Urolithiasis and urinary outflow obstruction

Urolithiasis

- **Common** clinical problem (5-10% of people) → **1%** of individuals at autopsy.
- **Definition:**

"Calculus formation at any level in the urinary collecting system".

  - Most often arise in the **kidney**.
  - **Unilateral** in 80% of patients (commonly found at pelvis, calyx or urinary bladder).
  - **M>F***; peak age of 20-30 yrs.
  - Has **familial tendency**.**

Types of Renal Stones

Stone	Comment
Calcium Oxalate and/or Calcium Phosphate Idiopathic hypercalciuria (50%) Absorptive hypercalciuria (GI) Renal hypercalciuria Hypercalcemia and hypercalciuria (10%) Hyperoxaluria (5%) Hyperuricosuria* (20%) *No known* metabolic abnormality (15-20%)	**80%** Alkaline pH**
Struvite (Magnesium, Ammonium, Phosphate) → Due to renal infection by urea splitting bacteria as proteus & staphylococci**	**10%** Alkaline pH

Types of Renal Stones

Stone	Comment
Uric Acid Associated with hyperuricemia Associated with hyperuricosuria* Idiopathic (50% of uric acid stones)	**6-7%** Acidic pH < 5.5
Cystine Defect in the renal transport of cystine	**1-2%** Acidic PH

Pathogenesis
(obscure)

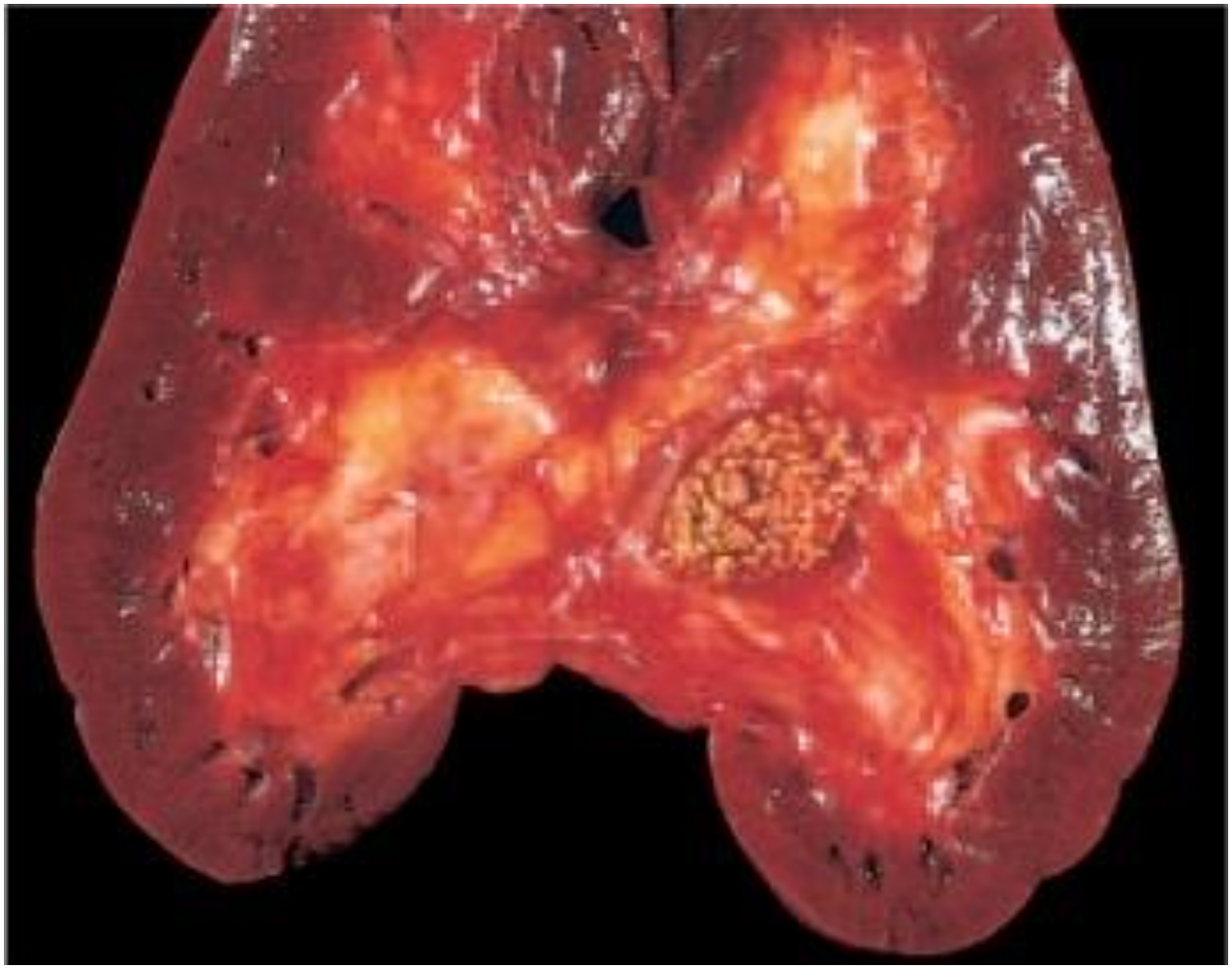
- The most important is ↑ *urine concentration of the stone's constituents* so that it exceeds their solubility in urine (**supersaturation**).
- In all cases, an organic matrix of *mucoprotein* makes up 2.5% of the stone (? **nidus**).
- **Predisposing factors:**
  - Change of urine pH.
  - Decreased urine volume.
  - Presence of bacteria.
  - Deficiency of inhibitors of crystal formation in the urine (as *Tamm-Horsfall* protein).

