Tubulointerstitial disease
Part 1

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Tubulointerstitial **diseases**

Two major processes are included

- Acute tubular **injury** (ATI)-

  Causes: Ischemia and toxins
  Result tubular injury

  Clinical manifestation : Acute renal failure

- Tubulointerstitial **nephritis**:

  Inflammatory injuries of the tubules and interstitium
  Could be 1ry or 2ry.

- Most forms of tubular injury involve the interstitium as well.
- Therefore, diseases affecting these two components are discussed together

Tubulointerstitial nephritis

Objectives

- List the causes of tubulointerstitial nephritis.
- Describe the marosocpy , microscopy and complications of acute pyelonephritis.
- Describe the macroscopy and microscopy of chronic pyelonephritis.
- Describe the pathology of tubulointerstitial nephritis due to drugs and toxins.

- List the causes for obstruction to the urinary tract.
- Describe the pathology of hydronephrosis.

Tubulointerstitial nephritis

Group of renal diseases with histological and functional alterations involving the **tubules and the interstitium**.

- In this group the primary involvement is the interstitium and the tubules
- Tubular functions affected.
- Glomerular changes are absent/minimal

  (except at the advanced stages)

- Secondary involvement of the tubules and interstitium may be seen with glomerular and other disorders.

  (2ry Tubulointerstitial nephritis)

Tubulo Interstitial nephritis

	Acute	Chronic
Inflammation	Neutrophils Eosinophils	Mononuclear cells
Interstitium	Oedema	Fibrosis
Tubules	Focal tubular necrosis	Tubular atrophy

Causes of tubulointerstitial nephritis

- Infections
- Toxins
- Metabolic disease
- Neoplasms – myeloma nephropathy
- Immunological reactions
- Vascular disease
- Others-radiation,idiopathic

(Refer robbins pathology text book for the detailed list)

Infection

- Lower UTI – Mostly asymptomatic
  Limited to the bladder

- Risk of spread to the kidney and the collecting system

UTI and pyelonephritis

Organisms

E.coli,Proteus,Klebsiella,Enterobacter

Streptococcus faecalis

Immunosupressed – Viruses

Routes –

- Ascending infection – most common
- Haematogenous –in septicaemia/endocarditis

Pathogenesis

- Colonization of the distal urethra – bacterial factors contribute

- Entry to the bladder

- UT obstruction and stasis of urine

- Vesicoureteral reflux

- Intrarenal reflux – Upper and lower poles of the kidney

Acute pyelonephritis

Suppurative inflammation of the kidney

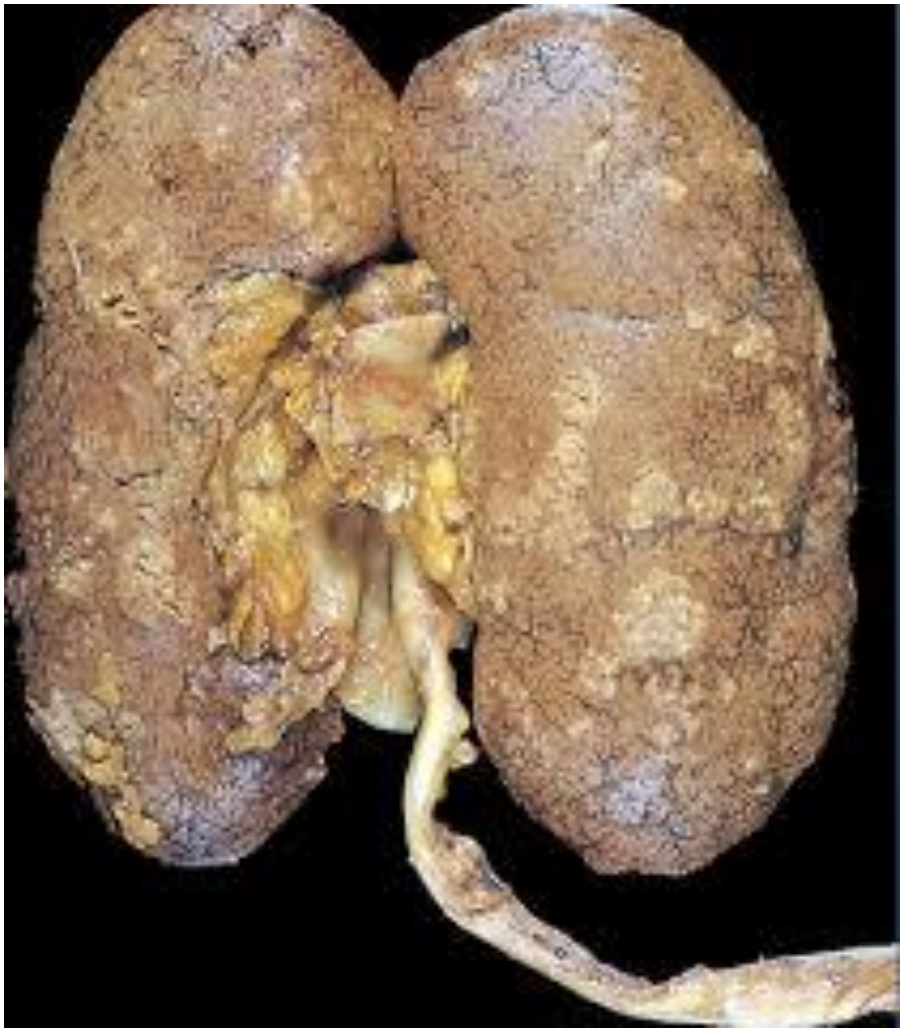
- Bacterial
- Haematogenous/Ascending infection

Acute pyelonephritis

Macroscopy

- Enlarged kidneys
- Bulging cut surface
- Focal abscesses , wedge shaped large abscesses
- Haphazardly distributed
- Yellow streaks in the papillae
- Congested pelvis and calyceal mucosa
- With reflux –upper/lower poles more commonly affected

