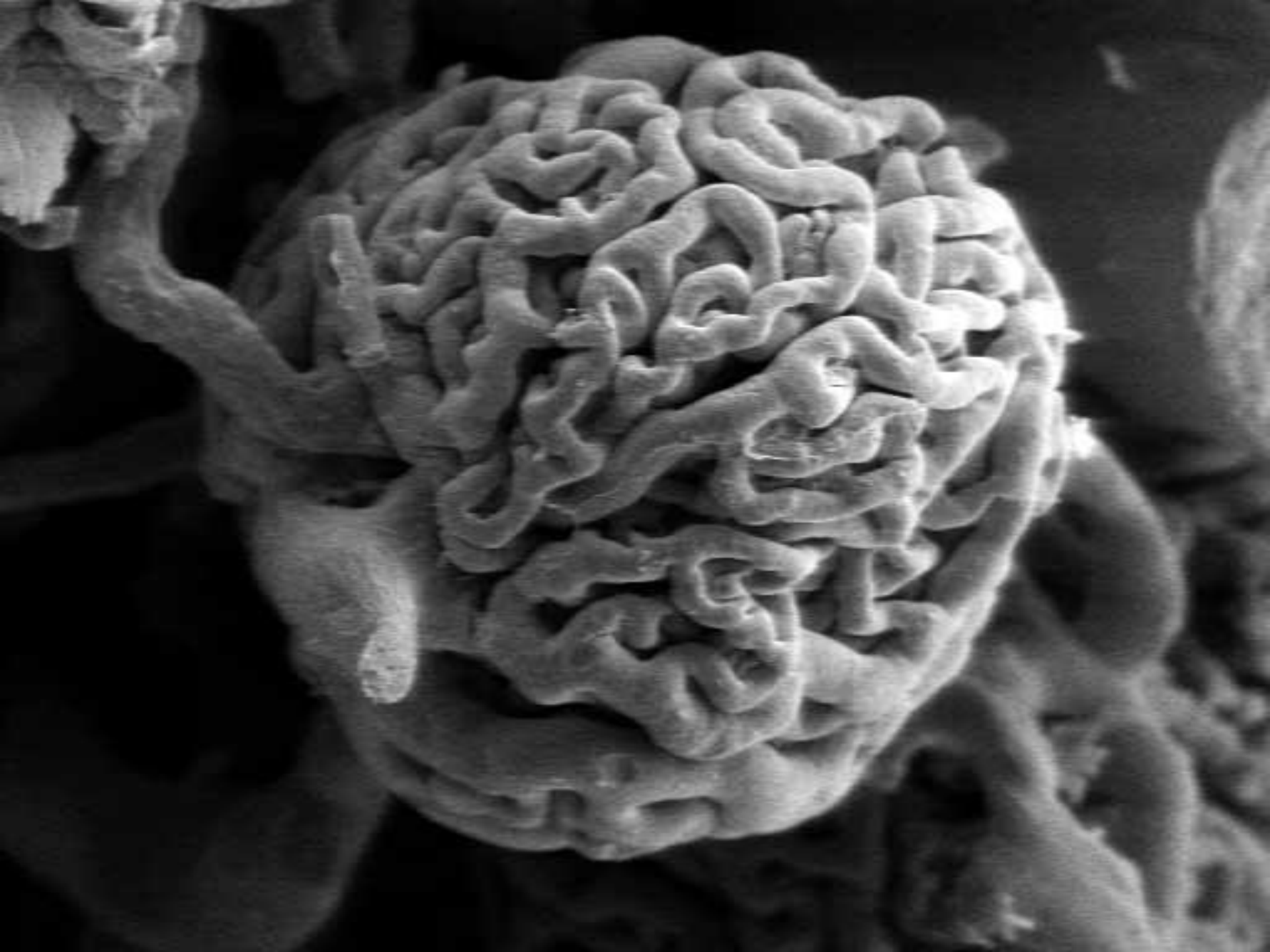
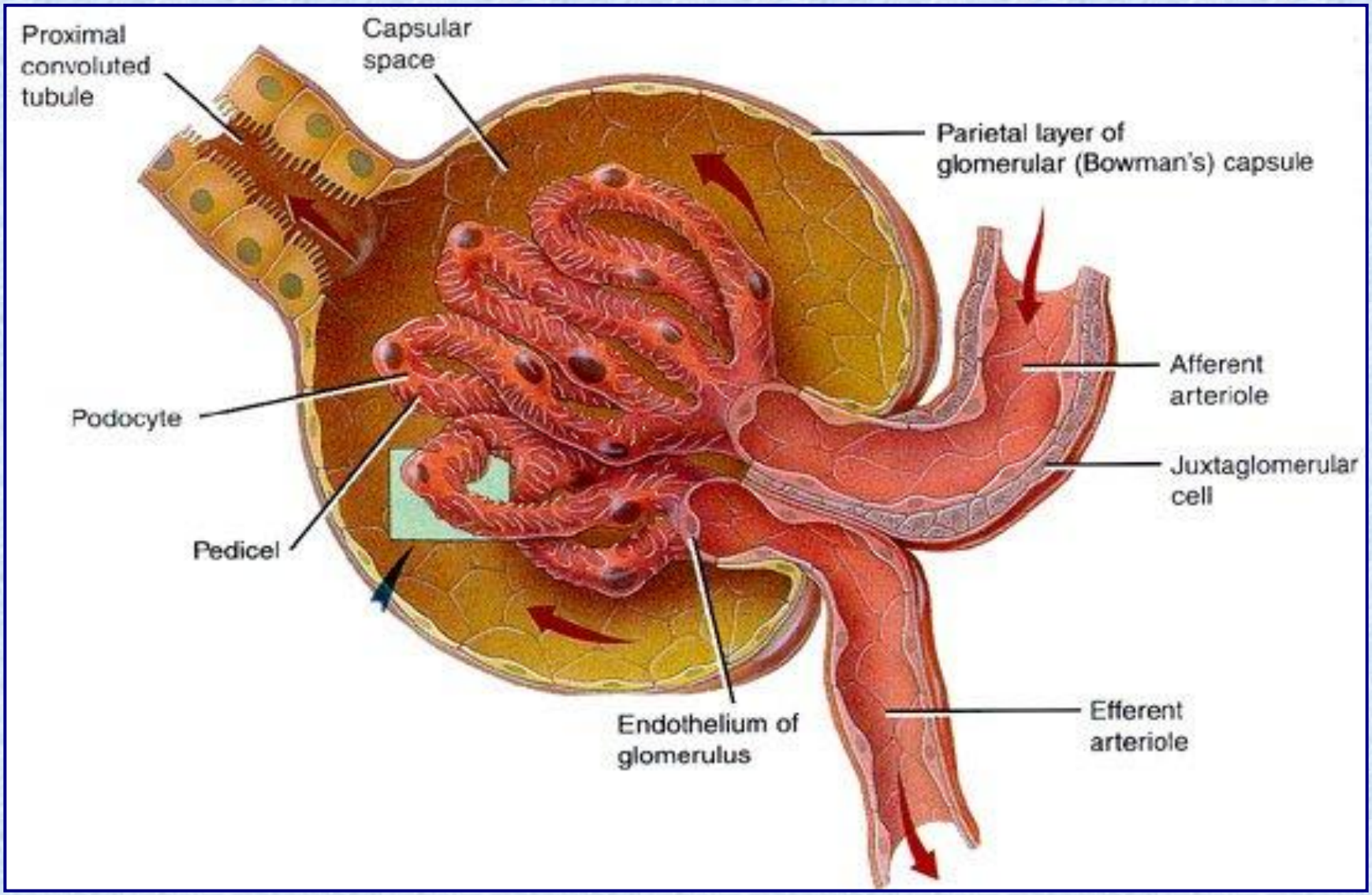
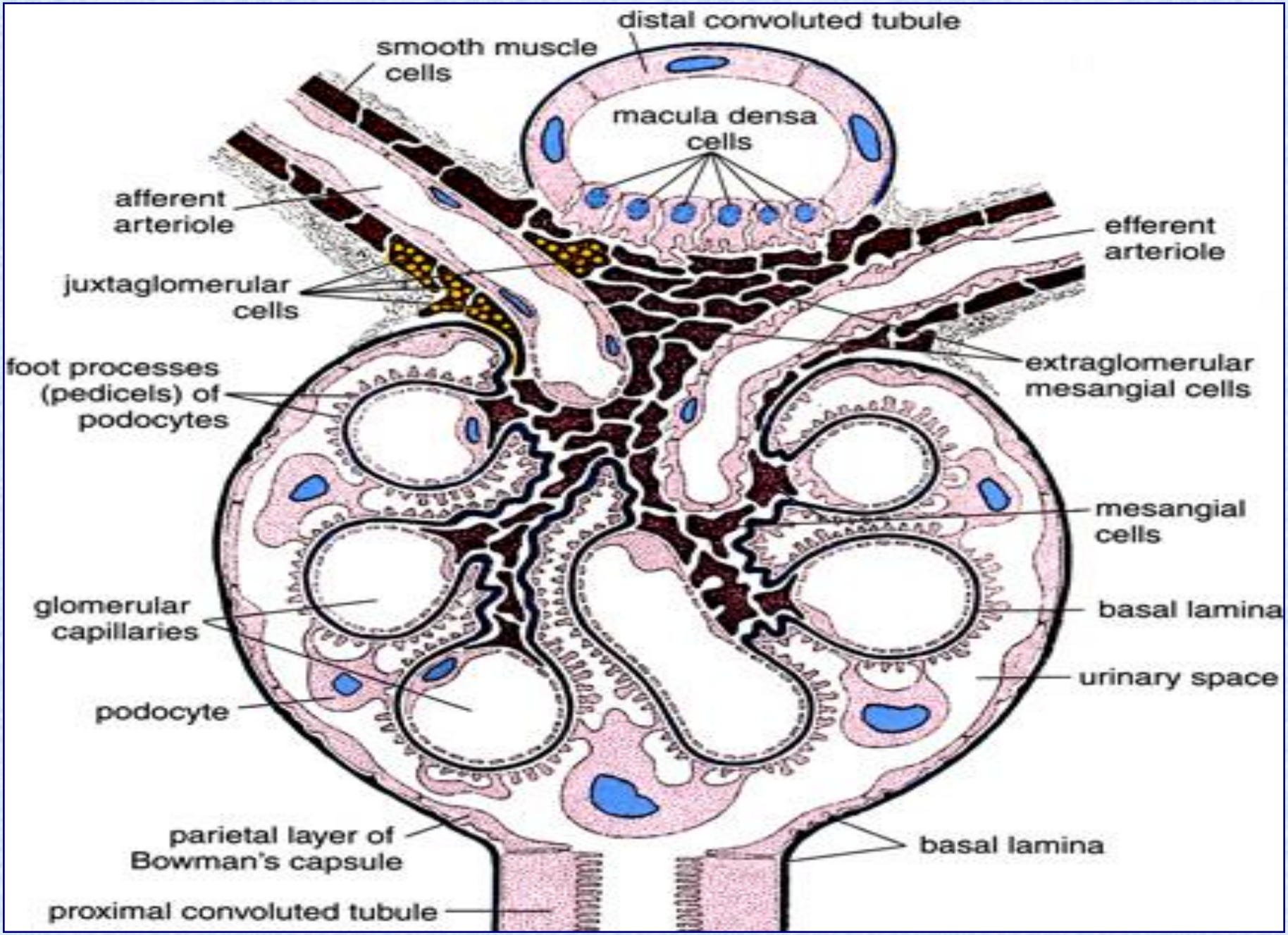
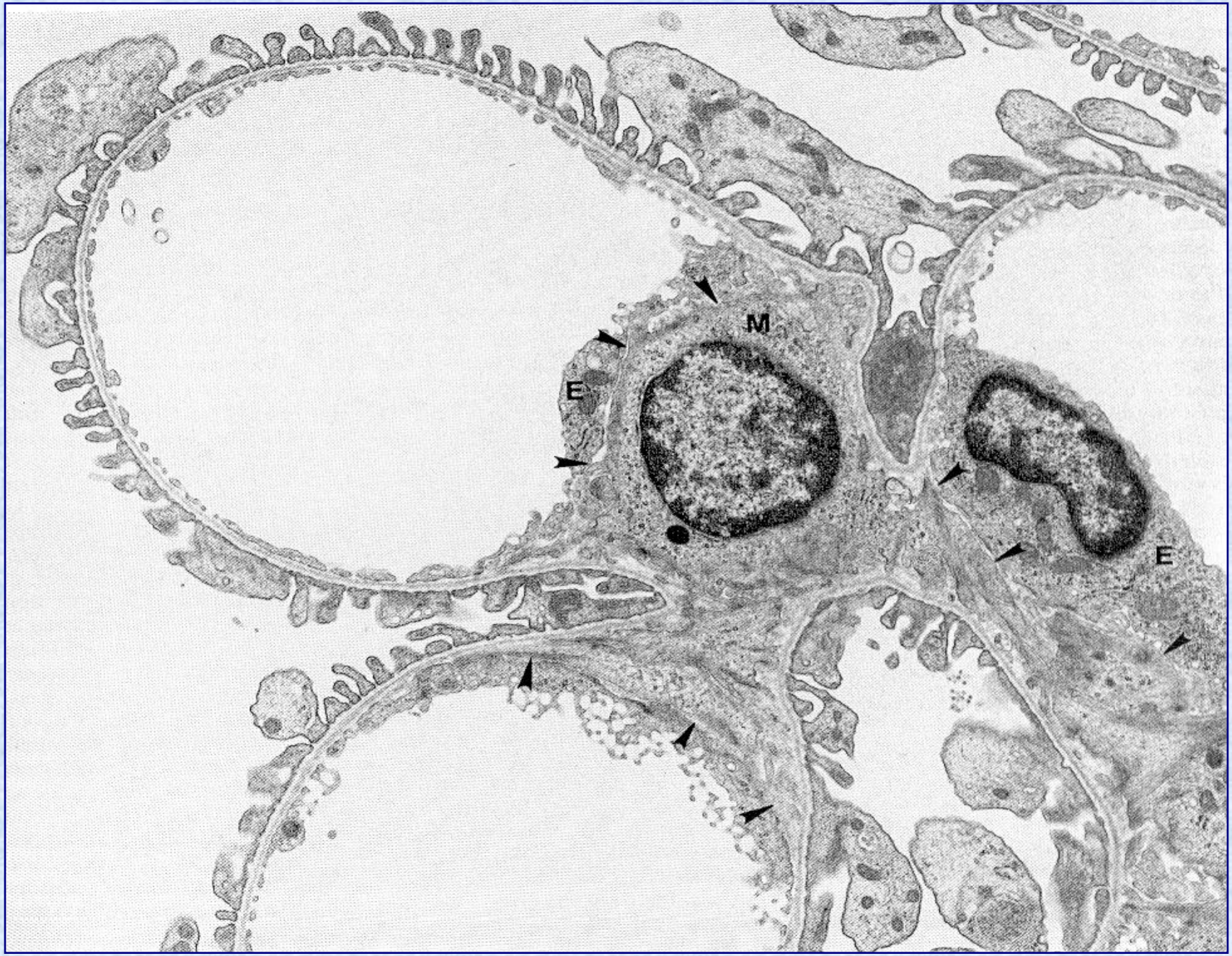
Glomerular diseases



Glomerulus


Proximal convoluted tubule
Capsular space
Parietal layer of glomerular (Bowman's) capsule
Afferent arteriole
Podocyte
Juxtaglomerular cell
Pedicel
Endothelium of glomerulus
Efferent arteriole


distal convoluted tubule
smooth muscle cells
macula densa cells
afferent arteriole
efferent arteriole
juxtaglomerular cells
extraglomerular mesangial cells
foot processes (pedicels) of podocytes
mesangial cells
glomerular capillaries
basal lamina
urinary space
podocyte
parietal layer of Bowman's capsule
basal lamina
proximal convoluted tubule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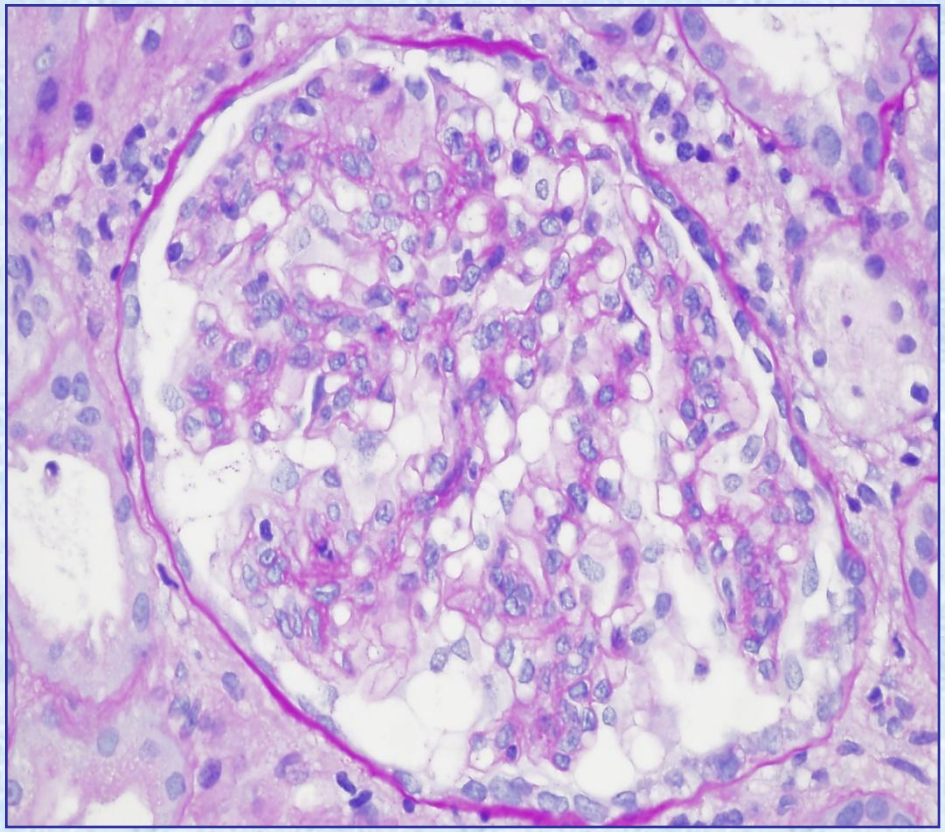
Mesangial cells

Pericytes with special functions

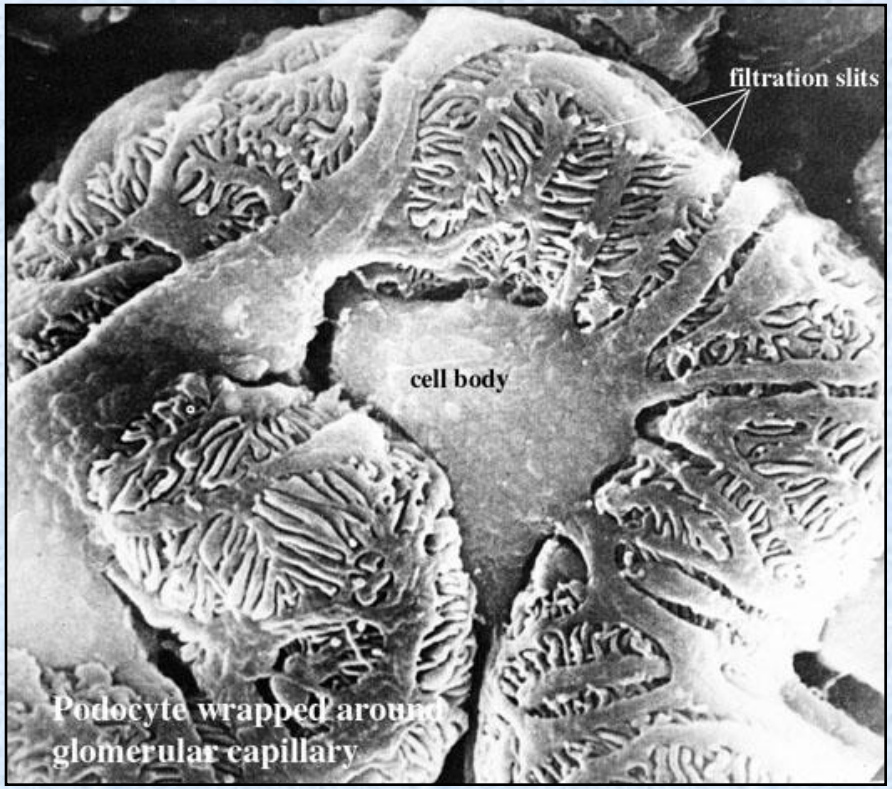
- Mesenchymal origin
- Contractile
- Phagocyte
- Proliferate
- Produce ECM and collagens
- Secrete biologically active inflammatory mediators
- Binde IgA- polymeres



Podocytes

Epithelial cells with special functions

- Synthesis of GBM components
- Regulate glomerular filtration by size, charge and shape

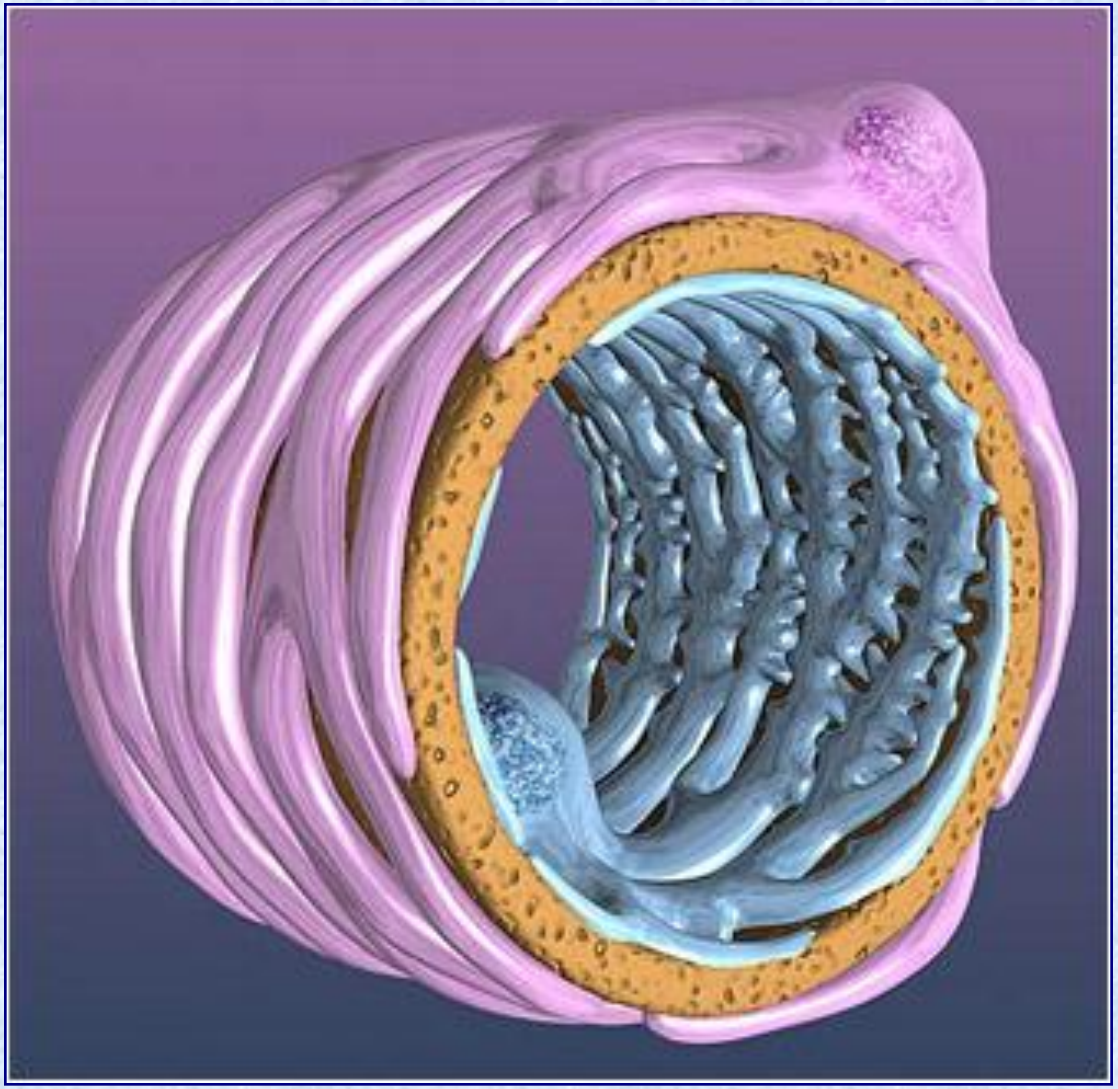


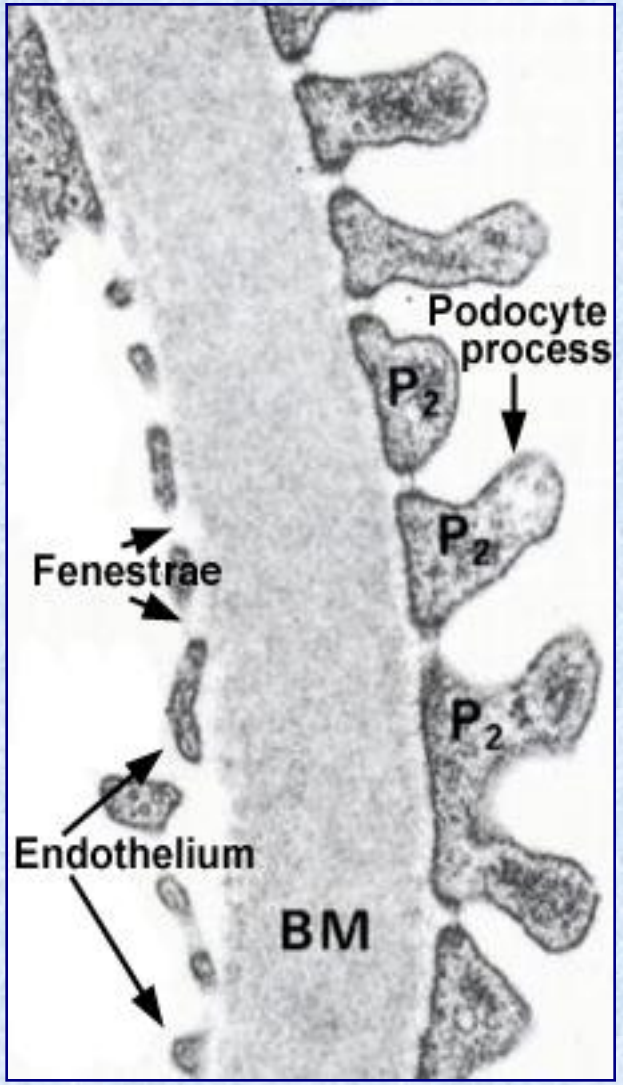
WT-1 supressor gene

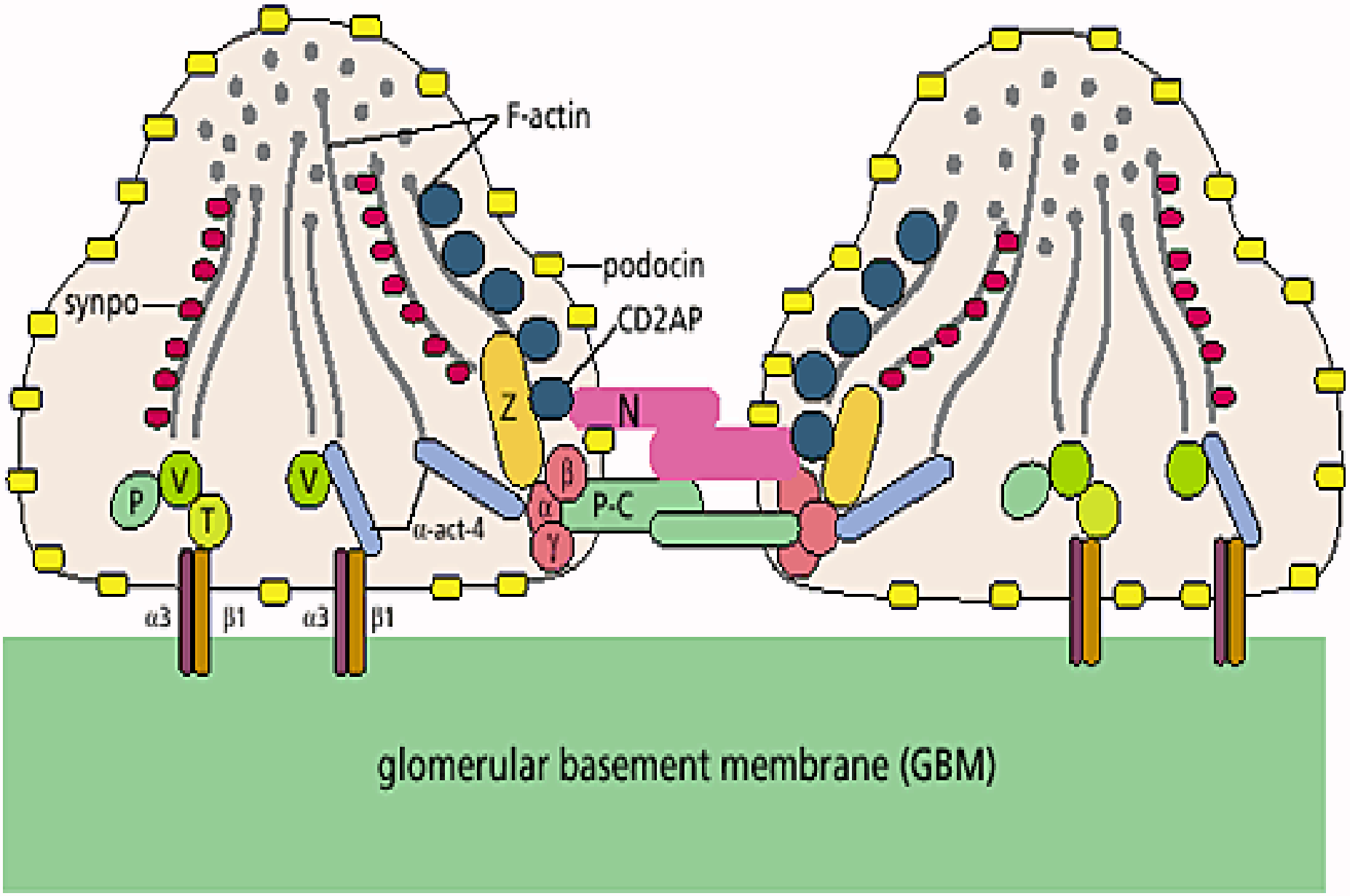
- Maintain the functions of podocytes
- Block the proliferation of podocytes

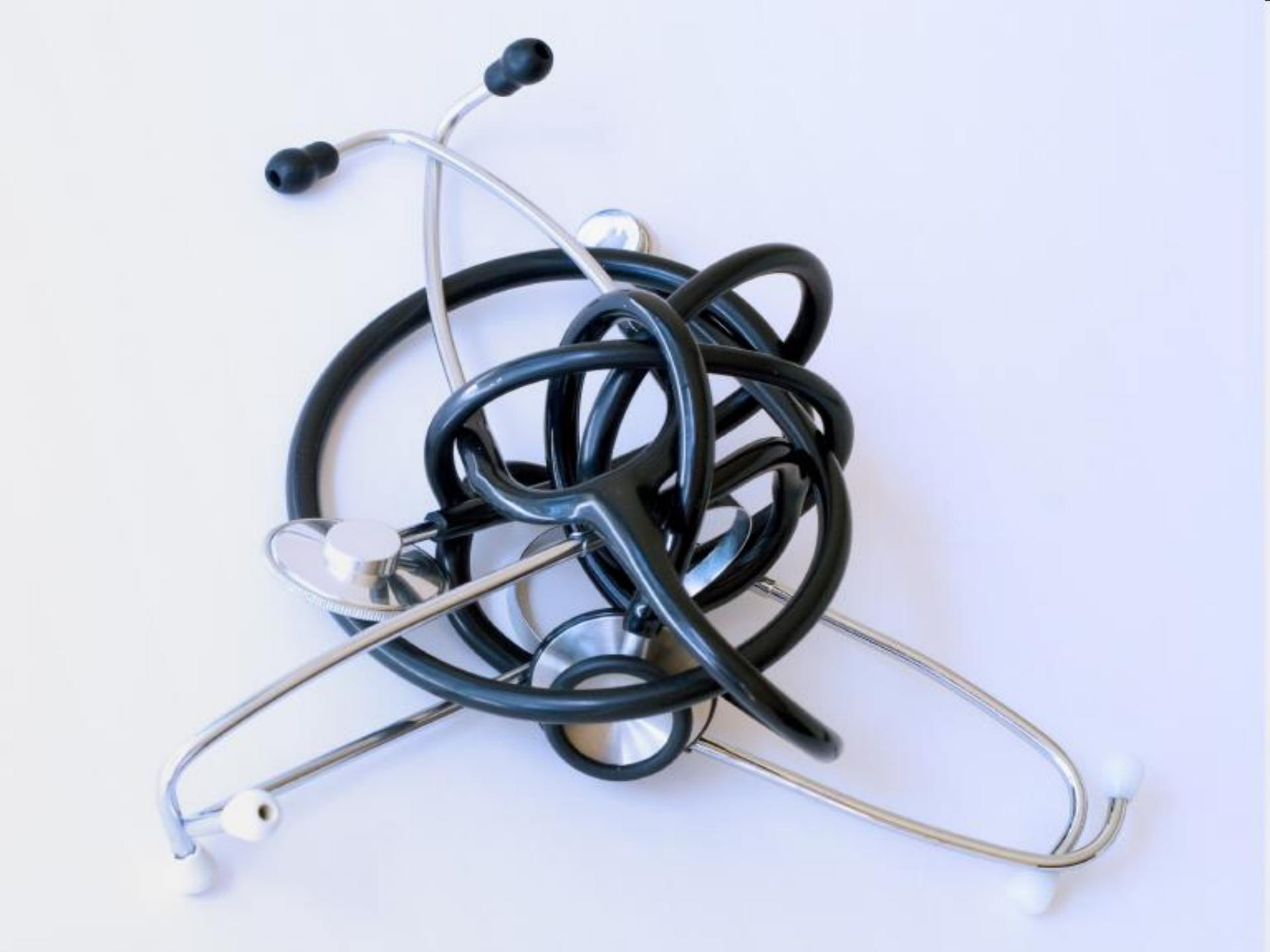
Prof.Iványi B. anyaga

Filtration



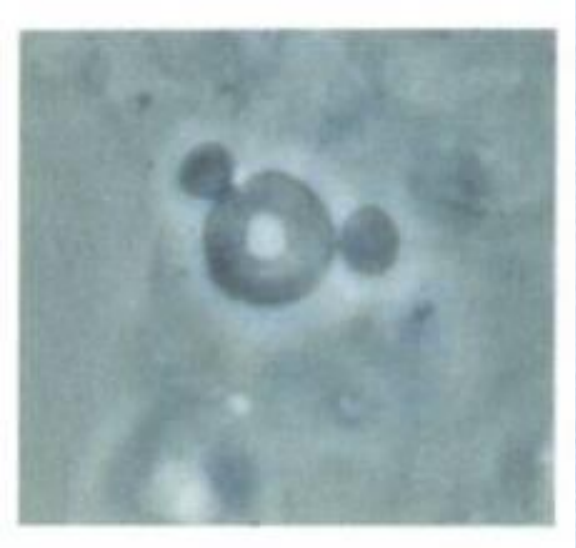



F-actin
podocin
CD2AP
synpo
Z
N
P
V
T
V
α-act-4
β
α
γ
P-C
α3
β1
α3
β1
glomerular basement membrane (GBM)



Asymptomatic hematuria and/or proteinuria

- Glomerular hematuria
  4-5 dysmorf red blood cell in urinary sediment



- Subnephrotic proteinuria

Nephrotic syndrome

- Proteinuria – 3,5 g/ day
- Hypoalbuminemia
- Oedema
- Lipiduria
- Hyperlipidaemia

Acut nephritic syndrome

- Haematuria
- Azotemia
- Oliguria
- Edema
- Proteinuria - 0,5-3 g / day
- Hypertension

Rapidly progressive renal failure

- Acut nephritic syndrome
- Proteinuria
- Acut renal failure

Chronic renal failure

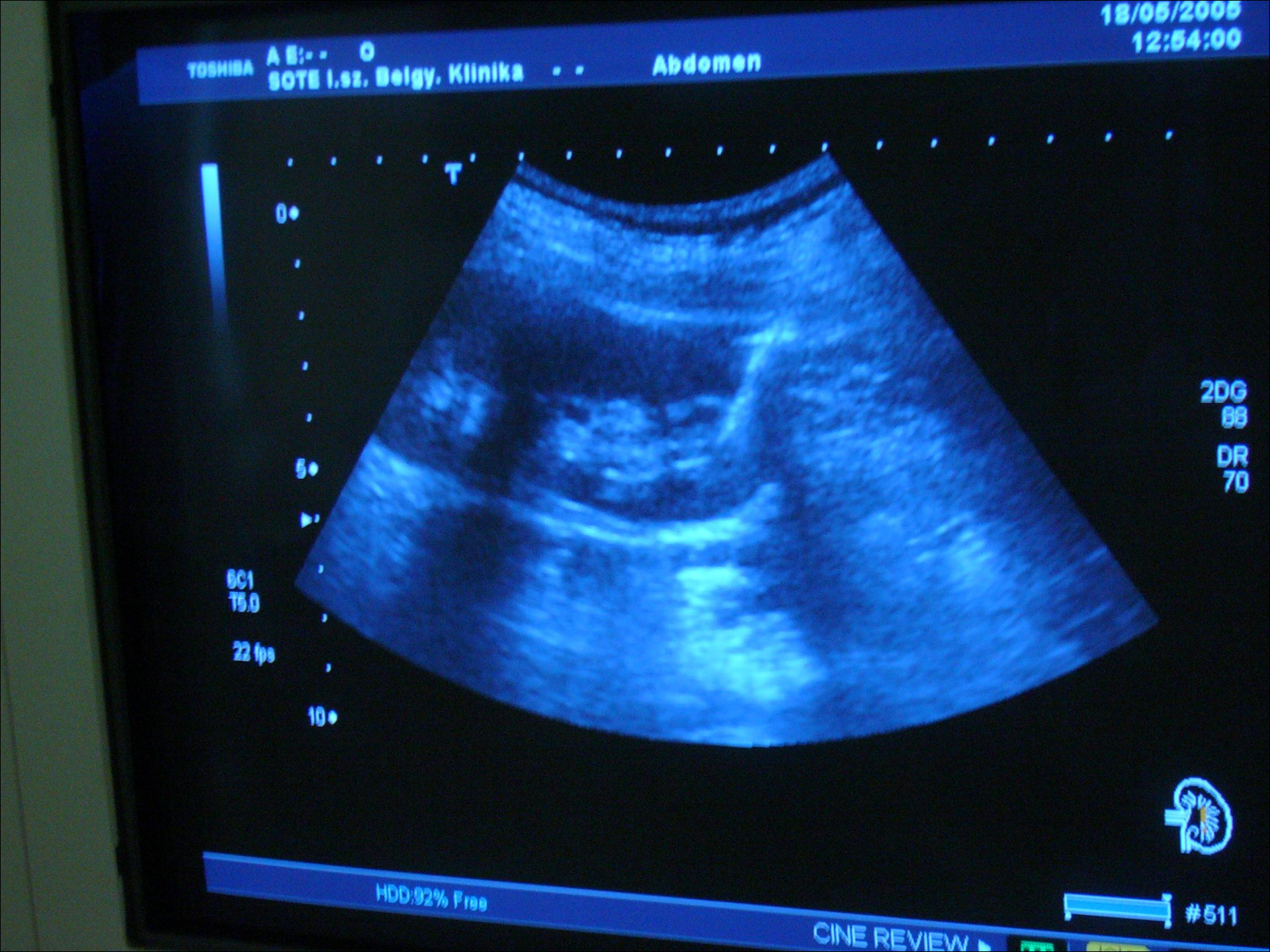
- Azotaemia → uraemia

  urea >36mmol/l GFR<30

- seKreatinin ↑ > 450 umol/ l
- Hypertension
- Atrophic kidneys

What is the next step?

