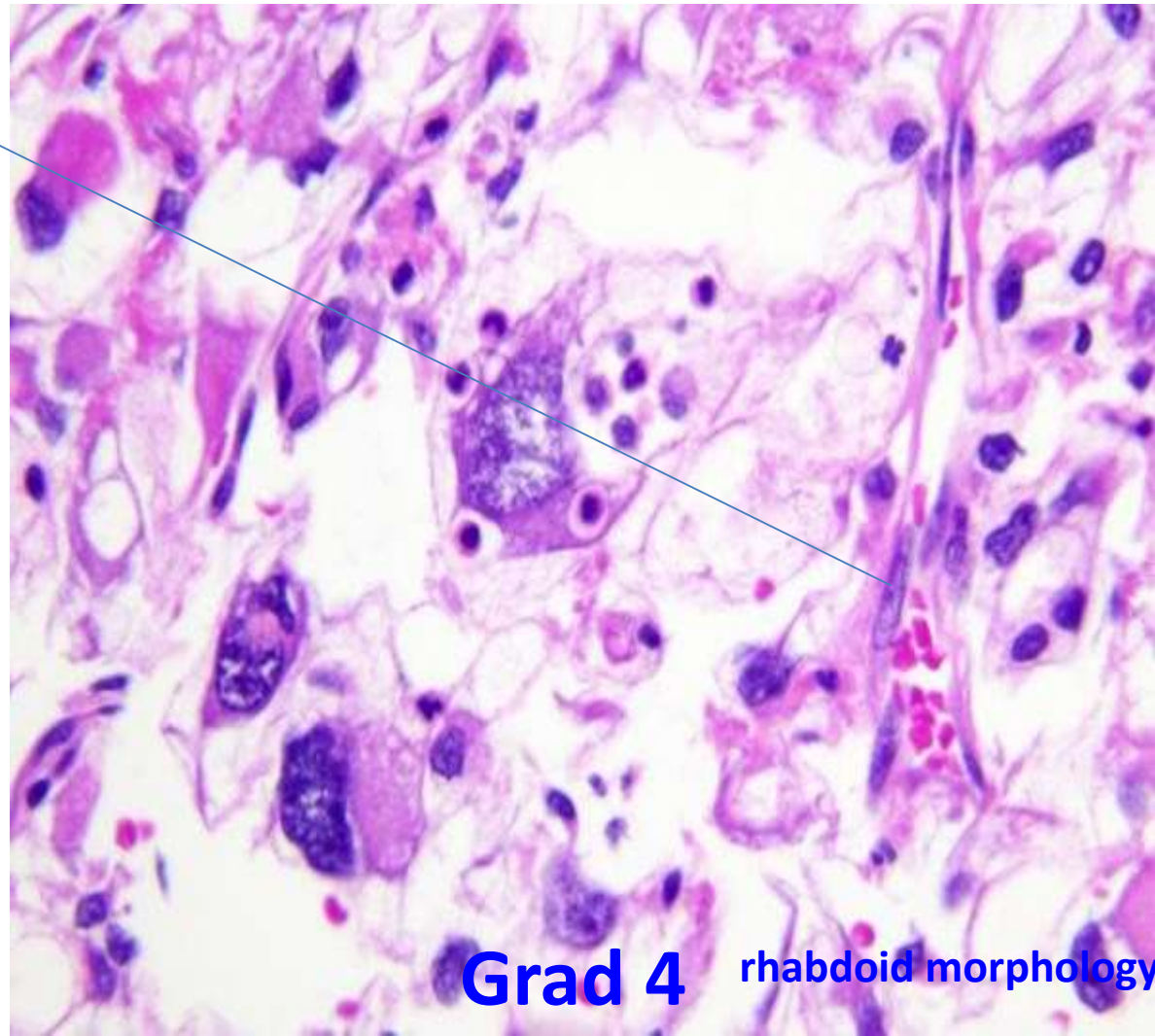
Cortical mass with **golden yellow** cut surface **Lipid contain**



1-Clear Cell Carcinomas

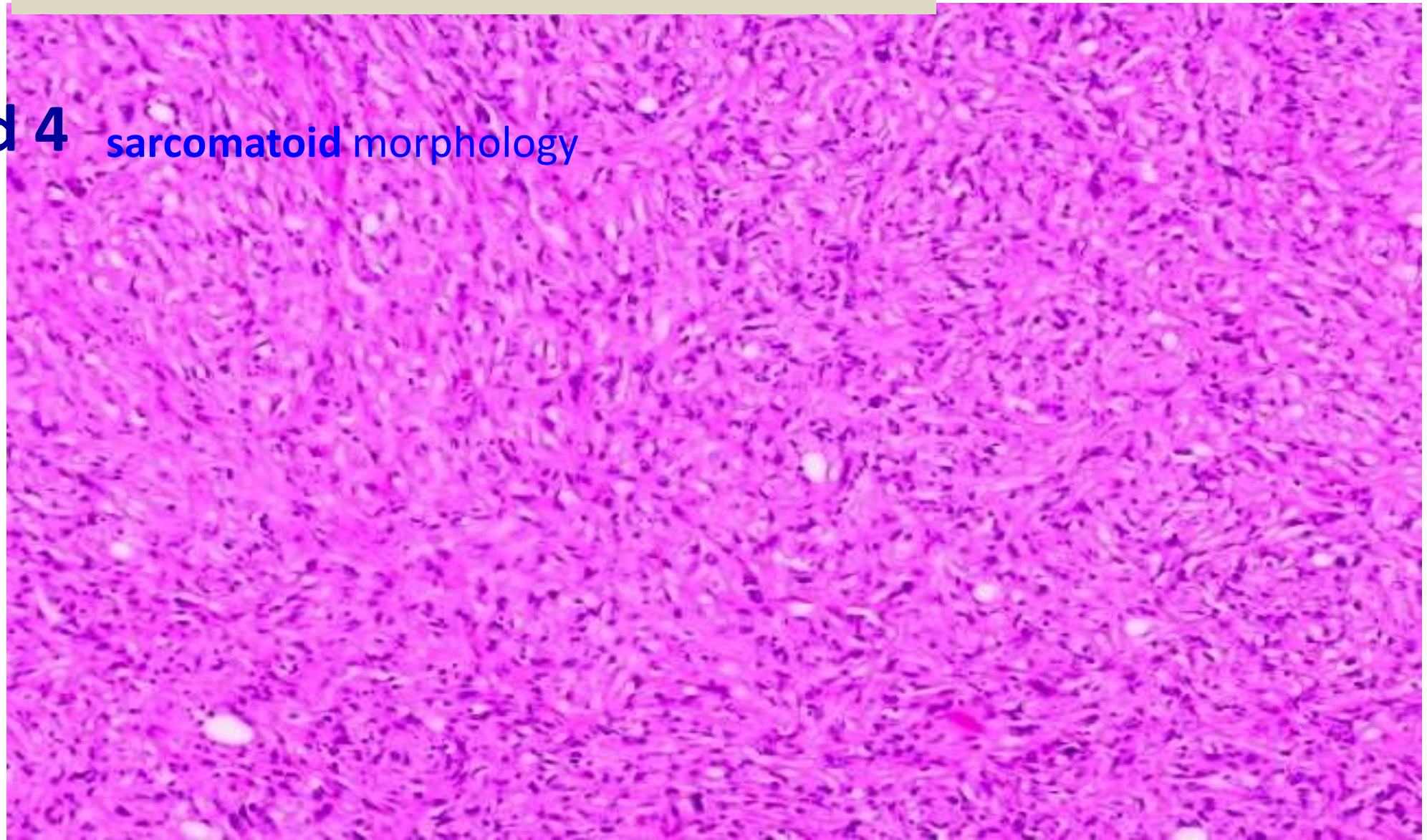
Clear or granular eosinophilic cytoplasm and prominent nucleus but delicate capillary network



