# KIDNEY - 4

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# CHRONIC GLOMERULONEPHRITIS

- End stage glomerular disease. By the time CGN is discovered in middle aged adults, it is difficult to discern the nature of original lesion.
- MORPHOLOGY-Kidneys are symmetrically contracted, having diffusely granular cortical surfaces.
- On C/S: Cortex is thinned out and increase in peripelvic fat.

# Kidneys and aorta, C.G.N. - Gross

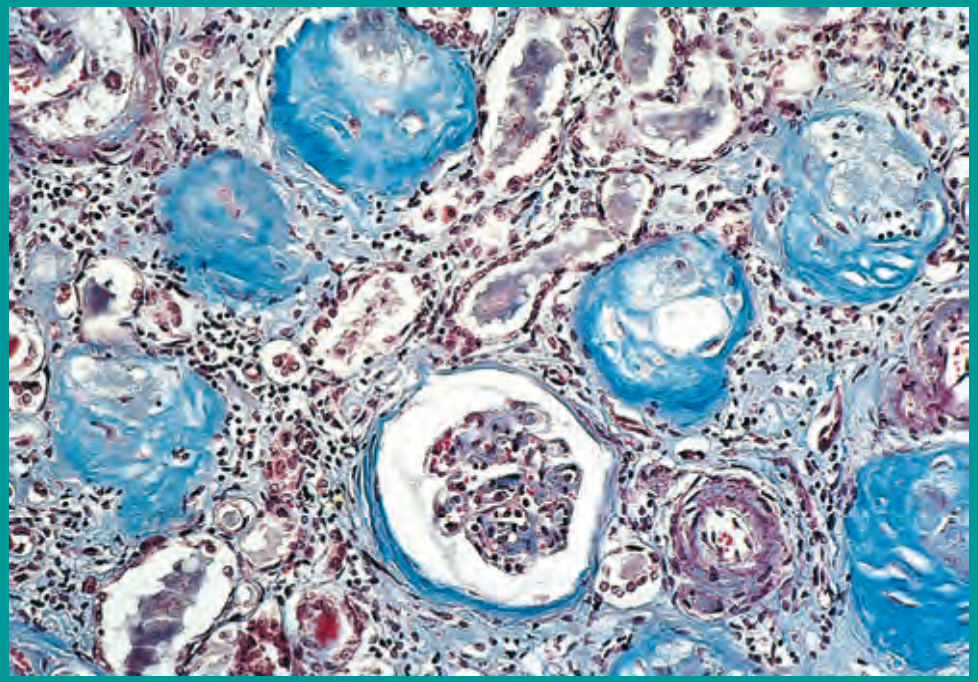

Ref: https://www.slideshare.net/benishajulian/chronic-glomerulonephritis-51301804

- Areas of atrophy and scarring with retraction alternating with normal areas. This produces the finely granular appearance of the kidneys, as the retracted scar tissue accentuates the preserved areas

# Microscopy of CGN

- Glomeruli may show e/o primary disease in early stages. Later on there is **hyaline obliteration of glomeruli** transforming them in to acellular eosinophilic masses.
- Hyaline represents combinations of trapped plasma proteins, increase mesangial matrix, basement membrane like material and collagen.
- Arterial or arteriolar sclerosis is seen.
- Marked atrophy of tubules.
- Irregular interstitial fibrosis and lymphocytic infiltration.

# Kidney, Chronic Glomerulonephritis



Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:925

- Masson trichrome preparation shows complete replacement of virtually all glomeruli by blue-staining collagen.

- **Dialysis changes** - Arterial intimal thickening by accumulation of smooth muscle like cells, calcium deposition in tubules and interstitium, acquired cystic diseases, renal adenoma and borderline adenocarcinoma, amyloidosis (beta 2 microglobulin is retained in circulation and deposited in synovium, joints and tendon sheath in 60-80% cases).

- If patients are not on dialysis or tranplant, outcome is invariably death during span of years.

# Chronic Pyelonephritis

## Def: Tubulointerstitial disorder

- Chronic pyelonephritis is defined as a morphologic entity in which predominantly interstitial inflammation and scarring of the renal parenchyma is associated with grossly visible scarring and deformity of the pelvicalyceal system.
- Chronic pyelonephritis is an important cause of chronic renal failure (10-20%).