Acute pyelonephritis - macroscopy

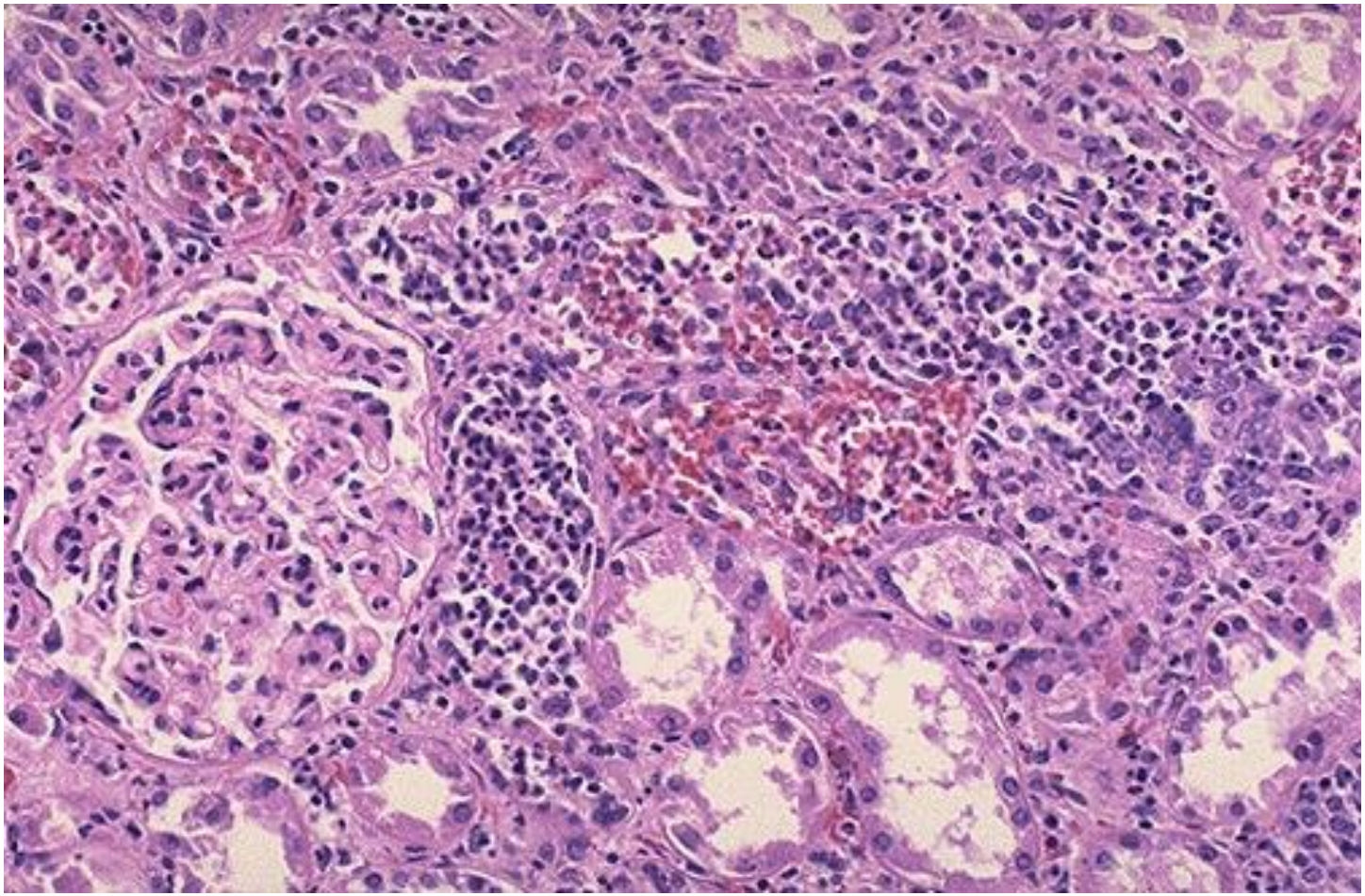


Abscess formation on the surface of the kidney

Acute pyelonephritis - microscopy

- Tubules infiltrate by PMN (Neutrophilic tubulitis)
- Destruction of the tubules(Tubular necrosis)
- Interstitial neutrophils (Interstitial inflammation)
- Large foci of suppurative Inflammation extends along collecting ducts.
- Glomeruli unaffected or affected with abscess formation.

