RENAL PATHOLOGY LECTURE 7

(II) PAPILLARY RCC

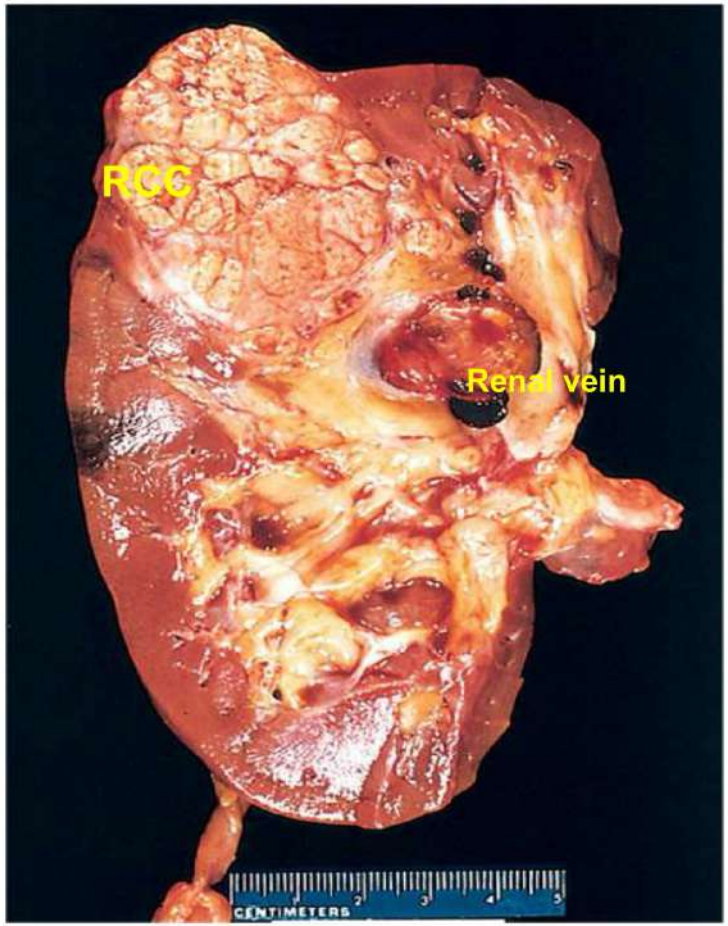
- Comprises 15%of RCC.
- • Shows **papillary growth** pattern.
- • Are frequently **multifocal & bilateral**;
- • Occurs in **familial & sporadic** forms,
- • The cause is the **MET proto-oncogene,** located on chromosome 7q31.
- • **Trisomy of chromosome 7 is seen commonly in both familial &sporadic cases,** with the addition of an activating mutation of the MET gene in the familial cases only.

(III) CHROMOPHOBE RCC

- **Rarest (5%)type of** RCC
- .• **Arise** from intercalated cells of collecting ducts.
- • Tumor cells **stain more darkly**(hence the name, i.e., they are less clear than cells in clear cell RCC).
- • **Unique** in having **multiple losses of entire chromosomes,** including chromosomes 1, 2, 6, 10, 13, 17, & 21.
- • In general, chromophobe RCC have a good prognosis.

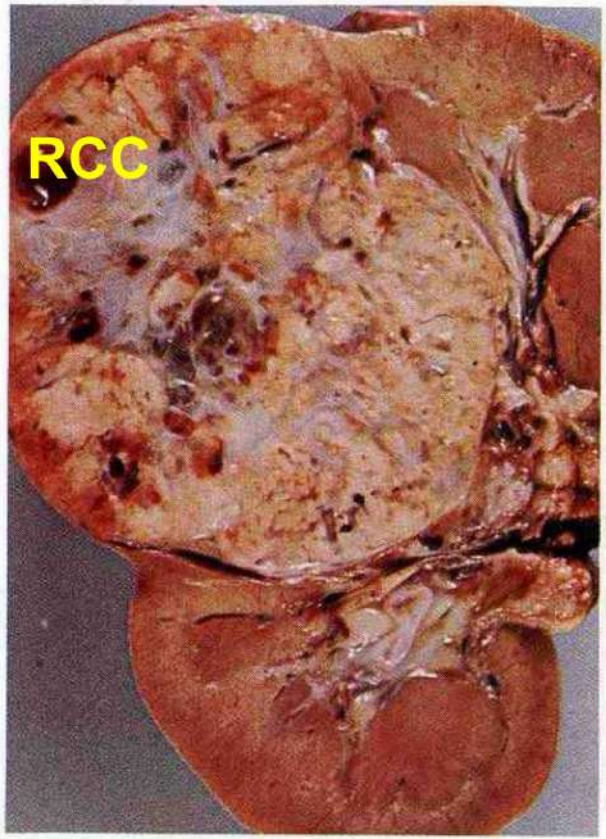
MORPHOLOGY (OF ALL TYPES)

- **Grossly (RCC)**
- **the clear cell RCC** is usually **solitary, spherical & large** mass, up to15 cm in ∅, arising anywhere in the cortex, & its cut surface is **yellow orange** with areas of **cystic necrosis &** fresh or old **hemorrhages.**
- As the tumor enlarges, it **frequently invades** the :
- (a)**renal vein** growing as a solid column within it, sometimes extending asfar as the inferior vena cava & even into the right side of the heart.
- Less frequently, it may invade through the:
- (b) Walls of the **calyces, pelvis & the ureter, & occasionally,**
- (c) in to the **perinephric fat & adrenal gland.**



Renal cell carcinoma (RCC): typical cross-section of ★yellowish, spherical tumor in the upper pole of the kidney.

