KIDNEY-5

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Hypertension and kidney

- Hypertension-Sustained increase in pressure more than 140/90 mm of Hg.
- Primary/Essential HT- 95% cases of HT are idiopathic and of uncertain origin.
- Secondary HT -Remaining 5% cases are secondary to renal diseases and less commonly to endocrine, vascular and neurogenic diseases.
- Both primary and secondary are benign and malignant according to clinical course.

- **Benign HT** -Most cases of HT remains stable over years to decades unless MI or CVA supervenes. Corresponding renal lesion is benign nephrosclerosis.

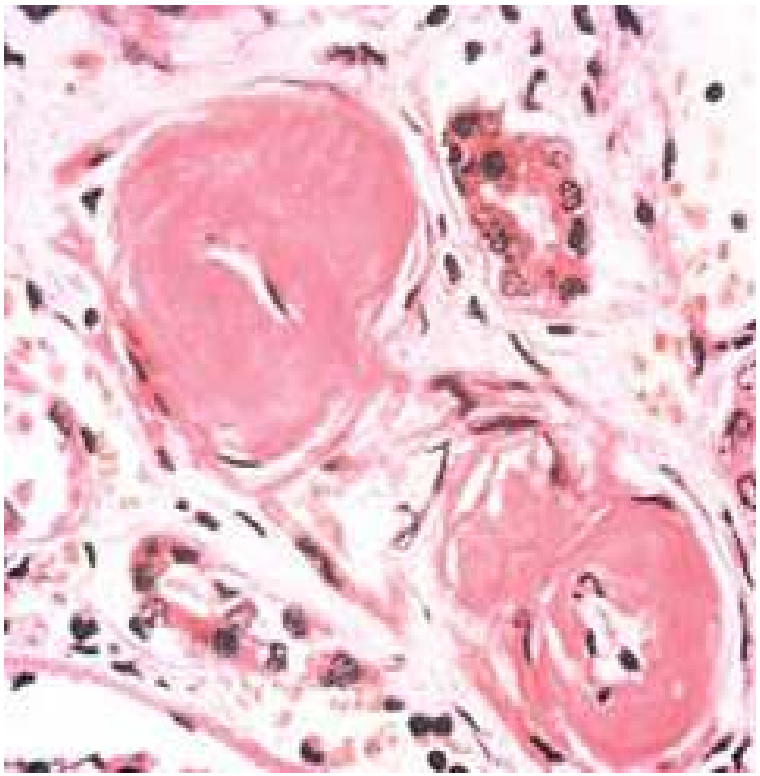
- **Malignant HT** -Few cases show rapidly rising BP which if untreated leads to death within a period of year or two is termed as accelerated or malignant hypertension and corresponding renal lesion is malignant nephrosclerosis.

Benign Nephrosclerosis

- Kidney lesion in benign hypertension, associated with sclerosis of small arteries and renal arterioles.
- Kidneys are either normal in size or moderately reduced to average weight. Cortical surface have fine even granularity that resembles grain leather with marked cortical narrowing.

Histology-

1.Hyaline arteriolosclerosis - Thickening and hyalinization of the walls of small arteries and renal arterioles.



Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:939

Benign Nephrosclerosis

- 2.Fibro elastic hyperplasia -Characteristic lesion seen in larger b.vessels (interlobular and arcuate arteries) which consists of reduplication of internal elastic lamina along with fibrous thickening of media and subintima with narrowing of lumen.
- Resultant ischemic atrophy consists of foci of tubular atrophy and interstitial fibrosis, periglomerular fibrosis, collapse of GBM and collagen deposition leading to total sclerosis of glomeruli.
- Clinically, uncomplicated cases rarely causes renal insufficiency.