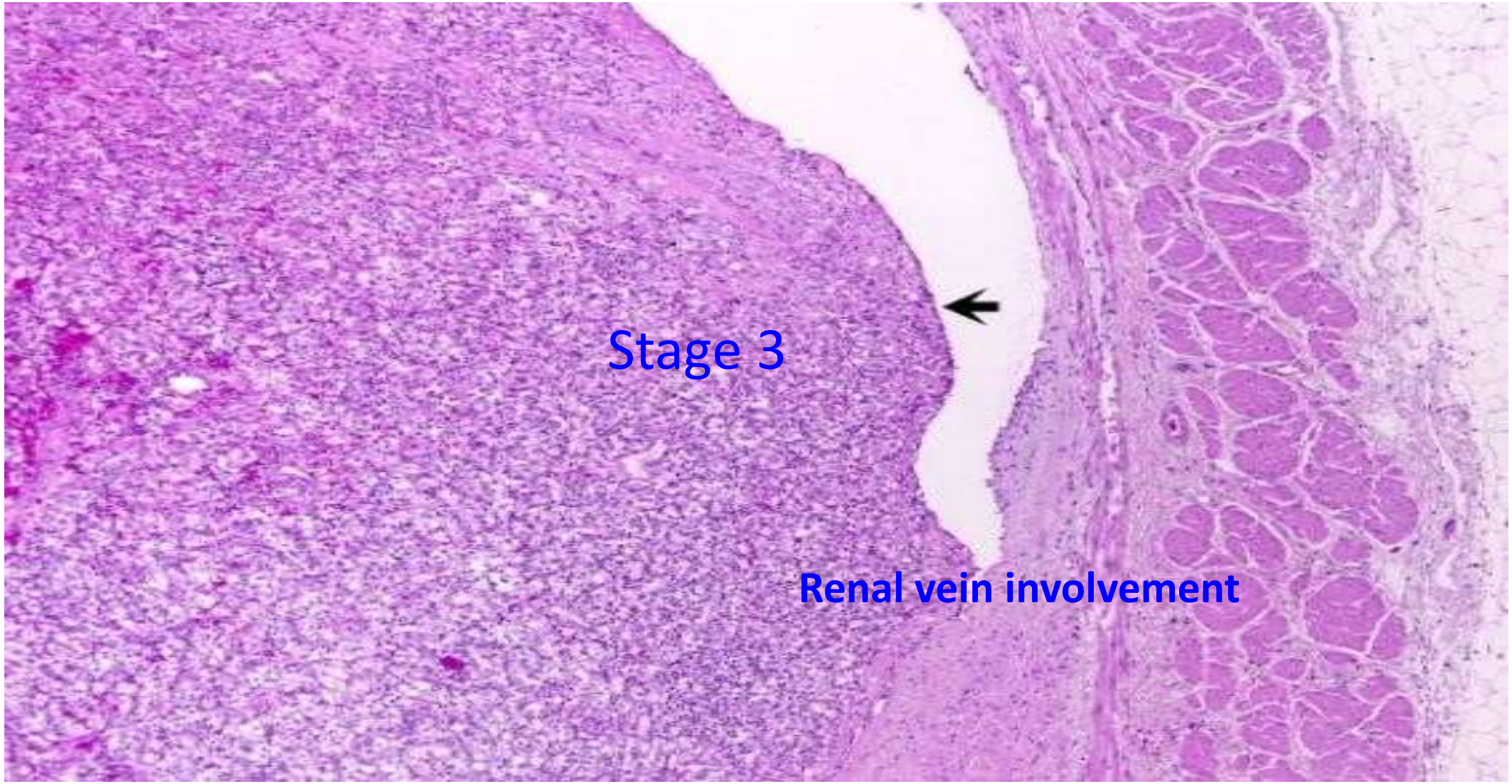


1-Clear Cell Carcinomas

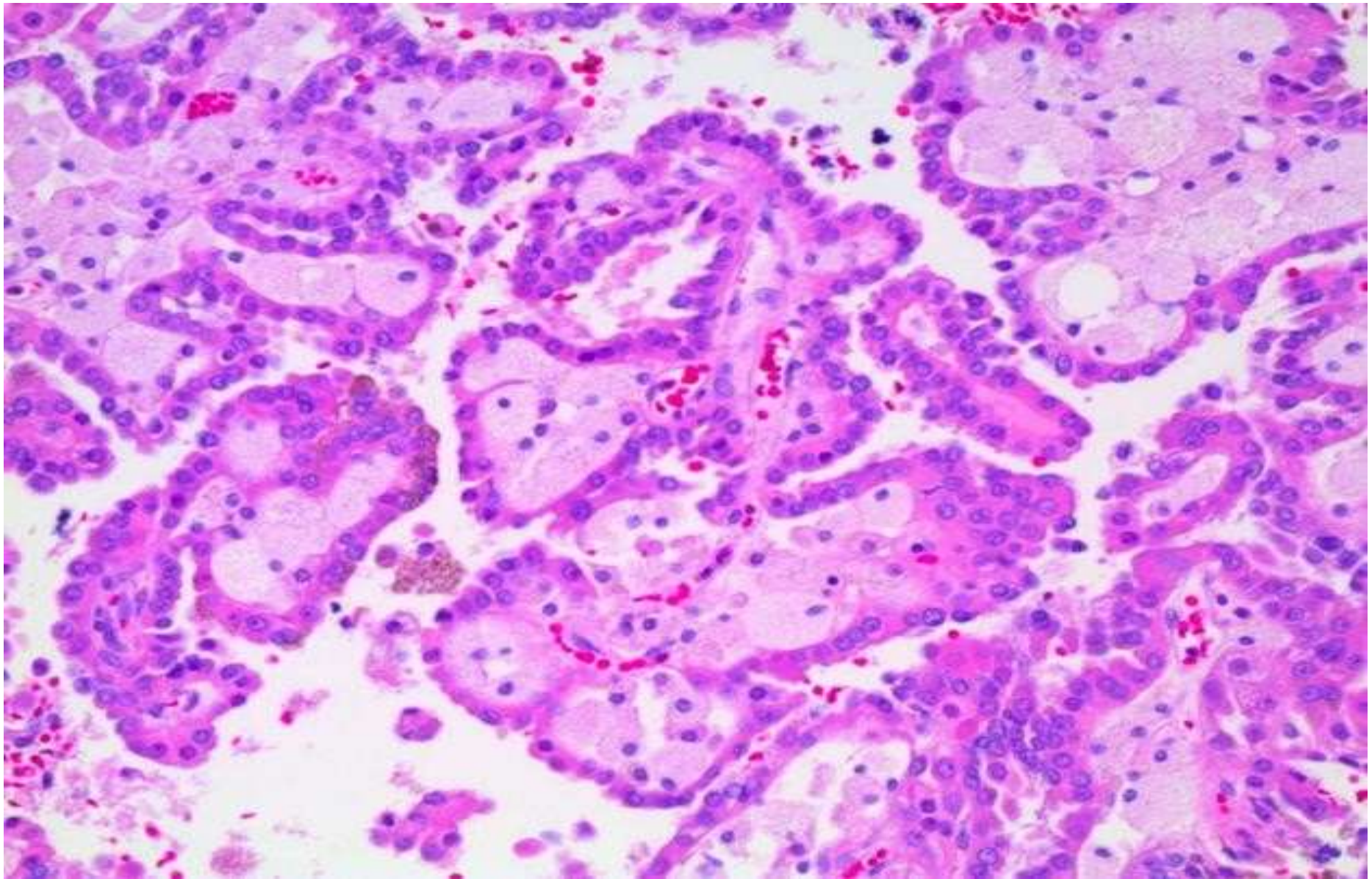
Grad 4 **sarcomatoid** morphology



1-Clear Cell Carcinomas



2-Papillary Renal Cell Carcinomas **TYPE 1**

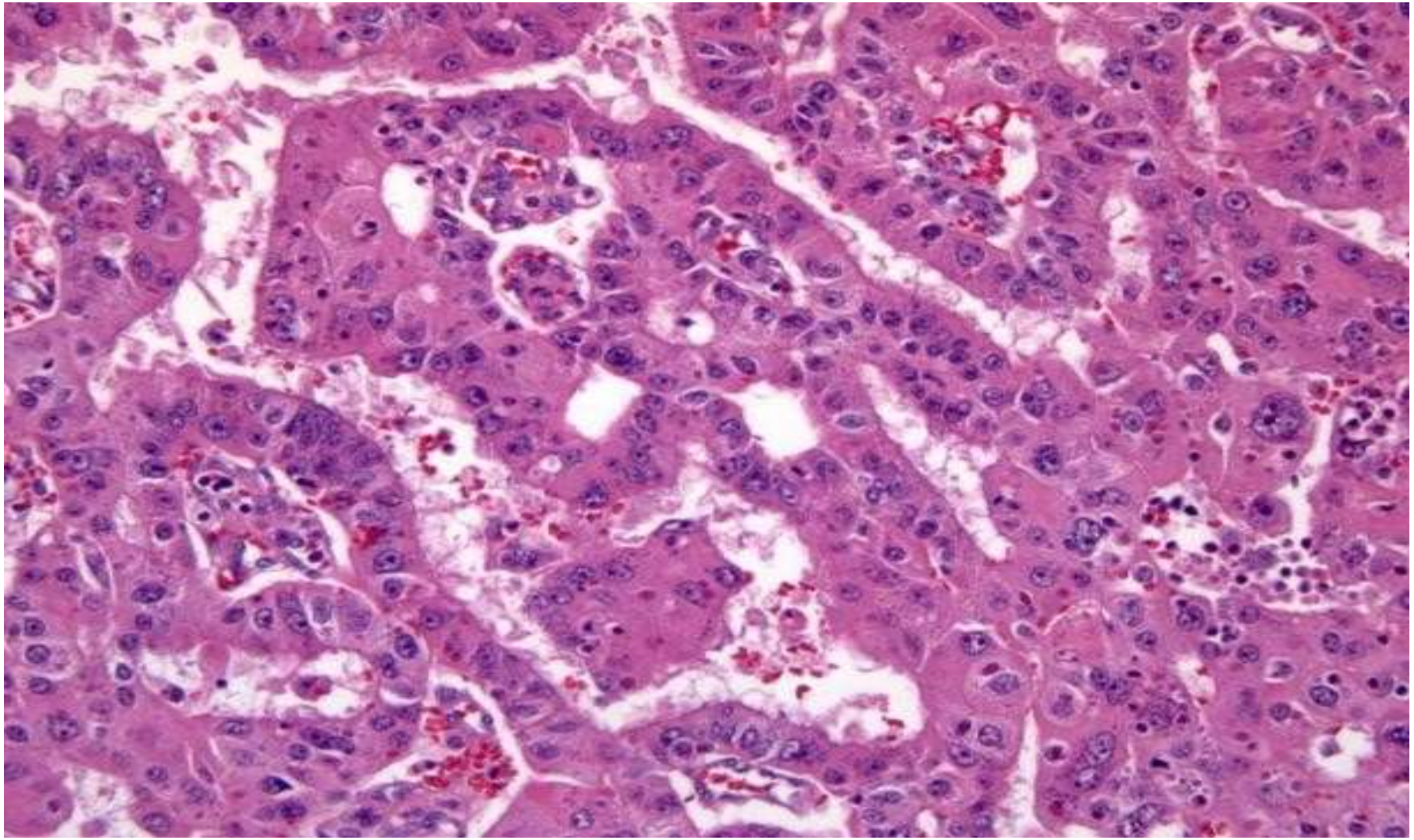


fibro vascular core

2-Papillary Renal Cell Carcinomas

TYPE 2

fibro vascular core



3-Chromophobe Renal Carcinomas

granular pale cells(ESINOPHILIC) with prominent cell borders, finely reticular cytoplasm, perinuclear (halos and wrinkled hyperchromatic nuclei (ABORMAL IN MITOCHENDIA