★Note the tumor invasion in the dilated thrombosed renal vein



10.54 Adenocarcinoma: kidney

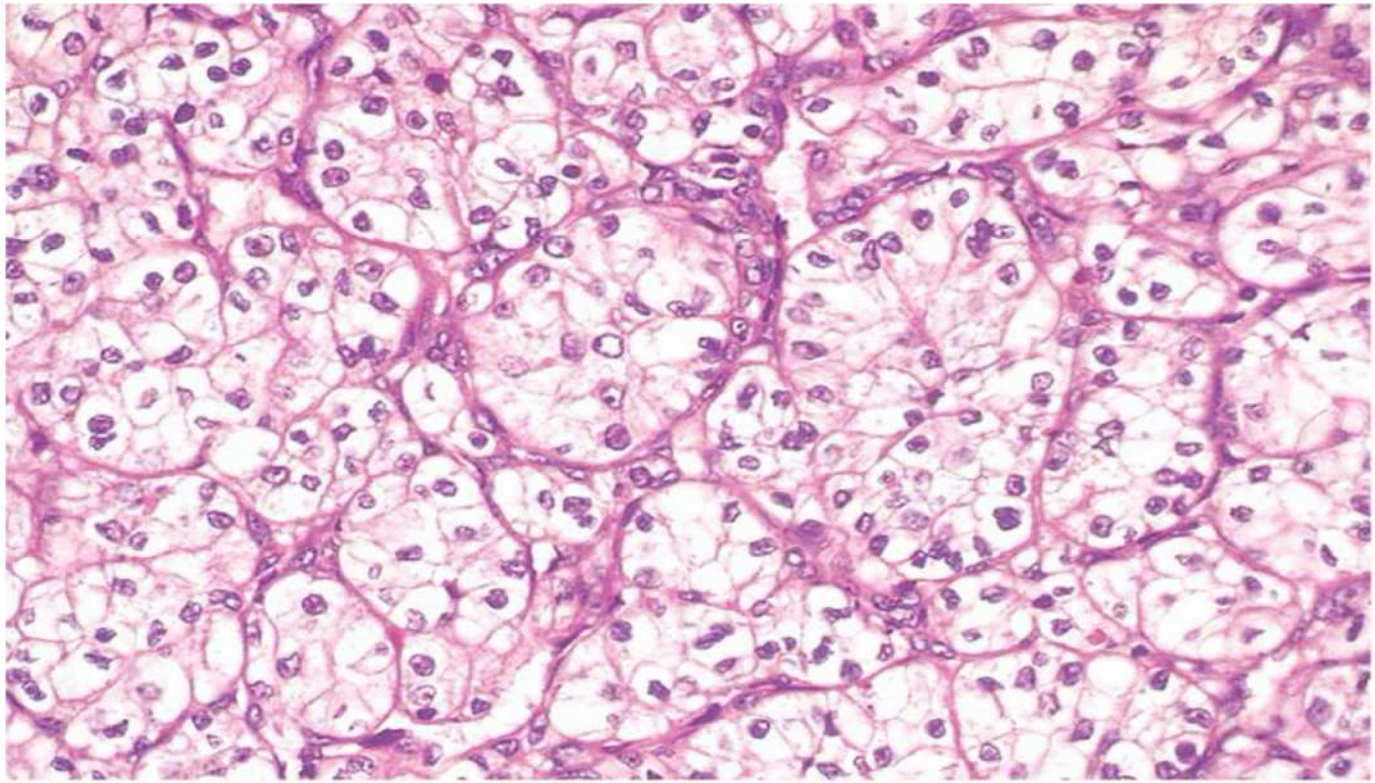
Smooth rounded tumor mass in the upper pole of the kidney invading the renal vein.
Yellow cut surface, with greyish fibrous septa, areas of hemorrhage & cystic necrosis

.

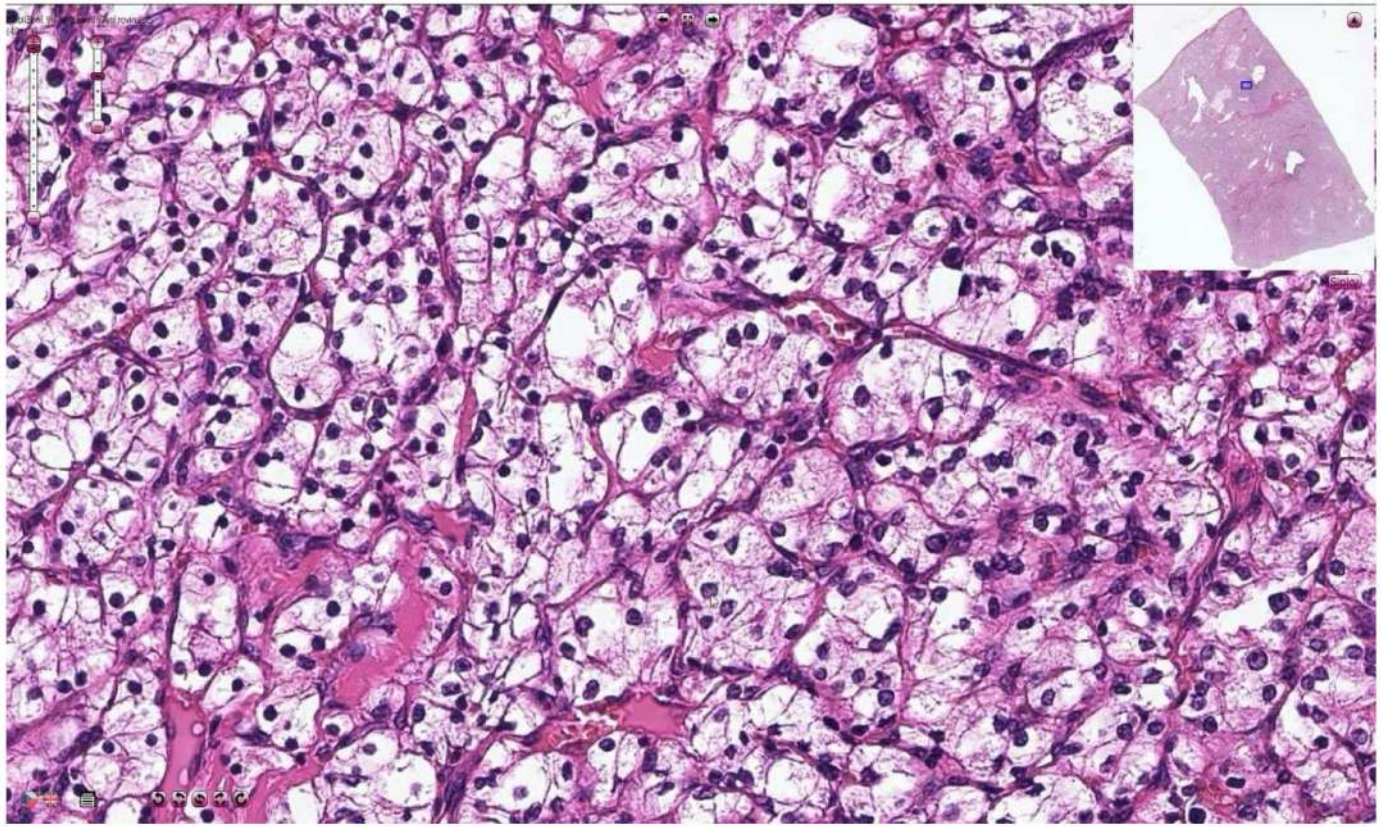
MORPHOLOGY (OF ALL TYPES)

- **Histologicaly (RCC):**
- Depending on the amounts of lipid & glycogen present, the tumor cells may appear:
- (a) Classically **vacuolated**, with lipid-laden **clear** cells, with small & round nuclei ,or
- (b)Granular cells, resembling the tubular epithelium, with granular pink cytoplasm.
- Some tumors exhibit marked degrees of **anaplasia**, with numerous mitotic figures & markedly enlarged, hyperchromatic, pleomorphic nuclei.
- The cellular arrangement, too, varies widely, with cells forming **tubules, cords or disorganized masses**. The stroma is usually scant, but highly vascularized

