PATHOLOGY TEAM 436

MEDICINE
KING SAUD UNIVERSITY

Tumors of the kidney

Revised by
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Objectives:

1. Recognize the benign tumors of the kidney.
2. Describe renal cell carcinoma and Wilms tumor.
3. Recognize transitional cell and squamous.
4. Carcinoma of the urinary bladder.

Black: Doctor's slides.

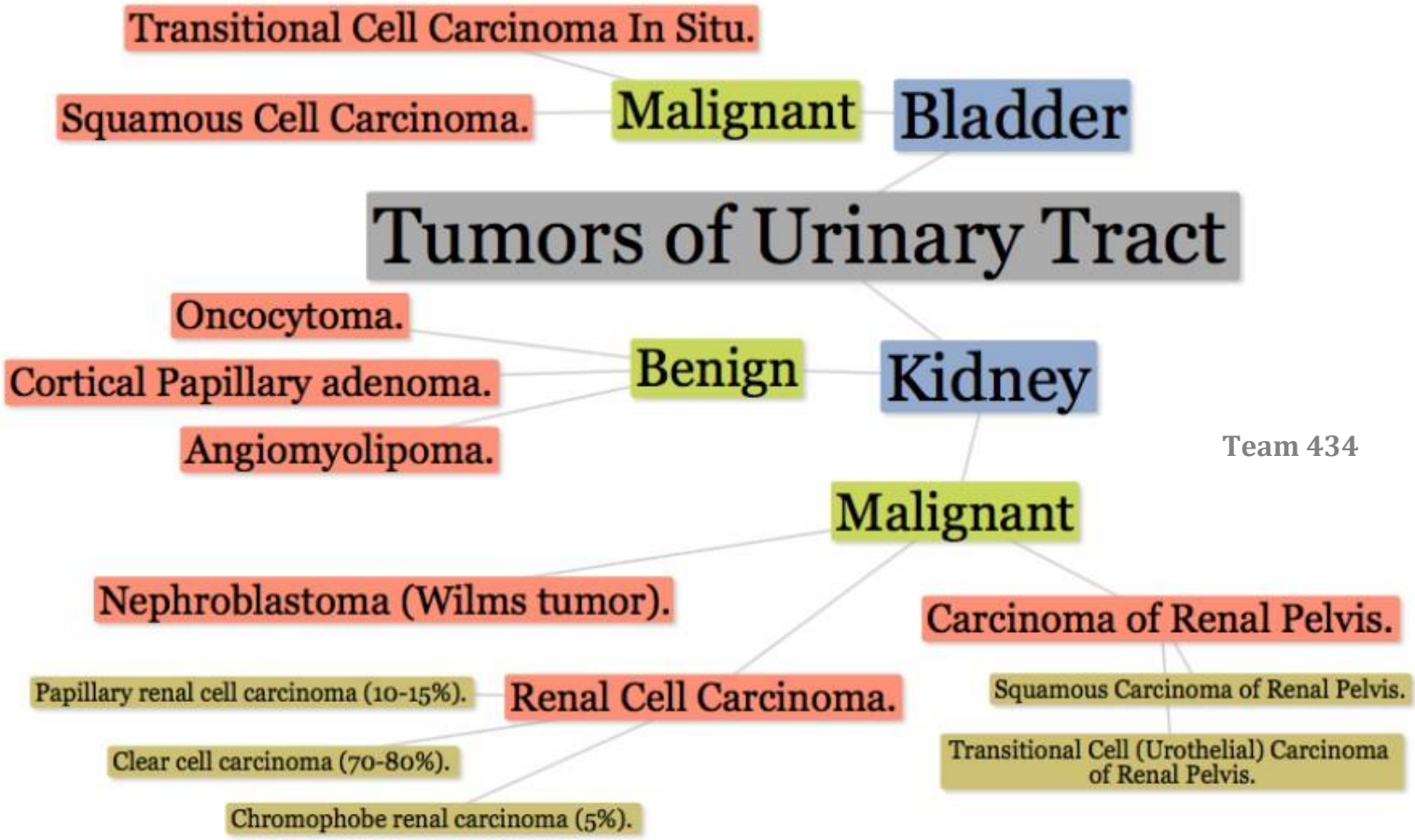
Red: important!

