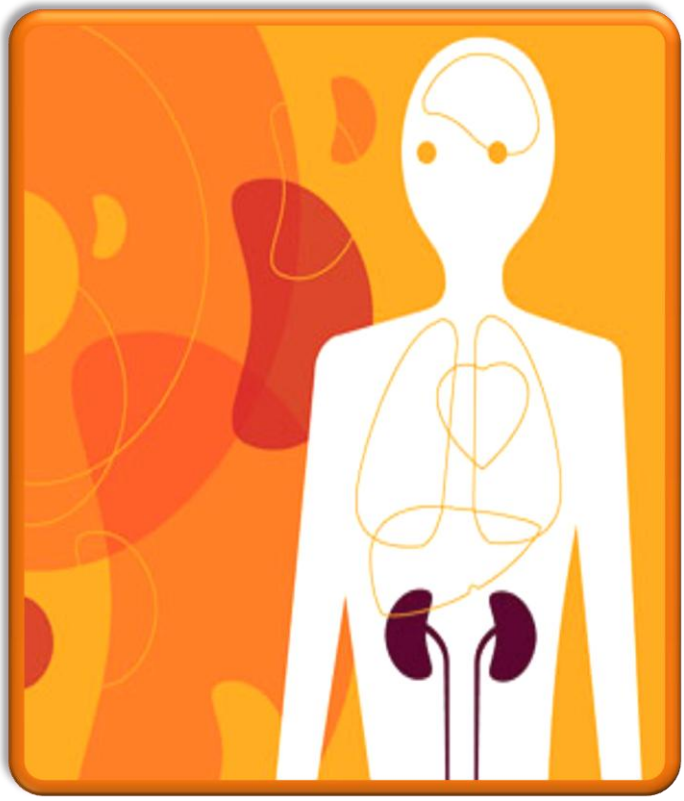

PATHOLOGY TEAM - 431 (renal block)

Pathology of Tumors

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Objectives:

- At the end of the lecture the students will be able to:
- Recognize the benign tumors of the kidney.
- Describe renal cell carcinoma and Wilm's tumor.
- Recognize transitional cell and squamous carcinoma of the urinary bladder.

Outlines:

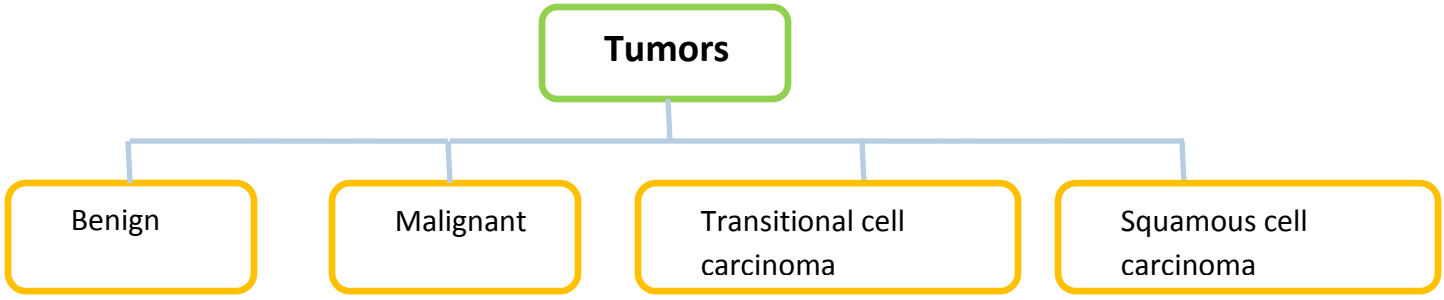
- Benign tumors of the kidney: Adenoma and Angiomyelipoma.
- Renal Cell Carcinoma: Incidence, Clinical Presentation, Histological Features and Prognosis.
- Wilm's tumor (nephroblastoma): Incidence, Clinical Features, Genetic and Histological Characteristics.
- Transitional Cell and Squamous Carcinoma: Predisposing Factors, Incidence, Clinical Pathological Features and Prognostic Indicators (Grade and Stage).

