Chronic Kidney Disease (CKD)

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CKD - Objectives

At the end of this lecture, you should be able to

- List the causes of CKD
- Describe briefly the pathophysiology of CKD
- Describe the macroscopic and microscopic changes of the kidney in CKD
- Briefly describe the extra renal manifestations of CKD

CKD - causes

- Congenital and inherited diseases
- Glomerular diseases
- Vascular disease
- Tubulointerstitial diseases
- Urinary tract obstruction

- **Congenital and inherited diseases**

  Polycystic kidney disease (adult and infantile forms)

  Medullary cystic disease

  Tuberous sclerosis

  Oxalosis

  Cystinosis

  Congenital obstructive uropathy

- **Glomerular diseases**

  Primary glomerulopathies

  Rapidly progressive GN

  Focal segmental GN

  Mesangiocapillary / membranoproliferative GN

  Membranous glomerulonephritis

  IgA nephropathy

- **Glomerular diseases**

  Secondary glomerulopathies

  SLE, Wegener granulomatosis, amyloidosis,
  diabetic glomerulosclerosis, accelerated hypertension, HUS, TTP,
  systemic sclerosis, sickle cell disease

- **Vascular diseases**

  Hypertensive nephrosclerosis

  Renovascular diseases

  Small and medium - sized vessel vasculitis

- **Tubulointerstitial diseases**

  Tubulointerstitial nephritis

  Reflux nephropathy

  Tuberculosis

  Schistosomiasis

  Nephrocalcinosis

  Multiple myeloma

  Renal papillary necrosis

- **Urinary tract obstruction**

  Urinary calculi

  Prostatic disease

  Pelvic tumours

  Retroperitoneal fibrosis

  Schistosomiasis

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Chronic renal impairment

Loss of renal tissue / nephrons

↓ Kidney attempts to maintain the normal intrarenal environment

Hypertrophy and continuous activation of remaining nephrons

↓

Increased blood flow to the hypertrophic glomeruli

↓

Increase in individual GFR

↓

Total GFR is low

Try to stabilize the nitrogenous waste products in the blood, but at a higher level

Effects of chronic kidney disease

Water and sodium balance

- Initially normal sodium balance is maintained by increased fractional excretion of sodium

- Later ,reduced GFR and poor reabsorption by tubules cause retention of water and sodium

FENa - percent of filtered sodium that is excreted in the urine

Tubular damage

↓

Decreased sodium and chloride reabsorption

↓

Reduced hypertonicity in medulla

↓

Poor concentration ability

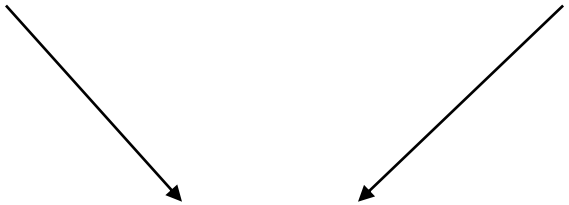
Osmotic diuresis

↘ ↙

Production of urine with **fixed specific gravity**

Reduced tubular production of ammonia and reduced secretion of ammonia into the tubule

Reduced HCO_3 reabsorption



Metabolic acidosis (↓ pH)

Reduced excretion of H^+ ions

Poor reabsorption in tubules

↓

Reduced excretion of potassium

↓ Exacerbated by acidosis

Hyperkalaemia

Chronic kidney disease

- Occurs in all age groups
- Underlying causes vary

- Renal damage is progressive and irreversible

- The rate of progression varies depends on the underlying renal pathology

- Systemic hypertension may both result from, and contribute to, CKD

Chronic kidney disease

- Underlying causes vary
- Occurs in all age groups

- **Renal damage is progressive and irreversible**

- The rate of progression varies depends on the underlying renal pathology

- **Systemic hypertension** may both result from, and contribute to, CKD

Progression of CKD

- The end stage kidney , regardless of cause, shows a common histological appearance
  - **Glomeruli** show diffuse sclerosis
  - **Interstitium** show fibrosis with scattered chronic inflammatory cells
  - **Tubules** are often dilated and filled with eosinophilic protein casts ("thyroidization“)
  - **Blood vessels** show thickening of the vessel wall

- This suggests a common final pathway of progressive renal damage

- The progression is most likely be due to **scarring and loss of renal parenchyma**

- The progression of CKD is postulated to result from a self-perpetuating vicious cycle of **fibrosis** activated after initial injury

- The **renin-angiotensin-aldosterone system** (RAAS) plays a major role in many of the pathophysiologic changes that lead to progression of renal disease.

Intrarenal activation of renin- angiotensin system – Angiotensin II

Possible mechanisms

- Efferent arteriolar vasoconstriction
- Increased intraglomerular capillary pressure
- Adaptive glomerular hypertrophy
  - Increased glomerular blood flow
  - Causes glomerular hyperfiltration

- Effect on mesangial cells and podocytes
  - Increases pore sizes

- Also modulates cell growth
  - Upregulates TGF –β which is fibrogenic
  - Myofibroblastic differentiation results in matrix formation and collagen synthesis

- **Proteinuria** alone also promotes secretion of pro- inflammatory mediators

  - Promotes interstitial inflammatory cell infiltrate and fibrosis

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CKD - Macroscopy

Depends on the underlying pathology

CKD - Macroscopy - vary according to the underlying pathology

Chronic Glomerulonephritis (CGN)

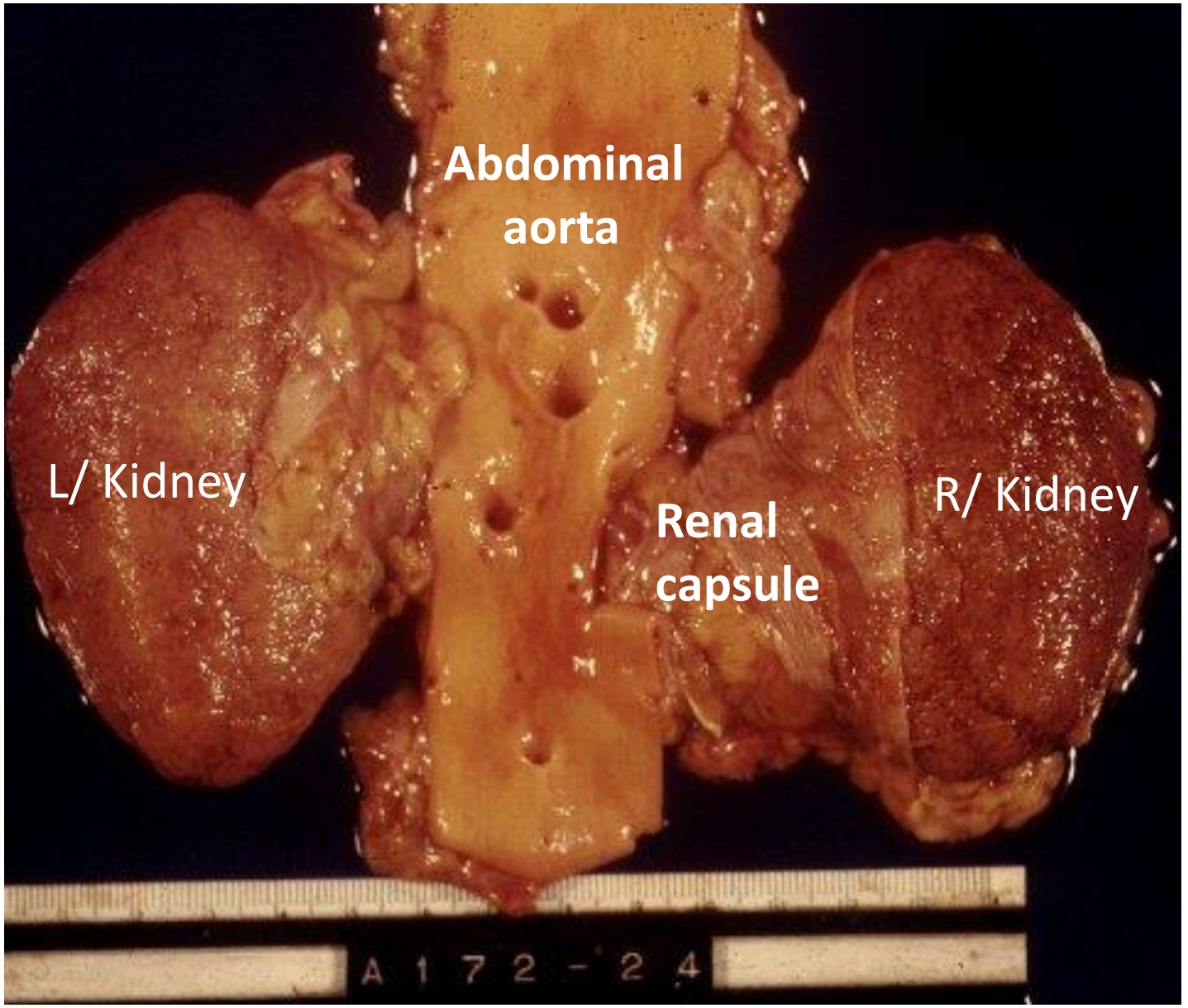
Hypertensive nephrosclerosis

Kidneys

- Symmetrically contracted / small kidneys
- Capsule - firmly adherent
- Cortical surface - Granular