Kidney biopsy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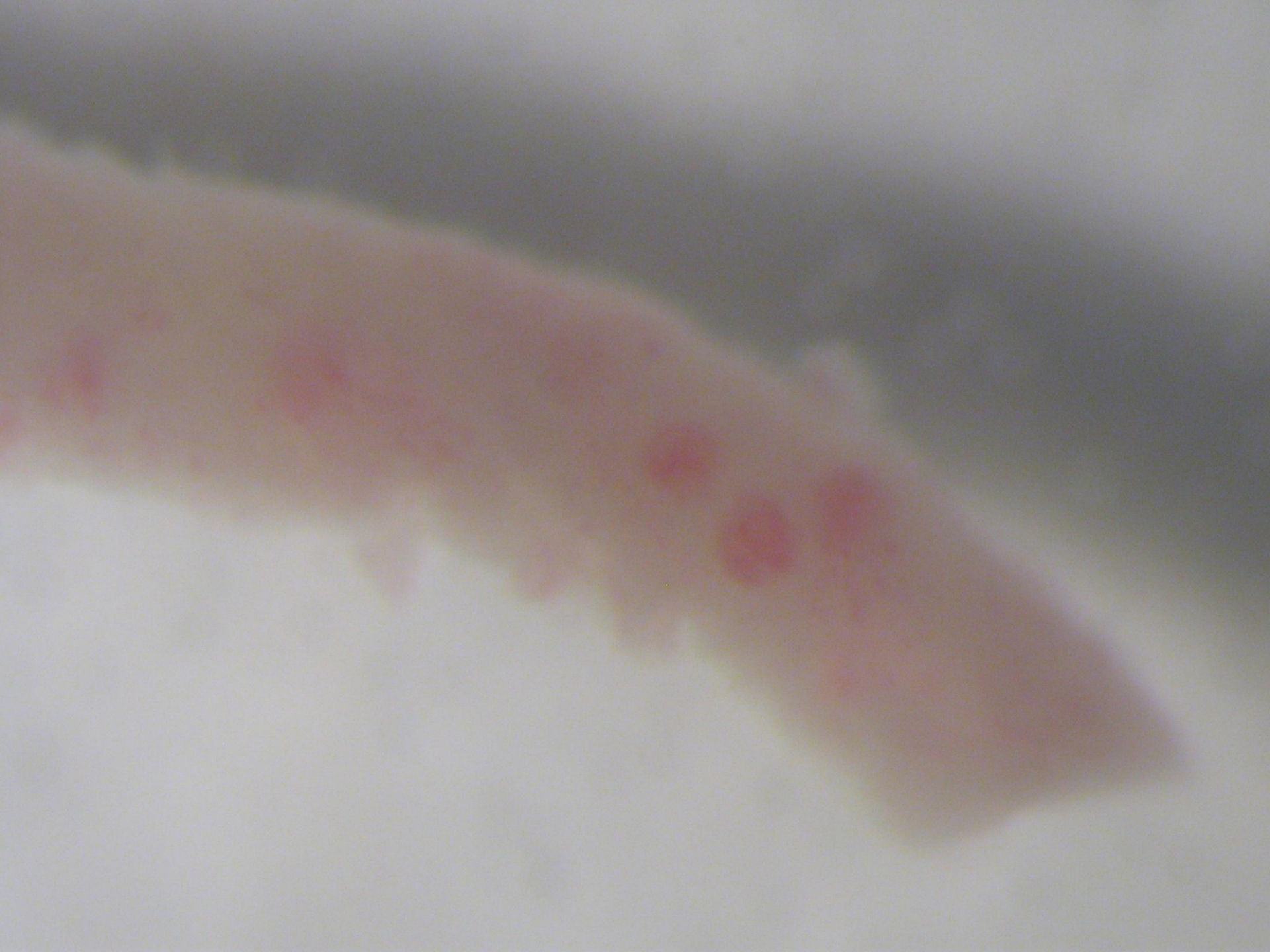
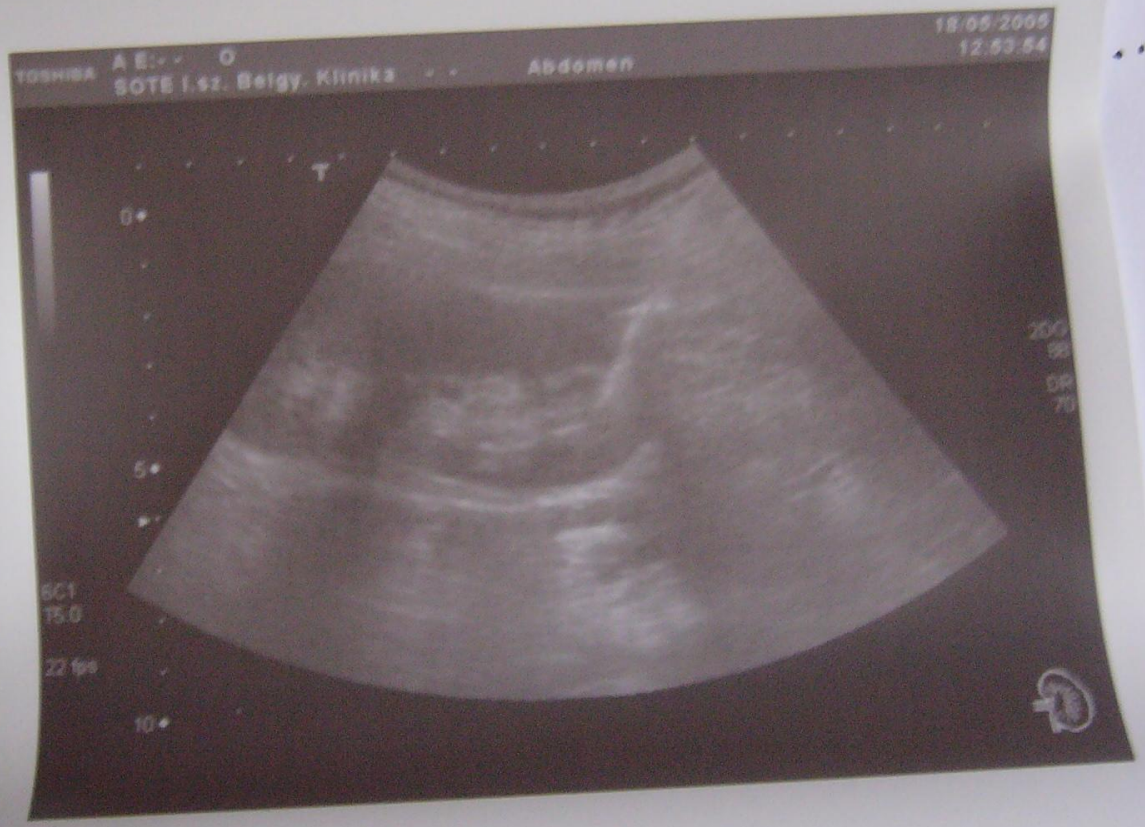
SOTE I.sz. Belgy. Klinika
Abdomen
18/05/2005
12:54:00
2DG
88
DR
70
6C1
T5.0
22 fps
HDD:92% Free
#511
CINE REVIEW




TOSHIBA
SOTE I.sz. Belgy. Klinika
Abdomen
18.05.2005
12:53:54
6C1
15.0
22 fps

Kidney biopsy

- Immunflourescens examination

  IgA, IgG, IgM, C1q, C3, C4, Kappa, Lambda, Fibrinogén

- Histological examination

  HE, PAS, Trichrom-staining, Jones, Congo

- Elektronmicroscopy

Guideline to examination of kidney biopsy

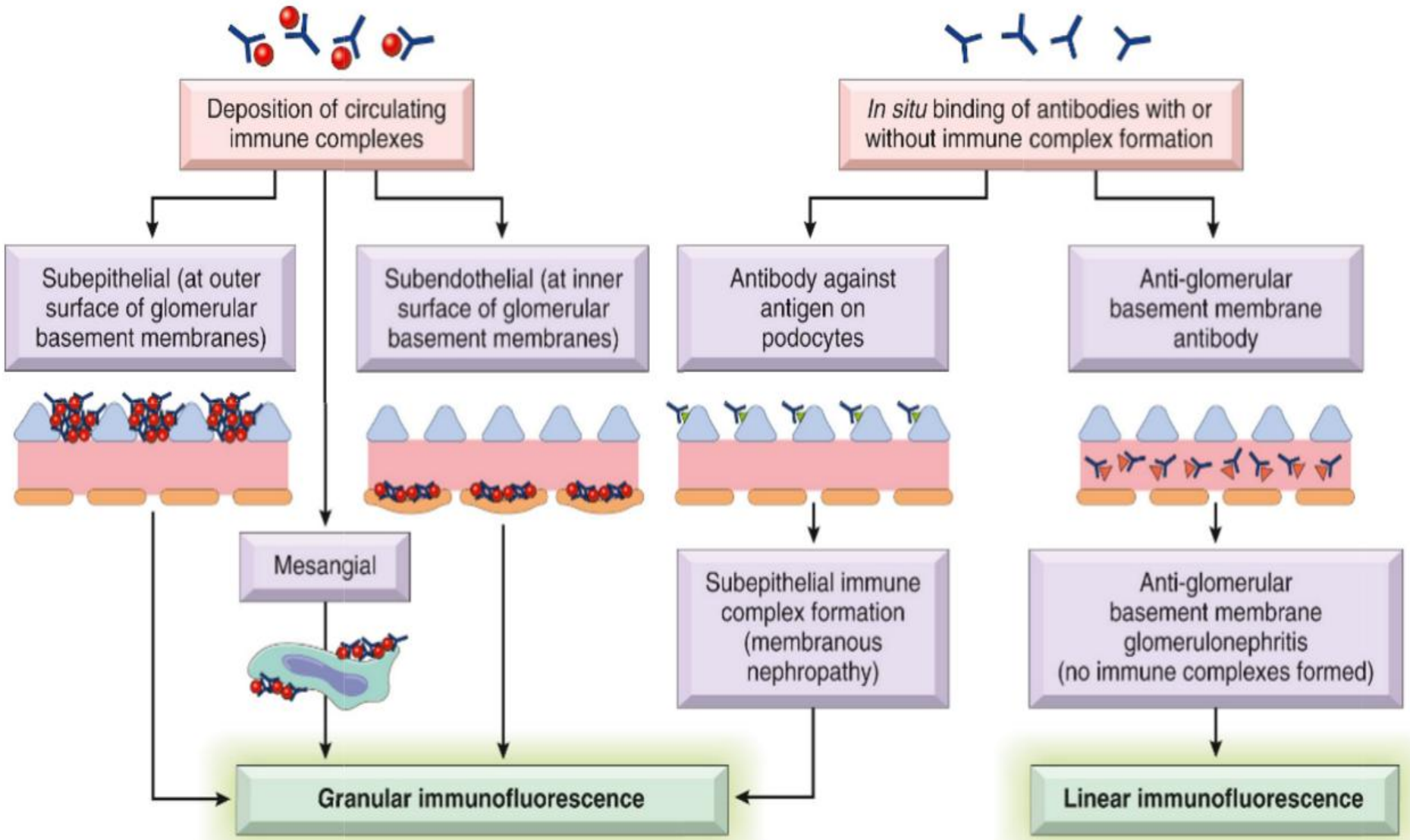
LM: localization and feature of the diagnostic lesion (HE, PAS, trichrome, Silver)

IF and EM: pathogenesis of the lesion

Dr. Iványi

Mechanisms of glomerular Injury

- Circulating immune complex
- In situ formed immune complex
- Anti-GBM antibody-mediated process
- Complement activation
- Mediators of immune injury
- Non-immune mechanisms
  - podocyta injury
  - nephron loss



Robbins: Basic Pathology

INTERRELATIONSHIP OF PATHOLOGIC AND CLINICAL MANIFESTATIONS OF GLOMERULAR INJURY

NEPHROTIC SYNDROME

MINIMAL CHANGE GLOMERULOPATHY

MEMBRANOUS GLOMERULOPATHY

FOCAL SEGMENTAL GLOMERULOSCLEROSIS

MESANGIOPROLIFERATIVE GLOMERULOPATHY

MEMBRANOPROLIFERATIVE GLOMERULONEPHRITIS

PROLIFERATIVE GLOMERULONEPHRITIS

ACUTE DIFFUSE PROLIFERATIVE GLOMERULONEPHRITIS

CRESCENTIC GLOMERULONEPHRITIS

NEPHRITIC SYNDROME

Classification of glomerular diseases

- Primary glomerular diseases
- Glomerulonephritis in systematic diseases
- Glomerular lesions in vascular diseases
- Hereditary nephropaty and miscellaneous glomerular lesions

TABLE 14.1 Glomerular Diseases

Primary Glomerular Diseases
Minimal-change disease
Focal segmental glomerulosclerosis
Membranous nephropathy
Acute postinfectious glomerulonephritis
Membranoproliferative glomerulonephritis
IgA nephropathy
Dense deposit disease
C3 glomerulonephritis
Glomerulopathies Secondary to Systemic Diseases
Lupus nephritis (systemic lupus erythematosus)
Diabetic nephropathy
Amyloidosis
Glomerulopathy secondary to multiple myeloma
Goodpasture syndrome
Microscopic polyangiitis
Granulomatosis with polyangiitis
Henoch-Schönlein purpura
Bacterial endocarditis–related glomerulonephritis
Thrombotic microangiopathy
Hereditary Disorders
Alport syndrome
Fabry disease
Podocyte/slit-diaphragm protein mutations

Robbins:Basic Pathology ábra

Primary glomerular diseases

1. Minimal change disease
2. Focal segmental glomerulosclerosis
3. Membranous nephropathy
4. Membranoproliferative GN
5. Mesangioproliferative GN
6. Crescentic GN

Nephrotic syndrome in childhood

Disease	Gene	Locus	Protein	Age at onset	Mode	Nephrin	WT1	Lamb2	Ki-67	Podocin	Steroid resistance
MCD	*NPHS1*	19q13.1	Nephrin	Congenital	AR	−	+	+	−	+	✓
	NPHS2	1q25–31	Podocin	Congenital, 1 year	AR	+	+	+	−	?	✓
	WT1	11p13	WT1	Congenital, 1 year	AD	+	Unknown	+	−	+	✓
DMS	*WT1*	11p13	WT1	1–4 years	AD	+	↓	+	↑	+	✓
	LAMB2	3p21	Lamb2	3 months–1 year	AR	+	+	−	↑	+	✓
	PLCE1	NPFS3	PLCe1	4 months–1 year	AR	+	+	+	Unknown	−	✓
FSGS	*NPHS2*	1q25	Podocin	Childhood	AR	+	+	+	−	−	✓
	CD2AP	6P12	CD2AP	Congenital (1 case)	AR						✓
	WT1	11p13	WT1	2–18 years	AD						✓
	PLCE1	10q.23.32-q24.1	PLCe1	2–8 years (rare)	AR	+	+	−	−	+	✓
CG	*COQ2*	4q21	Para-hydroxybenzoate-polyprenyl-transferase	Congenital (rare)	AR				+		✓

MCD indicates minimal change disease; DMS, diffuse mesangial sclerosis; FSGS, focal segmental glomerulosclerosis; CG, collapsing glomerulopathy; AR, autosomal recessive; AD, autosomal dominant.

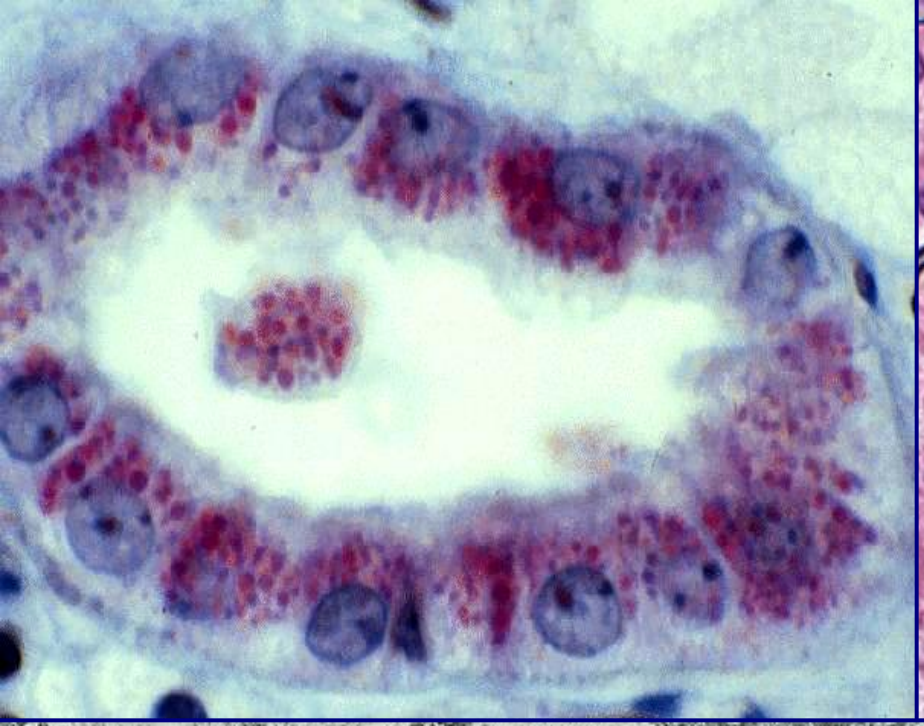
Pediatric and Developmental Pathology 11, 254-263, 2008
Helen Liapis

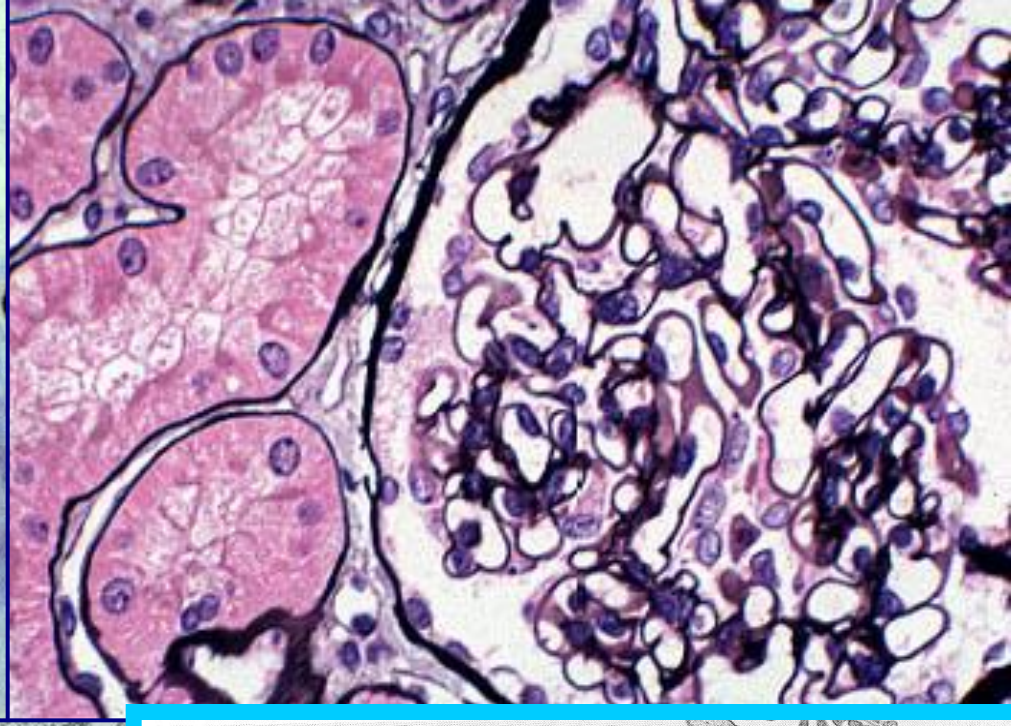
Glomerulopathies associated with nephrotic syndrome

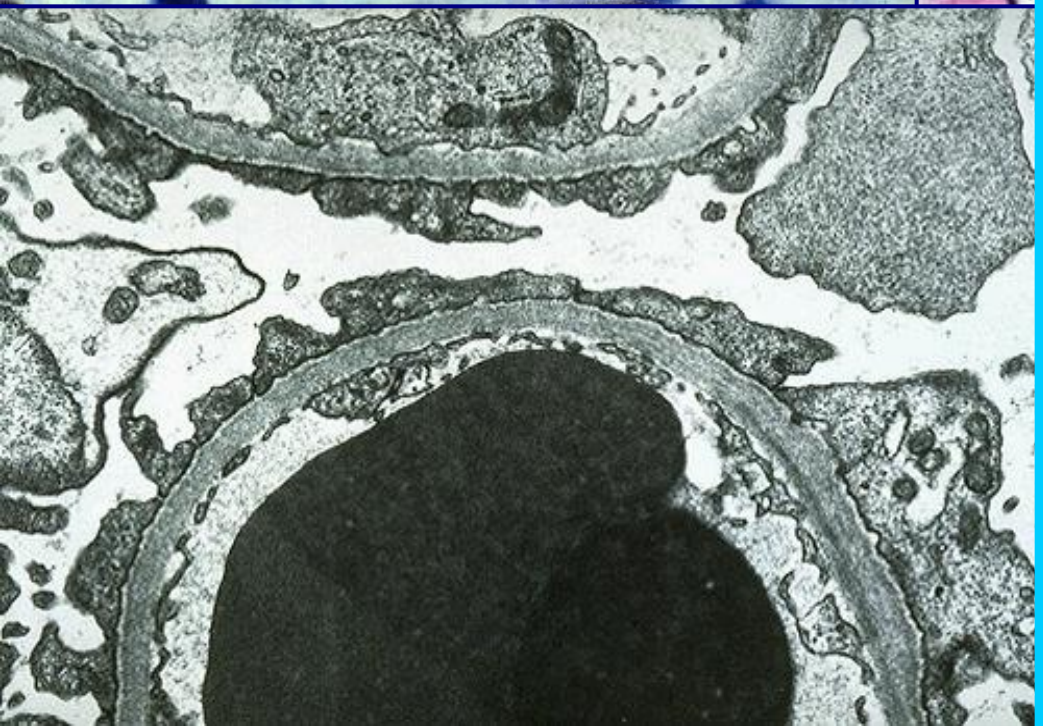
- Minimal change disease
- FSGS
- Membranous nephropathy

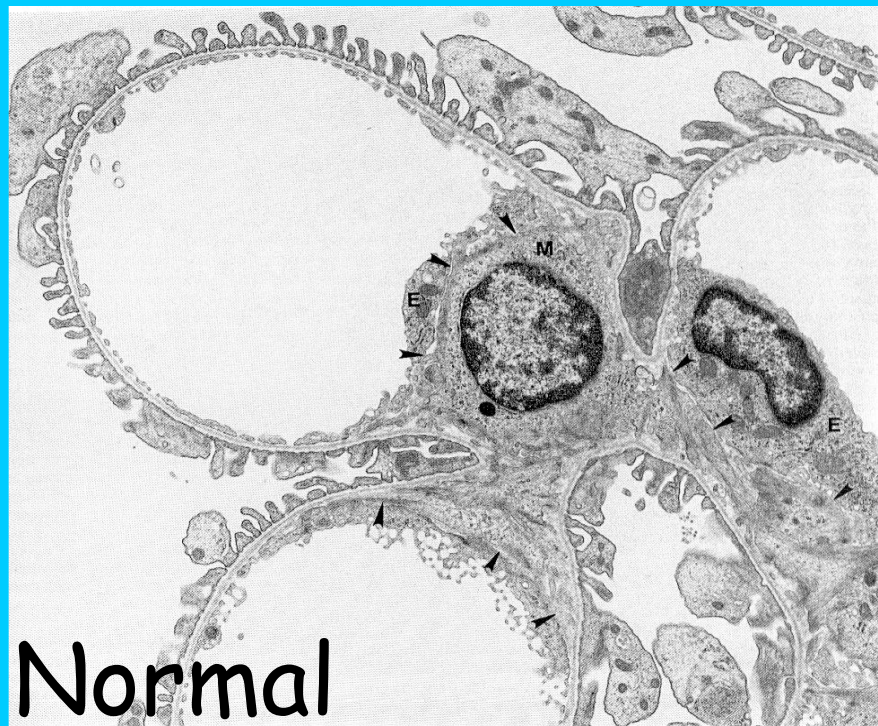
Minimal change disease

- Lipoid nephrosis
- Peak incidence is between 2-6 years
- Highly selective proteinuria
- IF and histology are negative
- EM:diffuse effacement of footprocesses
- Pathogenezis: unknown
- Response to corticosteroid therapy
- Good prognosis

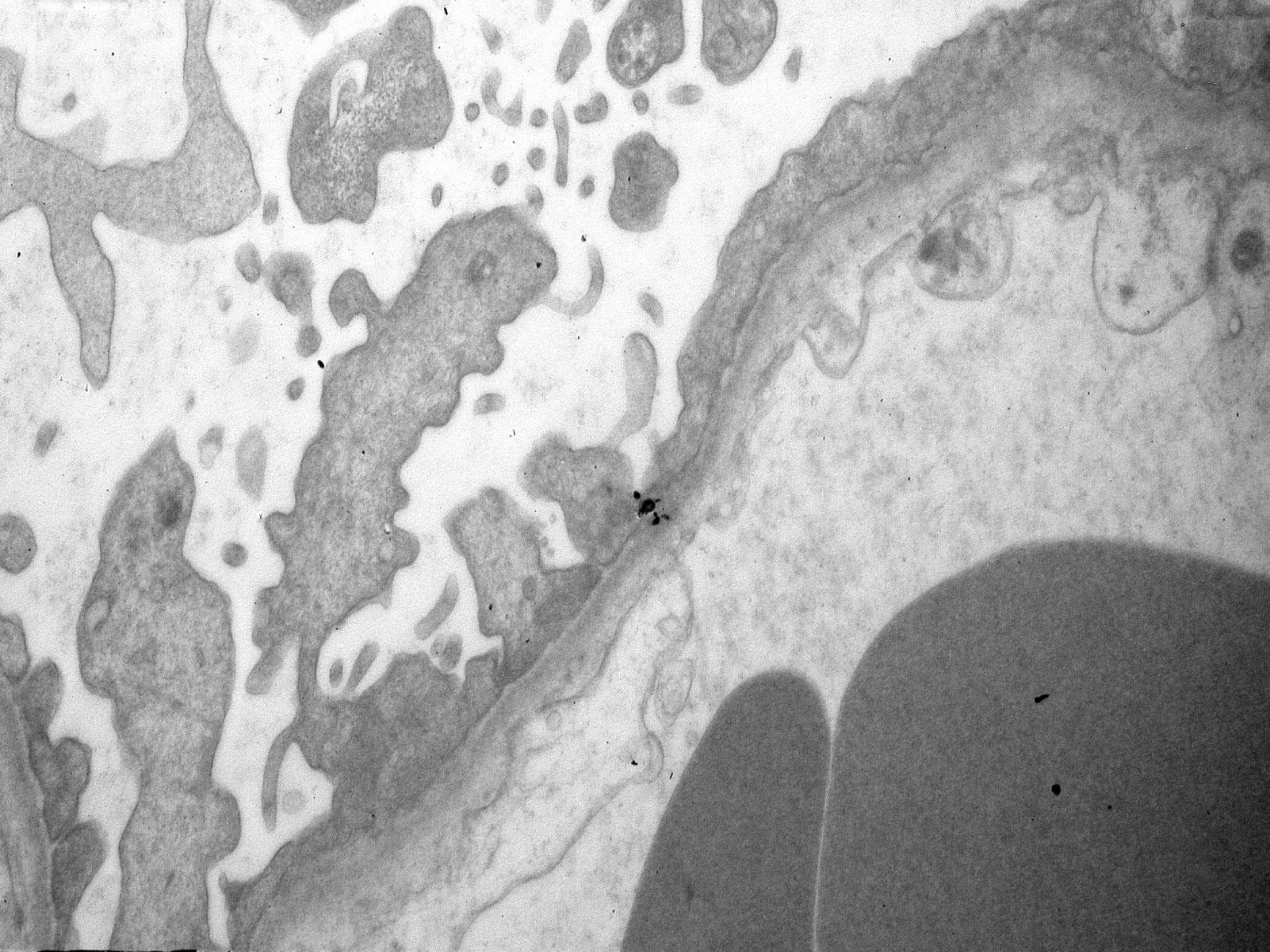








Normal

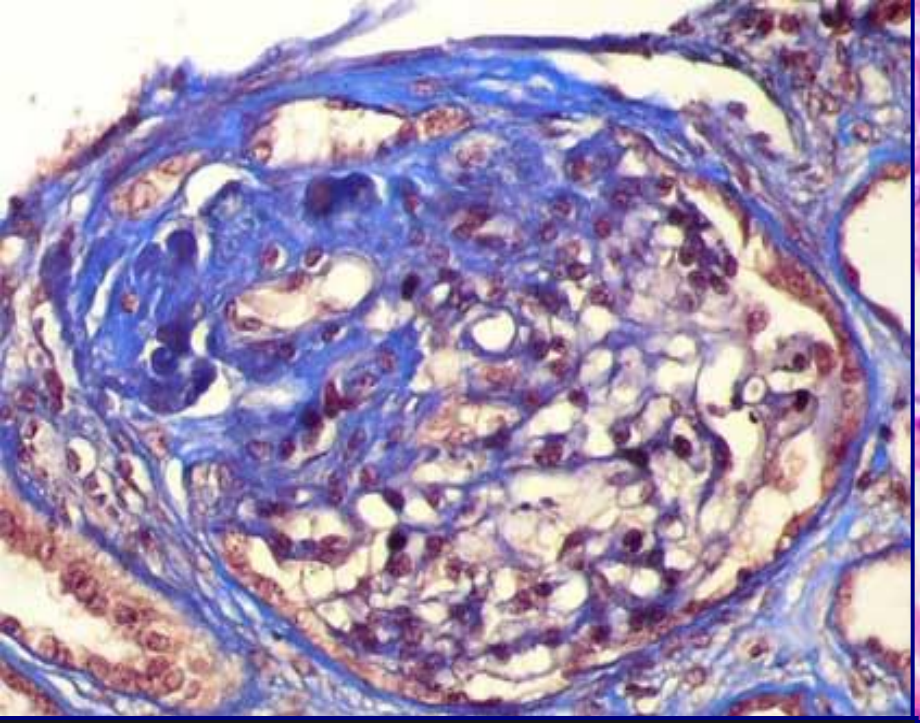


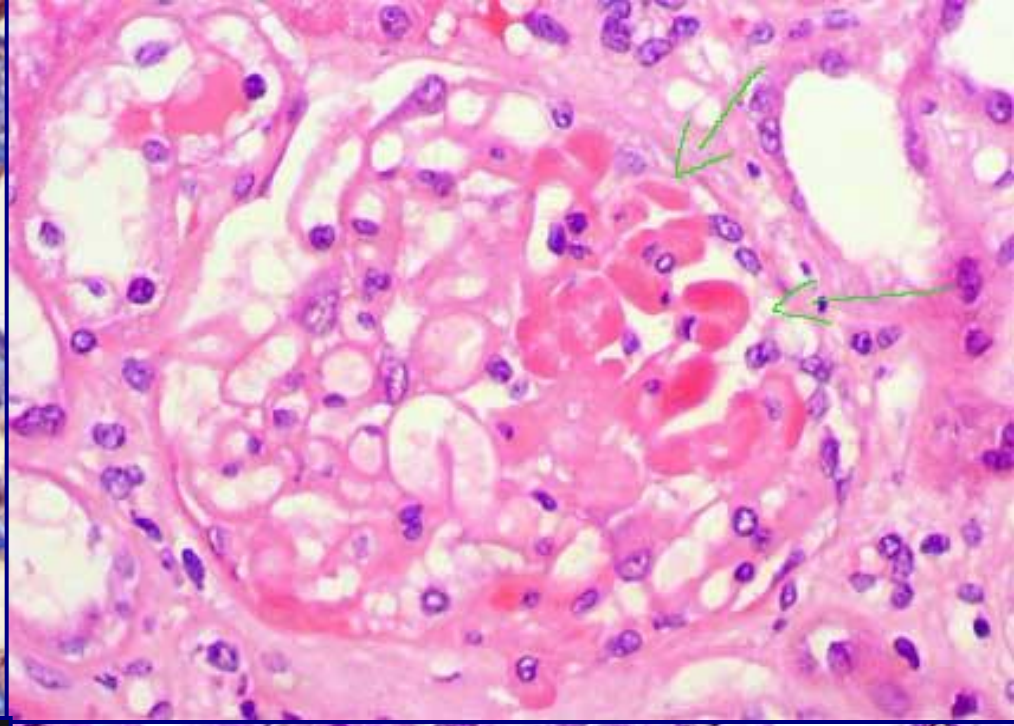
Secundary MCD

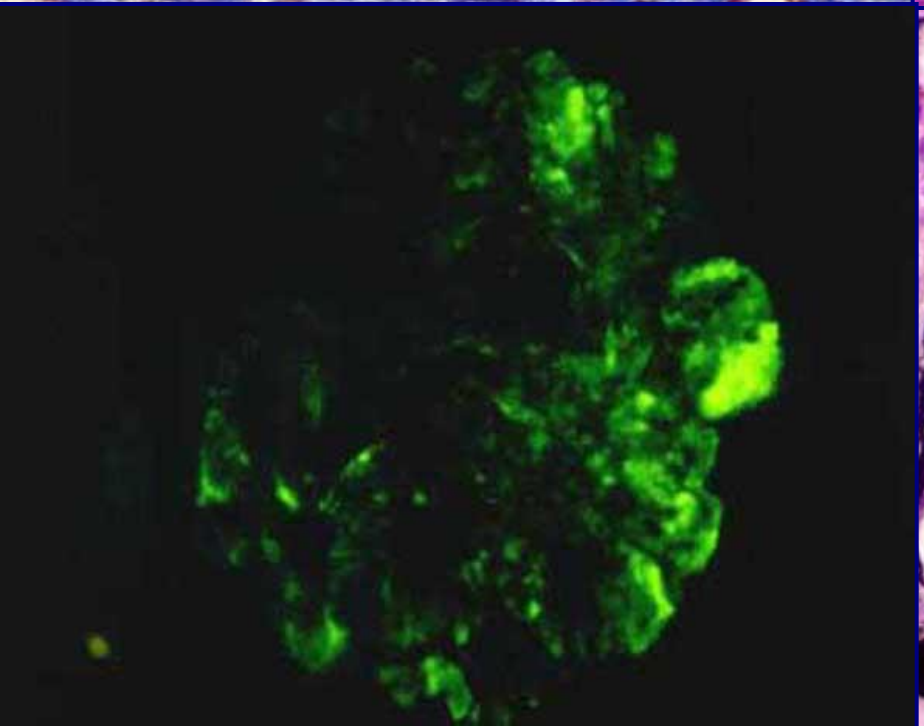
- Medications: NSAID, Lithium etc.
- Malignant tumors: Hodgkin-kór, non-Hodgkin ly., Mycosis fungoides, AML, CML, T-sejtes leukemia etc.
- Miscellaneous: bee sting, foodallergy, EBV,HIV

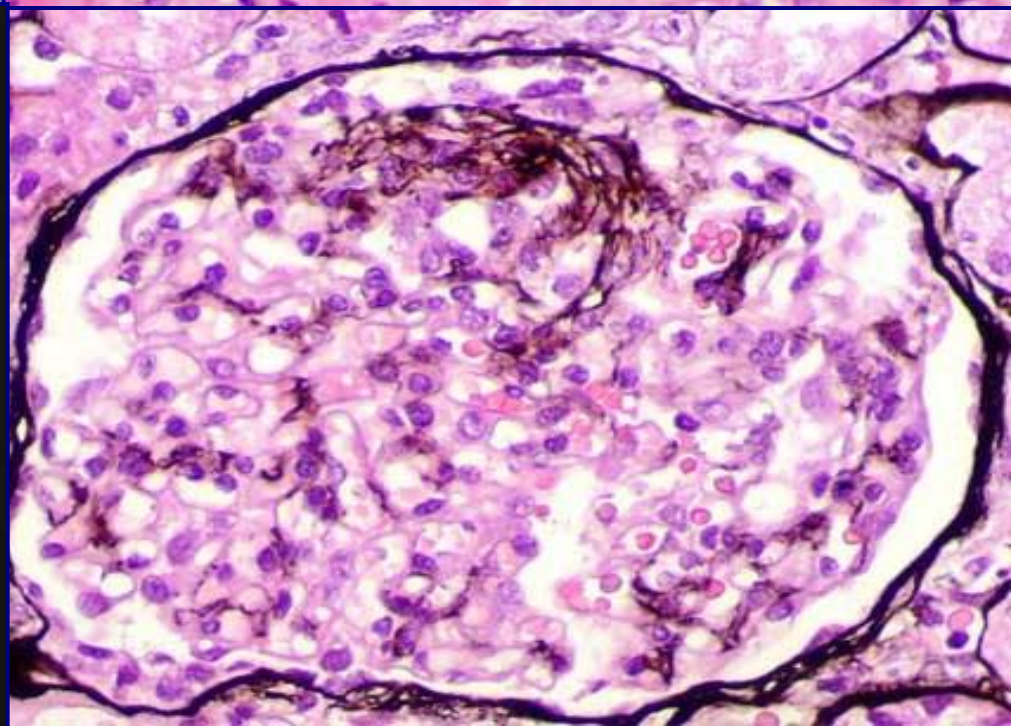
Focalis segmentalis glomerulosclerosis - FSGS

- Greatest prevalence: under 5 years of age or 30-40 years of age in adults
- Haematuria
- IF: IgM és C3 – granular, mesangial/GBM
- Histology: focal, segmental sclerosis
- EM: effacement of foot process and detachment
- Pathogenezis: circulating podocyte toxic agent?
- 40-60% of patients develop end stage kidney
- Recurrance following transplantation 15-50%



