

Involvement of kidney in some systemic diseases

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At the end of this lecture the students will be able to

- Describe the pathogenesis and pathology of renal involvement in following diseases
 - Diabetes mellitus
 - Amyloidosis
 - SLE in brief
 - Multiple myeloma



The kidneys are affected in many systemic diseases with different pathogenesis

- Systemic hypertension
- Vasculitides
 - Wegener granulomatosis(WG), Microscopic polyangitis, Goodpasture syndrome (GPS), PAN
- Immunologically mediate diseases
 - Infective endocarditis
 - SLE
 - Amyloidosis
- Metabolic
 - Diabetes mellitus
- Neoplastic
 - Multiple myeloma (MM)

The renal manifestations in these could be different

- Nephrotic syndrome – DM, SLE, amyloid ,MM
 - Nephritic syndrome – SLE
 - Isolated haematuria /isolated proteinuria –GPS, PAN, SLE, MM, amyloidosis, hypertension
 - RPGN- GPS, WG
 - Chronic renal failure –DM, MM, Amyloidosis
- Sometimes the renal symptoms could be the first clinical manifestation of the disease

Involvement of kidney in some systemic diseases

We will discuss the renal involvement in

- Diabetes mellitus
- SLE in brief
- Multiple myeloma
- Amyloidosis
- You have already learnt about the renal involvement in,
 - Hypertension
 - GPS, WG, infective endocarditis

Read by your own on

- Renal involvement in
 - Polyarteritis nodosa (PAN)
 - Microscopic polyangitis
 - Systemic sclerosis
 - Haemolytic uraemic syndrome
- Pregnancy and renal disease



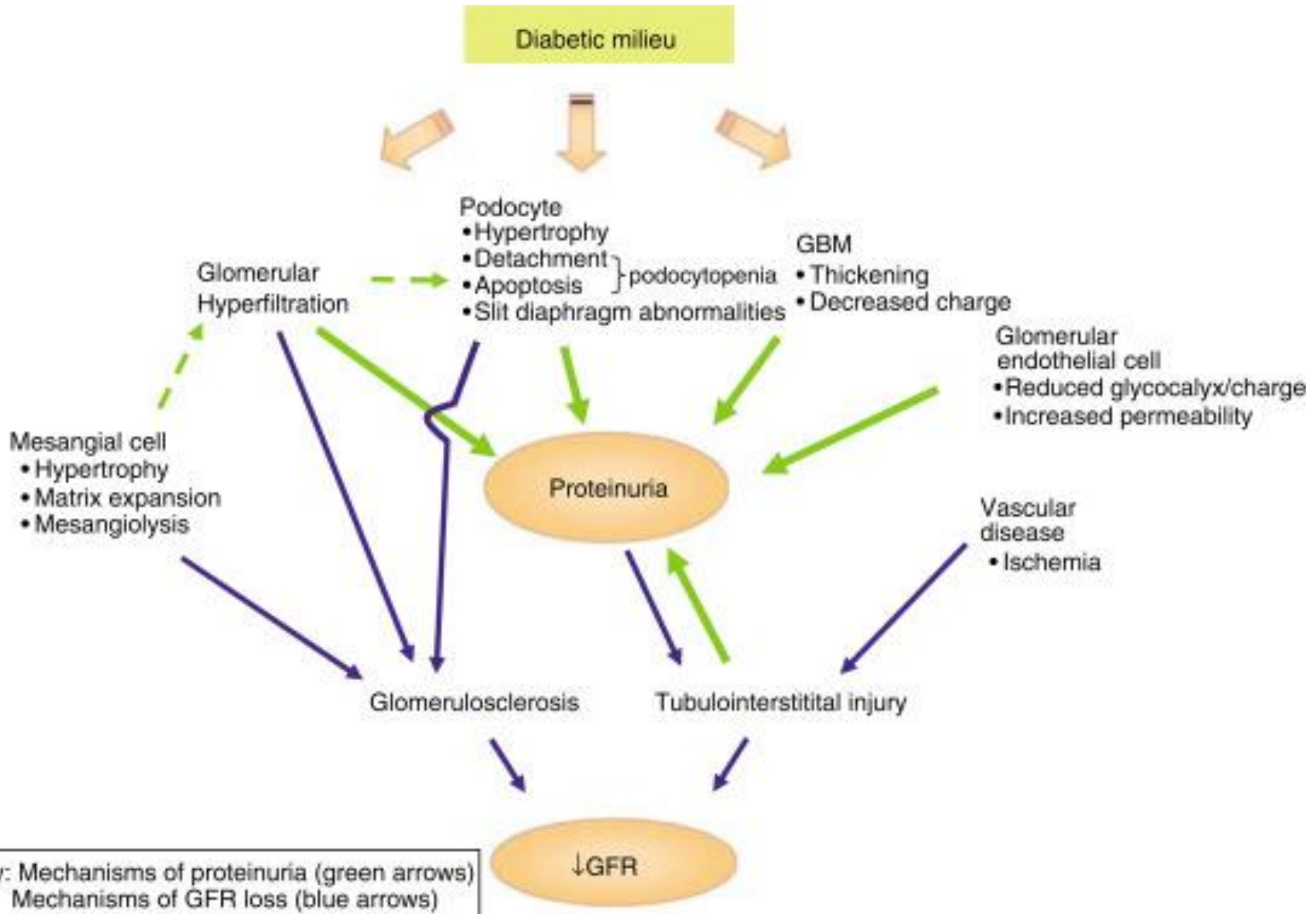
Diabetic Nephropathy

- A significant cause of advanced/ end-stage renal disease
- Occurs in both type 1 and type 2 DM
- Diabetic nephropathy is applied to a collection of lesions which include,
 - Glomerular compartment
 - Non-nephrotic proteinuria
 - Nephrotic syndrome
 - Chronic renal failure
 - Vascular compartment
 - Hyaline arteriolar sclerosis
 - Tubulo-interstitial compartment
 - Pyelonephritis and papillary necrosis