Green: Doctor's notes.

Grey: Extra.

Purple: Female's slides.

Blue: Male's slides.



Team 434

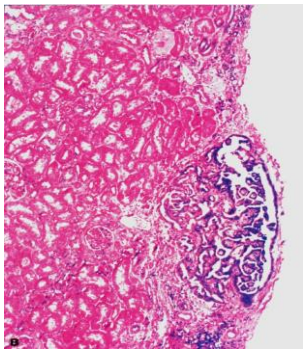
Benign tumors of the kidney:

1. Adenoma:

Adenoma = gland + benign

- This tumor is most often small and asymptomatic. It is derived from renal tubules.
- It may be a precursor lesion to renal carcinoma.
- It occurs in the cortex of the kidney and the outcomes are usually good.

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



Histology of a subcapsular papillary **adenoma** shows tubules arranged in a papillary fashion.

2. Angiomyolipoma:

It is often associated with the **tuberous sclerosis syndrome**[1].

Angiomyolipoma:
angio = blood vessel.
myo = smooth muscle.
lipoma = lipid.

3. Oncocytoma:

It's a benign tumor that arises from **the intercalated cells of collecting ducts**. These tumors are associated with genetic changes (loss of **chromosomes 1, 14, and Y**).

Malignant tumors of the kidney:

Neoplasms of the Renal Parenchyma:

A. **Renal cell carcinoma** (renal adenocarcinoma; hypernephroma).
B. Nephroblastoma **(Wilms tumor)**.
C. Transitional cell (urothelial) carcinoma.

Tumors of the lower urinary tract are about **twice as common** as renal cell carcinomas.

The most common **malignant tumor** of the kidney is renal cell carcinoma, followed in frequency by nephroblastoma (Wilms tumor) and by primary tumors of the calyces and pelvis.

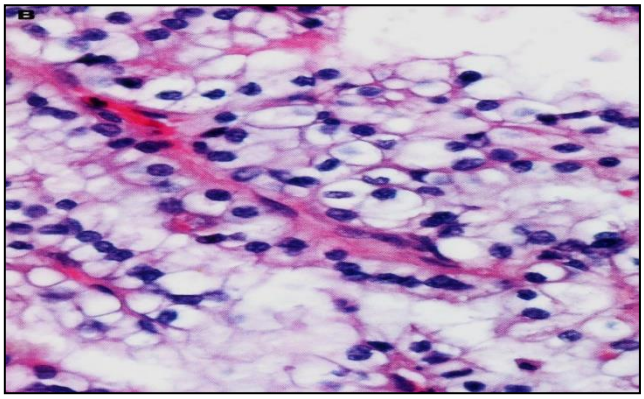
Renal cell carcinoma:

Etiology:

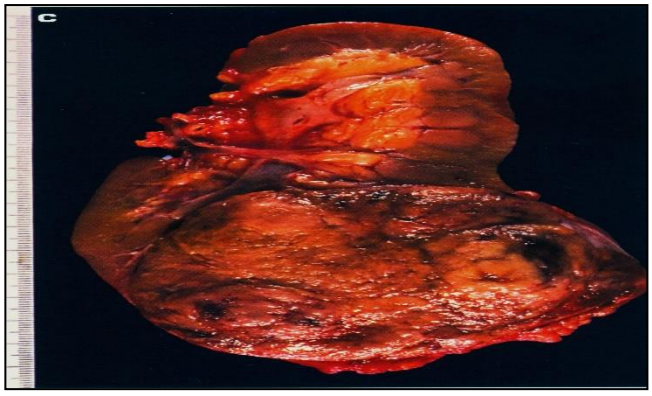
It is more common in **men**, occurs most often from 50-70 years of age and may be occult.