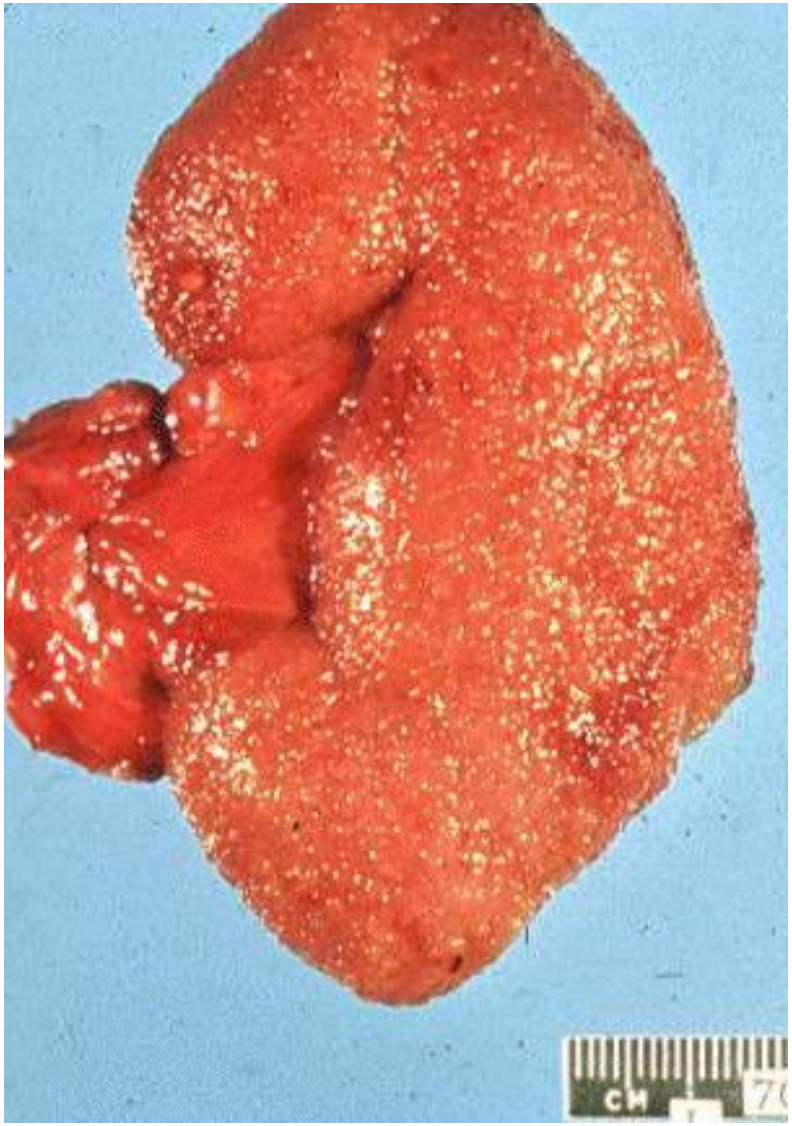
Cut surface

- Cortex - diffusely thin
- Increased peripelvic fat



Bilateral contracted kidneys with fine granular surface

Normal kidney
– Smooth surface



Cortical surface - Granular

Diabetes mellitus

- Kidneys may be normal or enlarged

Polycystic diseases

- Kidneys are enlarged with cysts

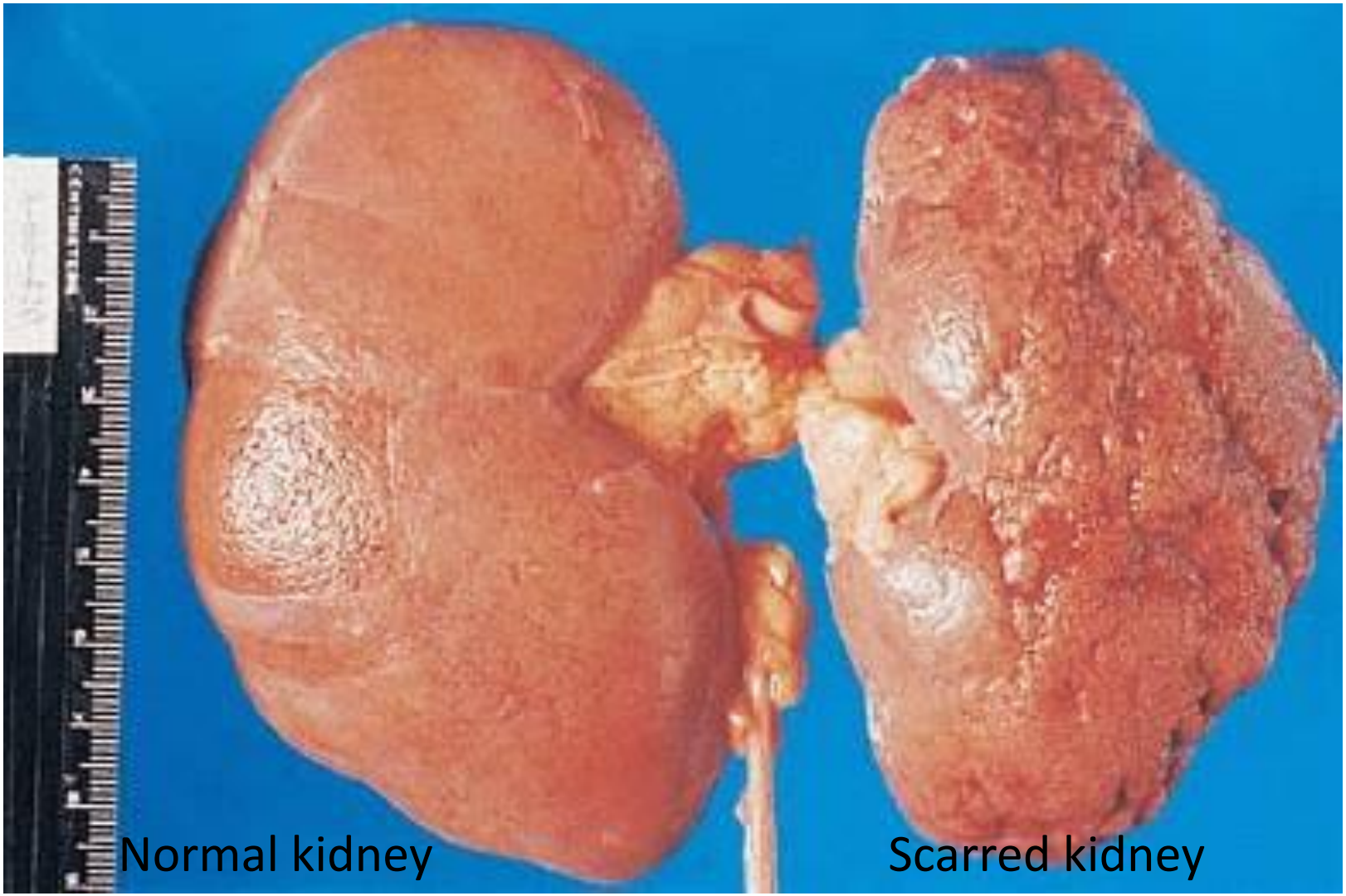
Chronic pyelonephritis

- Surface scarring of the kidney

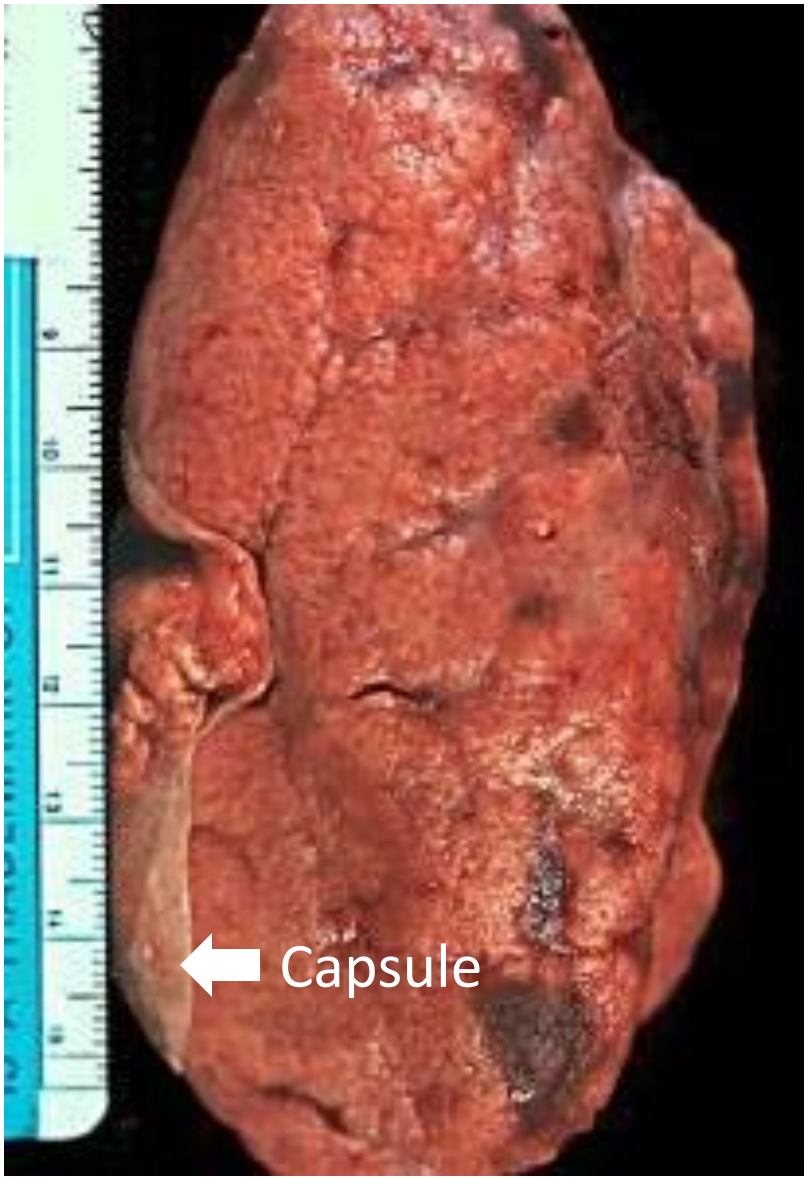
Amyloidosis

- Usually kidneys are enlarged

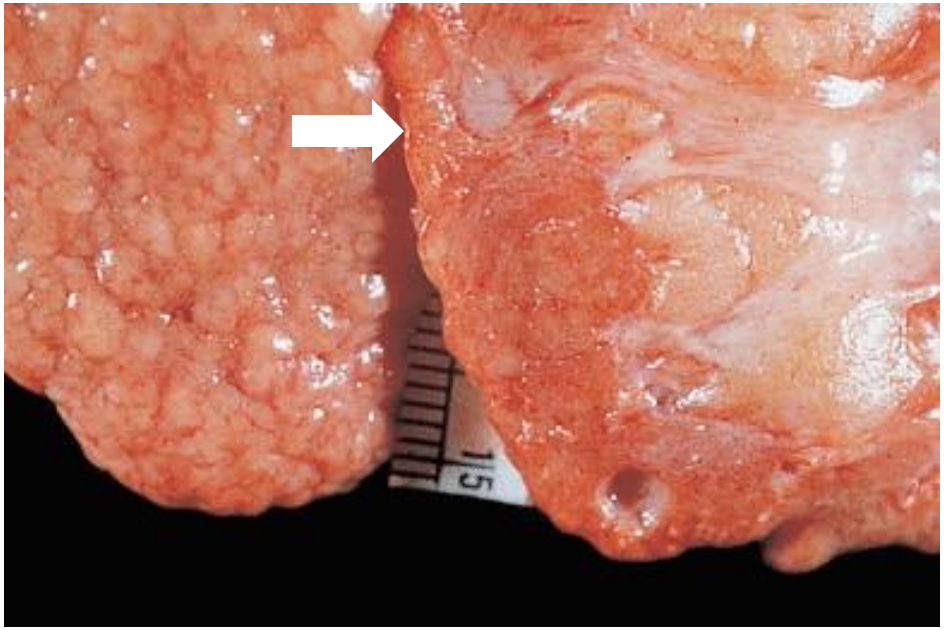
Chronic pyelonephritis



Chronic pyelonephritis - Macroscopy



Coarsely granular surface, discrete scars

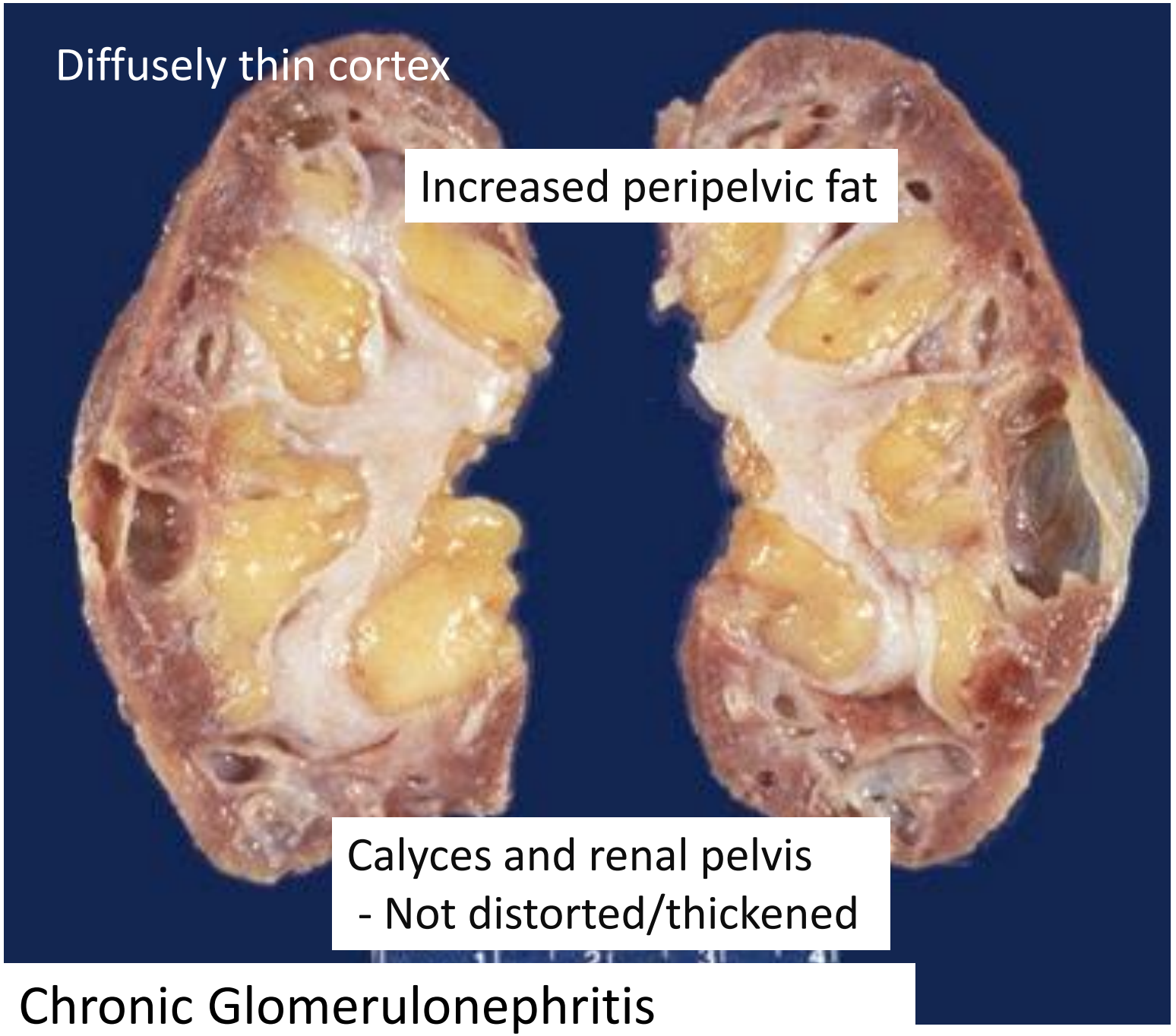


Cut surface shows discrete scars

Calyces and renal pelvis

- Appearance depends on the underlying pathology

- **CGN, hypertensive nephropathy**
  - Calyces and the renal pelvis is usually not affected
  - Increased peripelvic fat
- **Chronic pyelonephritis**
  - Dilated , distorted and thickened calyces
- **Urinary tract obstruction**
  - Hydronephrosis



