

PATHOLOGY OF TUMORS OF THE KIDNEY & URINARY TRACT

April 2021

Reference: Robbins & Cotran Pathology and Rubin's Pathology

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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.

Key Outlines:

- Benign tumors of the kidney.
- Renal Cell Carcinoma.
- Wilm's tumor (nephroblastoma).
- Transitional Cell and Squamous Carcinoma of bladder.



LECTURE OUTLINE

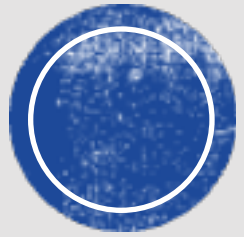
Tumors of Kidney

- Benign tumors of the kidney
 - Oncocytoma
 - Angiomyolipoma
- Malignant tumors of the kidney
 - Renal Cell Carcinoma
 - Wilm's tumor (nephroblastoma)

Tumors of urinary tract

- Transitional cell neoplasms of urinary bladder
- Squamous cell carcinoma of urinary bladder





NEOPLASMS OF KIDNEY

TUMORS OF THE KIDNEY

Benign Tumors

1. RENAL ONCOCYTOMA
2. ANGIOMYOLIPOMA

Malignant Tumors

1. RENAL CELL CARCINOMA
2. WILM'S TUMOR



RENAL ONCOCYTOMA

Benign tumors that arises from the intercalated cells of the collecting ducts in the kidney.

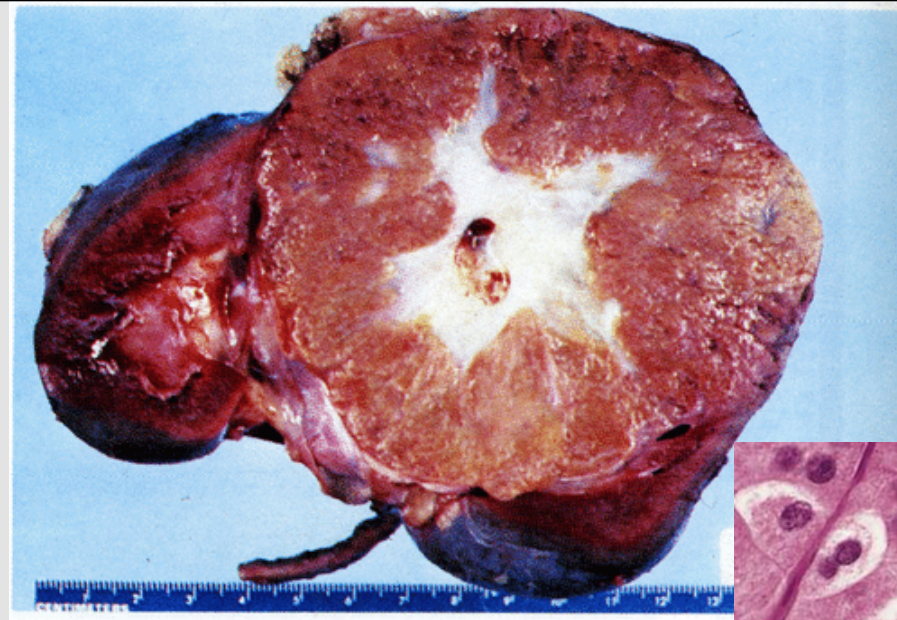
Grossly: well circumscribed mahogany-brown colored tumor with a central stellate scar.

Microscopically: they are composed of uniform round polygonal cells with abundant, intensely eosinophilic and granular cytoplasm with uniform round and central nuclei. These cells are called as oncocytes or oncocytic cells.

Electron microscopy: there are numerous mitochondria in the cytoplasm.

Radiologically: they mimic renal cell carcinoma.

Complications: spontaneous hemorrhage.



Ali et al. Annals of Saudi Medicine, Vol 4 No. 4; 1984

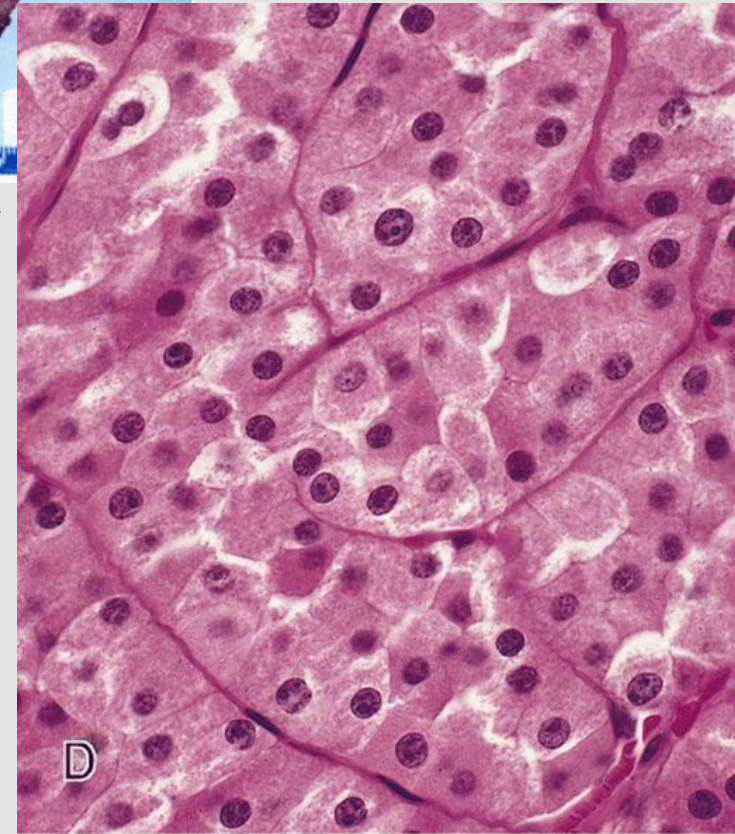
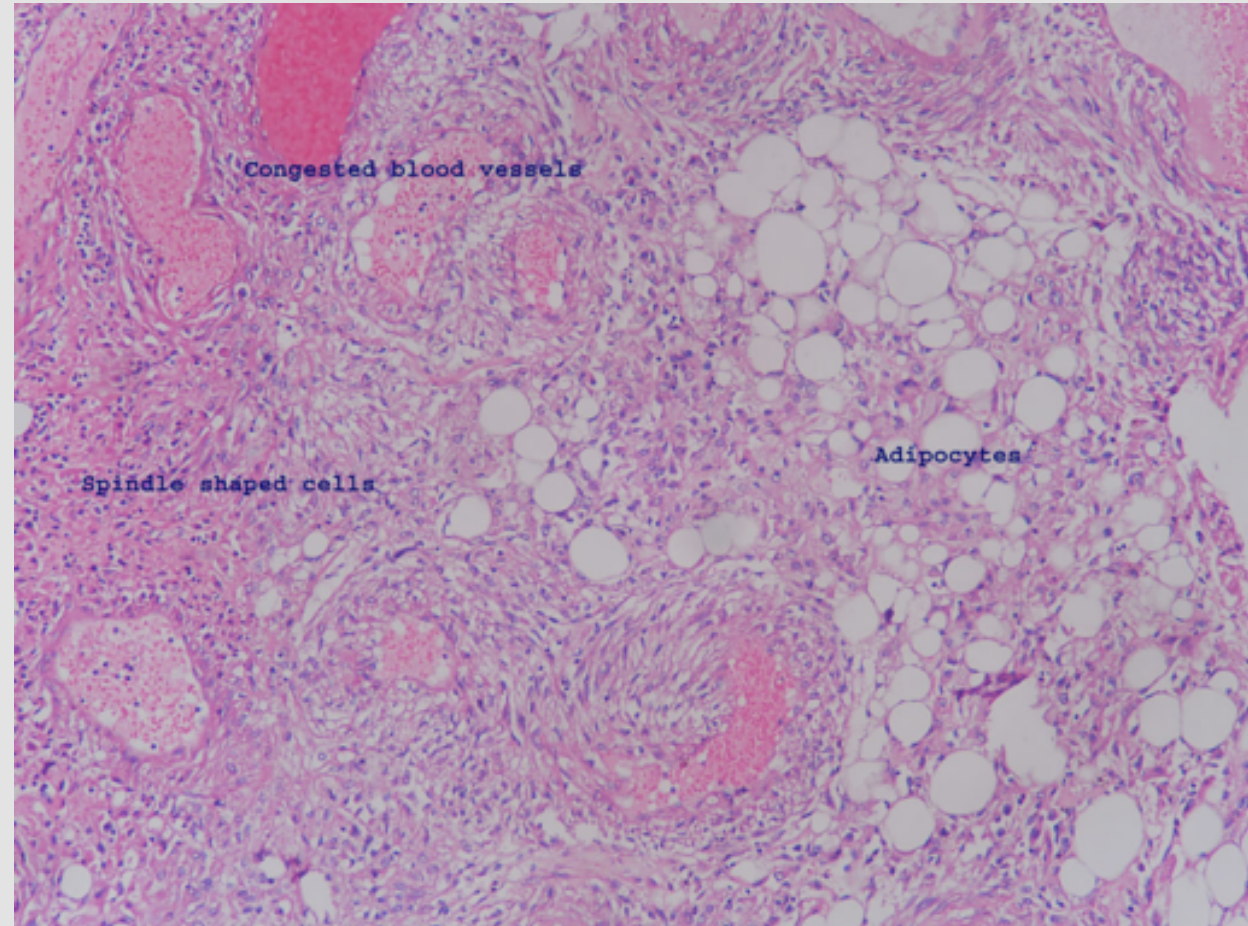