High power detail of the **clear cell pattern of renal cell carcinoma**



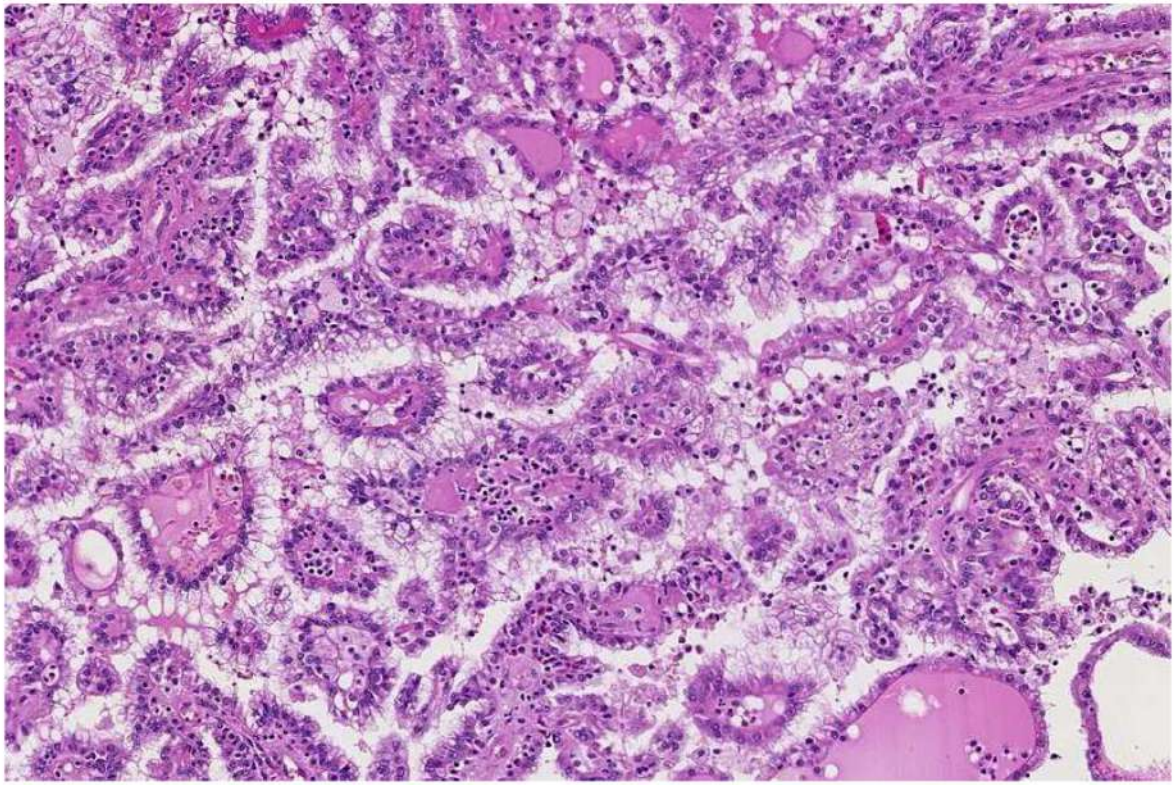
RCC



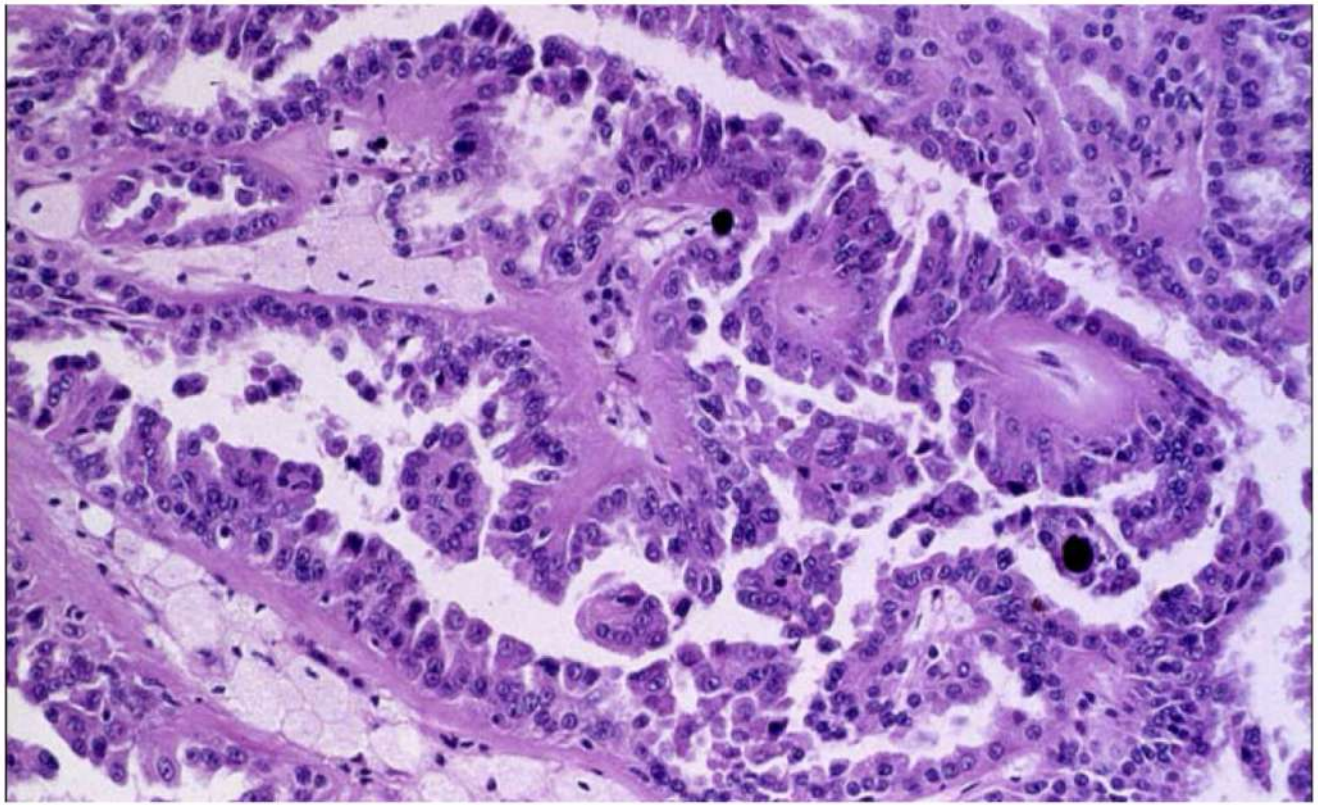
MORPHOLOGY (OF ALL TYPES)

- **Grossly**
- **the papillary RCC;**
- **exhibit papillally formation with fibrovascular cores.**
- **They tend to be bilateral & multiple, & may show gross evidence of cystic degeneration, necrosis & hemorrhage; but because of their lower lipid content, they are less orange-yellow in color.**
- **The cells can have clear or pink cytoplasm.**
- **Chromophobe RCC:**
- tends to be **tan-brown grossly.**
- **Their cells usually have clear, flocculent cytoplasm with very prominent, distinct cell membranes.**
- **The nuclei are surrounded by halos of cleared cytoplasm.**
- **By EM, large numbers of characteristic macrovesicles are seen.**