Diabetic nephropathy -pathogenesis

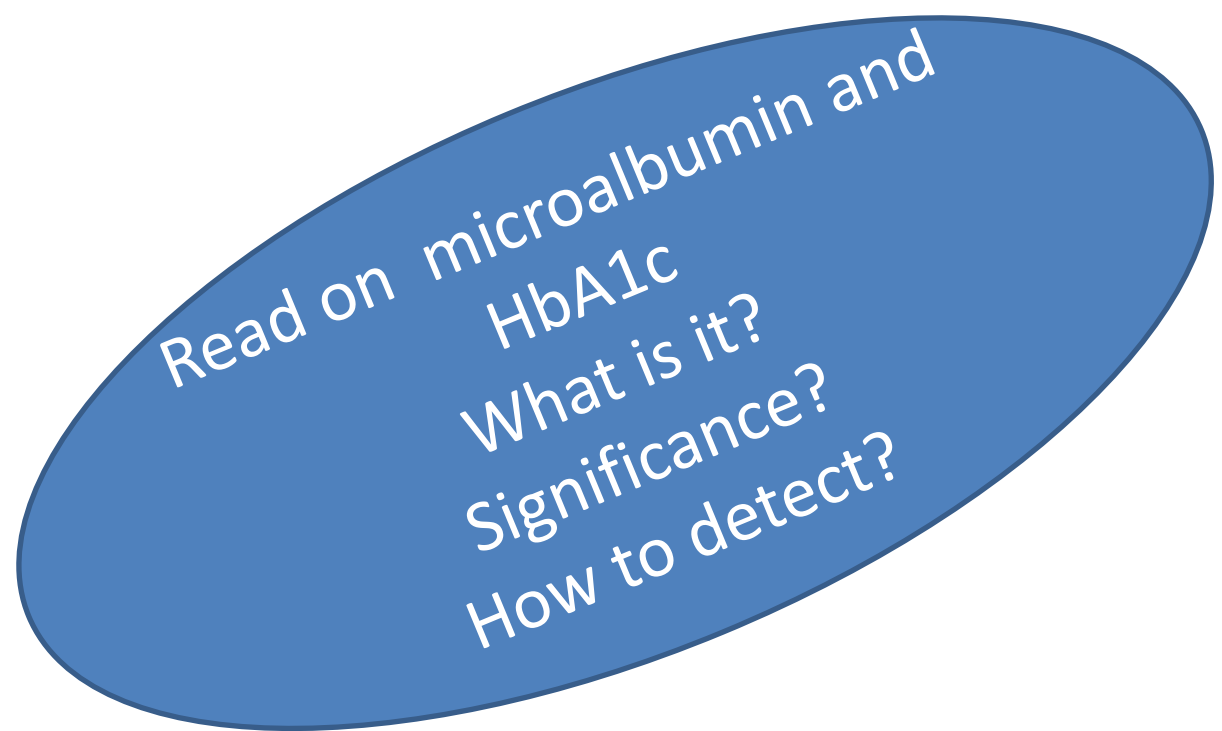
- Not fully understood
- Primary defect is a leaky basement membrane(BM)
- Glomerular hypertrophy
- Mesangial cell hypertrophy
- BM thickening
- Deficiency of proteoglycans in the BM causing altered charge

Diabetic nephropathy -pathogenesis



Diabetic nephropathy -mediators

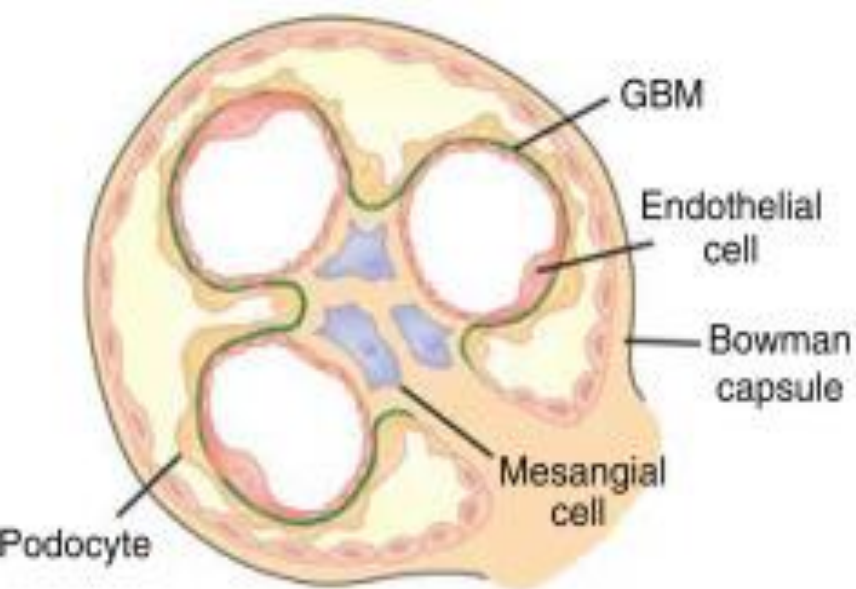
- Hyperglycaemia
- Hyperfiltration at glomeruli
- Non enzymatic glycosylation of proteins in BM
- Growth factors
- cytokines