Fig. 1-166D AFIP 3rd Series, Vol. 11
RENAL CELL CARCINOMA, CHROMOPHOBE CELL TYPE AND
ONCOCYTOMA
Renal oncocytoma: The cells are in tight alveolar arrangements and feature acidophilic cytoplasm. The nuclei are round and regular and exhibit no or single small nucleoli.

ANGIOMYOLIPOMA

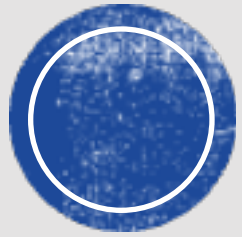
- Angiomyolipomas benign neoplasm composed of admixture of blood vessels, spindle shaped smooth muscle cells and adipose tissue
- The amount of each component is variable
- They are usually associated with tuberous sclerosis syndrome.

(Note: adipose tissue = fat cells)



<http://www.histopathology.guru/wp-content/uploads/2018/05/DSCN3356-p-1024x768.jpg>





RENAL CELL CARCINOMA (RCC)

RENAL CELL CARCINOMA (RCC)

- Renal cell carcinoma is the most common primary cancer of the kidney. It accounts for 80% of all renal cancers.
- It arises from renal tubular epithelial cells.
- Seen in men ranging from 50-60 years of age.
- Men affected more than women.
- Types of RCC

TYPES OF RCC	FREQUENCY (%)
Clear cell type	65%
Papillary type	10-15%
Chromophobe type	5%
Others	15%



RCC

- Risk factors include:
 - Tobacco (smoked or chewed).
 - Acquired cystic kidney disease due to end stage renal disease → they predispose to papillary RCC (as a complication of chronic dialysis)
 - Chronic hypertension
 - Obesity
 - Occupational exposure to cadmium
 - Genetic: about 5% are inherited. Hereditary RCCs tend to be multifocal & bilateral & appear at a younger age than sporadic RCC.
 - ✓ Hereditary clear cell RCC → associated with Von Hippel-Lindau (VHL) Syndrome in which there is an autosomal dominant germline mutation of VHL gene at chromosome 3 (VHL syndrome is characterized by cerebellar hemangioblastomas, retinal angiomas, clear cell RCC, pheochromocytoma and cysts in kidney).
 - ✓ Hereditary papillary RCC → associated with mutations in the c-MET protooncogene at chromosome 7. There is no association with the VHL gene.



RCC: CLEAR CELL TYPE

These are the most common type and arises from proximal tubular epithelial cells.

The majority of them are sporadic. Uncommonly associated with VHL disease.

Gross:

- usually solitary and large.
- cut surface: well circumscribed solid heterogenous partly yellow and partly hemorrhagic mass. May be cystic and necrotic.
- Tumor commonly invades the renal vein. There may be direct invasion into the perinephric fat and adrenal gland.



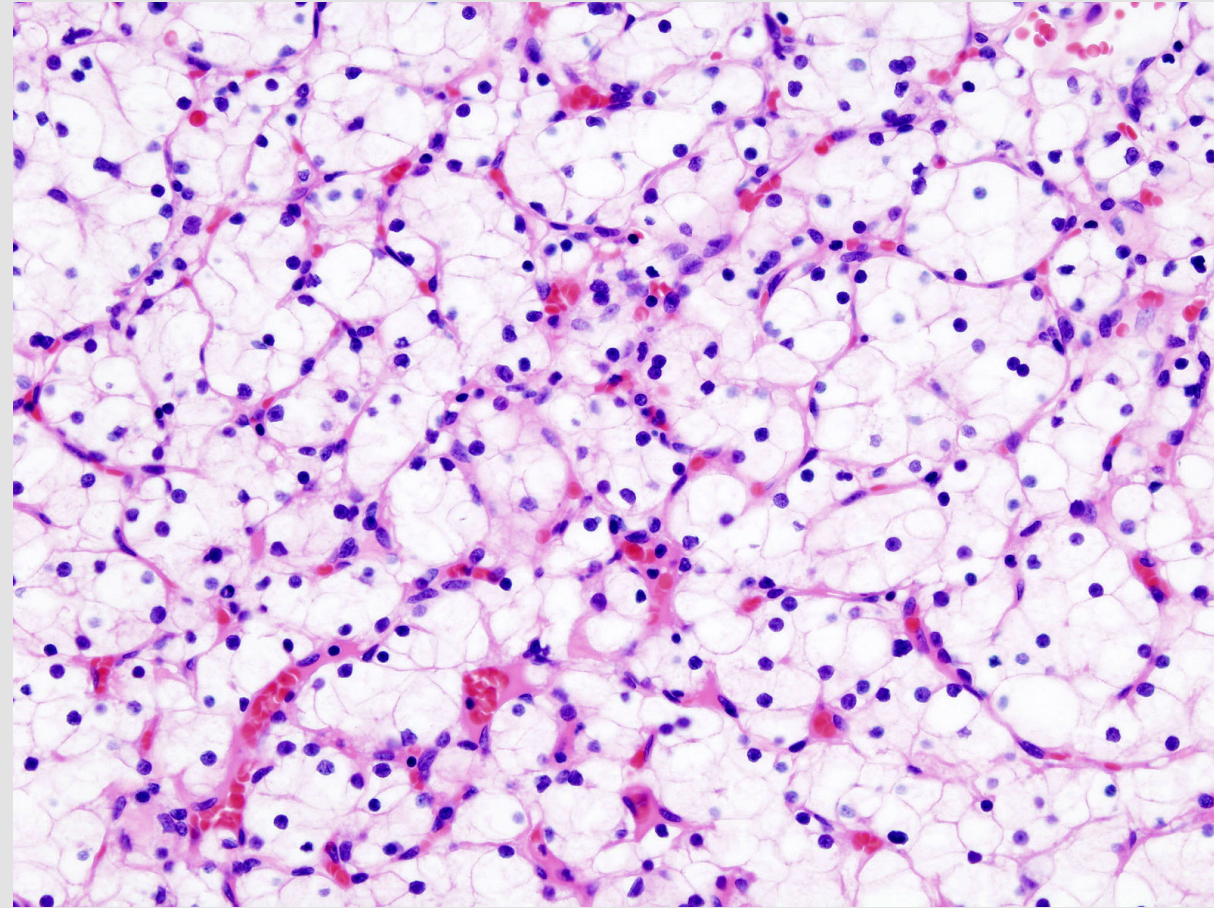
http://web2.airmail.net/uthman/specimens/images/renal_cell_ca.html



RCC: CLEAR CELL TYPE

Microscopically:

- Tumor is made up of cells with clear cytoplasm and sharp cell membrane. The cells are often arranged in sheets or nests. The stroma is highly vascularized. The nuclei can range from no atypia to marked atypia/pleomorphism. Some tumors exhibit marked degrees of anaplasia.



https://upload.wikimedia.org/wikipedia/commons/thumb/6/6d/Renal_clear_cell_ca_%281%29_Nephrectomy.jpg/1591px-Renal_clear_cell_ca_%281%29_Nephrectomy.jpg



RCC: papillary cell type

- The tumors have a papillary growth pattern.
- They can be sporadic or familial.
- The familial forms are uncommon and show mutation in the *MET* proto-oncogene.

