The Renal Biopsy Demystified

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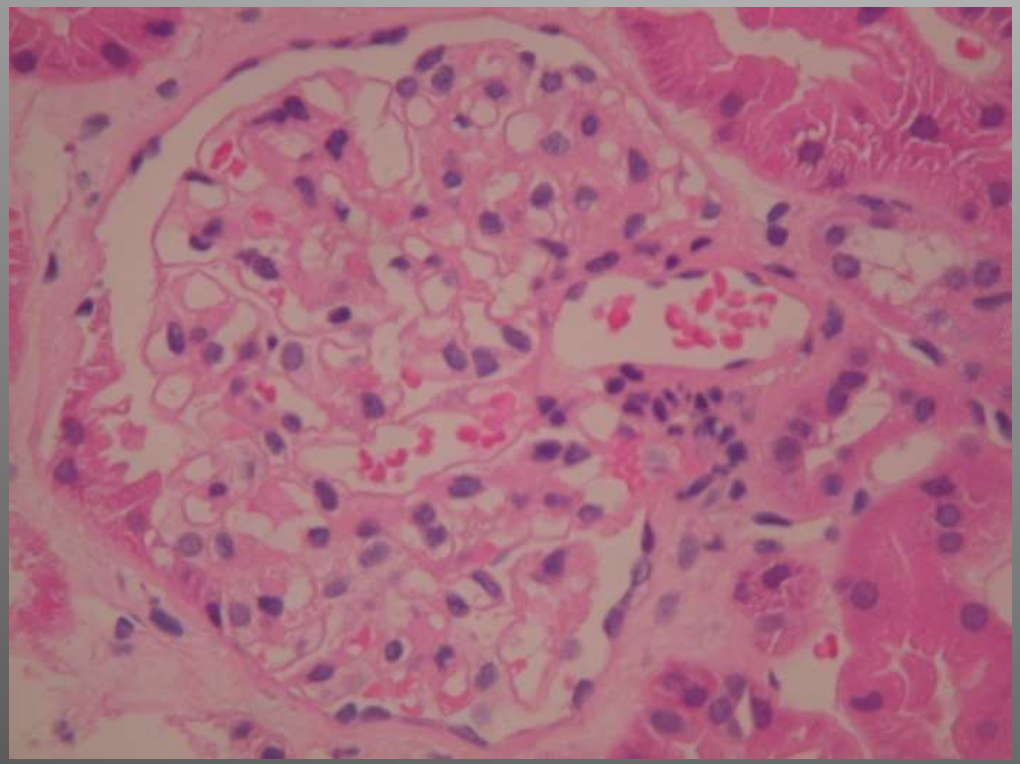
How this Presentation Works

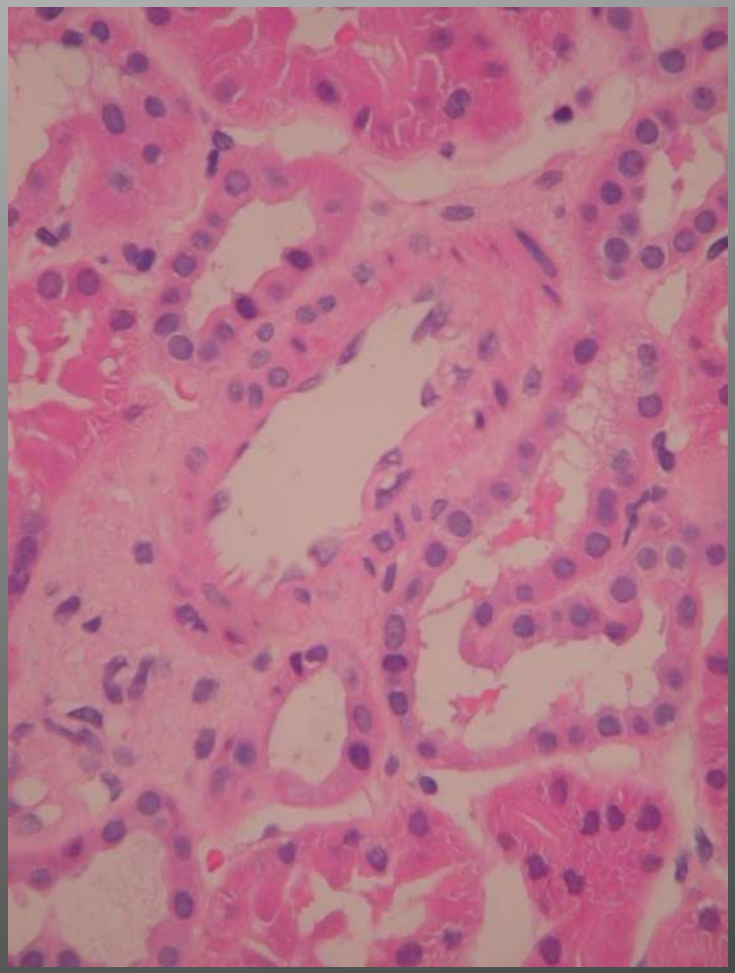
- Clinical context
- Modalities used
- Normal features
- Primer on glomerular disease patterns
- Examples of glomerular disease
- Assessment of biopsy adequacy
- Assessment of disease severity (grade)
- Assessment of disease chronicity (stage)

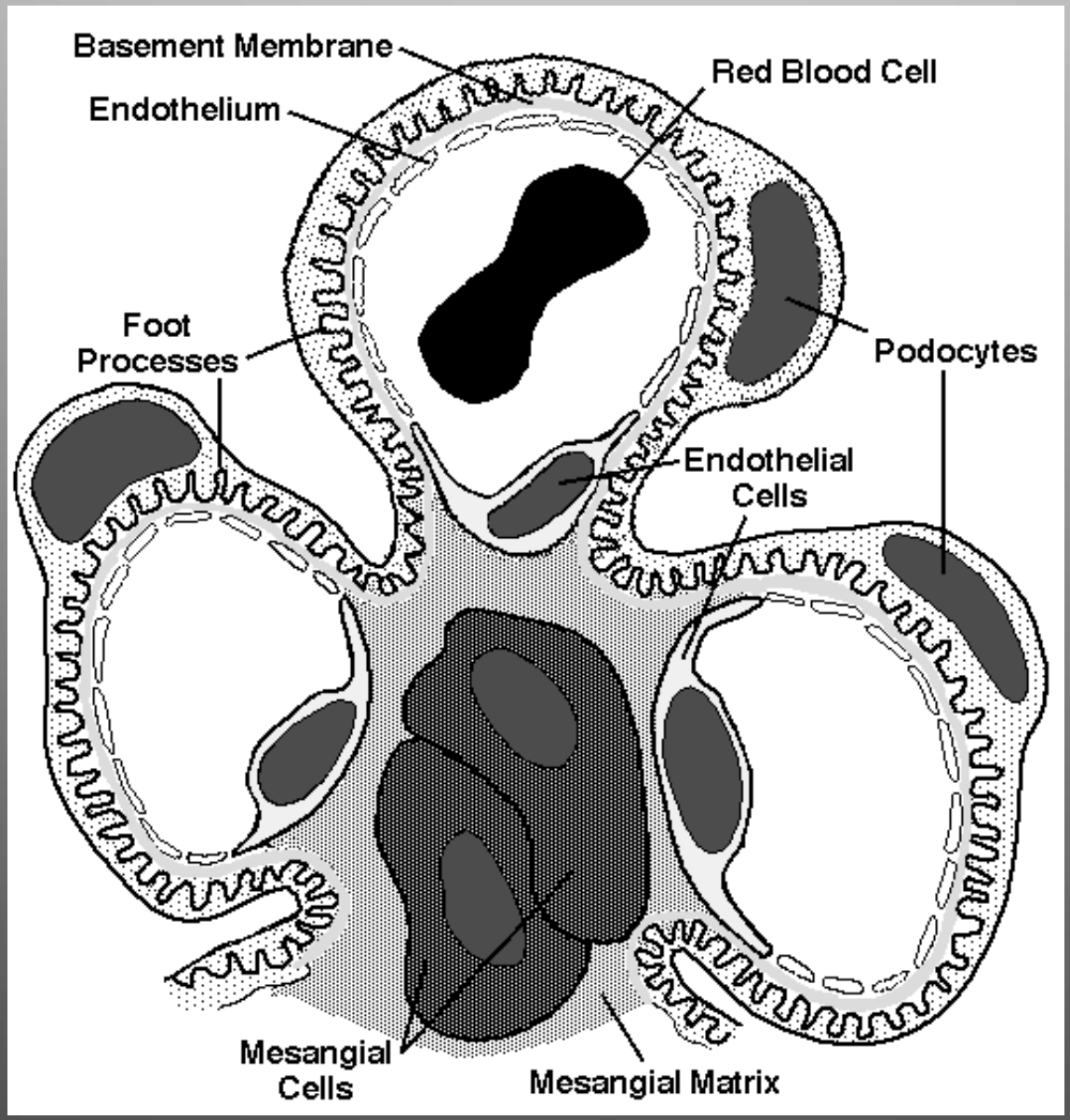
Considerations

- Clinical
  - Acute renal failure
  - Chronic renal failure
  - Nephrotic syndrome
  - Nephritic syndrome
  - Haematuria/proteinuria
  - Microscopic haematuria
- Pre renal
- Post renal
- Renal
  - Vascular
  - Tubulointerstitial
  - Glomerular
    - Primary
    - Immune complex
    - Non immune complex
    - Other
  - Systemic

Normal Histology

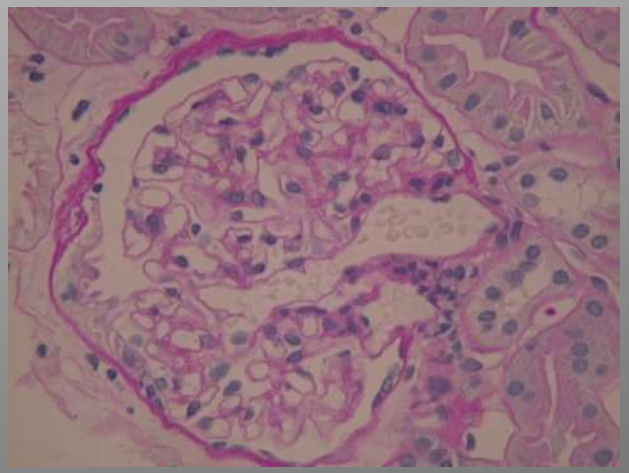


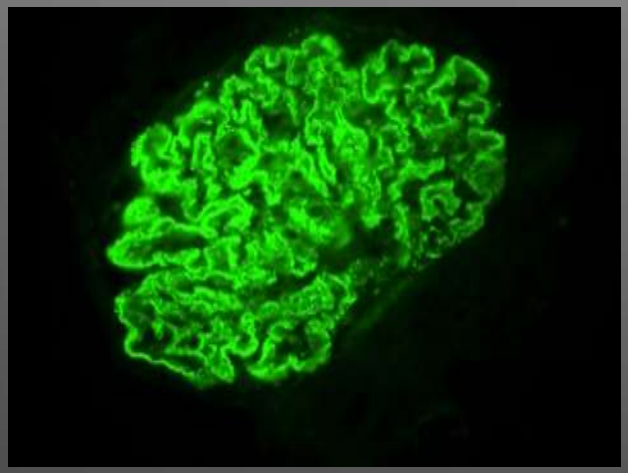


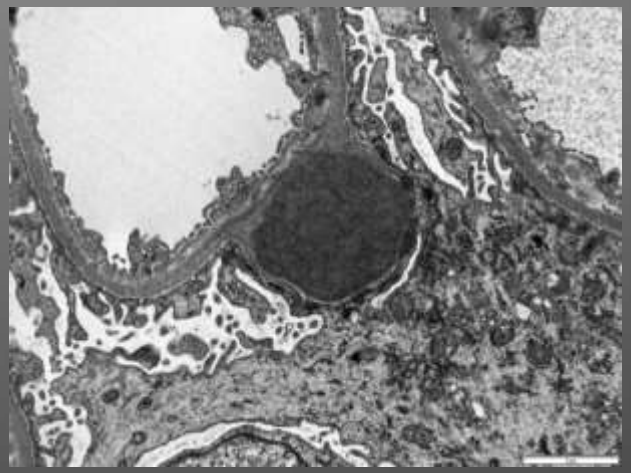

Basement Membrane
Endothelium
Red Blood Cell
Foot Processes
Podocytes
Endothelial Cells
Mesangial Cells
Mesangial Matrix

Techniques Used

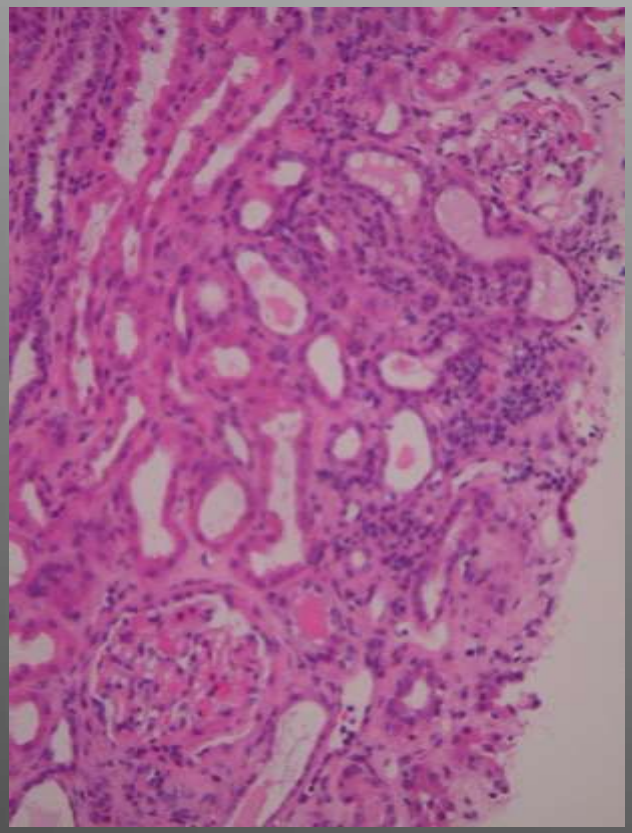
- Light microscopy
- Immunofluorescence
- Electron Microscopy

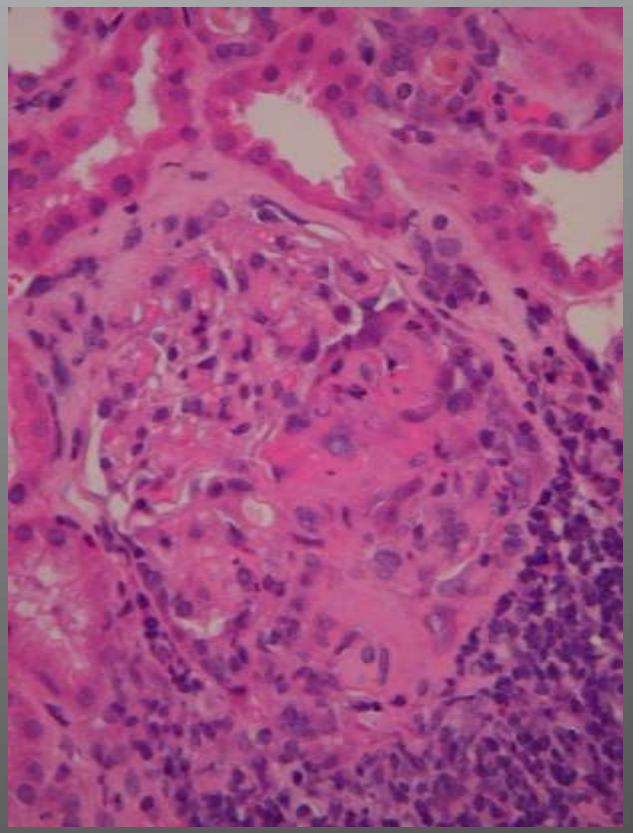


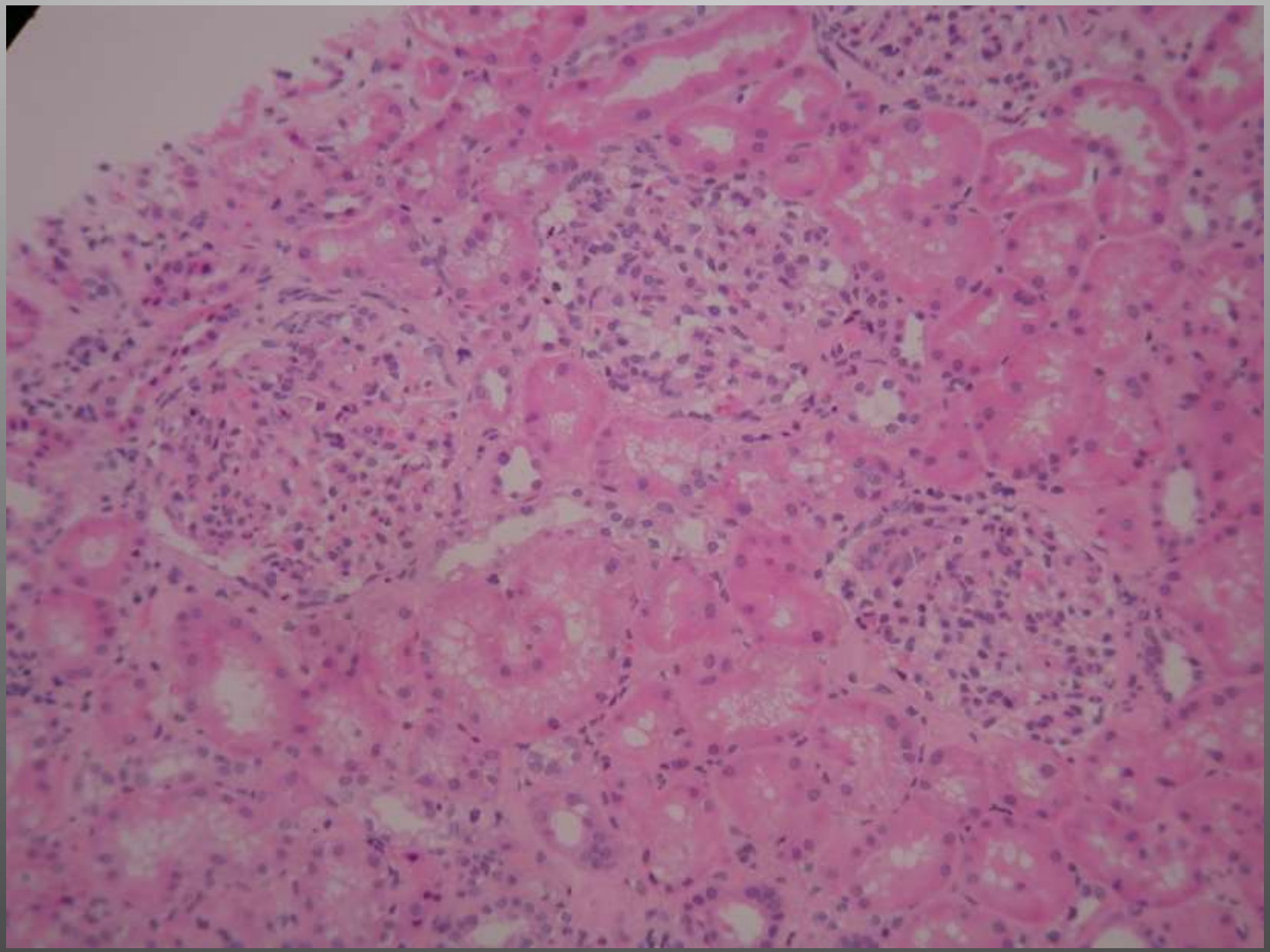


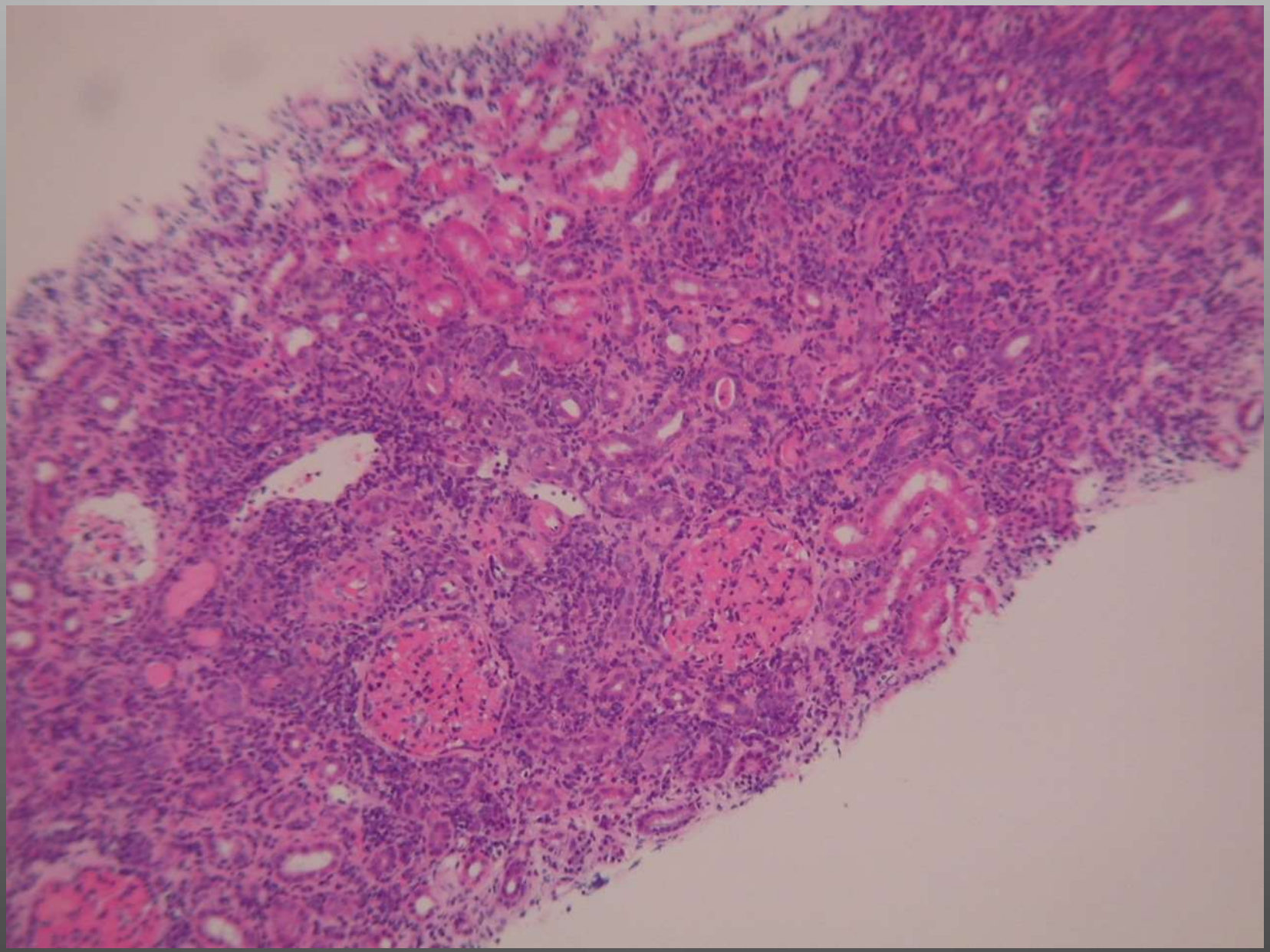


Haematoxylin and Eosin Stain

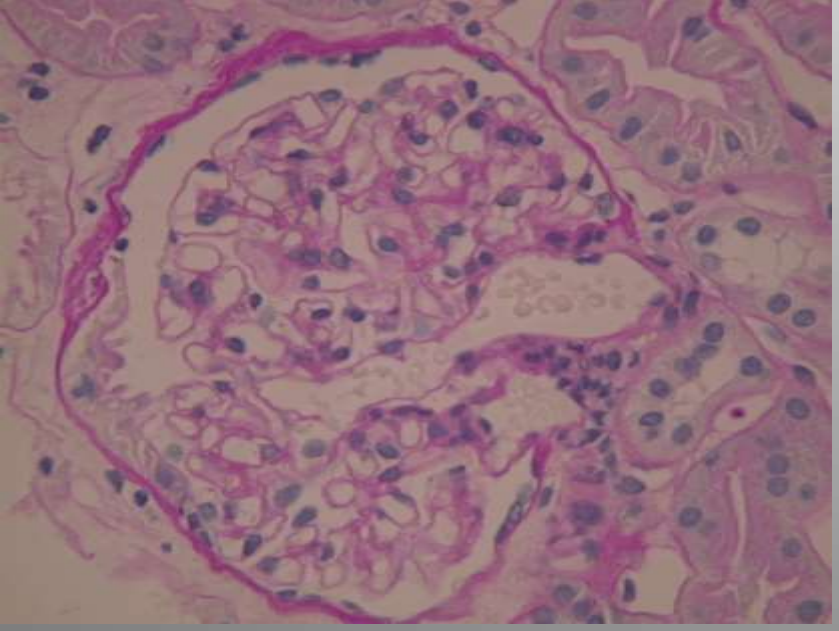


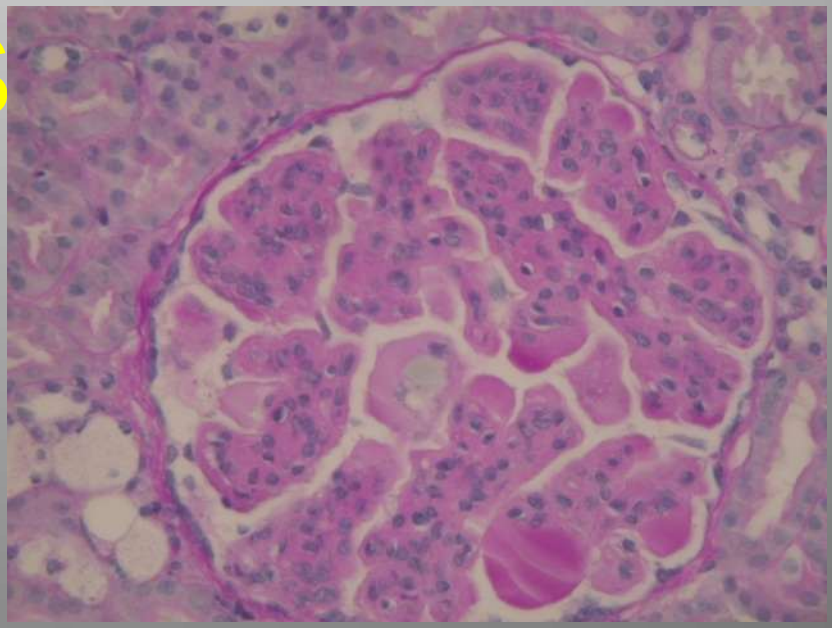


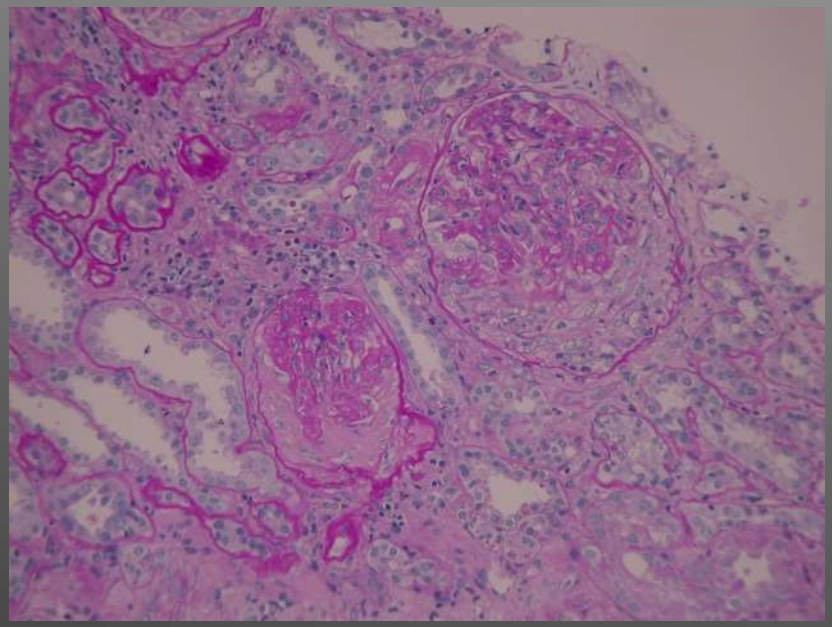


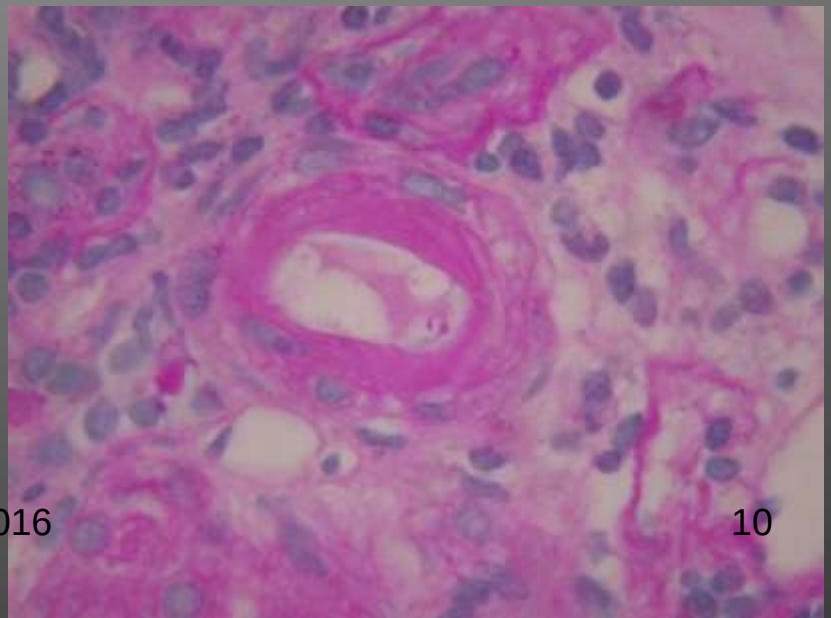


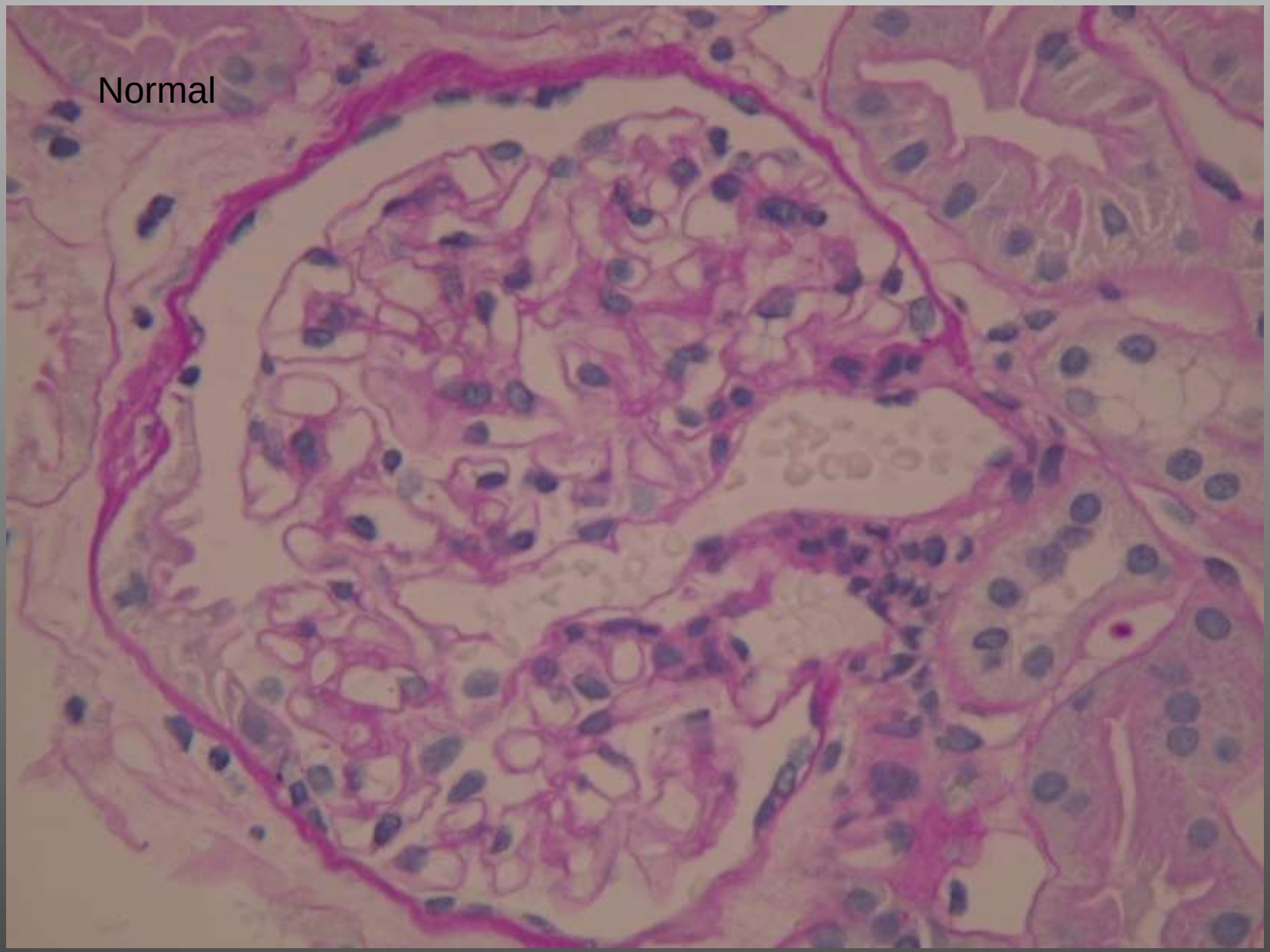
PAS

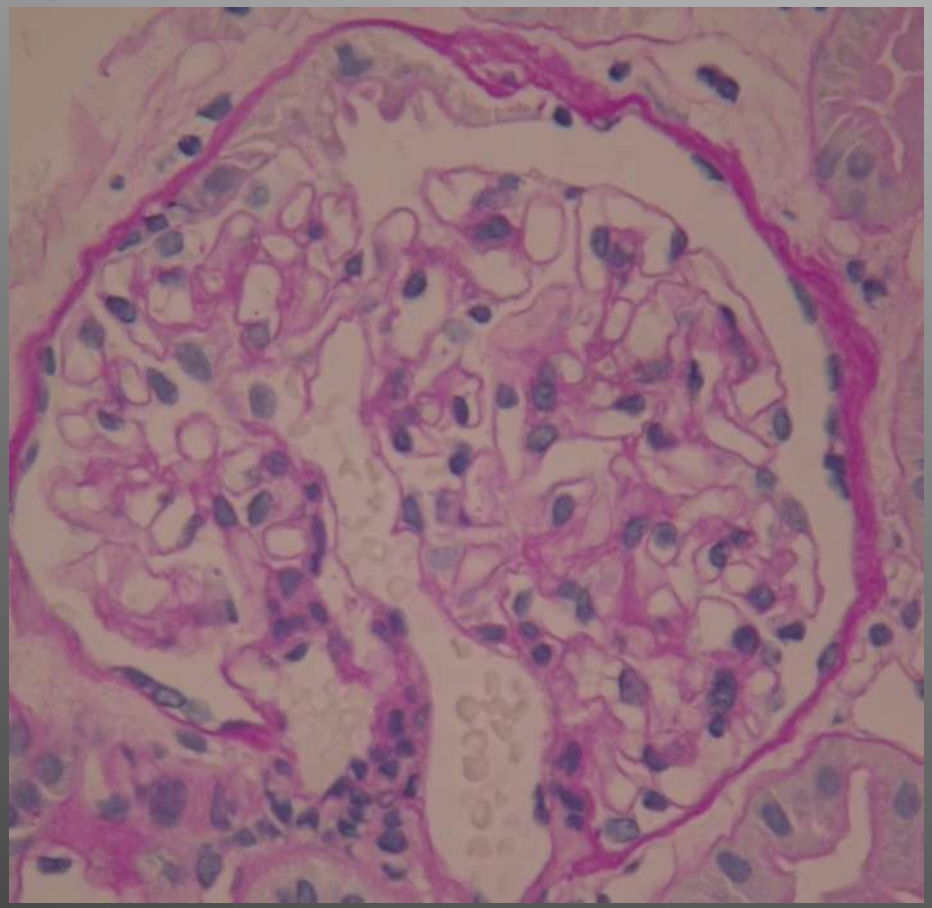


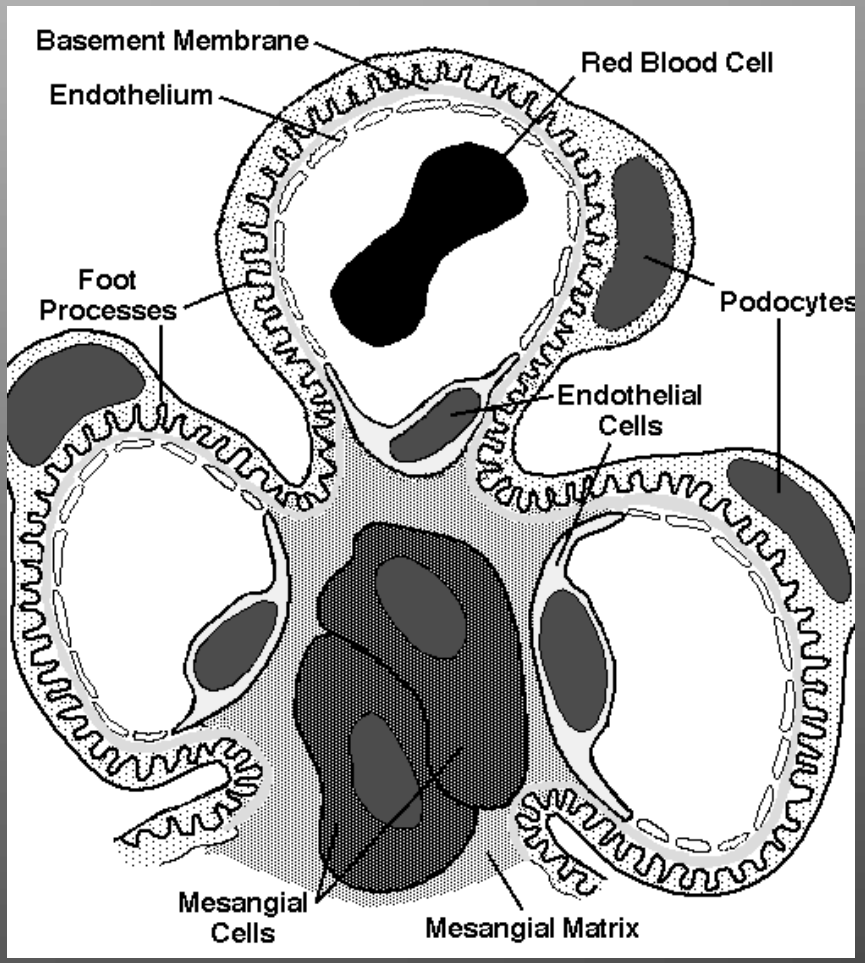







Normal

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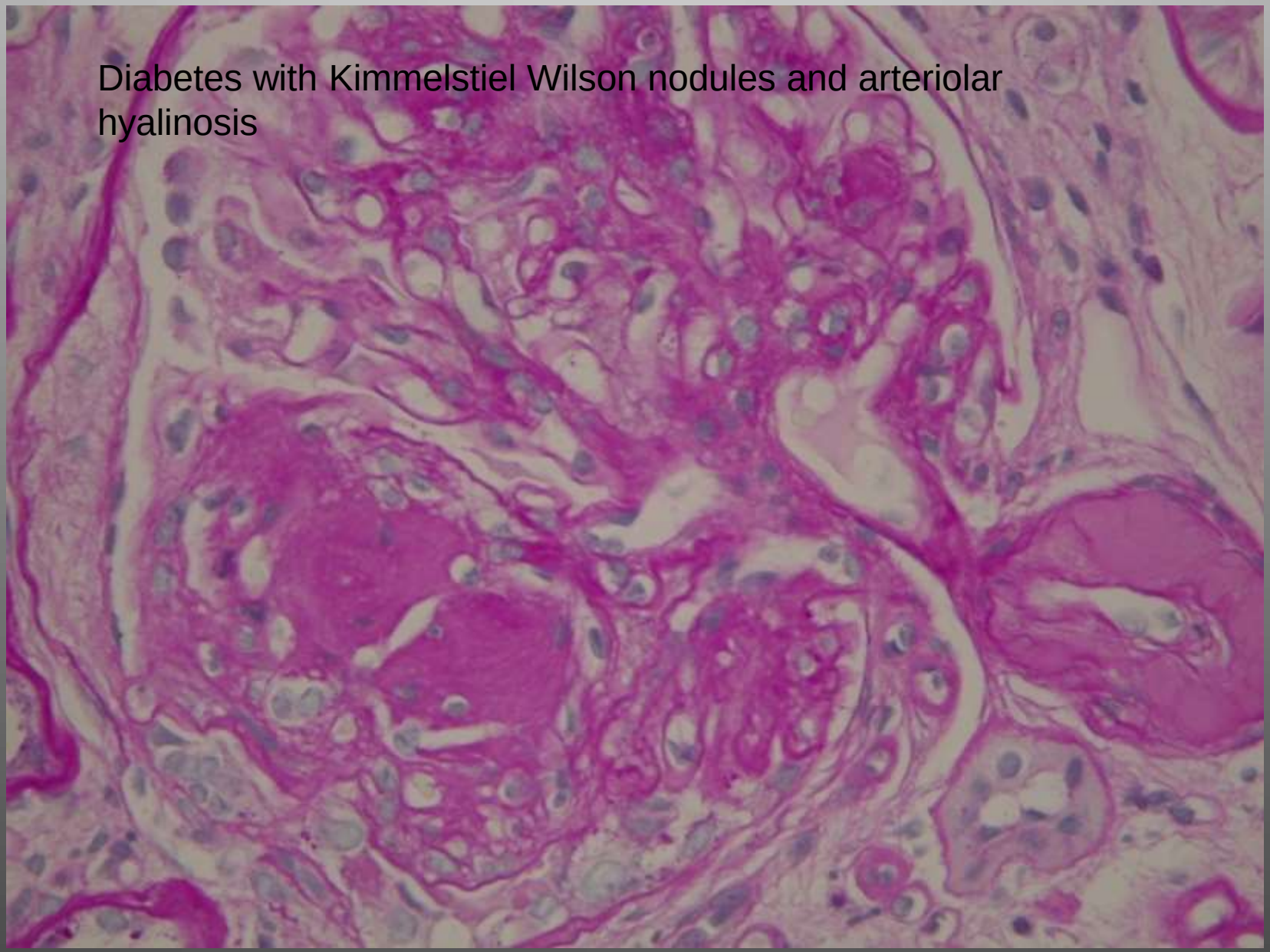
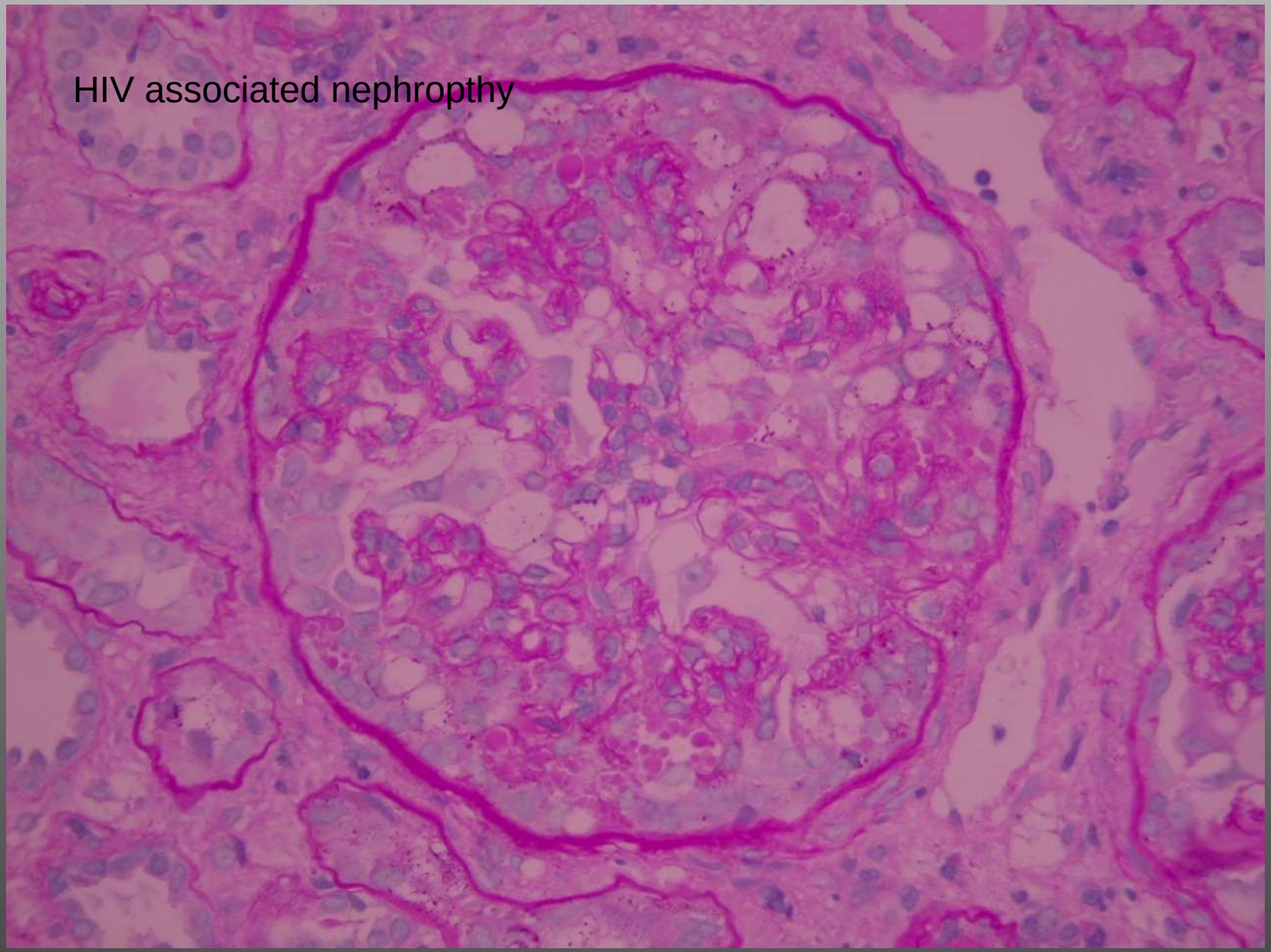
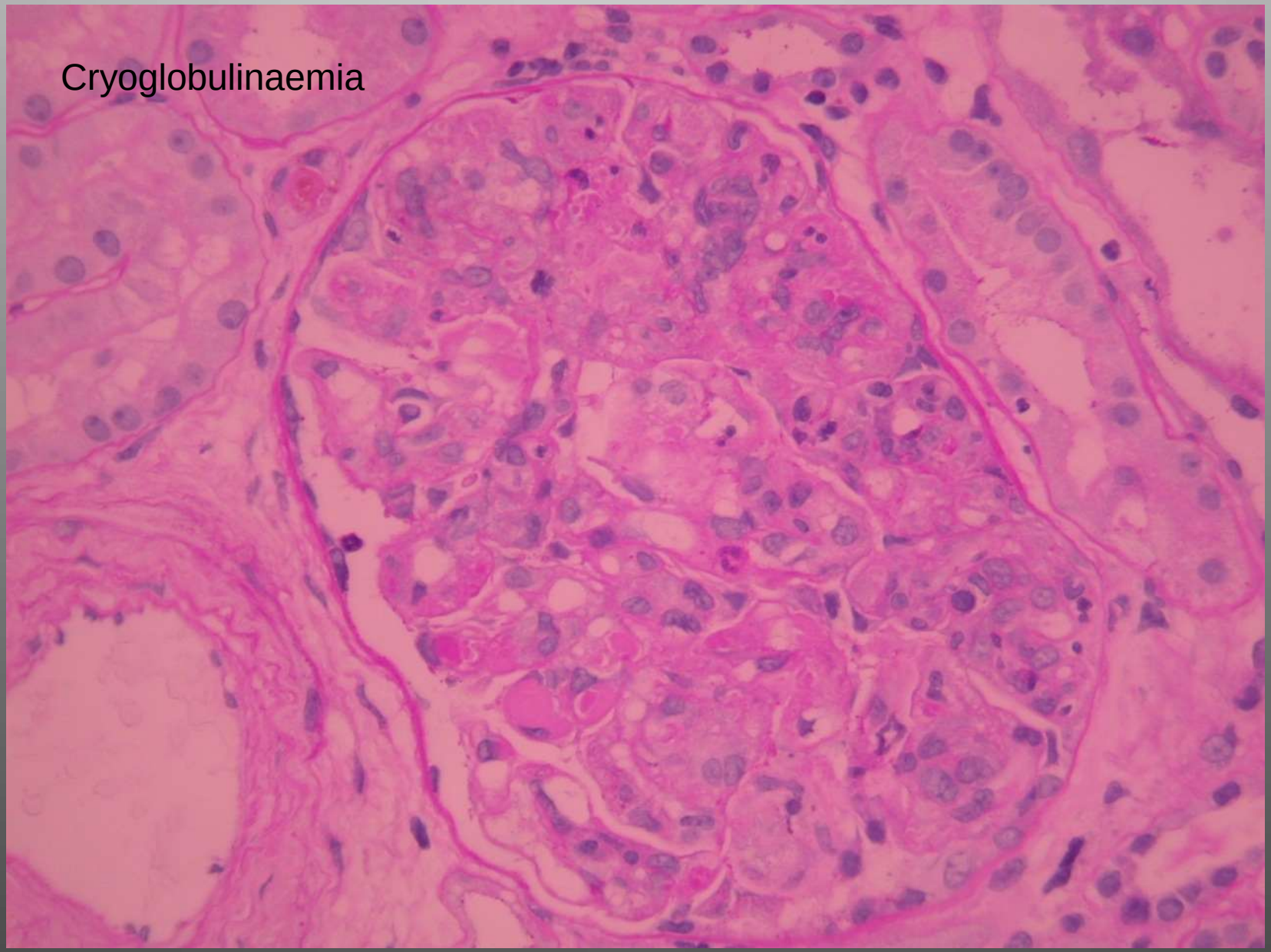
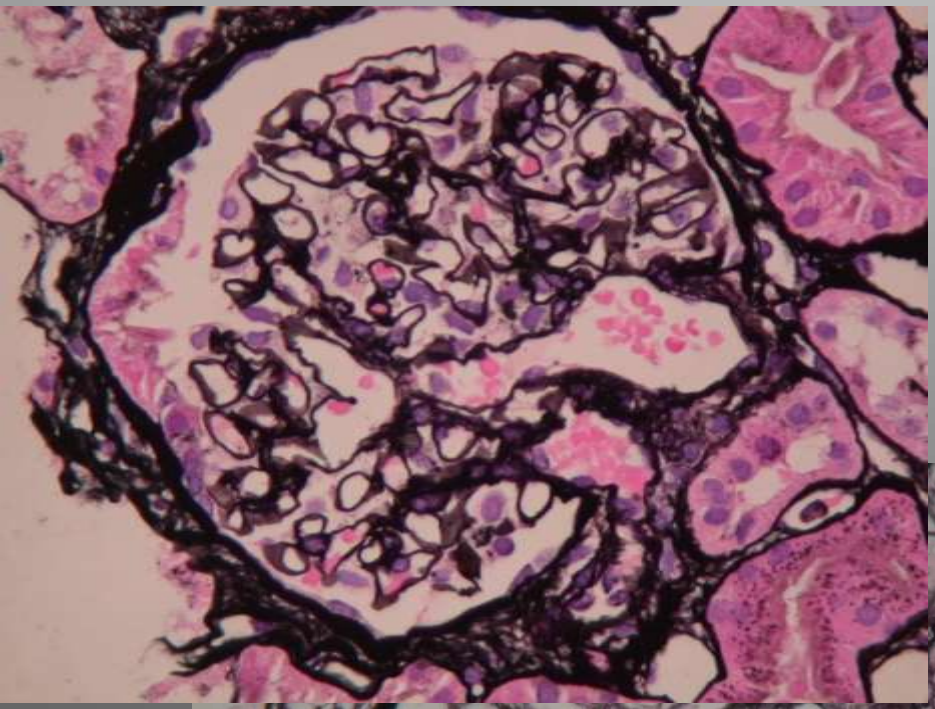
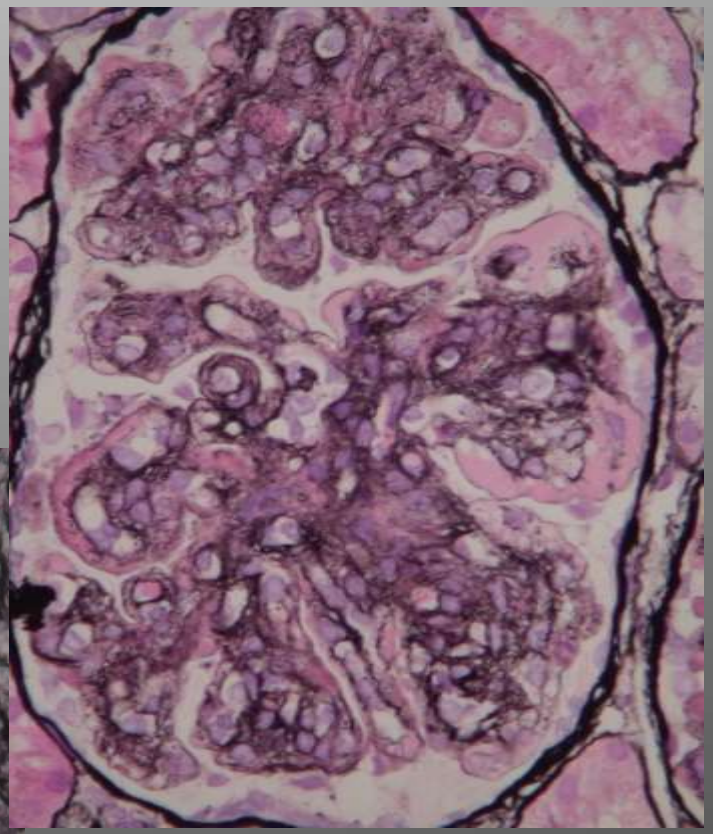

