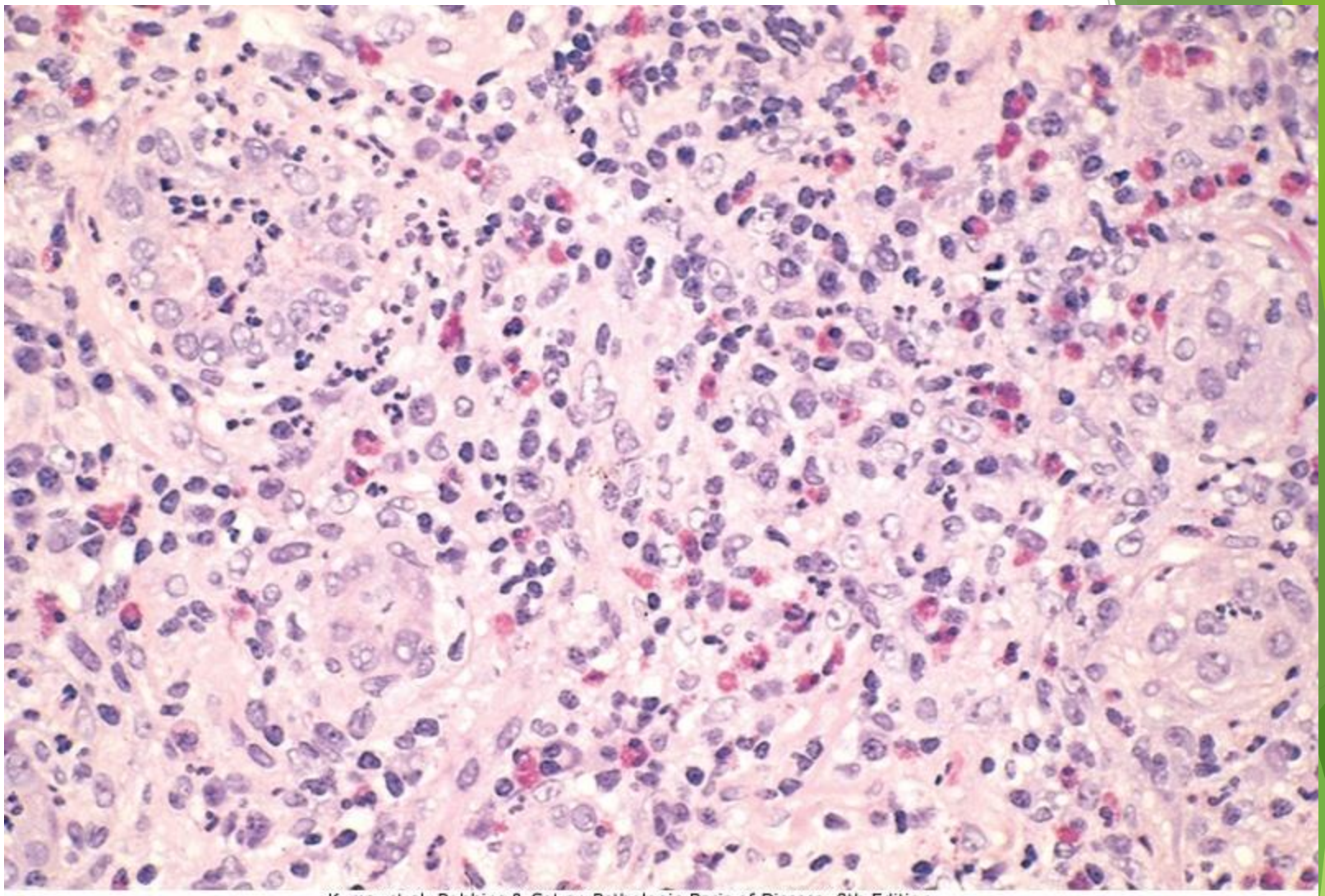
TUBULES, INTERSTITIUM OBSTRUCTION

Diseases of tubules & Interstitium

- Group of diseases characterized by:
- 1. Inflammatory involvement of tubules & Interstitium (tubulointerstitial nephritis).
- 2. Acute tubular necrosis (ischemic or toxic renal injury).

Tubulointerstitial nephritis: characterized by

- ▫ Mainly affect tubules & Interstitium.
- ▫ Glomeruli are usually spared & only affected late in the disease.
- ▫ causes:
- Most of cases are caused by bacterial infection in association with pyelonephritis
- Some cases are due to drugs(e.g. NSAID), hypokalemia, irradiation
- ▫ tubulointerstitial nephritis can be either Acute OR Chronic.



ATN

- It is a clinicopathological entity characterized morphologically by destruction of tubular epithelium and clinically by acute renal failure(ARF).

ATN PATHOGENESIS

- **BLOOD FLOW DISTURBANCES (ISCHEMIC)**
- **TUBULAR INJURY (NEPHROTOXIC)**

- Acute Renal Failure (ARF):
- Acute suppression of renal functions, with urine flow falling within 24 hours to less than 400cc / 24hours (Oliguria).
- Causes of ARF:
- 1. ATN.
- 2. Severe Glomerular diseases such as rapid progressive glomerulonephritis.
- 3. Polyateritis nodosa
- 4. Acute papillary necrosis.
- 5. Diffuse cortical necrosis.

Clinical features of ATN:

- Clinical course of ATN It is highly variable, symptoms depend on degree of damage

- but in classical cases is divided into three phases:

1. **Initiating phase:**
   - Last for 36 hours.
   - Usually due to medical, surgical, & obstetric critical events.
   - The only renal abnormality is decline in renal output(mild oliguria) & mild azotemia(rise in blood urea).
2. **Maintaining phase:**

- From second to sixth day.

- Urine output further fall (between 50 cc to 400cc / day).

- Features of Uremia, fluid overload.
- Without treatment patient may die within this phase, while with good care the survival is the rule.
- More OLIGURIA
- More AZOTEMIA
- DIALYSIS NEEDED

Recovery phase:

- Steady increase in urine volume, reaching up to 3 liters per day over a period of 3 weeks. increase in output ▫ cannot concentrate urine
- Serious electrolytes imbalance due to tubular function dysfunction.
- Increased susceptibility to infection.
- 25% of death due to ATN is occurred in this phase.
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- HYPOKALEMIA main problem

Urinary Tract Infection
Pyelonephritis (PN)

- It is one of the most common diseases of the kidney.