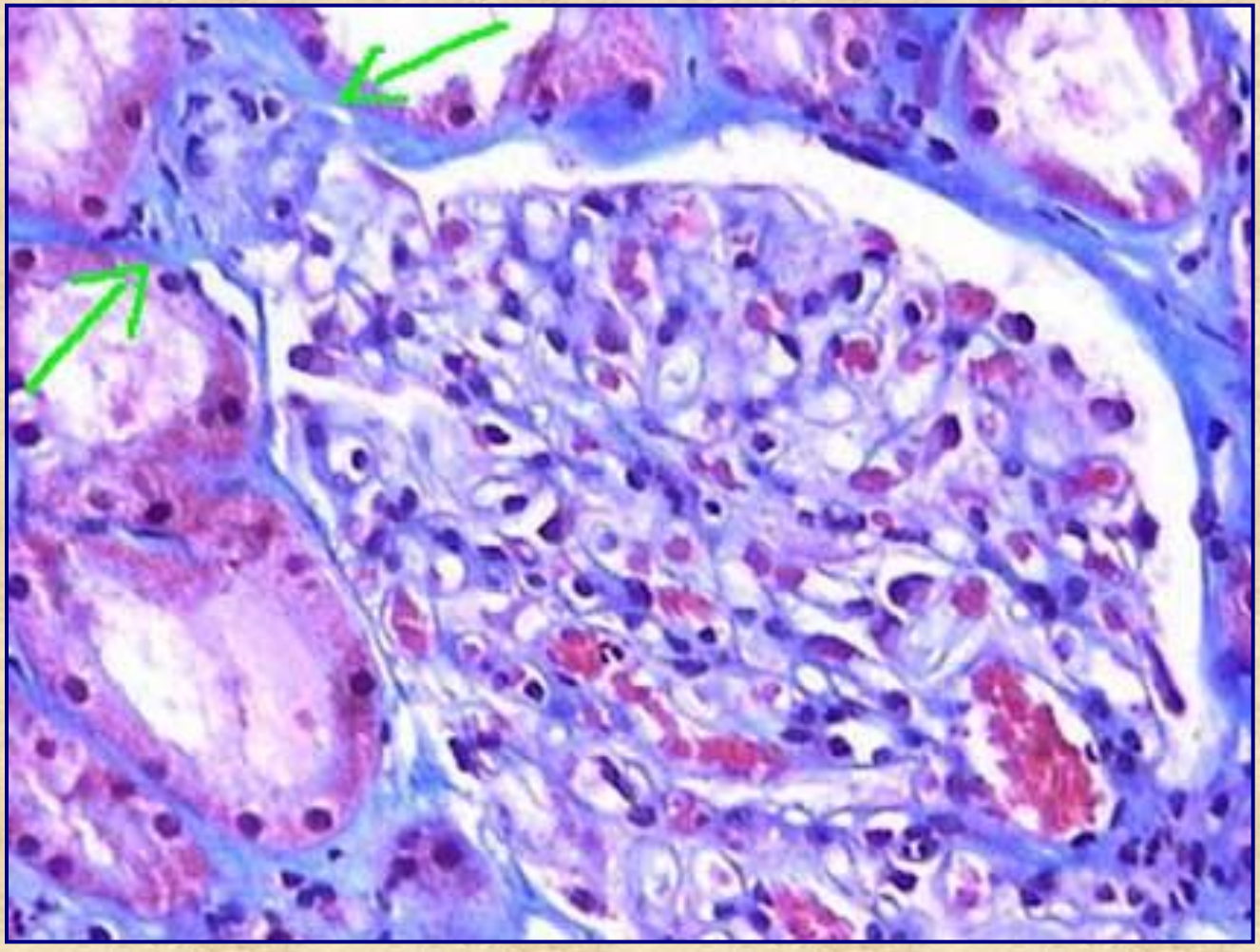






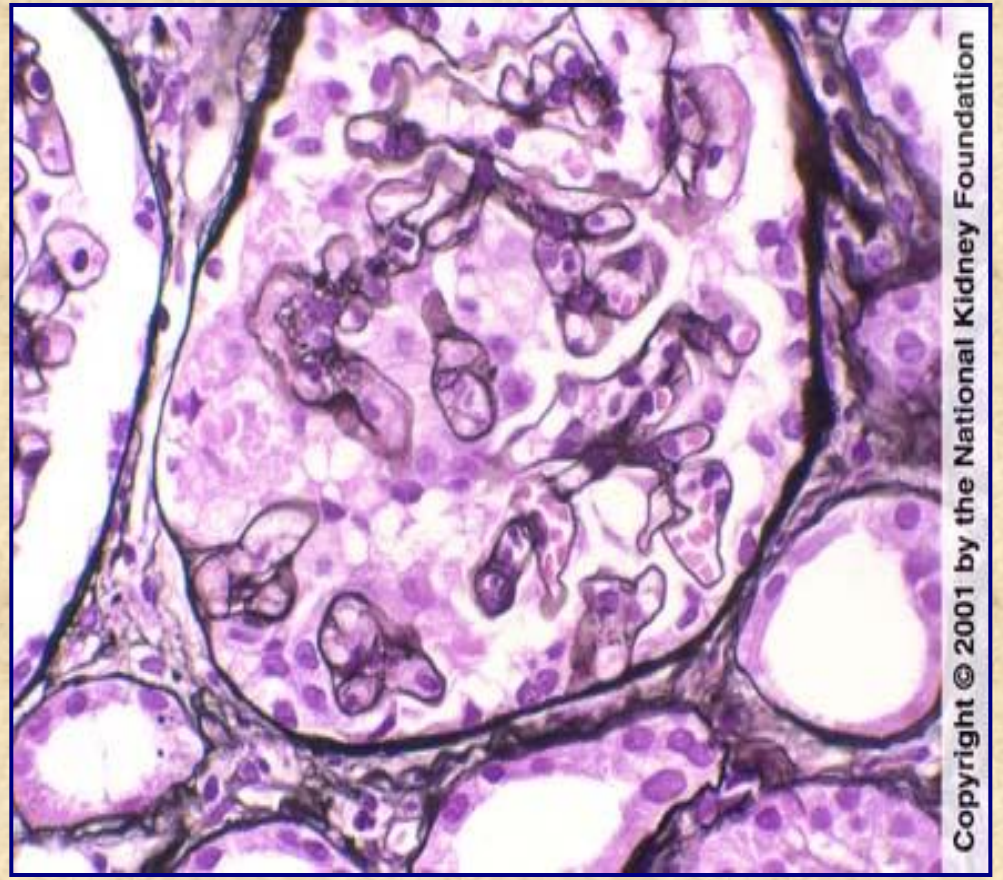
„Tip" lesion

- At proximal tubule
- Good response to steroid therapy



Collapsing glomerulopathia

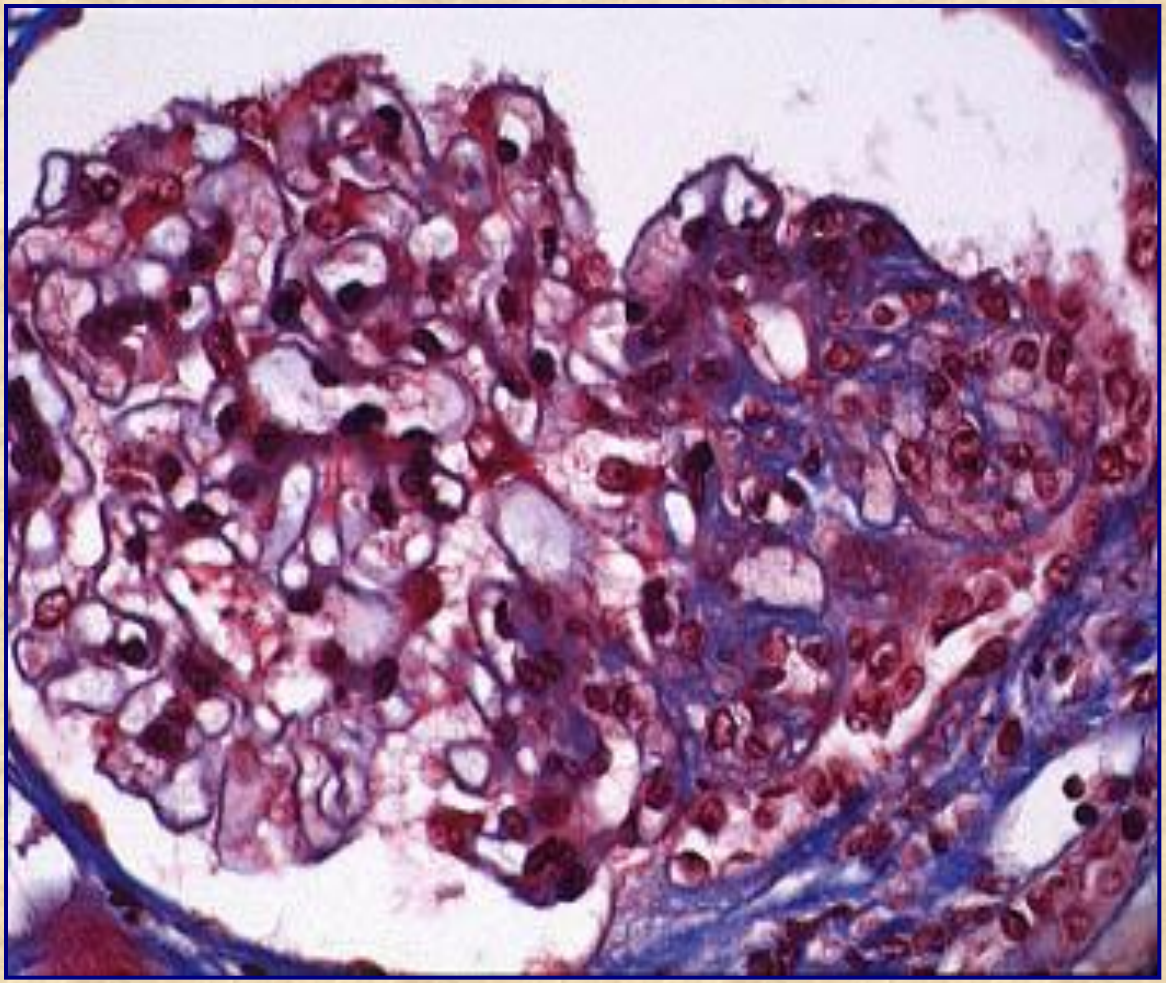
- Collapse of capillary loops
- Hyperplasia of podocytes
- Poor prognosis
- Rapid loss of renal function
- No response of therapy
- HIV infection and iv. drog abuse associated



Perihilar type

- Most common form
- Secundary

- Oligomeganephronia
- Healed proliferative necrotizing GN
- obesity
- VUR
- Cyanotic congenital heart disease
- Sickle cell disease
- Aging kidney

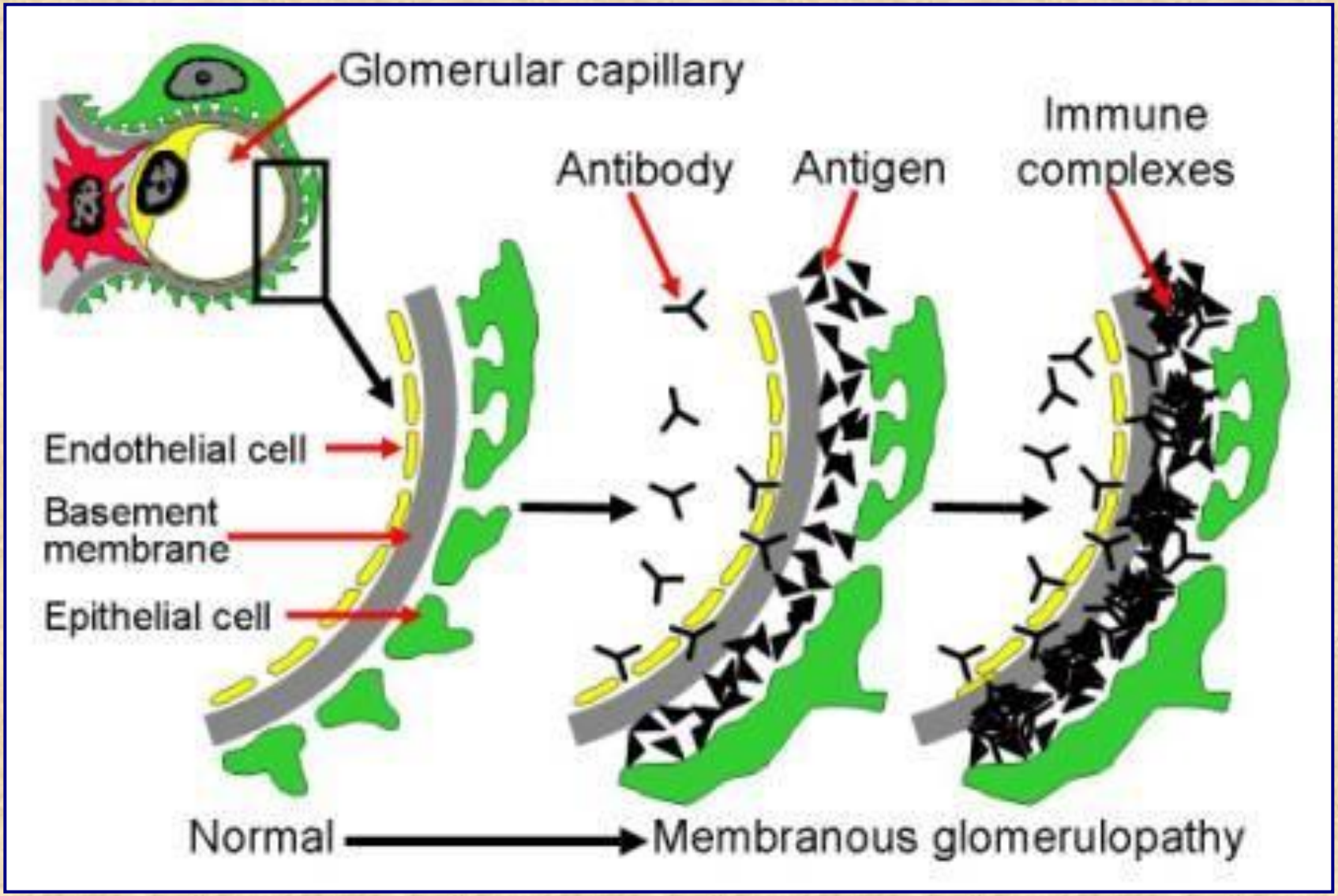


Membranous nephropathy

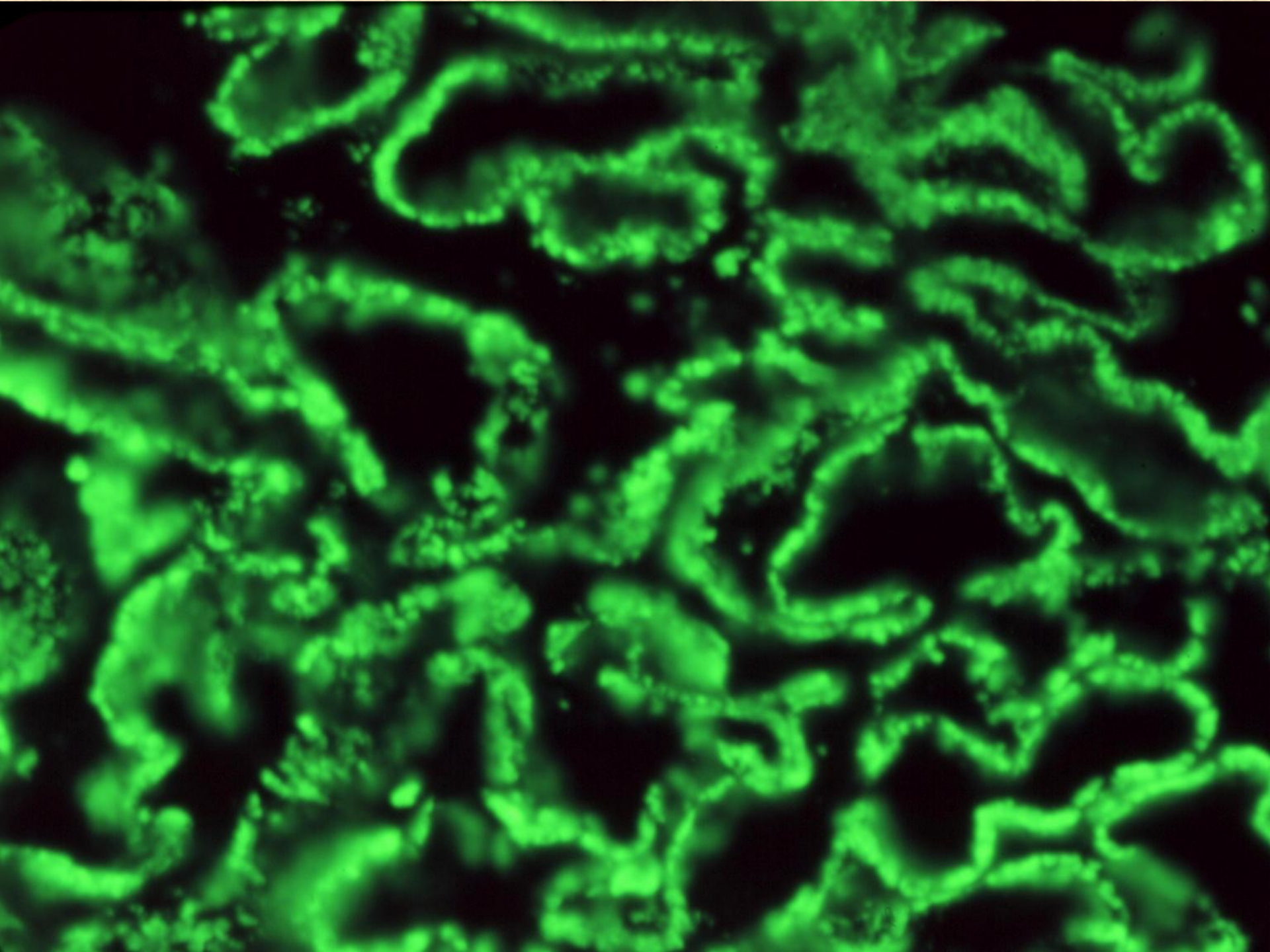
- Peak incidence beetwen 30-40 years of age
- IF: IgG, C3 – granular, along GBM
- Histology: diffuse GBM thickening
- EM: subepithelial deposits
- Pathogenesis: in-situ immuncomplexes

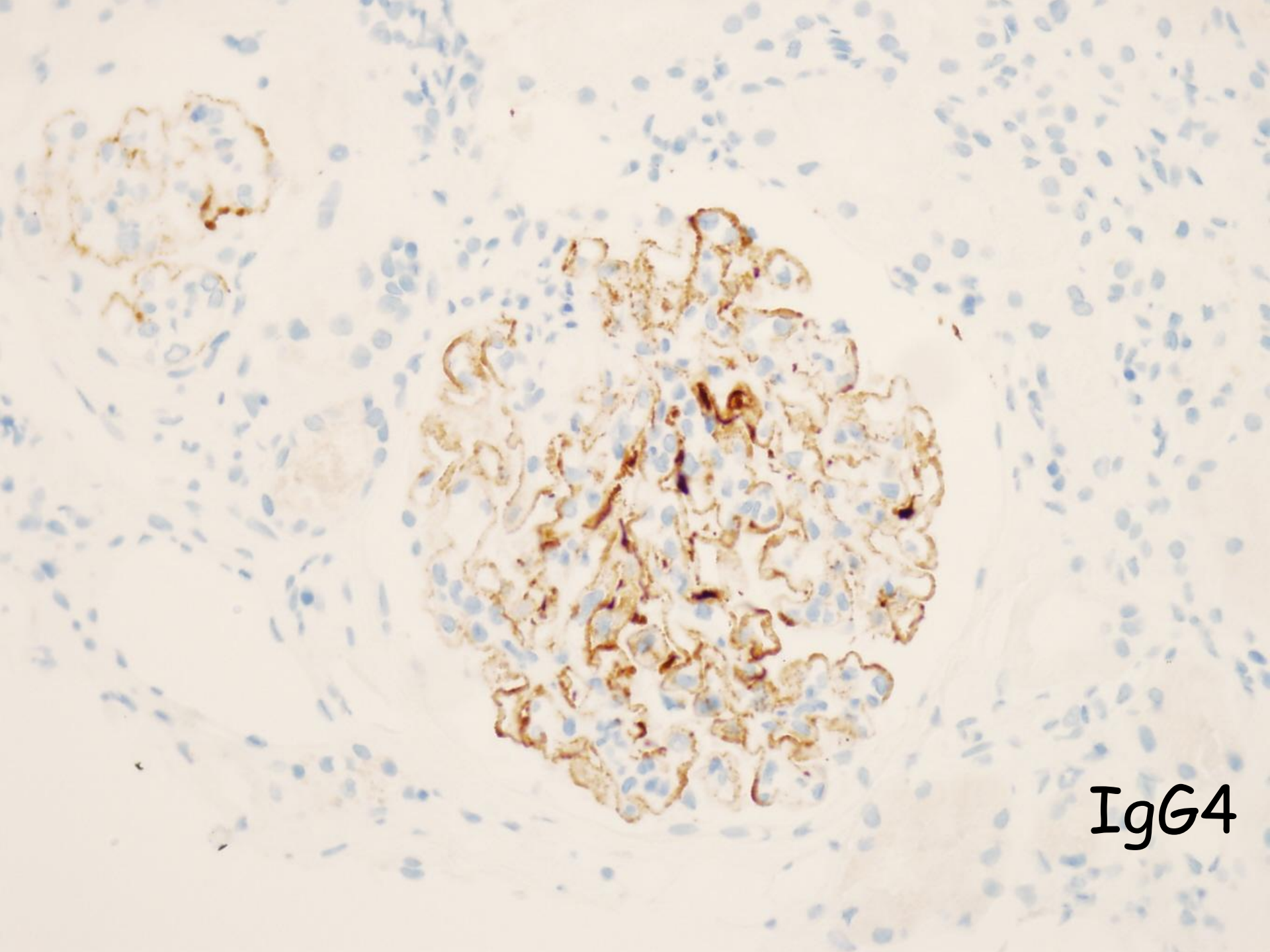
  PLA2R- Ag on podocyte IgG4 – Ab in serum
- Prognosis: variant

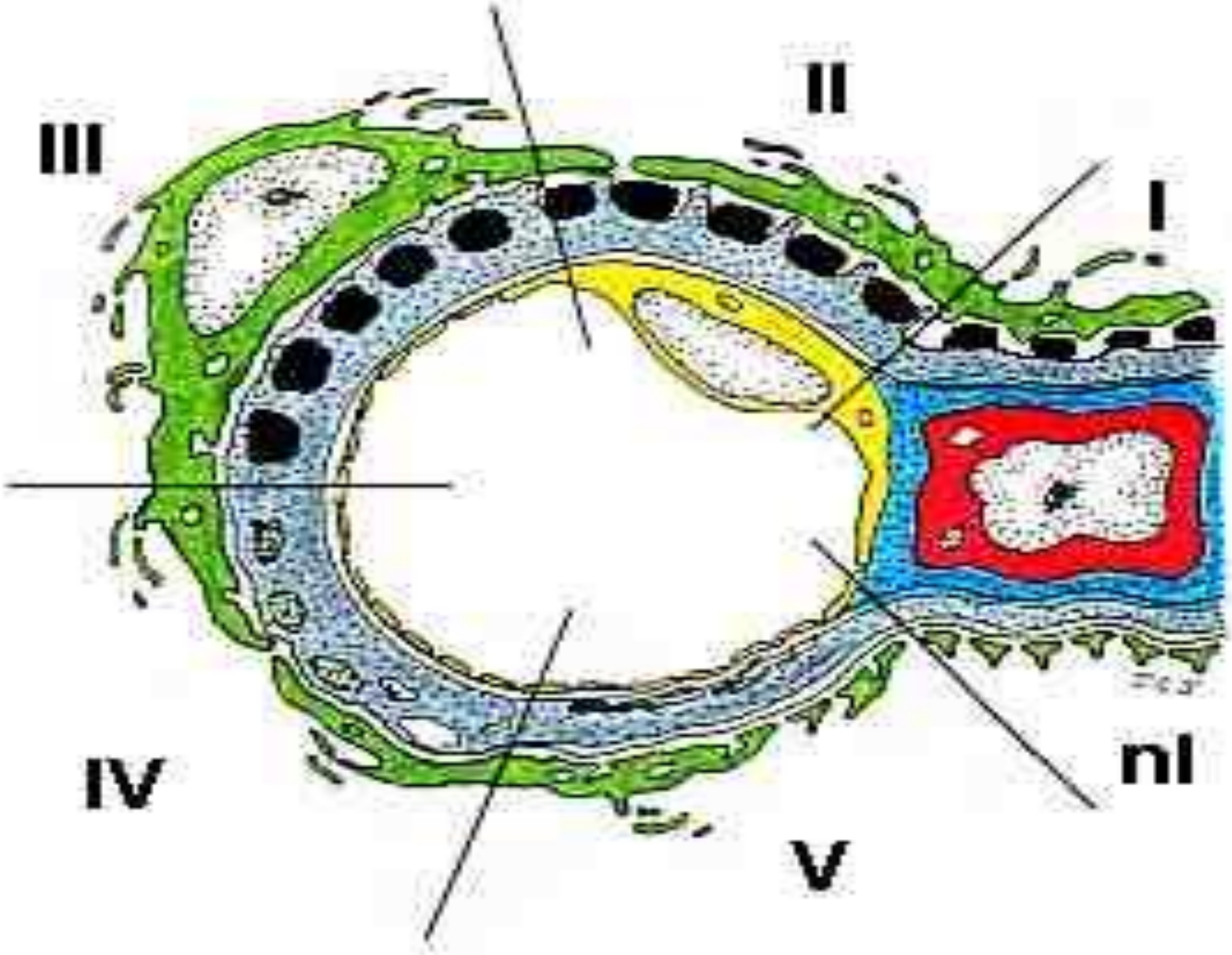
  20- 25 % of patients progress to renal failure terminating in end-stage renal disease.



Gp330-Ag located in coated pits on the podocyte cell basal surface.
Complement activation and antibody binding to the cell membrane.
Numerous granular subepithelial ICs and deposits.




IgG4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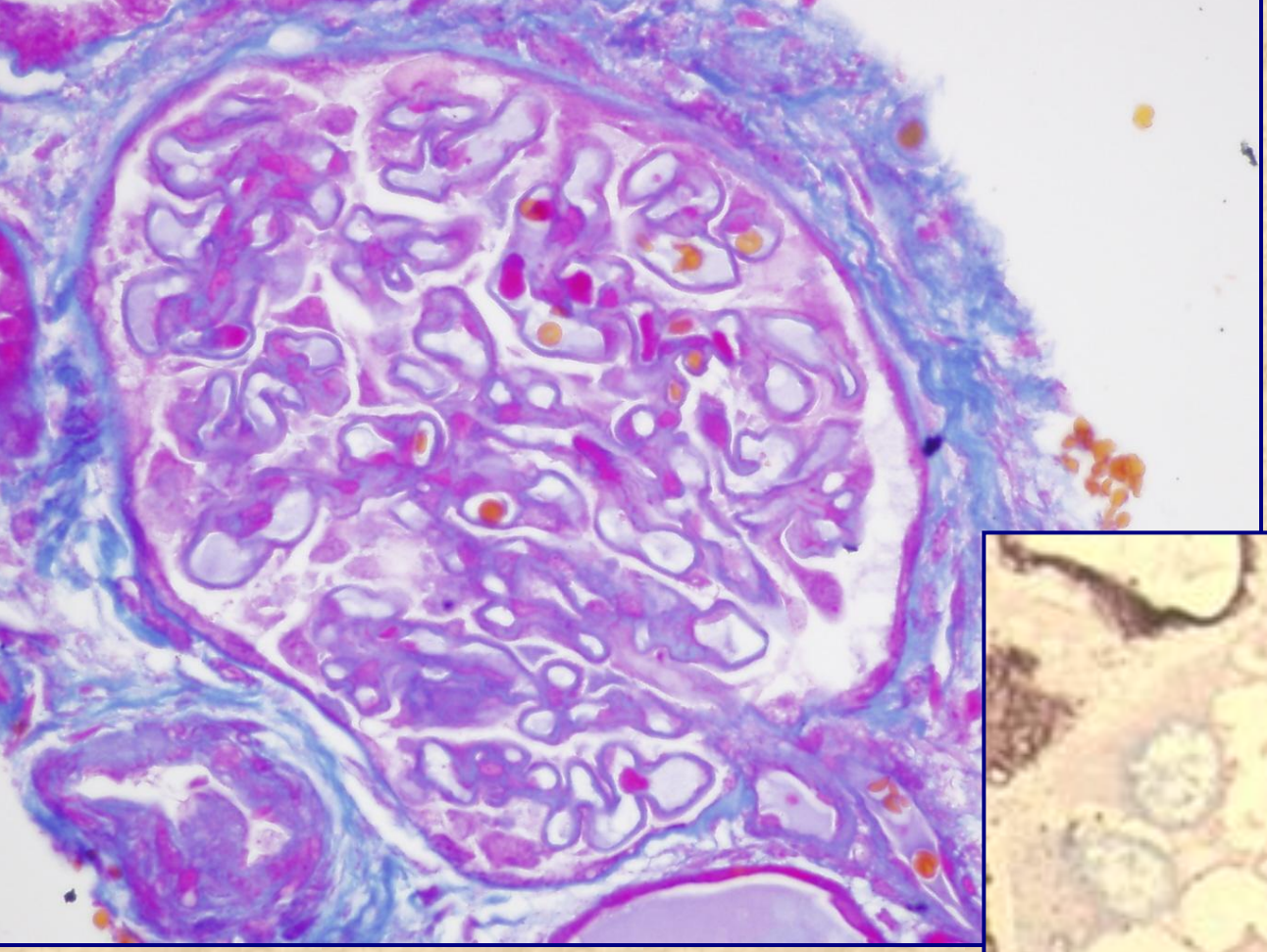
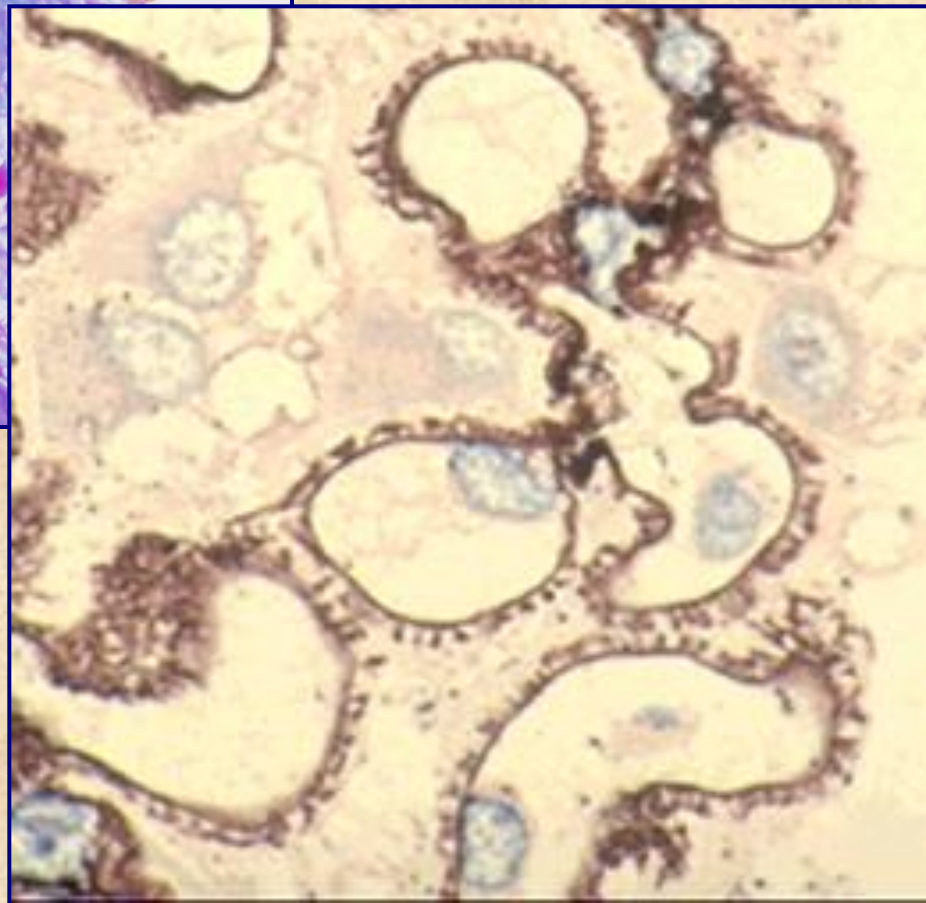
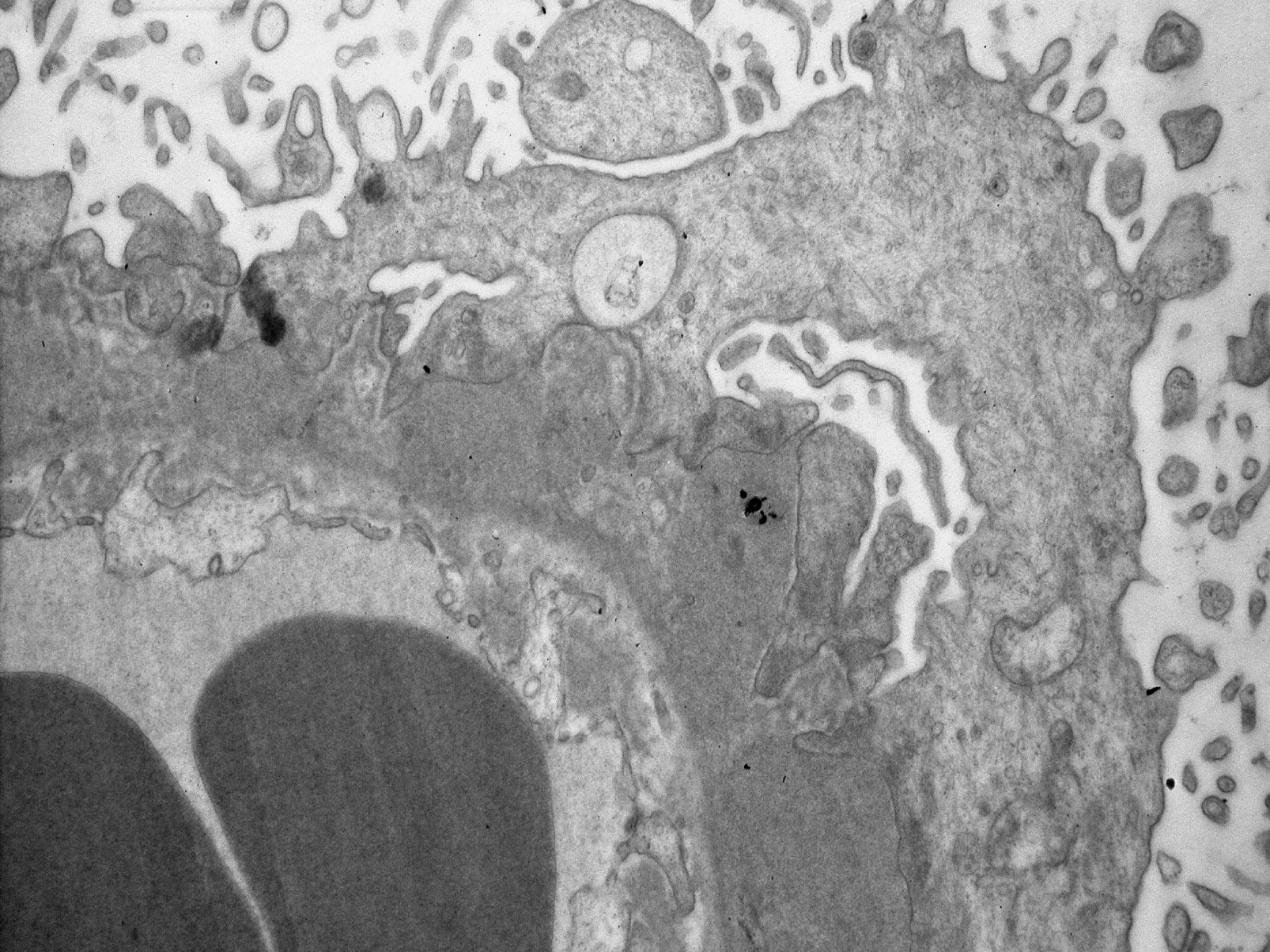






Secondary MGN

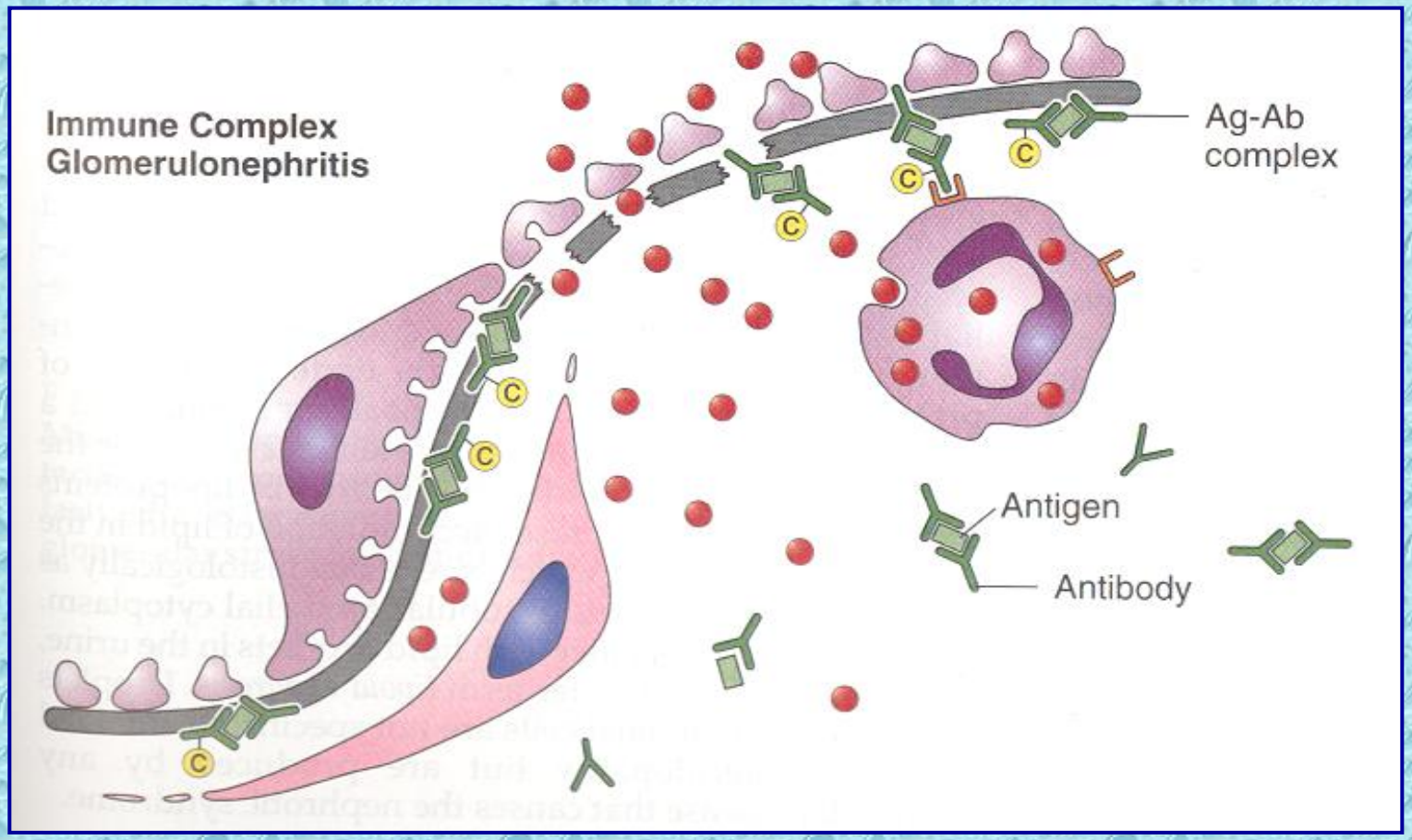
- Infections: HBV, HBC, syphilis, malaria
- Immunologic disorders: SLE, RA, Hashimoto-thyreoditis, Sjögren-syndroma, PBC
- Medications: gold, penicillinamin, diclofenac
- Neoplastic diseases: non-Hodgkin-lymphoma, carcinoma(lung,breast,prostate,GI tract etc.)
- Egyéb: renal vein thrombosis, diabetes mellitus, Guillan-Barré sy, etc.

Glomerulonephritis associated with nephritic syndrome

- Endocapillary proliferative GN
- Membranoproliferative GN
- Crescentic GN

Endocapillary proliferative GN

- Acute proliferative,poststreptococcalis, postinfectív
- After infection of béta-haemolytic Streptococcus
- Primiarly disease of childhood
- Circulating immun komplexes
- AST elevated, C3 level reduced
- IF: IgG és C3- granular, subepithelial and mesangial
- Histology: neutrophiles,endothelial and mesangial cell proliferation, lobular glomerular pattern
- EM: humps, increased mesangial matrix, mesangial hypercellularity
- Prognosis: good



Glomerulus is innocent „baystander".

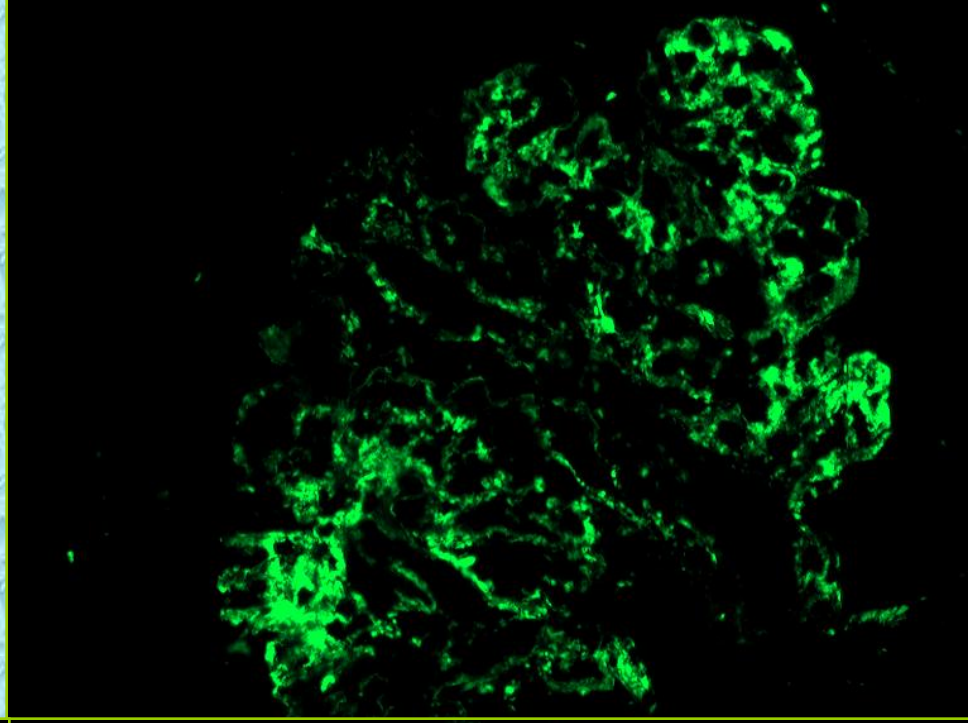
Antigen is either exogenous or endogenous.