Malignant Nephrosclerosis

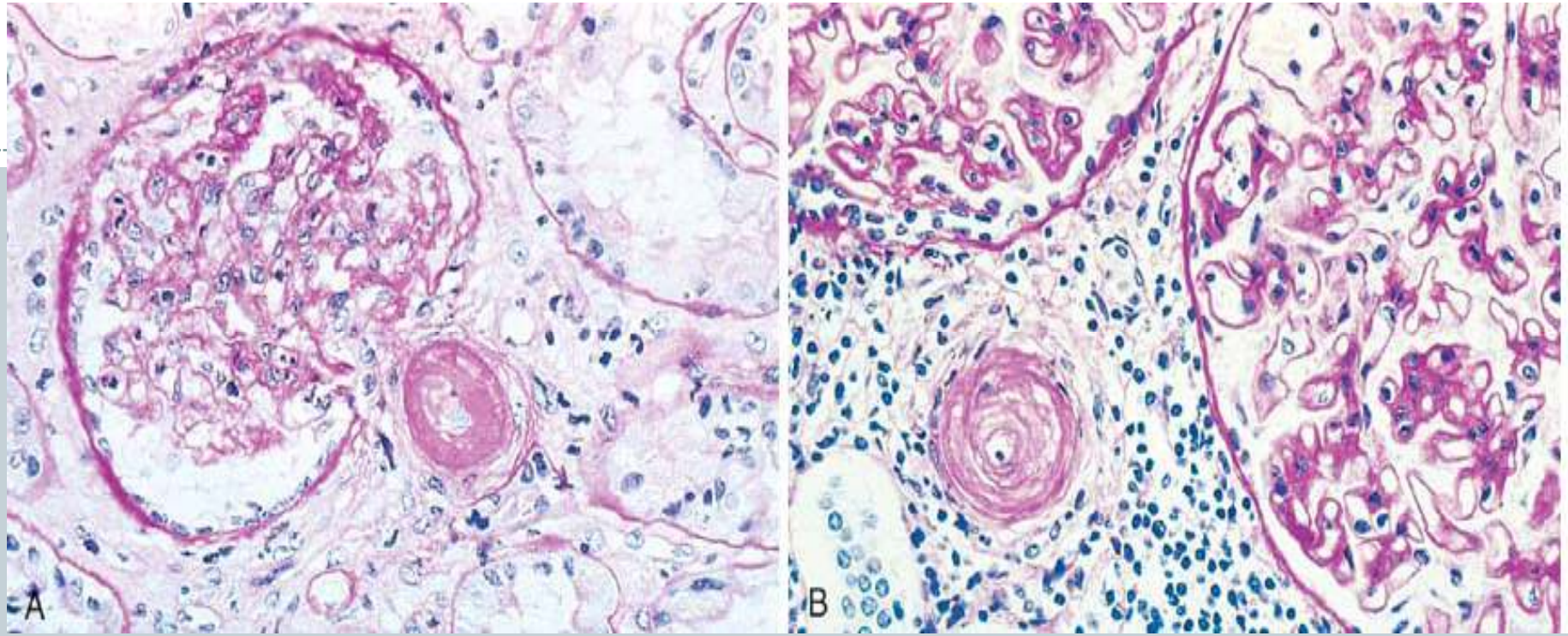
- Renal lesion associated with malignant hypertension (Diastolic BP more than120 mm of Hg).Relatively uncommon disorder, affects younger individuals. Usually superimposed on preexisting hypertension or chronic renal diseases.
- Early manifestations are related to increased intracranial pressure like headache, nausea, vomiting and visual impairment. Papilledema, retinopathy, encephalopathy, cerebrovascular abnormality & RF. Loss of consciousness or convulsions are common in hypertensive crisis.

MORPHOLOGY

- GROSS-Kidney size varies according to duration and severity of the disease. Small pin point hemorrhages appear on cortical surfaces from rupture of arterioles or glomerular capillaries, termed as flea bitten kidney.
- HISTOLOGY-
- *1.Fibrinoid necrosis of arterioles* - Eosinophilic granular change in blood vessel wall which is positive for fibrin by histochemical or immuno fluorescent technique.

- *2.Hyperplastic arteriolitis* -In interlobular arteries and arterioles, intimal thickening by proliferation of elongated concentrically arranged smooth muscle cells along with fine concentric layers of collagen, termed as onion skinning
- All this changes leads to ischemic atrophy and infarction distal to abnormal vessels.
- Clinically, there is marked proteinuria and hematuria without much alteration of renal function. It is a medical emergency, aggressive & prompt treatment is required before the development of irreversible renal damage.

Benign and malignant hypertension



Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:940

Tumors of kidney

- **Benign** –Renal papillary adenoma, Renal fibroma, Angiomyolipoma, Oncocytoma.

- **Malignant** -RENAL CELL CARCINOMA: Tumor derived from renal tubular epithelium. Because of gross yellow color and resemblance of tumor cells to clear cells of adrenal cortex, previously it was termed as HYPERNEPHROMA.
- Commonly affects adult males in 6^{th} or 7^{th} decade. Risk factors are smoking, occupational exposure to cadmium & after chronic dialysis.