COLLOID iRON STAIN +

3-Chromophobe Renal Carcinomas

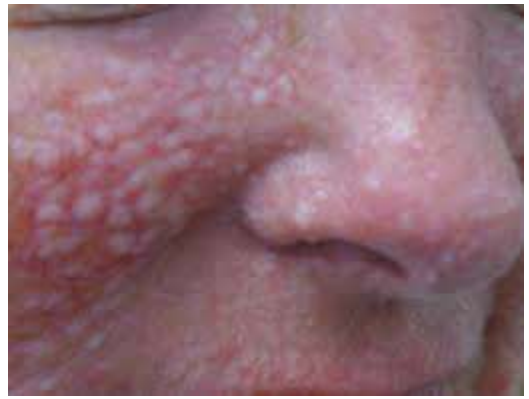
Birt-Hogg-Dubé syndrome

Multiple tumors (mean 5.3); mean age 51 years at first renal tumor diagnosis

Bilateral multifocal ChRCC, oncocytomas or hybrid oncocytic chromophobe tumor (HOCT), also may have oncocytosis

Autosomal dominant syndrome: small dome shaped papular fibrofolliculomas of face, neck and upper trunk, renal tumors, lung cysts and spontaneous pneumothorax

Mutations in the ***folliculin gene*** (*FLCN*) at 17p11.2.



