RENAL PATHOLOGY 6

MEDULLARY CYSTIC DISEASE

- 2 major types:
- **1-medullary sponge kidney**
- common and innocent (Harmless ,Inoccuous) condition.
- **2- nephronophthisis-medullary cystic disease complex**
- almost always associated with renal dysfunction.
- usually begins in childhood.
- **Cysts are at cortico-medullary junction**
- **In aggregate**, the various forms of nephronophthisis are now thought to be **the most common genetic cause of end-stage renal disease in children & young adults.**

MEDULLARY CYSTIC DISEASE

- • Four variants of this disease complex are recognized on the basis of the time of onset: **infantile, juvenile, adolescent, & adult.**
- **The juvenile form is the most common.**
- **• 5% to 20% of individuals with juvenile nephronophthisis have extra-renal manifestations, which mostly appear as retinal abnormalities.**

MORPHOLOGY OF MEDULLARY CYSTIC DISEASE

- **Grossly**
- **the kidneys are small & contracted.**
- **Histopathology:**
- numerous small cysts lined by flattened or cuboidal epithelium are present, **typically at the cortico-medullary junction.**

CLINICAL MANIFESTATIONS OF MEDULLARY CYSTIC DISEASE

- **Clinical features:**
- polyuria and polydipsia (↓ tubular function).
- renal failure over 5- 10- year
- The disease is difficult to diagnose, Because
- (1) no serologic markers &
- (2) the cysts may be too small to be seen with radiologic imaging or
- (3) cysts may not be apparent on renal biopsy if the cortico- medullary junction is not well sampled.
- **A positive family history & unexplained CRF in young patients** should lead to suspicion of **nephronophthisis-medullary cystic disease complex.**

URINARY OUTFLOW OBSTRUCTION

- **Renal Stones (Urolithiasis)**
- Stone formation at any level in the urinary collecting system.
- Most common in kidney.
- • (1%) of all autopsies.
- Symptomatic more common in men .
- Familial tendency toward stone formation.
- Unilateral in 80%.
- • Variable sizes.
- Stone = inorganic salt (98%) + organic matrix (2%)

RENAL STONES (UROLITHIASIS)

- **Types are according to inorganic salt:**
- 1- calcium oxalate/ calcium oxalate+ calcium phosphate- - (80%) .
- 2- Struvite (magnesium ammonium phosphate)
- 3- uric acid (6- 7%)
- 4- cysteine stones (2%)

RENAL STONES (UROLITHIASIS)

- **Causes of Renal Stones**
- **1-increased urine concentration of stone's constituentsexceeds solubility in urine (supersaturation).**
- 50% of calcium stones pts have hypercalciuria with no hypercalcemia.
- 5% to 10% hypercalcemia and hypercalciuria due to hyperparathyroidism, vitamin D intoxication, or sarcoidosis.
- **2-The presence of a nidus:**
- **Urates provide a nidus for calcium deposition.**
- **Desquamated epithelial cells**
- **Bacterial colonies**
- **3-urine pH**
- **4-infection**

RENAL STONES (UROLITHIASIS)

- Magnesium ammonium phosphate (struvite) stones staghorn shaped stones (**almost always occur in persons with persistently alkaline urine due to UTIs, specially, due to urea-splitting bacteria, such as Proteus vulgaris& the staphylococci.**
- Uric acid stones form in acidic urine (under pH 5.5).
- **Gout** & diseases involving rapid cell turnover, such as the leukemia's, lead to high uric acid levels in the urine & the possibility of **uric acid stones.**
- **However 50% of the individuals with uric acid stones have neither hyperuricemia nor urine urate but, an unexplained persistent excretion of acidic urine.**
- **Cystine stones** are almost invariably **associated with a genetically determined defect** in the renal transport of cysteine amino acid.

