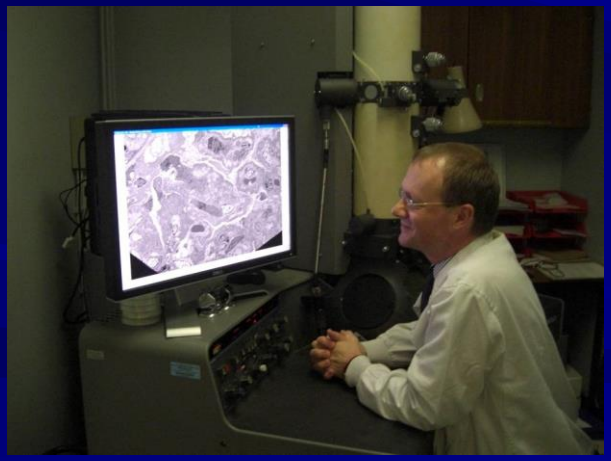
Basic Renal EM workshop

Southampton

September 30th 2011

Renal Ultrastructural Pathology
Lecture 1 C - D



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Renal Ultrastructural Pathology Lecture 1 - Topics

1. Crescentic nephritis
2. Cryoglobulinaemic glomerulonephritis
3. Crystals
4. Diabetic nephropathy

Crecsentic Glomerulonephritis

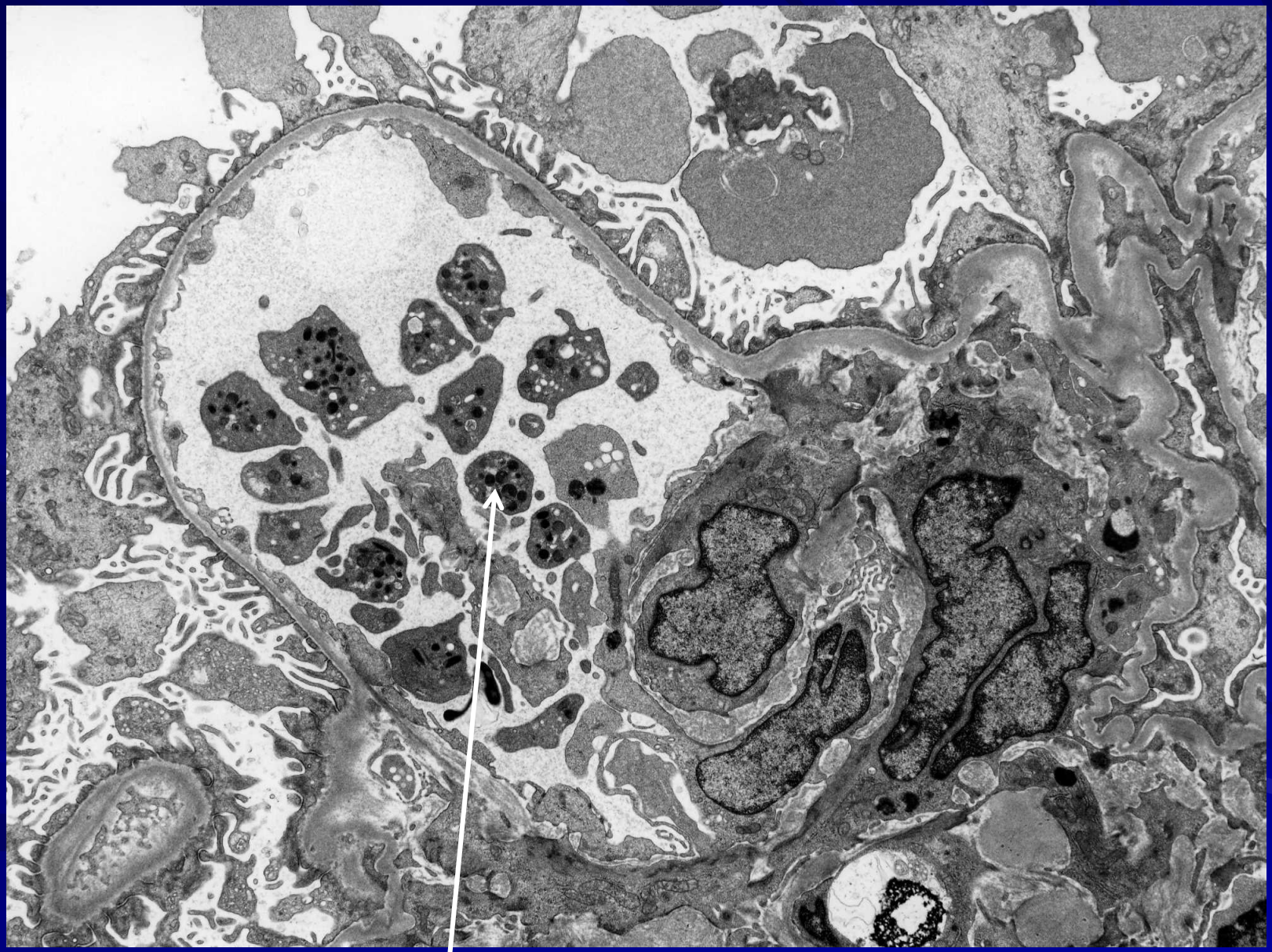
Crescentic Glomerulonephritis

- Most commonly caused by a pauci-immune autoimmune vasculitis, like Wegener's Granulomatosis, microscopic polyarteritis.
- Examples of non-pauciimmune crescentic GN are: SLE, IgA disease.
- Typically present with macroscopic haematuria and acute renal failure

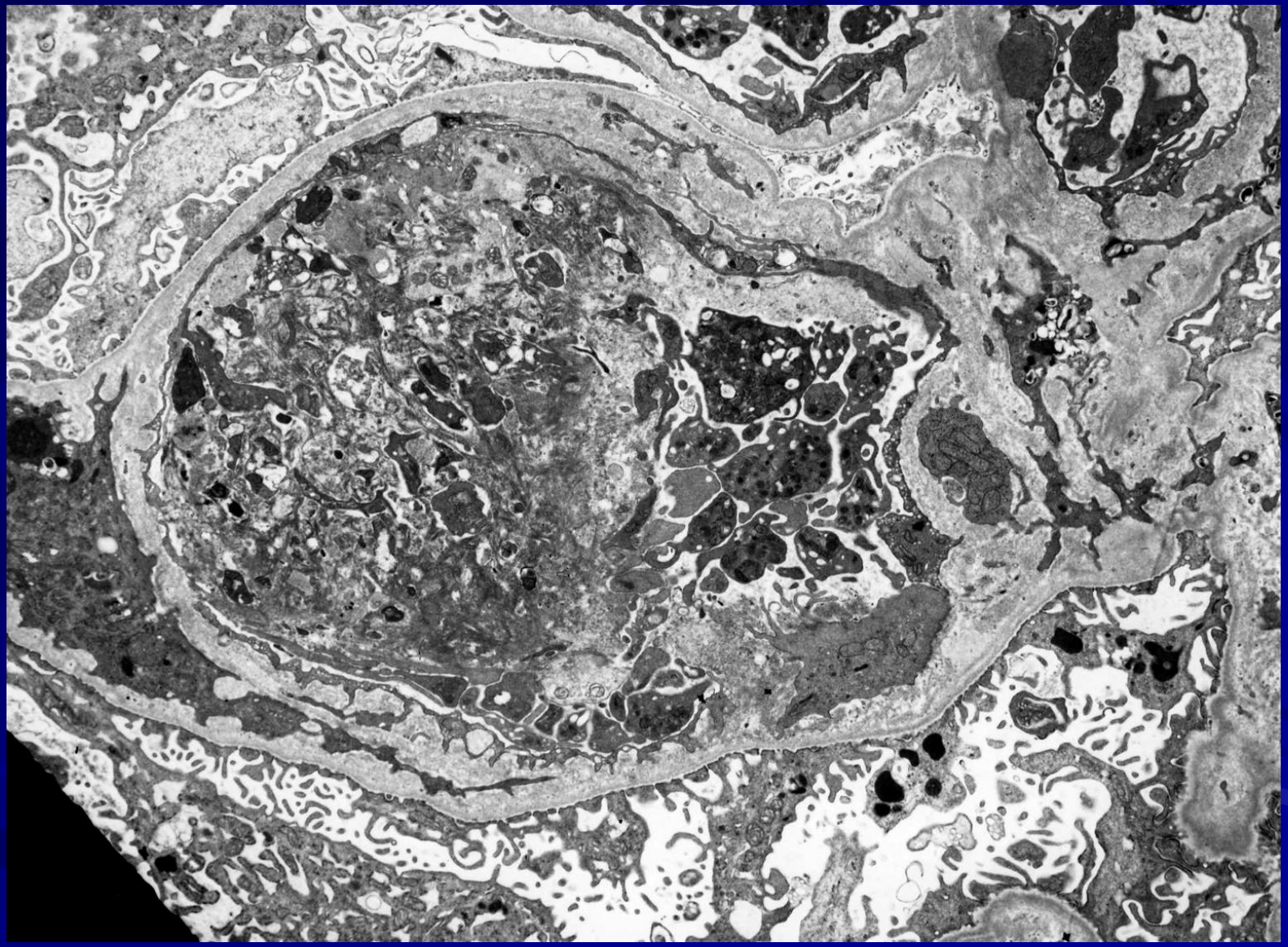
Crescentic Glomerulonephritis
Stage 1
Acute/segmental necrosis

- Endothelial cell damage
- Platelet and fibril clot in glomerular capillary loop
- Microinfarction
- Rupture of capillary loop
- Spillage of fibril into part of Bowman’s space

Pauci-immune vasculitis



Laminated thrombus within capillary loop



Laminated thrombus

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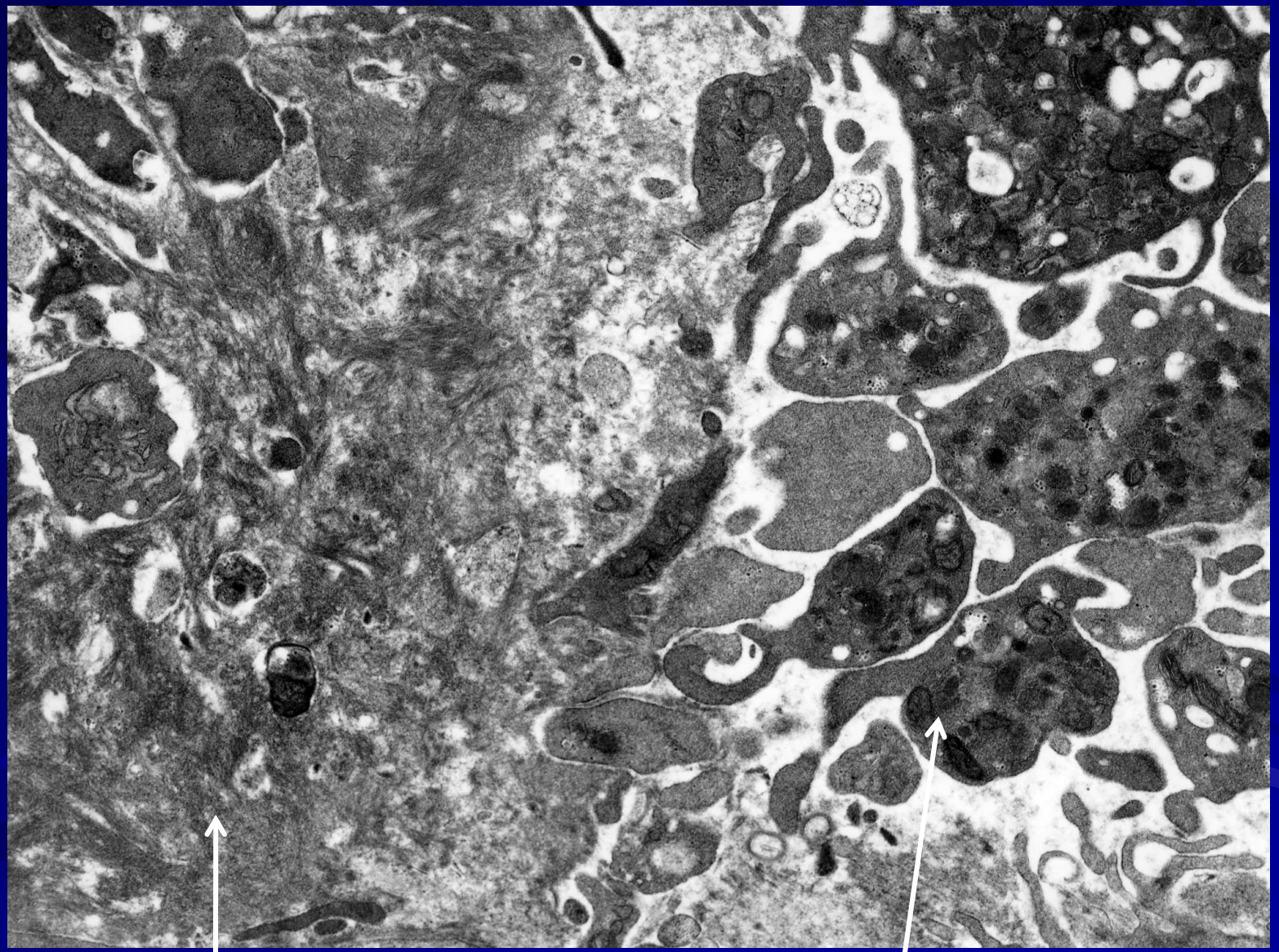
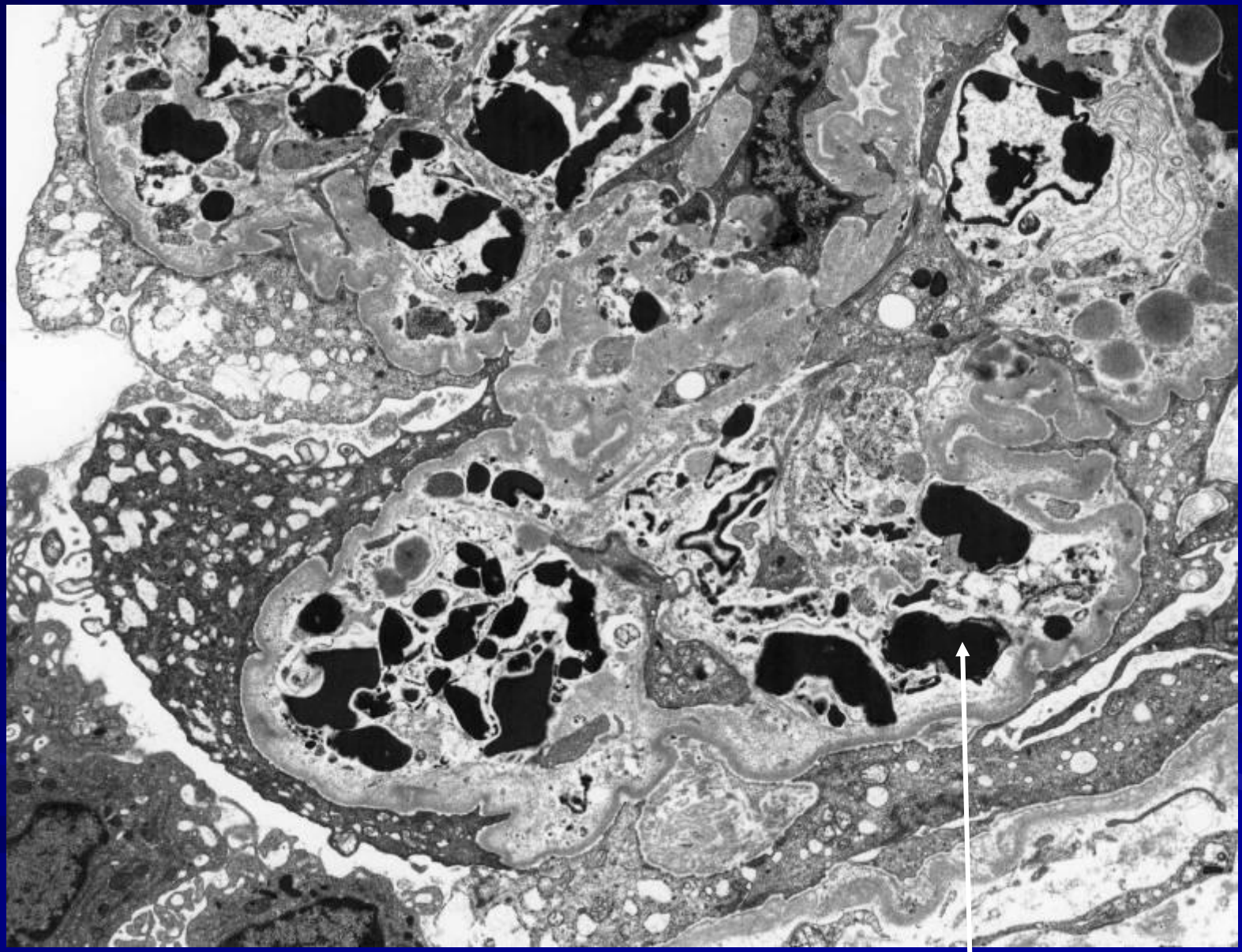
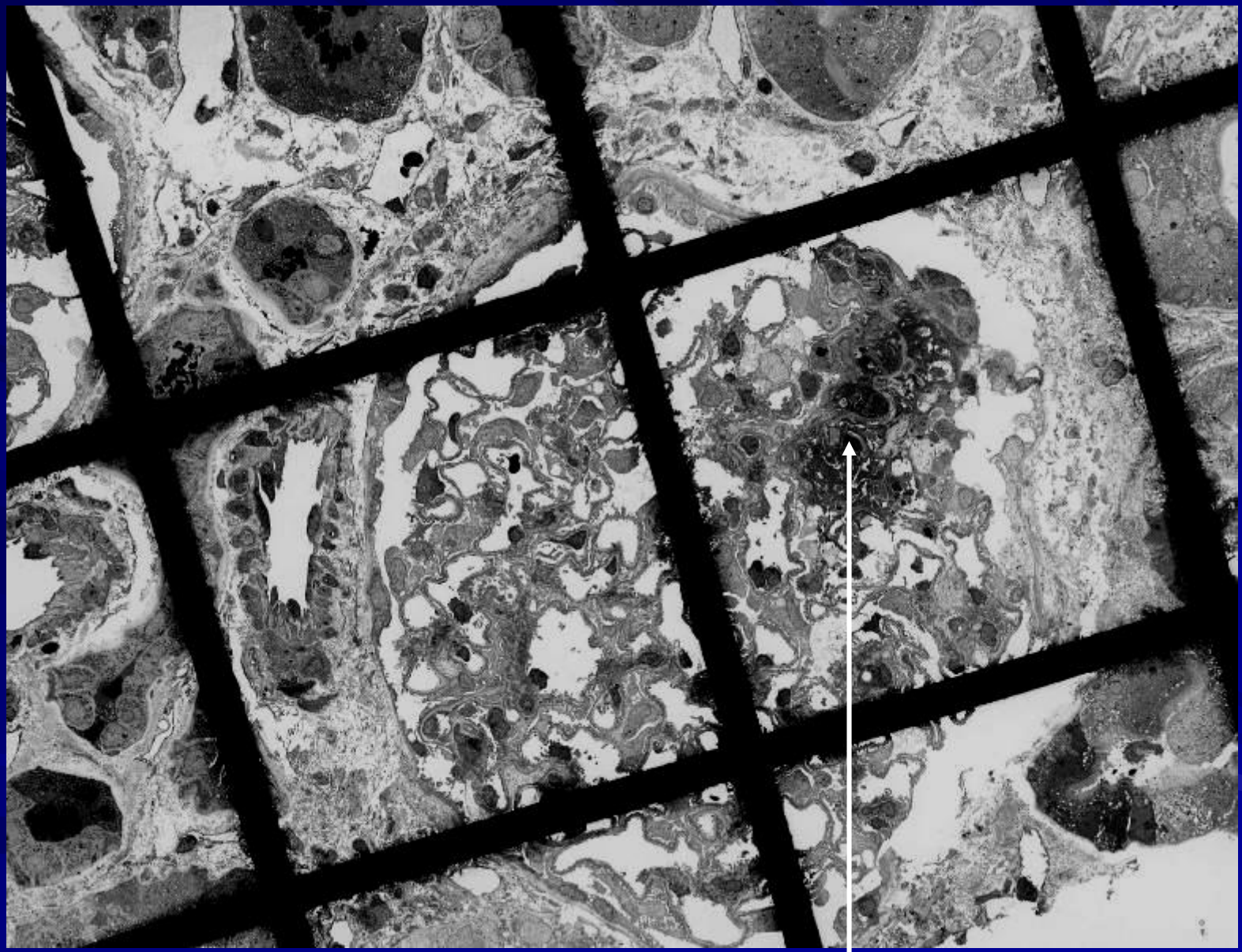


Platelet and fibrin thrombus

Aggregated platelets

Pre-crescentic lesion. Segmental necrotic lesion/micro infarct





Precrescentic pathology – segmental necrotic/fibrinous lesion

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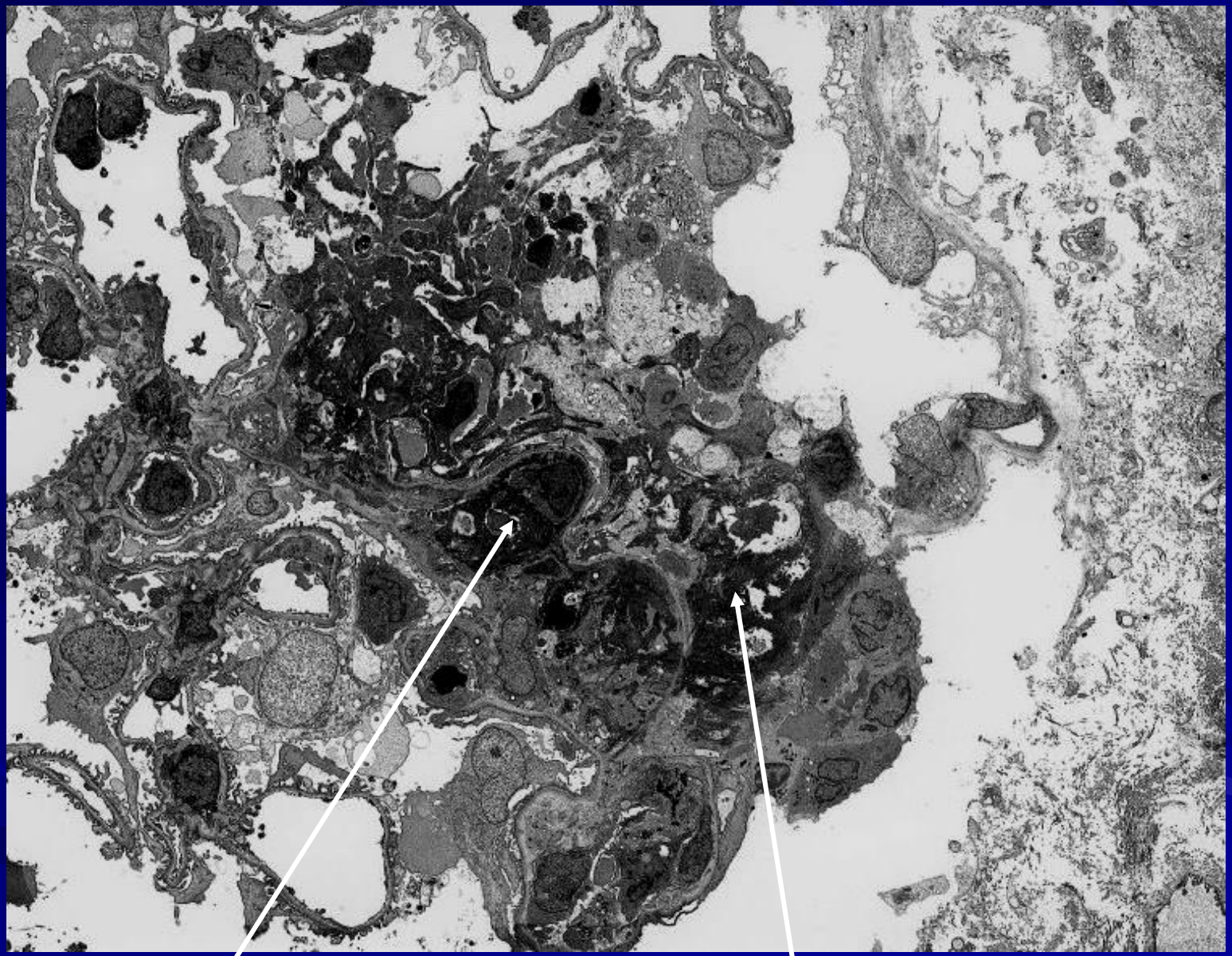
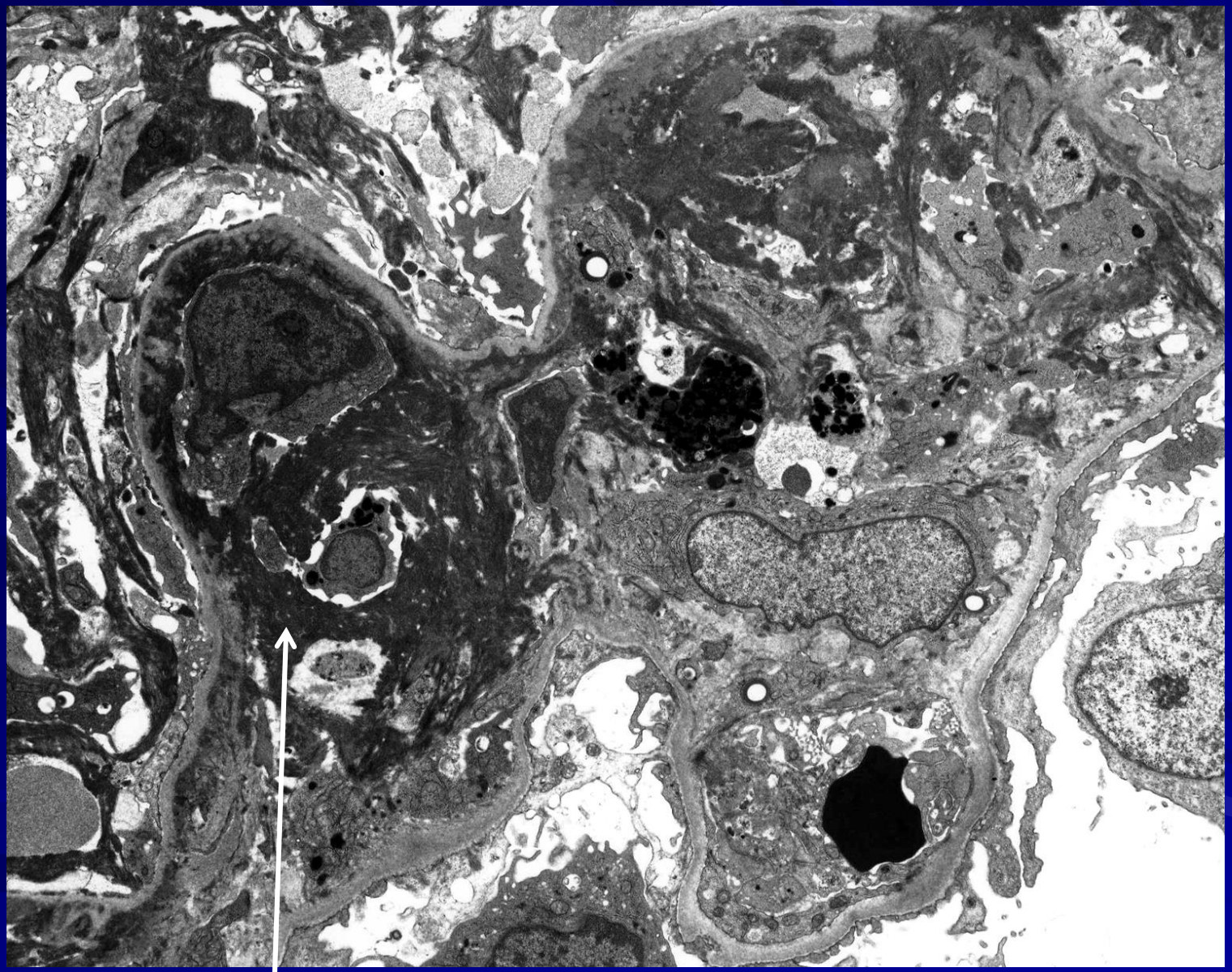
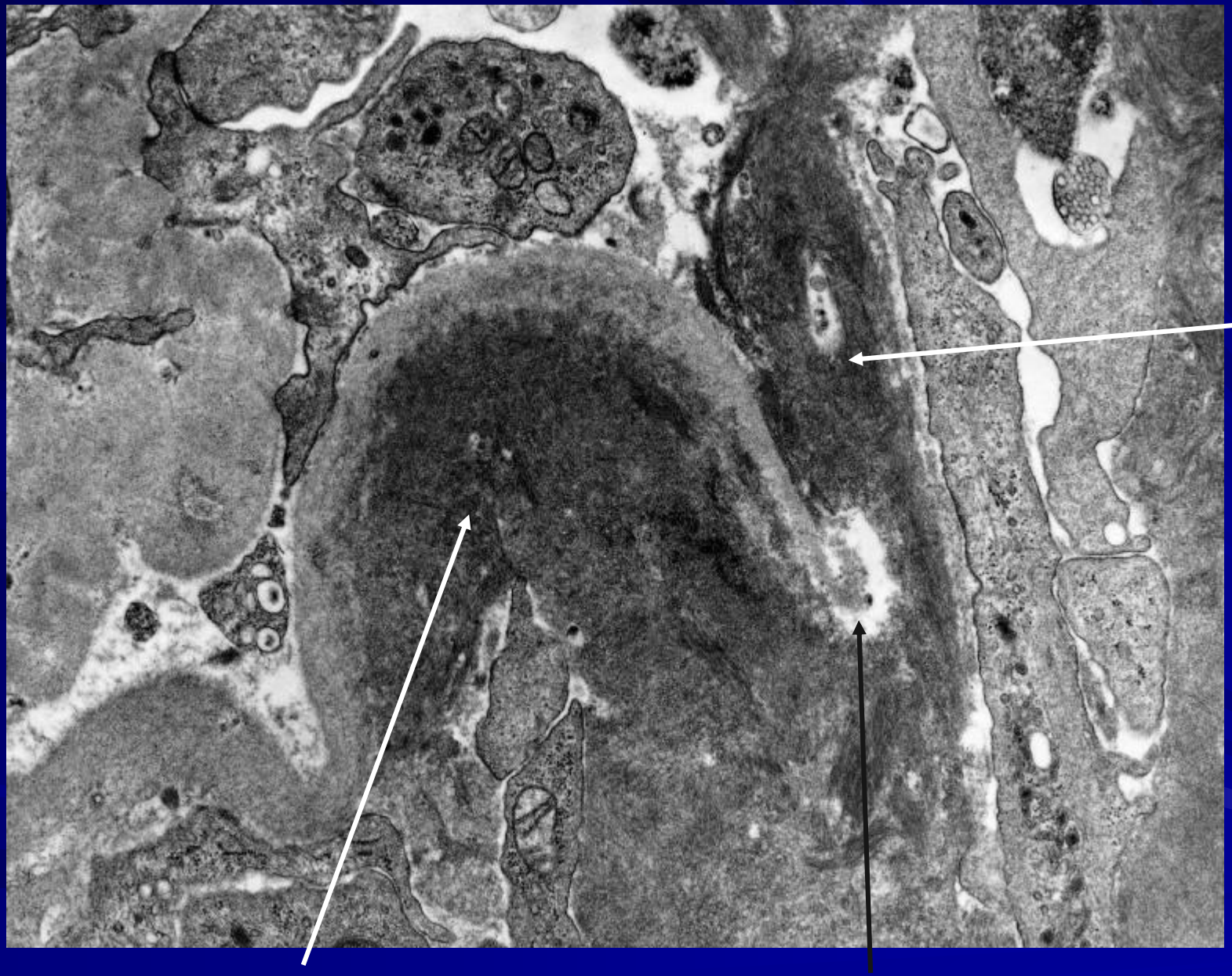