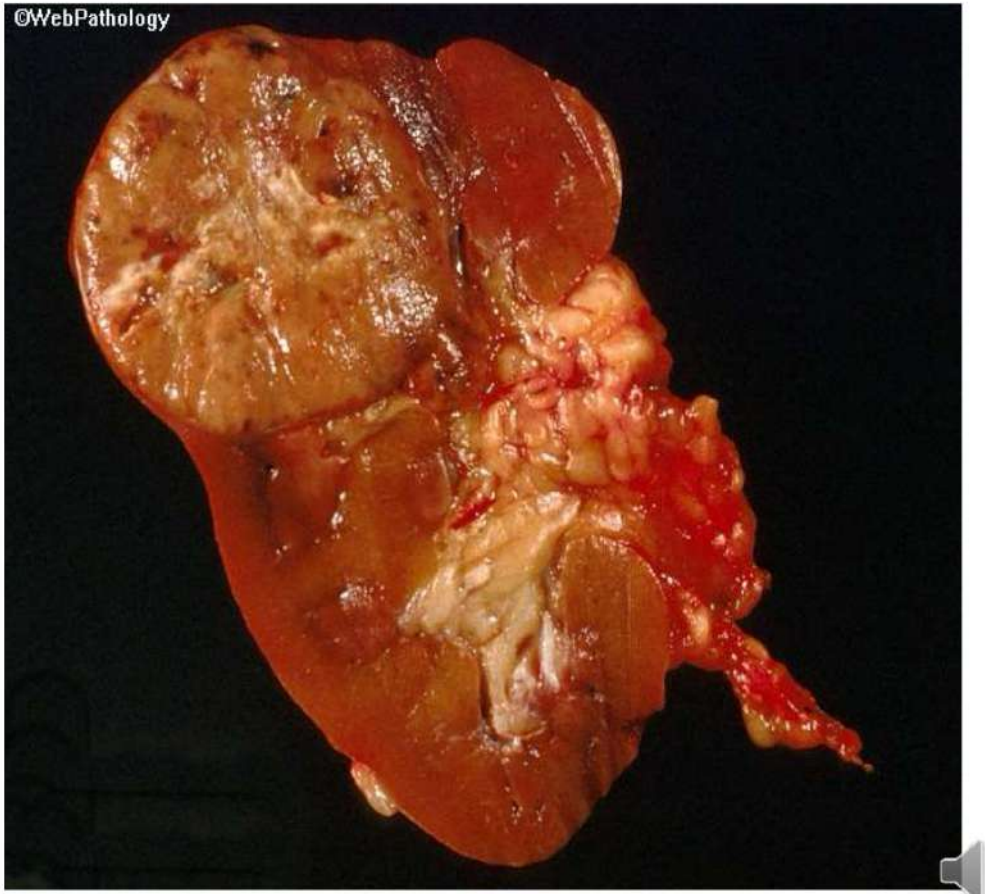
Papillary RCC



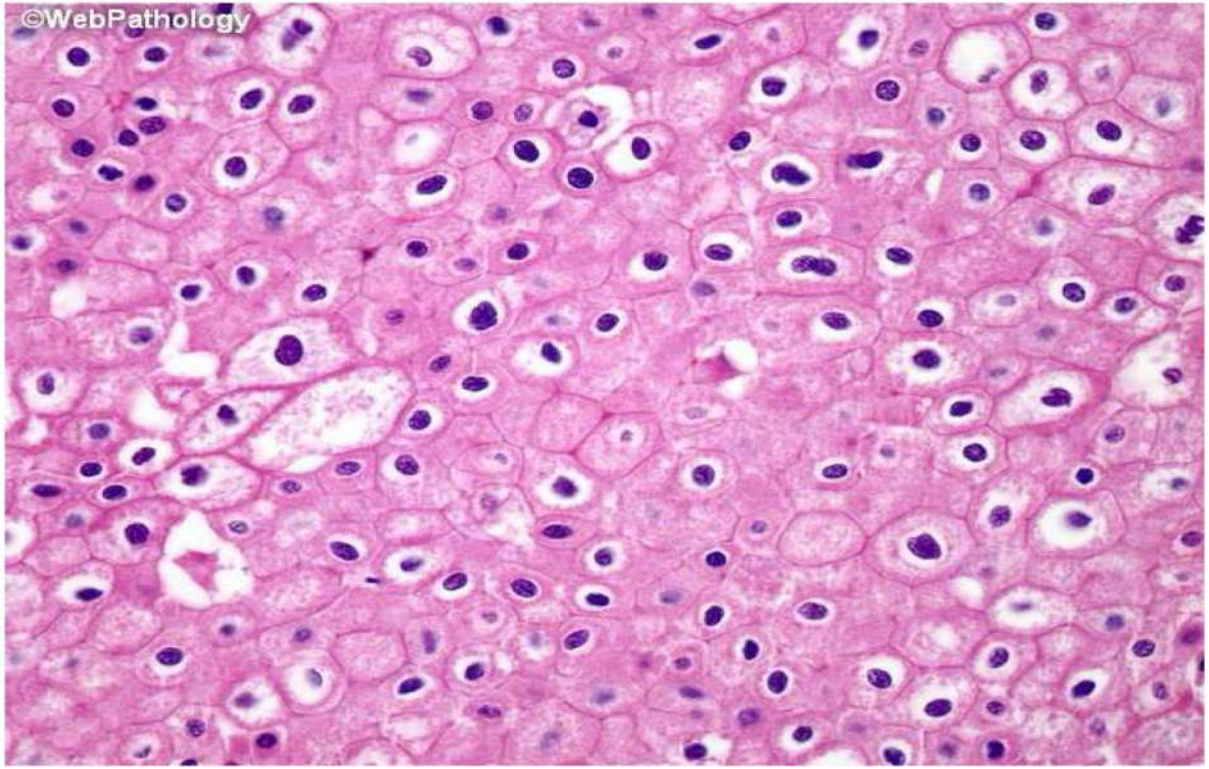
Papillary RCC



The upper pole of the kidney shows a well-circumscribed, mahogany brown tumor with central scar. The mass bulges the renal capsule but appears to be contained within it. Microscopically, it had classic features of a chromophobe renal cell carcinoma.