1. Acute pyelonephritis, caused by bacterial infection.

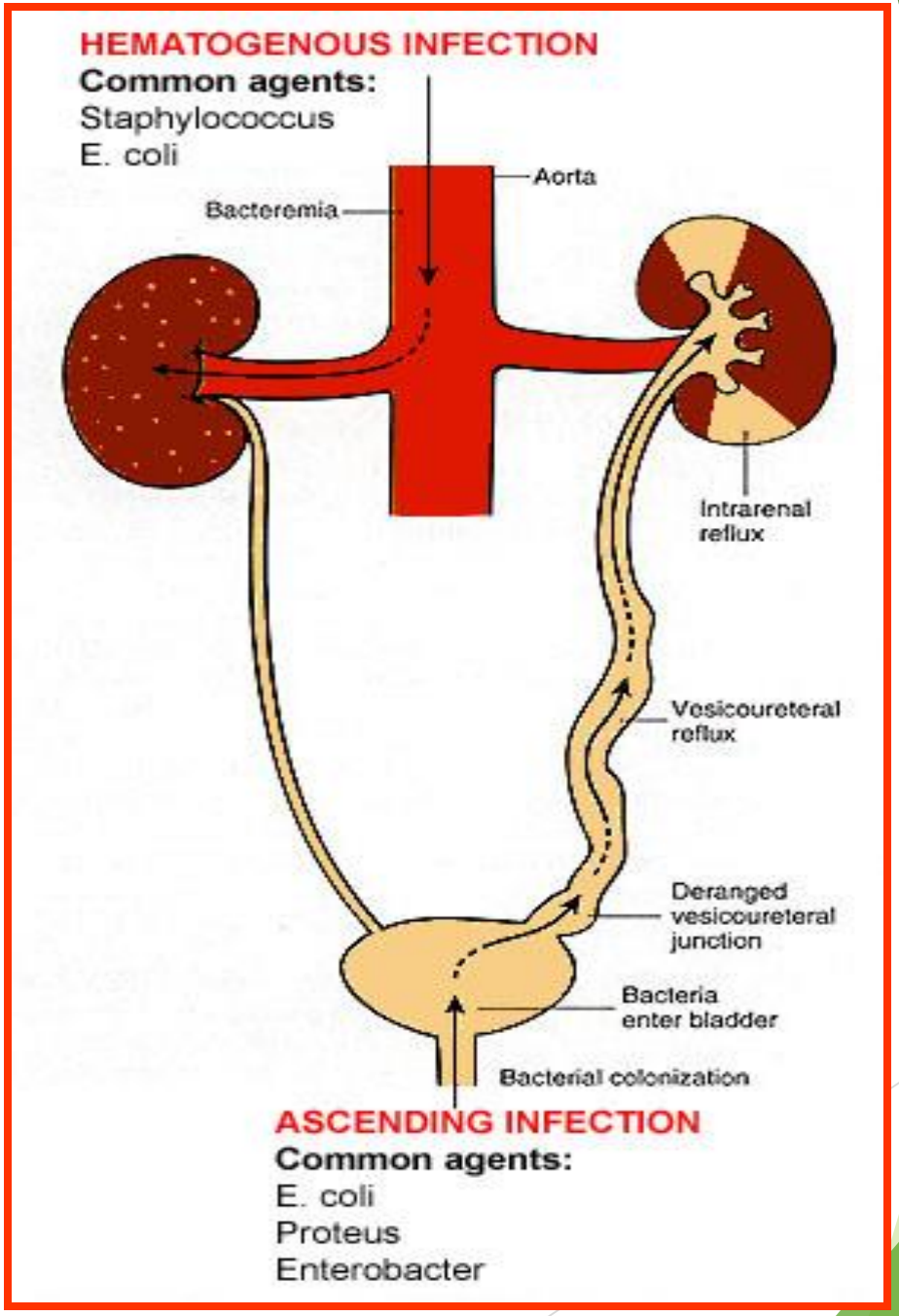
2. Chronic PN, is more complex disorder, bacterial infection plays a dominant role, but other factors (Vesicoureteral reflux, obstruction), are involved also in the pathogenesis.

Urinary Tract Infection Pyelonephritis (PN)

- Is a common suppuritive inflammation of kidney & renal pelvis caused by bacterial infection.
- It is a part of UTI (UTI either lower UTI like cystitis, prostatitis, urethritis) or (Upper Pyelonephritis) OR both.

- **Pathogenesis of pyelonephritis (UTI):**
- Commonest causative organism is E. coli (Other like Proteus, Klebsiella, and Enterobacter).
- **Routes of infection:**
- 1. Hematogenous (by blood stream).
- 2. Ascending infection (from lower urinary tract) ……. (Commonest).

Pathways of Renal Infection



Predisposing factors of UTI:

- 1.Female > male (short urethra, close proximity of urethra to the rectum).
- 2.Congenital abnormality of urinary tract.
- 3.immundeficiency
- 4.Urinary tract Catheterization.
- 5.Urinary tract obstruction (stone, tumors, & benign prostatic hyperplasia).
- 6.Vesicoureteric reflux disease (either congenital or Acquired).
- 7.Pregnancy.
- 8. Diabetes mellitus.
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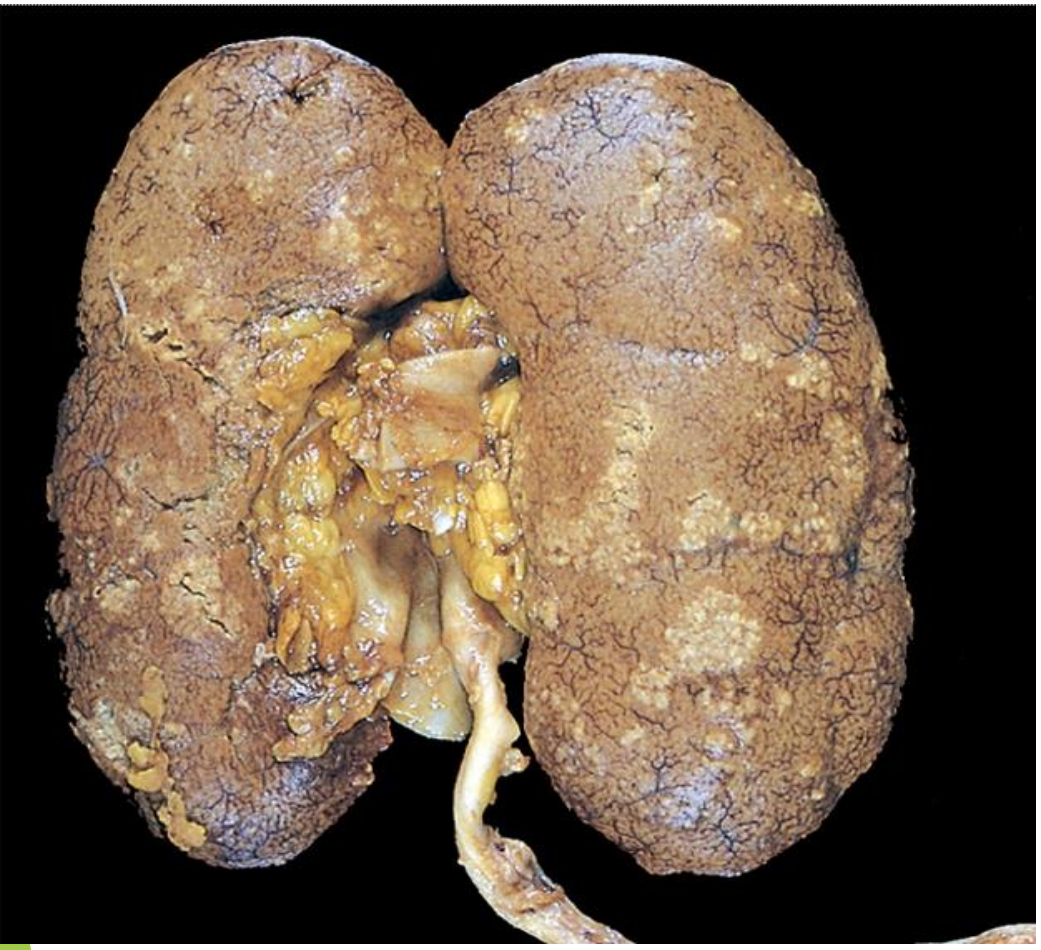
Morphology of acute pyelonephritis:

- **Gross**: Kidney (single or bilateral) may be normal in size or enlarged.
- Discrete, raised abscesses on the renal surface.
- **MIC:**
- The hallmark is patchy interstitial suppurative inflammation(large masses of neutrophils) within the renal parenchyma,
- tubular leukocyte casts and
- tubular necrosis.
- Typically the glomeruli are resistant to the infection.
- If there is superadded obstruction, the exudate fills the renal pelvis, calyces, & ureter (pyonephrosis).

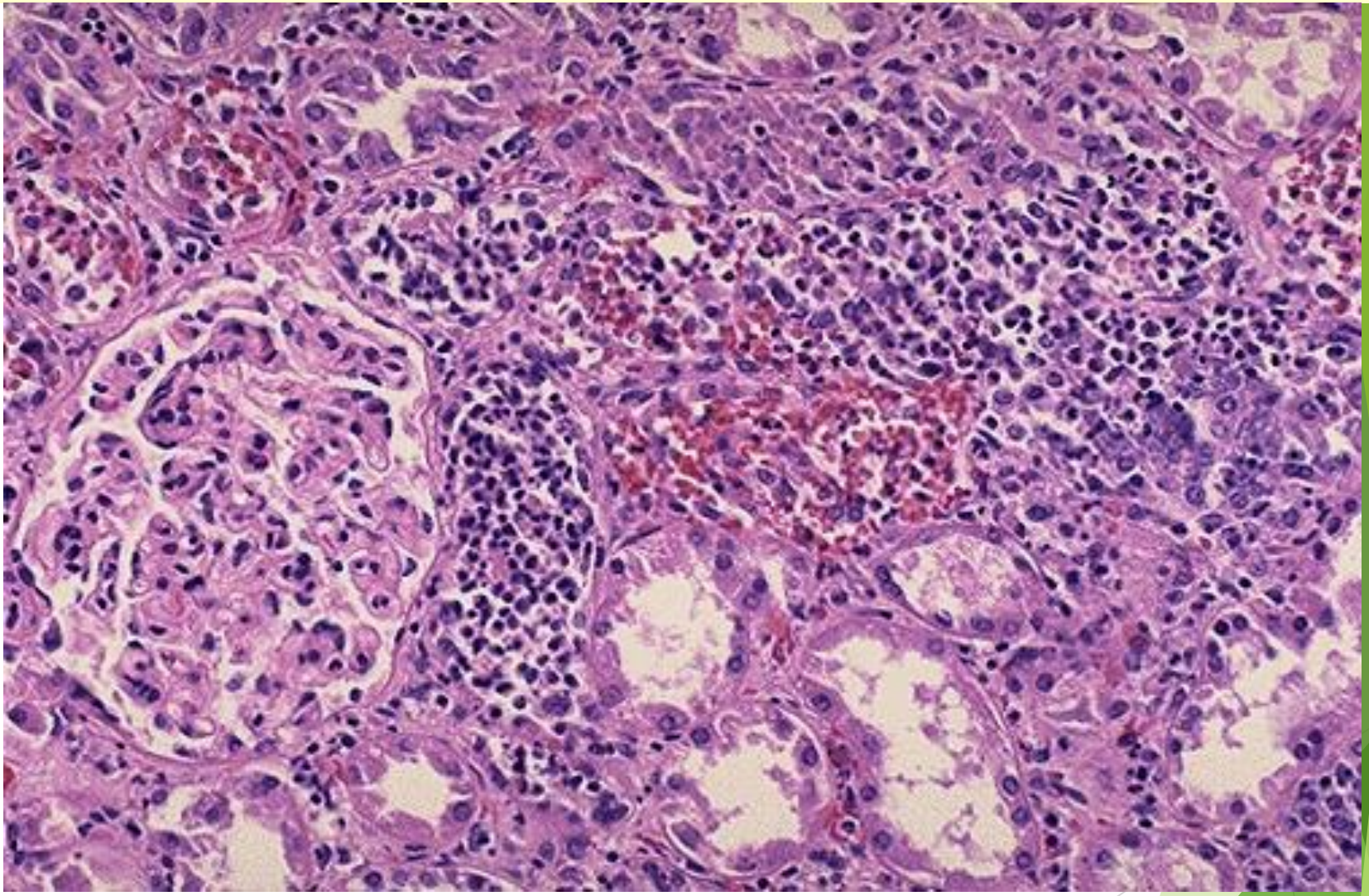
Acute pyelonephritis



Rt. The cortical surface is studded with focal pale abscesses, more numerous in the upper pole and middle region of the kidney; the lower pole is relatively unaffected. Between the abscesses there is dark congestion of the renal surface.