Acute pyelonephritis - microscopy



Neutrophils within the tubules and in the interstitium

Complications of acute pyelonephritis

A) Pyonephrosis

- With total/complete obstruction
- Pus fills the renal pelvis and the calyces

B) Perinephric abscess

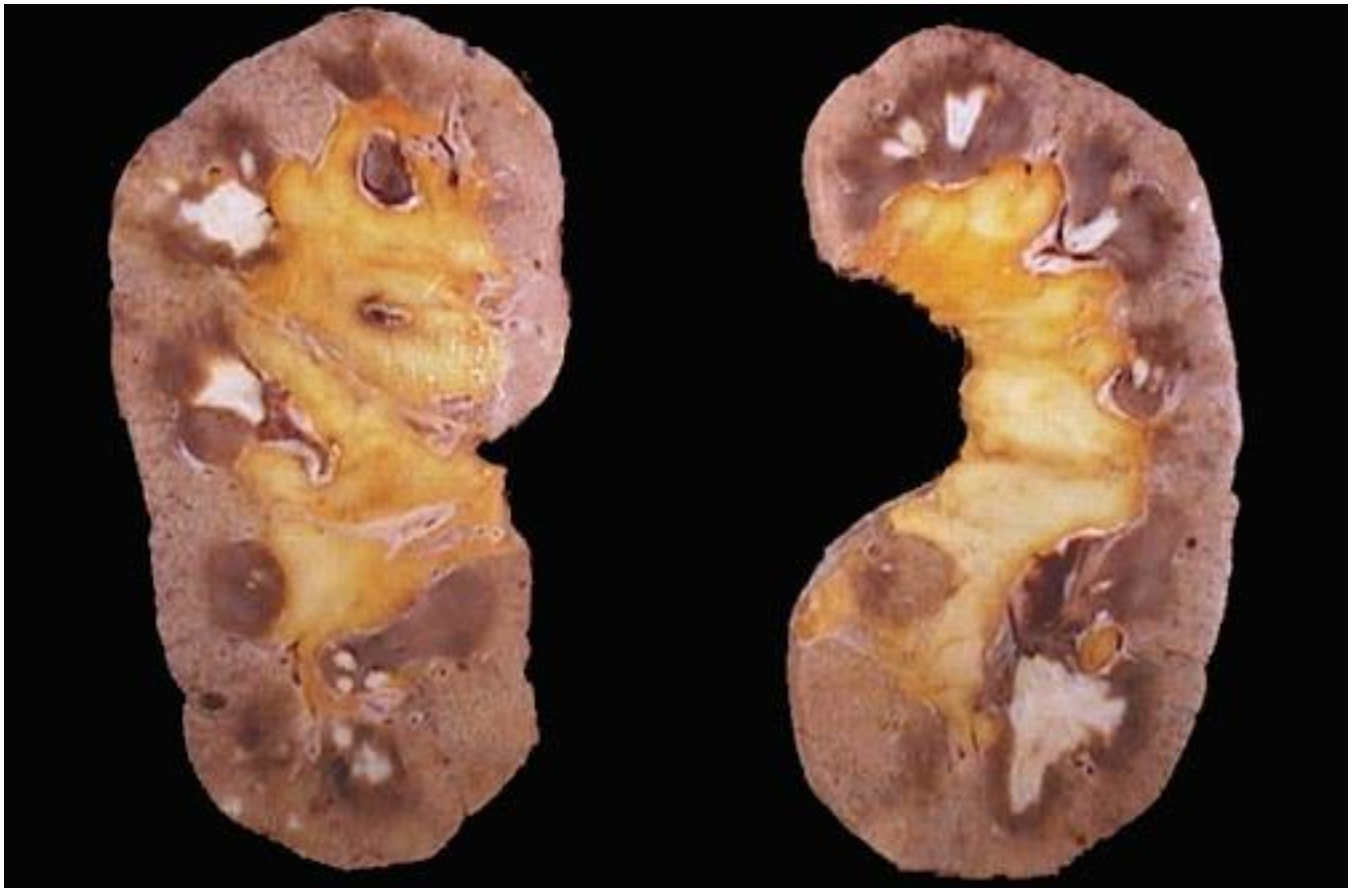
Complications of acute pyelonephritis Cont…

C) Papillary necrosis

- In diabetics, sickle cell disease /with UT obstruction
- Tip (distal 2/3) of the papillae necrose (grey- white)
- One or all papillae may involve.
- Undergo coagulative necrosis.
- Sharply demarcated from the rest of the tissue

Assignment: What are the other causes for renal papillary necrosis???

Papillary necrosis



Chronic pyelonephritis

A disorder in which **chronic** tubulointerstitial inflammation and **scarring involve** the cayces and pelvis.

Key features

- Tubulointerstitial inflammation

  (Produced by many diseases)

- Pathological involvement of the calyces and pelvis

  (only in Chronic pyelonephritis and analgesic nephropathy)

Chronic pyelonephritis

Can be divided into 2 forms

A)Reflux nephropathy

- Common
- In children with congenital vesico-ureteral reflux , intrarenal reflux and associated UTI

Chronic pyelonephritis cont.

B) Chronic obstructive pyelonephritis

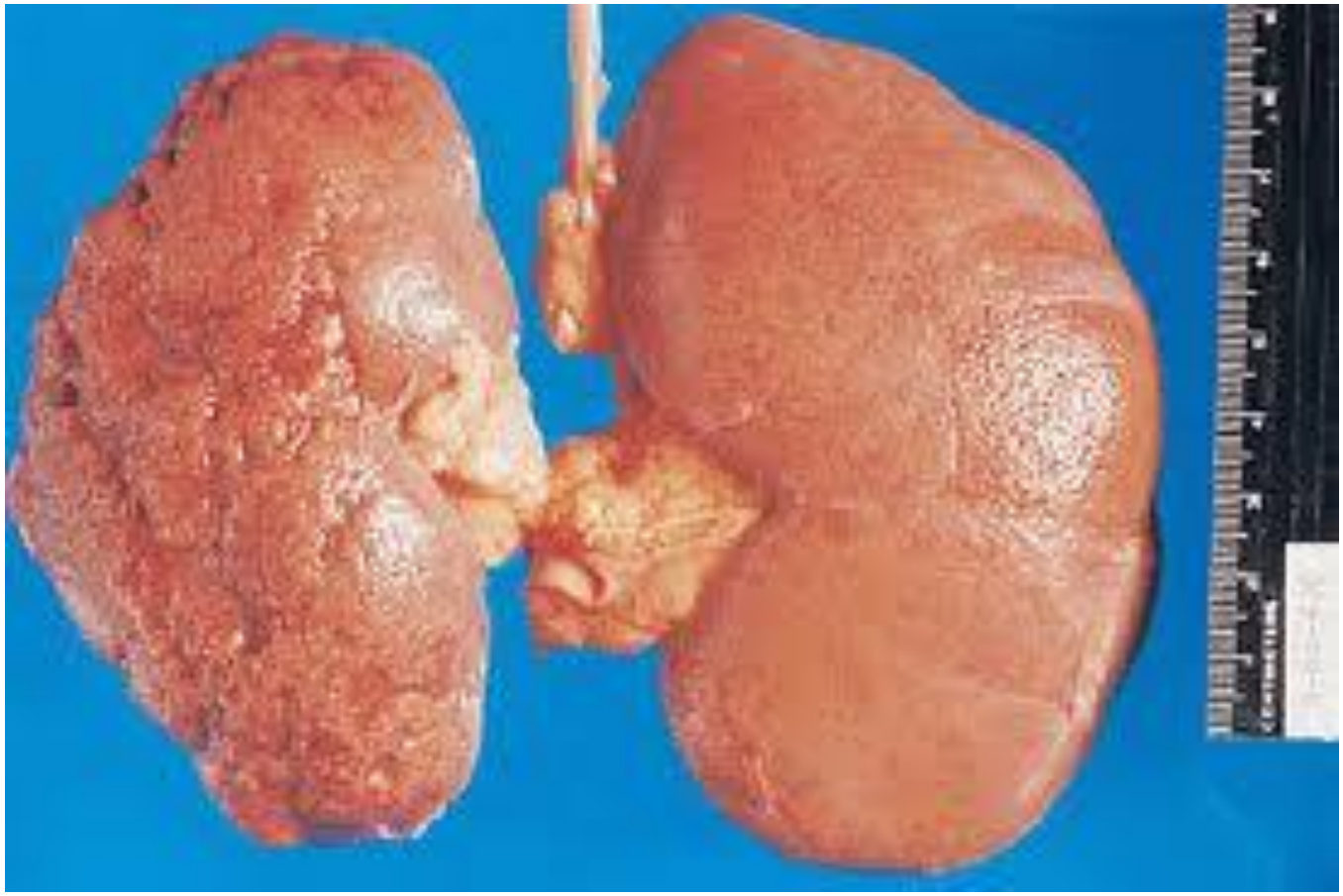
- Obstruction predispose to infection
- Recurrent renal inflammation and scarring
- Obstruction damage the parenchyma
- Bilateral/unilateral