Risk factors:

Cigarette smokers, hypertensive, obese patients and those who have had occupational exposure to cadmium.



(hypernephroma, Grawitz tumor) is spreading into perirenal adipose tissue.

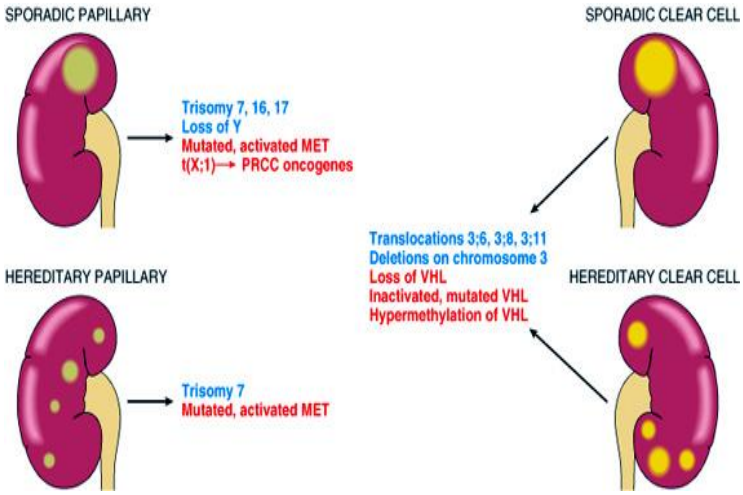


Typical lobulated, whorled, tan-colored cut surface of renal cell carcinoma.

[1] A rare, multi-system genetic disease that causes benign tumors to grow in the brain and on other vital organs such as the kidneys, heart, eyes, lungs, and skin. It usually affects the central nervous system and results in a combination of symptoms including seizures, developmental delay, behavioral problems, skin abnormalities, and kidney disease.

Pathogenesis:

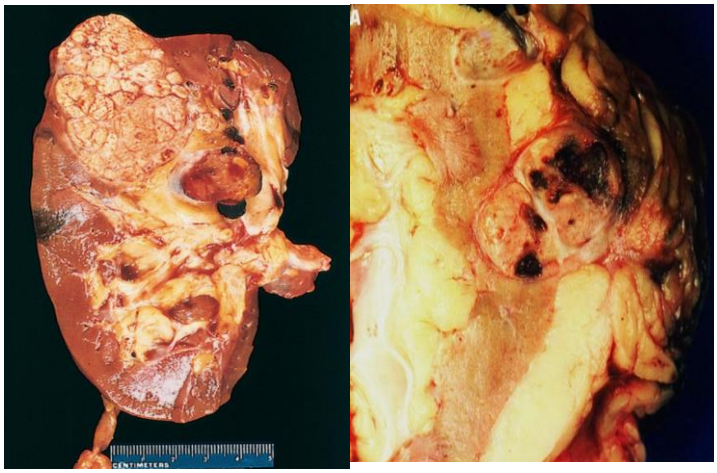
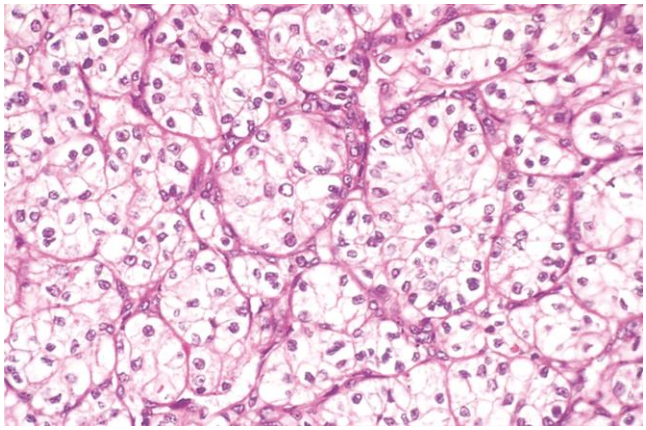
- it is associated with **gene deletions in chromosome 3**, it can also be associated with **Von Hippel-Lindau disease (VHL)**[2] which is caused by alterations in a gene localized in **chromosomes 3.**
- The carcinoma originates in **renal tubules**. Most often it arises in one of **the renal poles**, frequently the **upper pole.**
- Frequently the tumor invades **renal veins or the vena cava** and can extend up the vena cava.