In GREEN, mentioned by the doctor

In a BLUE box, student's notes

In PINK, from female slides

In RED, important information



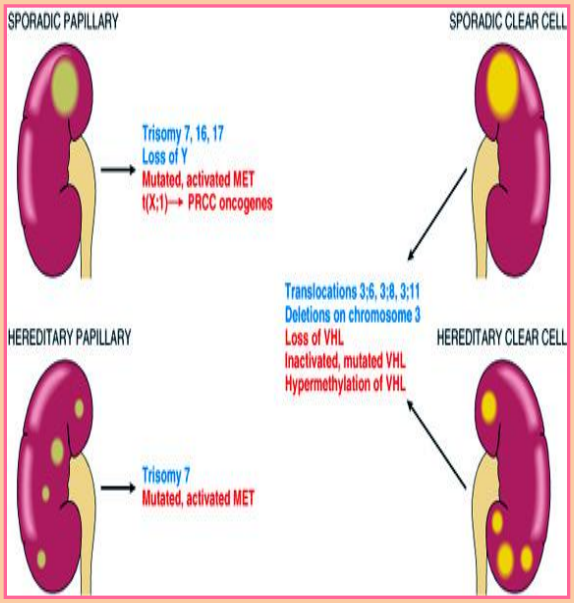
I. Benign Tumors of The Kidney

a) Adenoma	b) Oncocytoma	c) Angiomyolipoma
- The most small tumor. - Asymptomatic. - Derived from renal tubules. - A precursor lesion to renal carcinoma. -The adenoma can either show in a papillary formation or regular tubular epithelium lining. -The tumor is cortical, usually subscapular, and is generally well circumscribed.	- it is tubular adenoma , large 3-4 cm, well circumscribed and oval in shape. - by oncocetic cells : cells with deep esinophilic cytoplasm(in wiki is different)(in weki : An oncocyte is an epithelial cell characterized by an excessive amount of mitochondria, resulting in an abundant (eosinophilic) acidophilic, granular cytoplasm.) and contain a central scar(it is not found in renal cell carcinoma), In gross appearance, the tumors are tan or mahogany brown, well circumscribed and contain a central scar. They may achieve a large size (up to 12 cm in diameter).	- Associated with the tuberous sclerosis syndrome. - affect the CNS,epilipcy, lejins in the brain, sejers نوبات الصرع . Tuberous sclerosis is an inherited genetic disorder that affects the skin, kidneys, heart, and mainly brain/nervous system. This disease can cause tumors to grow. - The lesion of this tumor consists of blood vessels, adipocytes, and smooth muscle cells. - Angiomyolipoma is usually a big tumor where it can be mistaken as Renal Cell Carcinoma RCC. - The tumor can enlarge greatly to the extent where it can effect kidney function, or even rupture a vessel causing hemorrhage. Also it can be bilateral

** Kidney with ischemic atrophy also bears very small subcapsular **adenomas** near to each pole.

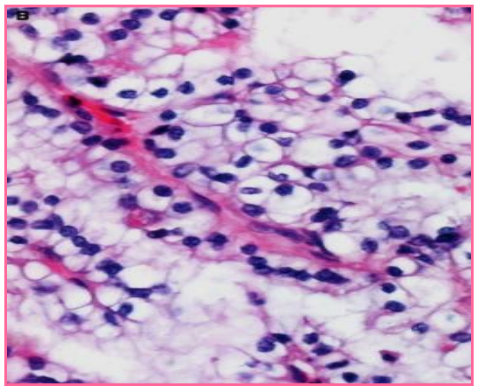
II. Malignant Tumors of The Kidney

	a) Renal cell carcinoma	b) Wilms tumor (nephroplastoma)
Location	- Renal tubules. - One of the renal poles (frequently upper). That is why it was called HYPERNEPHROMA.	- Wilms tumor originates from primitive metanephric tissue.
Incidence	- More common in men (50-70 years of age). - Cigarette smokers. - Other risk factors include: cadmium exposure (a substance most notably found in zinc batteries) and acquired polycystic disease that results form chronic renal failure.	- It's the most common renal malignancy in childhood. - Incidence peaks in children 2-4 years.
Characteristics	- Most common renal malignancy. - Associated with: o In some instances (5-10% runs between families), gene deletions in chromosome 3 (in the short arm). o von Hippel-Lindau disease, which is caused by alterations in a gene localized to chromosome 3. o (called VHL gene (**von Hippel-Lindau disease**) which is a tumer suppressor gene) - Carcinoma invades renal veins or the vena cava.	- It is often associated with deletions of the short arm of chromosome 11. The WT-1 and WT-2 genes localized to this chromosome are cancer suppressor genes. - The disease can be part of the AGR (or WAGR) complex (Wilms tumor, Aniridia [absence of the choroid layer in the eye], genitourinary malformations and mental retardation). These anomalies are associated with deletion of the WT-1 tumor suppressor gene and the other nearby genes. - It can also be associated with hemihypertrophy (gross asymmetry due to unilateral muscular hypertrophy), macroglossia, organomegaly neonatal hypoglycemia and various embryonal tumors. This set of anomalies along with Wilms tumor if collectively reffered to as the Bechwith-Wiedemann syndrome and is associated with deletion of the WT-2 gene.