Chromophobe RCC



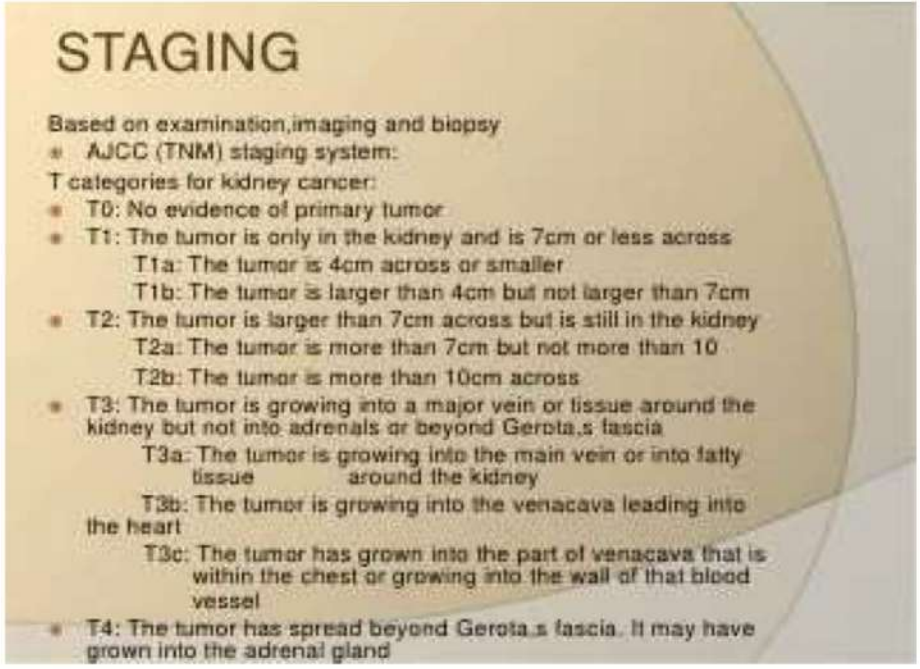
CLINICAL MANIFESTATIONS OF RCC

- **Clinically**
- the most frequent & characteristic presenting manifestation of all RCCs is ((PAIN,HEMATURIA ,MASS)):
- **(I)Hematuria, occurring in more than 50% of cases.**
- Less commonly as;
- **(II)painful, palpable flank mass,or may**
- **(III) present with metastases, in which the primary T may remain silent &is discovered only after it metastasis to other sites, the commonest arethe lungs & bones.**
- **Extra-renal nonspecific effects (manifestation)of RCC are (1) fever, (2) polycythemia affecting 5% to 10% of persons with RCC resulting from elaboration of erythropoietin by tumor cells.**
- Uncommonly, RCC may cause **(3) paraneoplastic syndromes due to their production of a variety of hormone-like substances, resulting in hypercalcemia, hypertension, Cushing syndrome, feminization or masculinization.**

IMMUNOHISTOCHEMICAL TECHNIQUES IN RENAL NEOPLASMS

- Immunohistochemical techniques with a variety of markers have been applied more frequently in diagnostic pathology of renal neoplasm
- Some of the most important and useful markers for the diagnosis of renalneoplasm include **cytokeratins, vimentin, PAX2, PAX8, RCC marker, CD10**, Eachmarker has its diagnostic role in a specific diagnostic setting.
- The common diagnostic situations that call for immunohistochemical stainingare differential diagnoses of renal versus non renal neoplasms,

Staging of RCC

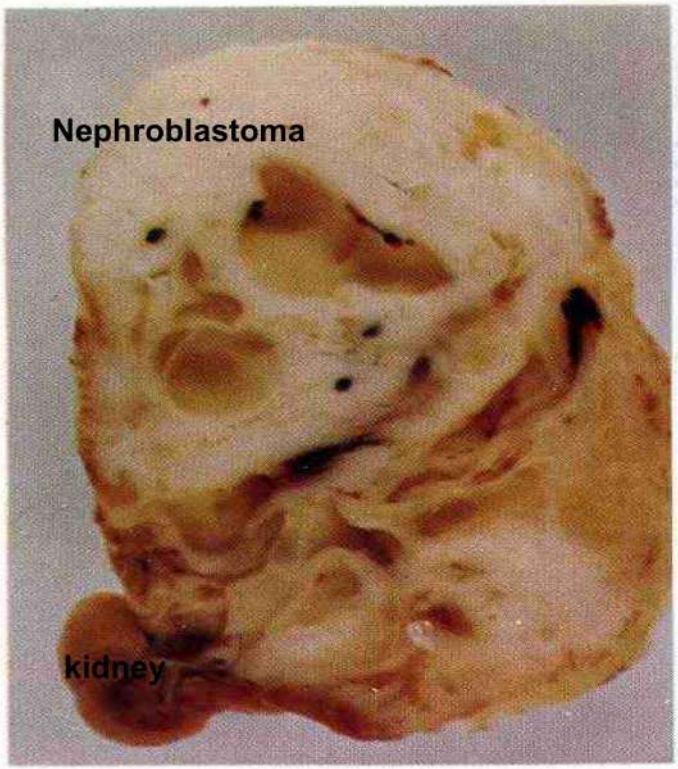


NEPHROBLASTOMA (WILM'S TUMOR)

- Represent **10%** of all renal cancers.
- The **3rd most common solid cancer in children** younger than 10 years ;it occurs rarely in adults,
- A mixed tumor, contain a variety of cell & tissue components (epithelial & mesenchymal), **all derived from the mesoderm.**
- Triphasic tumour
- blastemal tissue
- stromal cells
- epithelial cells (premature tubule and glomeruli)
- Like retinoblastoma, it may arise sporadically or be familial, inherited as an autosomal dominant trait.

CLINICAL PRESENTATION AND DIAGNOSIS

- Abdominal mass, painless palpable mass ,non-tender , homogenous or by incidental finding of abdominal mass by physician during rout in examination of healthy child or by mother during bathing .
- Hematuria when tumor rupture and invade collecting ducts
- Hypertension due to renin secretion.
- Intestinal obstruction
- Fever , anemia
- Diagnosis
- Ultrasound (initially)
- CT scan , MRI



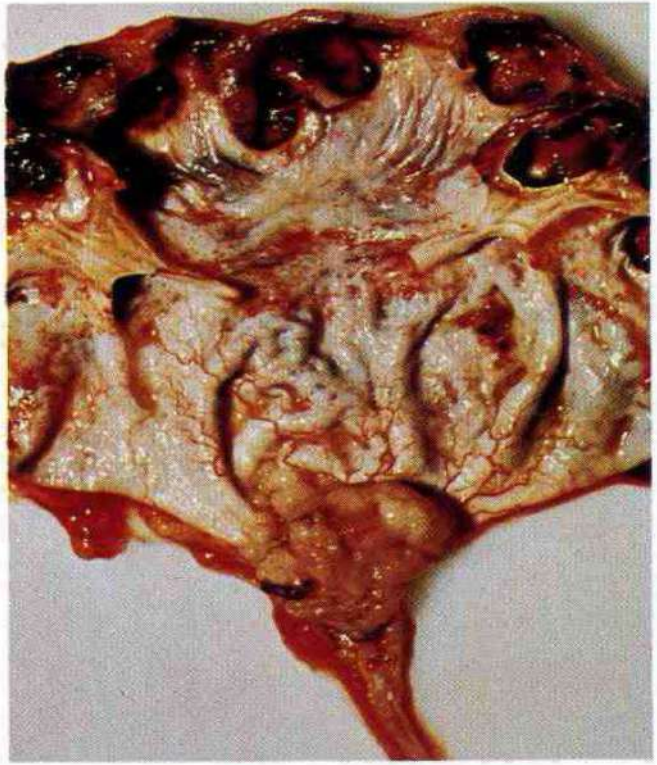
10.55 Wilms' tumour (nephroblastoma): kidney

Nephroblastoma(Wilms Tumor).

A creamy-white tumor has largely replaced the kidney, a small portion of which is visible at the lower left. Numerous cysts & focal hemorrhages are present within the tumor.