Classification:

1. Clear cell carcinoma (70-80%).
2. Papillary renal cell carcinoma (10-15%).
3. Chromophobe renal carcinoma (5%).

1. Clear cell carcinoma:

Gross	Microscopic
	
- May arise anywhere in the kidney (Mostly **poles**). - **Solitary**[3] unilateral and large lesions (spherical masses). - **Marginated**. - Composed of yellow-gray-white tissues that distorts the renal outline. - Foci of hemorrhagic discoloration. - Grey-white necrosis. - Invasion of the renal vein. - thin fibrovasculer septa.	- Depending on the amounts of **lipid** and **glycogen** present, the tumor cells may appear almost vacuolated or may be solid. - Nuclei are small and round. - Clear cells with clear or granular pink cytoplasm. (***Clear*** renal cell) - Spreading into perirenal adipose tissue. - translocation or deletion or loss of VHL

[2] Is a disease which results from a mutation in the von Hippel–Lindau tumor suppressor gene on chromosome **3p25**

2. Papillary renal cell carcinoma:

- Exhibit papilla formation with **fibrovascular** cores.
- They tend to be **bilateral and multiple.**
- most common cytogenetic abnormalities are **trisomies 7, 16 and 17**.
- Easily metastasize.
- Pink cytoplasm.

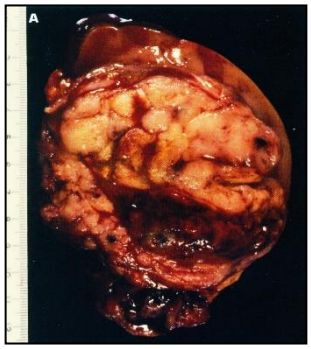
Clinical presentation:

- **Fever.**
- **Hematuria.**
- **Flank pain.**
- **Mass.**
- **Polycythemia.**

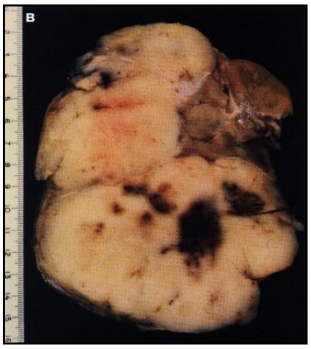
Chromophobe Renal Carcinomas:

- The least common.
- They arise from intercalated cells of collecting ducts.
- Tumor cells stain more darkly, so they are less clear than cells in clear cell carcinomas.
- Shows extreme hypodiploidy, by losing entire chromosomes, including chromosomes 1, 2, 6, 10, 13, 17, and 21.
- Grossly, they tend to be tan-brown.
- Have a goof prognosis.

Wilms tumor (nephroblastoma):



Solid, bulging, fleshy tan-white, partially necrotic tumor has replaced much of the kidney and is encompassed by a thin rim of renal tissue.



This **Wilms' tumor** appears whiter due to formalin fixation and has extended beyond the confines of the kidney

Etiology:

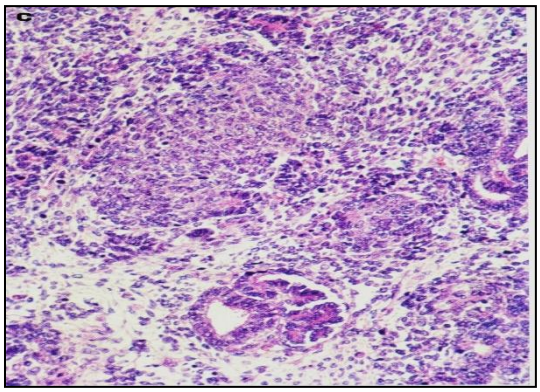
- This cancer is the most common renal malignancy of early childhood.
- Incidence peaks in **children 2-4 years** of age. Inherited as an autosomal dominant trait.