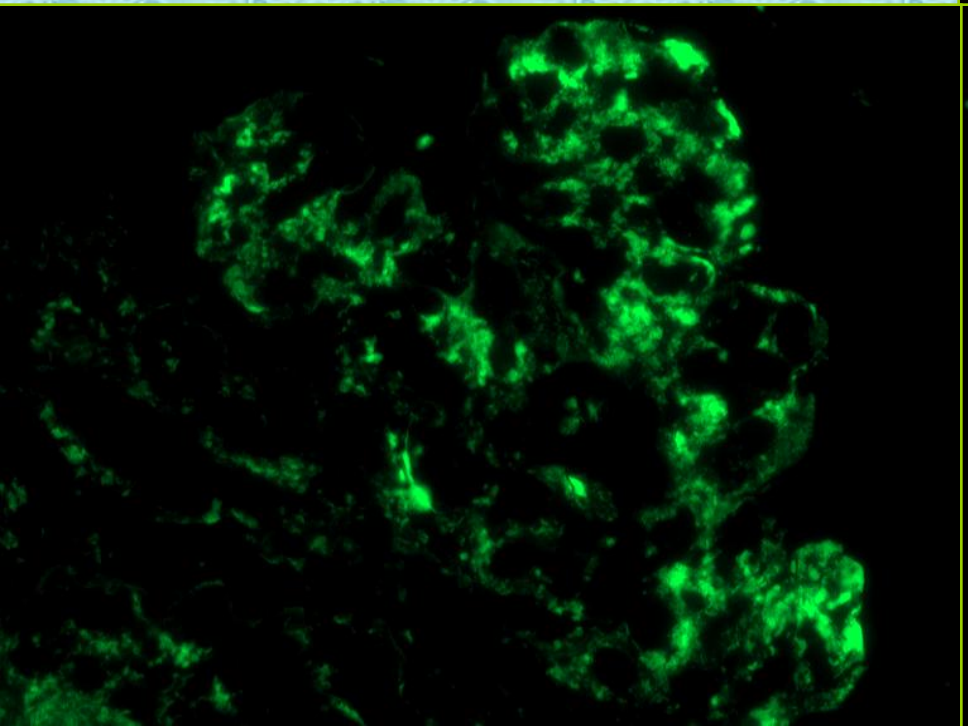
exogenous: *Streptococcus, Staphylococcus, Gold, HCV, HBV*

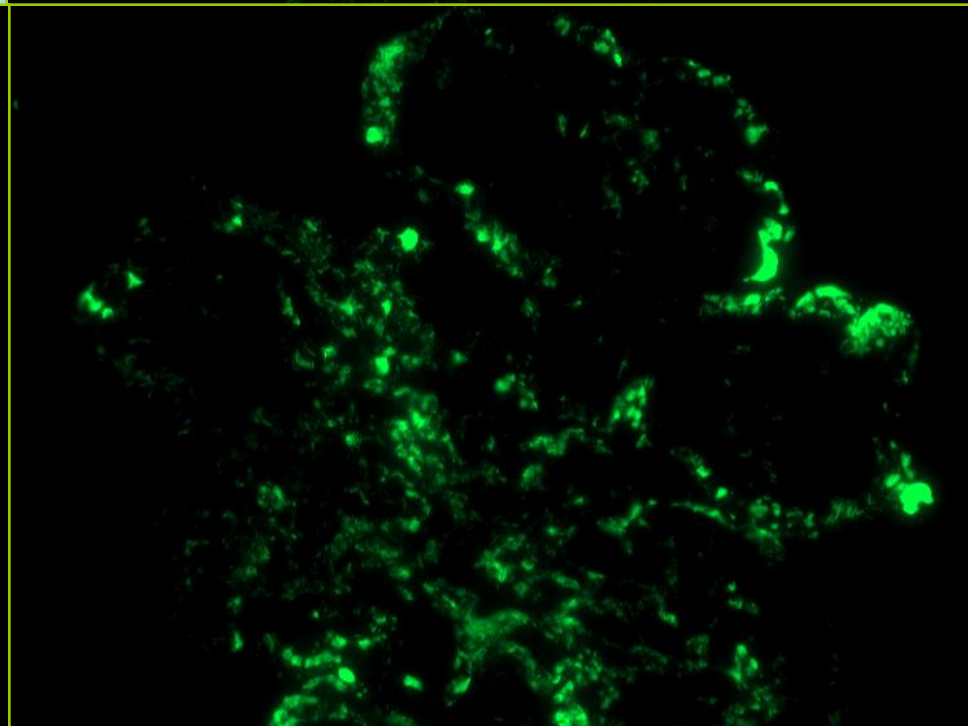
endogenous: *DNA (lupus), thyreoglobulin, tumor Ag.,etc.*

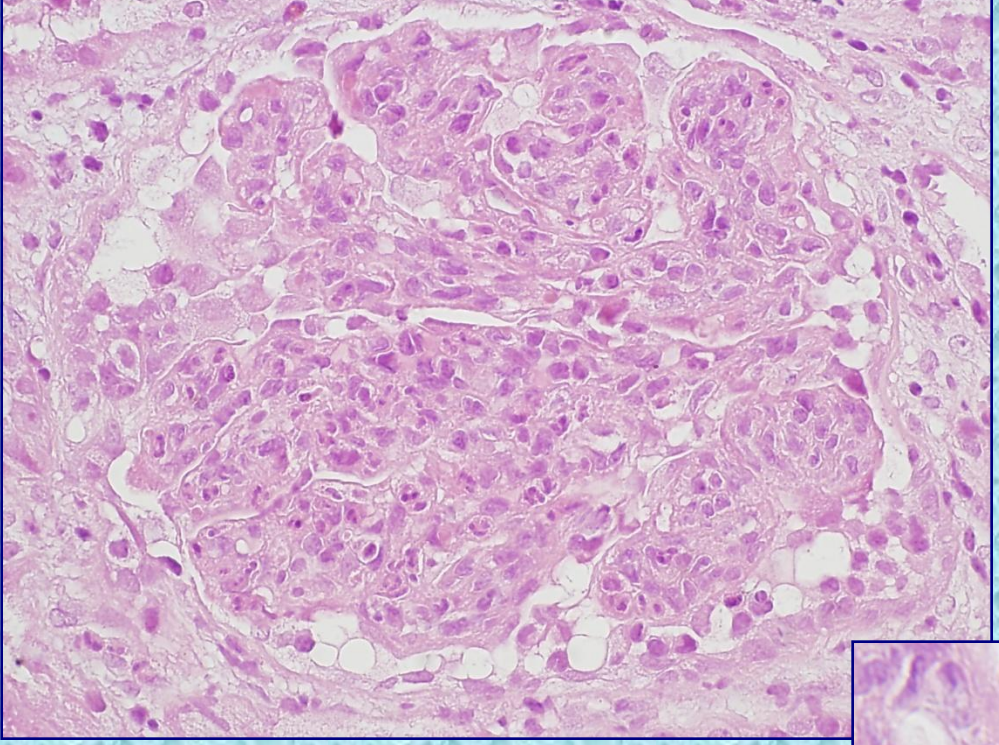
Antigen-antibody complexes trapped in glomeruli.

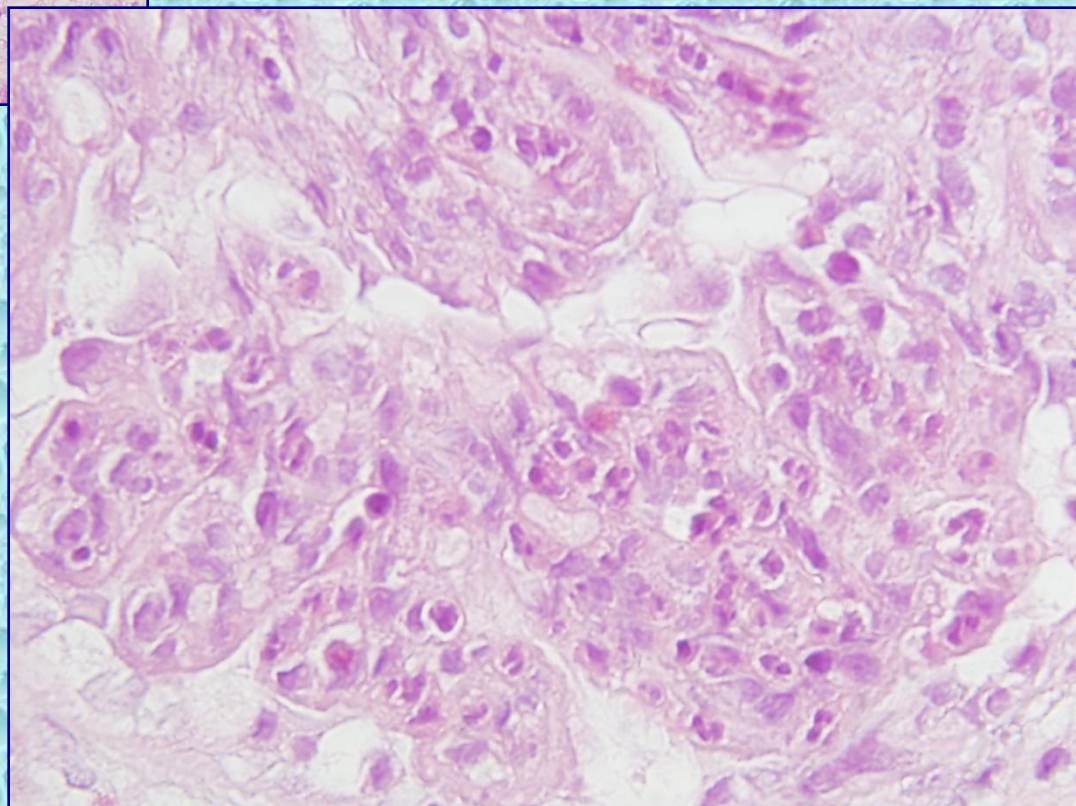
IgG
Complement 3

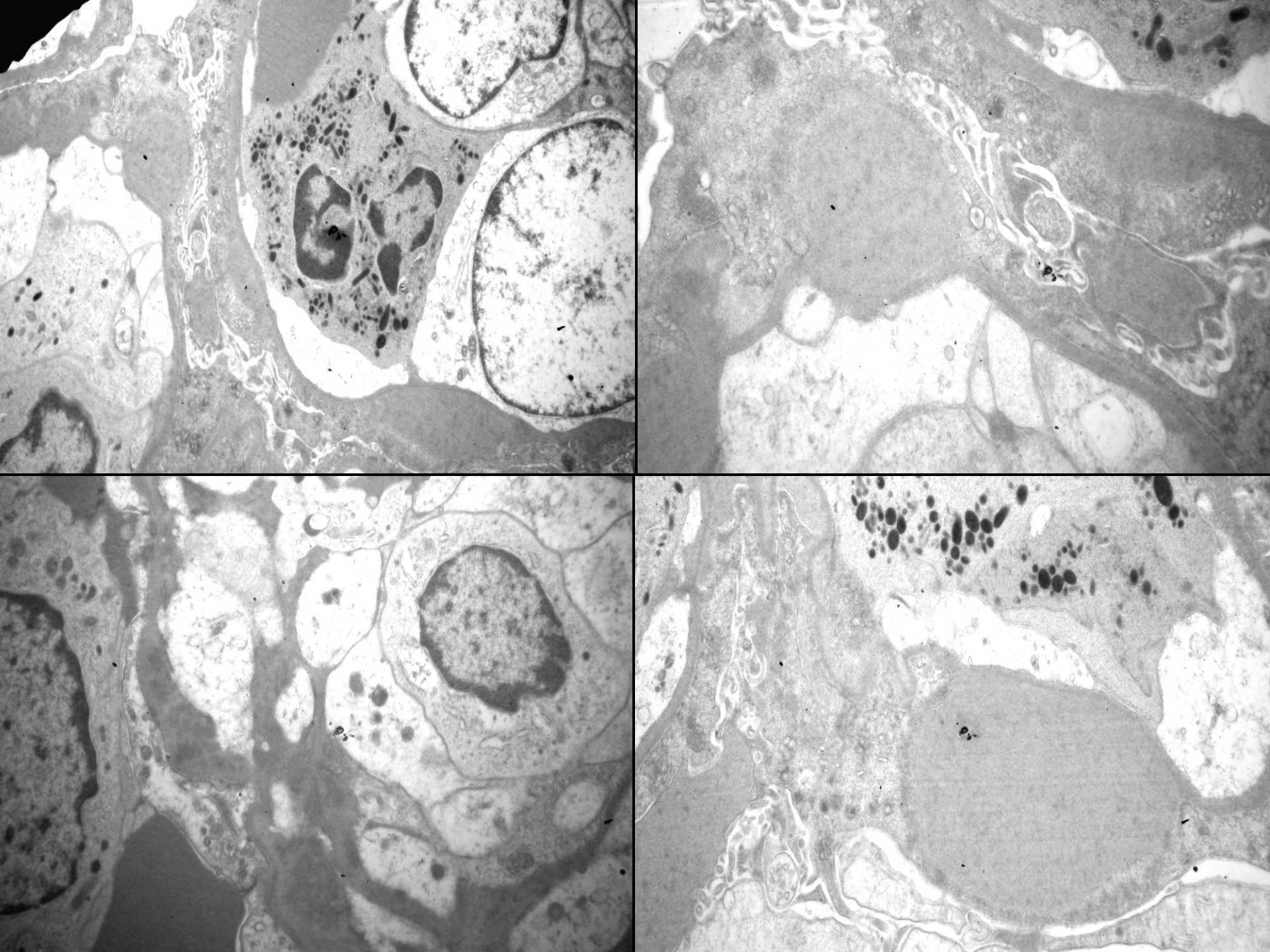












Membranoproliferative GN

- 2 group
- Children and young adults are affected
- Nephrotic sy.
- Hypocomplementaemia
- GBM és mesangium involved
- Poor prognosis
- Recurrance after transplantation

- **C3 Glomerulopathies**

Dense Deposit Disease (DDD) previously:type II

C3 glomerulonephritis

Familial C3 glomerulopathy

CFHR5 nephropathy

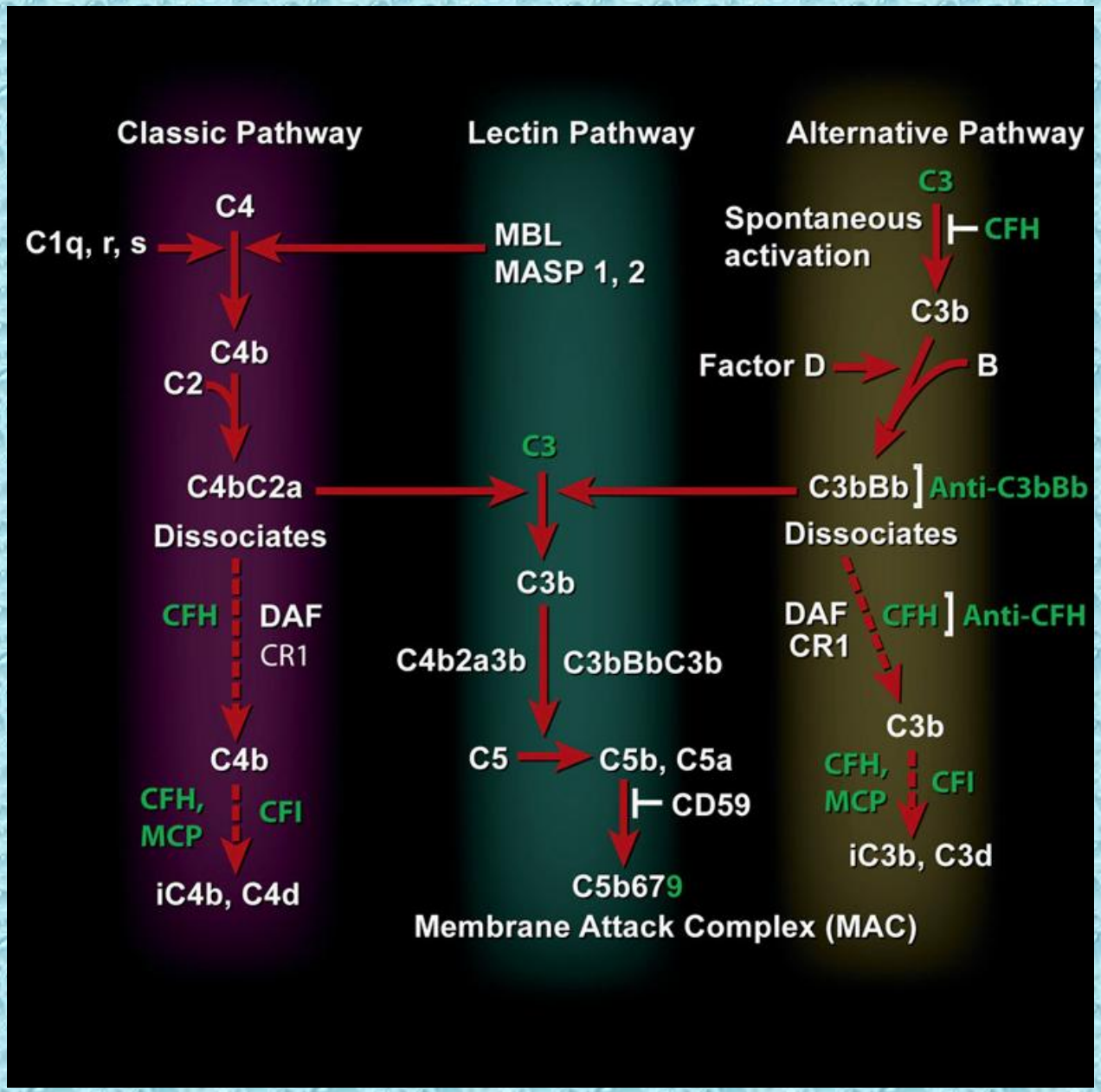
Atypical acute glomerulonepritis

- **Idiopathic MPGN with IC deposition**

Type I

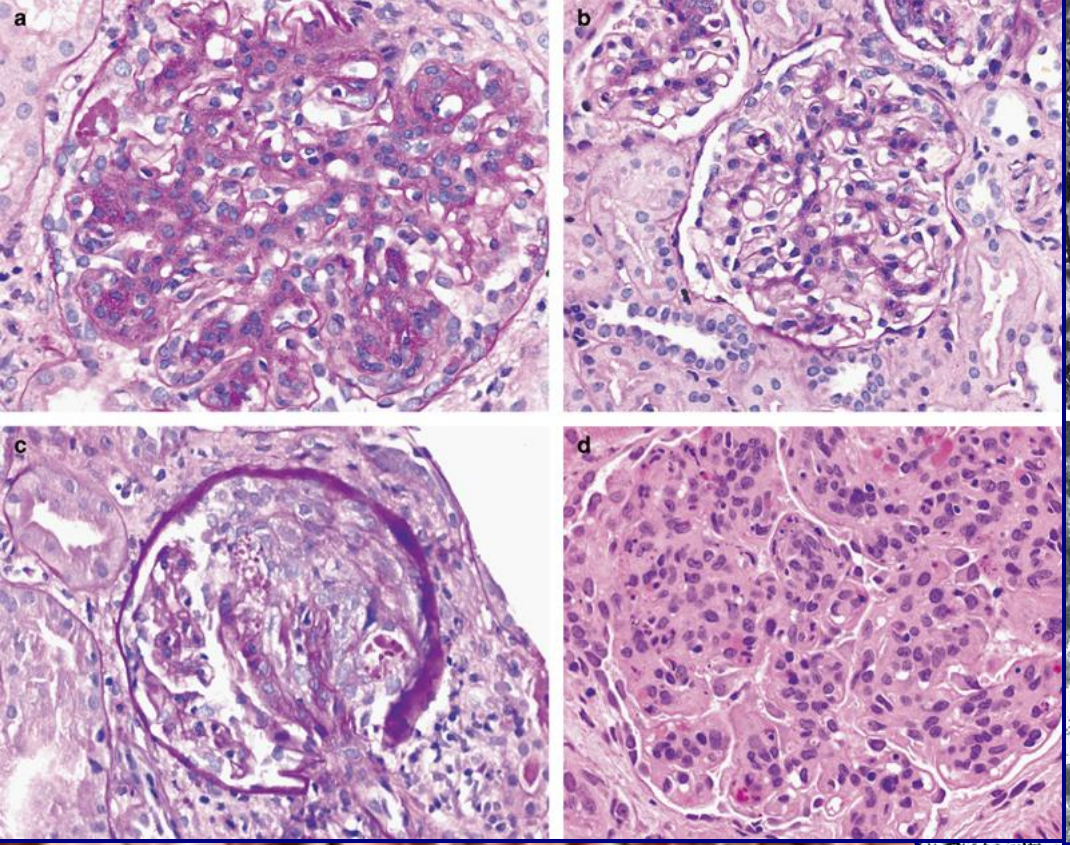
Type III

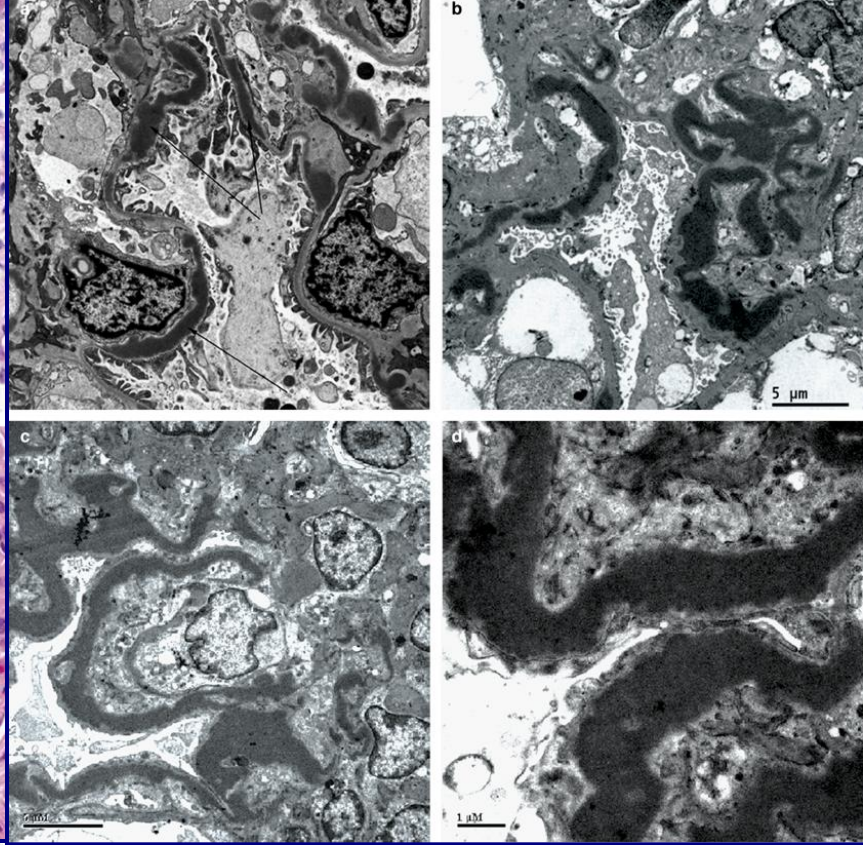
Complement Dysregulation in C3 Glomerulopathies

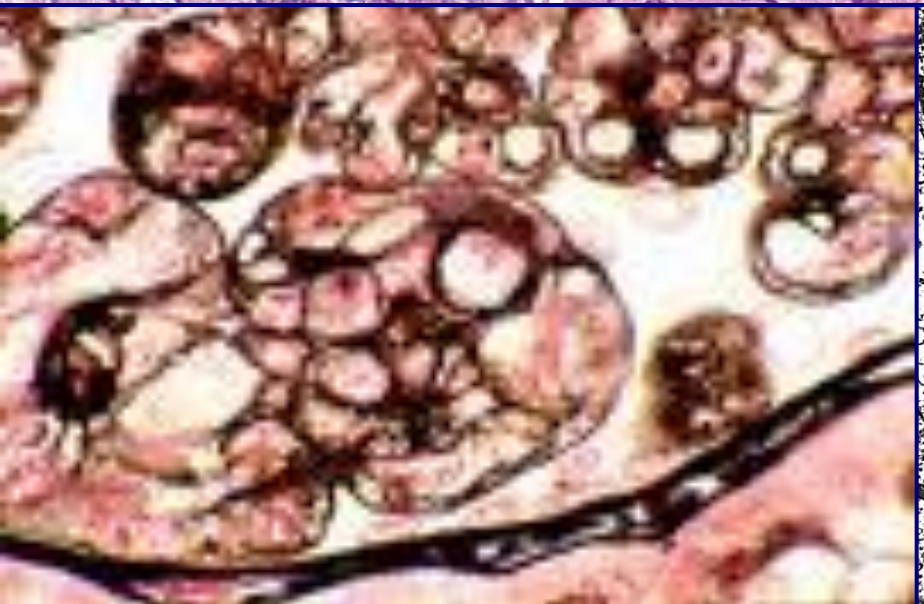


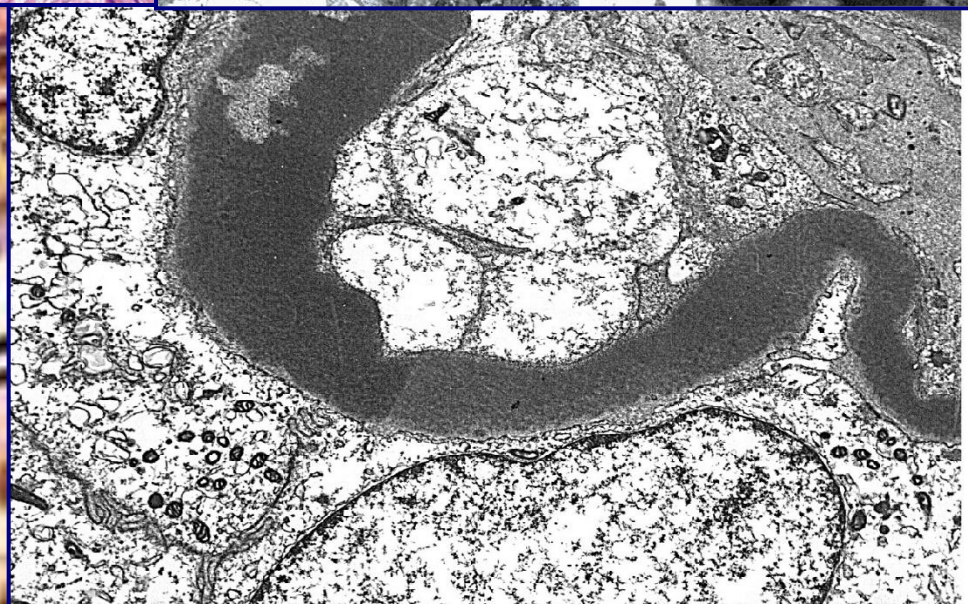
Dense Deposit Disease

- Patogenesis is unknown
- Rare (10% of all cases of idiopathic MPGN)
- C3 nephritic factor (C3NeF) - IgG autoantibody
- IF: ribbon-like C3 sign along GBM
- Histology: membranoproliferative lesions, necrosis, crescents may occur.
- Em: elektron denz material deposition in the GBM, Bowman-capsule and tubular bm.
- Poorer prognosis than typeI,
  50%-ESKD within 10 years



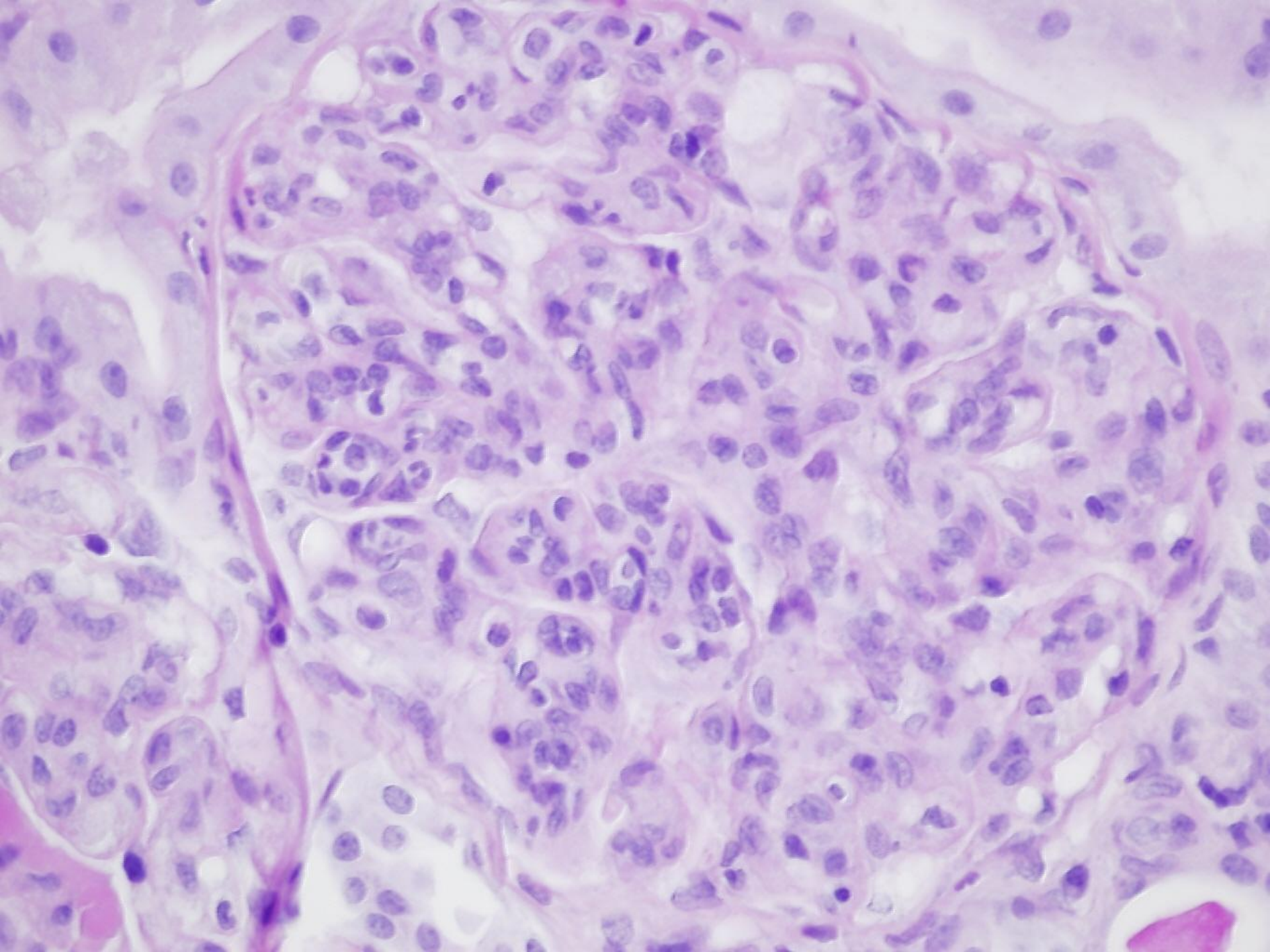


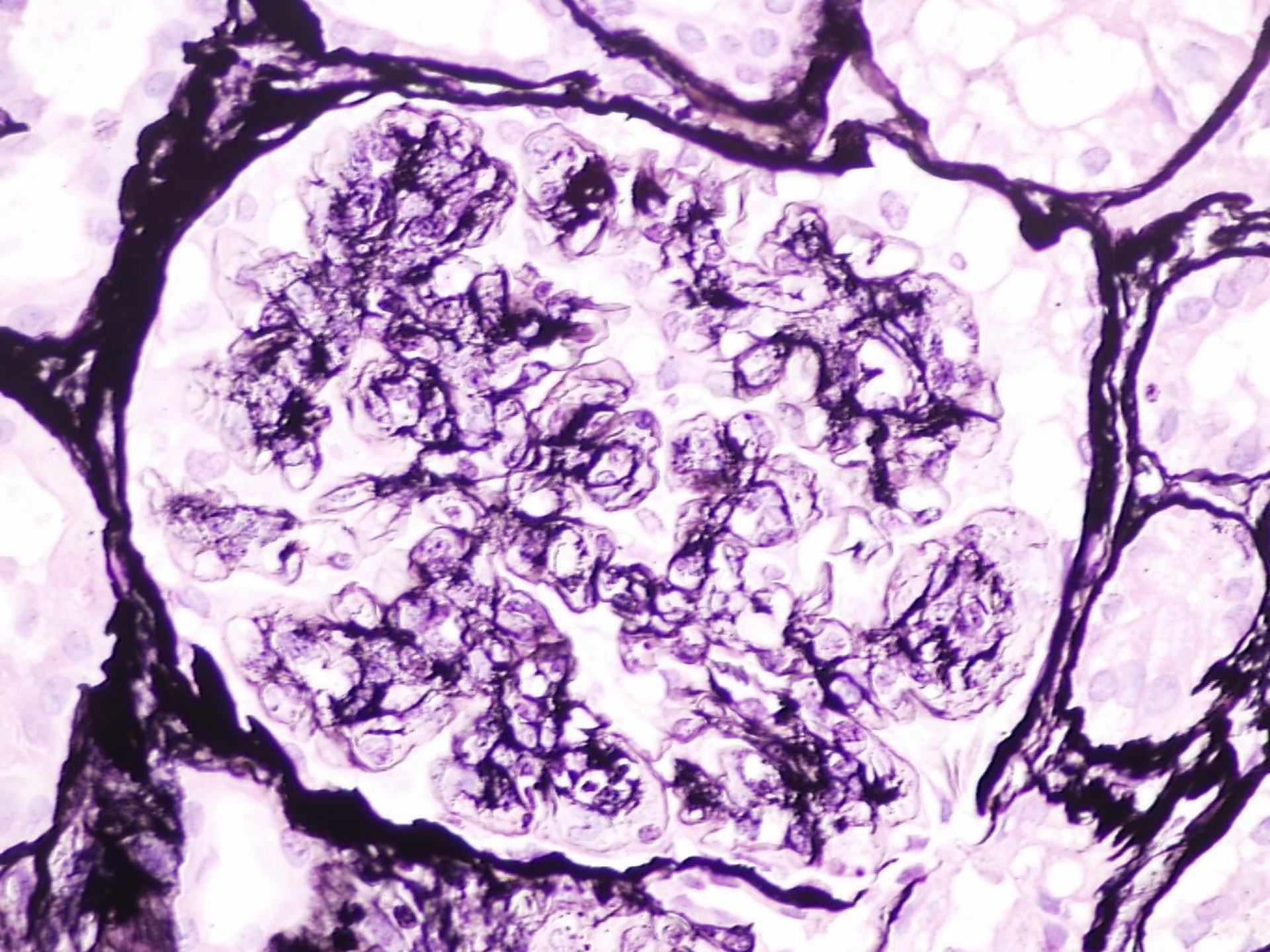


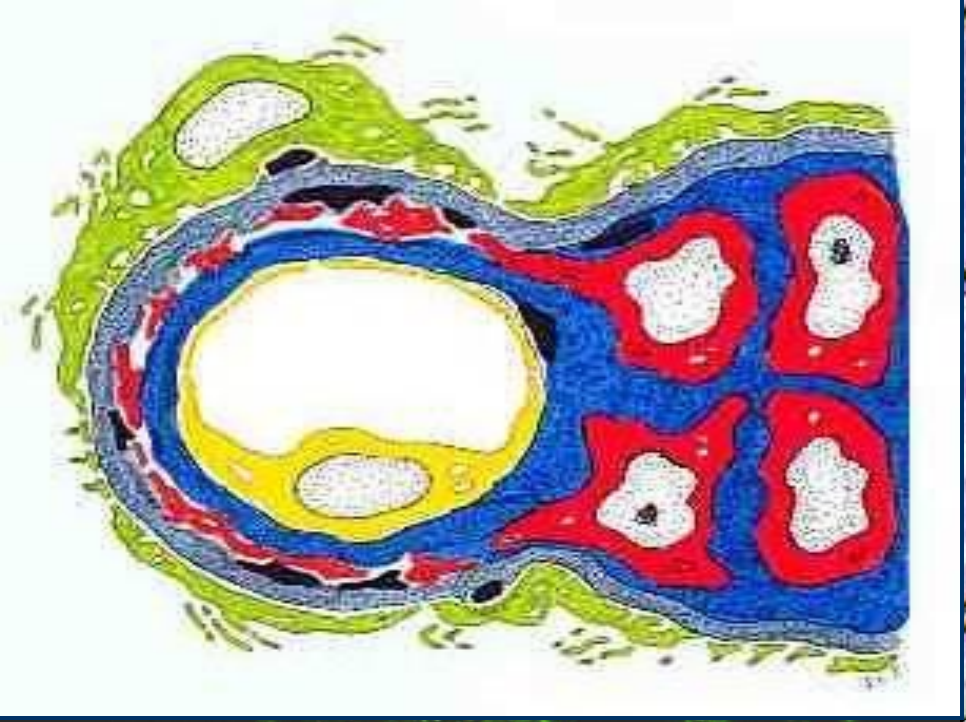


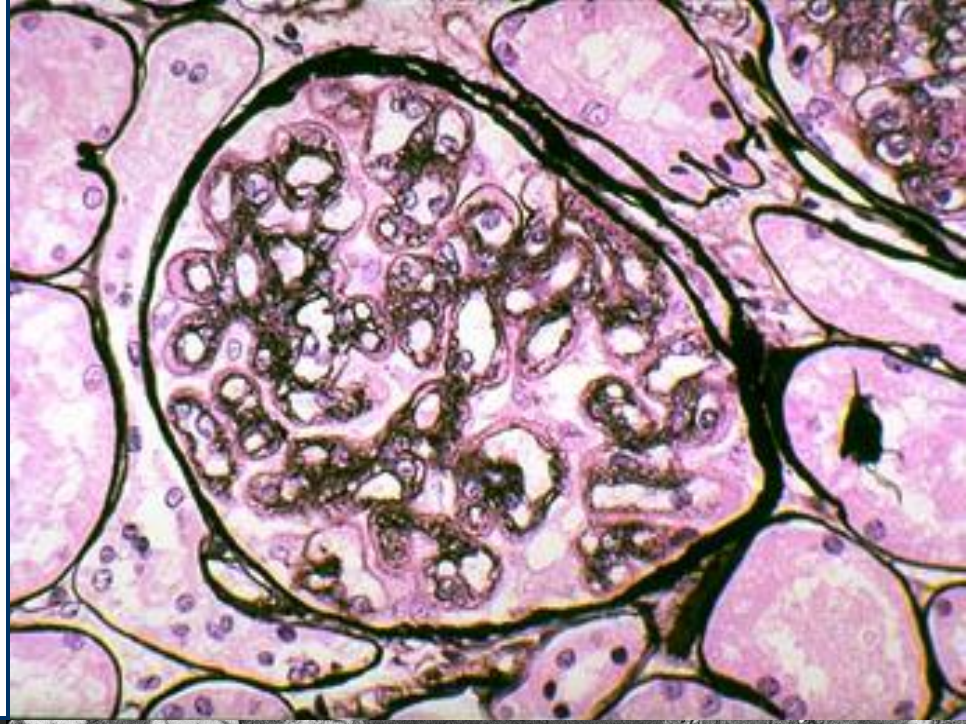
Membranoproliferative GN

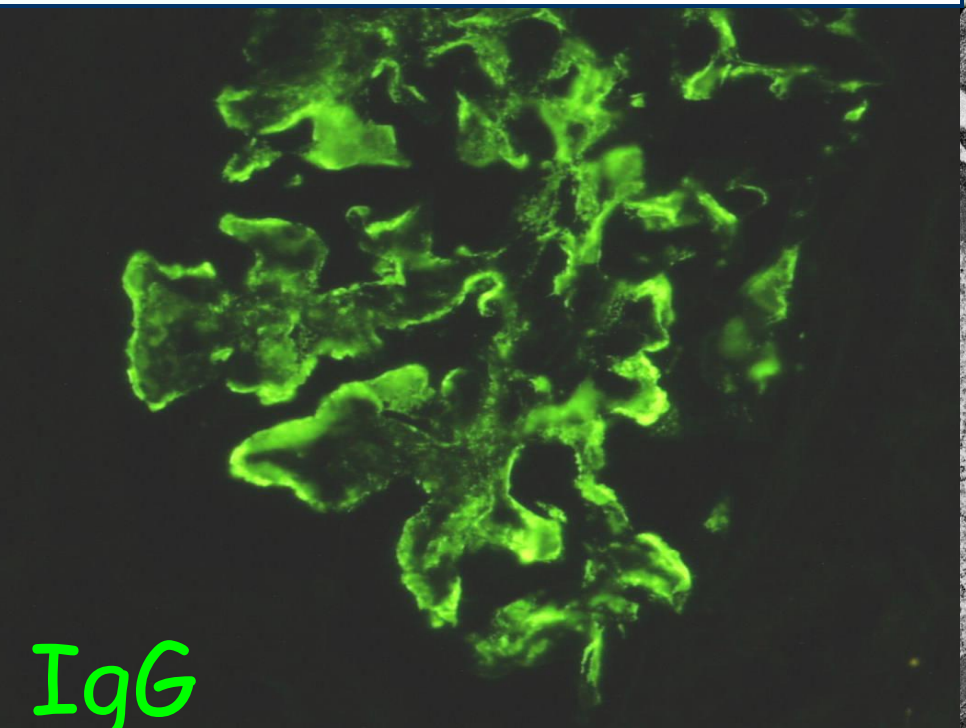
- More common
- Circulating or in situ immuncomplexes
- Ag unknown, complement activation
- IF: IgG, C3,C1q,C4 granular,subendothelial
- Szövettan: mesangial interposition, „tram-track", proliferation, lobular pattern
- EM: subendothelial deposits