Classification of RCC

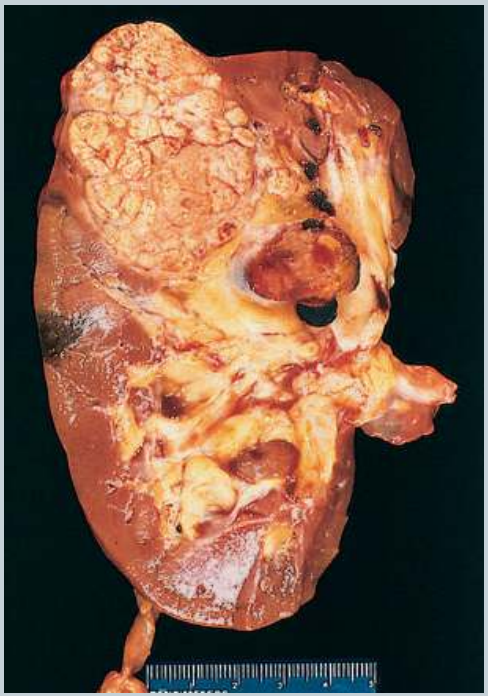
- With the better understanding of advanced genetics ,newer classification is based on molecular origins of tumor.

- **Clear cell RCC (70-80%)-**Association with Von Hippel Lindau disease (A.D.disorder) is common. Patients inherit a germ line mutation of VHL gene on chromosome 3p25 and loss of 2nd allele by somatic mutation. Loss of both copies of tumor suppressor gene give rise to clear cell RCC.
- **Papillary RCC (10-15%)-** Culprit is MET protooncogene, located on chromosome 7q31.
- **Chromophobe RCC (5%)-** Multiple losses of entire chromosomes, having excellent prognosis.
- **Collecting duct carcinoma (<1%)**

GROSS MORPHOLOGY

- It arises from upper pole of cortex as a solitary well defined lesion of 3-15 cm in diameter with bright yellow to gray white cut surface. Areas of cystic softening, haemorrhage and necrosis are common.
- It is a very aggressive tumour, may fungate through collecting system extending through calyces, pelvis and ureter. Commonly invade the renal vain as a solid column extending even up to right side of the heart.

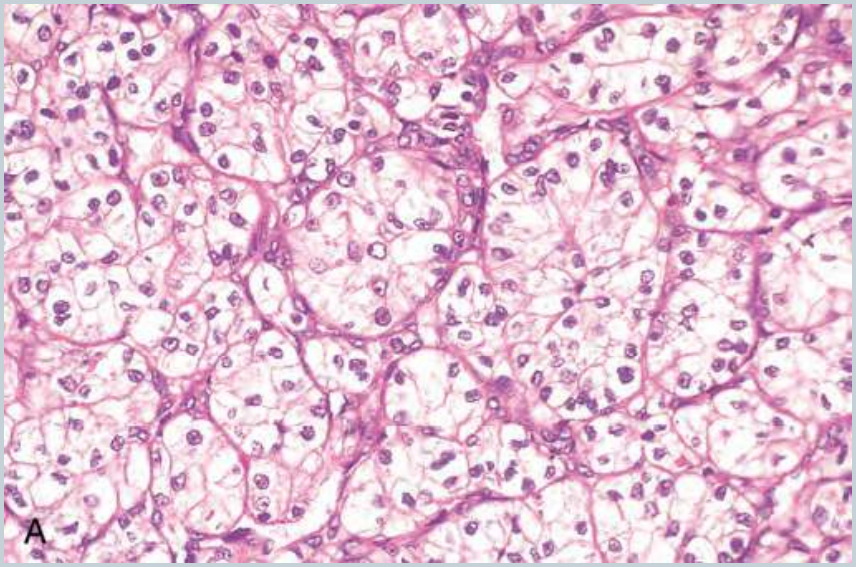
Renal cell carcinoma: GROSS



- spherical neoplasm in one pole of the kidney. Note the tumor in the dilated, thrombosed renal vein.

Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:954

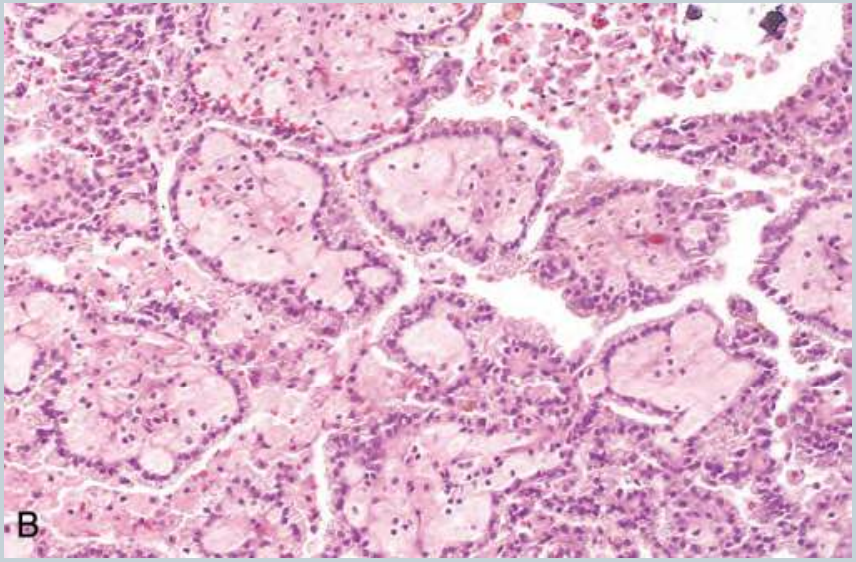
Histopathology



- **Clear cell RCC-** Solid, trabecular (cord like) or tubular pattern separated by vascularised stroma. Cells are large and polygonal. Nuclei are small & round. Depending upon the amount of lipid or glycogen present, cells may appear clear or granular. Anaplastic features with mitosis are seen.

Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:955

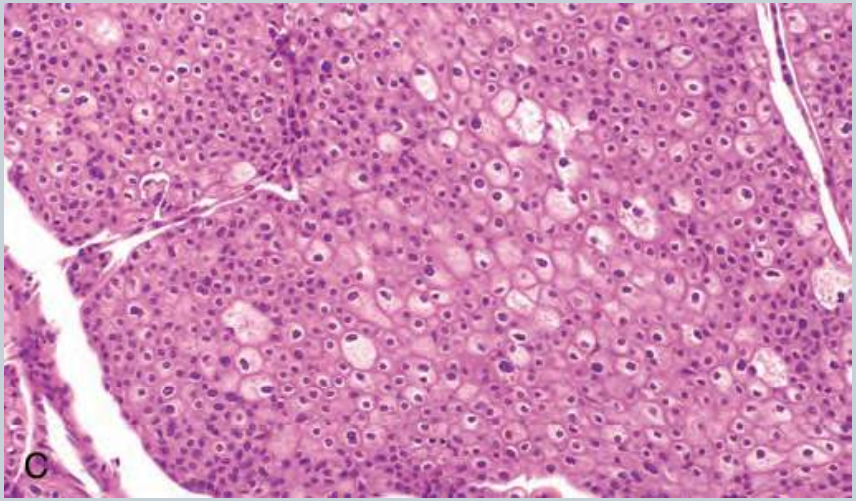
Histopathology



- **Papillary RCC-** Multifocal and bilateral with papillary pattern lined by cuboidal and low columnar epithelial cells. Foam cells are common in papillary cores. Psammoma bodies may be present

Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:955

Histopathology



- **Chromophobe carcinoma-** Cells stain darkly eosinophilic with perinuclear halo.

Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:955

Clinical behaviour

- **C/F:** hematuria, flank pain and palpable mass are common.Paraneoplastic syndrome like polycythemia, hypertension, hypercalcemia,Cushings syndrome etc.
- Tendency to metastasize widely before giving rise to local symptoms.