Morphology

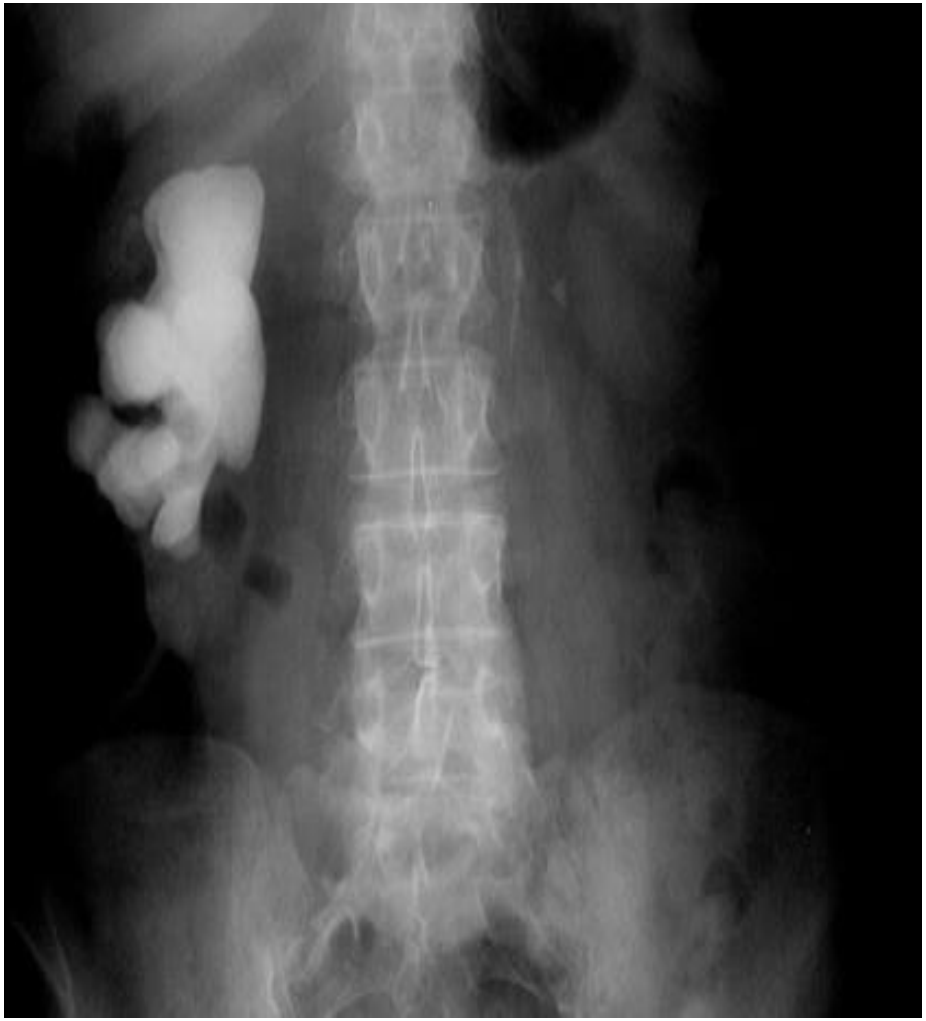
- **Number & Size:**
  - Usually *multiple*.
  - Tend to be *small* (smooth or jagged).

- **Staghorn calculi:**
  - Progressive accretion of salts leads to the development of branching structures → Lead to formation of massive stone filling the renal pelvis and calyceal system (cast of pelvis and calyceal system).
  - They are usually composed of ***struvite***.

Nephrolithiasis



KUB



Kidneys, ureters, bladder (KUB) film showing right staghorn calculus

Staghorn stone

Clinical Course

- **Large** stones are *asymptomatic.*
- **Smaller** stones may pass into the ureter, producing *renal (or ureteral) colic* & *gross hematuria*.

- Renal stones predispose to bacterial infection, obstruction & UT bleeding.

Urianary outflow obstruction

- **Importance of UT obstruction:**
  - Increases susceptibility to *infection & stone formation*.
  - If unrelieved lead to permanent renal atrophy (*Hydronephrosis or obstructive uropathy*)
  - Many causes are surgically *correctable* or medically treatable.

- It can occur at any level of urinary tract (intrinsic & extrinsic causes).

- Sudden or insidious, partial or complete, unilateral or bilateral

Urinary outflow obstruction

Causes

Congenital anomalies:
- Posterior urethral valves
- Urethral strictures
- Meatal stenosis
- Ureteropelvic junction obstruction
- Severe vesicoureteral reflux