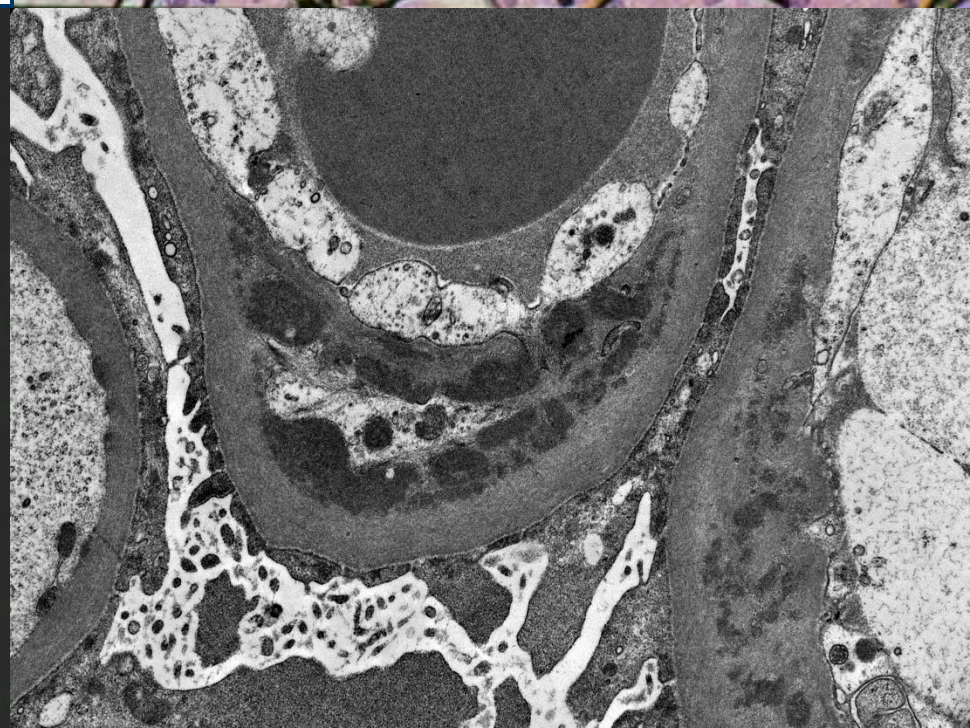









IgG



Secondary MPGN

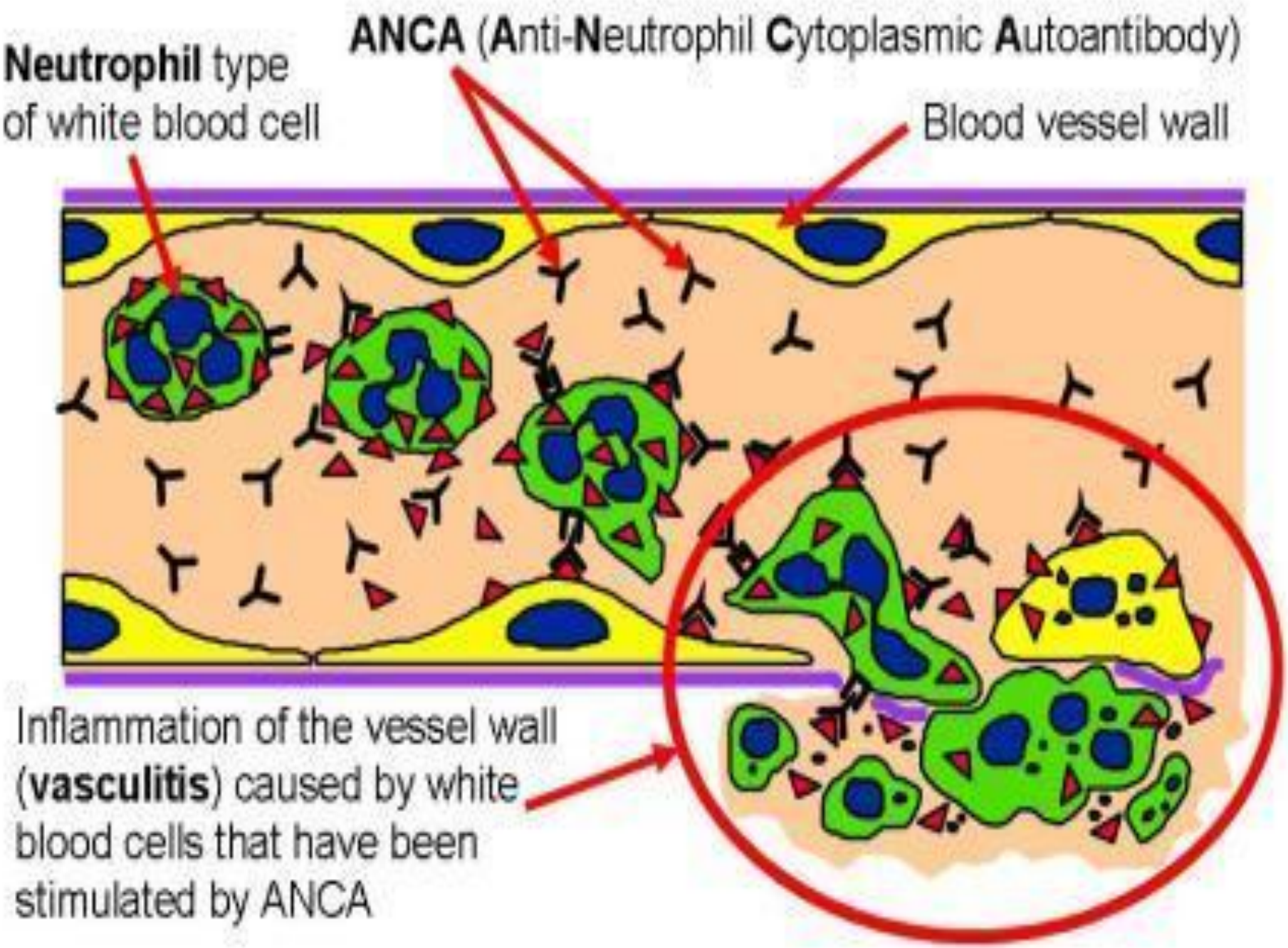
- Infections: HBV, HCV, HIV,EBV, mycoplasma, endocarditis, malaria
- Neoplastic diseases: carcinomas, CLL, melanoma, non-Hodgkin lymphoma
- Immunological diseases: SLE, SS, RA, Sjögren sy.,sarcoidosis,cryoglobulinaemia
- Miscellanous: drog abusus,Turner sy., Down's syndrome

Crestentic GN

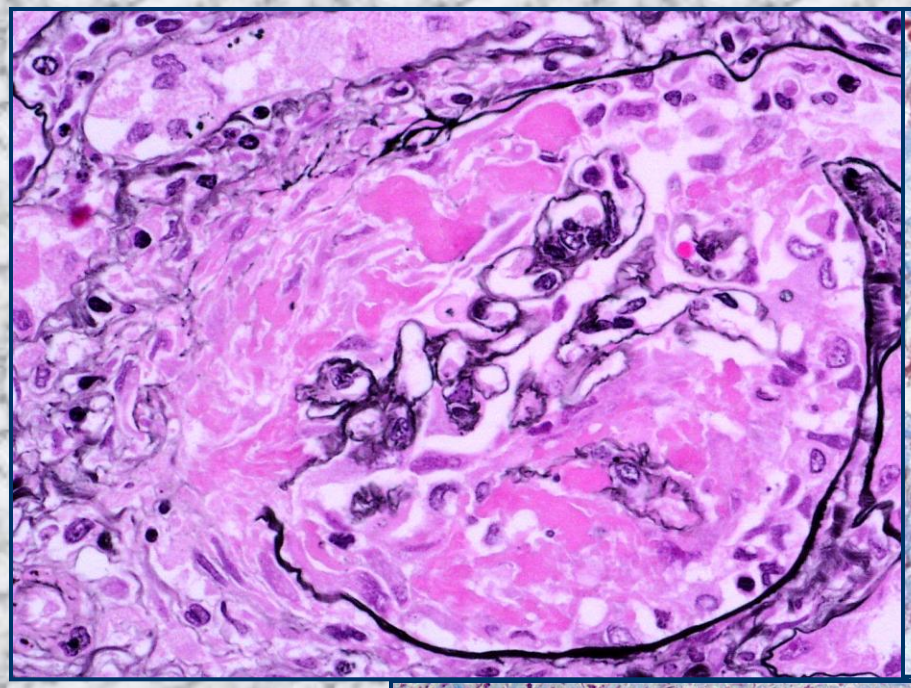
- ANCA-associeted, pauci-immun
- Immuncomplex-mediated
- Anti-GBM-nephritis

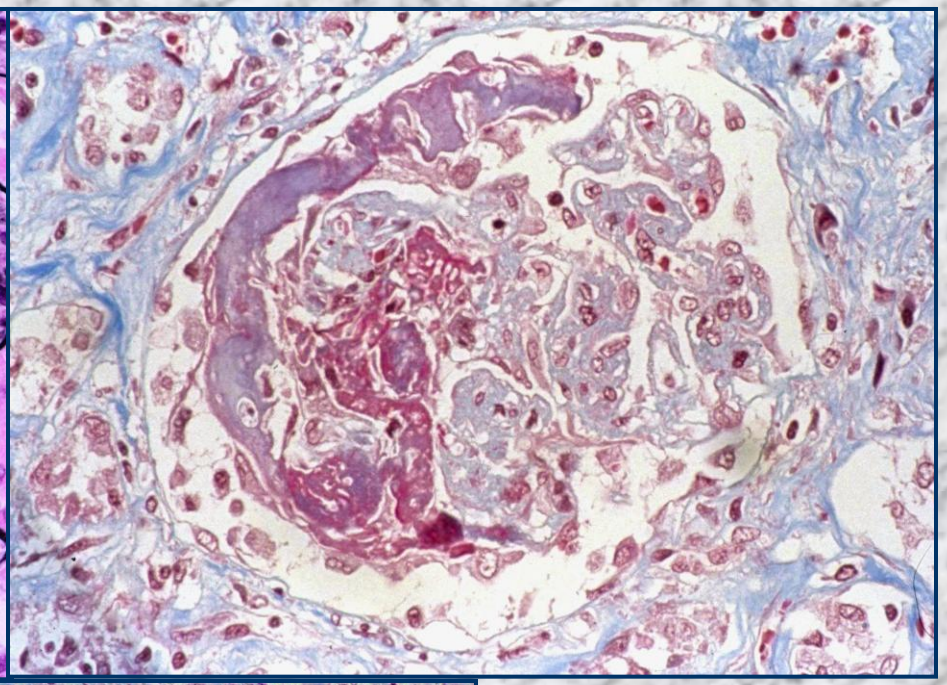
ANCA-associated, pauci-immun glomerulonephritis

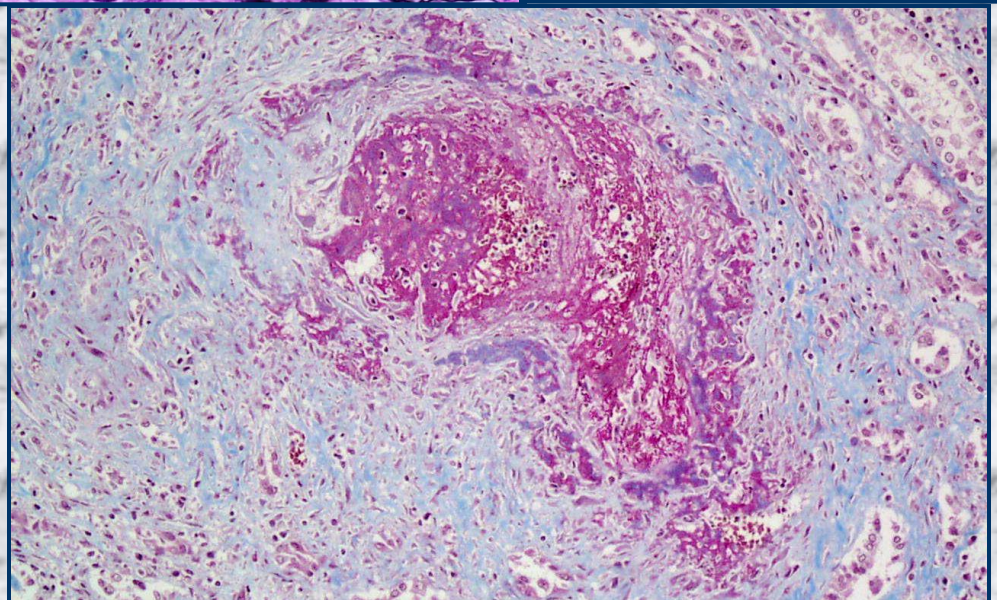
- Small vessel vasculitis
- cANCA –granulomatosis with polyangiitis (Wegener)
- pANCA – mikroscopic polyangitis
- IF: negative
- EM: negative
- Histology: crescent, fibrinoid necrosis in capillary walls and loops, granuloma
- Prognosis: poor, CRF


Neutrophil type of white blood cell
ANCA (**A**nti-**N**eutrophil **C**ytoplasmic **A**utoantibody)
Blood vessel wall
Inflammation of the vessel wall (**vasculitis**) caused by white blood cells that have been stimulated by ANCA

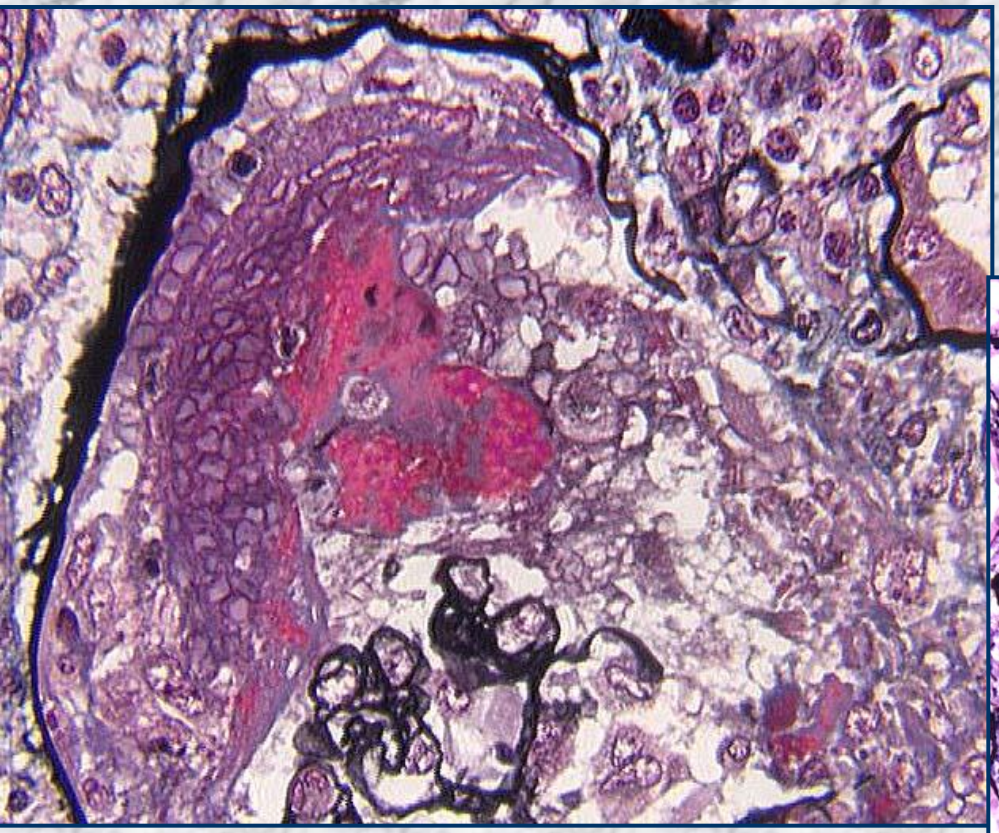
Microscopic polyangitis

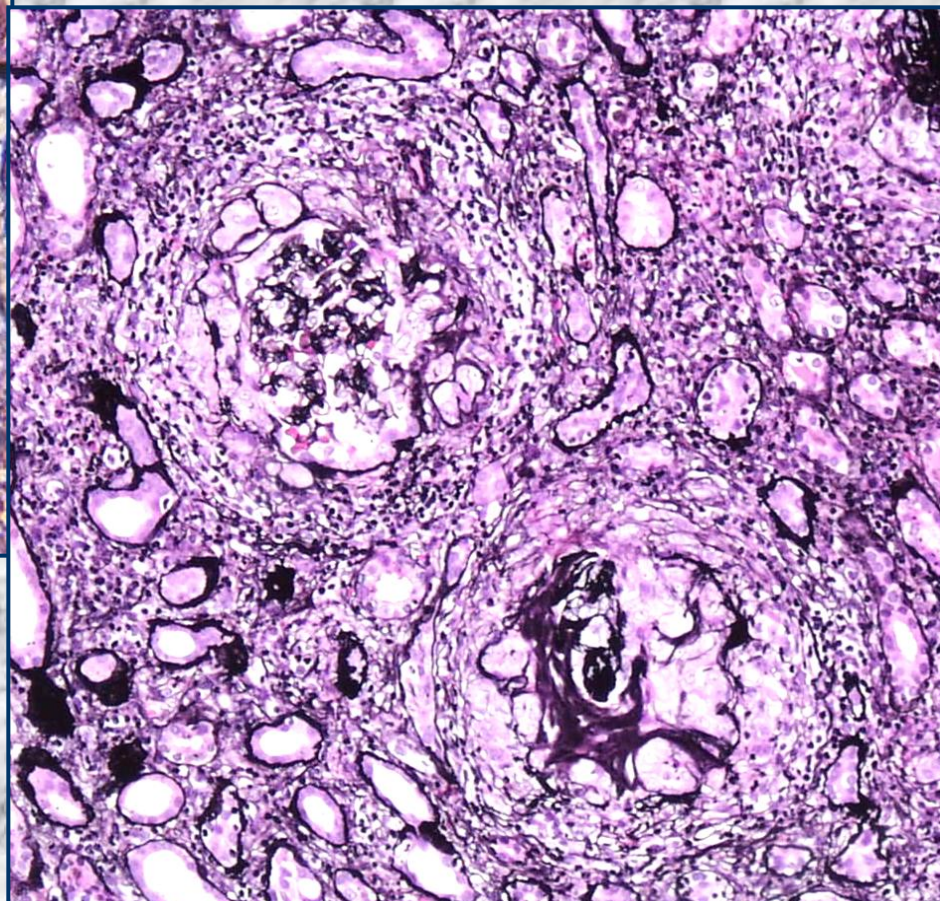






Granulomatosis with polyangiitis



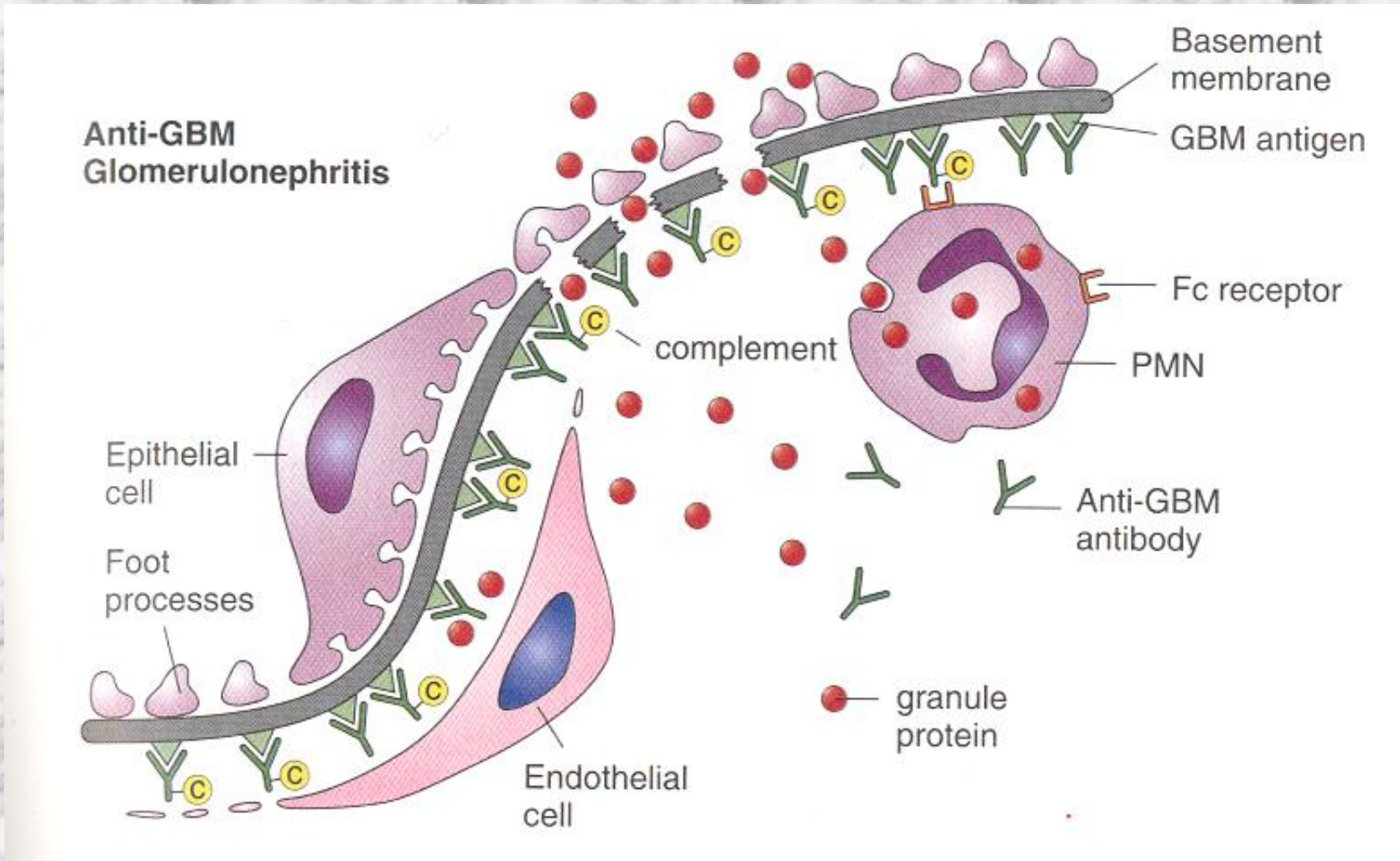


Immune complex crescentic glomerulonephritis

- Postinfective GN
- MPGN
- SLE
- Henoch-Schönlein Purpura
- IgA-nephropathia
- Cryoglobulinaemia

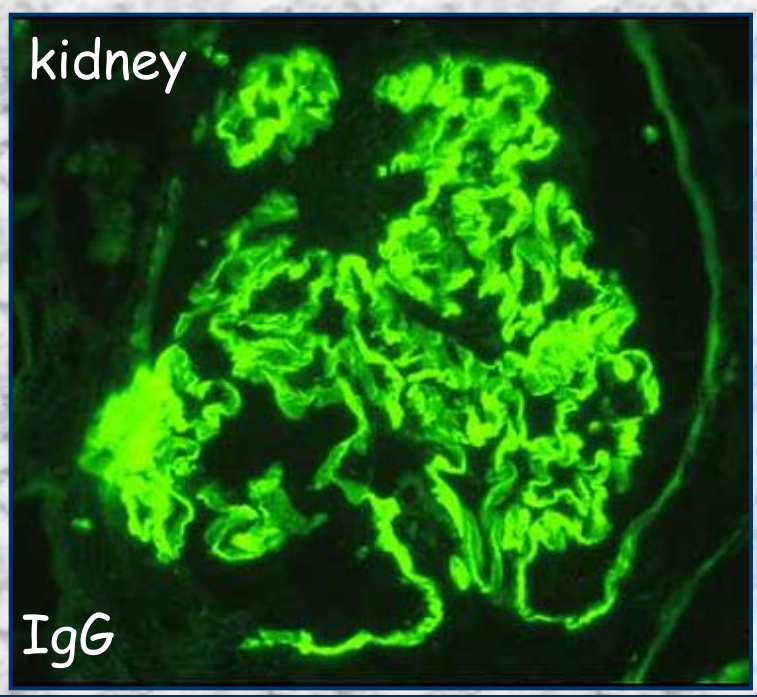
Anti-GBM nephritis

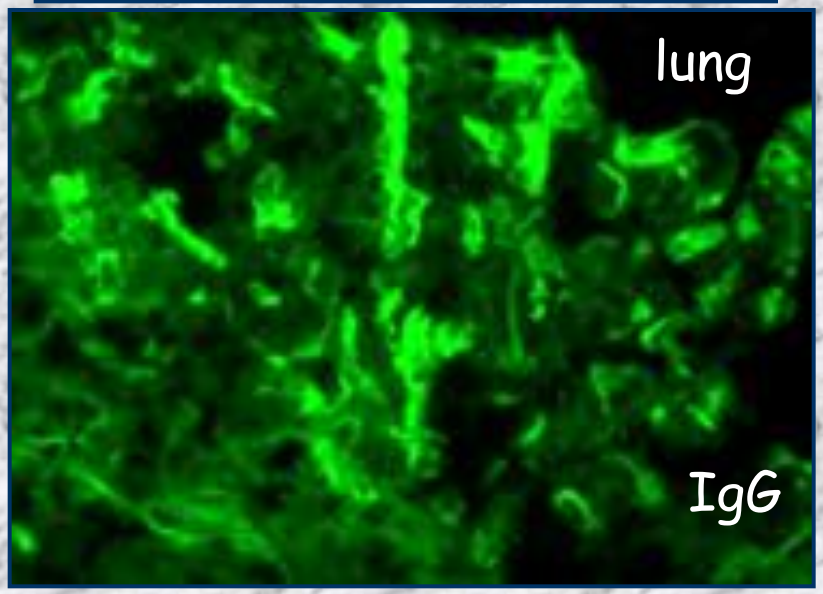
- alfa3-chain of type IV collagen of GBM : Goodpasture antigén
- Goodpasture-syndroma : with lung involvement
- In situ immune complexes
- Two peak incedens; 20-30 y.male; 60-70 y. female
- IF: IgG linear reaction along GBM and tubular BM
- Histology: crescent, necrosis, periglomerular infl.
- EM: negative
- Prognosis: poor

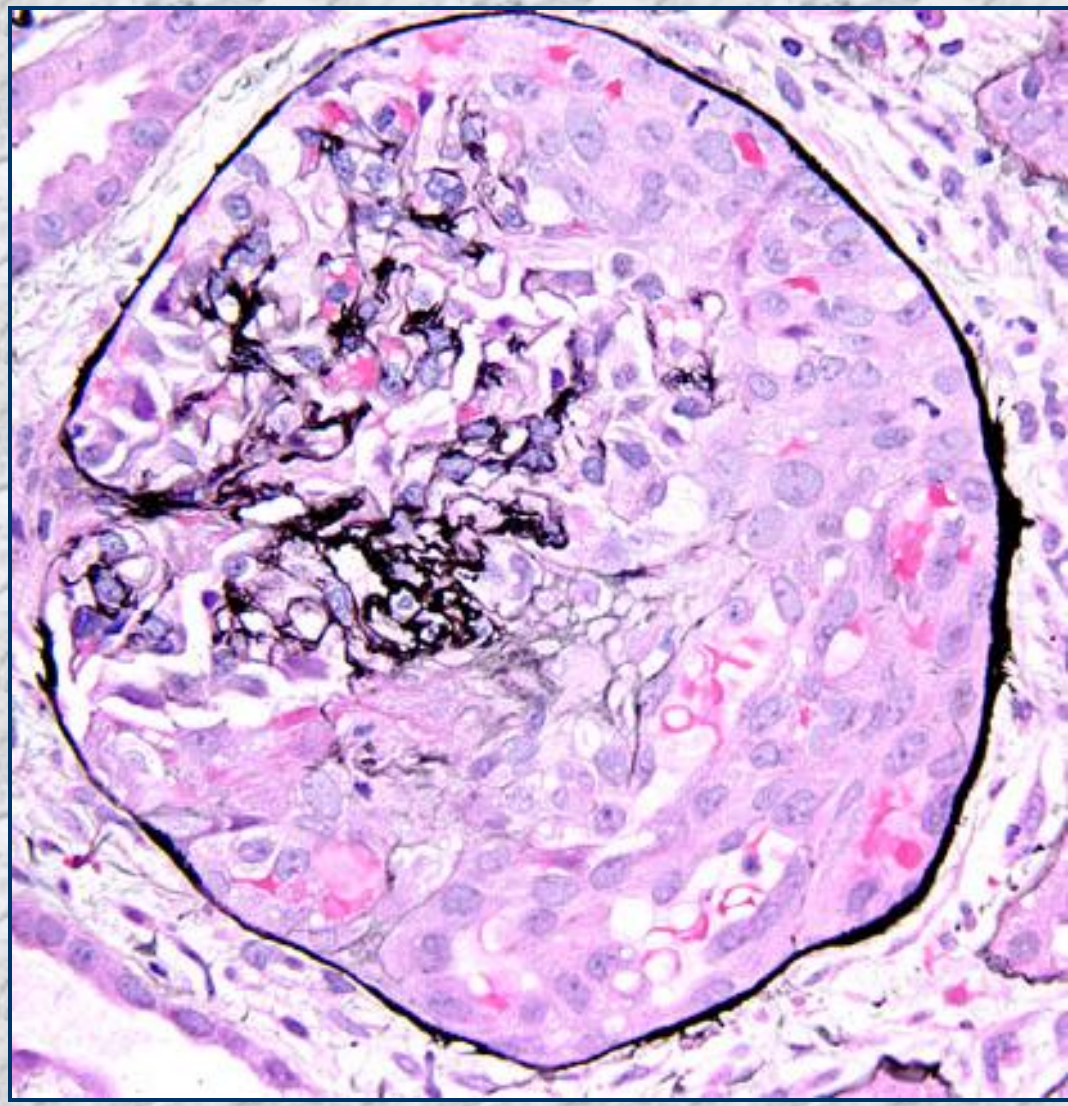


Antibodes are directed againts intrinsic fixed antigens in the GBM (type IV collagen) which induce a linear pattern of localization on IF microscopy

Goodpasture-syndrome





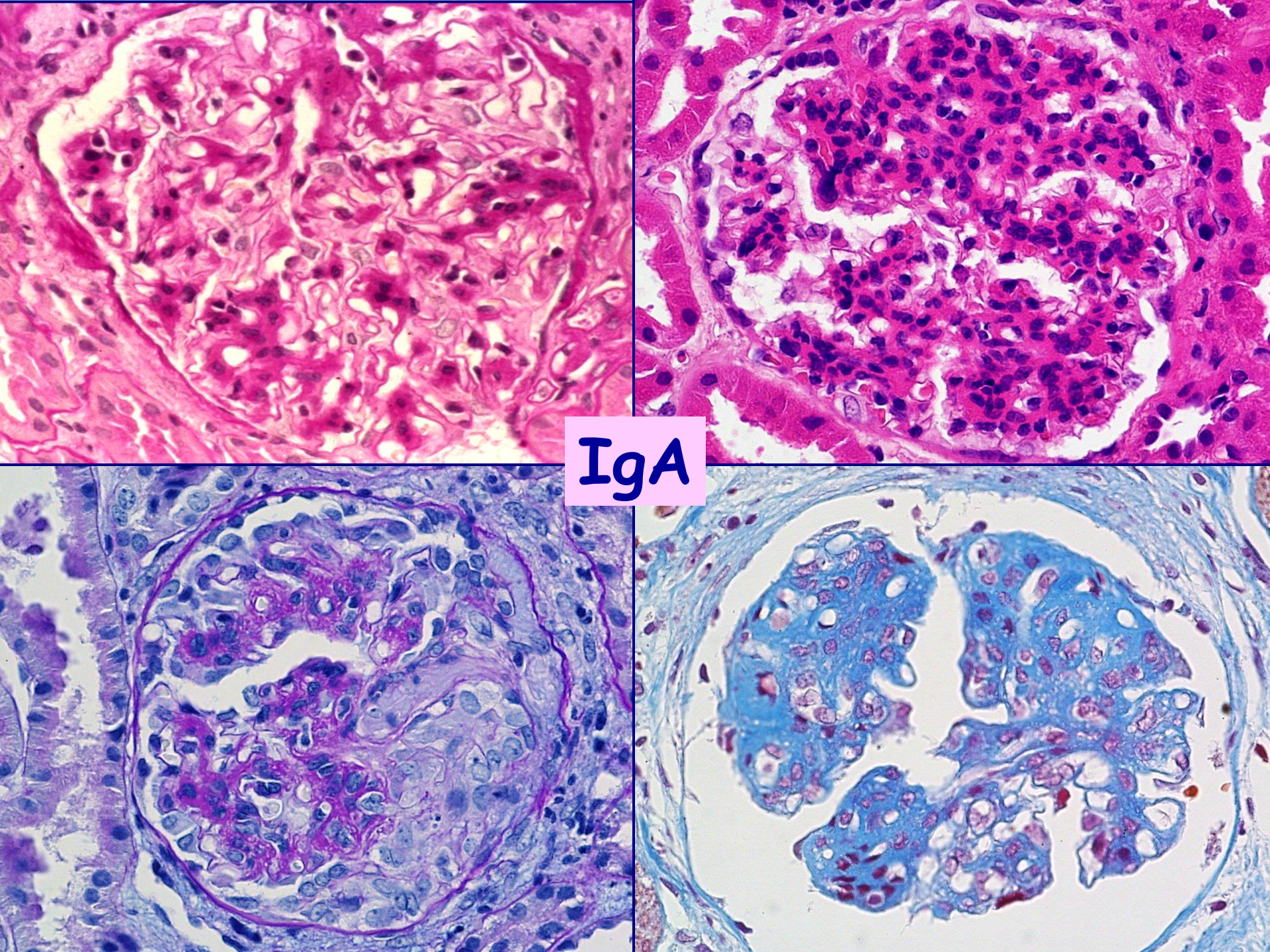


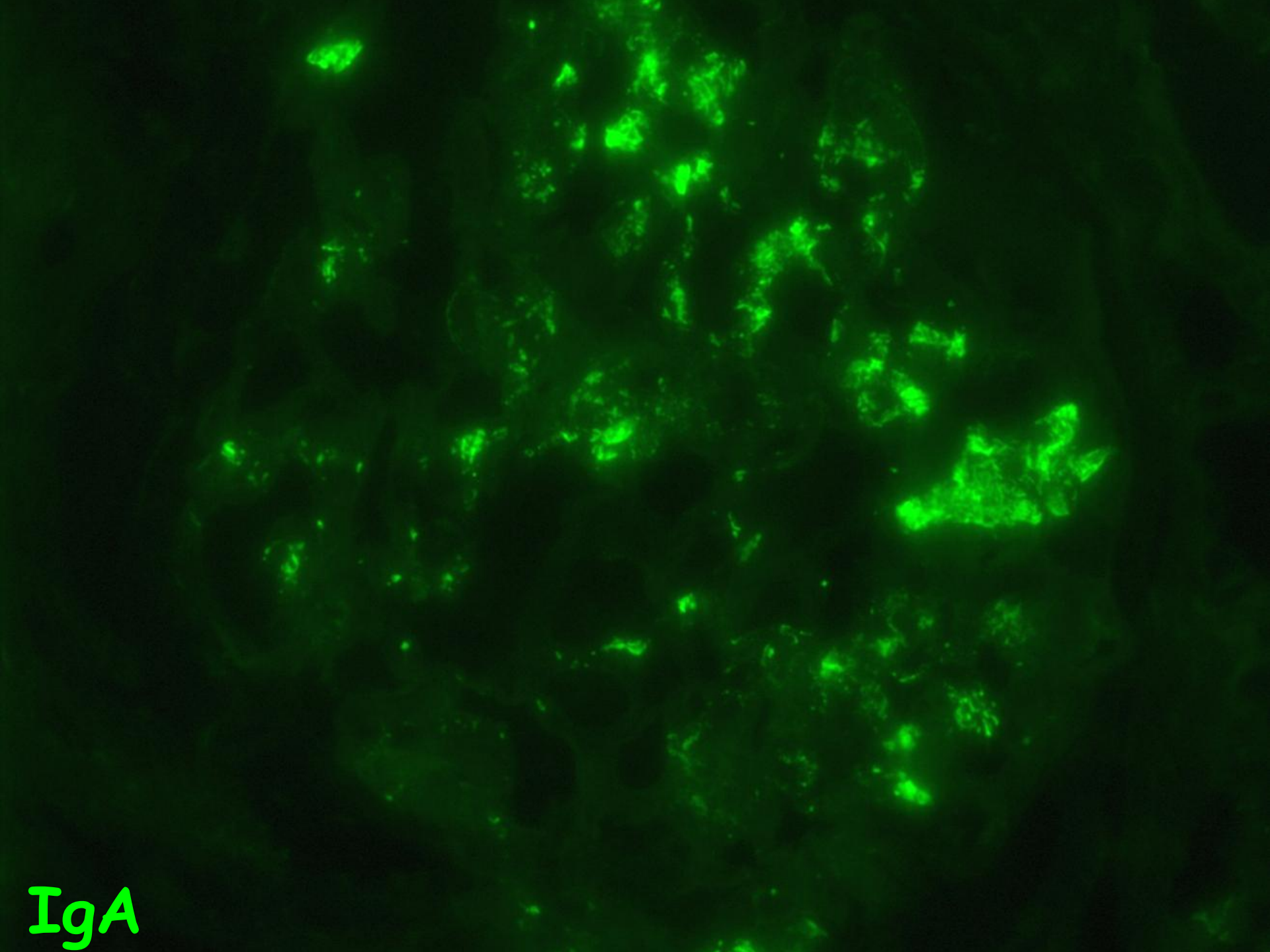
Glomerular diseases associated with haematuria

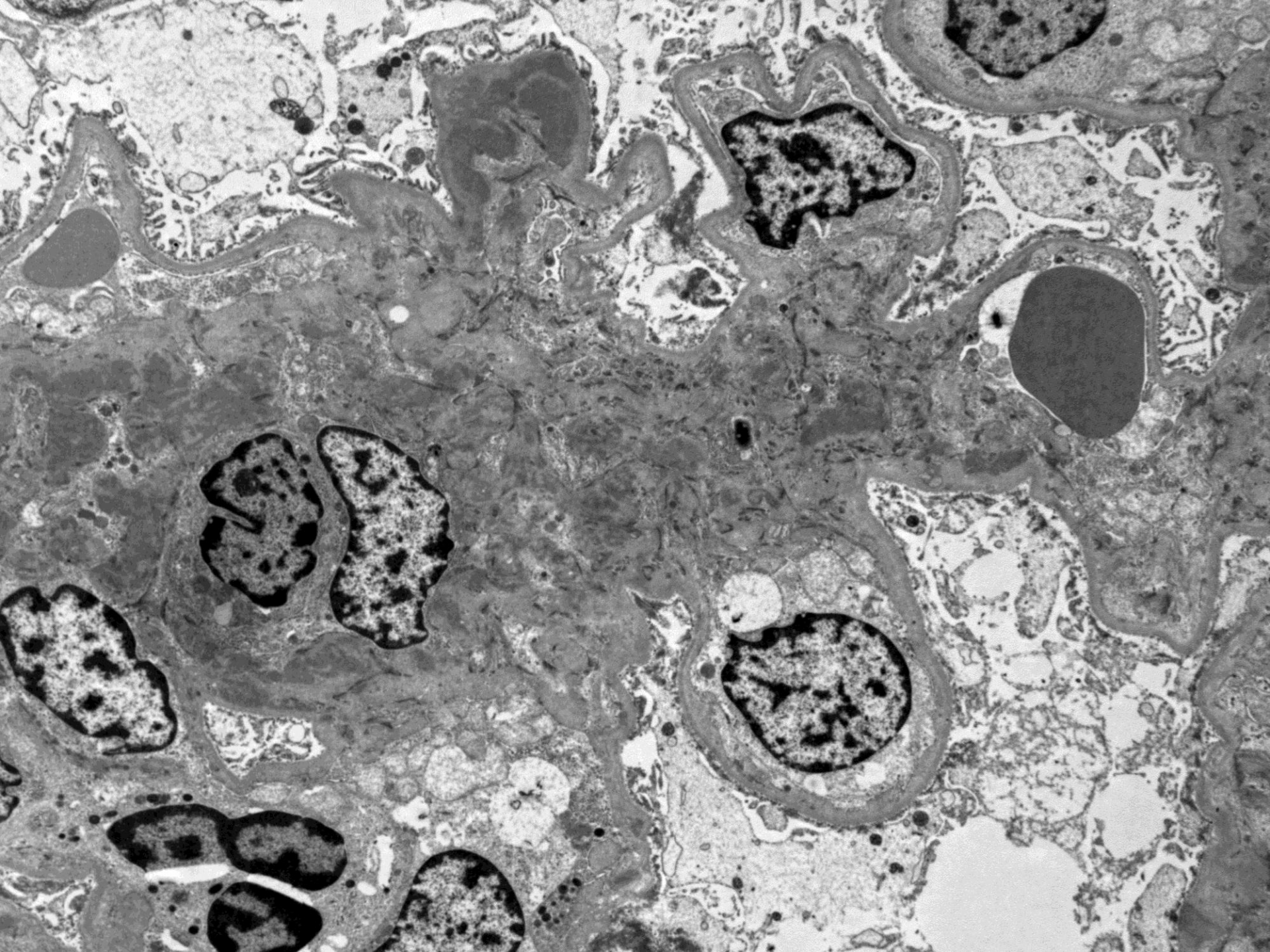
- IgA nephropathia
- Thin membrane disease
- Alport's nephropathy

IgA nephropathy

- Berger disease – primary form
- Systematic form: Henoch-Schönlein purpura
- 20-30 years of age; male predominance
- Most common form of primary GN
- From asymptomatic haematuria to RPGN
- IF: IgA,C3 granular, mesangial reaction
- Szövettan: mesangial proliferation – variable!
- EM: mesangial deposits
- Prognosis: 25-40% CRF within 20 years, 50%: Recurrence after transplantation