Chronic pyelonephritis

Macroscopy –

- Irregularly scarred (Coarse, discrete, cortocomedullary scars)
- More in the upper and lower poles
- Bilateral – asymmetrical involvement
- Coarse , discrete, corticomedullary scars overlying dilated blunted /deformed calyces
- Flattened papillae

Chronic pyelonephritis -macroscopy



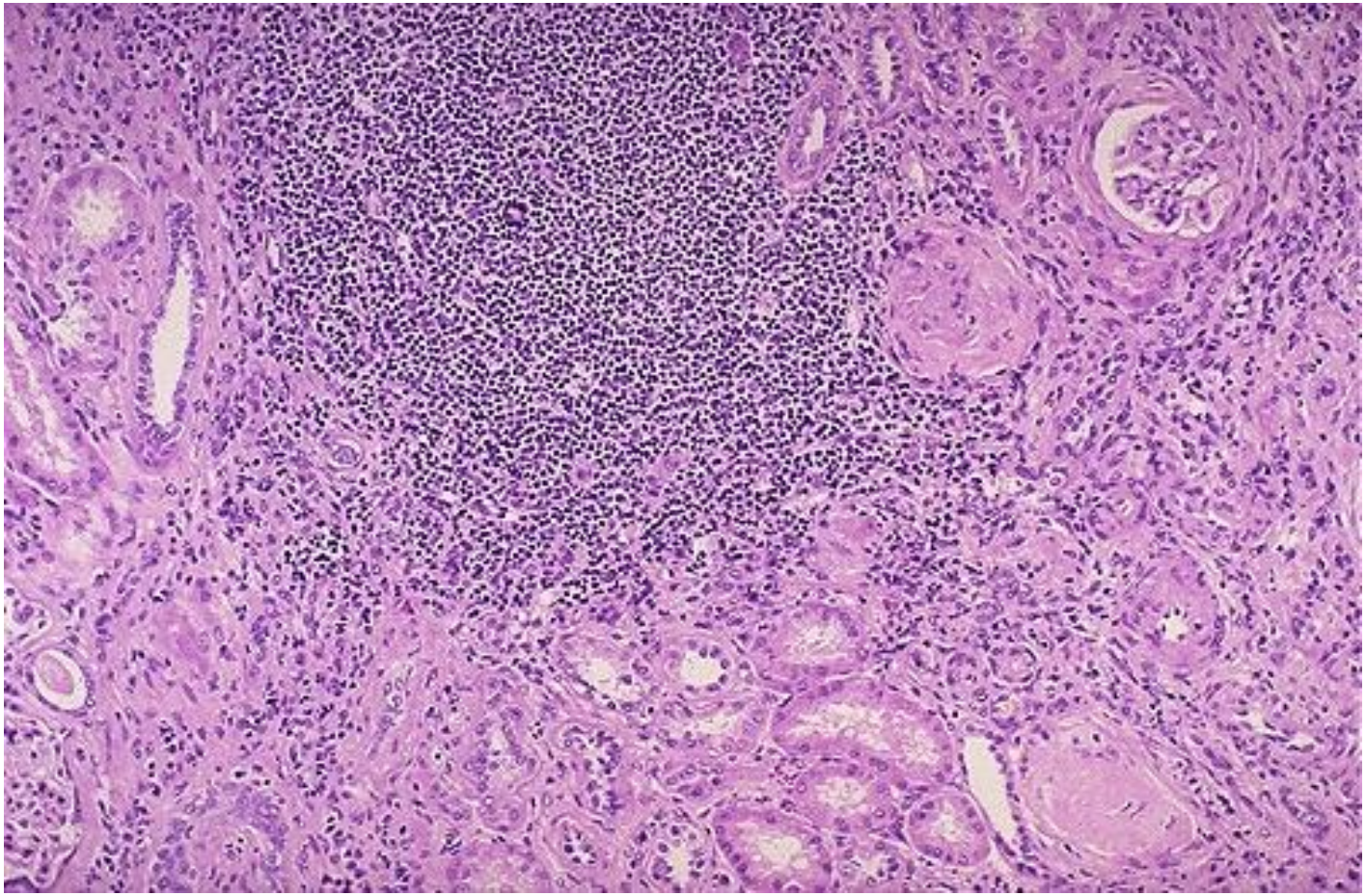
Irregularly scarred left kidney

Chronic pyelonephritis cont

Microscopy-

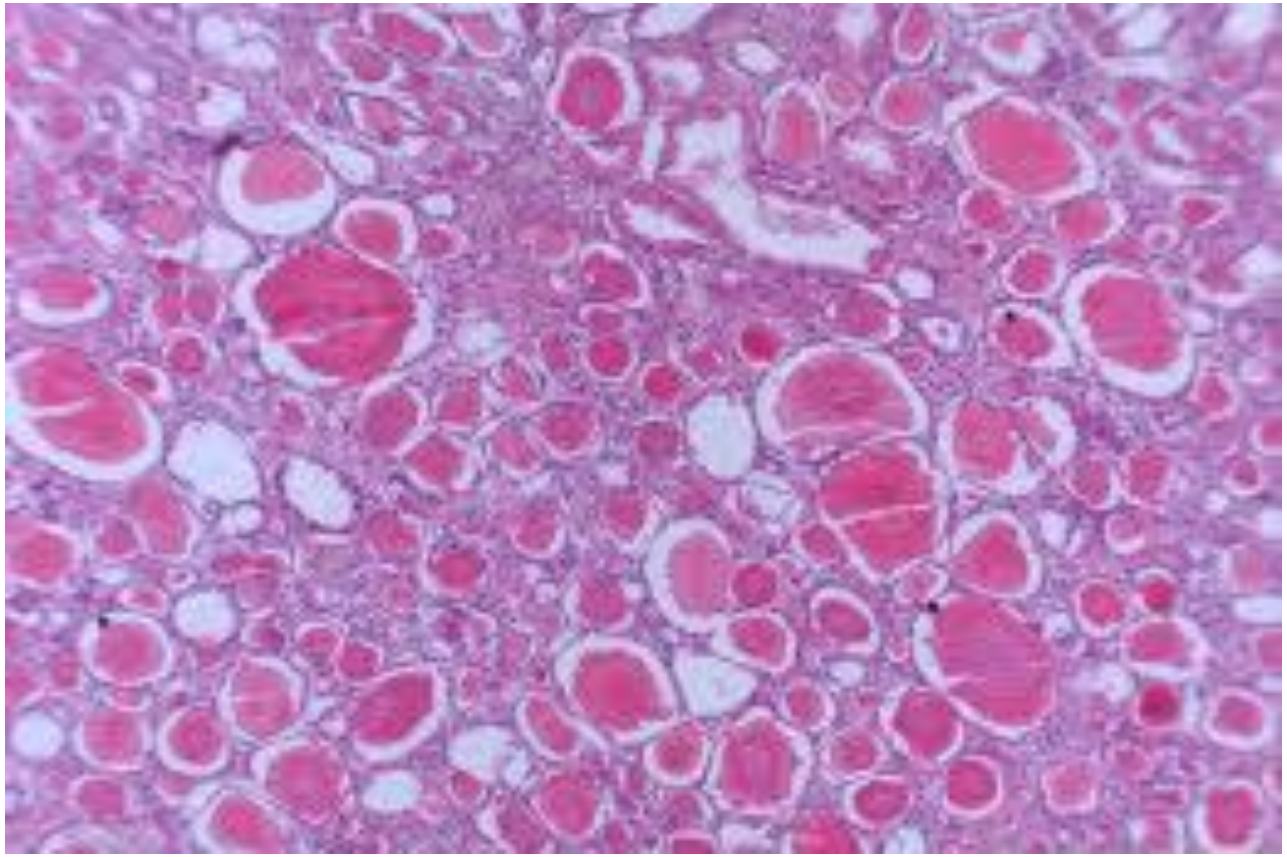
- Predominant changes – Tubules and interstitium
- Tubules – Atrophy and dilatation
- Dilated ones lined by flattened cells and filled with colloid casts – Thyroidization
- Chronic interstitial inflammation
- Fibrosis

Chronic pyelonephritis - microscopy



Heavy inflammation of the interstitium