Oxalate calculus. Large, hard, spherical stone with rough **spiny** surface

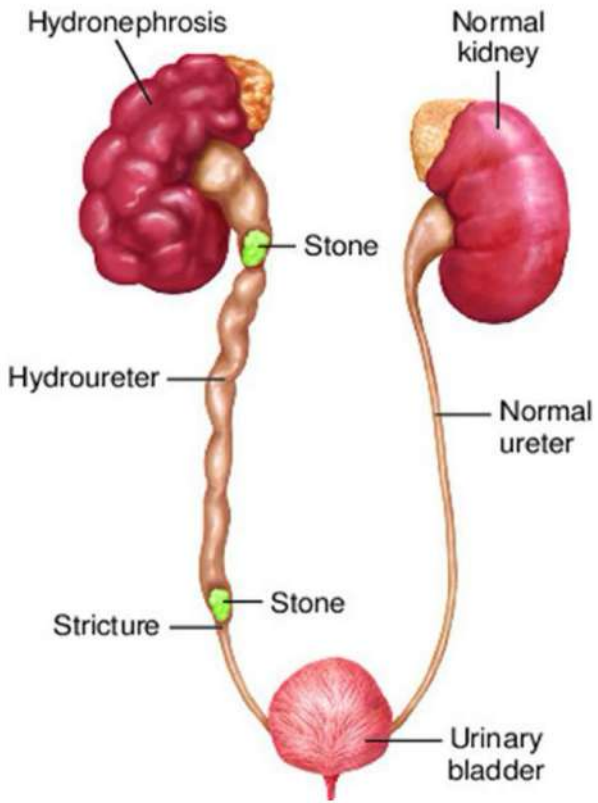
HYDRONEPHROSIS

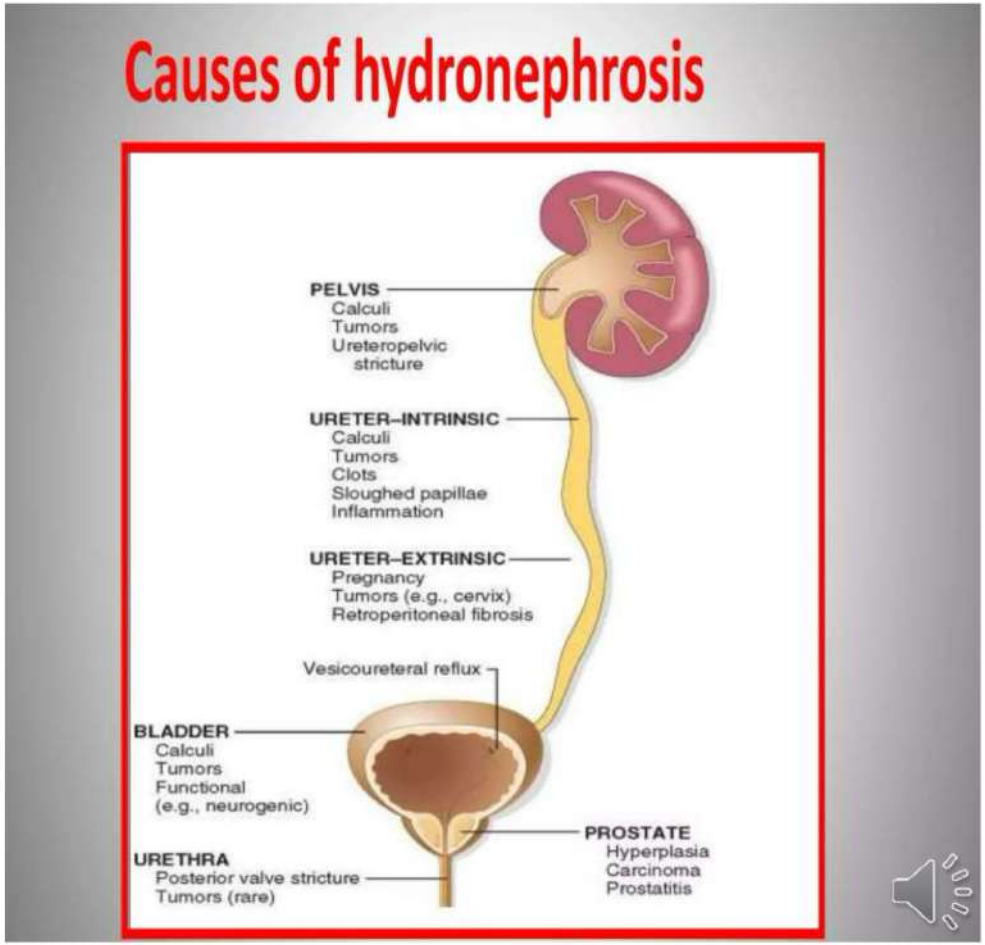
- Is dilation of the renal pelvis and calyces due to obstruction, with accompanying atrophy of kidney parenchyma.
- Sudden or insidious
- Obstruction at any level from the urethra to the renal pelvis.