Diabetes with Kimmelstiel Wilson nodules and arteriolar hyalinosis

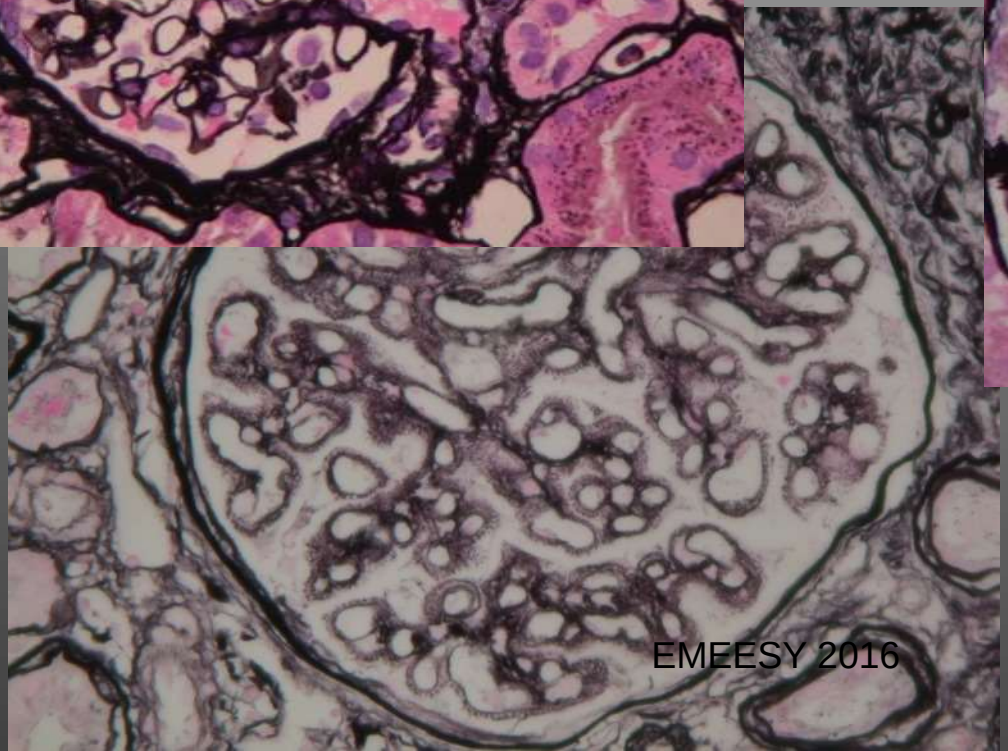

HIV associated nephropthy

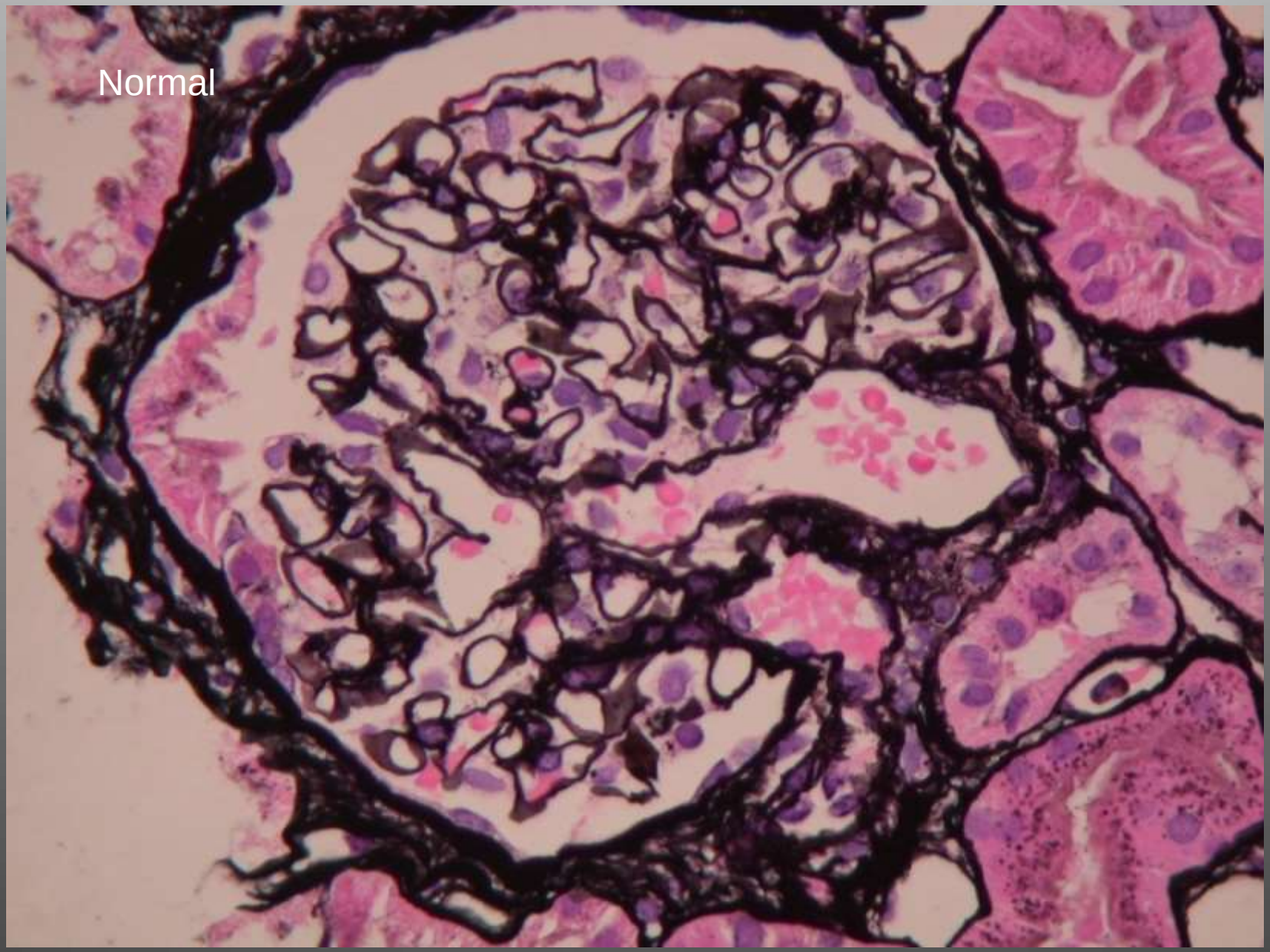

Cryoglobulinaemia

Methanemine Silver





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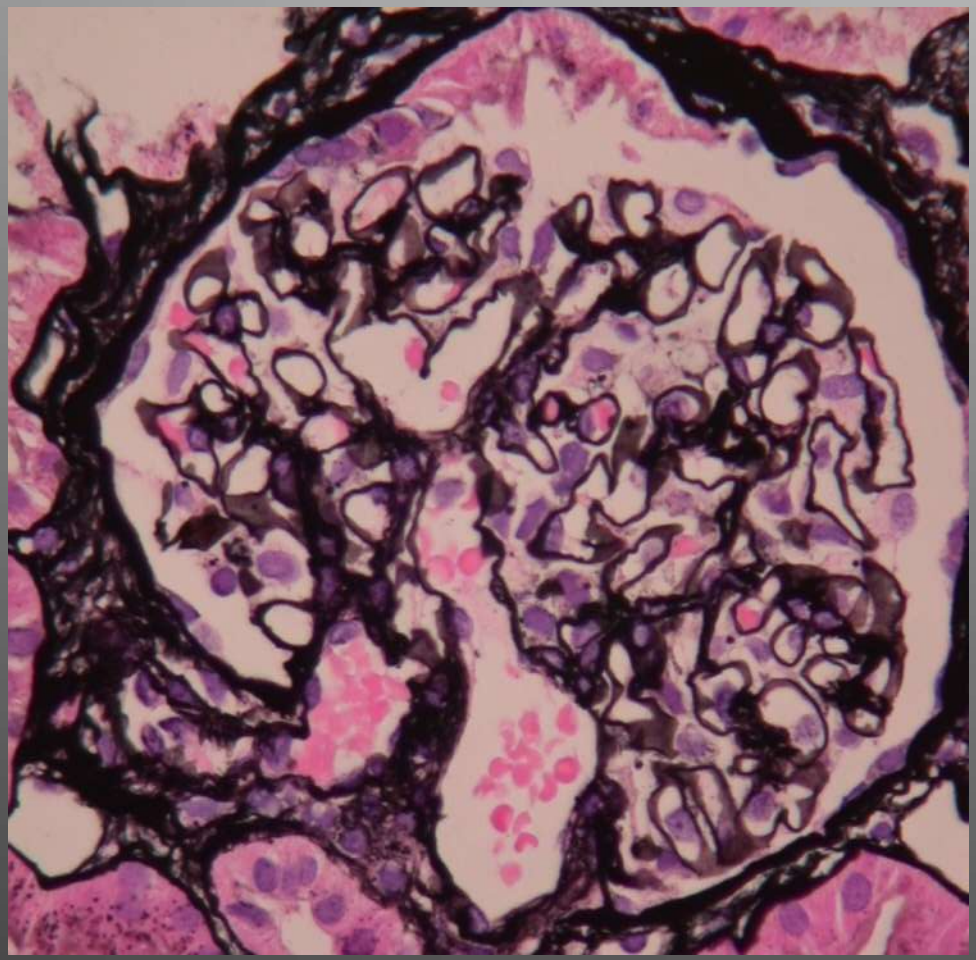

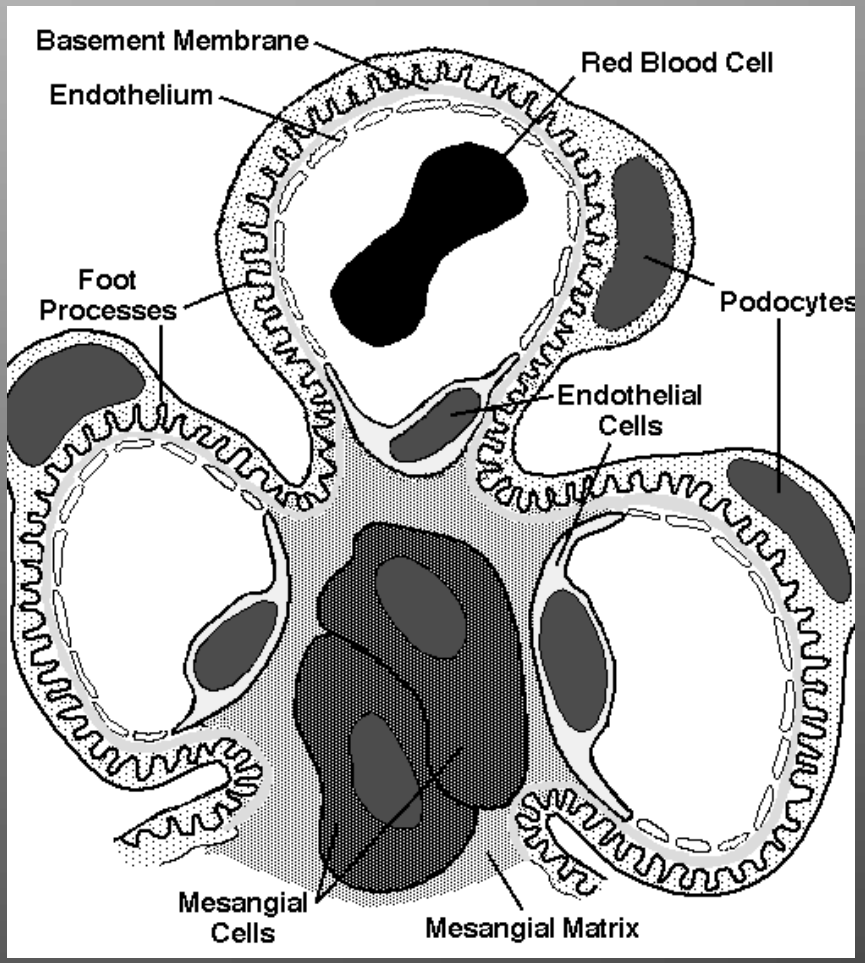
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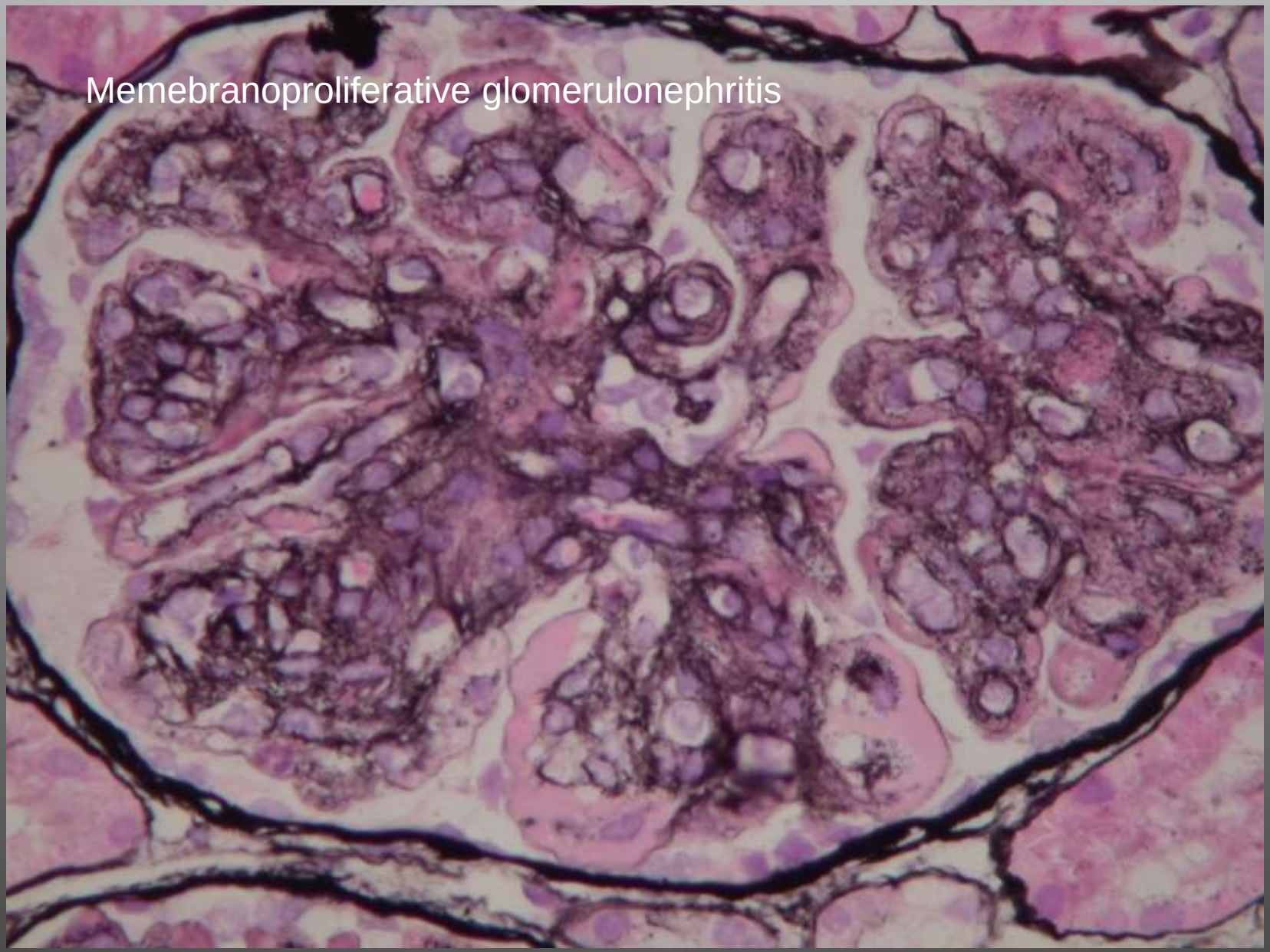
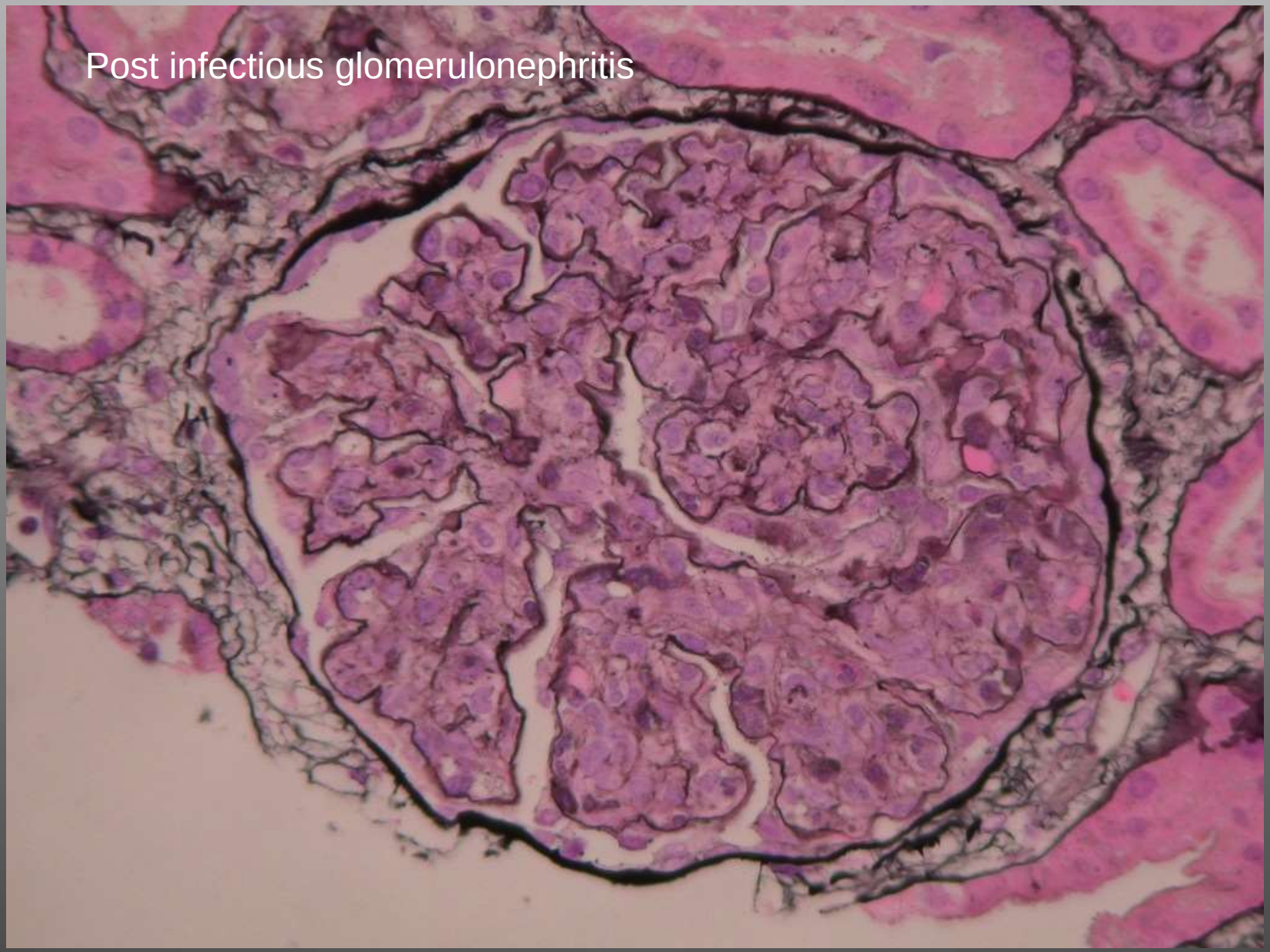
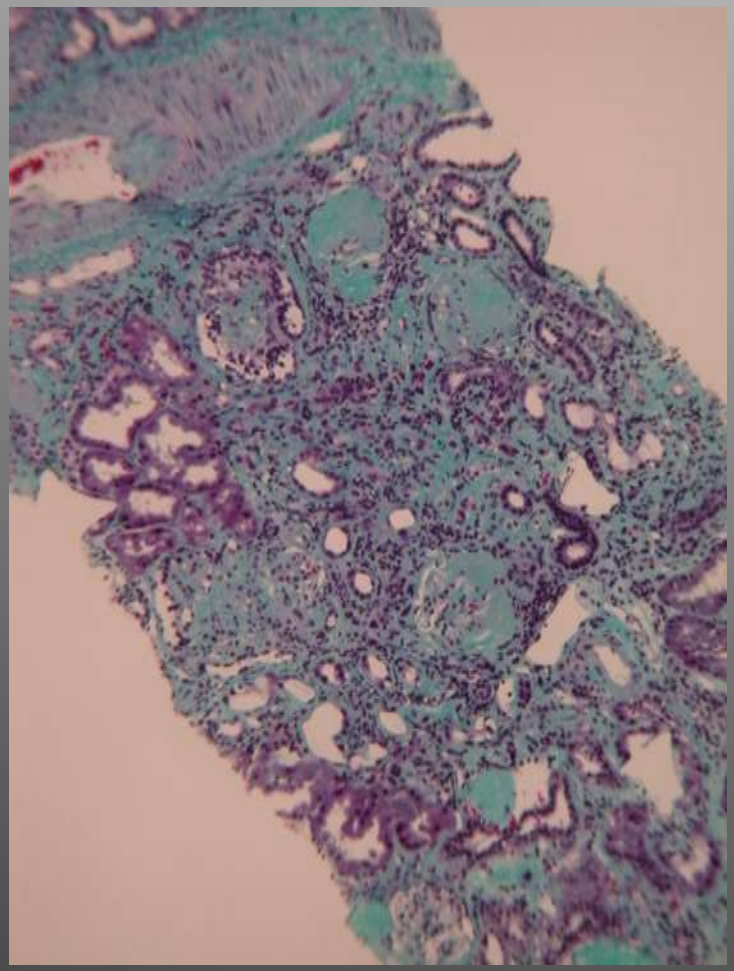
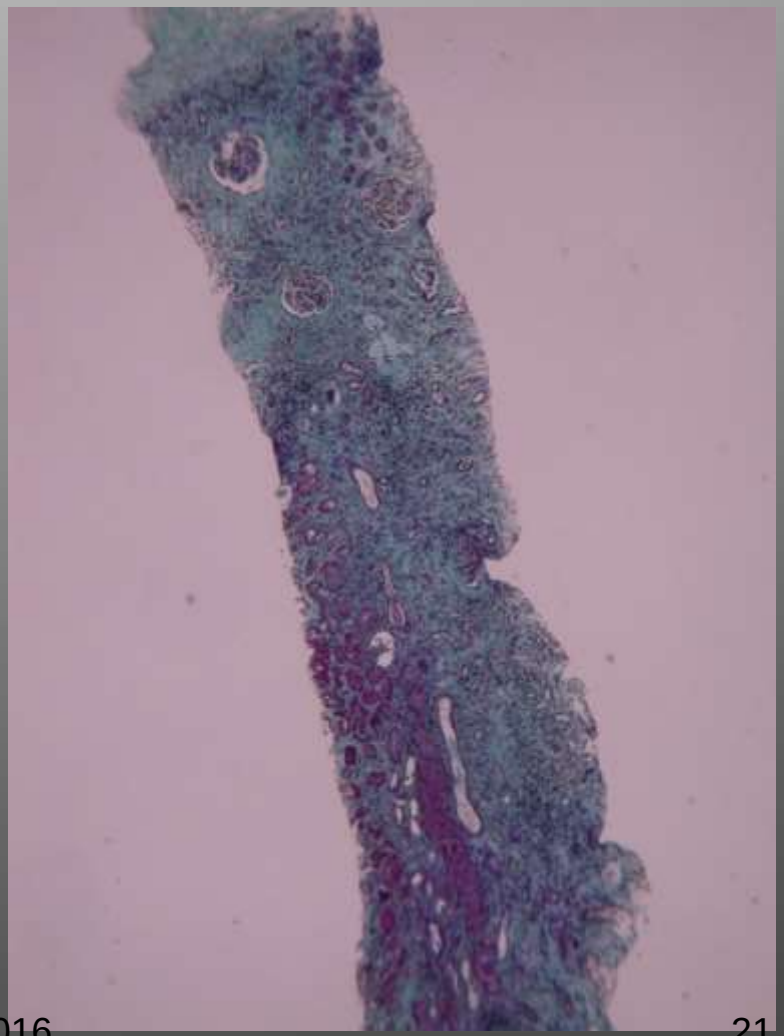

Memebranoproliferative glomerulonephritis

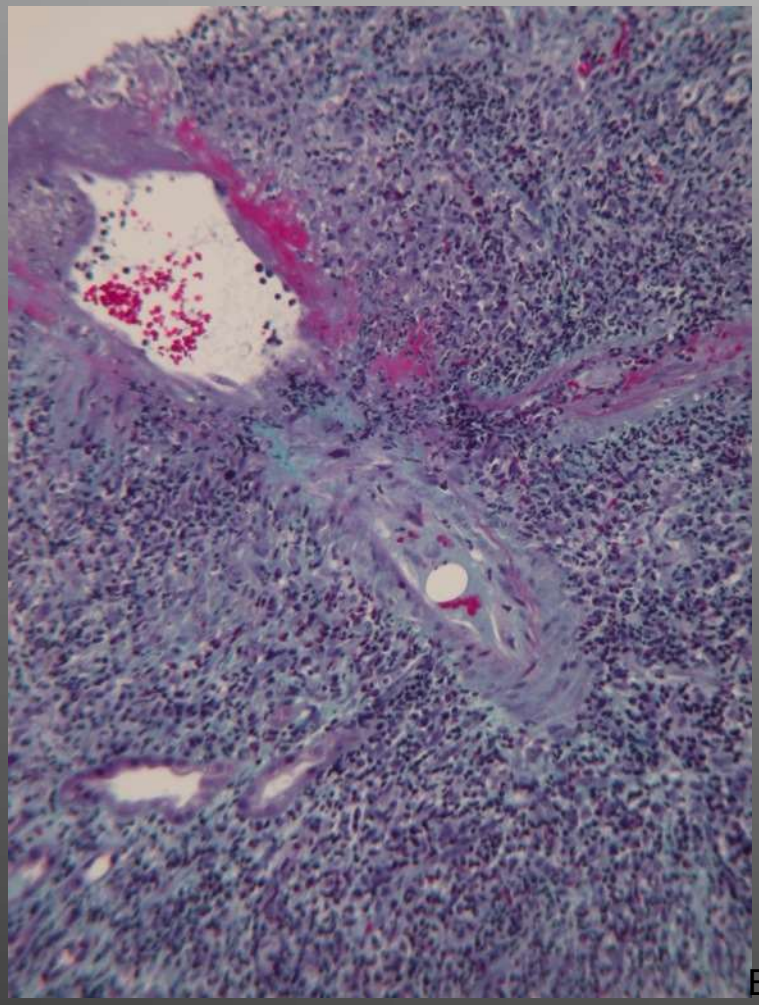

Post infectious glomerulonephritis

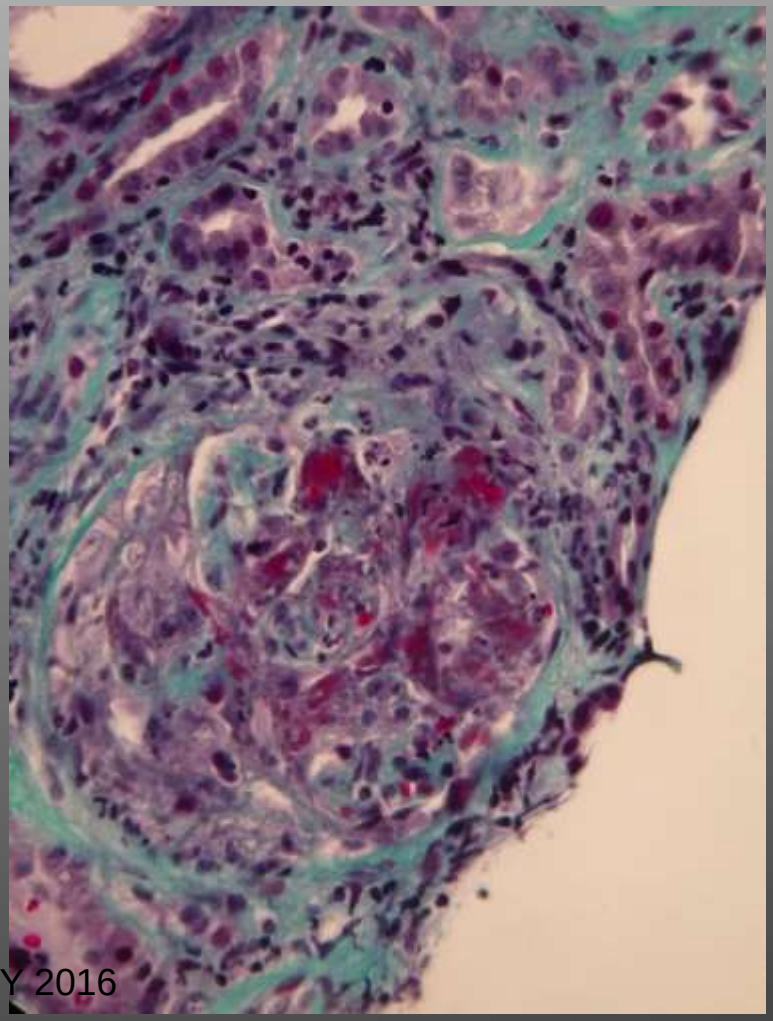
Masson Trichrome - Fibrosis



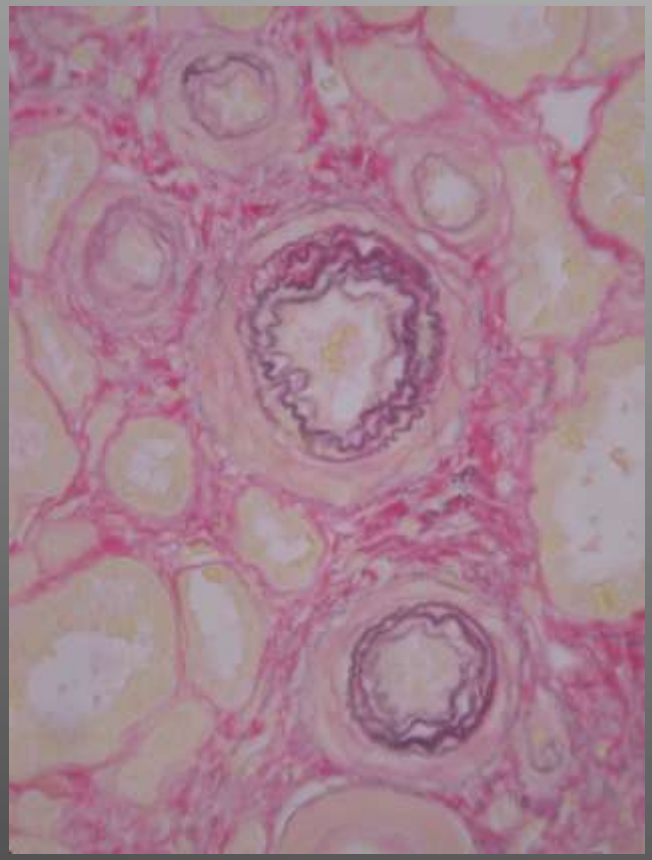


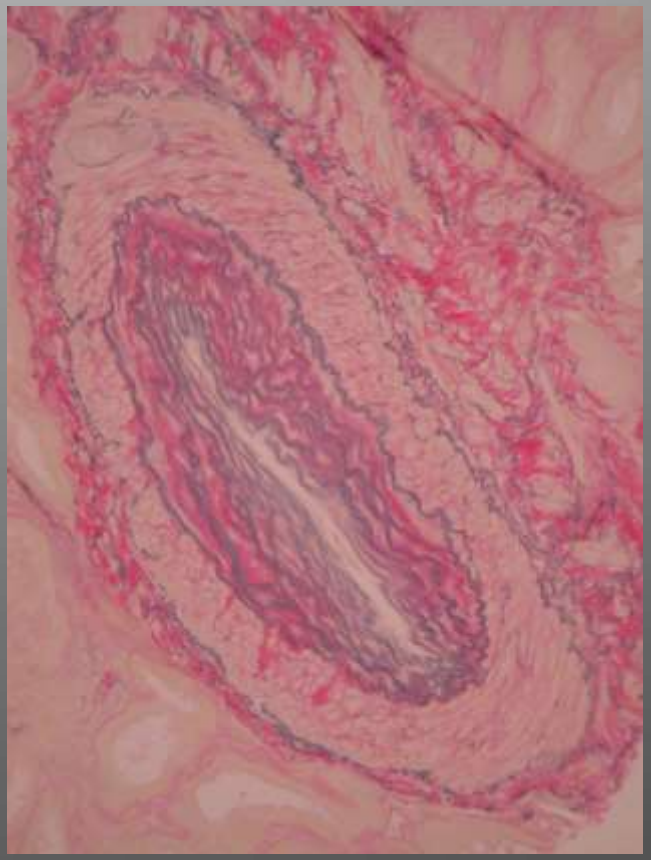
Masson Trichrome – Fibrinoid Necrosis



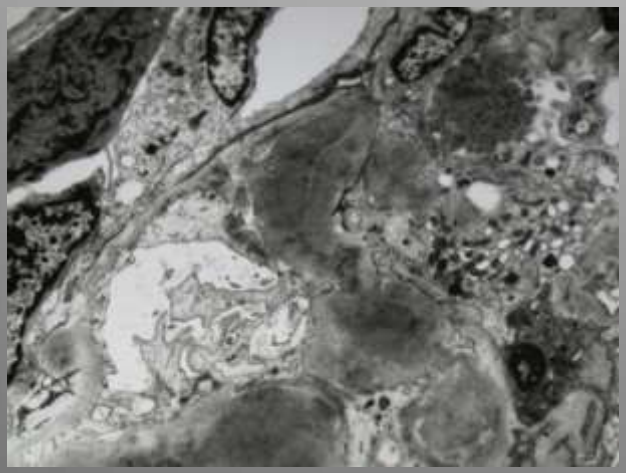


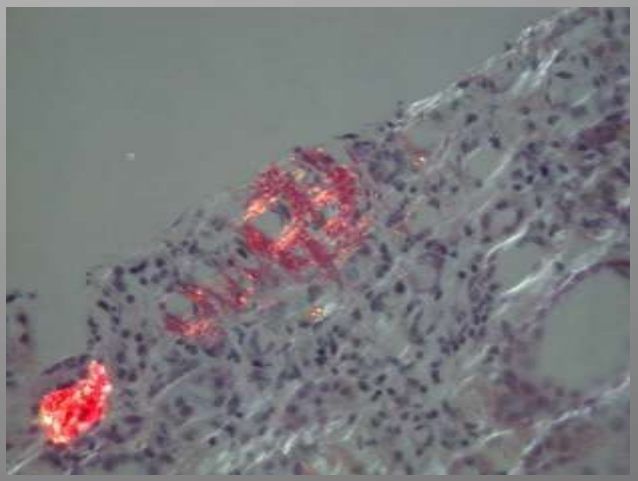
Elastin van Gieson

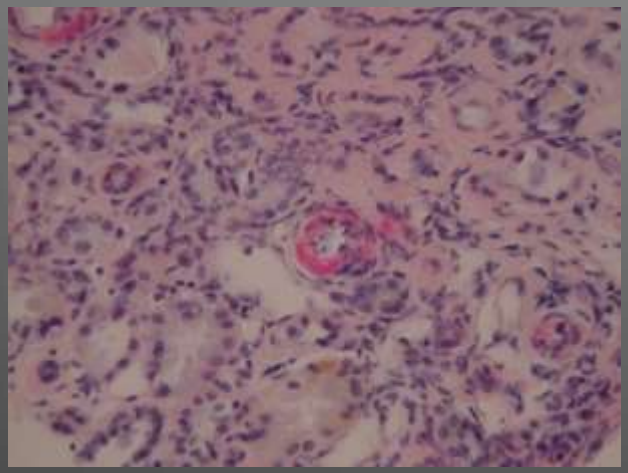




Congo Red - Amyloid

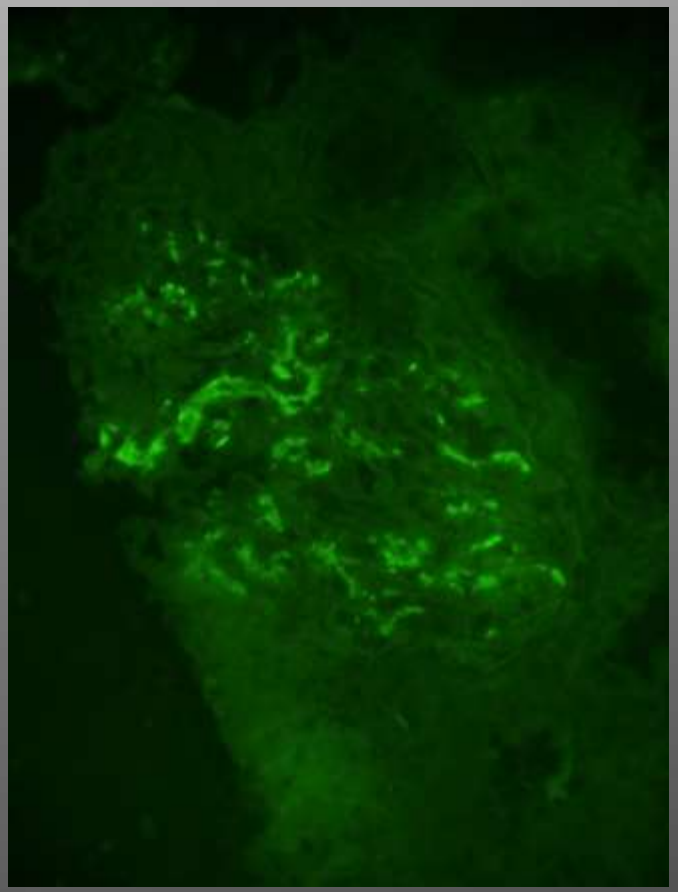


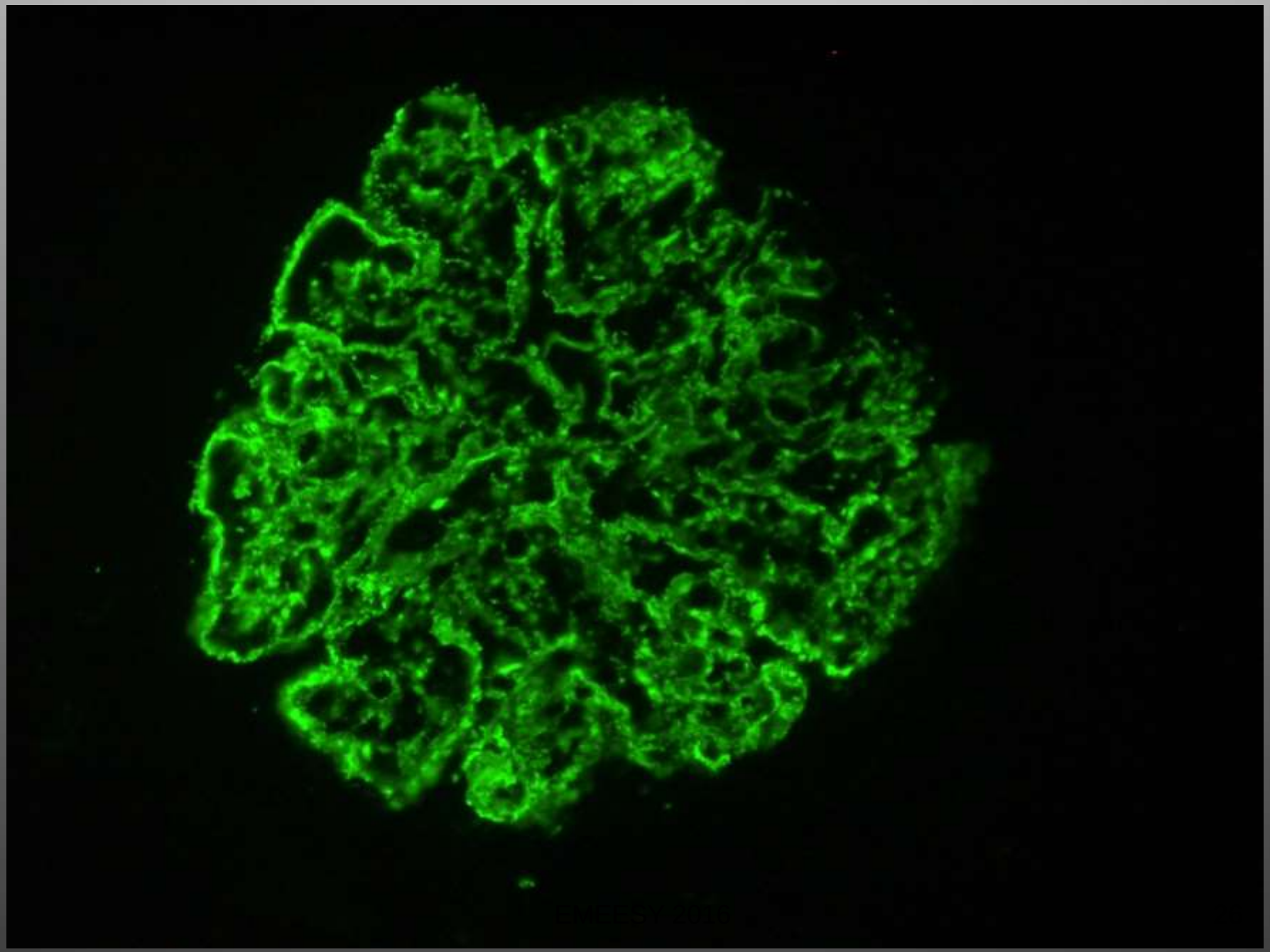




Immunofluorescence

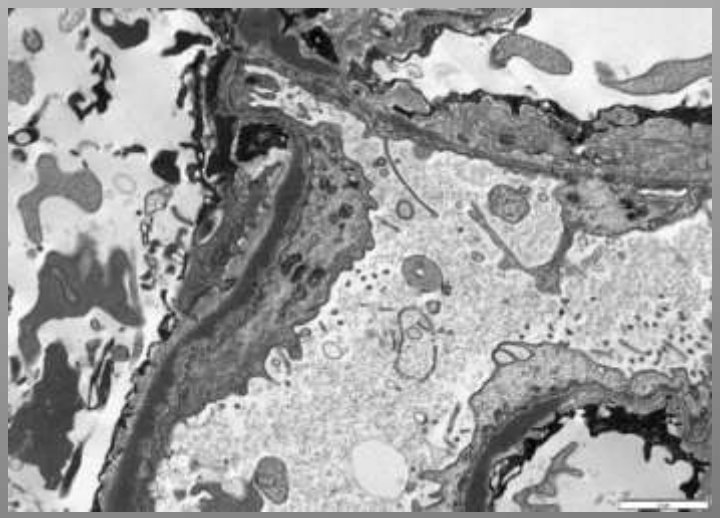
- Immunoglobulin
  - IgG, IgM, IgA,
- Complement
  - C3, C4, C1q
- Light Chain
  - Kappa, lambda
- Collagen type IV subunits (Alport's)

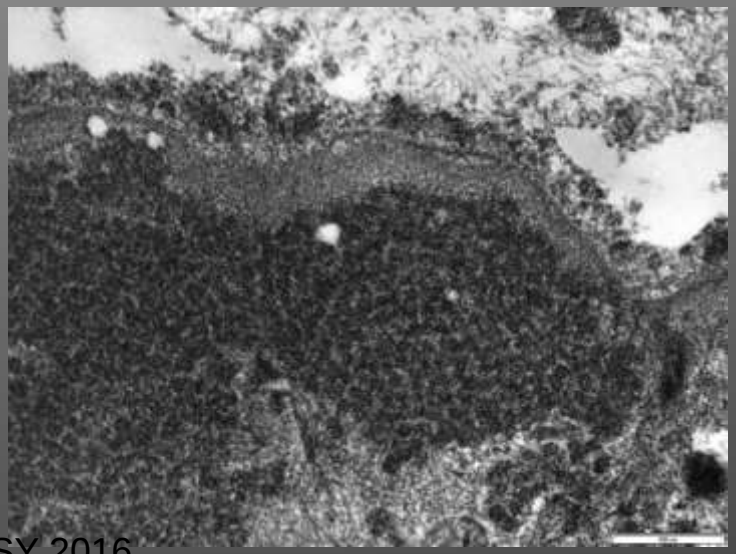




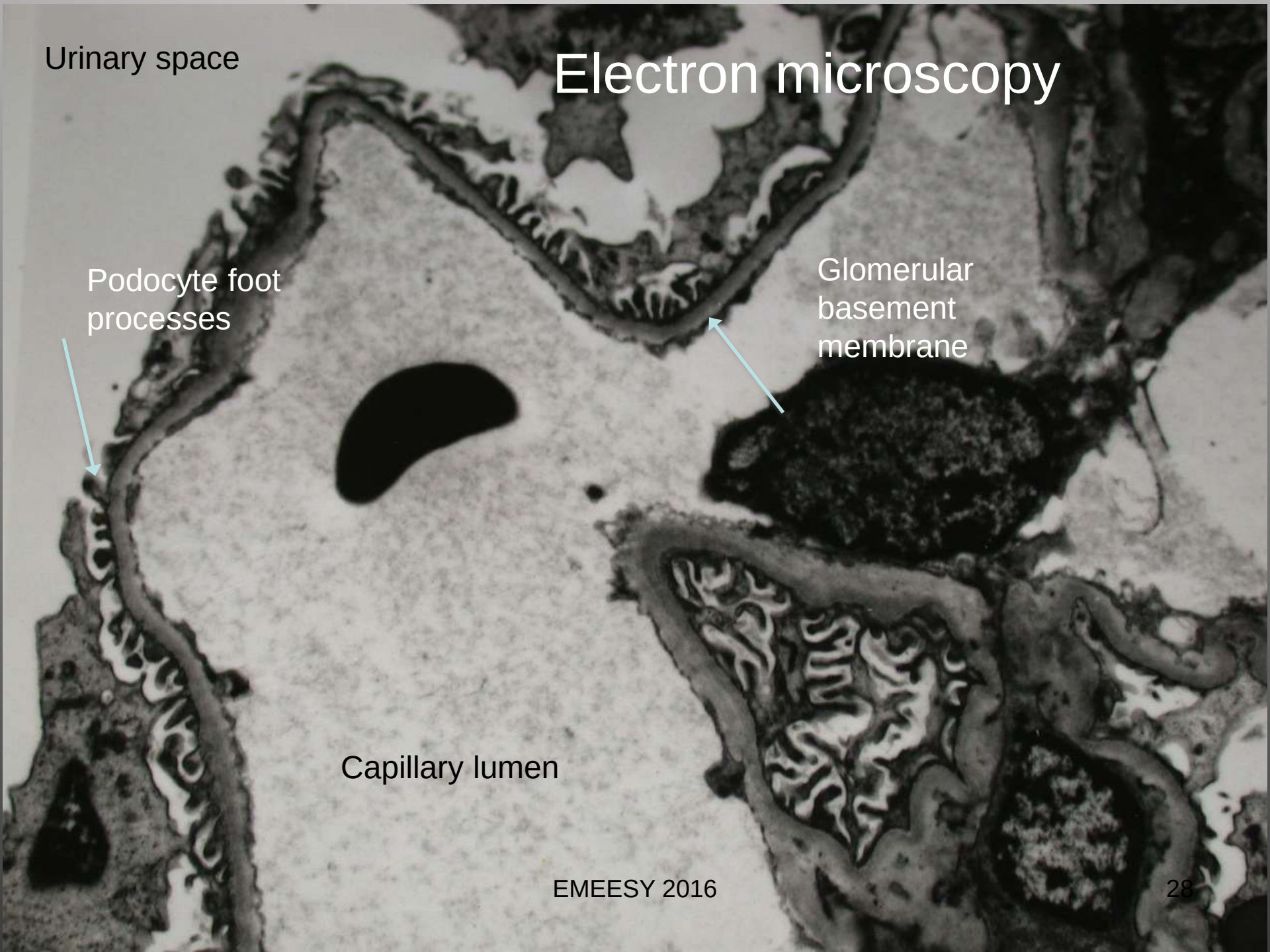
Electron Microscopy

- Deposits
  - Immune complex
- Podocyte morphology
  - Foot process effacement
- Glomerular basement membrane morphology
  - Alport's etc
- Organised deposits
- Amyloid etc