Inflammation:
- Prostatitis
- Ureteritis, urethritis
- Retroperitoneal fibrosis

Sloughed papillae or blood clots

Urinary calculi

Pregnancy

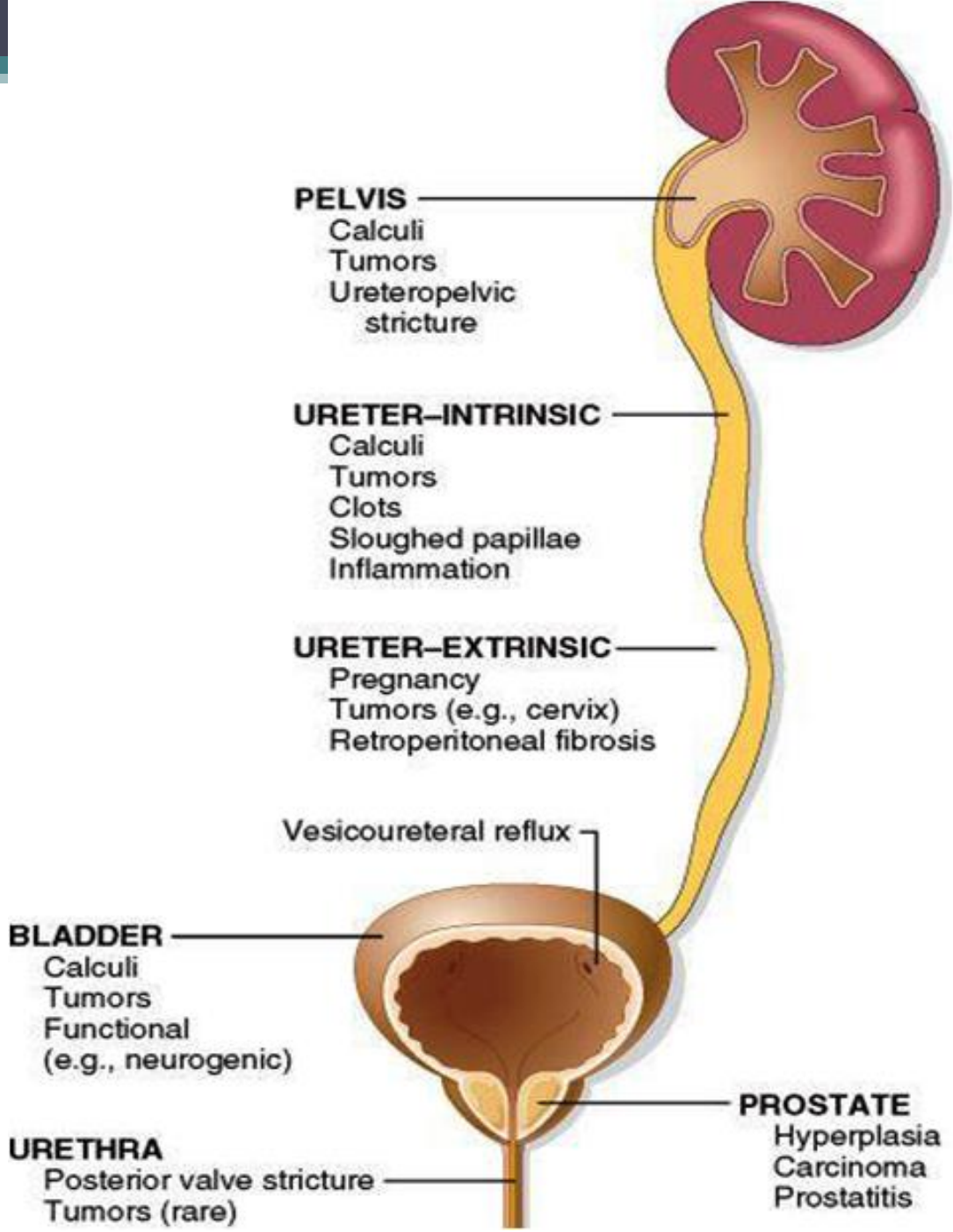
Benign prostatic hyperplasia

Uterine prolapse & cystocele

Tumors:
- CA of the prostate
- Bladder tumors
- Retroperitoneal tumors
- CA of the cervix or uterus

Functional disorders:
- Neurogenic (spinal cord damage or diabetic nephropathy)

Urinary outflow obstruction



Hydronephrosis

- **Definition:**

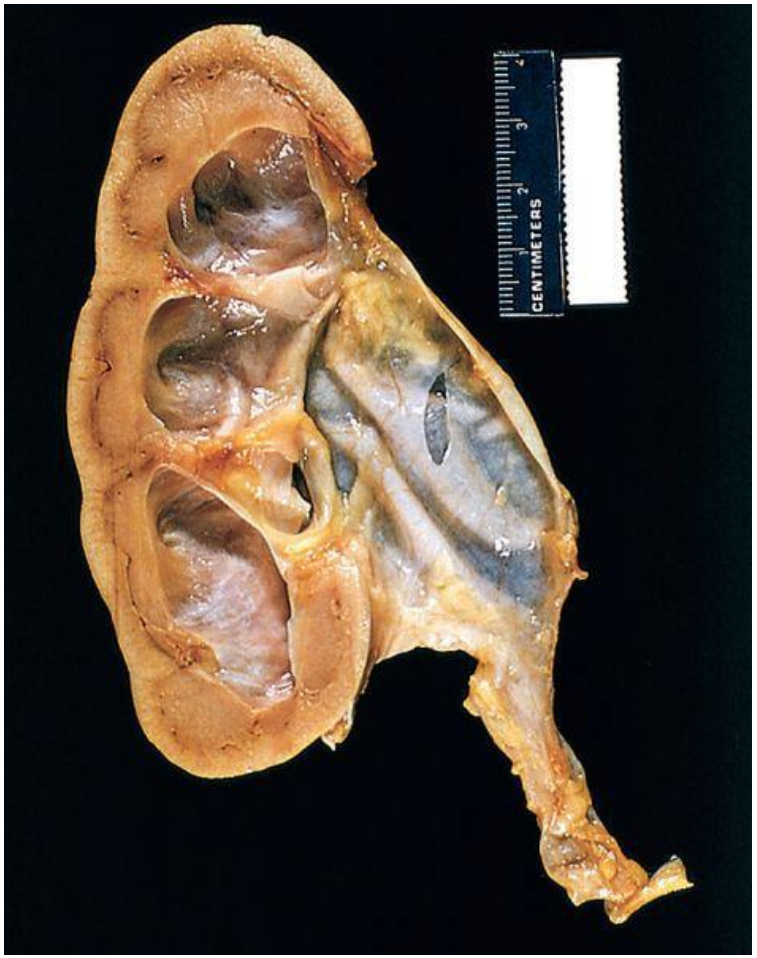
"Dilation of the renal pelvis and calyces, with accompanying atrophy of the parenchyma, caused by obstruction to the outflow of urine".

  - *Bilateral*: if obstruction is below the ureter.
  - *Unilateral*: if obstruction at the level of ureter or above.

Morphology

- **Gross:**
  - Slight to massive enlargement → early features include simple dilation of the pelvis and calyces and variable interstitial inflammation.
  - In chronic cases → cortical tubular atrophy with marked diffuse interstitial fibrosis.
  - Advanced cases transformed into thin-walled cystic structure 15-20 cm with striking atrophy and thinning of cortex

Hydronephrosis



Hydronephrosis of the kidney, with marked dilation of the pelvis and calyces and thinning of the renal parenchyma

Clinical features

- Depend on circumstances:
  - Acute Obstruction: pain.
  - Unilateral (complete or partial) Obstruction: may remain silent.
  - Bilateral partial Obstruction: features of TIN.
  - Bilateral complete Obstruction: ARF.