HYDRONEPHROSIS

- **The most common causes are :**
- **1-Congenital: examples**
- •Atresia of urethra
- •Valve formations in ureter or urethra
- •Aberrant renal artery compressing ureter
- •Renal ptosis with torsion or kinking of ureter.

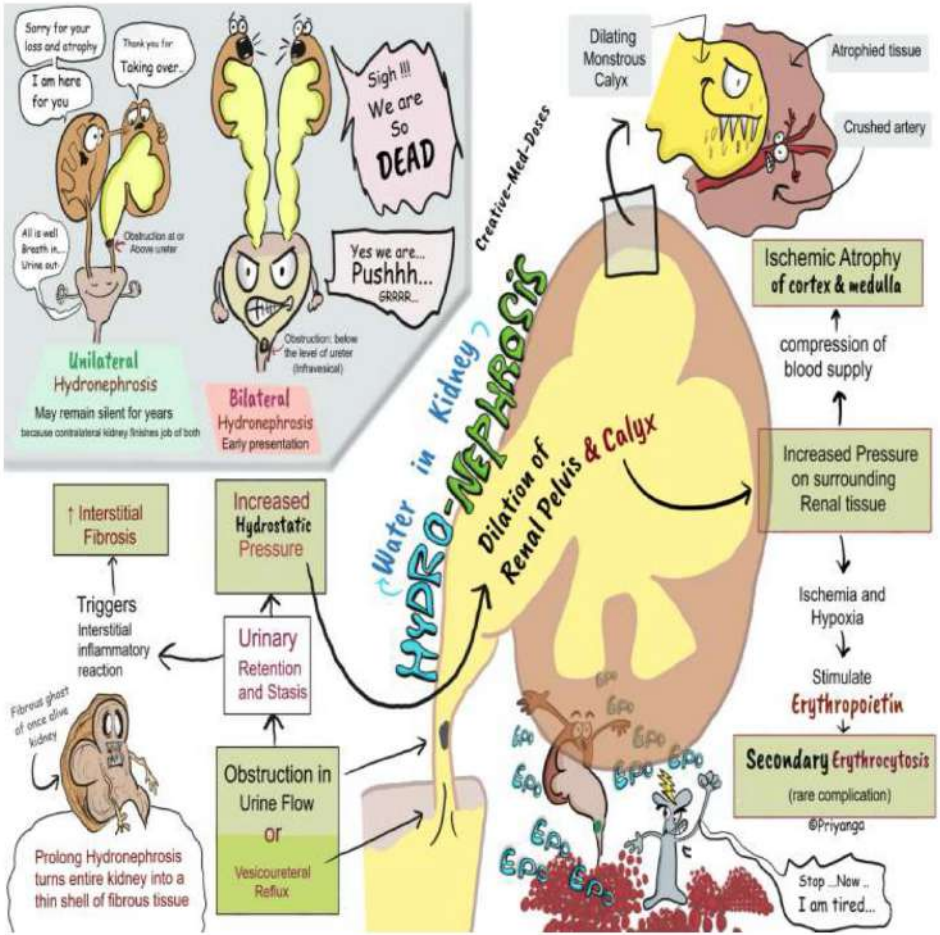
- **2-Acquired:**
- **Examples:**
- Foreign bodie
- Calculi
- necrotic papillae
- Tumors: prostatic hyperplasia, prostate cancer, bladder tumors, cervix or uterus cancer.
- Inflammation: Prostatitis, ureteritis, urethritis,
- Neurogenic: Spinal cord damage
- Normal pregnancy: rare, mild and reversible
- If blockage is at the ureters or above, the lesion is **unilateral**.
- **Bilateral HY** occurs only when the obstruction is below the level of the ureters.

