PATHOLOGY OF TUMORS OF THE KIDNEY & URINARY TRACT

April 2019

Reference: Robbins & Cotran Pathology and Rubin's Pathology

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
- 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 of the Kidney

They include:

1. RENAL ONCOCYTOMA
2. ANGIOMYOLIPOMA

Malignant Tumors of the Kidney

They include:

1. RENAL CELL CARCINOMA
2. WILM'S TUMOR

ONCOCYTOMA

Benign tumor of uniform round polygonal cells with abundant, intensely eosinophilic and granular cytoplasm with uniform round and central nuclei.

They arise from the intercalated cells of collecting ducts.

Grossly: characteristic well circumscribed mahogany-brown color with a central stellate scar.

Radiologically they mimic renal cell carcinoma.

Complications: spontaneous hemorrhage.

Electron microscopy: there are numerous mitochondria in the cytoplasm.

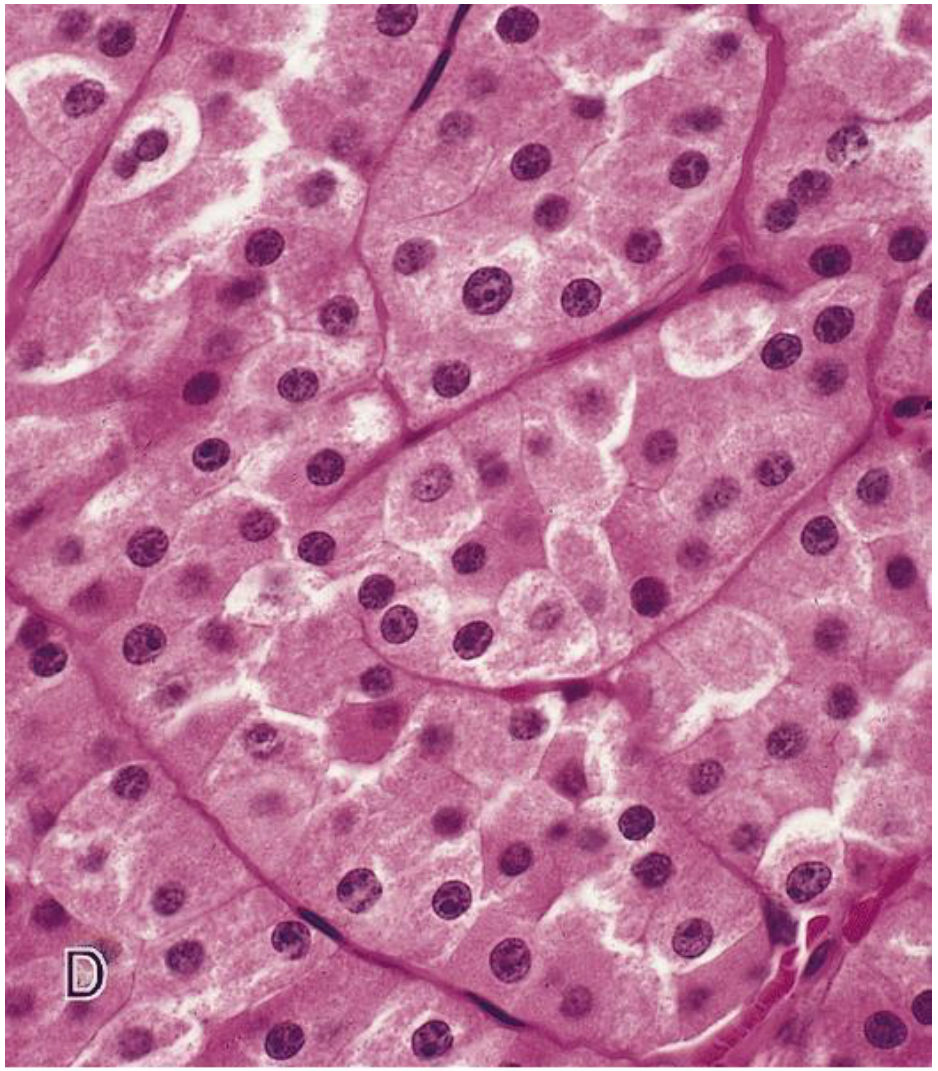
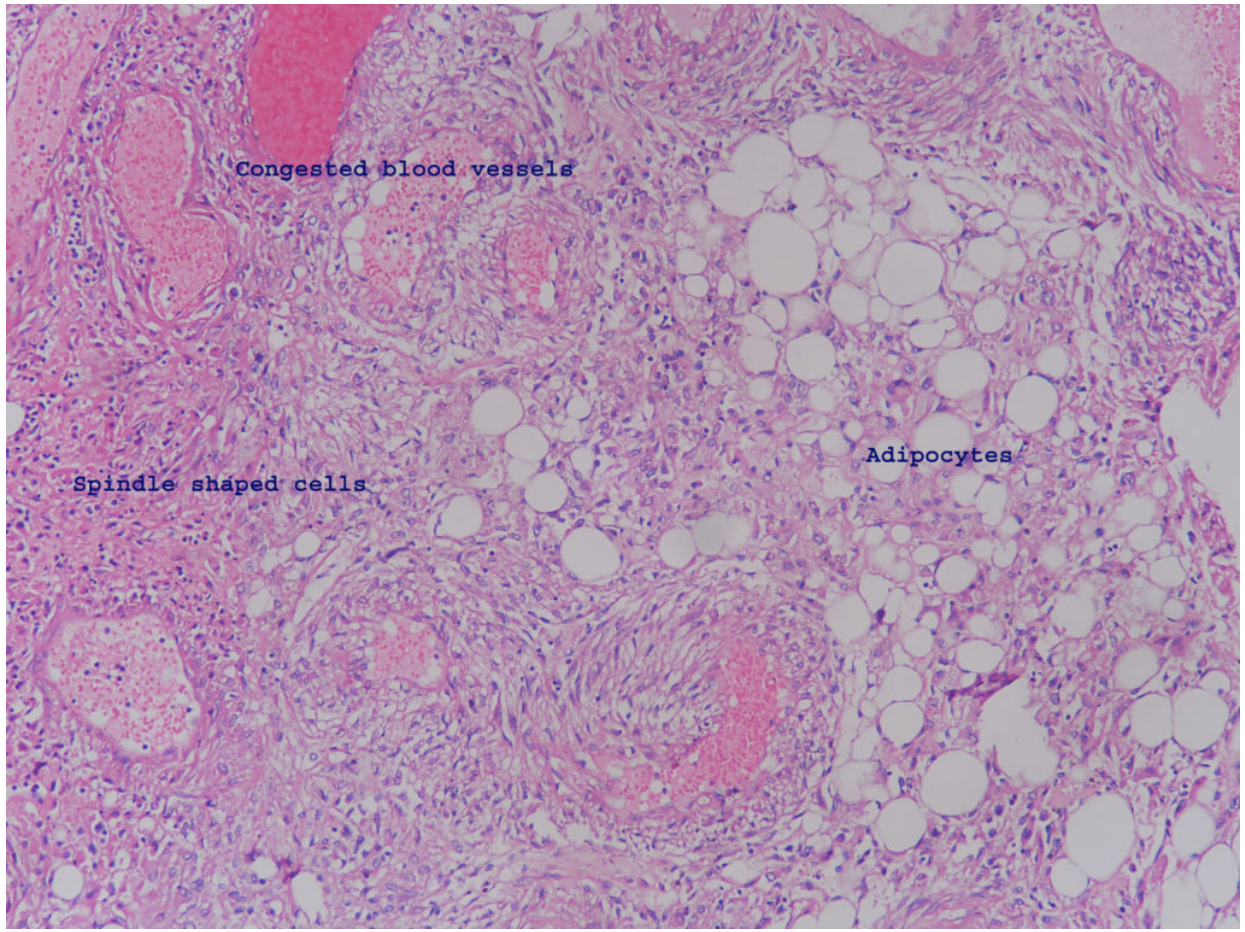


Fig. 1-166D AFIP 3rd Series, Vol. 11
RENAL CELL CARCINOMA, CHROMOPHOBE CELL TYPE AND ONCOCYTOMA
Renal oncocytoma: The cells are in tight alveolar arrangements and feature acidophilic cytoplasm. The nuclei are round and regular and exhibit no or single small nucleoli.