Tumors of the Kidney

Classification

(simplified)

PRIMARY

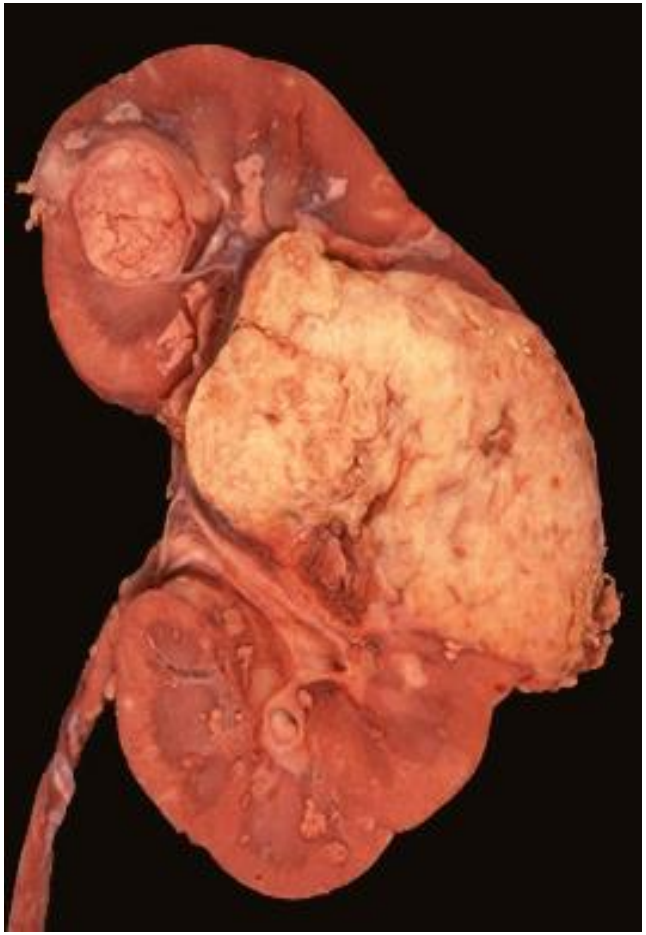
- *Benign:*
  - Papillary adenoma (in the cortex).
  - Oncocytoma.
  - Medullary fibroma (interstitial cell tumor).
- *Malignant:*
  - Renal cell carcinoma (most common):
    - Clear cell renal cell carcinoma.
    - Papillary renal cell carcinoma.
    - Chromophobe renal cell carcinoma.
  - Nephroblastoma (Wilms tumor).
  - Urothelial carcinoma of renal pelvis.

SECONDARY

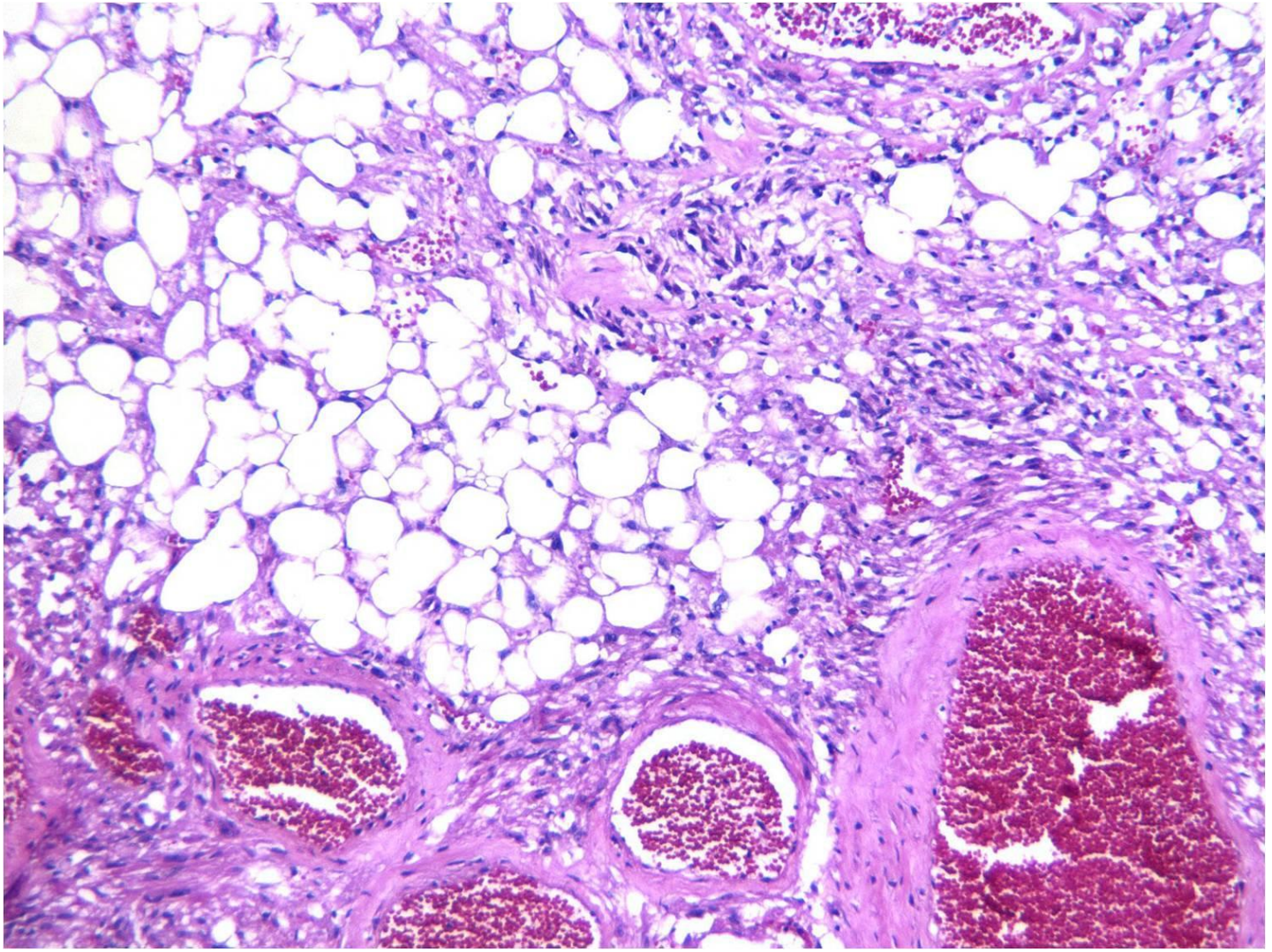
Benign renal tumors

2. Angiomyolipoma:

- Consists of vessels, smooth muscles & fat.
- Seen in 25-50% of patients with **(Tuberous Sclerosis).**



Angiomyolipoma



Malignant renal tumors

1. Renal cell carcinoma (RCC)

- Tumors are derived from the *renal tubular epithelium**.
- 2-3% of all visceral cancers. ~85% of all renal cancer.
- M:F = 2:1. commonly 60-70 years.
- Most cases are **sporadic**.