Periglomerular fibrosis

Chronic pyelonephritis - microscopy



Renal tubules filled with colloid material - Thyroidization

Chronic pyelonephritis cont.

- Active inflammation : PMN and pus casts
- Arcuate and interlobular vessels in scarred areas : Obliterative intimal sclerosis
- With hypertension : Hyaline arteriolosclerosis
- Around calyceal epithelium: Chronic inflammation and fibrosis
- Glomeruli : Periglomerular fibrosis
  Ischemic fibrous obliteration

Tuberculosis of the kidney

Involved by-

A) Generalized miliary spread from an active lesion

B) Solitary lesion – reactivation of a dormant lesion

Tuberculosis- macroscopy

Macroscopy –

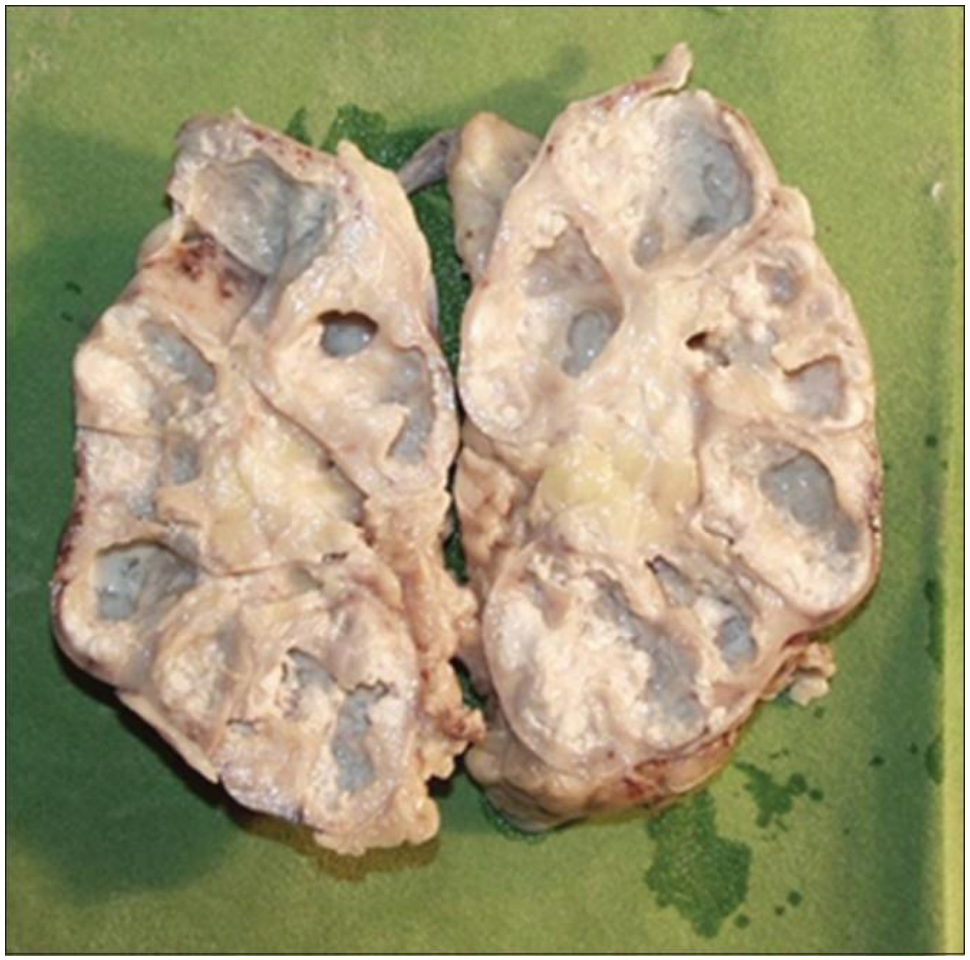
- Miliary form – Studded with pinpoint nodules
- Ulcerative/caseous form-