IgA


IgA

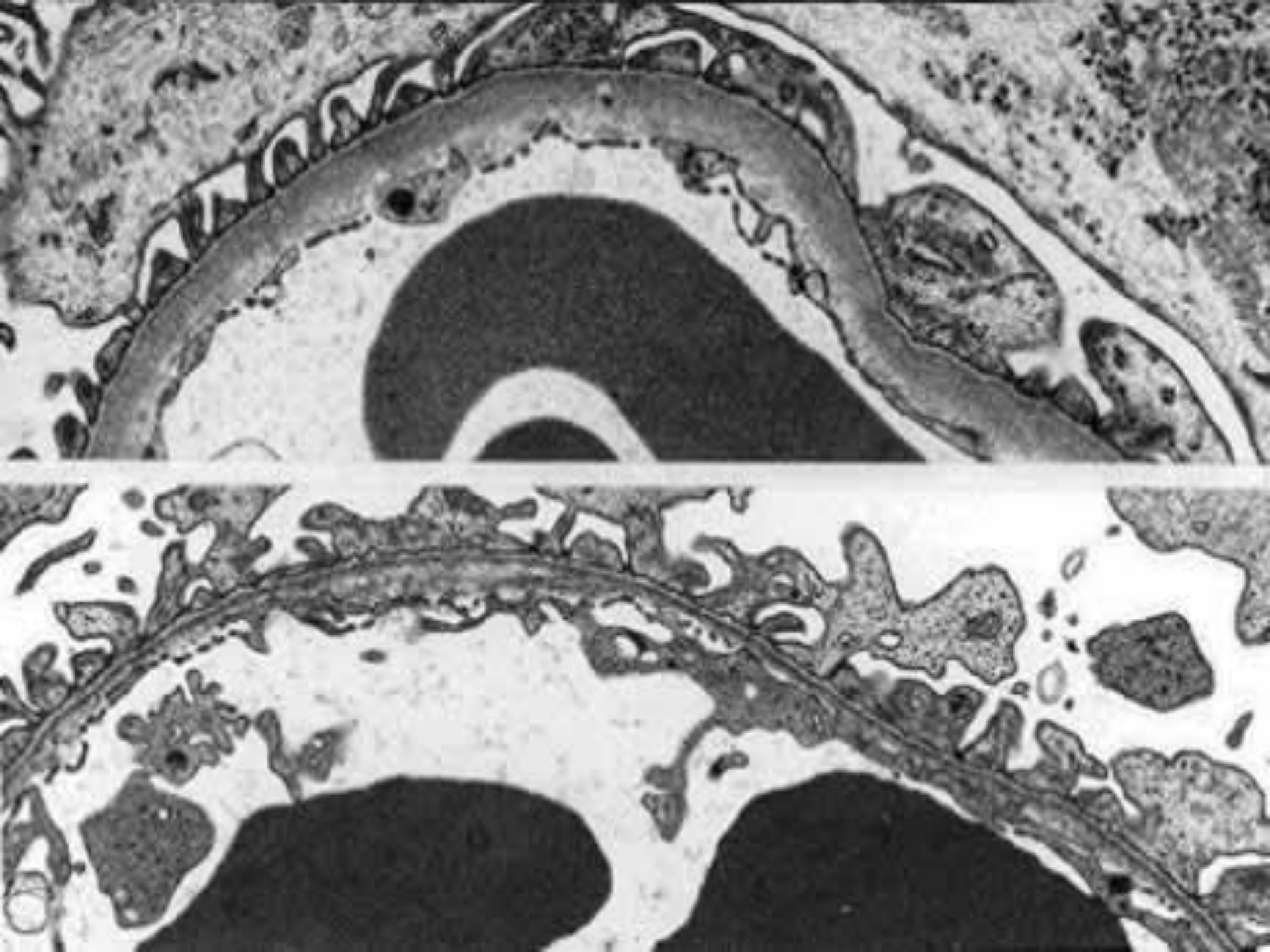


Secondary forms

- Chronic liver disease
- Celiac disease
- Dermatitis herpetiformis
- HIV infection
- Crohn' disease
- Carcinomas
- Mycosis fungoides
- Sjögren's syndrome

Thin membrane disease

- Benign familial haematuria
- Autosomal, dominant inheritance
- Uniform thinning of lamina densa ofGBM
- GBM: 200nm (normális: 310-380nm)
- Manifested in childhood
- No therapy
- No deterioration of renal function



Alport's nephropathy

- Mutation of gene codes for alfa3-5 chains of coll.IV.
- A3, A4 gene are situated on chromosoma 2,
  A5 gene is on X chromosome.
- Alport's sy: renal involvement, hearing impairment and ocular abnormalities
- IF: negative
- Histology : negative, mesangial widening, segmental and global sclerosis, interstitial foamy cells
- EM: GBM irregularity and splitting
- Prognosis: CRF
- After transplantation develop anti-GBM GN 3-4% M

Pathogenesis

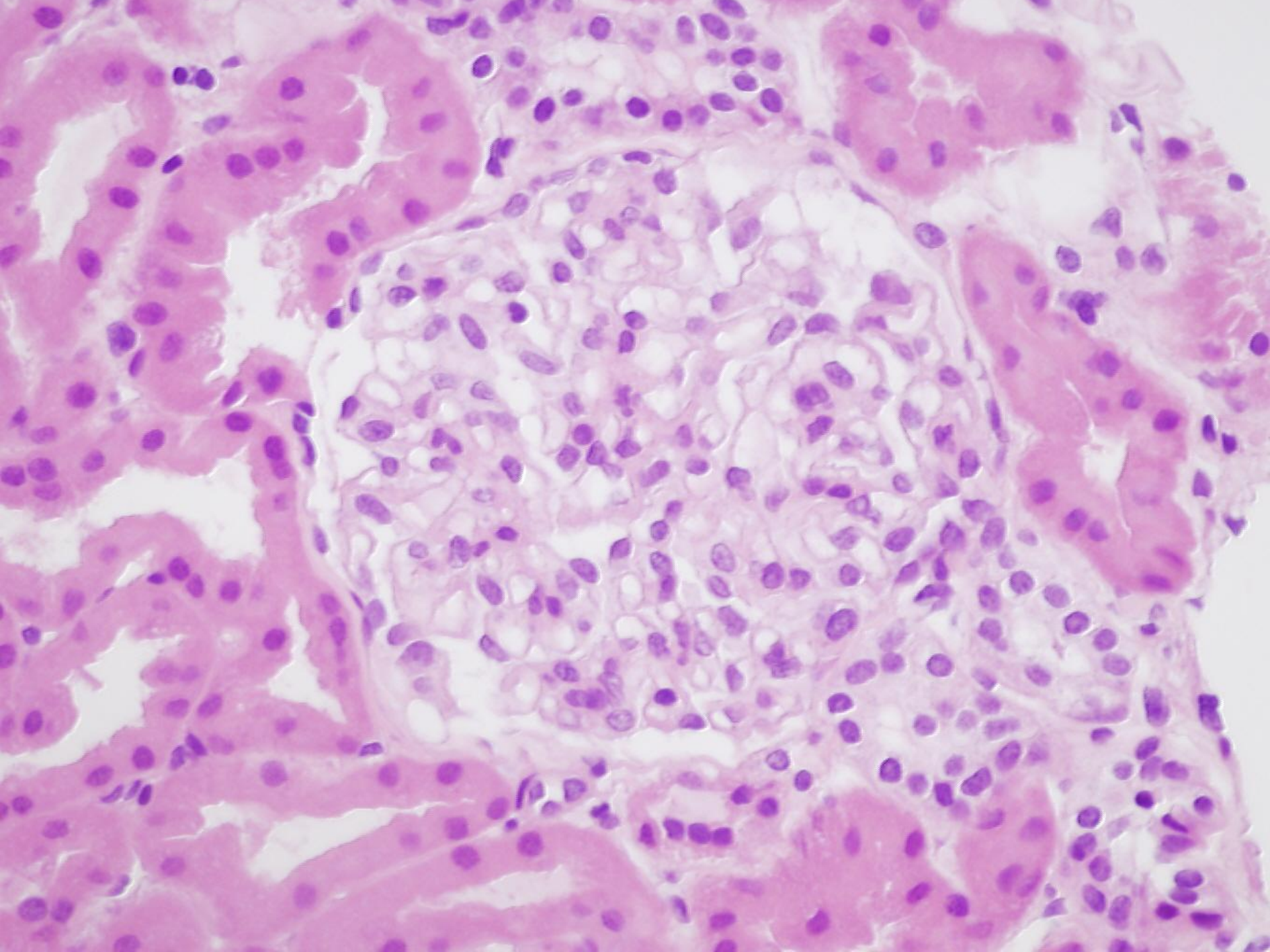
Embryonal GBM

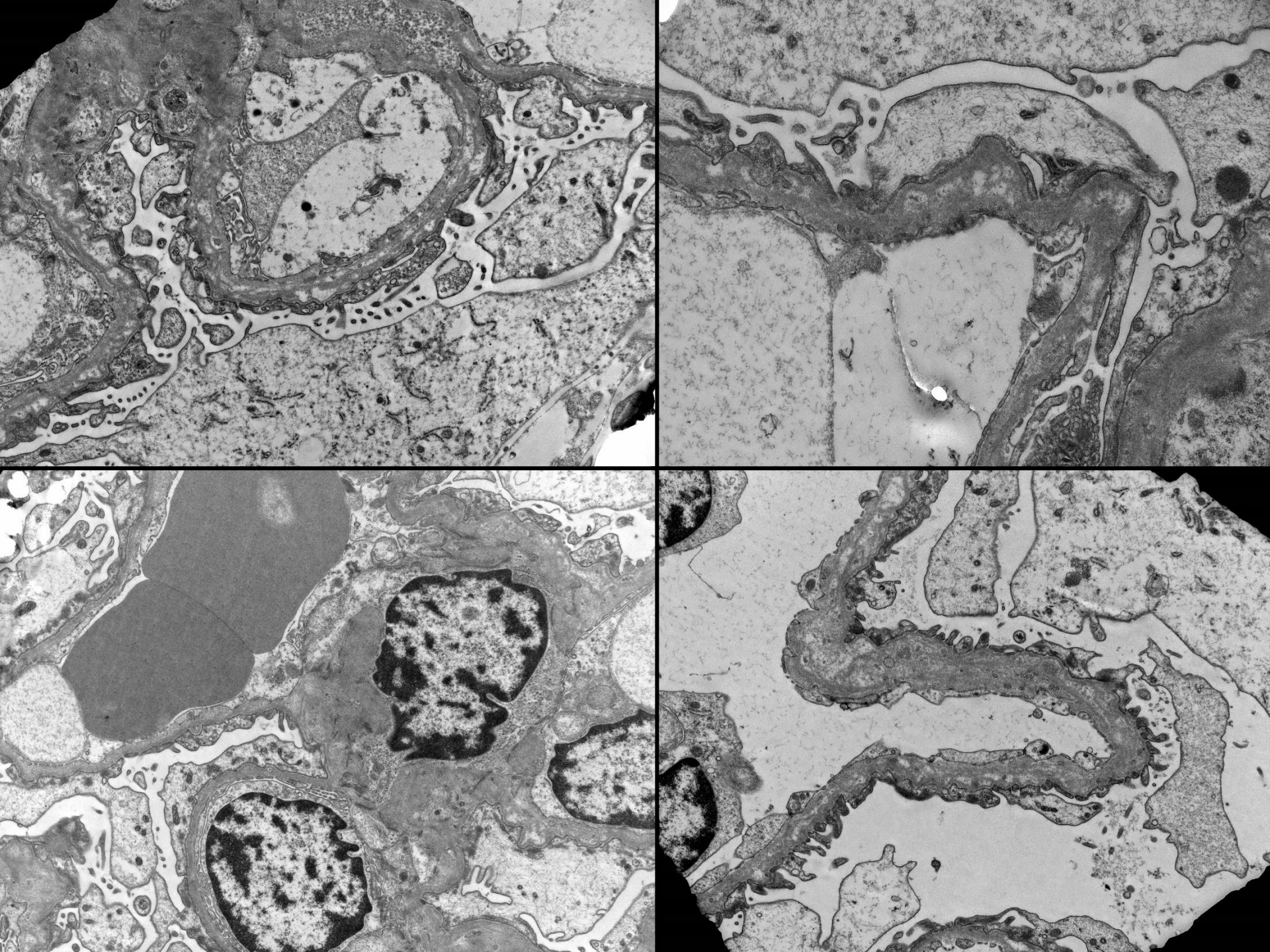
α1α1α1 network

after birth

Adult GBM

α3α4α5 network





Classification of glomerular diseases

- Primary glomerular diseases
- Glomerulonephritis in systematic diseases
- Glomerular lesions in vascular diseases
- Hereditary nephropaty and miscellaneous glomerular lesions

Diabetic nephropathy

- First symptom: microalbuminuria
- Glycosylation: vessels, tubules and glomerular basal membrane and mesangial matrix ↑
- Hyperfiltration
- IF: pseudolinear IgG
- Histology: diffuse or nodular pattern, aff. and eff. arteriola hyalinos art. scler.
- EM: GBM diffuse widening

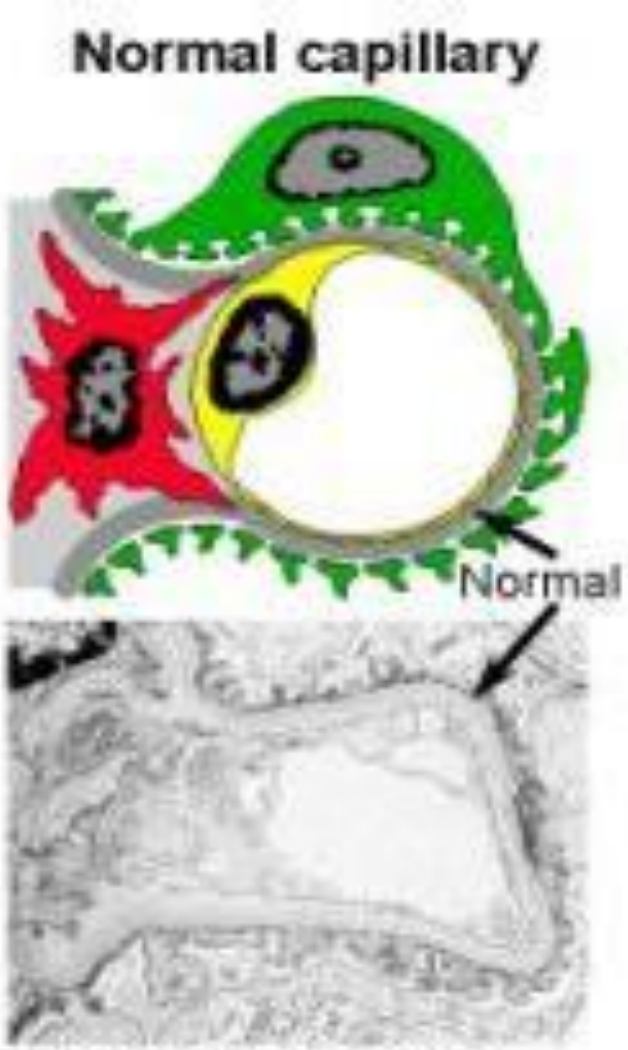
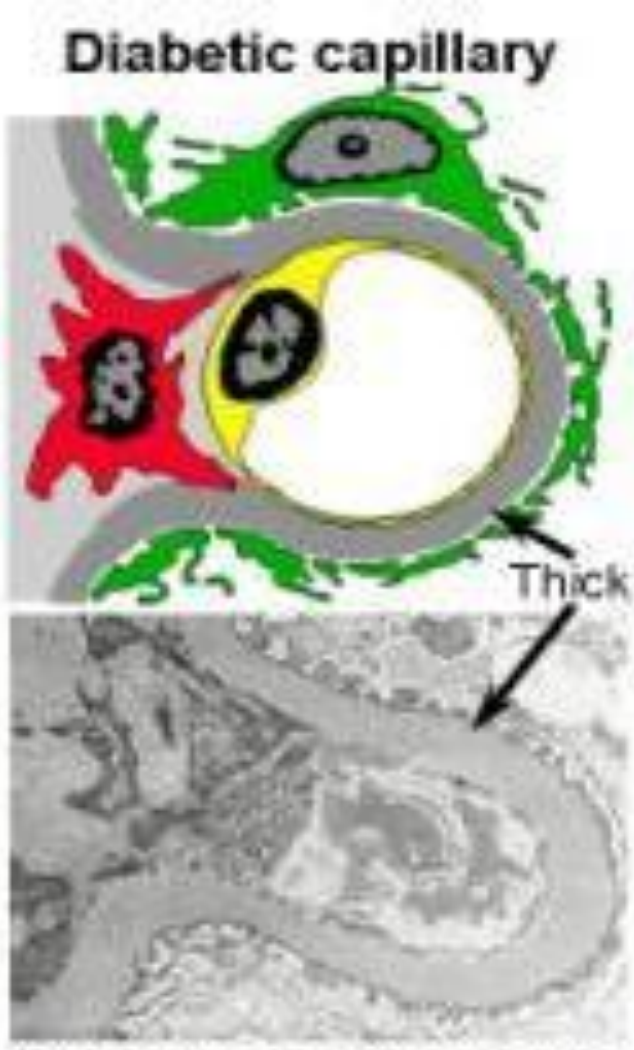
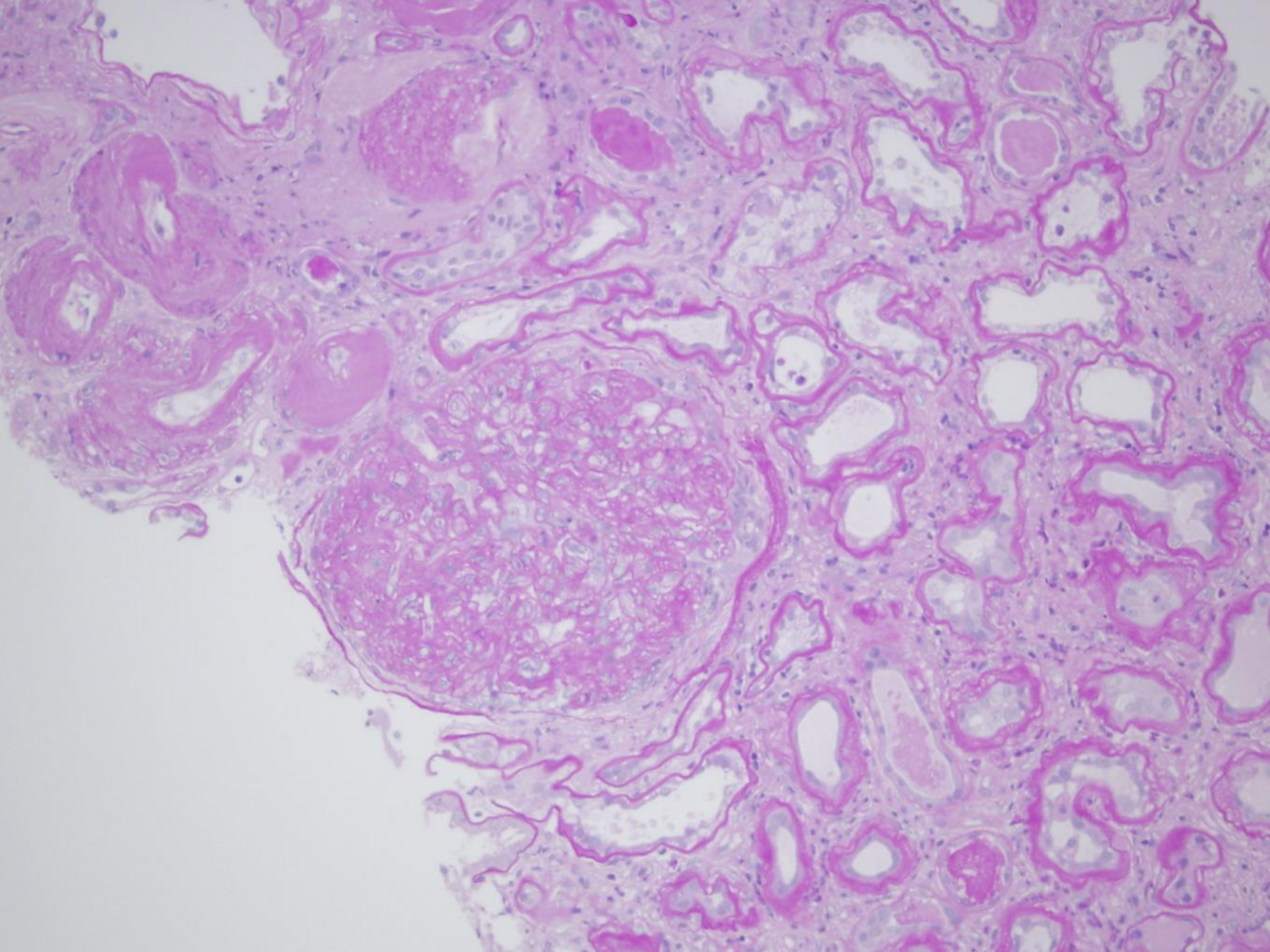
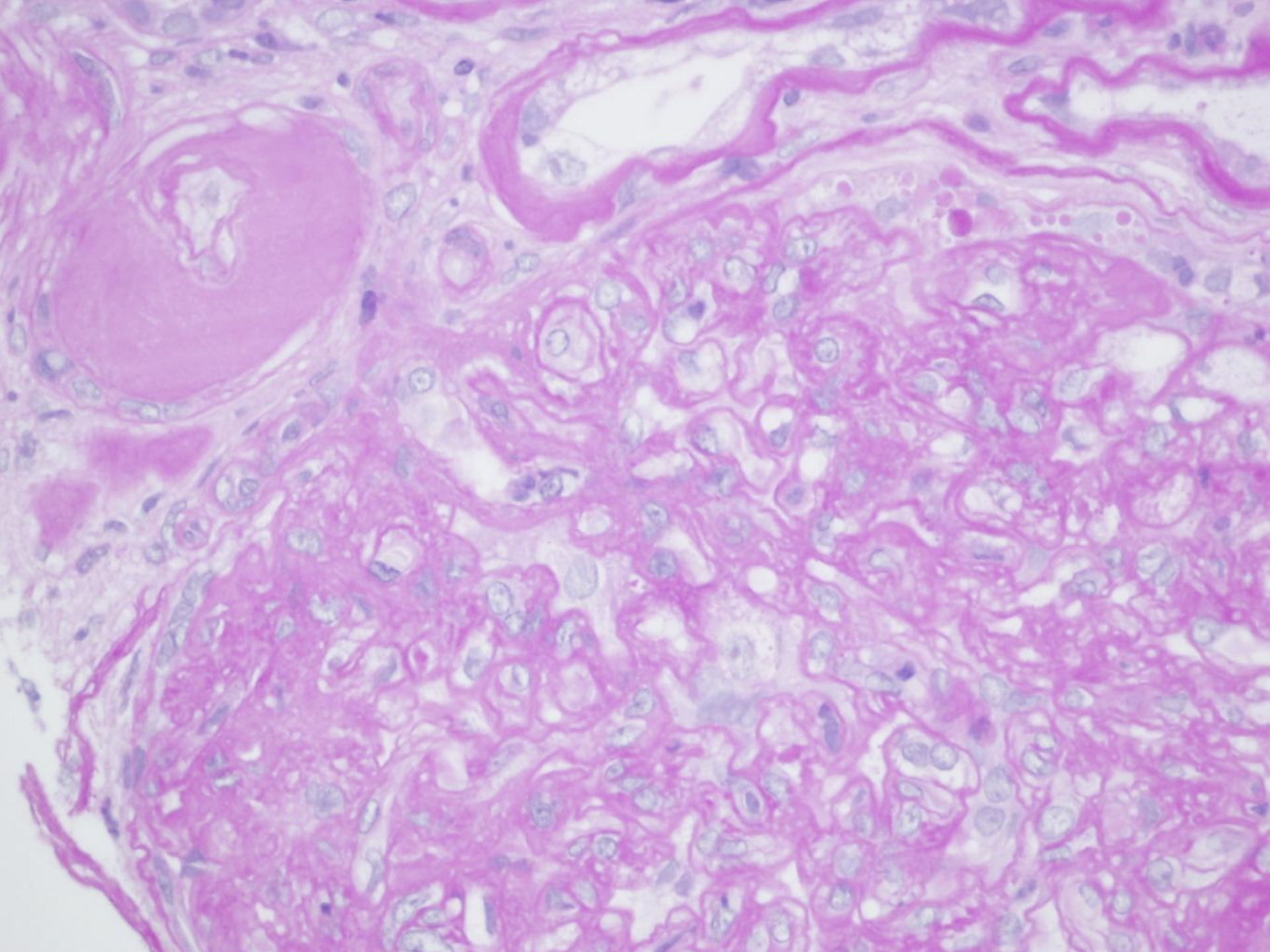


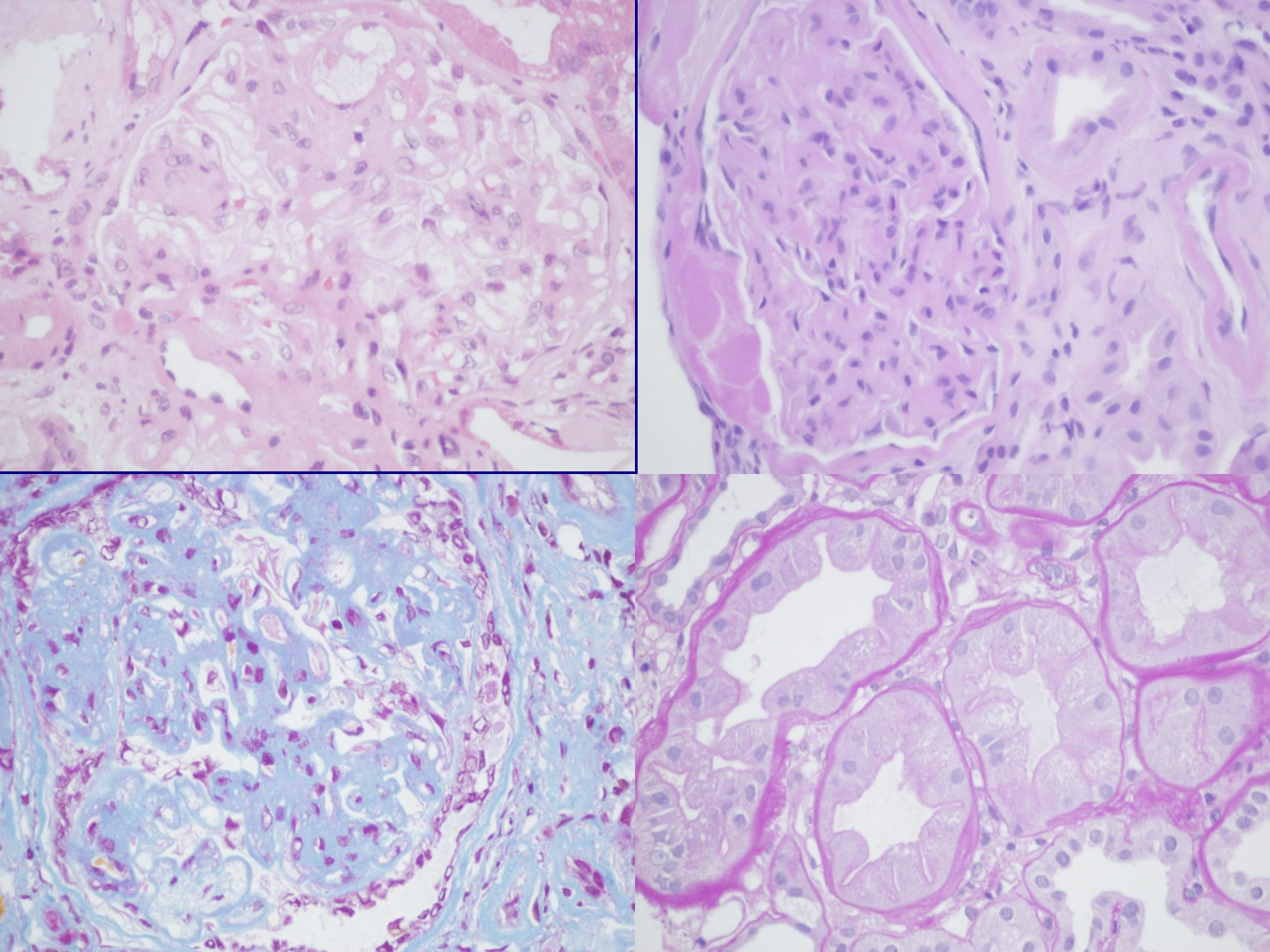
Diagram and electron microscopic photograph of a cross section of a normal glomerular capillary. The basement membrane is normal.



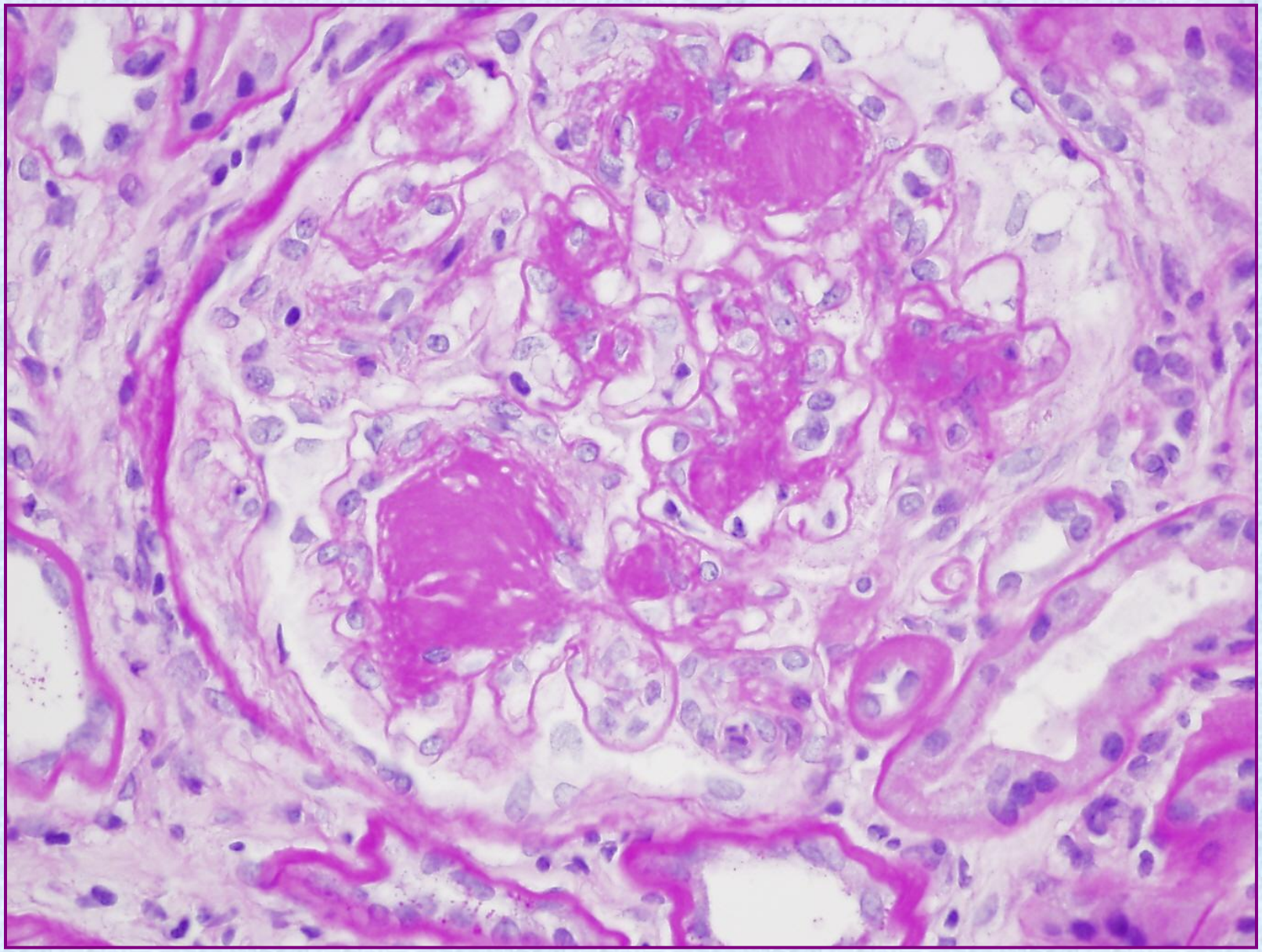
Cross section of a glomerular capillary injured by diabetes in a kidney biopsy specimen. The basement membrane is abnormally thick compared to normal.







Kimmelstiel-Wilson-syndrome

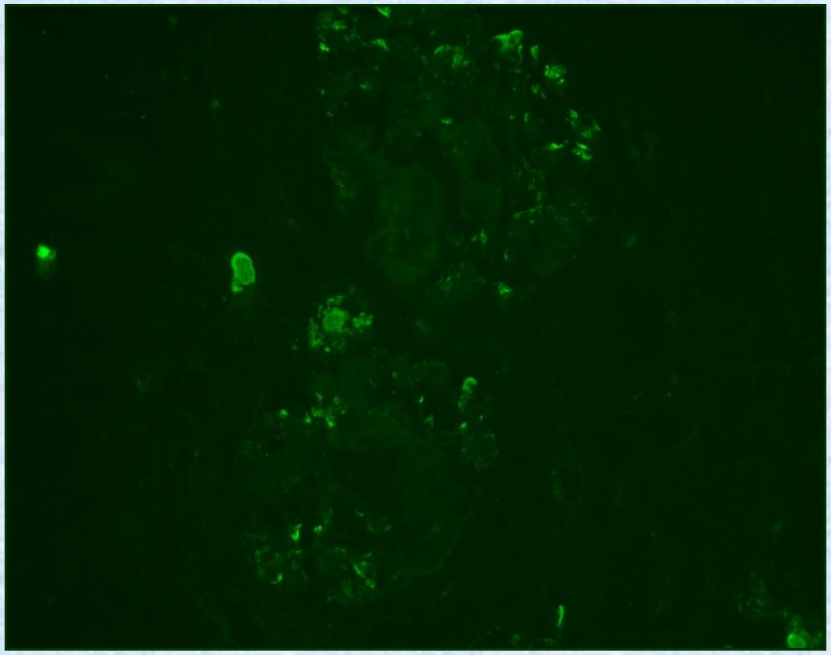


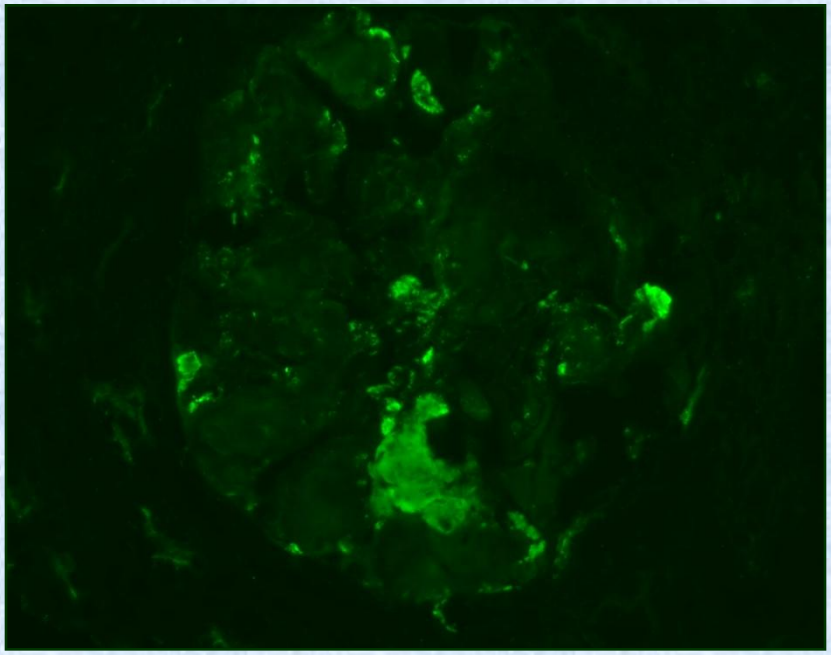
Sz.M. 80 years old lady

Clinical datas:

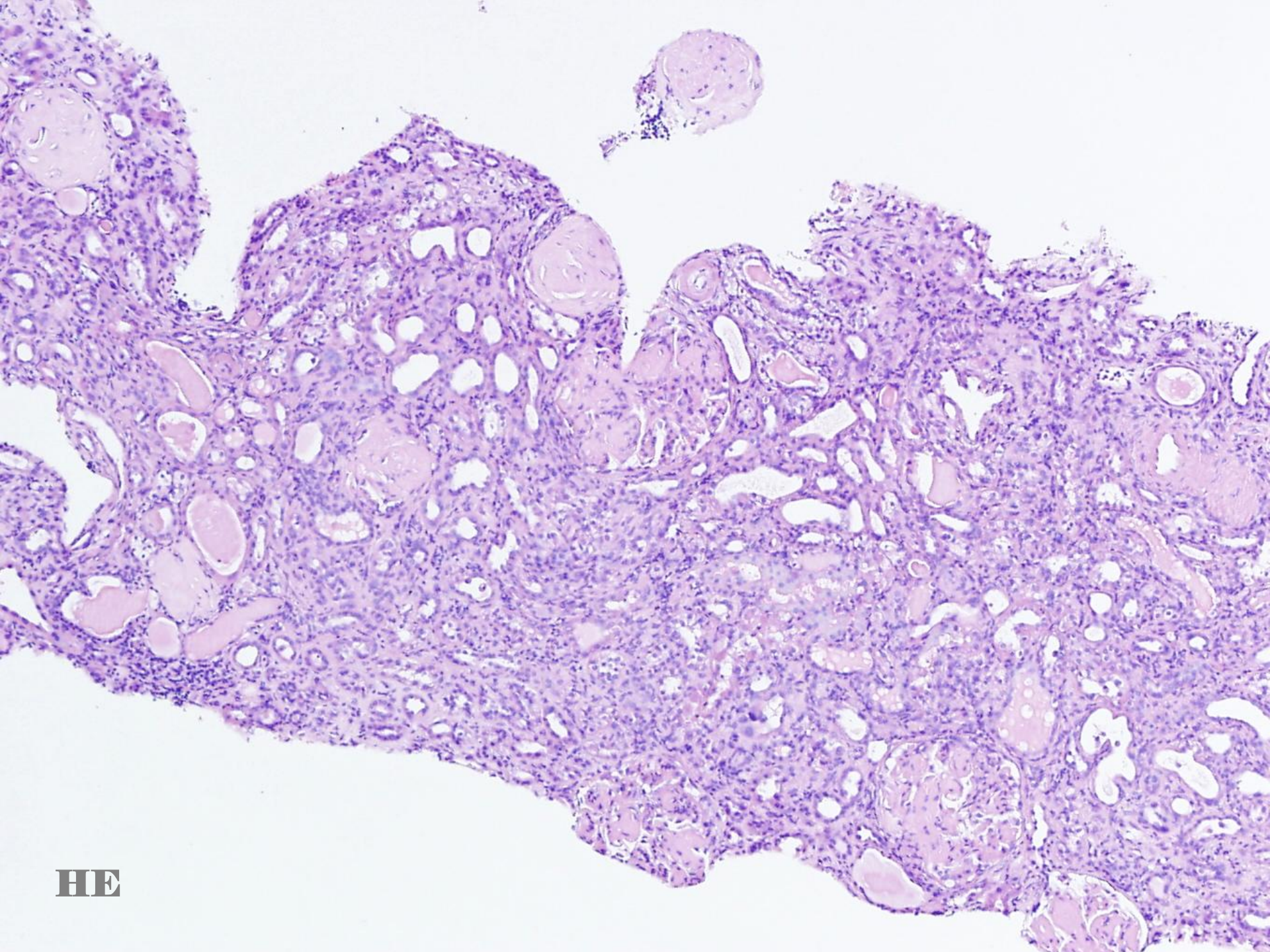
HT, IHD, RA, tu. colontos?
proteinuria: 6.6 g/l/day,
se creatinin 325 umol/l
Nephrosis sy.