Endocapillary polymerised fibrin

Polymerised fibrin spilling out into urine space



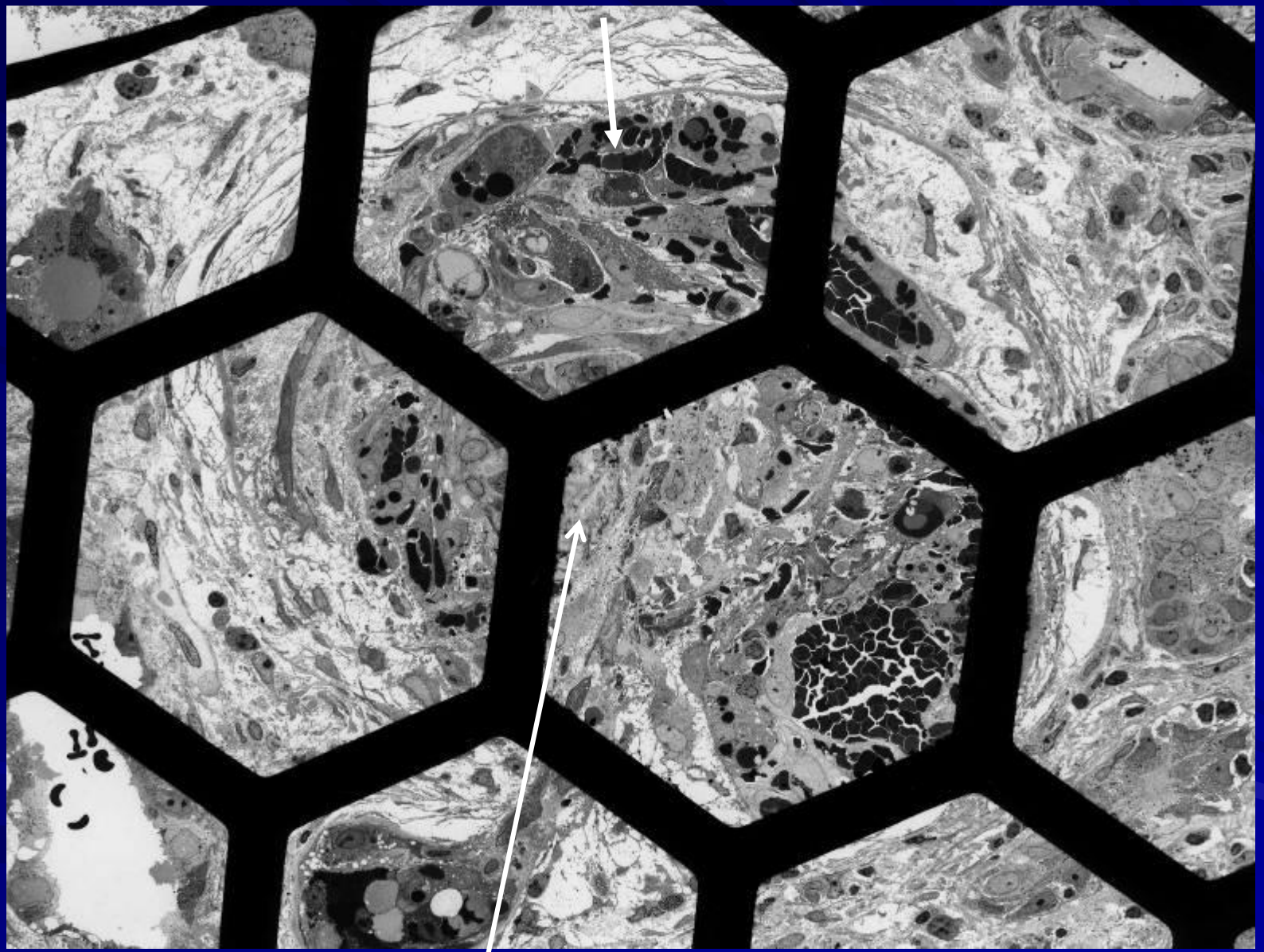
Polymerise fibrin in capillary loop


Polym-
erised
fibrin in
urine
space
Polymerised fibrin within capillary lumen
Point of GBM rupture

Crescentic glomerulonephritis
Stage 2
Cellular crescent

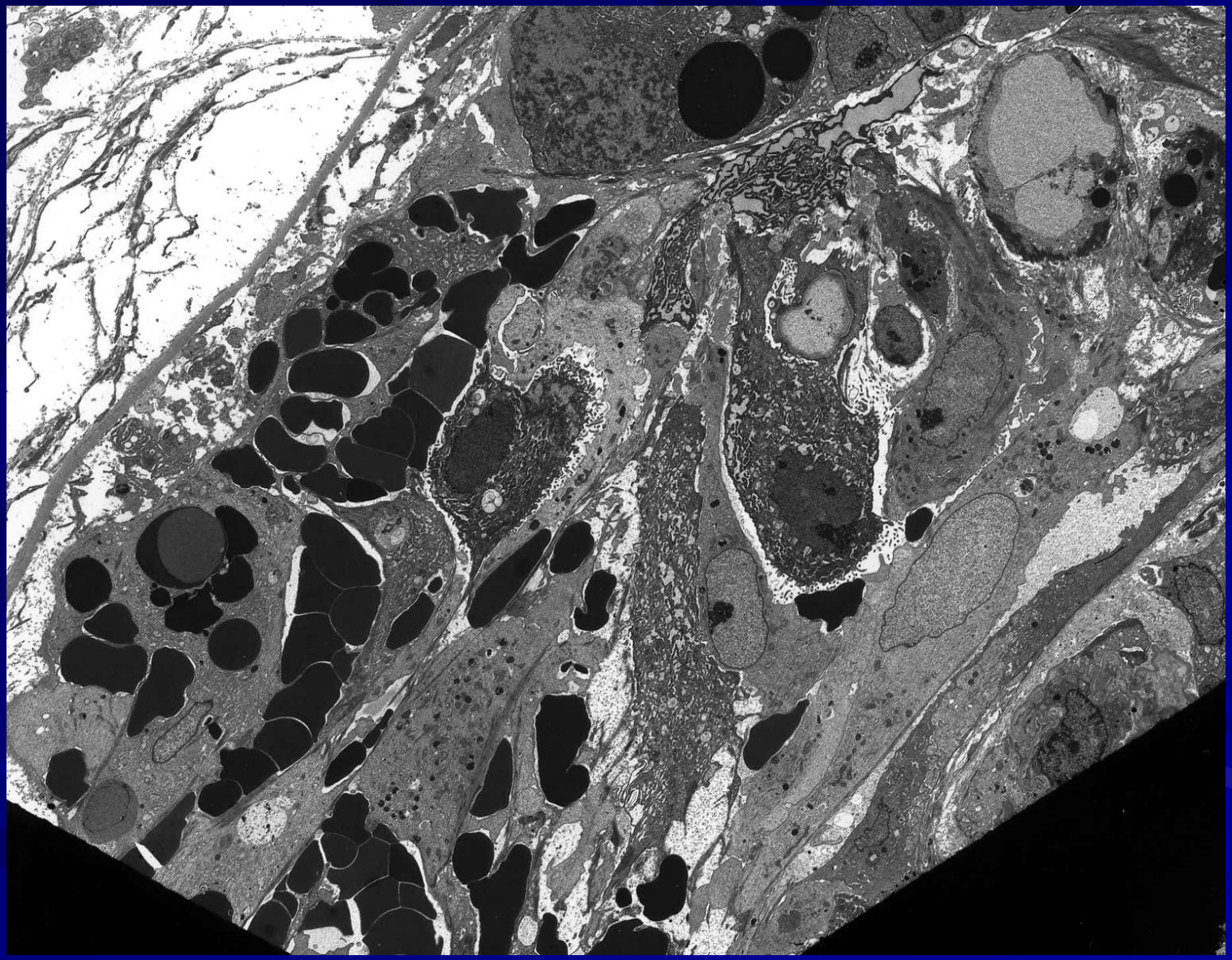
- Recruitment of inflammatory cells into fibrin filled Bowman's space
- Transformation of epithelial cells into facultative fibroblasts

Cellular crescent with extensive haemorrhage into Bowman's space



Collapsed glomerular tuft

Cellular crescent in Bowman's space



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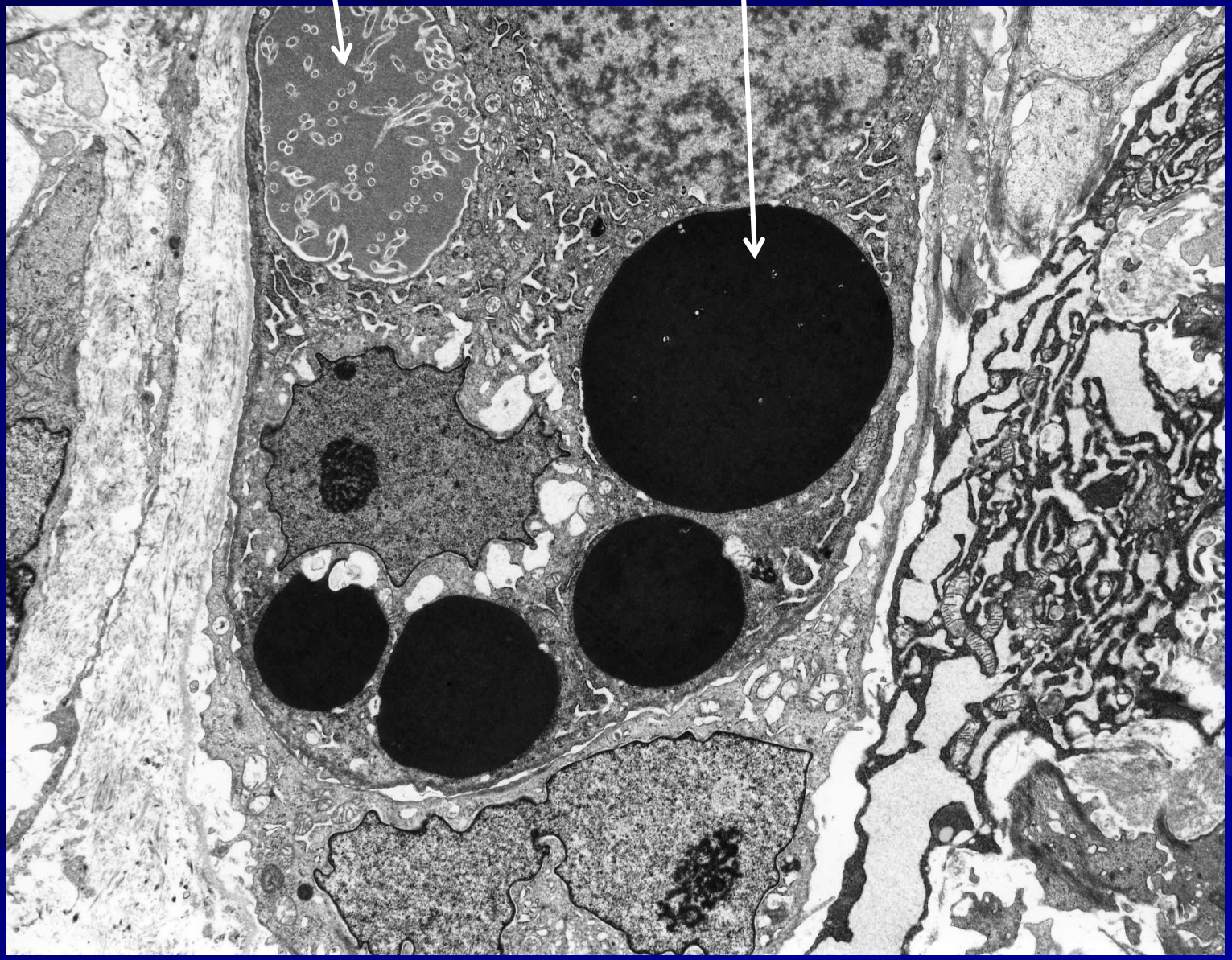
Microvilli lined vacuole

Erthrophagocytosis



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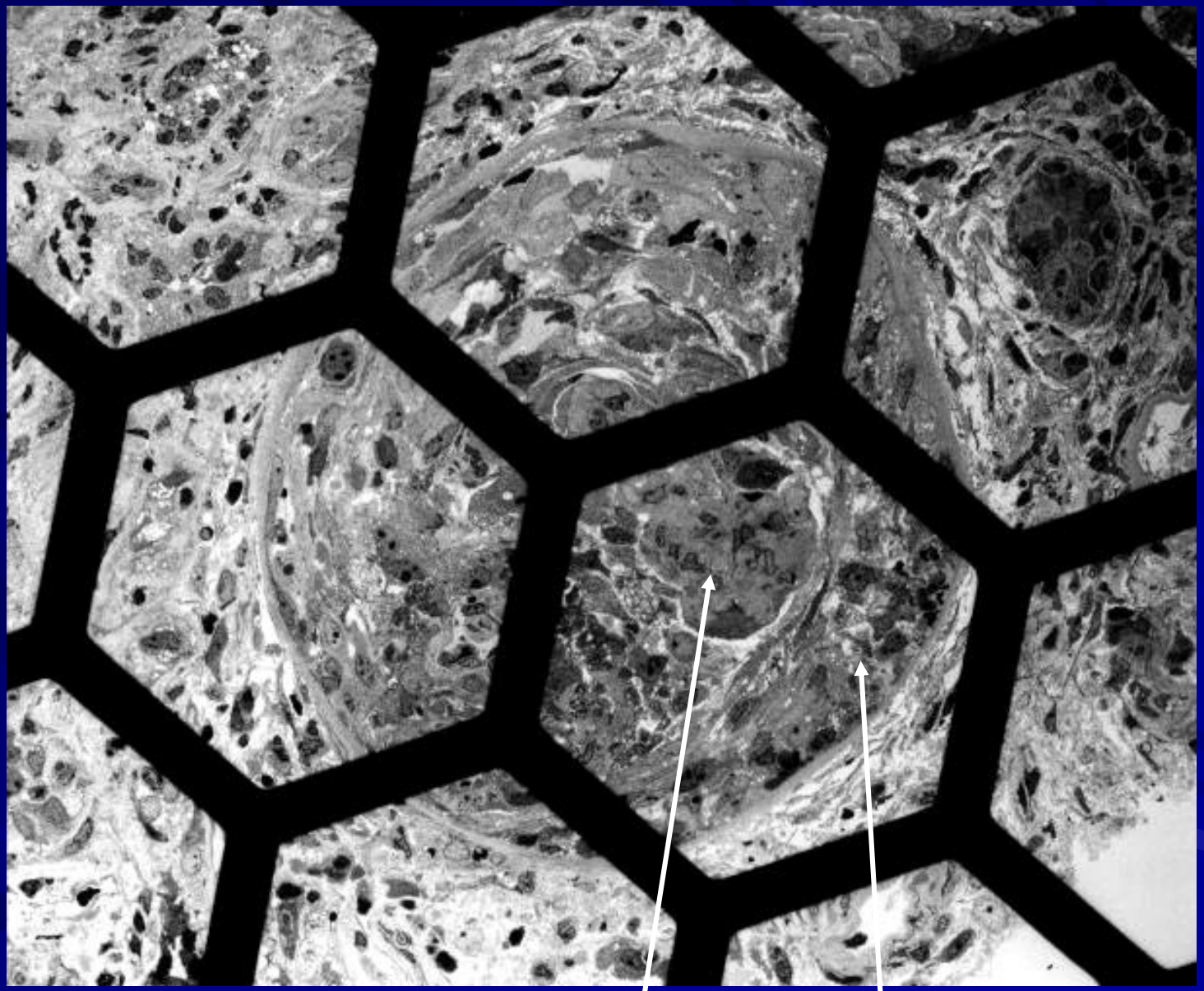
Collapsed tuft
Cellular crescent

Cellular crescent

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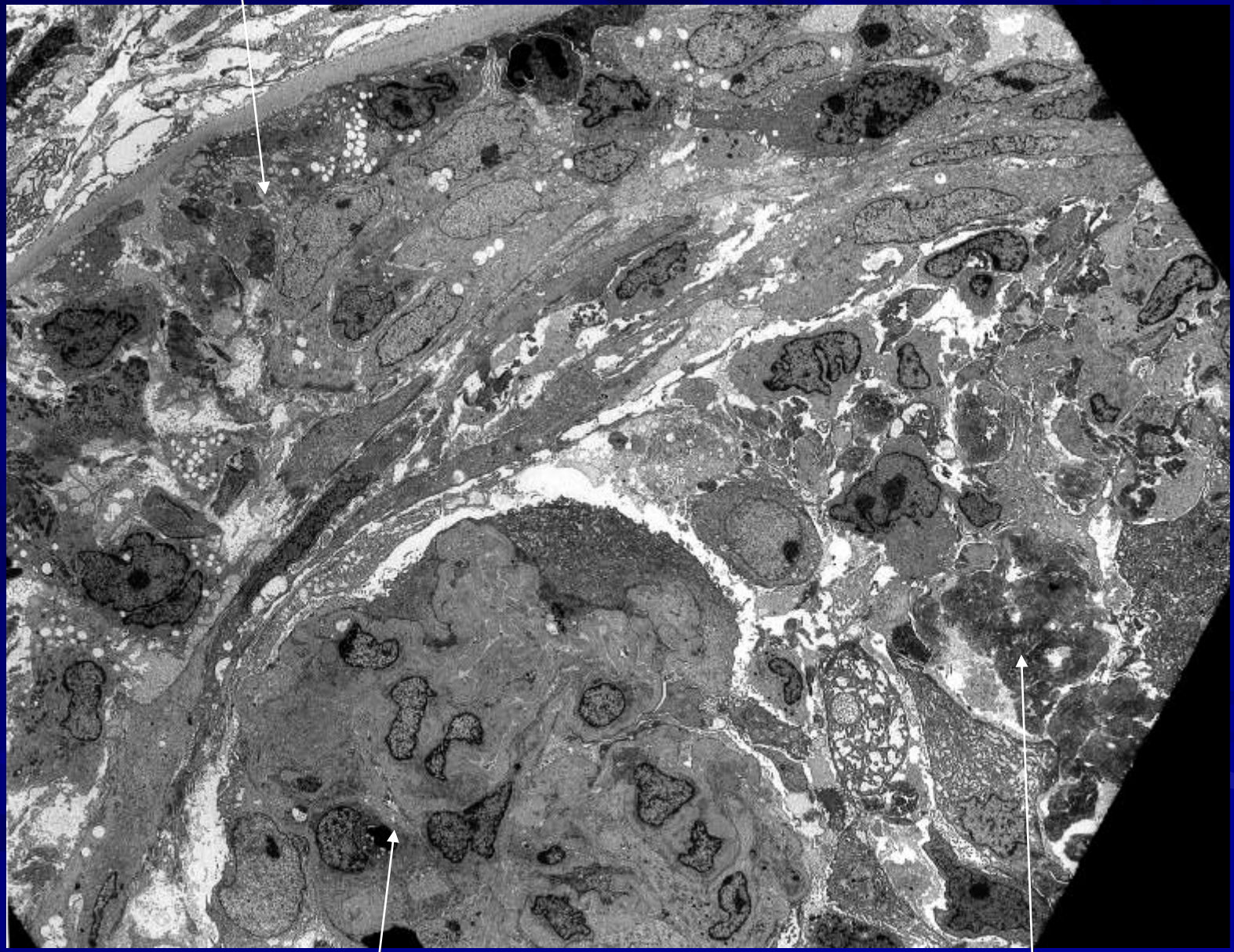
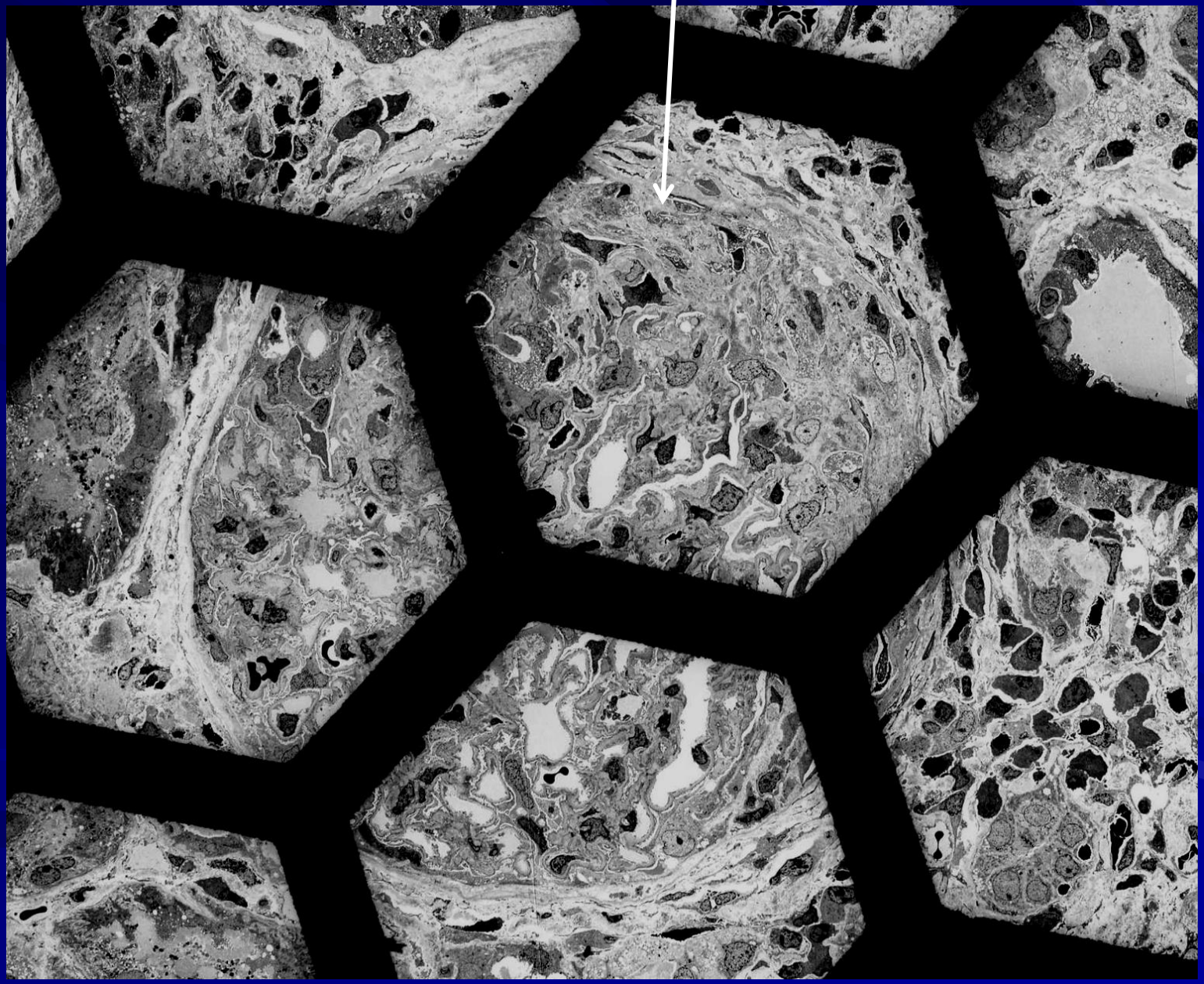


Collapse of glomerular tuft

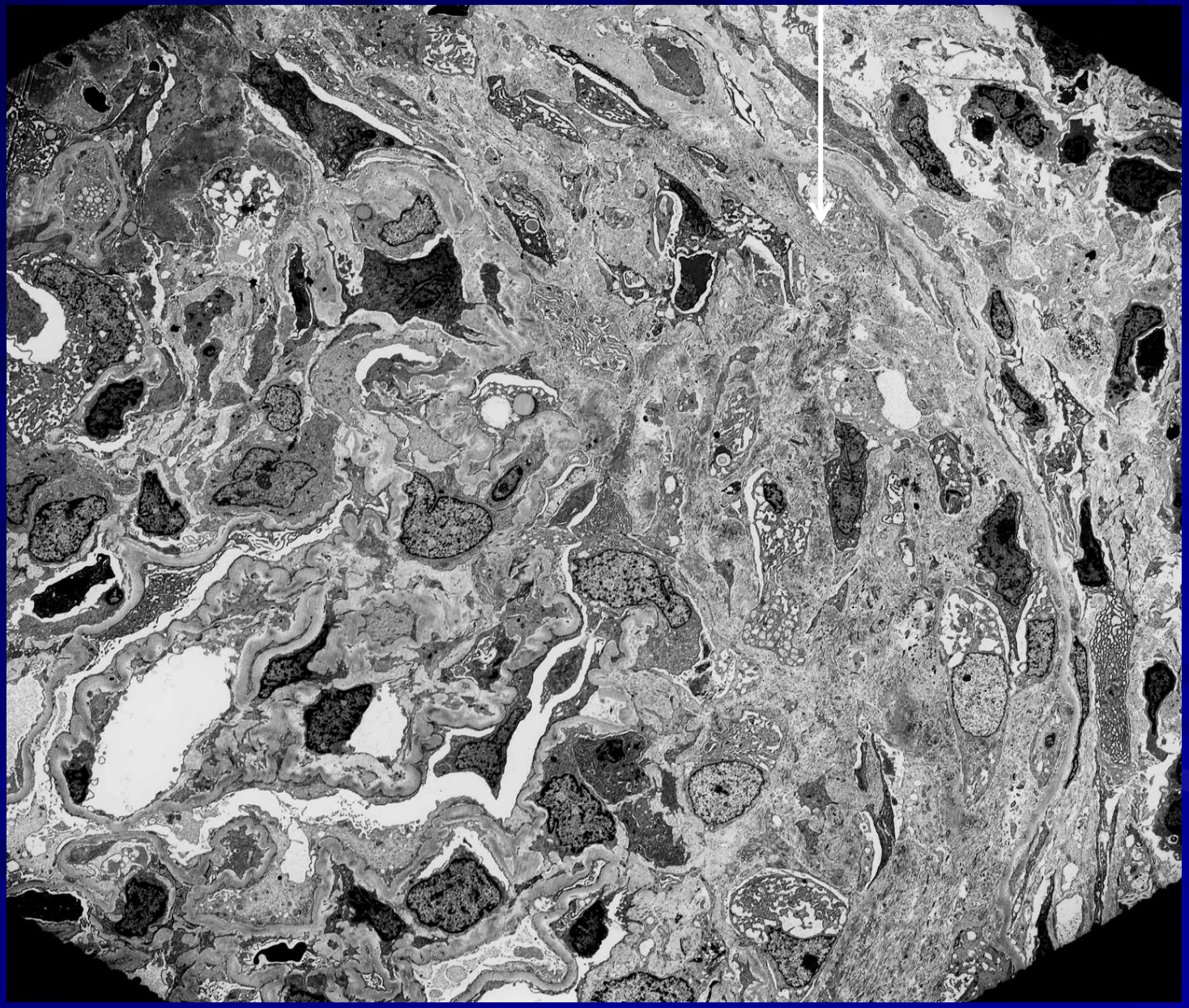
Polymerised fibrin

Crescentic glomerulonephritis
Stage 3
Fibrous crescent

- Synthesis of extracellular matrix
- Full dissolution of polymerised fibrin


Fibrous crescent

Fibrous crescent



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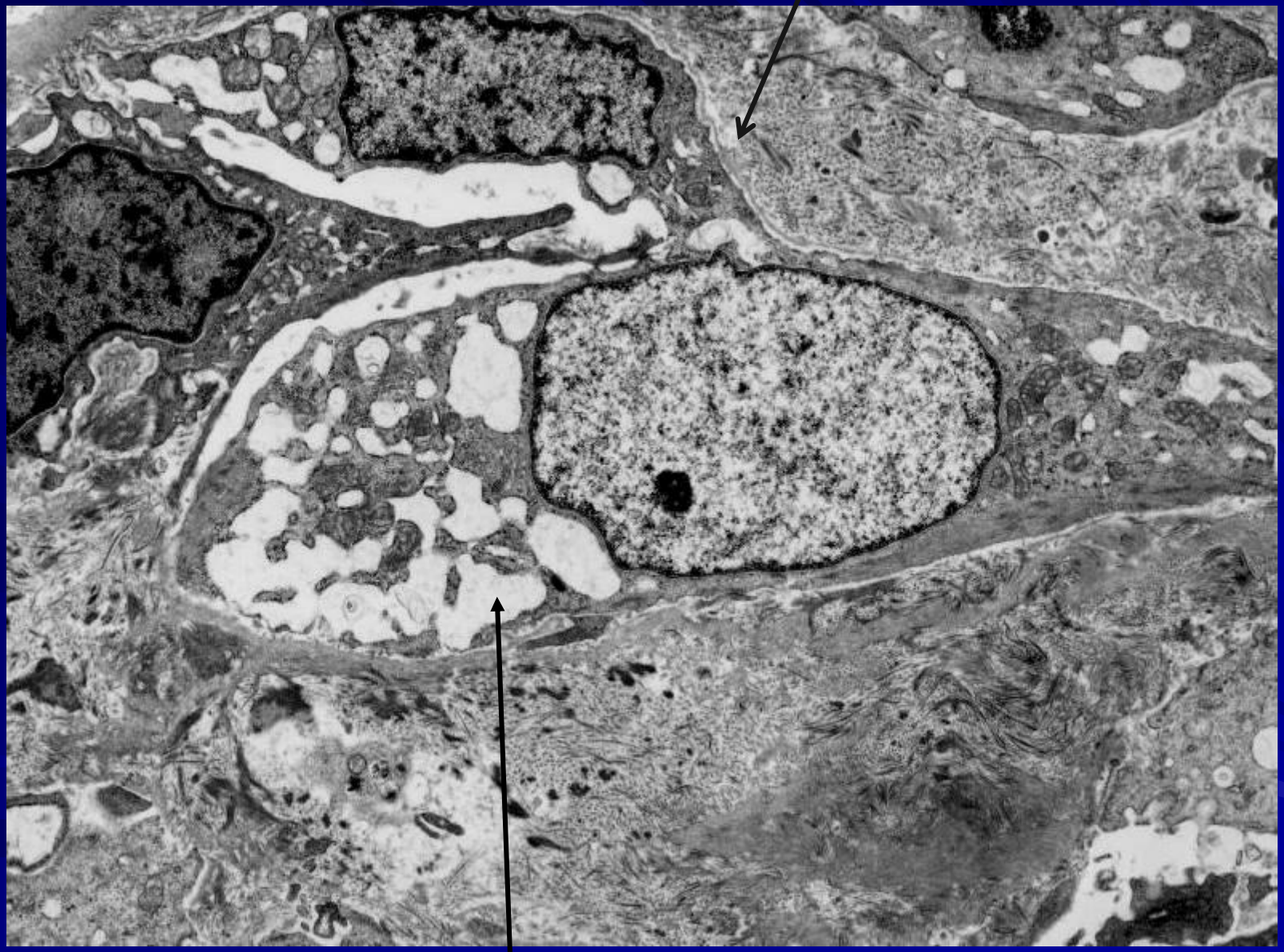
Thin new basement membrane