  Destruction of the renal parenchyma

  Caseous material

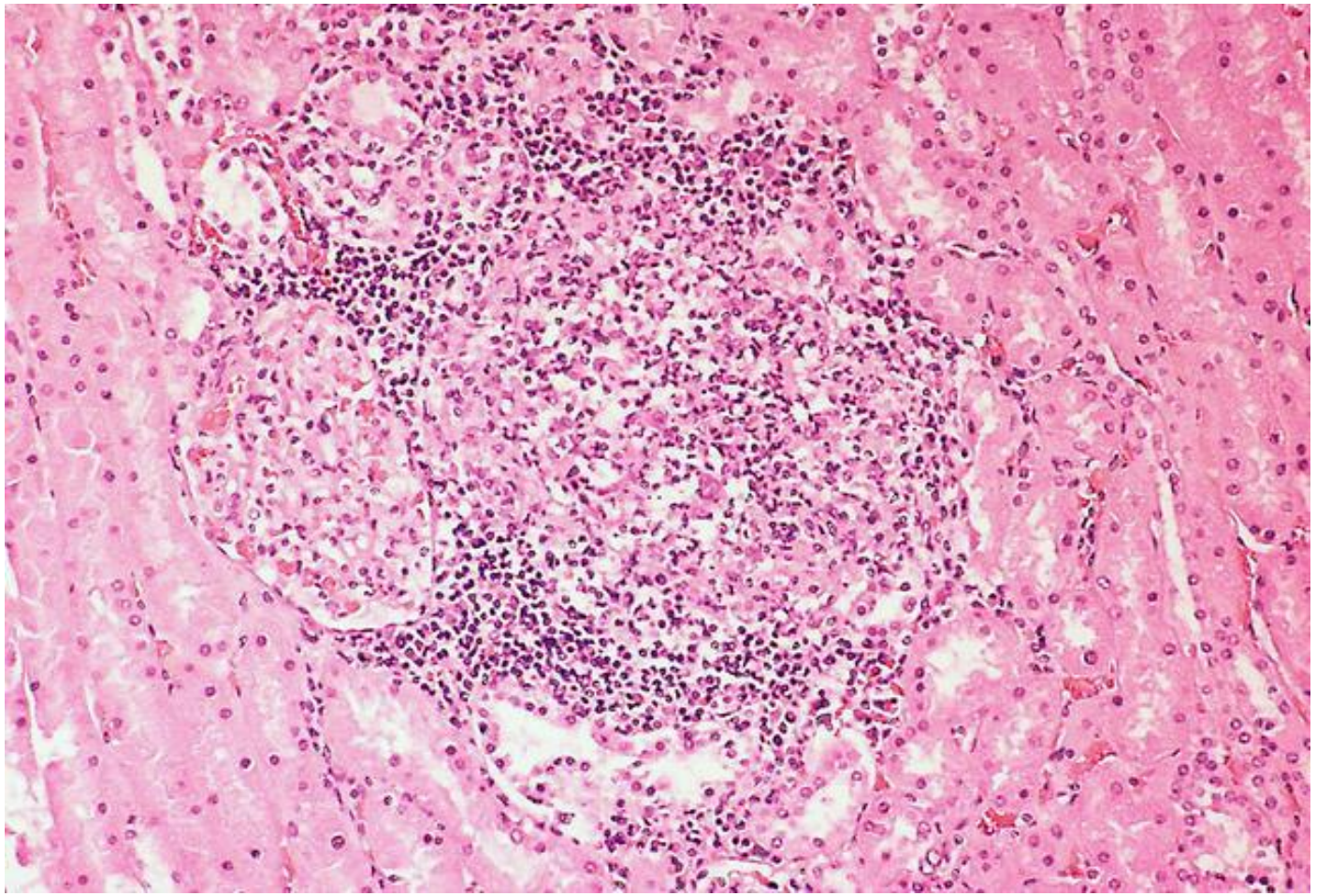
  Surface may show small tubercles

Renal tuberculosis - macroscopy



Breaking-down caseous material extensively involving the kidney

Renal tuberculosis -microscopy



Miliary tuberculosis

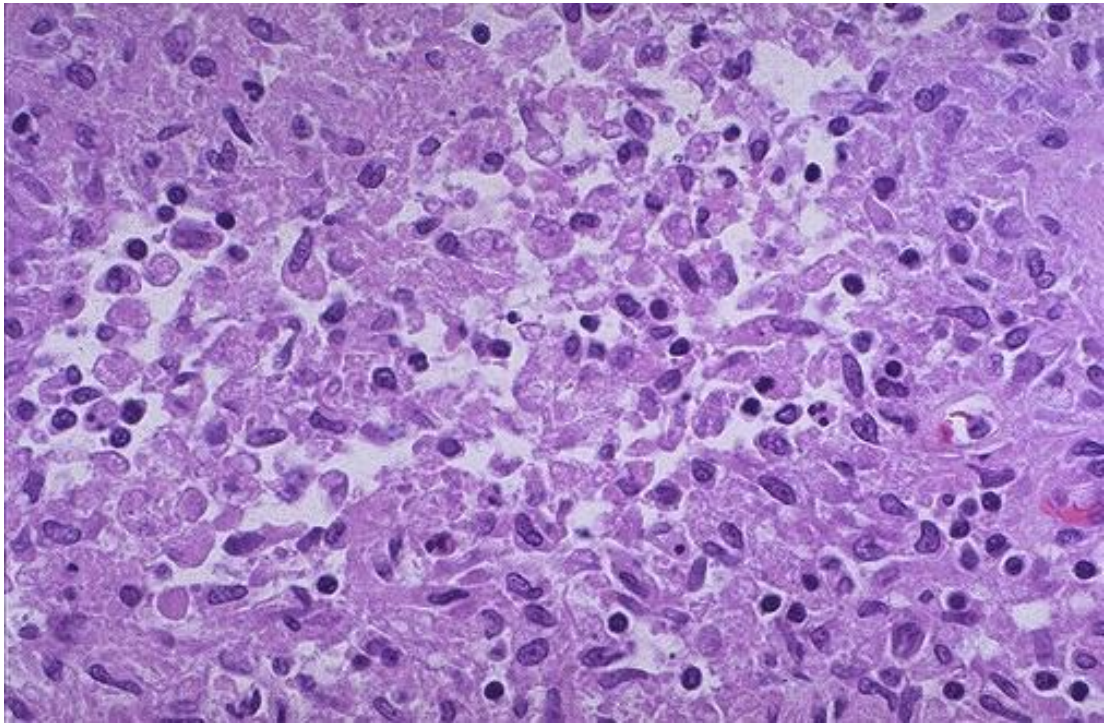
Xanthogranulomatous pyelonephritis

- Rare
- Associated with proteus infection
- Macro- yellowish nodules
- Microscopy - Foamy macrophages ,plasma cells and lymphocytes, PMN, occ- MNGC

Xanthogranulomatous pyelonephritis

Macroscopy

Microscopy



Drugs and toxin

Drugs and toxins induced TIN is second common cause of AKI.

Can injure kidneys by,

A) Acute hypersensitivity nephritis

B) Acute kidney injury

C) Chronic kidney disease

Acute drug induced interstitial nephritis

- Drugs –Many drugs give rise to this condition

  Sulphonamids,Ampicillinn/methicillin
  Thiazides,NSAIDs,Cimedtidine

- Clinically manifest –About 2weeks after the exposure

  Fever , eosinophilia , rash

  ARF with oliguria

Pathogenesis

- Immune mediated
- Suggestive of Type 1 (Ig E)or Type 4 (Cell mediated)

Microscopy

- Oedema
- Inflammatory cells – lymphocytes , macropahges , eosinophils , PMN,plasma cells and basophils