TUMORS OF THE (RENAL CALYCES, PELVIS, URETER, URINARY BLADDER & URETHRA)

- **The entire urinary collecting system, from renal calyces to urethra is lined by transitional epithelium, so its epithelial tumors assume transitional or"urothelial" patterns.**
- **Clinically, the most common presentation of all these tumors is painless hematuria.**
- A small tumor in the ureter may cause **urinary outflow obstruction& hydro nephrosis ,**
- have greater clinical significance than a much larger mass in the bladder.
- **Renal pelvis papillary TCC a carcinomas** (comprising 5% of all kidney ca),are much less frequent than bladder ca. Usually causes painless hematuria; but if they cause obstruction, it may result in hydronephrosis and pain in the costovertebral angle.
- **Infiltration of the walls of the pelvis, calyces, & renal vein worsens the prognosis**



10.59 Transitional cell carcinoma: renal pelvis

A sessile papillary yellowish-grey TCCa at the pelvi-ureteric junction lead to obstructing the ureter and producing severe hydronephrosis, with… marked pelvic mucosal congestion & extensive calyceal hemorrhage

BLADDER CANCER

- **Bladder cancer is a disease in which malignant (cancer) cells form in the tissues of the bladder.** Smoking can affect the risk of bladder cancer. Signs andsymptoms of bladder cancer include blood in the urine and pain during urination. Tests that examine the urine and bladder are used to diagnose bladder cancer.
- Bladder ca affect men 3 times as frequently as women. It usually develop in the 50 to 70 years age group.
- 50 times more common in aniline dye workers, duo to carcinogenic effect of β- naphthylamine
- It is more common in:
- • Schistosomiasis of the bladder
- • Chronic cystitis,
- • Cigarette smoking,
- • Certain drugs (e.g., cyclophosphamide) are also believed to induce higher rates of bladder cancer

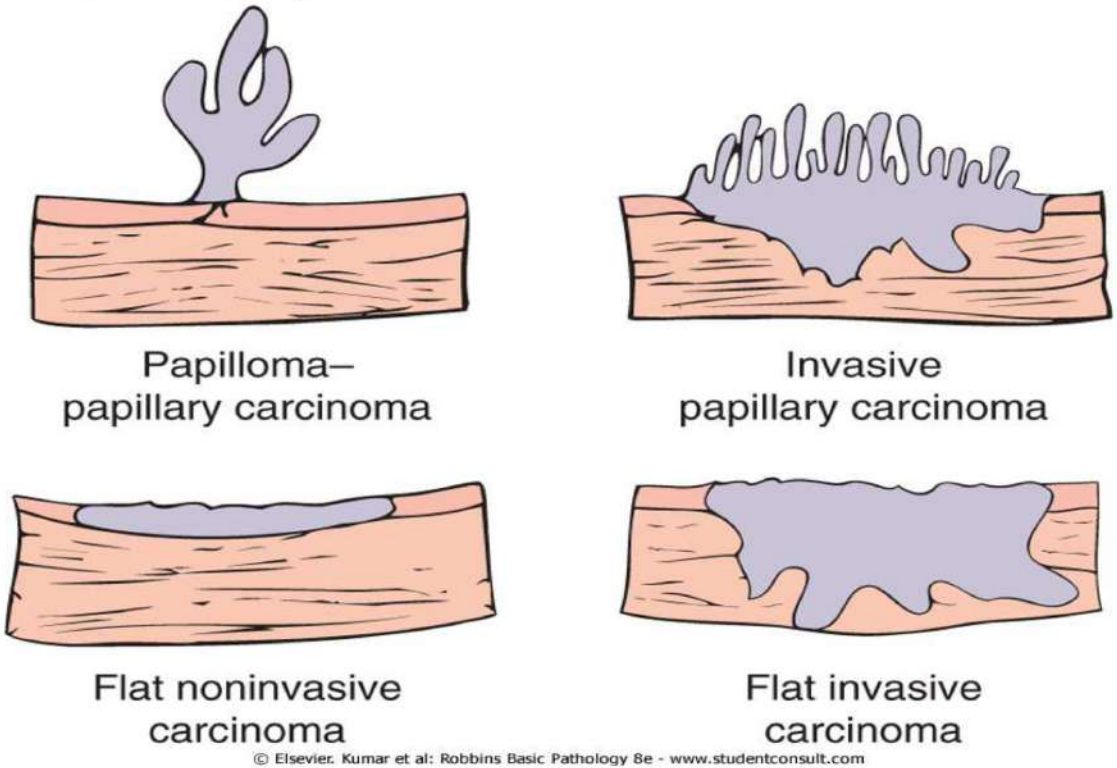
BLADDER TUMORS CLASSIFIED INTO:

- **(1) Very rare benign papillomas,usually solitary,** 0.2-1.0 cm frond like structures having a delicate fibrovascular core covered by multilayered completely normal looking transitional epithelium. They are noninvasive & rarely recur once removed.
- **(2) Papillary urothelial tumors of low malignant potential.**
- **(3) Transitional(Urothelial) carcinoma (TCCa)** may be papillary orflat, noninvasive or invasive & low or high grade.
- Pathologists divide urothelial carcinoma into two grades – low and high based on how the tumour cells look when examined under the microscope.
- Low-grade tumours are made up of cells that look more like normal urothelial cells while high-grade tumours are made up of more abnormal looking cells that tend to be larger, darker, and less organized than normal urothelial cells.
- The grade is important because high-grade tumours are more likely to re-grow after treatment and spread to other parts of the body.

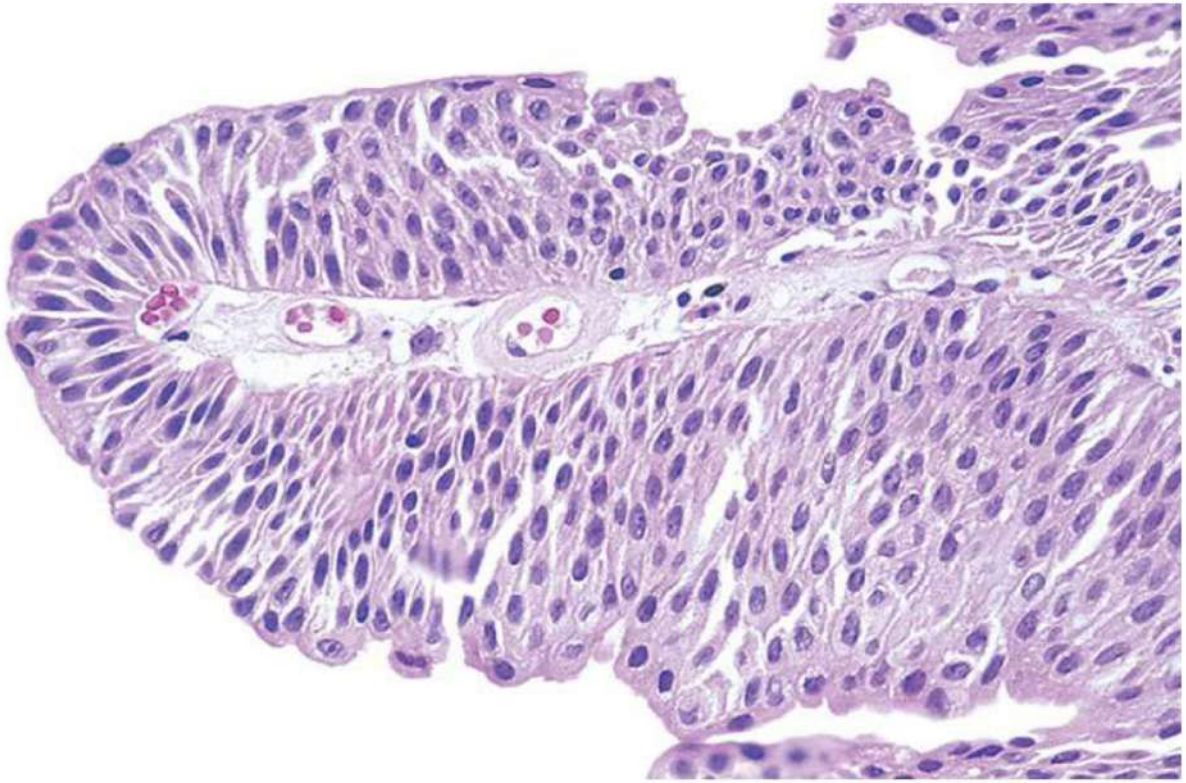
GRADING OF BLADDER CANCERS:

- **Low-grade (Grade I) ca :are always papillary& rarely invasive, may recur after removal. Increasing degrees of cellular atypia & anaplasia are seen in papillary exophytic tumors accompanied by an increase in the size of the tumor & evidence of invasion of the submucosal.**
- **High-grade (Grades II & III) ca** can be **papillary or flat** may cover larger areas of the mucosa, invade deeper **in the muscular layer,** may ulcerate, & may show foci of squamous differentiation.
- **5% of bladder ca in US** (BUT up **50%** else where in world) are usually associated with Schistosomal cystitis are **true squamous cell ca**
- Grades II & III ca infiltrate surrounding structures, spread to regional LNs & occasionally metastasize.
- In addition to overt ca, an in situ (pre-invasive) stage of bladder carcinoma can be recognized, often in individuals with previous or simultaneous papillary or invasive tumors.

Four morphologic patterns of bladder tumor

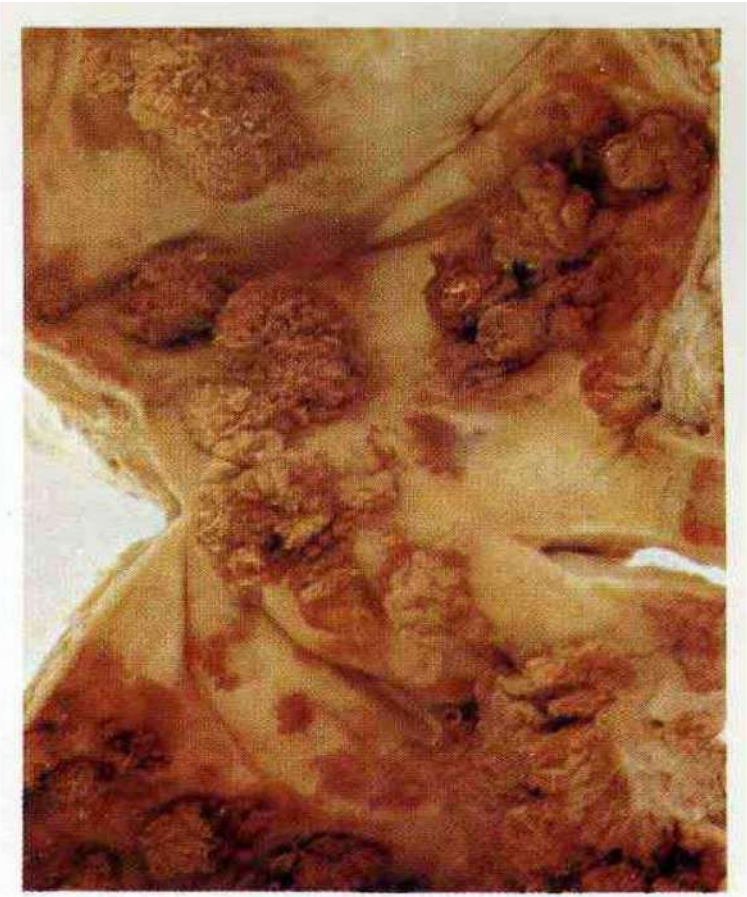


Low-grade papillary urothelial carcinoma of the bladder. The delicate papilla is covered by orderly transitional epithelium.



BLADDER CANCERS

- The most common genetic abnormalities seen in bladder cancers are mutations, involving several genes, on chromosome 9 (including p16), p53, & FGFR3.
- Bladder tumors prognosis depends most importantly on the depth of the invasion of the ca (muscular invasion usually treated by total cystectomy) & on their histological grade.
- Except for the clearly benign papillomas , all bladder tumors tend to recur after removal.
- Tumors invading ureteral or urethral orifices cause UT obstruction.
- Prognosis of low-grade shallow bladder tumors, after removal isgenerally good, but when...
- Deep penetration of the bladder wall muscles has occurred; the prognosis is poor with less than 20% 5-year survival rate

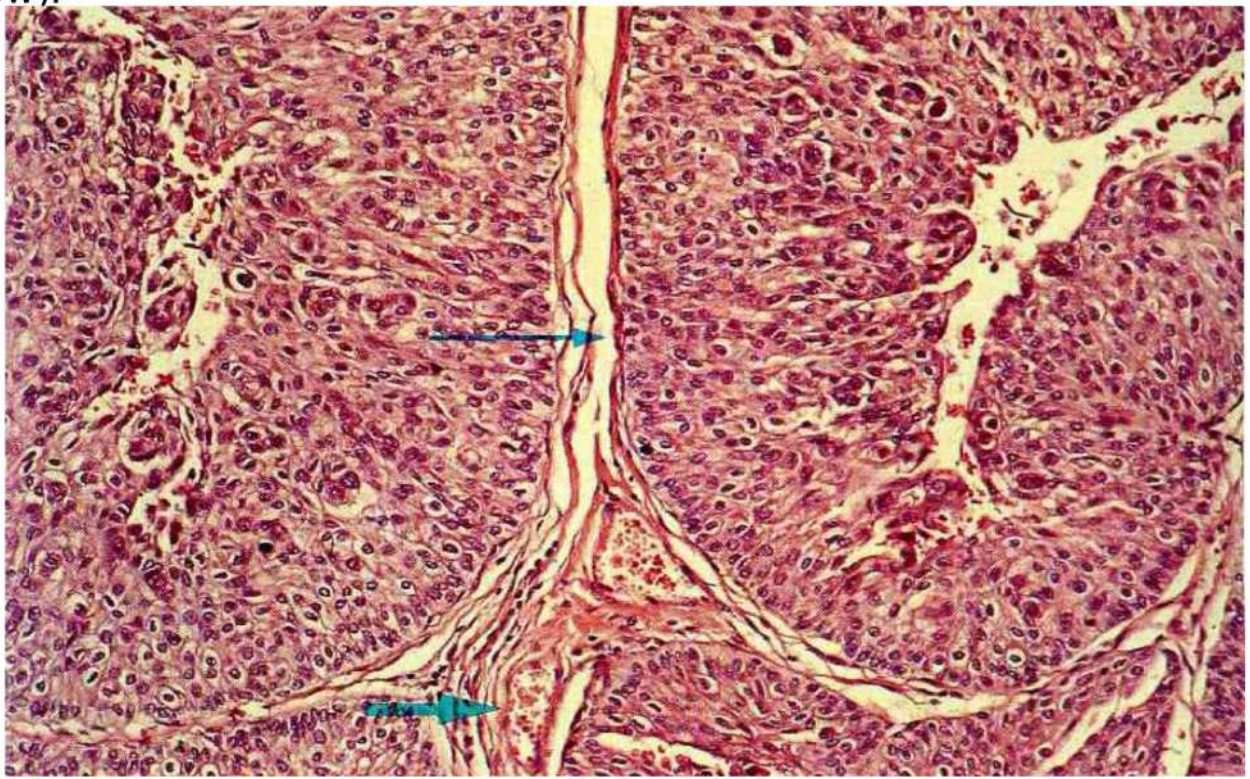


10.63 Papillomas: bladder

Low-grade papillary urothelial carcinoma: bladder.