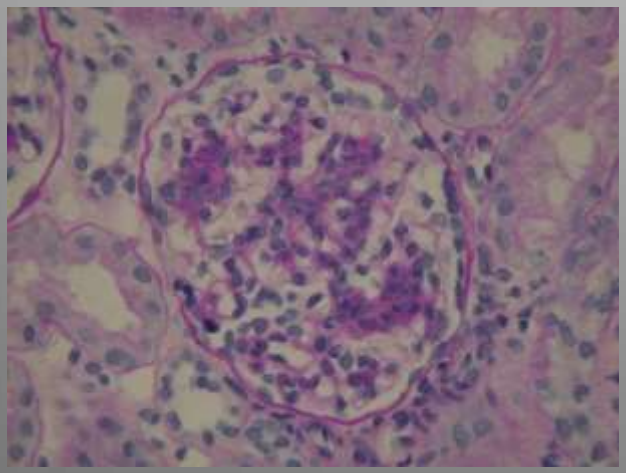


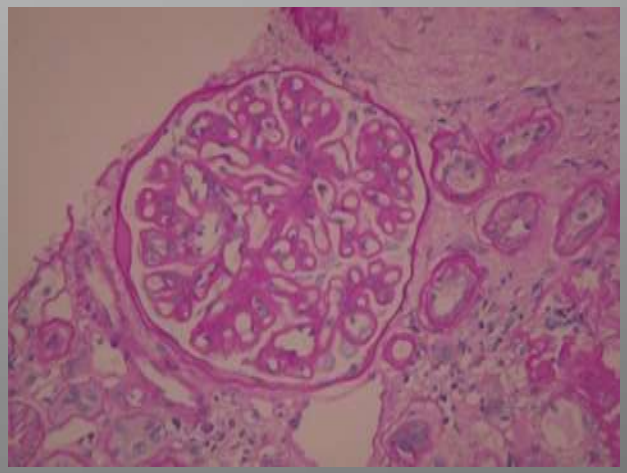
Electron microscopy

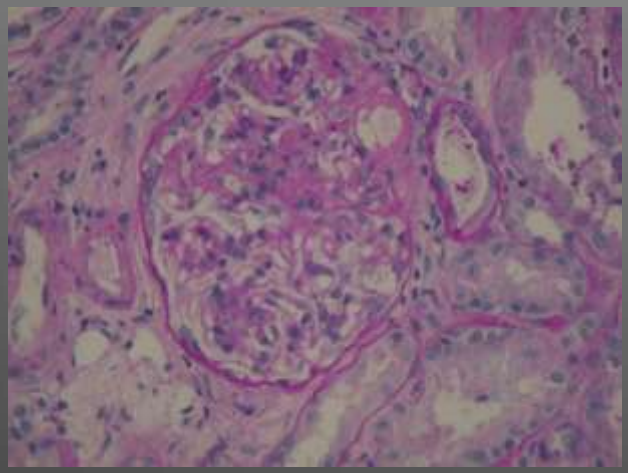


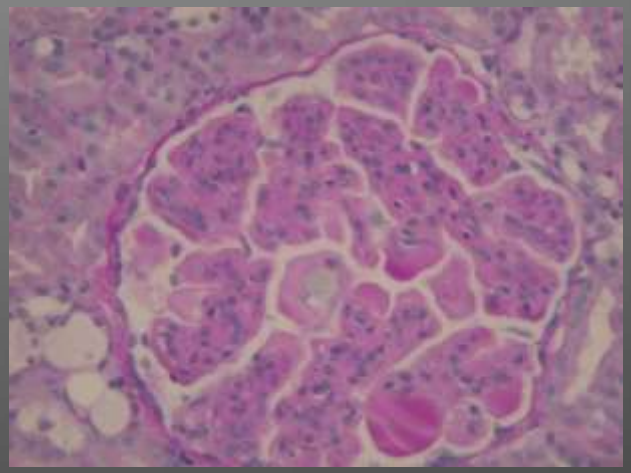

HSBC

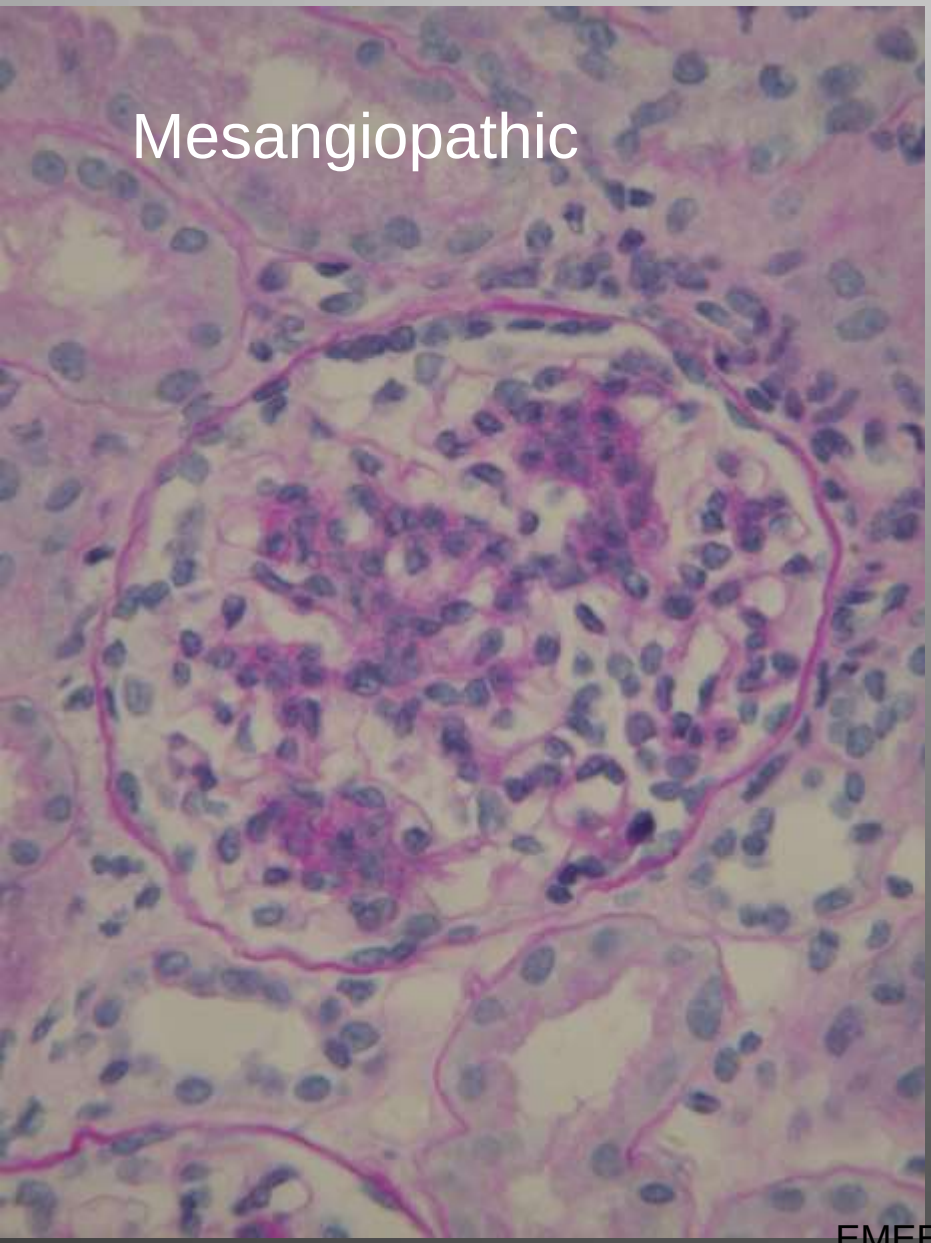
Patterns of Glomerular Disease

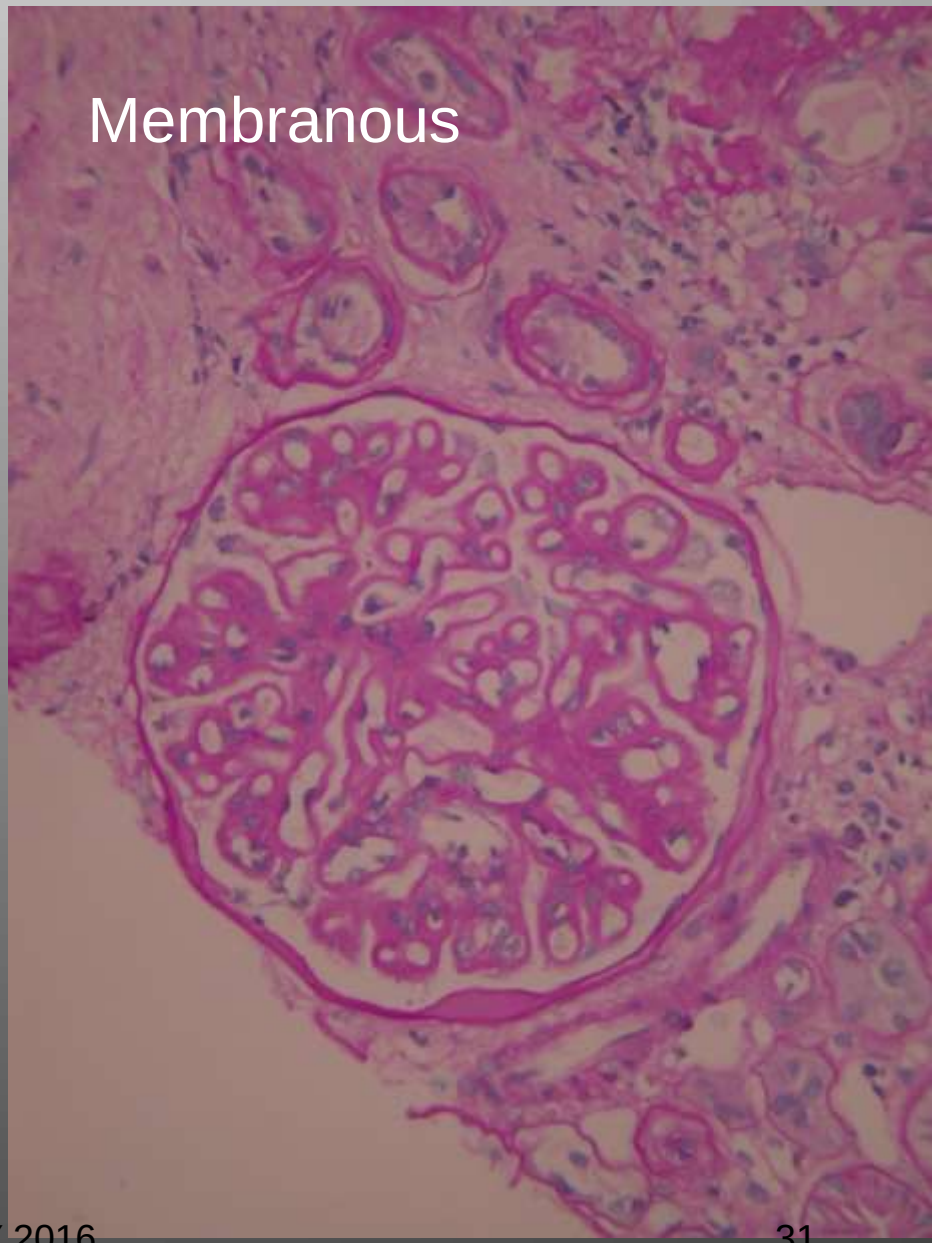


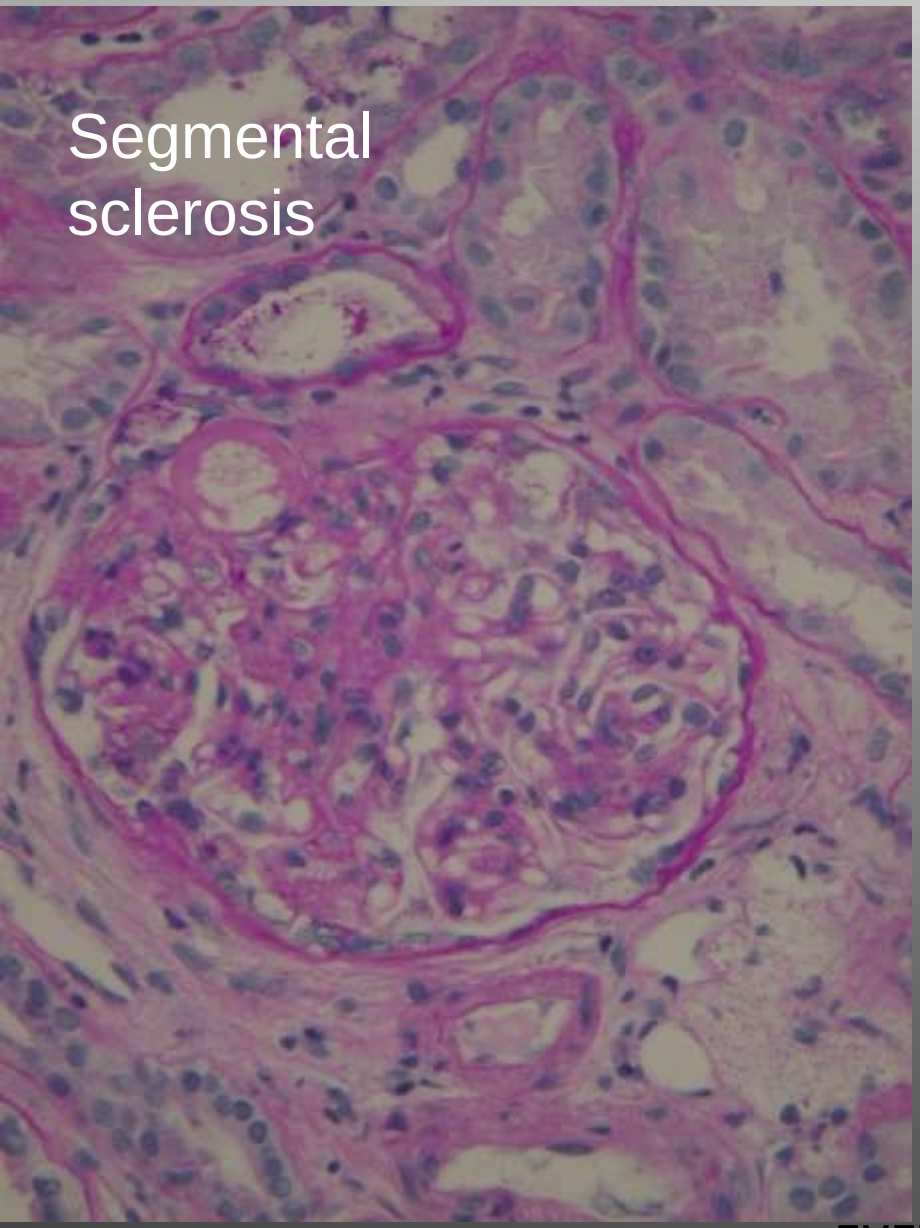


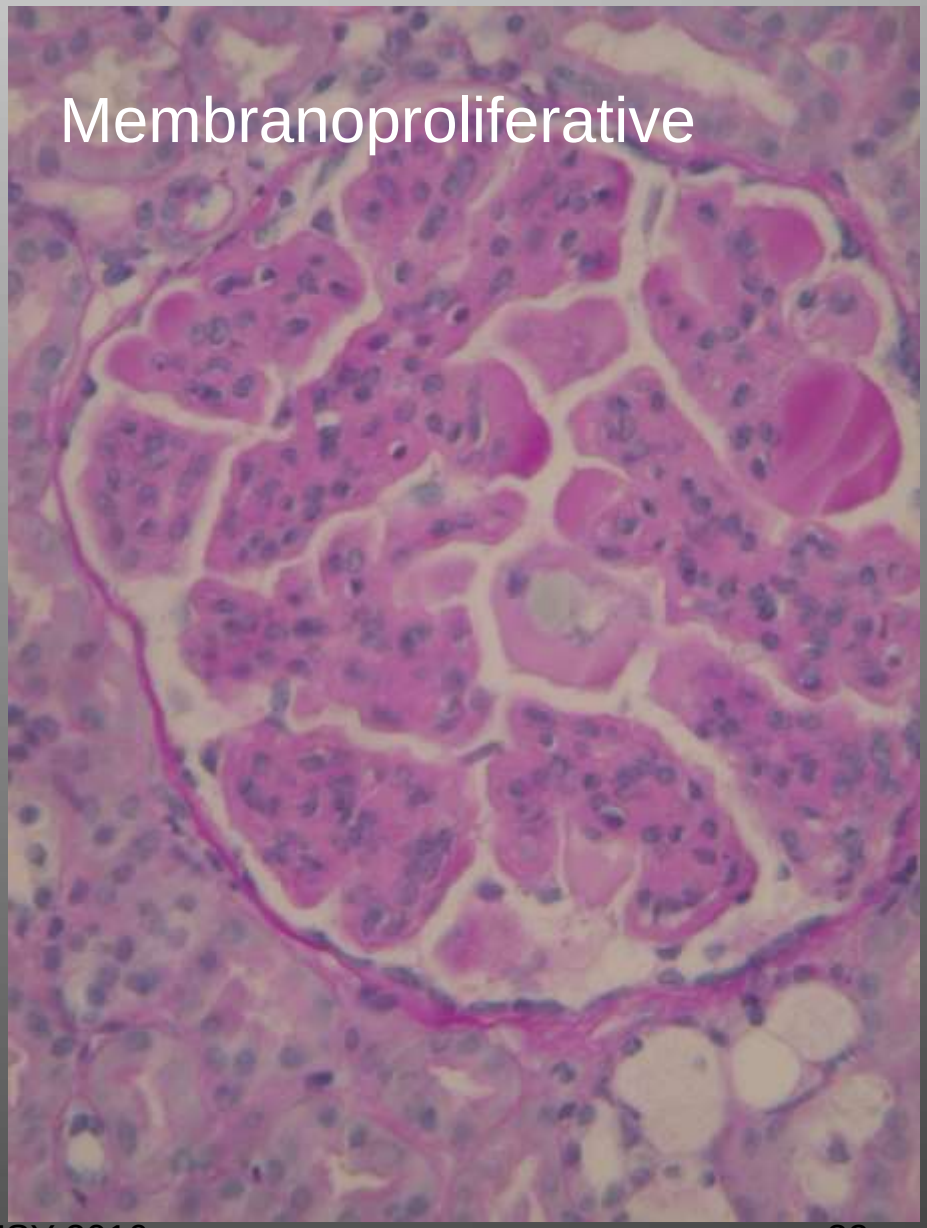




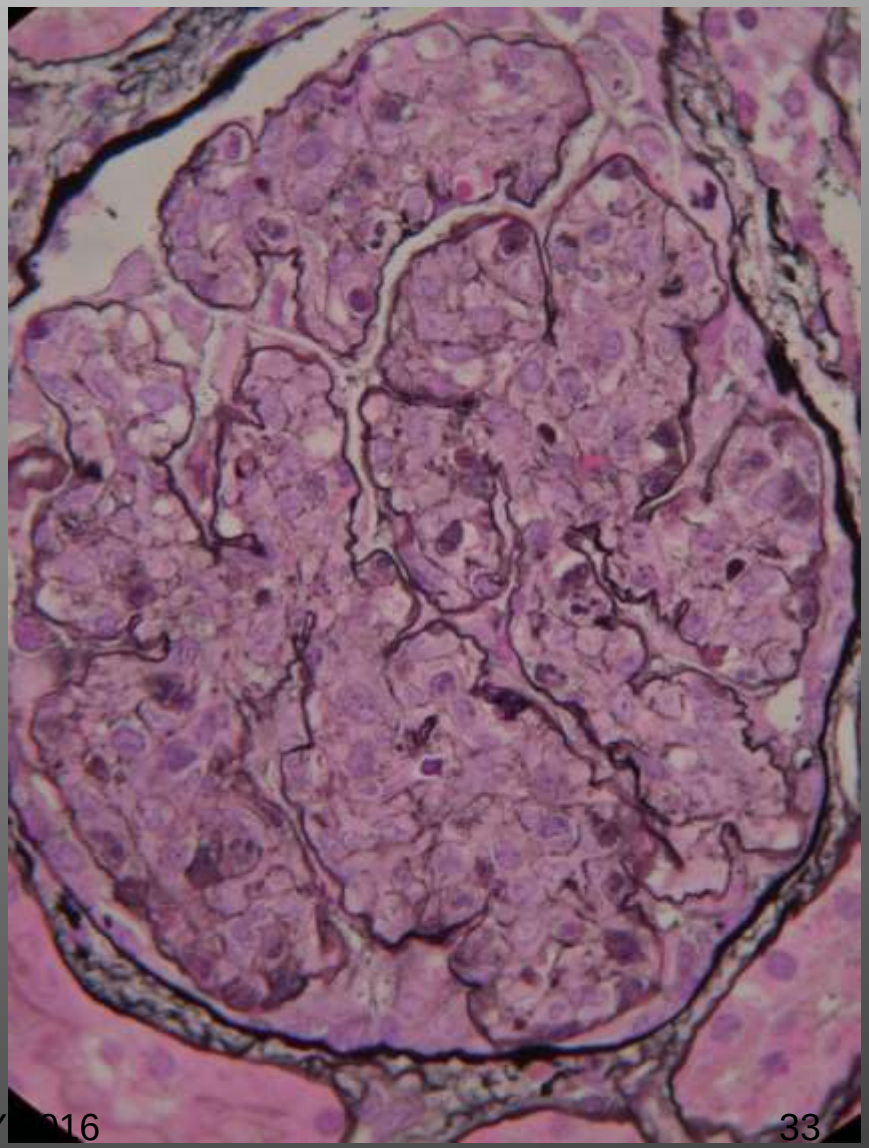

Mesangiopathic


Membranous

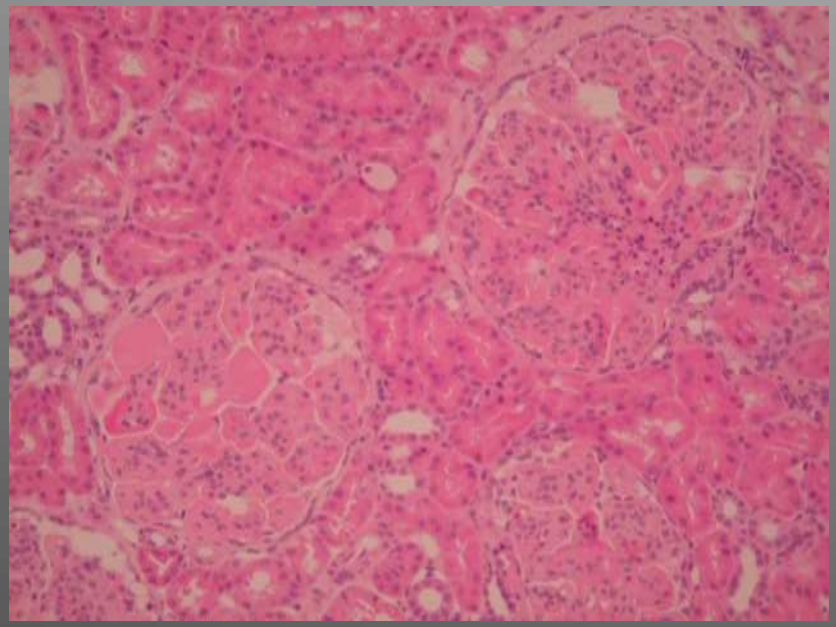

Segmental
sclerosis

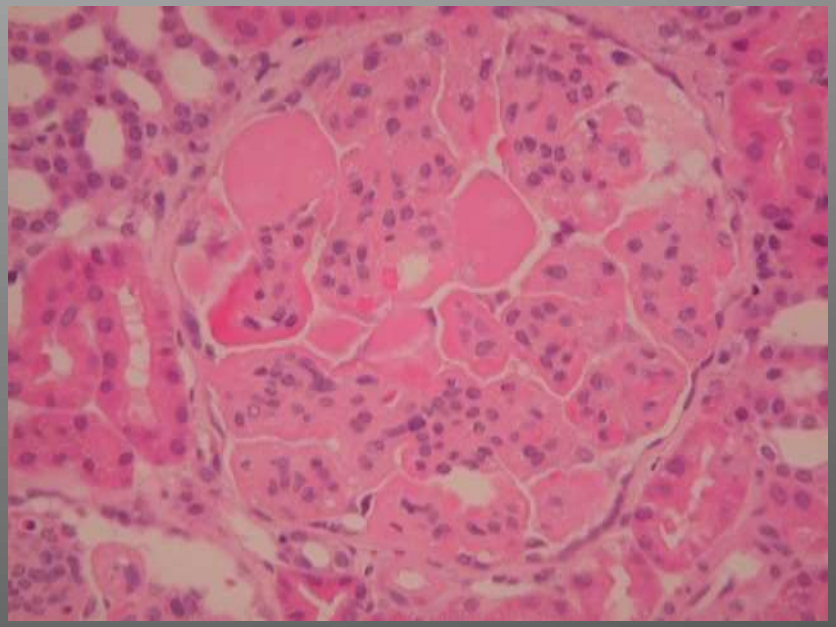

Membranoproliferative

Diffuse endocapillary

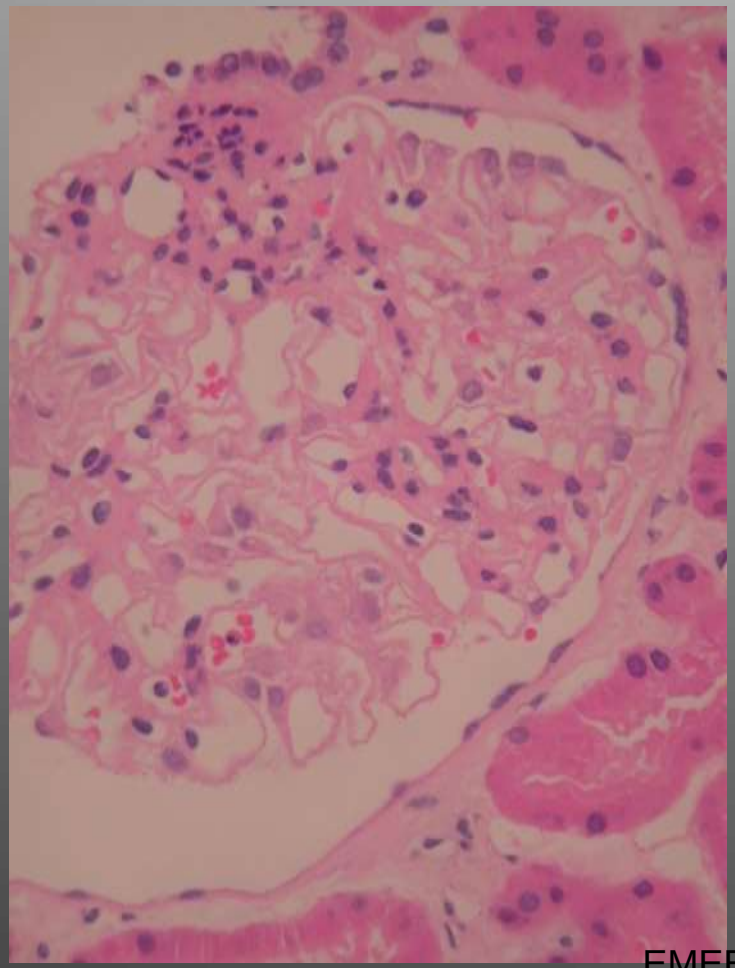


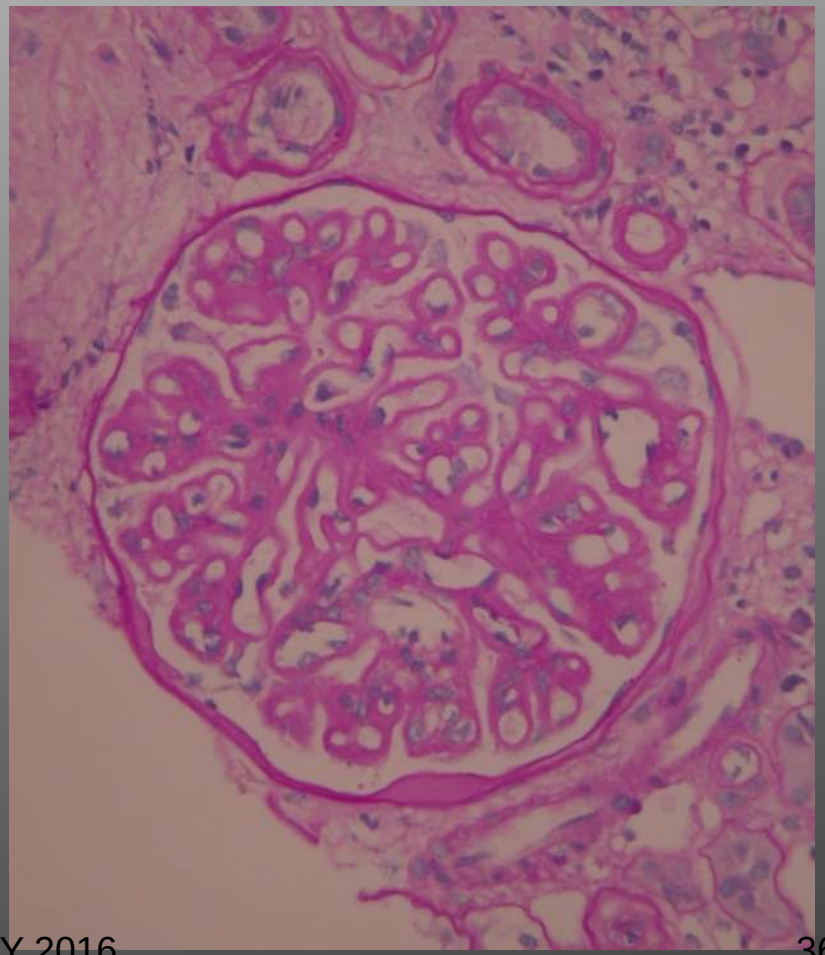
Examples

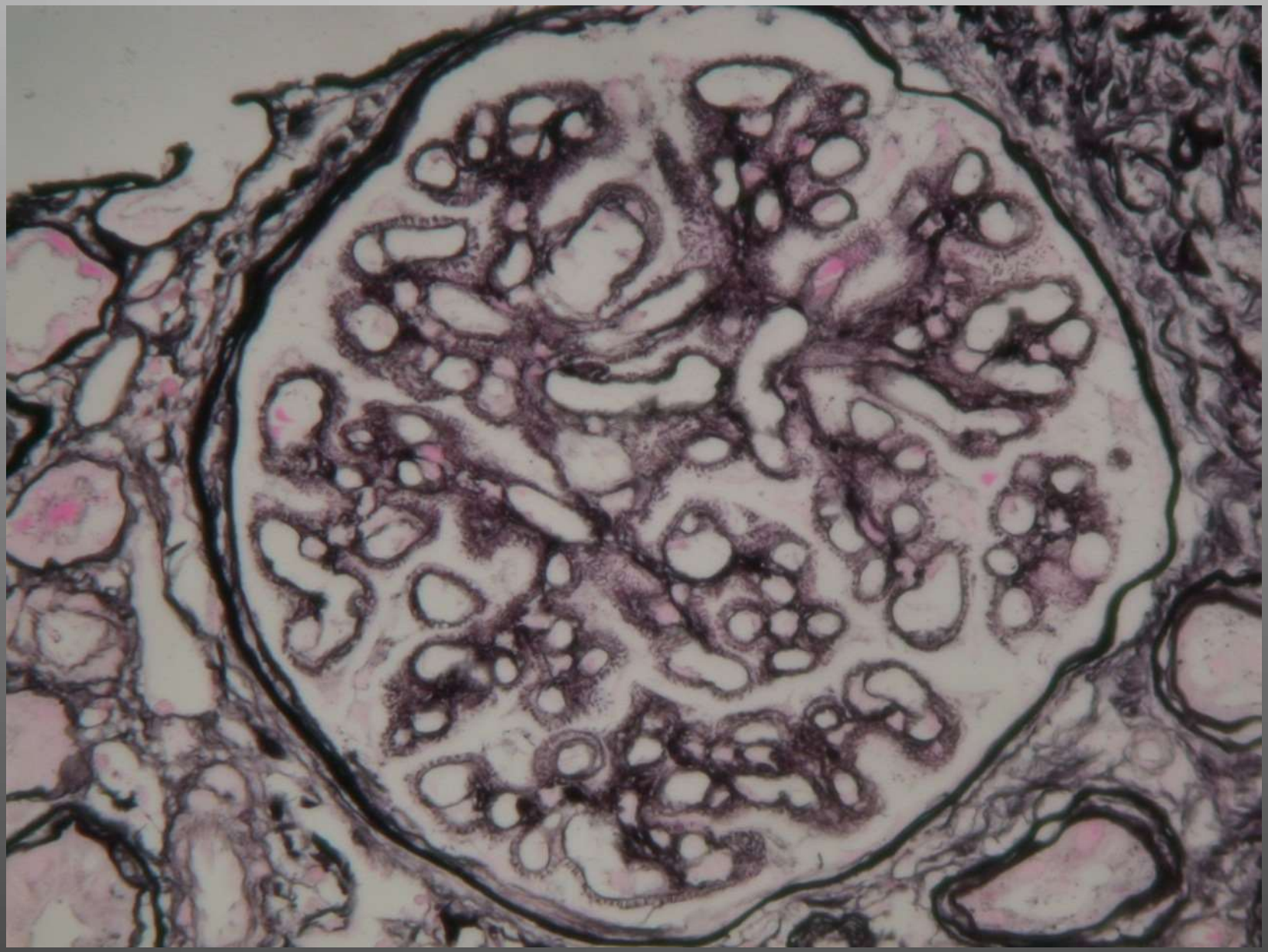


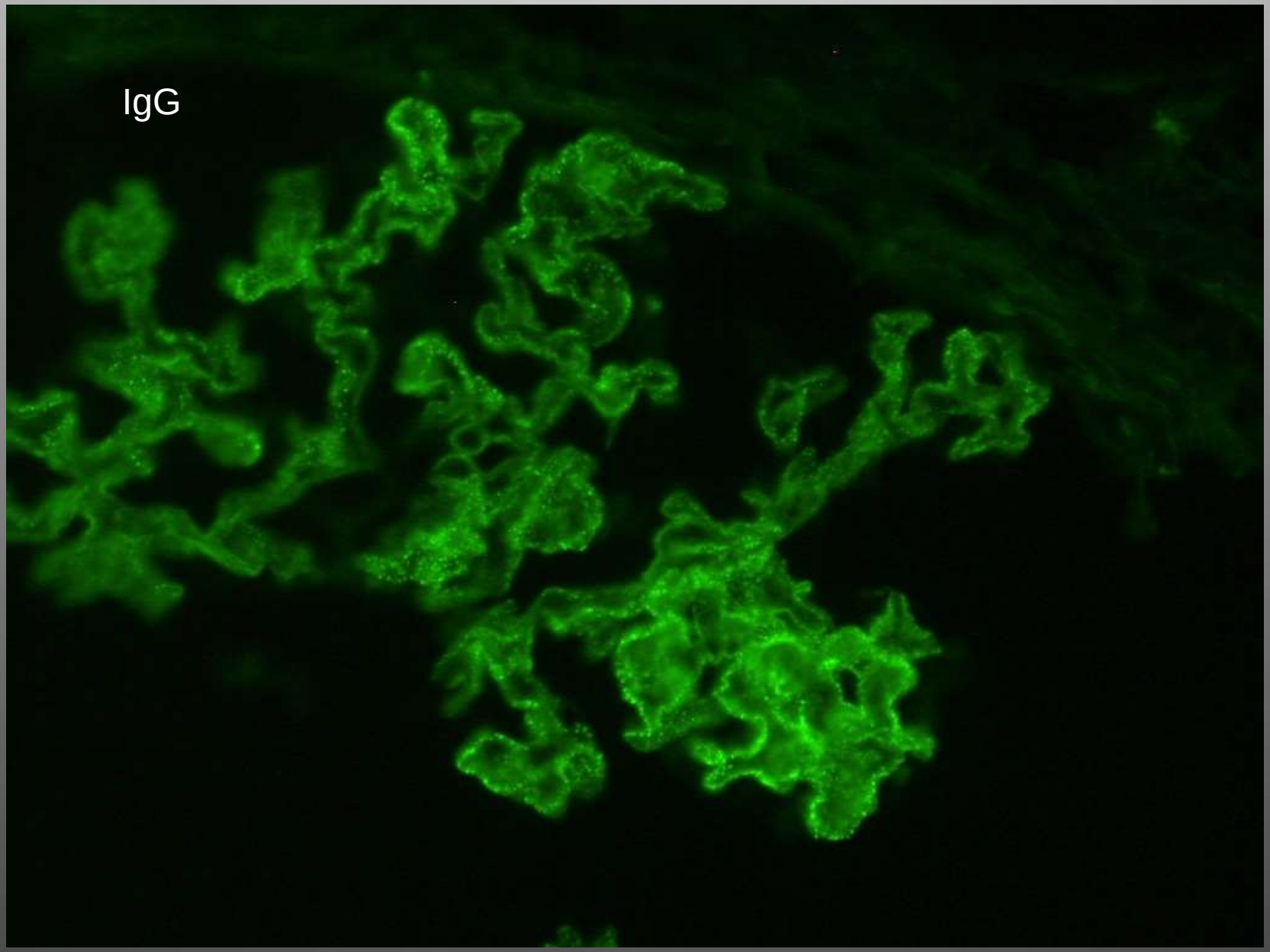


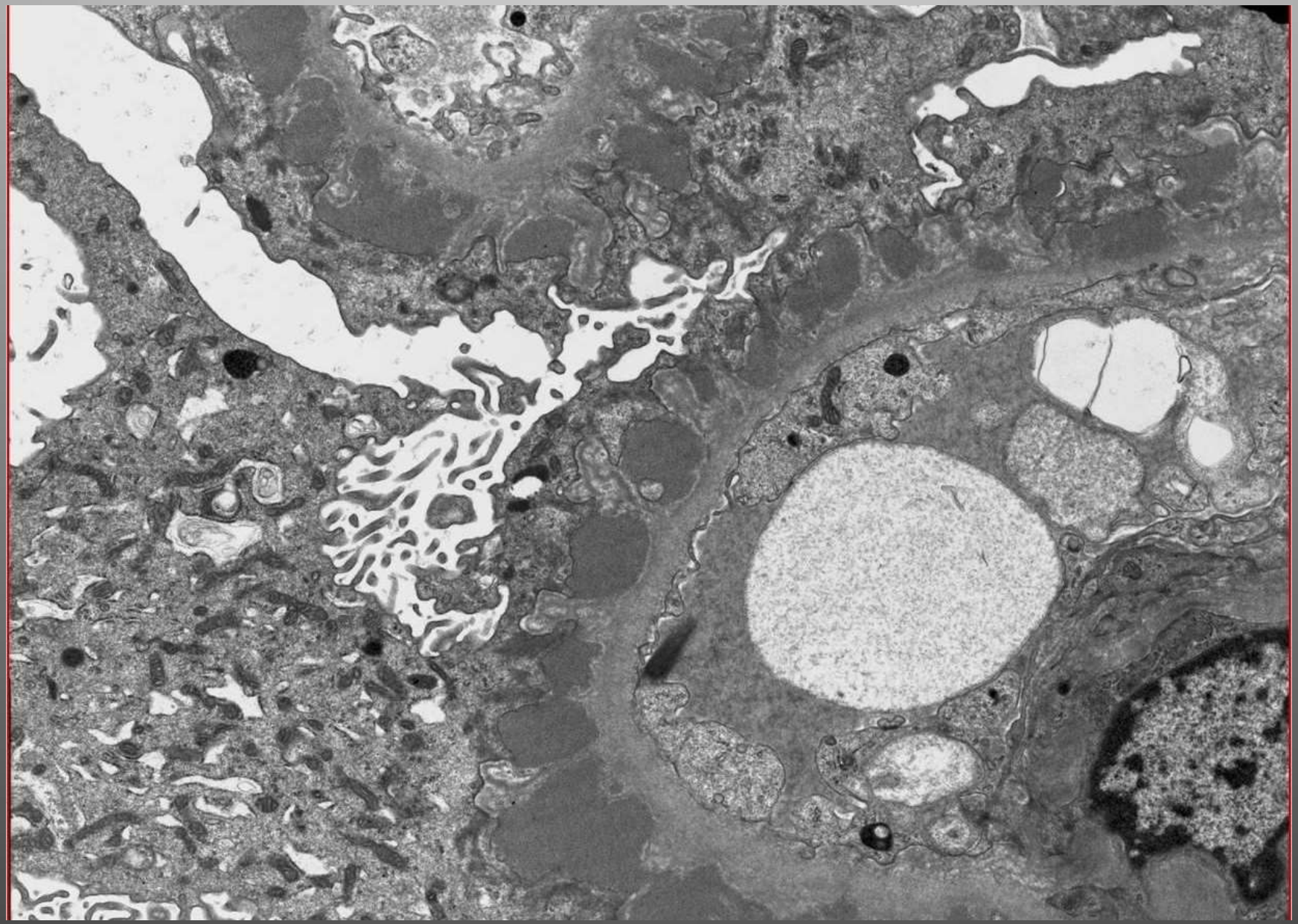
Example 1. Nephrotic Syndrome







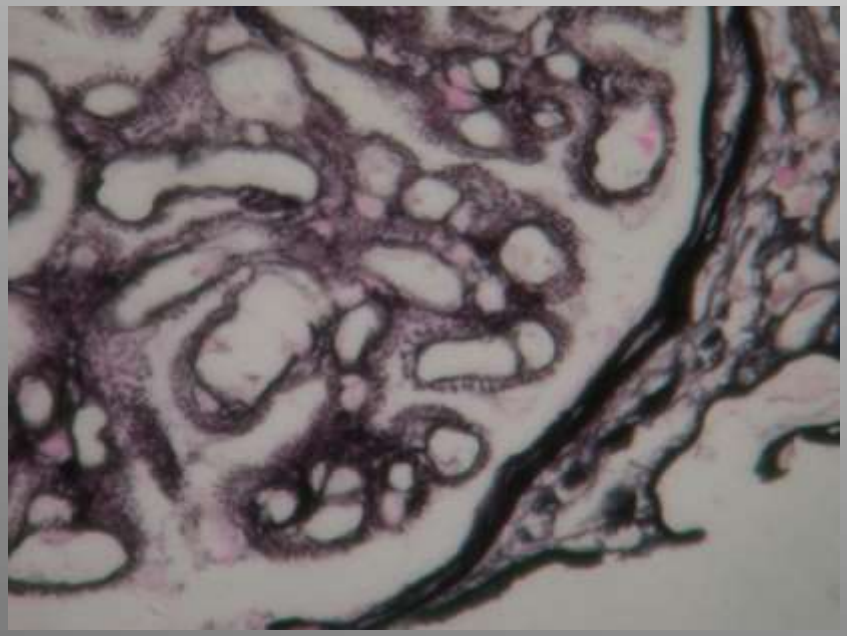

IgG

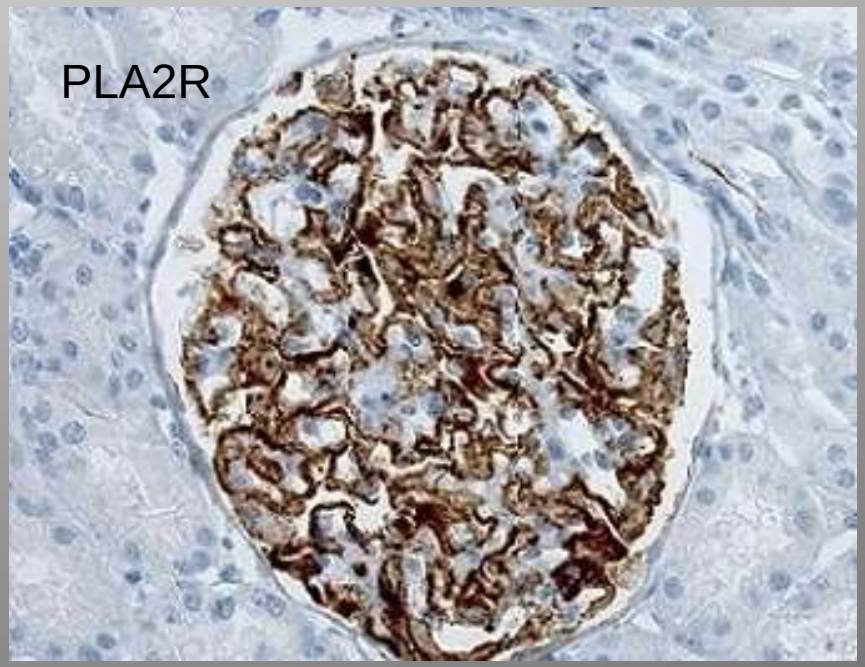


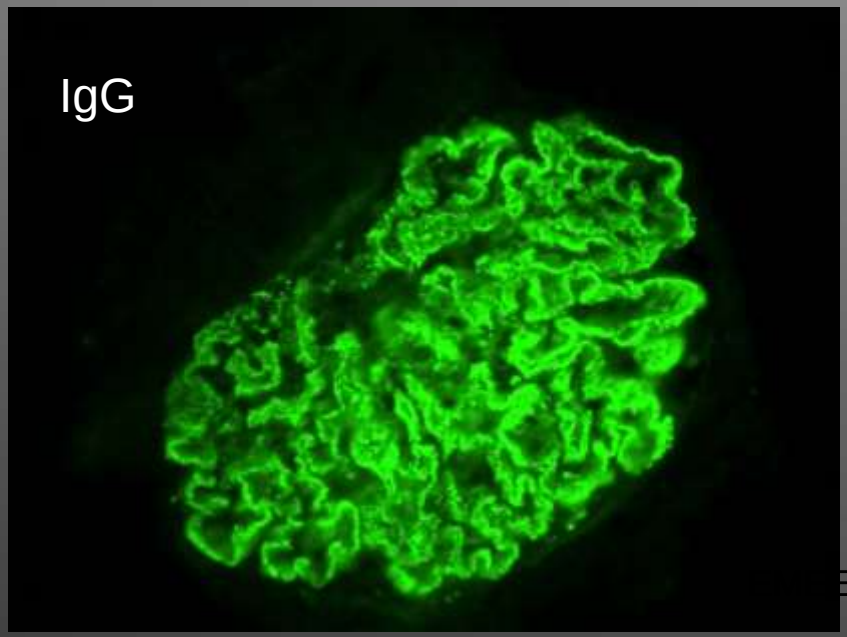
Example 1

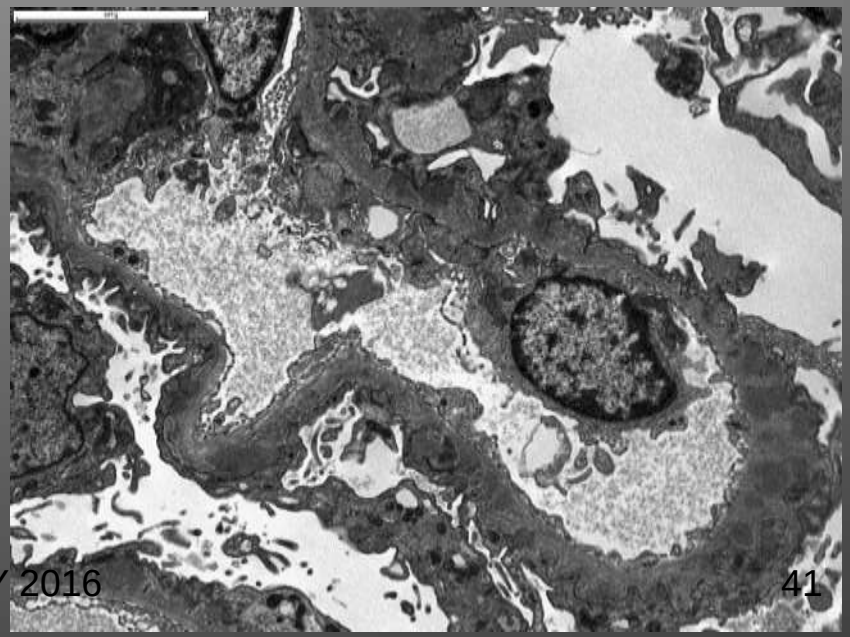
- Nephrotic patient
- Thick loops
- Spikes on silver
- Granular IgG on IMF
- Subepithelial deposits on EM