Fibrous crescentic epithelial cell with abundant dilated rough endoplasmic reticulum

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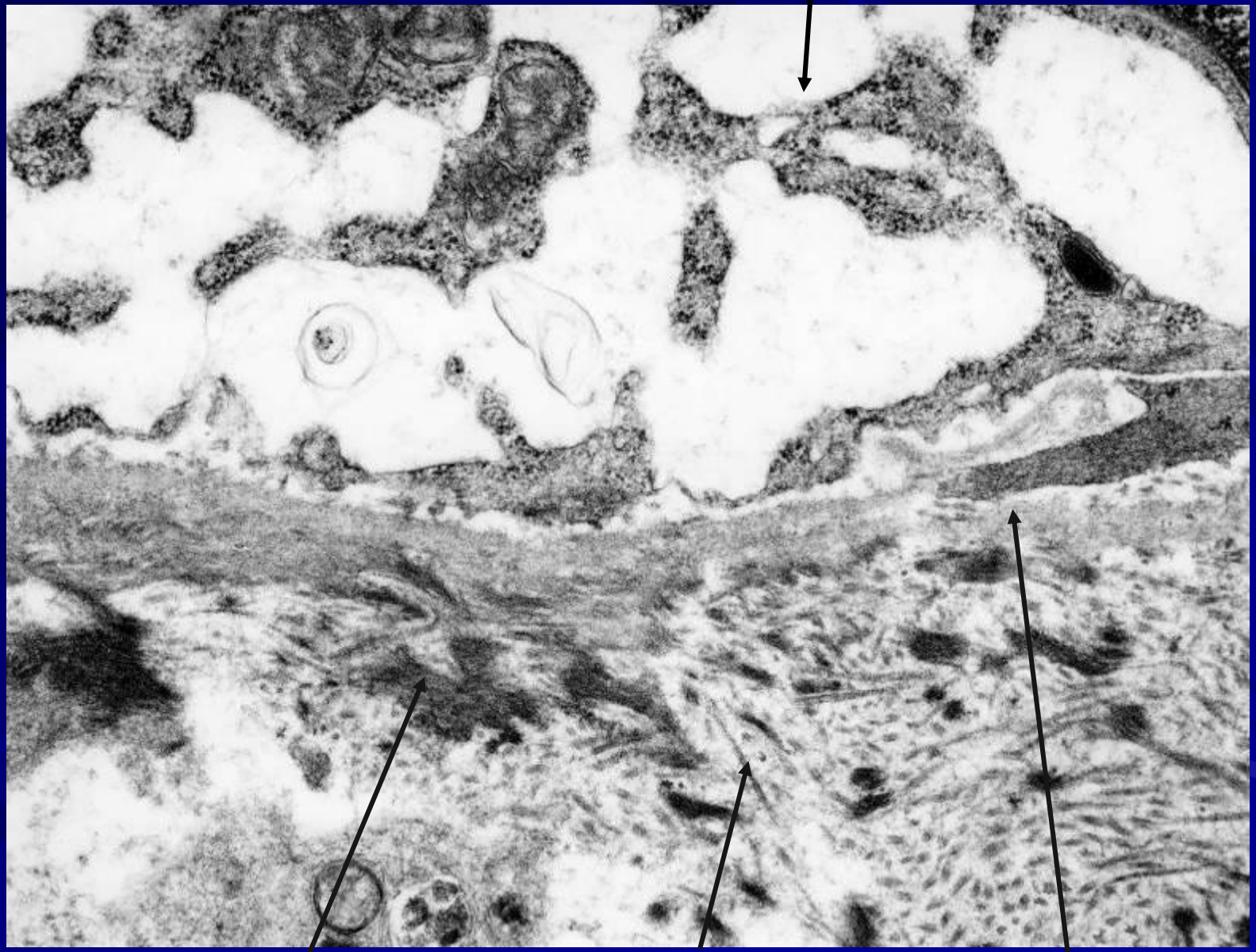
Dilated rough endoplasmic reticulum

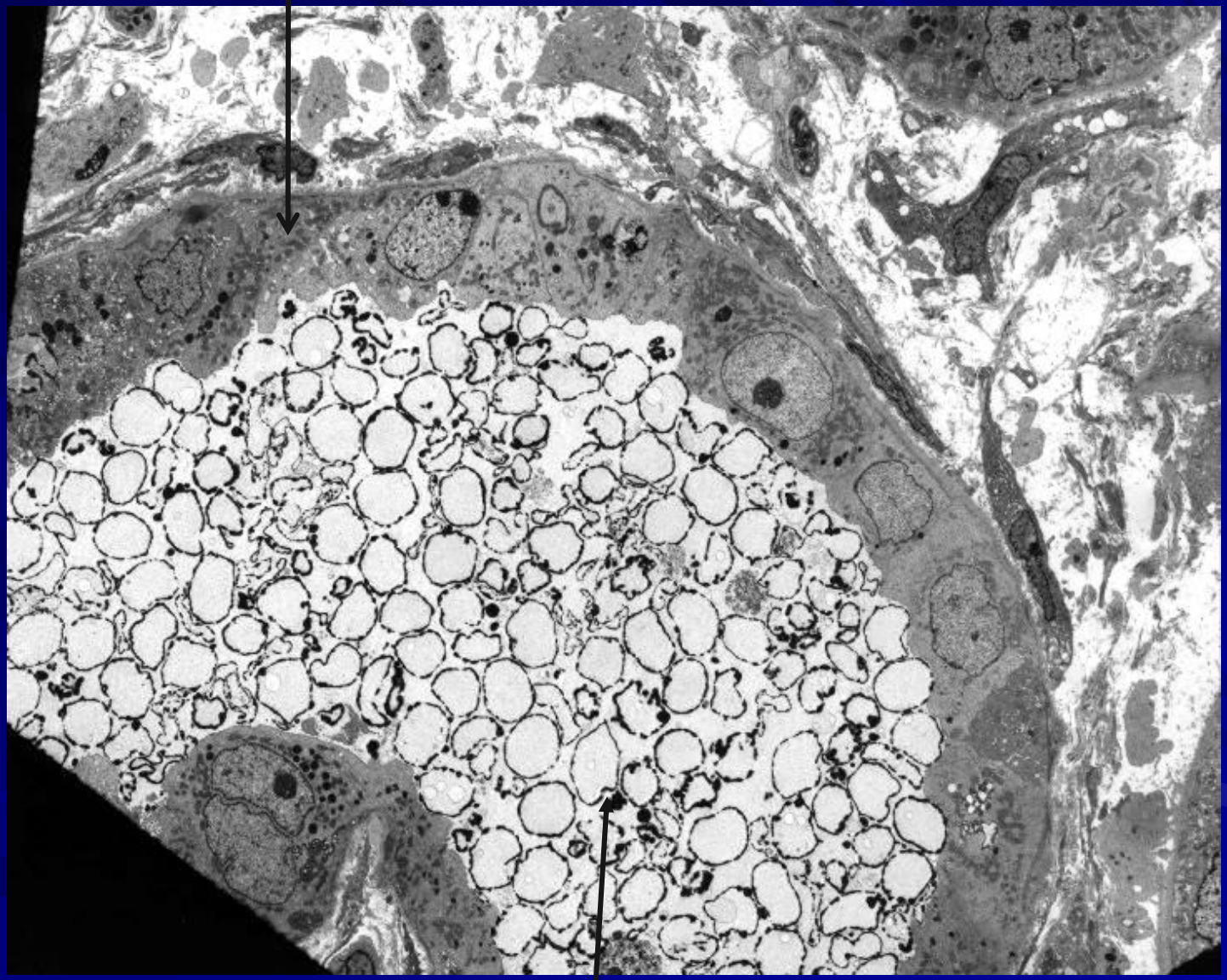


Partially lysed polymerised fibrin

Fibrous collagen

New basement membrane

Frank haematuria



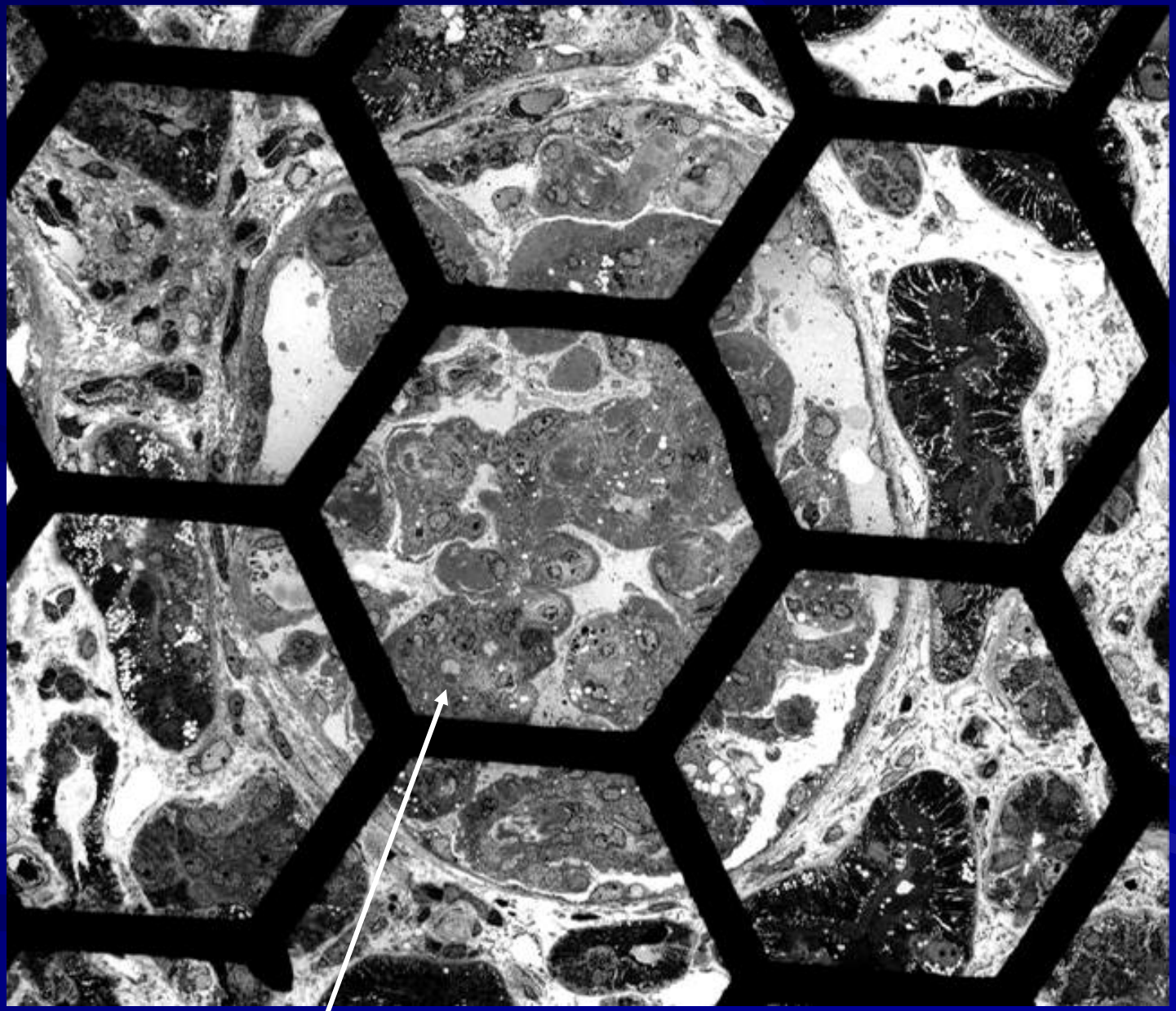
Cryoglobulinaemic glomerulonephritis

Cryoglobulinaemic glomerulonephritis

- Type 1 is associated with monoclonal gammopathies, usually IgM
- Type 2 is associated with a monoclonal component, usually IgM, which exhibit activity against the Fc portion of polyclonal IgG
- Type 3 is associated with polyclonal immunoglobulins of more than one isotype, and not associated with underlying plasma cell dyscrasias. Most commonly chronic Hepatitis C infection.

Cryoglobulinaemic glomerulonephritis

- Histology - Mesangiocapillary pattern of glomerulopathy, with, PAS positive, hyaline thrombi in capillaries. Hyaline means glass like or acellular.
- Immunoflorescence – Intracapillary immunoglobulin, and subendothelially IgG most commonly
- Electron Microscopy – Intracapillary hyaline thrombi, subendothelial deposited protein mainly. Macrophages phagocytosing cryoglobulin within glomerulus.



Accentuation of lobular architecture

Higher magnification of previous slide

Hyaline ‘thrombus’ – cryoglobulin within glomerular capillary loop

Infarcted capillary and perivascular mononuclear inflammatory cell infitrate

Normal peritubular capillary

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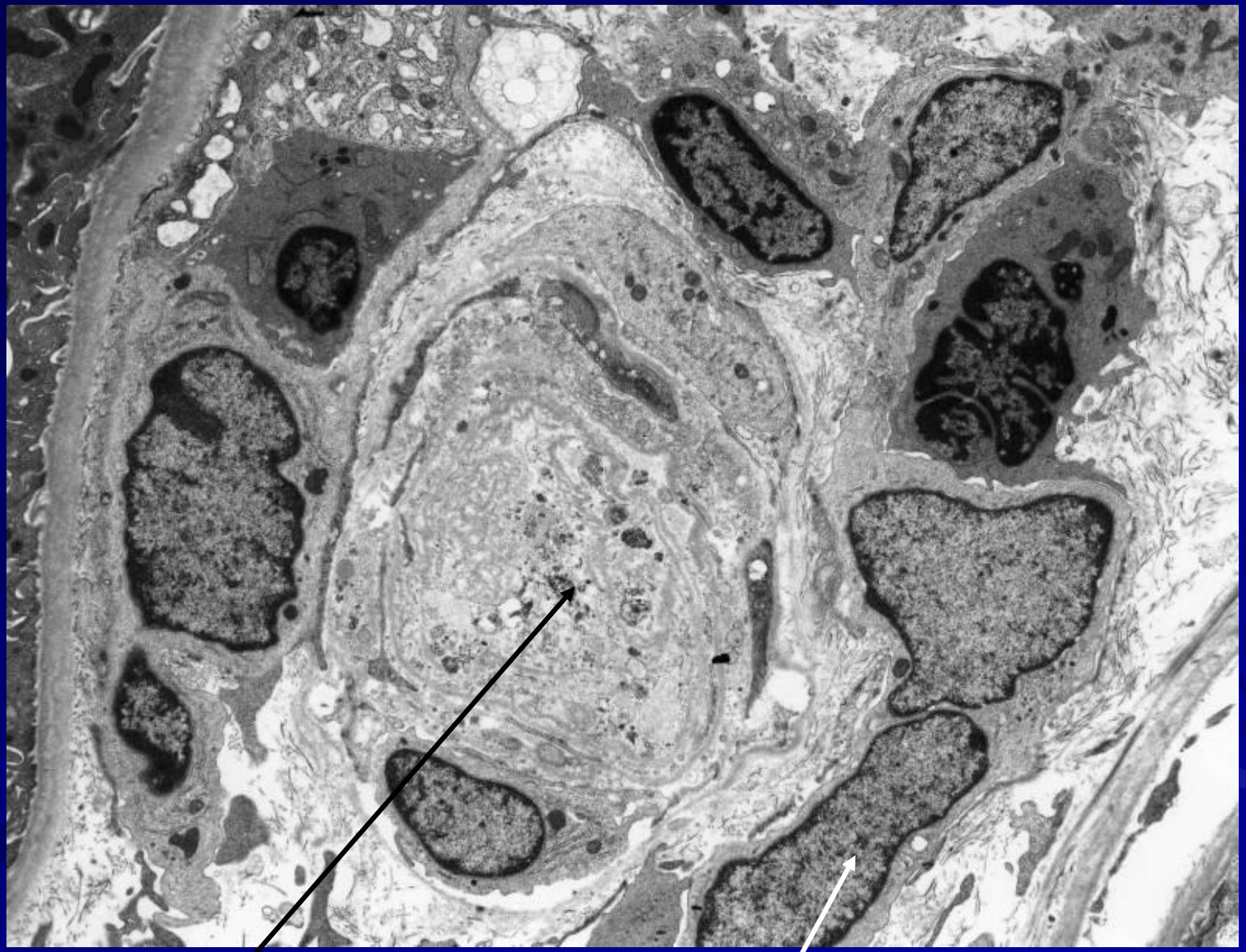
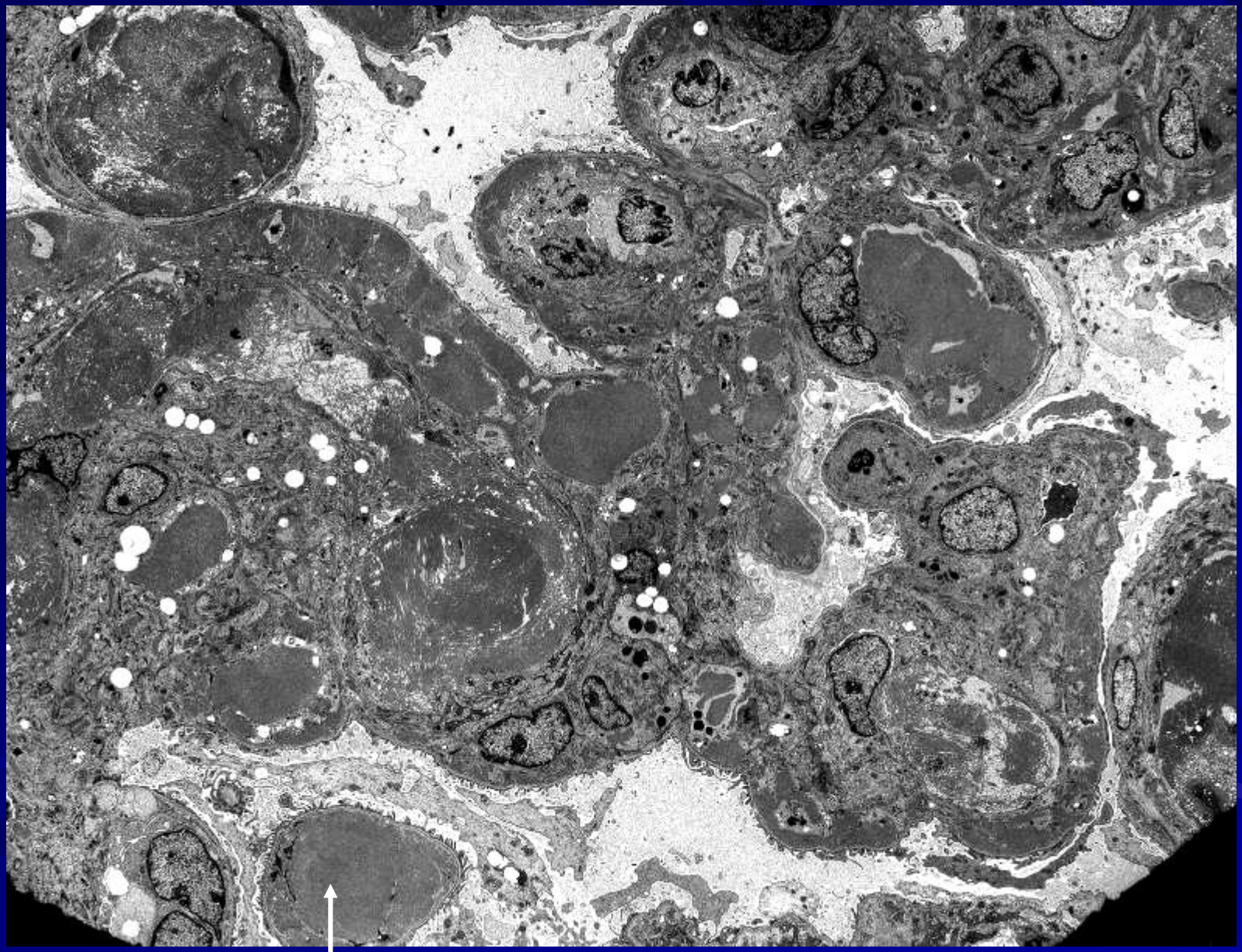


Infarcted endothelium

Pericapillary mononuclear cell inflammatory cell infiltrate

Higher magnification of two slides back



Endocapillary hyaline thrombus in glomerulus

Mesangial cell with interpositioning

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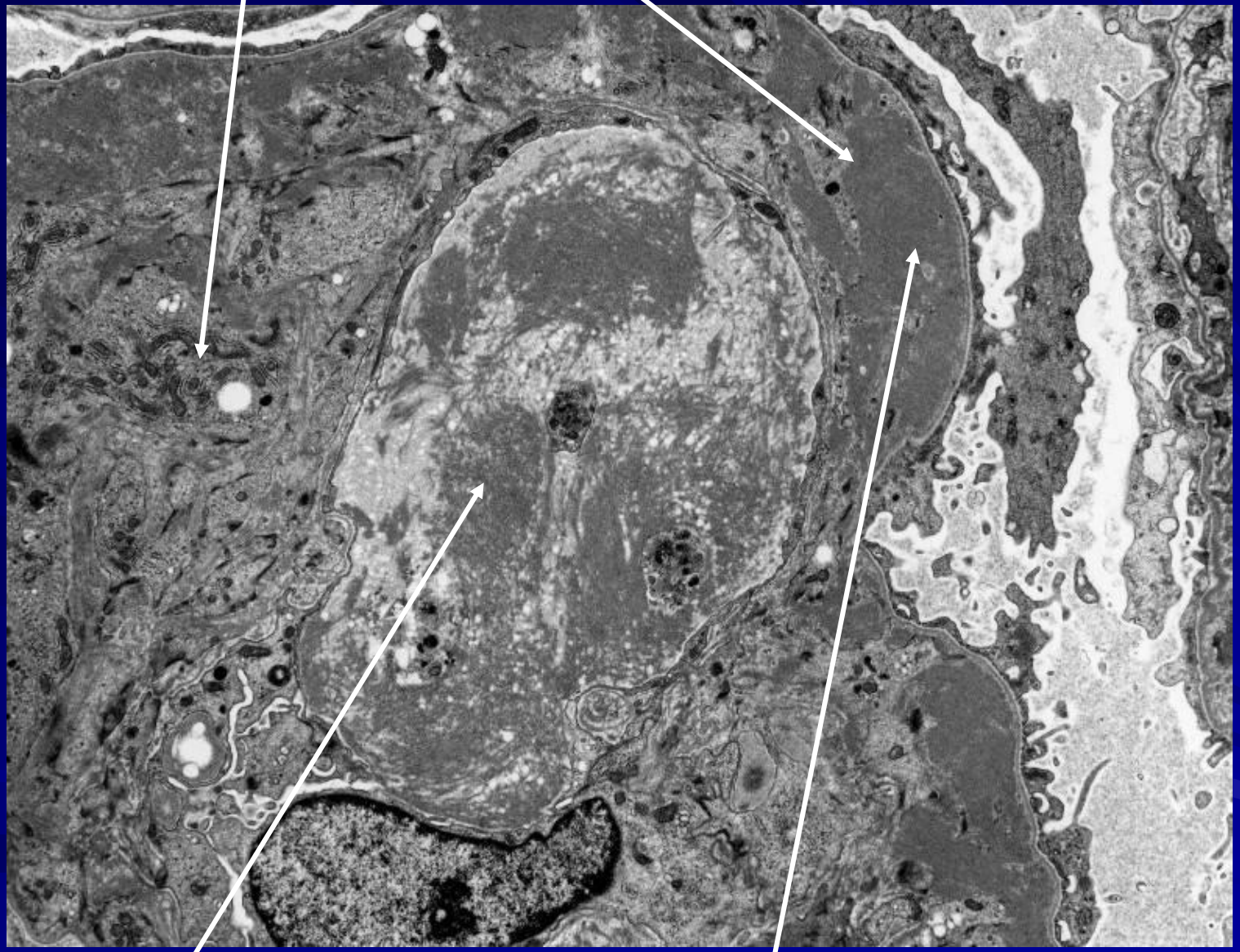
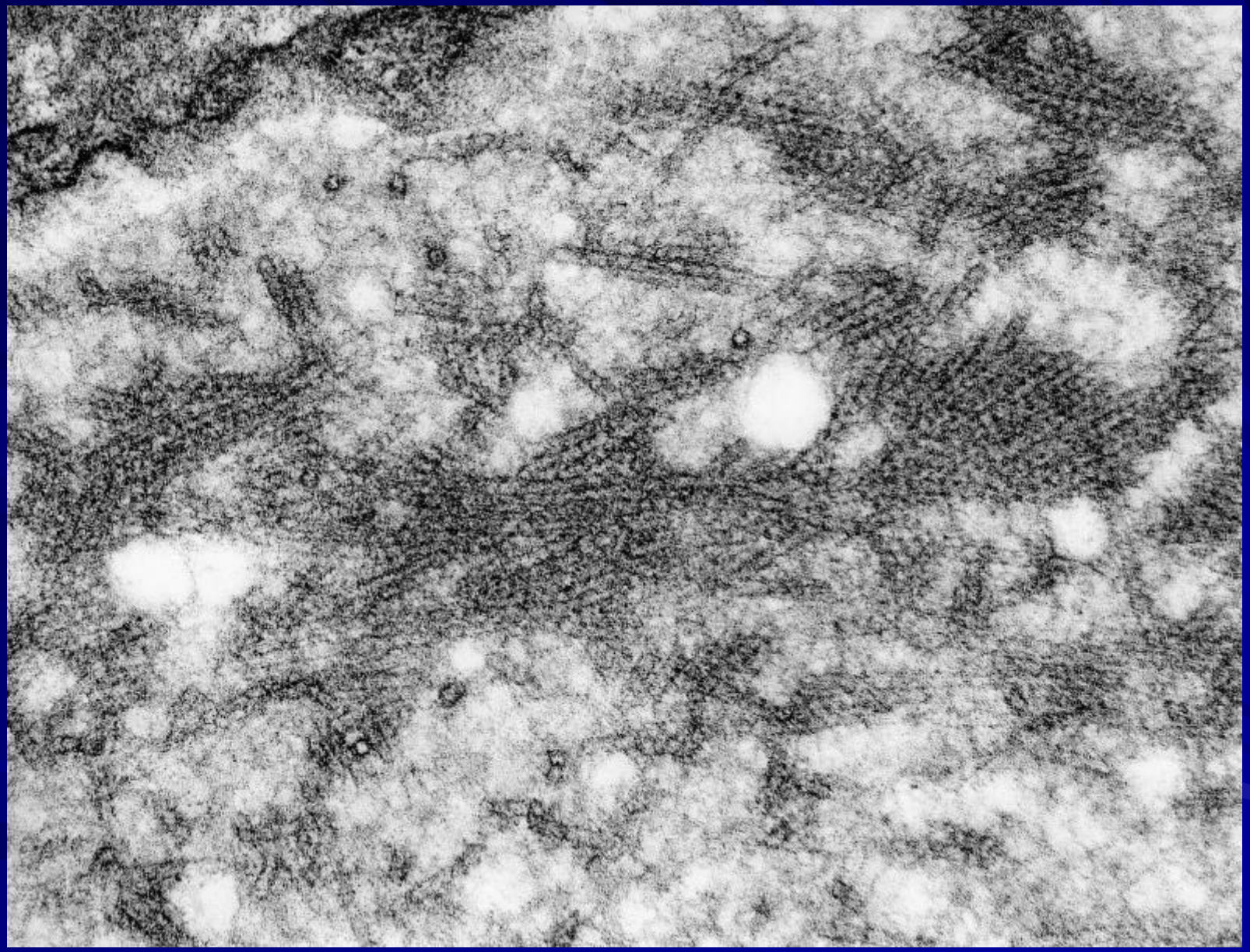


