

The background features several stylized illustrations. In the top left, there are three purple neurons with yellow centers and branching dendrites. In the top right, there is a large green cell with yellow and purple internal structures. In the bottom left, there is another large green cell with similar internal structures. In the bottom right, there is a single green neuron with a dark blue center and branching dendrites.

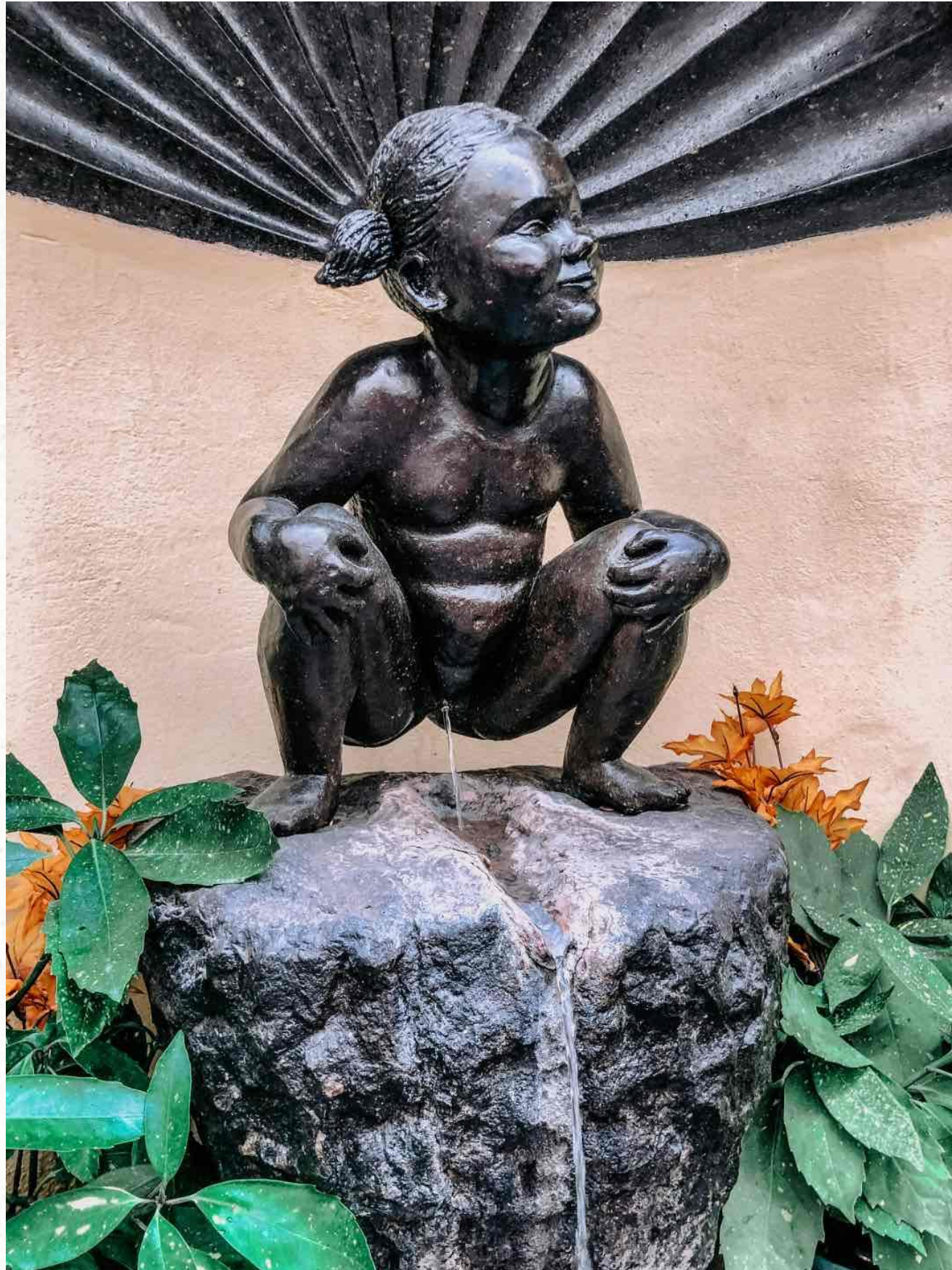
OLD CASE, NEW DIAGNOSIS

DR ANNIE KRET

QUINTESSENTIAL BELGIAN ICON?

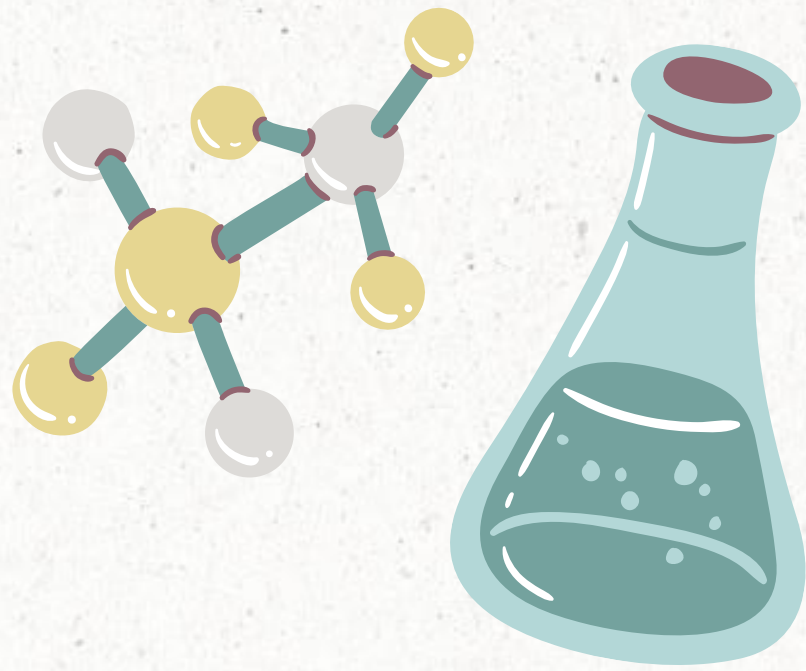






THE PATIENT

- 30 year old female
- Presented with nystagmus
- Head CT – micro-infarcts
- Atrial septal defect
- PMH: primary hypothyroidism, learning difficulties, iatrogenic adrenal insufficiency
- Developed lower limb oedema



WORK UP



BLOODS

Total protein 55 g/L (63–79 g/L)
Albumin 24 g/L (35–50 g/L)
Complement C3 2.03 g/L (0.75–1.65 g/L)
Polyclonal increase in IgM to 5.43 g/L (0.5–2.0 g/L)
Renal function otherwise normal
Negative serological autoantibody screen