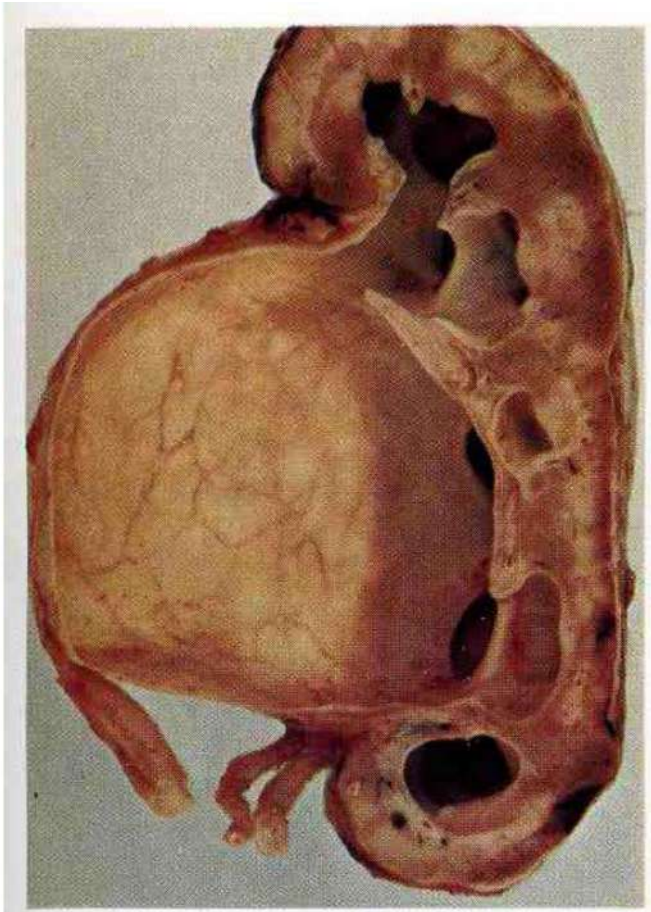

Hydronephrosis
Normal kidney
Stone
Hydroureter
Normal ureter
Stone
Stricture
Urinary bladder


Causes of hydronephrosis
PELVIS
Calculi
Tumors
Ureteropelvic stricture
URETER–INTRINSIC
Calculi
Tumors
Clots
Sloughed papillae
Inflammation
URETER–EXTRINSIC
Pregnancy
Tumors (e.g., cervix)
Retroperitoneal fibrosis
Vesicoureteral reflux
BLADDER
Calculi
Tumors
Functional (e.g., neurogenic)
PROSTATE
Hyperplasia
Carcinoma
Prostatitis
URETHRA
Posterior valve stricture
Tumors (rare)

PATHOGENESIS OF HYDRONEPHROSIS

- **Even with complete obstruction, GF persists for some time**,& the filtrate subsequently diffuses back into the renal interstitium & prerenal spaces,. Because of the **continued filtration,** the affected calyces & pelvis become dilated.
- The unusually high pressure thus generated in the renal pelvis, as well as that transmitted back through the collecting ducts, causes compression of the renal vasculature, with both venous stasis & arterial insufficiency.
- The most severe effects are seen in the papillae, because they are subjected to the greatest increase in pressure.
- **Accordingly,(a) the initial functional disturbances are largely tubular, manifested primarily by impaired concentrationOnly (b) later does G filtration begin to diminish.**


Sorry for your loss and atrophy
I am here for you
Thank you for Taking over..
All is well Breath in... Urine out
Obstruction at or Above ureter
Unilateral Hydronephrosis
May remain silent for years
because contralateral kidney finishes job of both
Sigh !!! We are So DEAD
Yes we are... Pushhh... SRRRR..
Obstruction: below the level of ureter (Infravesical)
Bilateral Hydronephrosis
Early presentation
Creative-Med-Doses
Water in Kidney
HYDRO-NEPHROSIS
Dilation of Renal Pelvis & Calyx
Dilating Monstrous Calyx
Atrophied tissue
Crushed artery
Ischemic Atrophy of cortex & medulla
compression of blood supply
Increased Pressure on surrounding Renal tissue
Ischemia and Hypoxia
Stimulate Erythropoietin
Secondary Erythrocytosis
(rare complication)
©Priyanga
Stop ..Now .. I am tired...
↑ Interstitial Fibrosis
Increased Hydrostatic Pressure
Triggers Interstitial inflammatory reaction
Urinary Retention and Stasis
Obstruction in Urine Flow
or
Vesicoureteral Reflux
Fibrous ghost of once alive kidney
Prolong Hydronephrosis turns entire kidney into a thin shell of fibrous tissue