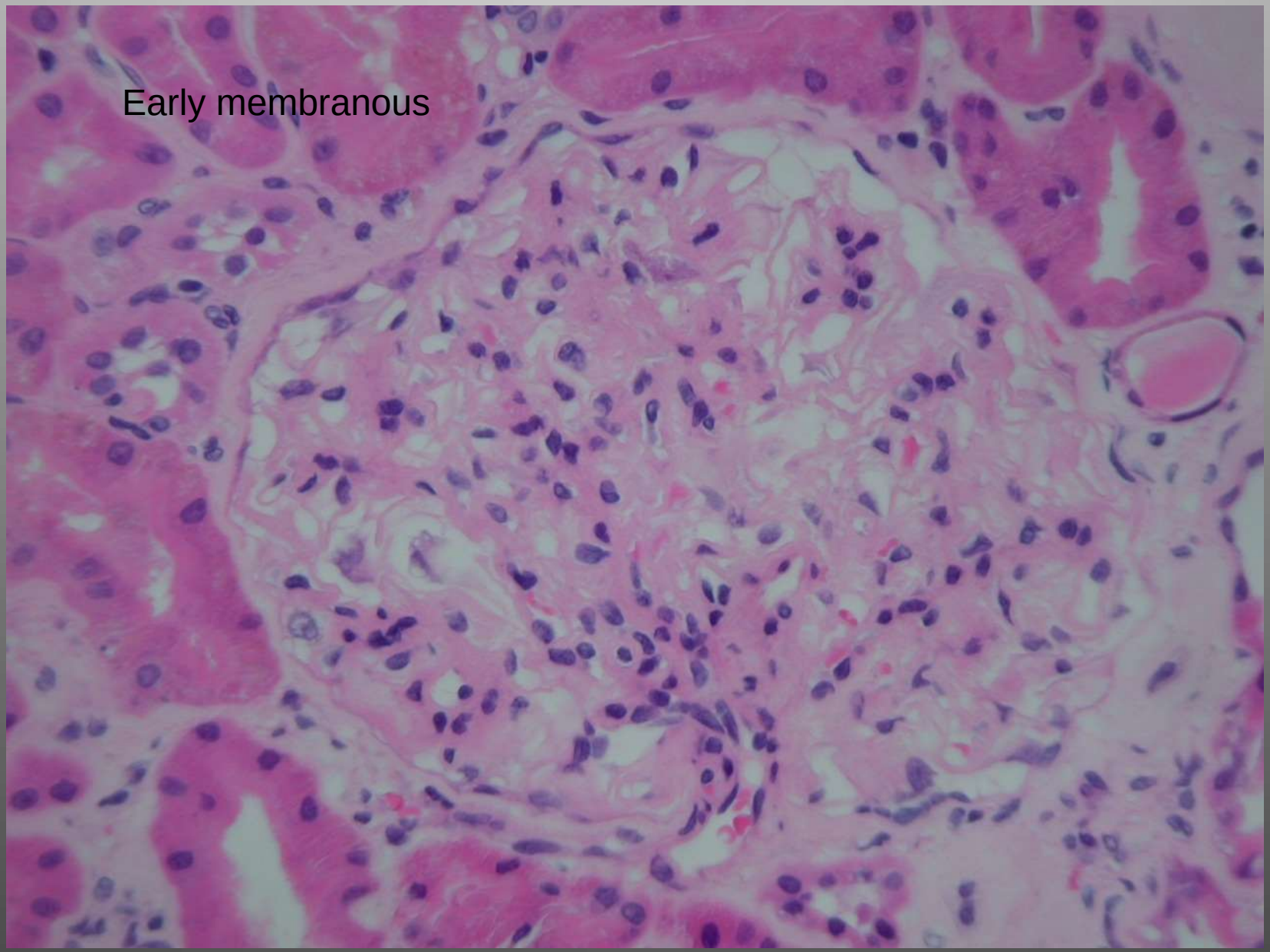
- = MEMBRANOUS NEPHROPATHY

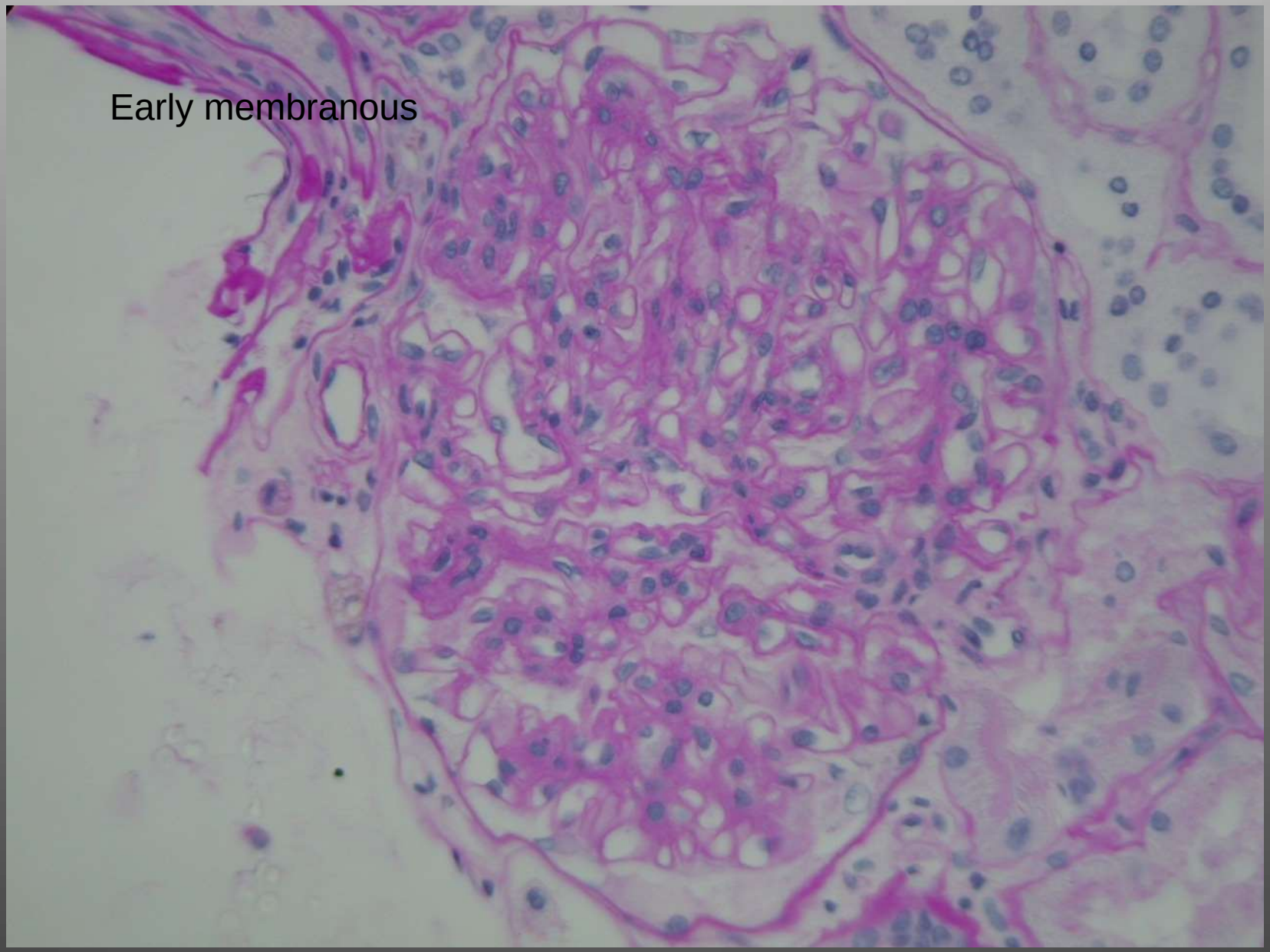


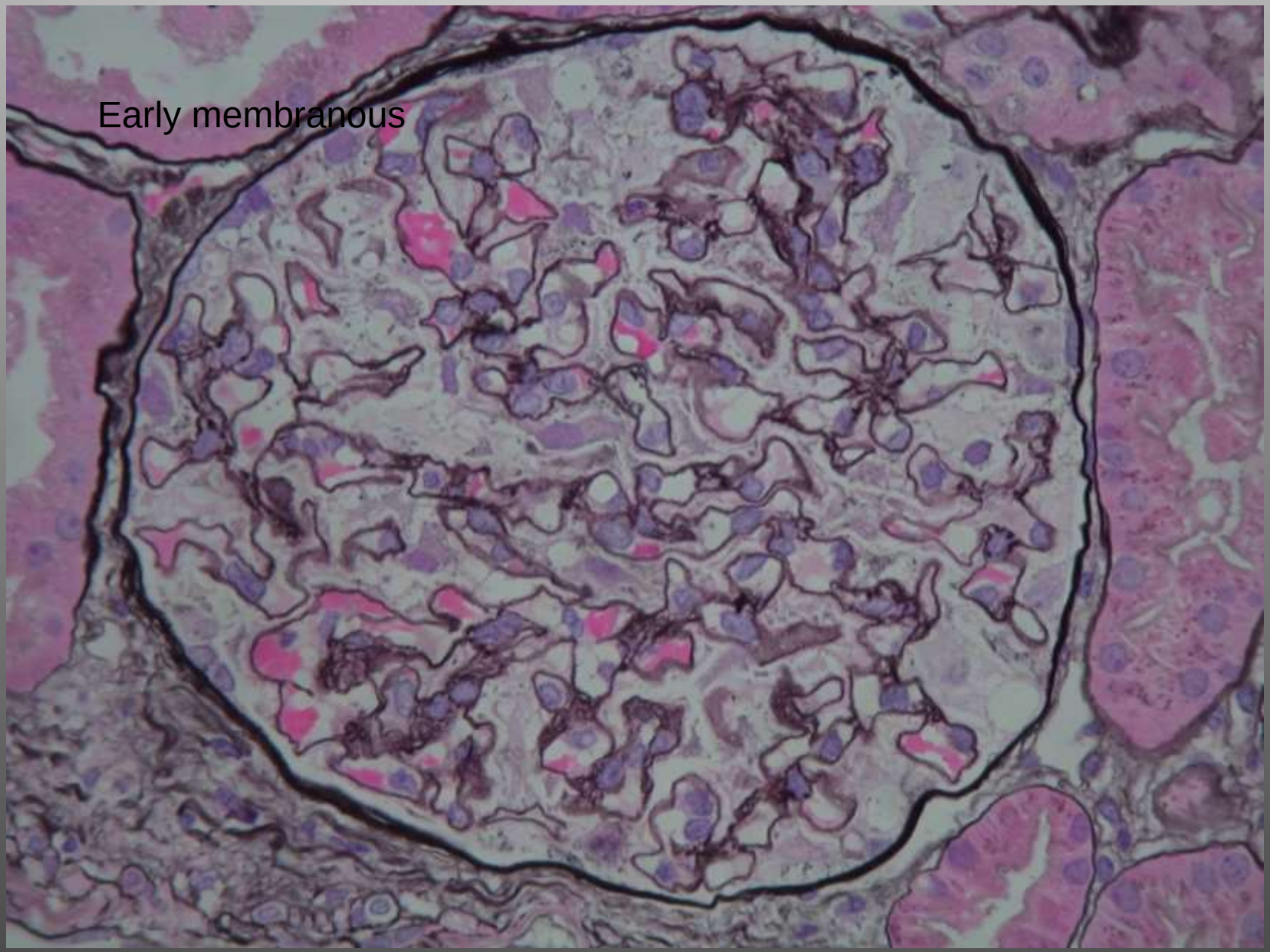

PLA2R

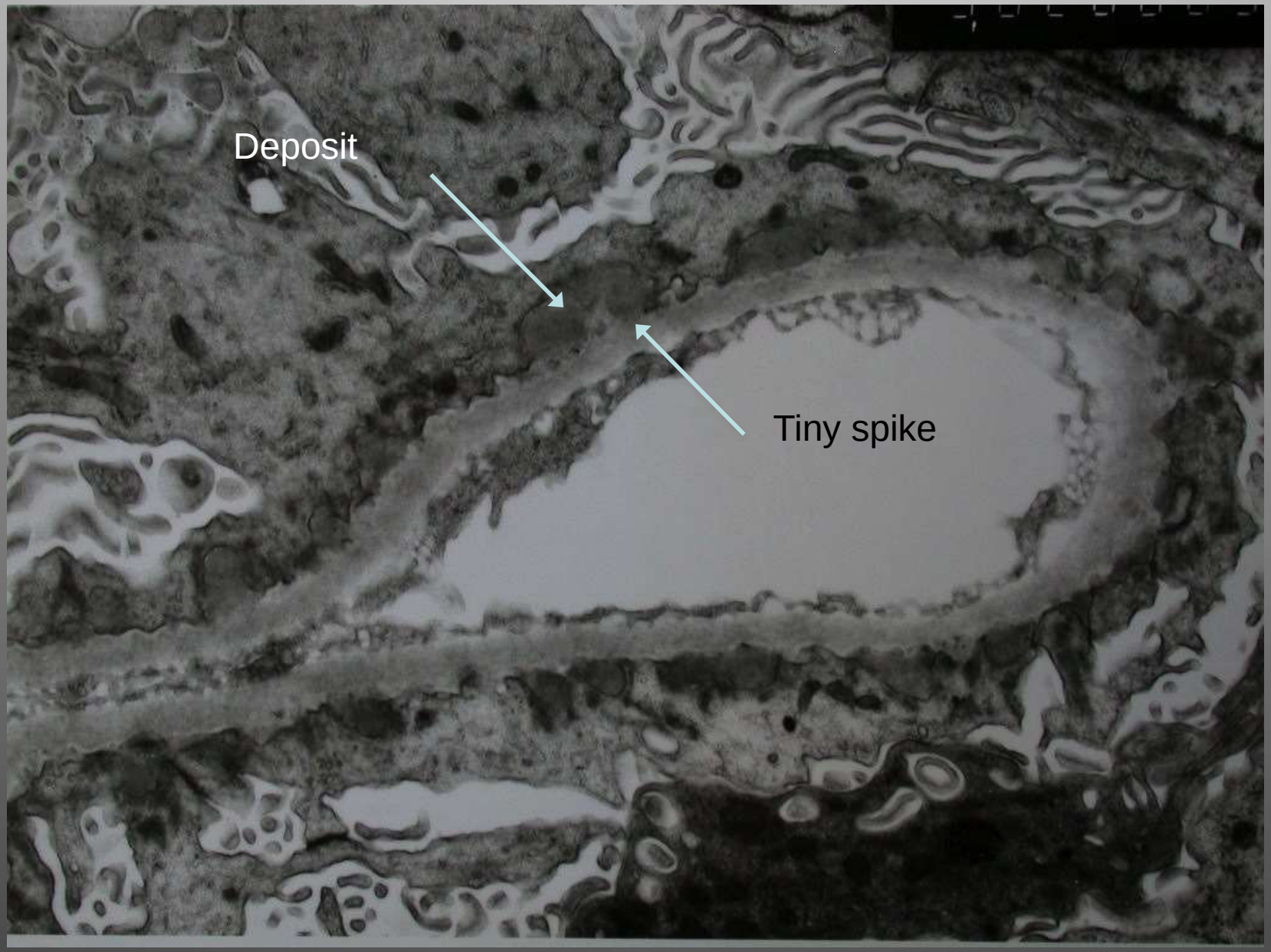

IgG

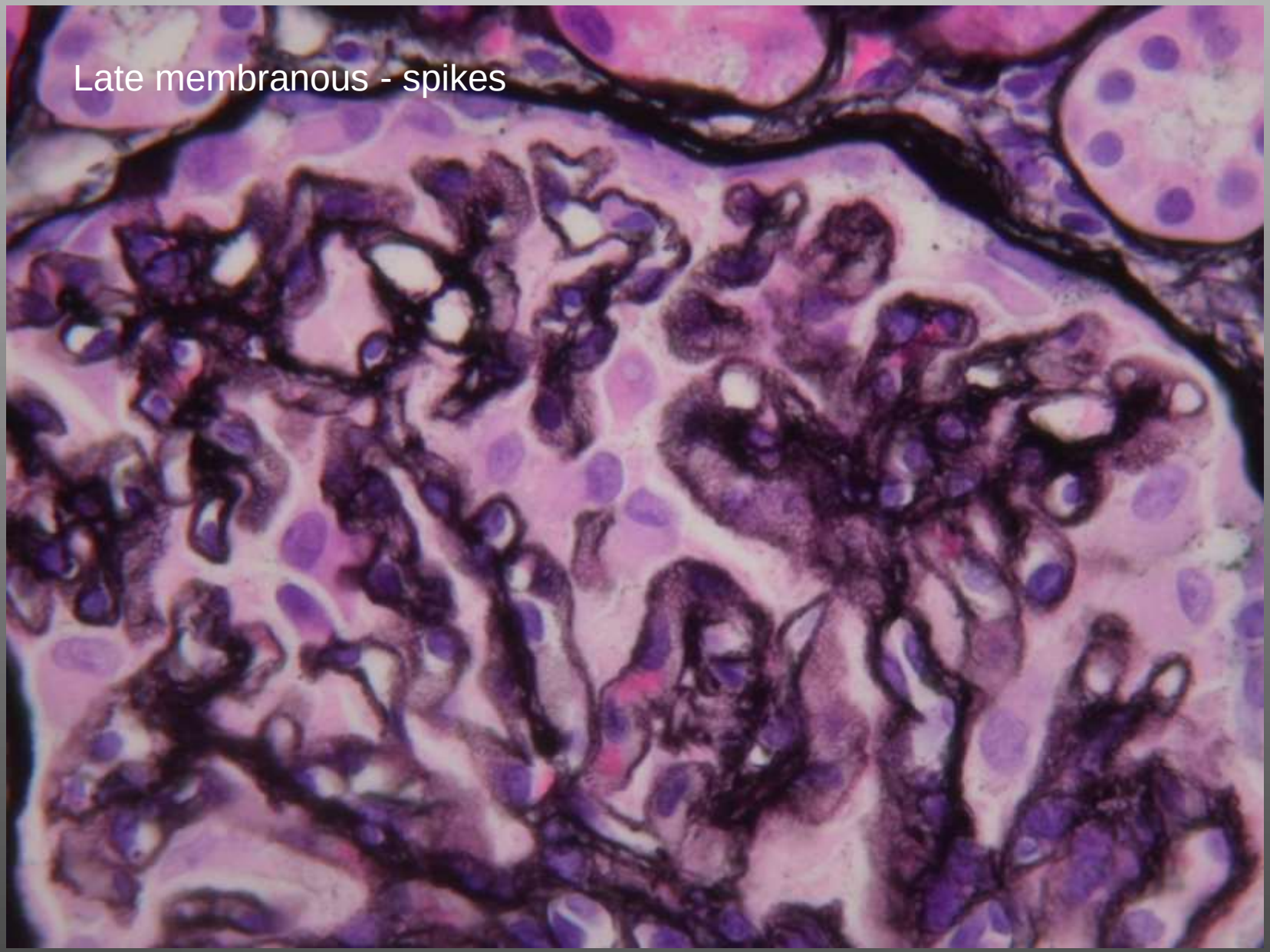


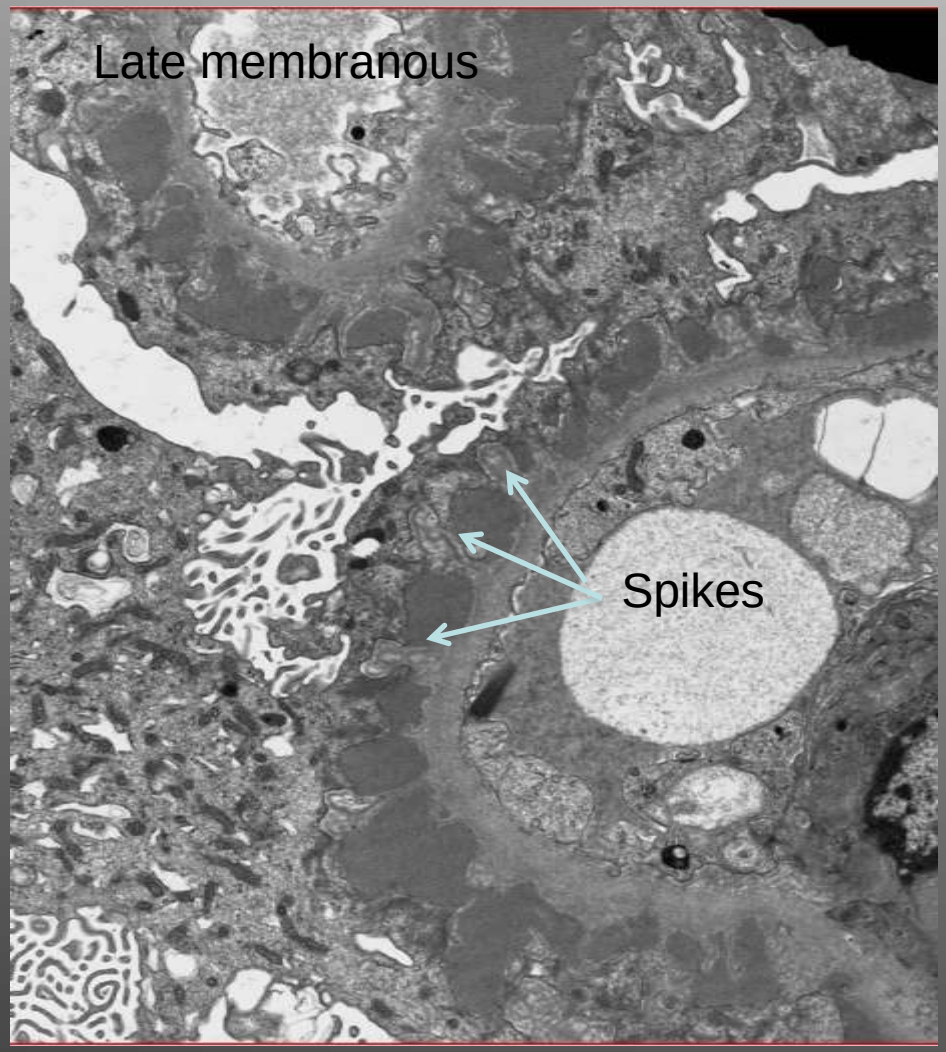

Early membranous

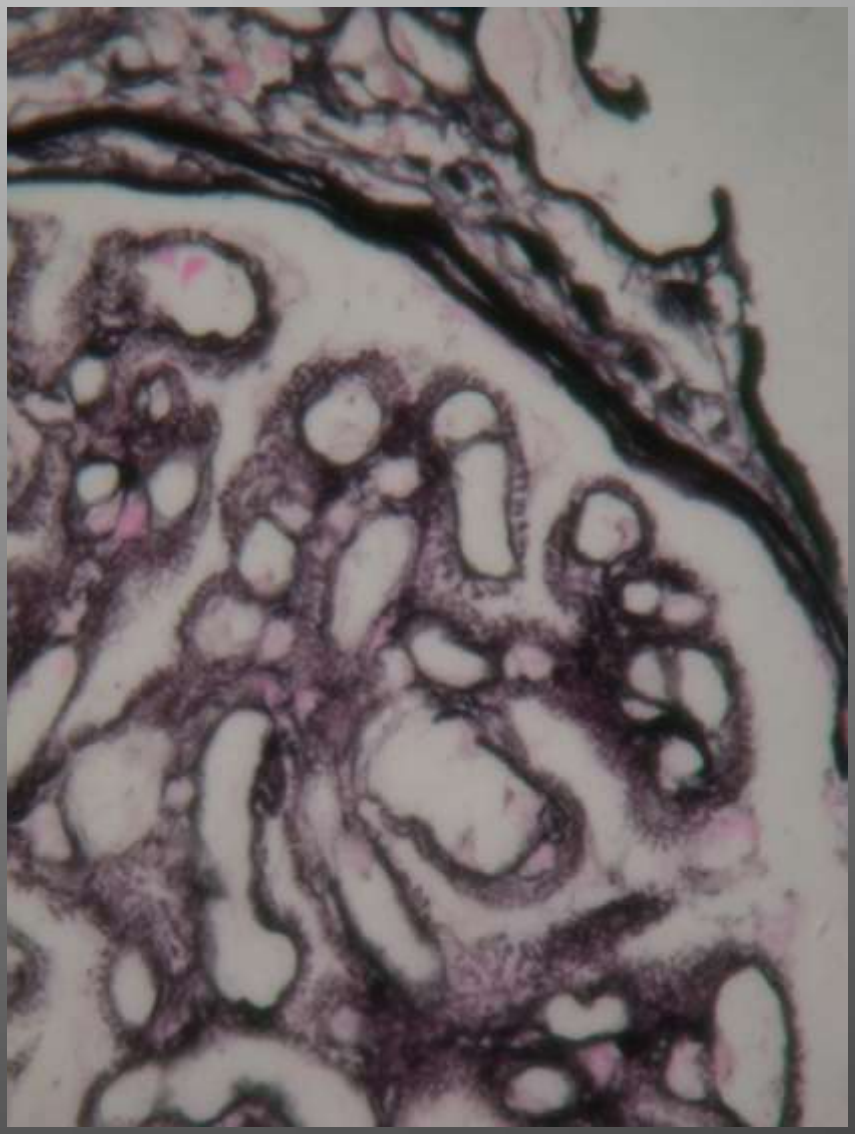

Early membranous


Early membranous


Deposit
Tiny spike

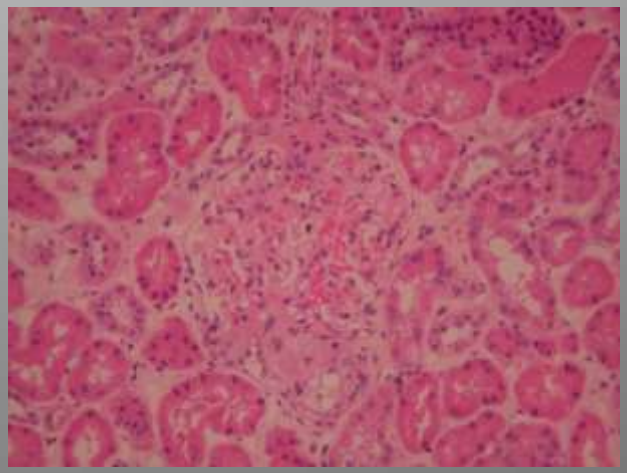

Late membranous - spikes

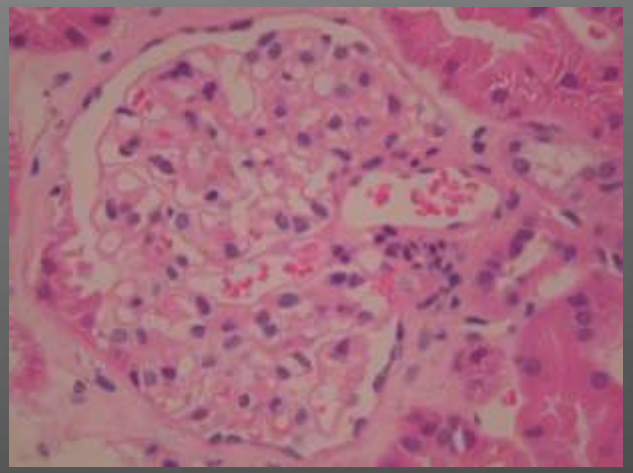

Late membranous
Spikes

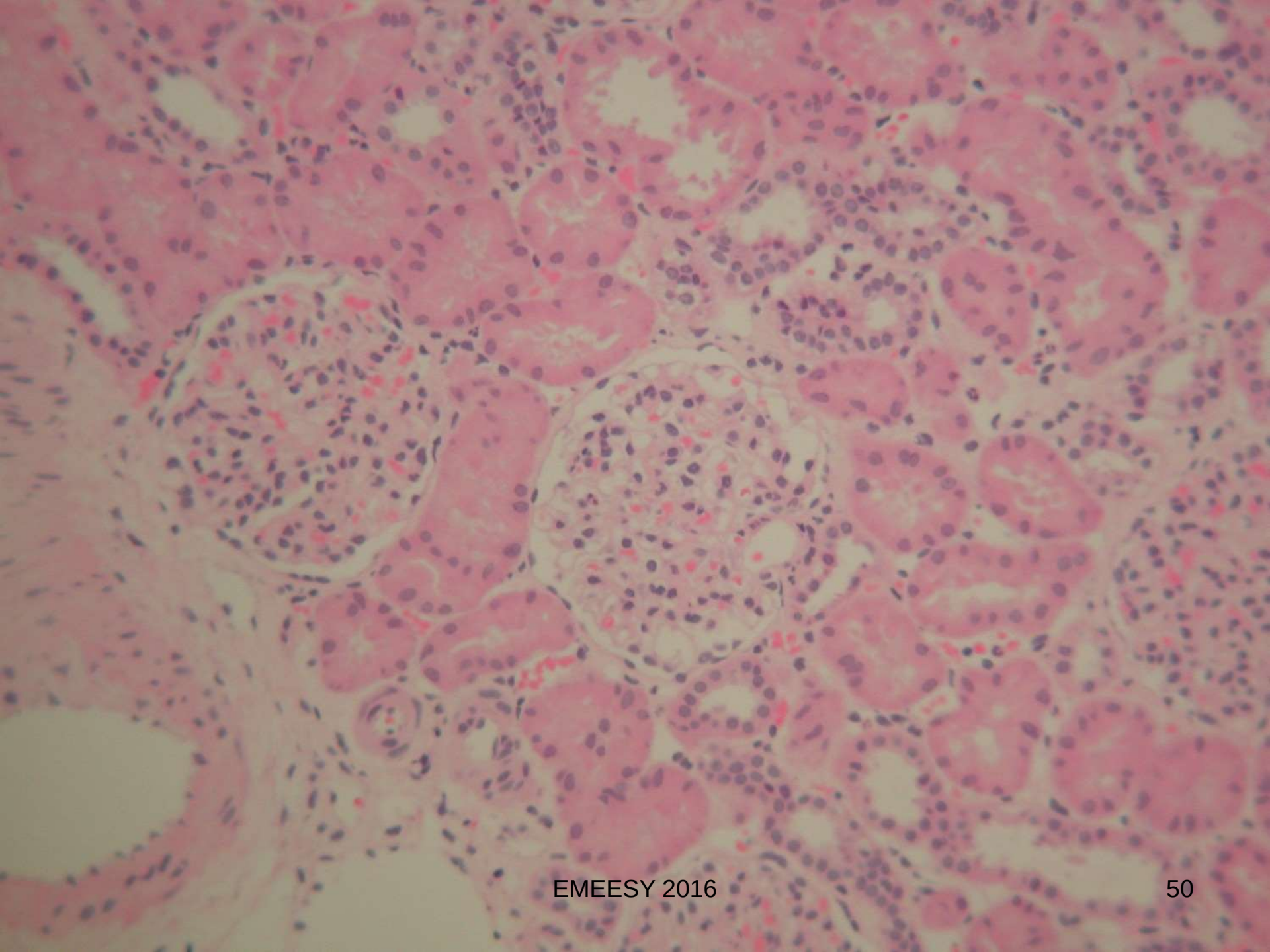


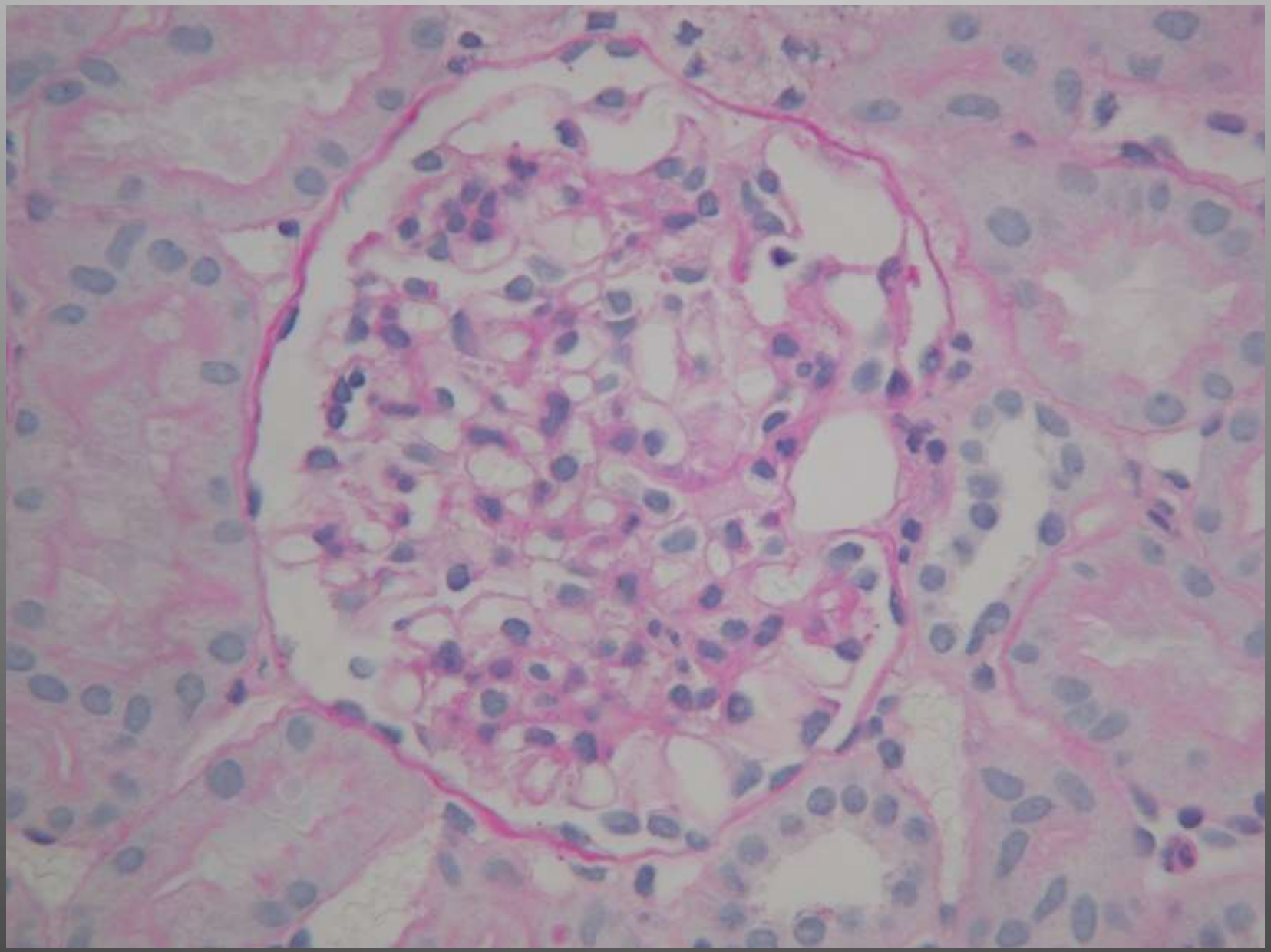
Example 2

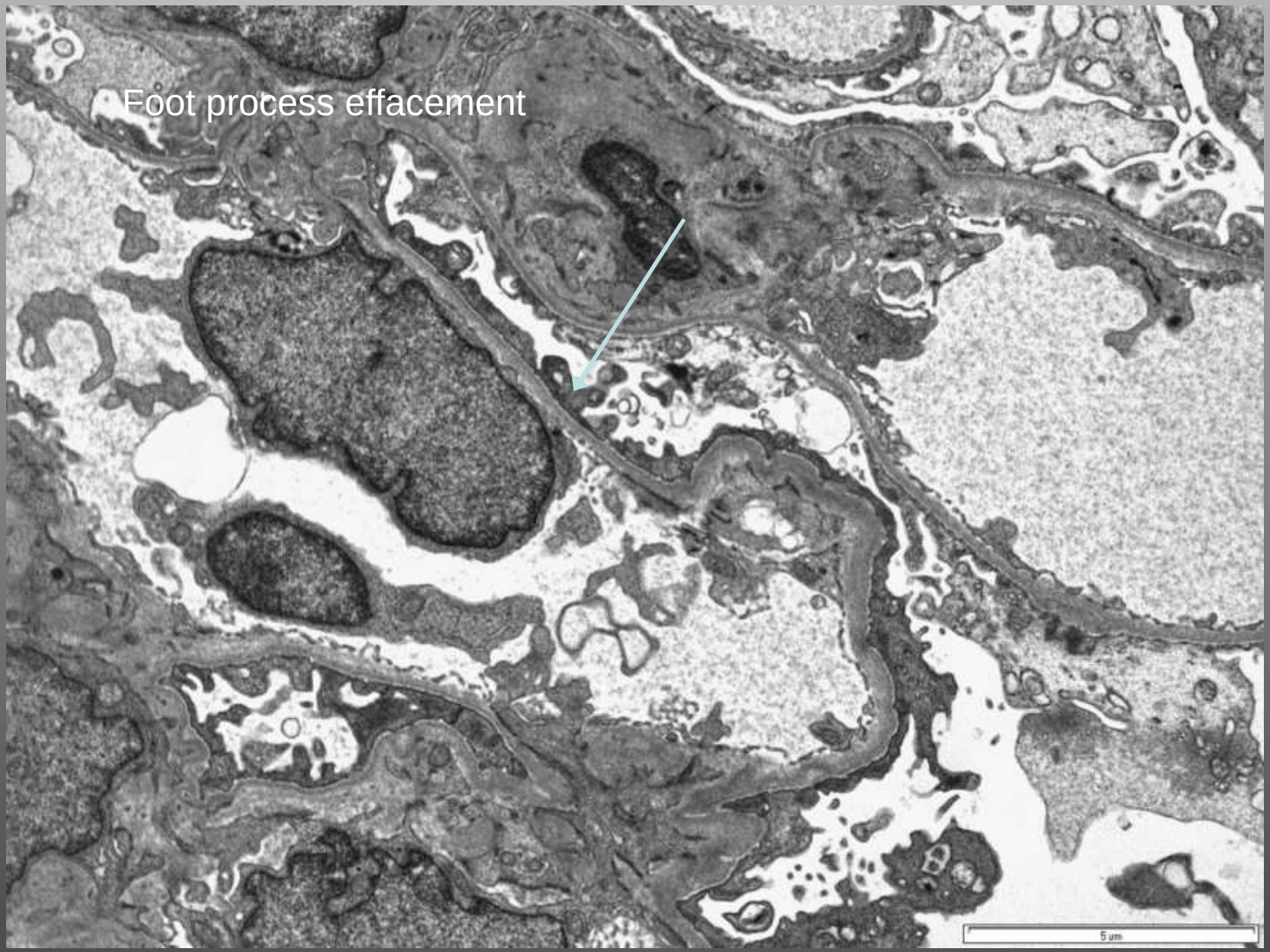
- 7y old boy
- Nephrotic syndrome
- Steroid resistant
- Normal renal function





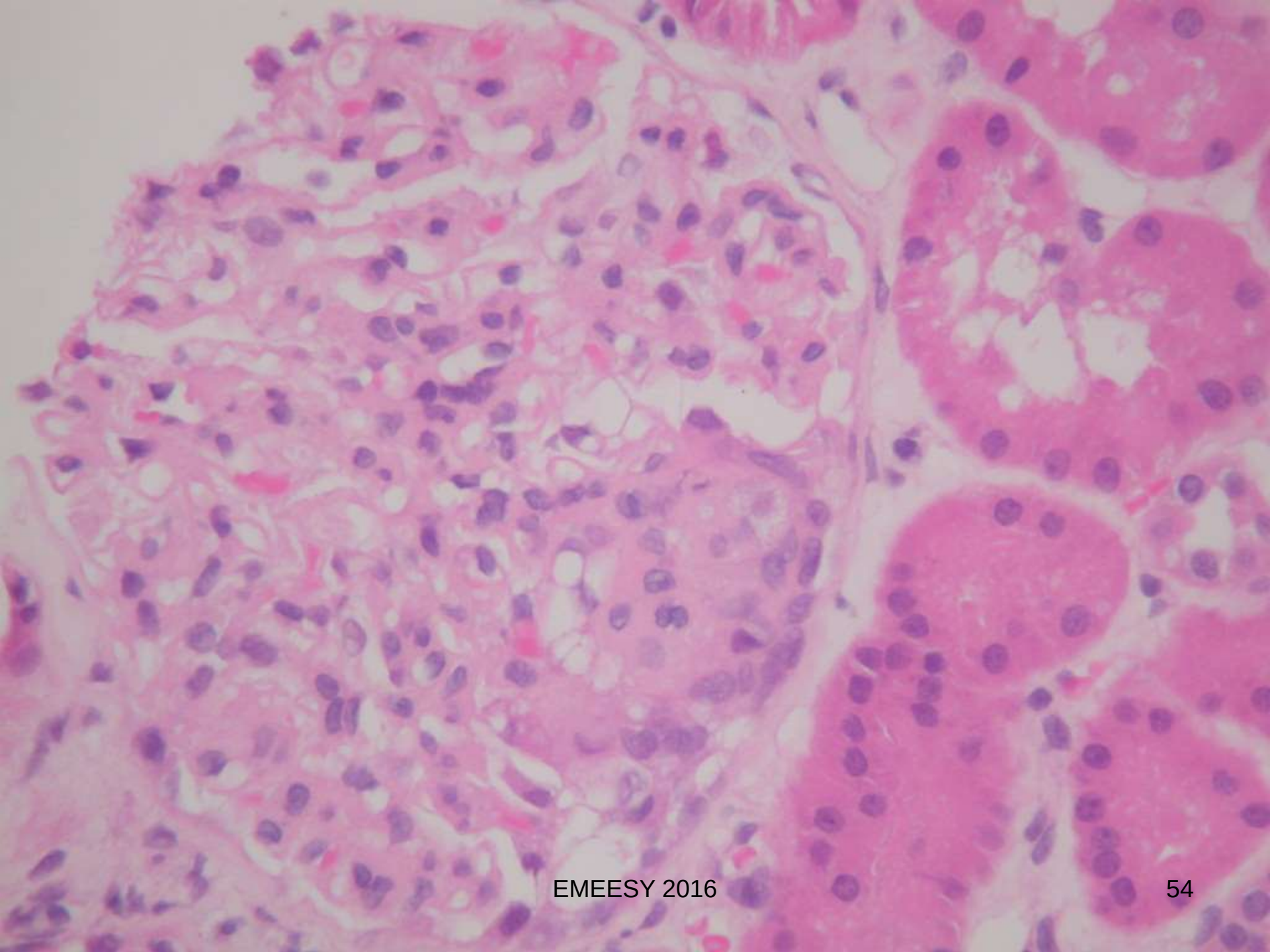


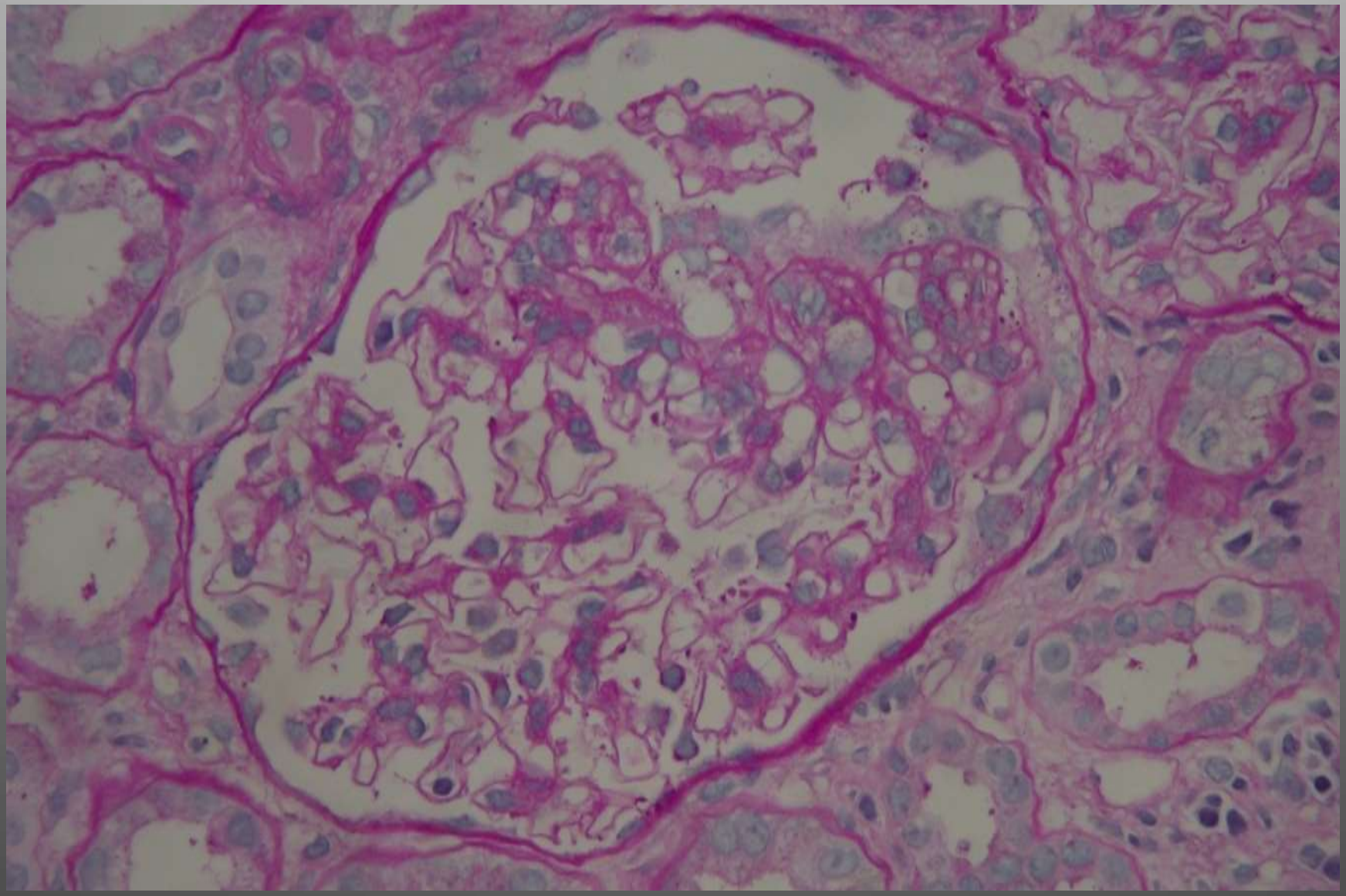


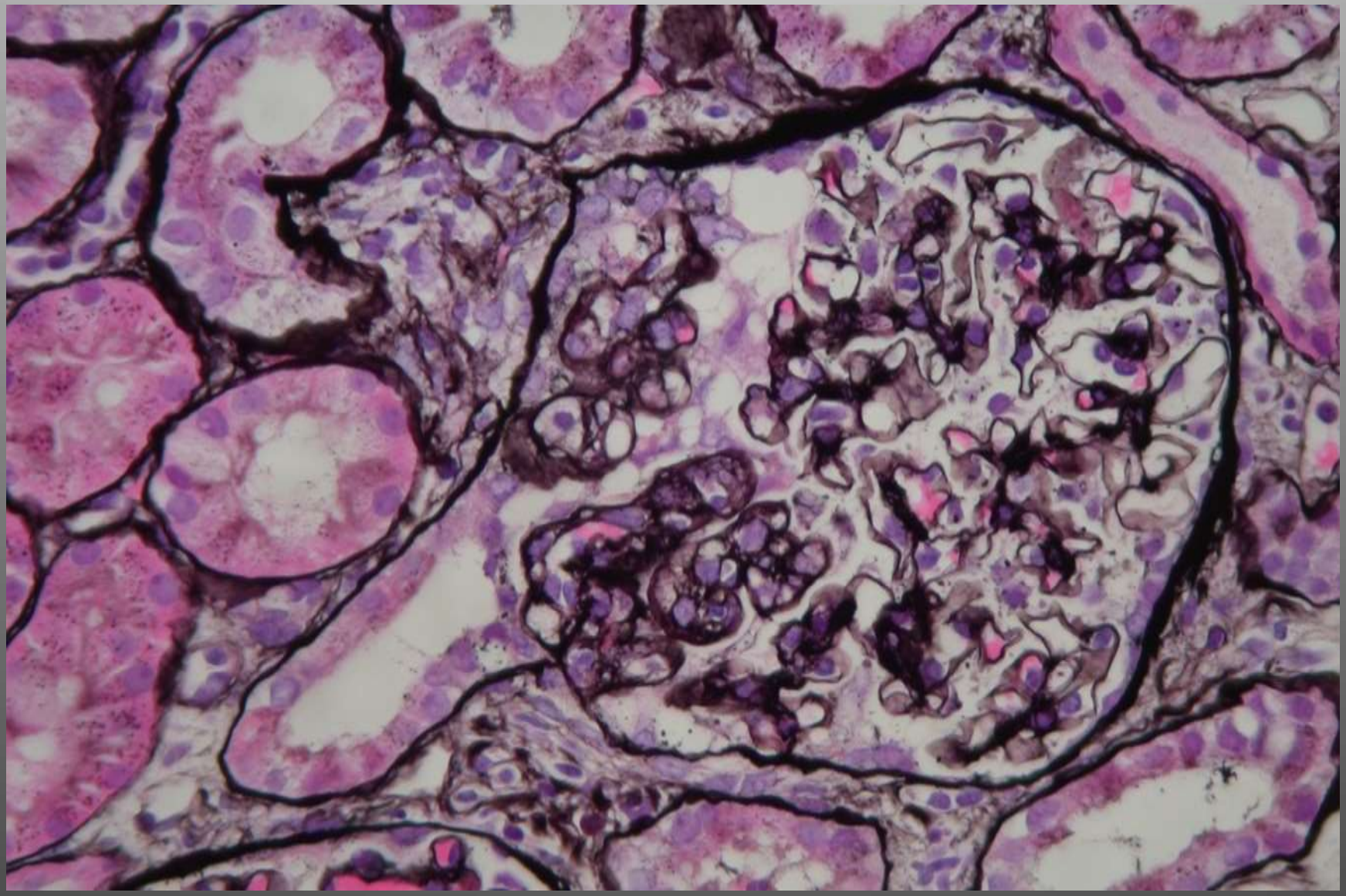

Foot process effacement
5 µm

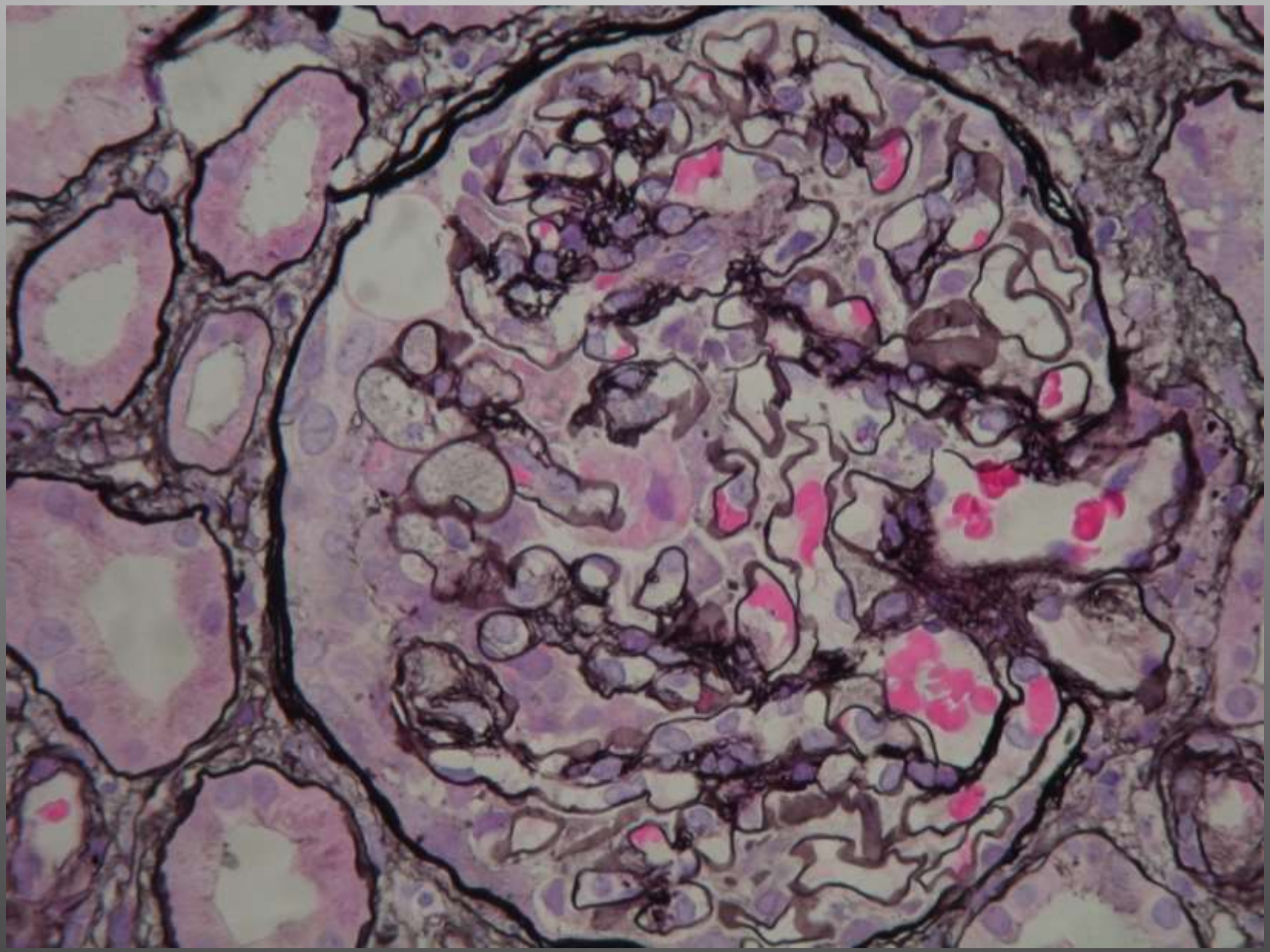
What is the Diagnosis

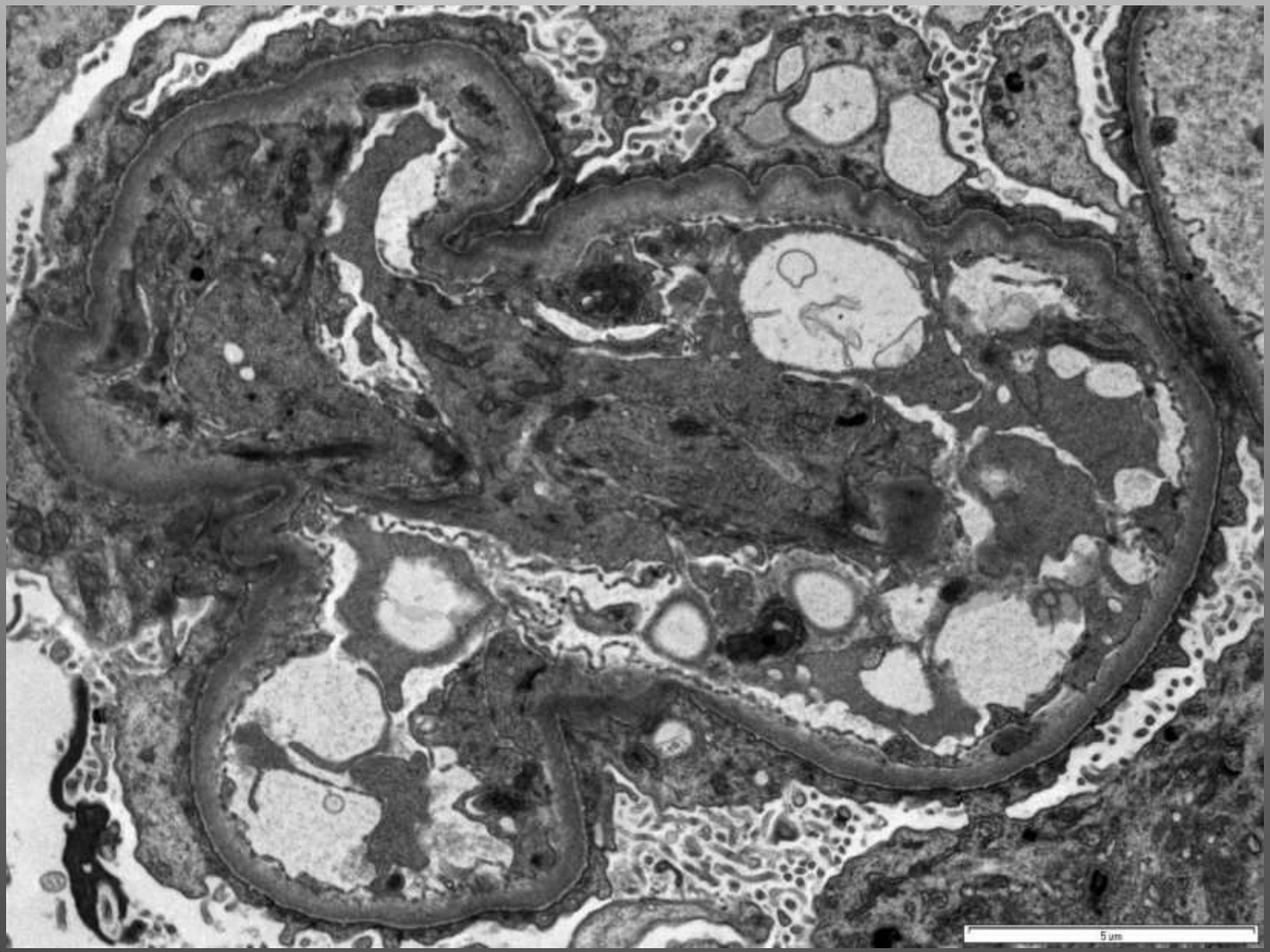
- ?minimal change disease?
- ?are we sure?



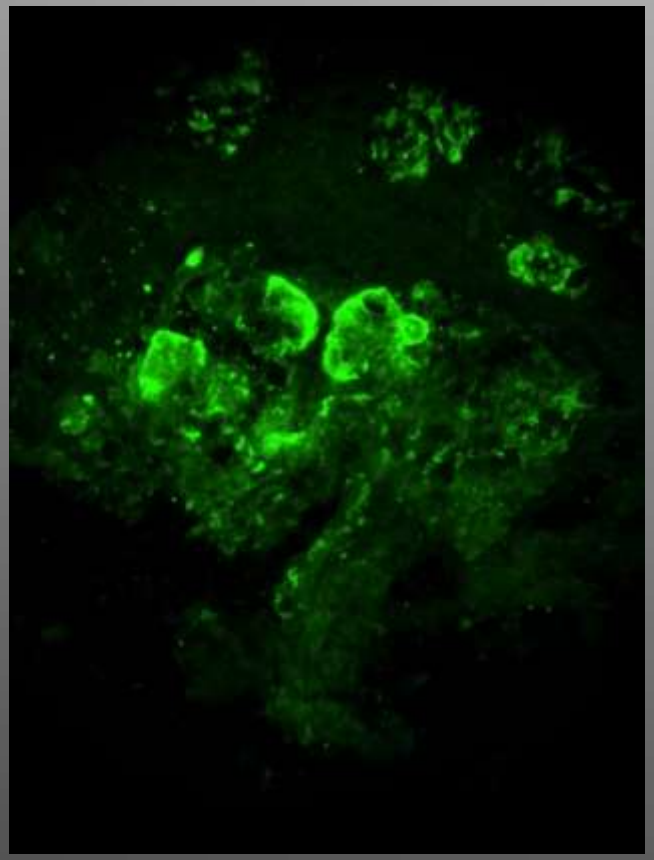




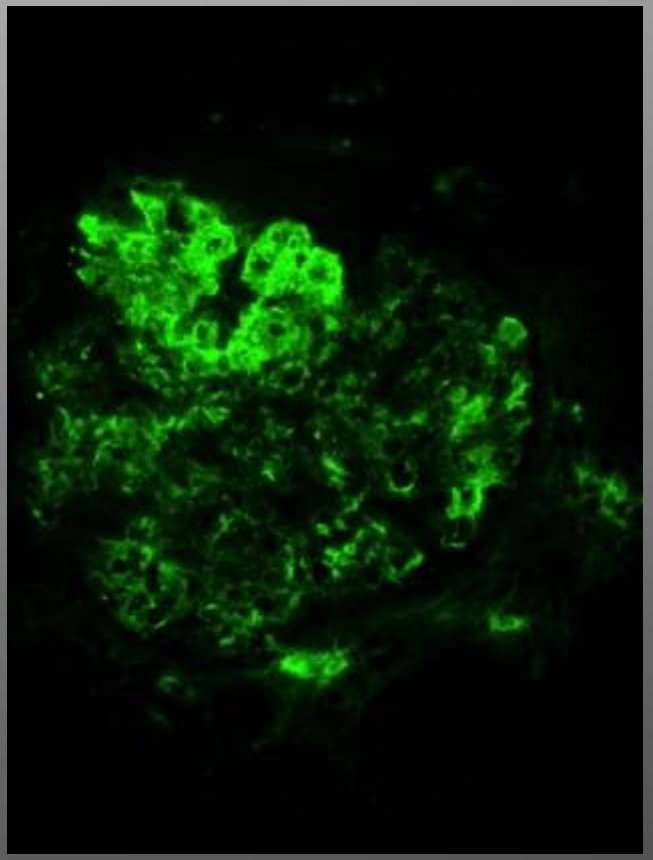



5 µm

C3



IgM

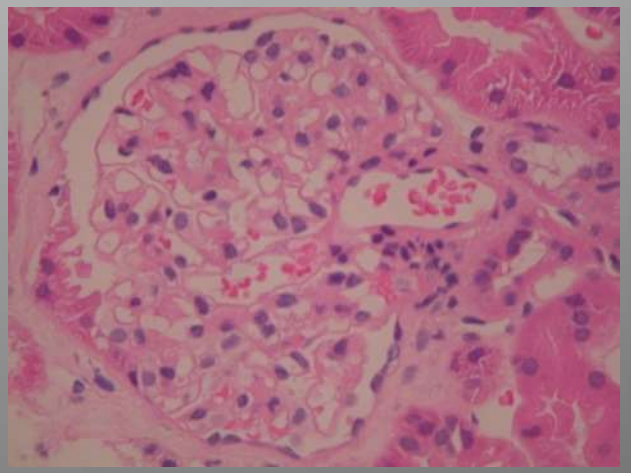


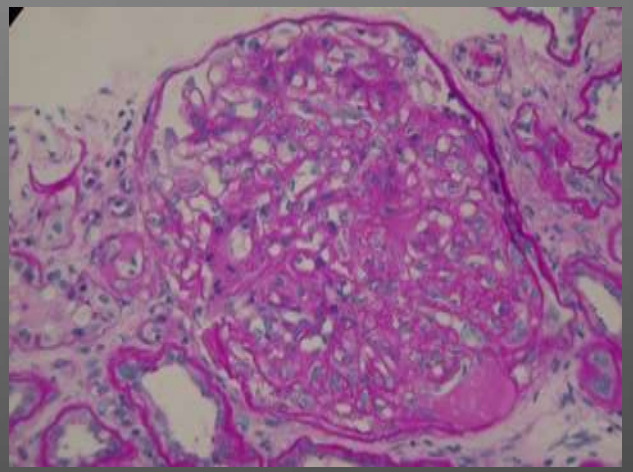
Example 2

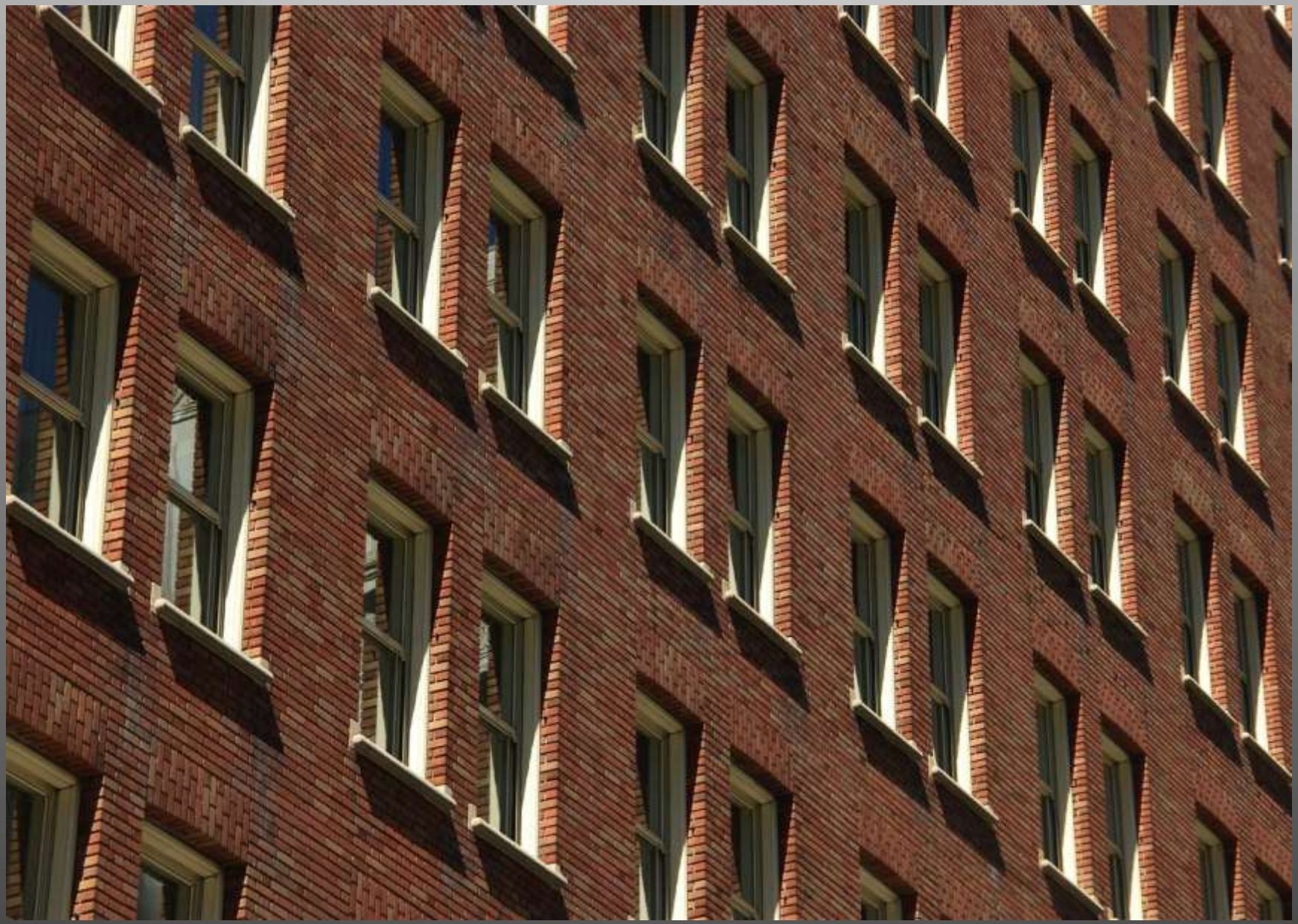
- Initially normal light microscopy
- Foot process effacement on EM
- Minimal change disease?
- But steroid resistant
- Further sections taken show segmental sclerosis in one glomerulus
- Diagnosis: Focal segmental glomerulosclerosis

Focal Disease: Focal Segmental Glomerulosclerosis

- How many glomeruli will be needed?
  - 10?
  - 20?
  - More?
- Distribution is relevant
  - Affected glomeruli are at the corticomedullary junction







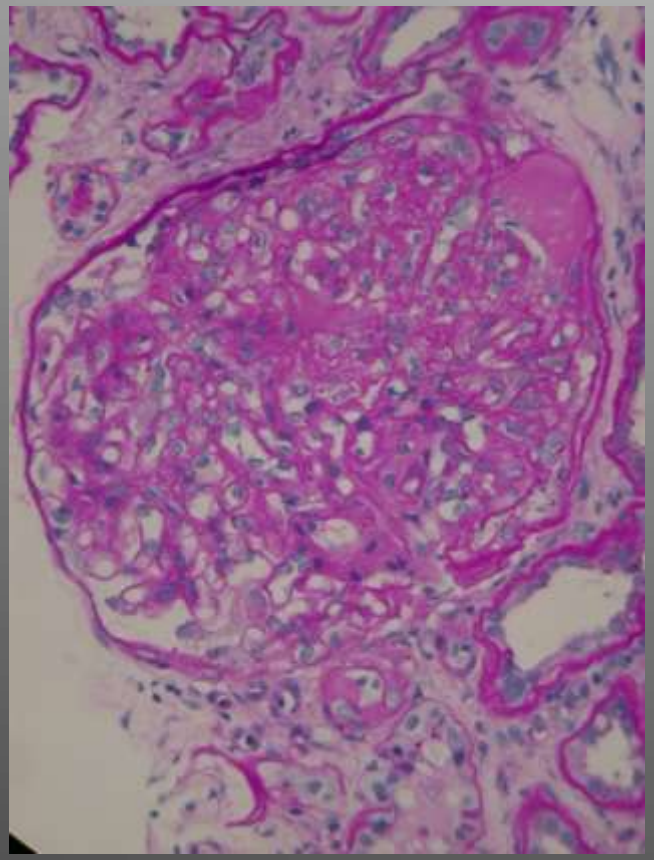
Specimen Adequacy

- What is adequate
- Depends on the disease present
  - Focal or diffuse

Glomerular Disease

- Diffuse
  - >50% of glomeruli involved
- Focal
  - <50% of glomeruli involved
- Global
  - The whole glomerulus is involved
- Segmental
  - Only part of the glomerulus (one or more segments) is involved

Sample Adequacy



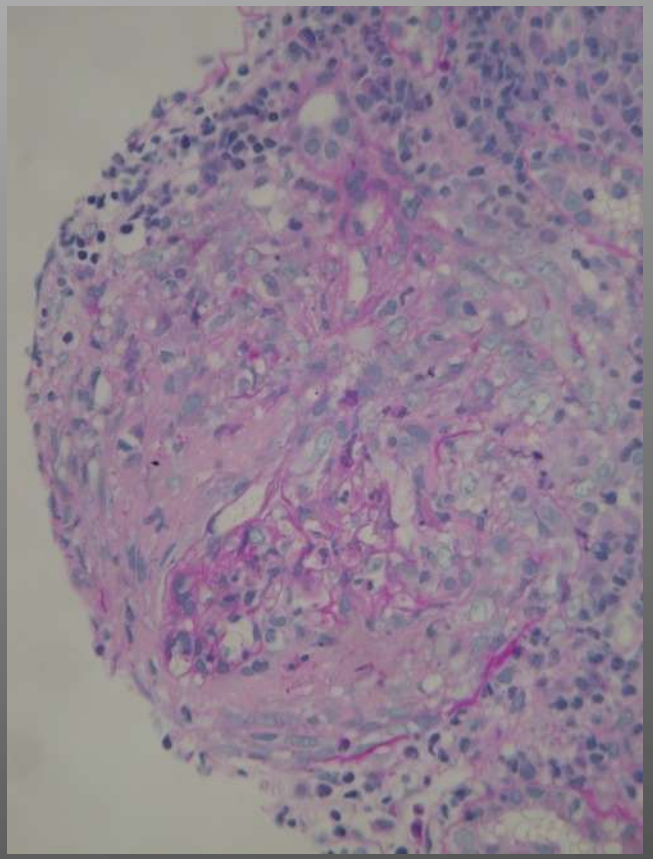
- In general
- 10 glomeruli considered adequate
- 7 borderline

- Vessels need to be represented

- Important role of tubulointerstitium

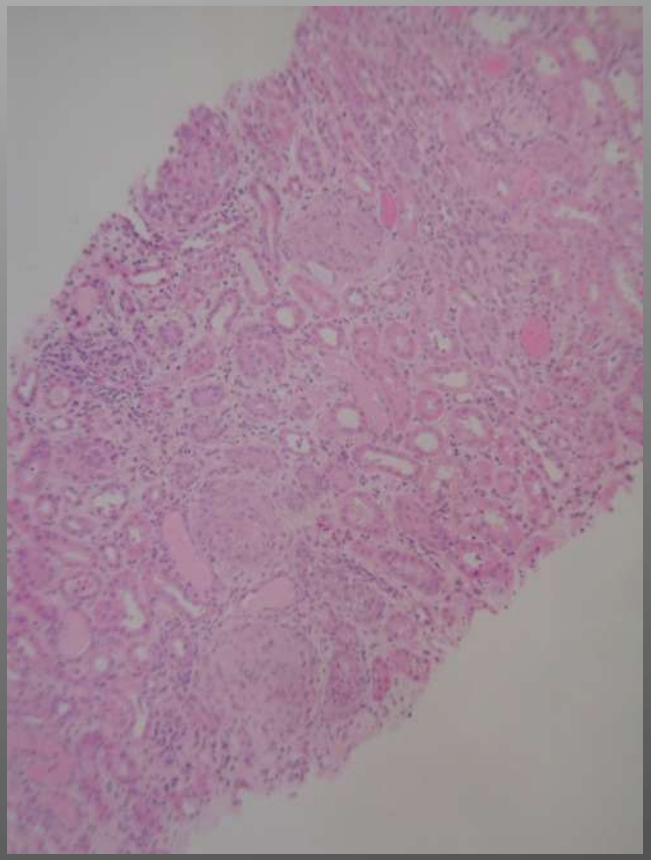
Sample Adequacy

- 1. Will have an effect on the likelihood on making the diagnosis in focal pathologies
  - Eg FSGS
  - Vasculitis
- 2. Will have an effect on assessing the severity (grade) of a pathology
  - Eg. Number of crescents in glomerulonephritis