ANGIOMYOLIPOMA

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



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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%

RISK FACTOR OF RCC

- Risk factors include:
  - Tobacco (smoked or chewed).
  - Acquired cystic kidney disease due to end stage renal disease (especially papillary RCC as a complication of chronic dialysis)
  - Chronic HTN
  - Obesity
  - Occupational exposure to cadmium
  - Genetic: about 5% are inherited. Hereditary RCCs tend to be multifocal and bilateral and appear at a younger age than sporadic RCC.
    - ✓ Hereditary form of clear cell RCC → associated with homozygous loss of Von Hippel-Lindau (VHL) tumor-suppressor gene. (VHL syndrome is an autosomal dominant syndrome characterized by cerebellar hemangioblastomas, retinal angiomas, clear cell RCC, pheochromocytoma and cysts in kidney and various organs). The mutation of VHL gene is on chromosome 3.
    - ✓ Hereditary form of papillary RCC shows no association with the VHL gene. Mutations in the c-met protooncogene (MET) → development of hereditary papillary RCC.
    - ✓ Duplications or trisomy of chromosome 7 → can also leads to papillary carcinomas

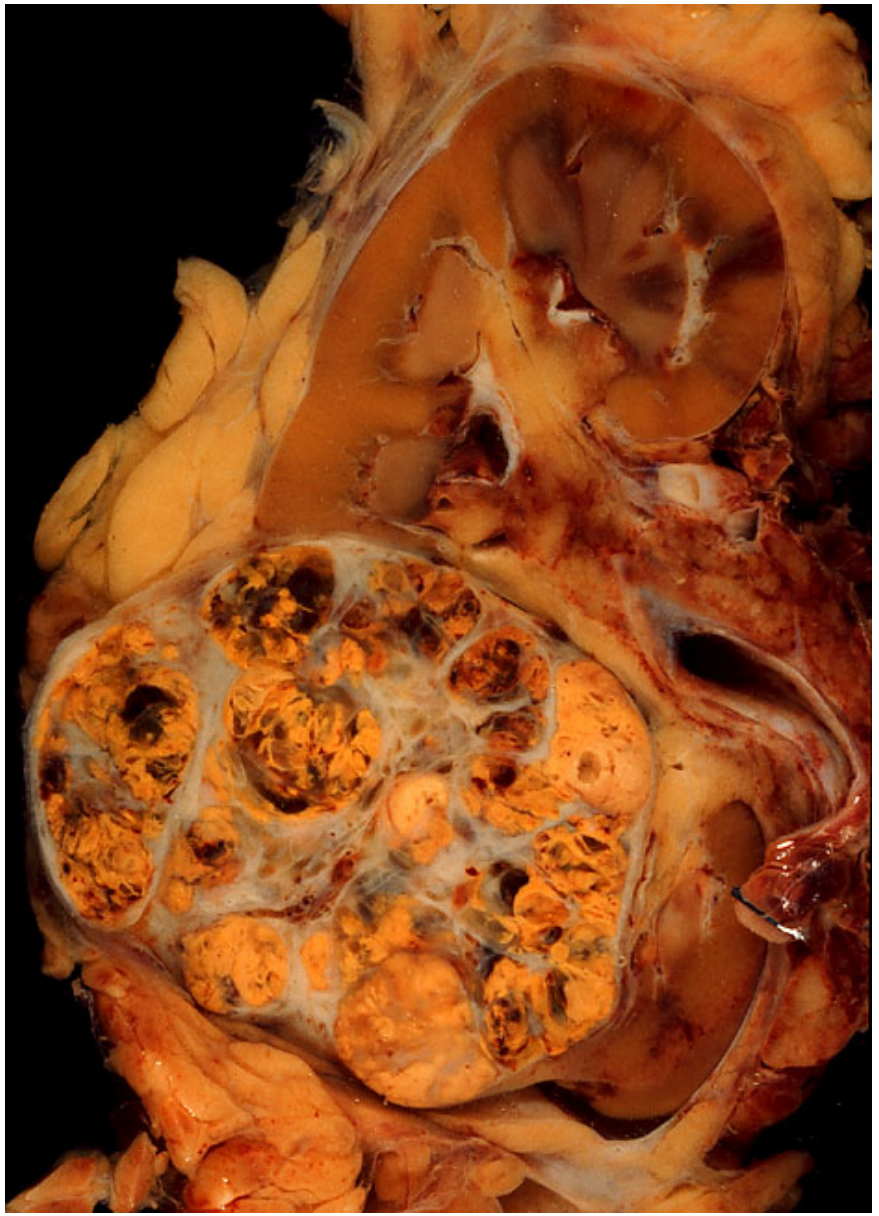
RCC: CLEAR CELL TYPE

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 is solid and focally cystic yellow-orange with hemorrhage and necrosis. The margins of the tumor are well defined.
- Tumor commonly invades the renal vein. There may be direct invasion into the perinephric fat and adrenal gland.



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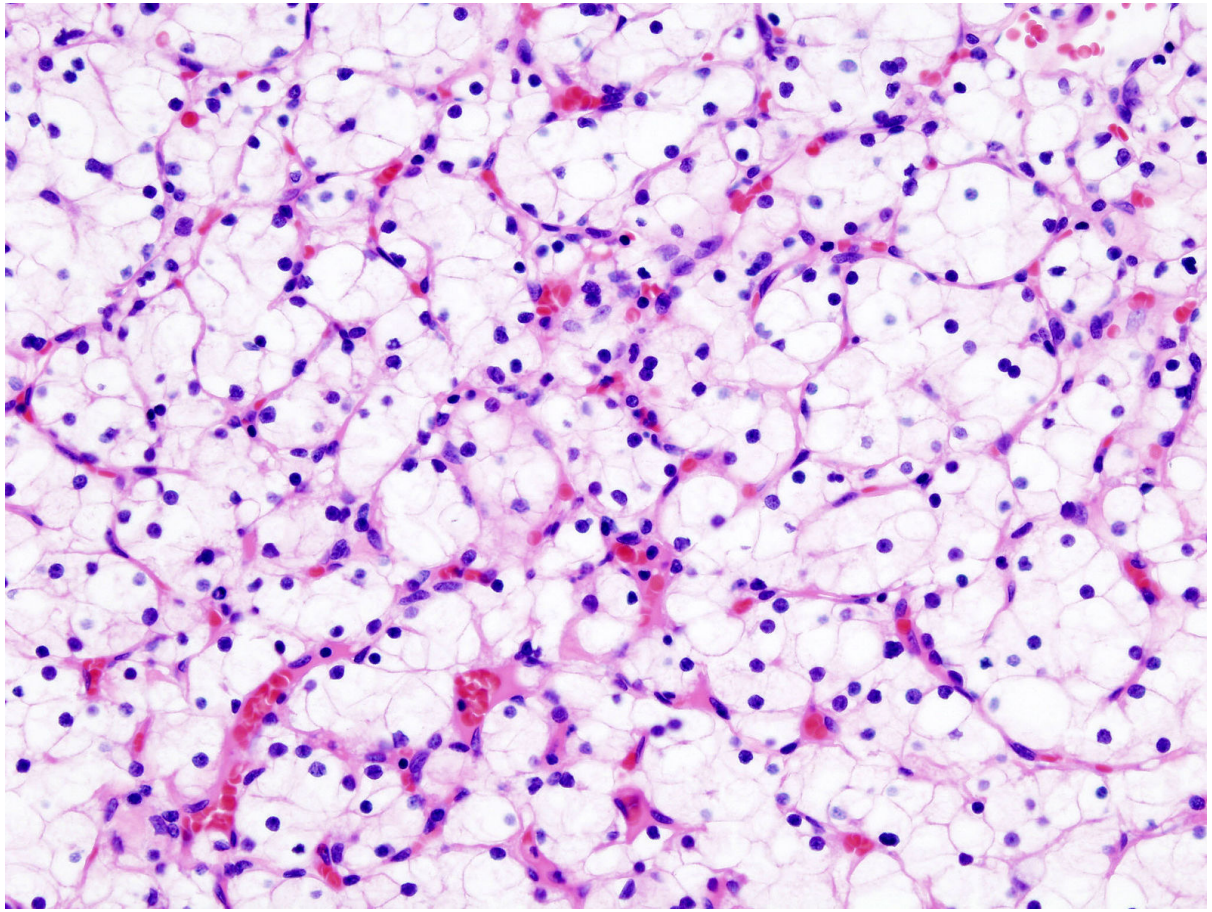
RCC: CLEAR CELL TYPE

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 are usually small and round with little to no pleomorphism. Some tumors exhibit marked degrees of anaplasia.