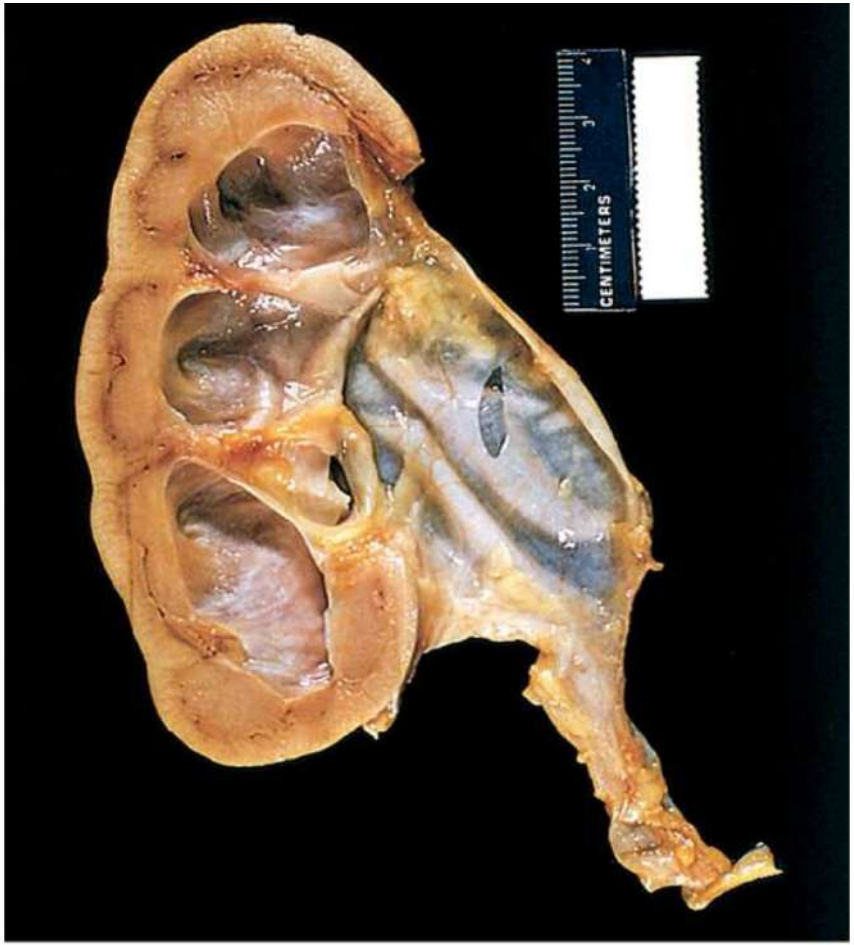
10.16 Hydronephrosis

Hydronephrosis.

Bisected kidney, showing:

(I) An **aberrant accessory renal artery** to the lower kidney pole (lower center, arrowed), which, by pressing upon & obstructing the upper end of the ureter, has caused……