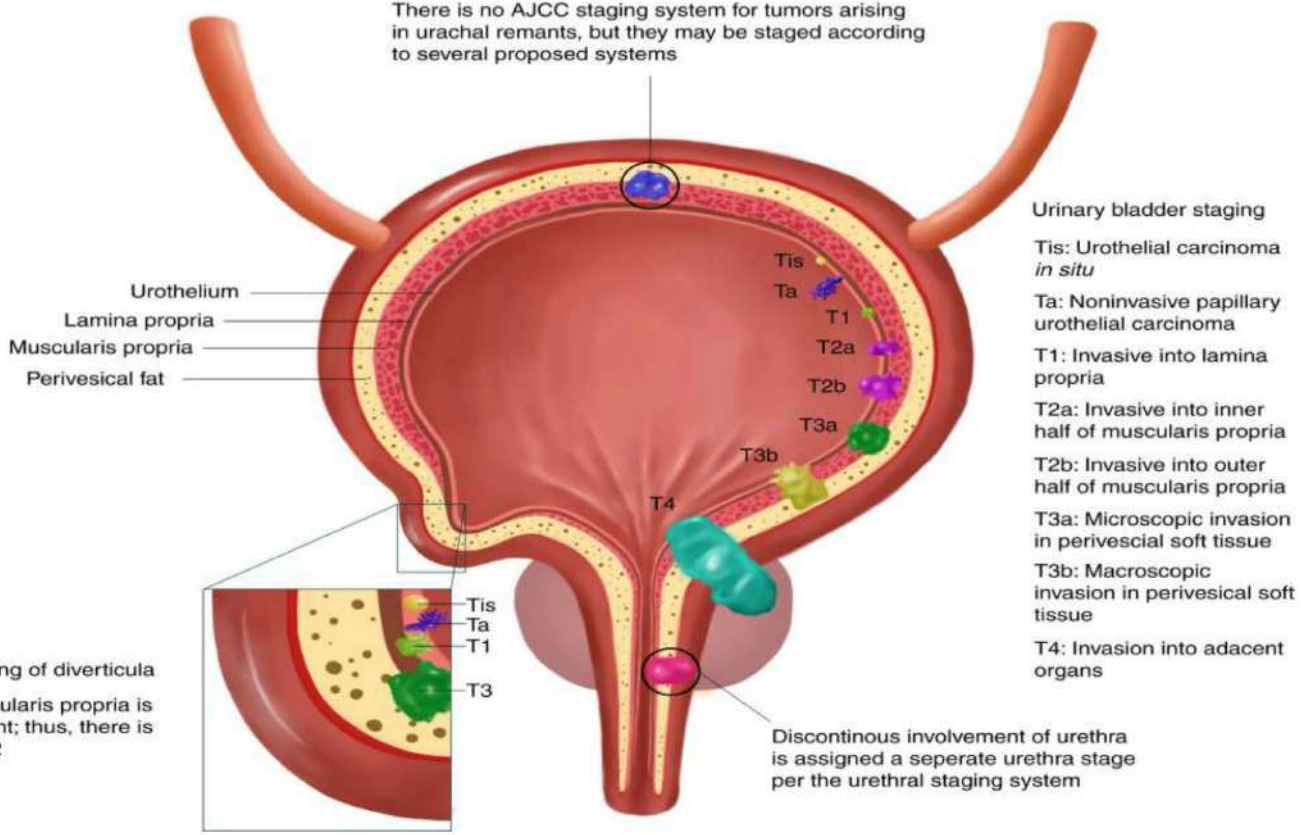
- Multiple small sessile papillary tumors, covering large areas of the bladder.
- The patient worked for many years in the rubber industry.

Transitional cell carcinoma, Grade II X150. Papillae, covered by transitional epithelium, several times thicker than normal (thin arrow) & with a fibrovascular core (thick arrow).



Staging of urachal tumours

There is no AJCC staging system for tumors arising in urachal remants, but they may be staged according to several proposed systems



Urinary bladder staging

Tis: Urothelial carcinoma *in situ*

Ta: Noninvasive papillary urothelial carcinoma

T1: Invasive into lamina propria

T2a: Invasive into inner half of muscularis propria

T2b: Invasive into outer half of muscularis propria

T3a: Microscopic invasion in perivescial soft tissue

T3b: Macroscopic invasion in perivesical soft tissue

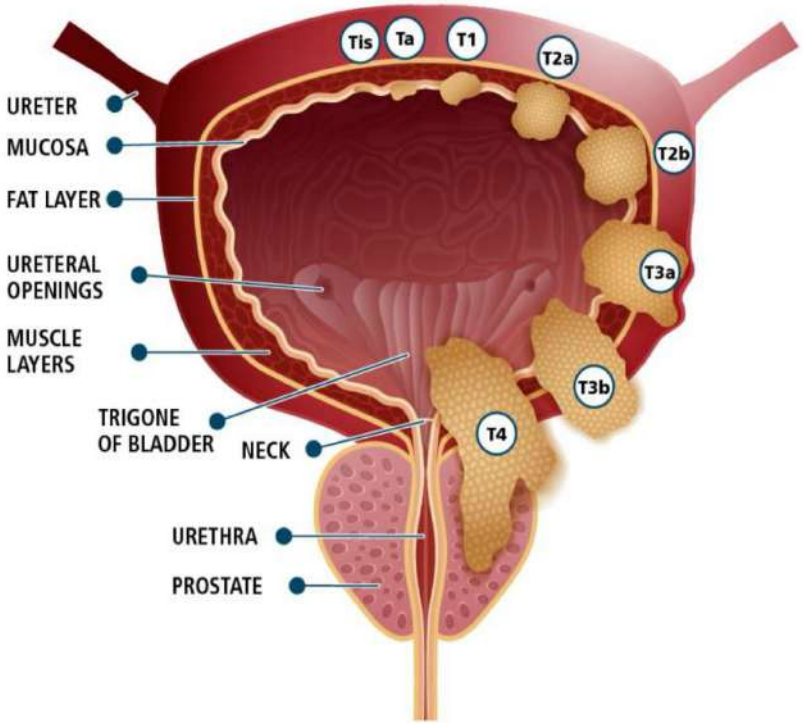
T4: Invasion into adacent organs

Staging of diverticula

Muscularis propria is absent; thus, there is no T2

Discontinous involvement of urethra is assigned a seperate urethra stage per the urethral staging system

Staging of Urothelial ca of Urinary bladder



STAGES

Stage 0 (Tis)	Flat cancerous cells within the cells lining the bladder
Stage 0 (Ta)	Inner lining of the bladder
Stage 1 (T1)	Into first deep bladder layer
Stage 2 (T2a)	Into bladder muscle
Stage 2 (T2b)	Deeply into bladder muscle
Stage 3 (T3a)	Into bladder fat
Stage 3 (T3b)	Deeply into bladder fat
Stage 4 (T4)	Invading other organs around the bladder (prostate, cervix, vagina)