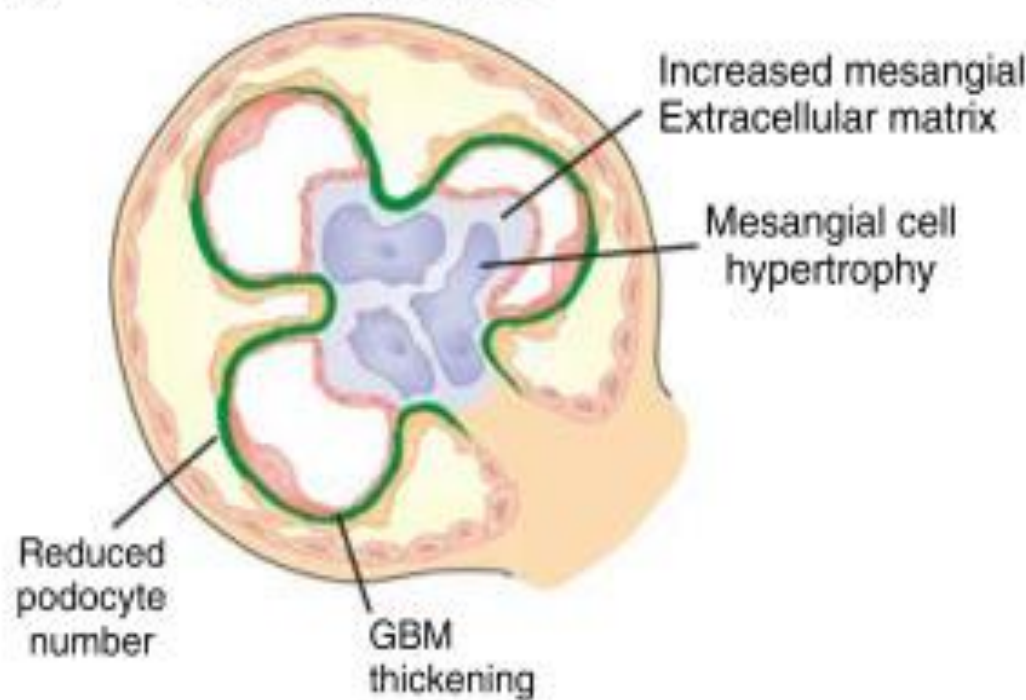
Diabetic glomerular lesions

- A manifestation of microangiopathy
- 3 important lesions
 - Capillary basement membrane thickening
 - Wide spread thickening of GBM
 - Leaky to plasma proteins
 - Diffuse mesangial sclerosis
 - Nodular glomerulosclerosis

a Normal glomerulus

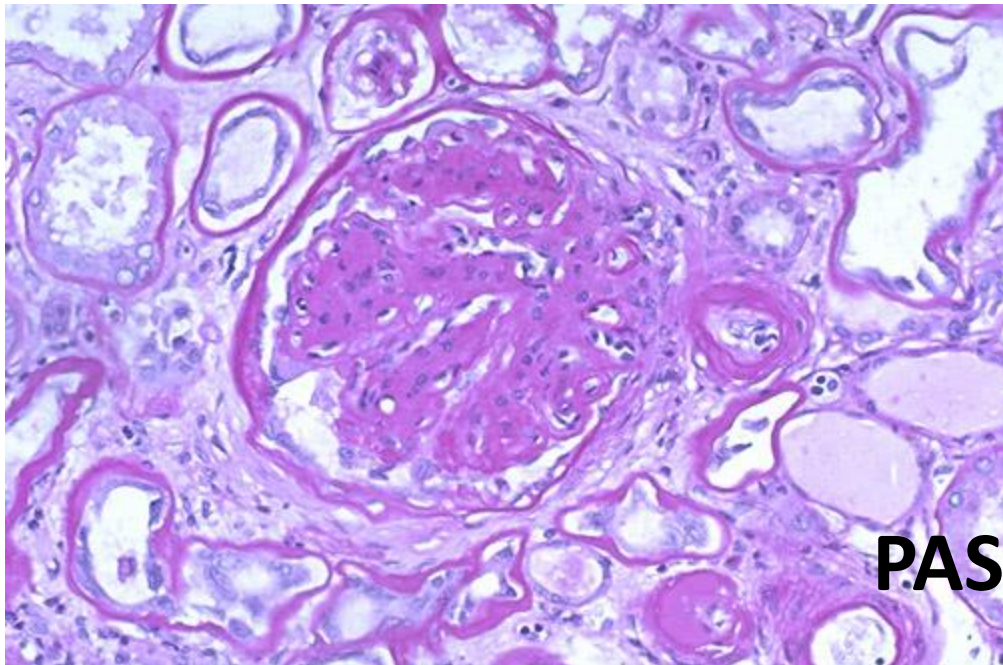


b Diabetic glomerulus



Diffuse mesangial sclerosis

- Diffuse increase of mesangial matrix
- The matrix depositions are PAS stain positive
- Associated with thickened GBM
- Mesangial cell proliferation is minimal