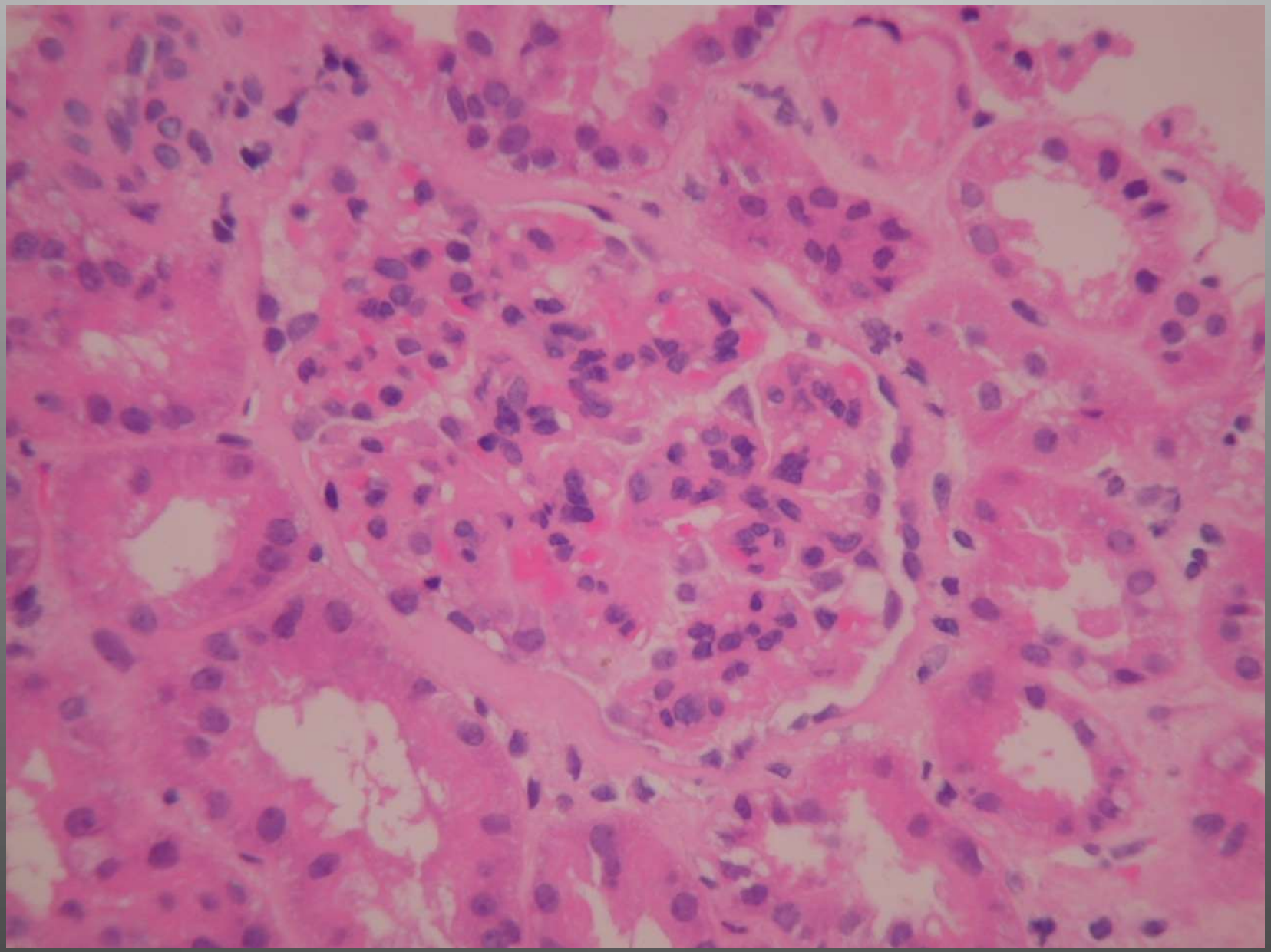
Sample Adequacy

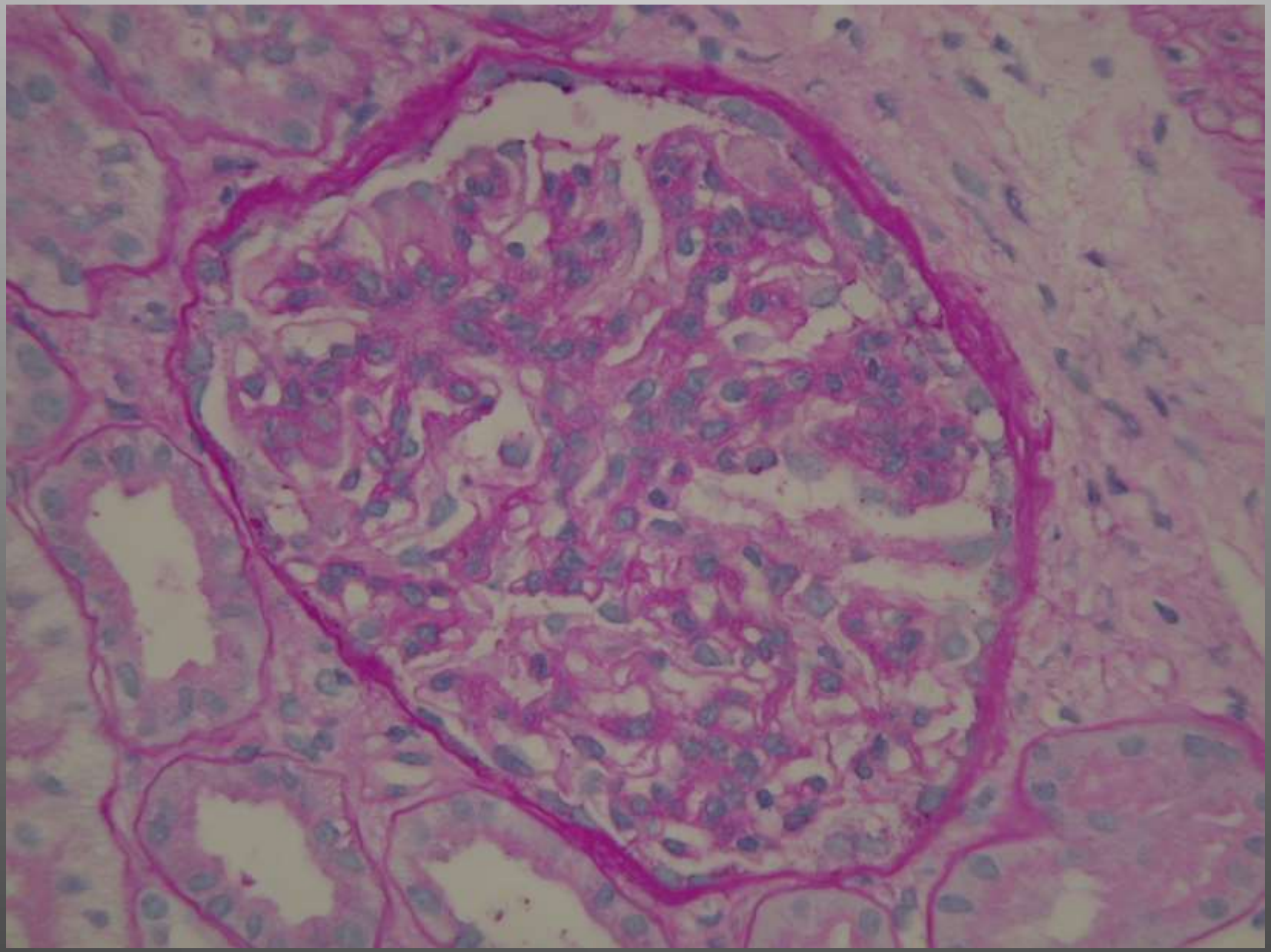
- We need enough to:
  - Diagnose the condition
  - Estimate the severity of the condition
    - Cf percentage of glomeruli with crescents
- But also:
  - To assess the level of chronic damage

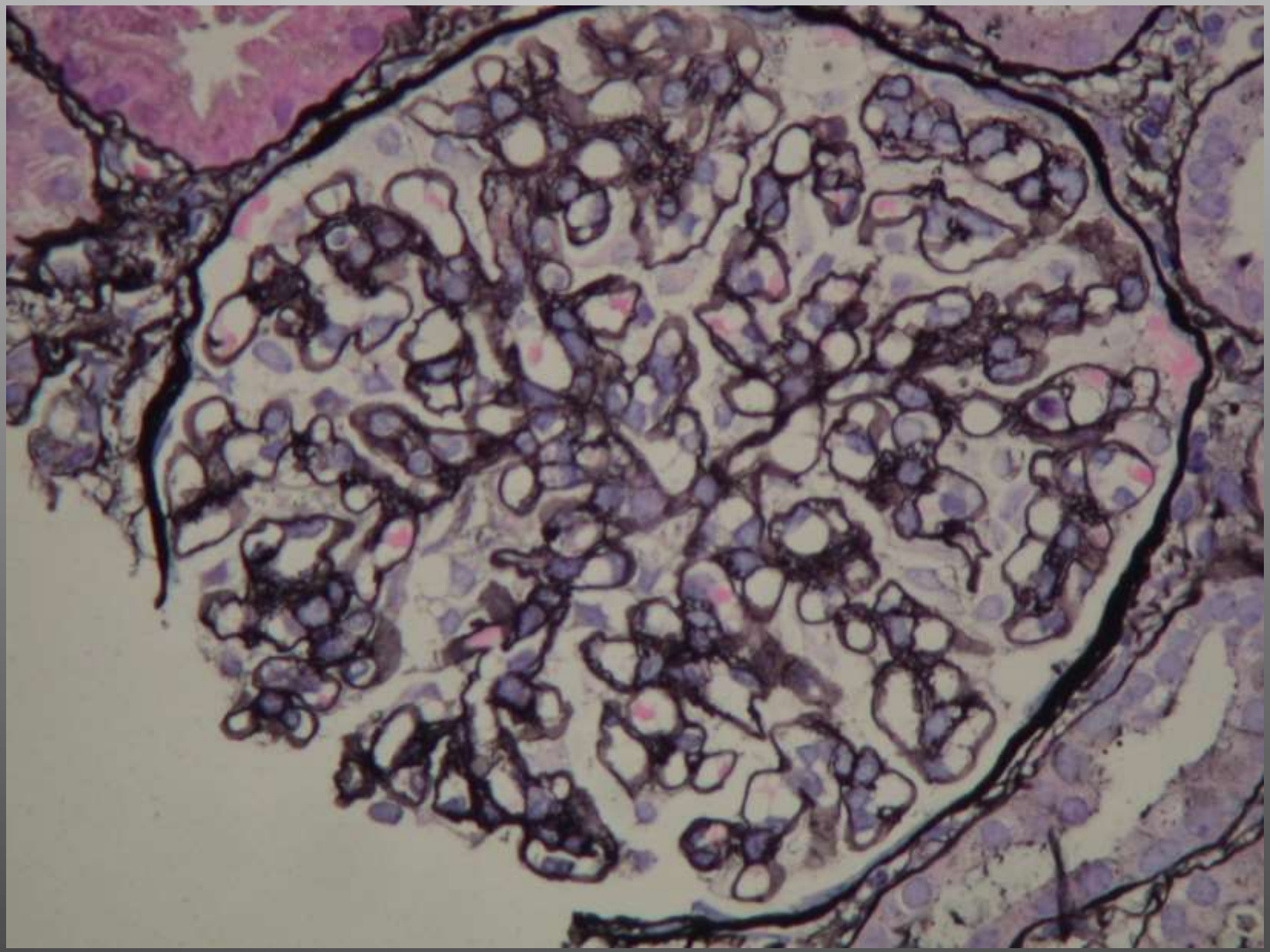


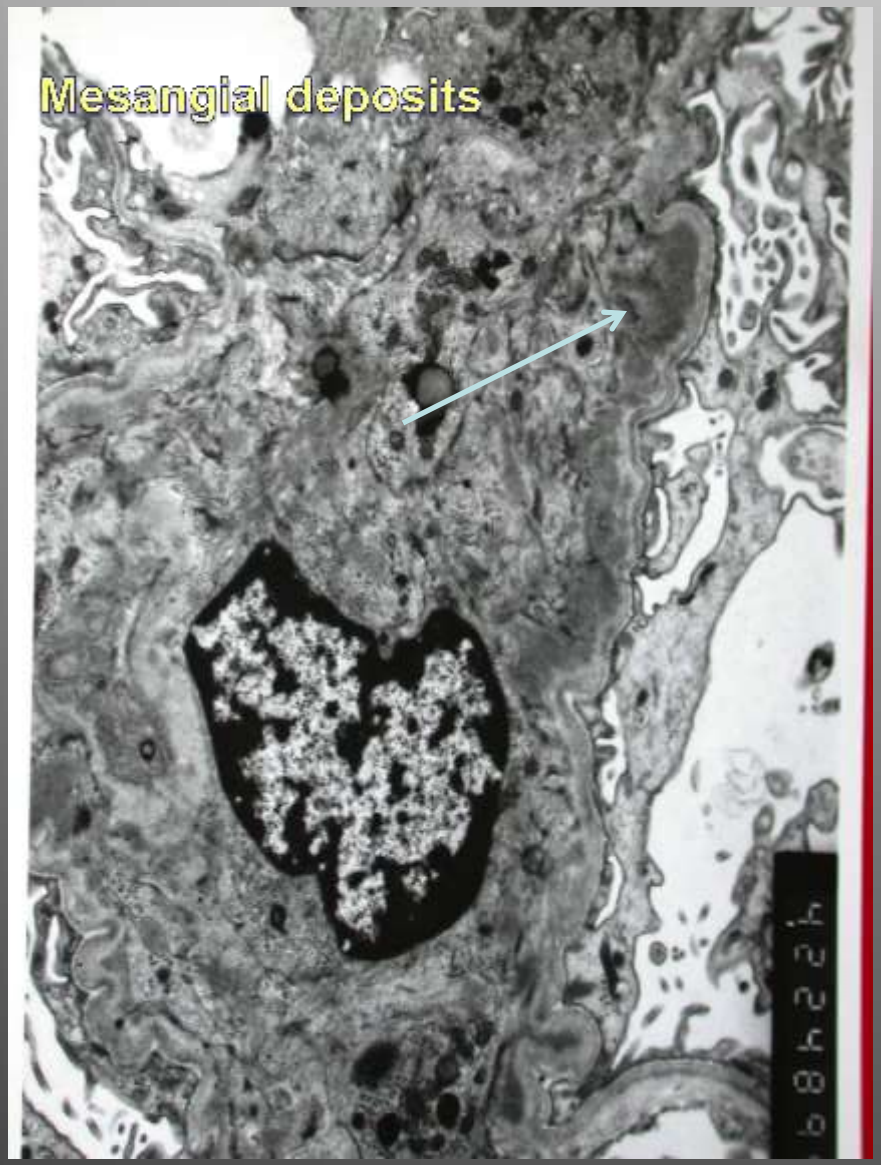
Example 3

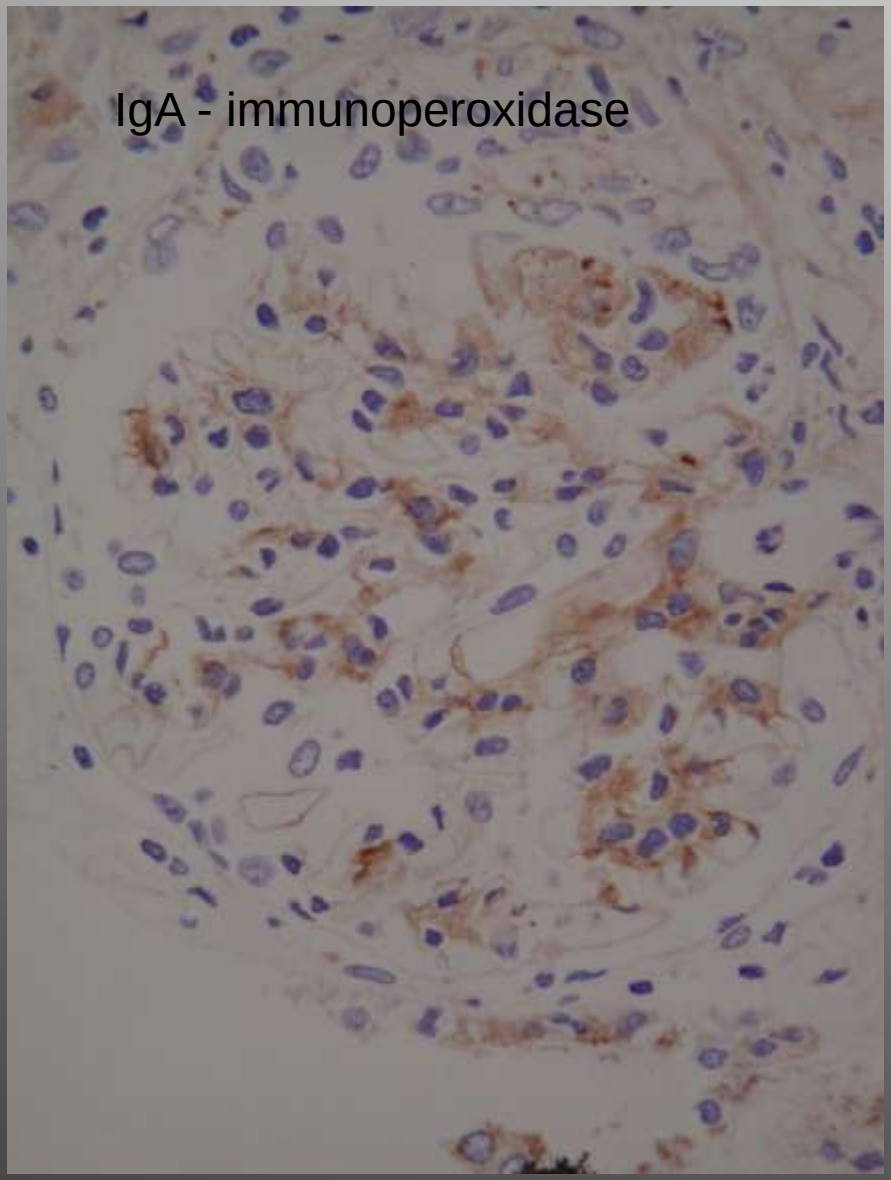
- Male 27
- Microscopic haematuria
- Proteinuria
- Mild renal impairment

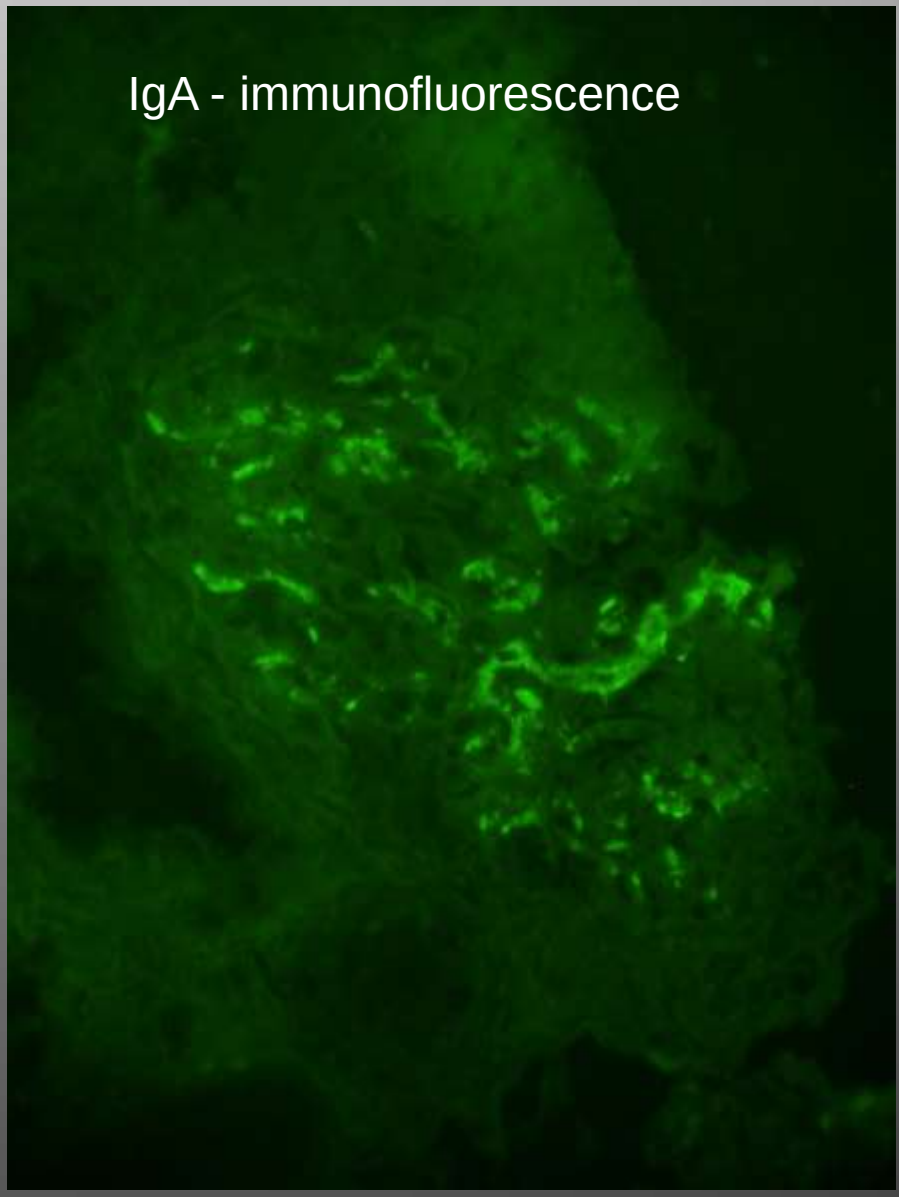






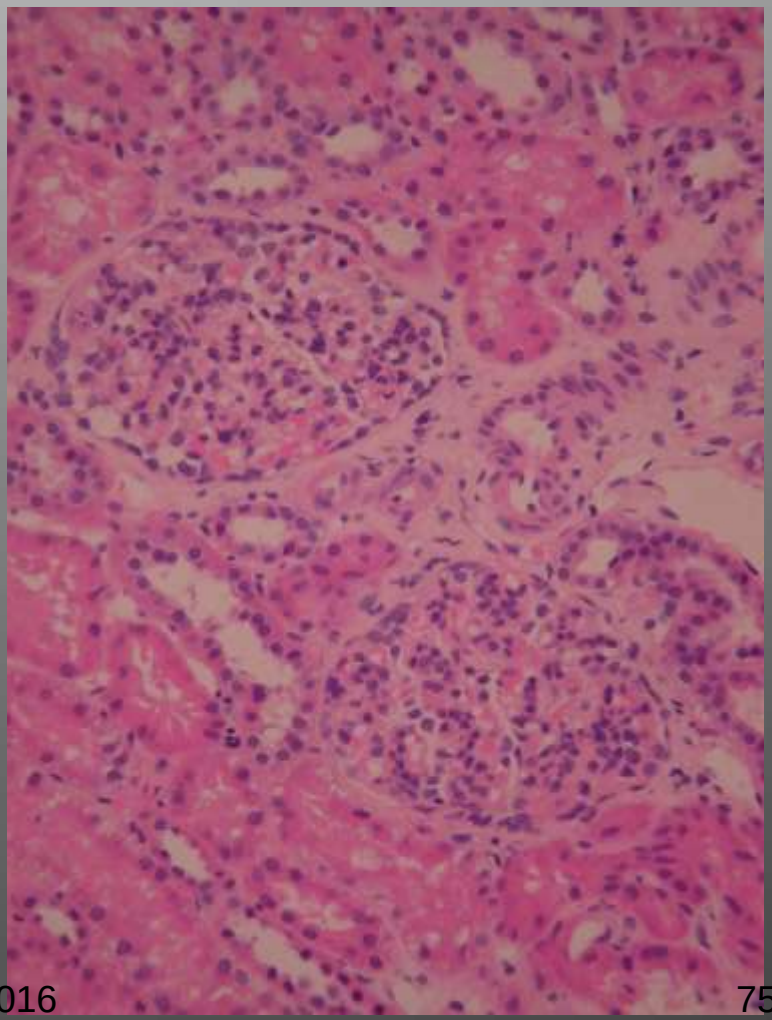

Mesangial deposits


IgA - immunoperoxidase


IgA - immunofluorescence

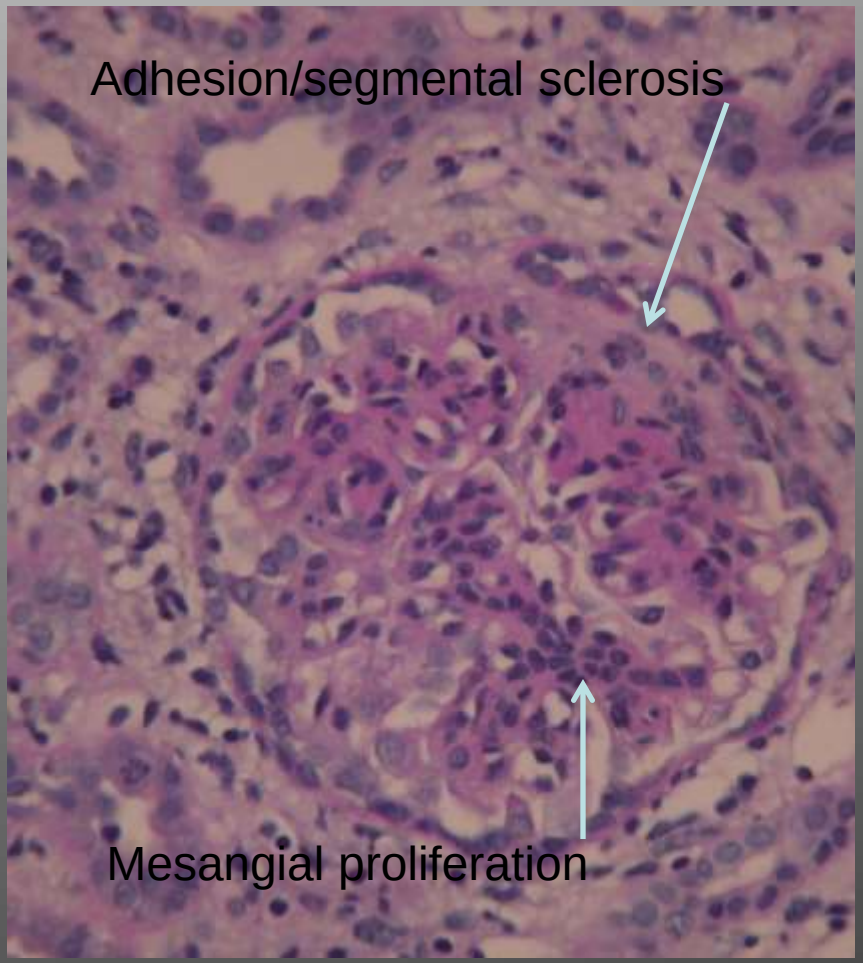
IgA nephropathy

- Mesangial hypercellularity
- Sometimes proliferation in the loops
- Sometimes crescents
- Defined by the imunohistochemistry



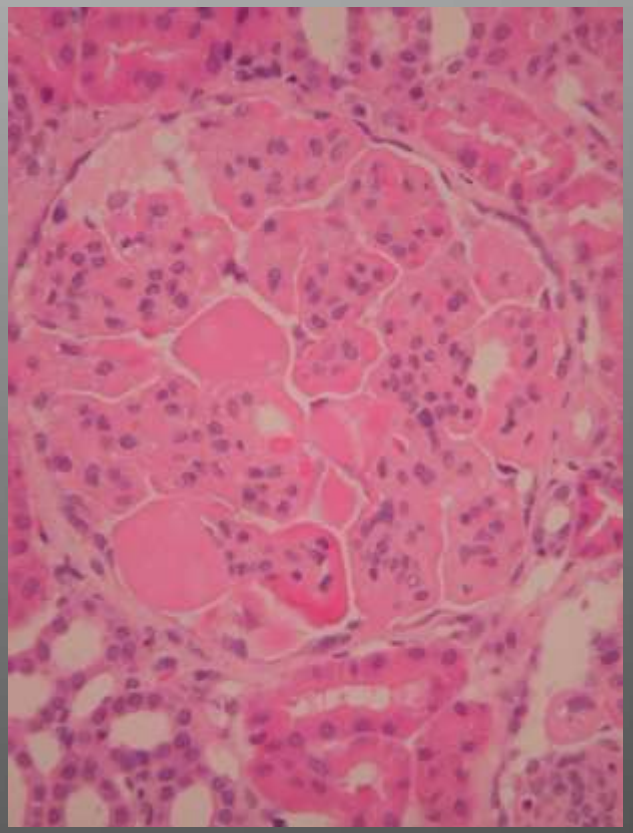
IgA nephropathy

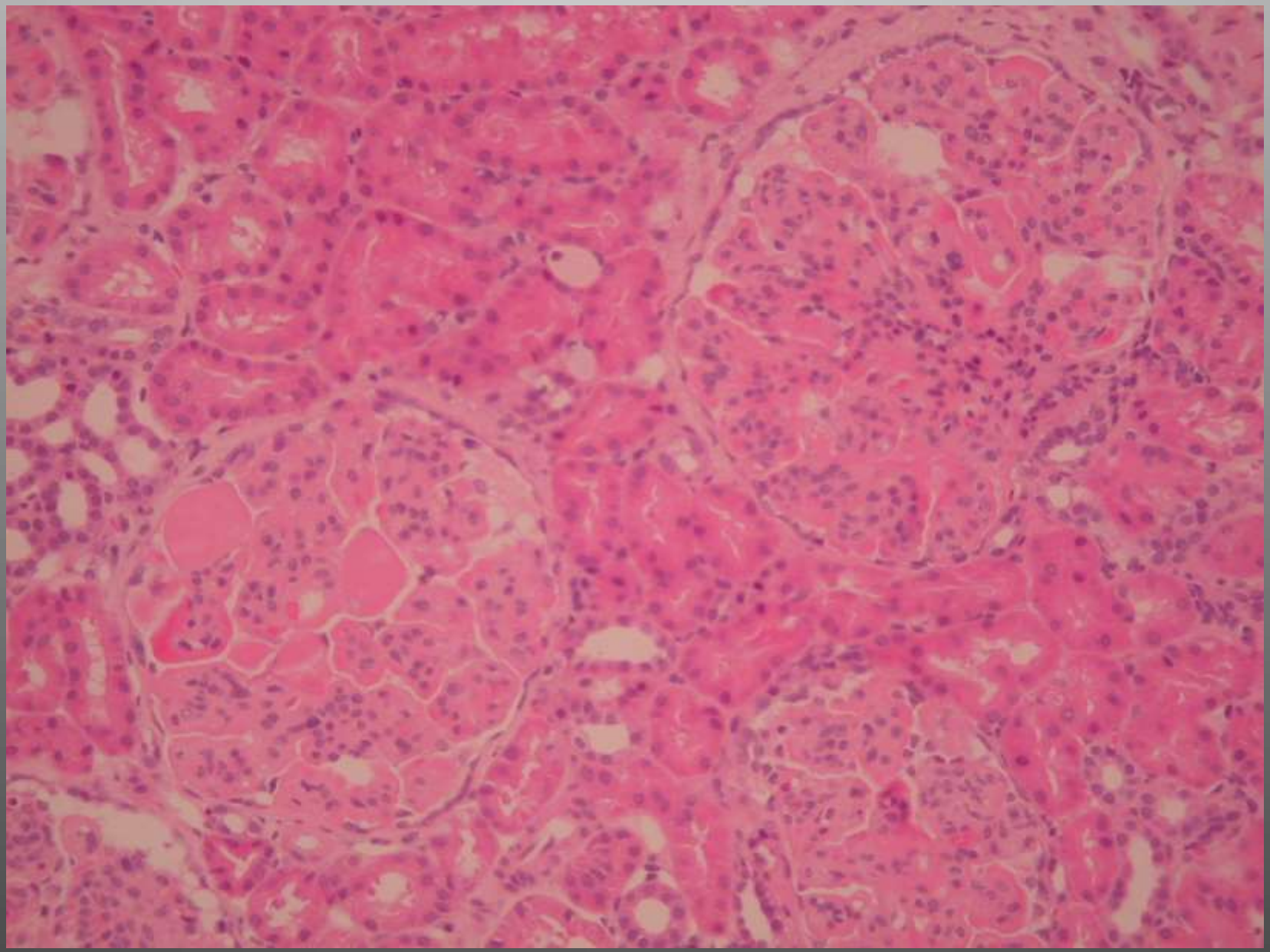
- Prognostic features
- Degree of mesngial proliferation
- Presence of endocapillary proliferation
- Presence of segmental sclerosis or adhesions
- Level of interstitial fibrosis
- Oxford Score
- M, E, S, T



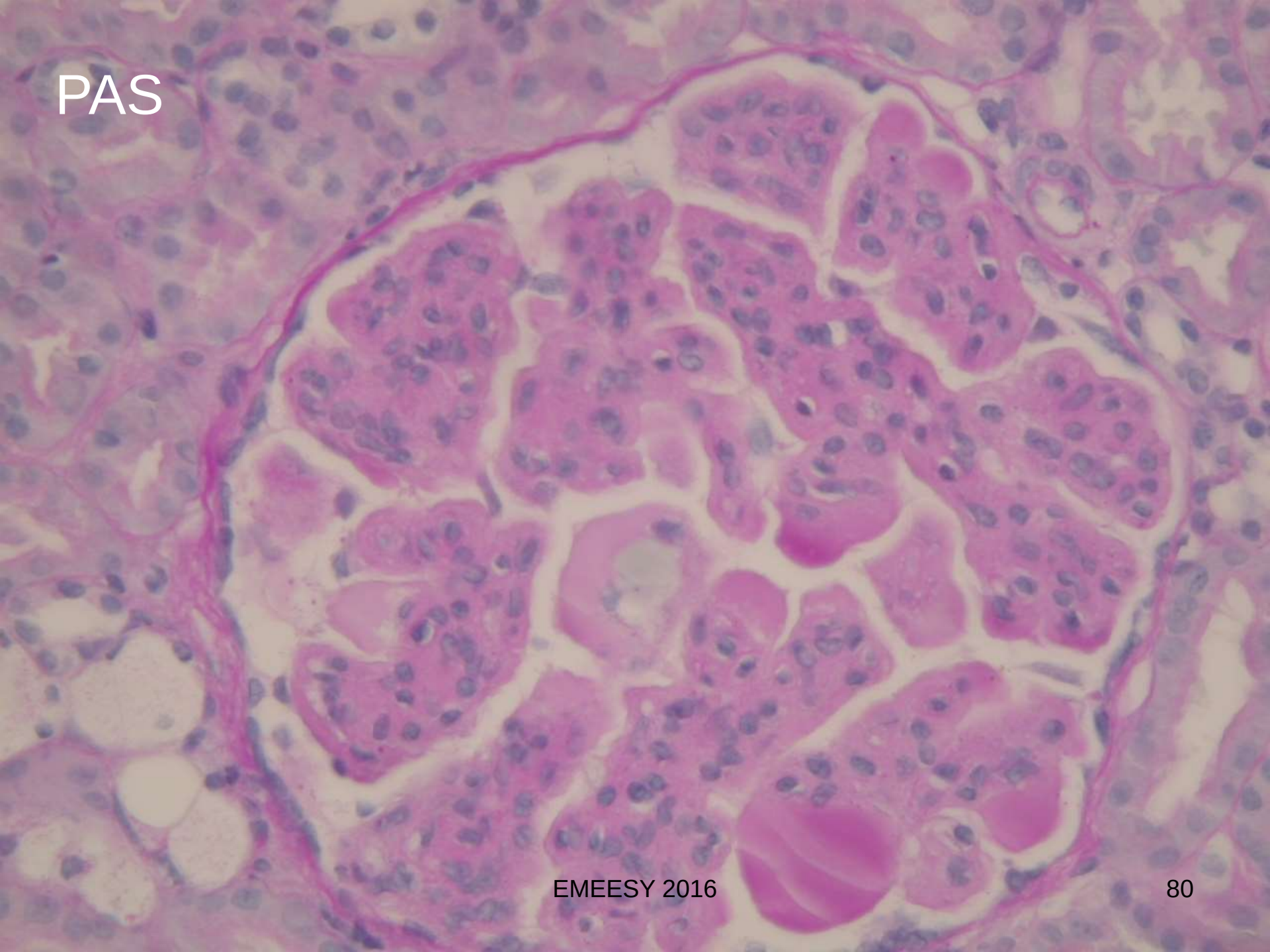
Example 4.

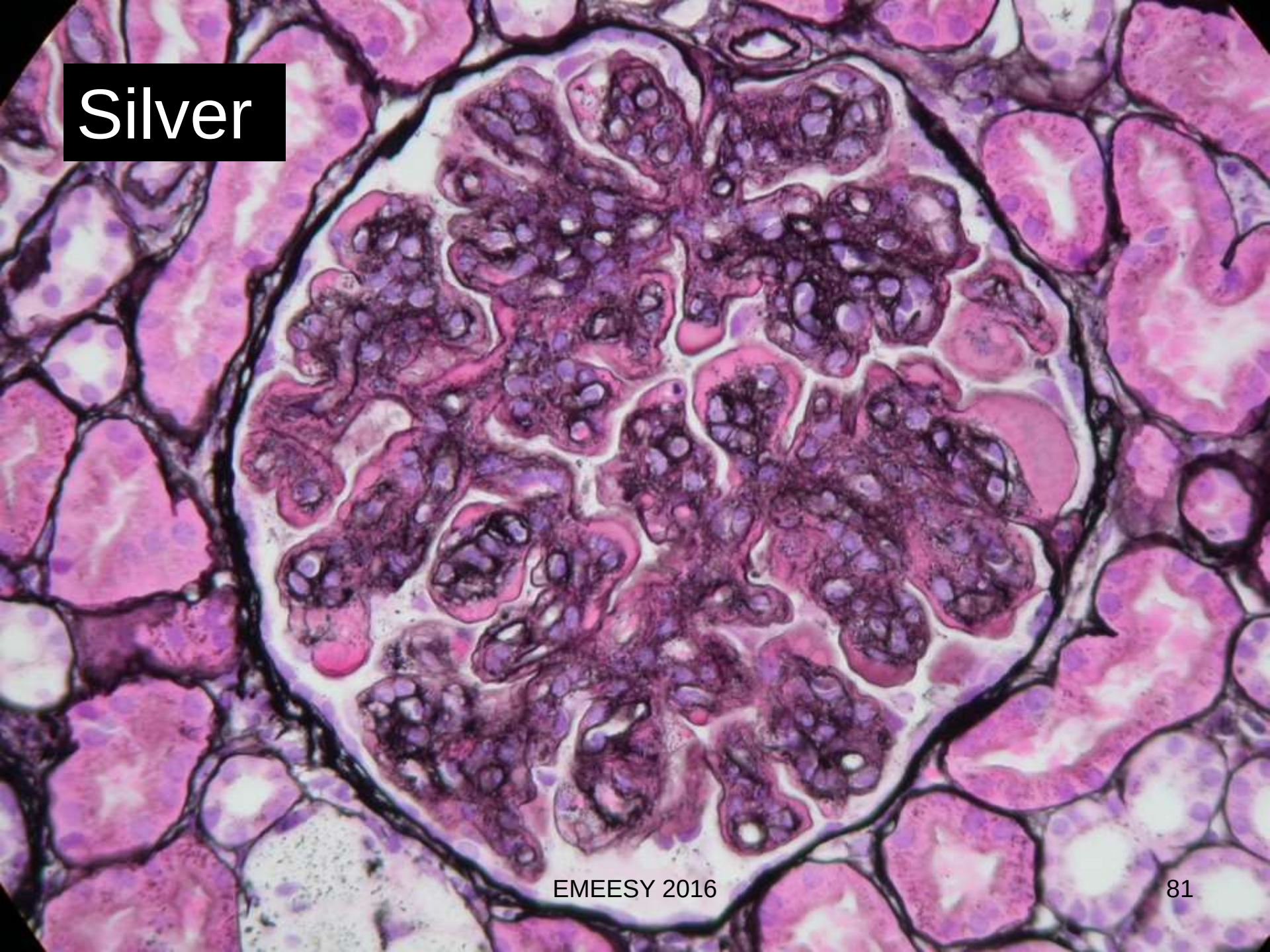
- Female 12
- Nephrotic syndrome
- Haematuria
- Some renal impairment
- Complement levels low
- ANA negative

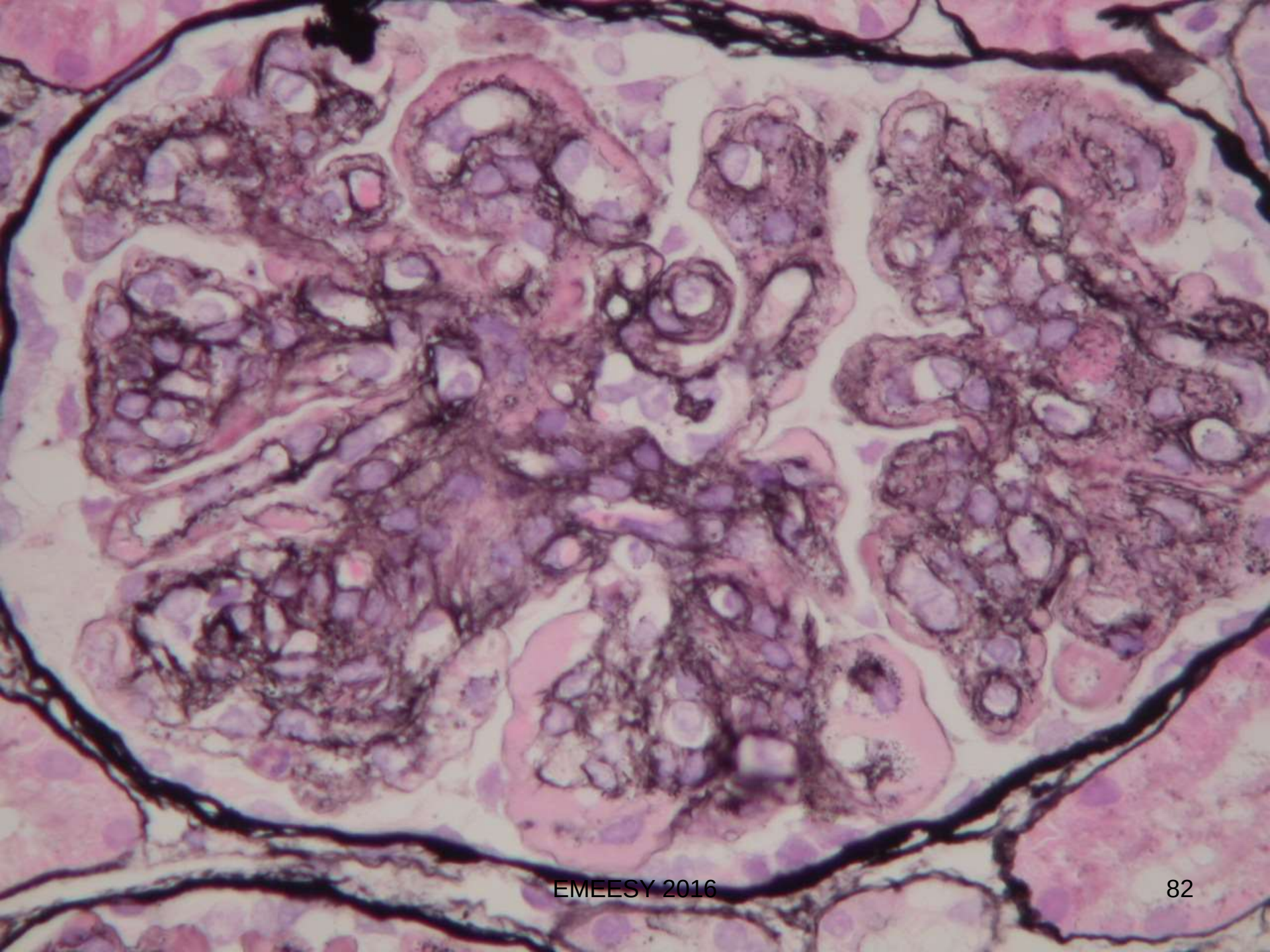


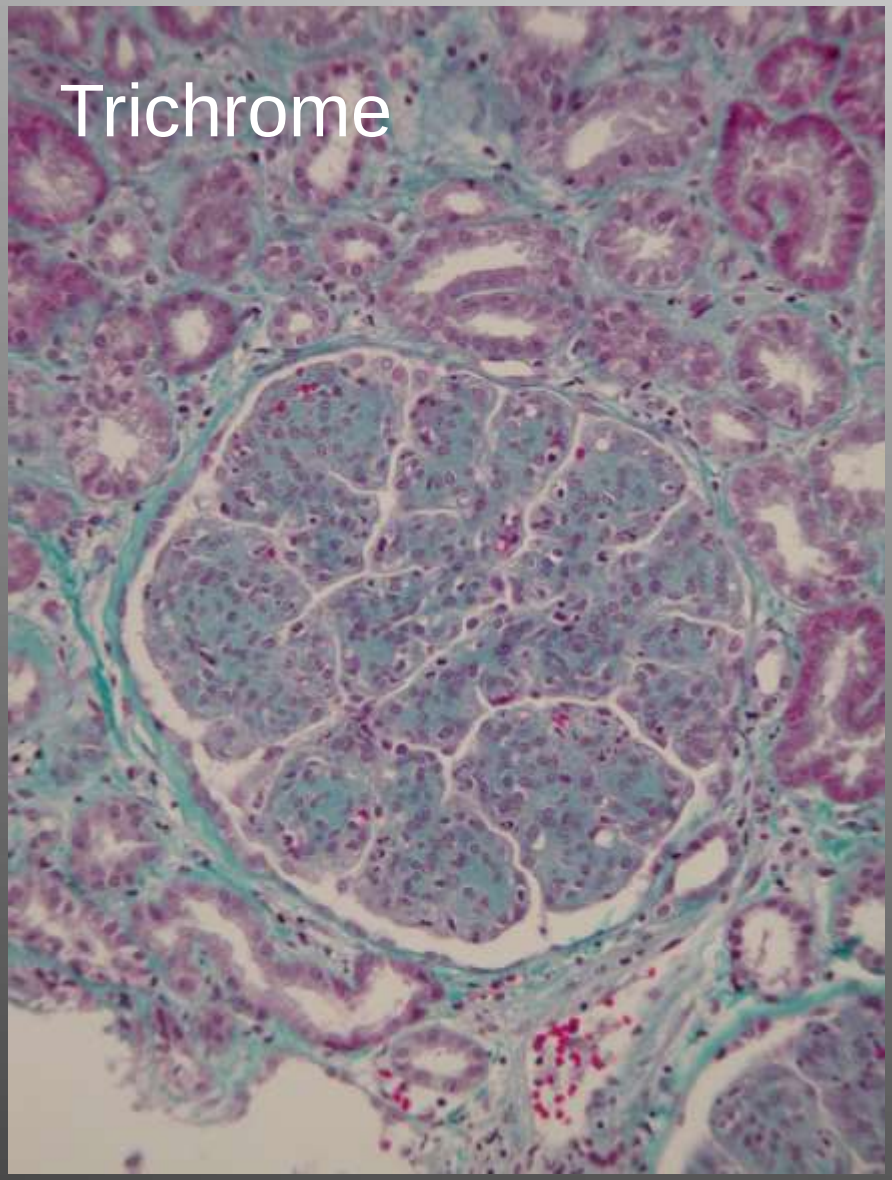


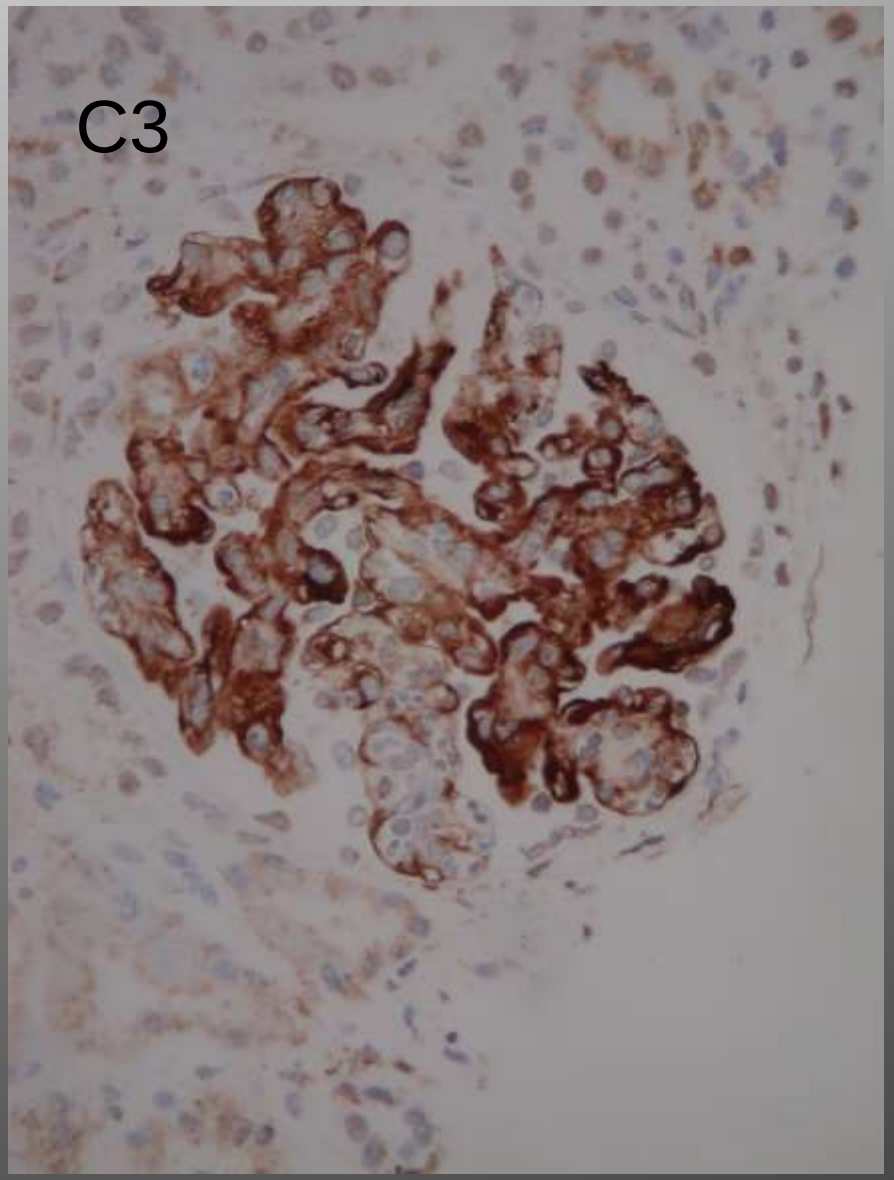
PAS



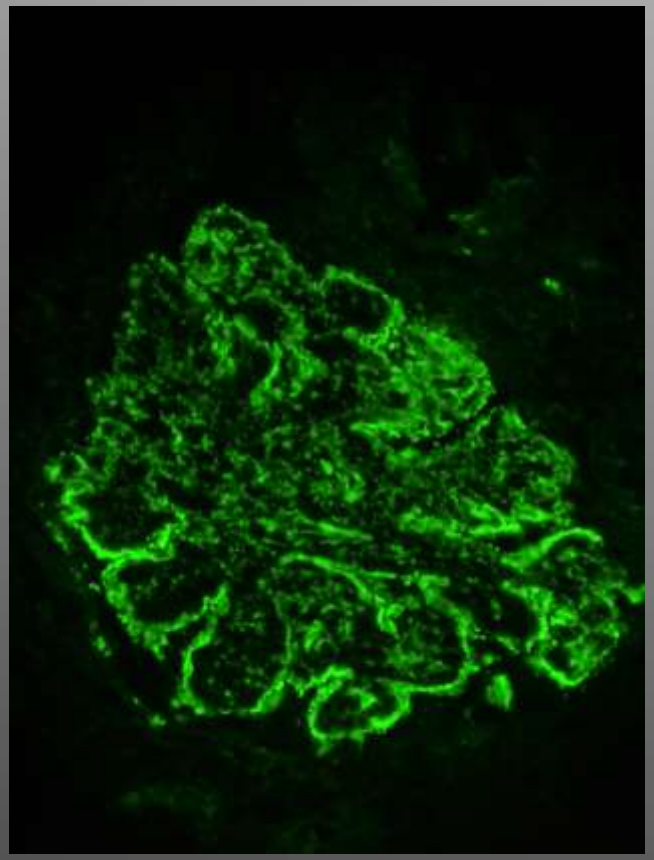

Silver



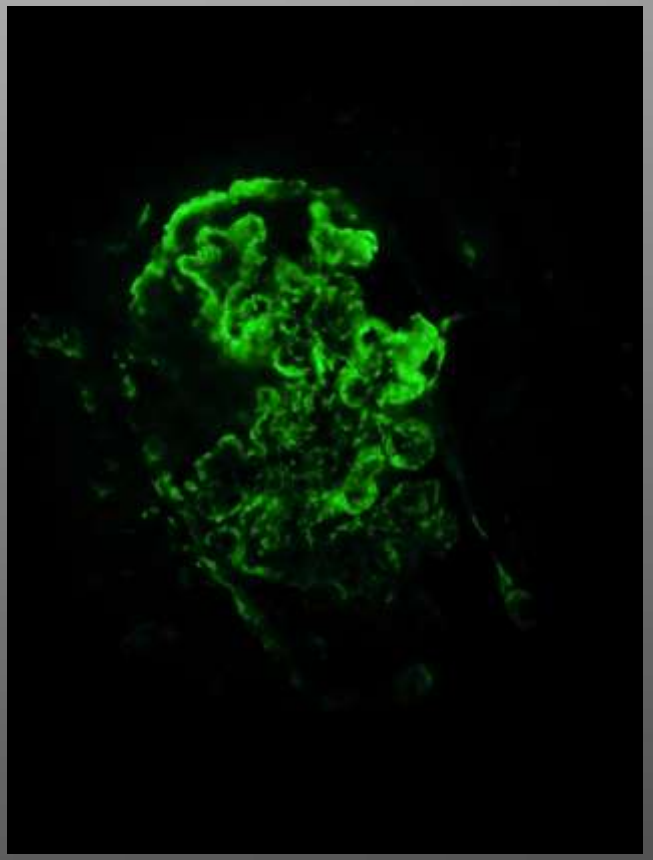

Trichrome

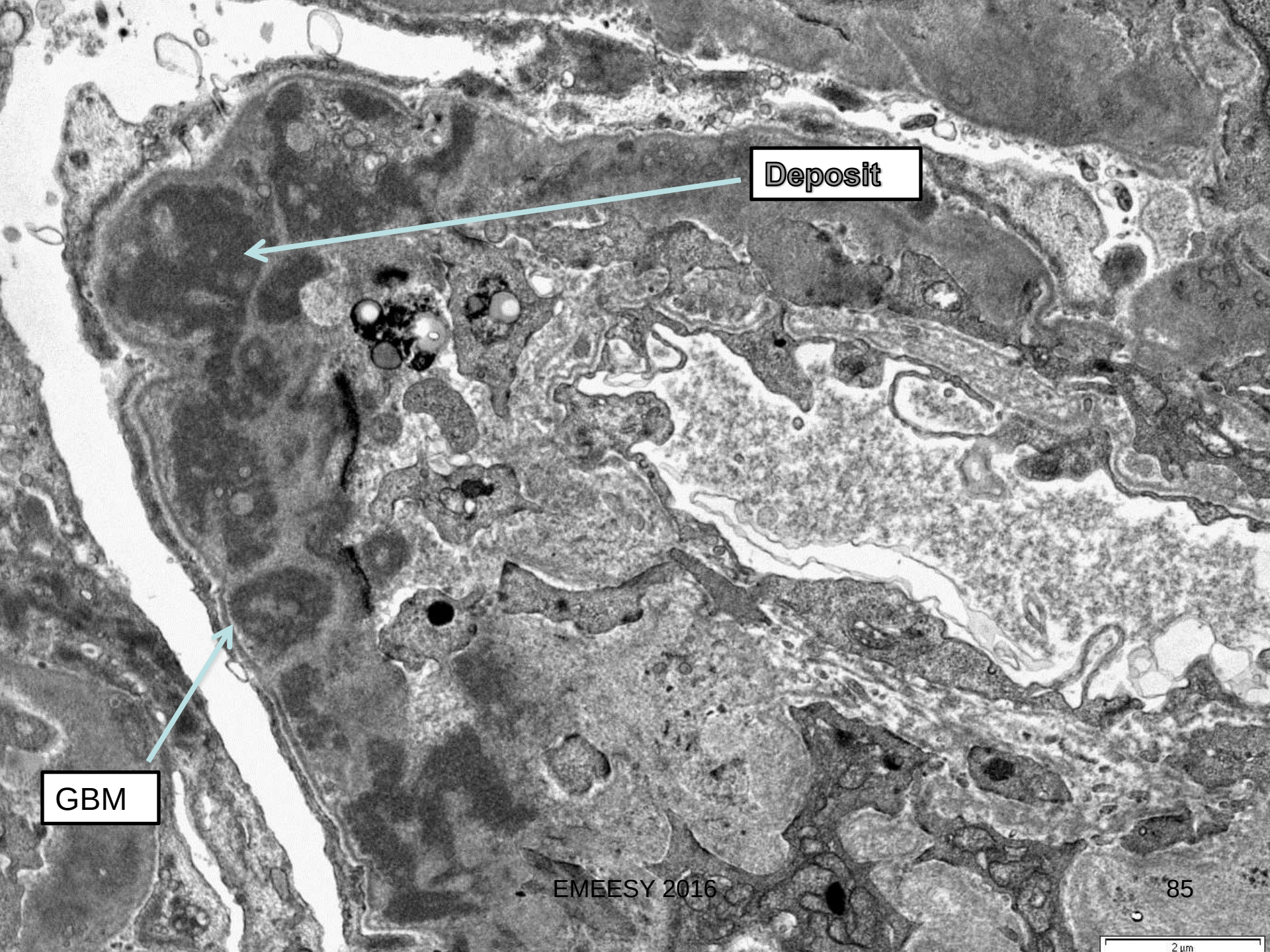

C3

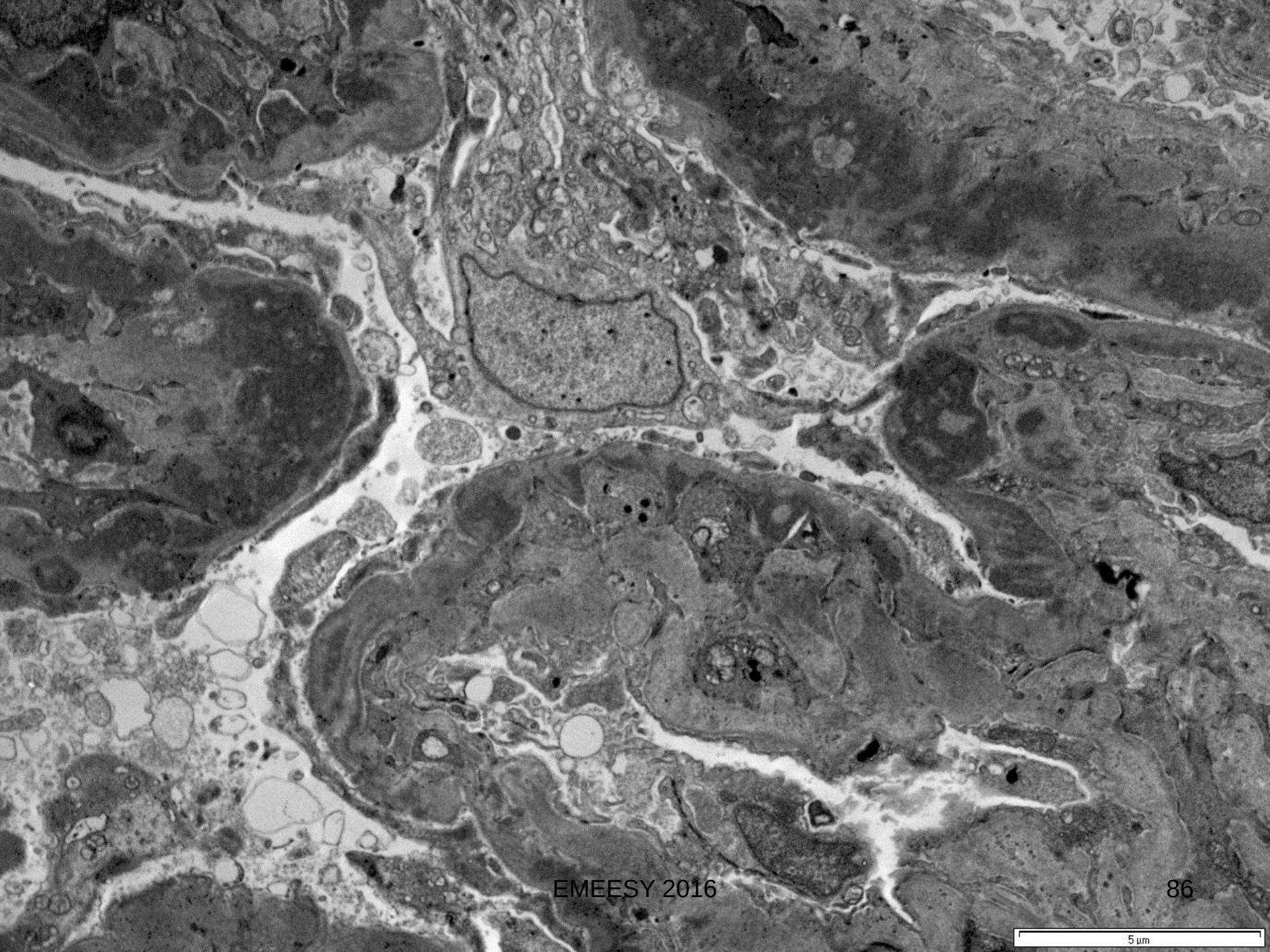
IgG



C3




Deposit
GBM
2 µm


5 µm

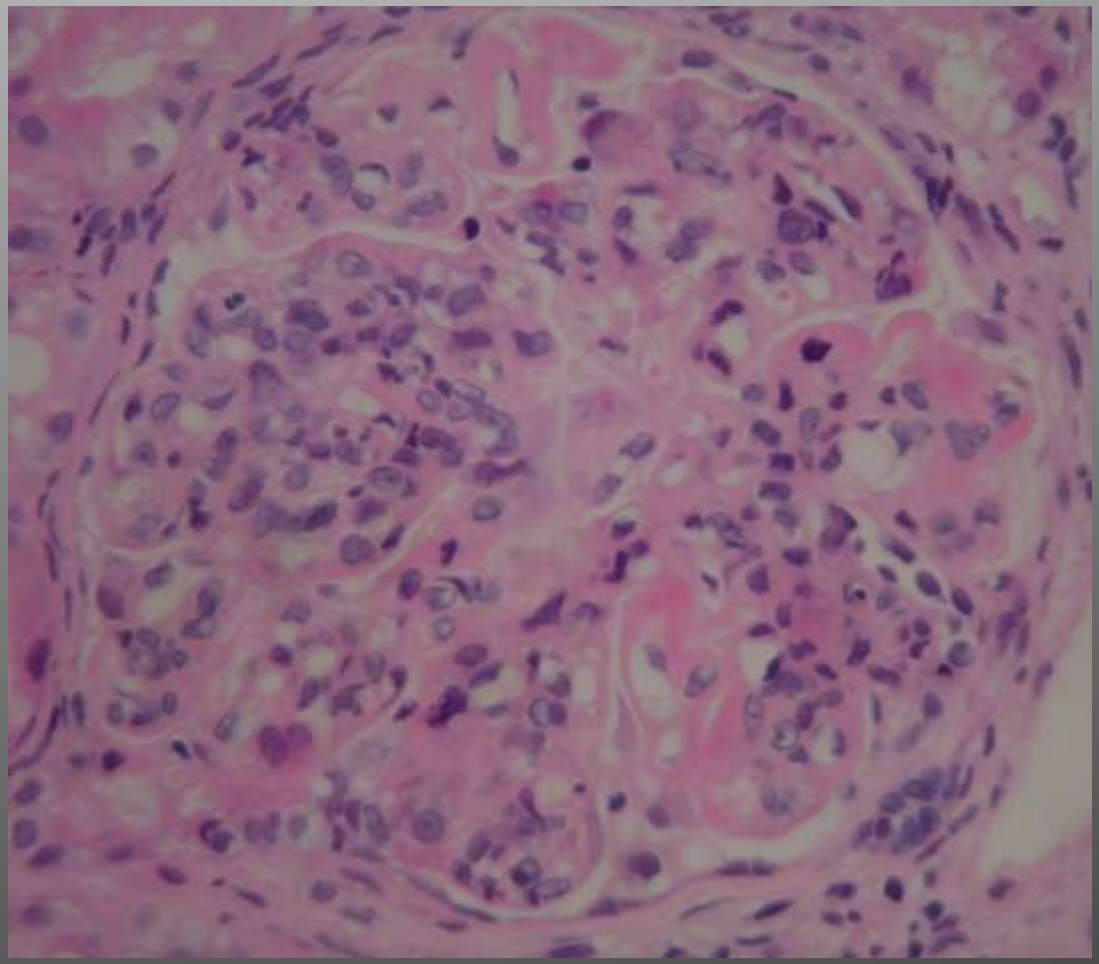
Example 4.