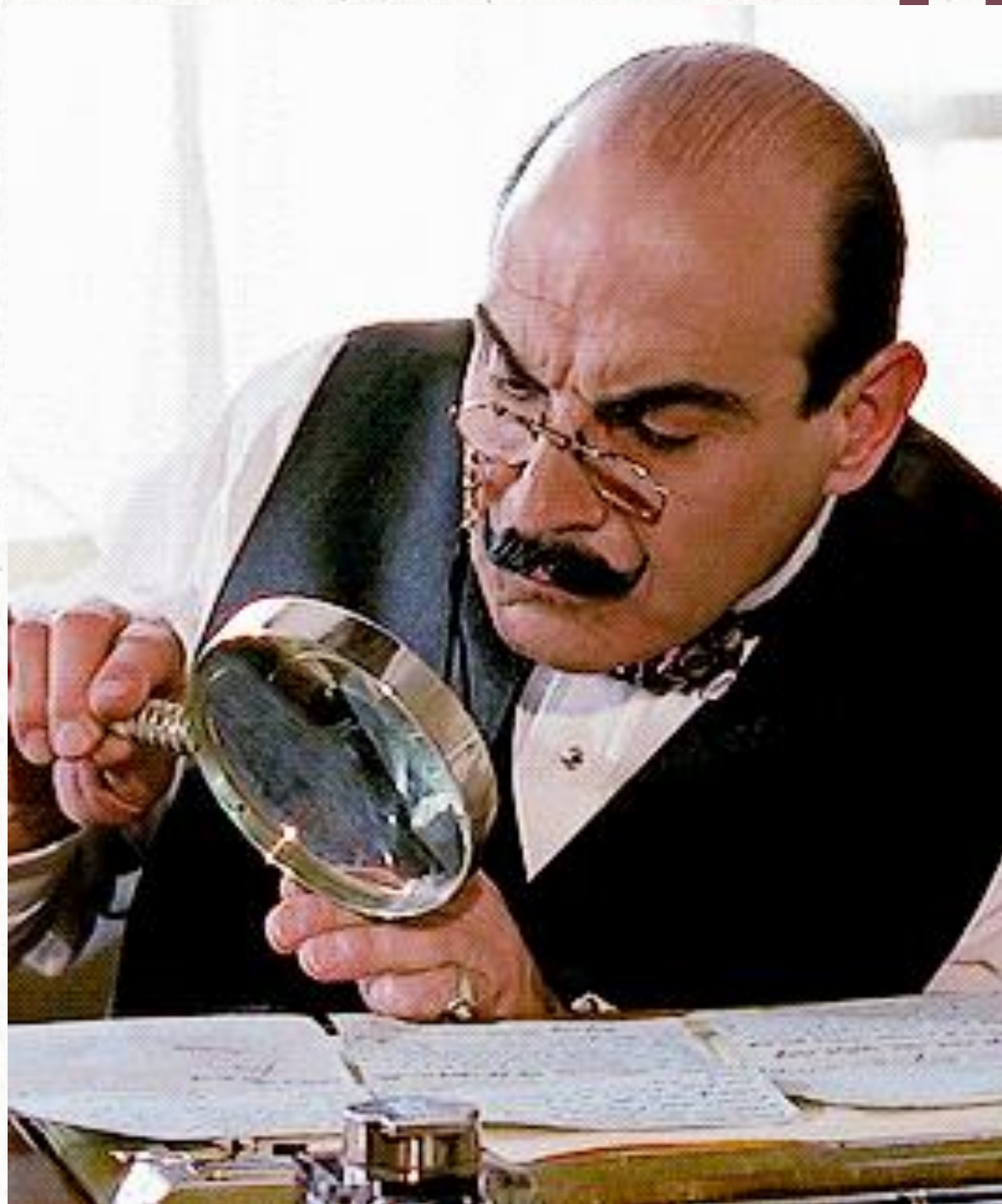
RADIOLOGY

Mildly dilated calyces but otherwise normal

URINE

24 hour protein excretion 7g → 14g

THE BIOPSY

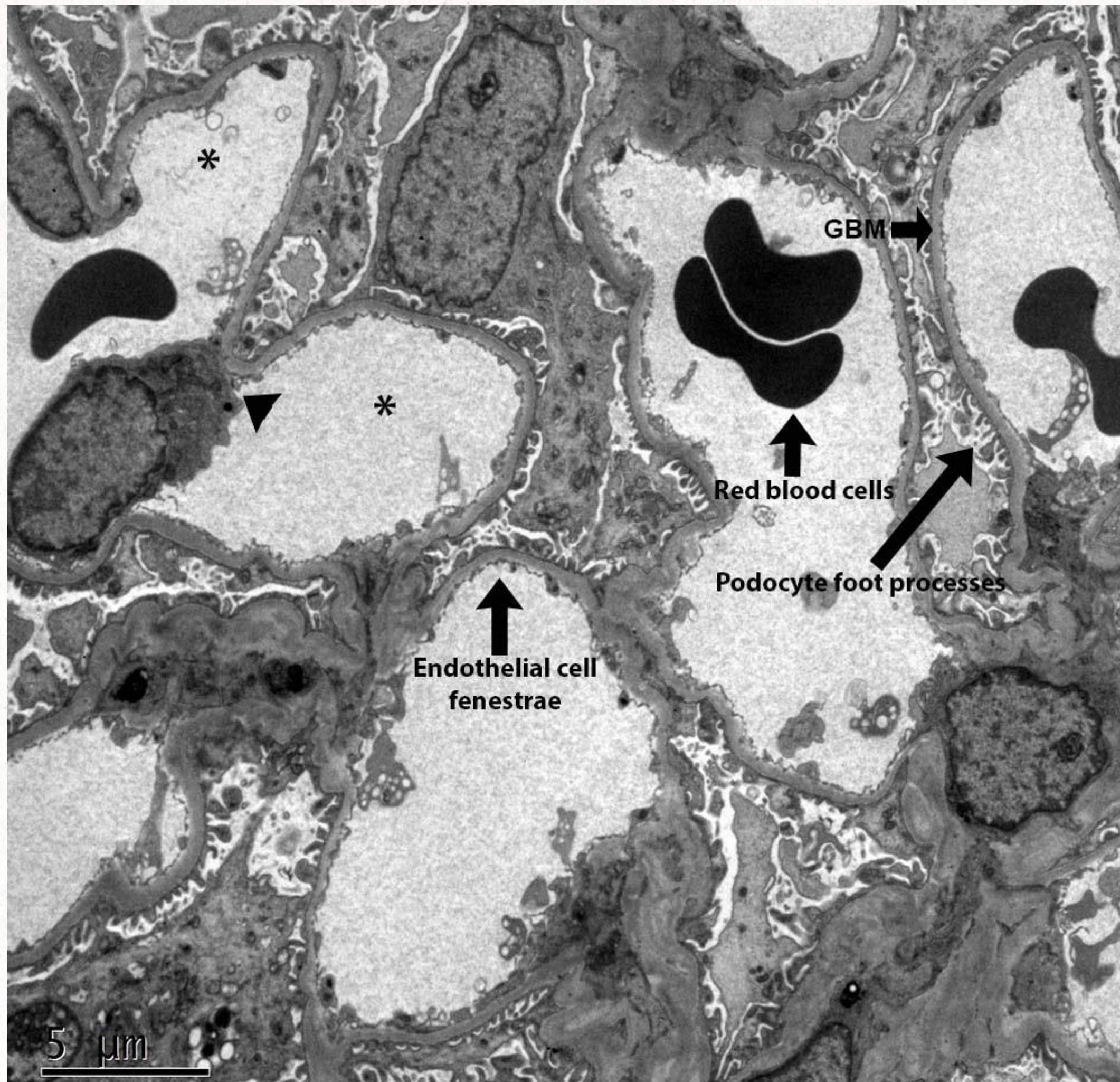


LM

- 10 gloms
- Mild mesangial prominence and hypercellularity
- Capillary loops are prominent
- Silver – “essentially normal peripheral profiles”
- Mild interstitial fibrosis