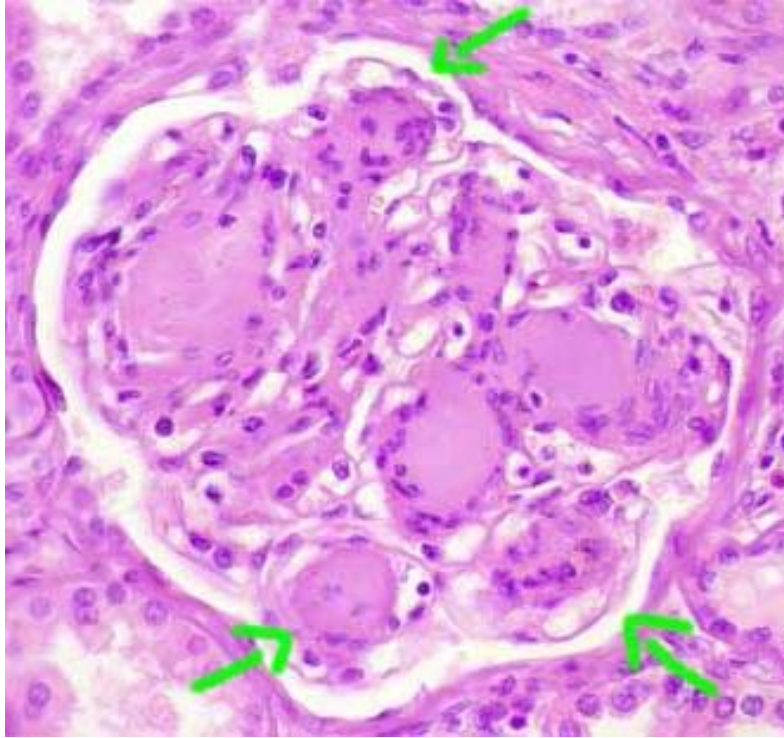


PAS stain

Nodular glomerulosclerosis

- Nodular expansion of the mesangial matrix
- Surrounded by patent peripheral capillary loops
- With disease progression –obliteration of the capillary tuft
- Called Kimmelstiel-Wilson lesion – characteristic of diabetic glomerulopathy

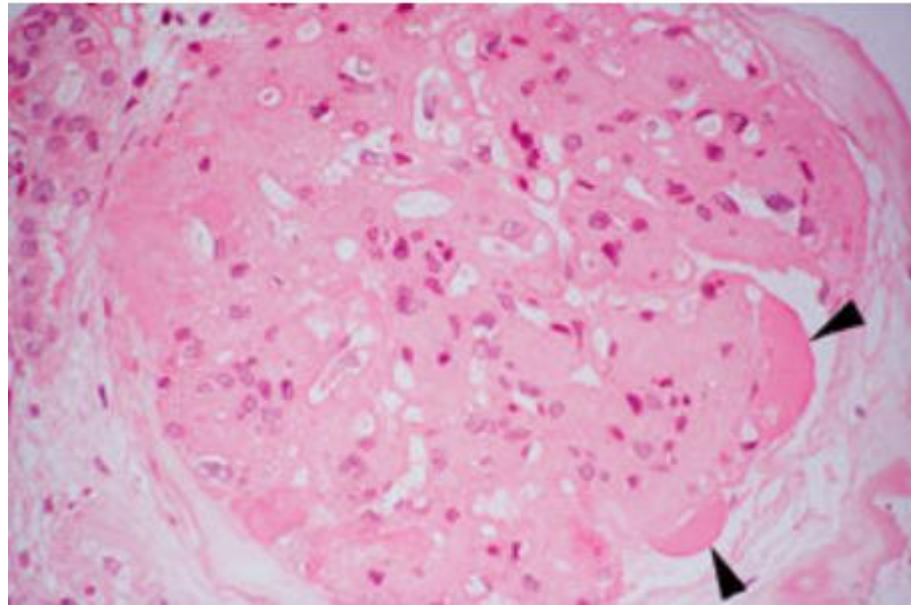
Nodular glomerulosclerosis - Kimmelstiel-Wilson lesion



- Kimmelstiel-Wilson Nodules highlighted with PAS stain;
- Glomerular nodules in amyloidosis and light chain deposit disease have a similar but more weak stain with PAS

Nodular glomerulosclerosis

- This is also accompanied by
- Accumulation of hyaline material at capillary loops-
"fibrin caps"



- -adhesion to bowman capsule-"capsular drops"

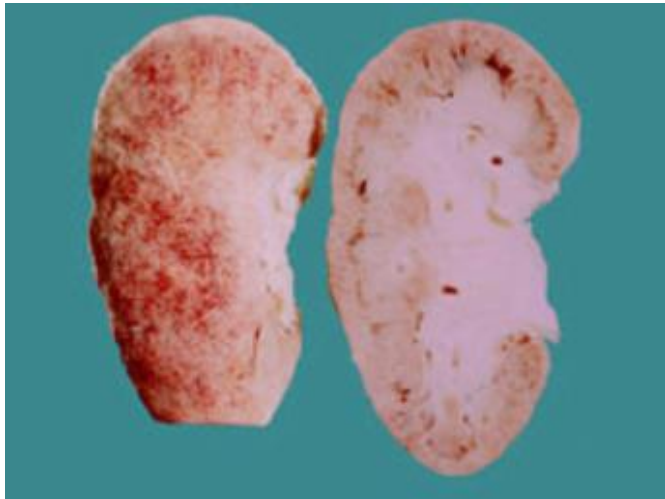
Pyelonephritis and Renal papillary necrosis



Read and refer the tubulo-interstitial diseases lecture

Diabetic nephropathy -macroscopy

What are the expected morphological changes in the kidneys of a diabetic patient?