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RCC: papillary cell type

- It is characterized by a papillary growth pattern with fibrovascular stalks.
- These tumors are frequently multifocal and bilateral
- They occur in familial and sporadic forms
- The familial forms → increased ecpression and mutation in the *MET* proto-oncogene.

RCC: chromophobe cell type

- Chromophobe RCC shows a mixture of acidophilic granular cells and clear cells.
- They arise from the intercalated cells of renal collecting ducts.

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. secretion of a parathormone-like substance leads to hyperparathyroidism and hypercalcemia; production of erythropoietin causes erythrocytosis; release of renin results in hypertension. They may present with Cushing syndrome, masculinization).
- Sometimes it is a silent condition and discovered only after metastasis.
- The tumor spreads most frequently to the lungs and bones

WILMS TUMOR (NEPHROBLASTOMA)

WILMS TUMOR (NEPHROBLASTOMA)

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

- Precursor lesion for the wilms tumor are – Nephrogenic rests

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

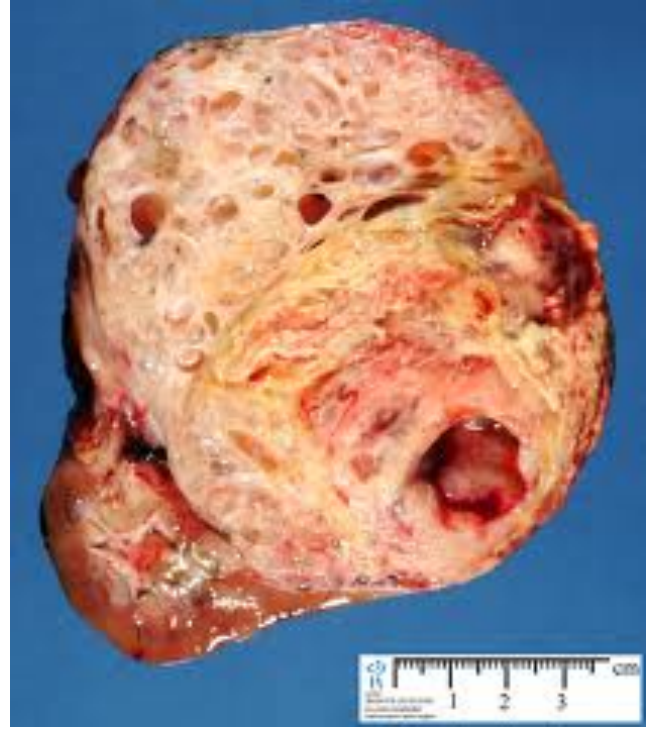
  In most cases the Wilms tumor is sporadic and unilateral.

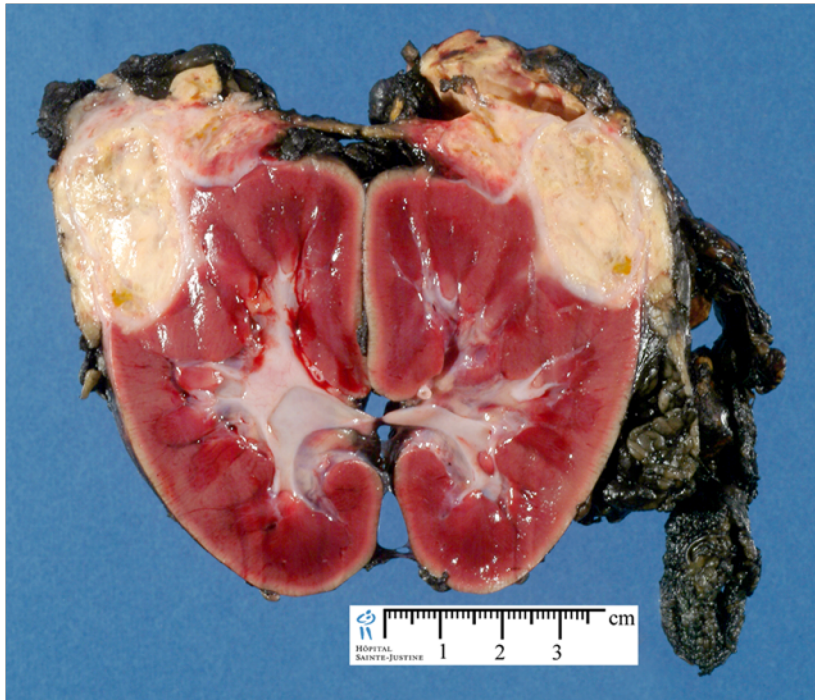
- Some cases of Wilms tumor are familial. There is deletion of WT1 gene on chromosome 11p13.
- Associated with WAGR syndrome, Denys Drash syndrome and Beckwith weidmann syndrome

WILMS TUMOR: MORPHOLOGY

Gross:

- Unilateral (10% bilateral), solitary, well circumscribed lesion.
- Wilms tumor tends to be large when detected, with a bulging, pale tan
- Cut section uniform, pale gray or tan – pink and soft in consistency (Fish flesh like)
- The tumor is soft, tan with foci of hemorrhage, cystic degeneration and necrosis





WILMS TUMOR: MORPHOLOGY

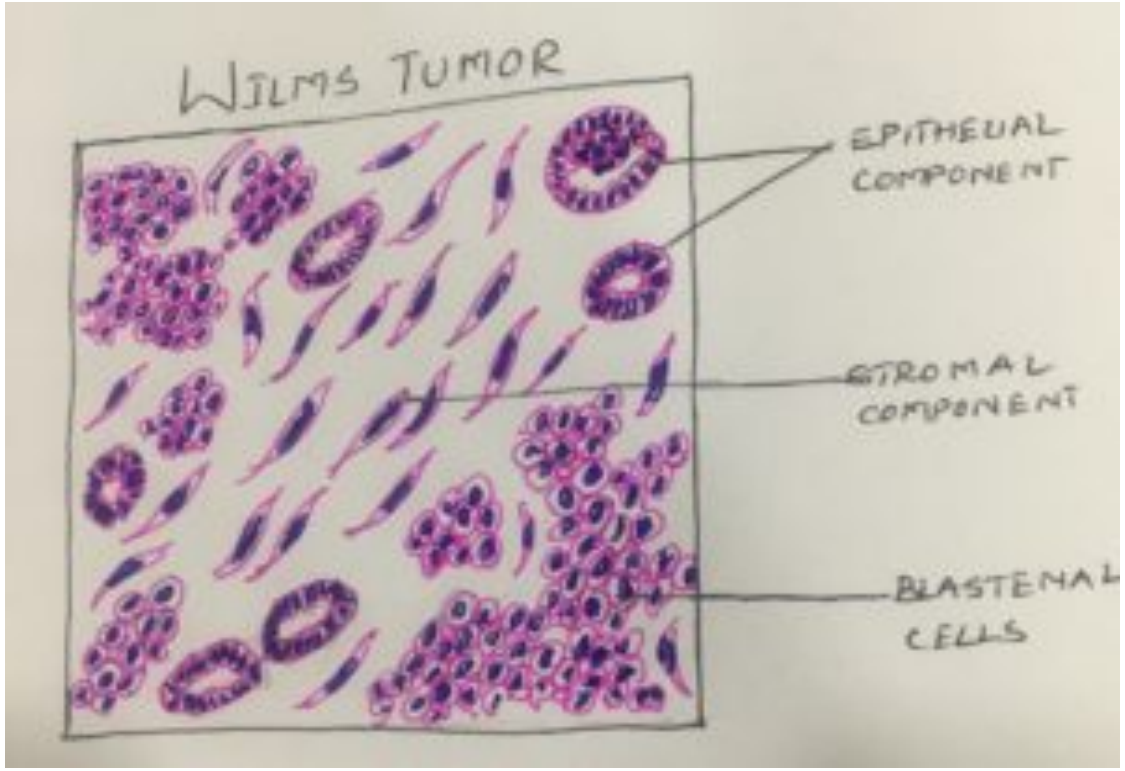
Microscopy:

the tumor is cellular and composed of triphasic classical triphasic combination of:

1. Blastemal component: composed of small ovoid cells with scanty cytoplasm and brisk mitosis
2. Epithelial component: appears as immature primitive tubular structures and immature glomeruli.
3. Stromal component: loose immature stroma of undifferentiated mesenchymal cells (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.