# Etiopathogenesis

- It can be divided into two forms:

a) chronic obstructive pyelonephritis

b) chronic reflux-associated pyelonephritis.

# a) Chronic Obstructive Pyelonephritis

- Obstruction predisposes the kidney to infection.
- Recurrent infections superimposed on diffuse or localized obstructive lesions lead to recurrent bouts of renal inflammation and scarring, which eventually cause chronic pyelonephritis.
- Bilateral-- as with congenital anomalies of the urethra (posterior urethral valves)
- Unilateral-- calculi and unilateral obstructive lesions of the ureter.

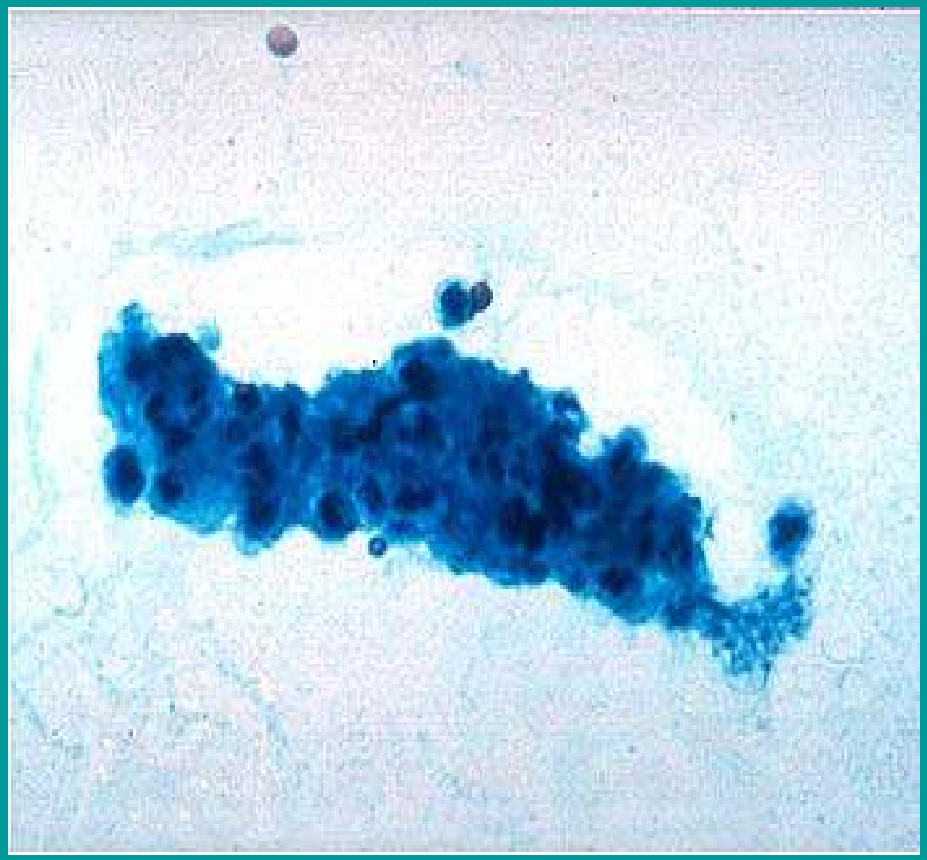
# b) Chronic Reflux-Associated Pyelonephritis (Reflux Nephropathy)

- More common form
- Results from superimposition of a UTI on congenital vesicoureteral reflux and intrarenal reflux.
- Reflux may be unilateral or bilateral & may affect one / both kidneys

# CHRONIC PYLONEPHRITIS

- Kidneys are irregularly scarred, asymetric involvement. Corticomedullary scars overlying dilated and blunted calyx.
- Glomeruli usually appears normal except for periglomerular fibrosis. Tubular atrophy, some dilated tubules filled with colloid casts(thyroidization),varing degree of interstitial inflammation and fibrosis.