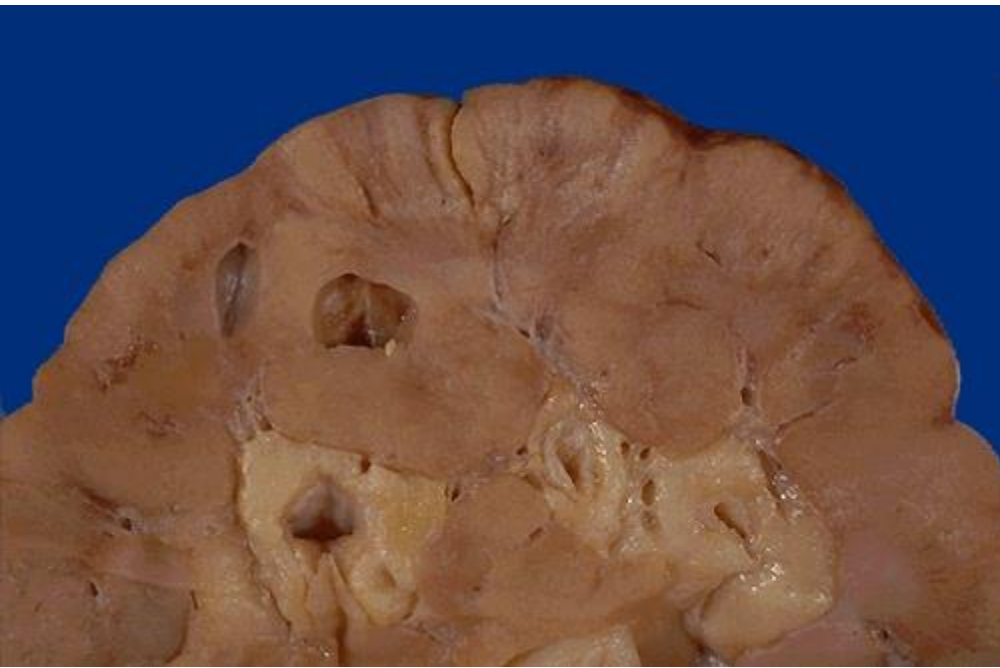


Renal Amyloidosis

- Kidneys are one of the most frequently involved organ in amyloidosis
- Presentation-proteinuria and nephrotic syndrome
- Deposition of amyloid proteins in glomerular mesangium
 - Along the capillary BM
 - As large nodules
 - **Differential diagnosis?**
- Amyloid is also deposited in BM of
 - Arterioles
 - Tubules

Renal Amyloidosis

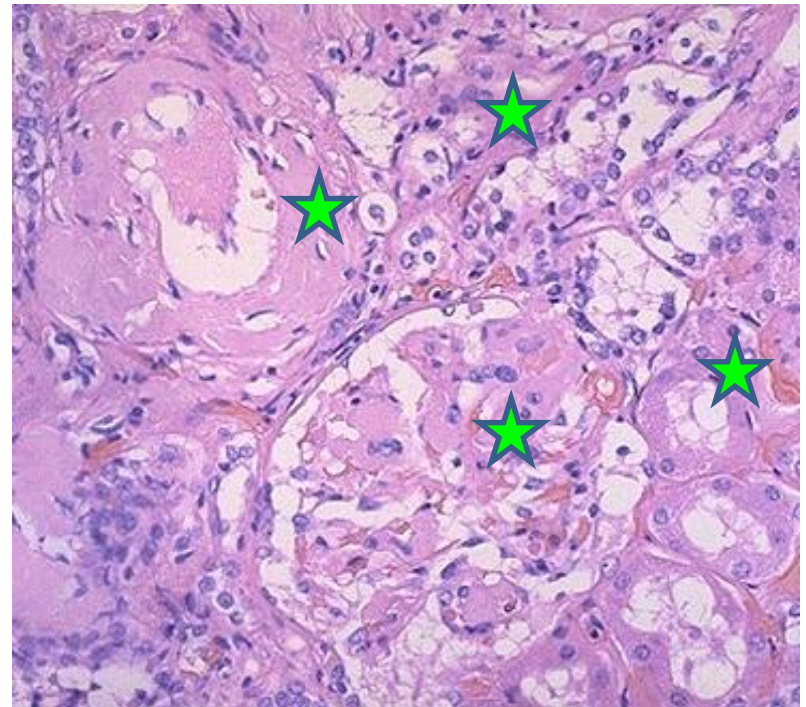
- The kidneys are enlarged
- Pale white nodular deposits in the cortex are due to amyloid.



The amorphous pink deposits

- around arteries,
- in interstitium,
- in glomeruli
- Tubular BM

➤ Confirmation with **Congo Red stain** and apple green birefringence under polarized light