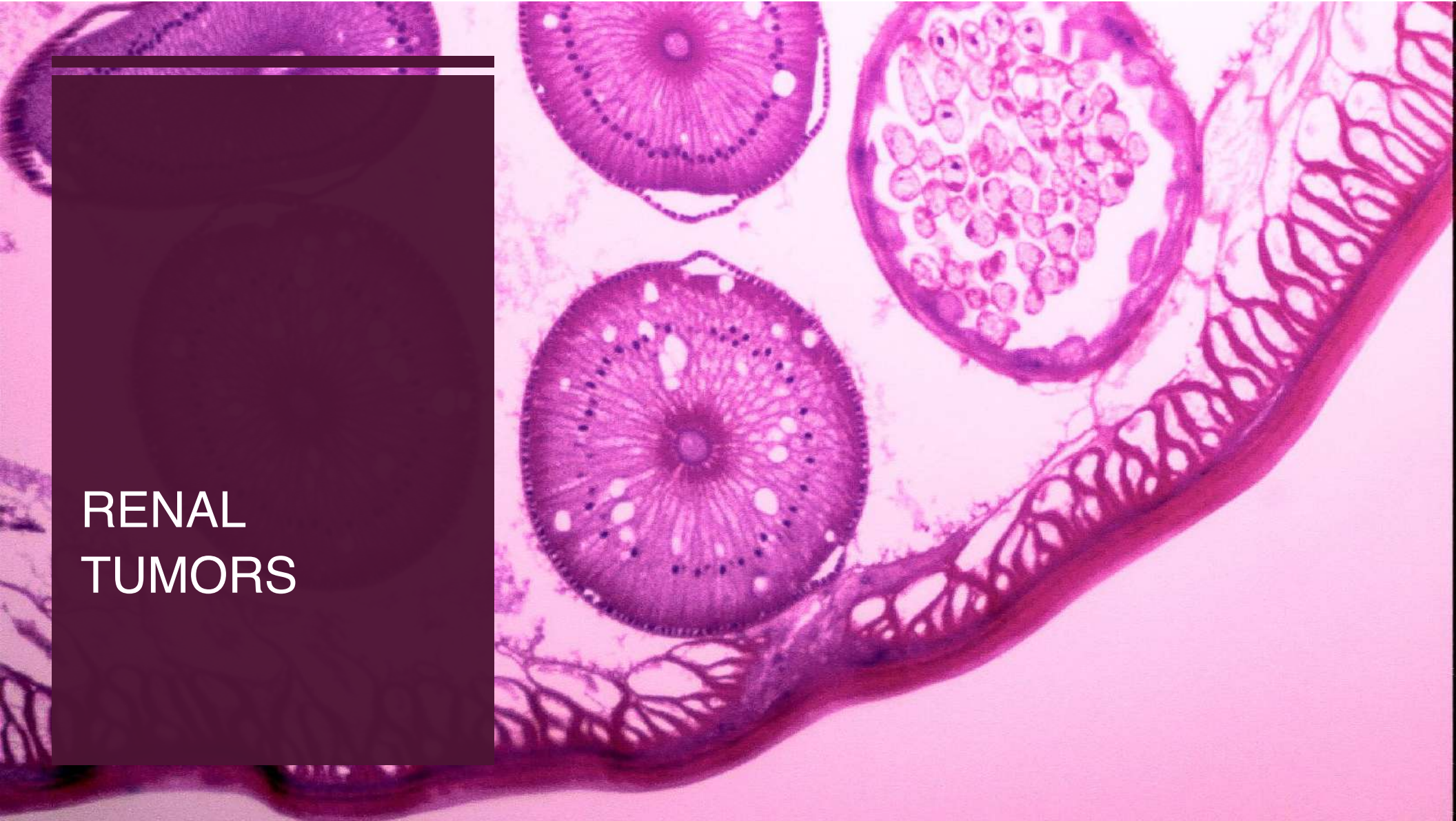
(II) **hydronephrosis,**with dilation of the pelvis, calyces, & upper ureter. ☺The lower ureter, below the obstruction, is normal



Hydronephrosis of the kidney,

★with marked dilation of the pelvis & calyces &

★thinning of the renal parenchyma



RENAL TUMORS

Classification of renal tumour

Benign

Cyst
Leiomyoma
Lipoma
Hemangioma
Angiomyolipoma
Adenoma
Juxtraglomerular cell tumour

Malignant

- RCC
- Transitional Cell Ca
- Oncocytoma
- Sarcoma
- Lymphoma
- Metastasis(Lung, Breast, GIT,Prostate, Pancreas, Melanoma)

RENAL TUMORS

- Either Benign Tumours arising either from epithelial component of kidney or from mesenchymal tissue
- Malignant tumour either epithelial (Renal cell carcinoma) arise from tubules or nephroblastoma arising from Pluripotential stem cells (Children).
- The commonest malignant T of the kidney is the
- (1) **Renal cell carcinoma =RCC (85%)**,followed by
- (2) **Nephroblastoma = Wilm's tumor (10%)**& by
- (3) **Carcinoma of the renal calyces & pelvis (5%).**
- Benign renal T, such as small (<0.5 cm) **cortical papillary adenomas** or interstitial cell medullary **fibromas** have no clinical significance.