Lt. Cut section showing multiple small yellow abscess mainly in the cortex but also in the medulla. Note the markedly congested parenchyma & pelvic mucosa.

Acute Pyelonephritis



There is intense acute neutrophilic infiltration within tubules and the renal substance.

Complications of Pyelonephritis:

- 1-Necrotizing Papillitis
- This is mainly seen in D.M, important characteristics are sharply defined gray- white to yellow necrosis of the apical two thirds of the pyramids (Coagulative necrosis at the tip of papillae), indicate poor prognosis & end in renal failure.
- 2-Pyonephrosis, when there is total or almost complete obstruction, especially when it is in the upper part of the urinary tract.
- 3-Perinephric abscess.
- 4-Septicemia.
- 5-The end-result is healing of chronic cases by scars formation, almost always associated with deformity of the underlying calyces and pelvis.

Clinical features:

- ▫ Sudden onset of pain at costophrenic angle (renal angle), and systemic evidence of infection, such as fever , chills and malaise.
- There is also dysuria, frequency and urgency.
- GUE (Pyuria, bacteriuria),urine contains pus cells and leukocyte casts and bacteria

- Prognosis:
- • It needs treatment with antibiotics .
- • The disease become chronic if there is predisposing factors & bilateral disease

Chronic Pyelonephritis

- It is characterized by chronic tubulointerstitial inflammation and renal scarring associated with pathologic involvement of the calyces and pelvis.
- It is an important cause of end-stage kidney disease.

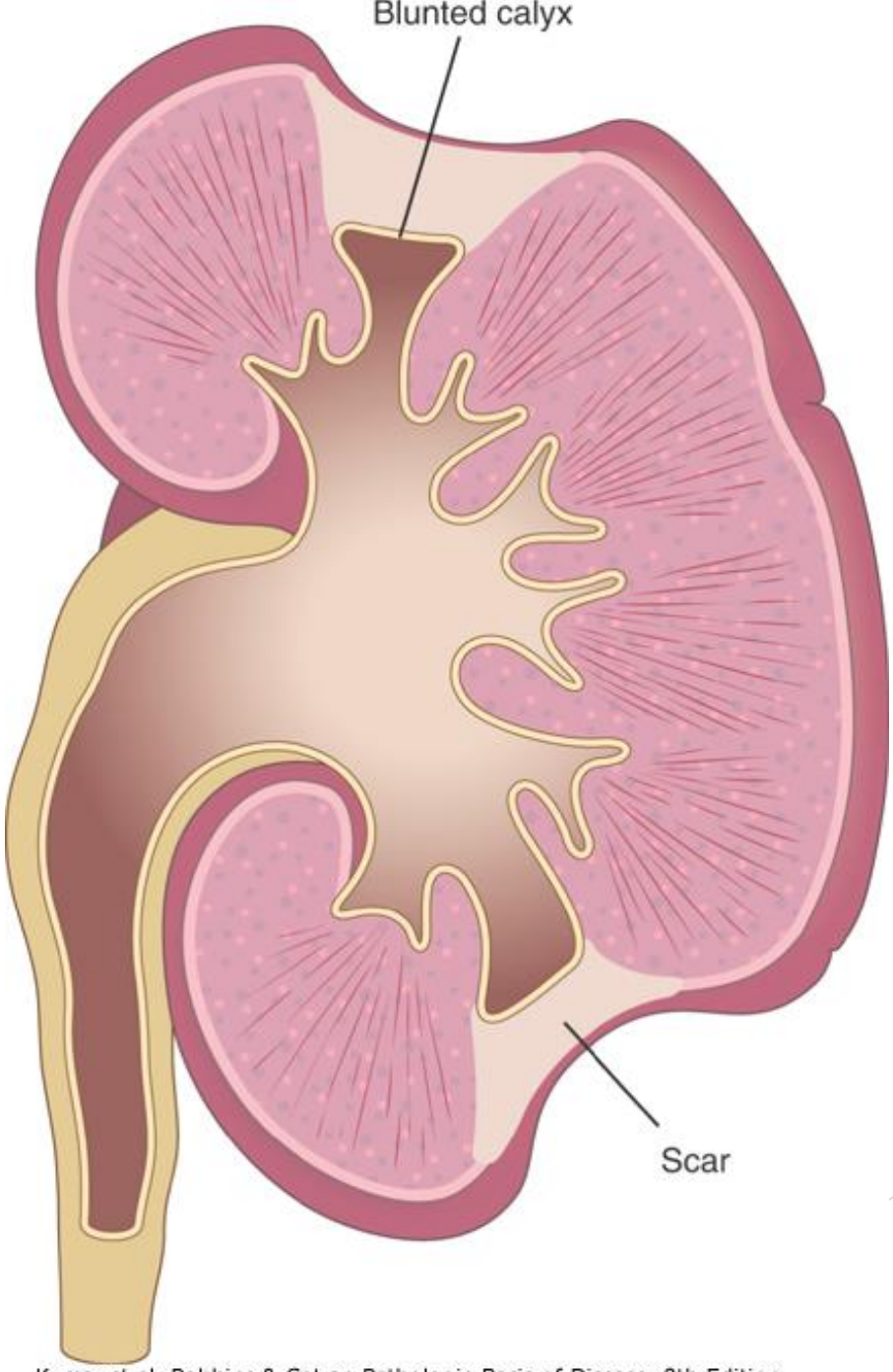
- It can be divided into 2 forms:

1. Reflux nephropathy, which is the more common. It occurs early in childhood.

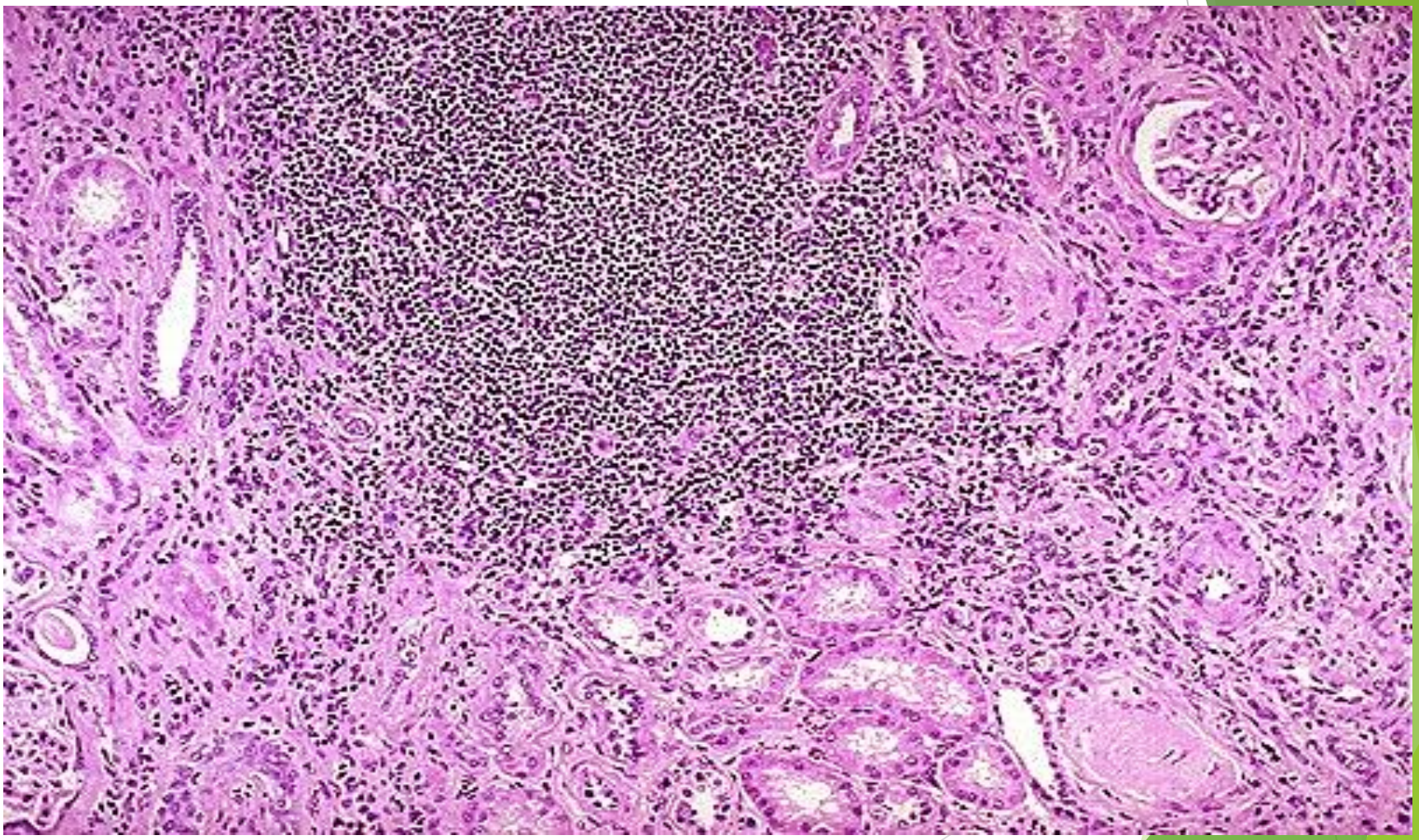
2. Obstructive nephropathy, which could be unilateral or bilateral.

Morphology,

- The characteristic changes are seen grossly. The kidneys are irregularly scarred; if bilateral, the involvement is asymmetric.
- The scars overlie dilated, blunted or deformed calyces, mostly in the upper and lower poles.
- Microscopically, tubules are atrophic and dilated in others. There are varying degrees of chronic interstitial inflammation and fibrosis in the cortex and medulla.



Chronic pyelonephritis



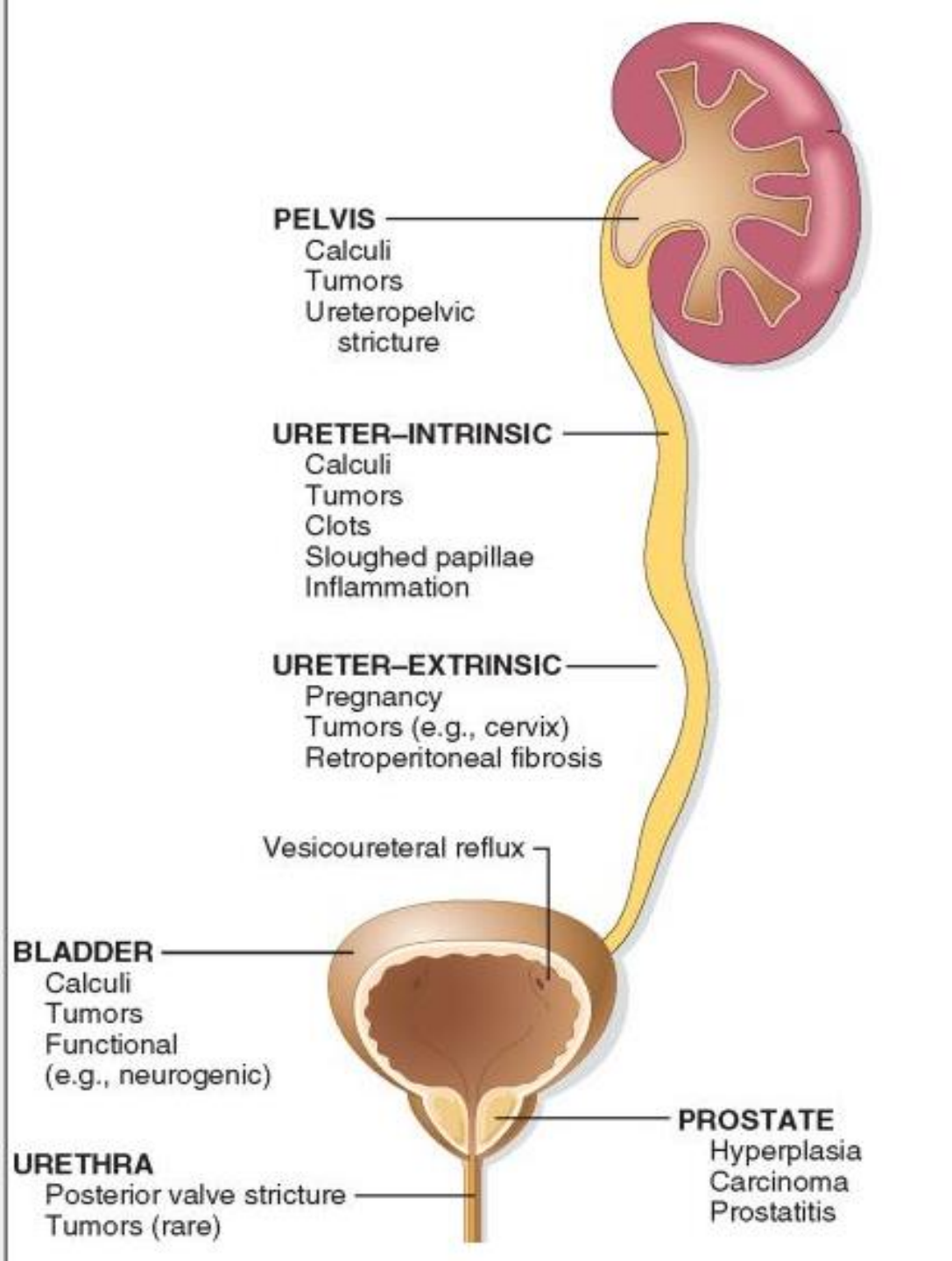
Urinary Tract Obstruction (Obstructive Uropathy)