- Hyperlobular glomeruli
- Double contouring on silver
- C3 and IgG aroud loops
- Subendothelial deposit on EM
- Membranoproliferative glomerulonephritis type 1.

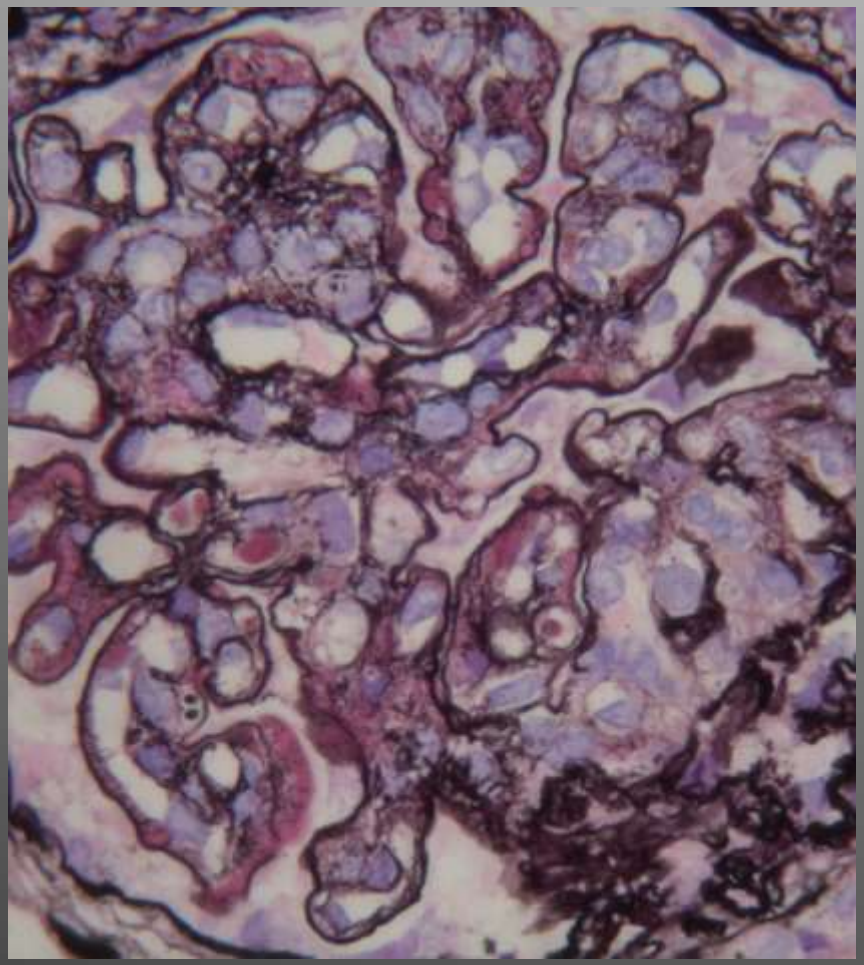

CITY CRUISES

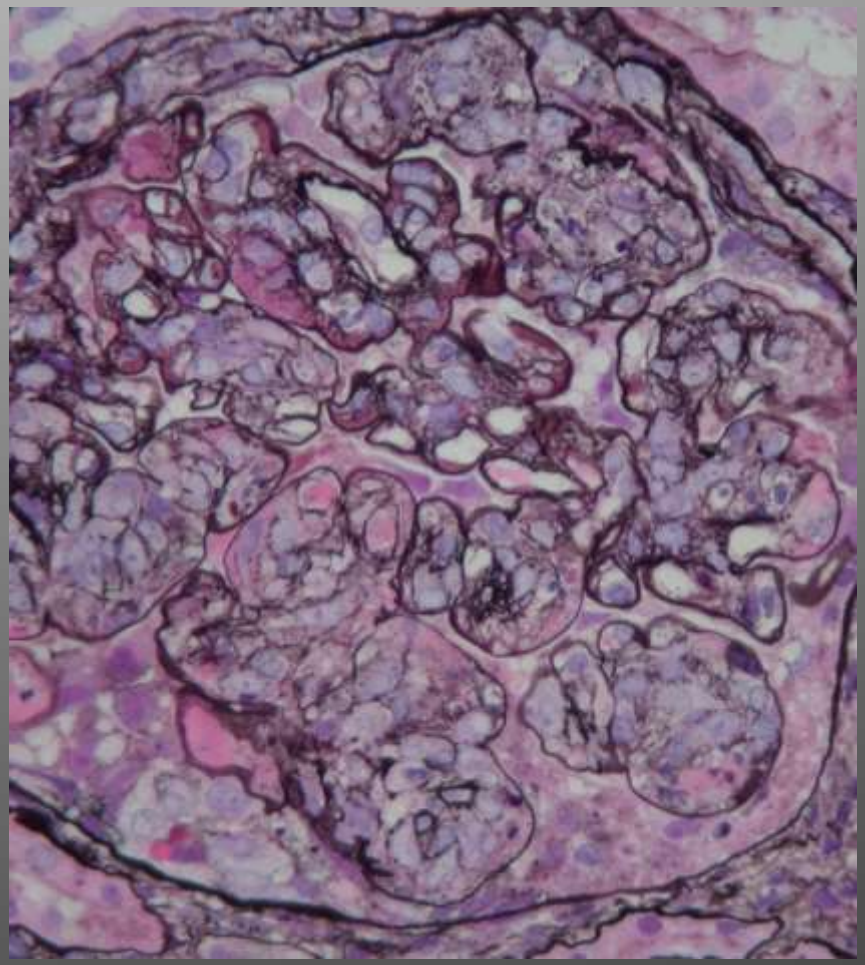
Example 5

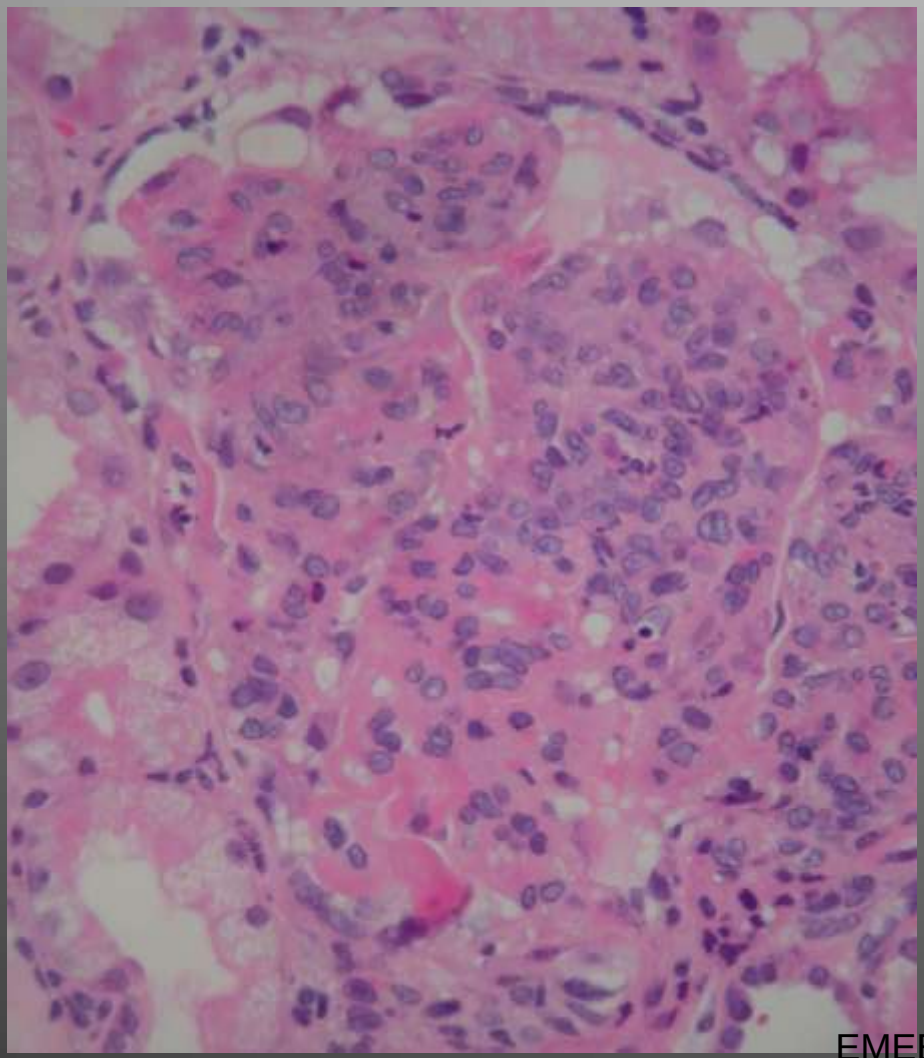
- 33 y female
- Nephrotic
- Active urine sediment
- ANA +ve

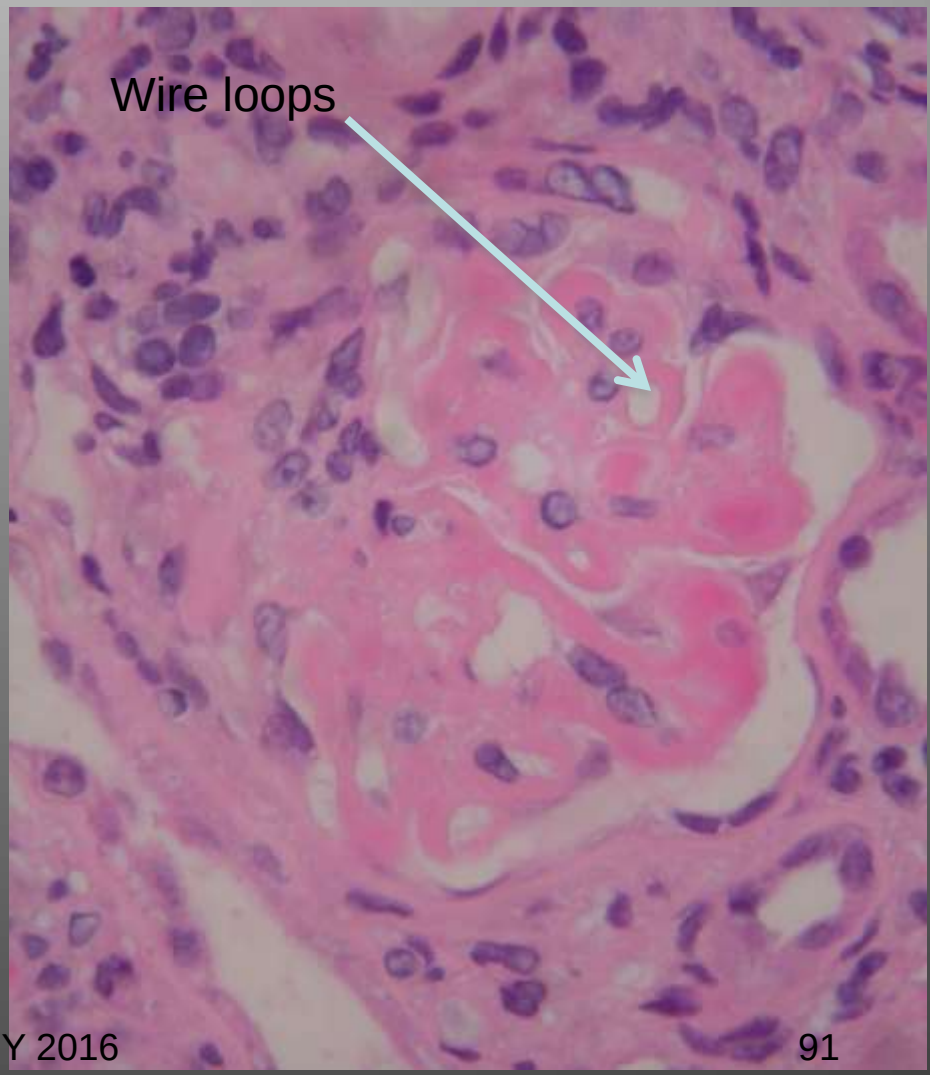


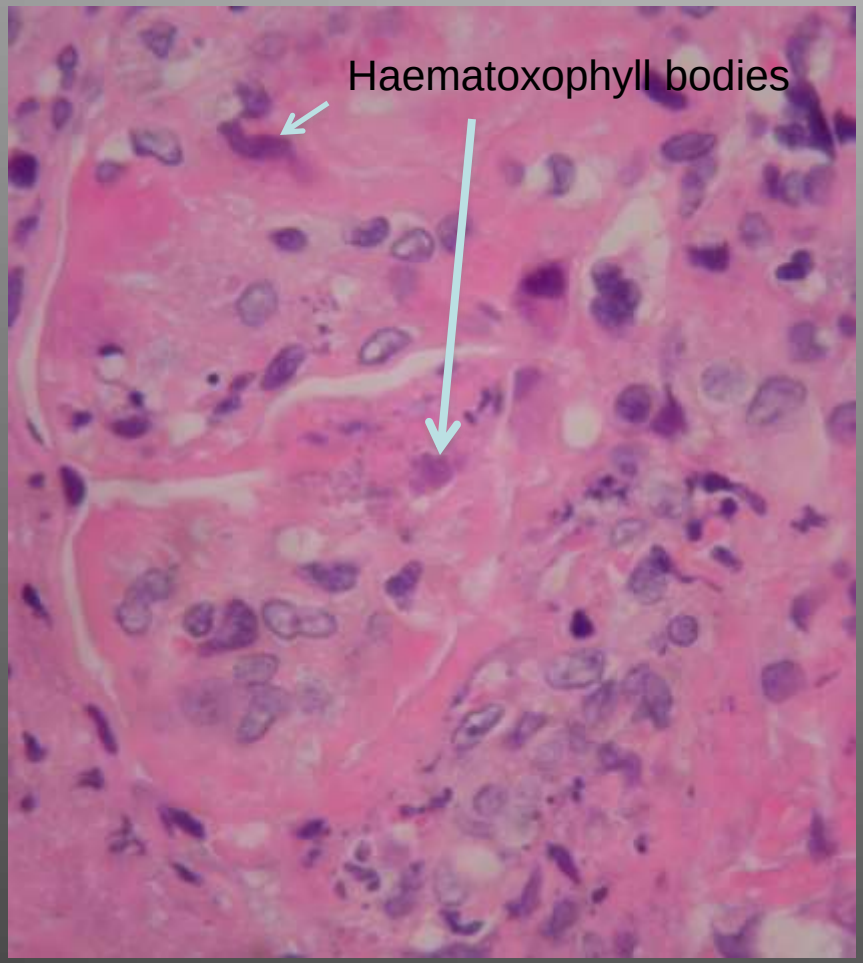
Endocapillary proliferation

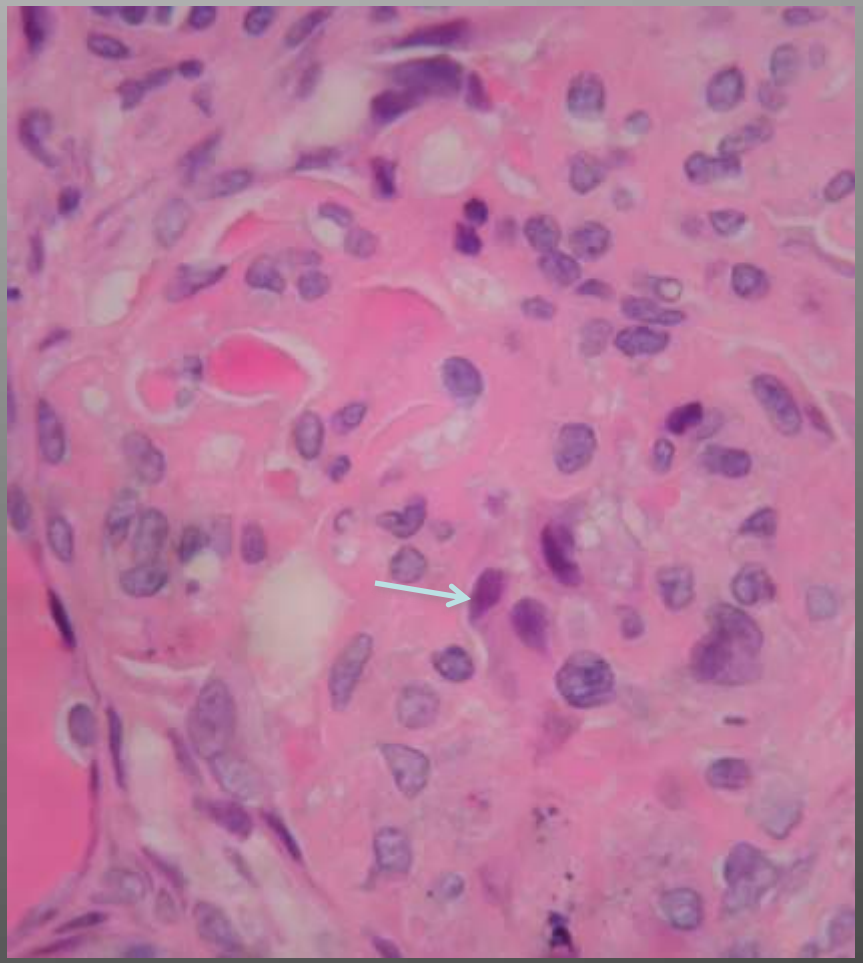




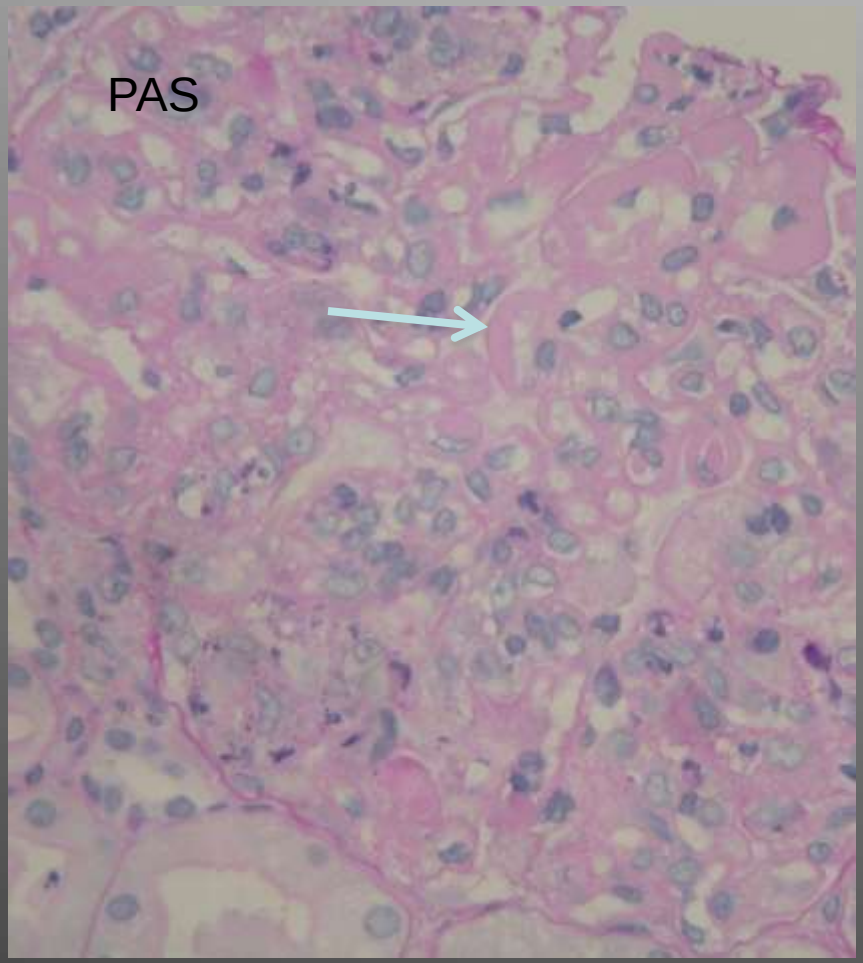


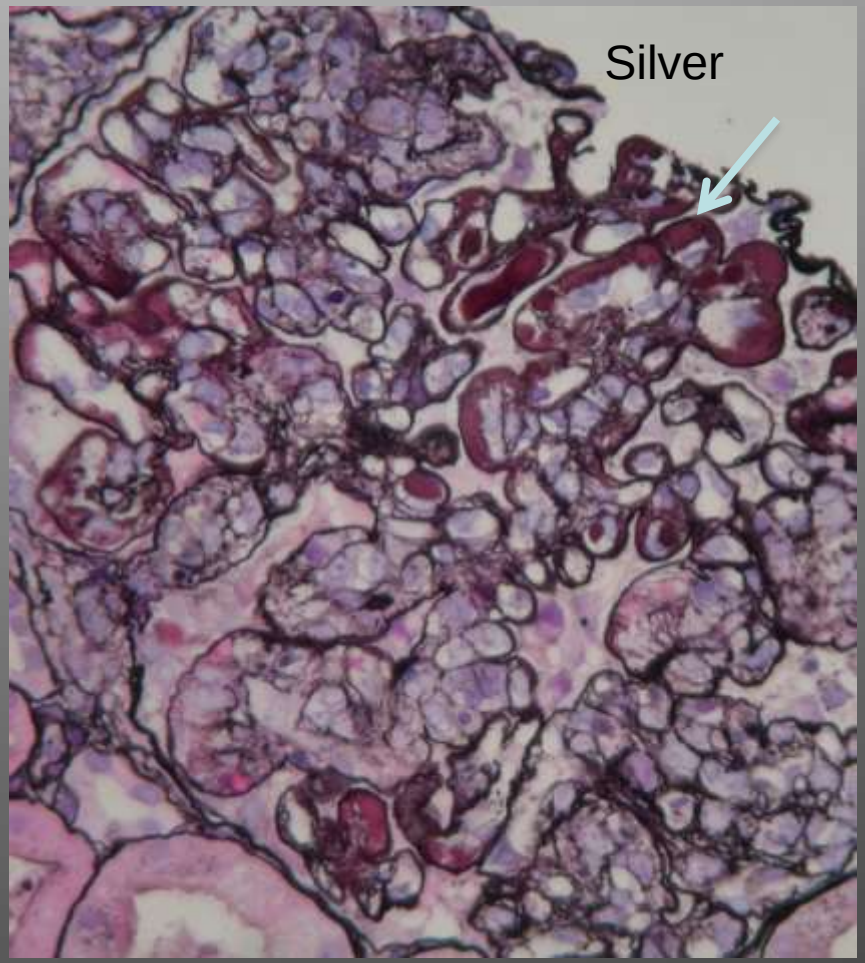

Wire loops


Haematoxophyll bodies

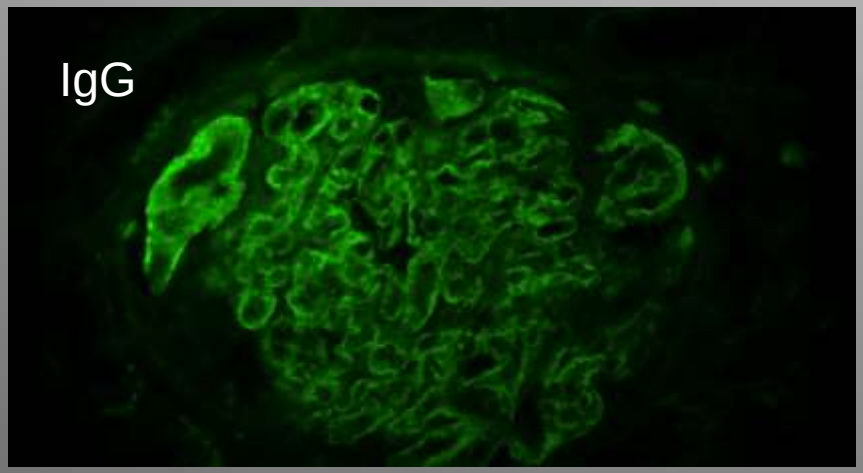


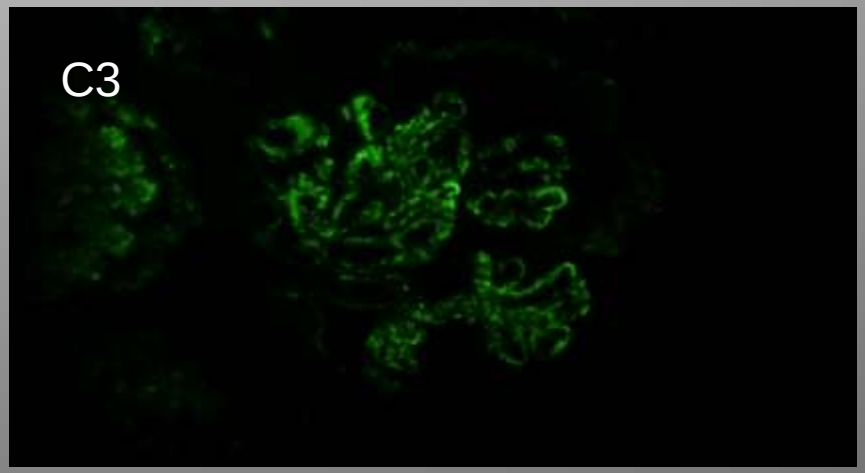
Deposits in loops

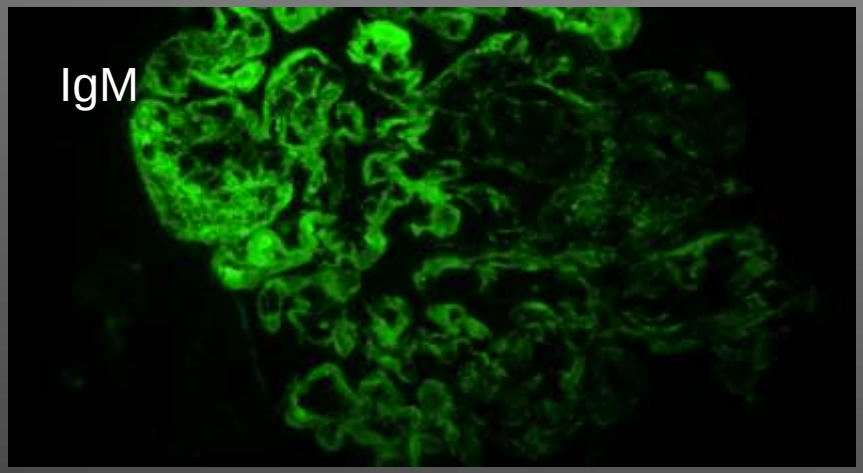


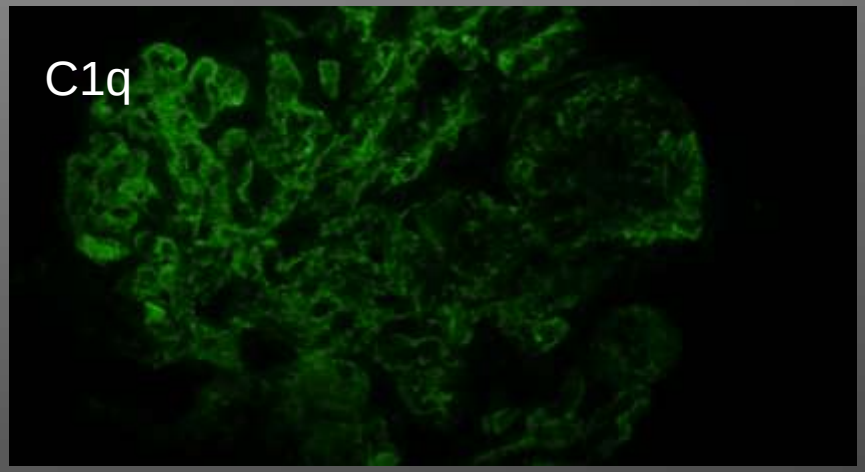


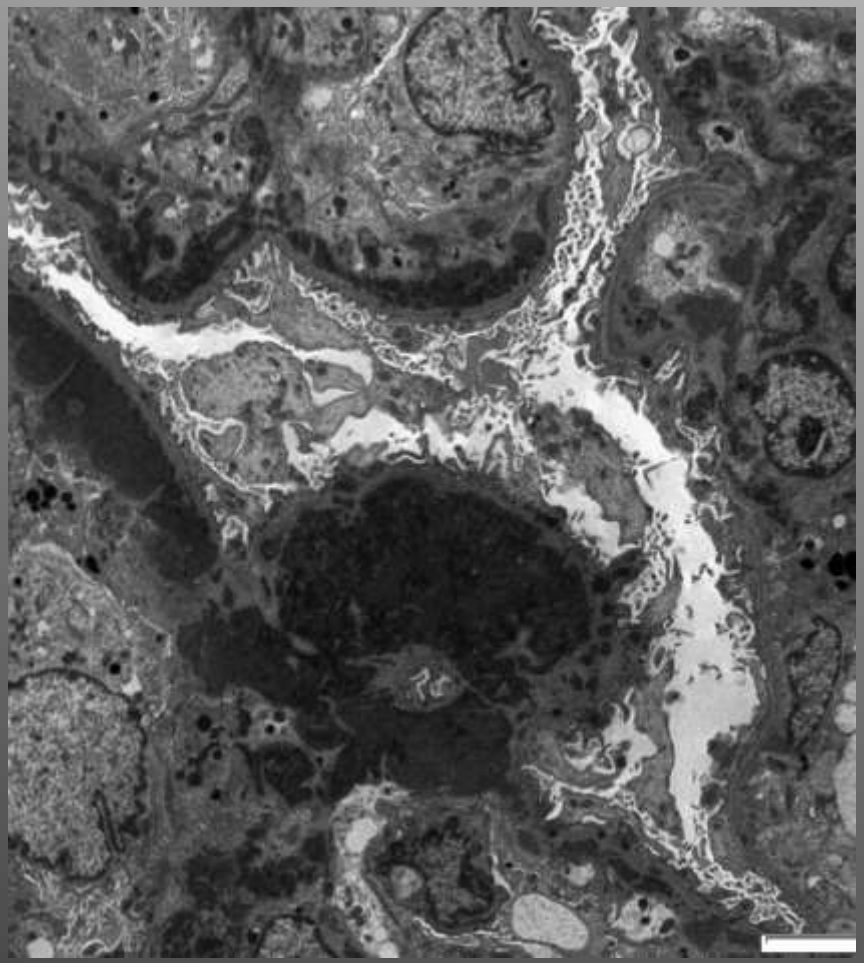
Immunofluorescence

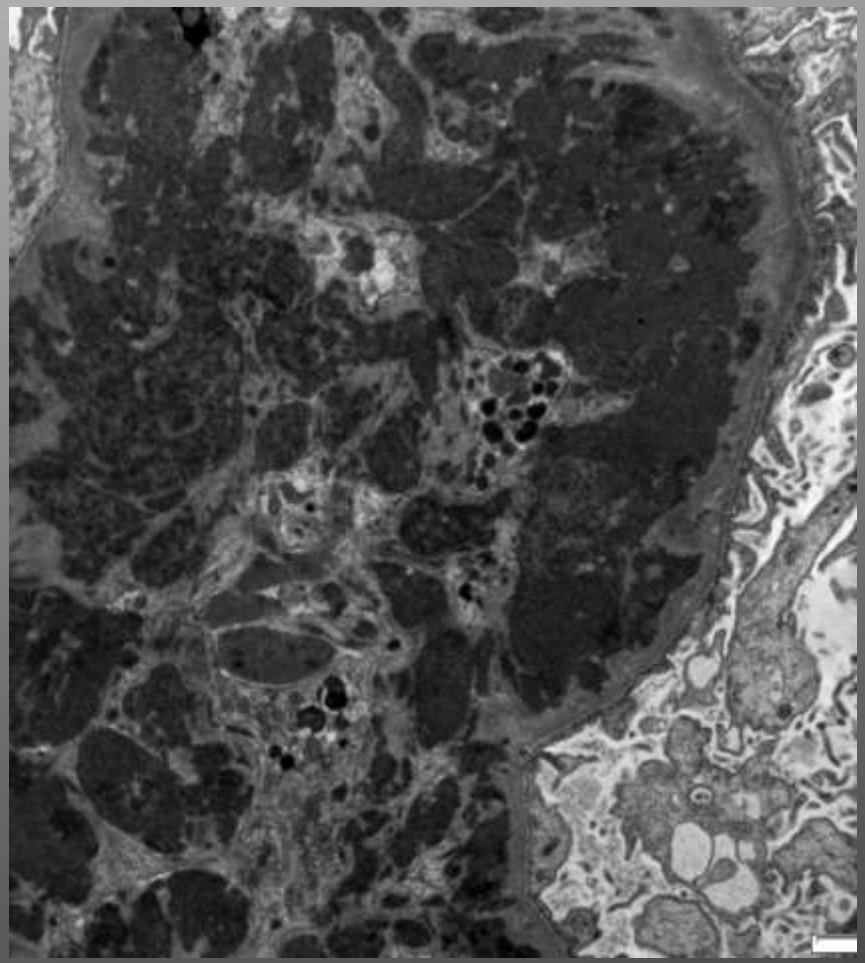












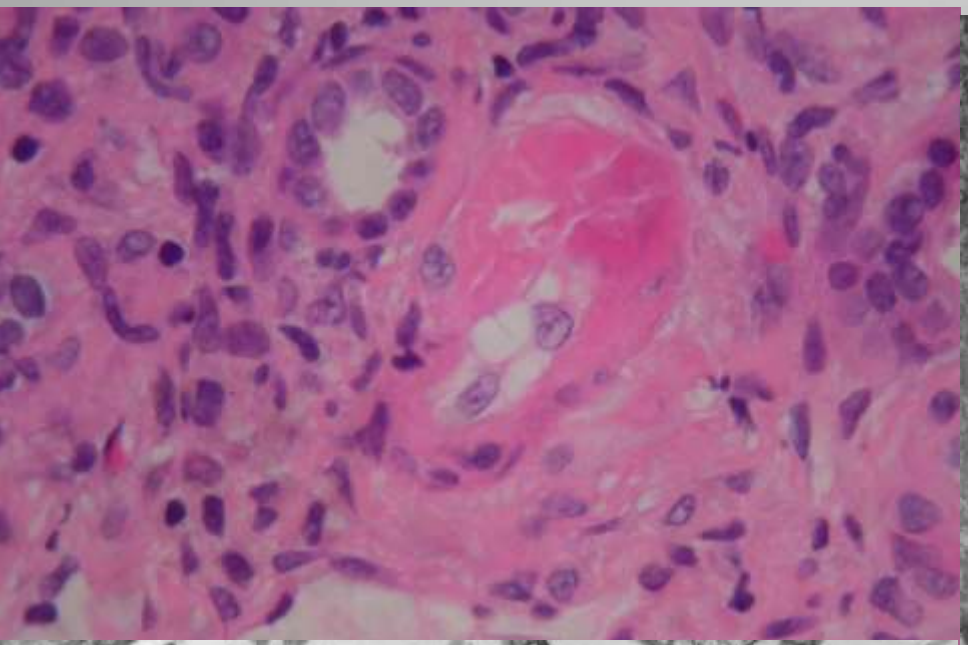
Example 5

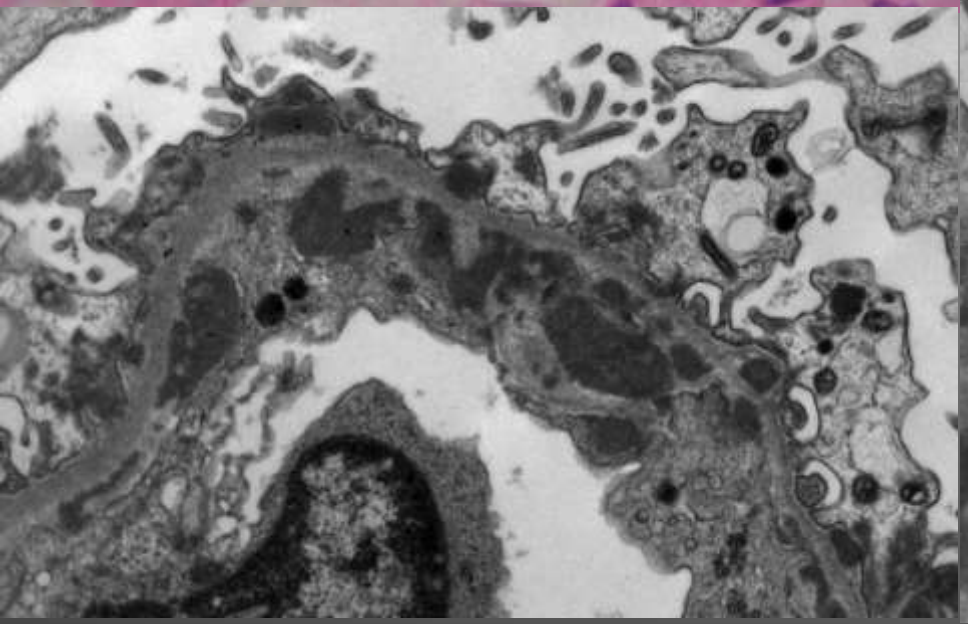
- Immune complex glomerulonephritis
- “Full house” IMF
- Full Monty of morphological features!

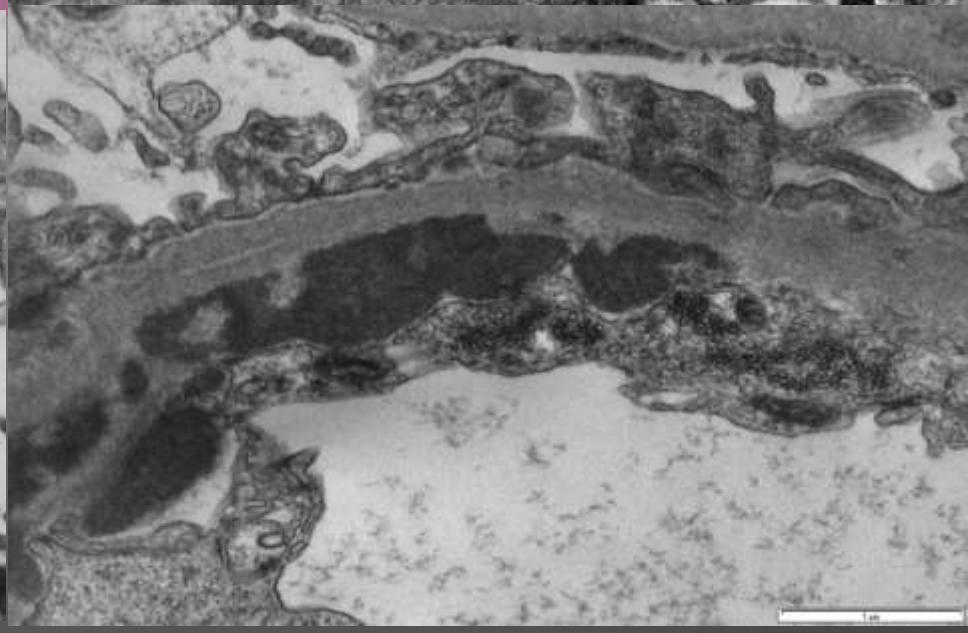
- = Lupus nepritis

- Affects more than 50% of glomeruli
  - All in this case
- Generally the whole glomerulus is affected
  - Global
- It is acute
- No membranous component

- Class IV-G (A)

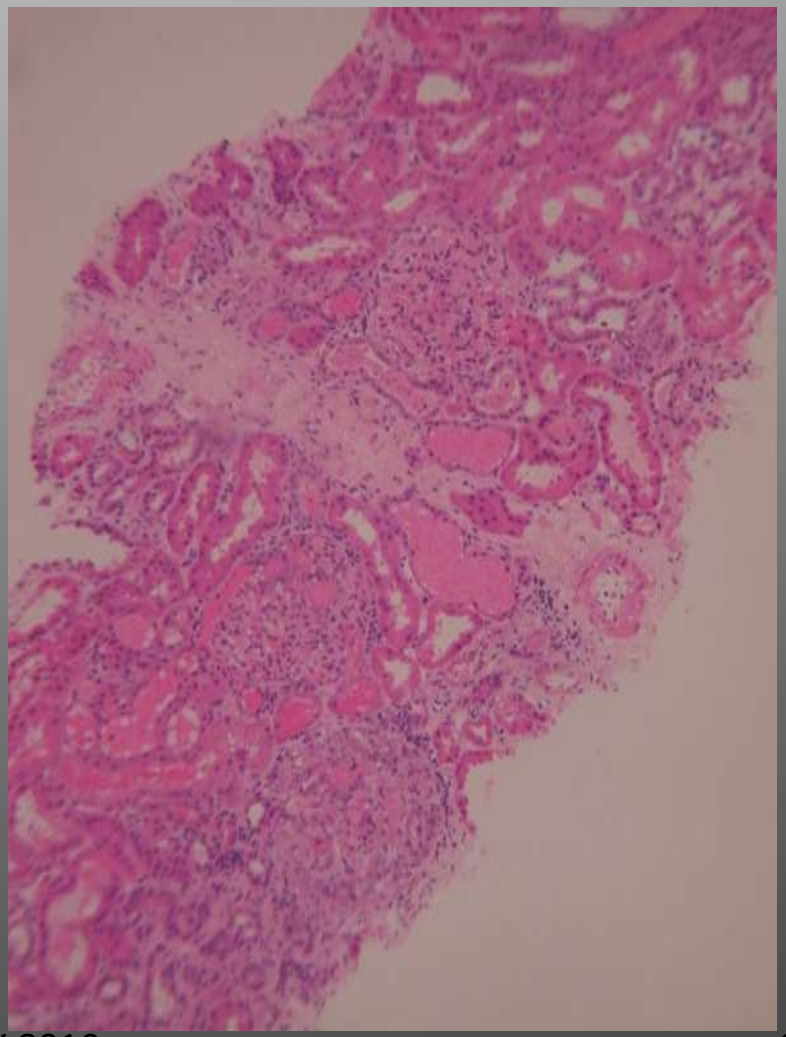


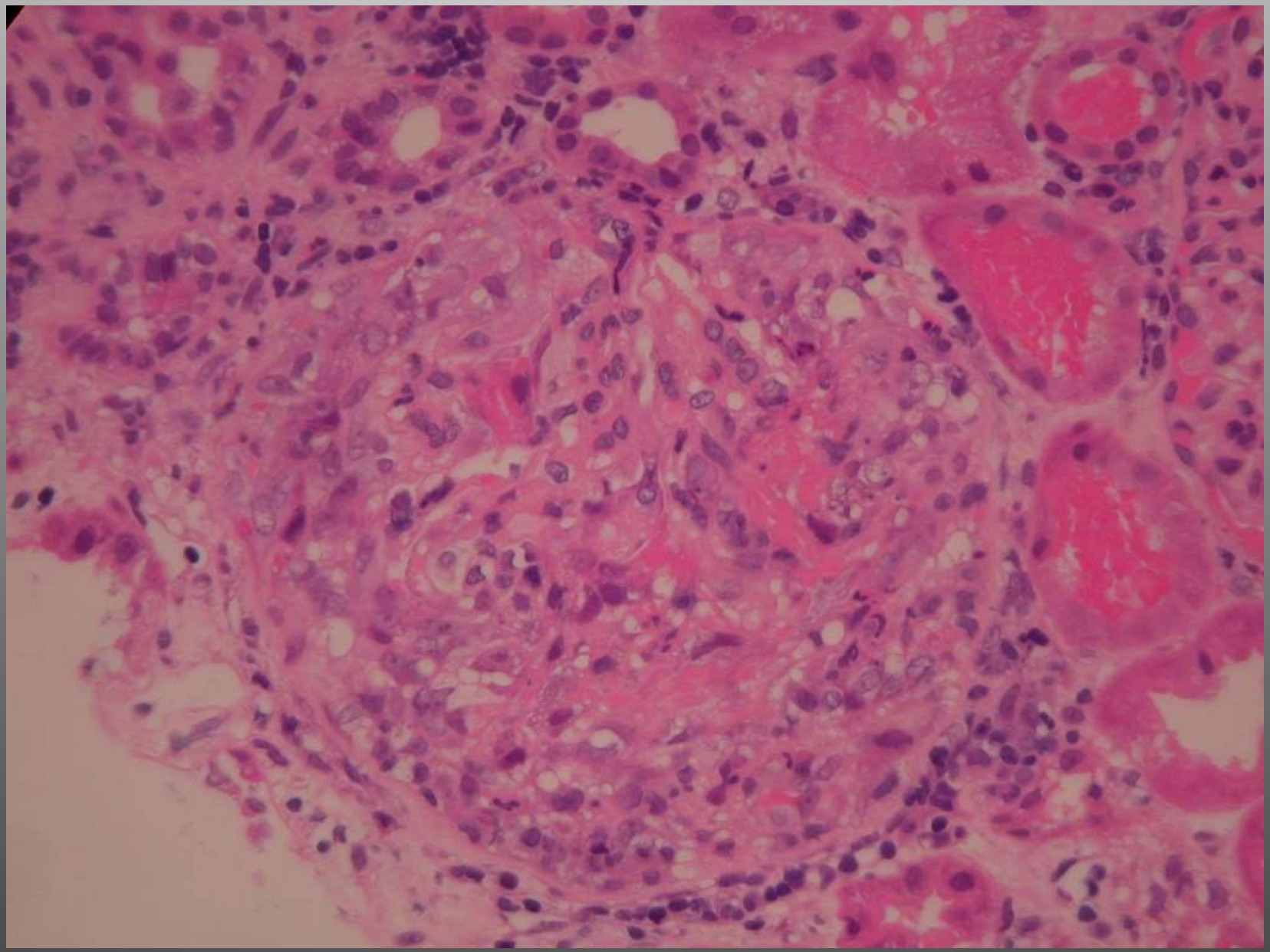


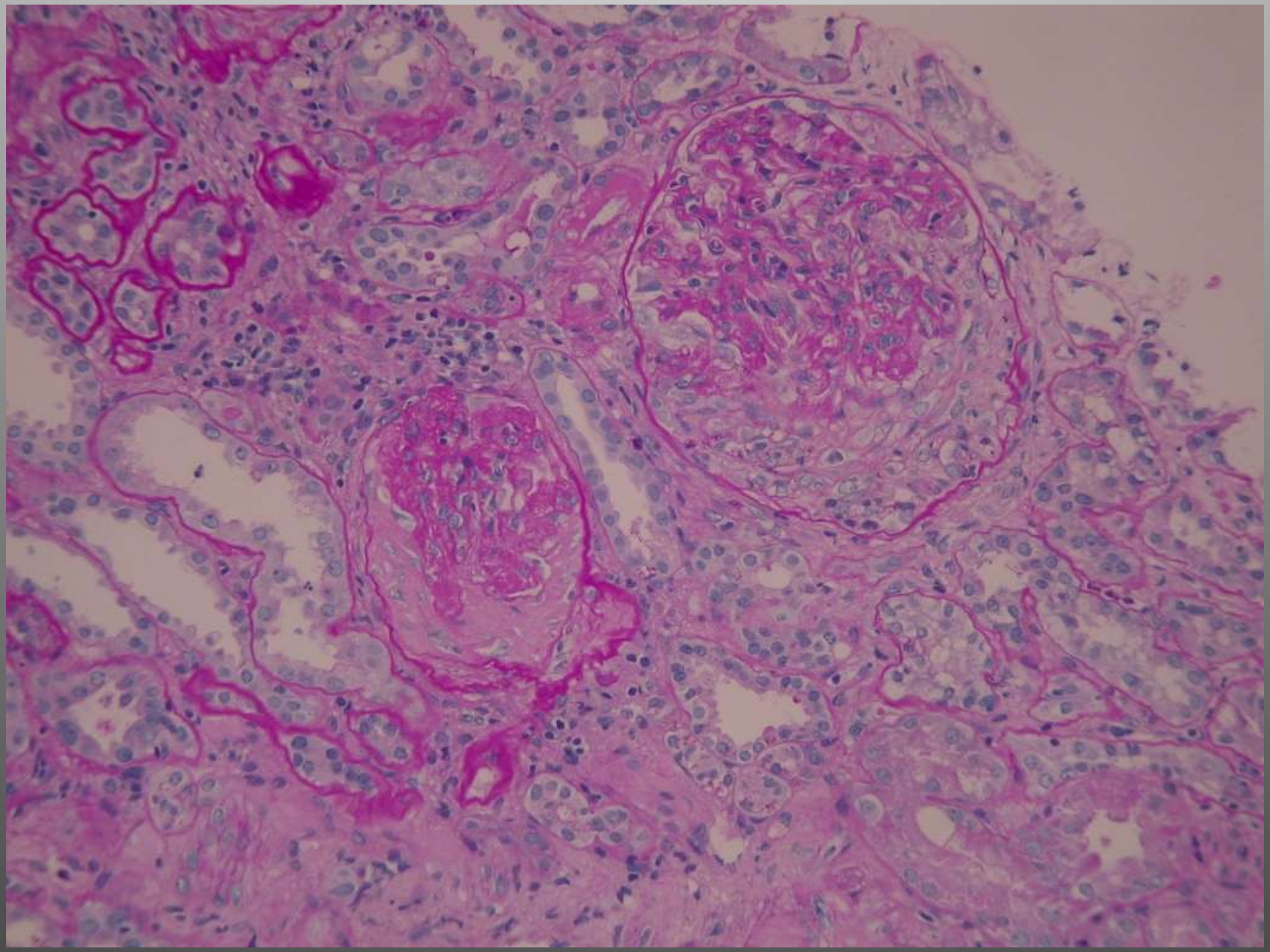


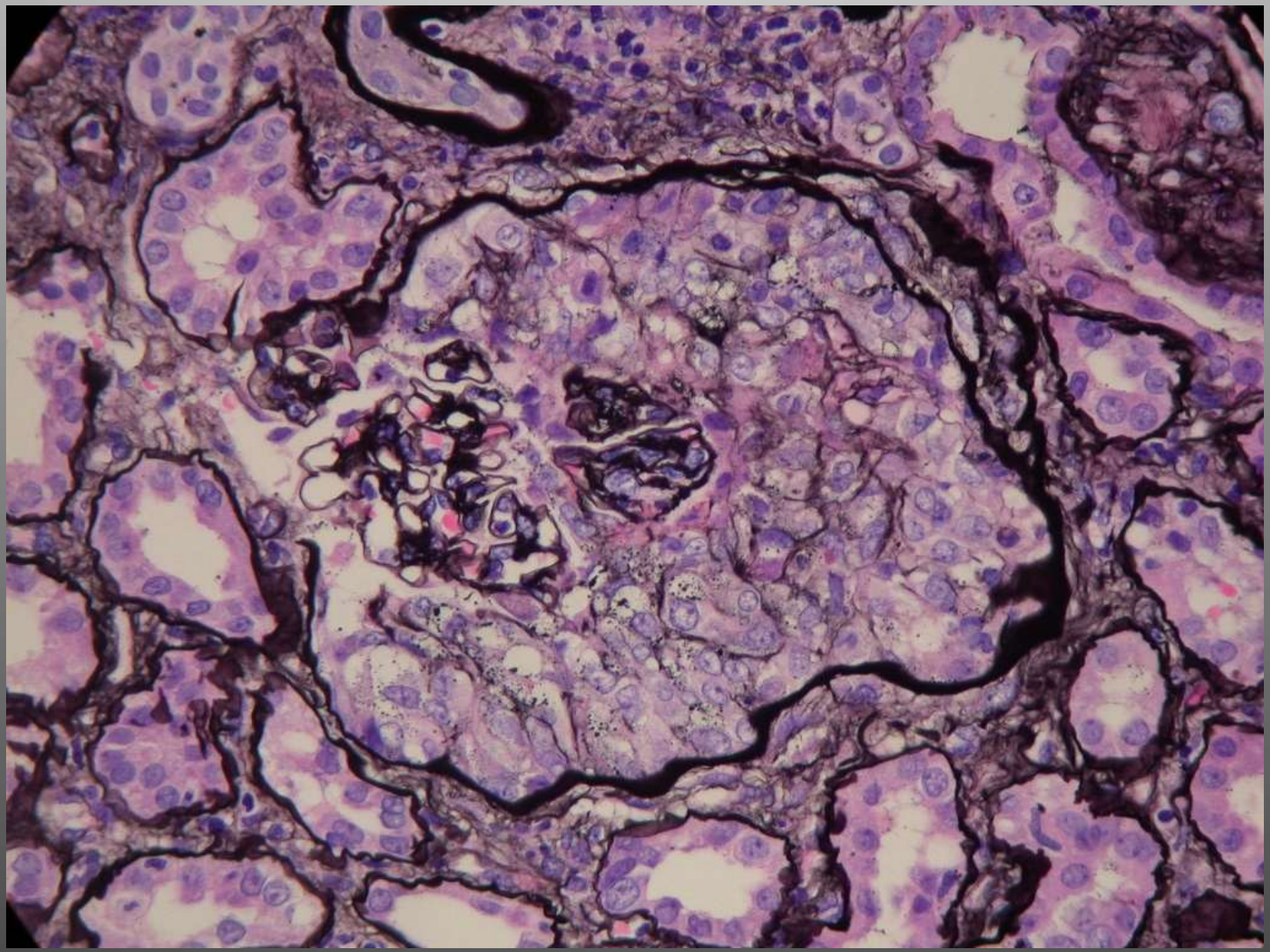
Example 6

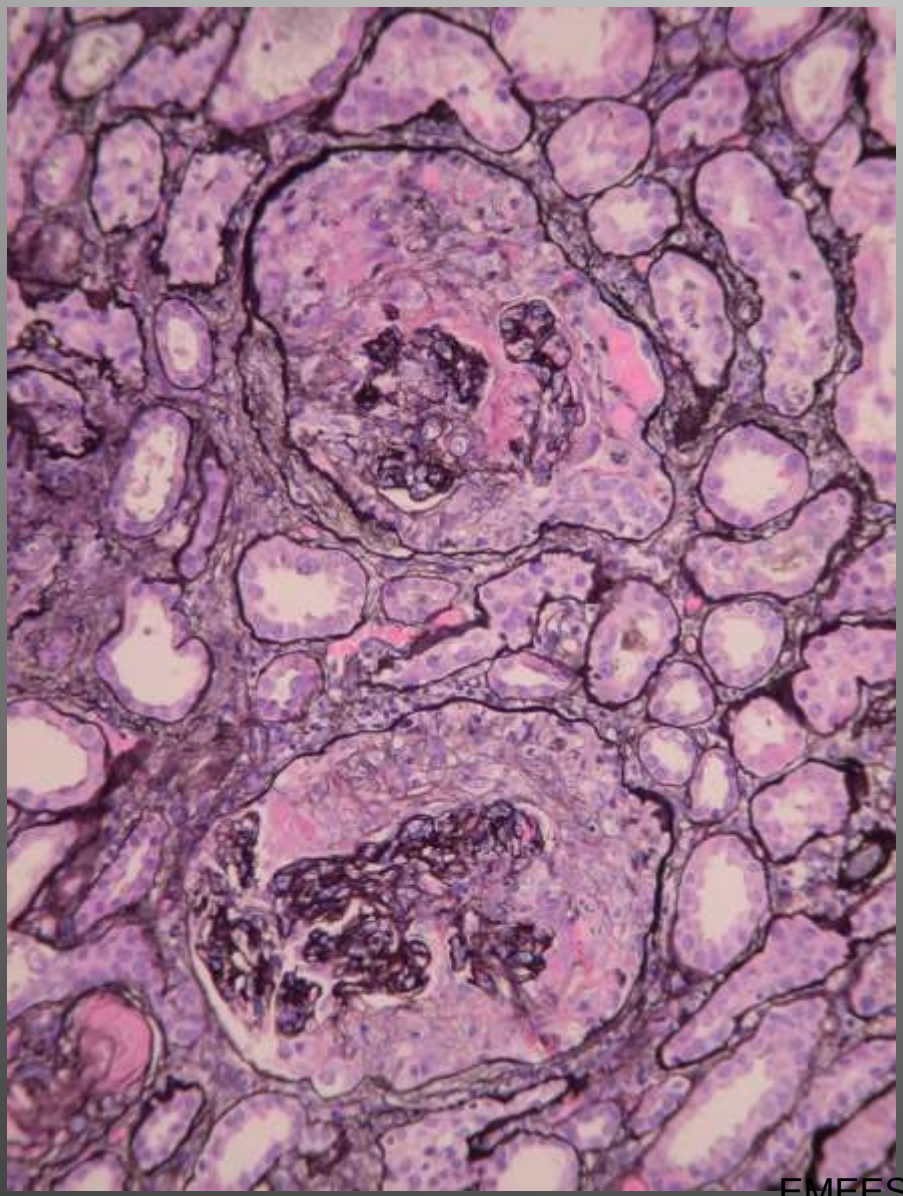
- 78y man
- Unwell for six weeks
- Nasal stuffiness
- Creatinine 600