Endocapillary cryoglobulin

Subendothelial deposited cryoglobulin



Endocapillary tubular structured cryoglobulin

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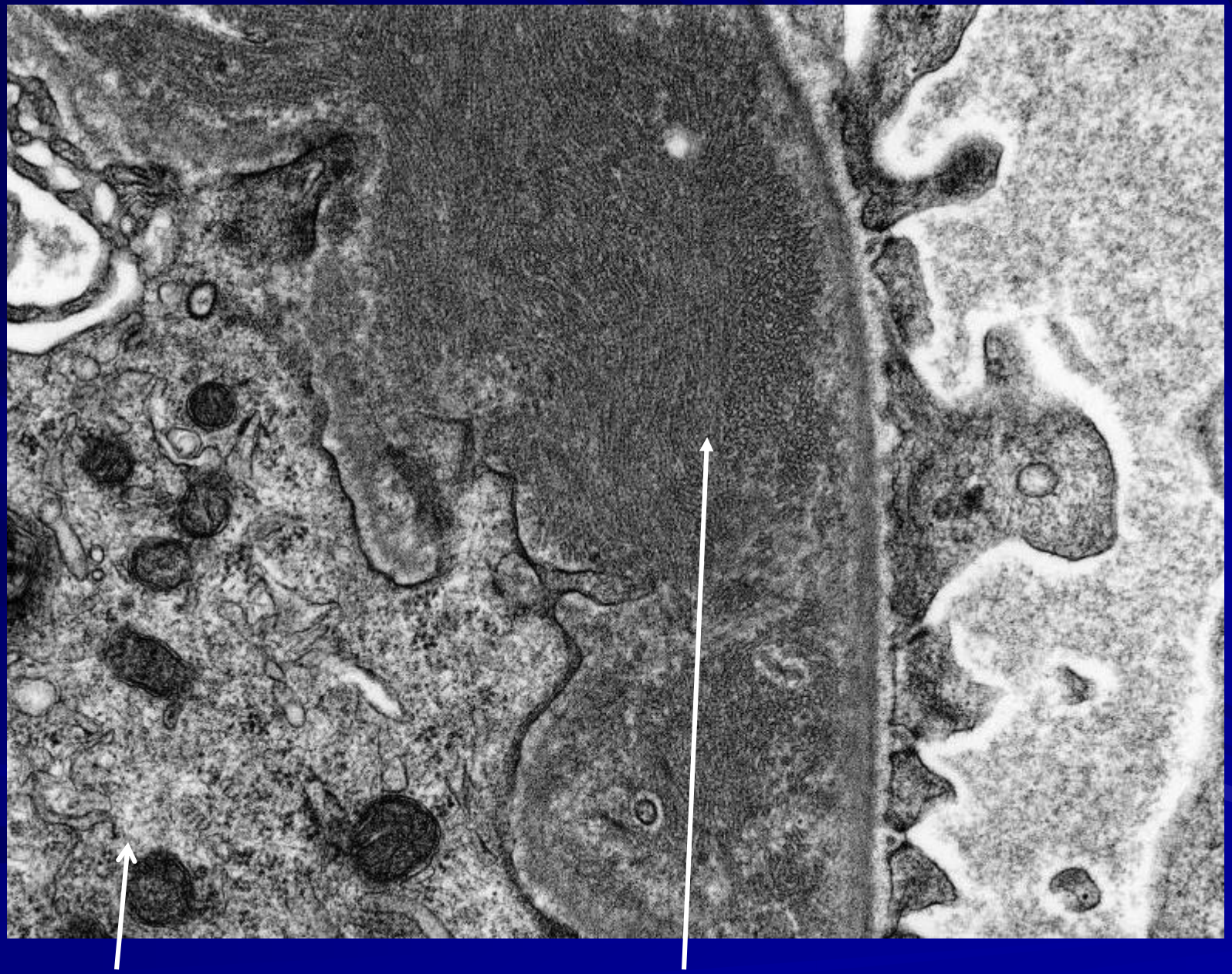

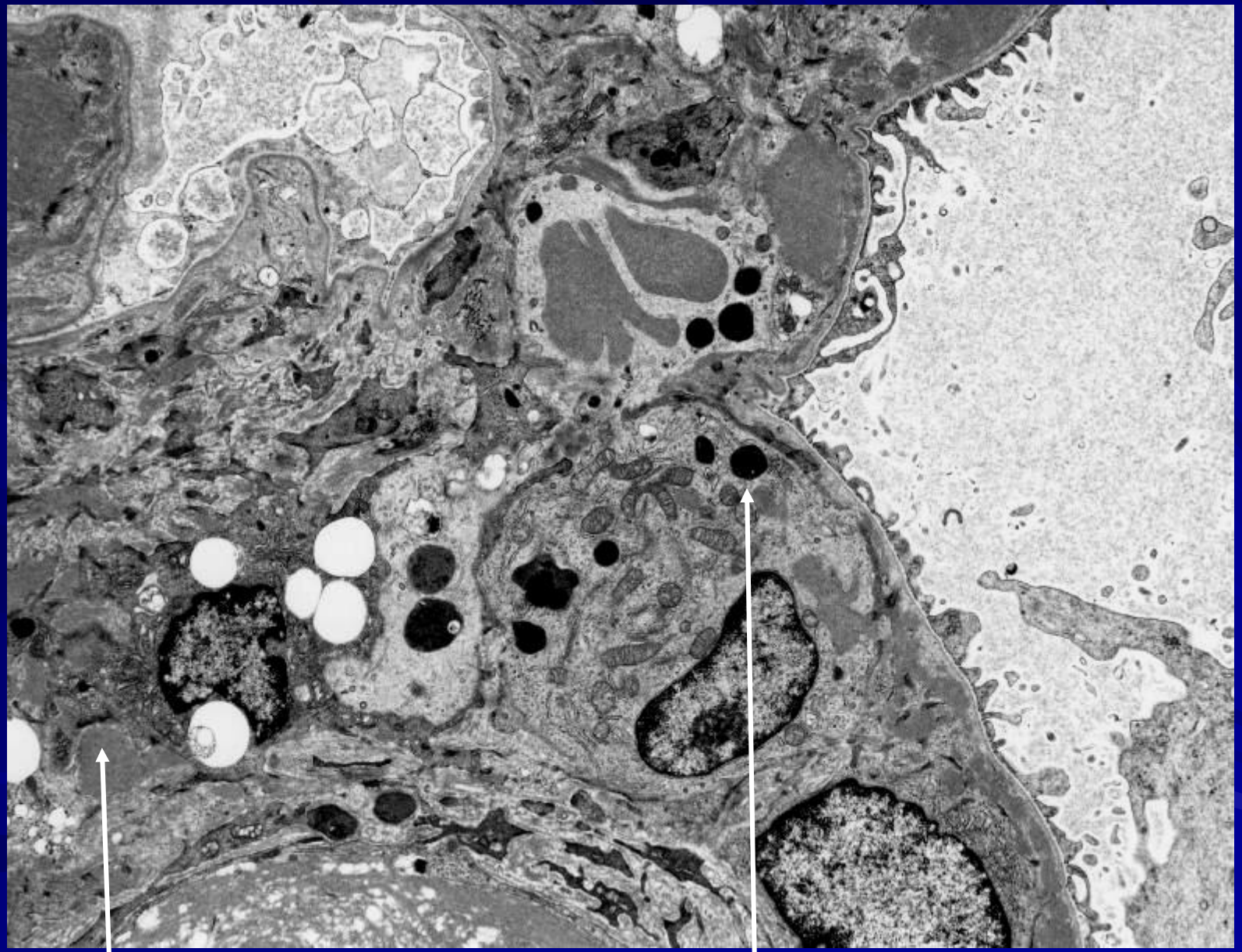

Mesangial deposits

Macrophage digesting cryoglobulin intralysosomally

Tertiary lysosomes

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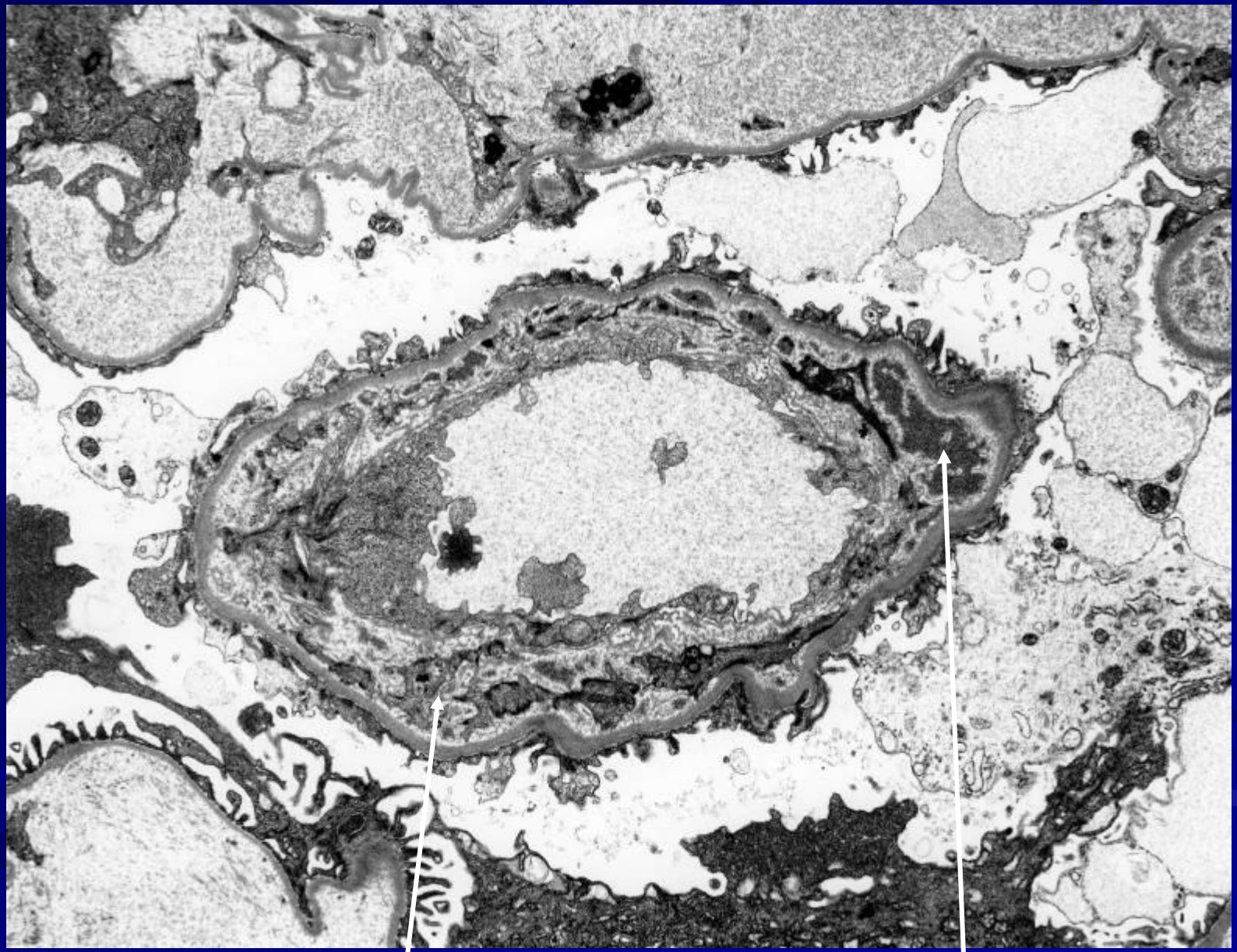
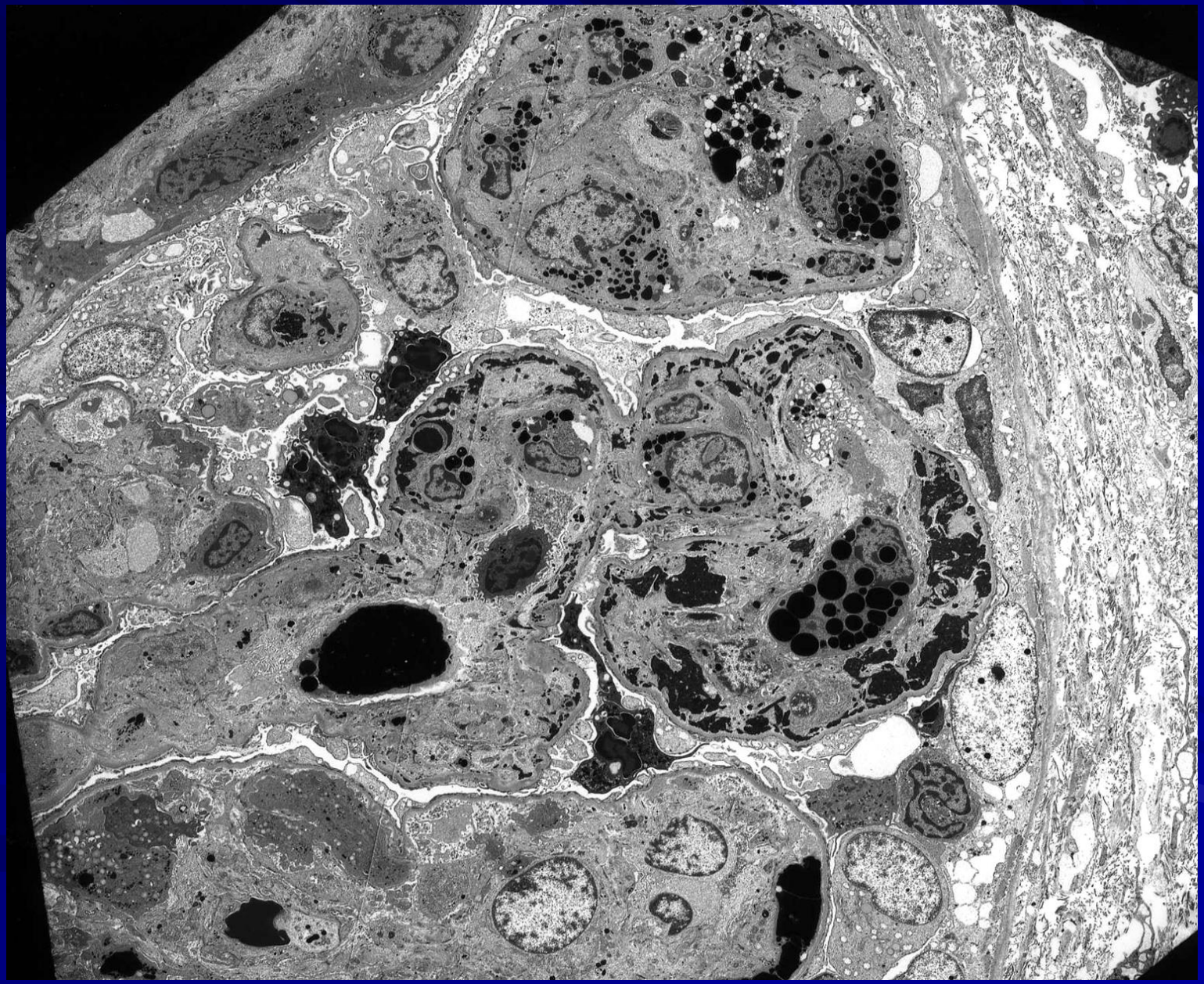
Tubular cryoglobulin in mesangium

Macrophage secondary lysosomes with partially digested tubular cryoglobulin


Mesangial interpositioning
Subendothelial deposits

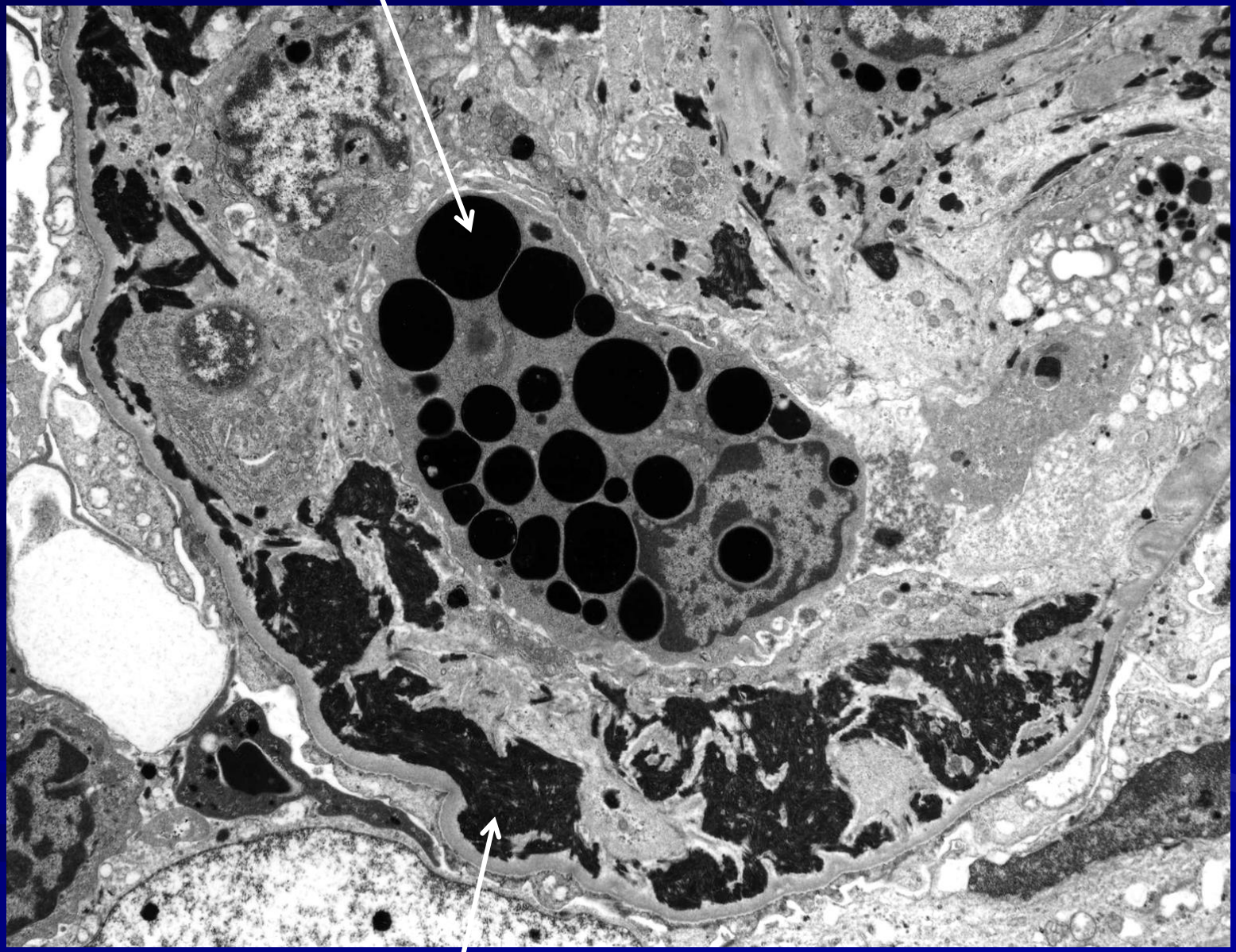
Structured cryoglobulin Different case



Accentuation of lobular architecture

Numerous macrophages

Intracapillary macrophage with cryoglobulin filled lysosomes



Subendothelial electron dense cryoglobulin

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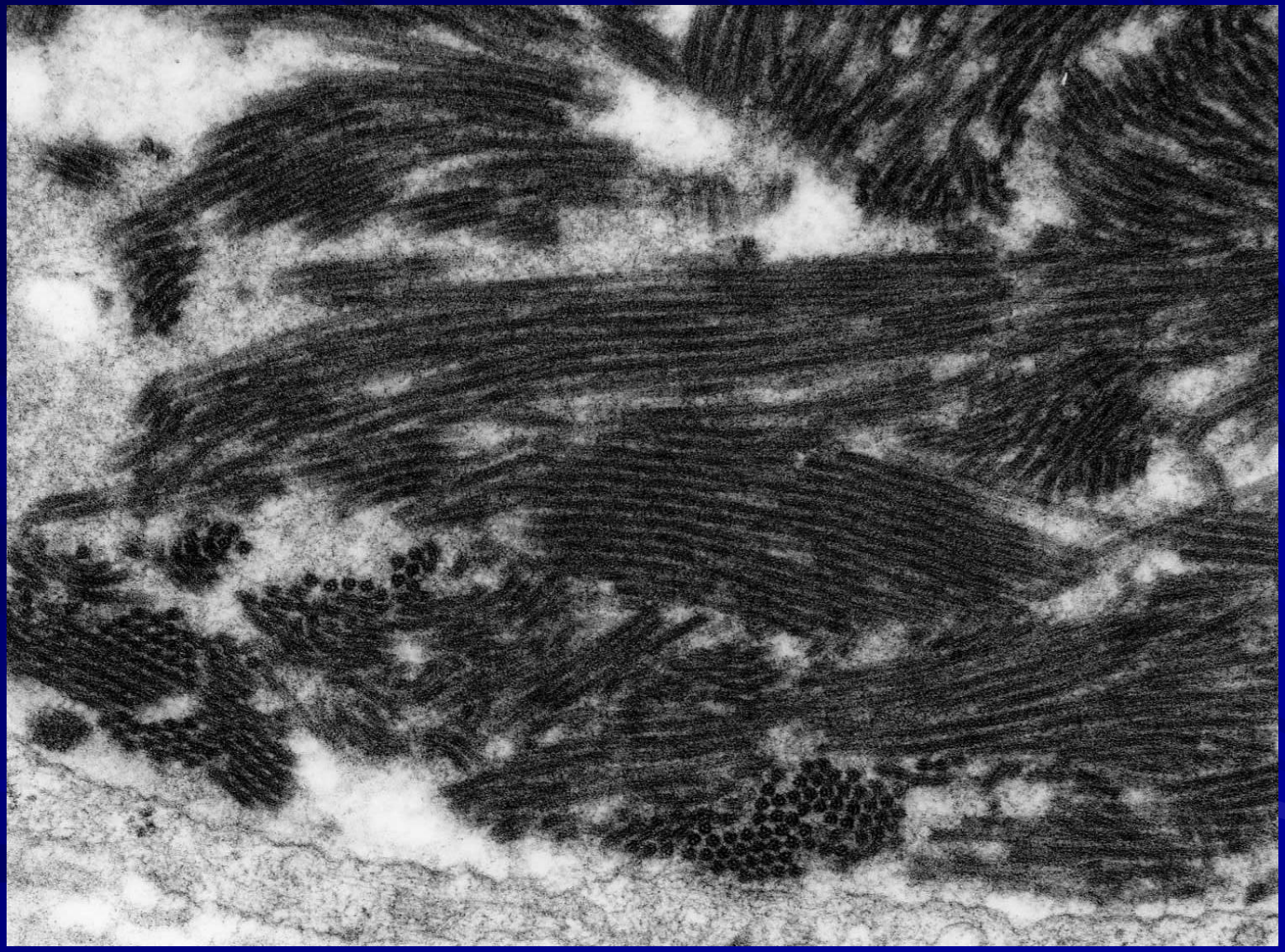
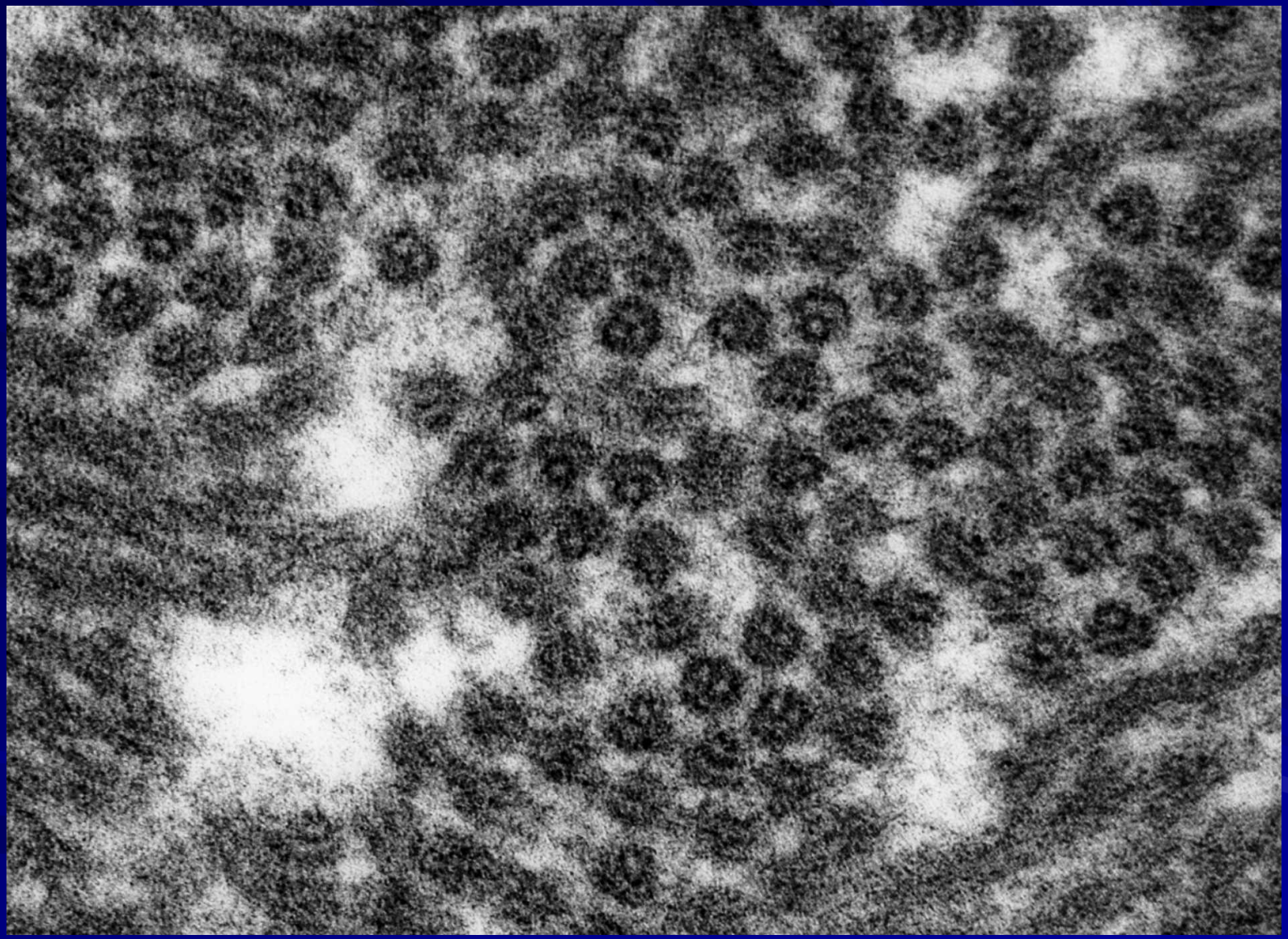
Tubular structured cryoglobulin