- Recognition of obstruction is important, because it increases susceptibility to infection and to stone formation, and if unrelieved, it leads to permanent renal atrophy, termed hydronephrosis.
- The obstruction may be sudden or insidious, partial or complete, unilateral or bilateral, and it may occur at any level.
- The most common causes are:

1. Congenital anomalies, posterior urethral valves and urethral strictures.

2. Urinary calculi.
3. Prostatic hyperplasia.
4. Tumors.
5. Inflammation.
6. Pregnancy.
7. Functional disorders, neurogenic bladder.

- **Pathogenesis,** even with complete obstruction, glomerular filtration persists for sometimes. This continued filtration leads to pelvicalyceal dilation, which leads in turn to renal atrophy and hydronephrosis


PELVIS
Calculi
Tumors
Ureteropelvic stricture
URETER–INTRINSIC
Calculi
Tumors
Clots
Sloughed papillae
Inflammation
URETER–EXTRINSIC
Pregnancy
Tumors (e.g., cervix)
Retroperitoneal fibrosis
Vesicoureteral reflux
BLADDER
Calculi
Tumors
Functional (e.g., neurogenic)
PROSTATE
Hyperplasia
Carcinoma
Prostatitis
URETHRA
Posterior valve stricture
Tumors (rare)

Morphology,

- When the obstruction is sudden and complete, there is mild hydronephrosis, but if the obstruction is subtotal or intermittent, there is more severe hydronephrosis.
- Depending on the level of urinary block, the ureter and the bladder may be affected too.
- In advanced cases, the kidney may become transformed into a thin-walled cystic structure .

Hydronephrosis:

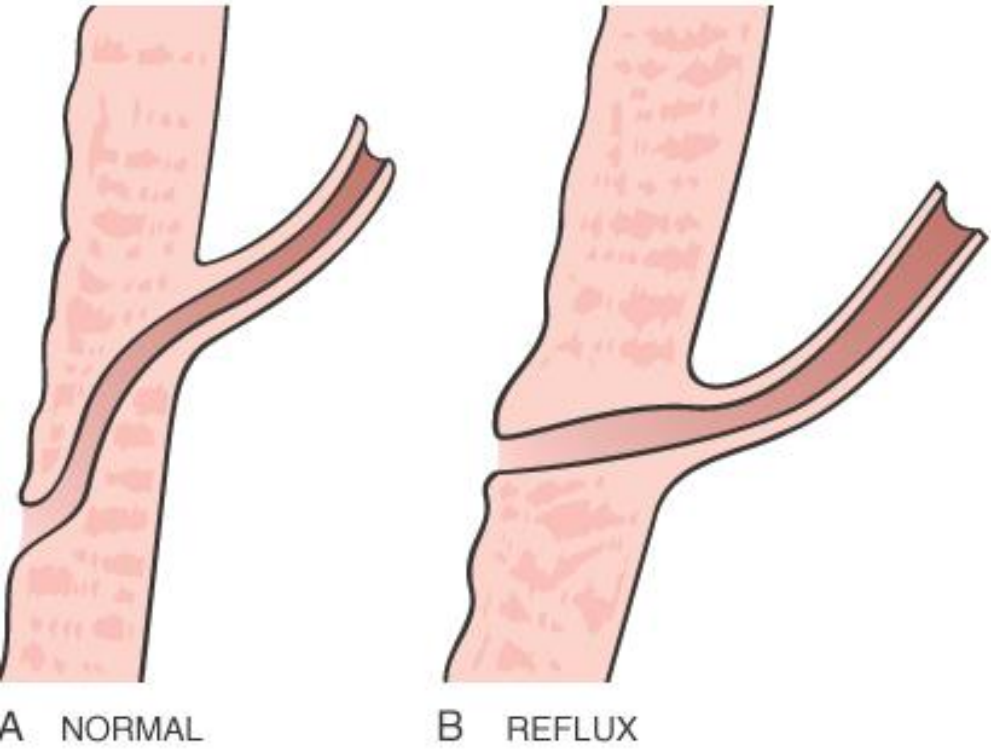
- Dilatation of renal pelvis and calyces associated with progressive atrophy of the renal parenchyma due to obstruction of urine out flow.

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

Chronic Pyelonephritis & Reflux Nephropathy:

- • More common form characterized by recurrent pyelonephritis associated with congenital Vesicoureteric reflux.
- • Can be uni or bilateral diseases.
- • Predominantly interstitial inflammation & scarring of the renal parenchyma.
- • Associated with grossly visible scarring & deformity of pelvicalceal system