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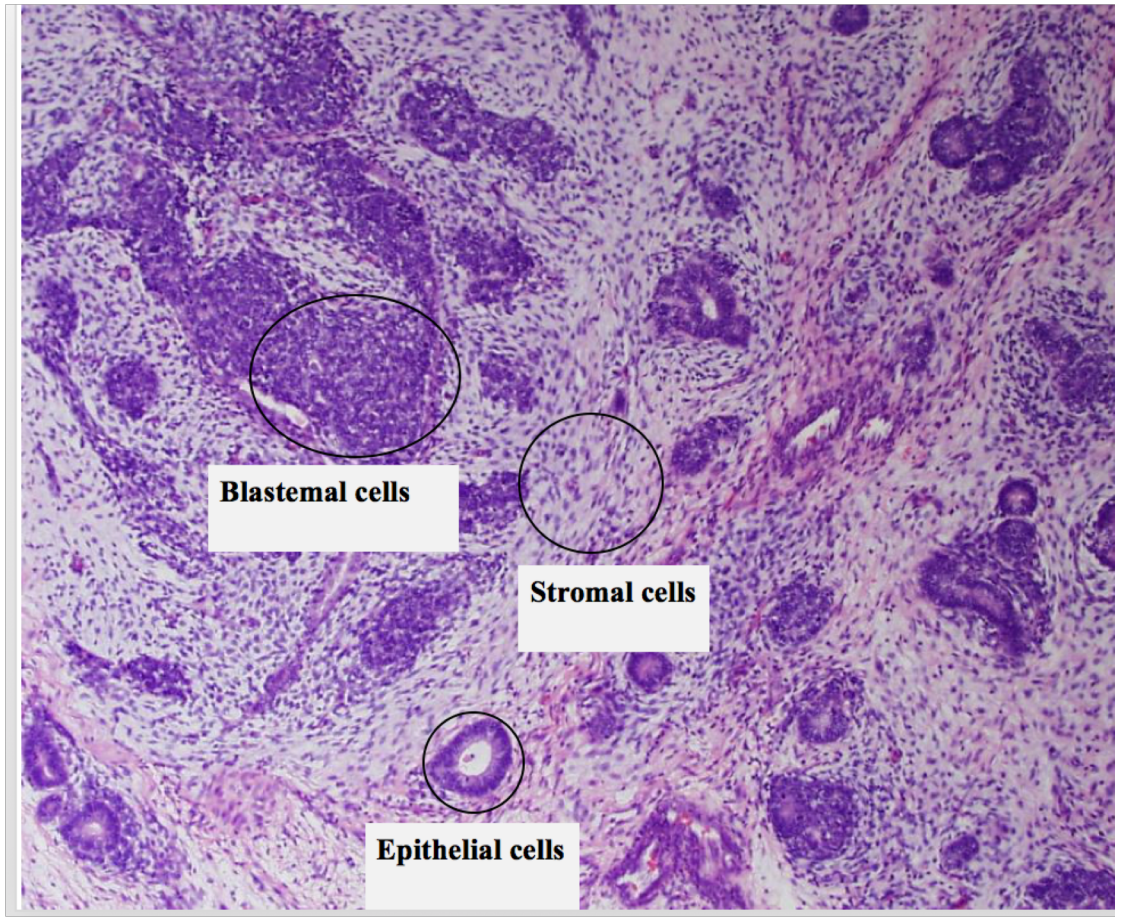
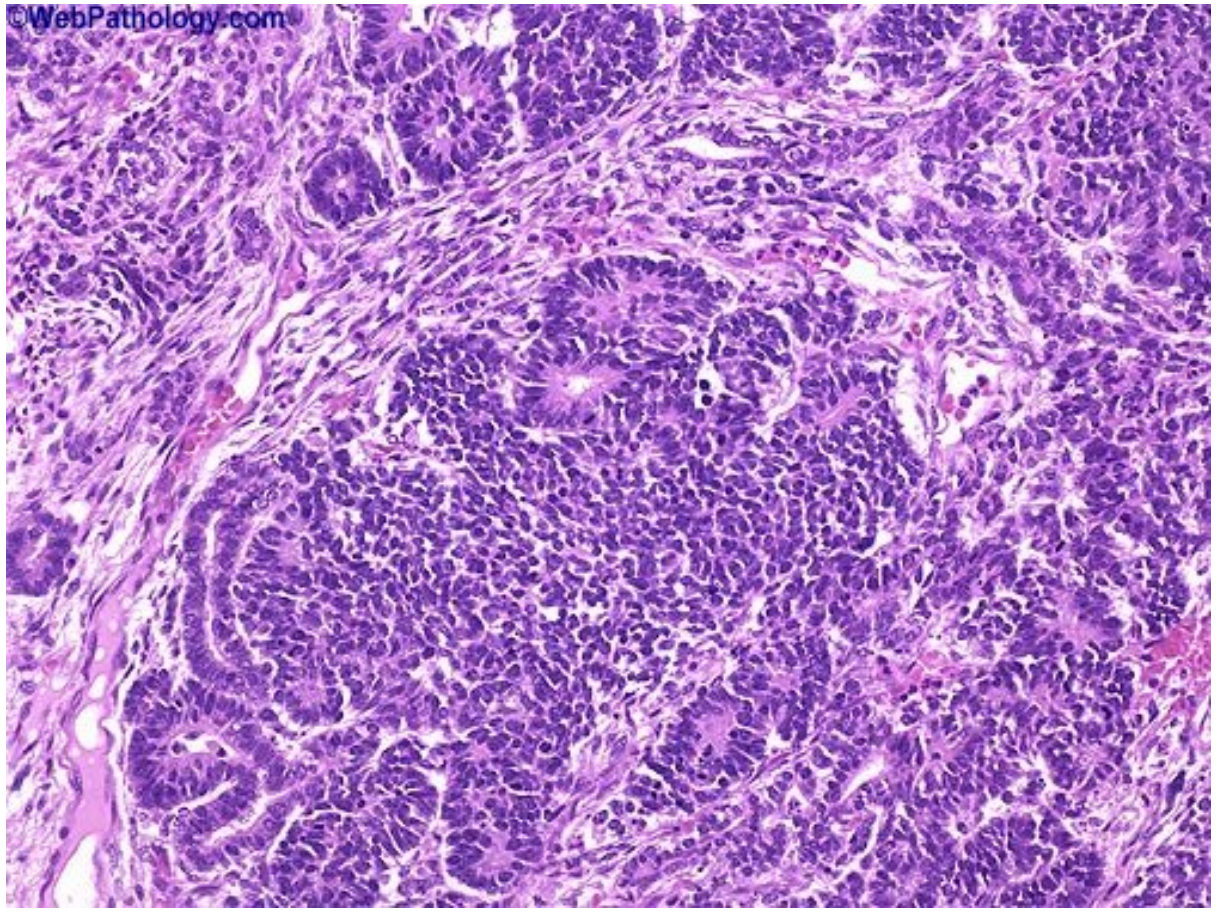