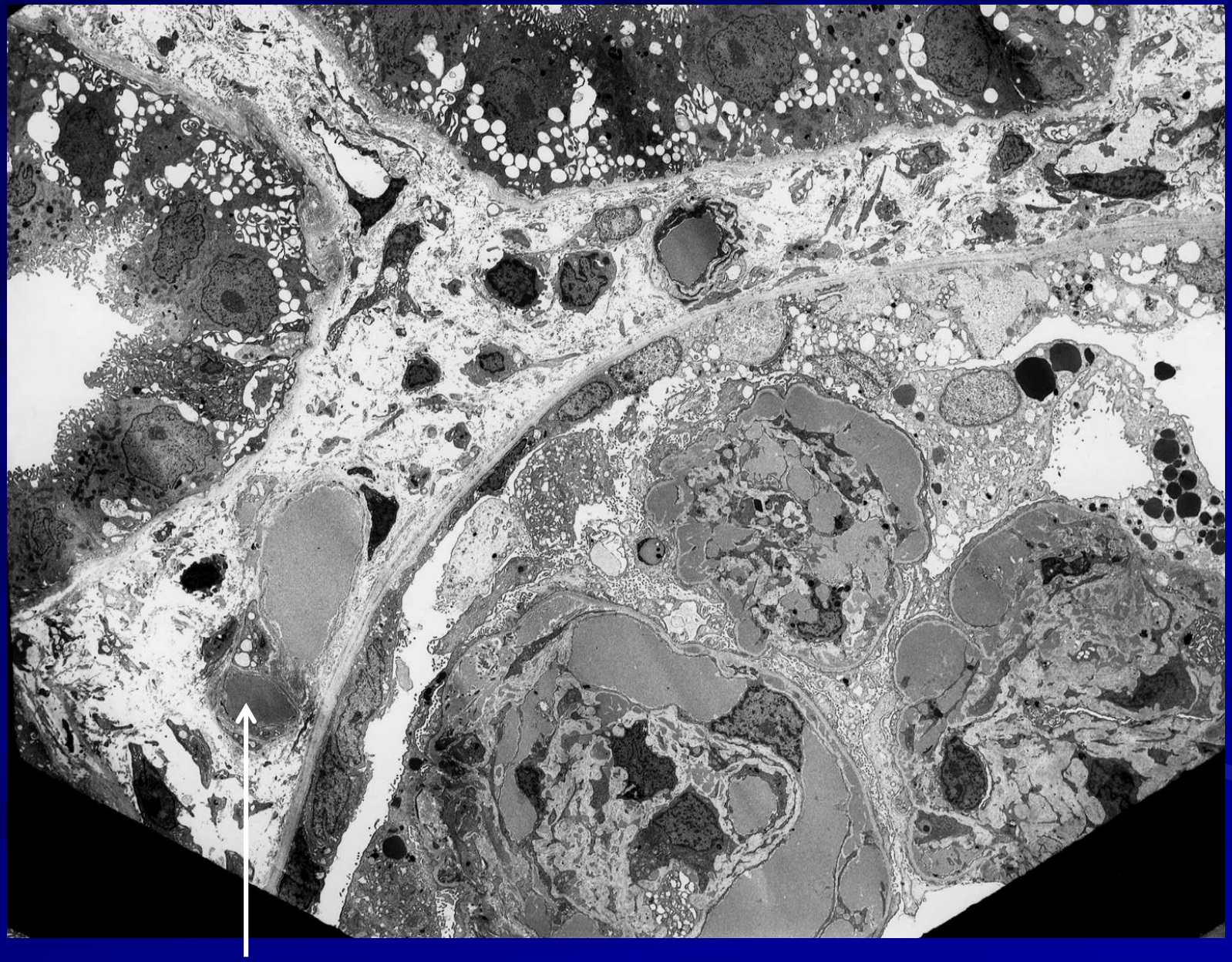
Structured cryoglobulin



Three tubules fused together

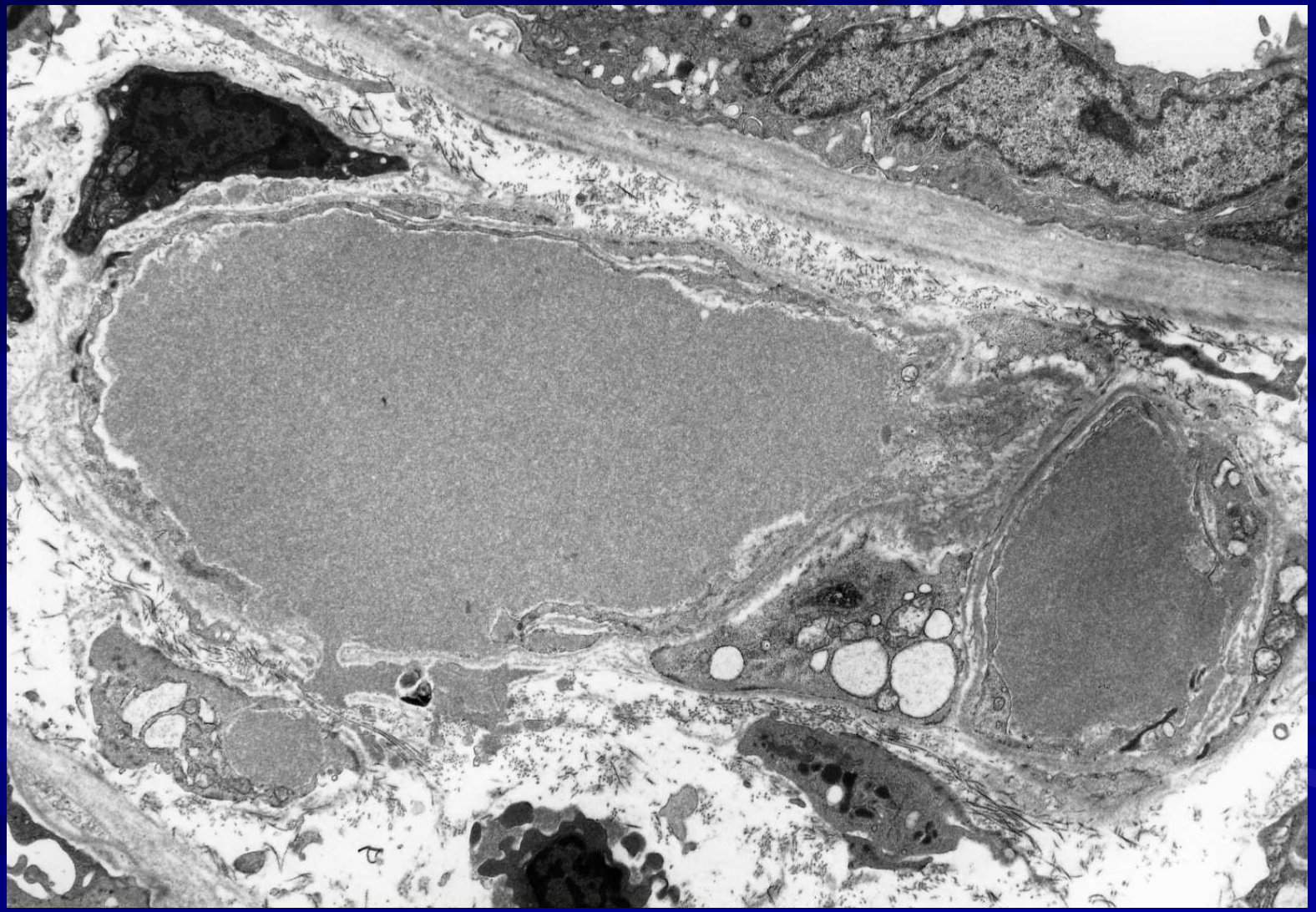
The Mercedes-Benz of cryoglobulins

Unstructured cryoglobulin



Hyaline thrombus in capillary lumen

Unstructured cryoglobulin in lumen of capillary



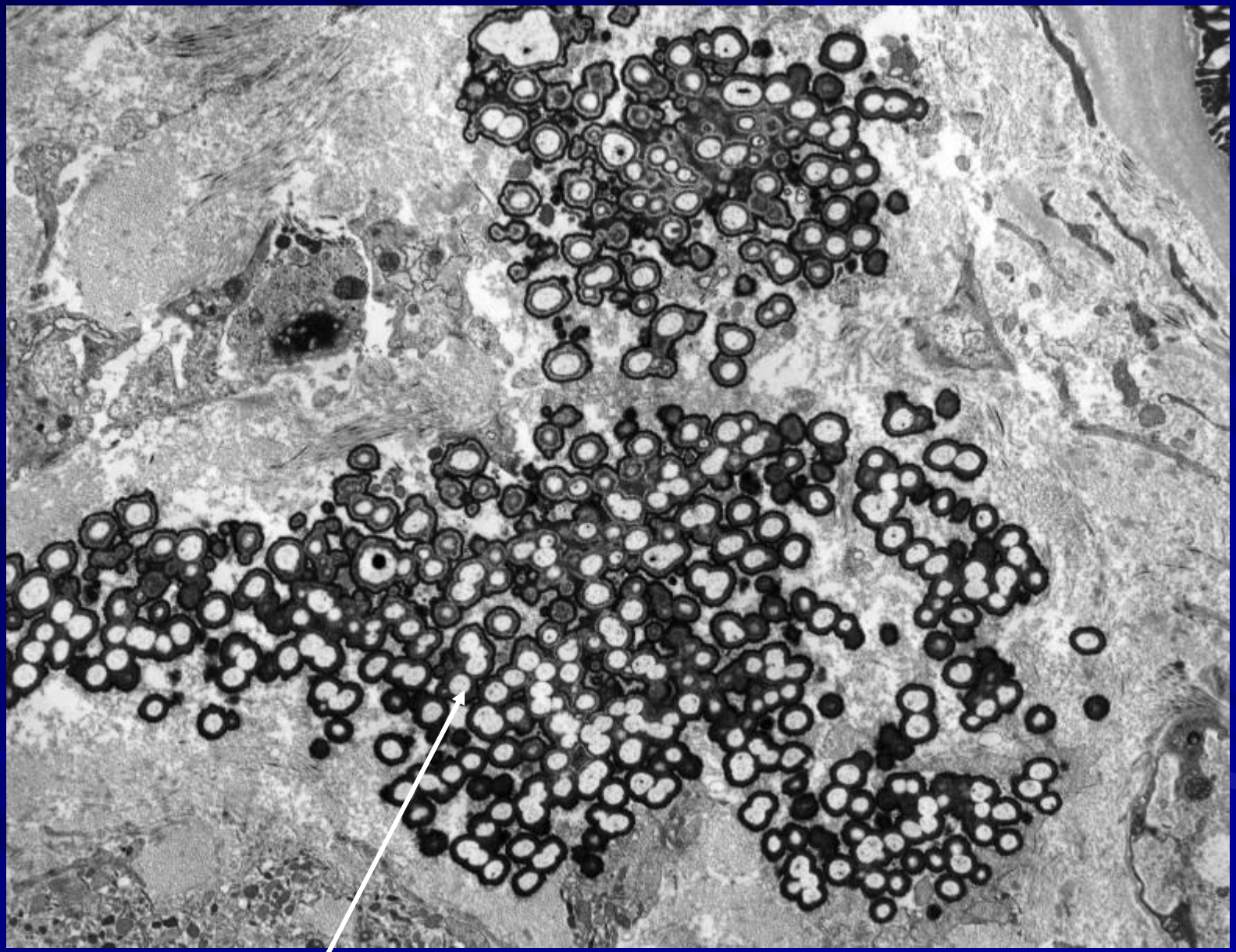
Periglomerular capillary

Crystals

Crystals

- Nephrocalcinosis – electron dense in renal interstitium - basophilic/dark purple on H&E
- Cholesterol – rectangular space (cleft) in vascular lumen – not retained during fixation and processing.
- Oxalate – in tubular lumen – rotates polarised light – calcific rim
- Uric acid – in tubular lumen – needle shaped - not retained during aldehyde fixation

Nephrocalcinosis

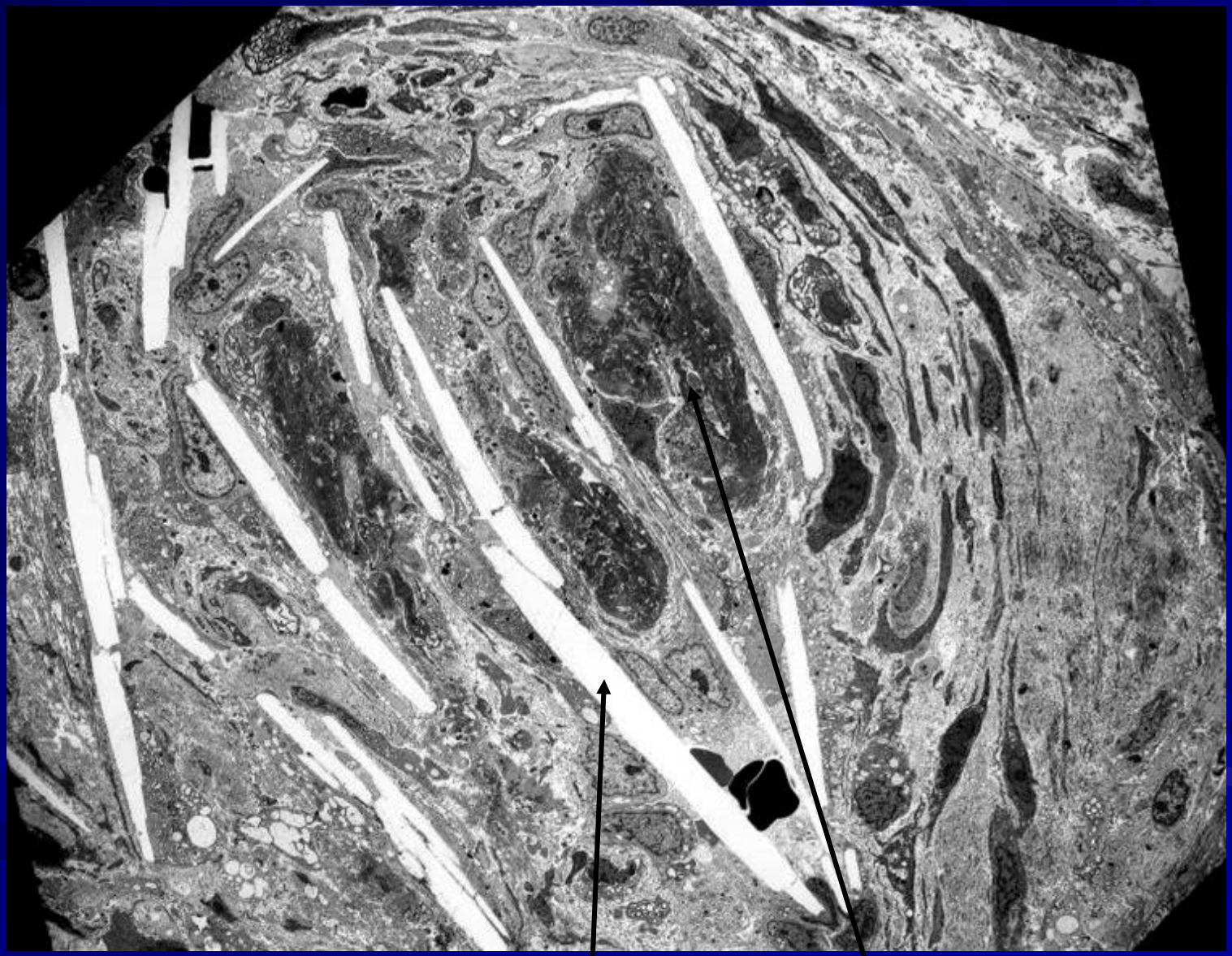


Interstitial nephrocalcinosis

Concentrically deposited calcific body

Cholesterol embolus

Previous episode of aortic atheromatous plaque rupture



Vascular smooth muscle cell

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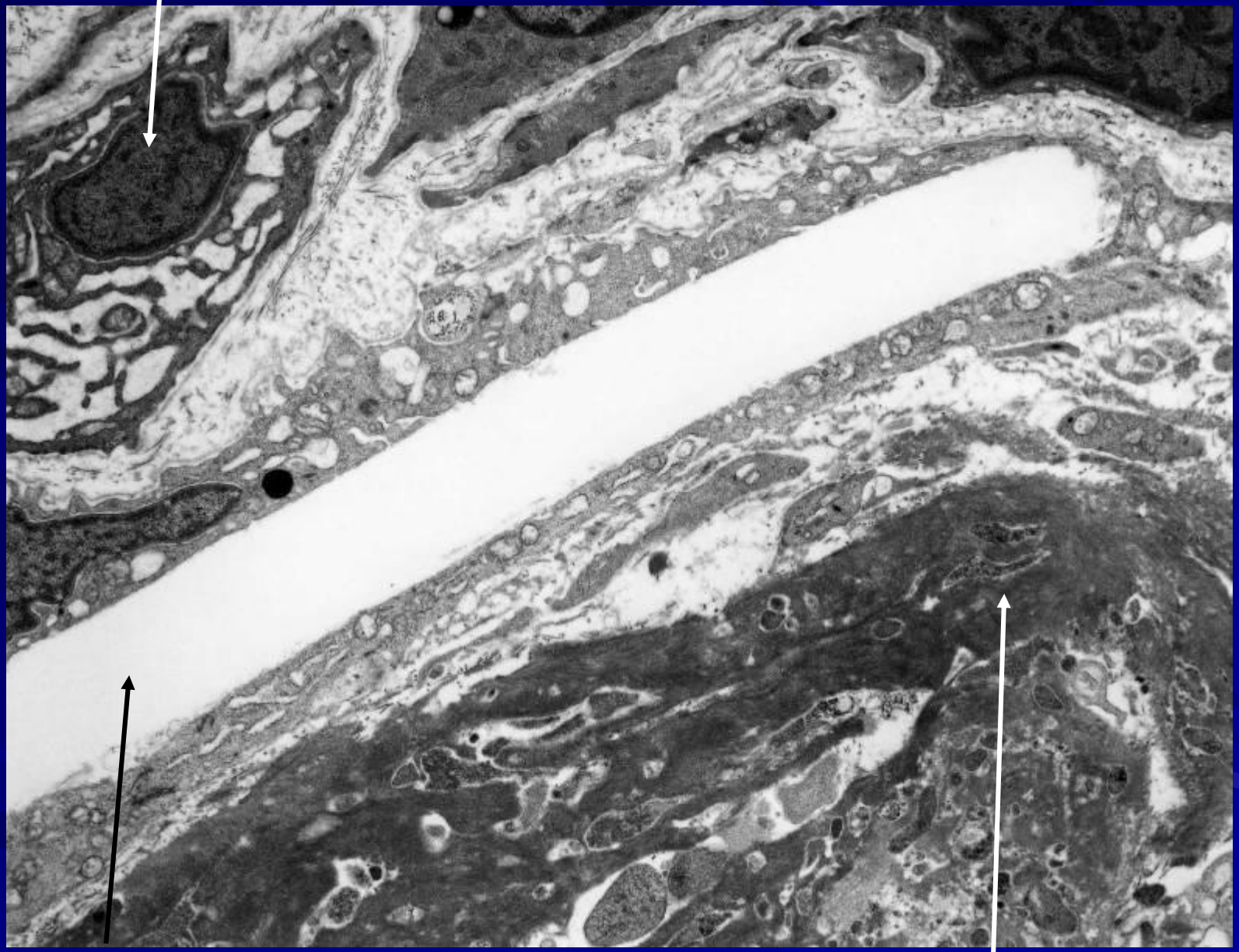
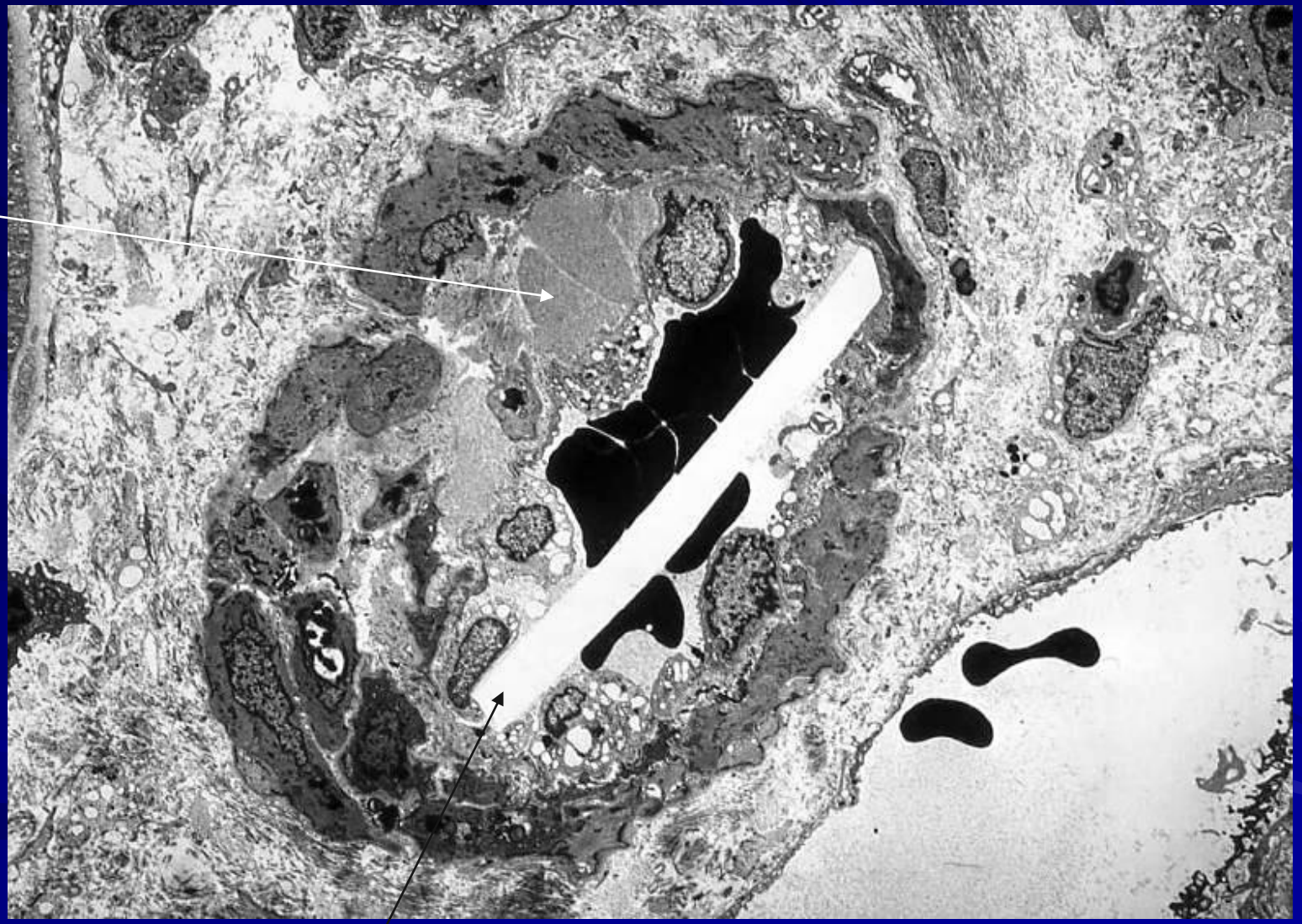
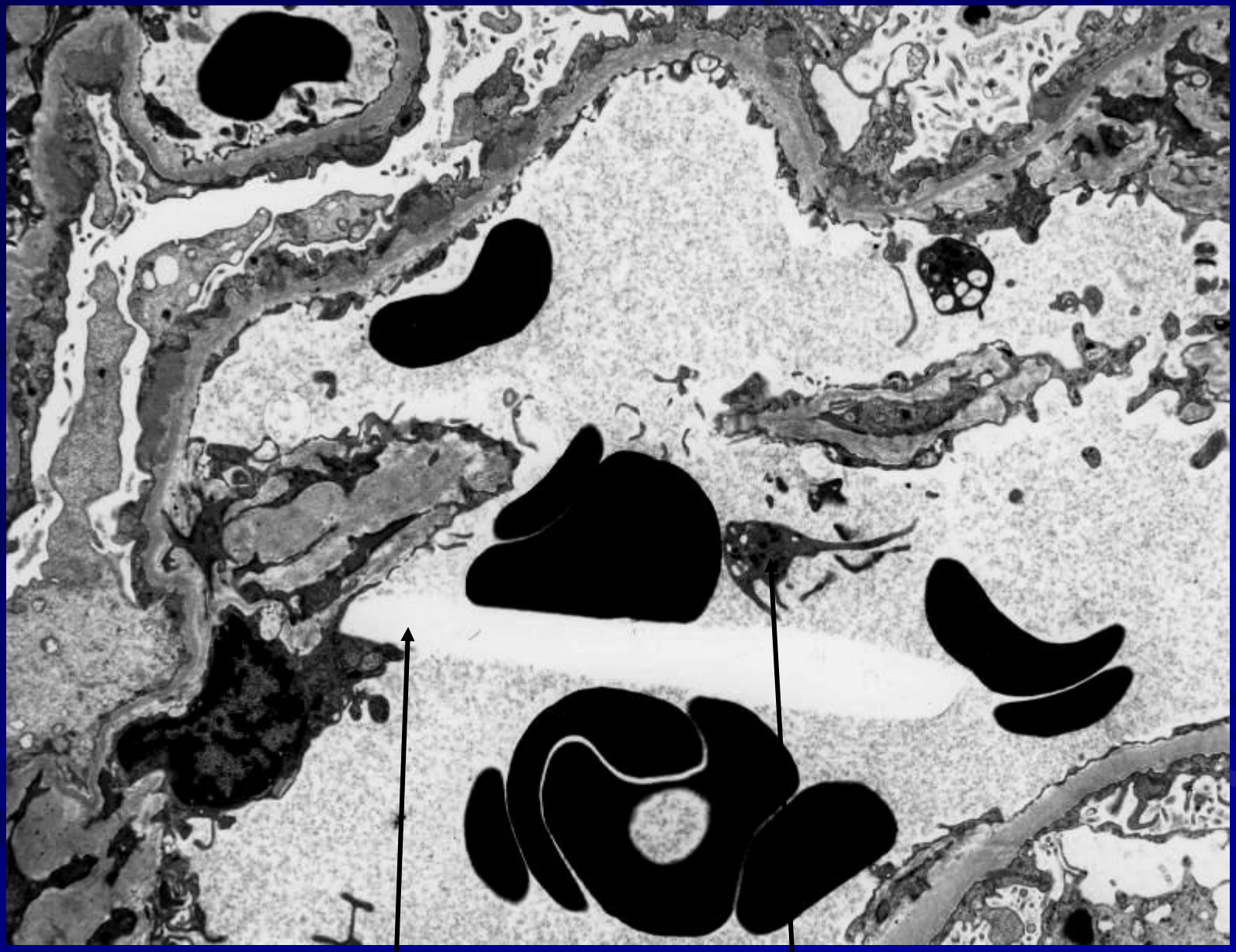


Intracellular cholesterol crystal cleft

Fibrin clot

Cholesterol embolus within intrarenal arteriole



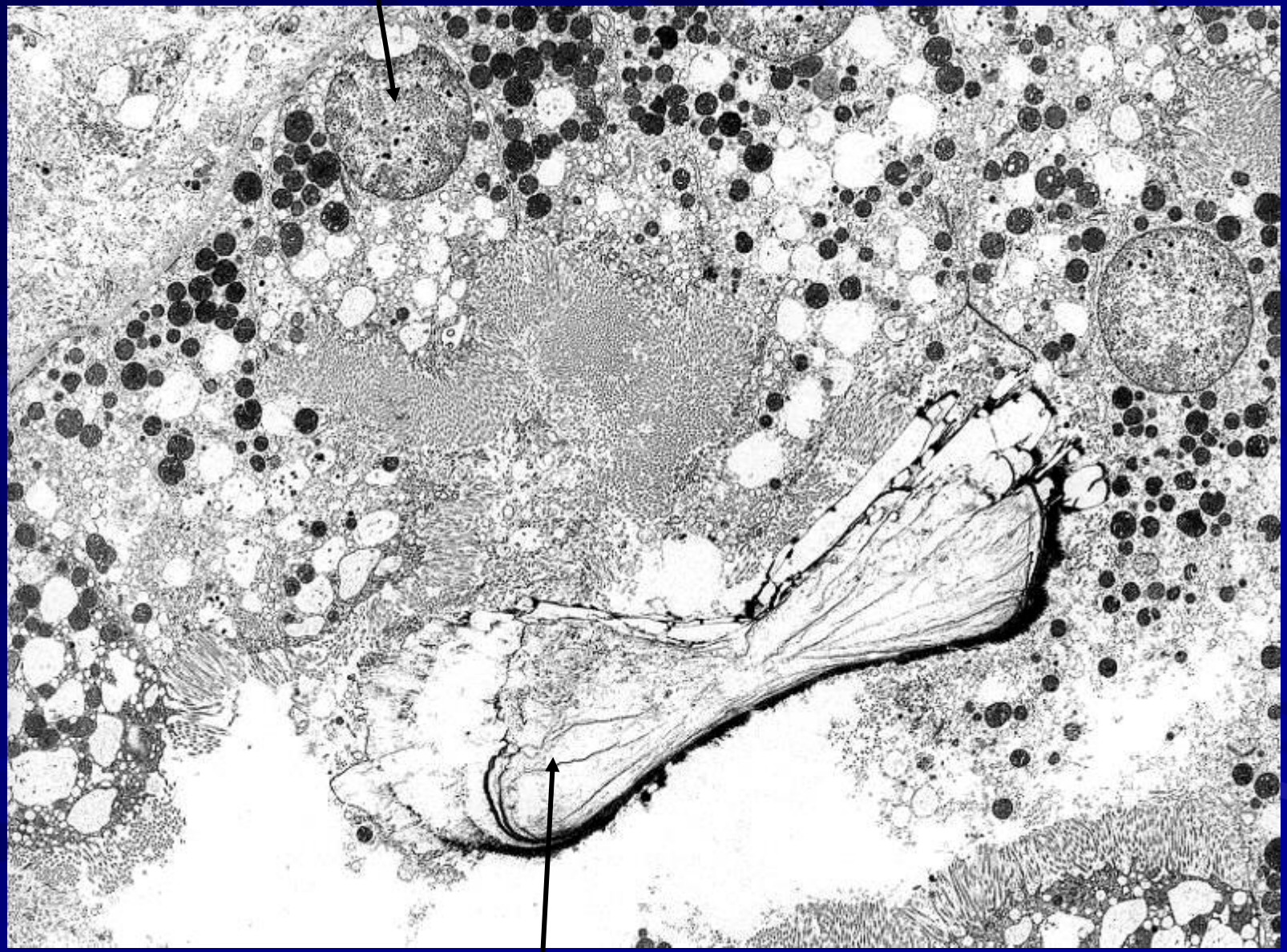


Intravascular cholesterol crystal

Activated platelet with pseudopodia

Calcium oxalate

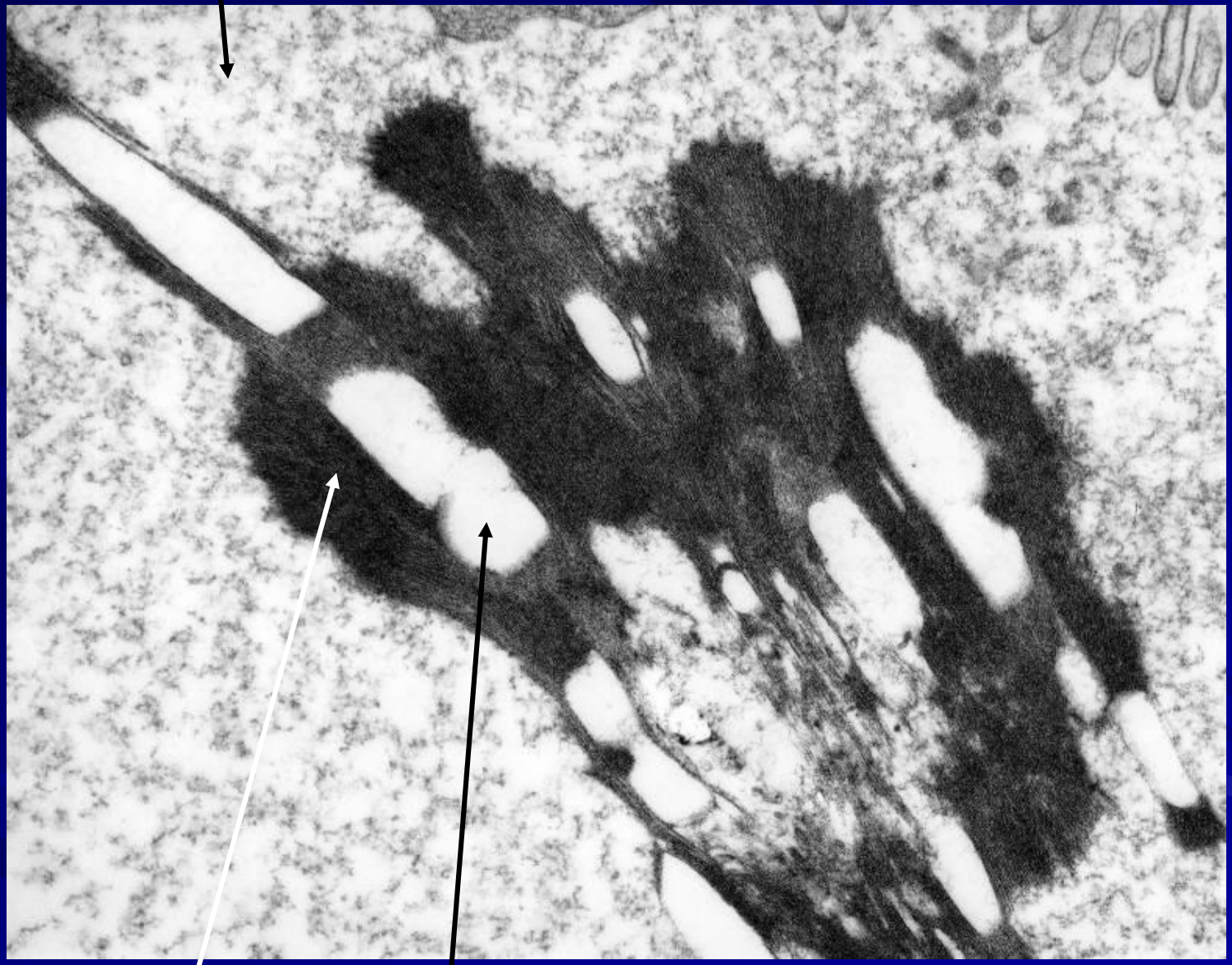
Acute necrosis of proximal convoluted tubule – following ethylene glycol poisoning