Pathogenesis (mutated genes):

- Originates from **primitive metanephric** tissue (derived from the mesoderm).
- 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 WAGR syndrome (i.e., Wilms tumor, aniridia, enital abnormalities, and mental retardation)→ deletion of **WT1.**
- Denys-Drash syndrome (DDS) approximately 90% → deletion of **WT1.**
- Beckwith-Wiedemann syndrome (BWS), enlargement of individual body organs → deletion of **WT2** (11p15.5)

The prognosis is very good with a **combination of nephrectomy and chemotherapy.**

Morphology:



- Characteristics are varied with **immature stoma, primitive tubules and glomeruli,** and **mesenchymal elements** such as fibrous connective tissue and cartilage bone.
- In most lesions, **triphasic combination** of blastemal, stromal and epithelial cell types is observed.
- The tumor is large, **solitary**, and **well-circumscribed** mass.
- the tumor is **soft, homogenous**, and **tan to gray,** with occasional
- foci of *hemorrhage*, **cystic degeneration, and necrosis**.
- **Nephrogenic rests**[3] are precursor lesions of Wilms tumors.

Histology shows hypercellular areas comprising undifferentiated blastema, **loose stroma with undifferentiated glomeruloid body.**

Presenting Features:

- Most often, the presenting feature is palpable flank mass, which may extend across the midline and down to the pelvis (often huge).
- Less often, the patient will present with fever, abdominal pain, hematuria, or intestinal obstruction as a result of pressure from tumor.

Transitional cell (Urothelial) carcinoma:

This cancer is the most common tumor of the urinary collecting system **but can occur elsewhere** thus it's central not peripheral. It's often multifocal in origin. Malignant tumor arising from the transitional cells.

- In the renal pelvis, transitional cell carcinoma has been associated with **phenacetin abuse.**
- This carcinoma is likely to **recur** after removal.
- Most often, the presenting feature is **hematuria**.
- There is tendency to spend by local extension to surrounding tissues.
- Associated toxic exposures may sometimes be involved, including the following:
  - Industrial exposure to **benzidine** or **β-naphthylamine**, which is an
  - **aniline dye.**
  - Cigarette **smoking**.
  - Long term treatment with **cyclophosphamide**

Papillary urothelial (transitional cell) carcinoma of renal pelvis. Note the exophytic, multifronded nature of the tumor.

Malignant tumors of the bladder:

- More common in male.
  - Transitional Cell Carcinoma In Situ (90%).
  - Squamous Cell Carcinoma (3-7%).

[3] A fragment of embryonic tissue in the kidney retained after the period of embryonic development

Pathogenesis:

- **first pathway:** The tumor is initiated by deletions of tumor-suppressor genes on 9p and 9q → formation of superficial papillary tumors →may then acquire TP53 mutations →invasion.
- **second pathway:** Initiated by TP53 mutations →carcinoma in situ →loss of chromosome 9 →invasion.

Morphology:

- Undifferentiated tumor.
- Could be invasive or noninvasive.

Clinical Features:

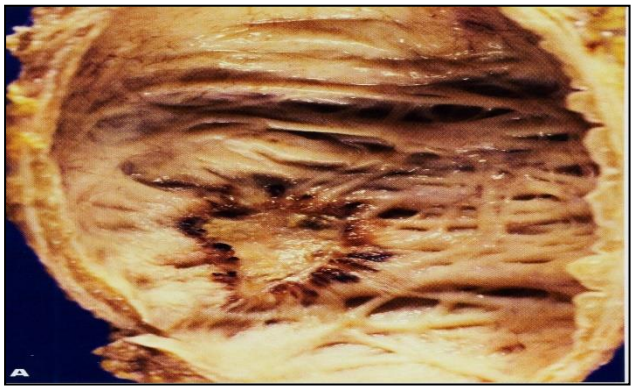
- All bladder tumors present with gross painless hematuria.
- Patients with urothelial tumors, have a tendency to develop new tumors after excision, and recurrences may exhibit a higher grade.