Blastemal cells
Stromal cells
Epithelial cells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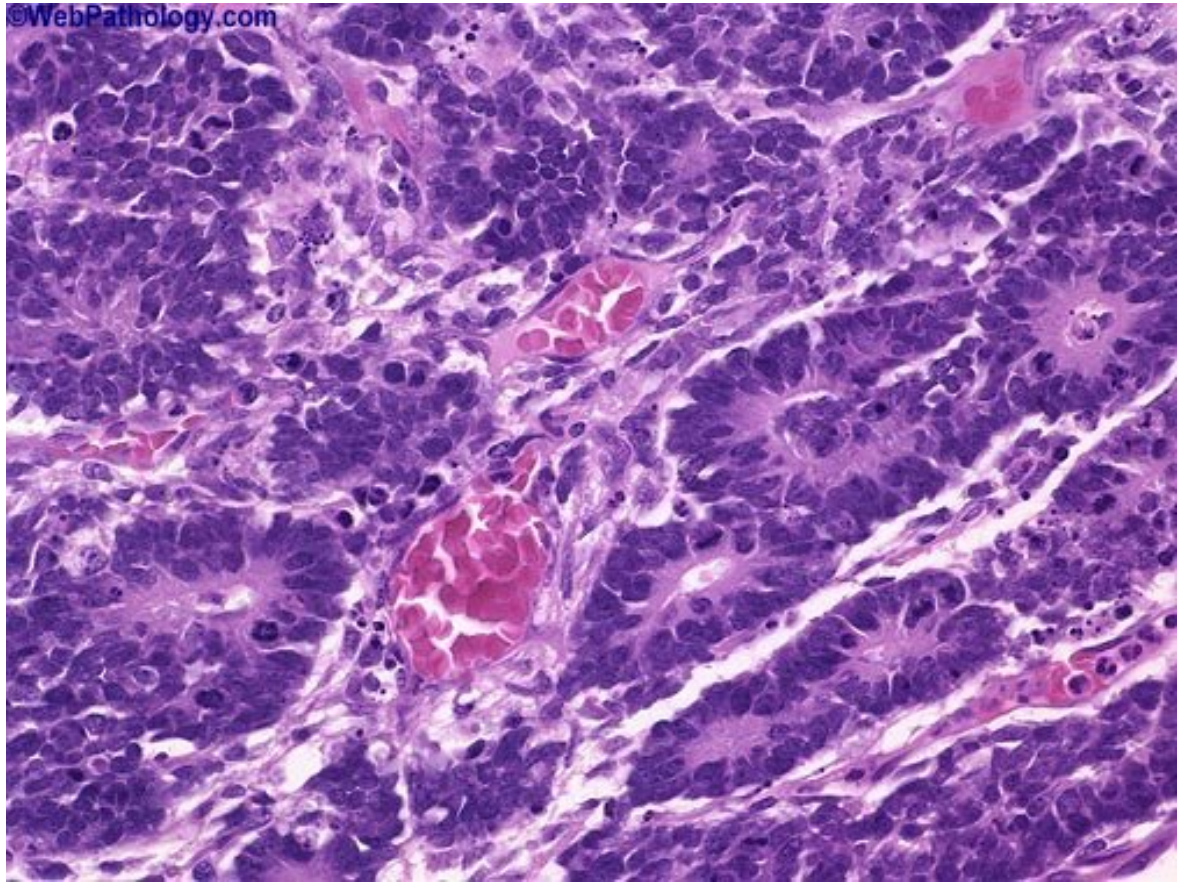
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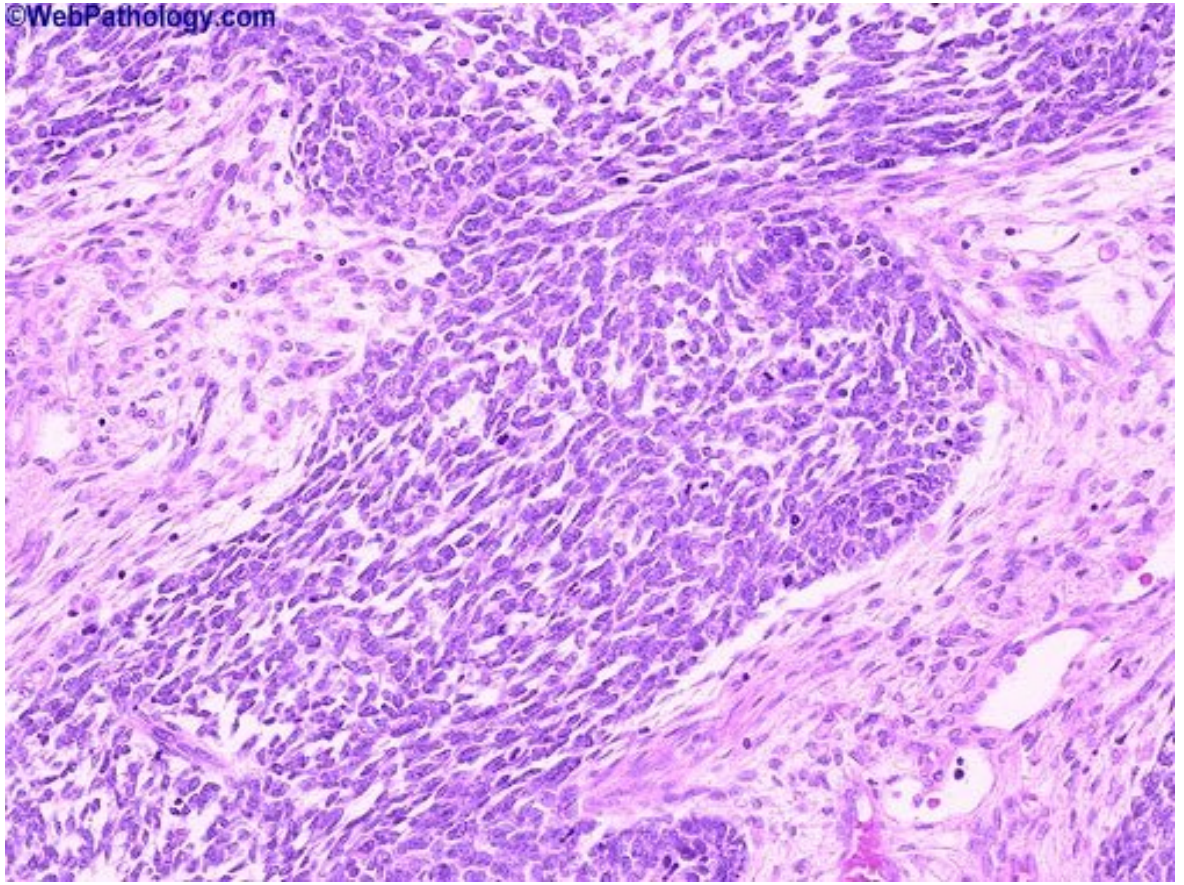
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WILMS TUMOR:CLINICAL FEATURES

Clinical features

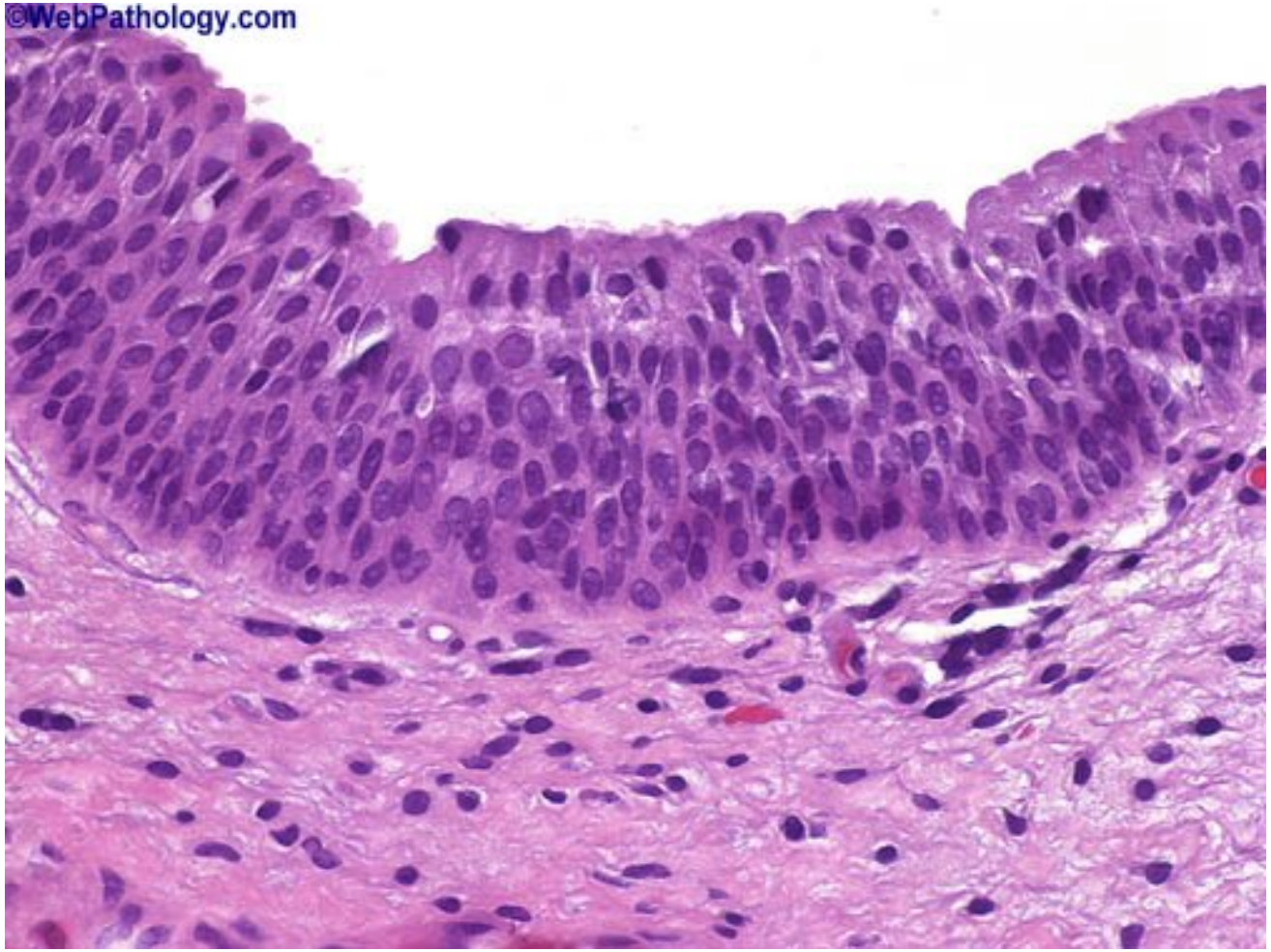
- Wilms tumor usually presents between 1 and 3 years of age, and 98% occur before 10 years of age.
- Abdominal mass (commonest sign)
- Hematuria
- Pain abdomen
- Hypertension