RCC: chromophobe cell type

- The tumors are made up of chromophobic cells (they are acidophilic granular cells).

Note: papillary and chromophobe RCCs have a better prognosis than the clear cell RCC.



RCC: CLINICAL FEATURES

- The incidence of RCC peaks in the sixth decade.
- RCC is twice as frequent in men as in women.
- Hematuria is the single most common presenting sign.
- The classic clinical triad → hematuria, flank pain and a palpable abdominal mass.
- Some patients develop polycythemia.
- Uncommonly, these tumors produce paraneoplastic syndromes e.g. [a] secretion of a parathormone-like substance leads to hyperparathyroidism and hypercalcemia; [b] production of erythropoietin causes erythrocytosis, polycythemia; [c] release of renin results in hypertension [d] may present with Cushing syndrome, masculinization.
- These tumor have a high tendency to invade the renal vein and metastasize.
- Sometimes RCC is a silent and discovered only after metastasis.
- The tumor spreads most frequently to the lungs and bones





WILMS TUMOR (NEPHROBLASTOMA)

WILMS TUMOR (NEPHROBLASTOMA)

It is malignant tumor arising from embryonic nephrogenic elements. It is composed of mixtures of blastemal, stromal, and epithelial cells.

The precursor lesion for the Wilms tumor is called as nephrogenic rests.

It is the most common primary tumor of the kidney in children

Most cases of Wilms tumor are sporadic and unilateral.

Some cases of Wilms tumor are familial with deletion of WT1 gene on chromosome 11p13.

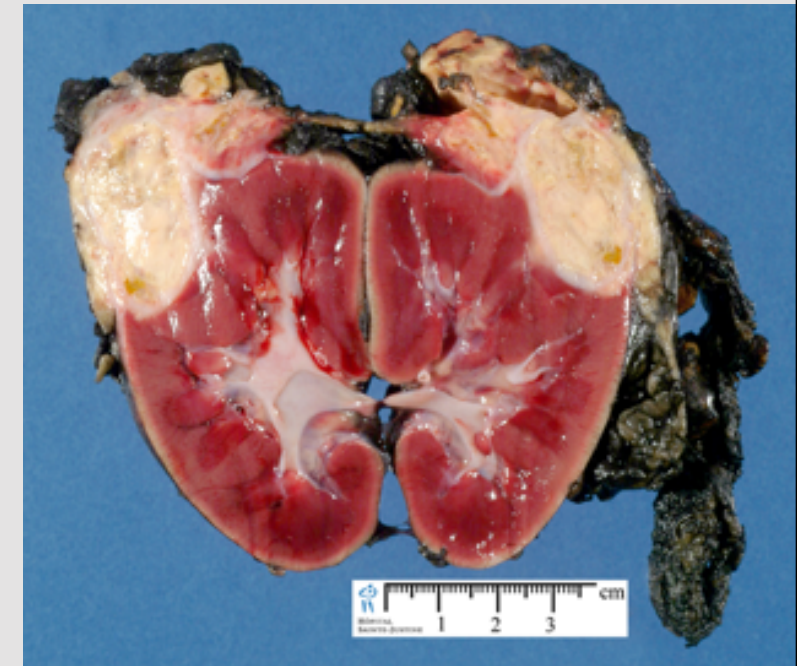
Can be associated with WAGR syndrome, Denys Drash syndrome and Beckwith weidmann syndrome.



WILMS TUMOR: MORPHOLO

Gross:

- Unilateral (10% bilateral), solitary, well circumscribed lesion.
- By the time Wilms tumor is detected it is large.
- Cut section: uniform, pale gray and soft in consistency (Fish flesh like)
- The tumor may show foci of hemorrhage, cystic degeneration & necrosis



WILMS TUMOR:

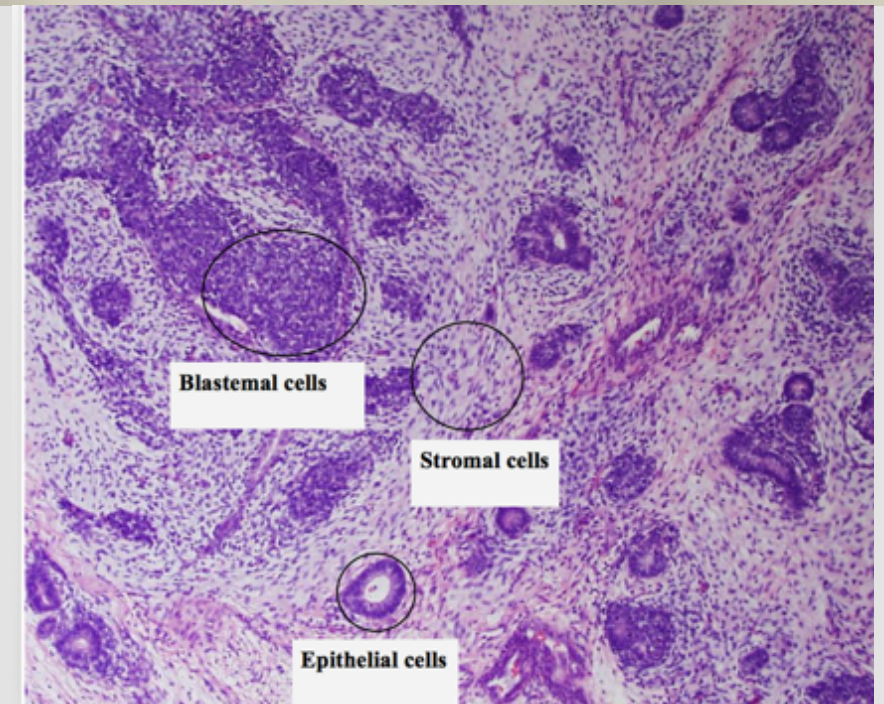
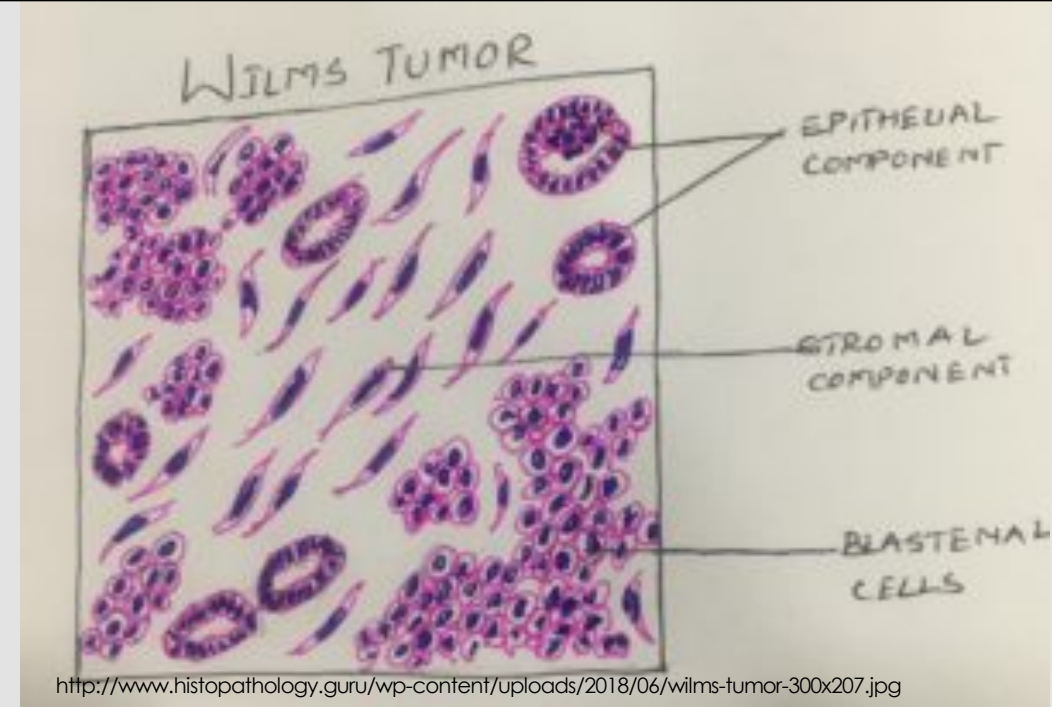
Microscopy:

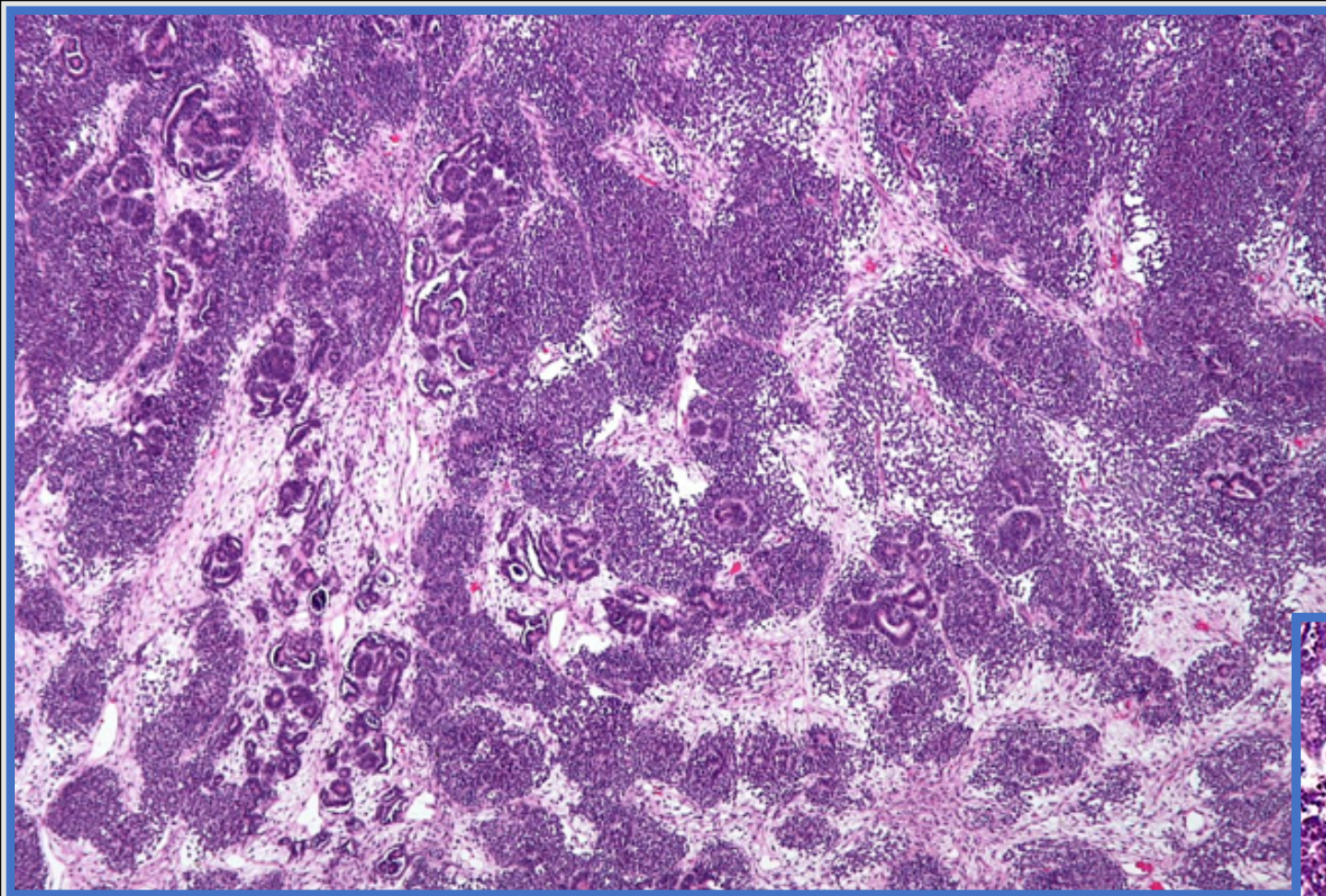
It is composed of the classical triphasic combination of (i.e. 3 patterns):

1. **Blastemal component /cells:** composed of densely packed small round blue cells with scanty cytoplasm and brisk mitosis
2. **Epithelial component (immature epithelial cells):** composed of immature primitive tubular structures (rosettes) and immature glomeruli.
3. **Stromal component/ cells:** composed of immature undifferentiated mesenchymal stromal cells (i.e. immature spindle cells and myxoid material).

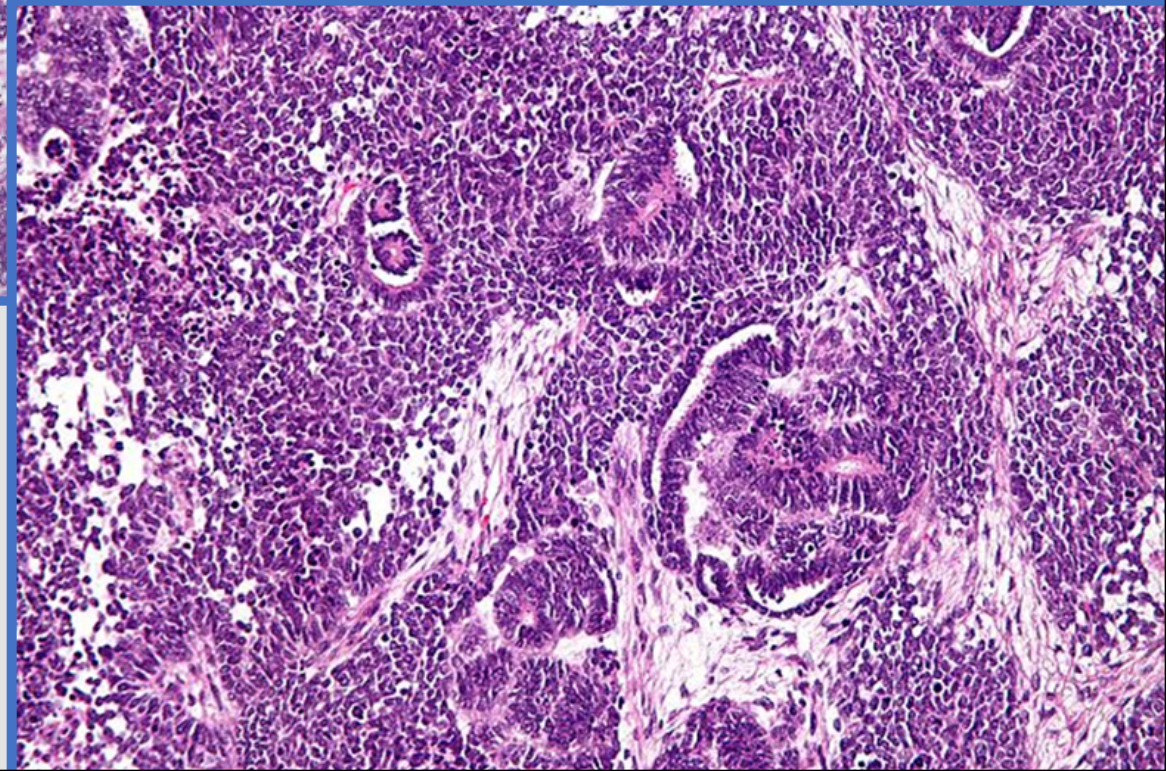
Biphasic and monophasic patterns can also occur.

5% of tumors contain foci of anaplasia. Anaplasia is an indication of poor prognosis.