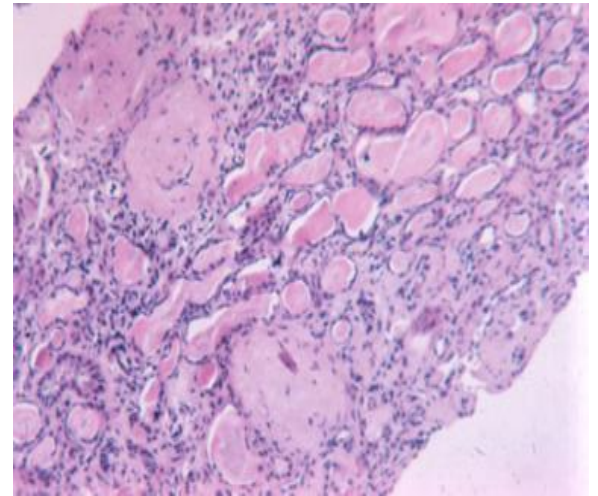
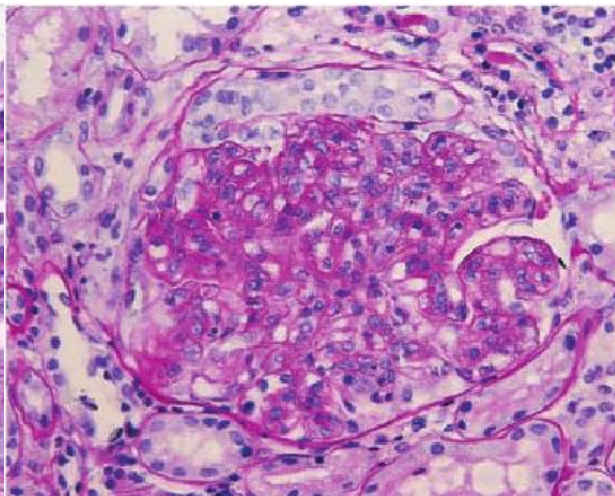
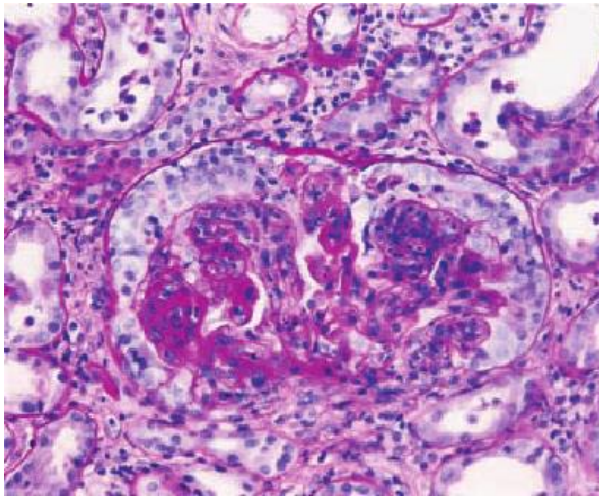
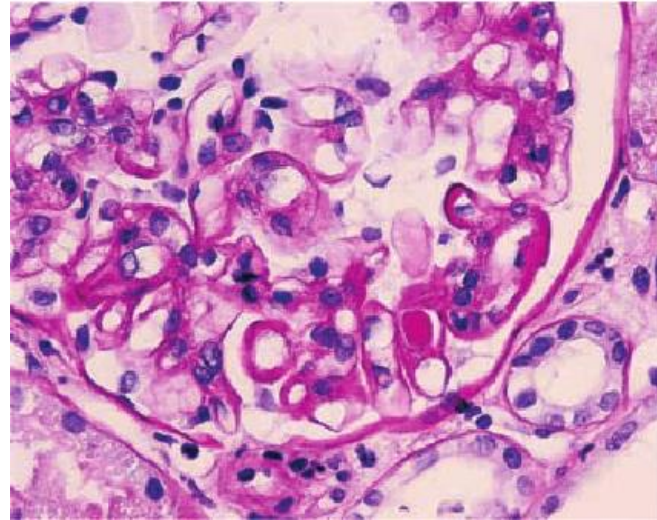
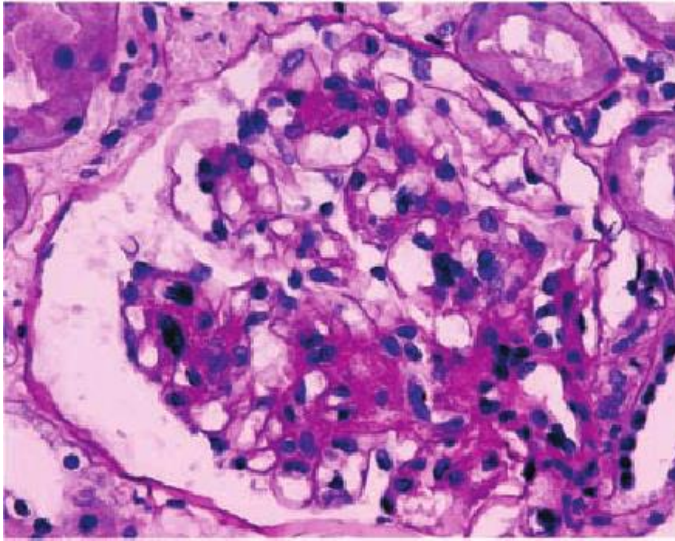
Renal involvement in SLE

- An autoimmune disease affecting mainly young females
- About 70% of SLE patients develop significant renal disease
- Carries a bad prognosis
- Renal manifestations
 - Nephritic syndrome
 - Nephrotic syndrome
 - Haematuria
 - Proteinuria
- Essential changes are in the glomeruli-a great variety of lesions

Lupus nephritis-common glomerular lesions

- Mesangial and endothelial cell proliferation
- “Wire loop” like capillary wall thickening
- Fibrinoid necrosis of capillaries
- Intra-capillary hyaline thrombi
- Deposition of immune complexes
- Glomerular scarring

Lupus nephritis-common glomerular lesions



Lupus Nephritis-WHO classification

- On the basis of glomerular morphology (LM, EM,IF)

WHO recognized following groups

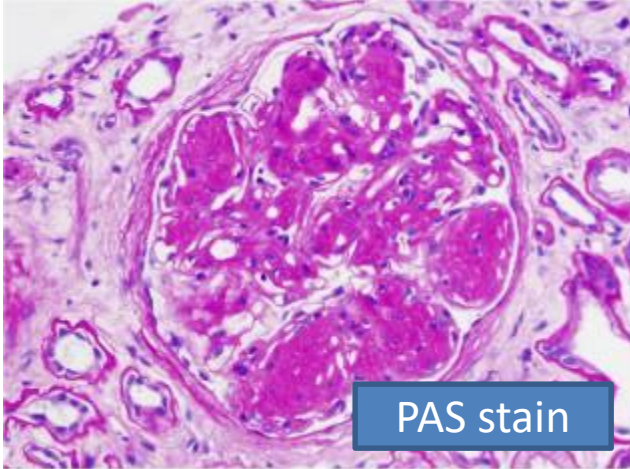
Class 1	No lesions by LM
Class 11	Mesangial expansion
Class 111	Focal and segmental proliferative GN
Class 1V	Diffuse proliferative GN
Class V	Membranous glomerulopathy
Class V1	Extensive glomerular sclerosis

Renal involvement in multiple myeloma [MM]

- MM is a neoplasm of immunoglobulin secreting plasma cells
- Produces high levels of circulating Igs and Ig light chains
- Light chains are excreted in urine- Bence –Jones protein

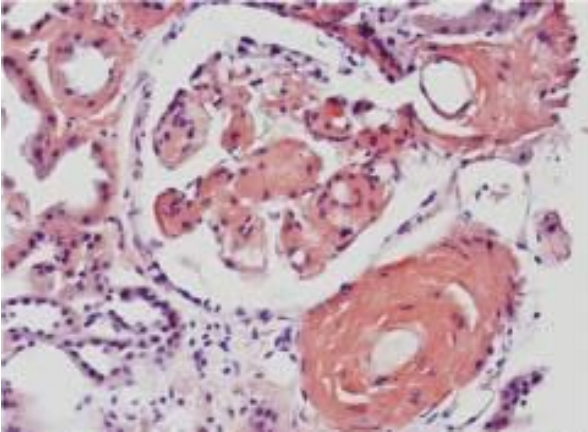
Glomerular lesions of MM

- Can take several forms
 - Deposition of monoclonal Ig or light chains in GBM
 - Nodular deposition of non fibrillar light chains
 - Amyloidosis – light chain deposition