Classification of kidney tumours

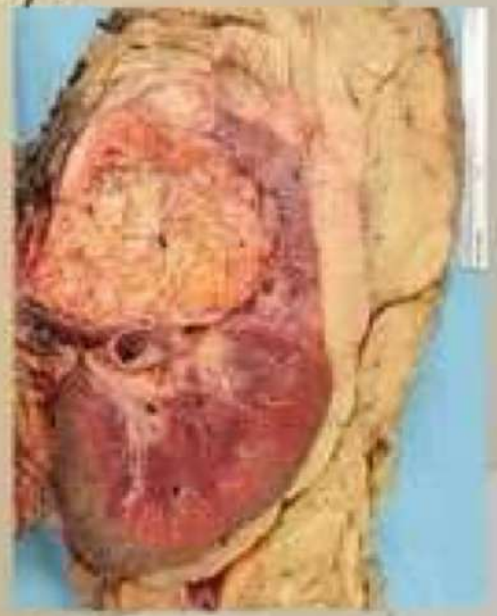
	BENIGN	MALIGNANT
A.	EPITHELIAL TUMOURS OF RENAL PARENCHYMA	
	Adenoma Oncocytoma	Adenocarcinoma (hypernephroma, renal cell carcinoma)
B.	EPITHELIAL TUMOURS OF RENAL PELVIS	
	Transitional cell papilloma	Transitional cell carcinoma
		Others (squamous cell carcinoma, adenocarcinoma of renal pelvis, undifferentiated carcinoma of renal pelvis)
C.	EMBRYONAL TUMOURS	
	Mesoblastic nephroma	Wilms' tumour (nephroblastoma)
	Multicystic nephroma	
D.	NON-EPITHELIAL TUMOURS	
	Angiomyolipoma	Sarcomas (rare)
	Medullary interstitial tumour (fibroma)	
E.	MISCELLANEOUS	
	Juxtaglomerular cell tumour (Reninoma)	
F.	METASTATIC TUMOURS	

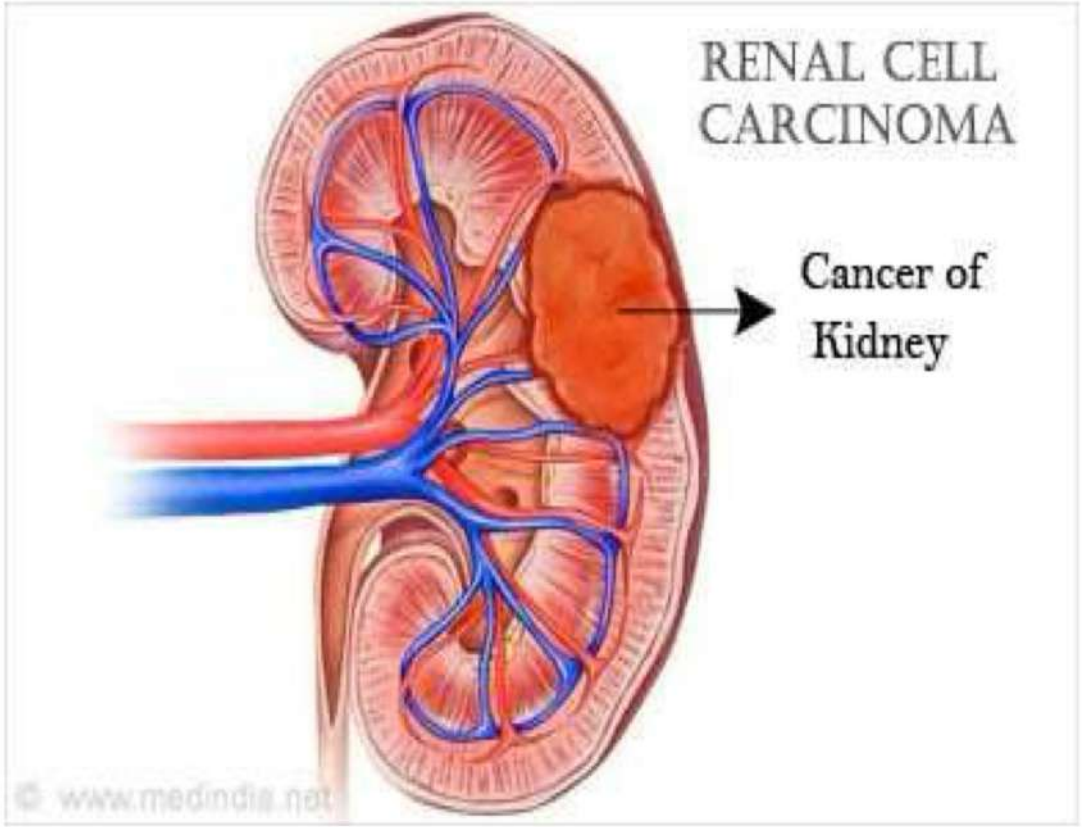
RENAL CELL CARCINOMA (RCC)