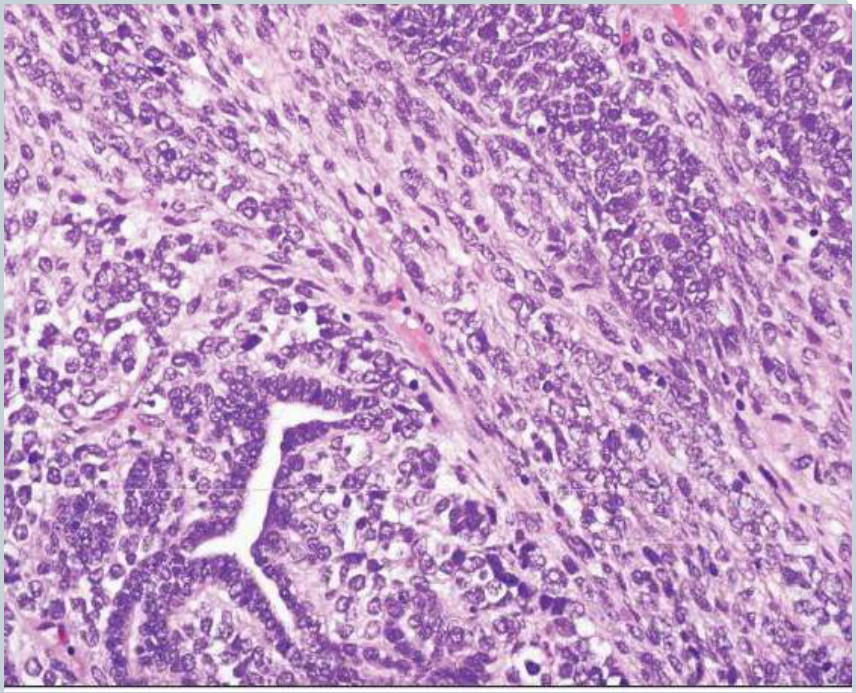
WILMS TUMOUR

- 6% of all renal cell tumor.
- Common childhood tumor that contain a mixture of renal epithelial and stromal elements as well as various heterogenous tissues all derived from mesoderm (mixed tumour).Association with WT-1 gene(tumour suppressor gene situated on chromosome 11p13).
- ***Grossly***, large solitary well circumscribed mass.10% are bilateral and multicentric. Variegated cut surface depending upon the tissue type produced. Soft homogenous tan to gray with occasional foci of cystic degeneration, haemorrhage and necrosis.

Microscopy of wilms tumor

- Characterized by recognizable attempts to recapitulate different stages of nephrogenesis.
- Classic triphasic combination of blastemal, stromal & epithelial types.
- Blastemal components- nests or sheets of dark blue primitive cells.
- Epithelial differentiation- Abortive tubules and glomeruli.
- Stromal cells- fibroblastic, myxoid or skeletal muscle differentiation are present.
- Heterogenous elements-squamous or mucinous epithelium, adipose tissue, cartilage, osteoid etc..

Wilms tumor



Ref: Heptinstall Pathology of the Kidney 7th Edition , Pg.1554

- Typical triphasic histology with epithelial, blastemal, and mesenchymal elements.

Wilms tumor

- Percentage of each component correlate with tumor aggressiveness.

- Predominant epithelial component –stage 1 or 2.

- Predominant blastemal component-stage 3 or 4 .

- Excellent prognosis.

- Urothelial tumor of calyces and pelvis (transitional cell carcinoma). 5-10% renal tumours. Ranges from benign papillomas to invasive urothelial (transional)carcinoma

CONGENITAL MALFORMATIONS

- 10% of all persons

I. Abnormalities in amount of renal tissue.

- anomalies with deficient renal parenchyma (e.g. unilateral or bilateral renal hypoplasia) or with excess renal tissue (e.g. renomegaly, supernumerary kidneys).

II. Anomalies of position, form and orientation.

- renal ectopia (pelvic kidney), renal fusion (horseshoe kidney)

III. Anomalies of differentiation. : *'cystic diseases of the kidney'*

CYSTIC DISEASES OF KIDNEY

- *congenital or acquired,*
- *non-neoplastic or neoplastic.*
- *Majority are* congenital & non-neoplastic.
- Clinical Features:

✓ abdominal mass

✓ Infection

✓ respiratory distress (due to accompanied pulmonary hypoplasia)

✓ Haemorrhage

✓ neoplastic transformation.

Classification of Cystic Lesions of the Kidney

A. NON-NEOPLASTIC CYSTIC LESIONS

I. Renal multicystic dysplasia

II. Polycystic kidney disease (PKD)

1. Adult (autosomal dominant) polycystic kidney disease (ADPKD)
2. Infantile (autosomal recessive) polycystic kidney disease (ARPKD)

III. Medullary cystic disease

1. Medullary sponge kidney (MSK)
2. Nephronophthiasis-medullary cystic disease complex

IV. Simple renal cysts

V. Acquired renal cysts

VI. Para-renal cysts

B. NEOPLASTIC CYSTIC LESIONS

I. Cystic nephroma

II. Cystic partially-differentiated nephroblastoma (CPDN)

III. Multifocal cystic change in Wilms' tumour

I. Multicystic Renal Dysplasia

- The term ‘multicystic renal dysplasia’ is used for disorganised metanephrogenic differentiation.
- Most common form of cystic renal disease in the newborn and infants.
- May occur sporadically or familial.
- It is commonly associated with obstructive abnormalities of the ureter and lower urinary tract such as obstruction of pelviureteric junction (PUJ), ureteral atresia and urethral obstruction.

Multicystic Renal Dysplasia

- *May be* **unilateral or bilateral**.
- ***Grossly:*** kidney or its affected part is replaced by disorderly mass of multiple cysts resembling a bunch of grapes. The ureter is invariably abnormal, being either absent or atretic.
- ***Histologically,***
- The cysts in the mass represent dilated tubules lined by flattened epithelium which are surrounded by concentric layers of connective tissue. There is *presence* of undifferentiated mesenchyme that contains smooth muscle, cartilage and immature collecting ducts.
- Glomeruli and tubules are scanty, primitive or absent.