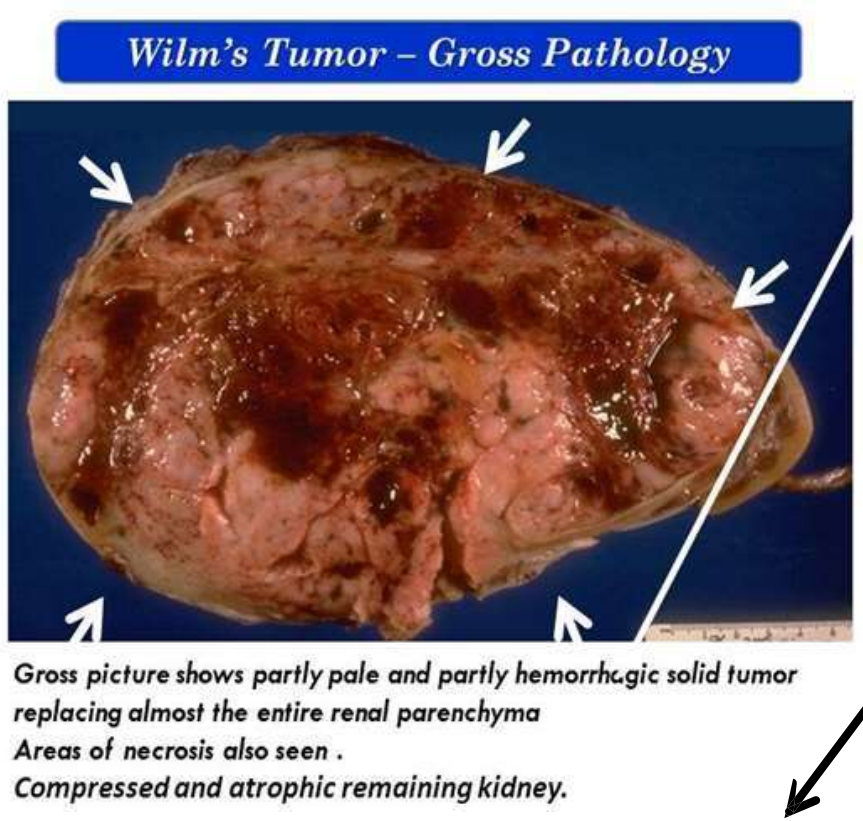
Wilms Tumor: Nephroblastoma

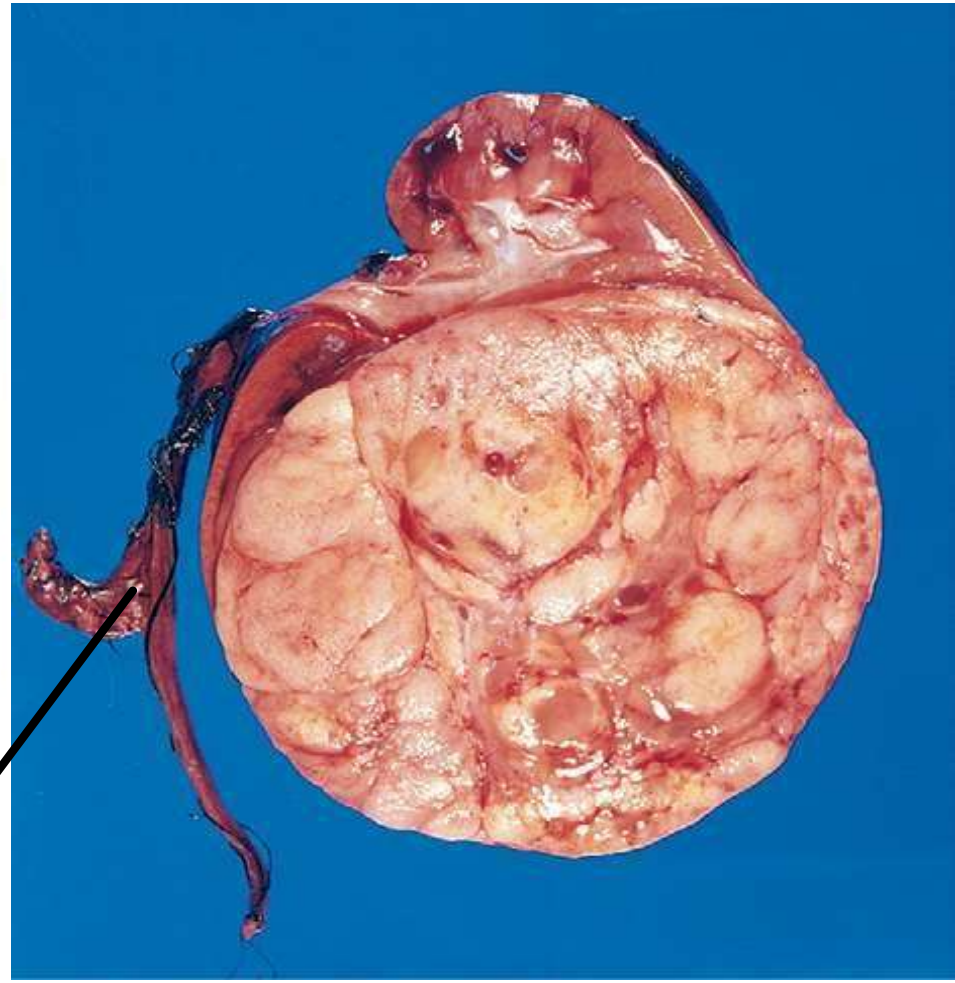
Morphology

Gross:

Large, solitary, well-circumscribed tan to gray mass.

Occasionally:Foci of Hg, cystic degeneration, necrosis.