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



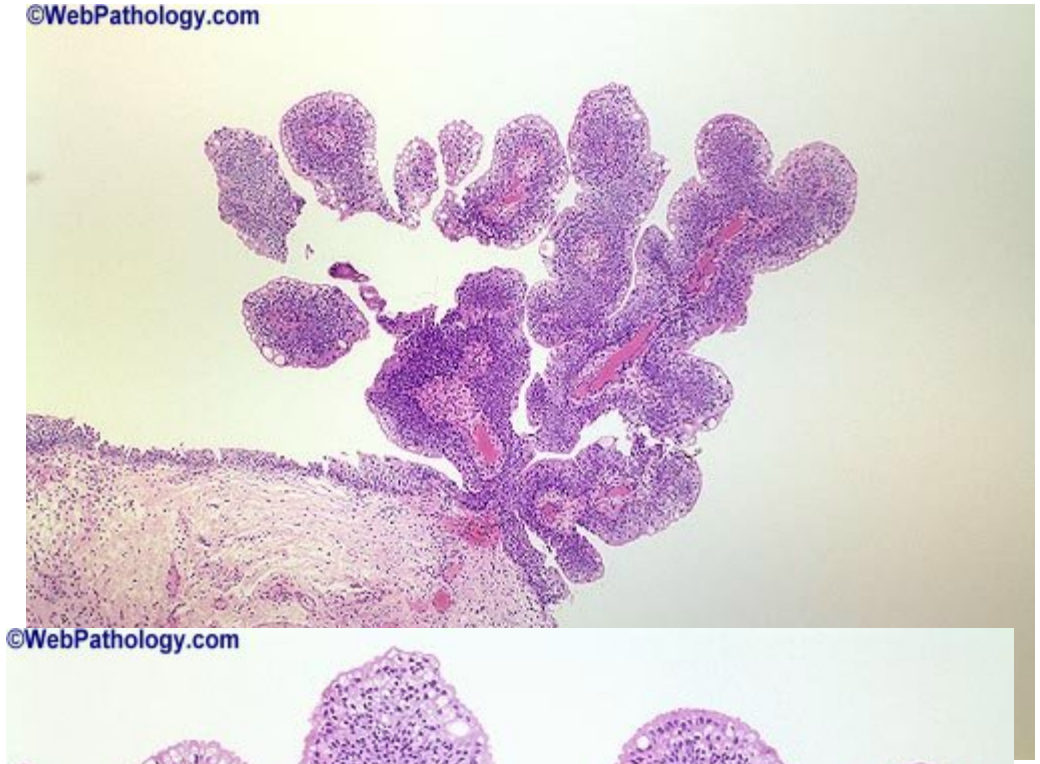
TUMORS OF THE LOWER URINARY TRACT

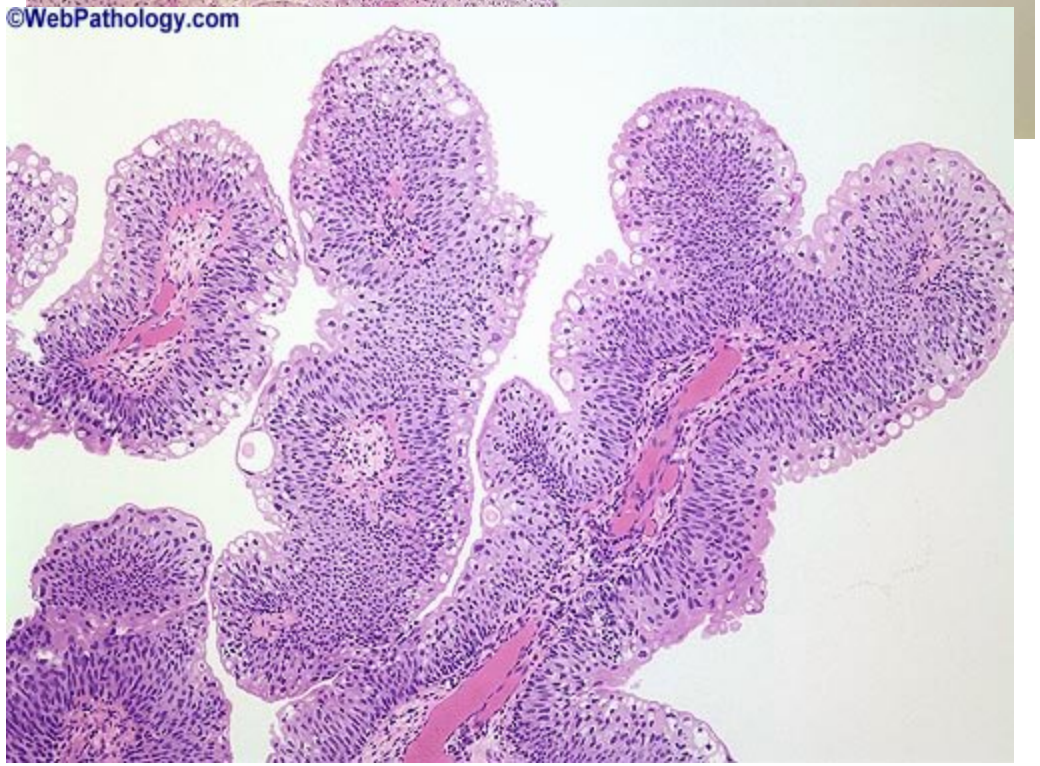
- Tumors in the collecting system above the bladder are relatively uncommon
- Malignant tumors in the bladder are a more common cause of death than kidney tumors.
- A small lesion in the ureter may cause urinary outflow obstruction and have greater clinical significance than a much larger mass in the large capacious bladder.
- The histological range of urothelial neoplasms include the following:
  - Papilloma
  - PUNLMP
  - Low grade papillary urothelial carcinoma
  - High grade papillary urothelial carcinoma
  - Urothelial carcinoma in situ
  - Invasive urothelial carcinoma.

TRANSITIONAL CELL NEOPLASMS OF URINARY BLADDER

PAPILLOMA

- are rare and benign.
- They measure 0.2 to 1.0 cm papillary structures covered by benign transitional epithelium.
- Usually solitary
- Noninvasive, benign and rarely recur once removed.
- 2 types: exophytic (common) and inverted (rare).





PAPILLARY UROTHELIAL NEOPLASM OF LOW MALIGNANT POTENTIAL (PUNLMP)

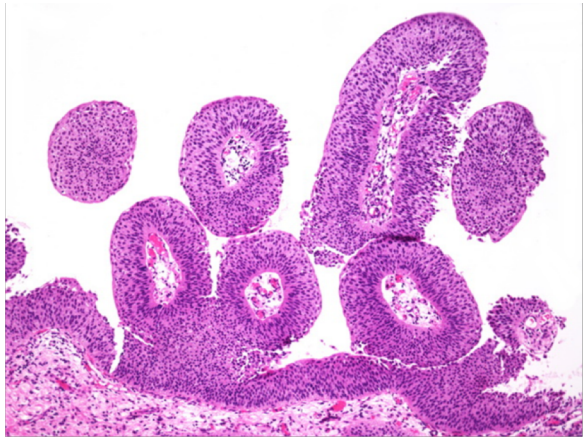
They are well differentiated urothelial tumors of low malignant potential.