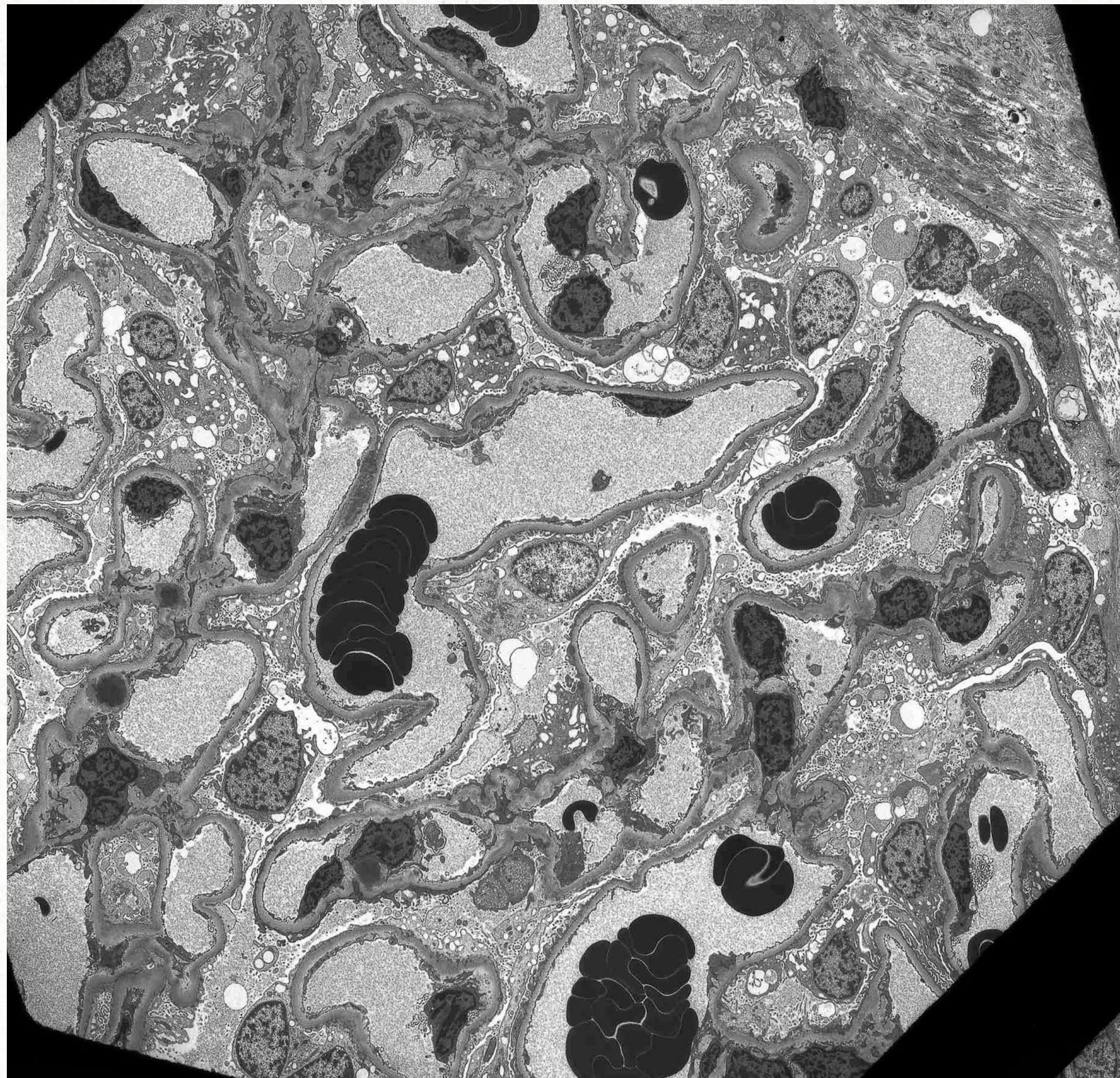
IF

No cortical tissue

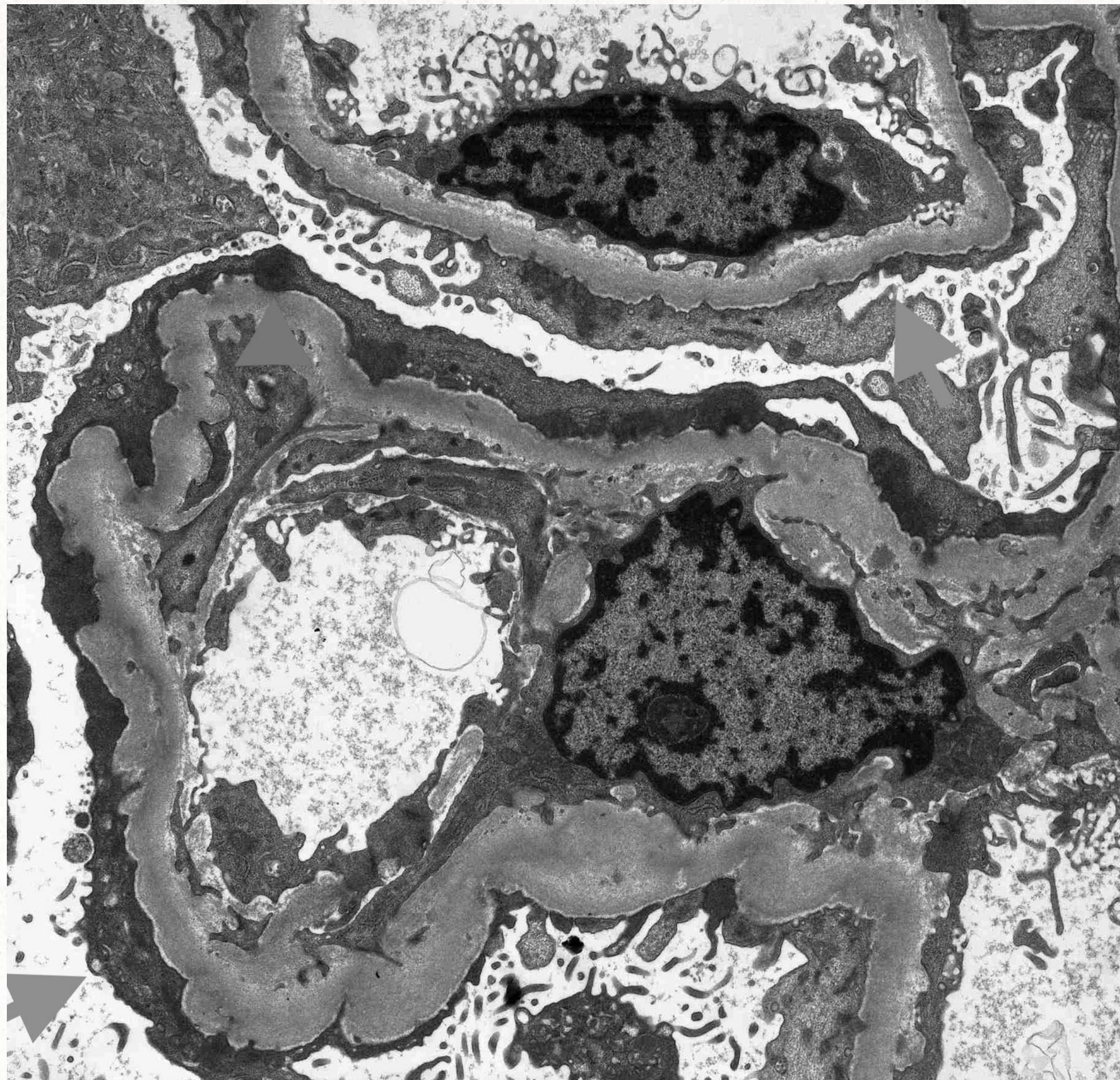


NORMAL EM

Image from Renal Fellow “Kidney Biopsy of the Month: What is Normal?”