Intralumenal calcium oxalate crystal

Lumen of proximal convoluted tubule

Same biopsy as previous slide

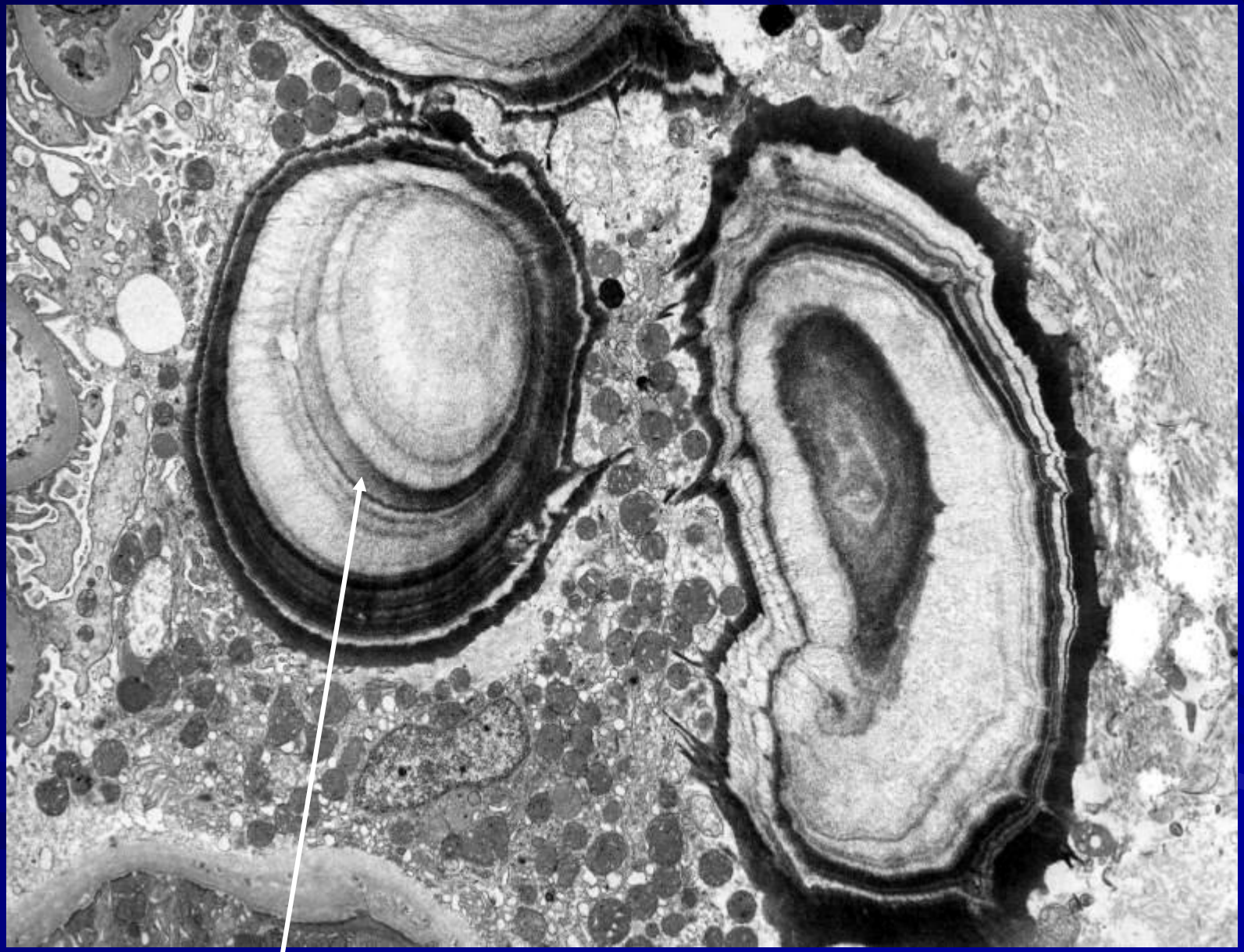


Calcium

Oxalate crystal

Example of hetrogenous nucleation

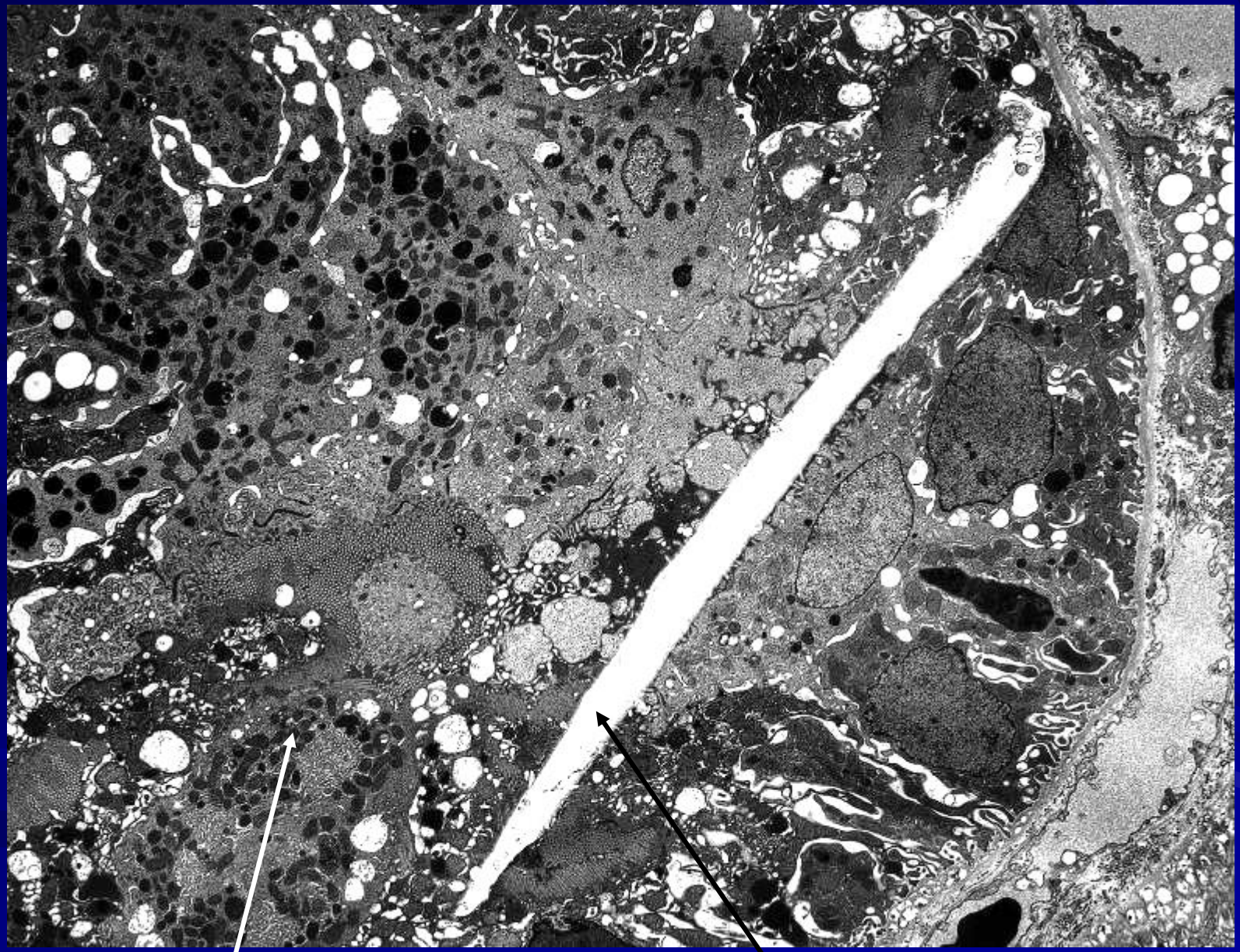
Calcium oxalate crystals in Bowman's space



Calcium oxalate concretion

Patient had multiple bowel resections

Uric acid



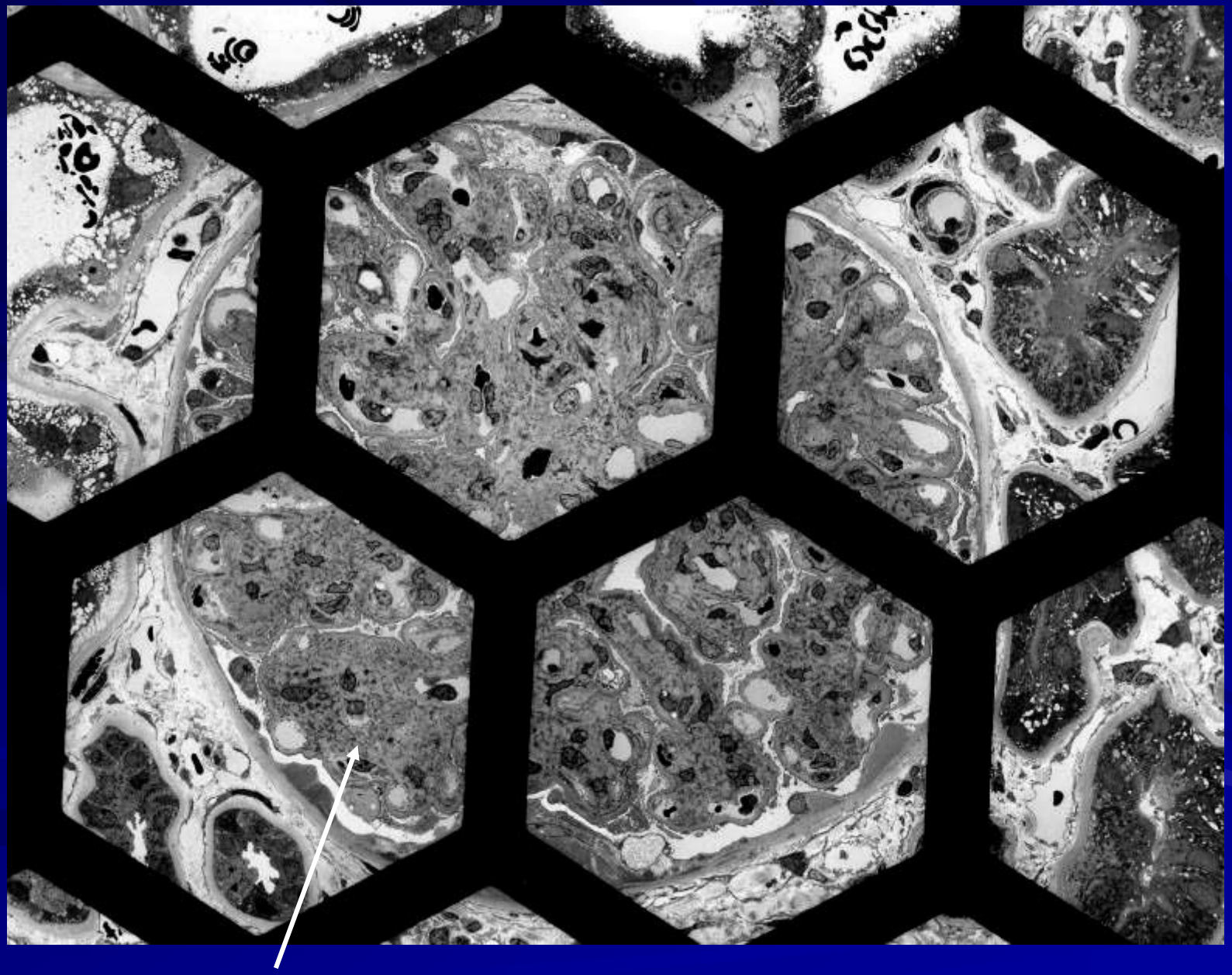
Proximal convoluted tubule with intralumenal uric acid crystal

Diabetes

Diabetic nephropathy

- Only biopsied if an additional pathology is suspected
- Diabetic change similar irrespective of type
- Early diabetic change occurs occasionally in patients not known to be diabetic
- Nodular glomerulosclerosis can be diabetic, amyloid, MIDD, or MCGN
- GBM's can be mildly thickened in capillary loops with GBM wrinkling but not diabetic

Diabetic nodular glomerulosclerosis



Kimmelstein-Wilson nodules

Kimmelstein-Wilson nodules

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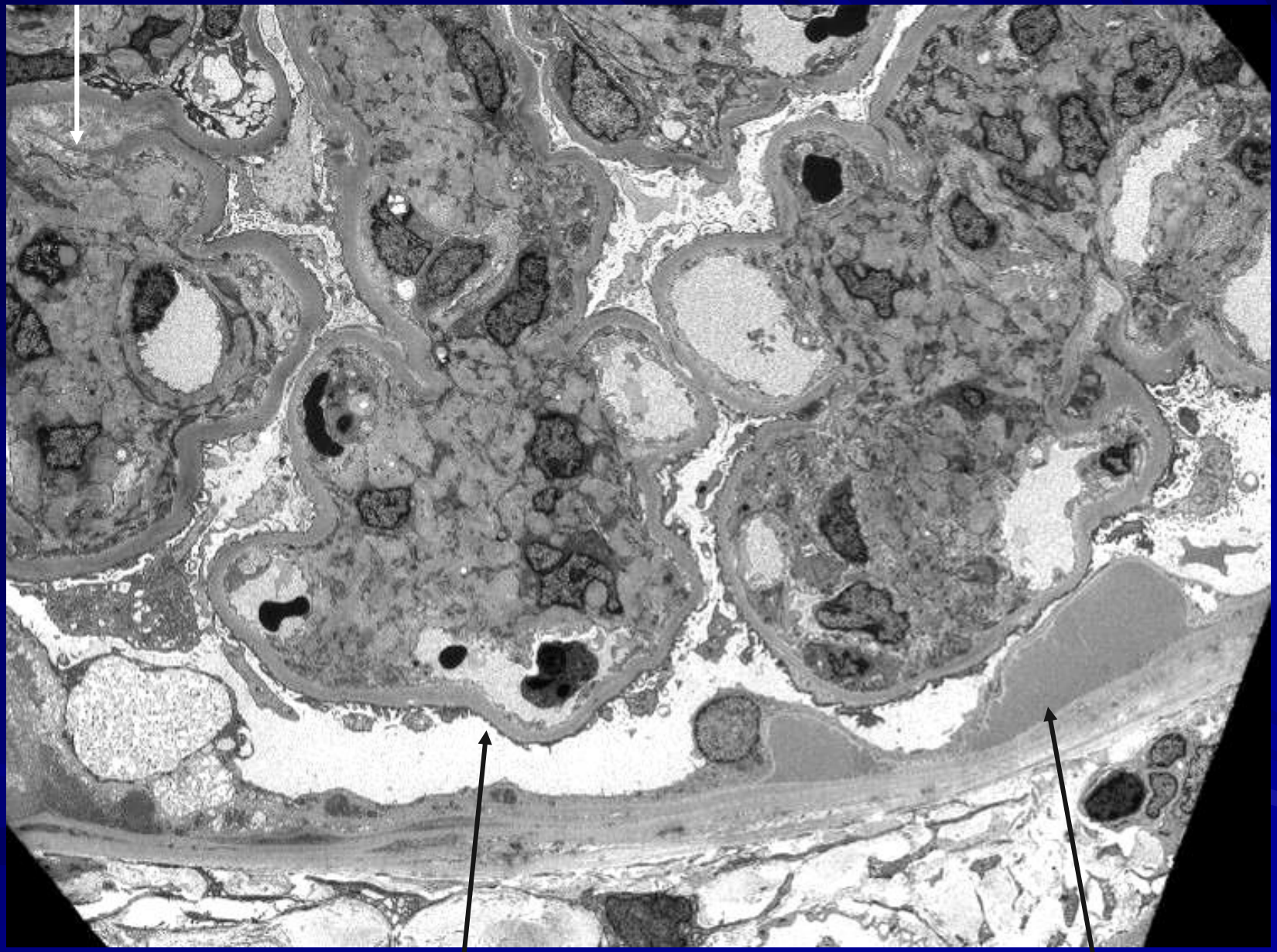
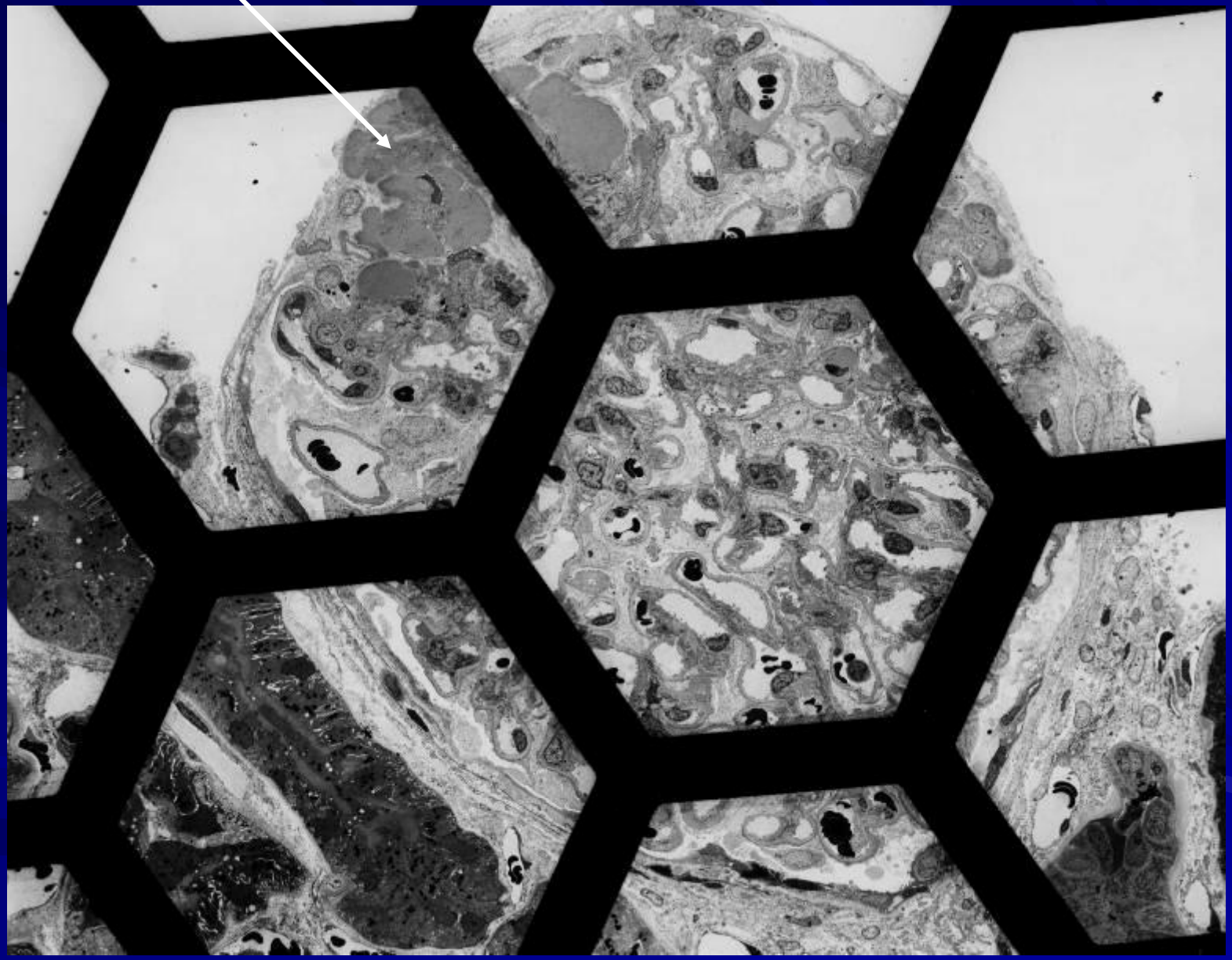


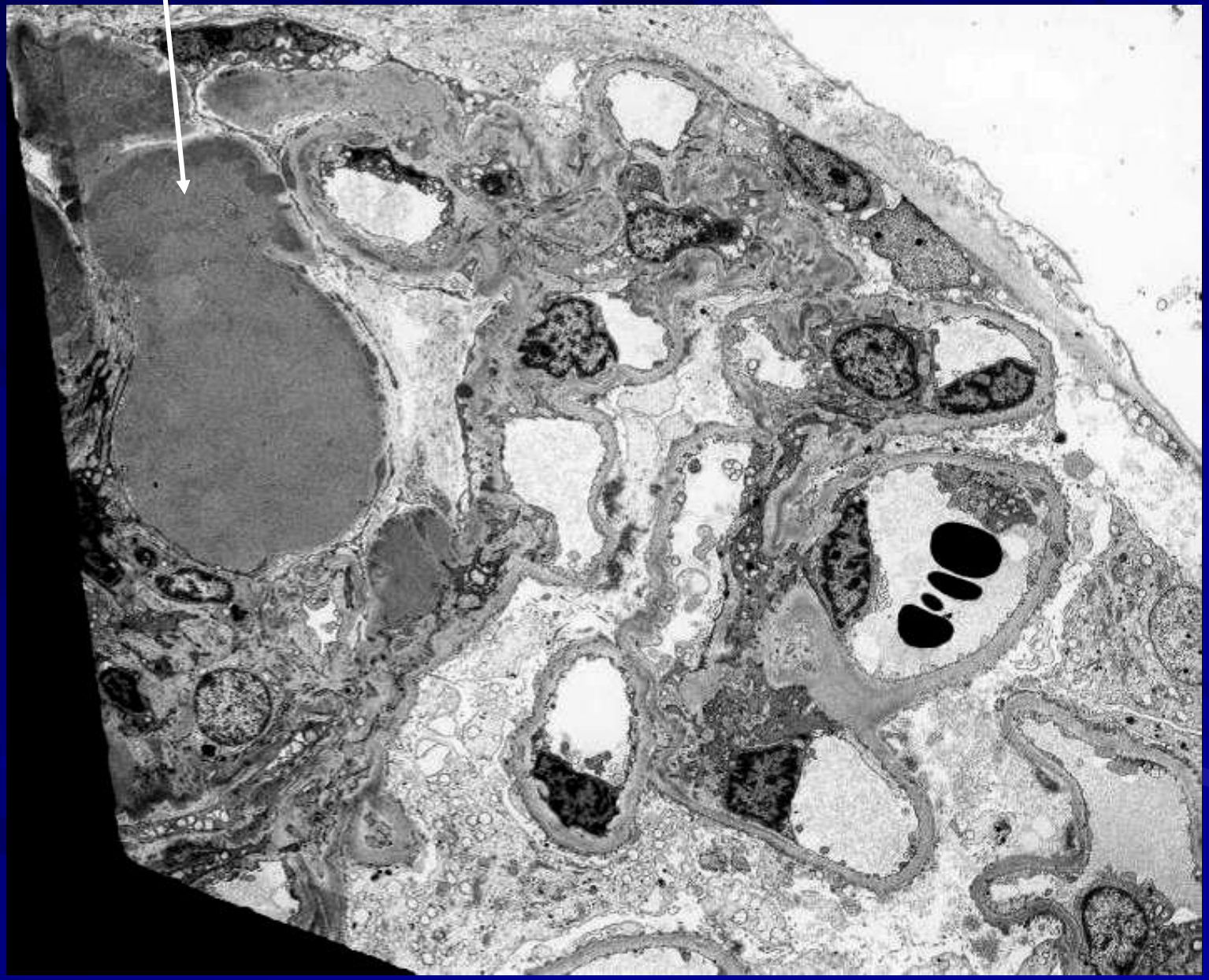
Thickened Glomerular Basement Membrane – linear IgG occasionally

Capsular drops IgM C3

Exudative segmental lesion IgM C3



Exudative lesion – also known as ‘fibrin caps’, which is a misnomer.



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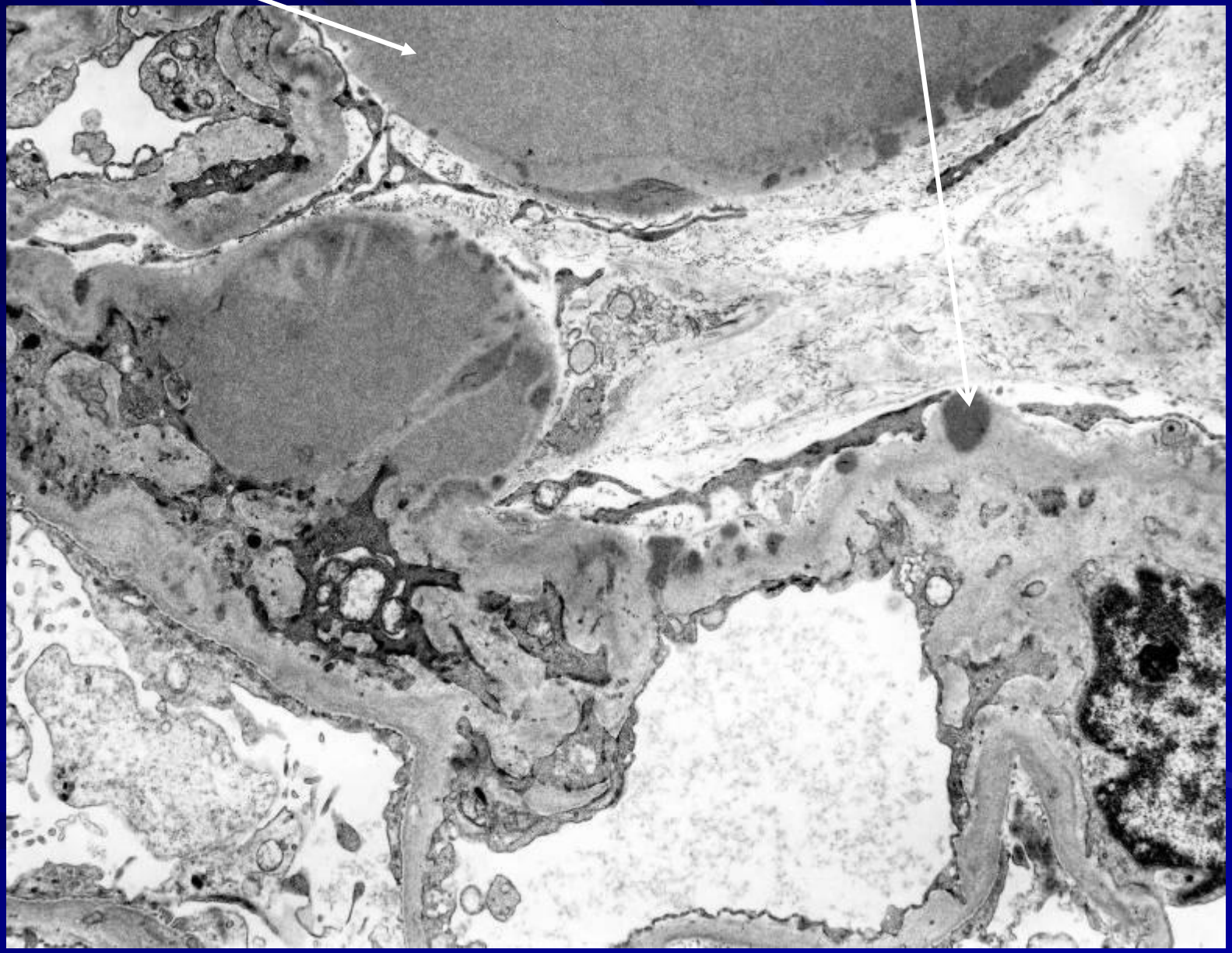
Exudative lesion – plasmatic material