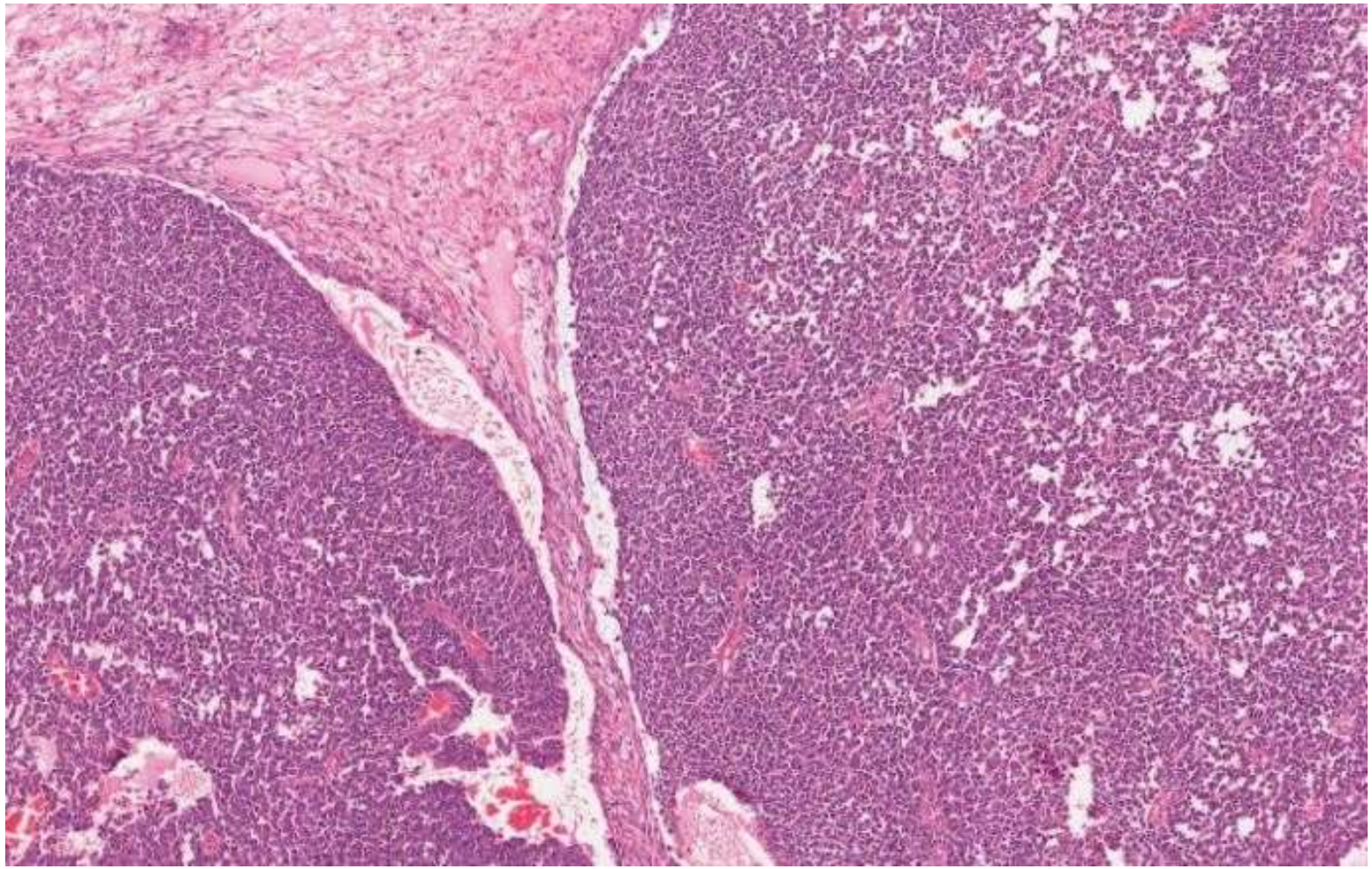




Wilms Tumor (nephroblastoma)

Blastemal component

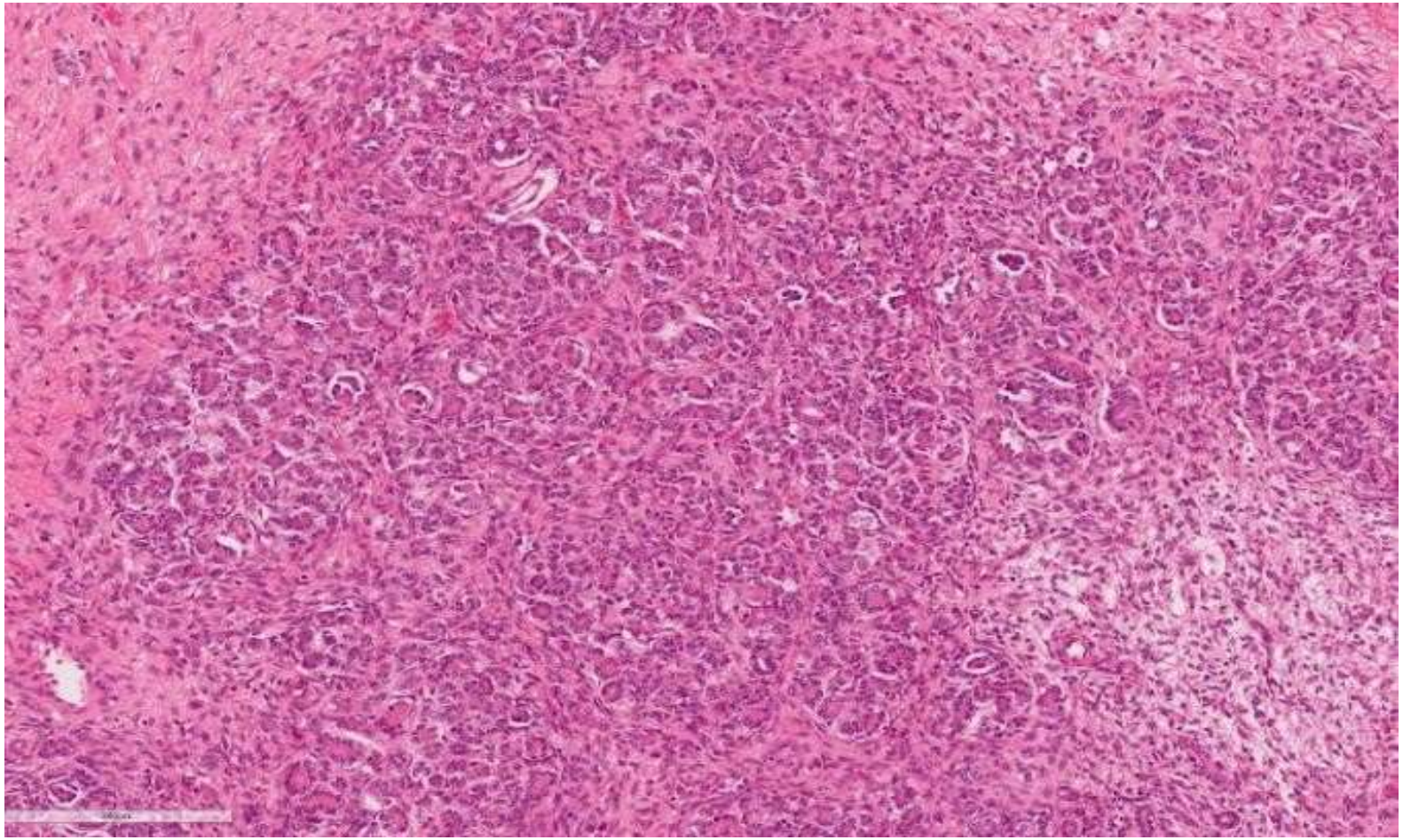
Sheets of small blue cells



*Wilms Tumor (*nephroblastoma)