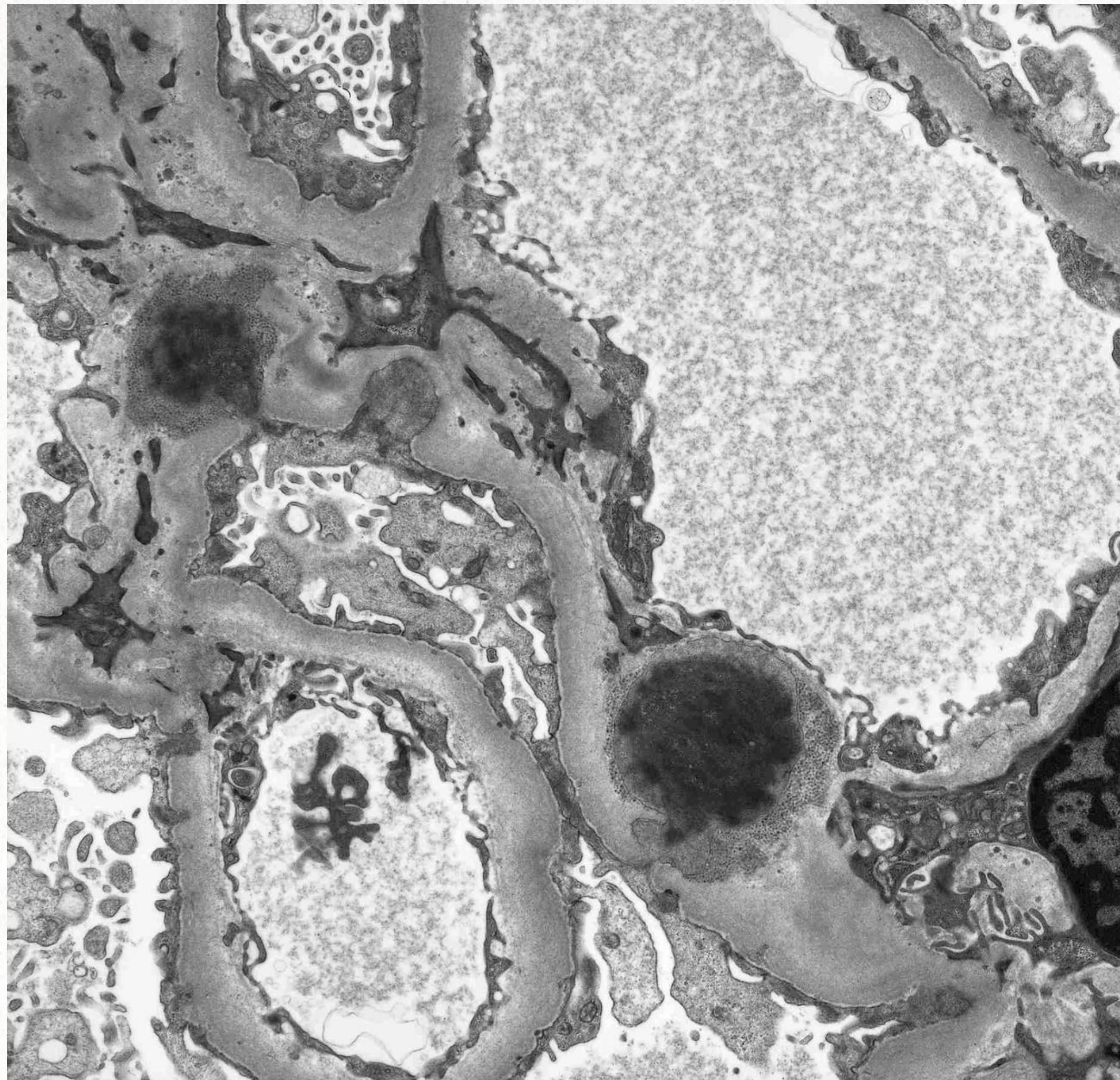
THE BIOPSY - EM



THE BIOPSY - EM

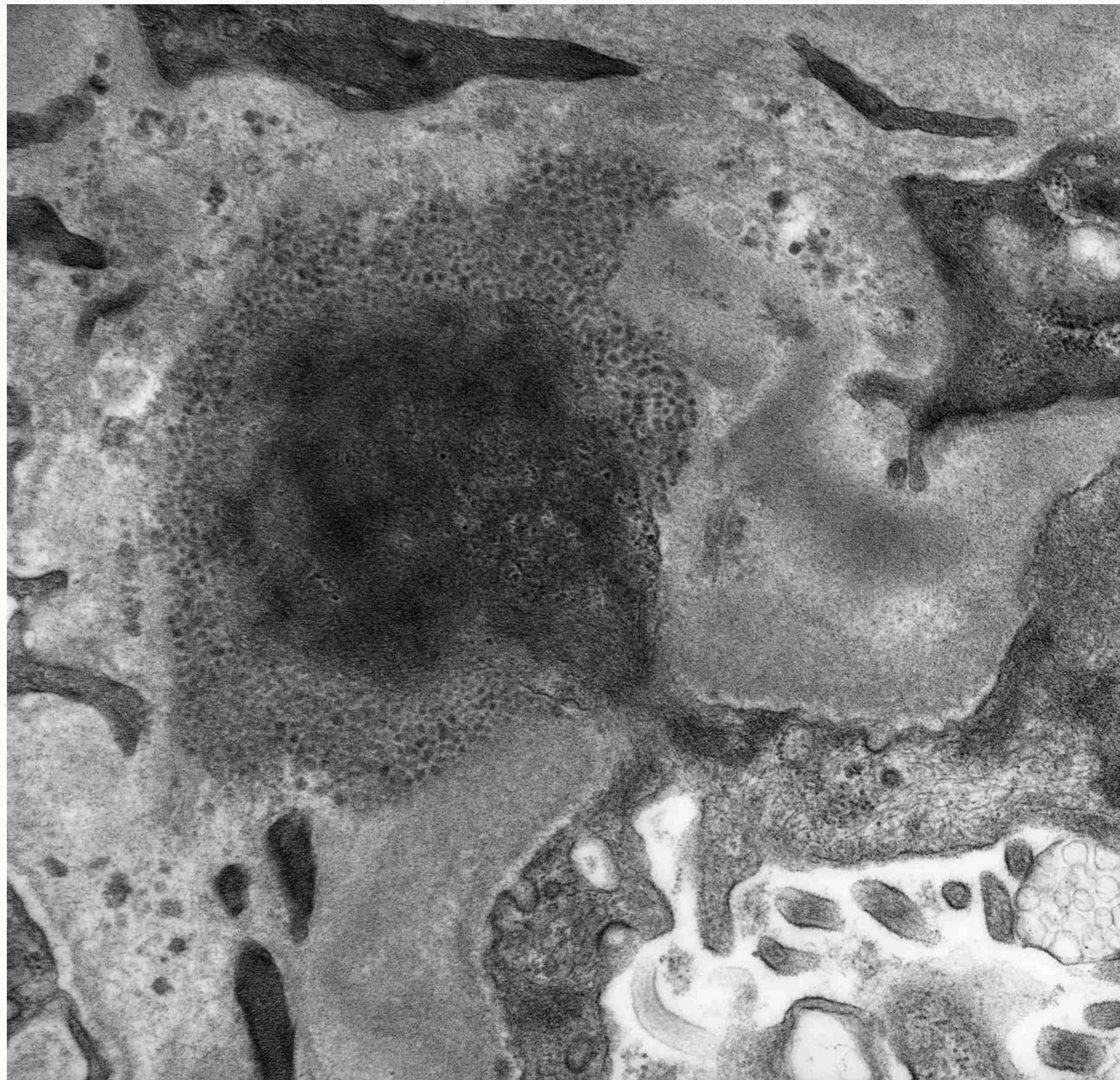
severe podocyte foot processes
effacement





THE BIOPSY - EM

podocyte cytoplasmic inclusions
extending into the GBM



THE BIOPSY - EM

spherical microparticle
degenerative change

WHAT IS IT?



**25 CASES
17 INSTITUTIONS
19 FEMALES : 6 MALES
20–69 YEARS OLD
17 HAD COLLAGEN DISEASES**

Clin Exp Nephrol (2008) 12:421–431
DOI 10.1007/s10157-008-0104-z

ORIGINAL ARTICLE

Special issue
Podocytic infolding glomerulopathy: a proposed new
disease entity

Proposal of podocytic infolding glomerulopathy as a new disease entity: a review of 25 cases from nationwide research in Japan

**Kensuke Joh · Takashi Taguchi · Hidekazu Shigematsu · Yutaka Kobayashi ·
Hiroshi Sato · Shinichi Nishi · Ritsuko Katafuchi · Shinsuke Nomura ·
Yoshihide Fujigaki · Yasunori Utsunomiya · Hitoshi Sugiyama ·
Takao Saito · Hirofumi Makino**



Fig. 3 Light microscopy of case 19 shows a non-argaffin hole (bubbling or stipple formation) in the GBM. Spike formation was not remarkable (PAM stain)

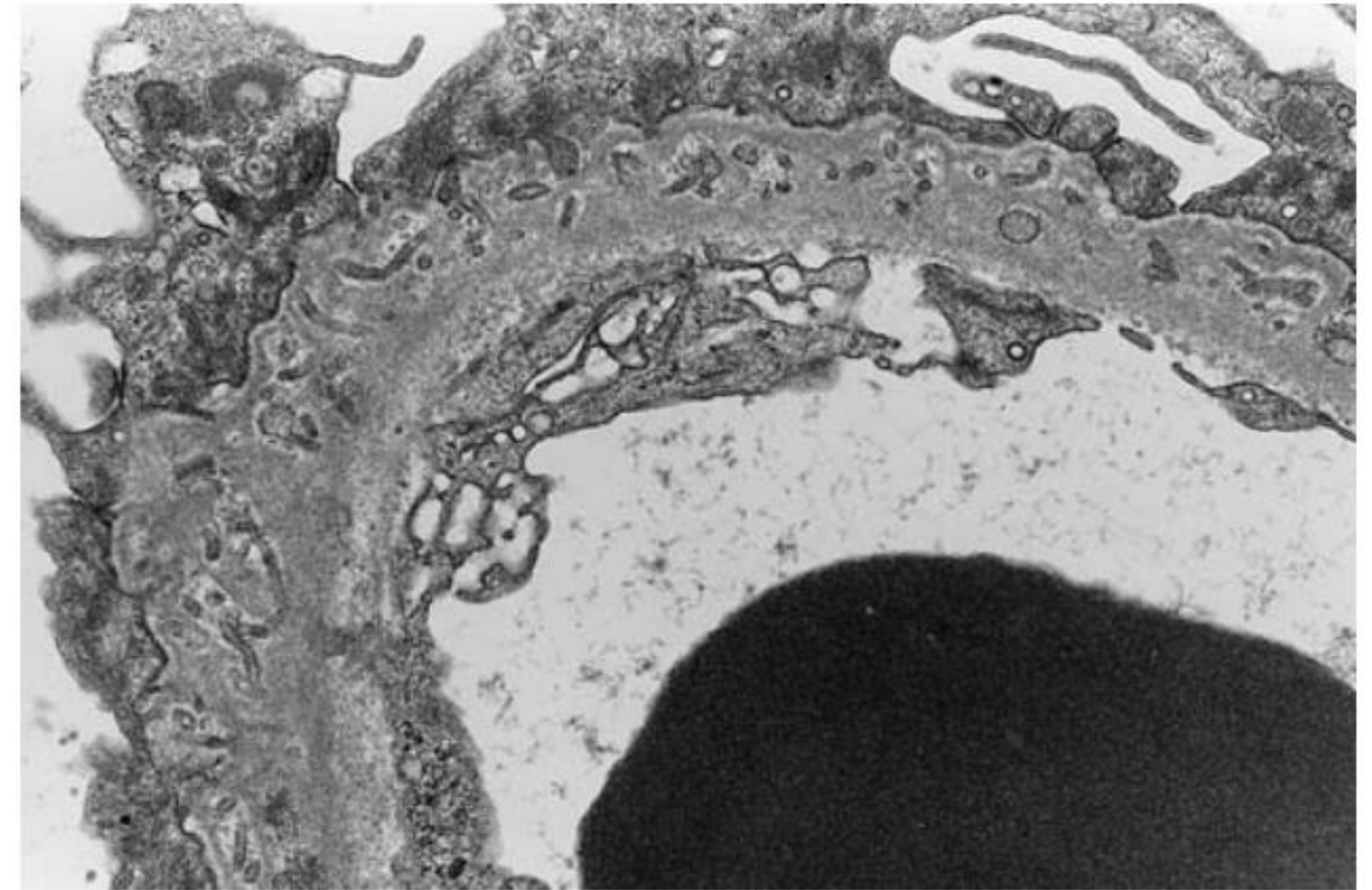


Fig. 2 Electron micrograph of case 3 shows microtubular structures with a diffuse distribution measuring 50–100 nm in width ($\times 10,000$)

Images from Joh K et al. Clin Exp Nephrol. 2008;12(6):421–31.