Treatment:

- Depends on tumor grade and stage and on whether the lesion is flat or papillary.

Transitional Cell Carcinoma In Situ:

Most common bladder cancer in **adult males**, rare and non-familial.



Urothelial (transitional cell) carcinoma in situ of the urinary bladder if untreated, up to 75% of cases go on to invasive cancer.

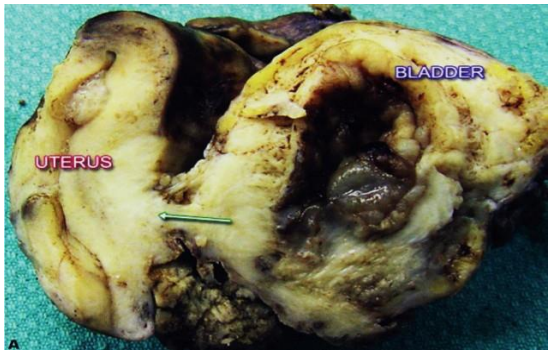
Squamous Cell Carcinoma:

- They typically show extensive keratinization.
- Associated with chronic bladder irritation and infection.

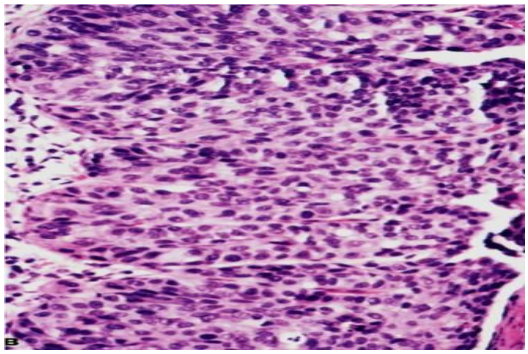
Risk factor:

Schistosoma haematobium infections in areas where it is endemic, such as Egypt.

Invasive urothelial carcinoma of the bladder is invading the muscle coat on the right side of the picture.



The invasion of the tumor up to the uterus.



Histology of carcinoma in situ (surface is to the right).

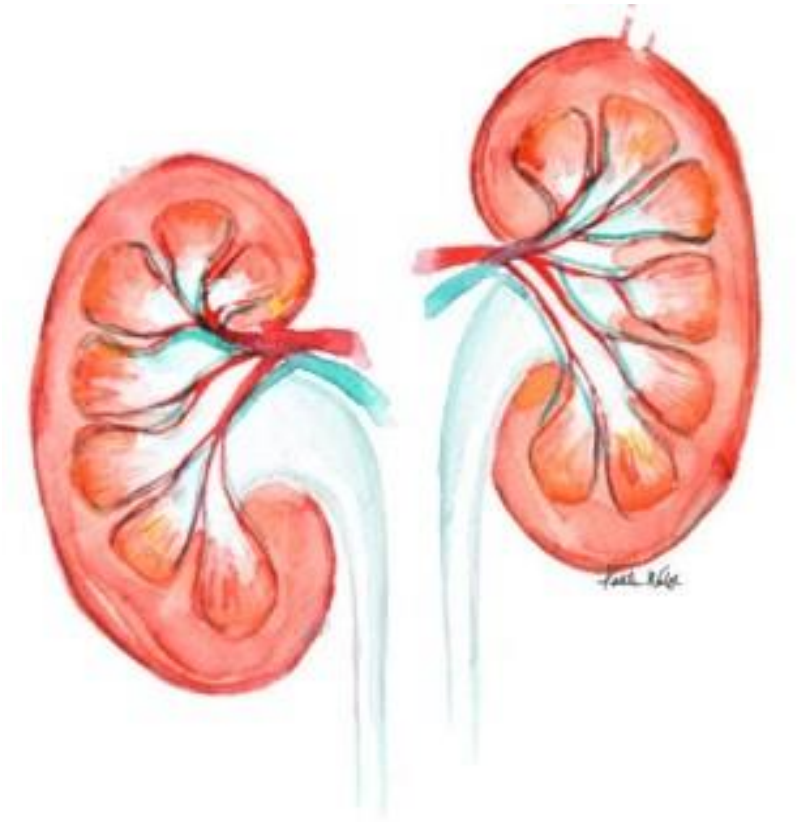
Box II. Grading and staging of bladder transitional cell carcinoma (TNM):