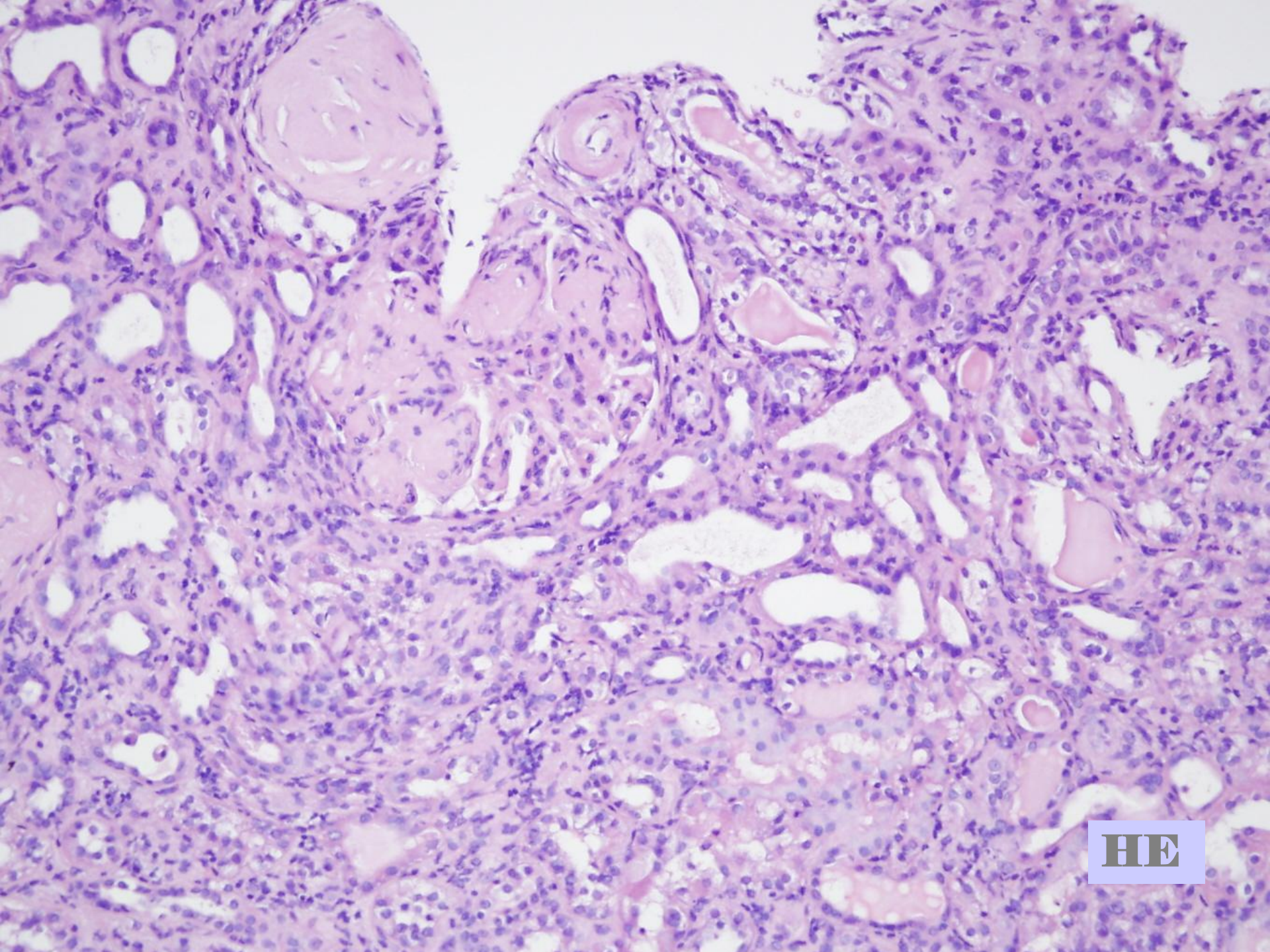
Immunflorescens examination





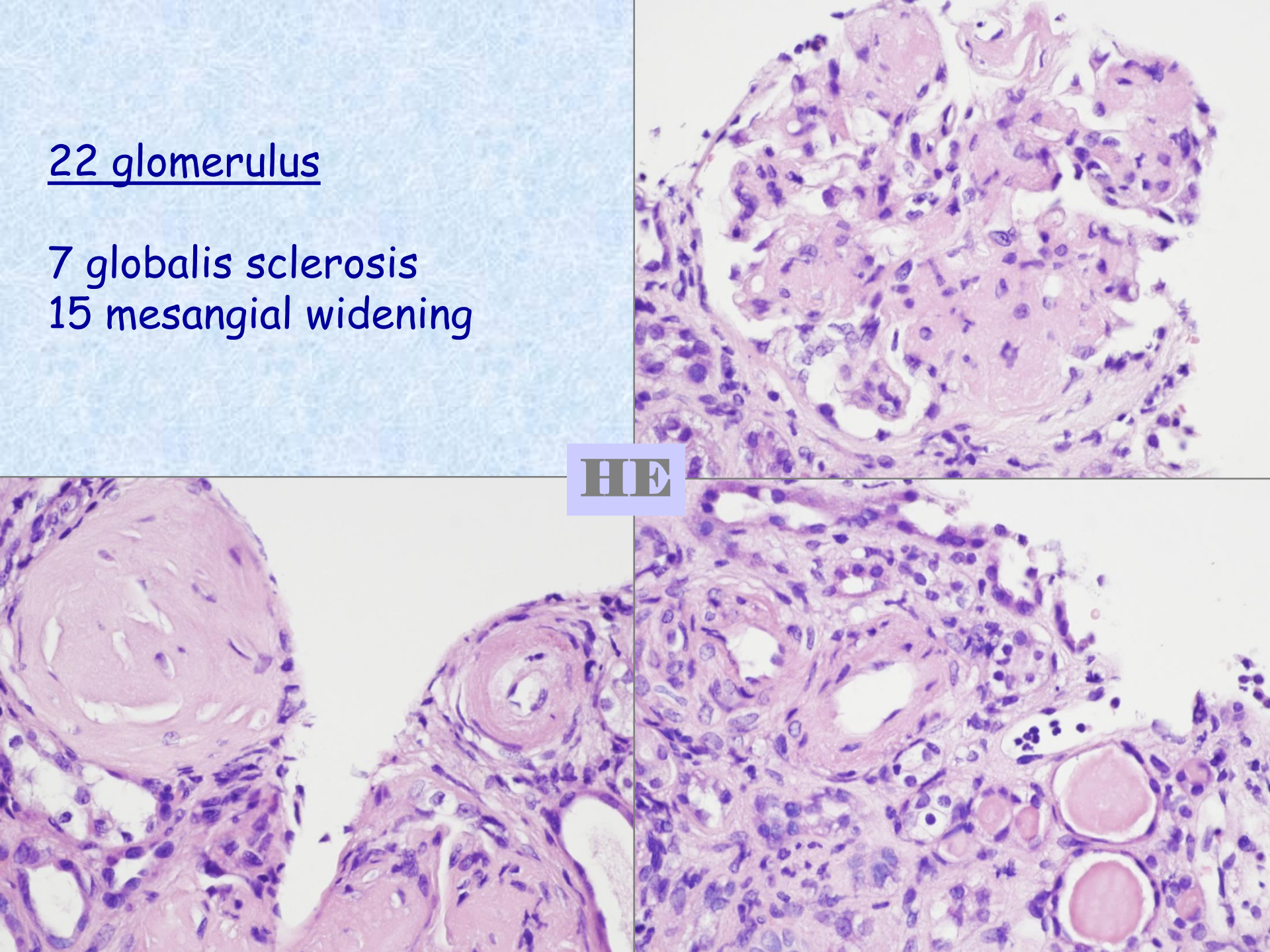
Non specific, middle intense, granular reaction against IgG, IgM, C3, C1q and kappa antibodies


HE

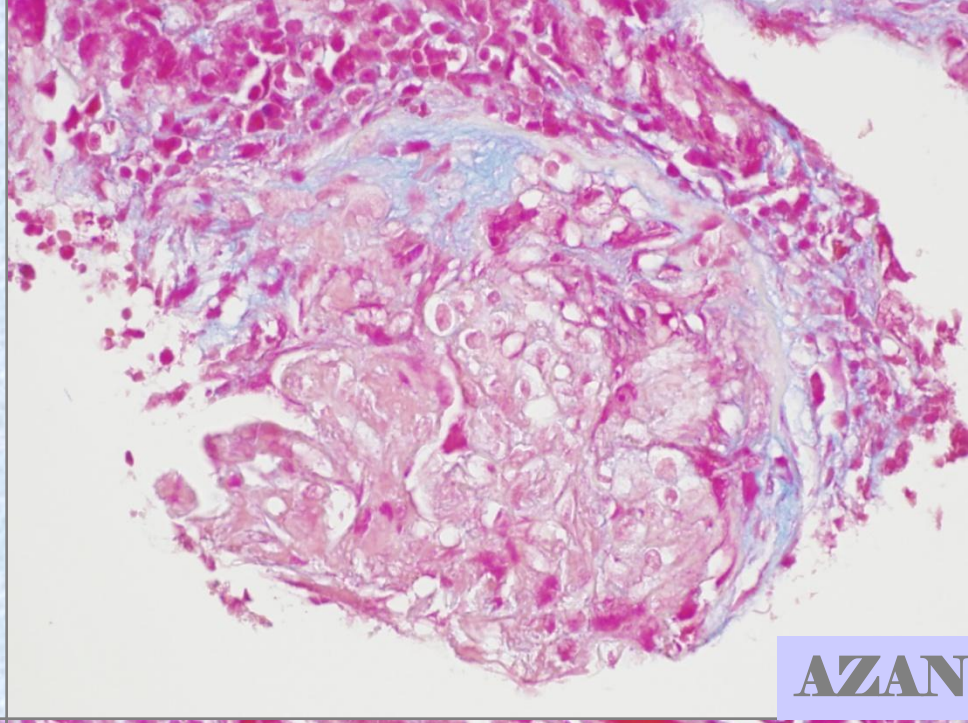

HE

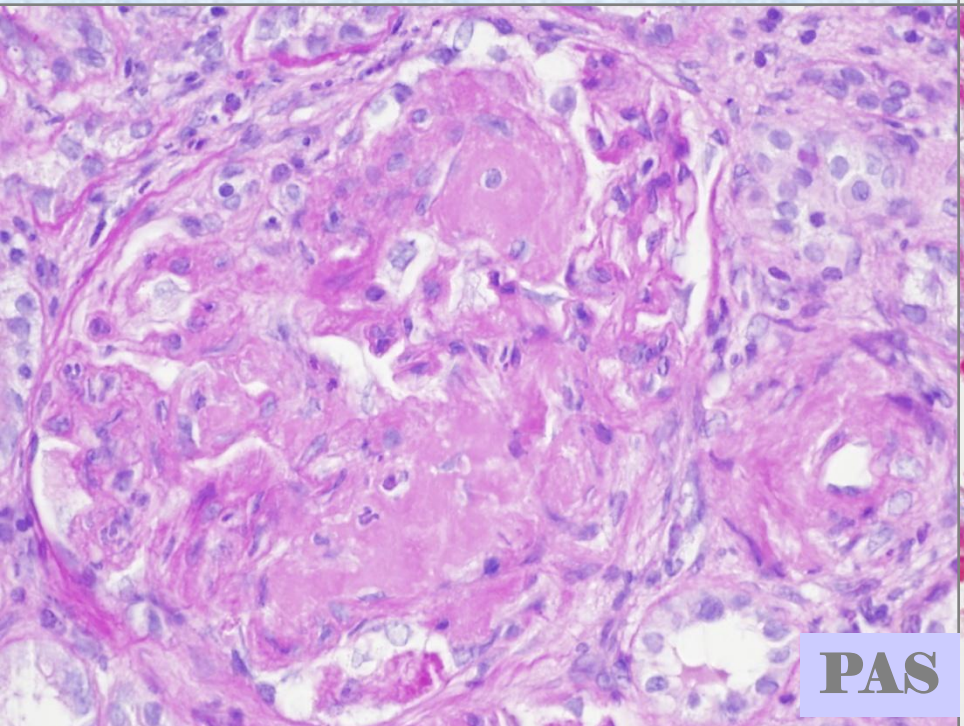
22 glomerulus

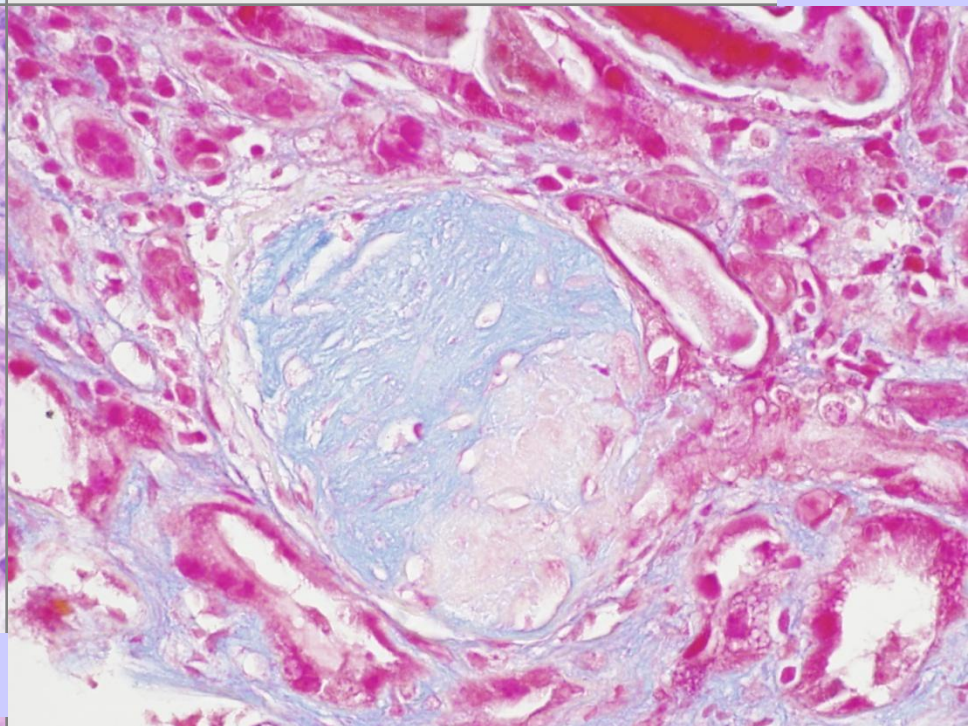
7 globalis sclerosis
15 mesangial widening



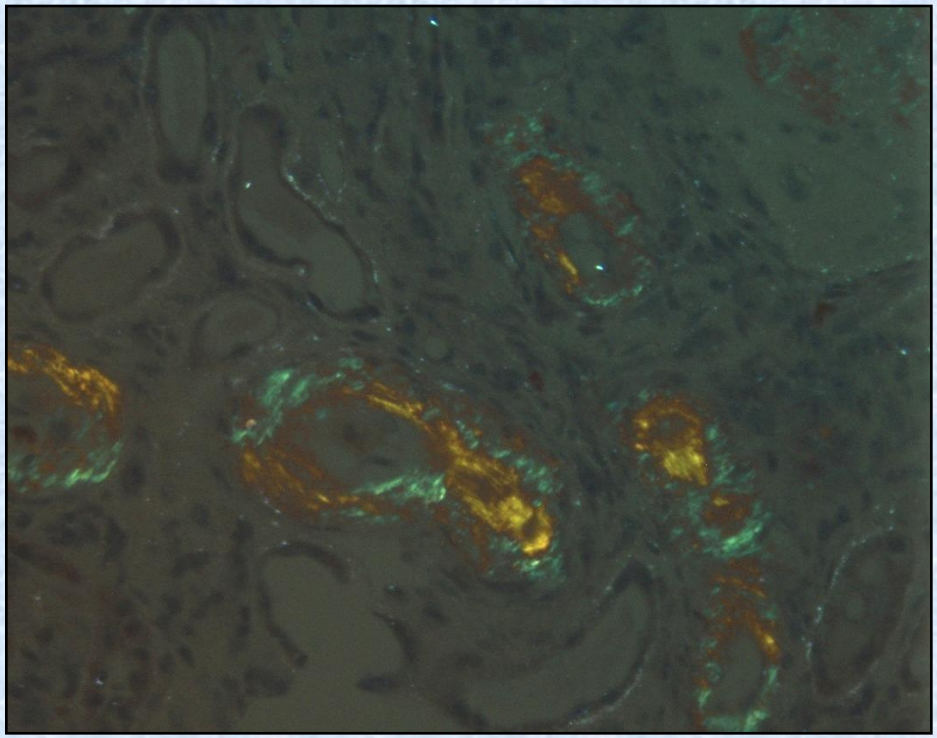
Special stainings



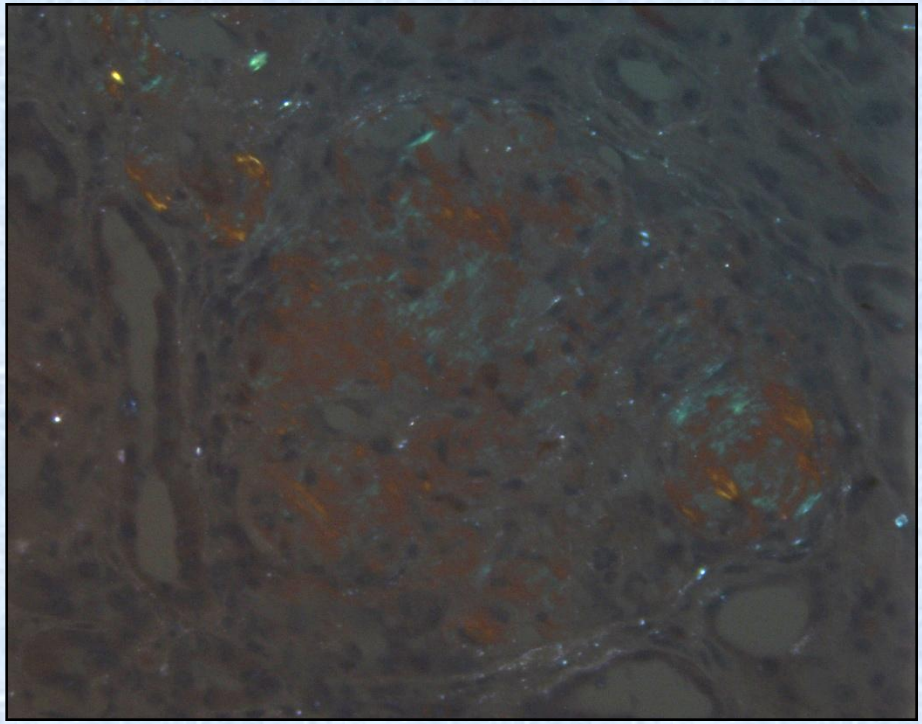




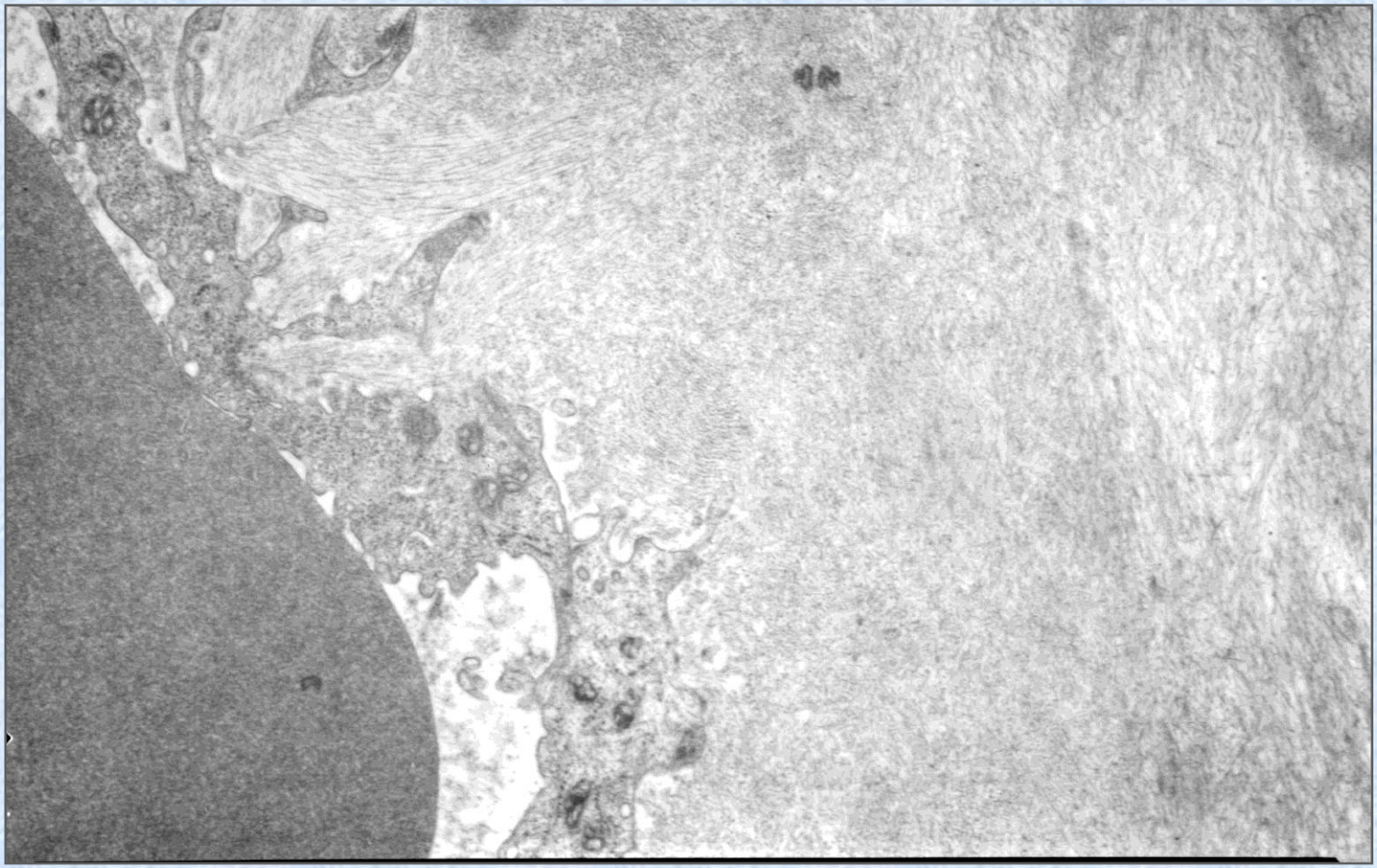
Under polarized light



Congo stain



Electronmicroscopy



Diagnosis

Rheumatoid arthritis associated with secunder amyloidosis

Interstitialis nephritis with fibrosis and tubular atrophy

Renal amyloidosis

- AA – amyloidosis (amyloid associated)

  chronic inflammatory conditions pl:

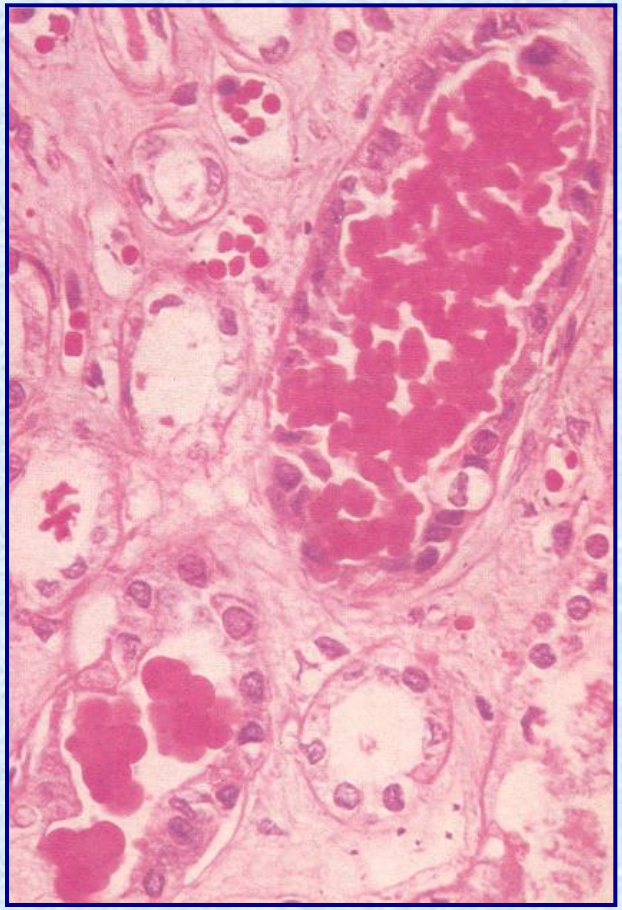
  tuberculosis, osteomyelitis, rheumatoid arthritis, bronchiectasia etc.

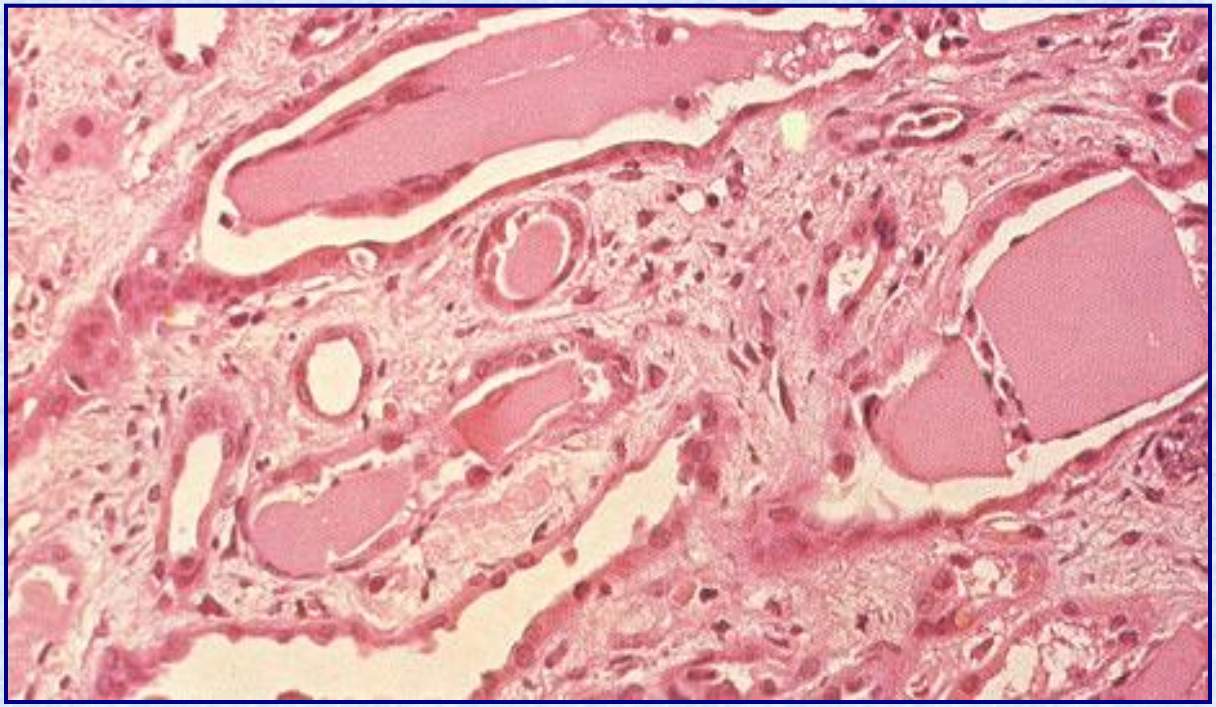
- AL – amyloidosis (light chain)

  Plazmacell – dyscrasia pl:

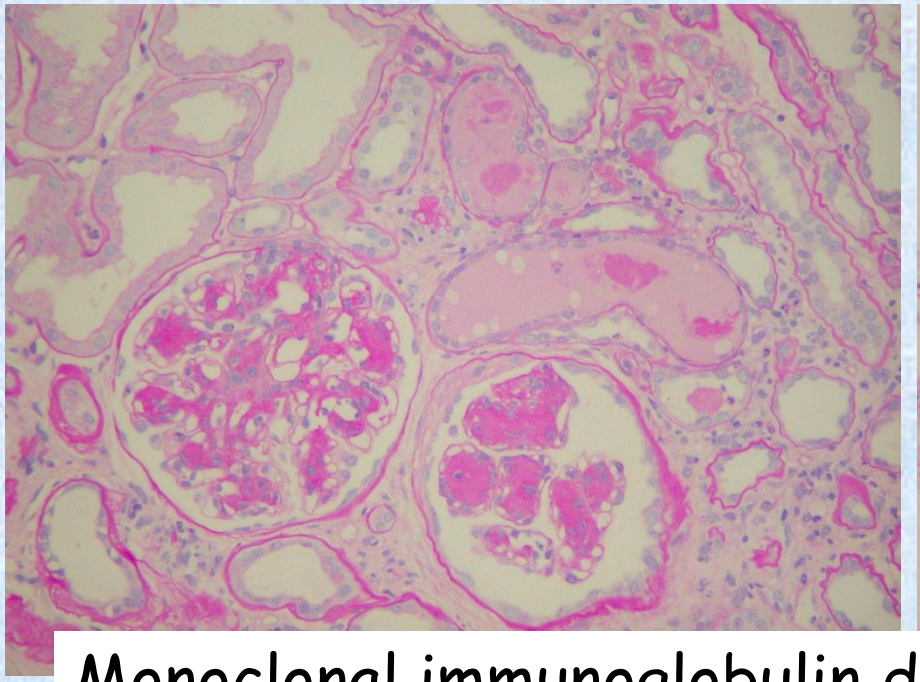
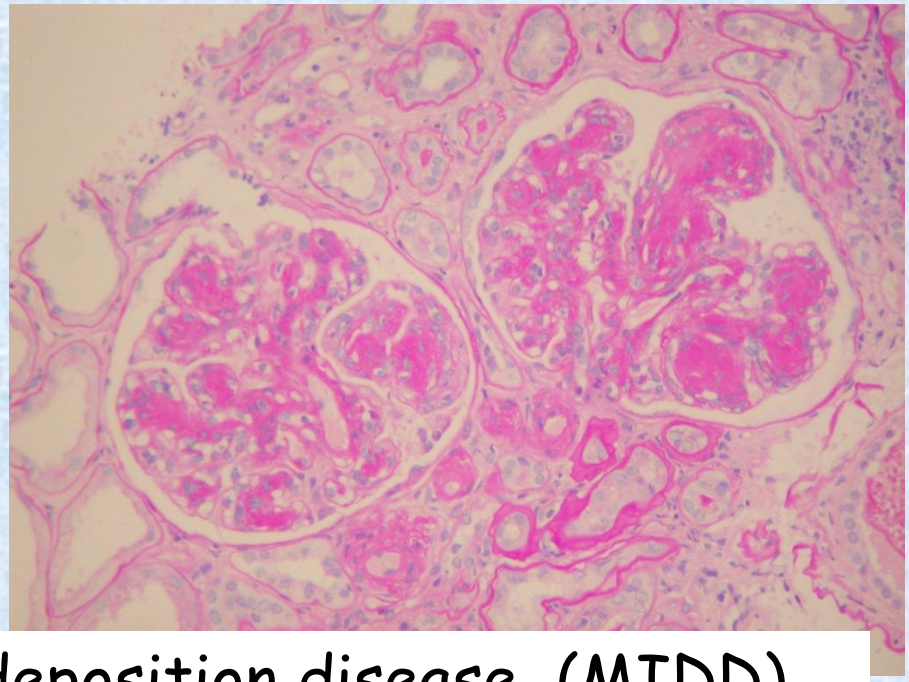
  myeloma multiplex,Waldenström-macroglobulinaemia monoclonal light chain disease

Myeloma kidney (Myeloma cast nephropathy)

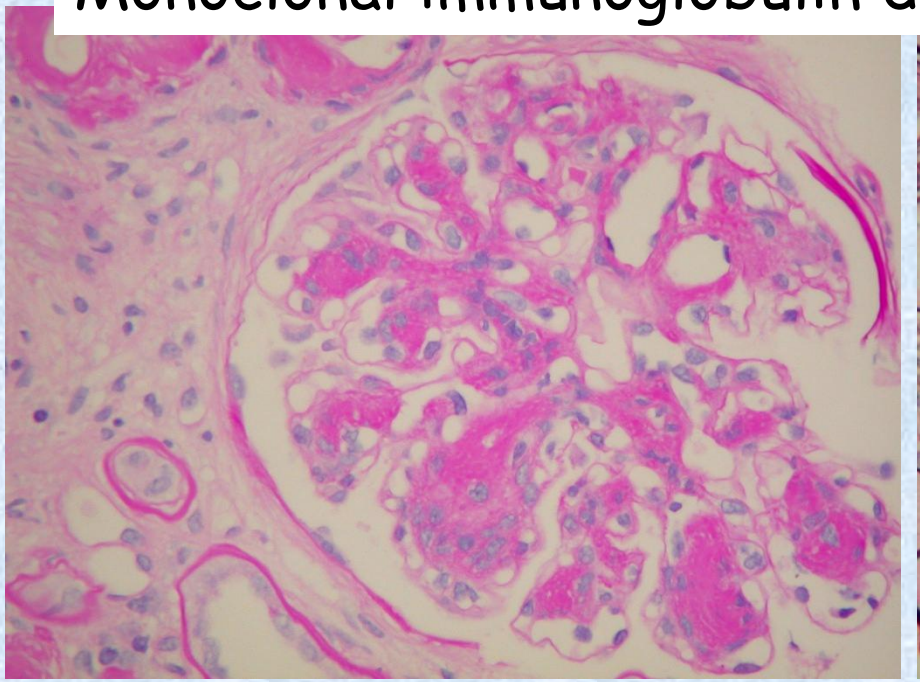
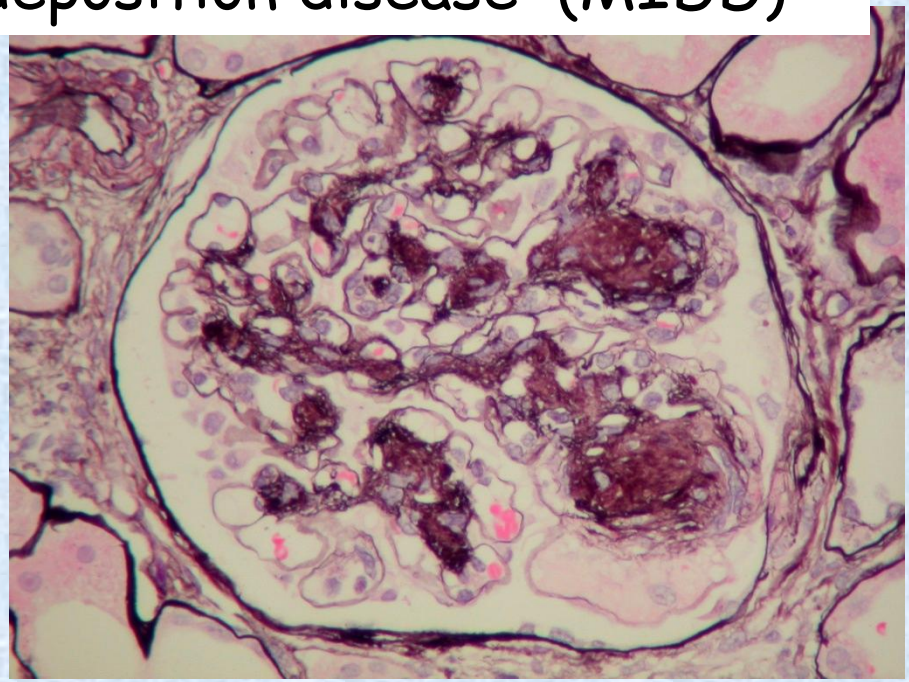


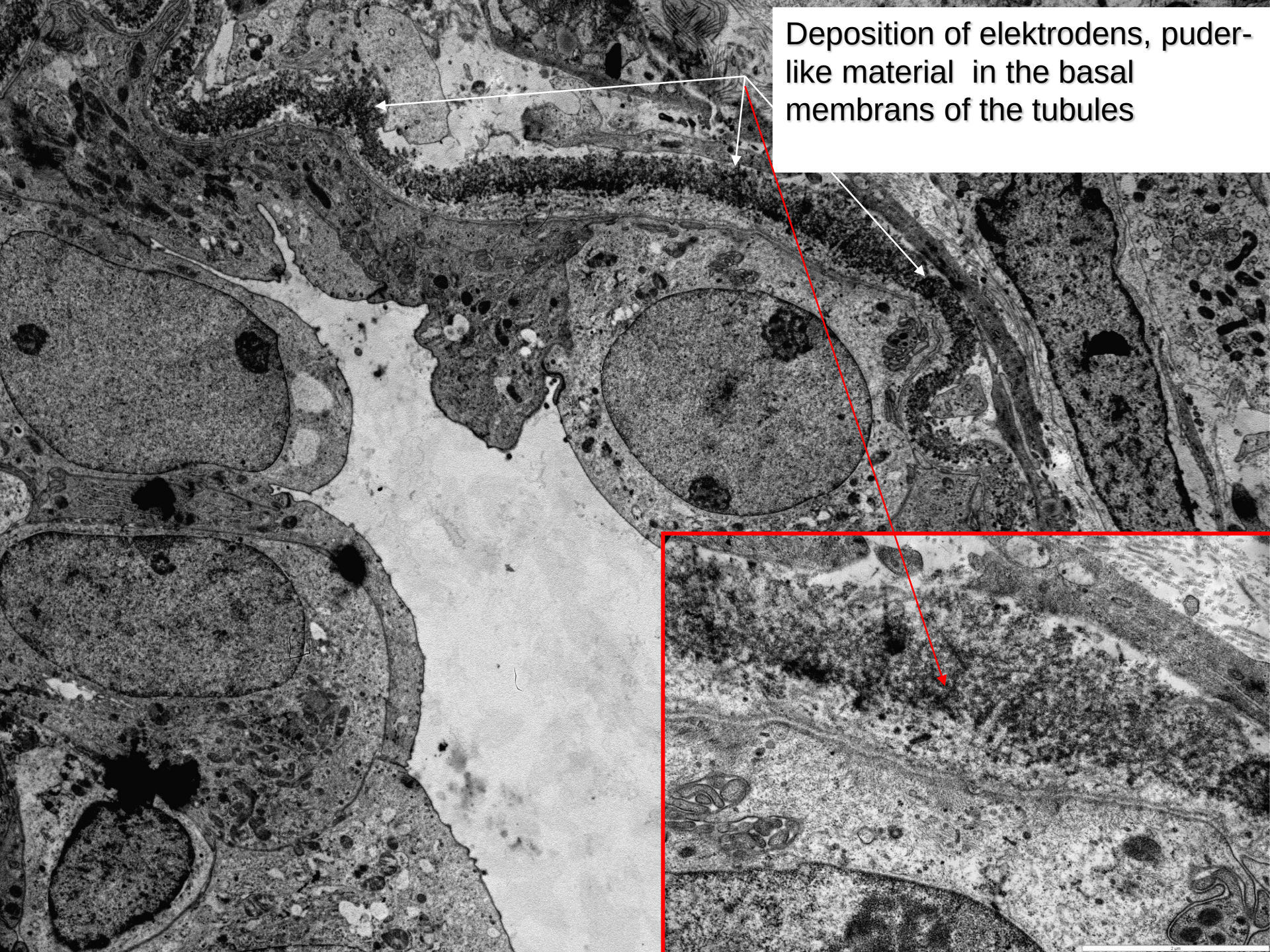


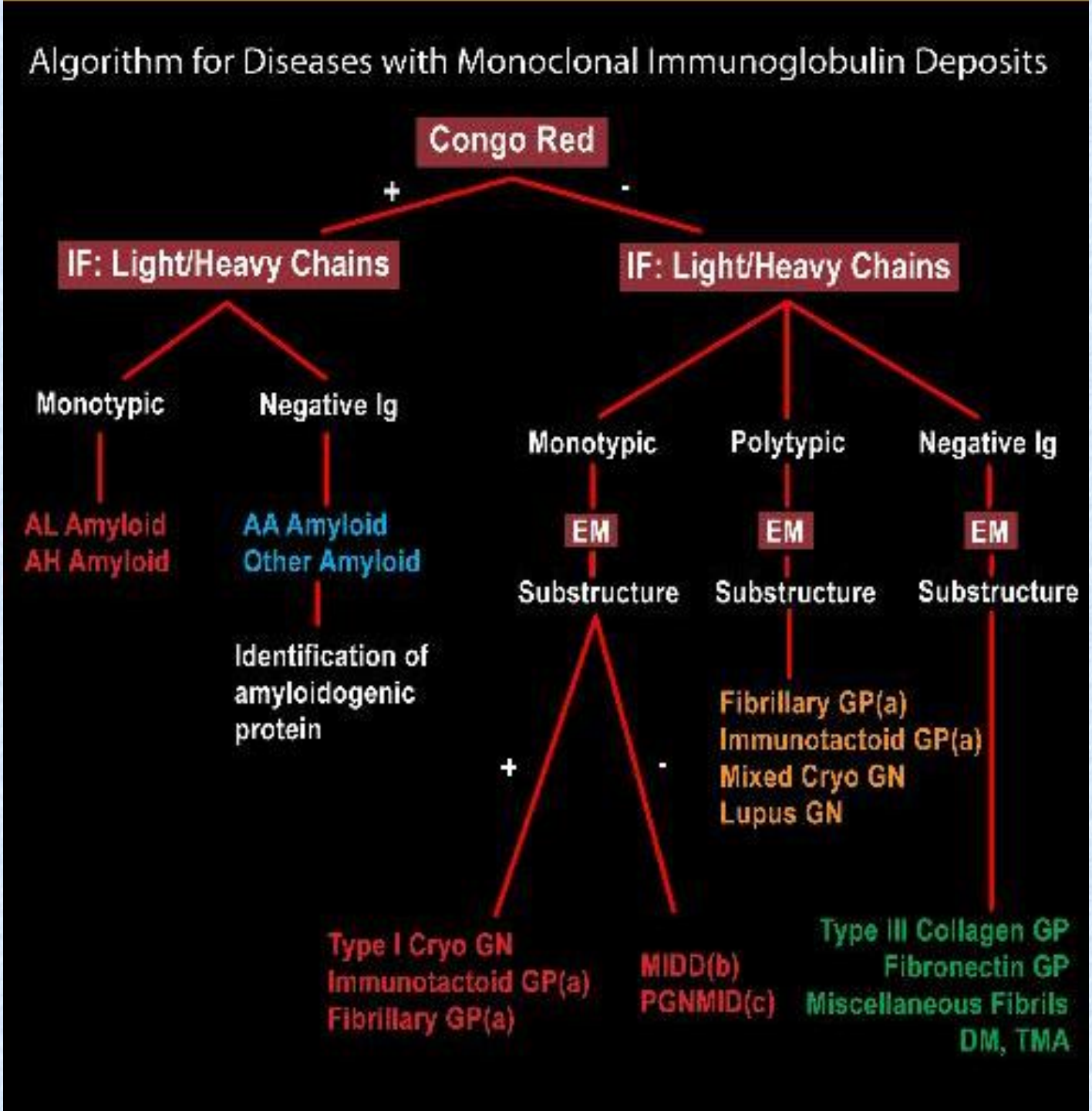
Multiple Myeloma is a plasma cell malignancy.The tumor cells secrete M-protein and Bence Jones protein. These proteins form tubular casts in the distal and collecting tubuli obstructing urine flow.
Tubular epithel cells form giant cells around the casts.