PROTENURIA **CAPILLARY LOOP GBM BUBBLES OR SPIKES USING** **SILVER STAIN**

Fig. 1 **a** Electron micrograph of case 19 shows global and diffuse distribution of microstructures in the GBM ($\times 3,000$). **b** The microstructures show microspheres measuring 50–150 nm in diameter ($\times 15,000$)

**GBM THICKENING
PODOCYTIC INFOLDING
INTO THE GBM
+/- MICROTUBULES OR
MICROSPHERES
VARIABLE IF
+/- ELECTRON-DENSE
DEPOSITS**

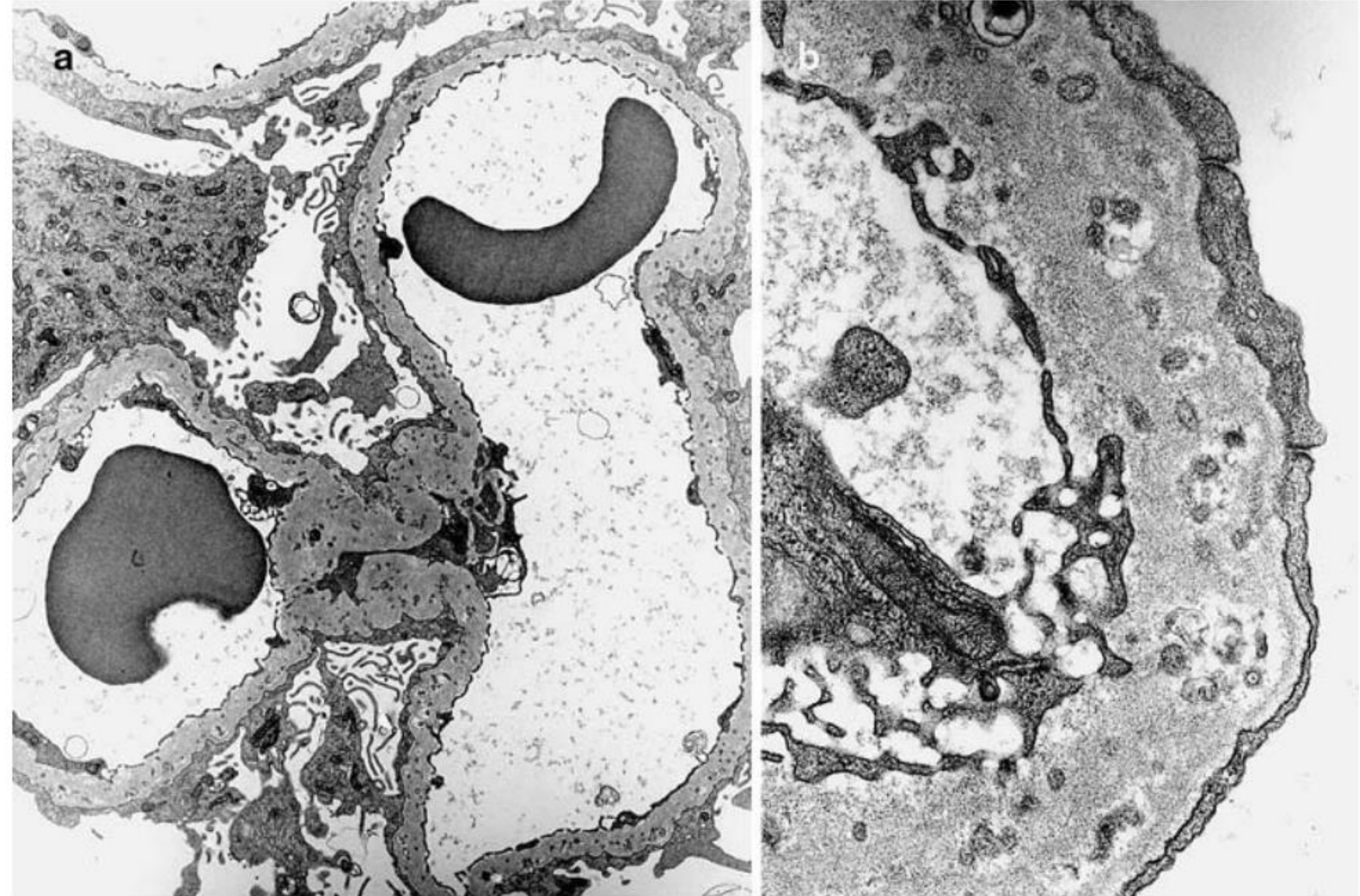


Image from Joh K et al. Clin Exp Nephrol. 2008;12(6):421–31.



- 116 PIG cases
- 89 (76.7%) had positive IF results
- Of these, 63 (70.8%) had SLE
- 51.9% with isolated PIG had no known underlying disease



Kidney International Reports
Volume 8, Issue 12, December 2023, Pages 2742-2753



Clinical Research

Podocyte Infolding Glomerulopathy: A Special Morphology of Podocyte Injury Caused by Heterogeneous Diseases

Ling Hong^{1 2 4}, Lin Wang^{3 4}, Honglei Wang², Qihua Wang², Shicong Yang², Tian Tian²,
Tianjiao Cui¹, Shuling Yue³, Xiaotao Hou³, Zhihua Zheng¹  , Wenfang Chen²  



- Diffuse GBM thickening
- Diffuse podocyte effacement
- Mesangial proliferation *
- Endocapillary proliferation *

*Significantly more common in IF positive group

- Proteinuria +/- haematuria
- 47.5% had Nephrotic syndrome
- Remission in 95.1% with glucocorticoid +/- immunosuppression treatment