Vesicoureteral reflux



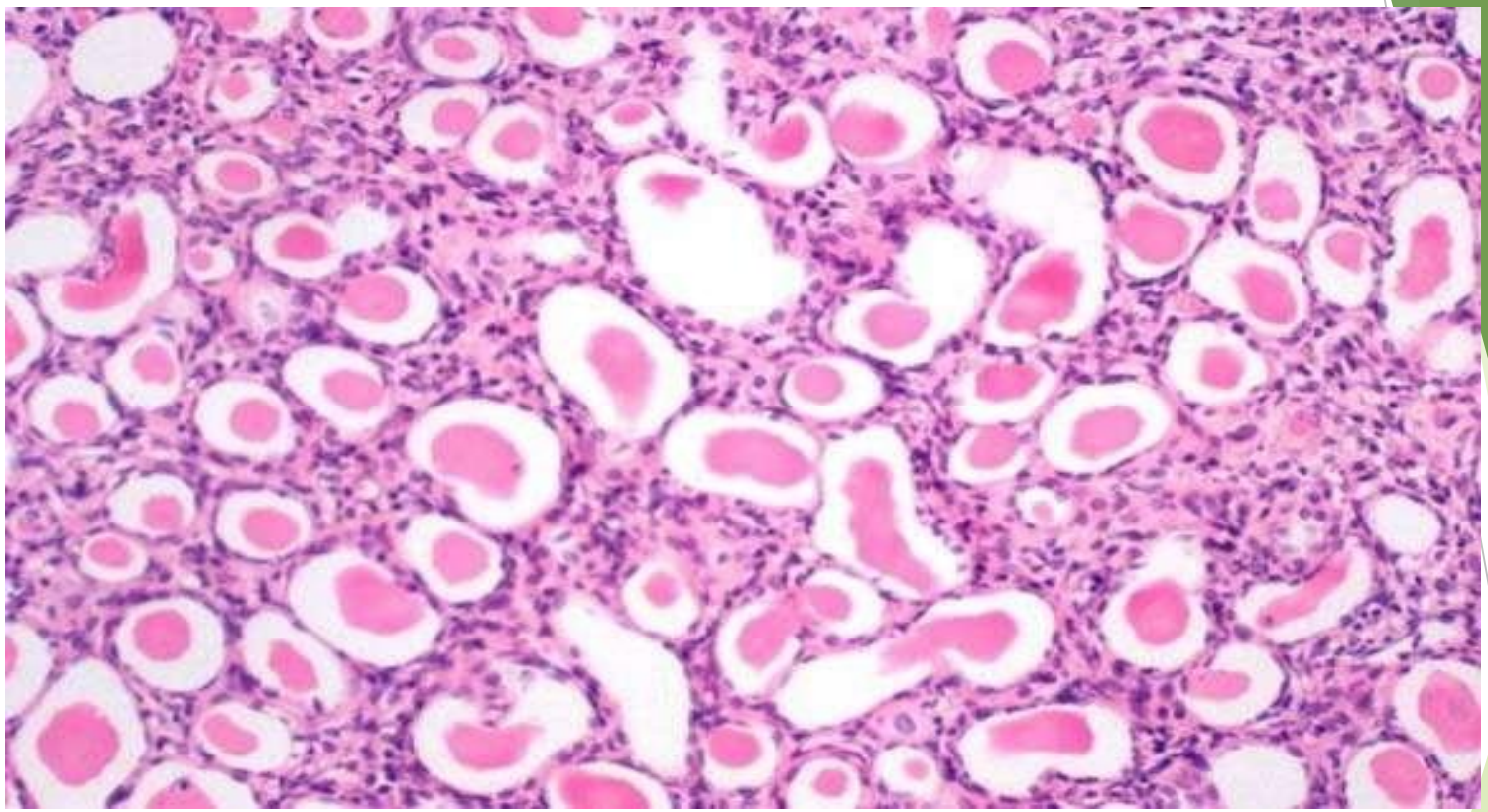
The vesicoureteral junction. In normal individuals (A), the intravesical portion of the ureter is oblique, such that the ureter is closed by muscle contraction during micturition. The most common cause of reflux is congenital complete or partial absence of the intravesical ureter (B).

Vesicoureteral reflux demonstrated by a voiding cystourethrogram. Dye injected into the bladder refluxes into both dilated ureters, filling the pelvis and calyces.

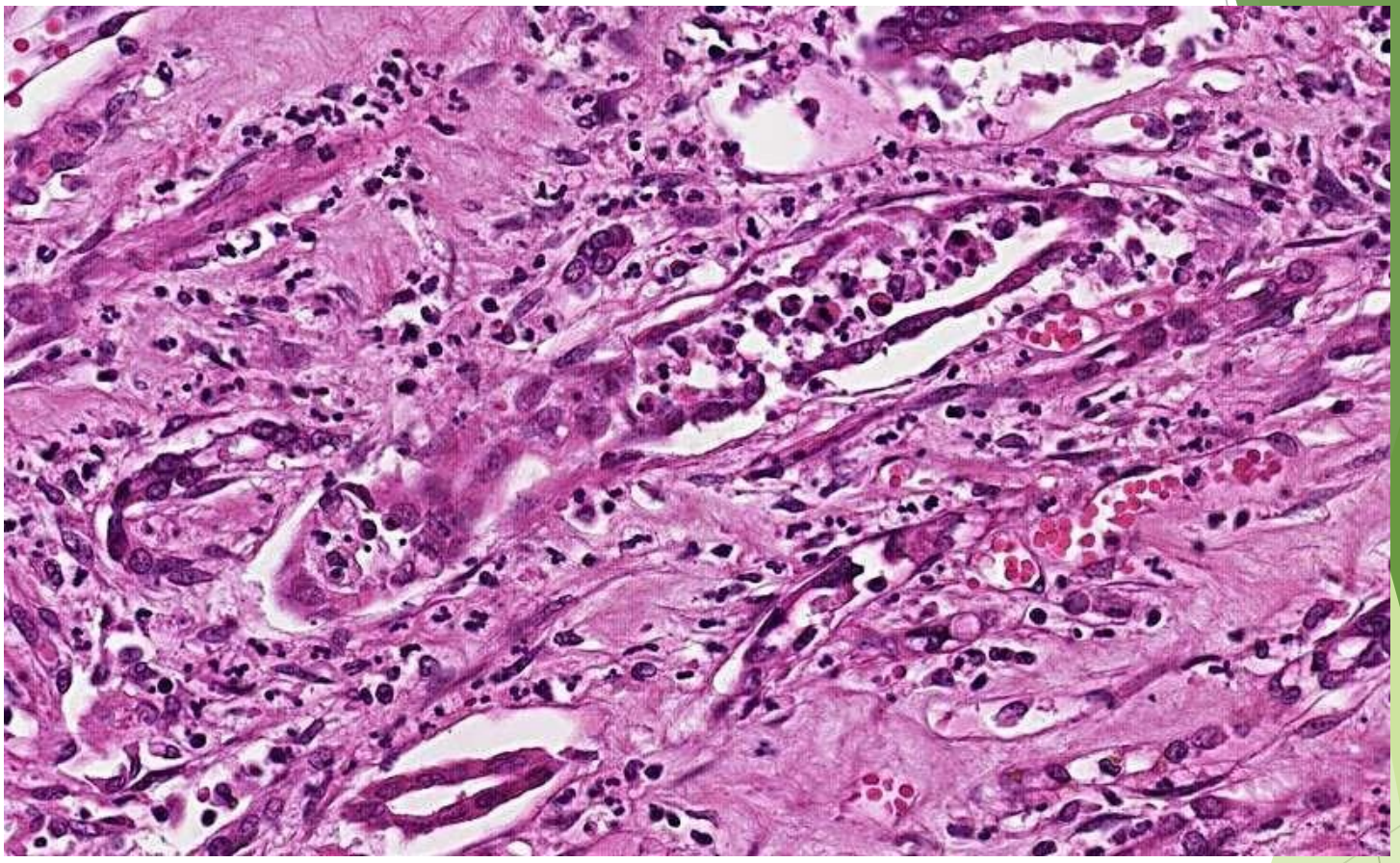
- Morphology:
- Gross:
- Unequal contracted kidneys (sometime only one kidney is involved).
- The hallmark of Pyelonephritis is scarring involving the pelvis or calyces or both leading to blunting of papillary blunting & marked calyceal deformity.