Monoclonal immunoglobulin deposition disease (MIDD)


Deposition of elektrodens, puder-like material in the basal membrans of the tubules


Algorithm for Diseases with Monoclonal Immunoglobulin Deposits
Congo Red
+
-
IF: Light/Heavy Chains
IF: Light/Heavy Chains
Monotypic
Negative Ig
Monotypic
Polytypic
Negative Ig
AL Amyloid
AH Amyloid
AA Amyloid
Other Amyloid
EM
EM
EM
Substructure
Substructure
Substructure
Identification of amyloidogenic protein
Fibrillary GP(a)
Immunotactoid GP(a)
Mixed Cryo GN
Lupus GN
+
-
Type I Cryo GN
Immunotactoid GP(a)
Fibrillary GP(a)
MIDD(b)
PGNMID(c)
Type III Collagen GP
Fibronectin GP
Miscellaneous Fibrils
DM, TMA

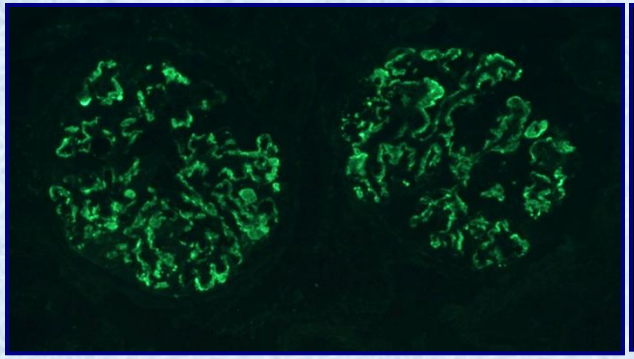
Systematic lupus erythematodes

- Generalised autoimmune disease
- 16-30 y. mostly females (10:1)
- Antinuclear antibody - ANA
- Double-stranded DNA antibody
- Prognosis is depend on the kidney and cerebral involvement

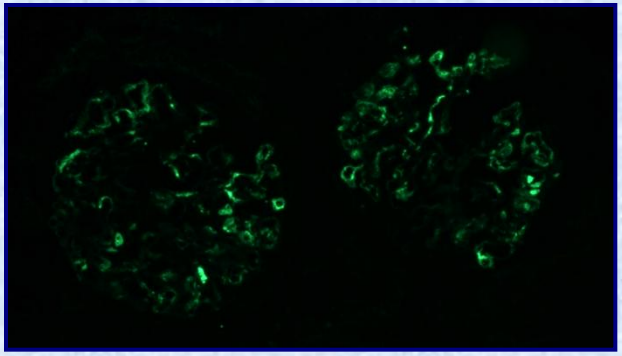
Lupusnephritis

- Circulating immuncomplexes
  Ag=nucleus + autoantibodies, complement
- Deposit: GBM, vessels, tubular BM
- Deposits: subendothelial
  subepithelial
  intramembranous
  mesangial
- IF: „full house"

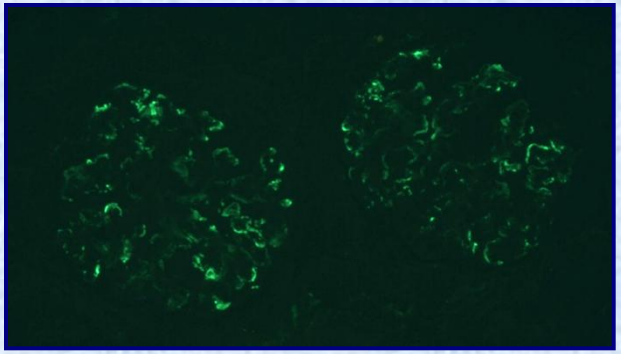
Immun reactions



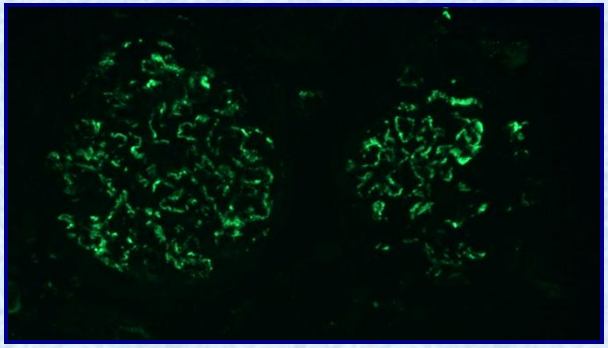
IgG



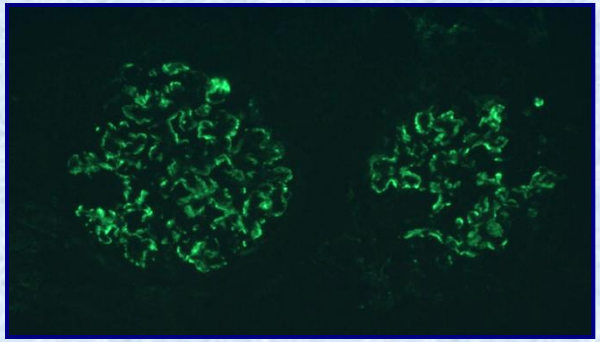
IgA



IgM

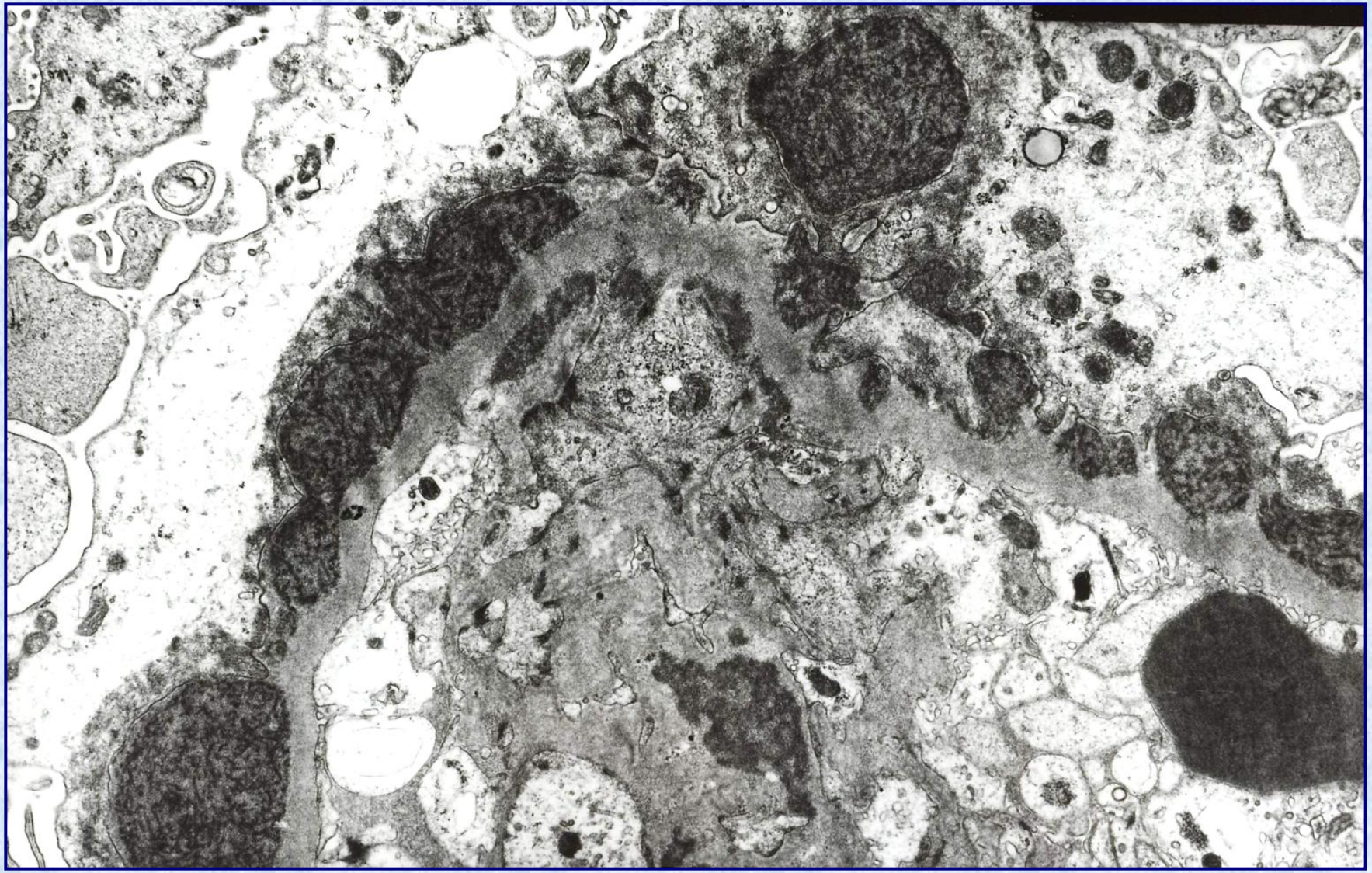


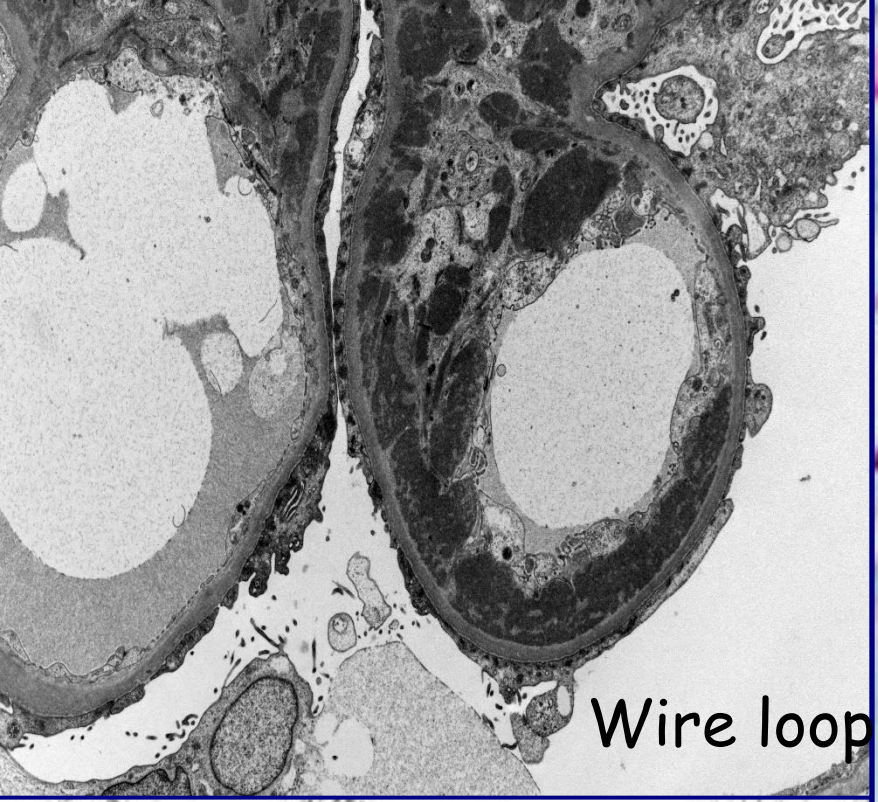
C3

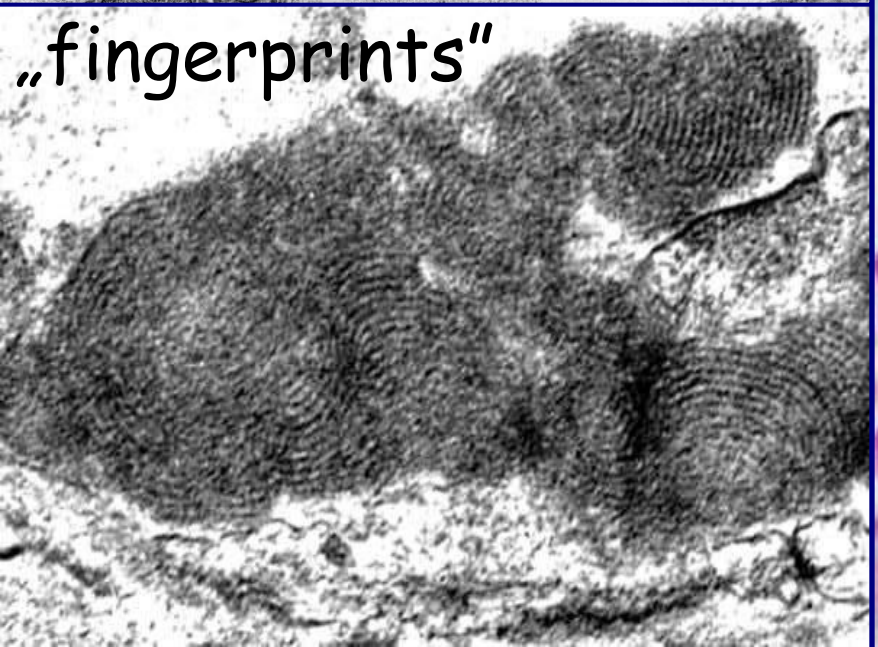


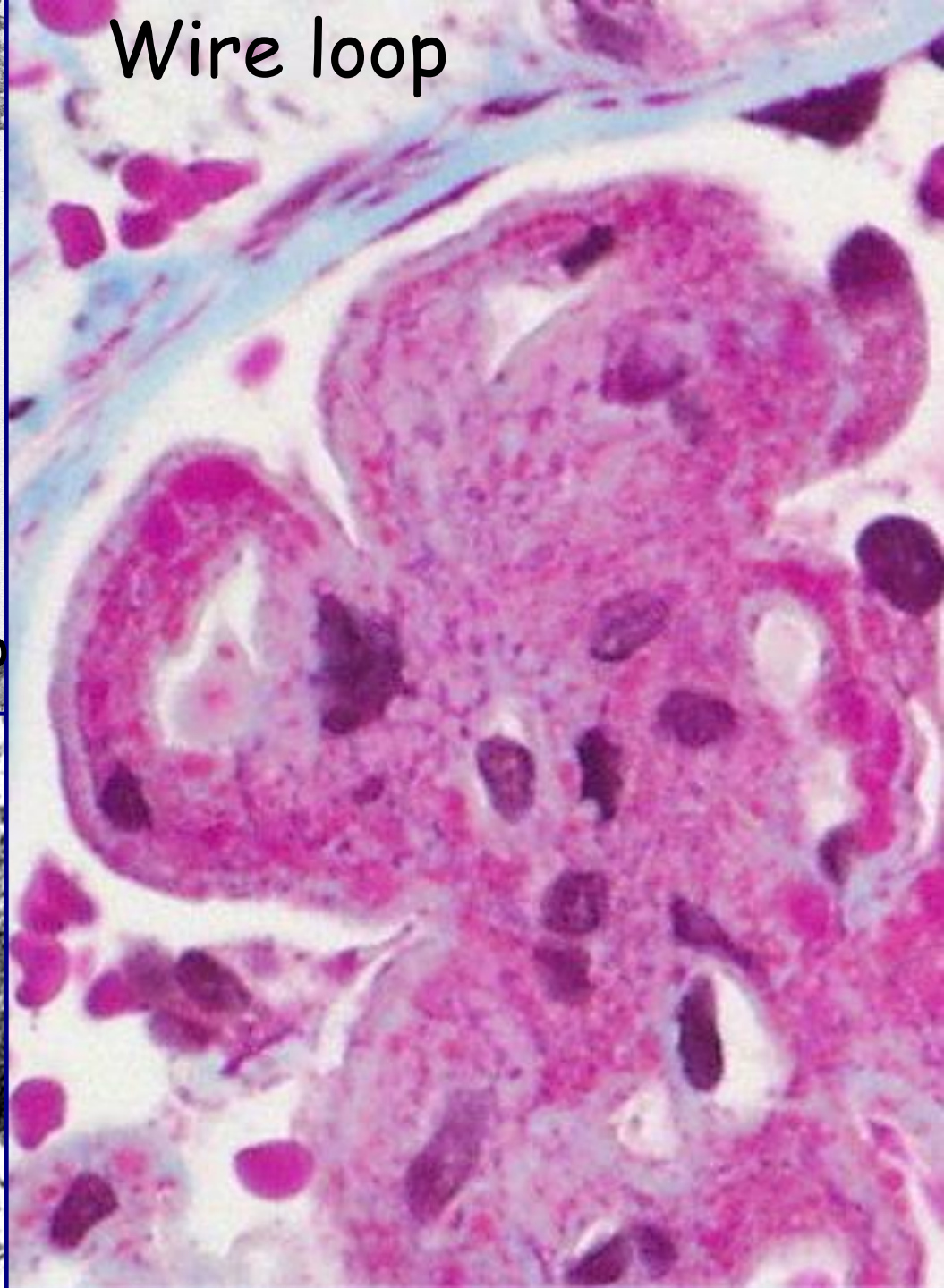
C1q

Electronmicroscopy




Wire loop


„fingerprints"


Wire loop

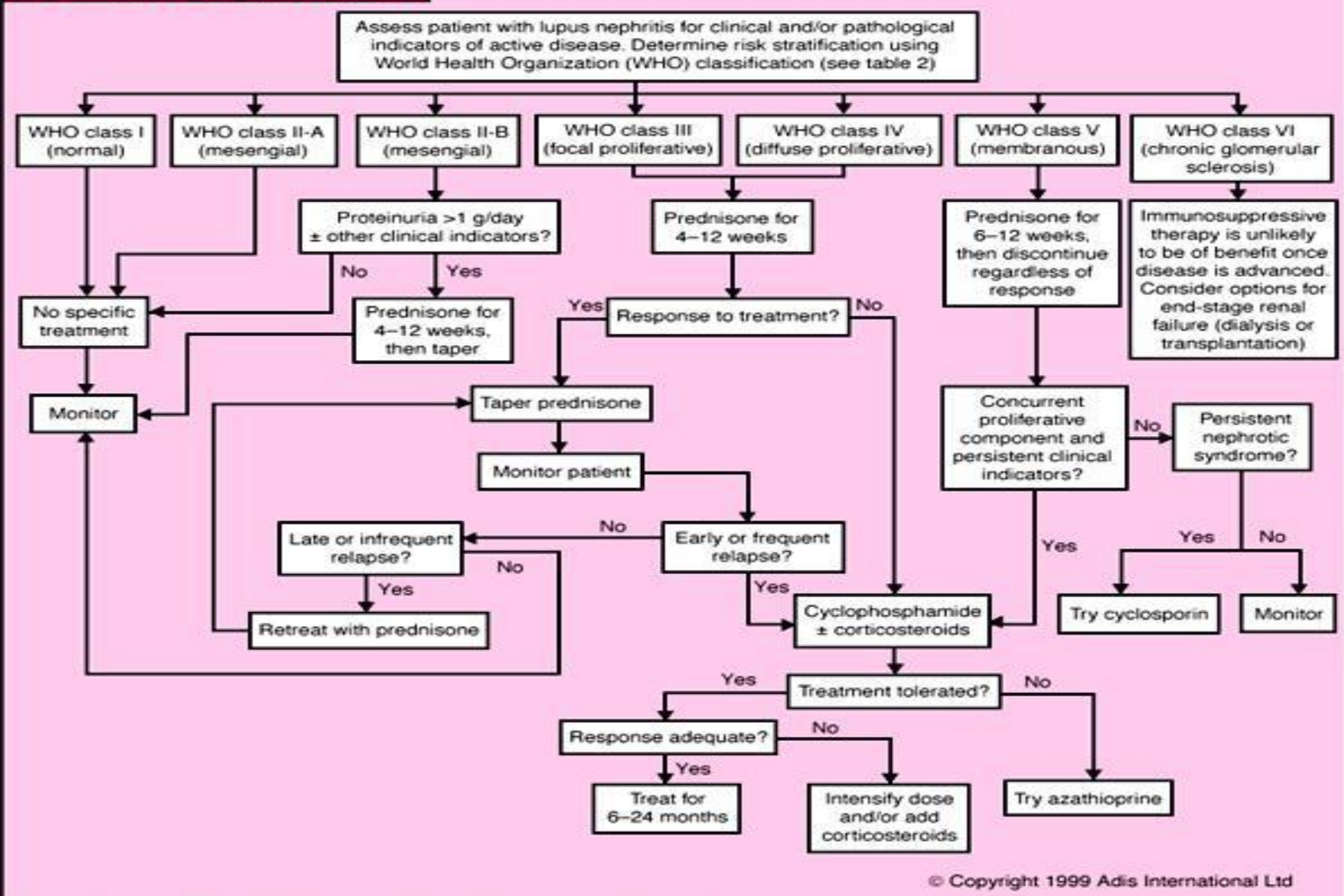
Abbreviated International Society of Nephrology/ Renal Pathology Society (ISN/RPS) classification of lupus nephritis (2003)

Class I	Minimal mesangial lupus nephritis -
Class II	Mesangial proliferative lupus nephritis -
Class III	Focal lupus nephritis[a] -
Class IV	Diffuse segmental (IV-S) or global (IV-G) lupus nephritis[b]
Class V	Membranous lupus nephritis[c] -
Class VI	Advanced sclerosing lupus nephritis

Morphology

- Active lesions: crescent, cellular proliferation, necrosis, wire loop, intracapillary leukocytosis, necrotising arteriolitis or hyalinosis, lymphocyte infiltration, tubular degeneration

- Chronic lesions: glomerular sclerosis, fibrotic crescent, interstitial fibrosis, tubulur atrophy



Possible treatment strategies for patients presenting with active lupus nephritis[1]

Classification of glomerular diseases

- Primary glomerular diseases
- Glomerulonephritis in systematic diseases
- Glomerular lesions in vascular diseases
- Hereditary nephropaty and miscellaneous glomerular lesions

Renal vascular diseases

Sclerosis proliferation

Arteriosclerosis
- primary
- secunder

Fibromuscular diseases

Infiltratio insudatio

Amyloidosis
MIDD
Storage

Hyalinosis
- Insudation: RR
- IC: Lupus
- Toxicus

TMA thrombosis

TMA
- HUS
- TTP
- DIC

Vasculitis

- ANCA
- IC

Causes of Tubulointerstitial Nephritis

Infection

Acut bacterial pyelonephritis

Chronic pyelonephritis (reflux nephropathy)

Other infections (viral, parasitic)

Toxins

Drugs

Acute hypersensitive nephritis

Analgesic nephropathy

Heavy metals

Lead, Cadmium

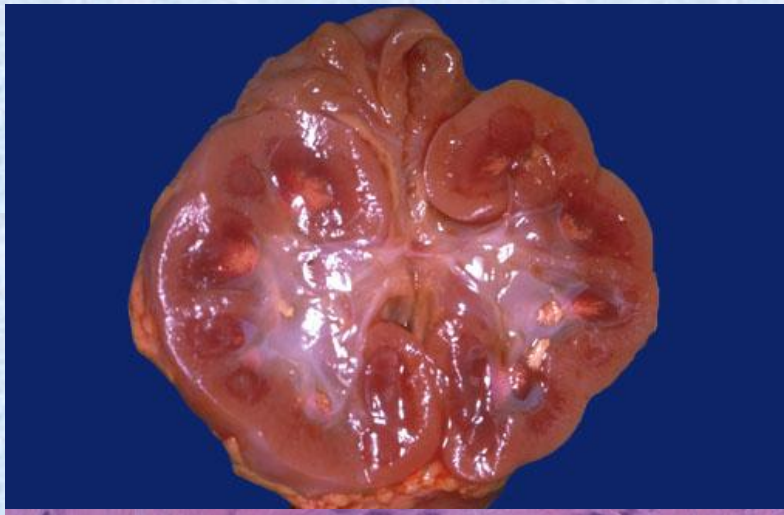
Metabolic diseases

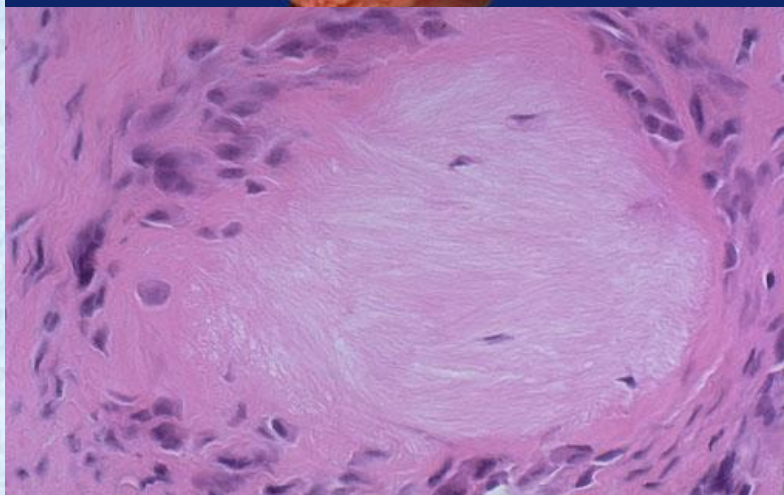
Urate nephropathy

Hypercalcaemic nephropathy

Hypokalaemic nephropathy

Oxalate nephropathy





Causes of Tubulointerstitial nephritis

Physical factors

Chronic urinary obstruction

Radiation nephropathy

Neoplasm

Myeloma multiplex

Immun diseases

Transplant rejection

Sjögren sy

Sarcoidosis

Vascular diseases

Others

Balkan nephropathy

Nephronophthisis – medullary cystic disease

„Idiopathic" interstitial nephritis

Tubulointerstitialis nephritis induced by drugs and toxins

- Antibiotics

SA,penicillin,cephalosporin,rifampin,erythromycin etc.

- Diuretics

thiazids, furosemide, triamterene

- NSAID

- Miscellaneous

phenytoin, allopurinol, cimetidine, Chinese herbal medicine, captopril, lithium, valproate, warfarin, antiviaral drugs

Tubulointerstitialis nephritis induced by drugs and toxins

Etiology/Pathogenesis

T-cell mediated hypersensitivity reaction

- Idiosyncratic reaction, not dose dependent

Clinical Issues

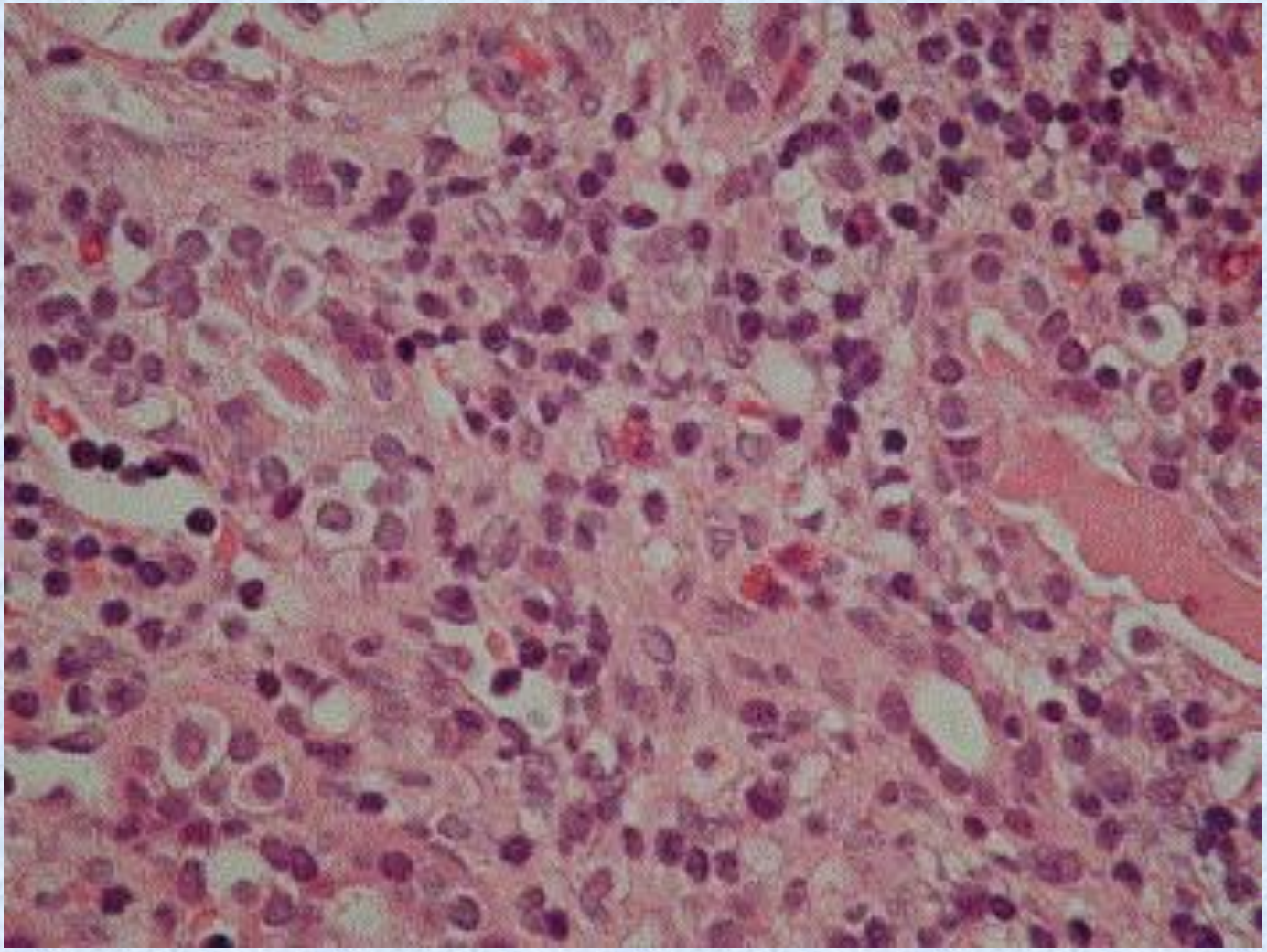
- Triad of fever, rash, eosinophilia in 50%
- Urine eosinophils
- Subnephrotic proteinuria
- Recovery of renal function in 60-90 %

Tubulointerstitialis nephritis induced by drugs and toxins

Microscopic pathology

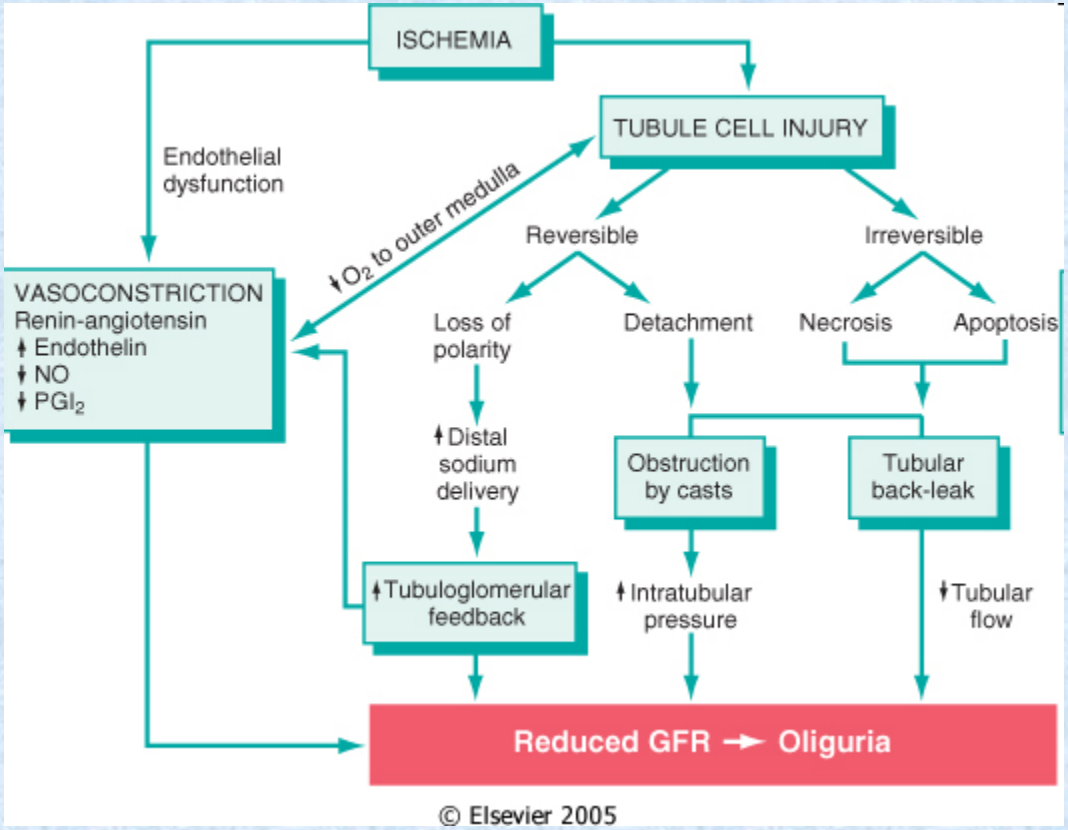
- Interstial inflammation with tubulitis, usually with eosinophils
- Granulomas
- Fibrosis and atrophy with prolonged drug exposure
- Minimal change disease: NSAIDs
- Papillary necrosis: NSAIDs

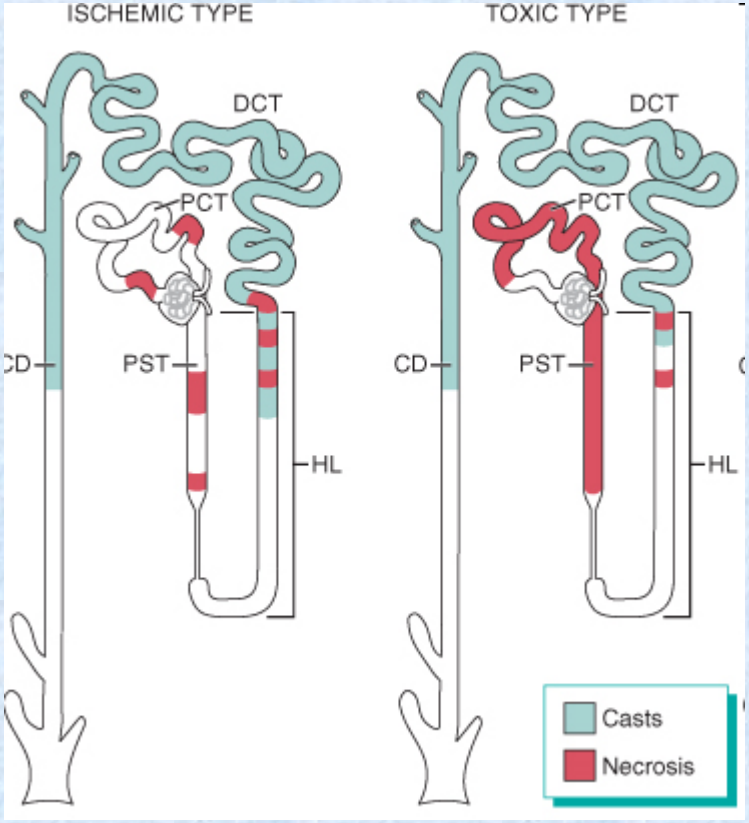
Tubulointerstitialis nephritis induced by drugs and toxins



http://www.sciencedirect.com/science/journal/09686053

Renal tubular injury





Acut tubular necrosis

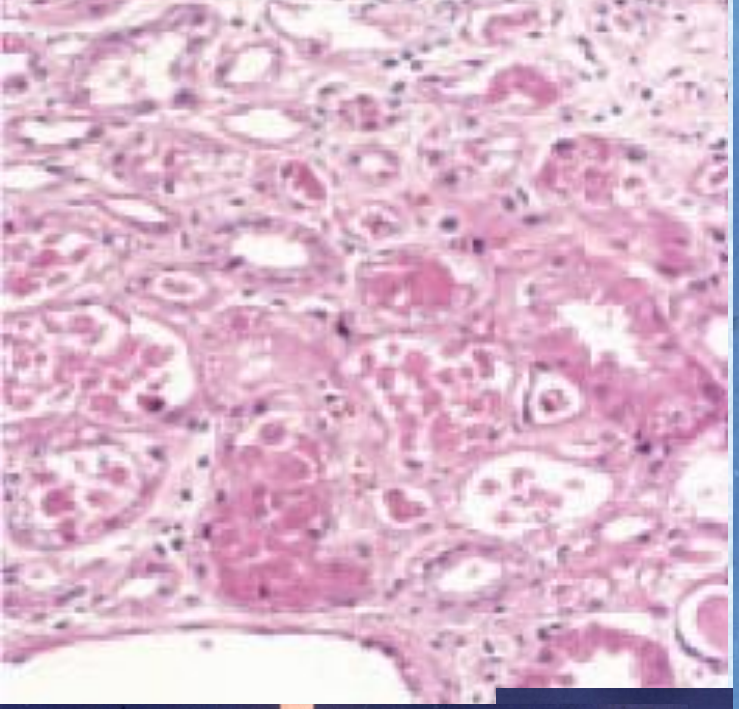
Ischaemic ATN

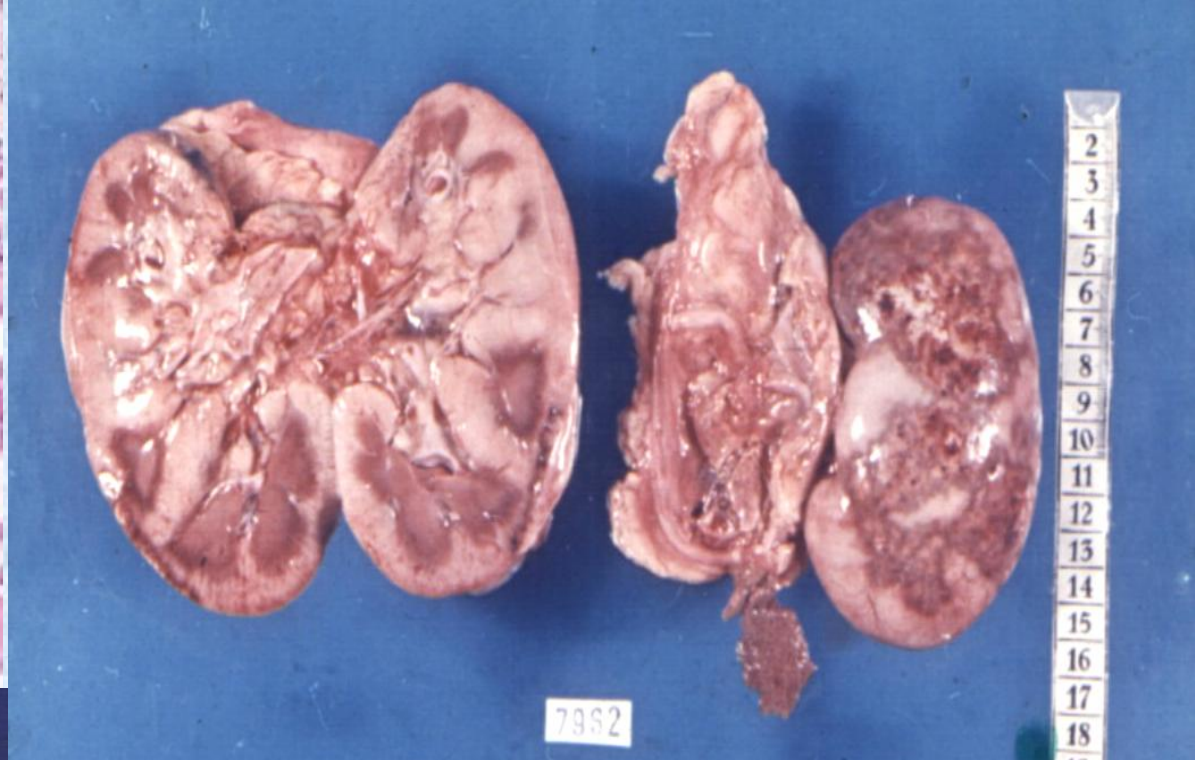
- Shock
- Traumatic damage of skeletal muscles: rhabdomyolysis, myoglobinuria

Nephrotoxic ATN

- AB
- RTG contrast material
- Poisons

etilenglicol, metilalcohol, insecticid, mushrooms





Renal tubular injury – shock kidney