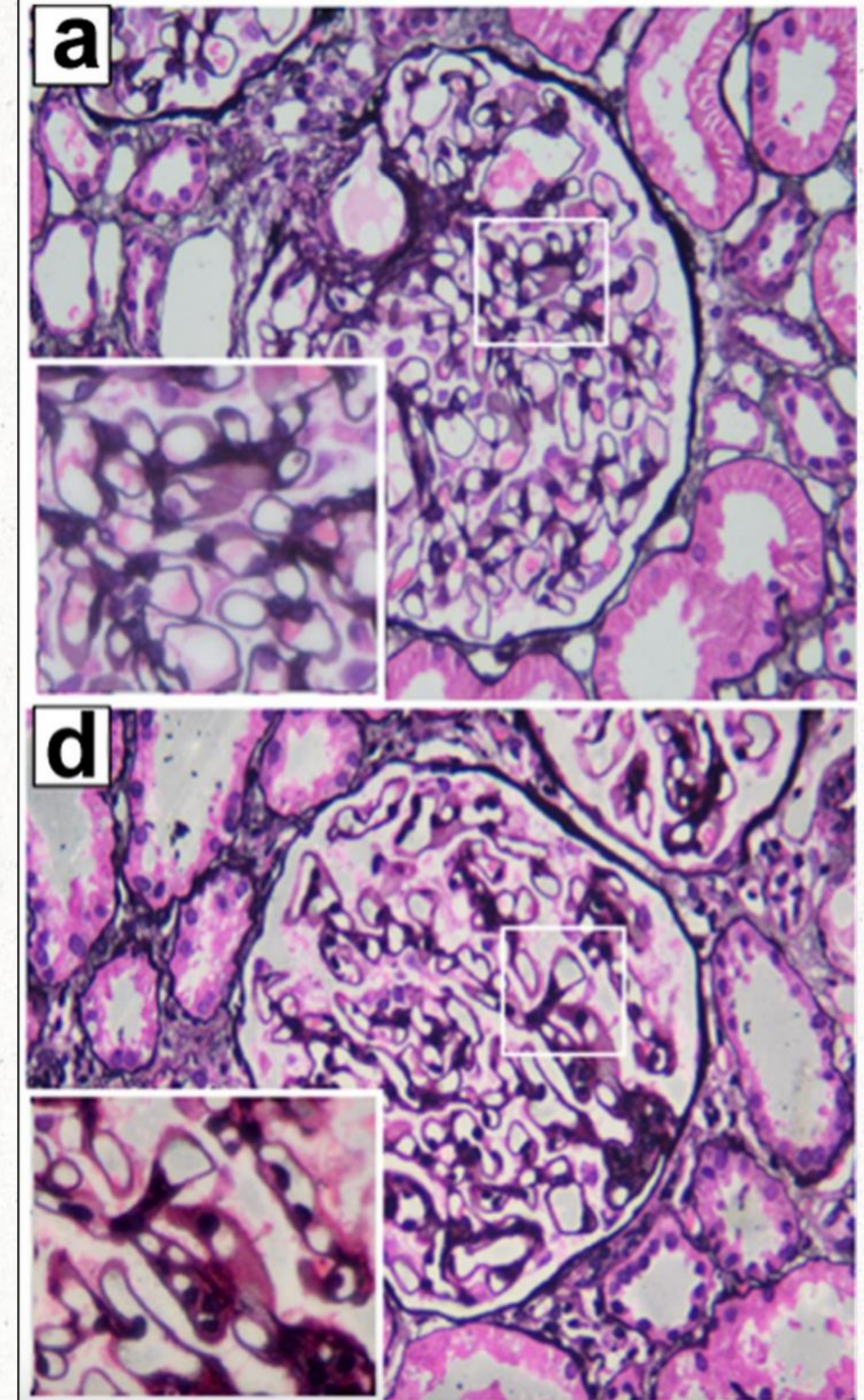
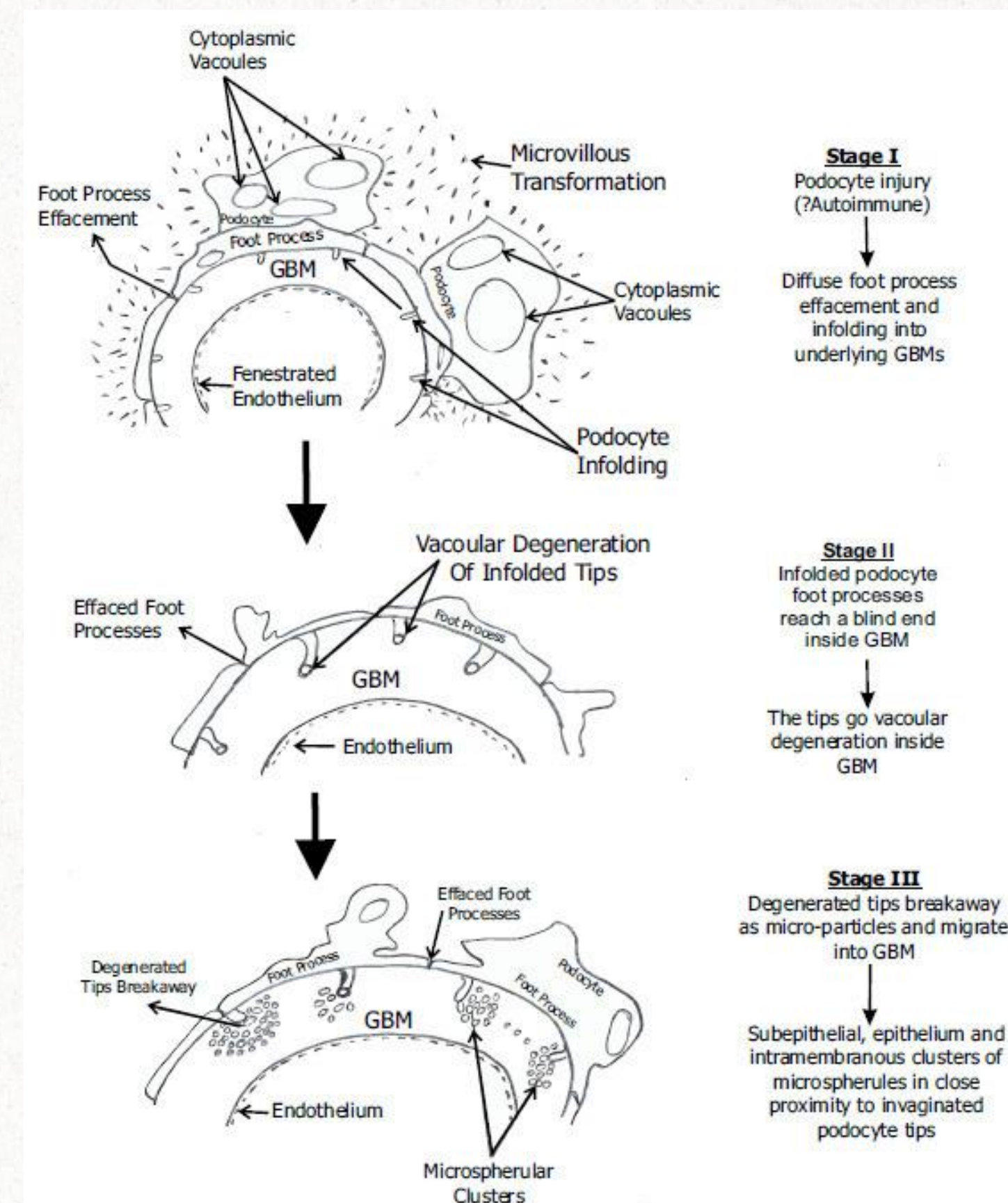
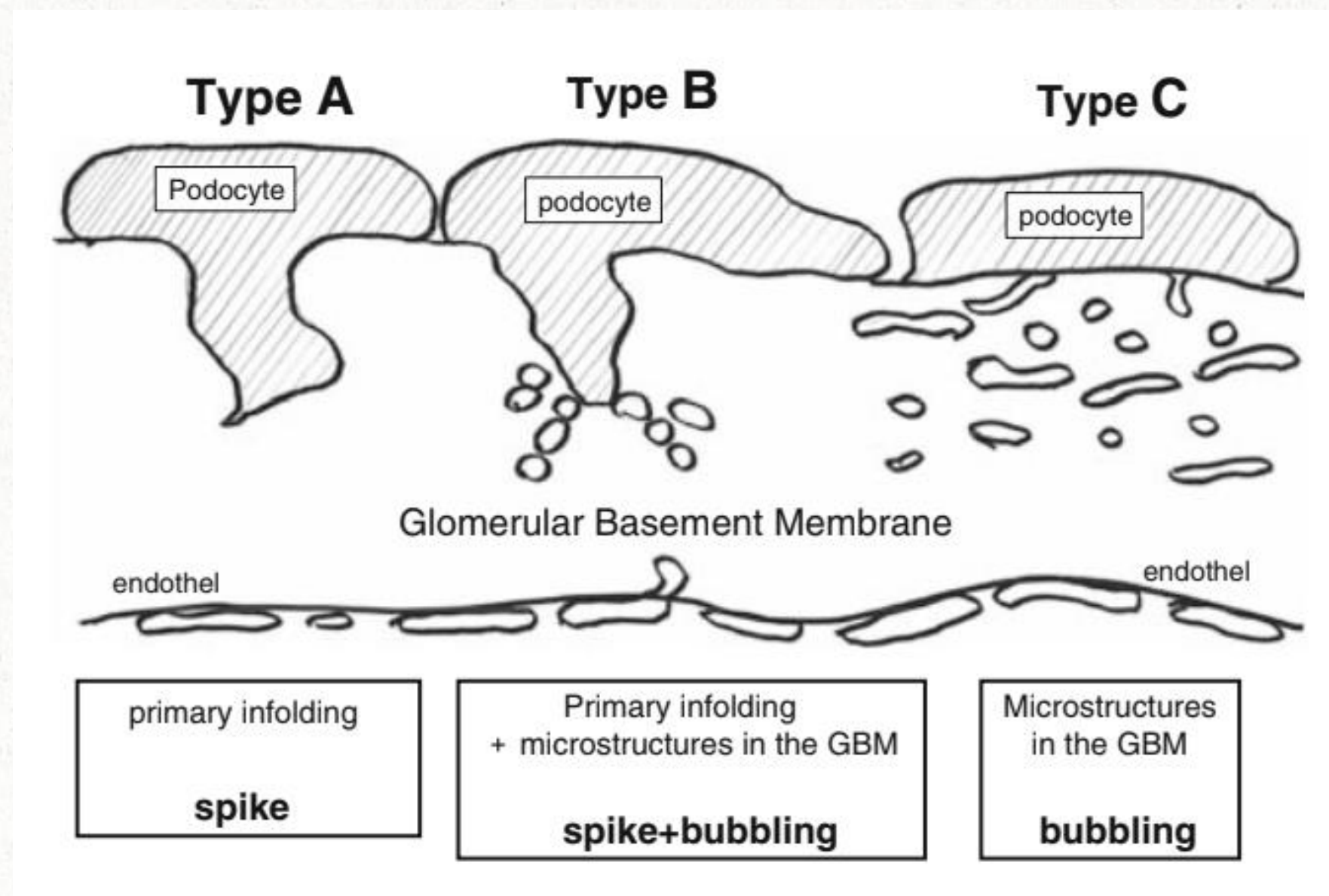


Image from Hong L et al. Kidney Int Rep. 2023;8(12):2742–53.