By Nephron - Own work, CC BY-SA 3.0, <https://commons.wikimedia.org/w/index.php?curid=14818887>



WILMS TUMOR:CLINICAL FEATURES

Clinical features

- Wilms tumor usually presents between 1 and 3 years of age, and 98% occur before 10 years of age.
- Most common presentation: abdominal mass with no other associated symptoms
- Other signs or symptoms (seen in about 20% of cases): abdominal pain, hematuria, hypertension and anemia

Treatment and prognosis

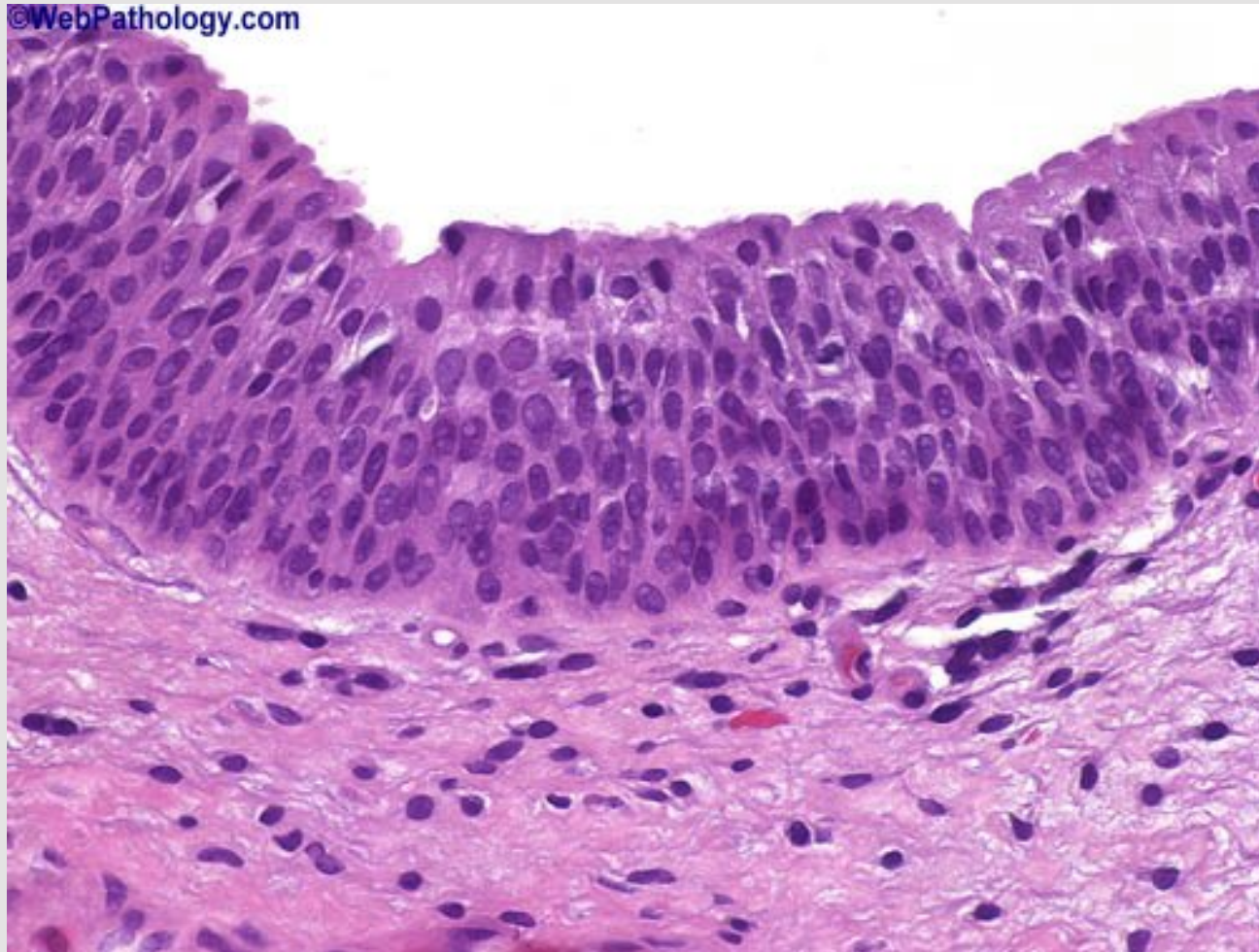
- Chemotherapy and radiation therapy combined with surgical resection, have dramatically improved the outlook of patients with this tumor.
- The prognosis for Wilms' tumor is generally very good



TUMORS OF THE LOWER URINARY TRACT



NORMAL UROTHELIUM



TUMORS OF THE LOWER URINARY TRACT

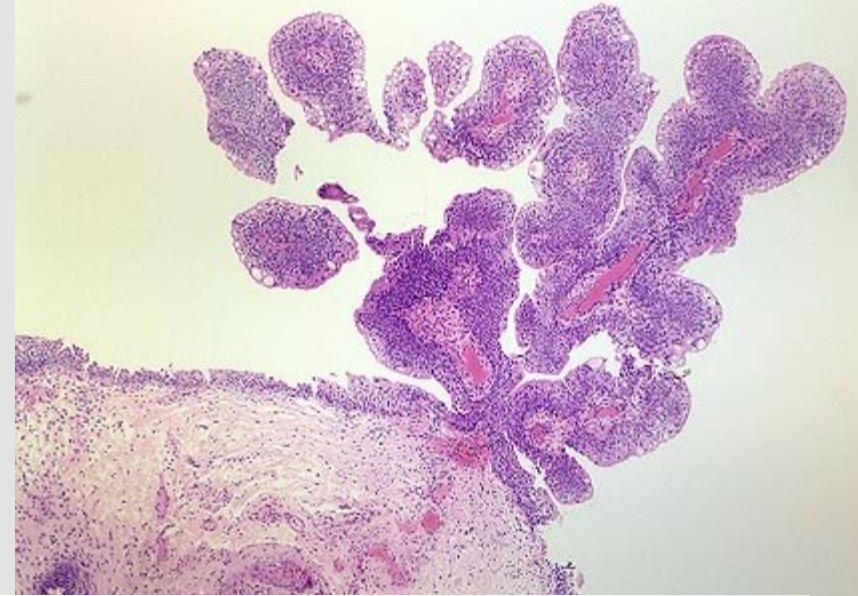
- Tumors in the collecting system above the bladder are relatively uncommon
- A small lesion in the ureter may cause urinary outflow obstruction and have greater clinical significance than a much larger mass in the large capacious bladder.
- The types of urothelial tumors include the following:
 - **Non invasive papillary lesions**
 - ✓ Papilloma (benign)
 - ✓ PUNLMP (borderline)
 - ✓ Noninvasive papillary urothelial carcinoma low grade (malignant)
 - ✓ Noninvasive papillary urothelial carcinoma high grade (malignant)
 - **Non invasive flat lesions**
 - ✓ Flat urothelial carcinoma in situ
 - **Invasive urothelial carcinoma (worst prognosis).**



PAPILLOMA

- are rare and benign.
- They are non-invasive papillary tumor lined by benign transitional epithelium.
- Usually solitary
- Do not recur once removed.

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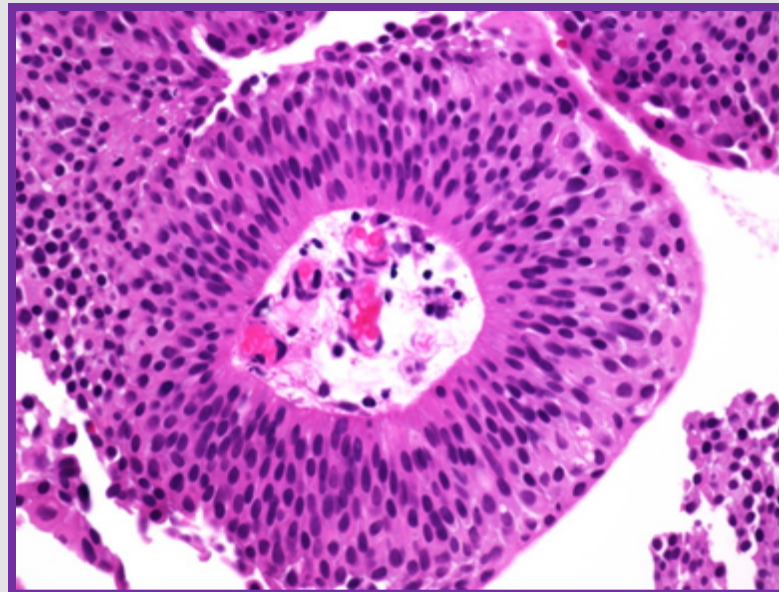
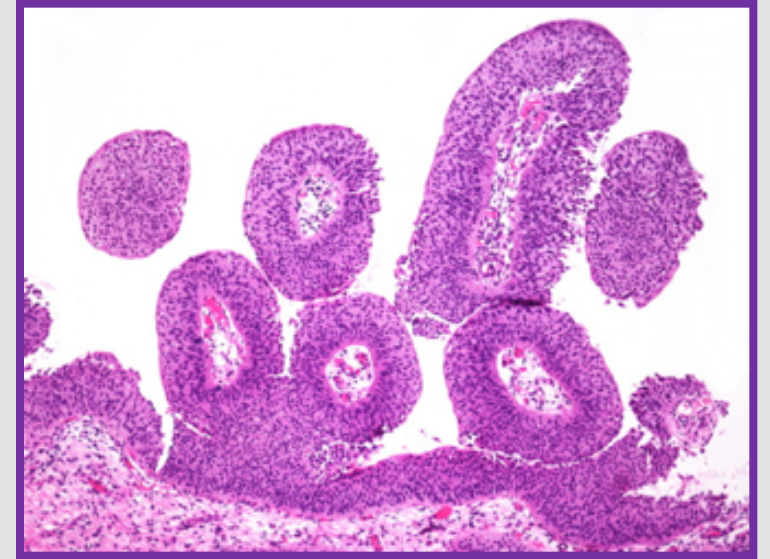