# White blood cell (WBC) cast, Papanicolaou stain - High power



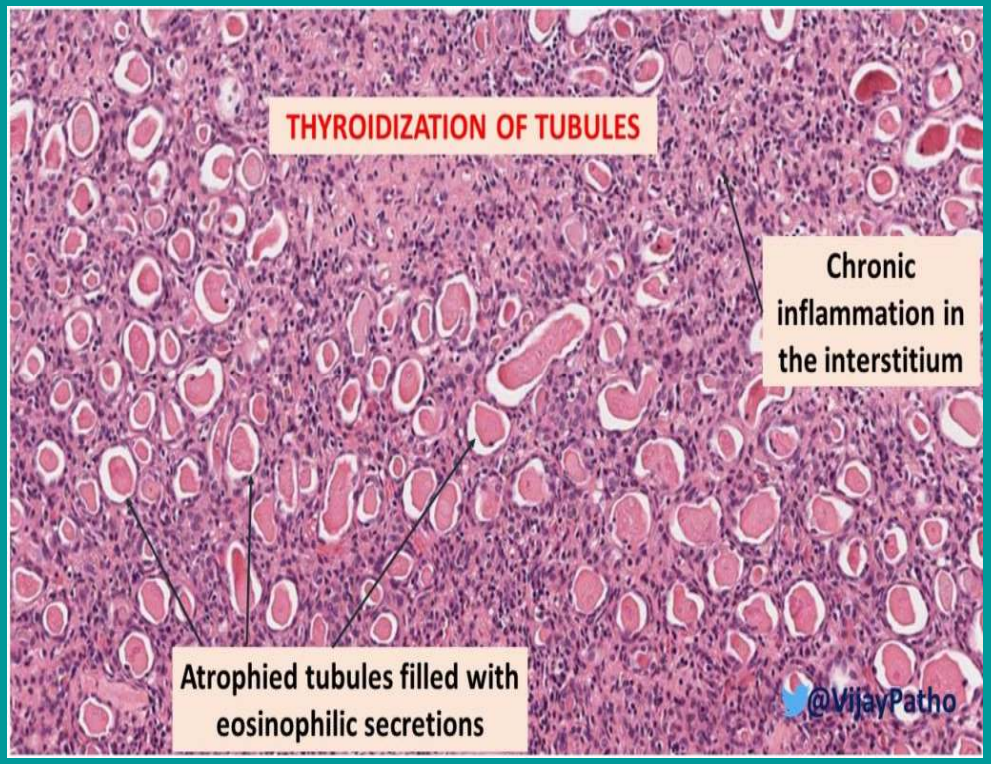
- Numerous neutrophils and degenerating epithelial cells are held together in a cylindrical cast by proteinaceous material.

# Kidney, chronic pyelonephritis - Gross


Ref: https://www.slideshare.net/LayaPillai/chronic-pyelonephritis-62970745

- The surface of the kidney is irregularly, depressed in the scarred areas with pseudobulging of the remaining intact parenchyma. Chronic pyelonephritis can affect both kidneys simultaneously; however, the scarring is asymmetrical. The cut surface would reveal dilated, blunted, or deformed calyces.

# Kidney, chronic pyelonephritis Medium power




- Many dilated "colloid"-filled tubules are present. This phenomenon is known, appropriately enough, as thyroidization of the kidney.

Ref: http://ilovepathology.com/chronic-pyelonephritis/

# Xantho Granulomatous Pylonephritis

- Unusual and rare form of CPN.
- Gross-Large yellowish orange nodules are present,mimicing RCC.
- Microscopy: Characterized by accumulation predominantly of foamy macrophages with plasma cells, lymphocytes and neutrophils.Giant cells are seen.
- Often associated with proteus infection.

# DIABETIC GLOMERULOSCLEROSIS

- Major cause of renal morbidity and mortality, leading cause of chronic renal failure.
- Occurs usually 12-22 yrs after clinical appearance of type 1 D.M, progressive CRF and death within a period of 4-5 yrs.
- Presented clinically as non nephrotic proteinuria, nephrotic syndrome or CRF.
- causes glomerular, tubular and vascular lesions. Arteriolar sclerosis, pylonephritis and papillary necrosis are common.