  (Prominent in medulla)
- Some drugs – Nonnecrotizing granulomas with giant cells
- Tubulitis
- Tubular necrosis and regeneration
- Glomeruli – normal

  (With NSAIDs -Minimal changes disease and nephrotic syndrome occurs)

Nephropathy associated with NSAIDs

NSAIDS Causes inhibition of cyclooxygenase induced PG synthesis.

Kidney also express COX 2.

NSAID Associated renal problems

- Acute kidney injury
- Acute tubulointerstitial nephritis
- Minimal change disease
- Membranous nephropathy

Read: Analgesic nephropathy (Pathogenesis, Morphology)

Other tubulointerstitial nephropathy

- Urate nephropathy
- Hypercalcaemia and nephrocalcinosis
- Acute phosphate nephropathy
- Light chain cast nephropathy

Read…….

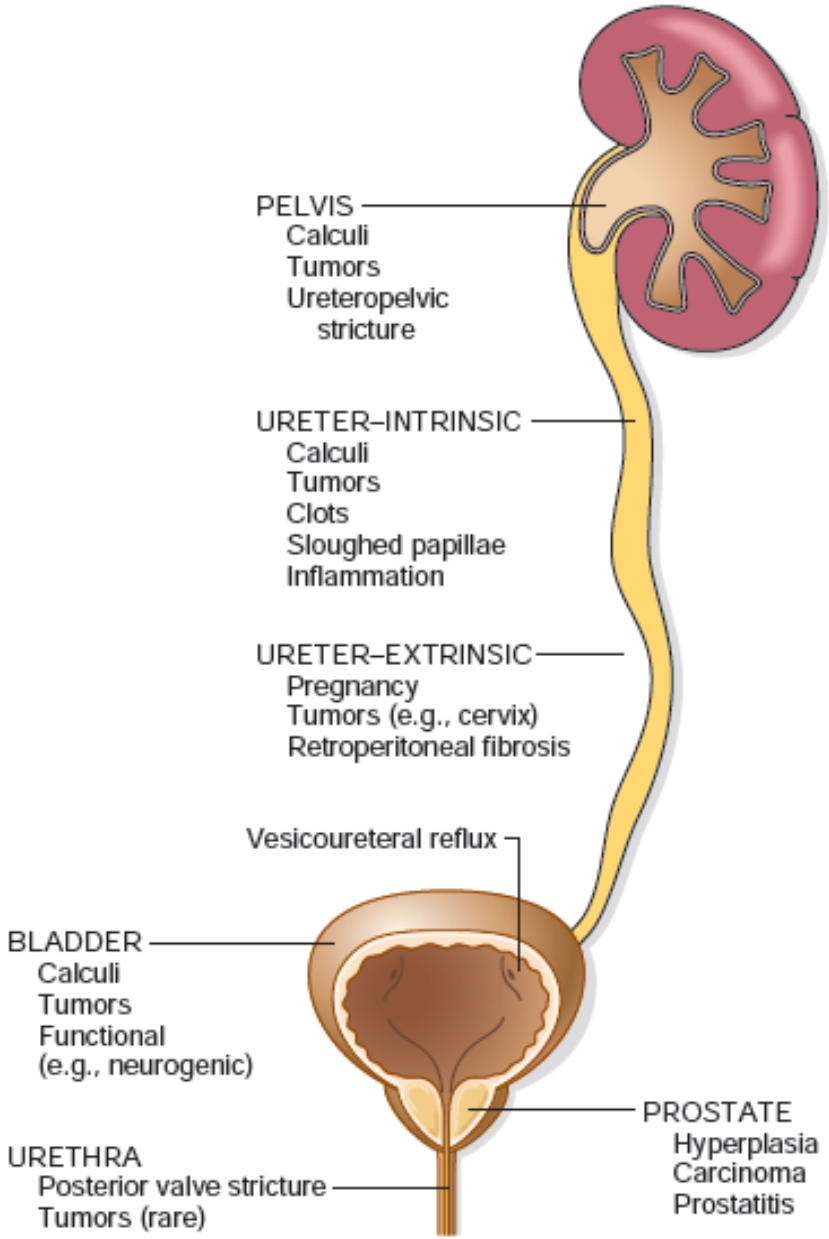
Urinary tract obstruction (Obstructive uropathy)

Obstruction could be

- Any site
- Sudden/slow onset
- Unilateral/bilateral
- Complete/partial

- **Causes**- Intrinsic
  Exstrinsic

Causes of urinary tract obstruction



Effects of UT obstruction

A) Infection
B) Formation of calculi
C) Renal atrophy and hydronephrosis

Hydronephrosis

- Dilatation of the renal pelvis and calyses
- High pressure in pelvis transmitted back
  - to the cortrex through collecting ducts.