Multicystic Renal Dysplasia

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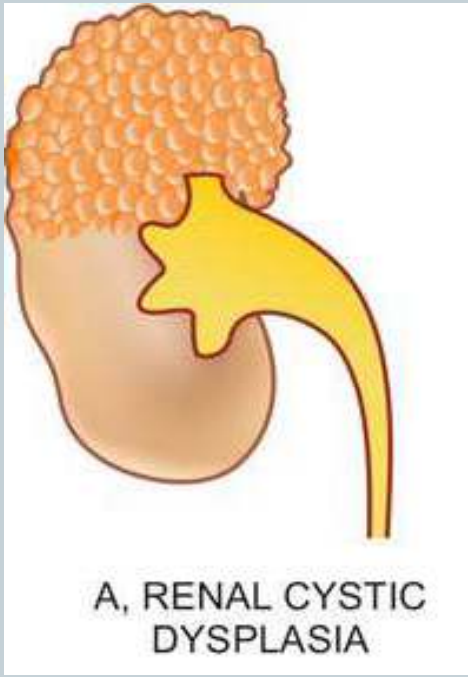
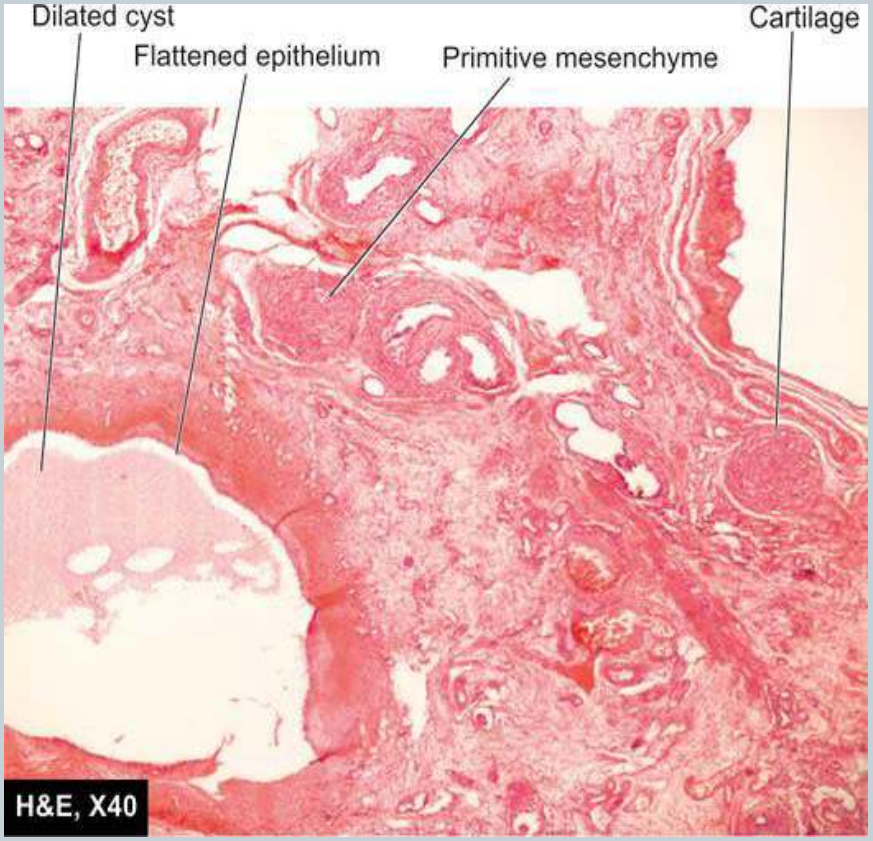


Ref: Harsh Mohan Textbook of pathology, 7th Edition Pg: 644

Renal cystic dysplasia.

There are cysts lined by flattened epithelium while the intervening parenchyma consists of primitive connective tissue & cartilage.