# PATHOGENESIS

- Caused by metabolic defect (insulin deficiency hyperglycemia / glucose intolerance)
- Linked to generalized microangiopathy.
- Nonenzymatic glycosylation of protein is known to occur in diabetics giving rise to advanced glycosylation end products, contribute to glomerulopathy.(process by which glucose chemically attaches to amino group of protein without the aid of enzymes, forms reversible Schiff base that may rearrange to form more stable amadori type reversible products that under go chemical rearrangement to form irreversible advanced glycosylation end products)

- Biochemical alterations in GBM include increase amount and synthesis of collagen type 4 and fibronectin with decreased synthesis of proteoglycan heparan sulphate causes basement membrane thickening and increase mesangial matrix.

- Hemodynamic changes like increase GFR, glomerular capillary pressure and glomerular hypertrophy are responsible for initiation and progression of diabetic glomerulosclerosis.

# MORPHOLOGY

- *1.Capillary basement membrane* thickening - Occurs in all diabetics because of diabetic microangiopathy.GBM thickening continues progressively with concurrent mesangial widening.

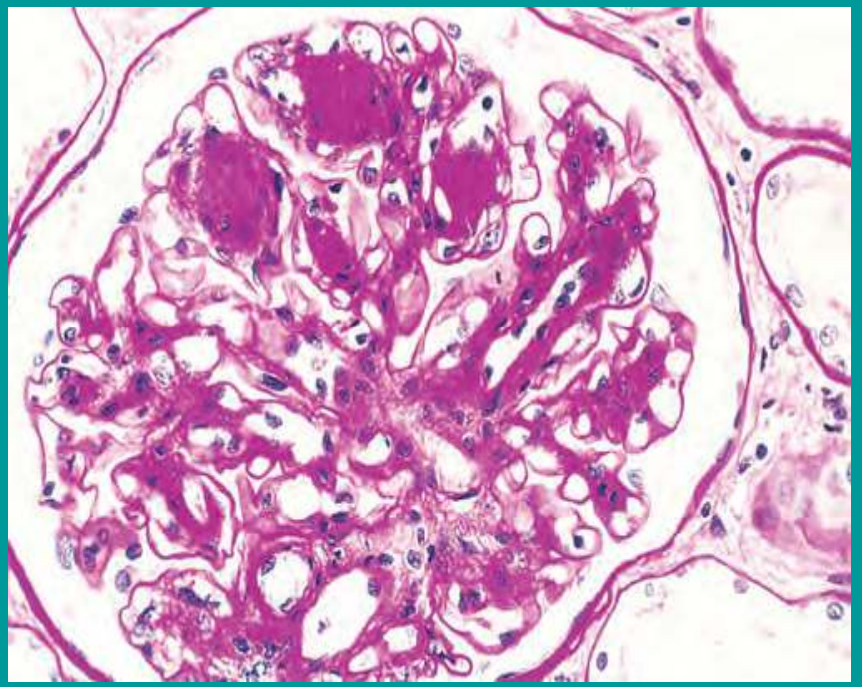
- *2.Diffuse glomerulosclerosis* -Appears 10-20 yrs. of DM, diffuse increase in mesangial matrix with mild proliferation of mesangial cells. With the advancement, mesangial areas expand further filling the entire glomerulus

  (obliterating diabetic GS)

- **3. Nodular glomerulosclerosis ;**
  **( Kimmelstiel Wilson disease.)**
- Ovoid or spherical often laminated hyaline masses situated in periphery of glomeruli within mesangial core of glomerular lobules often surrounded by peripheral patent capillary loops. As the disease advances, nodules enlarge ultimately obliterating the glomerular tuft.
- Although diffuse and nodular GS are similar lesions of mesangium, nodular GS is pathognomonic of DM. Often accompanied by Fibrin Caps & Capsular Drops
- Kidney suffers from ischemia, develops tubular atrophy, interstititial fibrosis and over all contraction in size

# Diffuse and Nodular diabetic glomerulosclerosis (PAS stain).

- Diffuse increase in mesangial matrix and characteristic acellular PAS-positive nodules.