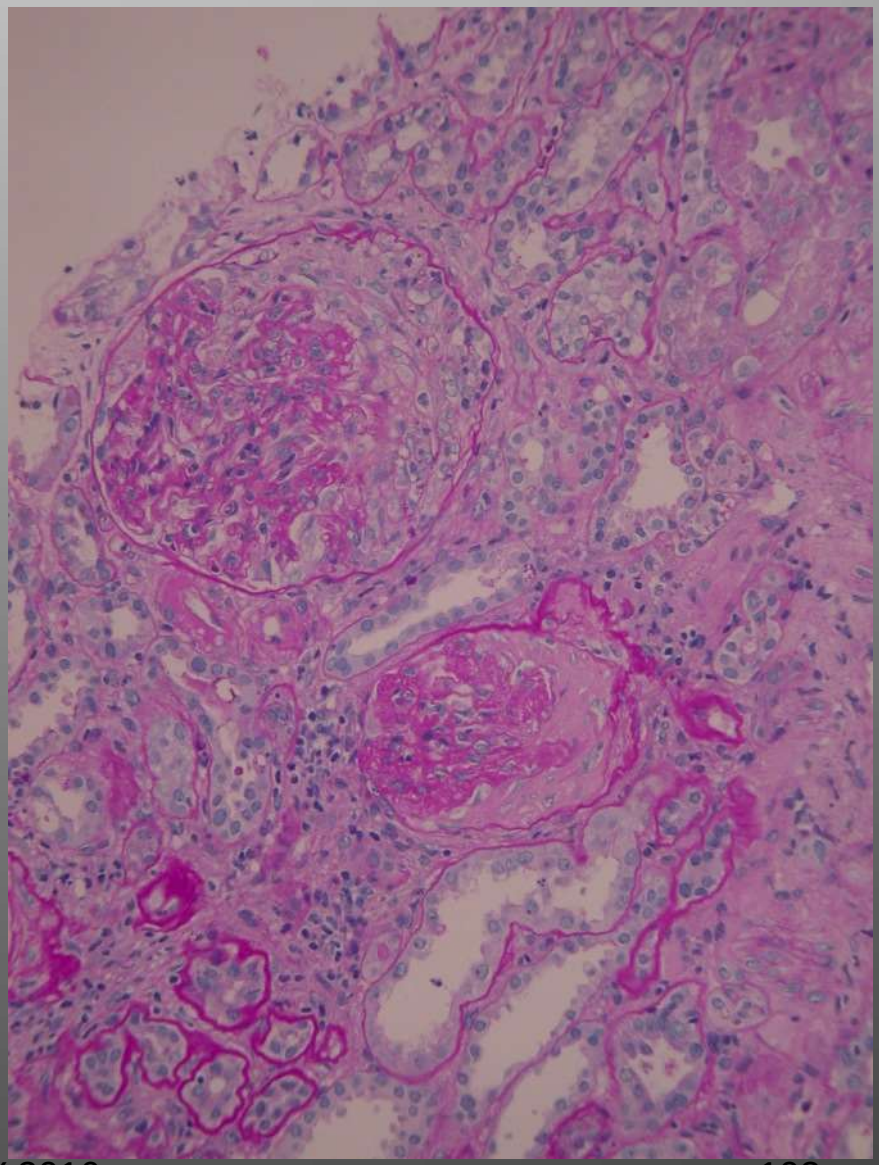


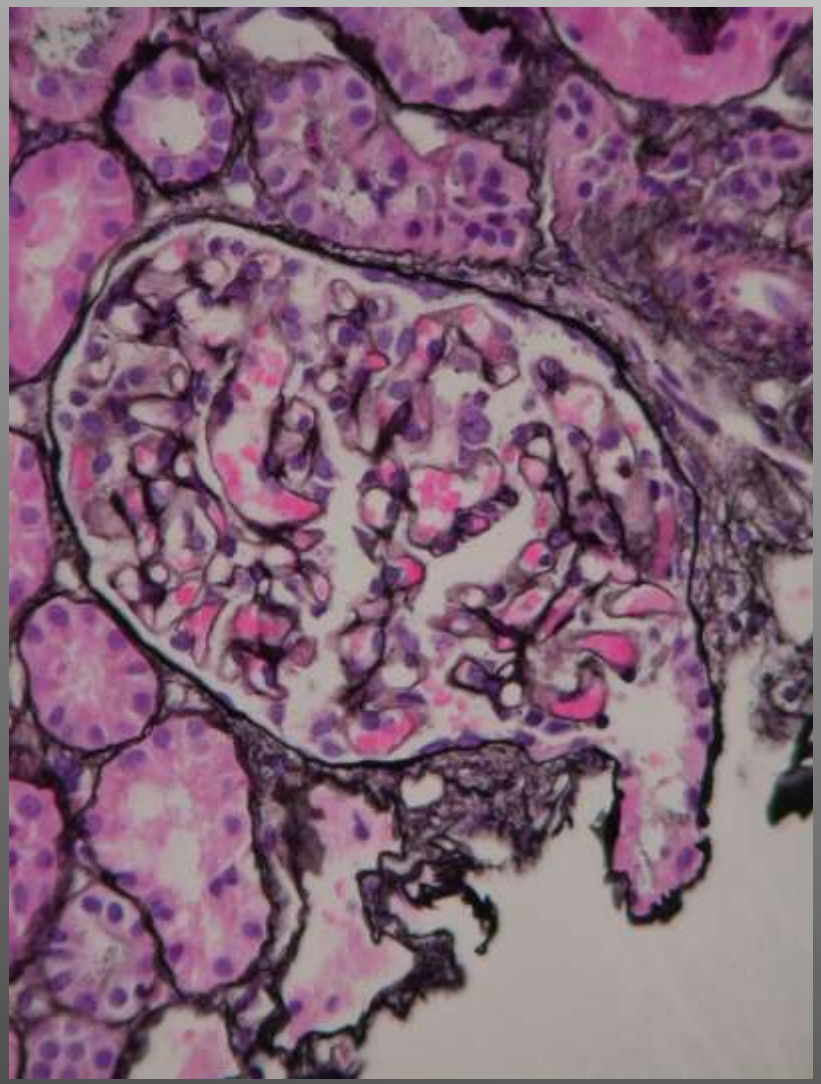


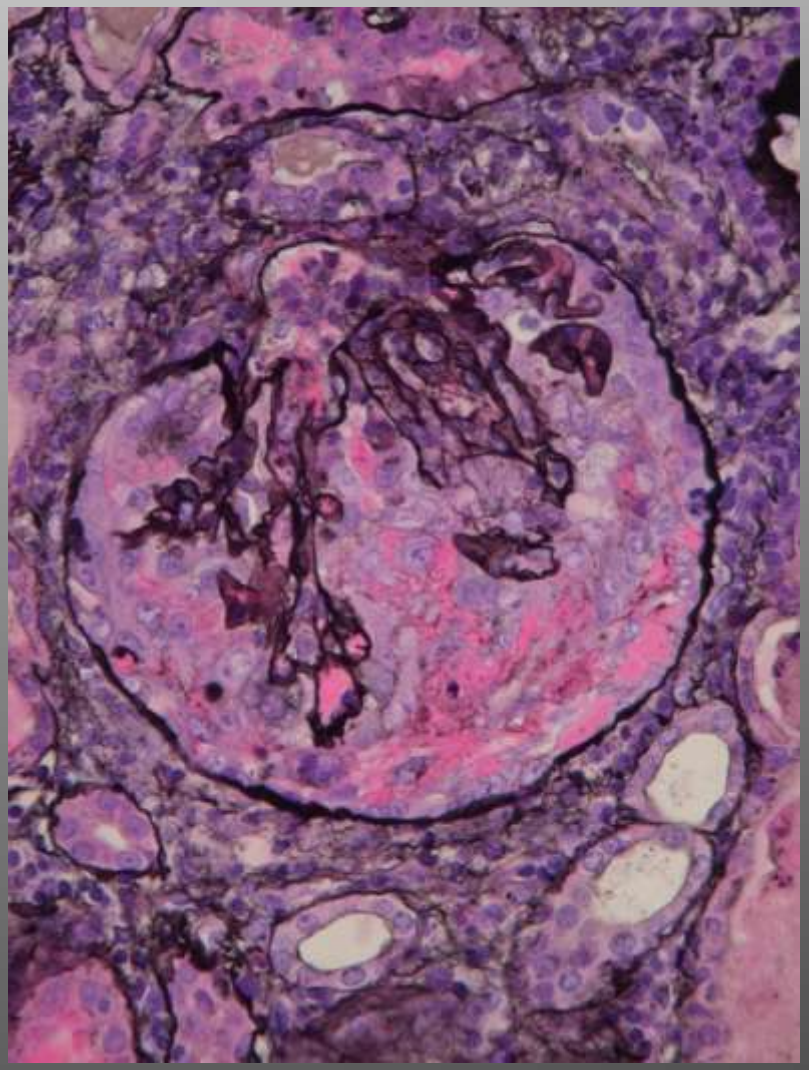


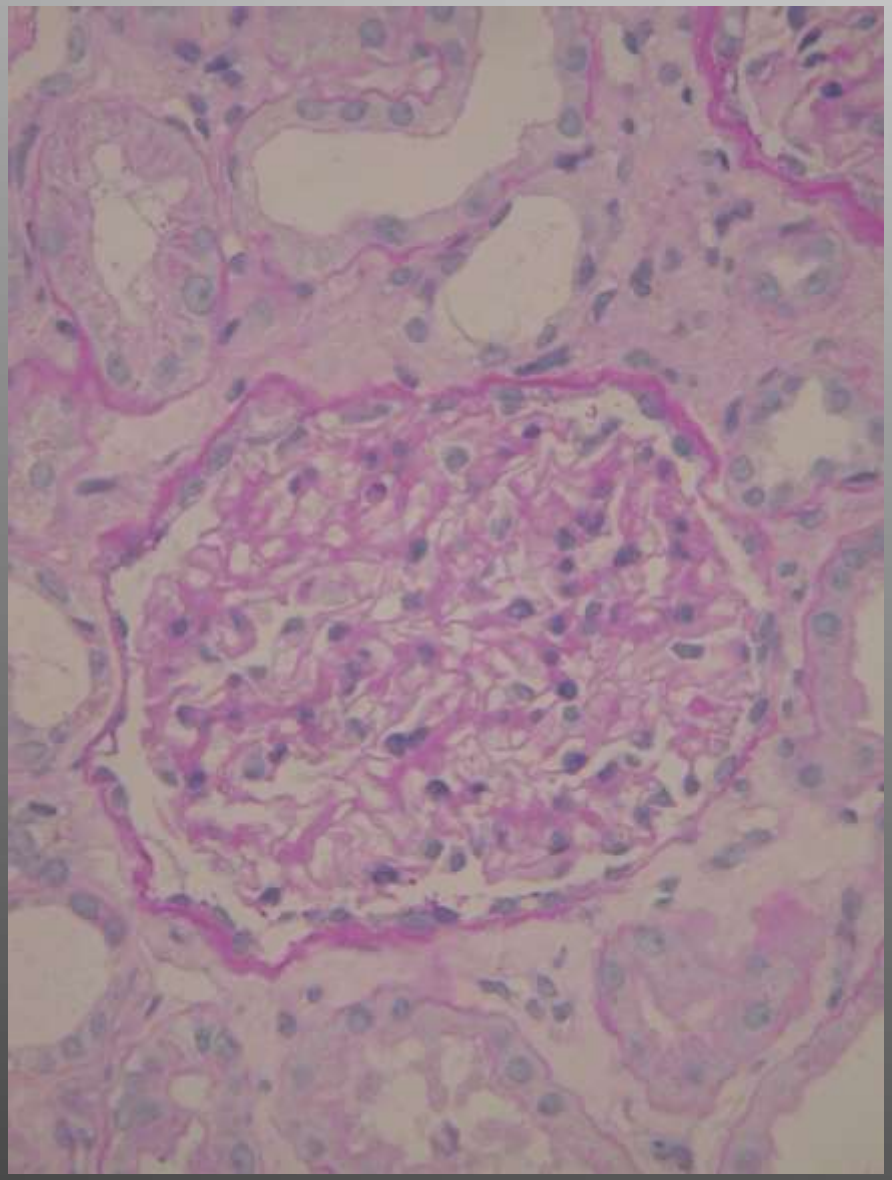


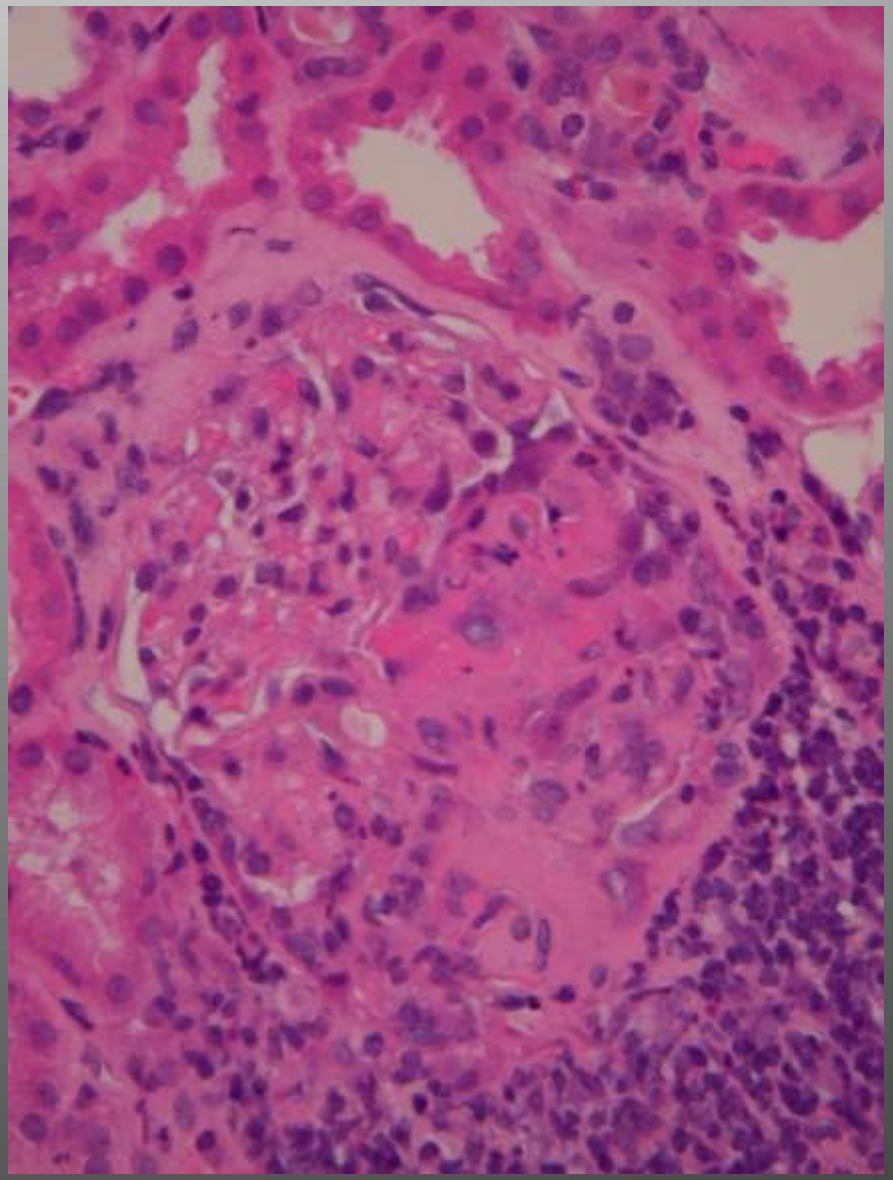


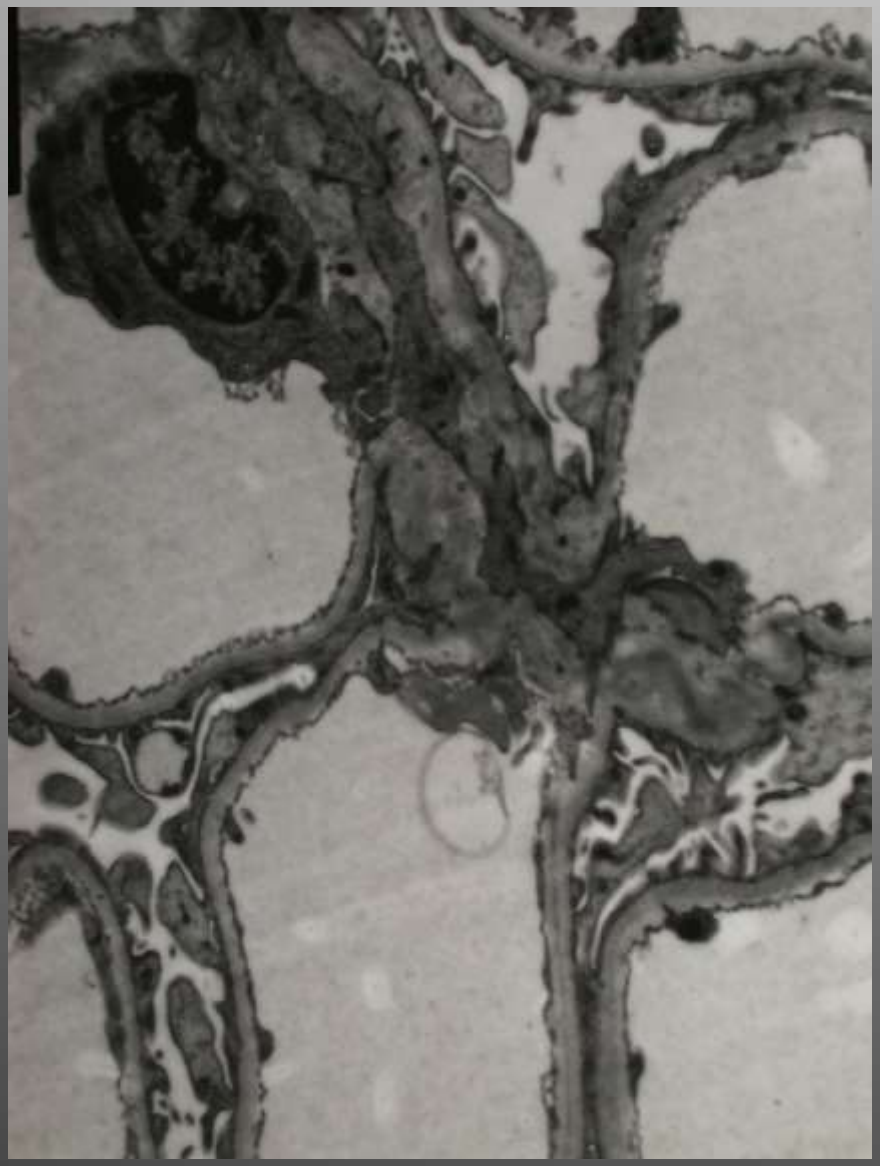


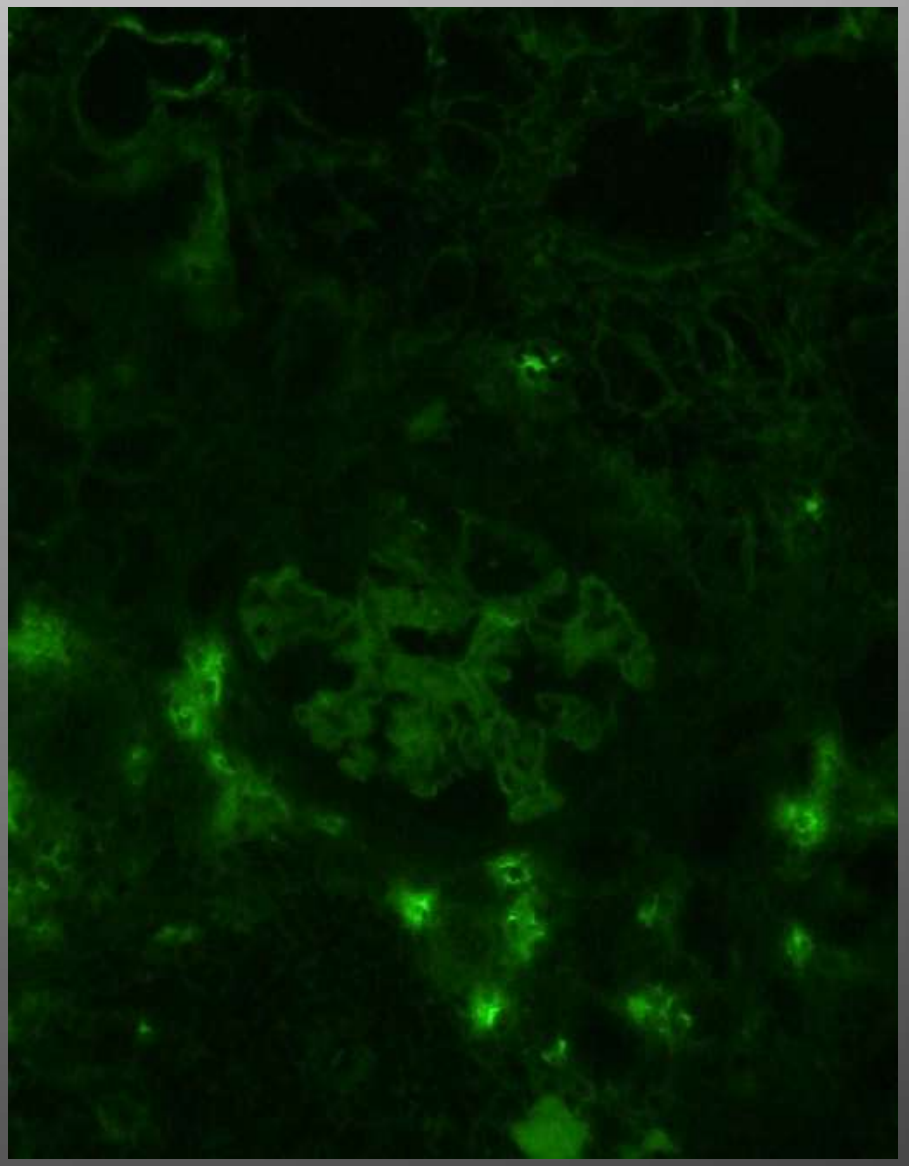






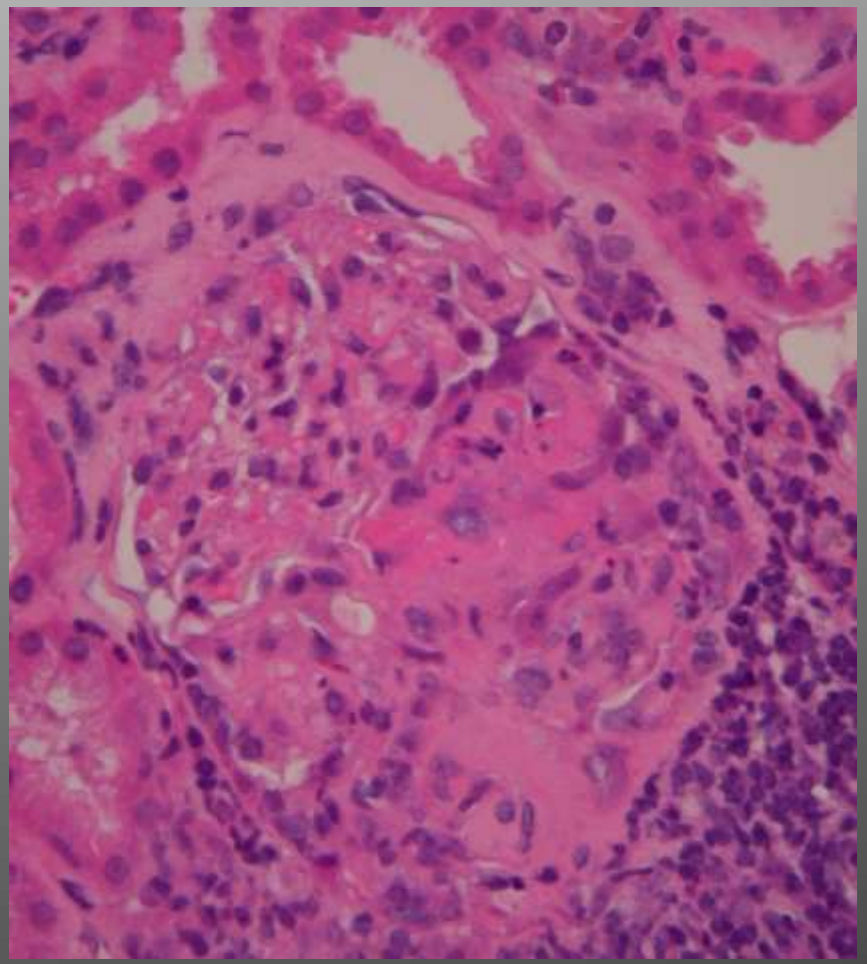




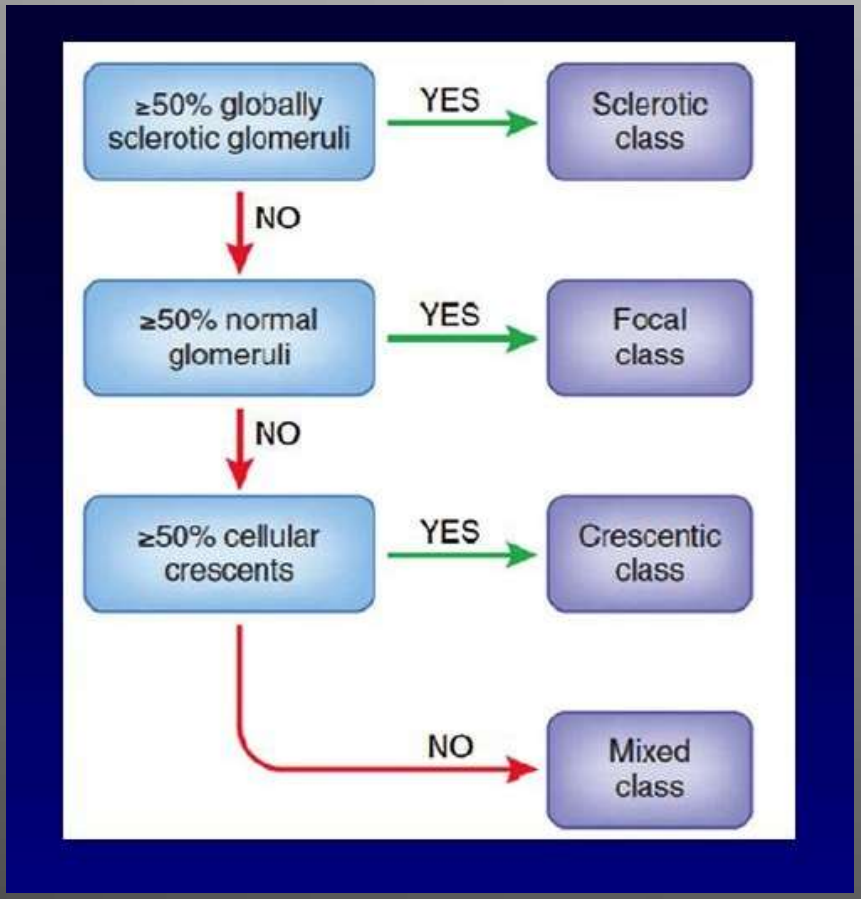


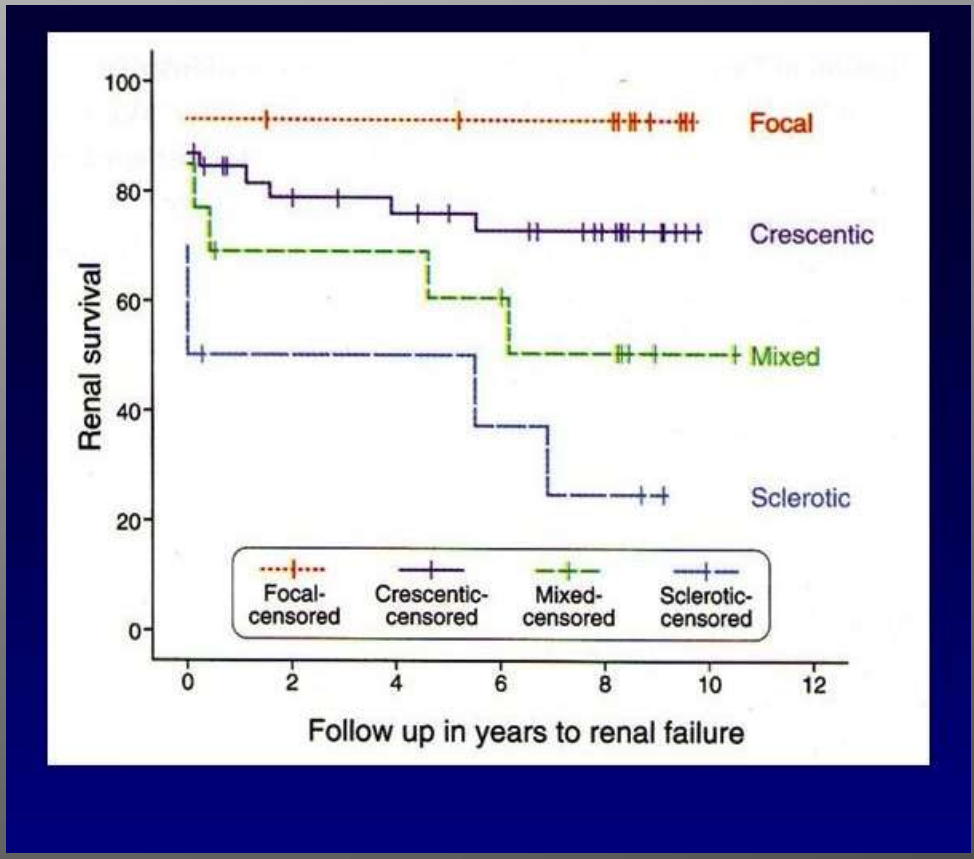
Example 6

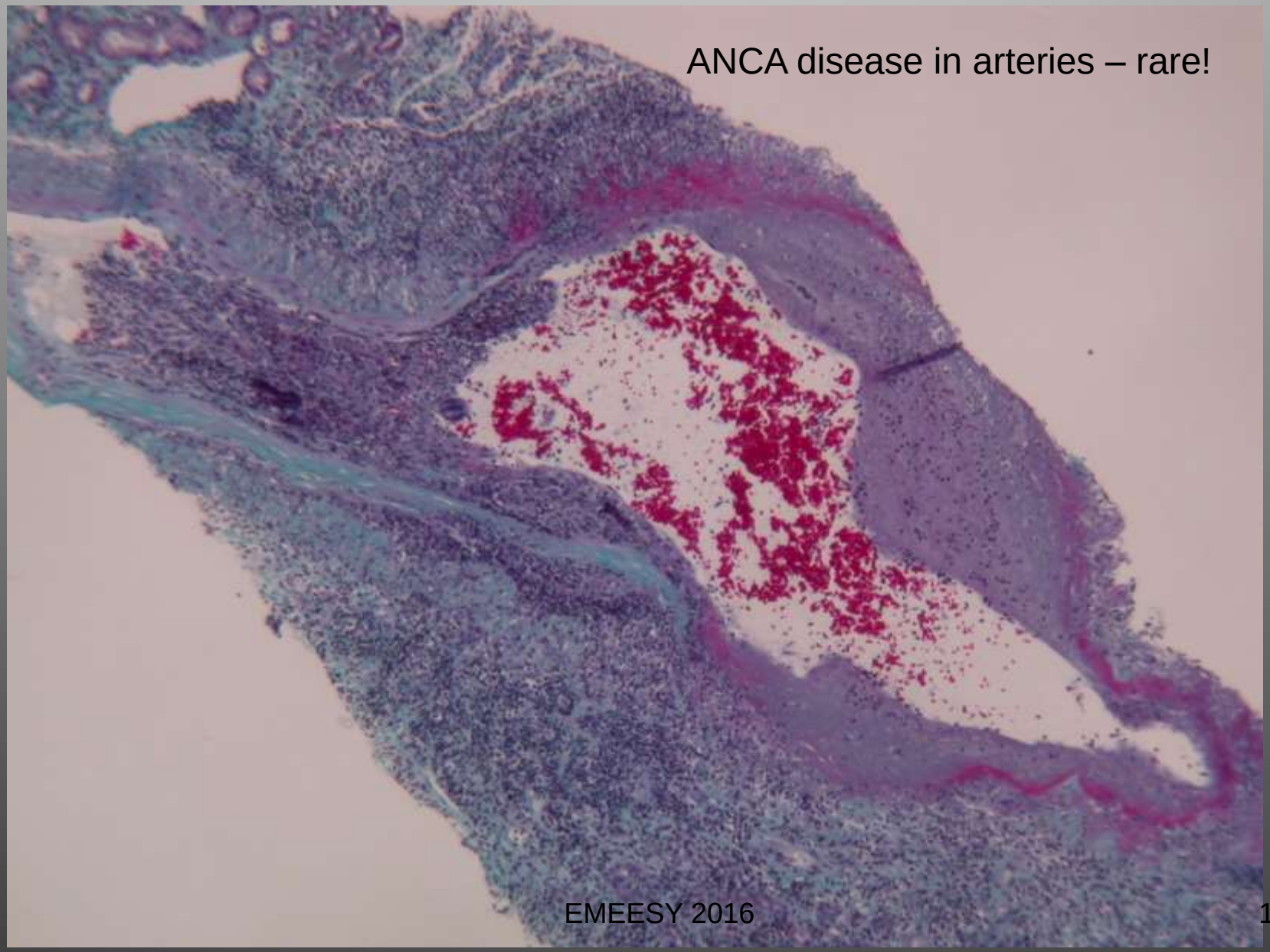
- Focal segmental necrotising glomerulonephritis
- Unaffected glomeruli normal
- No deposits on EM
- Negative immunofluoescence
- (Vasculitis)
- Diagnosis: Pauci-immune (ANCA associated) glomerulonephritis
  - Eg Wegener's granulomatosis



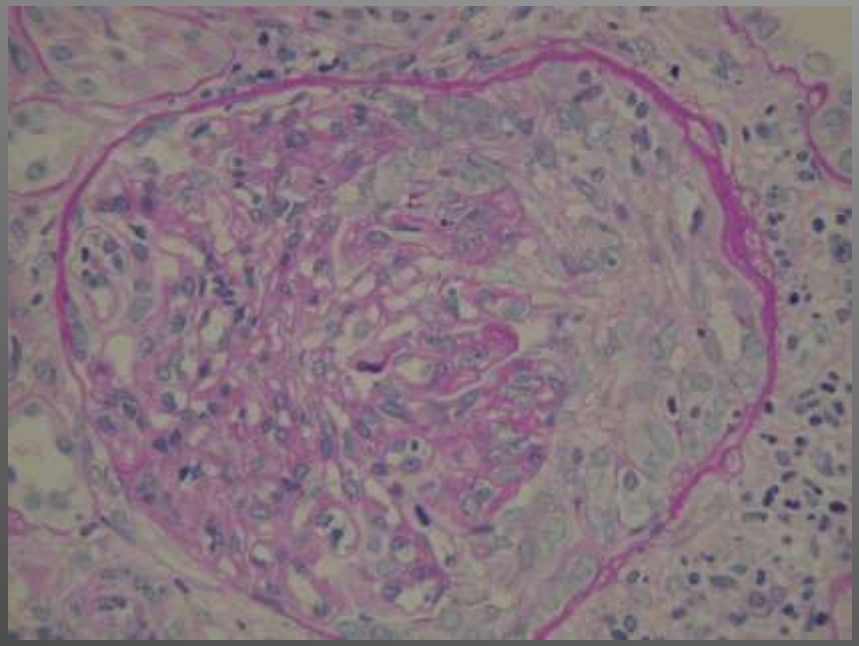
Leiden Classification in ANCA Associated Glomerulonephritis

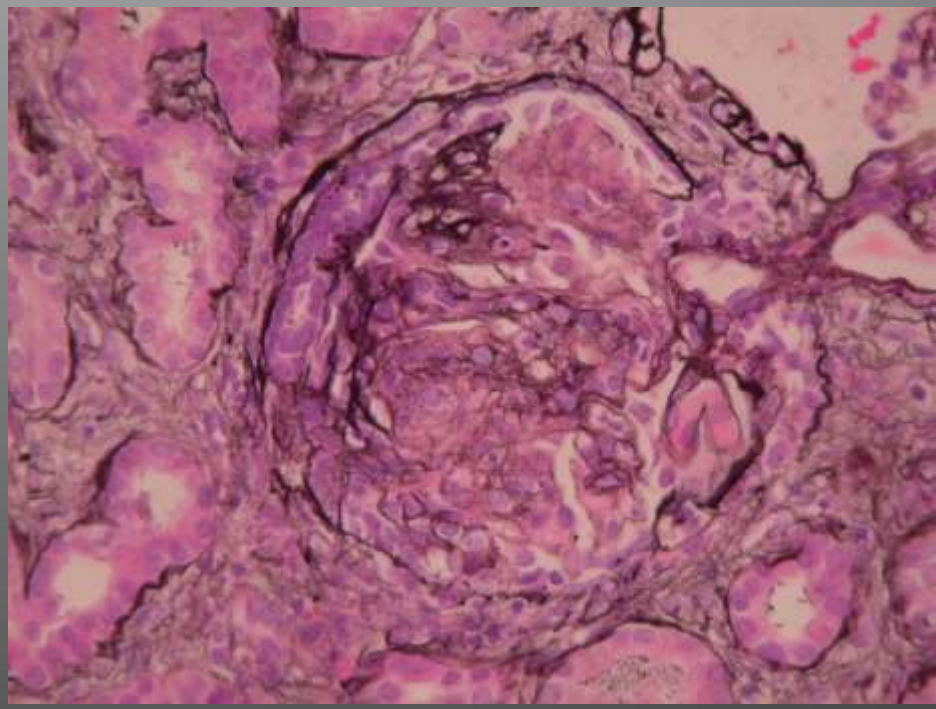





ANCA disease in arteries – rare!

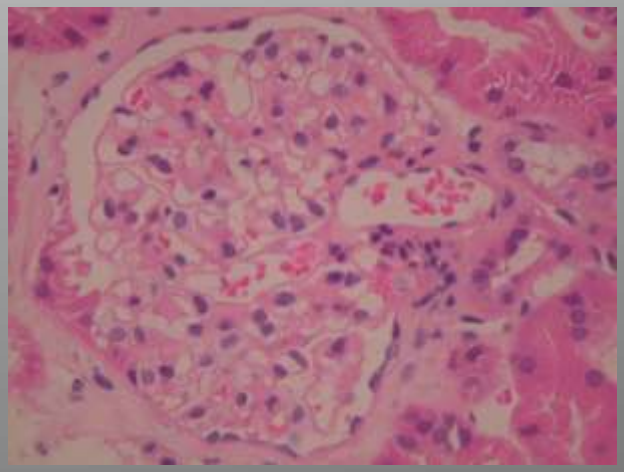
Assessment of Crescentic Glomerulonephritis



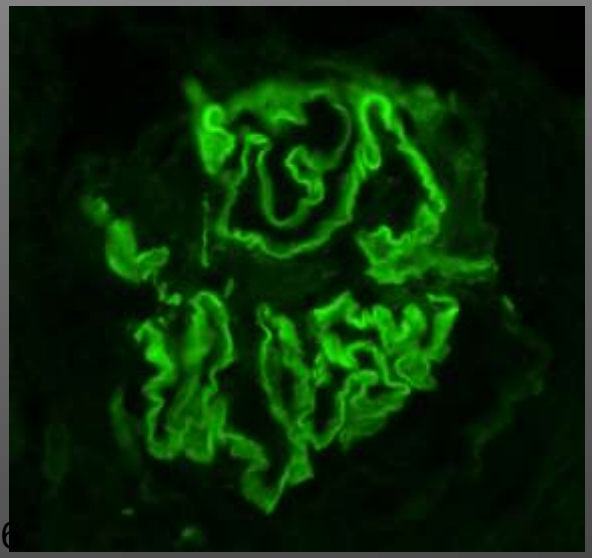


Non-affected glomeruli - normal

- ANCA

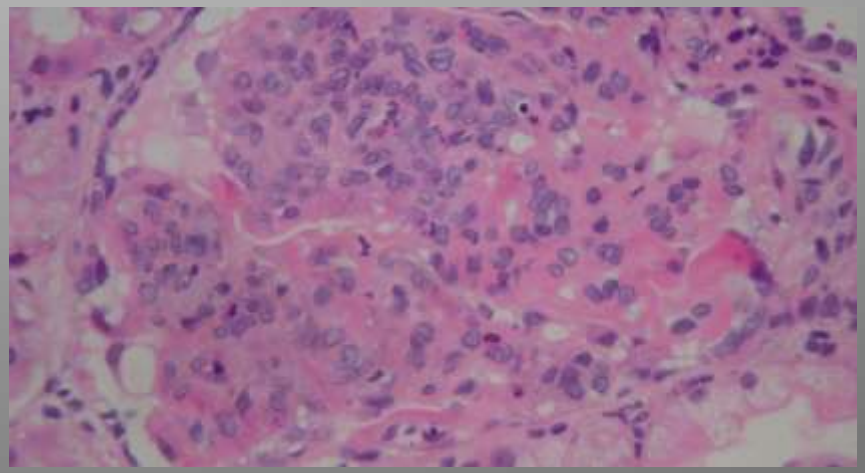


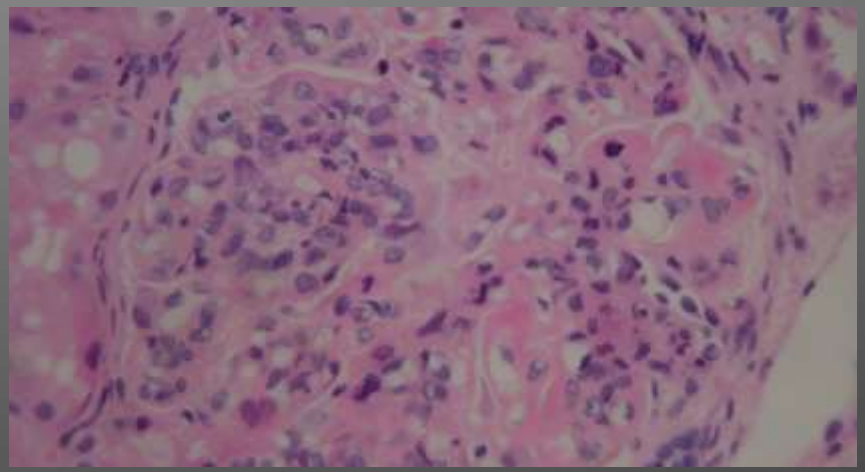
- Anti – GBM disease



Non-crescentic glomeruli show proliferation

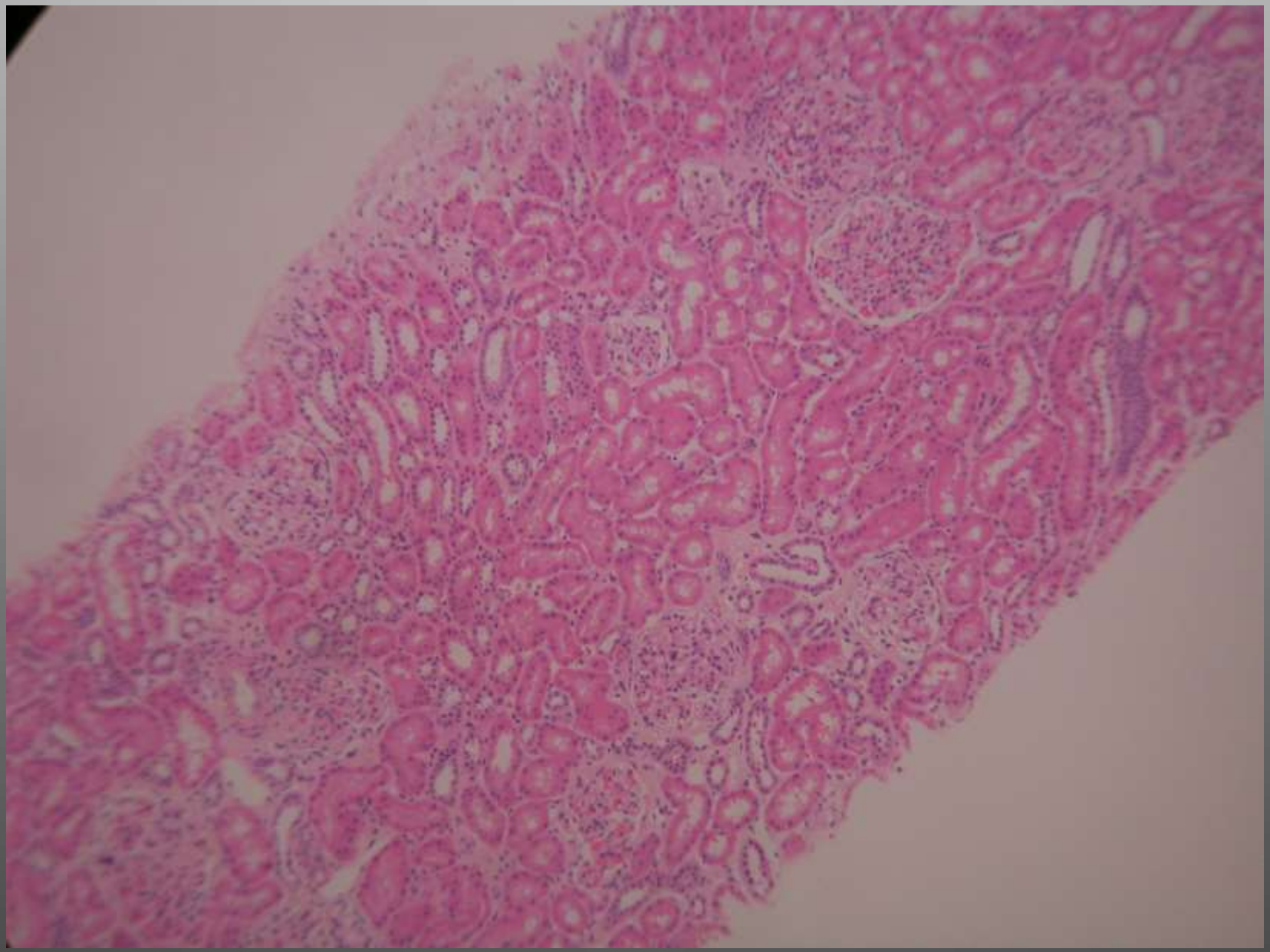
- Immune complex disease
  - IgA/HSP
  - Lupus
  - MPGN
  - Post infectious GN
  - Fibrillary GN
  - Cryoglobulinaemia