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II. Polycystic Kidney Disease

- Major portion of the renal parenchyma is converted into cysts of varying size.
- The disease occurs in two forms:

A. An *adult type inherited as an autosomal dominant disease*

B. An *infantile type inherited as an autosomal recessive* disorder.

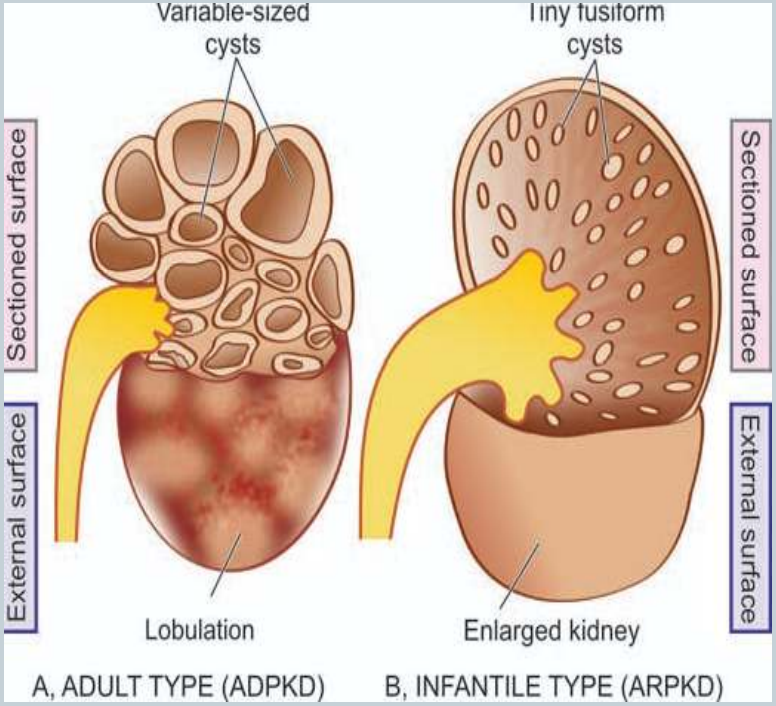
ADULT POLYCYSTIC KIDNEY DISEASE

- ADPKD is relatively common (incidence 1:400 to 1: 1:1000)
- Autosomal Dominant disorder, *family history of similar* disease may be present.
- symptoms appear in adult life, mostly between the age of 30 and 50 years.

Pathogenesis: Mutation in *PKD-1 gene located on chromosome 16 in over 85% cases* (ADPKD-1) while remainder 15% cases have mutation in *PKD-2 gene located on chromosome4 (ADPKD-2).*

MORPHOLOGIC FEATURES- ADPKD

- **Gross:** Kidneys are always bilaterally enlarged, usually symmetrically, heavy (weighing up to 4 kg)
- Lobulated appearance on external surface due to underlying cysts. Cysts varying in size from tiny cysts to 4-5 cm in diameter
- **The contents of the cysts-** clear straw-yellow fluid to reddish-brown material.
- ***Histologically:*** *The cysts arise from all parts of nephron.*



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CLINICAL FEATURES

- The most frequent and earliest presenting feature is a dull-ache in the lumbar regions. In others, the presenting complaints are hematuria , renal colic, hypertension, urinary tract infections and progressive CRF.
- ADPKD is considered a systemic disease. About a third of patients with ADPKD have cysts of the liver. Other associated congenital anomalies are cysts in the pancreas, spleen, lungs and other organs.
- Approximately 15% of patients have one or more intracranial berry aneurysms of the circle of Willis.

INFANTILE POLYCYSTIC KIDNEY DISEASE

- Less common (incidence 1:20,000 births).

Pathogenesis:

- transmitted as an *autosomal recessive trait*
- The condition occurs due to a mutation in chromosome 6; *6p21, PKHD1 (polycystic kidney* and hepatic disease 1).
- The age at presentation may be perinatal, neonatal, infantile or juvenile, but frequently serious manifestations are present at birth and result in death from renal failure in early childhood.

MORPHOLOGIC FEATURES.

Grossly: *The kidneys are* bilaterally enlarged with smooth external surface and retained normal reniform shape.

- Cut surface reveals small, fusiform or cylindrical cysts radiating from the medulla and extend to the outer cortex. This gives the sectioned surface of the kidney *sponge-like appearance*

Histologically:

- Since the cysts are formed from dilatation of collecting tubules, all the collecting tubules show cylindrical dilatations and are lined by cuboidal to low columnar epithelium. Many of the glomeruli are also cystically dilated.

CLINICAL FEATURES.

- The clinical manifestations depend on age of the child.
- In severe form, the gross bilateral cystic renal enlargement may interfere with delivery.
- In infancy, renal failure may manifest early.

  Almost all cases of infantile polycystic kidney disease have associated multiple epithelium-lined cysts in the liver and portal fibrosis with proliferation of portal bile ductules.
- In older children, associated hepatic changes develop into what is termed *congenital hepatic fibrosis which* may lead to portal hypertension and splenomegaly.