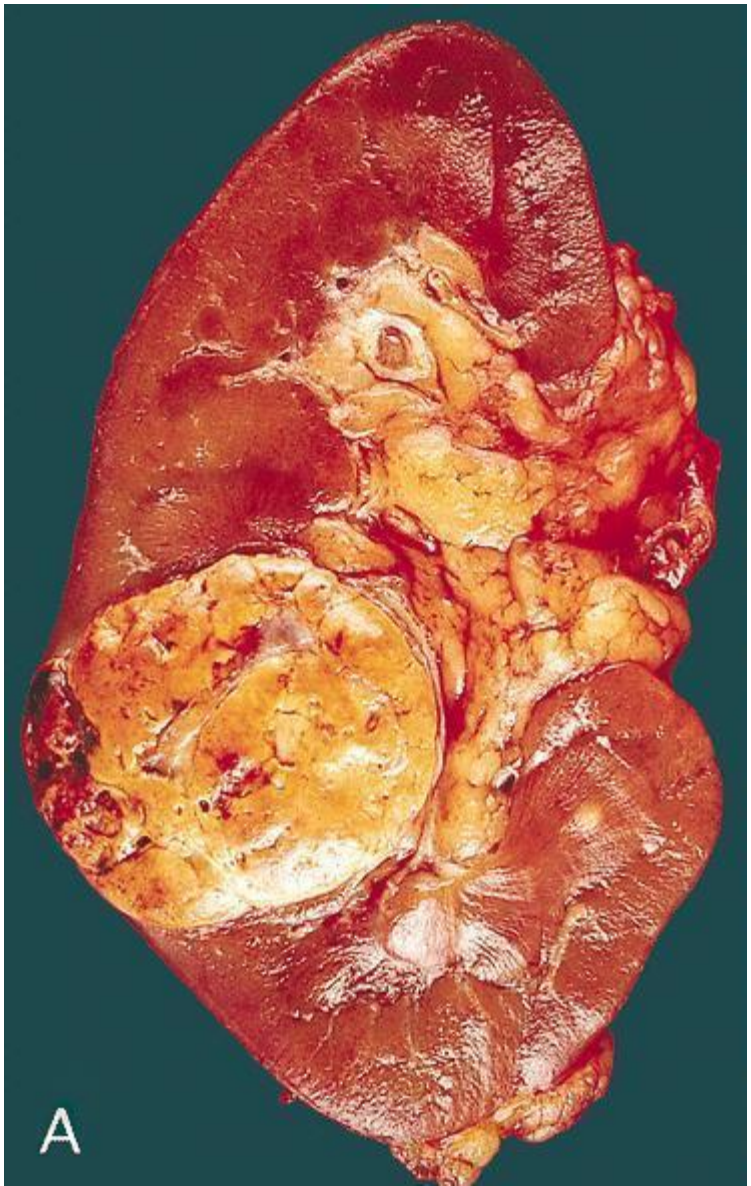
Risk factors

- Smoking (*most significant*), obesity*, HTN.
- Unopposed estrogen Rx
- Cadmium, petroleum products & heavy metals.
- CRF & acquired cystic disease** (30 folds)
- Familial (4%) → most are AD:
  - Von Hippel-Lindau (VHL) syndrome
  - Hereditary clear cell carcinoma
  - Hereditary papillary carcinoma