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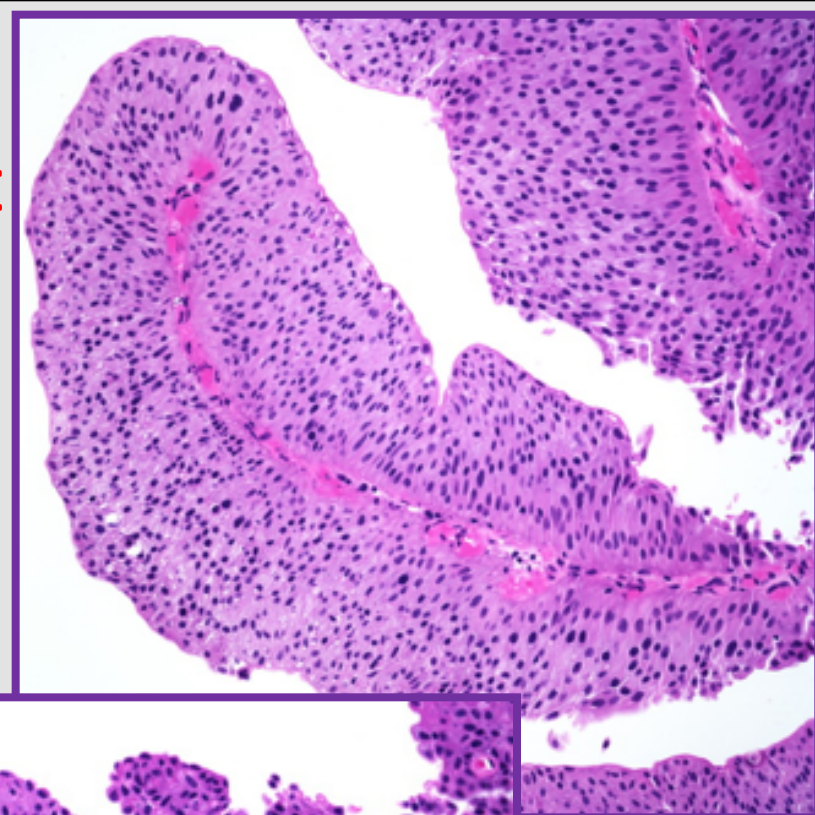
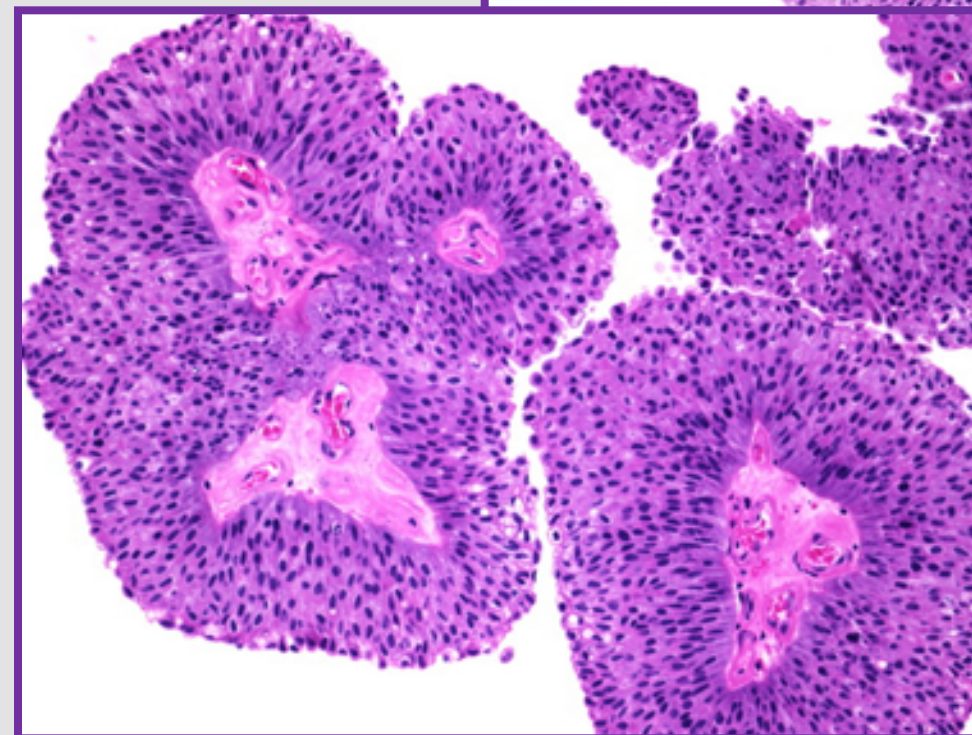
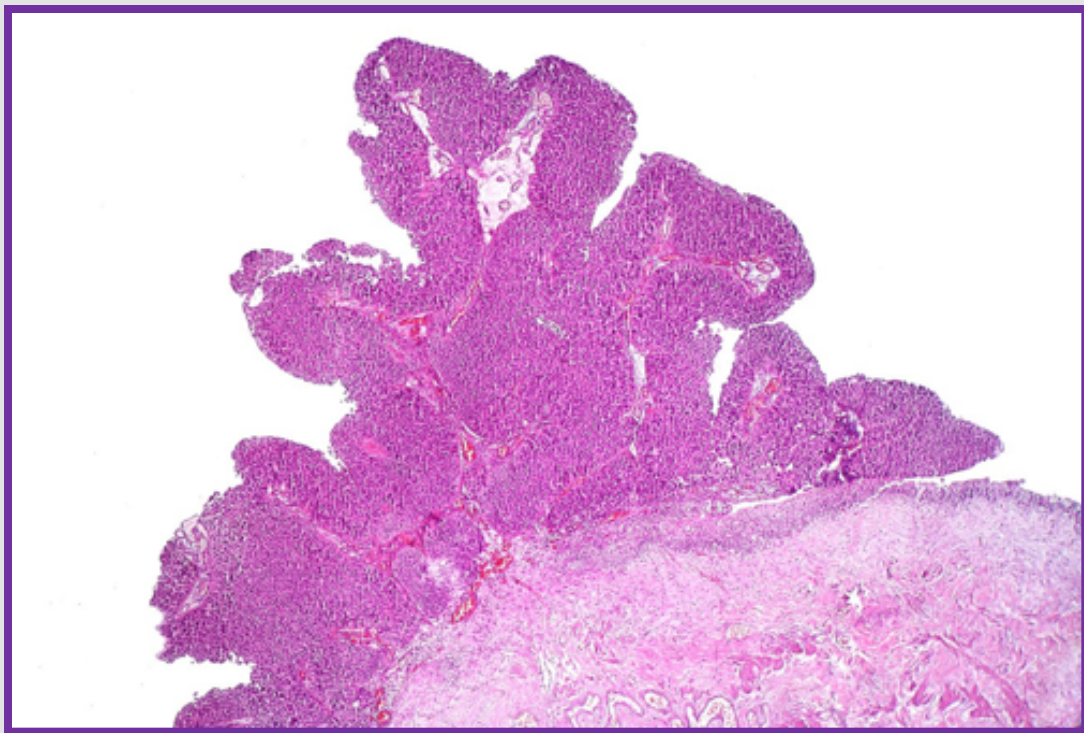
PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL (PUNLMP)

- Uncommon.
- They are non-invasive papillary tumors with nuclear features intermediate between papilloma and low grade papillary urothelial carcinomas
- They may recur after removal.