Not immune complexes



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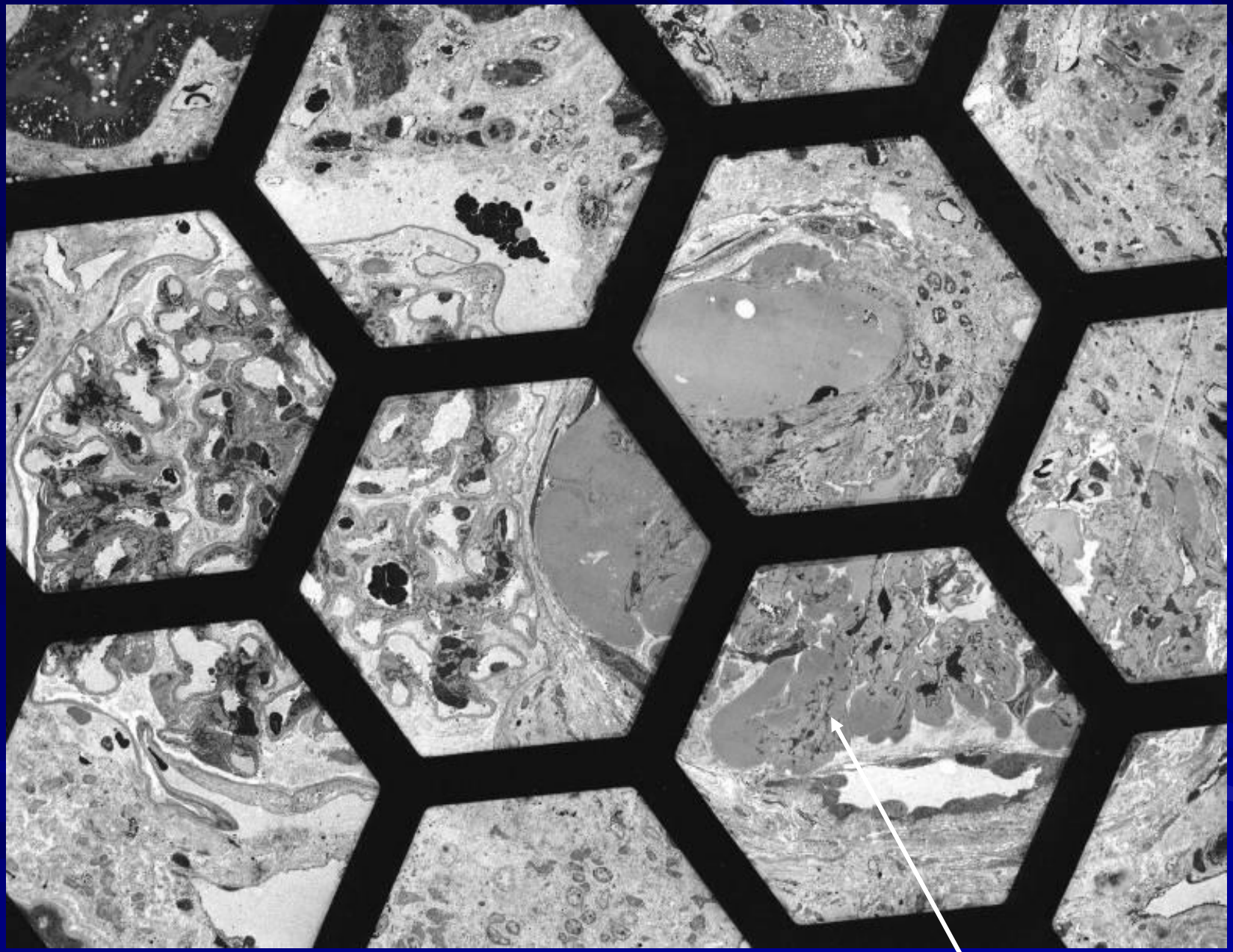
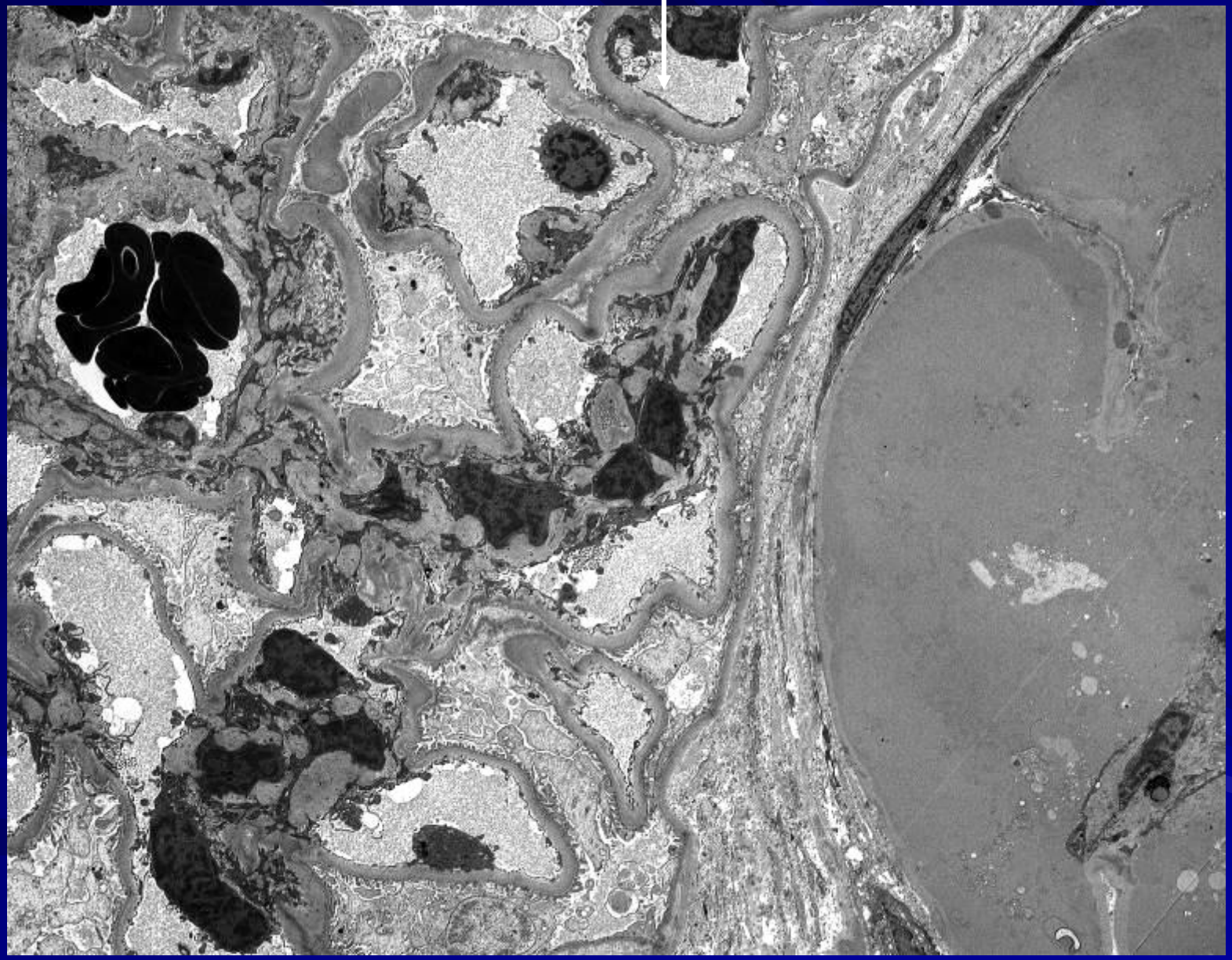
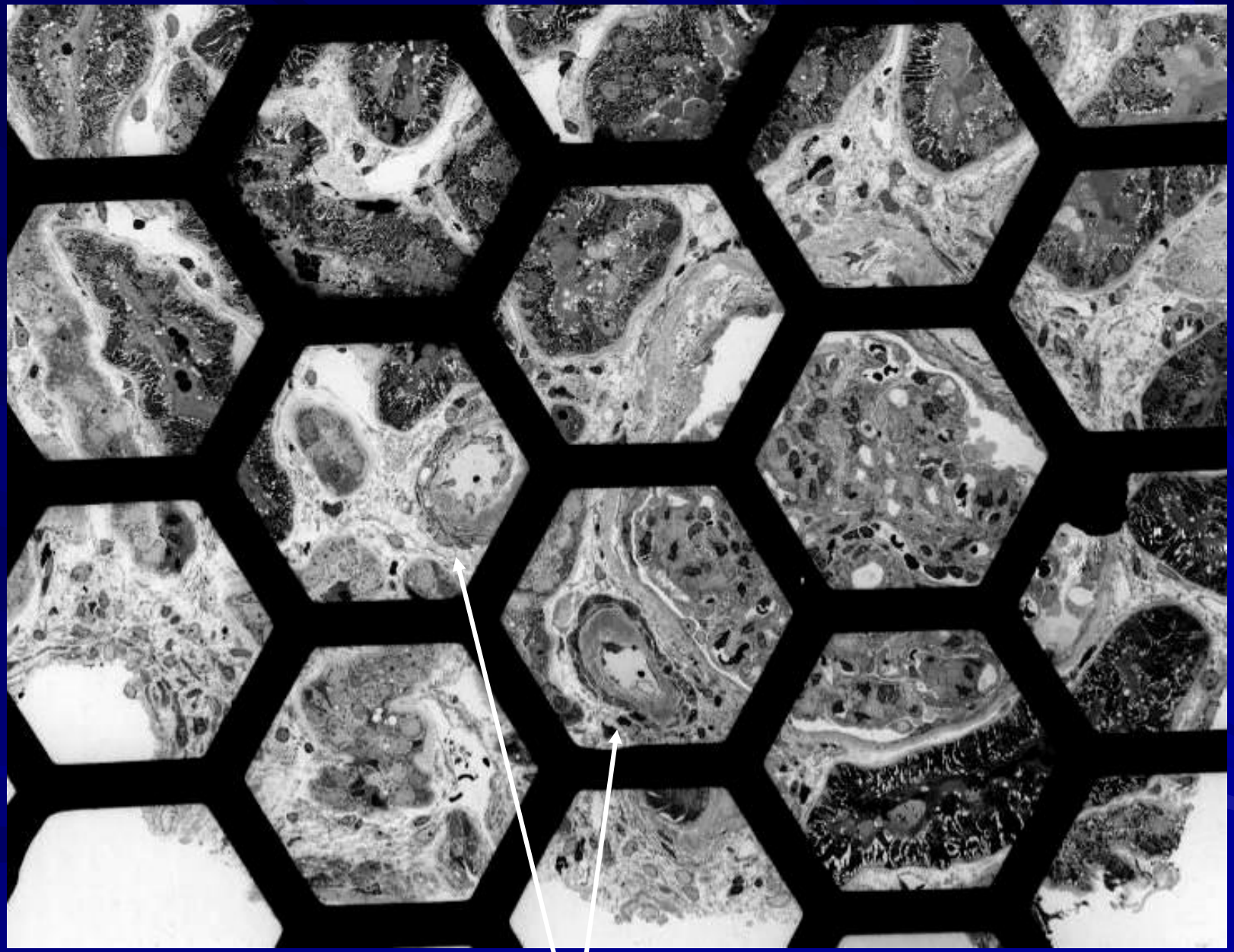


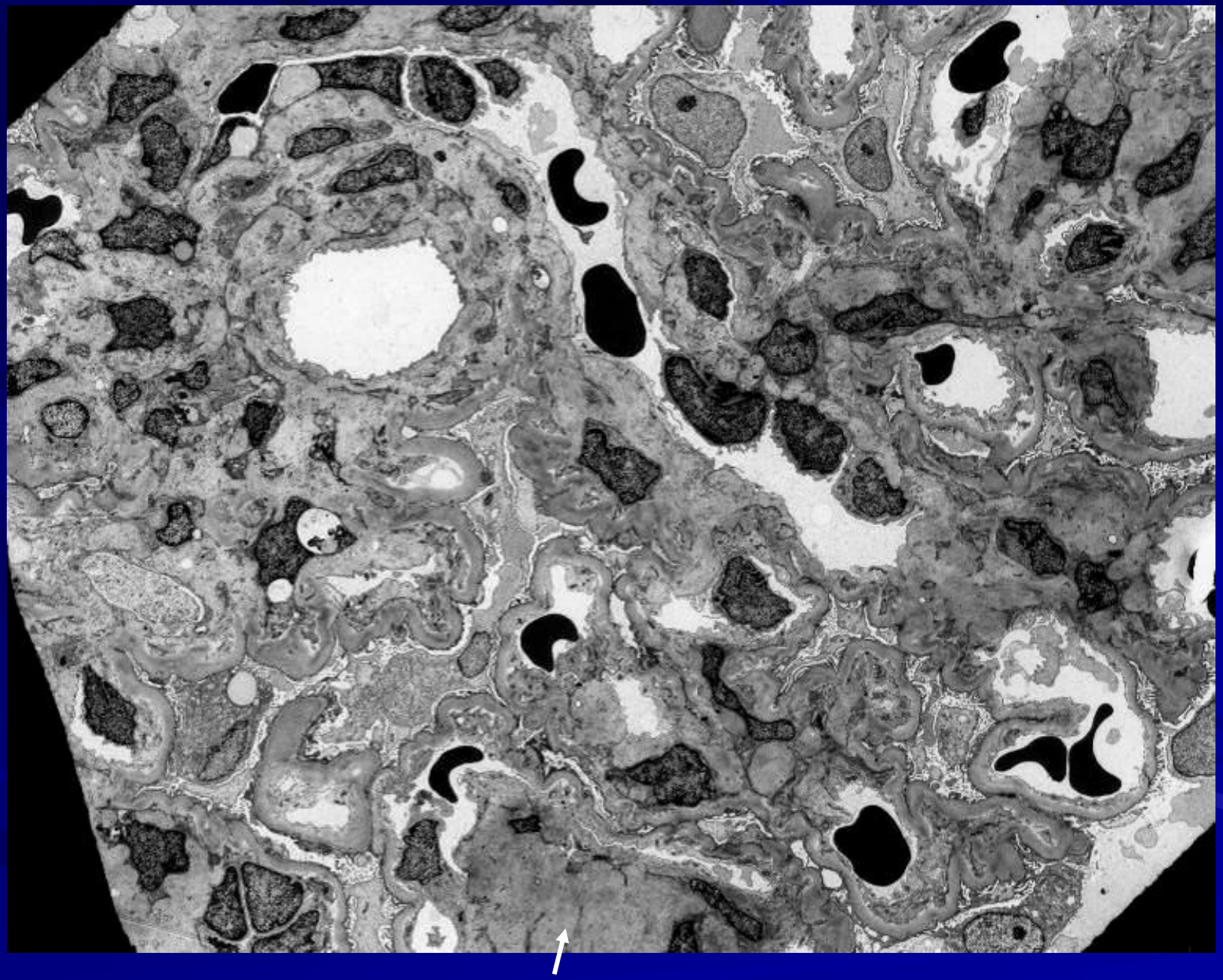
Obsolete glomerulus – numerous exudative lesions

Thickened GBM up to 600nm – normal is 300 to 350nm for adults

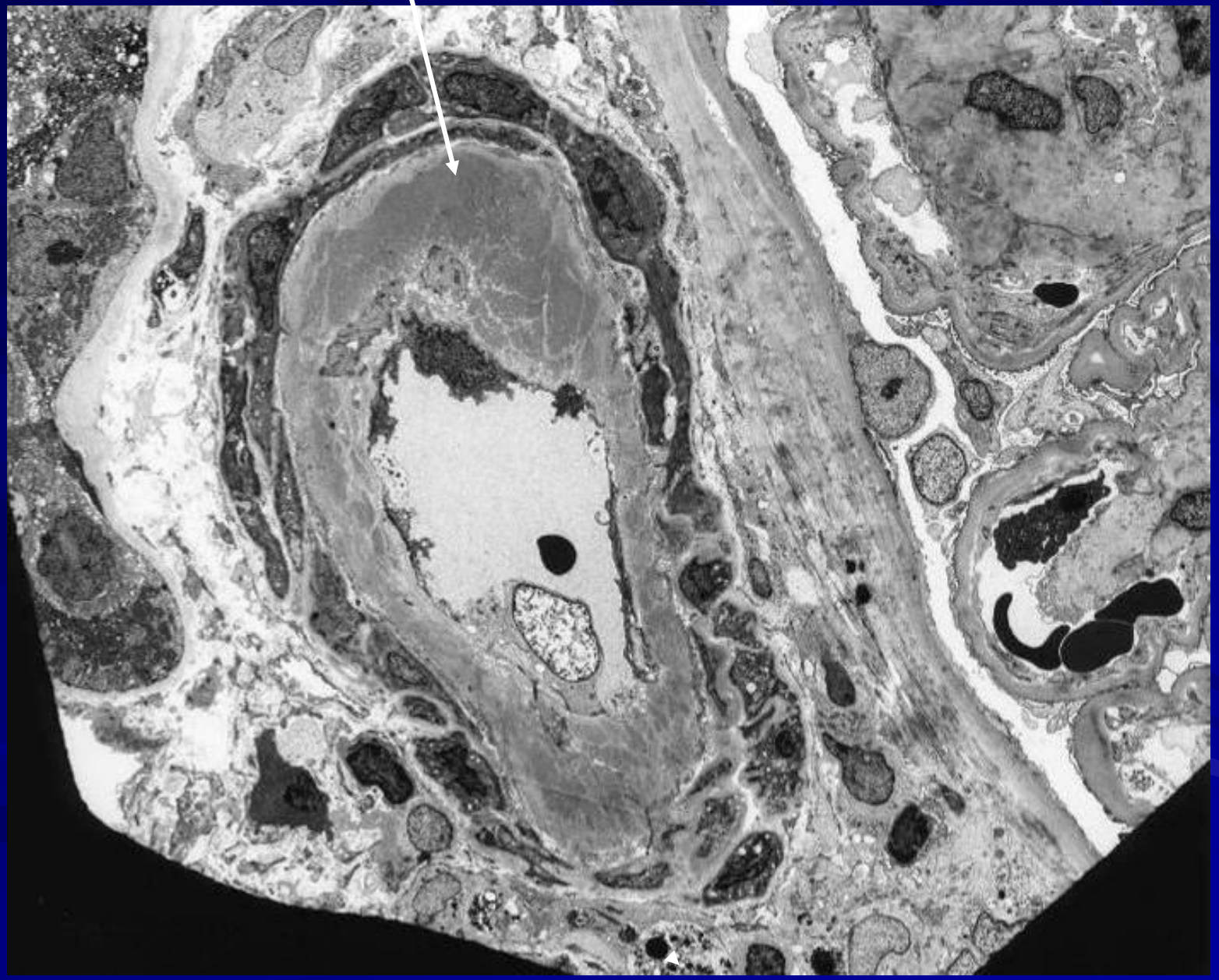


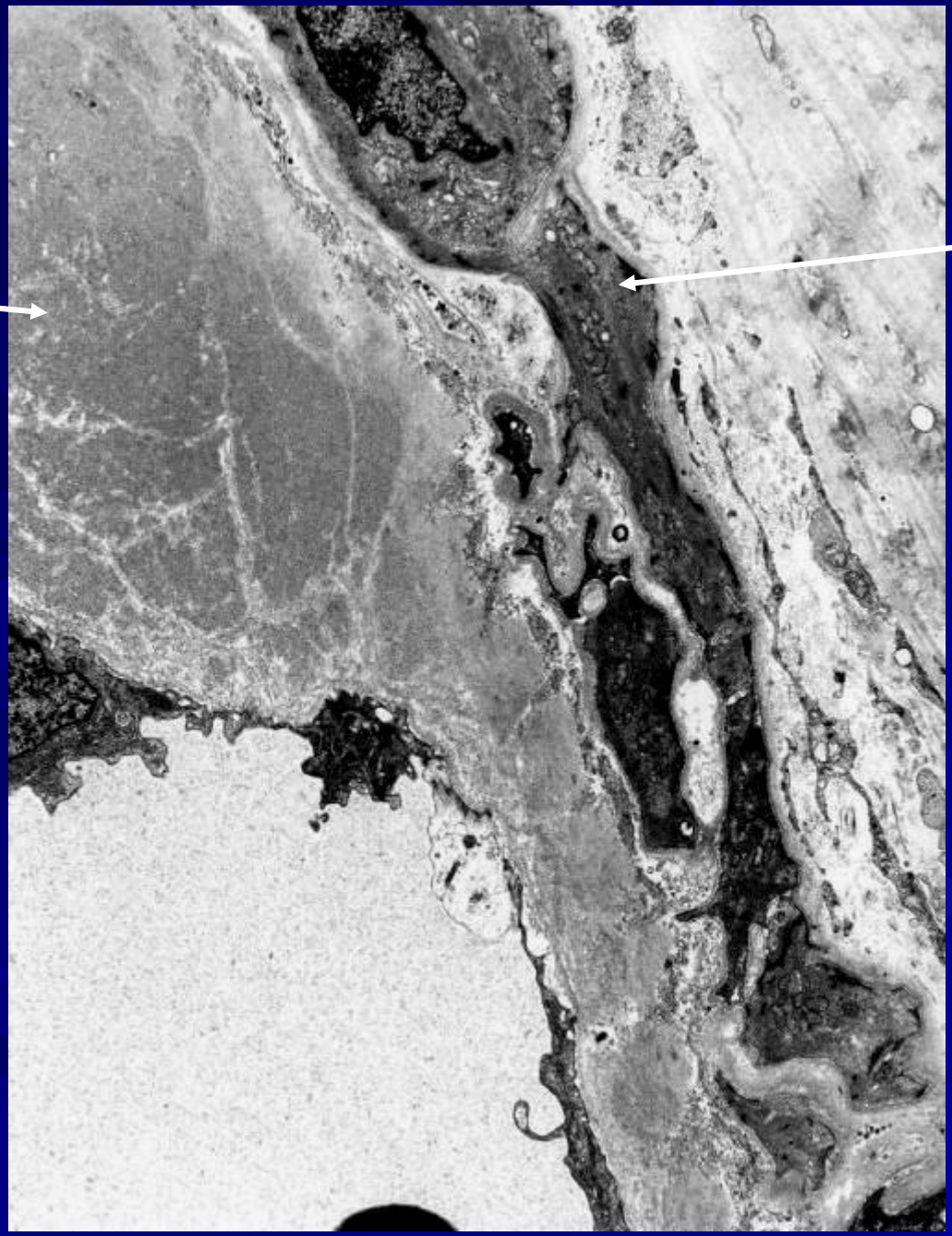


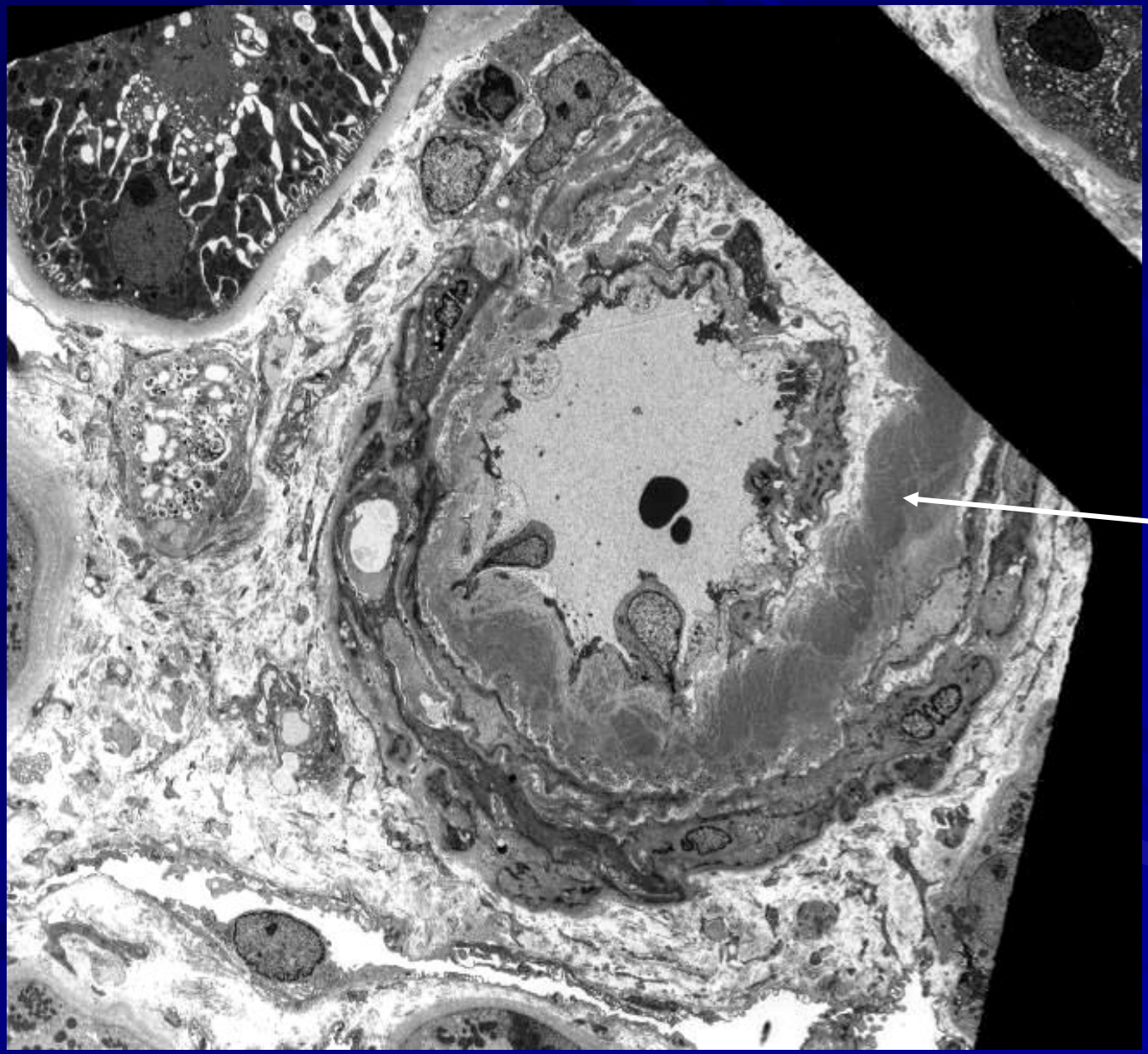
Afferent and efferent arteriolar hyalinosis


Mesangial matrix expansion

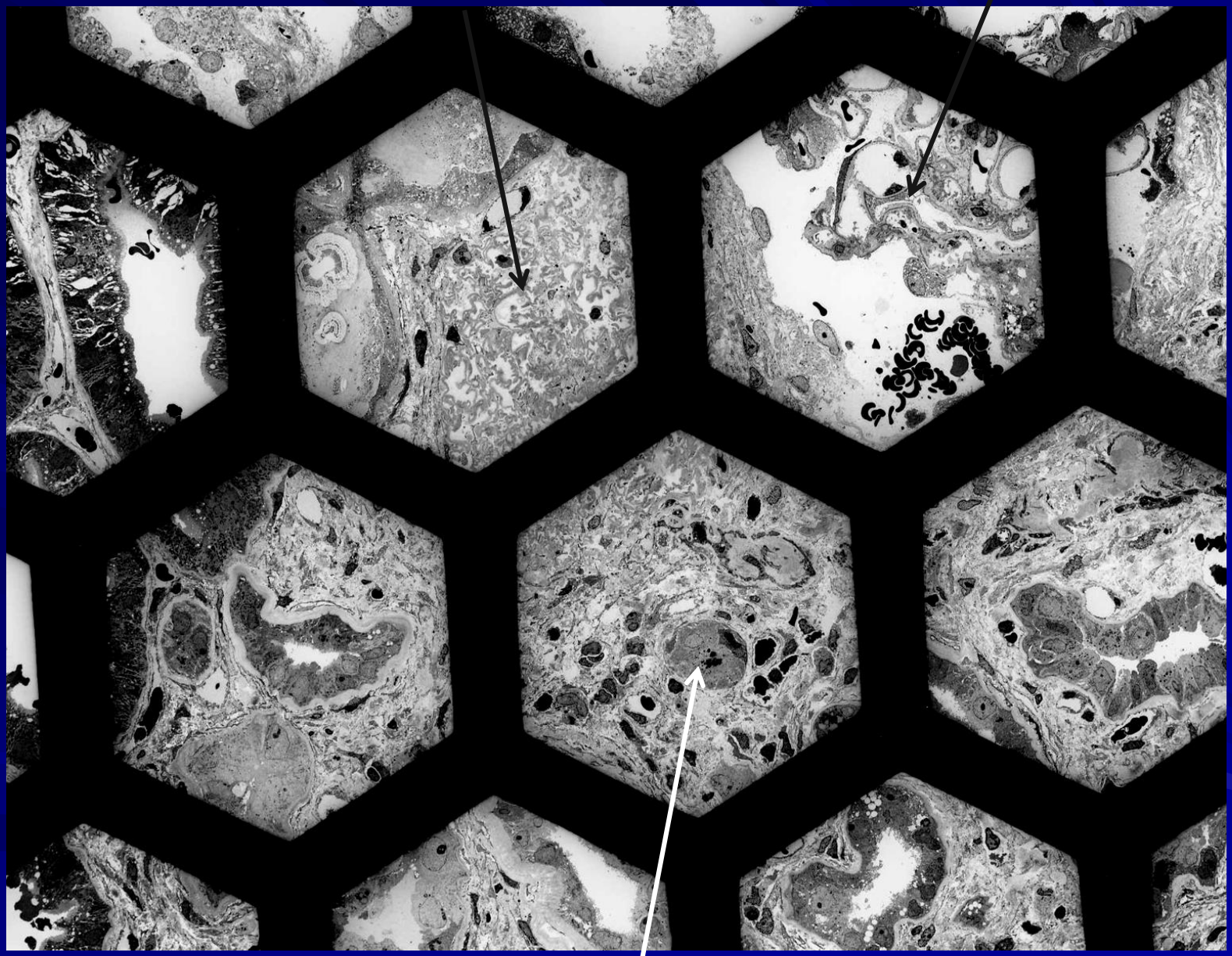
Arteriolar hyalinosis IgM & C3




Arteriolar hyalinosis
Arteriolar smooth muscle cell

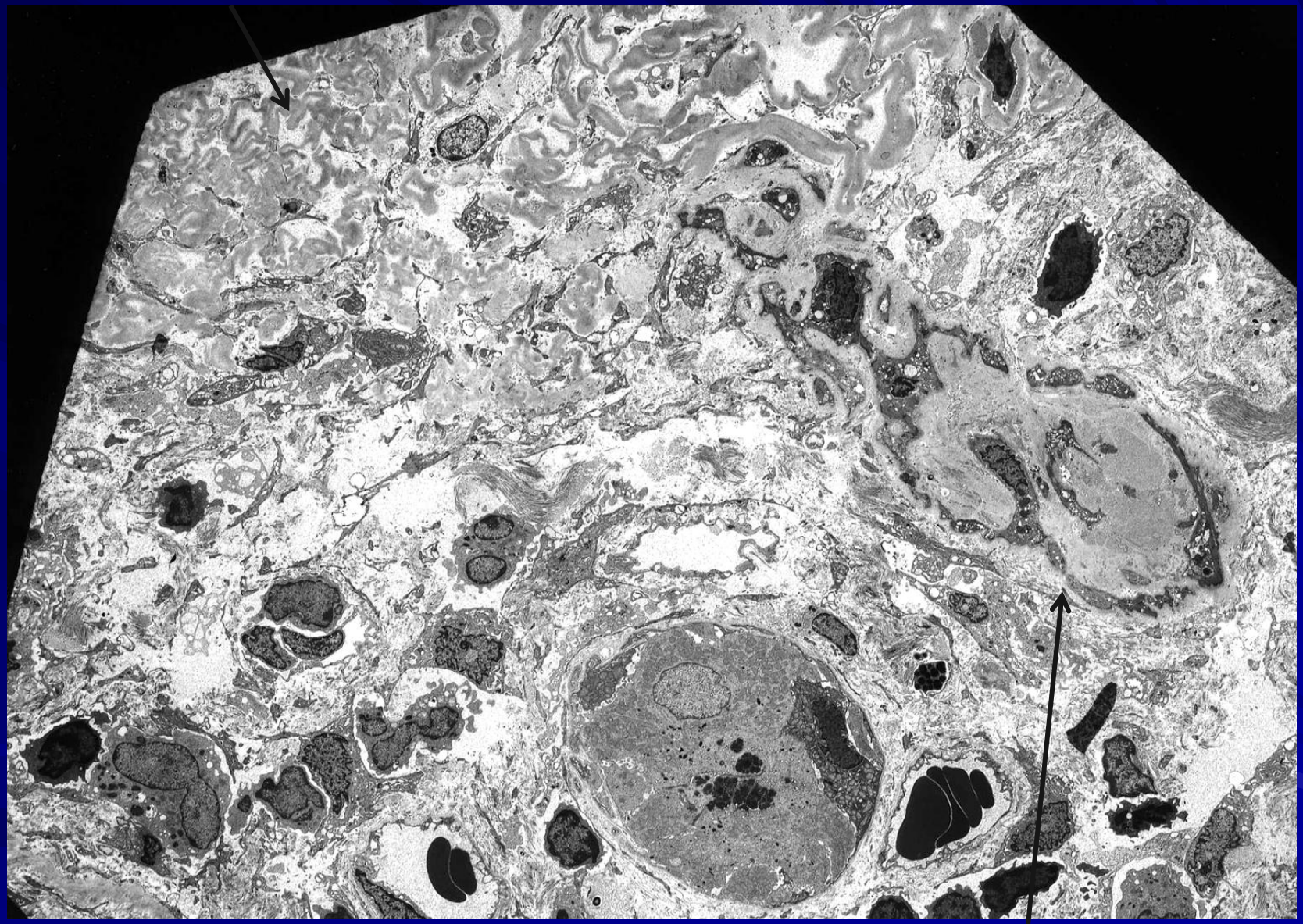


Other arteriole – see 4 slides up for low magnification


Infarcted glomerulus
Relatively unaffected glomerulus
Severe arteriolar hyalinosis