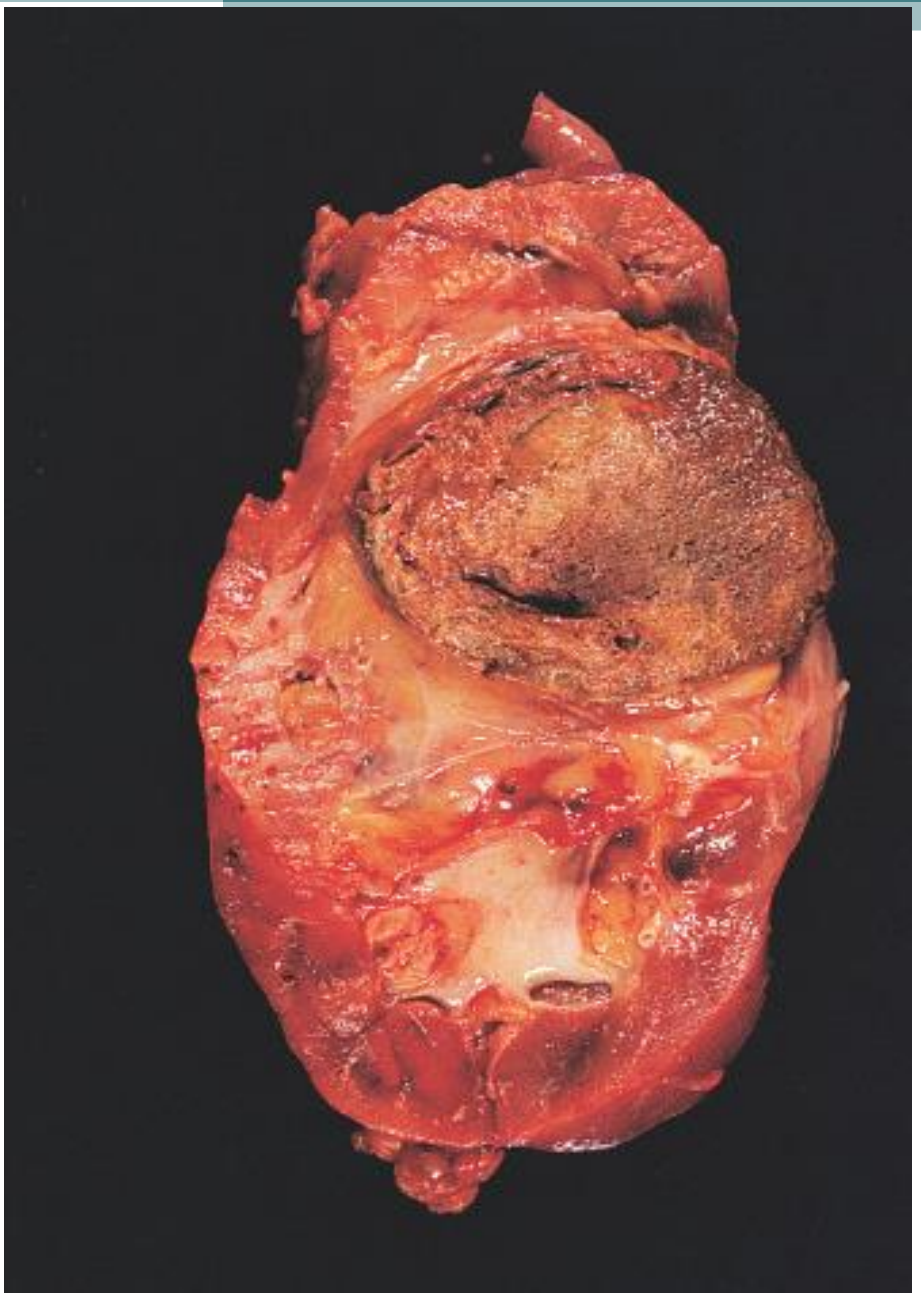
Morphology of RCC

- **Grossly:**
  - Mainly arise in cortex → polar & spherical.
  - Orange – yellow OR tan–brown*, variegated tumor with hemorrhagic, necrotic & cystic areas.
  - May extend into *renal vein*.
- Classified according to the **histological** picture:
  - Clear cell carcinoma (70-80%).
  - Papillary carcinoma (10-15%).
  - Chromophobe renal carcinoma (5%).
  - Sarcomatoid carcinoma.

Renal cell carcinoma



Chromophobe RCC



A. Clear cell carcinoma

- Most common RCC subtype.
- Arise from proximal convoluted tubules.
- Majority are *sporadic & unilateral*.
- Familial forms, associated with germ-line mutation of the *VHL* tumor suppressor gene on 3p:

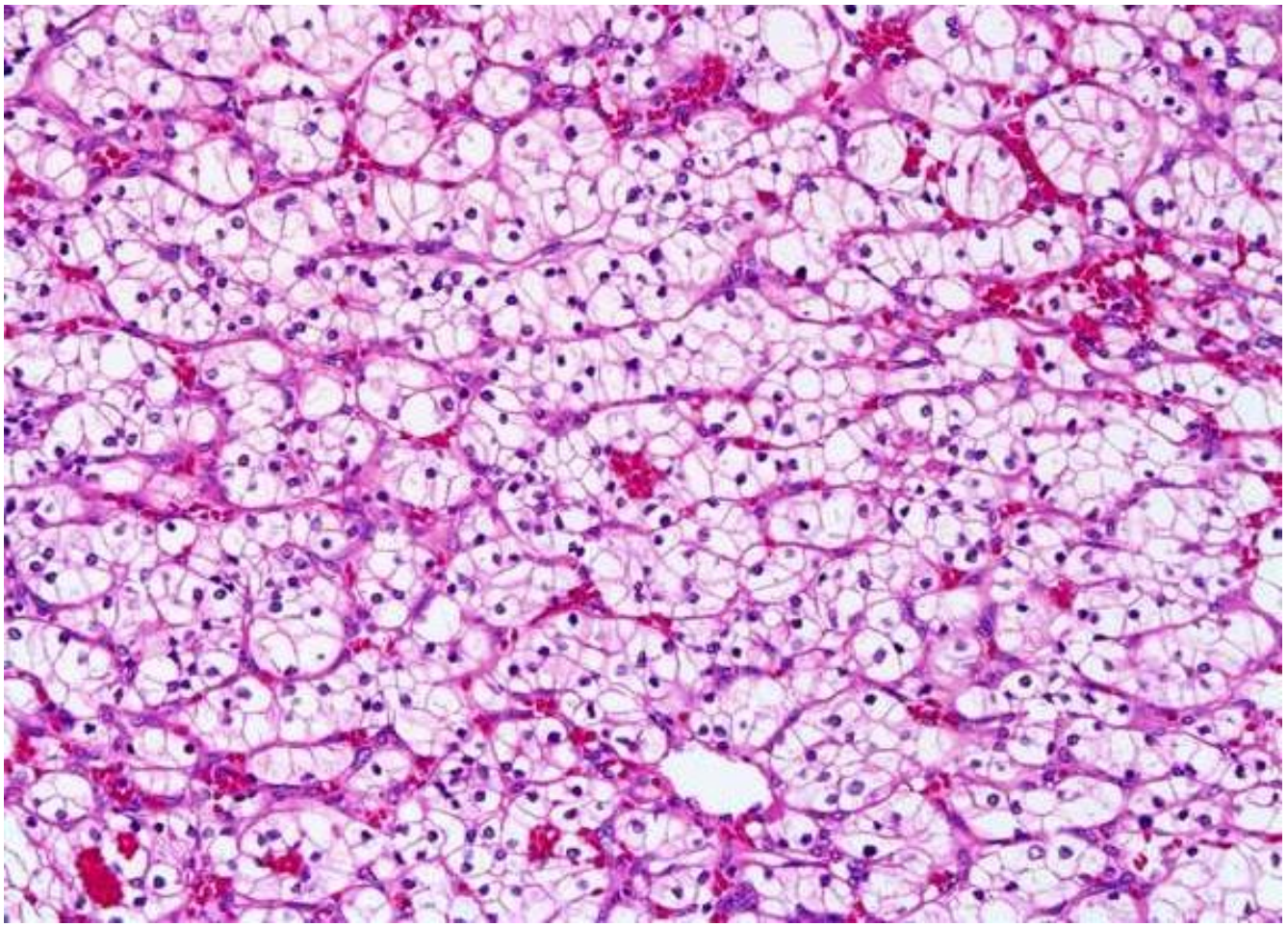
❖**von Hippel-Lindau:**

- Hemangioblastomas of cerebellum & retina.
- Bilateral, multiple renal cysts clear cell carcinomas (40-60%).
- Pheochromocytoma.

❖**Familial clear cell carcinoma:**

- Clear RCC confined to the kidney without other manifestations of VHL.