    Progressive atrophy of the kidney.
  - Compress renal vasculature

    Reduce medullary blood flow.

    Tubular functions are affected initially

    Later GFR is reduced.

Hydronephrosis -Macroscopy

Early

- Enlarged kidney
- Depending on the level of obstruction different parts of the UT dilated
- Dilatation of the renal pelvis and calyses
- Atrophy of the renal parenchyma

Late

- Interstitial fibrosis
- Progressive blunting of the apices of the pyramids
- Total obliteration of pyramids
- Marked thinning of the cortex
- Kidney is transformed into a thin walled cystic structure

Hydronephrosis - maroscopy

Dilated pelvi-calyseal system
Thinned cortex

Hydronephrosis - microcopy

- Tubular atrophy
- Interstitial inflammation
- Interstitial fibrosis

Urinary calculi

Reasons-

- Supersaturation of the stone forming constituents in the urine (main reason)
- Changes in the Urinary pH
- Infections
- Low urine volume
- Deficiency of inhibitors of crystal formation in the urine.(Eg: Pyrophosphate, nephrocalcin,osteopontin)

Urolithiasis

Main types of calculi

A) Calcium stones (70%)

B) Triple stone /Struvite stones (15-20%)

(Magnesium, ammonium, phosphate)

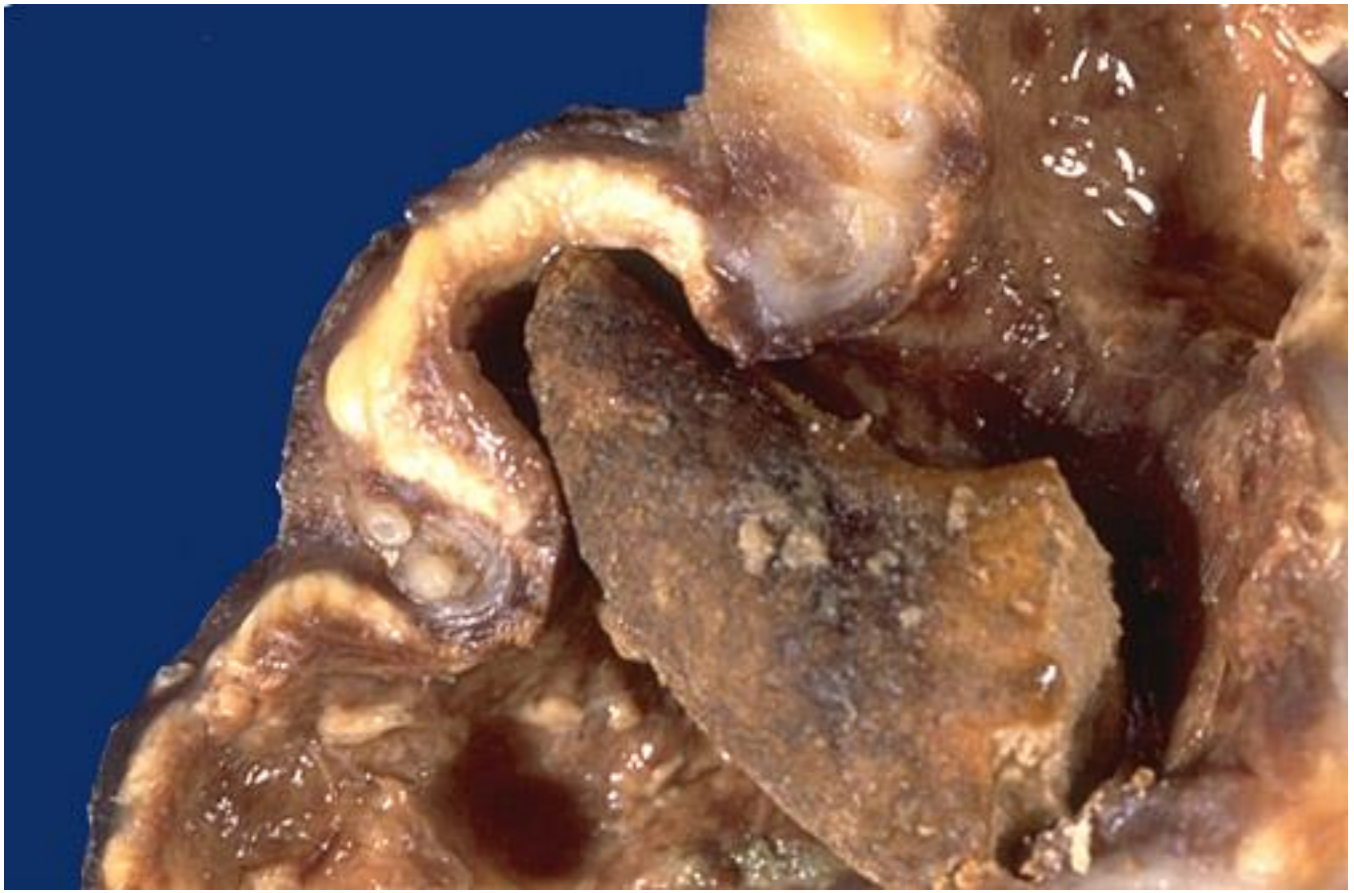
C) Uric acid stones

D) Cystine

Assignment: Find the reasons for formation of these specific types of calculi and how to identify each type.

Different types of calculi

Staghorn calculi



Assignment

- Describe the normal function of the tubules
- How to investigate a patient suspected of having tubular disease?