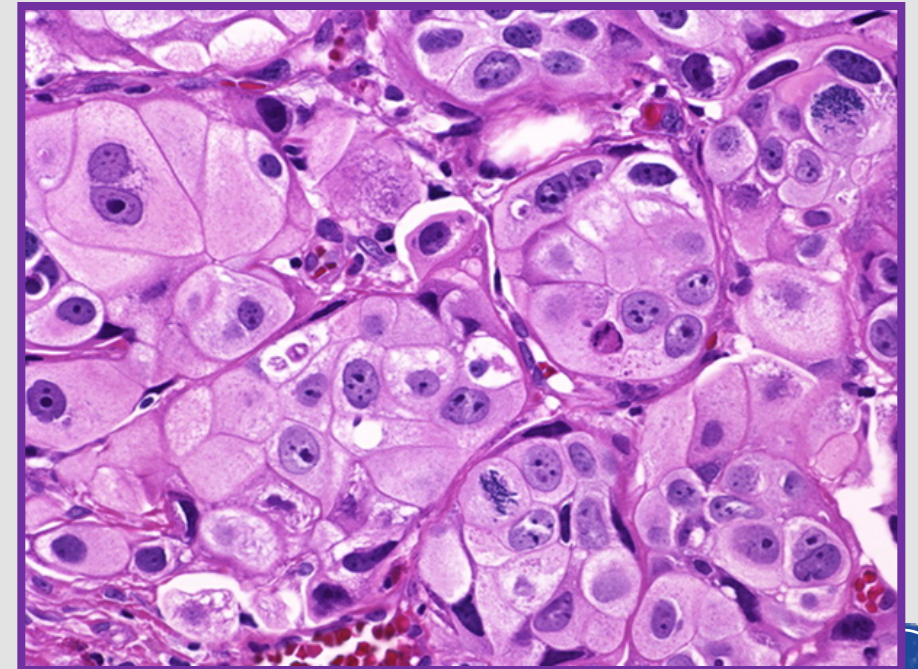
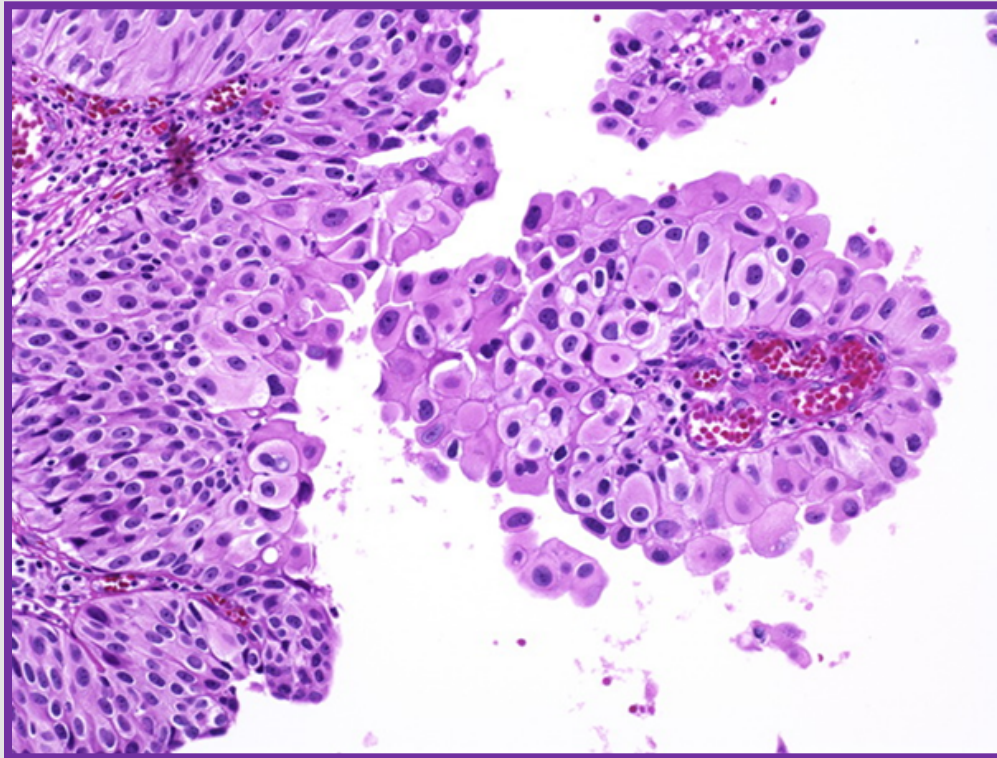
NONINVASIVE PAPILLARY UROTHELIAL CARCINOMA LOW GRADE

- Non-invasive papillary tumors made up of papillary projections lined by malignant urothelial cells with mild atypia/ pleomorphism and mild mitotic activity.



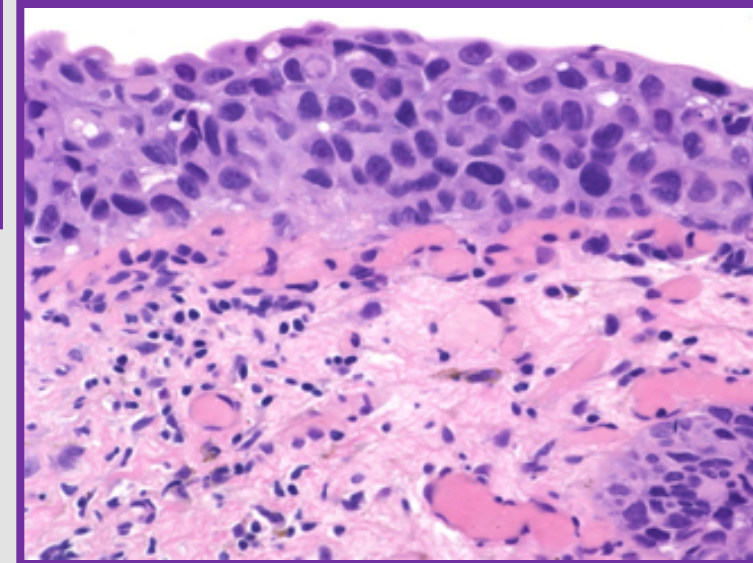
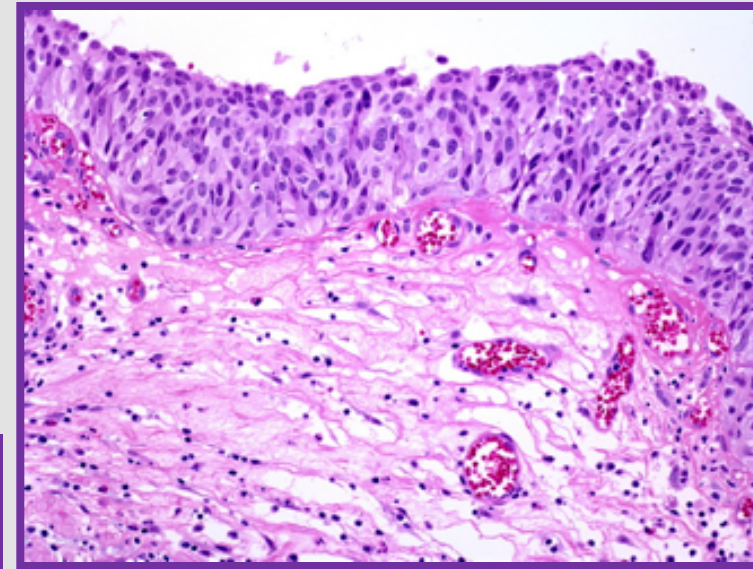
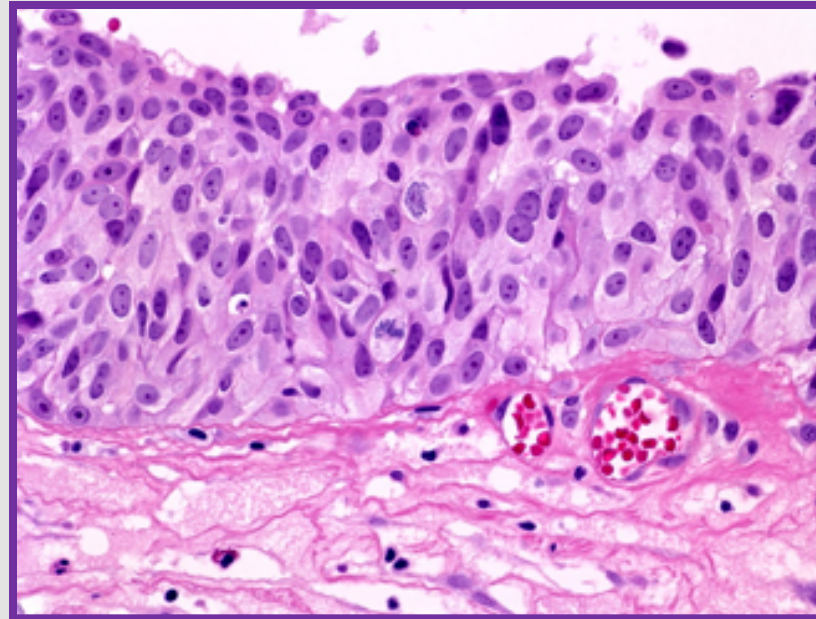
NONINVASIVE PAPILLARY UROTHELIAL CARCINOMA HIGH GRADE