Chronic Glomerulonephritis

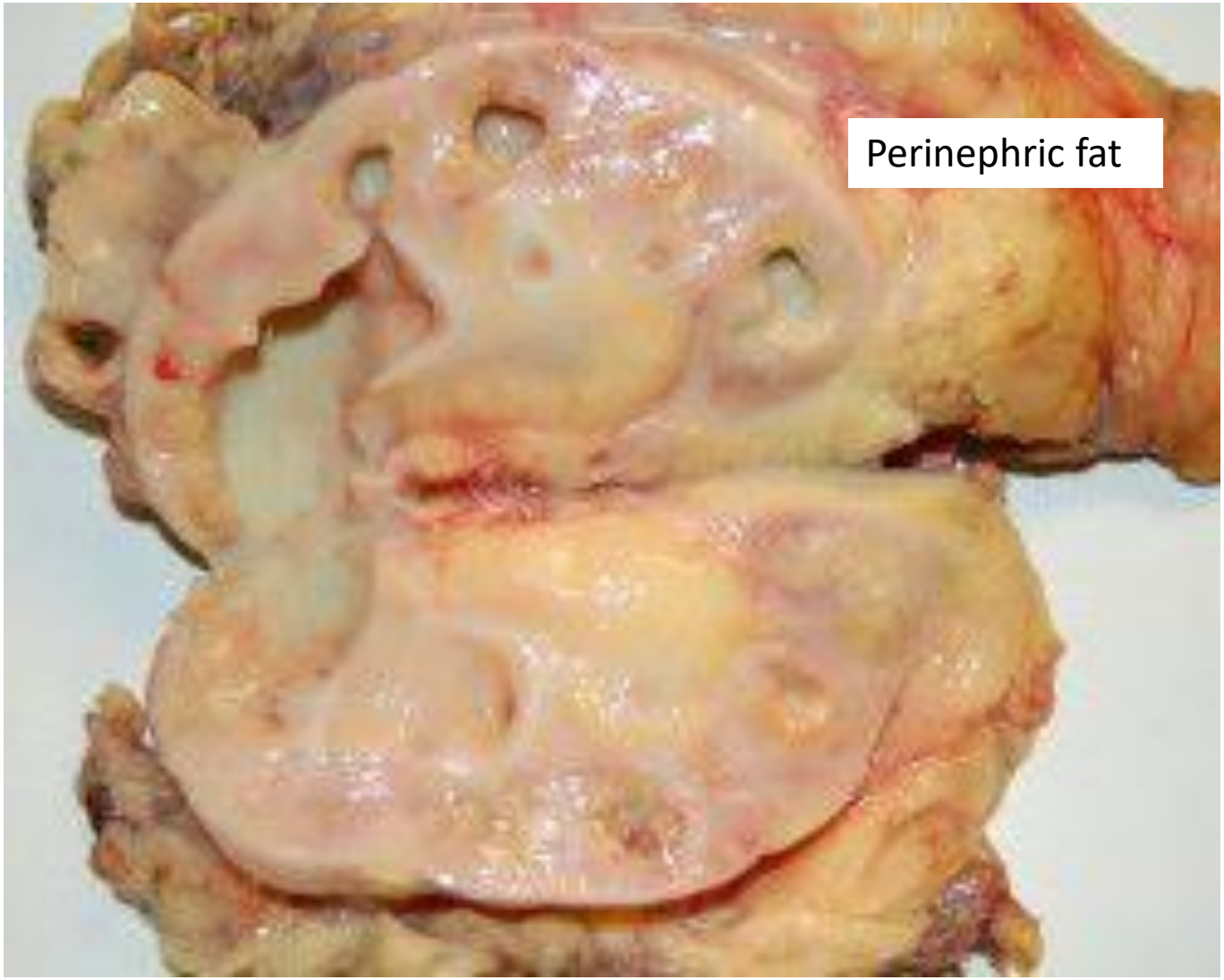
Normal kidney

Diffusely thin cortex

Increased peripelvic fat

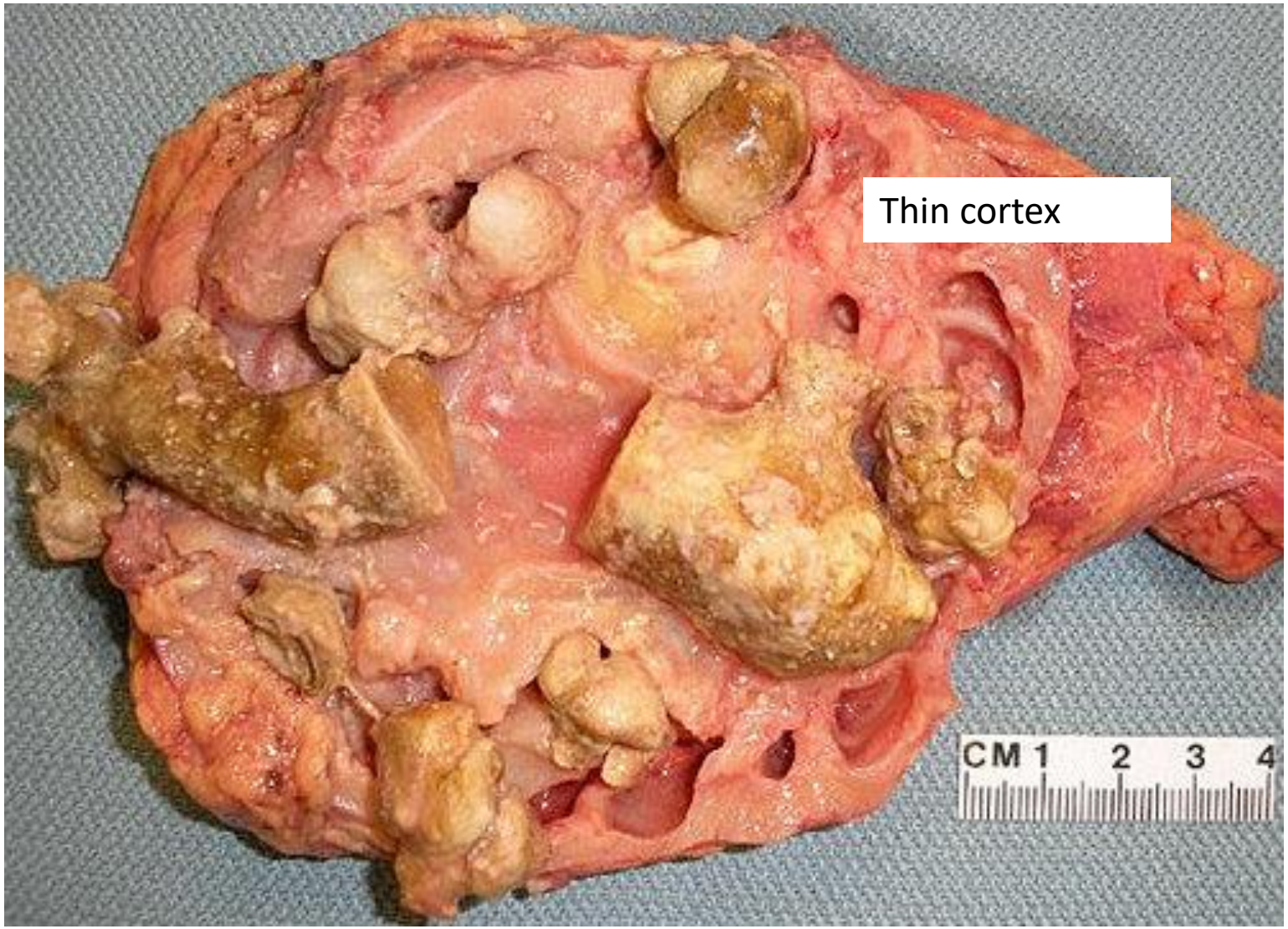
Calyces and renal pelvis - not distorted

Chronic pyelonephritis



Dilated and distorted pelvis and calyces filled with yellow-green material / pus

Renal calculi



Distorted renal pelvis and the calyces

CKD macroscopy

Obstructive uropathy

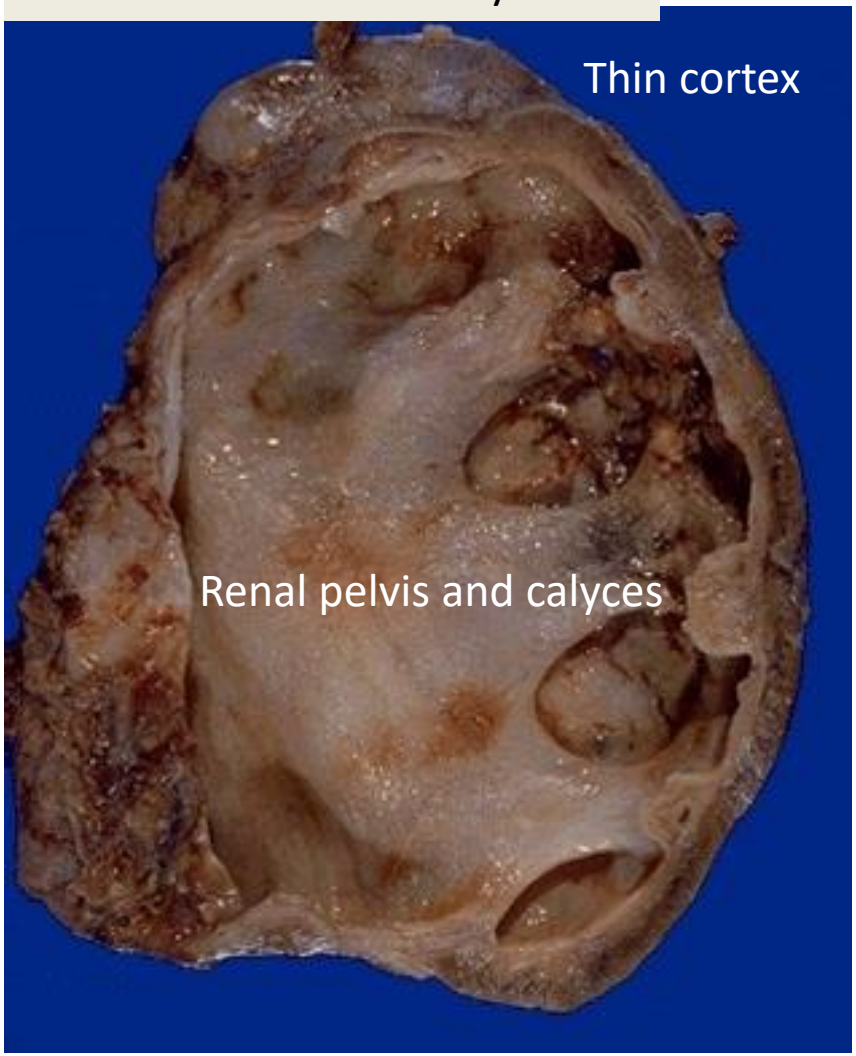
The cut surface of a kidney

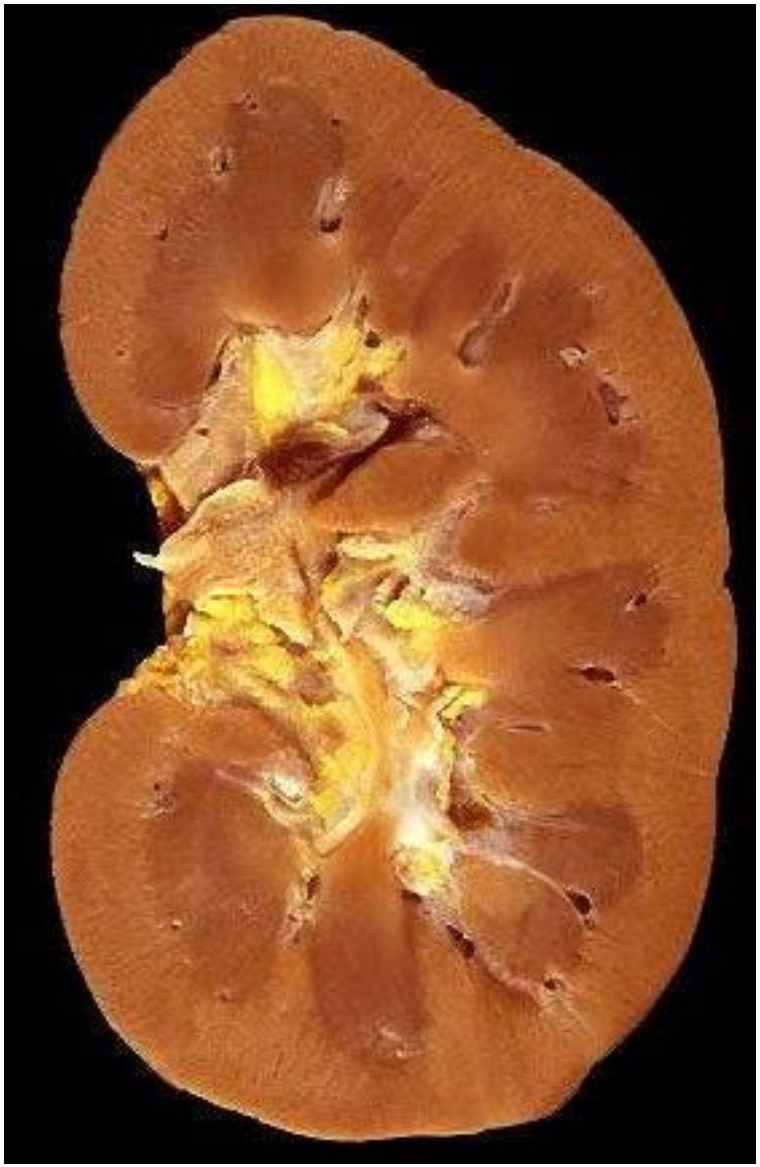
Note:

- Dilated pelvicalyceal system (Hydronephrosis)
- Markedly thin cortex

Obstructive uropathy

Cut surface of the kidney





-Distorted, dilated and thickened renal pelvis and calyces

CKD macroscopy

ADPKD

Both kidneys enlarged
Surface -Numerous cysts of variable size

Cut surface - Loss of renal parenchyma

End stage kidney disease Macroscopy

- Typically shrunken
- But usually not in DM and amyloidosis
- Surface is usually granular
- Adherent capsule
- Surface scarring
- Hydronephrosis
- Distorted pelvi-calyceal system
- Cysts
- Atrophic/ thin cortex
- Obscured cortico-medullary demarcation

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End stage kidney disease - Microscopy

- Shows loss of renal parenchyma
- Regardless of the cause, shows a common histological appearance

Glomeruli

- Reduced in number
- All glomeruli are sclerosed

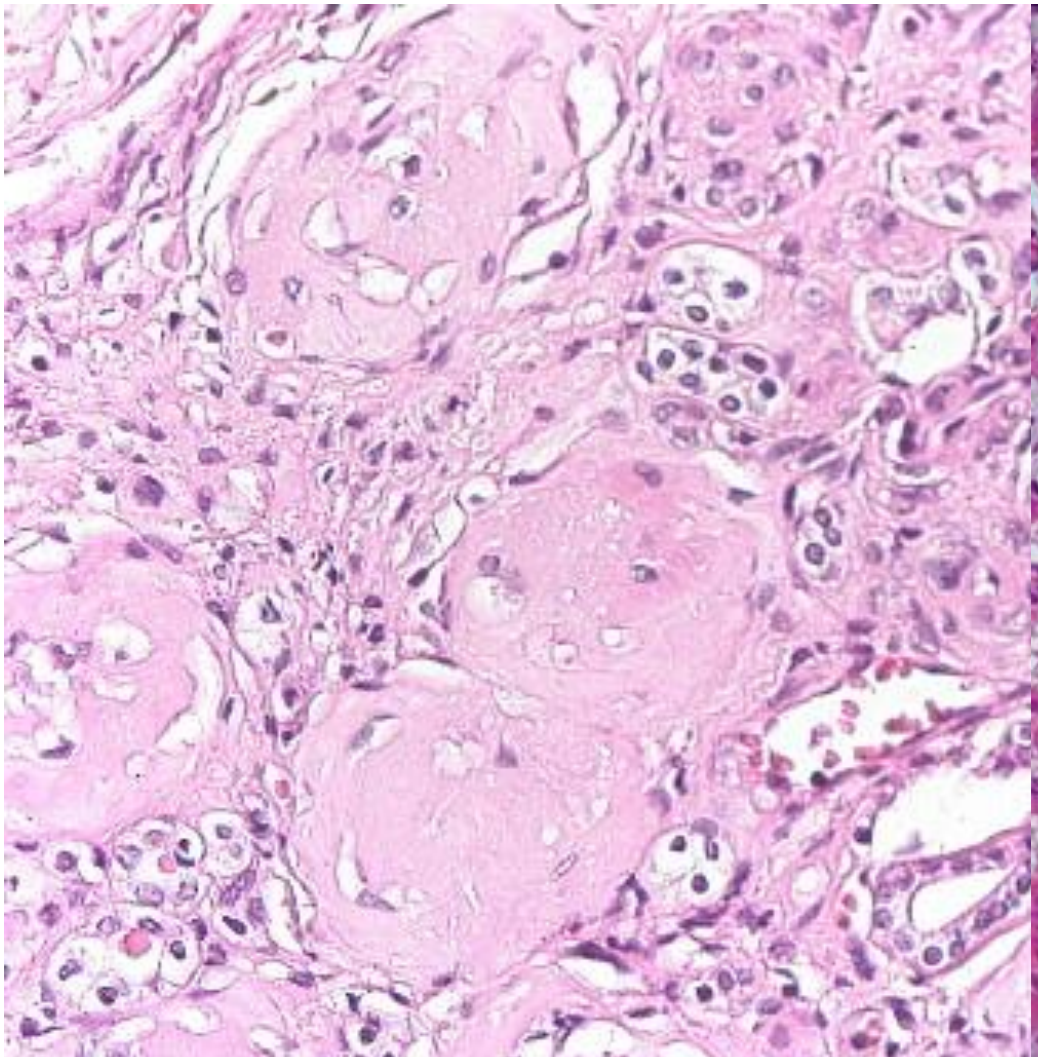
Tubules

- Dilated and filled with eosinophilic protein casts ("thyroidization“)
- Scarred areas show tubular loss and atrophy

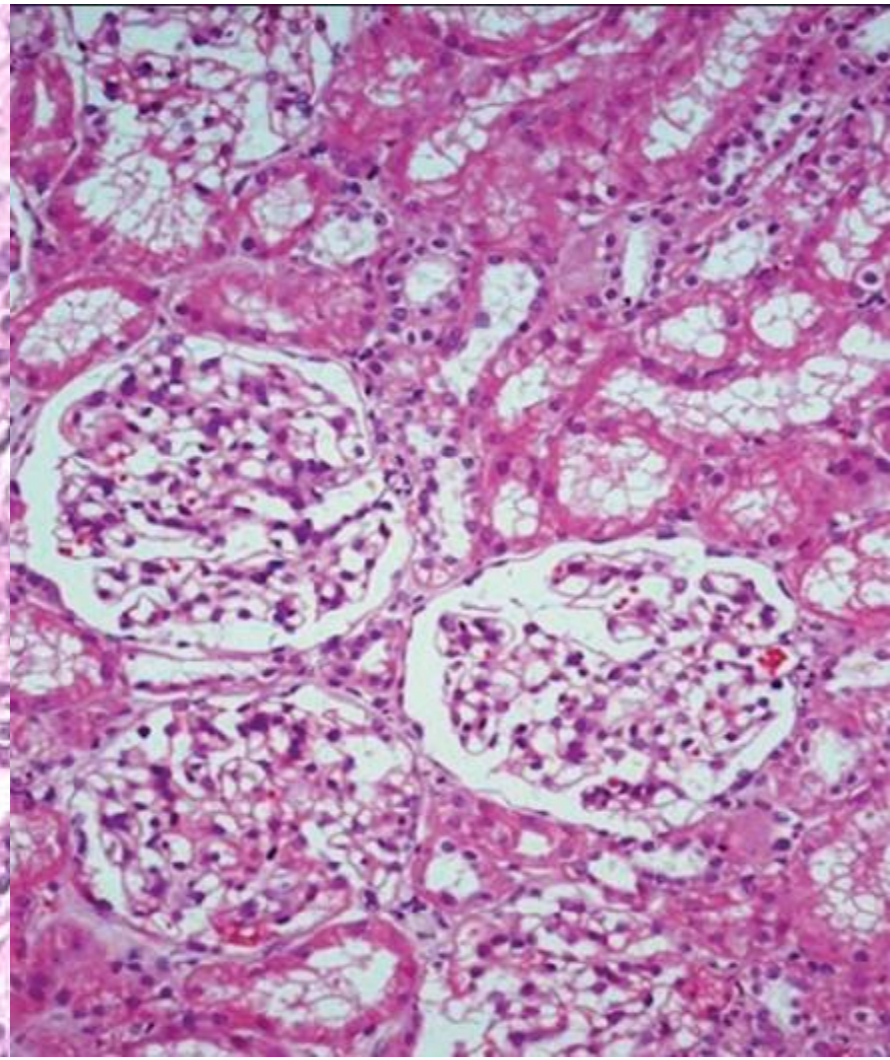
End stage kidney disease - Microscopy

- **Interstitium**
  - Interstitial fibrosis
  - Mononuclear cell/ lymphocytic infiltrate
- **Blood vessels**
  - Thickened vessel walls
  - Hyaline arteriosclerosis (hypertension)
  - Obliterative endarteritis