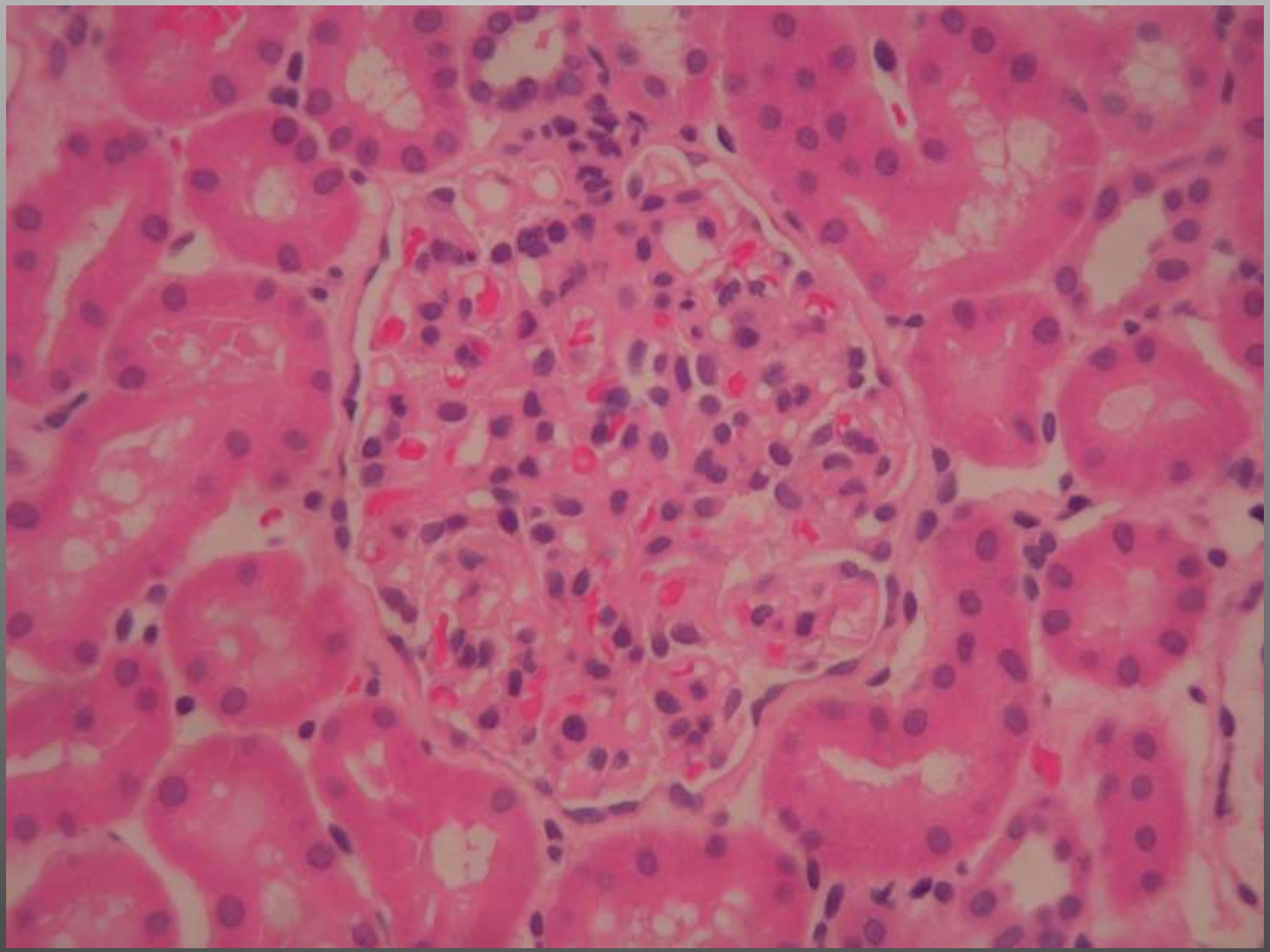


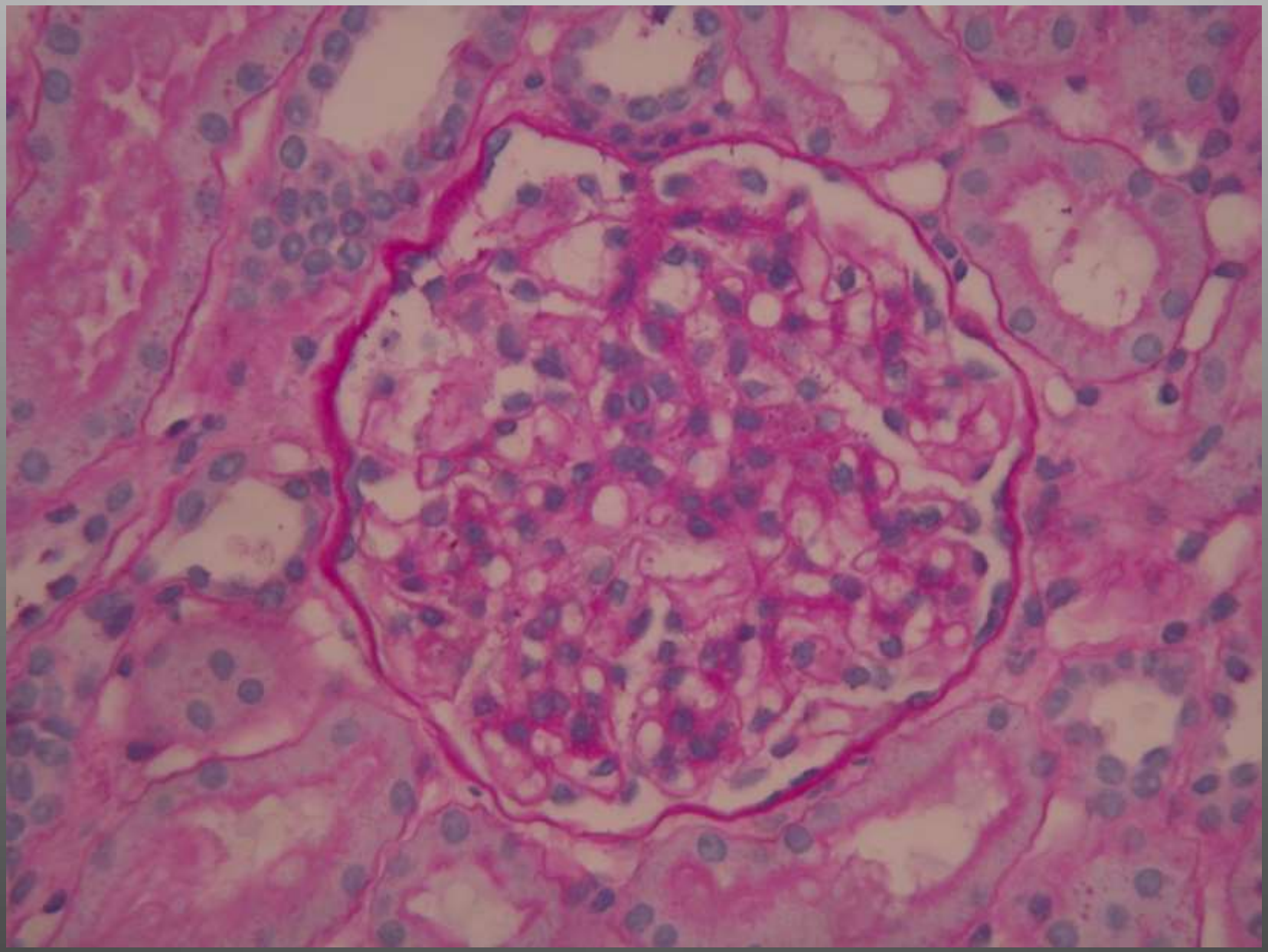


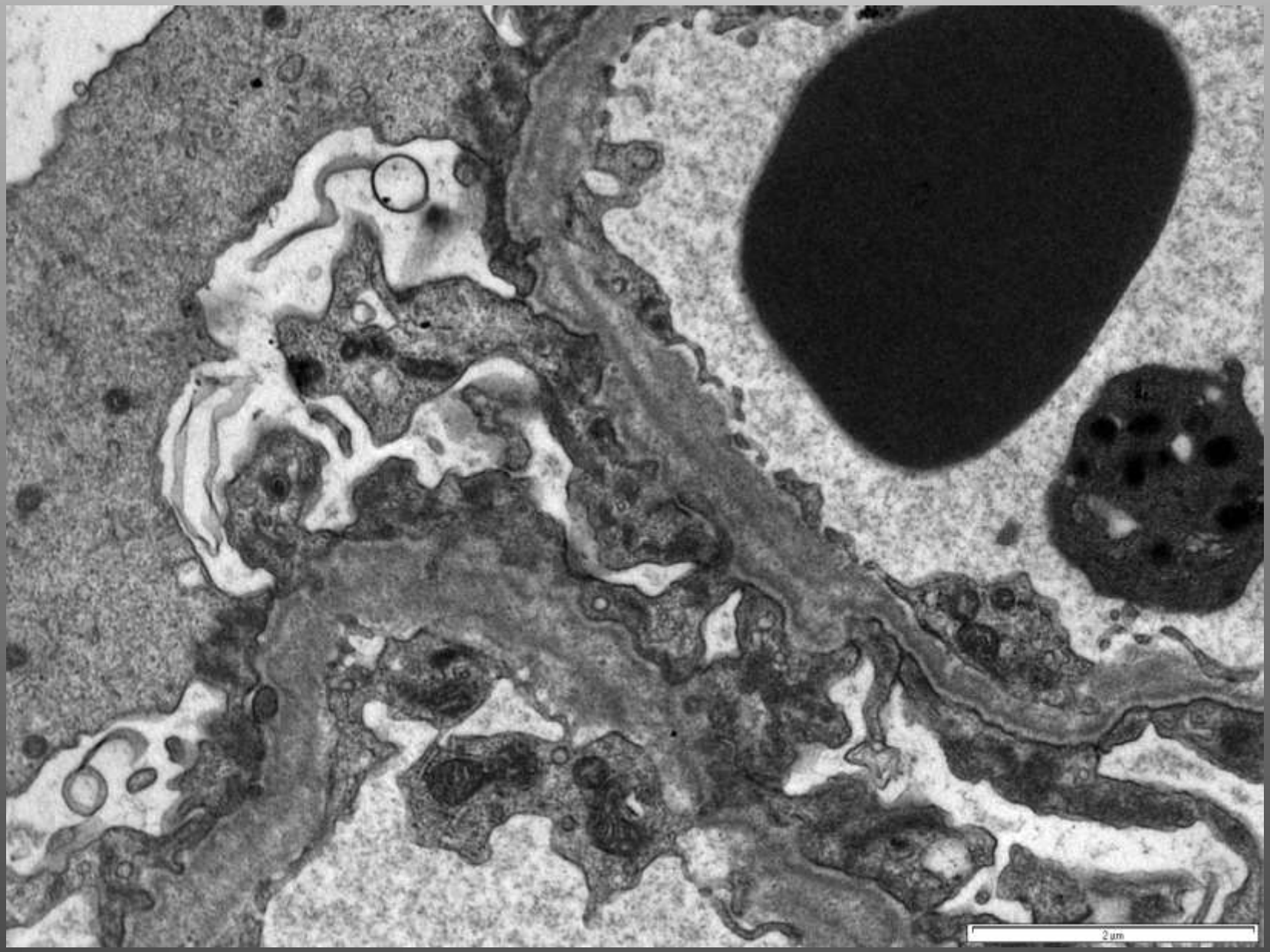
Example 7

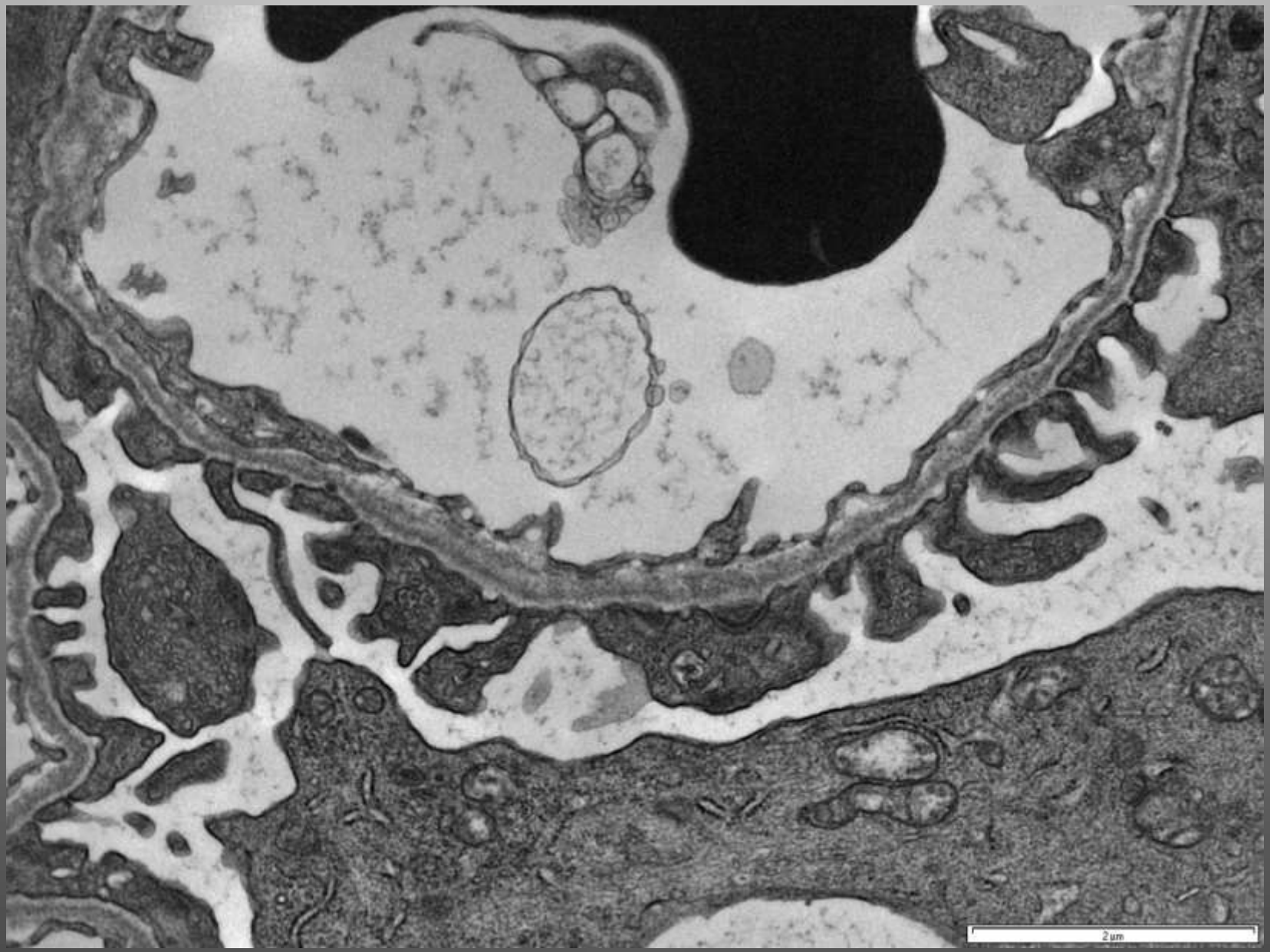
- 7y boy
- Heavy proteinuria
- Haematuria
- Renal impairment
- Family history or renal disease

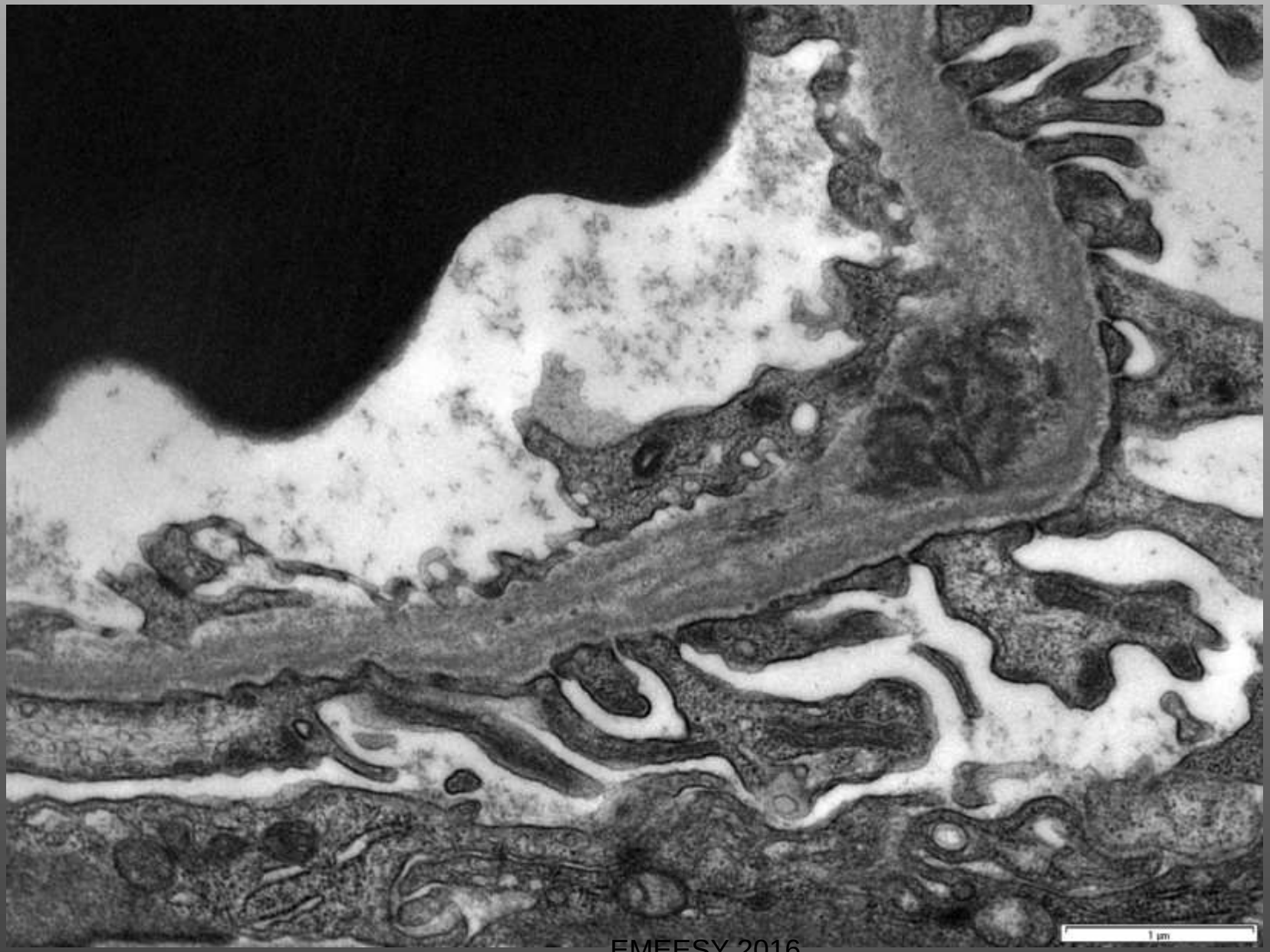




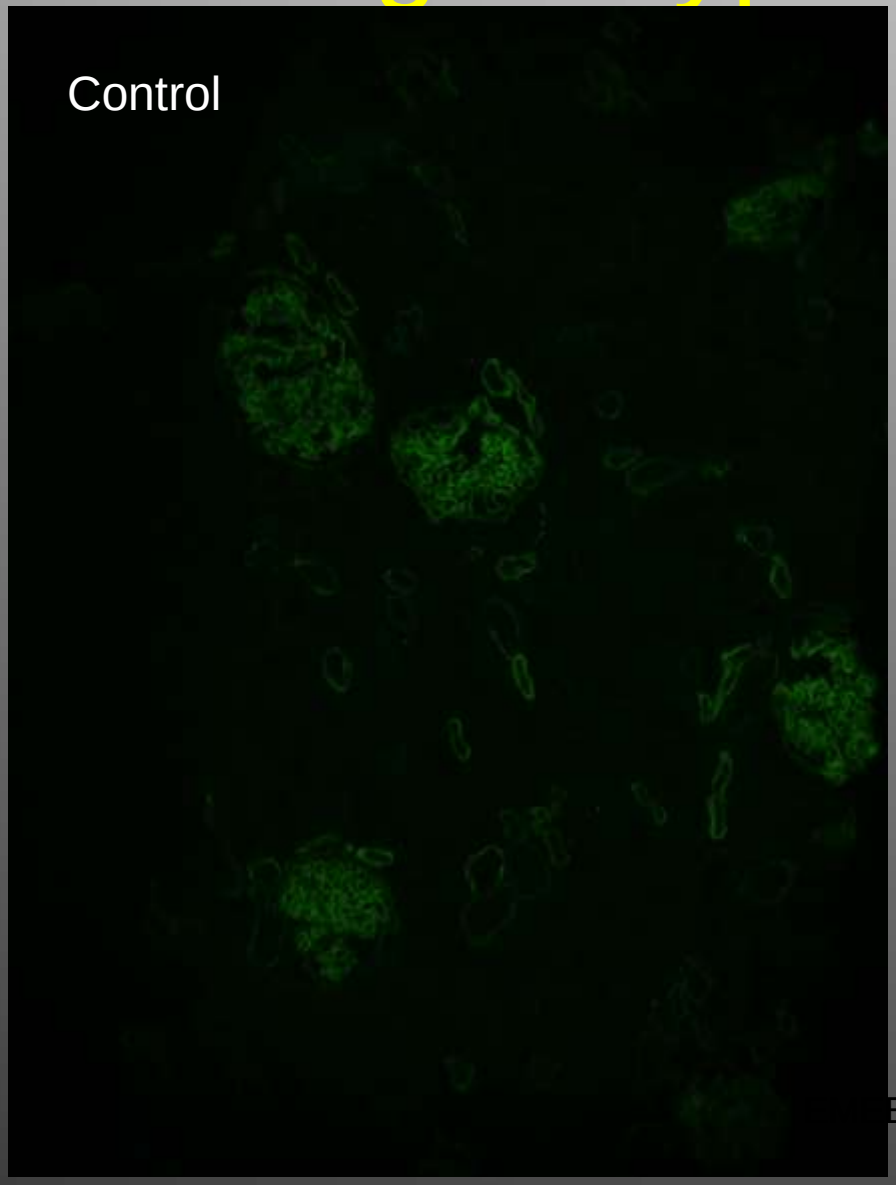


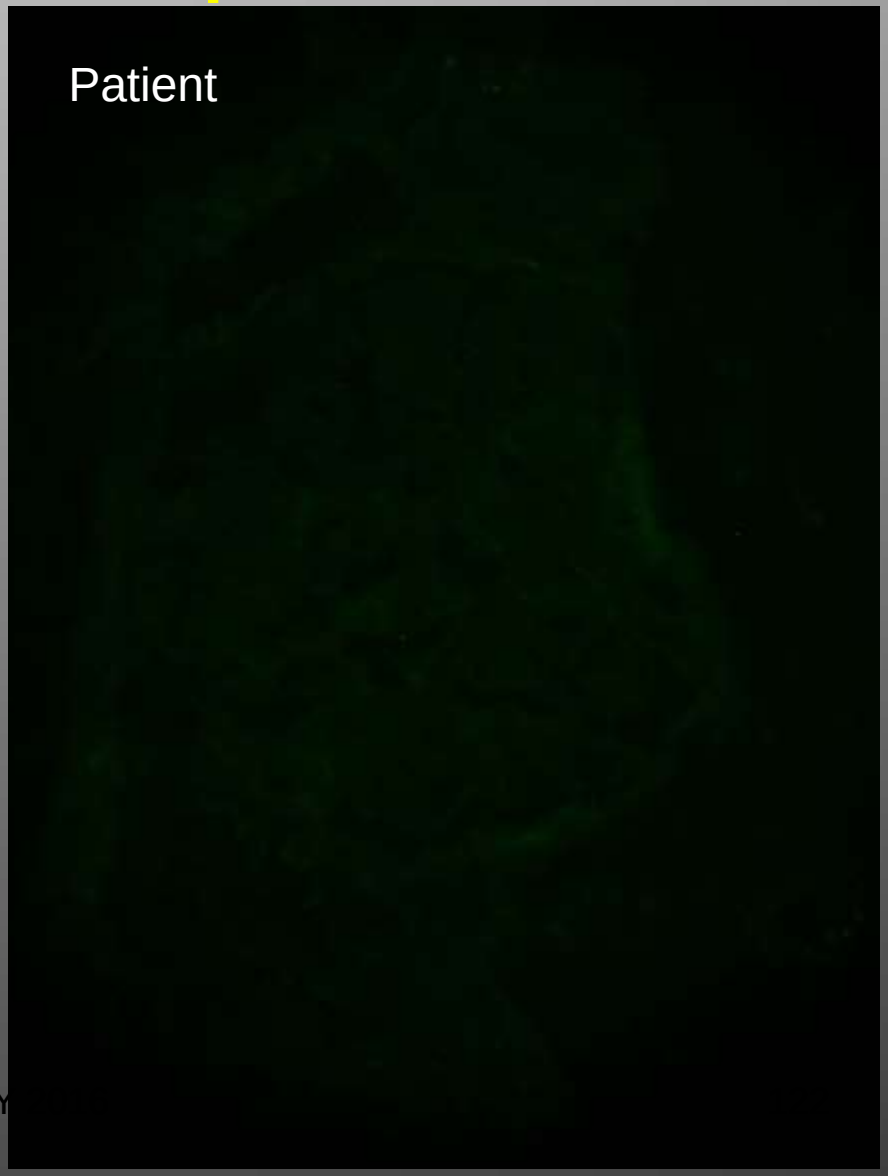

2 µm


2 µm

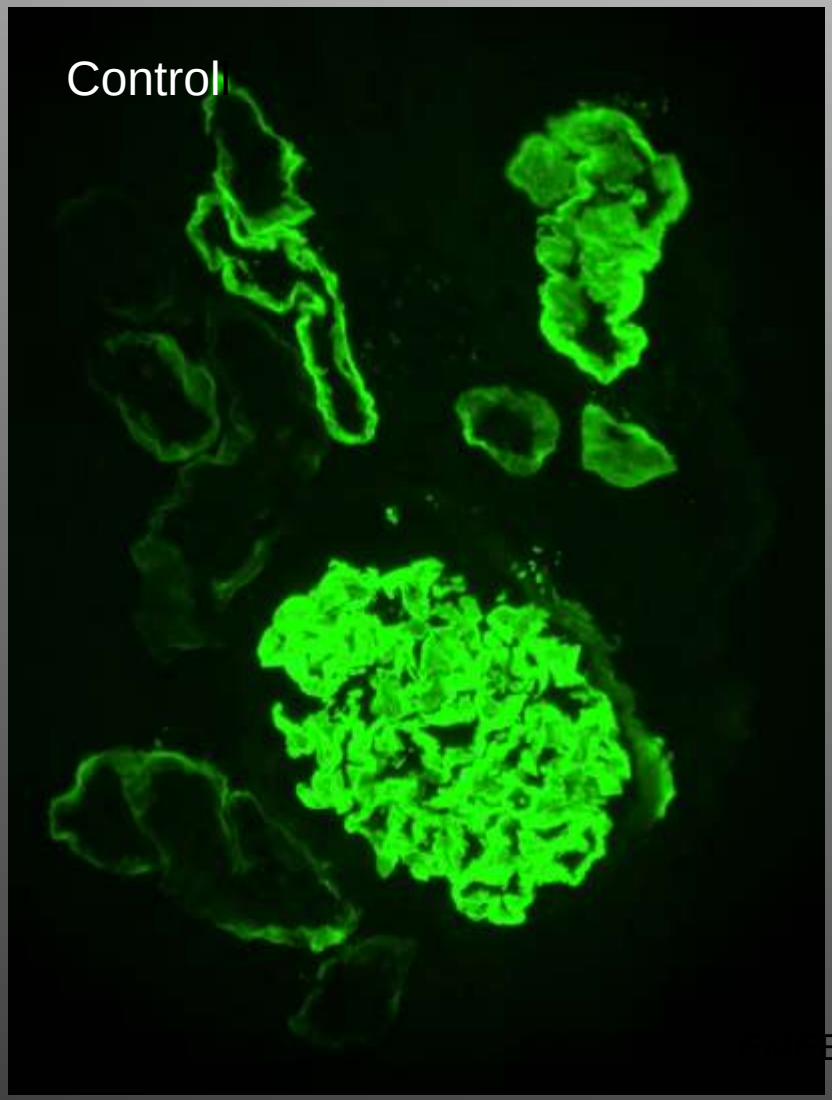

1 µm

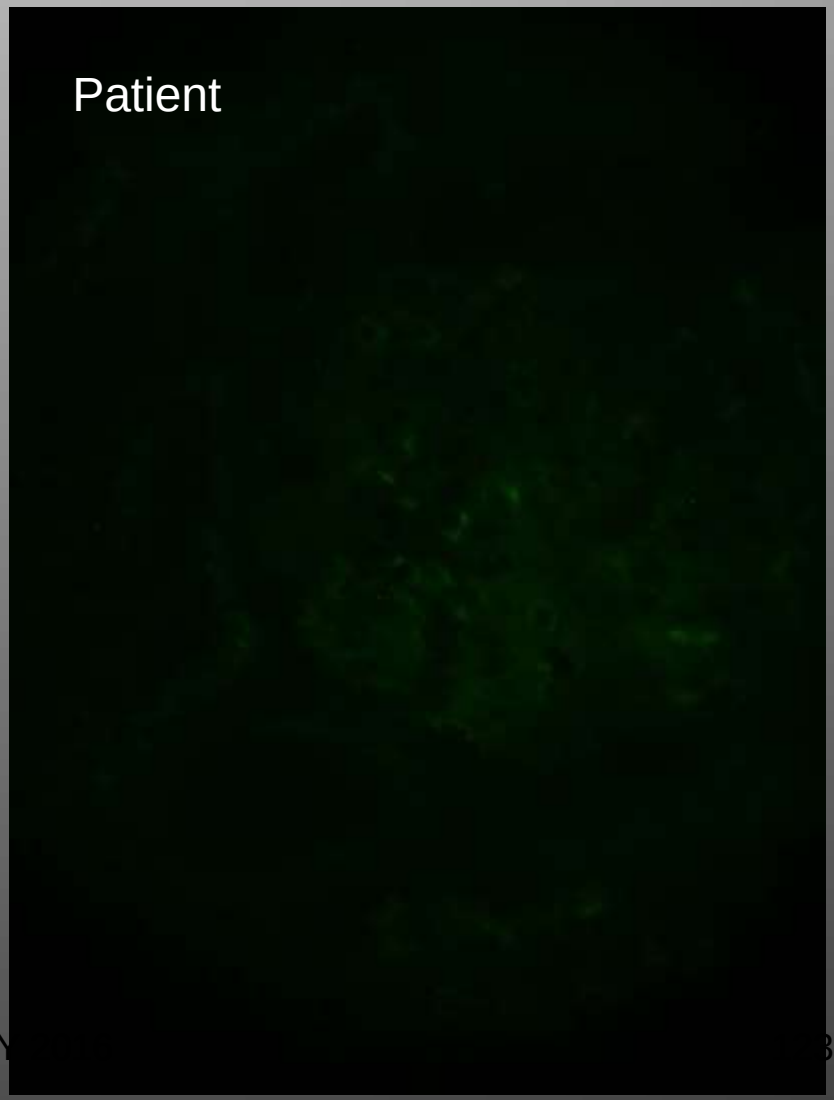
Collagen Type IV Alpha 5 chain





Alpha 3 Chain





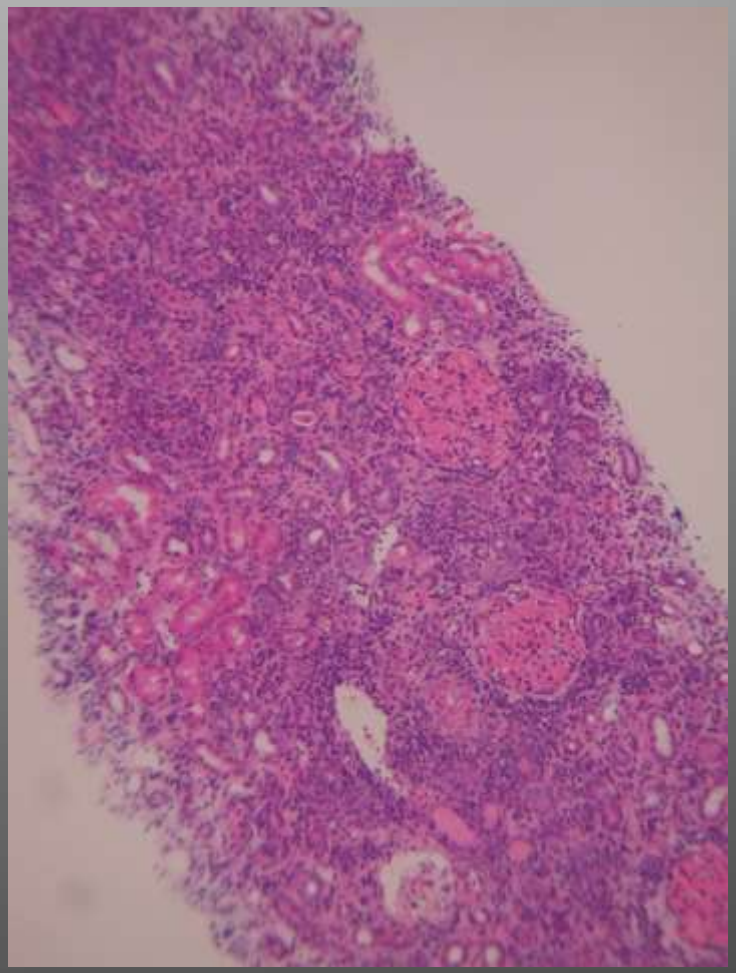
Example 7

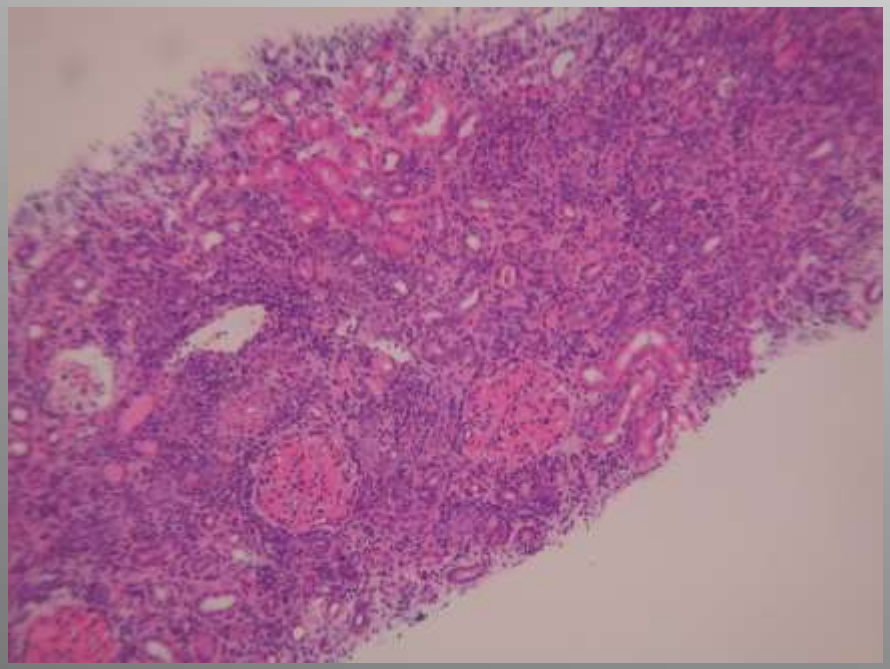
- Familial nephropathy
- Characteristic GBM abnormalities
- Absent collagen type IV subunits 3 and 5 from the GBM and TBM

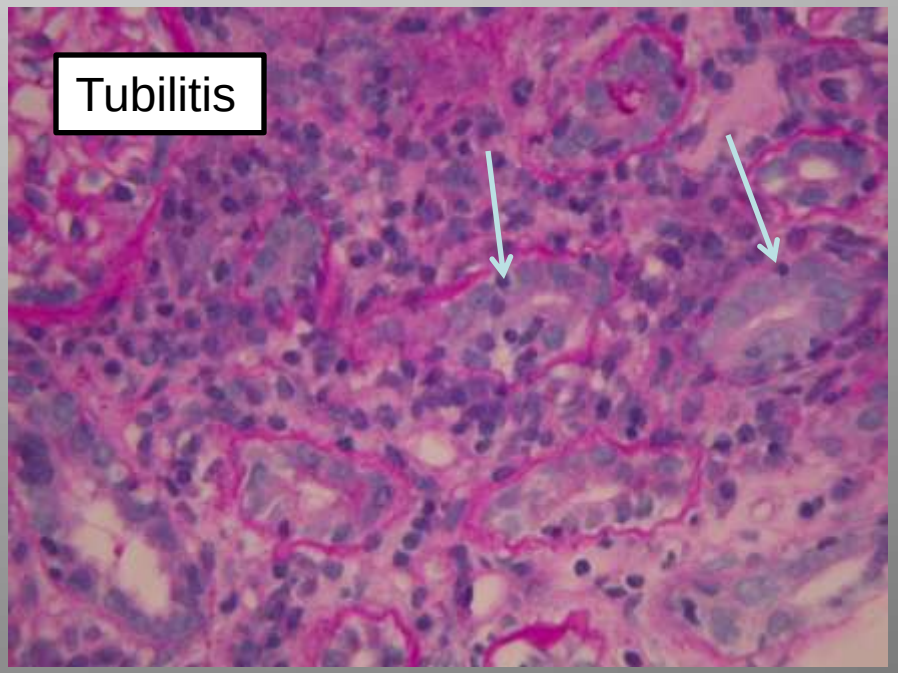
- = ALPORT'S DISEASE
  - X- linked variant

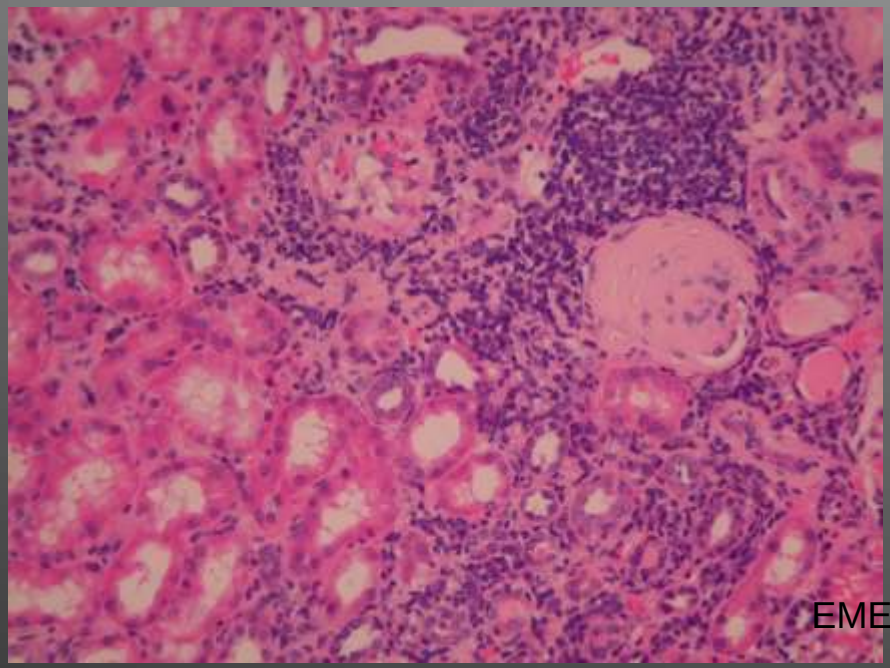
Example 8

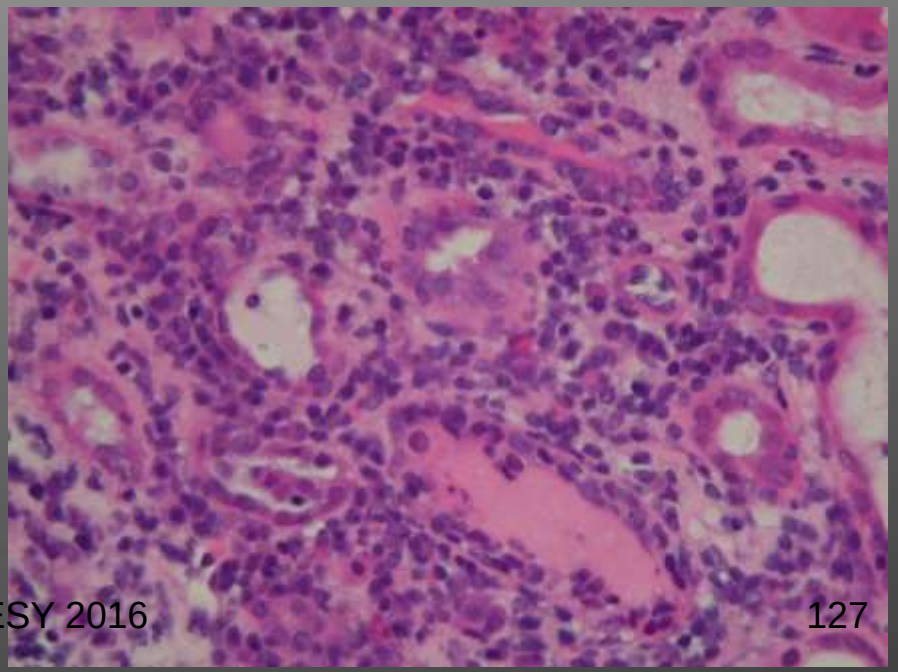
- 64y female
- recently started on omeprazole for gastro-oesphageal reflux disease
- Acute renal failure





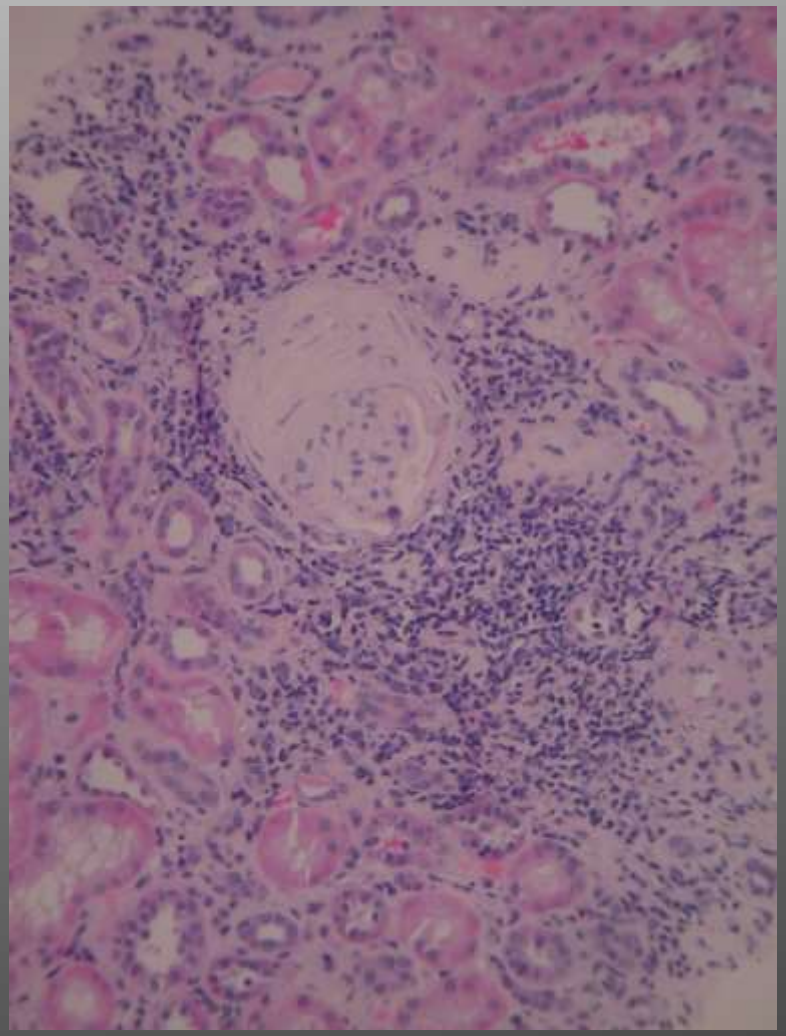

Tubilitis

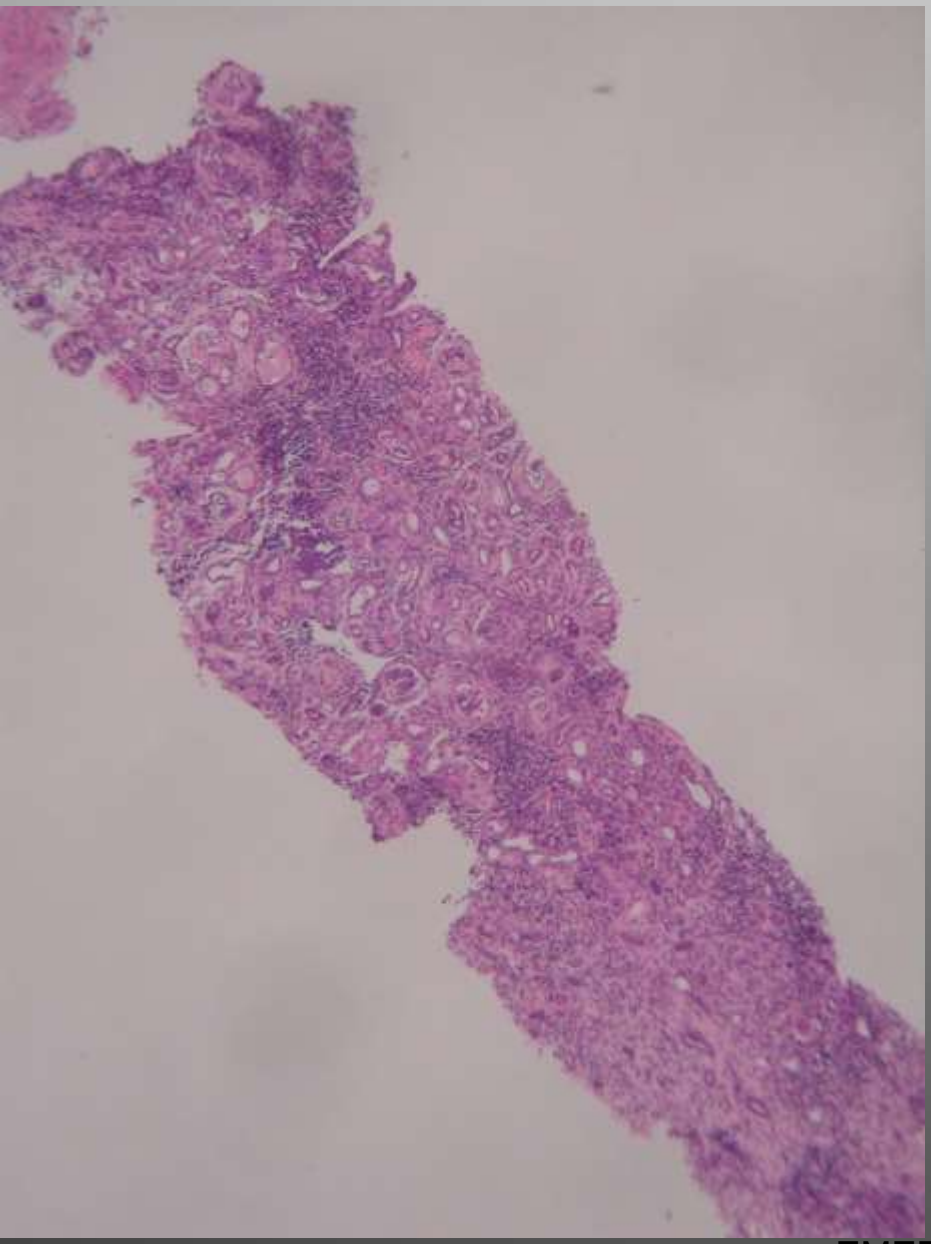


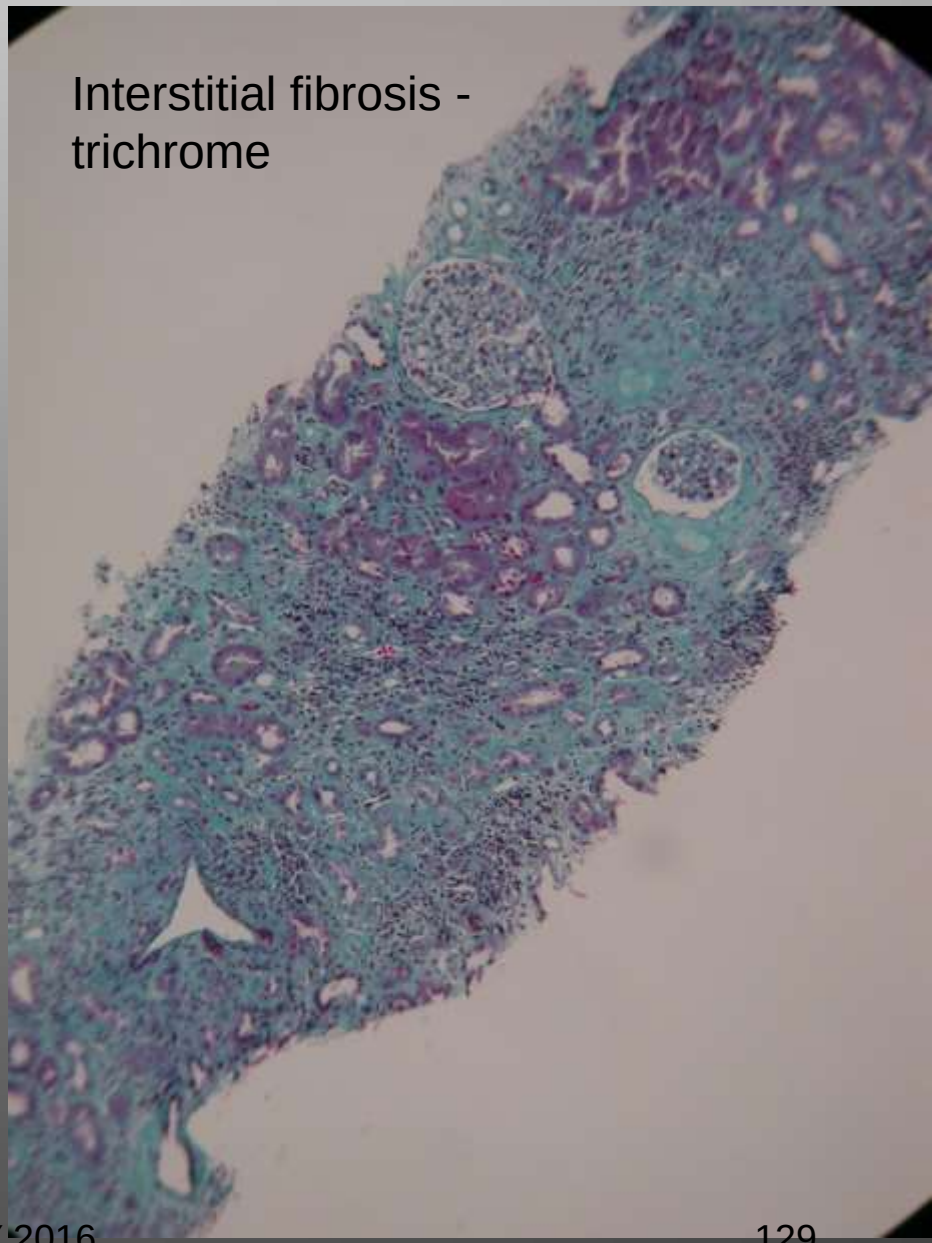


Example 9

- 44y man
- Known ulcerative colitis
- Low level proteinuria
- Creatinine 350
- On mesalazine

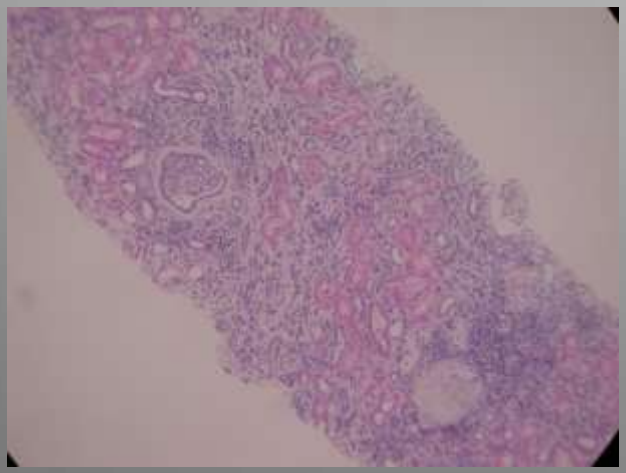


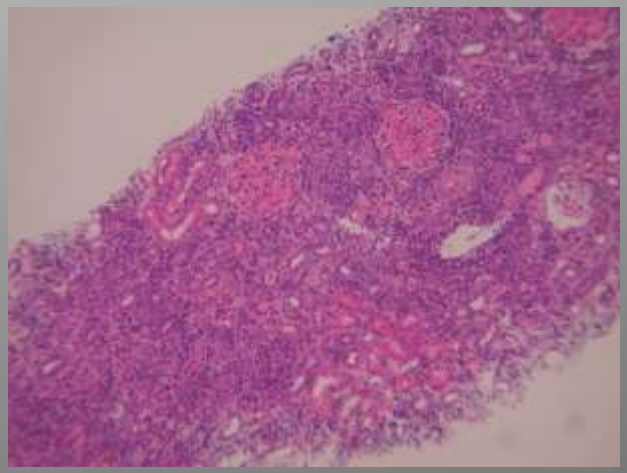




Interstitial fibrosis - trichrome

Examples 7 and 8 – acute and chronic tubulointerstitial nephritis





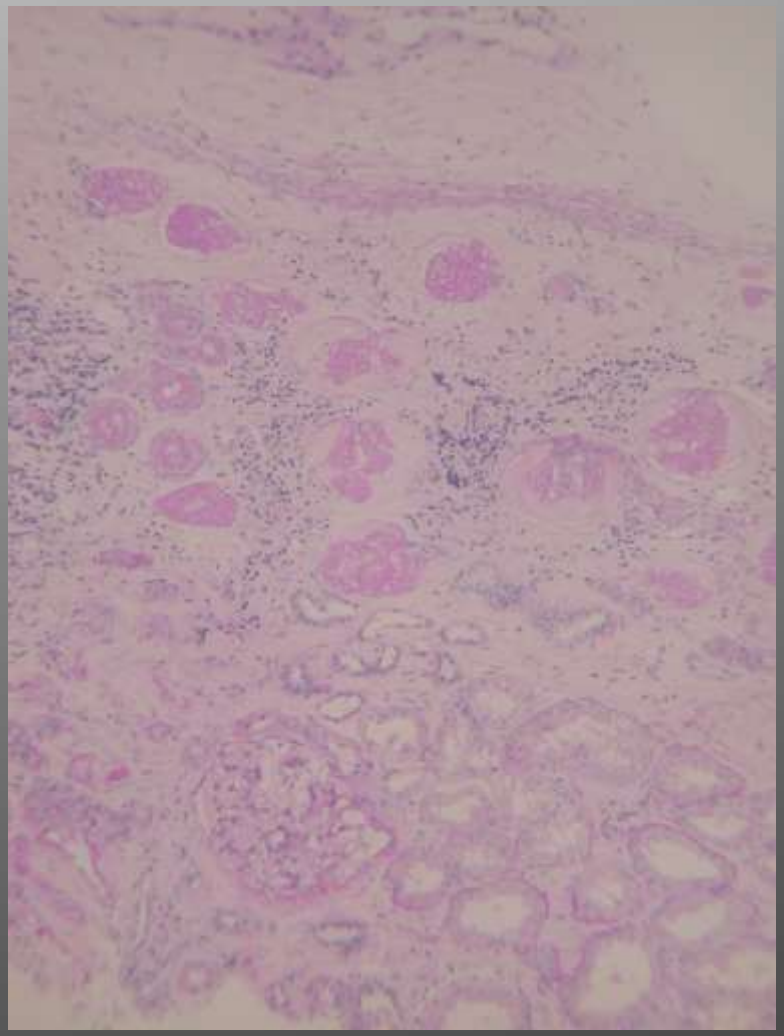
- Defined by the presence or absence of fibrosis
- We need enough tissue to estimate the level of fibrosis and tubular atrophy

Chronic Renal Disease

- All renal disease will progress to interstitial fibrosis and tubular atrophy (IFTA)
- In all renal disease the strongest predictor of prognosis is the level of IFTA
- We need enough tissue to estimate the level of fibrosis and tubular atrophy
- Pathologists are not very good at estimating the level of IFTA

Chronic Renal Disease

- Final outcome – end stage kidney disease (ESKD)
- May be impossible to determine the original pathology
- Sometimes we can suggest diagnosis or whether glomerular, TI or vascular in origin
- Very little effect on current treatment
- The importance is for transplantation

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Assessment of Renal Disease in the Human

- Assessment is multimodal
- Clinical setting highly important
- Knowledge of renal medicine is essential
- Consider wide variety of diseases
- Often several pathologies present in one biopsy (patient)
- These may be of differential importance
  - eg pauciimmune glomerulonephritis with incidental IgA nephropathy
- And may interact with one another
  - eg IgA nephropathy, diabetes and hypertension

Summary – Assessment of Renal Disease in the Human

- Adequate sample needed
  - To make the diagnosis
  - To assess the severity of the pathology (grade)
  - To assess the stage of the disease
- Clinicopathological correlation is paramount!

Thank you

Systemic Example

- Diabetes and hypertension