Clear cell carcinoma



Microscopic:

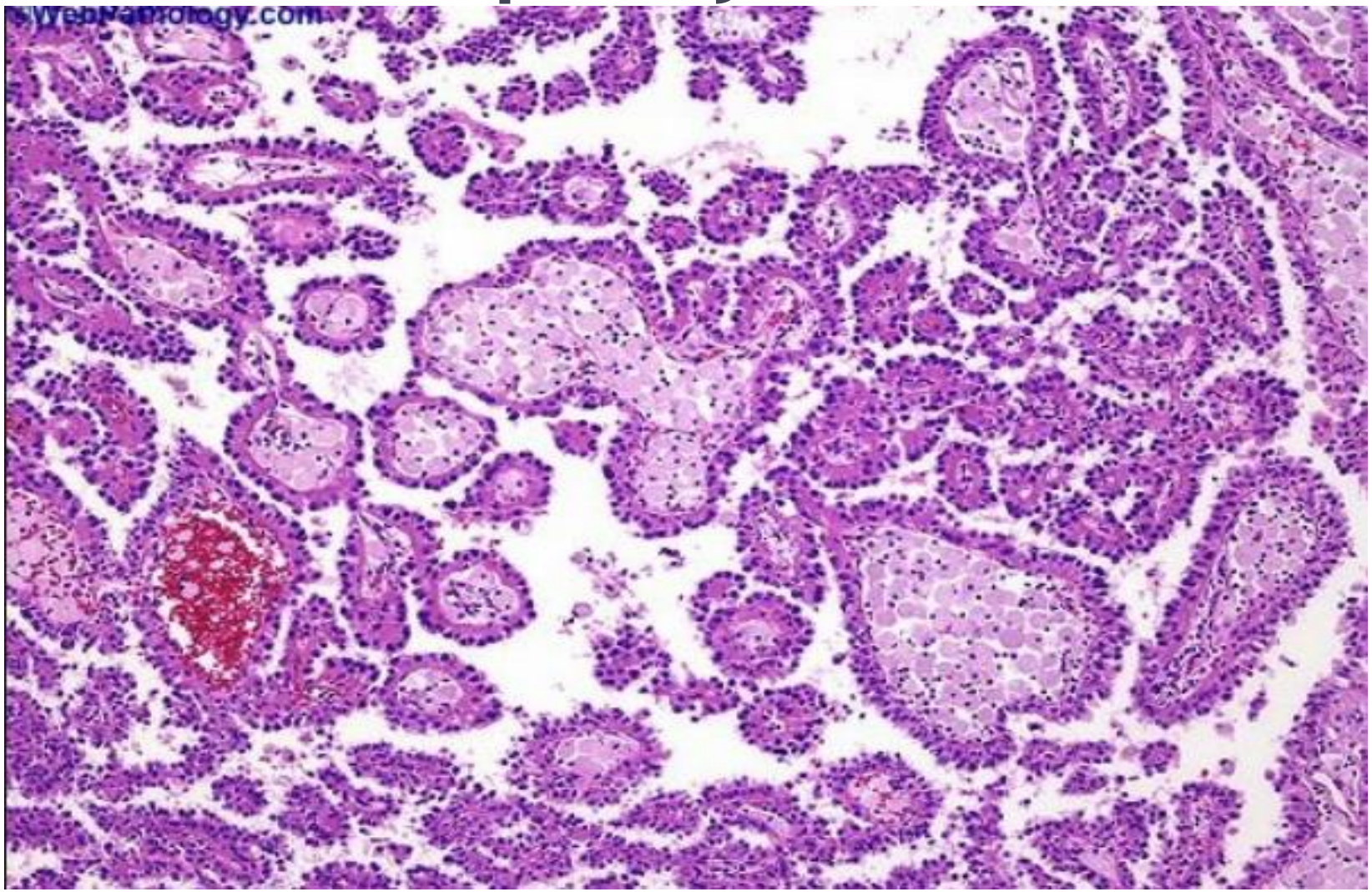
-Vaculated cells with clear or granular cytoplasm.

-Highly vascularized stroma

B. Papillary RCC

- Arise from distal convoluted tubules.
- Most are sporadic. Frequently *multifocal & bilateral.*
- Familial forms are associated with activitating mutation of **MET** protooncogene on 7q.