End stage kidney disease - Microscopy

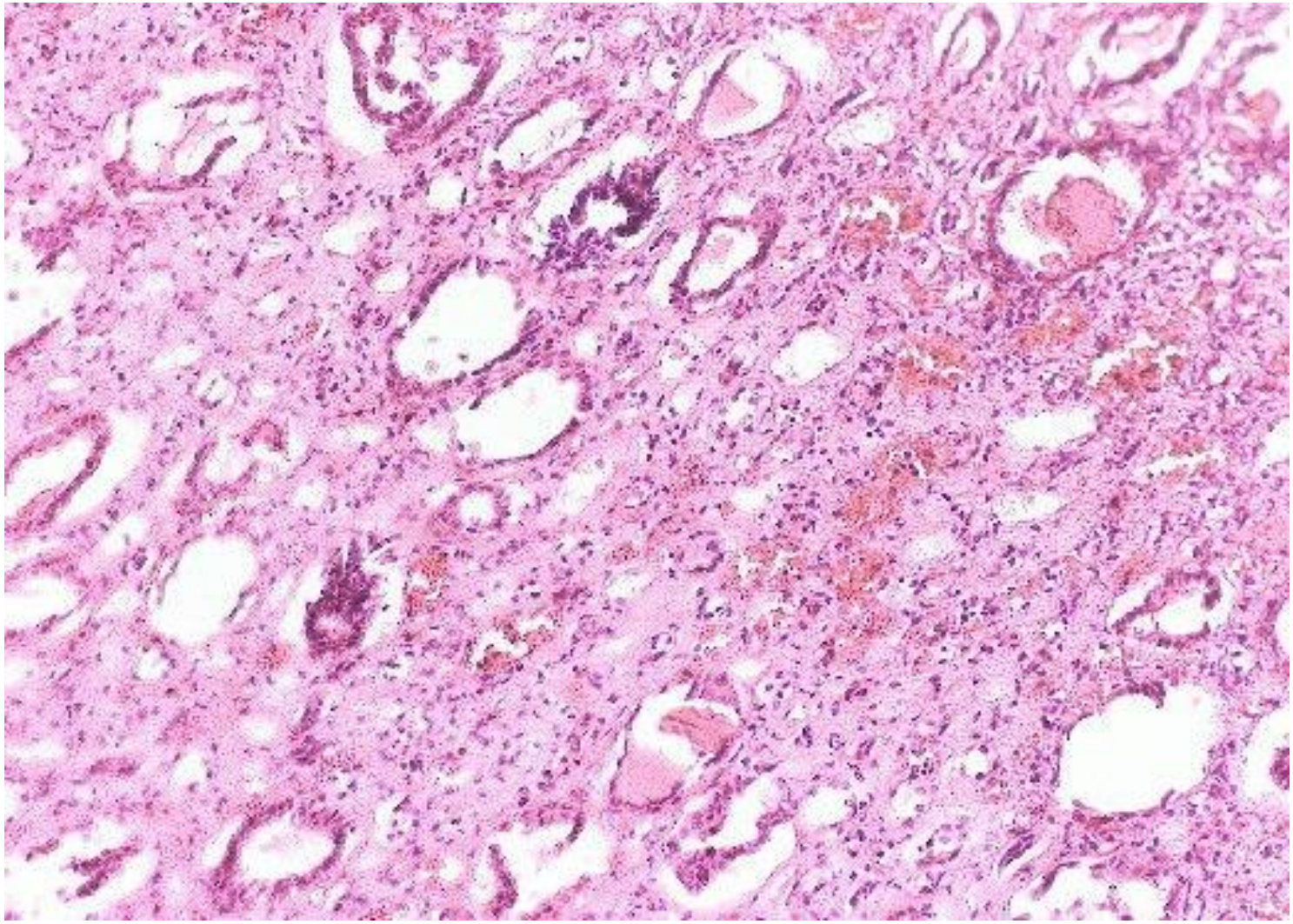


Diffuse glomerular sclerosis



normal glomeruli

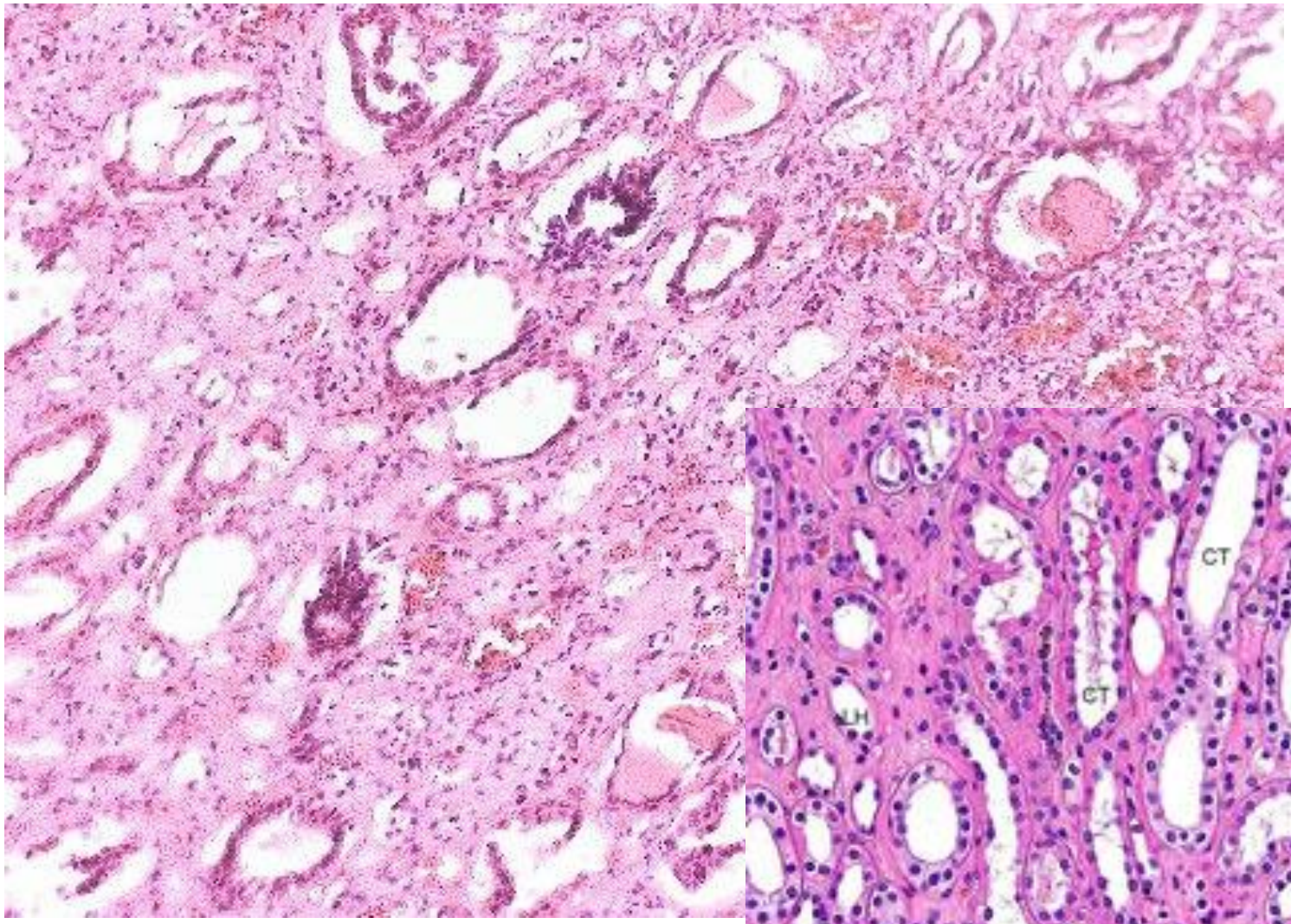
End stage kidney disease - Microscopy

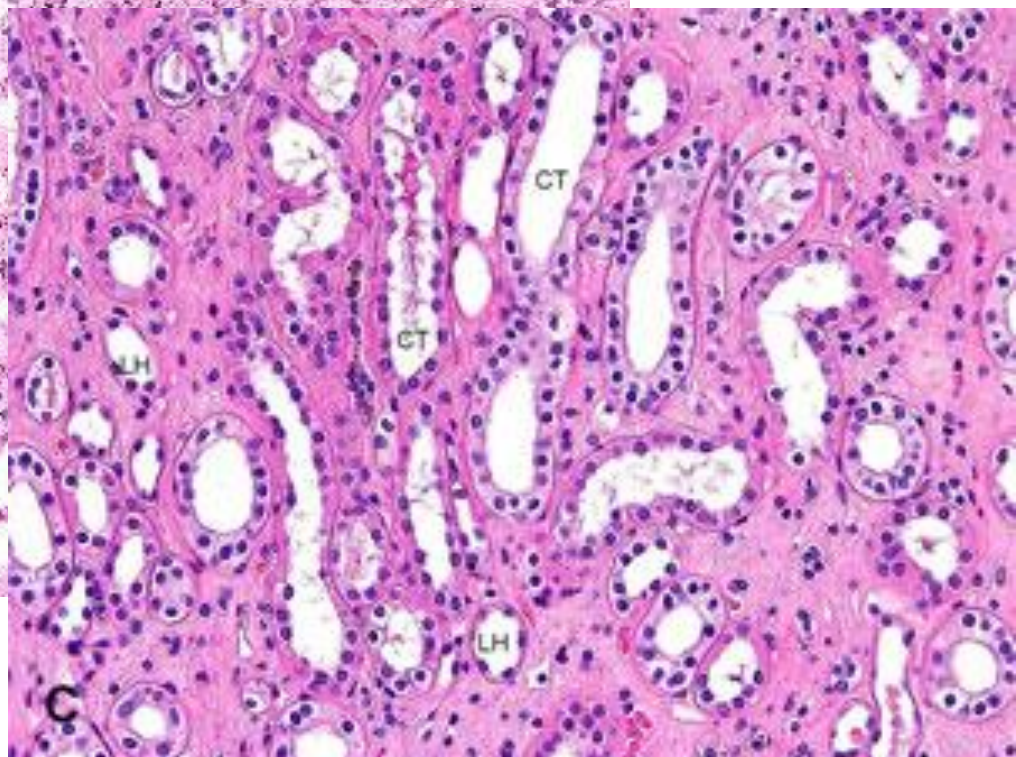


Tubules - Show atrophy

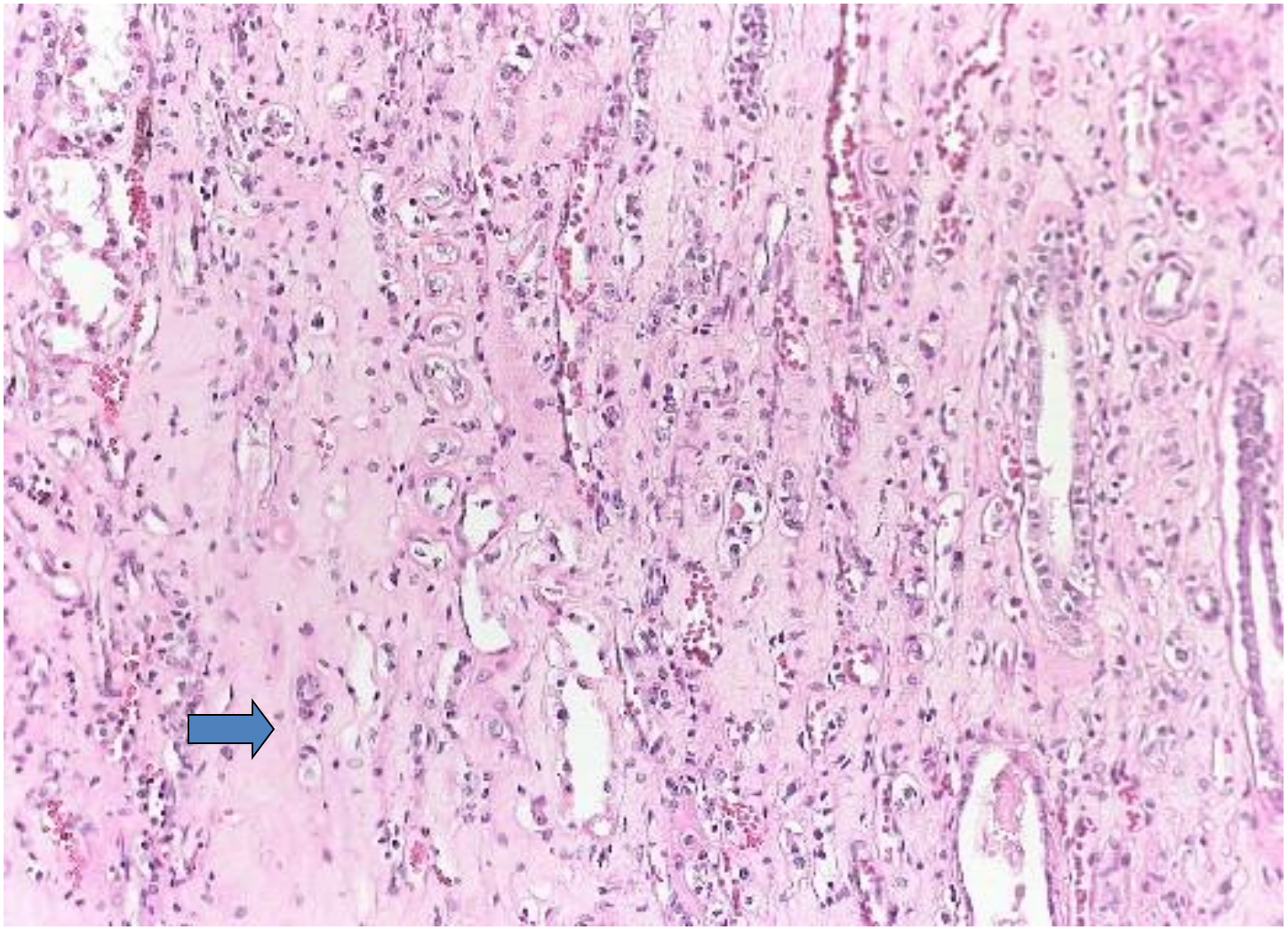
Interstitium - Shows fibrosis and a chronic inflammatory cell infiltrate