III. Medullary Cystic Disease

- Cystic disease of the renal medulla has two main types:

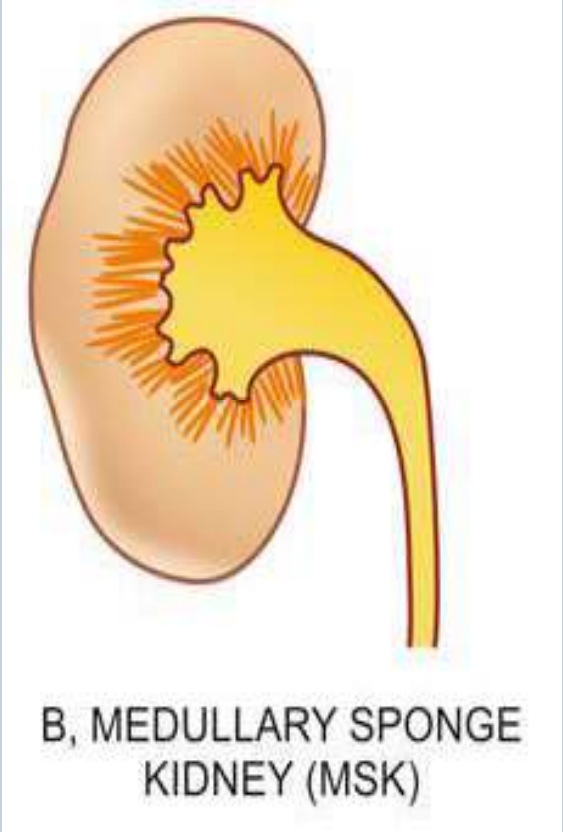
- A. *Medullary sponge kidney, a relatively common and* innocuous condition
- B. *Nephronophthiasis-medullary cystic disease complex, a* common cause of chronic renal failure in juvenile age group

Medullary Sponge Kidney

- Autosomal dominant transmission.
- The condition occurs in Adults
- Incidental radiographic finding or presented with colicky flank pain, dysuria, haematuria and passage of sandy material in the urine.
- Renal function remains normal or may be mildly impaired with secondary complications of infection and calculus formation.

Medullary Sponge Kidney

Grossly, *the kidneys may* be enlarged, normal or shrunken in size depending upon the extent of secondary pyelonephritis. On cut surface, the characteristic feature is the presence of several, small, cystically dilated papillary ducts, which may contain spherical calculi.



B, MEDULLARY SPONGE KIDNEY (MSK)

Ref: Harsh Mohan Textbook of pathology, 7th Edition Pg: 644

- ***Microscopically,*** *the cysts are lined by tall columnar,* cuboidal, transitional or squamous epithelium. Renal cortex may show secondary pyelonephritis but cortical cysts are never a component of medullary sponge kidney.

NEPHRONOPHTHIASIS-MEDULLARY CYSTIC DISEASE COMPLEX

- Also called *juvenile nephronophthiasis or uraemic sponge kidney*
- It is the most common form of genetic cause of end-stage renal disease in children and adolescents. The condition has an autosomal recessive inheritance.
- The clinical manifestations are due to impaired urinary concentration and consist of polyuria, polydipsia and enuresis. Other features include renal osteodystrophy, anemia and progressive renal failure leading to uremia

- ***Grossly,*** *the kidneys are* moderately reduced in size and granular and have narrow cortices. Cut surface reveals minute cysts, present at the cortico-medullary junction.
- ***Microscopically,*** *the cysts are lined by flattened or* cuboidal epithelium.
- There is widespread nonspecific chronic inflammatory infiltrate, interstitial fibrosis, hyalinised glomeruli & tubular atrophy

IV. Simple Renal Cysts

- very common postmortem finding, age of 50 yrs.
- Rarely responsible for symptoms. The association between simple cysts and hypertension is common

Grossly, *simple renal* cysts are usually solitary, commonly located in the cortex, size varies from a few millimeters to 10 cm. Wall of cyst is yellowish-white and translucent. The cyst usually contains clear straw-coloured fluid.

Microscopically, *the lining of the cyst is by flattened* epithelium. The cyst wall contains variable amount of collagenised fibrous tissue.

V. Acquired Renal Cysts

1. Patients with end-stage renal disease on prolonged dialysis (dialysis-associated cystic disease).
2. Hydatid (echinococcal) cyst.
3. Tuberculosis of the kidney.
4. Traumatic intrarenal haematoma

VI. Pararenal Cysts

Cysts occurring adjacent to a kidney are termed pararenal cysts. These include the following:

1. Pyelocalyceal cysts
2. Hilar lymphangiectatic cysts
3. Retroperitoneal cysts
4. Perinephric pseudocysts from trauma.

Thank You