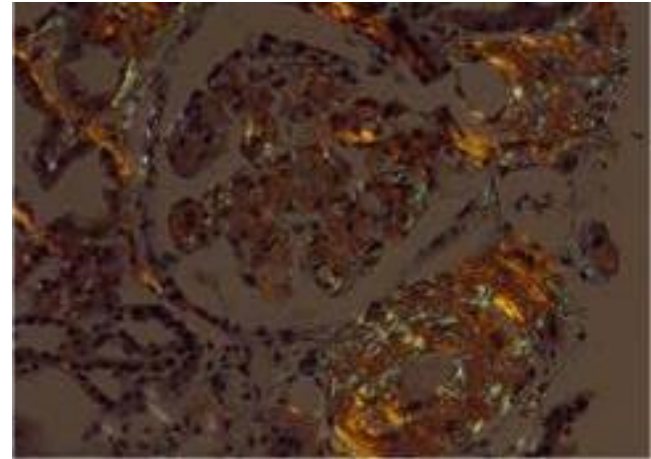


Nodular glomerular sclerosis due to kappa light chain deposition disease
Mimics diabetic nephropathy or amyloidosis

Amyloidosis of AL type



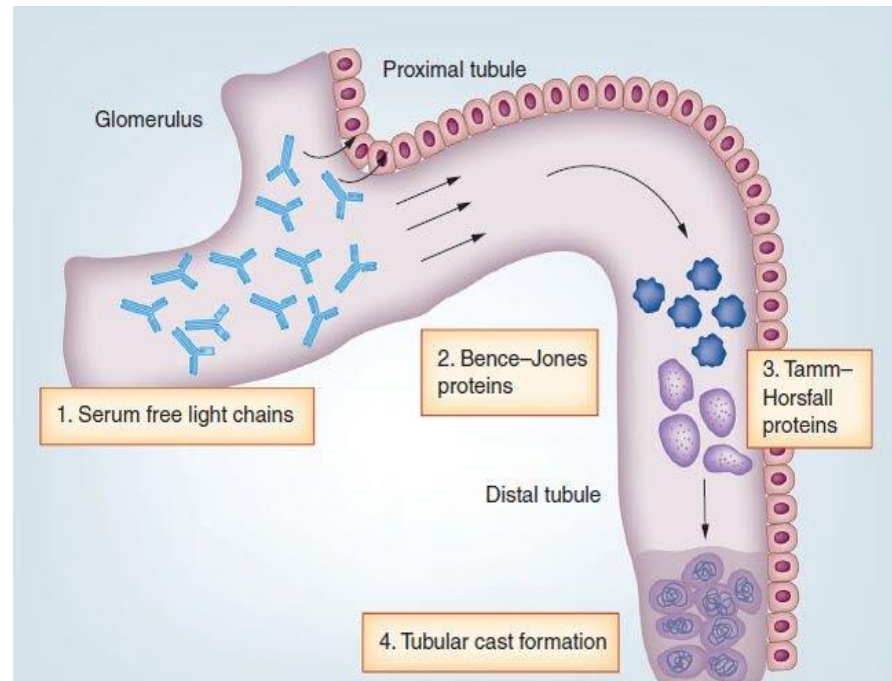
Extensive Congo Red positive amyloid deposition present in the glomeruli, in the vasculature and focally in the interstitium



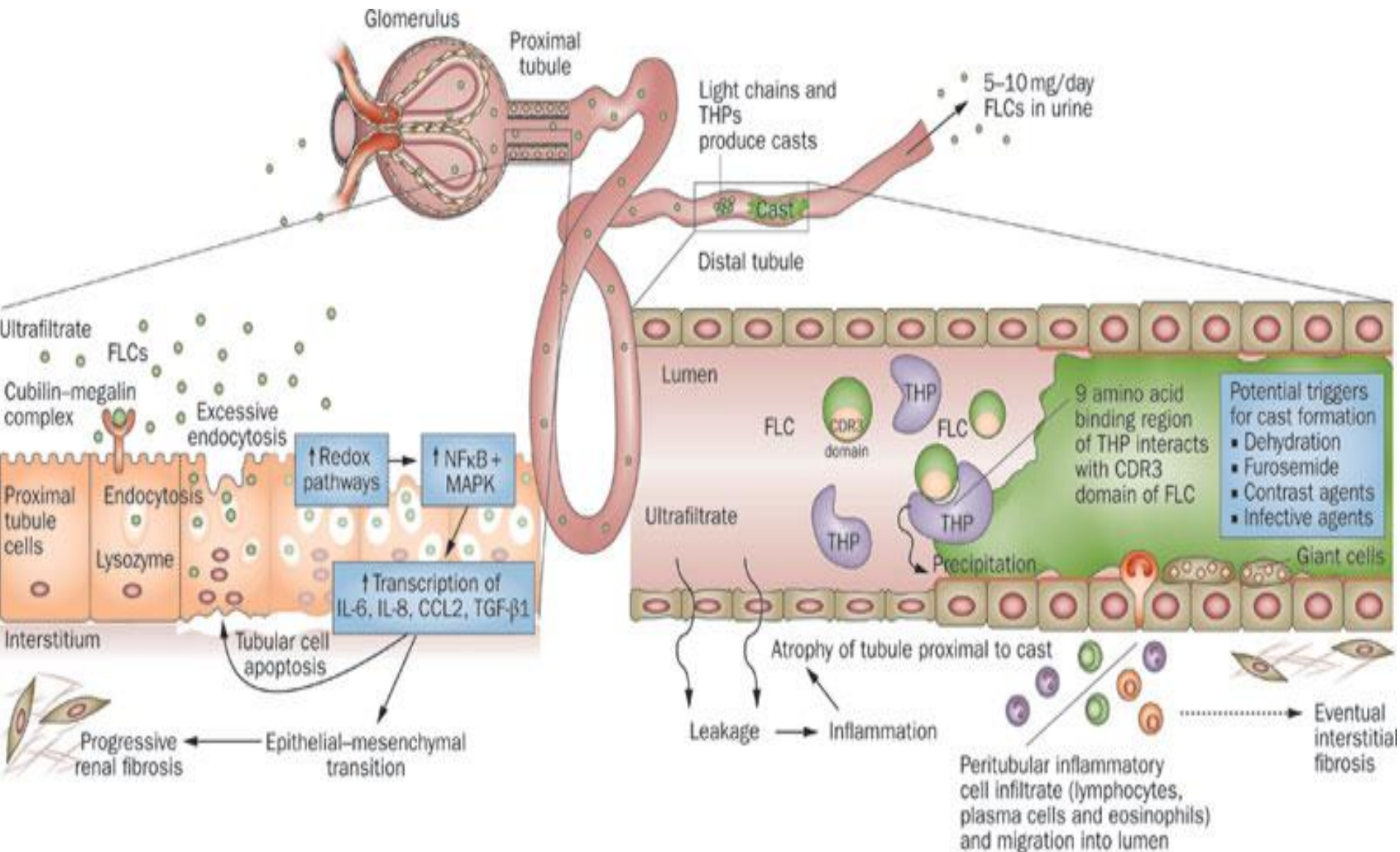
Apple green birefringence on polarized light confirms the presence of amyloid