End stage kidney disease - Microscopy



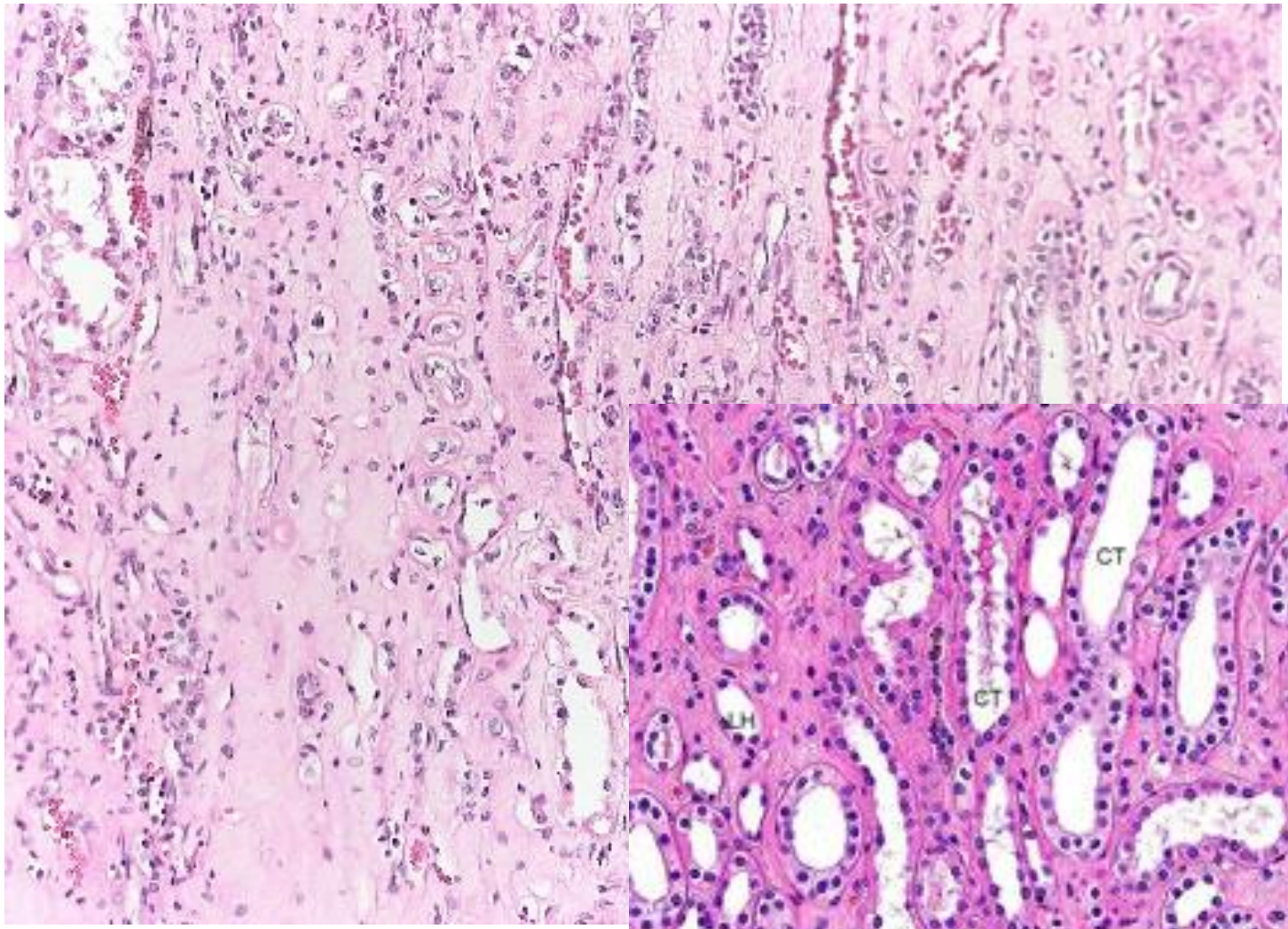


End stage kidney disease - Microscopy

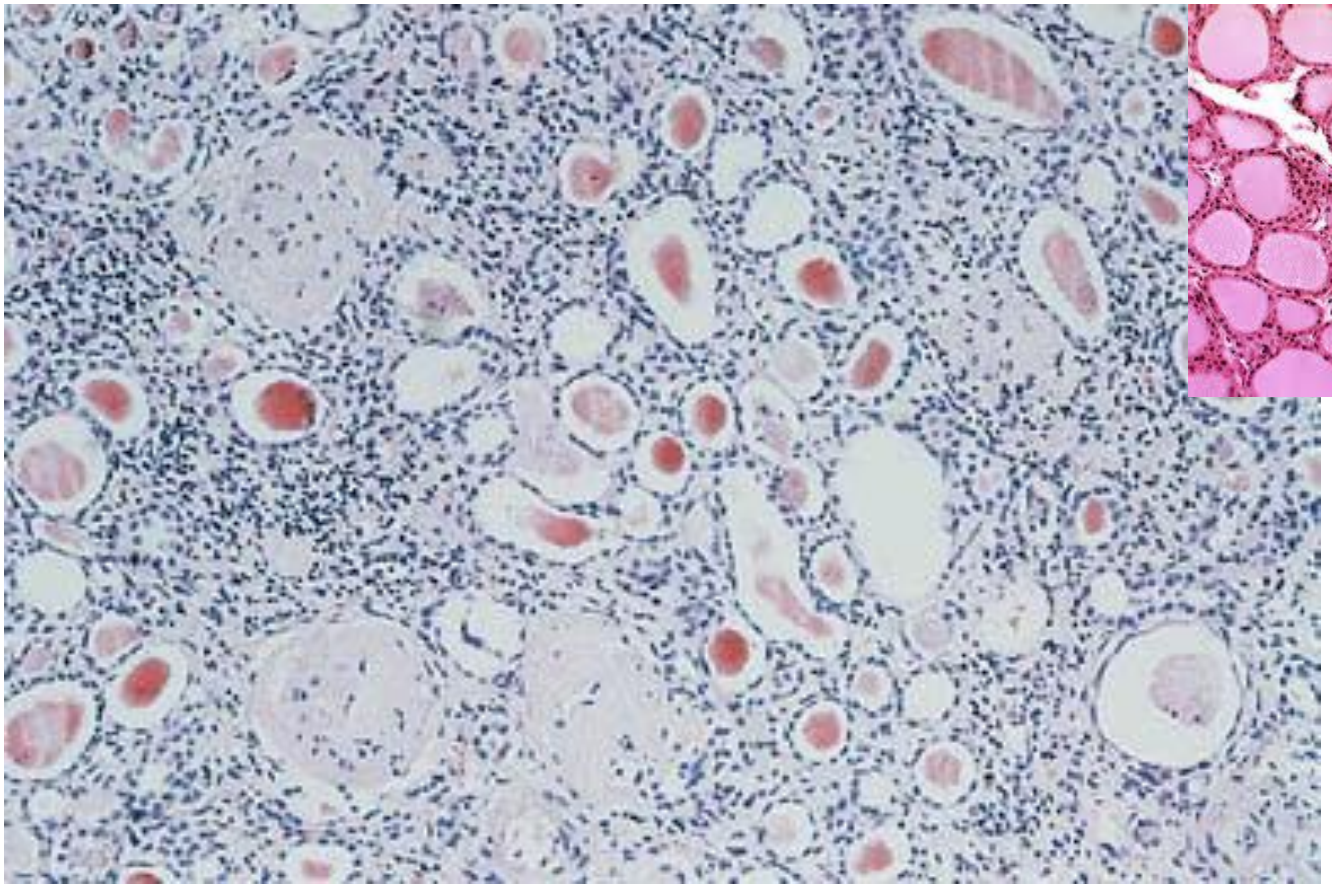


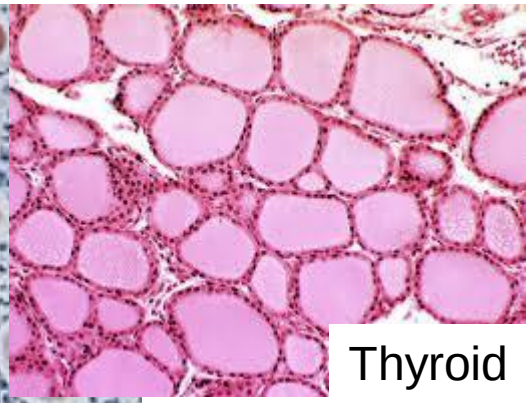
Note: Interstitial fibrosis

End stage kidney disease - Microscopy



“Thyroidization”



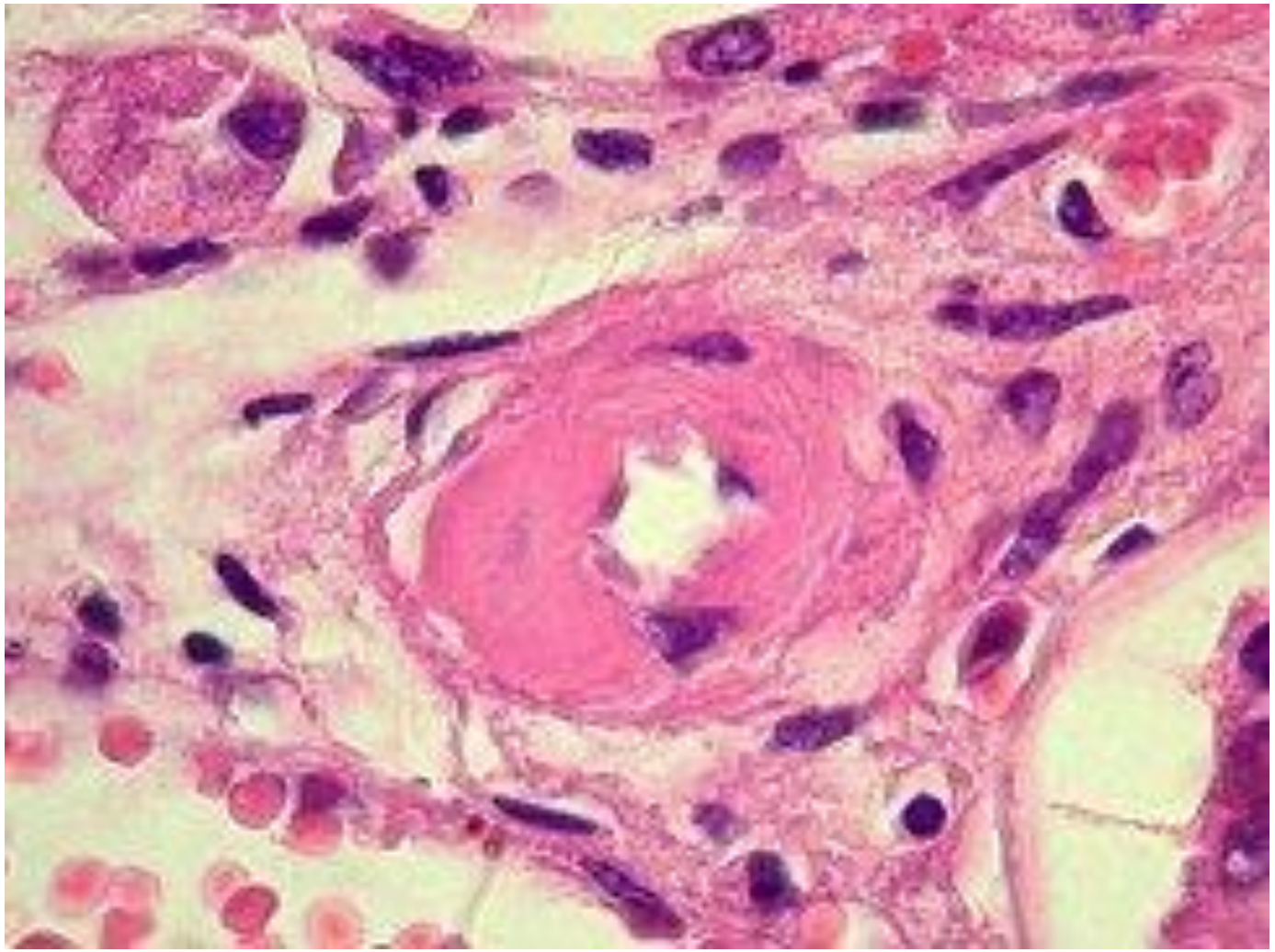


Thyroid

Note: Atrophic ad shrunken tubules, some are dilated.
These tubules are by a flattened epithelium
Tubules contain eosinophilic protein casts (“thyroidization”)
Variable lymphoplasmacytic infiltrate in the interstitium