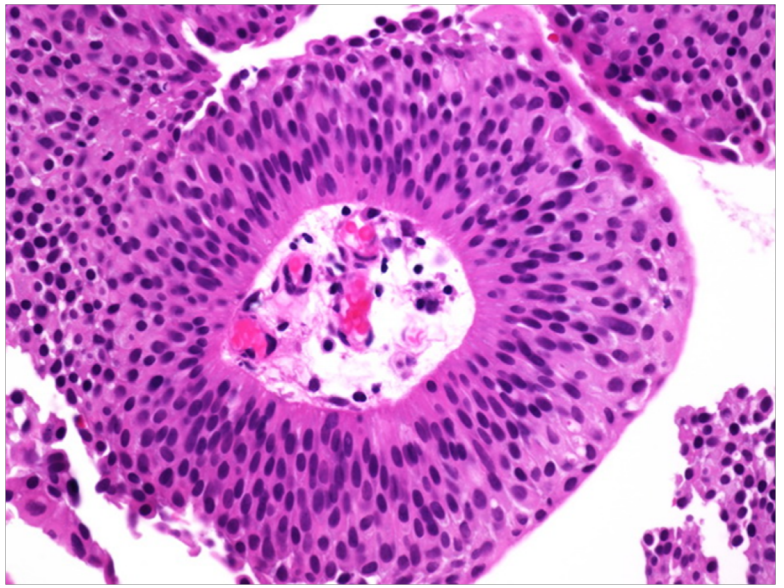
They are papillary

They may recur after removal.

Uncommon.

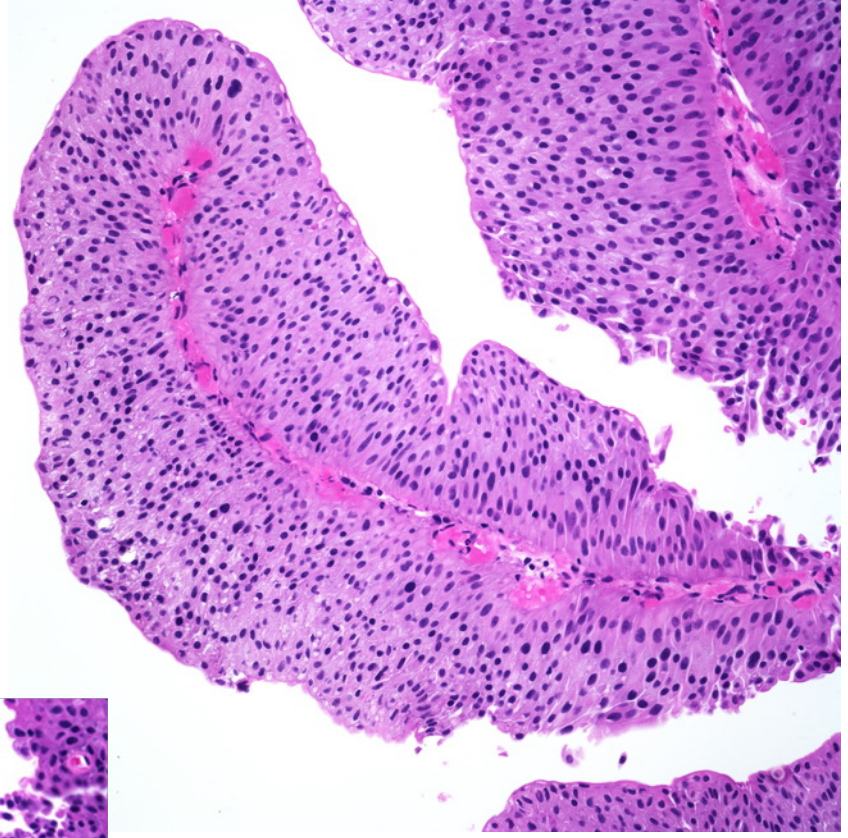
They are intermediate between benign papillomas and low grade papillary urothelial carcinomas.

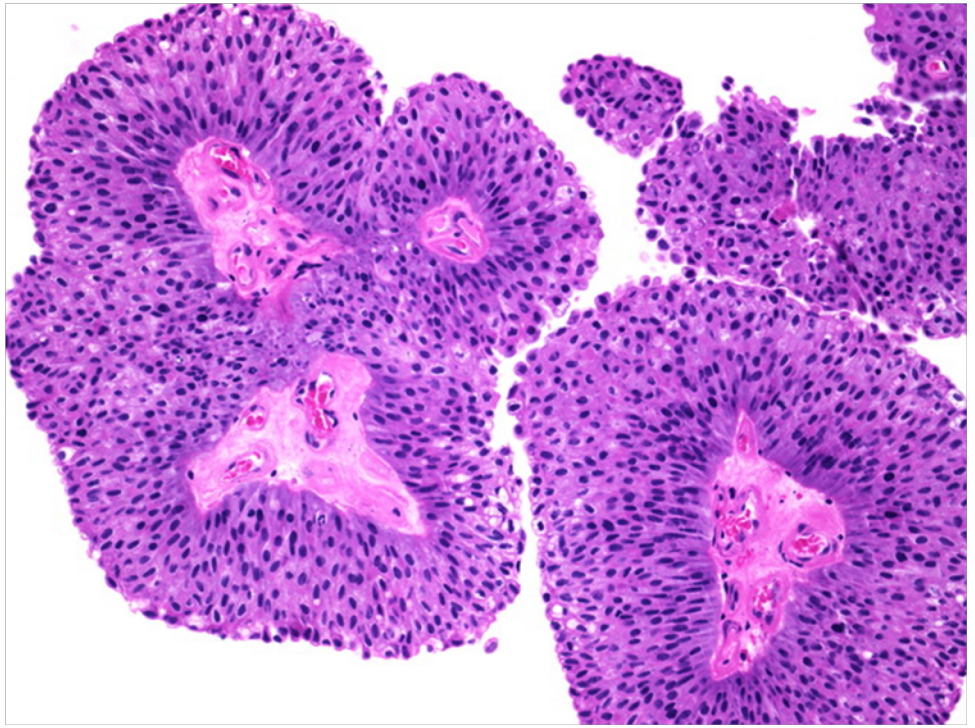




LOW GRADE PAPILLARY UROTHELIAL CARCINOMA

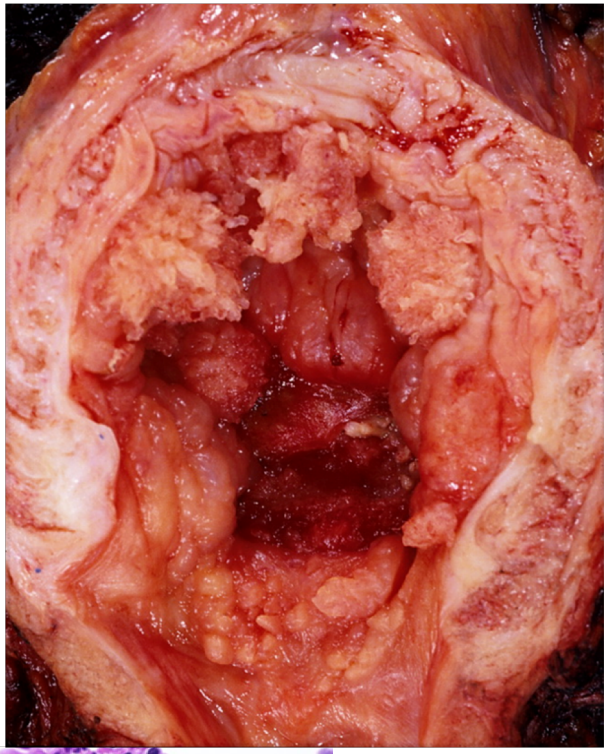
- **Low grade papillary urothelial carcinoma**: Papillary projections are lined by neoplastic transitional epithelium with minimal pleomorphism and minimal mitotic activity.