- Renal cell carcinoma (RCC) is the third most common cancer of the genitourinary tract and the most lethal urologic cancer, accounting for approximately 2% of all cancer deaths
- ***RCC*** are derived from the **renal tubular epithelium,** & hence they are located predominantly in the renal cortex.
- **RCC** represent **85%**of all primary renal cancers
- **RCC** are most common from the 6th to 7th decades, & men are affected about twice as commonly as women.

WHAT IS RENAL CELL CARCIMONA (RCC)?

- Cancer arising from the lining of proximal convoluted tubule.
- The most common type of kidney cancer.
- Also known as Renal Adenocarcinoma or Grawitz's Tumor.
- Most lethal of all the genitourinary tumors.




RENAL CELL
CARCINOMA
Cancer of
Kidney
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RENAL CELL CARCINOMA (RCC)

- Approximately **one-third of the patients with RCC** will present with metastases, and many patients will develop metastasis after surgical resection.
- Traditionally, RCC is known to be resistant to chemotherapy. However, there has been tremendous development in effective molecular targeted therapies in the past few years for specific types of RCC withwell- defined histology and molecular abnormalities.
- Therefore, accurate histologic diagnosis and classification is increasingly important.

RENAL CELL CARCINOMA (RCC)

- **The risk of developing RCC is higher in :**
- smokers, hypertensive,obese patients, & those who have had occupational exposure to cadmium;
- **30-fold in individuals who develop acquired polycystic disease as a complication of chronic dialysis.**

RENAL CELL CARCINOMA (RCC)

- The role of genetic factors in the causation of RCC is discussed below.
- **Based on their molecular origins, RCC are classified in 3 forms:**
- **• (I)Clear Cell RCC (80%)**
- **• (II) Papillary RCC (15%)**
- **• (III) Chromophobe RCC (5%).**

(I)CLEAR CELL RCC

- Commonest type, comprises **80%** of all RCC, Tumor cells show clear or granular cytoplasm. **Majority are sporadic**, also occur in **familial** forms or in association with... **An autosomal dominant von Hippel-Lindau (VHL) disease.**
- characterized by predisposition to a variety of tumors, but particularly to **hemangioblastomas** of the cerebellum & retina.
- People who have VHL disease may experience tumors and/ or cysts in up to ten parts of the body, including the brain, spine, eyes, kidneys, pancreas, adrenal glands, inner ears, reproductive tract, liver and lung.
- Hundreds of **bilateral renal cysts & bilateral, multiple, clear cell RCC** develop in 40% to 60% of **VHL disease** patients**.**
- **Those with VHL syndrome inherit a germ-line mutation of the VHL gene on chromosome 3p25& lose of the second allele by somatic mutation.**
- **Thus, the loss of both copies of this tumor suppressor gene gives rise to clear cell RCC.**

(I)CLEAR CELL RCC

- The VHL gene is also involved in the majority of **sporadic** clear cell RCC. Thus, **homozygous loss of the VHL gene** seems to be the common underlying molecular abnormality in **both sporadic & familial forms of clear cell RCC.**
- The VHL protein is involved in limiting the angiogenic response to hypoxia; thus, its absence may lead to angiogenesis & tumor growth.
- The mean age of onset of 26 years and 97% of people with a VHL gene mutation have symptoms by the age of 65.
- VHL disease affects males and females and all ethnic groups equally, and occurs in all parts of the world.