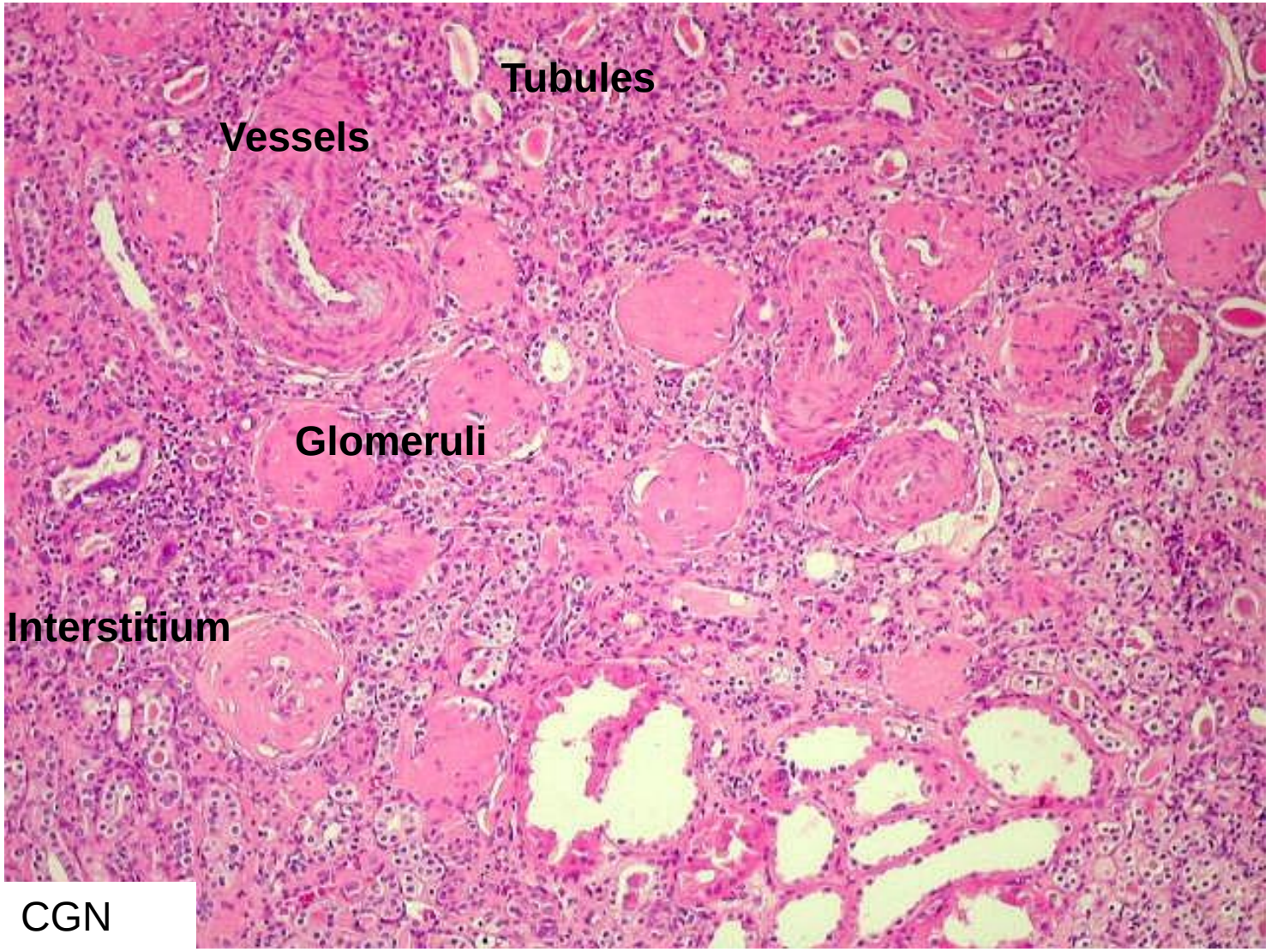
CKD

Vascular changes



Hyaline arteriolar sclerosis

End stage kidney disease - Microscopy



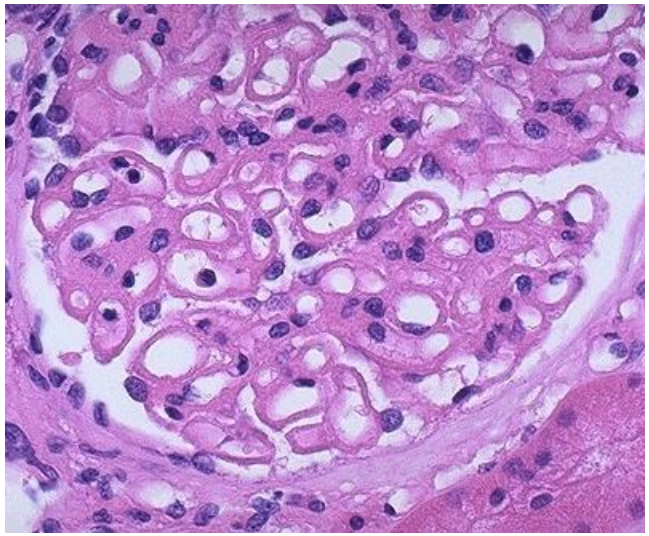
CGN

CKD microscopy

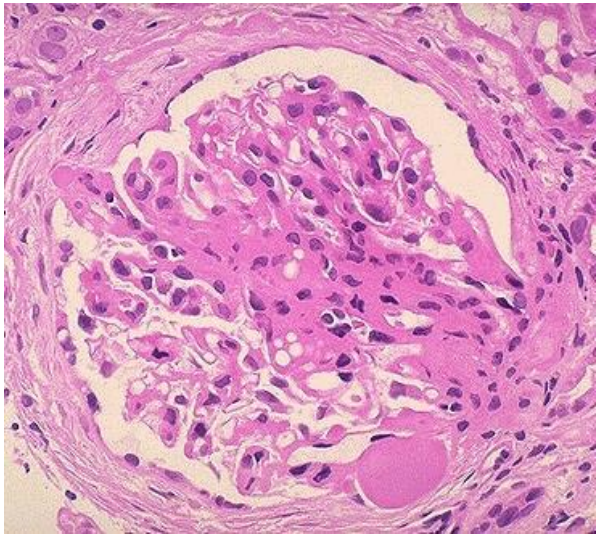
However, at early stages the preserved glomeruli (which are not totally sclerosed) may show variable pathological changes according to the underlying glomerulopathy

eg. CGN - Microscopy

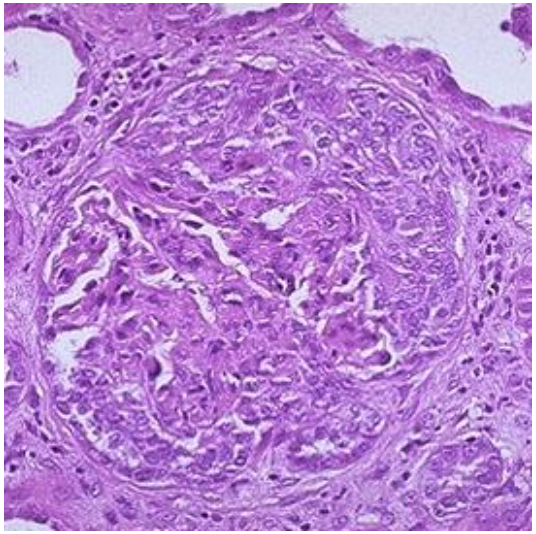
The remaining glomeruli may show features of the underlying glomerulopathy



Membranous GN

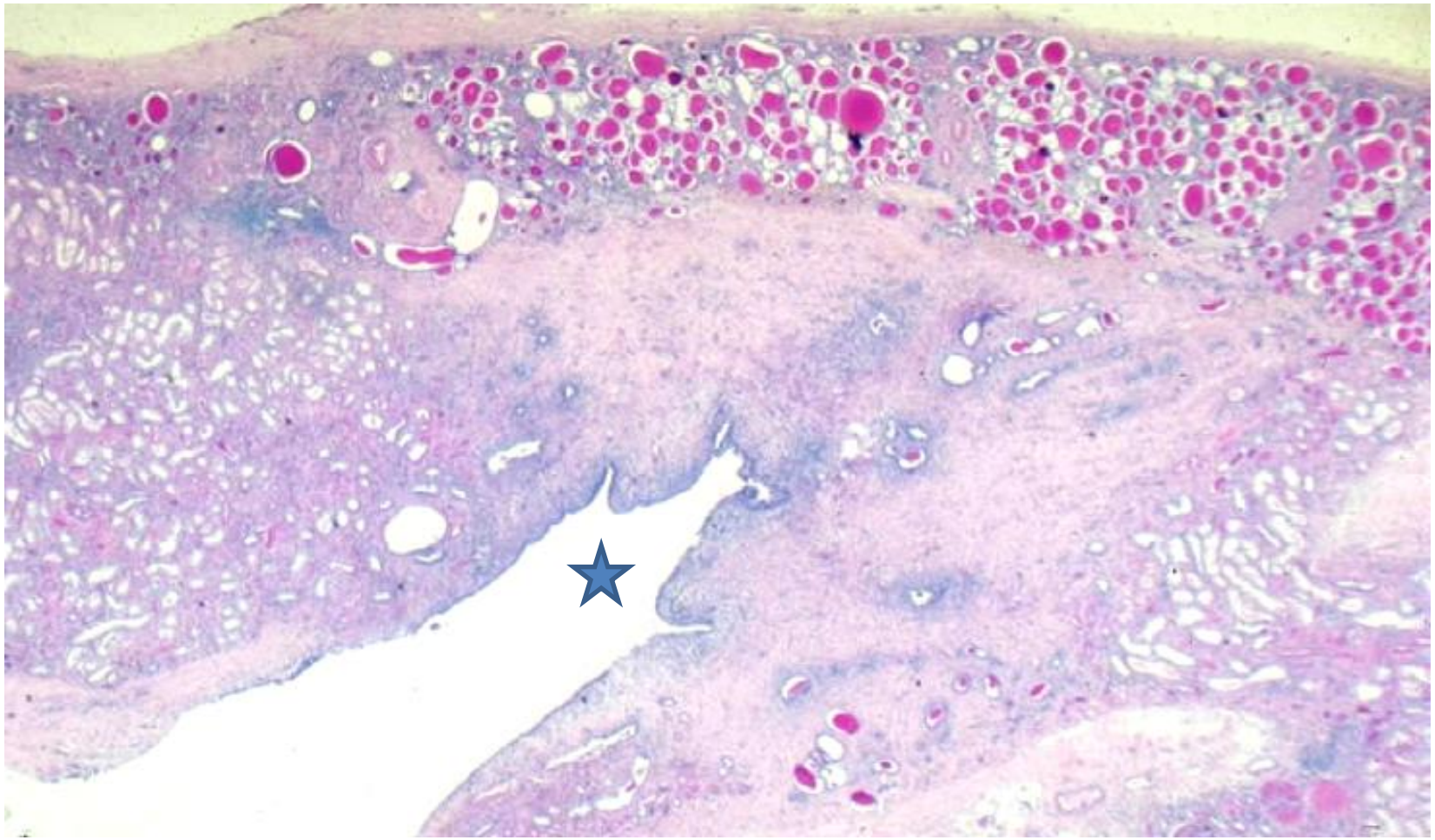


FSGS



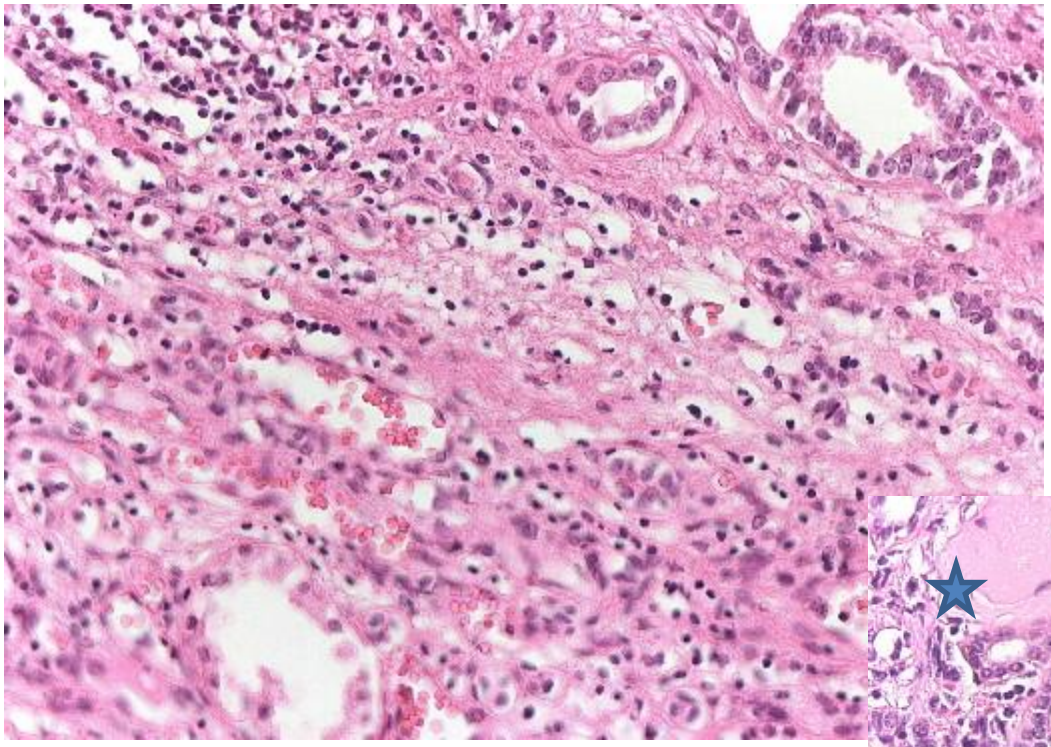
RPGN / Crescentic GN

eg. Chronic pyelonephritis



Note: - Cortical atrophy with "thyroidisation”
- Dilated tubules filled with eosinophilic protein casts
- Fibrosed and distorted papilla (Chronic pyelonephritis)