- Non-invasive papillary tumor made up of papillary projections lined by poorly differentiated malignant urothelial cells with marked atypia/ pleomorphism and significant (brisk) mitotic activity.
- Majority of high grade papillary urothelial carcinomas progress → and they invade into the underlying lamina propria and the muscularis propria becoming → invasive urothelial carcinoma.



UROTHELIAL CARCINOMA IN SITU

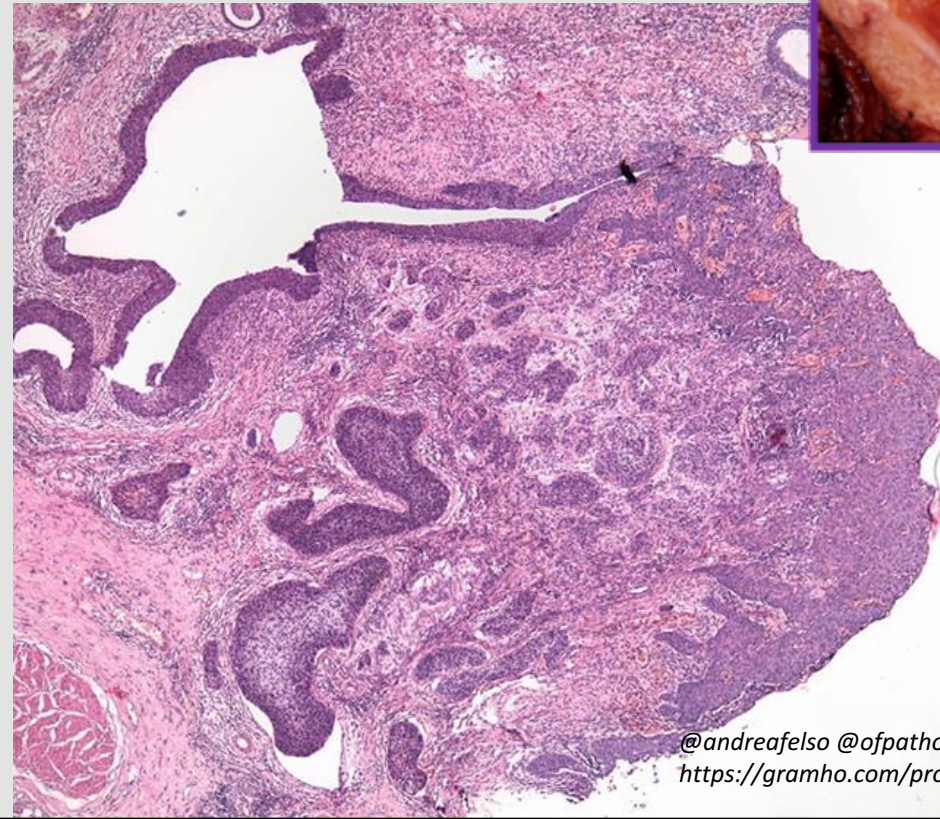
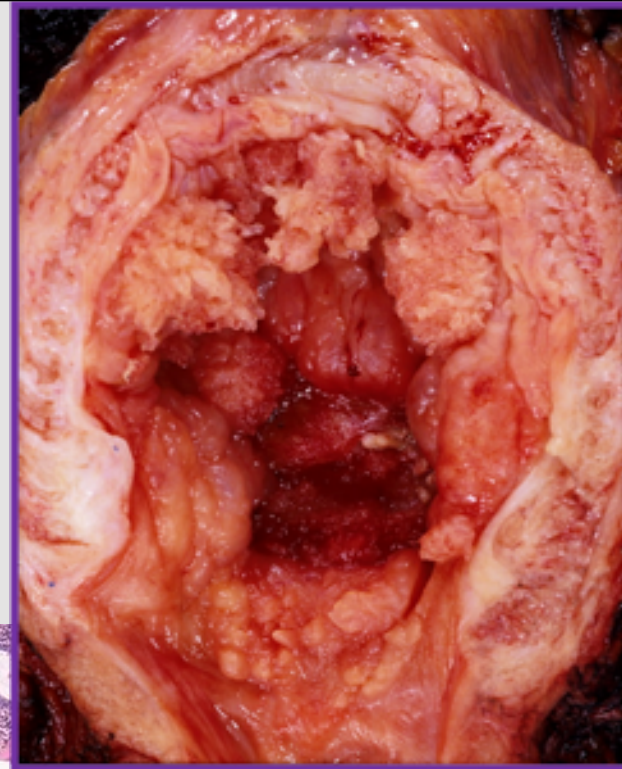
- Non-papillary, non-invasive flat lesions.
- Tend to be multifocal.
- There is the full-thickness dysplasia of the urothelium (hyperchromatic and pleomorphic cells with prominent nucleoli).
- There may be excessive shedding of malignant cells in urine.
- In about 50% of cases it is associated with subsequent invasion into the underlying lamina propria and the muscularis propria becoming → invasive urothelial carcinoma.



INVASIVE UROTHELIAL CARCINOMA

- Invasive urothelial carcinoma usually progresses from a
 - High grade papillary urothelial carcinoma
 - and flat urothelial carcinoma in situ.
- Among urothelial tumors they have the worst prognosis.

Microscopically, the tumor cells infiltrate beyond the basement membrane into the underlying tissue (the lamina propria and muscularis propria i.e. the detrusor muscle) in the form of irregular nests, lobules and single cells.



UROTHELIAL CARCINOMA

More common in men.

Age: 50 to 70 years.

Predisposing factors:

- Bladder tumors are more common in those exposed to chemicals called aromatic amines (arylamines) such as benzidine and beta-naphthylamine, which are sometimes used in the dye industry (aniline and Azo dyes).
- Cigarette smoking and chronic cystitis
- Chronic bladder irritation from stones or long term bladder catheters
- Chemotherapy (long-term use of cyclophosphamide) and
- Radiotherapy (previous exposure of the bladder to irradiation)

They are not familial.

Clinical Features

Painless hematuria is the dominant clinical presentation of all these tumors and less frequently as dysuria. Cystoscopy reveals the tumor.

Bladder cancers vary from exophytic, flat, ulcerated to deeply invasive.

Bladder cancer metastasize to regional lymph nodes, liver, lung, and bone.



NON-UROTHELIAL CARCINOMAS OF THE LOWER URINARY TRACT

are rare and have very poor prognosis.

- Squamous cell carcinoma.
- Adenocarcinoma.
- Small cell neuroendocrine carcinoma.
- Sarcomas (leiomyosarcoma, rhabdomyosarcoma)
- Metastatic (from cervix, prostate etc).



SQUAMOUS CELL CARCINOMA OF THE BLADDER

- Squamous cell carcinoma of the bladder develops in foci of squamous metaplasia.
- Long standing *Schistosoma haematobium* infections can predispose to squamous cell carcinoma of the urinary bladder.





END