Ref- Robbins and Cotran: Pathologic basis of disease: South Asia Edition, Pg:1118

# Laboratory diagnosis

- Microalbuminuria (urine alb-30-300 mg/day or 20-200 microgram/min) and increase GFR are important predictors of future diabetic nephropathy. Detected by nephelometry, RIA or HPLC.
- 10-15yrs after the onset of DM,stage of microalbuminuria appears. Rigorous control of b.glucose,B.P.or use of ACE inhibitors can prevent or even reverse the progression towards RF.Once the stage of macroalbuminuria (dip stick positive)develops,even meticulous sugar control is unlikely to prevent progression to RF.

# CHRONIC RENAL FAILURE (UREMIA)

- CRF is characterized by prolonged signs and symptoms of uremia.
- STAGES-

(1) Diminished renal reserve - GFR 50% of normal, asymptomatic patients are more susceptible to azotemia.

(2) Renal insufficiency - GFR 20-50% of N , azotemia, anemia and H.T, sudden stress may precipitate uremia.

(3) Renal failure - GFR less than 20%,overt uremia.

(4) End stage renal failure - GFR less than 5% of N, terminal stage of uremia.

## Calcium , phosphate & bone metabolism

- Serum phosphate levels rise when the glomerular filtration rate (GFR) falls to < 25%. This enhances calcium entry into bone, causing hypocalcemia. Hypocalcemia stimulates the parathyroid glands to undergo hyperplasia and secrete PTH, as they try to increase the serum calcium level by releasing it from bone. This cycle leads to renal osteodystrophy.

# CRF

- Renal osteodystrophy- Impaired bone growth in children and spontaneous fractures in adults.
- Dermatologic changes- Sallow colour of skin and itching because of accumulation of urinary pigment;urochrome in skin.
- Neuromuscular disturbances-

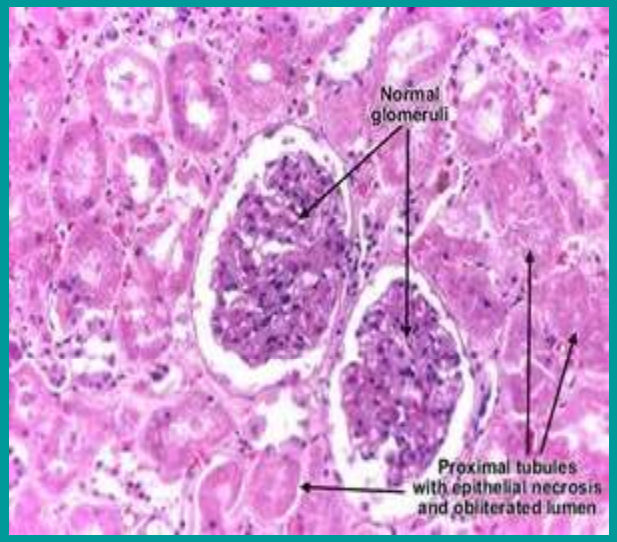
  Myopathy, encephalopathy and peripheral neuropathy leading to seizures, stupor and coma are common in terminal stage.

# ACUTE RENAL FAILURE

- Implies rapid and frequently reversible deterioration of renal function.
- Causes- Vascular obstruction (PAN,HUS…)
  -Severe glomerular disease as RPGN
  -Acute tubulointerstitial nephritis (drug)
  -Massive infection
  -DIC with cortical necrosis
  -Urinary obstruction by tumors

Acute tubular necrosis- tubular epithelial cells become totally necrotic and desquamated within the lumen. Interstitial inflammation, and evidence of epithelial regeneration are seen.

# Kidney, acute tubular necrosis (ATN) due to shock




Ref: https://www.pinterest.com/pin/471048442249162164/

- The glomeruli are normal.. Several of the proximal tubules show necrosis of the epithelium. In these tubules, the normal cuboidal epithelium has been replaced by eosinophilic, structureless debris in which cellular outlines as well as the nuclei are obscured. These tubules may be compared with normal (uninjured) tubules, which have a well-preserved layer of epithelial cells that show distinct nuclei.

# Thank You