Cast nephropathy

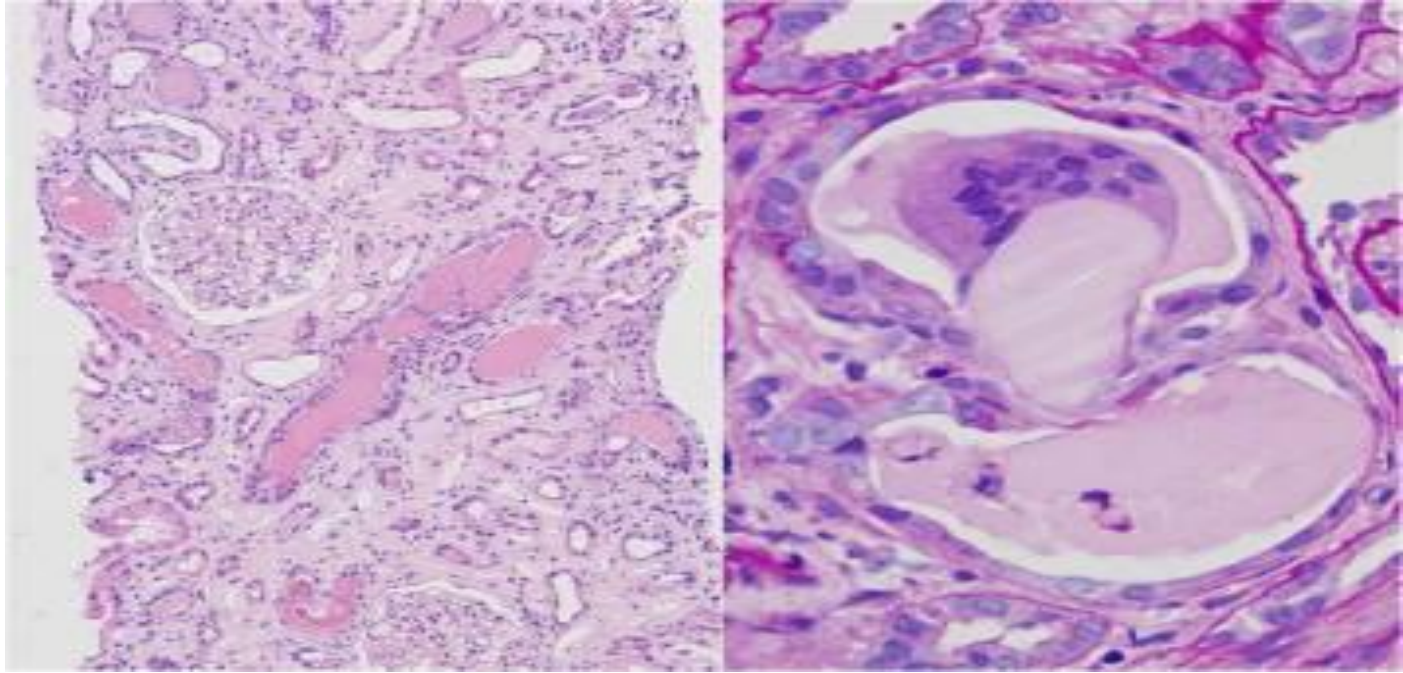
- The main cause of renal dysfunction is proteinuria related to light chains (B-J preprotein)
- Light chains are toxic to tubular epithelium
- They combine with tamm –Horsfall protein to form tubular casts



Renal involvement in MM -pathogenesis



Cast nephropathy



- The tubules are filled with protein containing casts that are glassy, refractile,
- Some casts are surrounded by inflammatory cells and giant cells
- Interstitium shows fibrosis

MM and kidney-Clinical features

- Proteinuria
 - B-J proteiuria
 - Albuminuria
- Chronic renal failure
- Acute renal failure
- Pyelonephritis
- Hypercalcaemia and nephrocalcinosis
- Hyperuricaemia



Read more