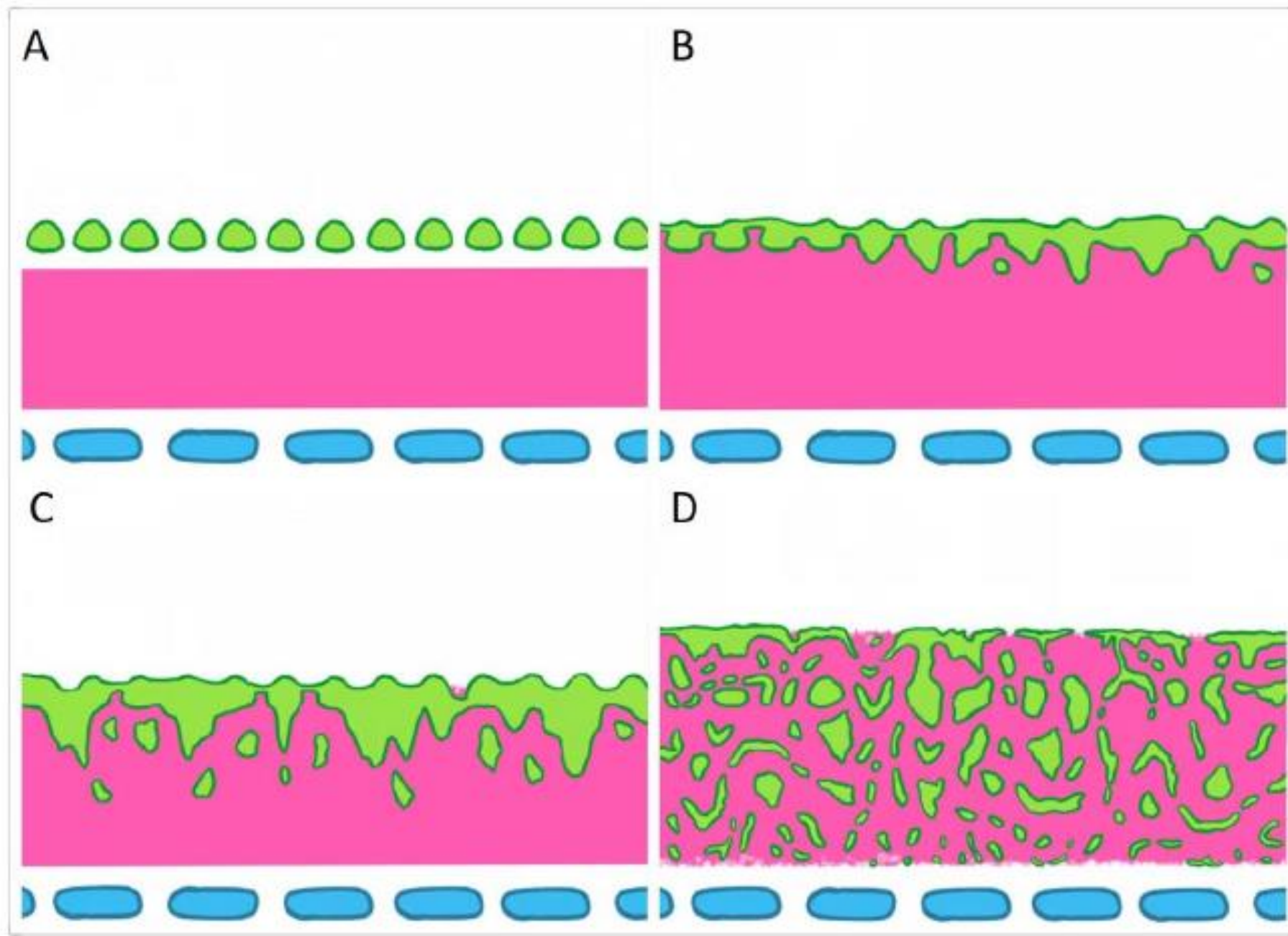


Above image from Joh K et al. Clin Exp Nephrol. 2008;12(6):421-31.

Left image from Matthai SM et al. Indian J Nephrol. 2024;34(4):397.

The severity of PIG correlates with worse treatment response

Image from Hong L et al. Kidney Int Rep. 2023;8(12):2742–53.



A, Normal filtration barrier. B, Mild PIG; C, Moderate PIG; D, Severe PIG.



Laser microdissection and mass spectrometry

Reduction in ACTN4

Podocyte injury →
dysfunction of the cytoskeleton →
its invasion into the GBM

► J Clin Med. 2023 Jan 30;12(3):1088. doi: [10.3390/jcm12031088](https://doi.org/10.3390/jcm12031088) 

Podocyte Infolding Glomerulopathy: A Case Series Report and Literature Review

[Yunlin Feng](#)^{1,2,3,†}, [Wei Wang](#)^{1,2,†}, [Yurong Zou](#)^{1,2}, [Tingyu Chen](#)⁴, [Wei Wang](#)^{1,2}, [Guisen Li](#)^{1,2}, [Amanda Y Wang](#)^{3,5,6},
[Ping Zhang](#)^{1,2,*}

Editor: Ernesto Paoletti

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PMCID: PMC9918010 PMID: [36769735](https://pubmed.ncbi.nlm.nih.gov/36769735/)

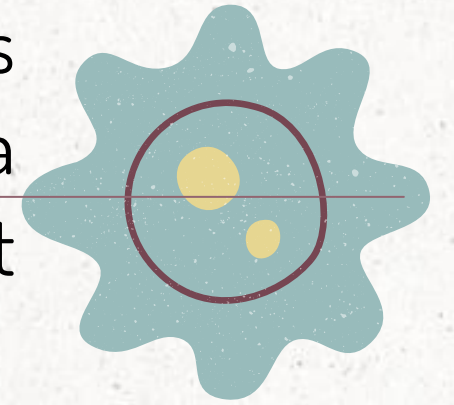
3 out of 4 cases had INF2 mutations

INF2 regulates actin cytoskeleton remodeling in podocytes

INF2 mutations lead to podocyte dysfunction

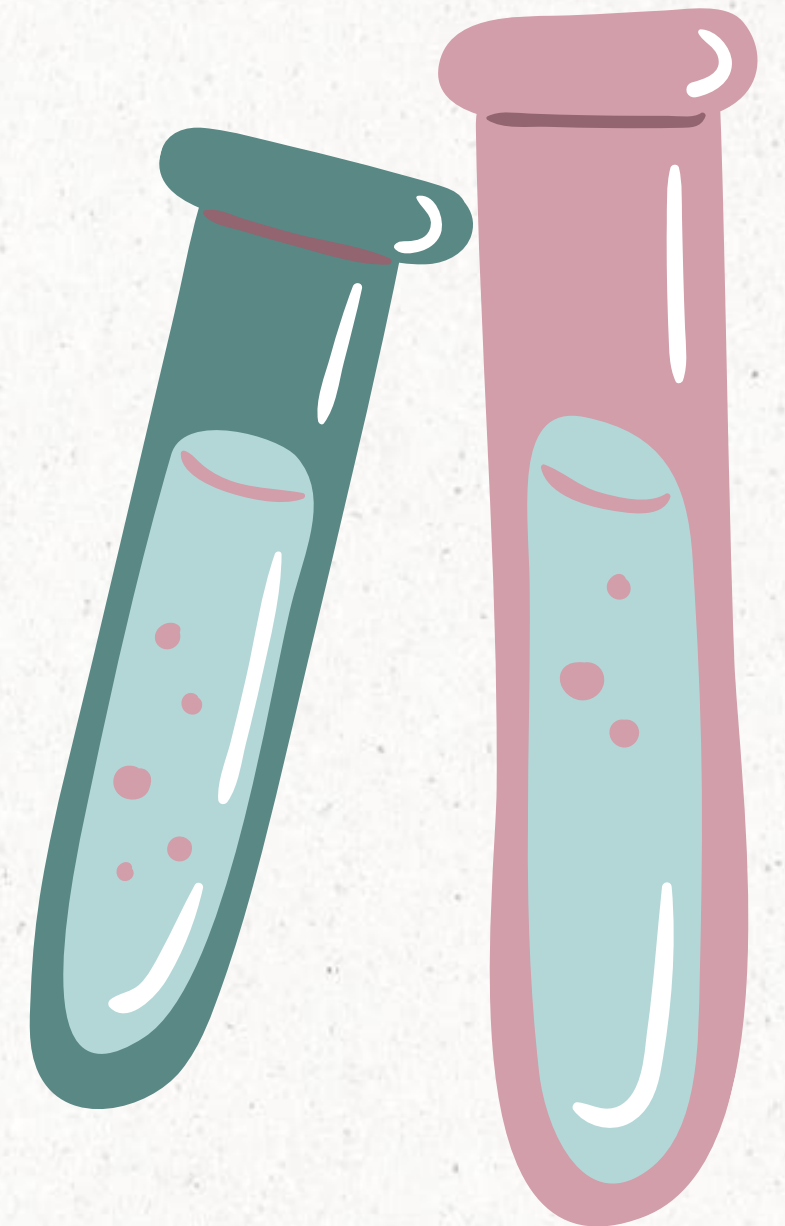
“Wherever there is human nature, there is
drama