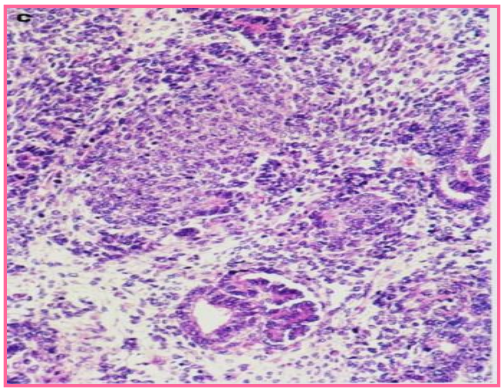
		- Solid, bulging, fleshy tan-white, partially necrotic tumor has replaced much of the kidney and is encompassed by a thin rim of renal tissue.
Histology Characteristics	- Polygonal clear cells. - Sometimes with vestigial (primitive) tubule formation. - Small clear cell renal cell carcinoma (hypernephroma, Grawitz tumor) is spreading into perirenal adipose tissue.	- Immature stroma. - Primitive tubules. - Glomeruli and mesenchymal elements (when they loss the sense of differentiation) such as; fibrous C.T, cartilage bone and rarely striated muscle. - hypercellular areas comprising undifferentiated blastema, loose stroma with undifferentiated glomeruloid body.
Presenting features	- Triad of flank pain. - Palpable mass. - Hematuria (most frequently presenting abnormality). - Fever. - Secondary polycythemia (from erythropoietin production). - Ectopic production of hormone or hormone-like substances e.g. ACTH, prolactin, gonadotropins and rennin. (paraneoplastic parathyroid-like hormone can also cause hypercalcemia)	- presenting feature is a palpable flank mass (often huge).

- Renal cell carcinoma (Clear Cell Carcinoma) (Hypernephroma) Has three types:

    1) Clear Cell Renal Cell Carcinoma with 70 – 80% of cases (detailed later)
    2) Papillary Renal Cell Carcinoma: Doses not occur with association with deletions of chromosome 3, but changes in or with chromosome 7 and trisomies of other chromosomes especially in sporadic cases.
    3) Chromophobe Renal Carcinoma: mostly affects the cortical collecting ducts or their intercalated cells. This type of renal carcinoma is associated with loss of multiple and full loss of certain chromosomes; therefore, the affecting loss of locus and gene cant be pinpointed. This type also has a good prognosis



Renal cell carcinoma



Wilms Tumor

III. Transitional cell carcinoma

Location	Renal calyces, pelvis, ureter or bladder. It is often Multifocal in origin.
Incidence	The most common tumor of the urinary collecting system. Usually affects patients from 50 – 70 years of age.
Characteristics	-In the renal pelvis, transitional call carcinoma has been associated with phenacetin abuse. So it would sometimes present as a medullary mass rather than the cortical masses in RCC where it arises from the tubules. - This carcinoma is likely to occur after removal. - There is a tendency to spread by local extension to surrounding tissues. - Associated toxic exposures may sometimes be involved, including the following: A. Industrial exposure to benzidine or β-naphthylamine which is an aniline dye. B. Smoking. C. Long-term treatment with cyclophosphamide.
Presenting features	-Most often, the presenting feature is hematuria. The hematuria here is intermittent in contrast to a continuous hematuria found in RCC. - It is present with: disgrowth in the renal pelvis (called: cauliflower or fungating growth), anemia, obstruction –with it is symptoms-.also it has papillary growth (finger-like)

IV. Squamous cell Carcinoma

- Constitutes a minority of urinary tract malignancies.
- This cancer may result from chronic inflammatory process, such as; chronic bacterial infection or Schistosoma haematobium infection.
- It can also be associated with renal calculi.