CHRONIC PYELONEPHRITIS

- Mic:
- ▫ Interstitial fibrosis (uneven).
- ▫ Inflammatory infiltrate (lymphocytes, plasma cells, & occasional Nutrophils).
- ▫ Dilated or Contracted of tubules, with atrophy of lining epithelium.
- ▫ Many of dilated tubules contain pink to blue, glassy appearing PAS Positive casts known as Colloid Casts that suggest appearance of thyroid tissue **(Thyroidization of renal tubules),**
- ▫



CHRONIC PYELONEPHRITIS



CHRONIC PYELONEPHRITIS

- Hyaline or hyperplastic arteriolosclerosis due to frequently associated Hypertension.
- ▫ Glomeruli are usually spared, sometime there is Focal glomeruloscleroais.

- Clinical Features:
- ▫ Gradual onset of renal insufficiency.
- ▫ Hypertension
- ▫ Asymmetrical contracted kidneys.

Urolithiasis(urinary stones):

- Is a stone formation at any level in the urinary collecting system. Most often arise in the kidney.
- The peak age at onset is 20-30 years. Male > female
- Some have familial tendency.

Types of renal stones:

- according to chemical composition
- 1. Calcium oxalate or Calcium oxalate mixed with Calcium phosphate (75%).
- 2. Magnesium ammonium phosphate (15%).
- 3. Uric acid & cystine stones (10%).
- Note: in all types there is an organic matrix of mucoprotein form about 2.5% of weight of stones.
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Causes of renal stones according to chemical types:

Causes of renal stones according to chemical types:

- 1. Calcium oxalate or Calcium phosphate
- Idiopathic hypercalciuria (50%).....(abnormal absorption of Ca+2 & abnormal reabsorption of Ca+2 by the kidney).
- Hypercalcemia & Hypercalciuria (as in hyperparathyroidism, vitamin D intoxication, or sarcoidosis).
- Hyperoxaluria (increased Ca+2 reabsorption).
- Hyperuricosuria (urate act as favored nidus for calcium deposition).
- Unknown metabolic abnormality.
- 2. Magnesium ammonium phosphate (struvite).
- Renal infection (mostly Proteus {urea splitting bacteria}, Staphylococci), bacteria act as nidi for stones formation.

3. Uric acid stones

- Hyperuricemia.
- Hyperuricosuria
- Idiopathic

UROLITHIASIS

- **CALCIUM (OXALATE or PHOSPHATE) 75%** → **CA↑↑↑**
- **MAGNESIUM AMMONIUM PHOSPHATE 15%** → **Bact.**
- **URIC ACID 10%** → **U.A. ↑↑↑**

Morphology of renal stones:

- Unilateral stones in about 80% of patients
- Common sites of stone formation are renal pelvis, calyces, & bladder.
- Some magnesium ammonium phosphate stone result in formation of Staghorn stone (branching stone, fill the renal pelvis & calyces).

- Clinical features:
- Symptomless like in staghorn stone.
- Renal colic & Uretric colic.
- Gross hematuria.

Renal stones

Upper left: Oxalate stone

Upper Rt. Uric acid stone

Lower Rt. A staghorn phosphate

Clinical course

- Stones are of importance when they
  - obstruct urinary flow
  - produce infection,
  - ulceration
  - bleeding.

- Complications are obstructive uropathy, recurrent UTI.
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- Hydronephrosis:
- Refer to dilatation of the renal pelvis & calyces, with accompanying atrophy of the parenchyma, caused by obstruction to the outflow of urine.
- It may occur at any level of urinary system from the urethra to the renal pelvis.

- Causes of Hydronephrosis:
- 1. Congenital:
- Atresia of the urethra.
- Aberrant renal artery compressing the ureter.
- Renal torsion.

- 2. Acquired:
- Foreign bodies: stones, necrotic papillae.
- Tumors: BPH, Carcinoma of prostate, bladder tumors (papilloma & carcinoma), Carcinoma of cervix.
- Inflammation: Prostatitis, Urethritis, Ureteritis.
- Nurogenic: Spinal cord damage with paralysis of the bladder.
- Normal pregnancy: mild & reversible.

- Morphology of Hydronephrosis:
- ▫ Bilateral hydronephrosis lead to renal failure.
- ▫ Unilateral hydronephrosis display wide range of morphological changes, which vary with the degree & speed of obstruction.
- I. Subtotal or intermittent obstruction,
- Kidney may be massively enlarged (20cm in length), & entirely distended pelvicalceal system.
- Compressed & atrophied renal parenchyma.
- Obliteration of papillae & flattening of pyramids.
- II. When obstruction is sudden & complete,
- 1. GFR is reduced while dilatation is still slight.
- 2. Unilateral or Bilateral hydroureter.

- Mic:
- ▫ Tubular dilation follows by tubular atrophy & fibrous replacement of tubular epithelium with relatively sparing of the glomeruli.
- ▫ Eventually in severe cases the glomeruli become atrophic & disappear, converting the entire kidney into a thin shell of fibrous tissue.
- Clinical features:
- In case of bilateral complete obstruction:
- 1. Anuria.
- 2. Bladder distention (obstruction below the level of bladder).
- 3. Polyuria due to defect in tubular concentrating mechanisms & incomplete obstruction.
- In case of unilateral hydronephrosis:
- Remain silent & diagnosed on routine examination as enlarged kidney.