~ Hercule Poirot



GEOGRAPHICAL VARIATIONS

- Genetics
- Environment
- Access to EM
- Awareness bias
- Under sampling as steroid-responsive



SUMMARY

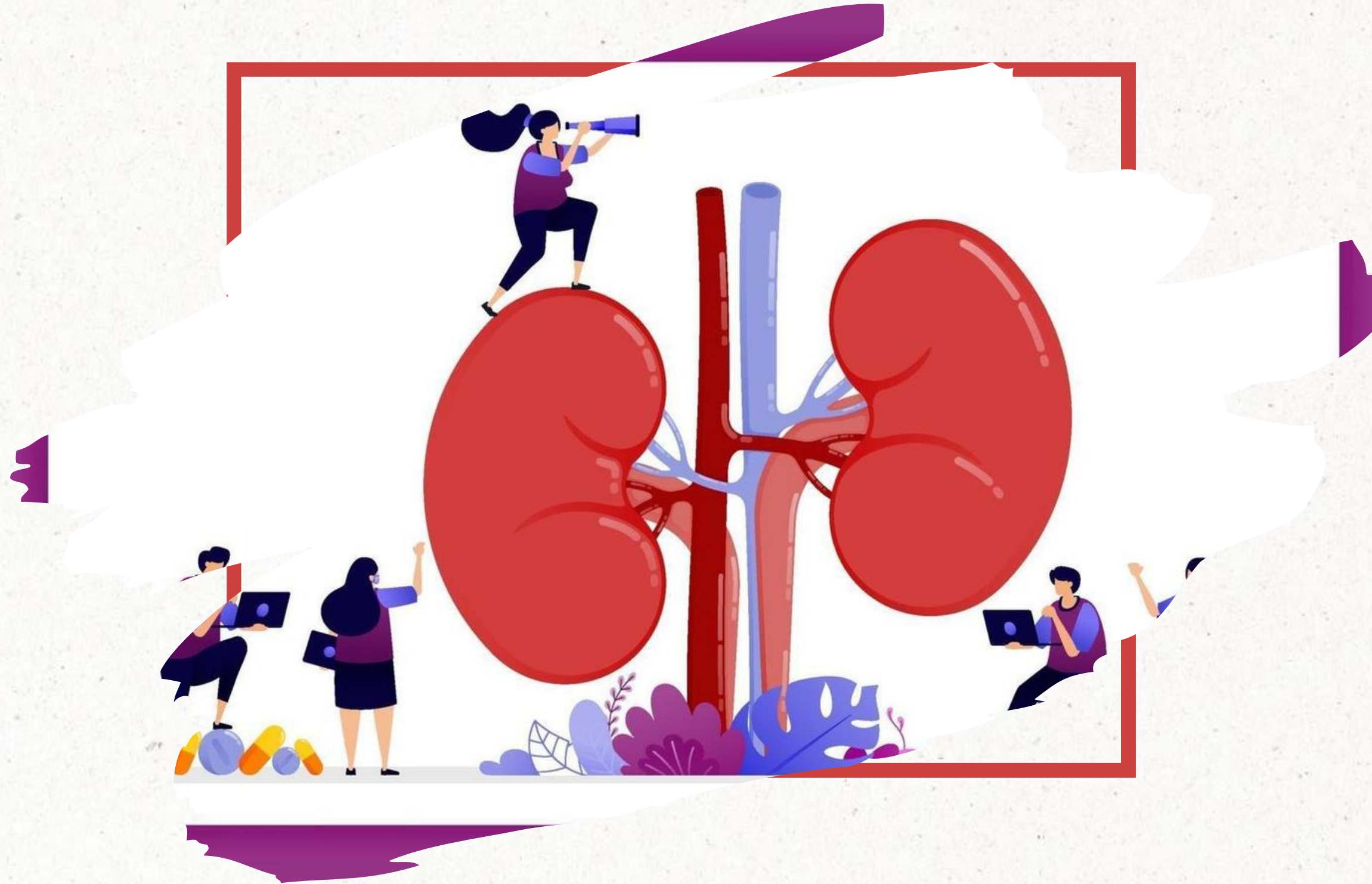
PIG is a rare glomerulopathy

Often associated with connective
tissue disorders

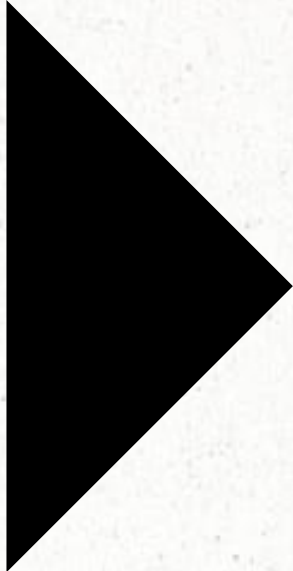
Can mimic membranous nephropathy

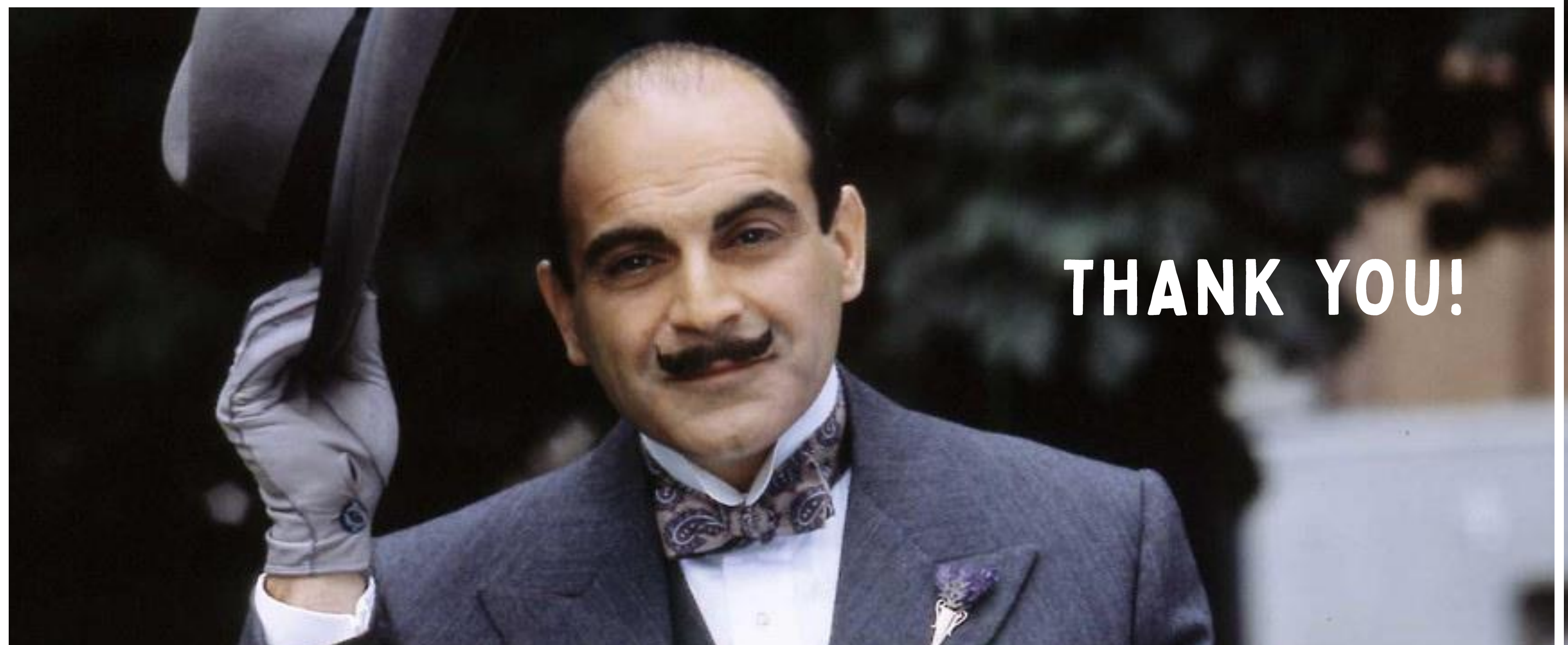
EM is paramount for diagnosis

Good response to steroids



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Any questions?