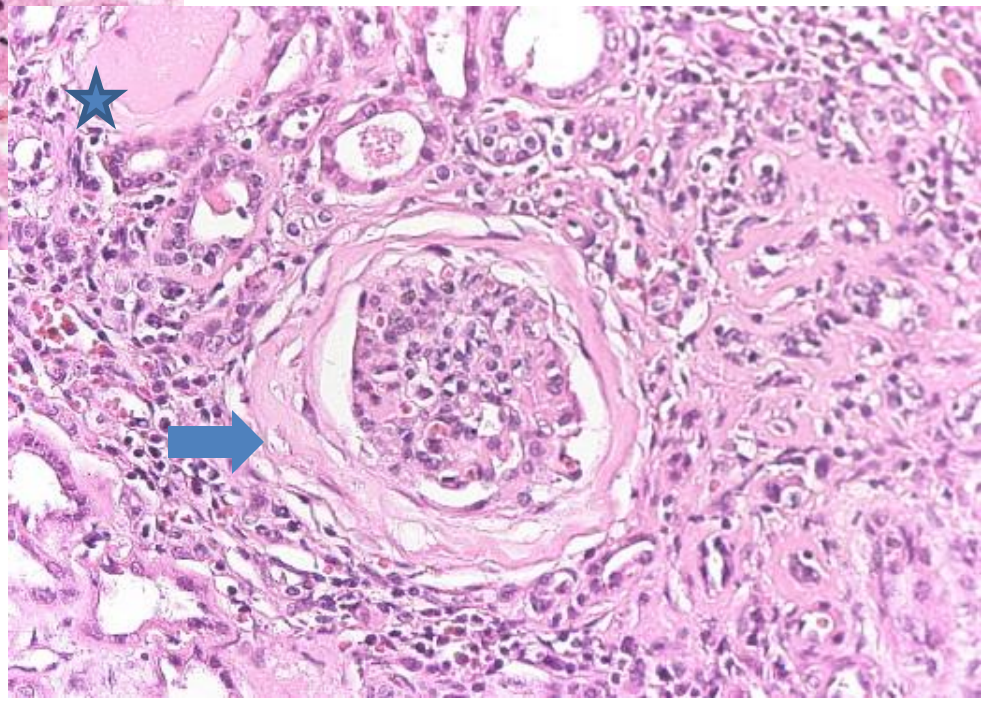
Chronic pyelonephritis



Tubular atrophy

Interstitial inflammation

Interstitial fibrosis

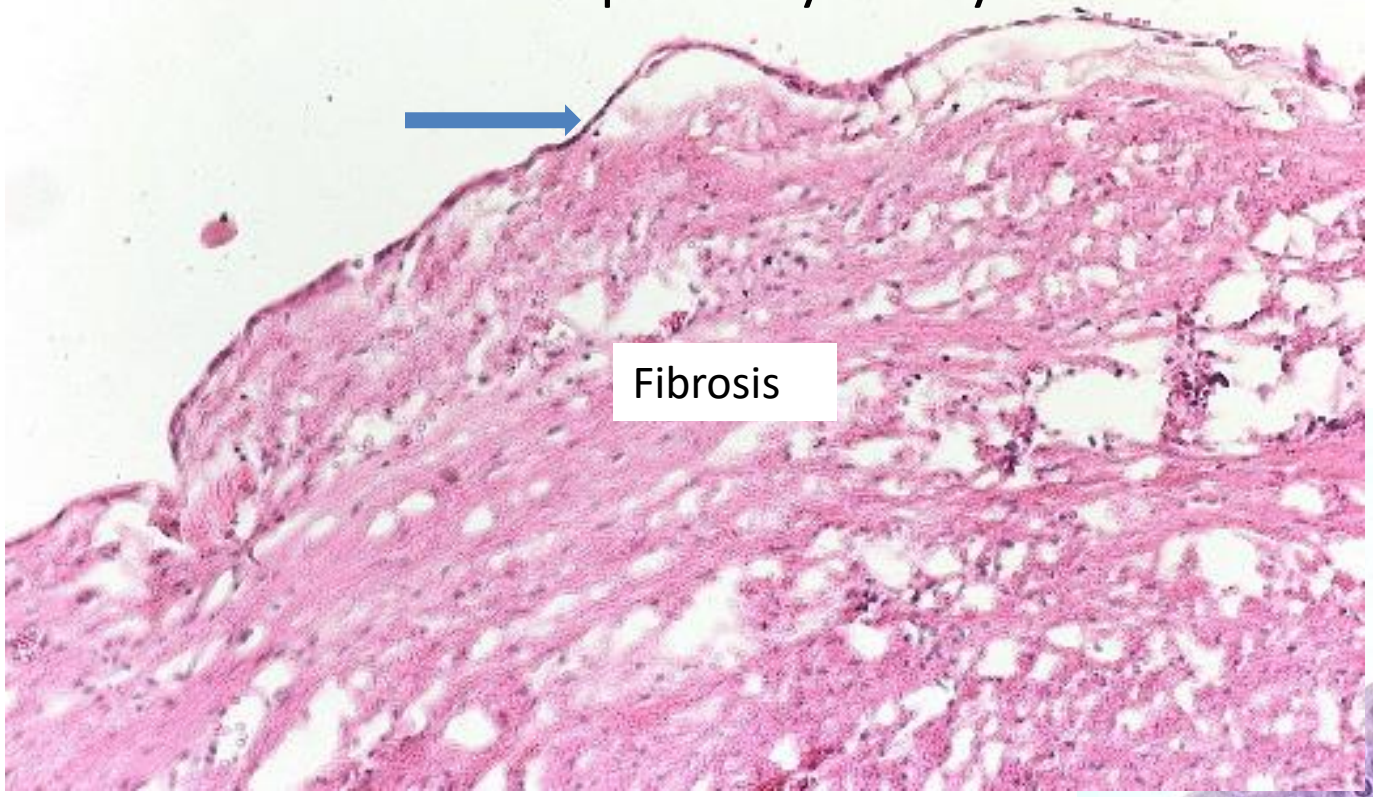


Saclerosed glomeruli (★)

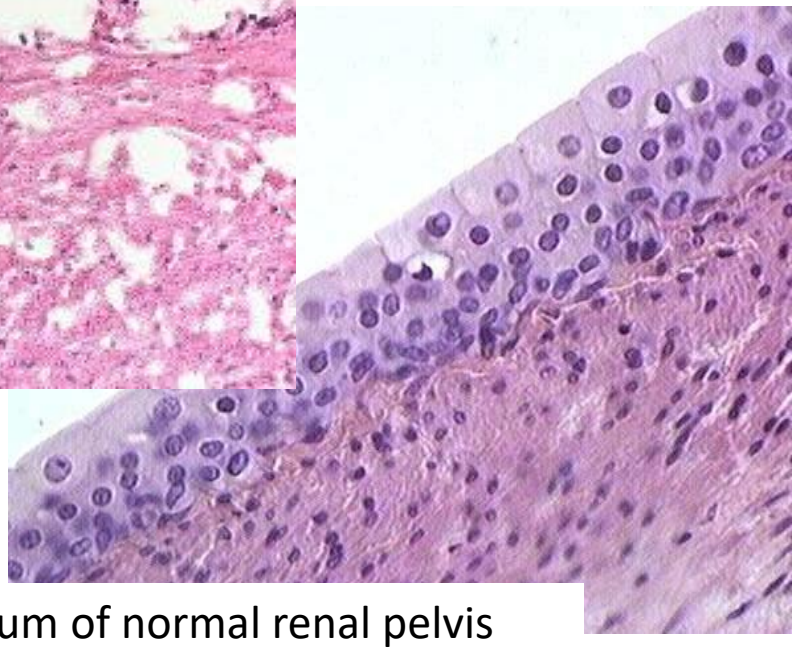
Periglomerular fibrosis (➡)

Chronic pyelonephritis

Flattened mucosa in the pelvicalyceal system



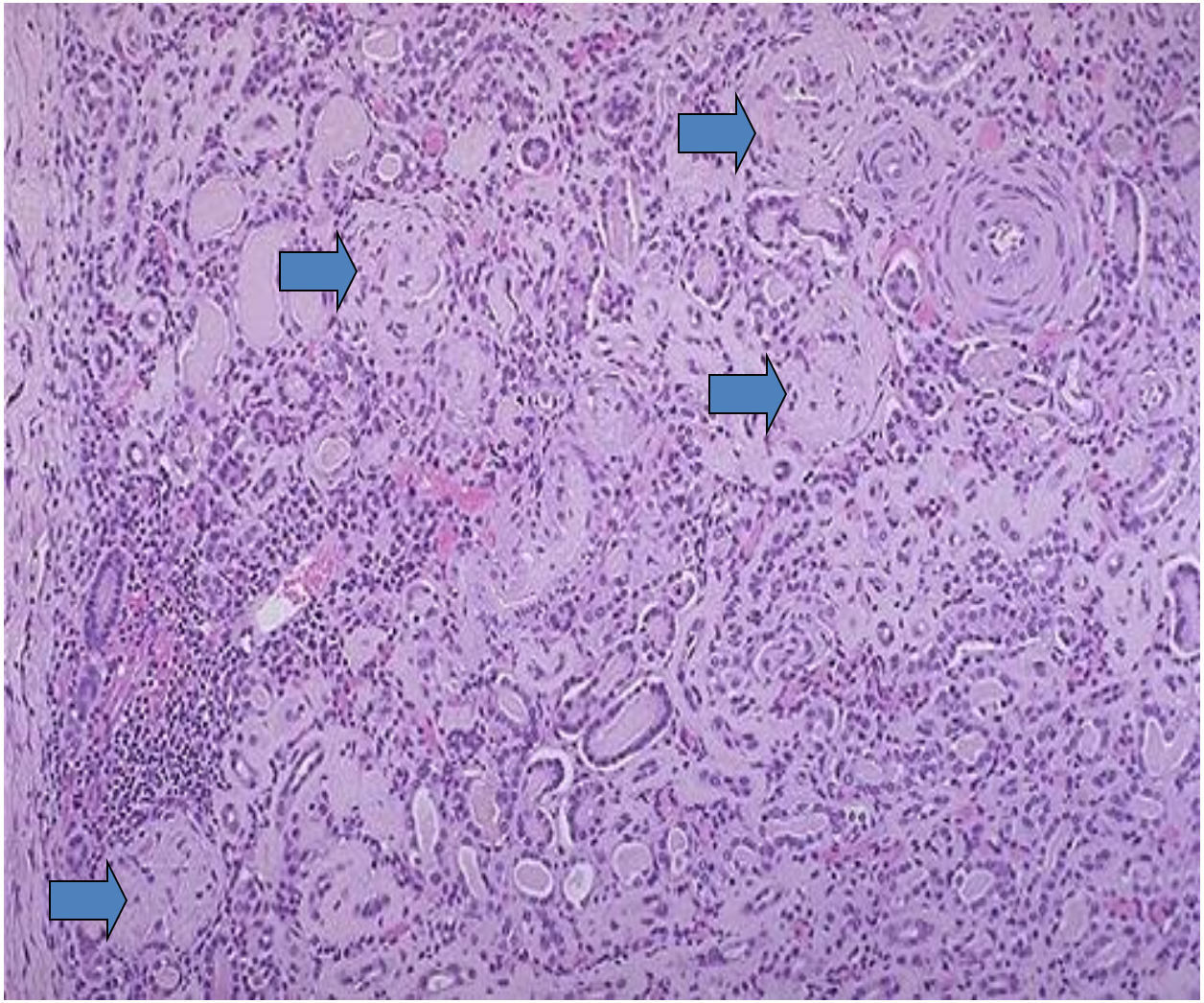
Fibrosis and patchy chronic inflammation



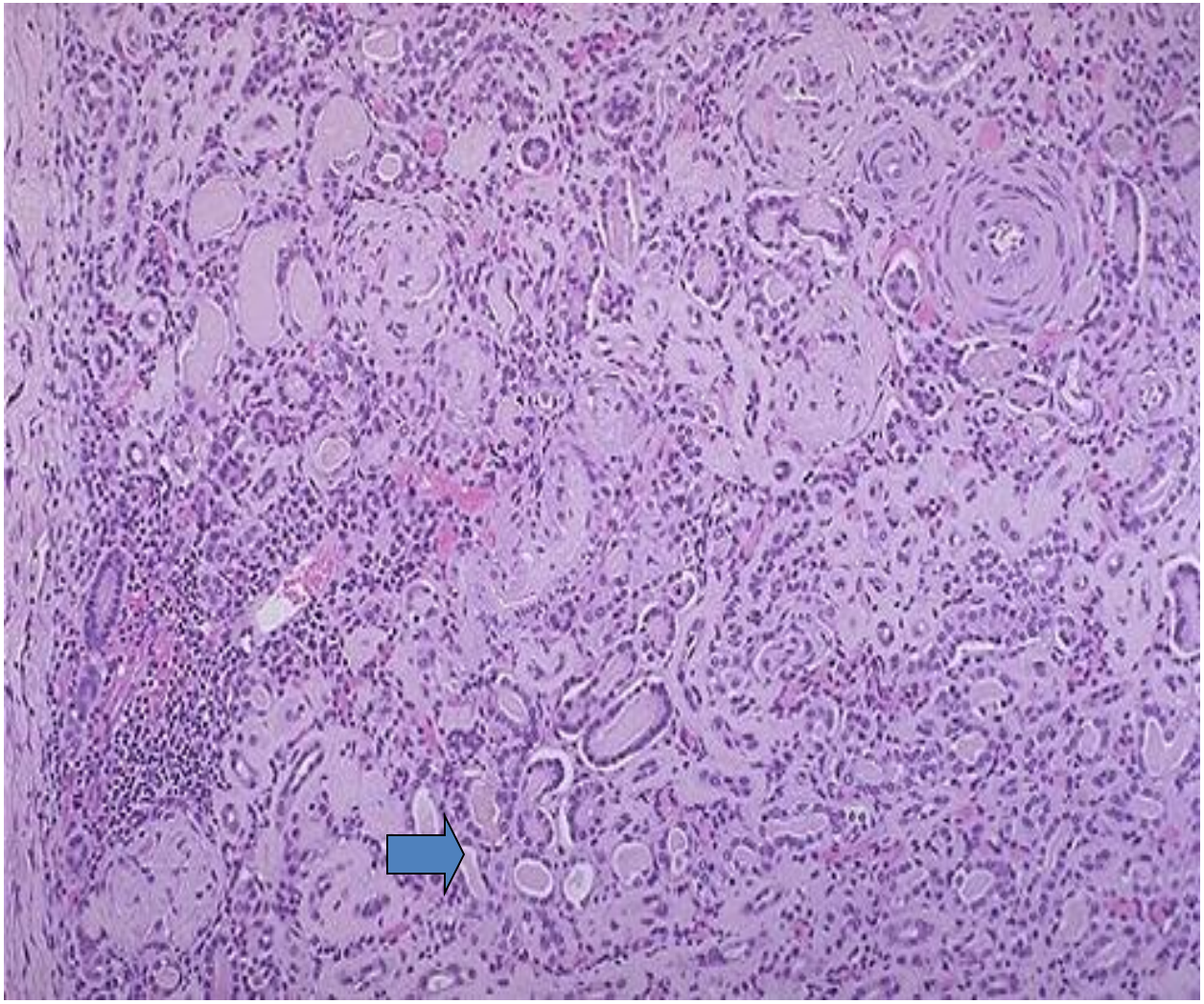
Transitional epithelium of normal renal pelvis