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 connective tissue
T2	Tumor invades muscularis propia
T3	Tumor invades beyond muscularis propia
T4	Tumor invades prostate, uterus, vagina or pelvic wall/abdominal wall
N1	Single lymph node metastases (≤2cm)
N2	Single metastasis (>2cm) or multiple metastases (≤5cm)
N3	Multiple metastases (>5cm)

The prognosis of TCC of the bladder depends largely on the grade and the stage of tumor but most patients with metastases bladder TCC die within five years of diagnosis.

Tumors			
Benign			
Tumor	**Info**		
Adenoma	○ This tumor is most often small and asymptomatic. It is derived from renal tubules. ○ It may be a precursor lesion to renal carcinoma.		
Angiomyolipoma	It is often associated with the tuberous sclerosis syndrome.		
Malignant			
Tumor	Definition	Characteristics	Info
Renal cell carcinoma	More common in men, cigarette smoking.	**Gene deletions in chromosome 3;** it can also be associated with **von Hippel-Lindau disease**	The three most common forms are: ▪ Clear cell carcinoma ▪ Papillary renal cell carcinoma ▪ Chromophobe renal carcinoma.
Clear cell carcinoma	Solitary, large and spherical masses, which may arise anywhere in the cortex.	The cut is yellow to orange to gray-white, with prominent areas of cystic softening or of hemorrhage.	**The tumor cells may appear almost** vacuolated or may be solid. At the other extreme are granular cells, which have small, round, regular nuclei and granular pink cytoplasm
Papillary renal cell	▪ Exhibit papilla formation with **fibrovascular** cores. ▪ They tend to be **bilateral and multiple.** ▪ They also show **necrosis,** hemorrhage, and cystic degeneration. ▪ The cells may have clear or, more commonly, pink cytoplasm		
Chromophobe Renal Carcinomas	▪ The least common, They arise from intercalated cells of collecting ducts. ▪ Tumor cells stain more darkly, so they are less clear than cells in clear cell carcinomas. ▪ Shows extreme hypodiploidy, by losing entire chromosomes, including chromosomes 1, 2, 6, 10, 13, 17, and 21. ▪ **Grossly, they tend to be** tan-brown. ▪ The cells usually have clear, flocculent cytoplasm with very prominent, distinct cell membranes, In general, they have a good prognosis		
Wilms tumor	Most common renal malignancy of early childhood Histology shows hypercellular areas comprising undifferentiated Blastema, loose stroma with undifferentiated glomeruloid body.	Associated with deletions of the short arm of chromosome 11.	**Can be part of the AGR (or WAGR) complex:** Associated with deletion of the **WT-1** **Associated with Beckwith-Wiedemann syndrome:** Associated with deletion of the **WT-2 gene.**
Transitional cell carcinoma	This cancer is the most common tumor of the urinary collecting system and can occur in renal calyces, pelvis, ureter, or bladder. It's often multifocal in origin.	○ In the renal pelvis its associated with **phenacetin abuse.** ○ This carcinoma is likely to recur after removal. ○ Most often, the presenting feature is hematuria.	
Bladder carcinoma	By far the common malignant tumor of the bladder in adults is the urthelial-delieverd transitional cell carcinoma (TCC). Not familial.	Two distinct precursor lesions to invasive urothelial carcinoma are recognized: The most common is a noninvasive papillary tumor, other is carcinoma in situ (CIS) Most commonly present with ***painless hematuria***	

"اللهم لا سهل إلا ما جعلته سهلًا و أنت تجعل الحزن إذا شئت سهلًا"



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القادة

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