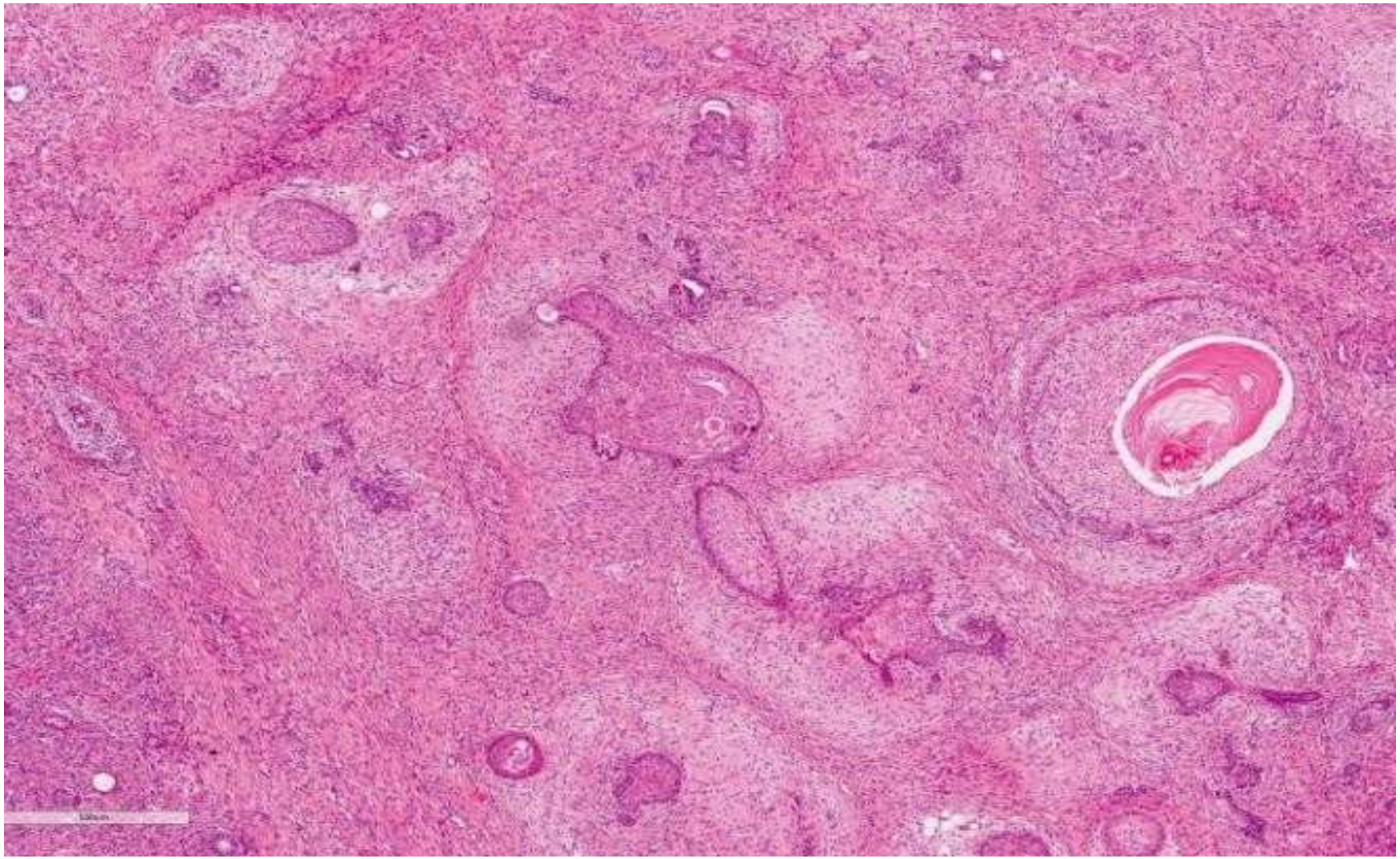
Epithelial component

usually takes the form of **abortive tubules or glomeruli**



Stromal component

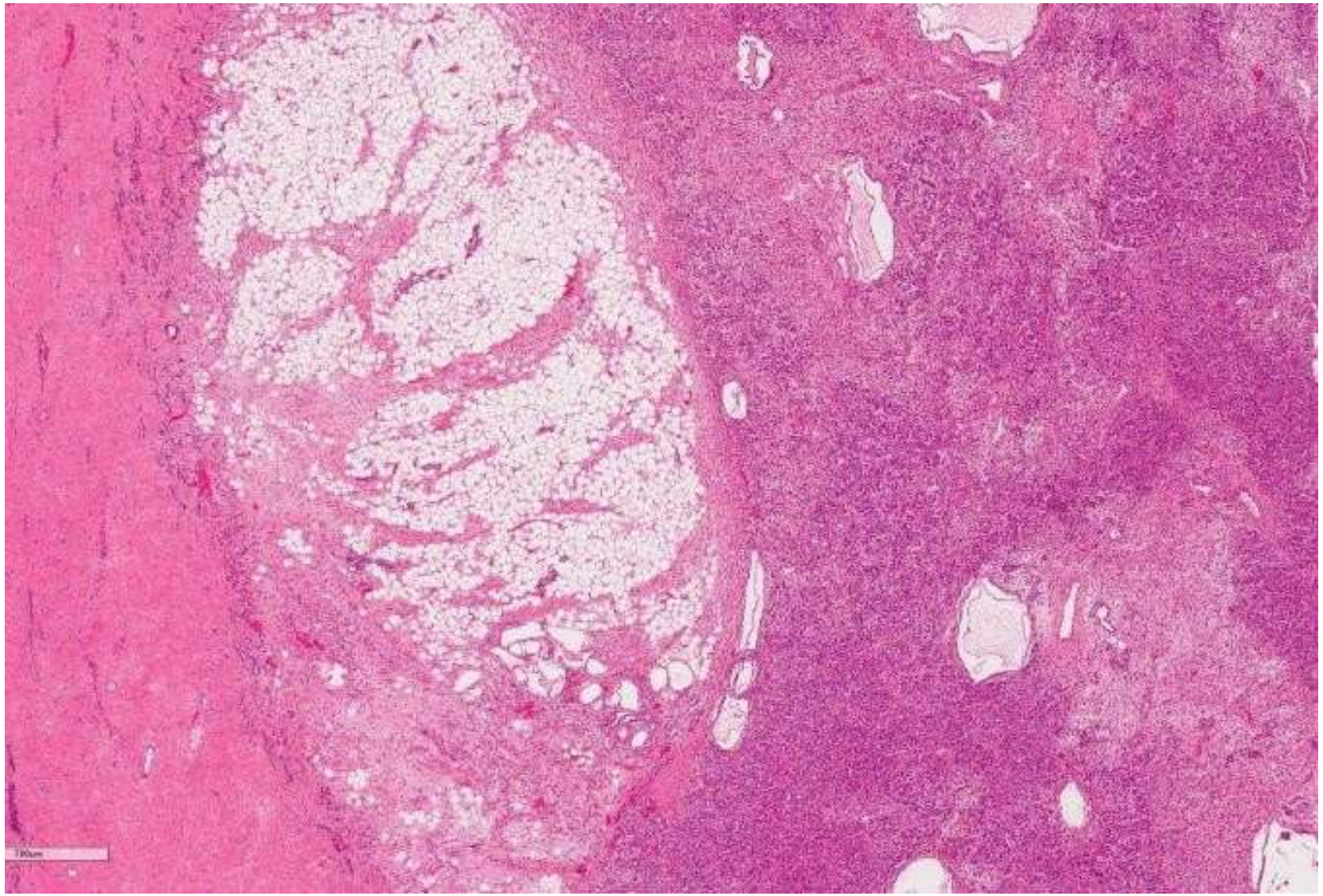
Fibrous myxoid cartilage muscle .