Malignant tumors of the bladder

- The most common malignant tumor of the bladder in adults is the urothelial delivered transitional call carcinoma. (TCC).
- The most common malignant tumor of the bladder in pediatric age is the rhabdomyosarcoma

Transitional cell carcinoma (TCC)	
General info about TCC	- Transitional cell carcinoma-in-situ (TCCis) is believed to precede the development of TCC in some patients (as evidence by the presence of TCCis in the majority of cases of TCC). - TCCis is characterized by flat and thickened or gently undulated full-thickness dysplastic urothelium (nuclear pleomorphism, abnormal mitoses and apoptic figures are seen). Often appearing as a red patch, the disease may be multifocal within the bladder.
Incidence	- TCC account for about 5% of all malignancies in adults in the U.K. - Most patients are over 50. - There are definite risk factors for development of TCC (Table one)
Presenting features	- Hematuria. - Frequency of urgency. - Maybe multifocal within the bladder or the urinary tract.
Characteristics	- As another part of the urothelium-lined urinary tract, the tumor can have

	a varied appearance both macroscopically (fronded and seaweed-like to solid) and microscopically (well differentiated and papillary to poorly differentiated and wildly muscle-invasive). - The grading and staging system along with the prognosis for bladder TCC is shown in (Table 2). - Numerous cytogenetic alterations and molecular alterations have been found in TCC, including monosomy or deletion of the short (p) or long (q) arm of chromosome 9, and deletion of 17p (which involves p53 gene). - Squamous metaplasia of the urothelium can occur in a variety of circumstances, for example as a response to bladder stones, indwelling catheters and infection by Schistosoma (Schistosoma haematobium egg because they have spines➔irritation of the bladder➔ *squamous metaplasia*) (schistosomiasis is endemic in countries such as Egypt). Under these circumstances, squamous cell carcinoma of the bladder can develop. Often this tumor has invaded the bladder wall at time of presentation.

Table One: Risk factors for TCC

Smoking	**Increases risk up to five times**
Analgesics, NSAID especially phenacitin over periods of time.	Mainly associated with renal pelvis TCC, but also bladder tumors
Occupation	Workers in aniline dye, rubber and chemical industries (textile industries) due to exposure to β-naphthylanine (which in the liver is converted to a carcinogen that must be activated in the bladder). benzidine + bentalaphedamine.other than as: nitrosamines + phenyl chloride These workers need regular bladder checks
Cyclophosphamide used in treats of lymphomas, leukemia, and Polyarteritis Nodosa.	Can cause bladder cancer in the long-term (although used for cancer treatment)
Schistosomiasis	Causes chronic inflammation and metaplasia (squamous) of the bladder mucosa (leading to squamous cell carcinoma)
Chronic infections/inflammation	Some authorities believe that any chronic inflammatory process may predispose to cancer

Table Two: Grading and staging of bladder TCC:

Grade	Definition
G1	Well differentiated
G2	Moderately differentiated
G3	Poorly differentiated/undifferentiated
Stage	**Definition**
Tis	In situ carcinoma
Ta	Non-invasive, papillary tumor
T1	Tumor invades subepithelial C.T
T2	Tumor invades muscularis propia
T3	Tumor invades beyond muscularis propia
T4	Tumor invades prostate, uterus, vagina or pelvic wall/abdominal wall
N0	Lymph node free (no cancer)
N1	Single lymph node metastases (≤2 cm)
N2	Single metastases (>2 cm) or multiple metastases (≤5 cm)
N3	Multiple metastases (>5 cm)
M0	No metatases
M1	Metastases

Prognosis of TCC of the bladder:

Depends largely on the grade and stage of tumor, but most patients with metastatic bladder TCC die within 5 years of diagnosis.

Summary (from Robbins):

- Renal cell carcinomas account for 2-3% of all cancers in adults; classified into 3 types.
  - Clear cell carcinomas are the most common; associated with homozygous loss of the VHL tumor suppressor protein; tumors frequently invade the renal vein.
  - Papillary renal cell carcinomas are frequently associated with increased expression and activating mutations of the MET oncogene; tend to be bilateral and multiple, and show varying papilla formation.
  - Chromophobe renal cell carcinomas are less common; tumor cells are not as clear as in the other renal cell carcinomas.