Papillary RCC

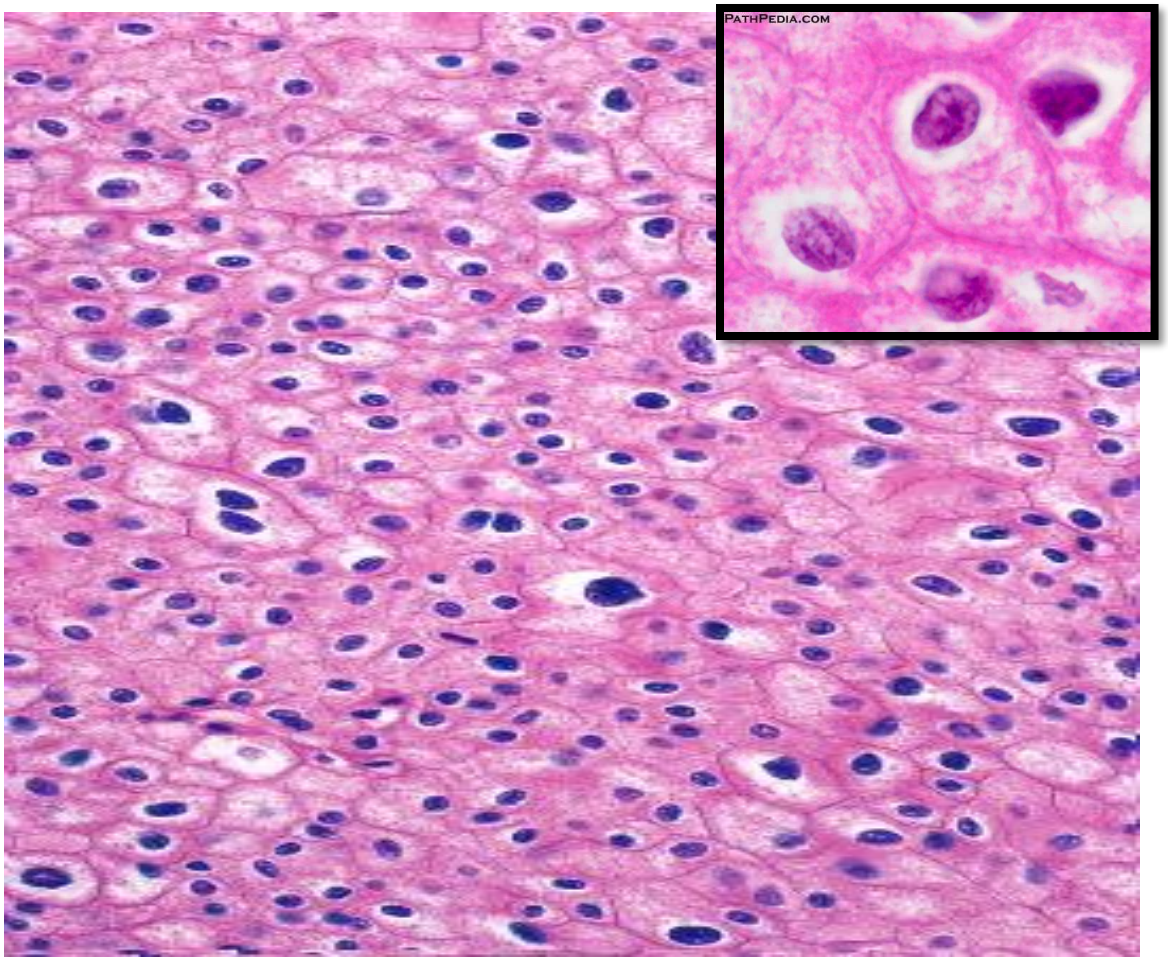


•**Microscopic:**
Papillae with fibrovascular cores

C. Chromophobe renal cell carcinoma

- Arise from cortical collecting ducts or their intercalated cells.
- Multiple losses of entire chromosomes (as:1,2,6,10,13,17,21) → extreme hypodiploidy
- General **good** prognosis.

Chromophobe RCC



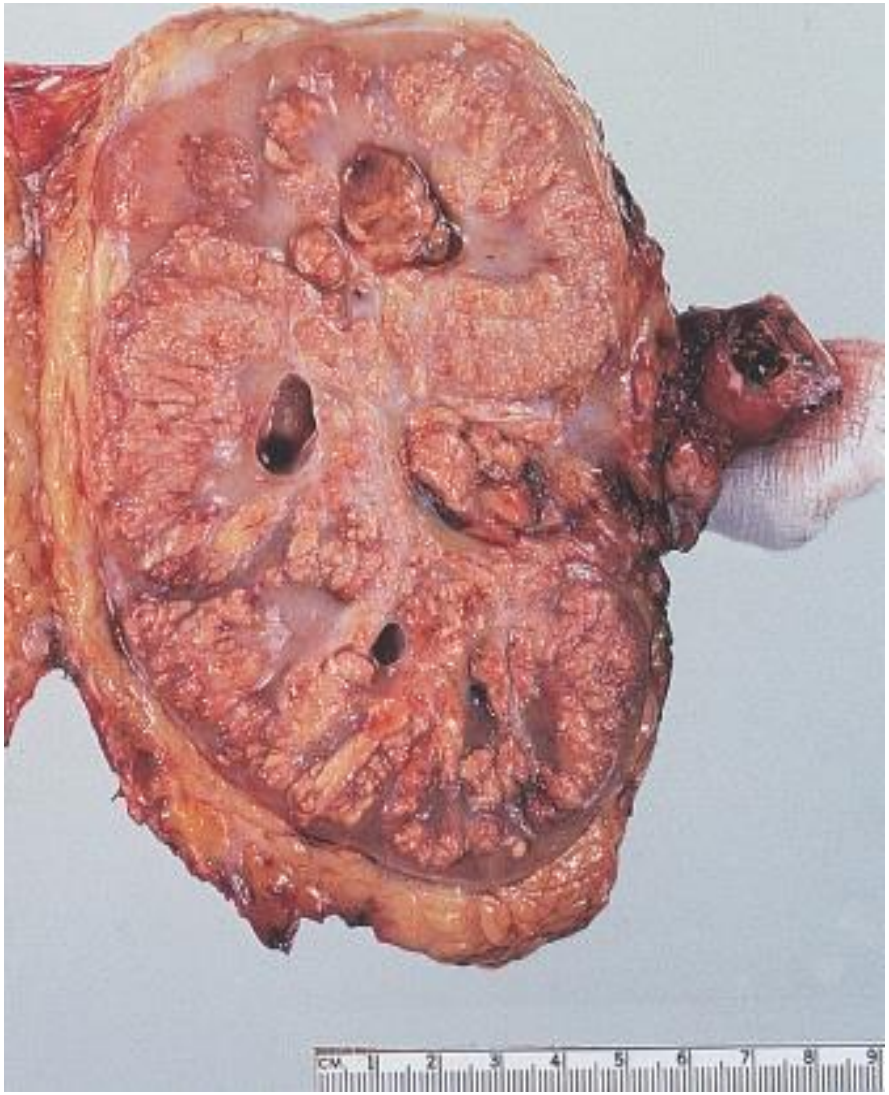
•Microscopic:

- Tumor cells have clear faint granular cytoplasm with prominent, distinct cell membranes
- The nuclei are surrounded by halos of clear cytoplasm → **Raisen-like**

Tumor spread

- Intra-renal → **small satellite nodules .**
- To pelvicalyceal system & ureter.
- Frequently the **tumor invades the renal vein** and grows in the **IVC** to **RT** side of the heart.
- Direct invasion to perinephric fat, renal sinus fat, regional LNs, or adrenal gland.

RCC extending into the renal vein



Clinical features of RCC

- **Hematuria** is the most frequent symptom (50%).
- Triad of 3 symptoms (in 10%) → characteristic:
  - Flank pain, palpable mass & hematuria.
- Asymptomatic/incidental finding.
- Constitutional symptoms (Fever, wt loss …)
- Present with mets (esp. lungs and bones)*.
- Paraneoplastic syndromes
  - Polycythemia 5-10%.
  - Hypercalcemia.
  - HTN.
  - Cushing's syndrome.
  - Feminization or masculinization.
- **Prognosis:** 5 yr survival is around 70%.