Wilms Tumor (nephroblastoma)

Stromal component

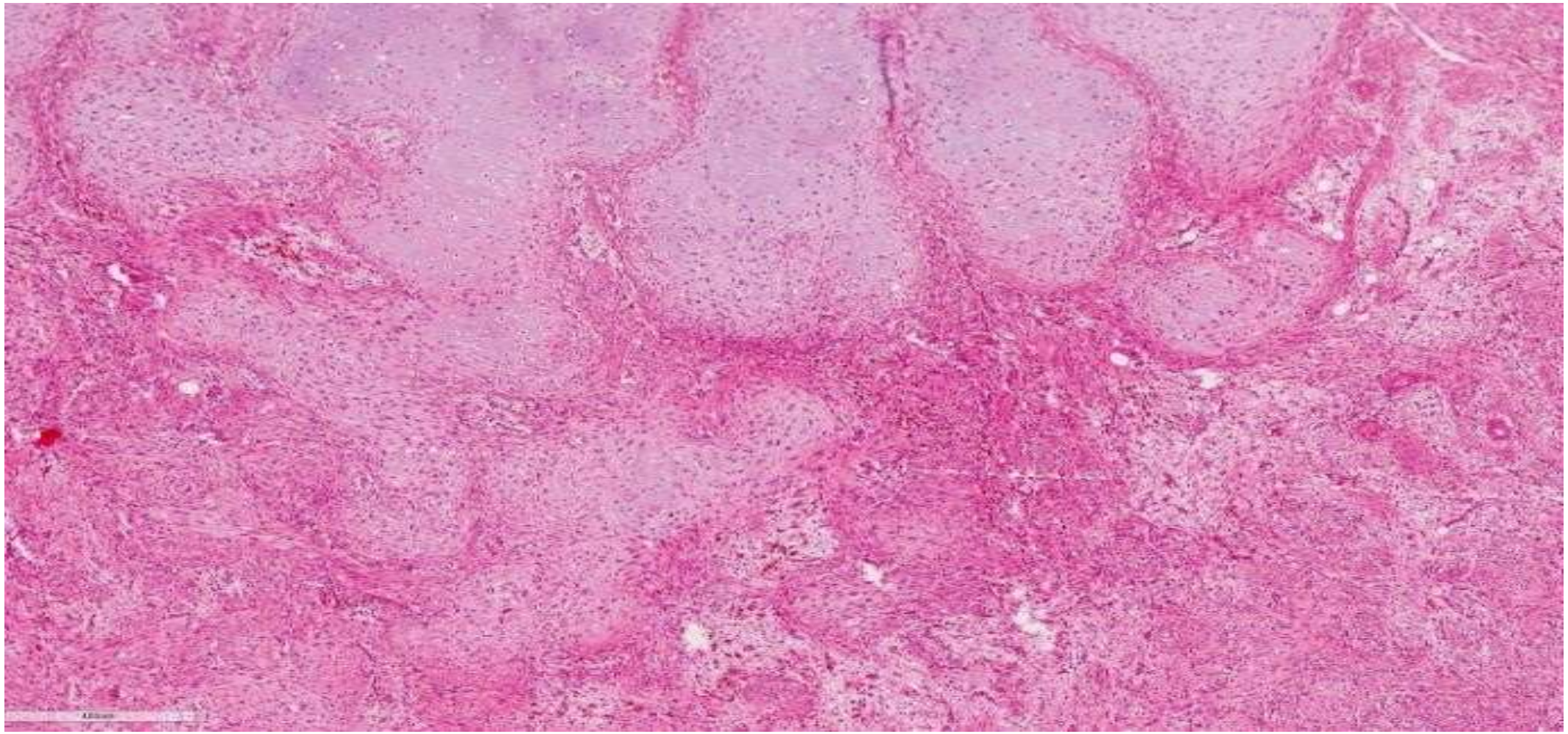
Fat



Wilms Tumor (nephroblastoma)