End stage kidney disease Microscopy

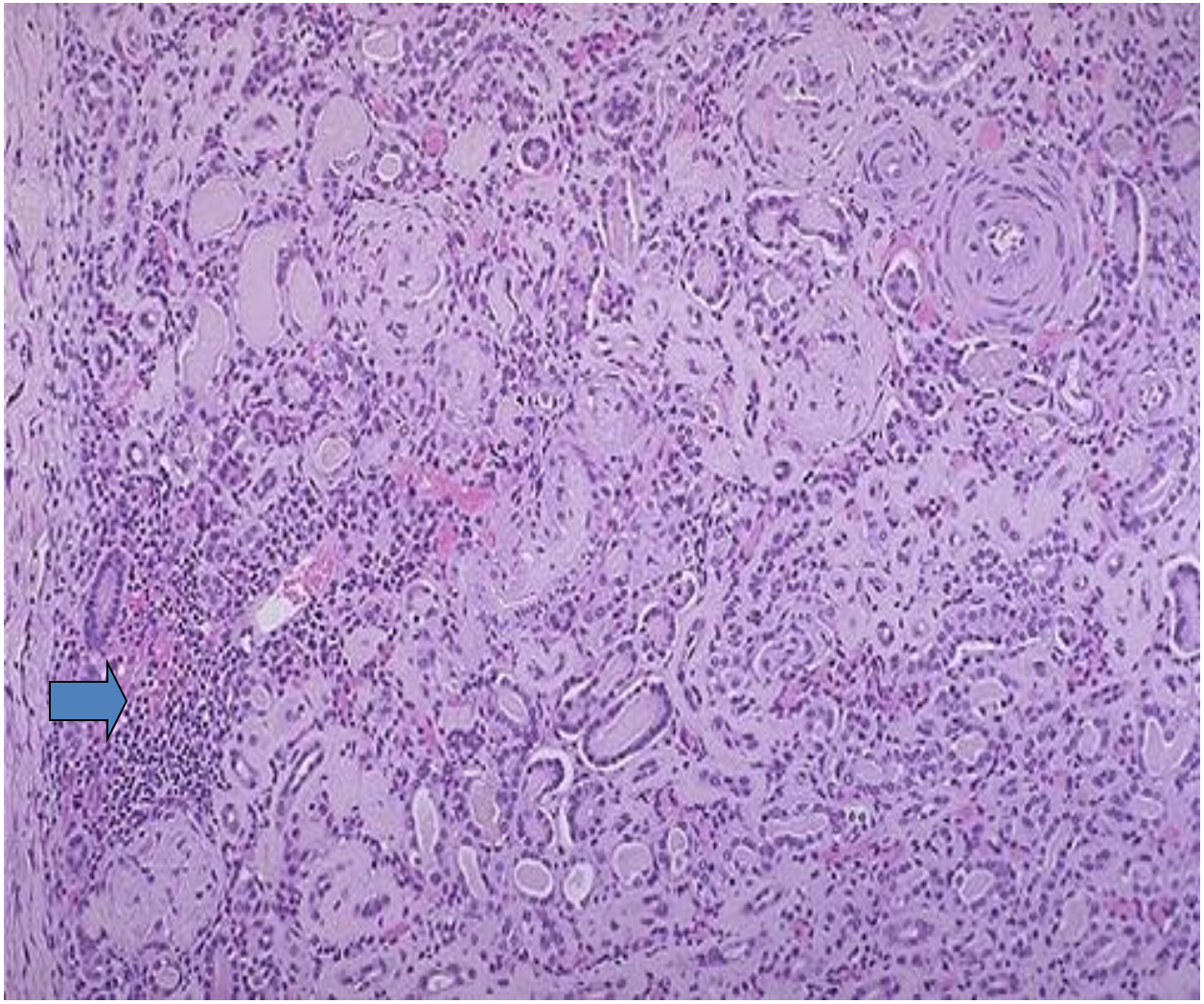
Diffuse glomerular sclerosis



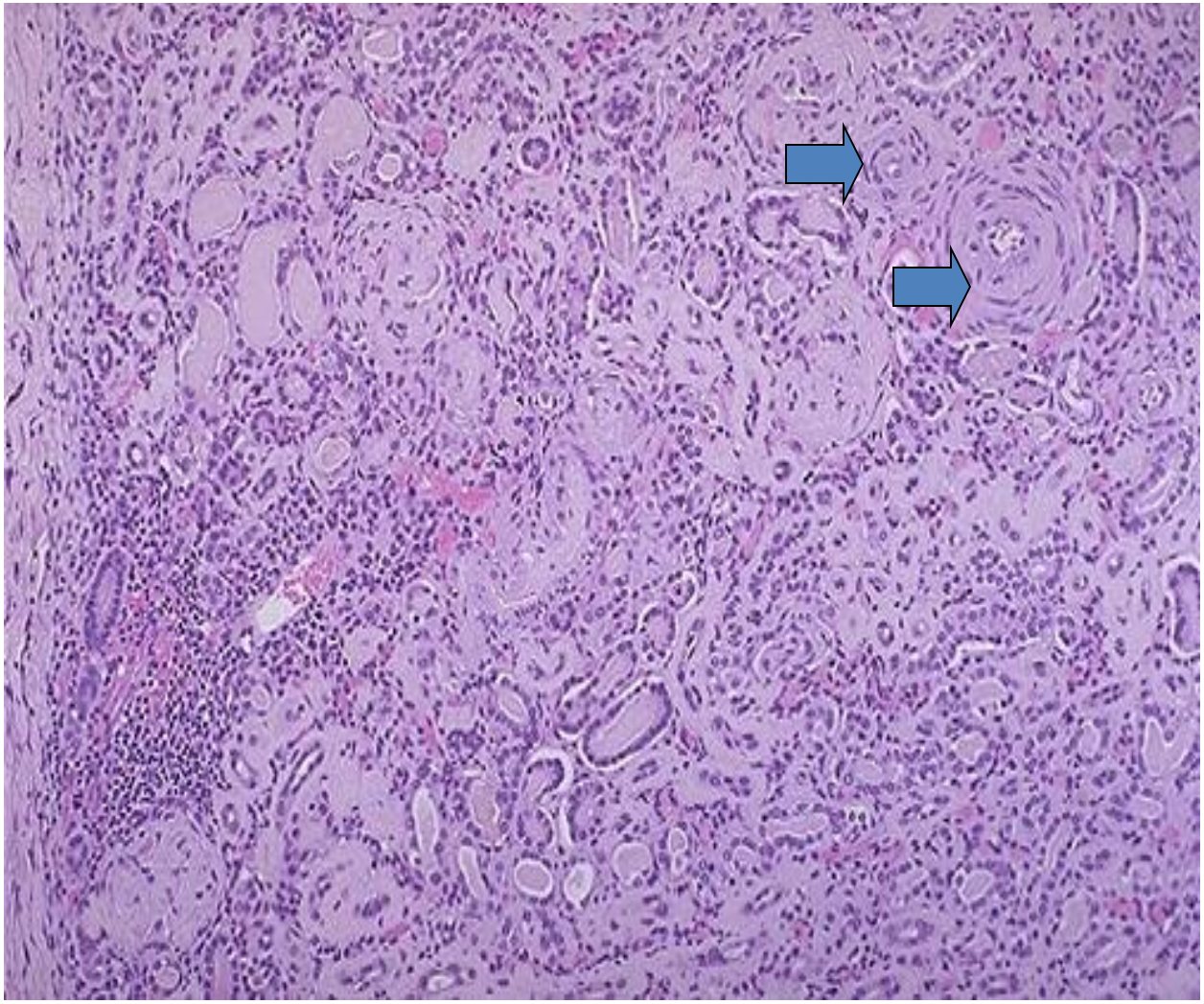
Tubular atrophy and “thyroidization”



Interstitial inflammtion



Vascular changes



Place of renal biopsy in CKD

- In advanced chronic stage it is difficult to determined the underlying primary nephropathology
- But attempts should be always made to identify it as it will influence the outcome of transplantation.

  eg. recurrent diseases will affect the

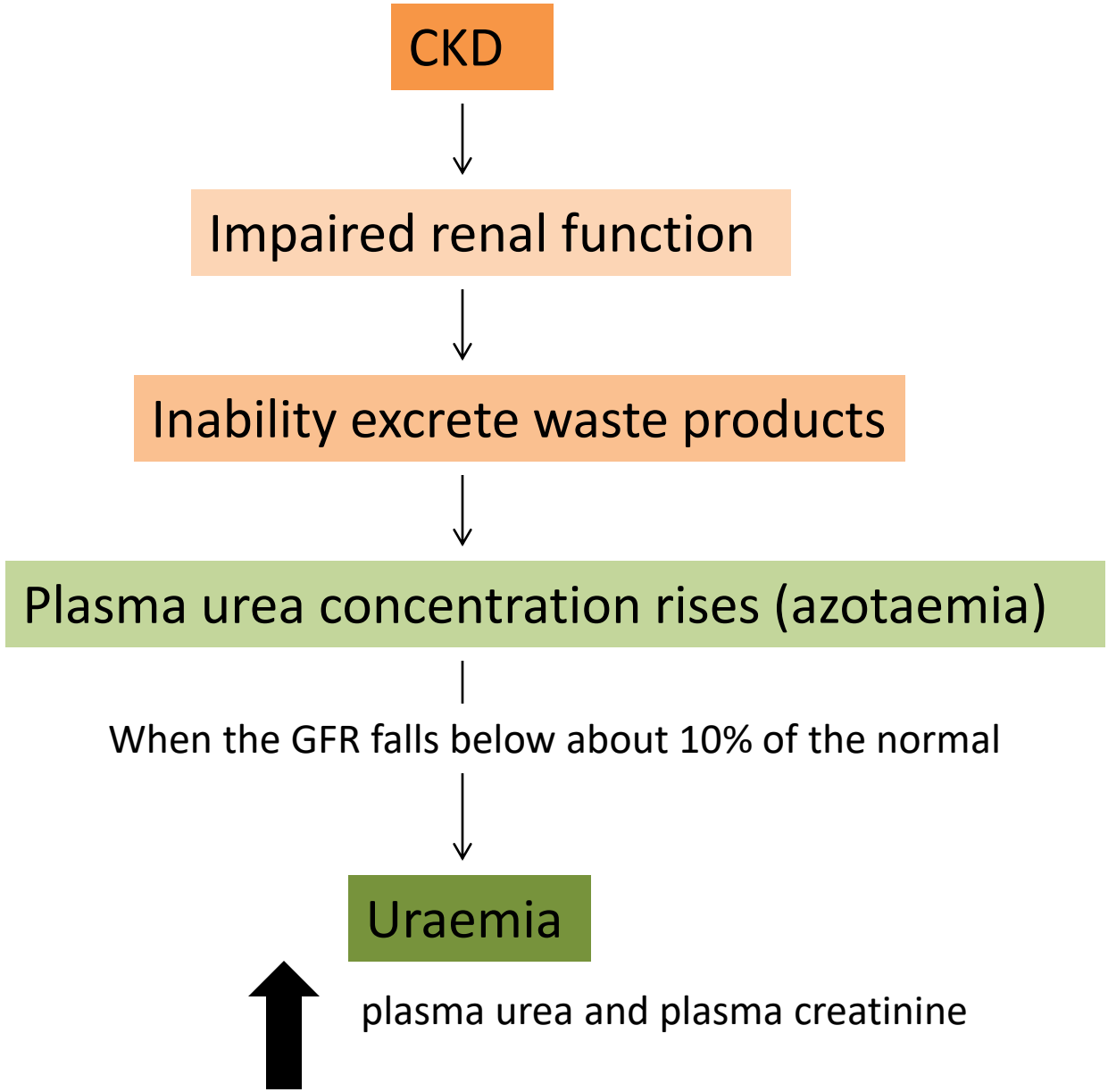
  transplanted kidney as well

CKD - Objectives

At the end of this lecture, you should be able to

- List the causes of CKD
- Describe briefly the pathophysiology of CKD
- Describe the macroscopic and microscopic changes of the kidney in CKD
- Briefly describe the extra renal manifestations of CKD

CKD - Extra-renal manifestations



Some of the extra-renal manifestations are related to uraemia

CKD - Cardiovascular complications

- Hypertension - a frequent complication
- Dyslipidaemia - Atheroma
- Cardiomegaly
- Diastolic dysfunction – Attributable to left ventricular hypertrophy
- Systolic dysfunction may be due to
  - myocardial fibrosis
  - Abnormal myocyte function due to uraemia
  - Calcium overload and hyperparathyroidism

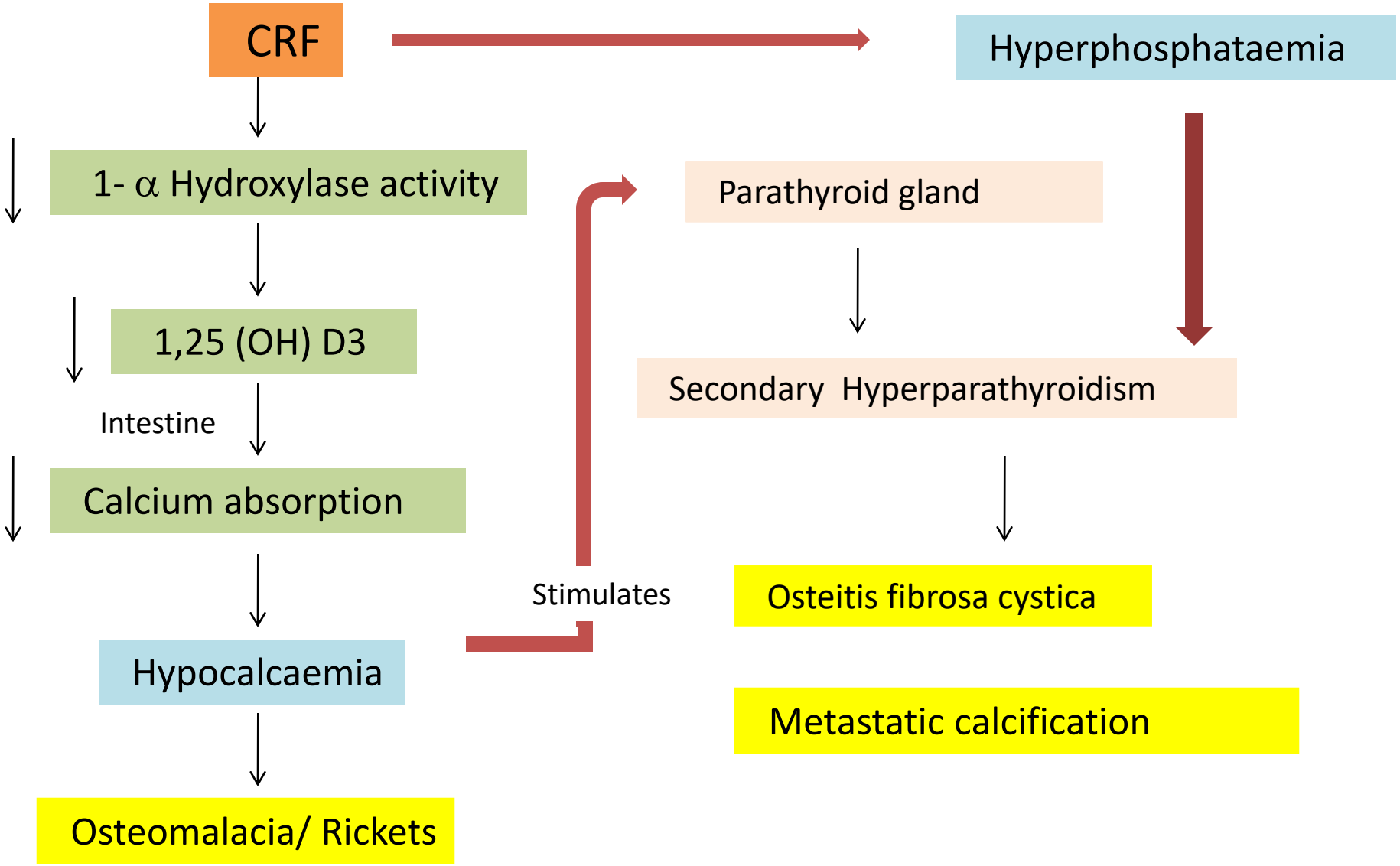
- Calcifications of the myocardium

  May involve AV node and conduction bundles
- Coronary artery calcification
- Pericarditis

Bone

Renal osteodystrophy/ bone mineral disorder

- A collective term which includes
  - hyperparathyroid bone diseases
  - Osteomalacia / rickets
  - Osteoporosis
  - Osteosclerosis
- Associated with uraemia
- Not specific for CKD


CRF
Hyperphosphataemia
1- α Hydroxylase activity
Parathyroid gland
1,25 (OH) D3
Secondary Hyperparathyroidism
Intestine
Calcium absorption
Stimulates
Osteitis fibrosa cystica
Hypocalcaemia
Metastatic calcification
Osteomalacia/ Rickets

Hematological changes

- **Anaemia**

  - Reduced erythropoetin production by diseased kidney
  - Bone ,marrow toxicity by retained waste products
  - Increased RBC destruction due to membrane abnormalities
  - Blood loss
    - Occult bleeding from GI tract
    - Haemodialysis
    - Platelet dysfunction

- **Immunologic abnormalities**
  - Uraemia causes suppression of both cell mediated and humoral immunity
  - Variable degree of immunodeficiency, predisposes to infection
- **GI Tract**
  - Uraemic oesophagitis, gastritis, duodenitis
  - Peptic ulceration
- **Neuromuscular abnormalities**
  - Peripheral neuropathy
  - Poor concentration

  But structural changes are not identified in the brain

CKD - Summary

Now you should be able to

- List the causes of CKD
- Describe briefly the pathophysiology of CKD
- Describe the macroscopic and microscopic changes of the kidney in CKD
- Briefly describe the extra renal manifestations of CKD

Reading assignment

- Progression of CKD
- Extrarenal mainifestations / complications of CKD

Reference :Kumar and Clark’s Clinical Medicine