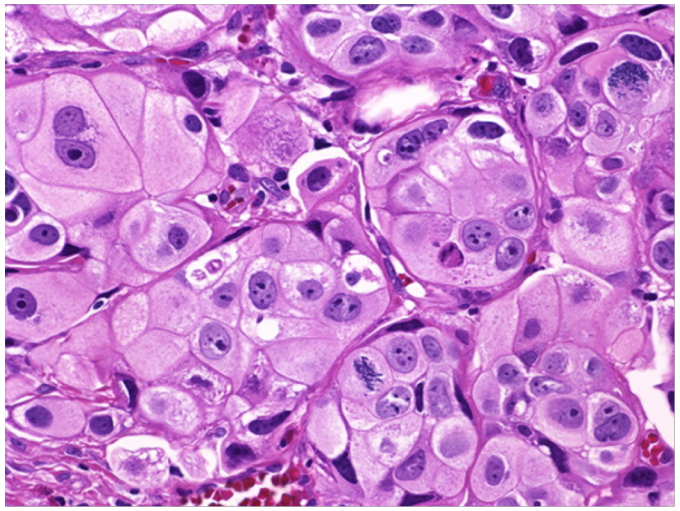


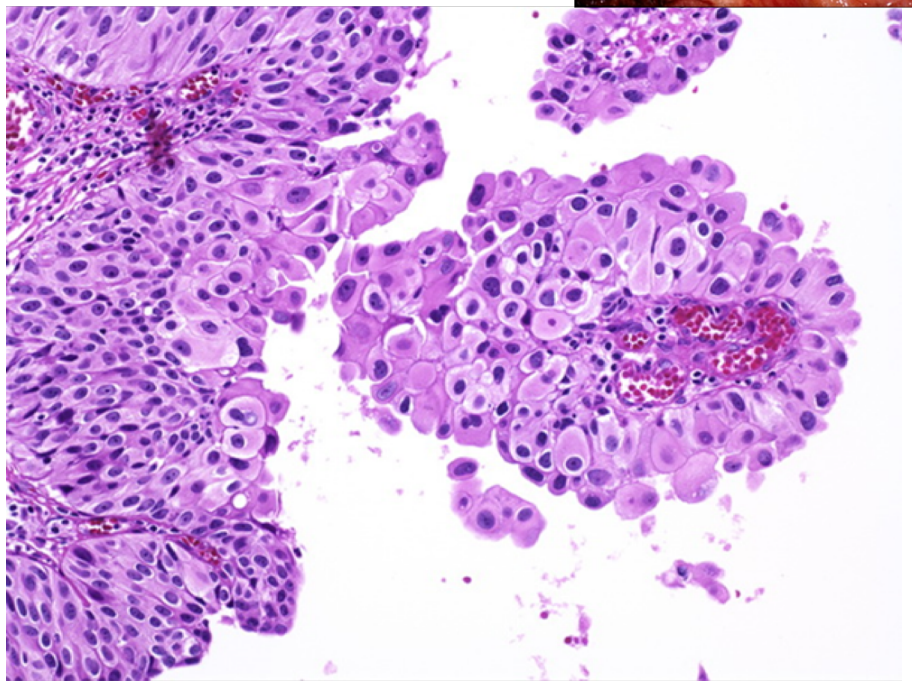


HIGH GRADE PAPILLARY UROTHELIAL CARCINOMA

- Papillary projections are lined by neoplastic transitional epithelium with marked hyperchromasia, pleomorphism and brisk mitotic activity. The epithelium is disorganized and there are mitoses in all layers. Majority of high grade tumors → invade into the lamina propria, and the muscularis propria.







UROTHELIAL CARCINOMA IN SITU

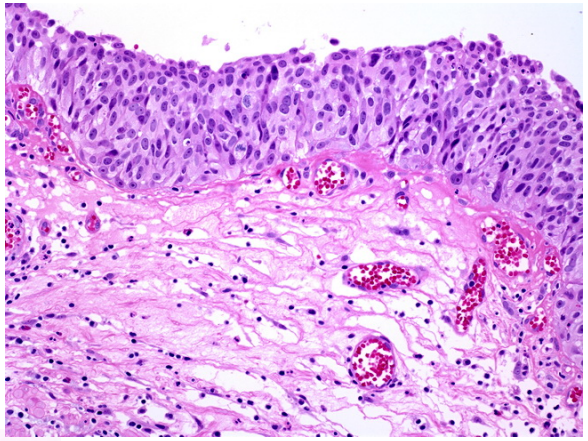
Multifocal, flat and nonpapillary.

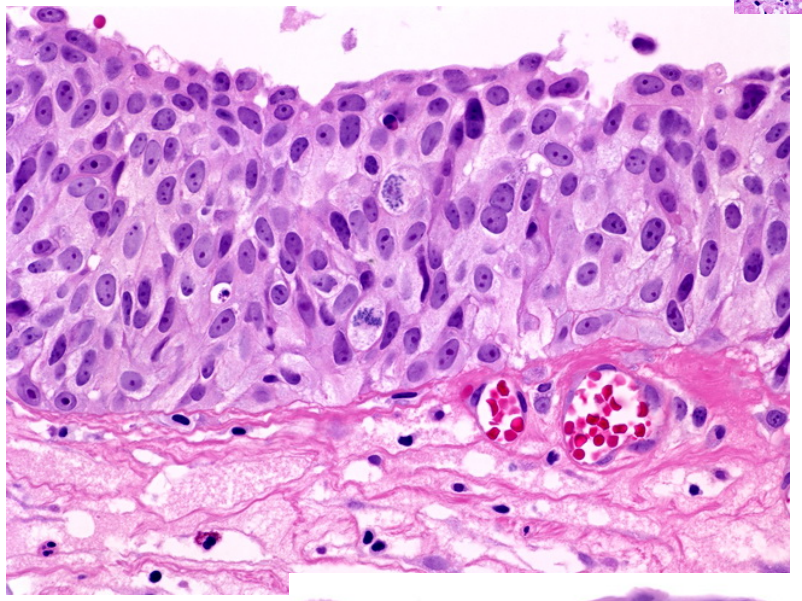
There is the full-thickness malignant changes of the urothelium (hyperchromatic and pleomorphic cells with prominent nucleoli).

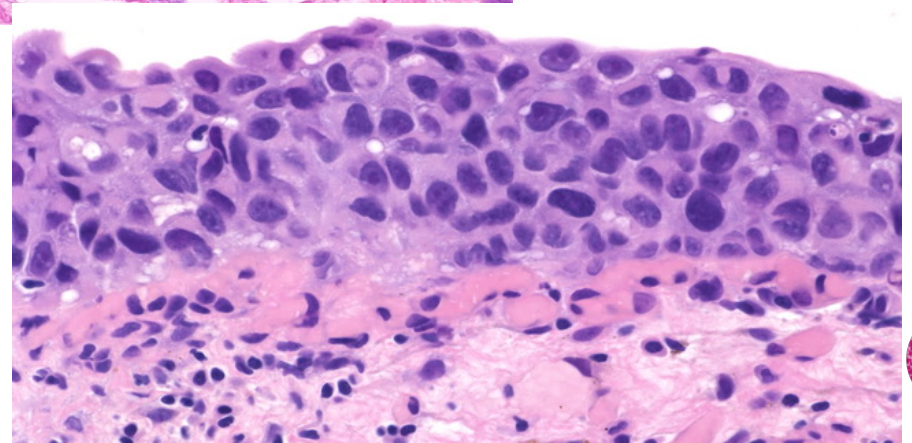
There may be excessive shedding of malignant cells in urine.

It may extend into the ureters and urethra

In about 50% of cases it is associated with subsequent invasive carcinoma.







INVASIVE UROTHELIAL CARCINOMA

- It is associated with
  - papillary urothelial cancer, usually high grade,
  - and CIS

CLINICAL FEATURES OF UROTHELIAL CARCINOMA

They affect men about three times as frequently as women.

usually between the ages of 50 and 70 years.

Predisposing factors:

- Bladder tumors are 50 times more common in those exposed to arylamines(β-naphthylamine)
- Cigarette smoking and chronic cystitis
- Schistosoma haematobium infections in endemic areas
- Long-term use of analgesics
- Heavy long-term exposure to cyclophosphamide
- Previous exposure of the bladder to irradiation

They are not familial.

Lesions that invade the ureteral or urethral orifices cause urinary tract obstruction with associated hydronephrosis or pyelonephritis

Painless hematuria is the dominant clinical presentation of all these tumors.

- Bladder cancers vary from exophytic, flat, ulcerated and deeply invasive.
- Urothelial carcinoma of the bladder typically manifests as sudden hematuria and less frequently as dysuria. Cystoscopy reveals single or multiple tumors.
- Bladder cancer metastasize to regional lymph nodes, liver, lung, and bone.

NON-UROTHELIAL CARCINOMAS OF THE LOWER URINARY TRACT

are rare and all the following have very poor prognosis.

- Squamous cell carcinoma.
- Adenocarcinoma.
- Neuroendocrine carcinoma.
- Rhabdomyosarcoma

SQUAMOUS CELL CARCINOMA OF THE BLADDER

- Squamous cell carcinoma of the bladder develops in foci of squamous metaplasia.
- Usually associated with schistosomiasis.

END