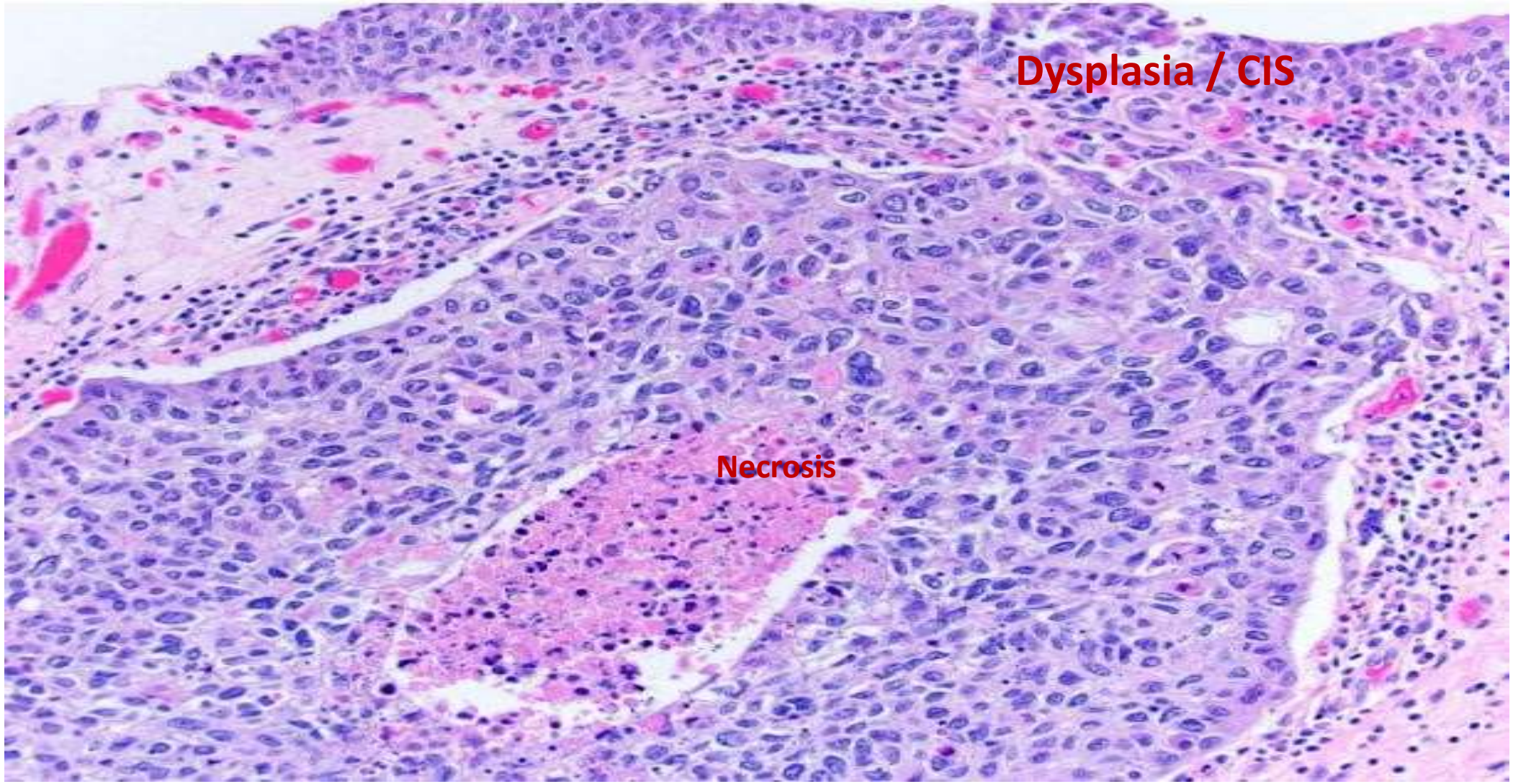
Stromal component

Cartilage



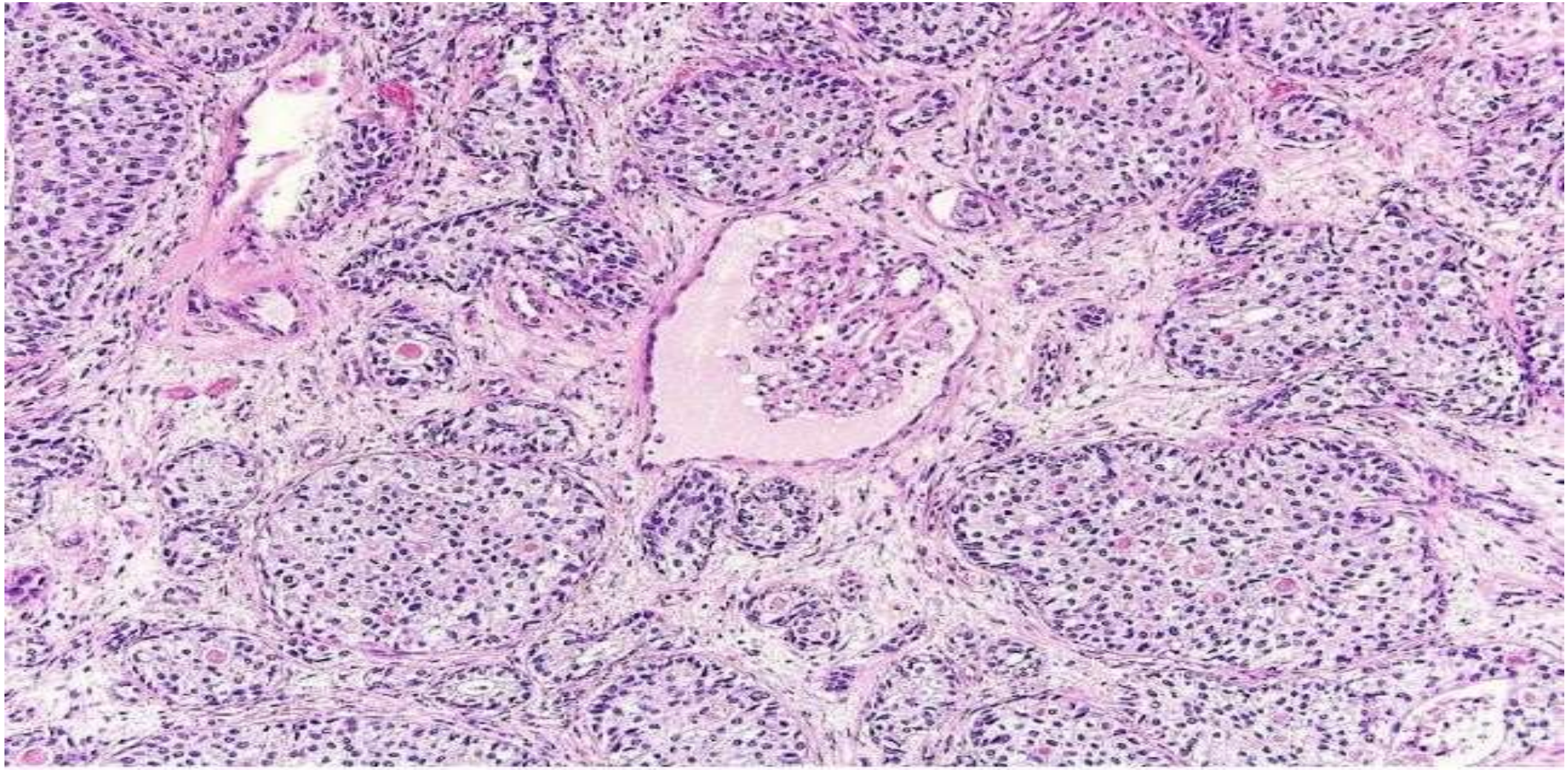
urothelial carcinomas

HIGH GRAD



urothelial carcinomas

LOW GRAD



Squamous cell carcinomas

related to Schistosoma infections in areas where it is endemic