Infarcted glomerulus

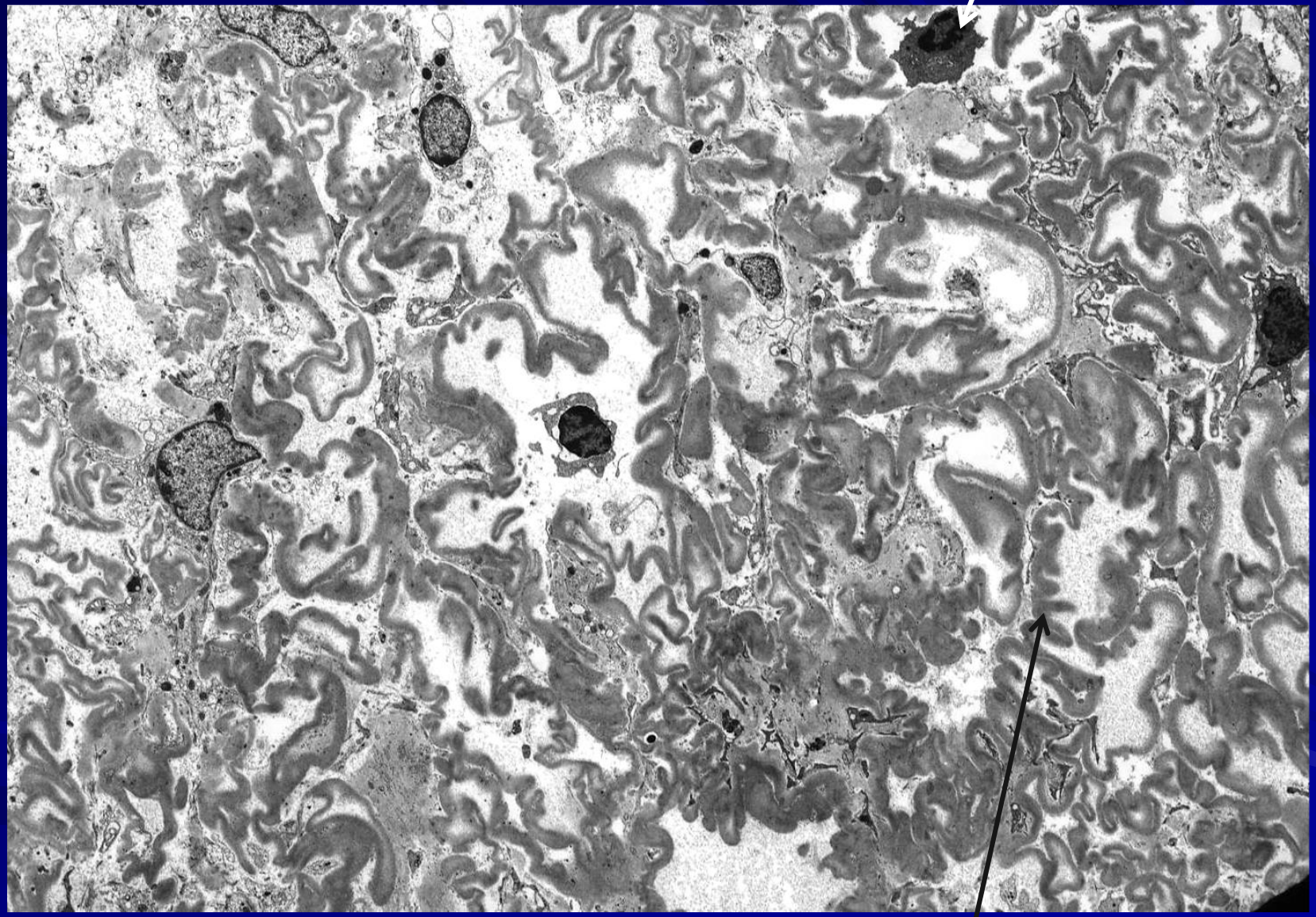
Higher magnification of previous slide



Severe arteriolar hyalinosis

Infarcted glomerulus

Occasional lymphocyte



Higher magnification of two slides earlier

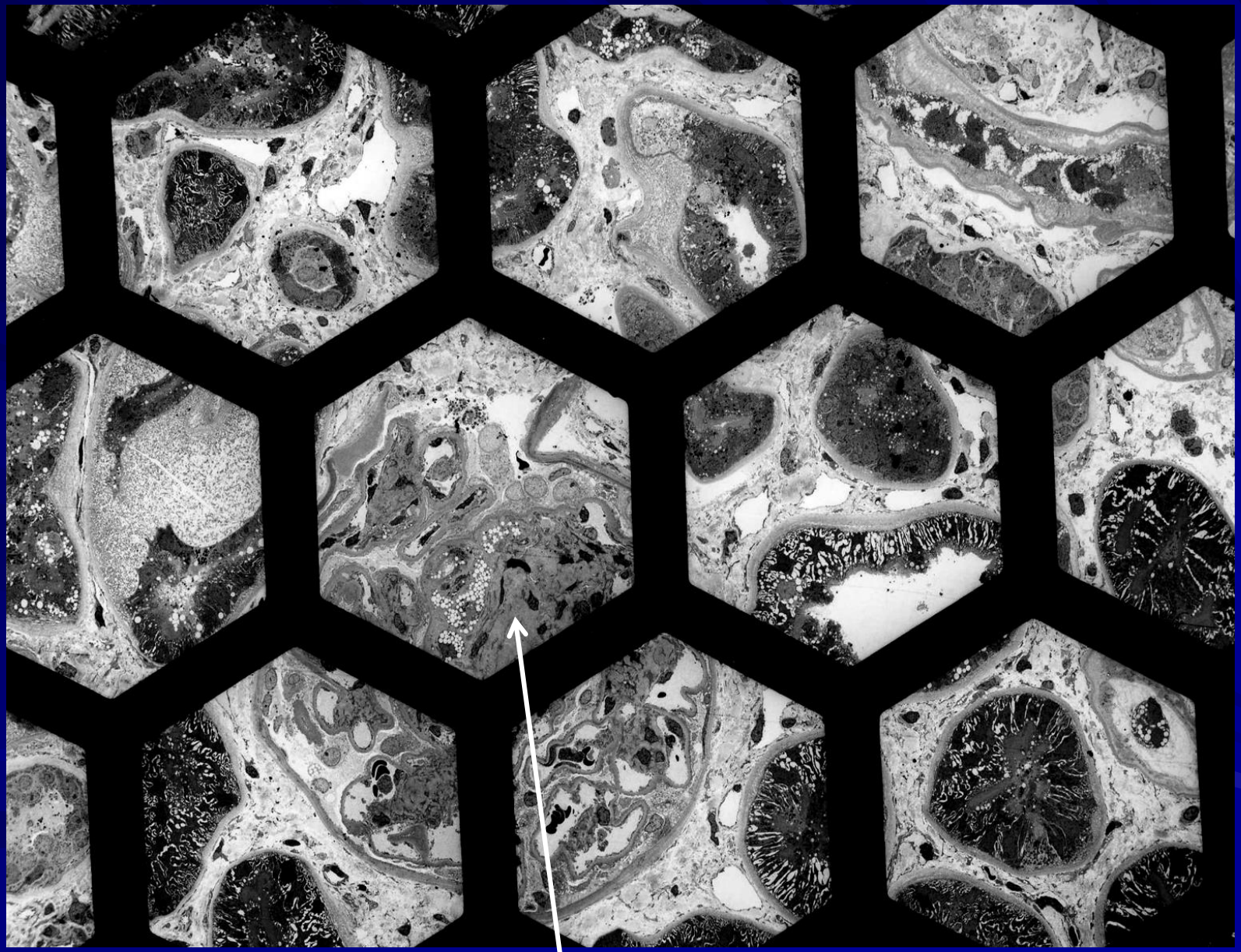
Severe GBM wrinkling

Patient with diabetic nephropathy and nephrotic syndrome

- Poorly controlled diabetes
- Early stage pregnancy
- Nephrotic

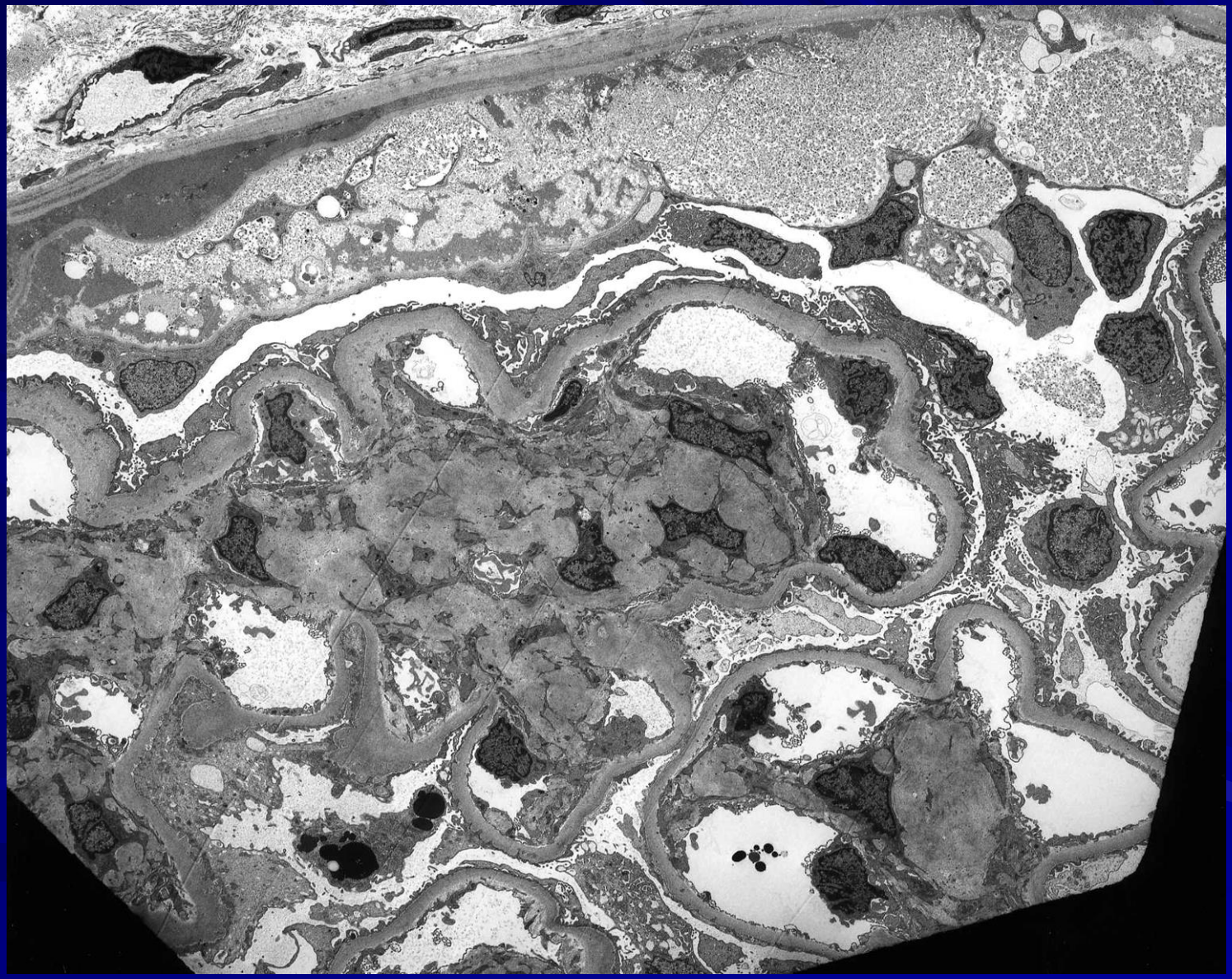
- Histology – diabetic change only
- IF – linear IgG – consistent with diabetes alone
- EM – diabetic and stage 1 membranous

Diabetic nephropathy and membranous glomerlonephritis



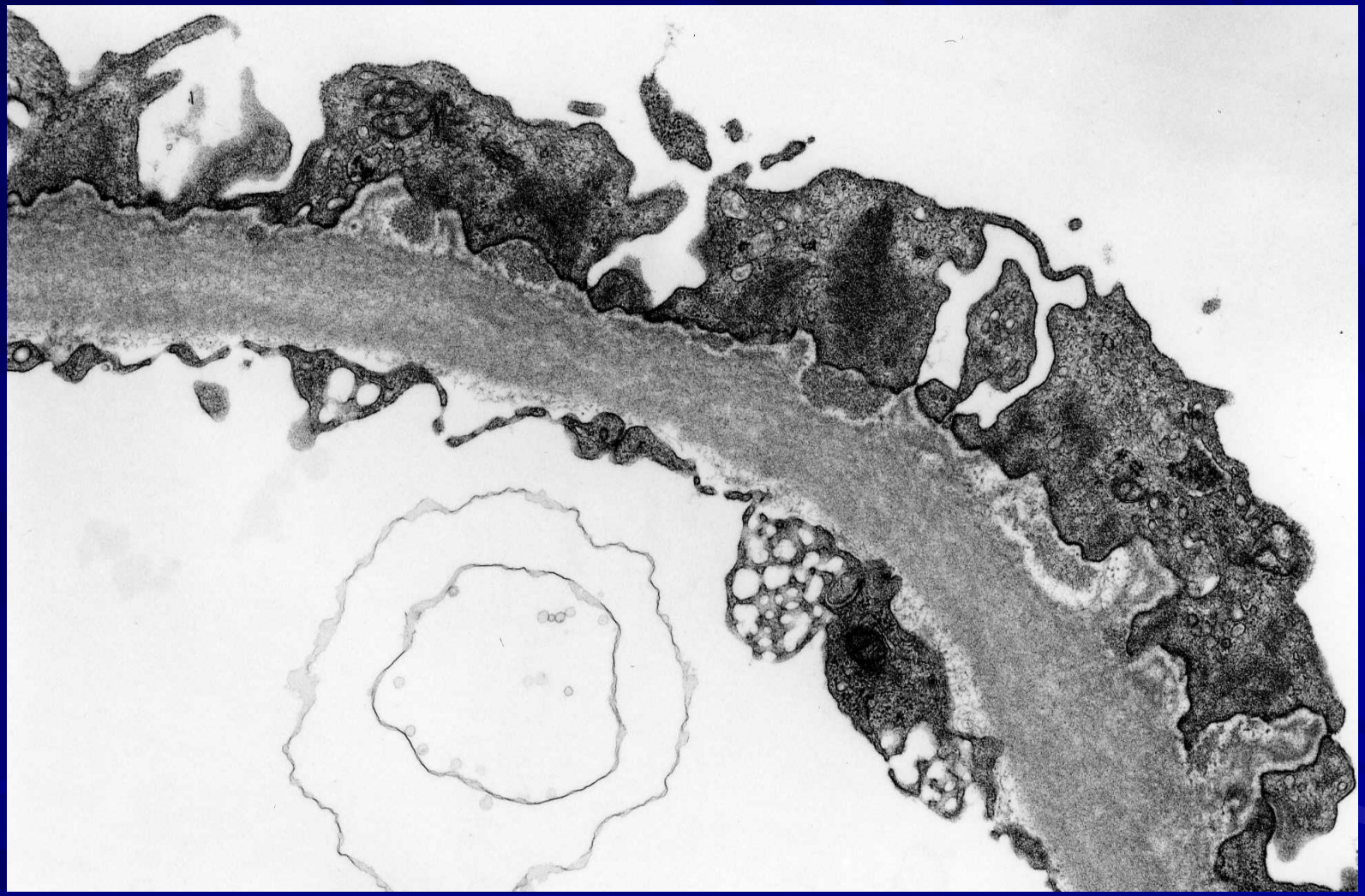
Nodular glomerulosclerosis

Diabetic and membranous glomerulonephropathy



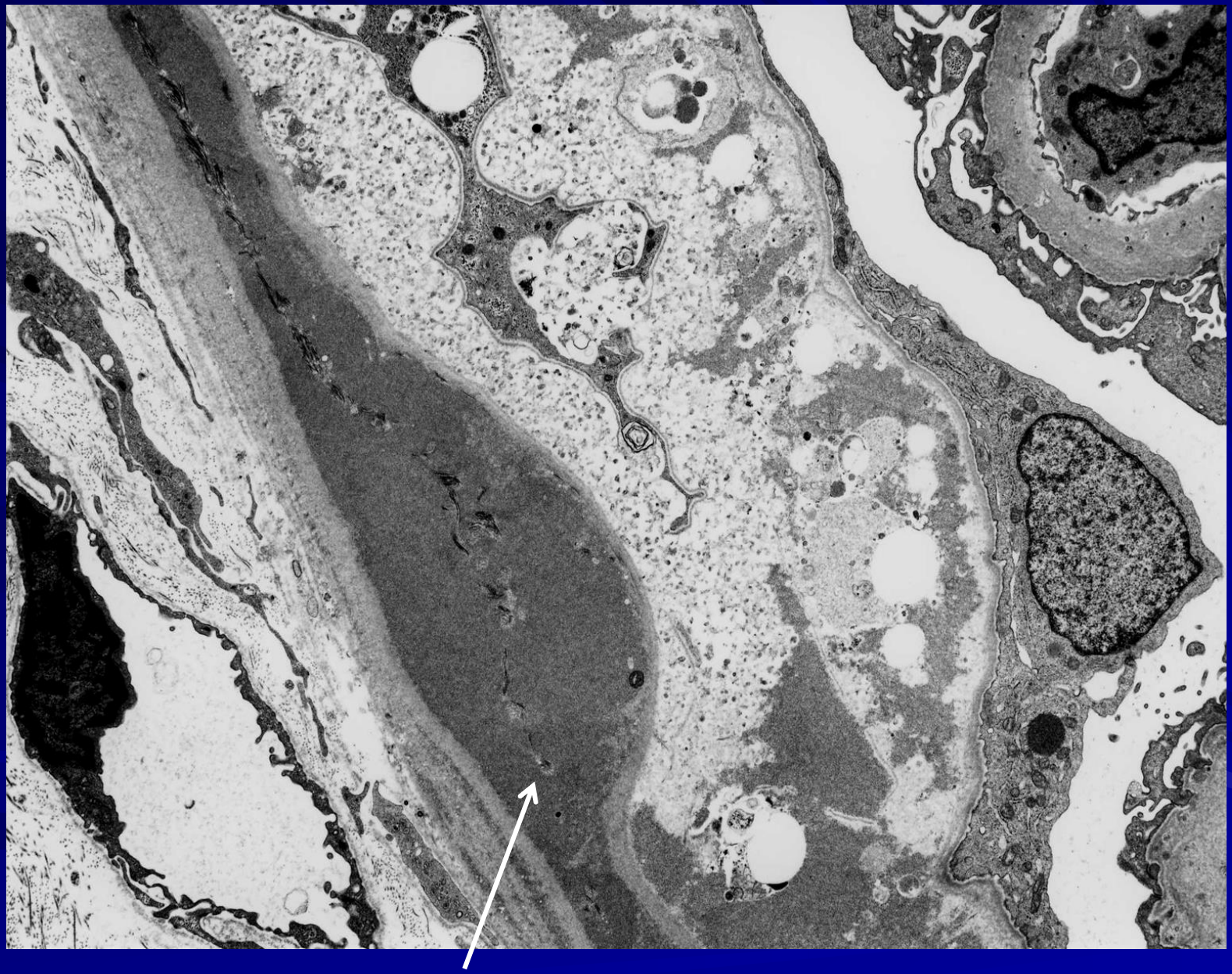
Thickened GBM and Kimmelsiel-Wilson nodules

Thickened GBM and numerous small subepithelial deposits



No spikes on MST, linear IgG on immunofuorescence

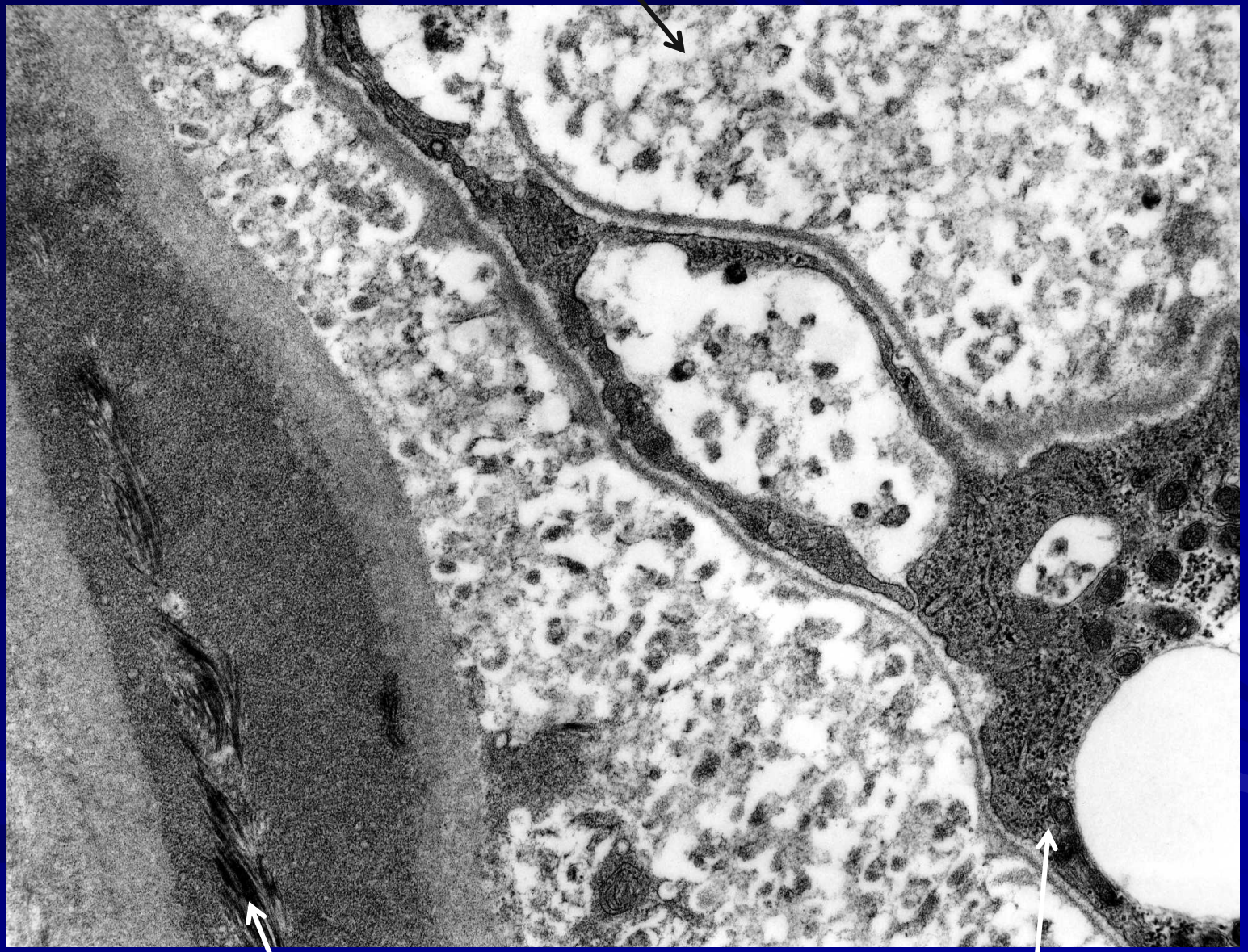
Thickened Bowman’s capsule with foamy structure



Capsular drop

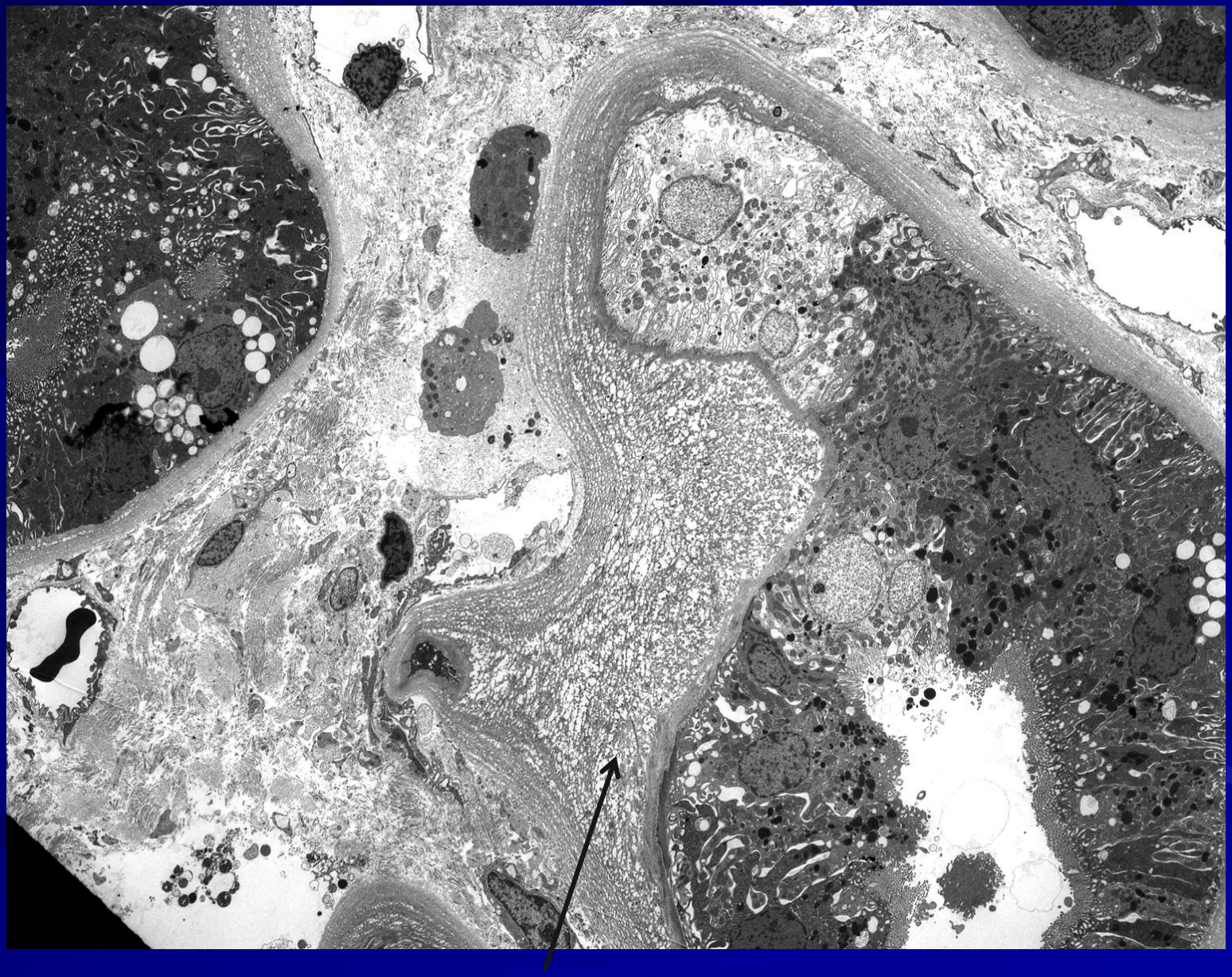
Higher magnification of two slides previous

Lipid laden new basement membrane

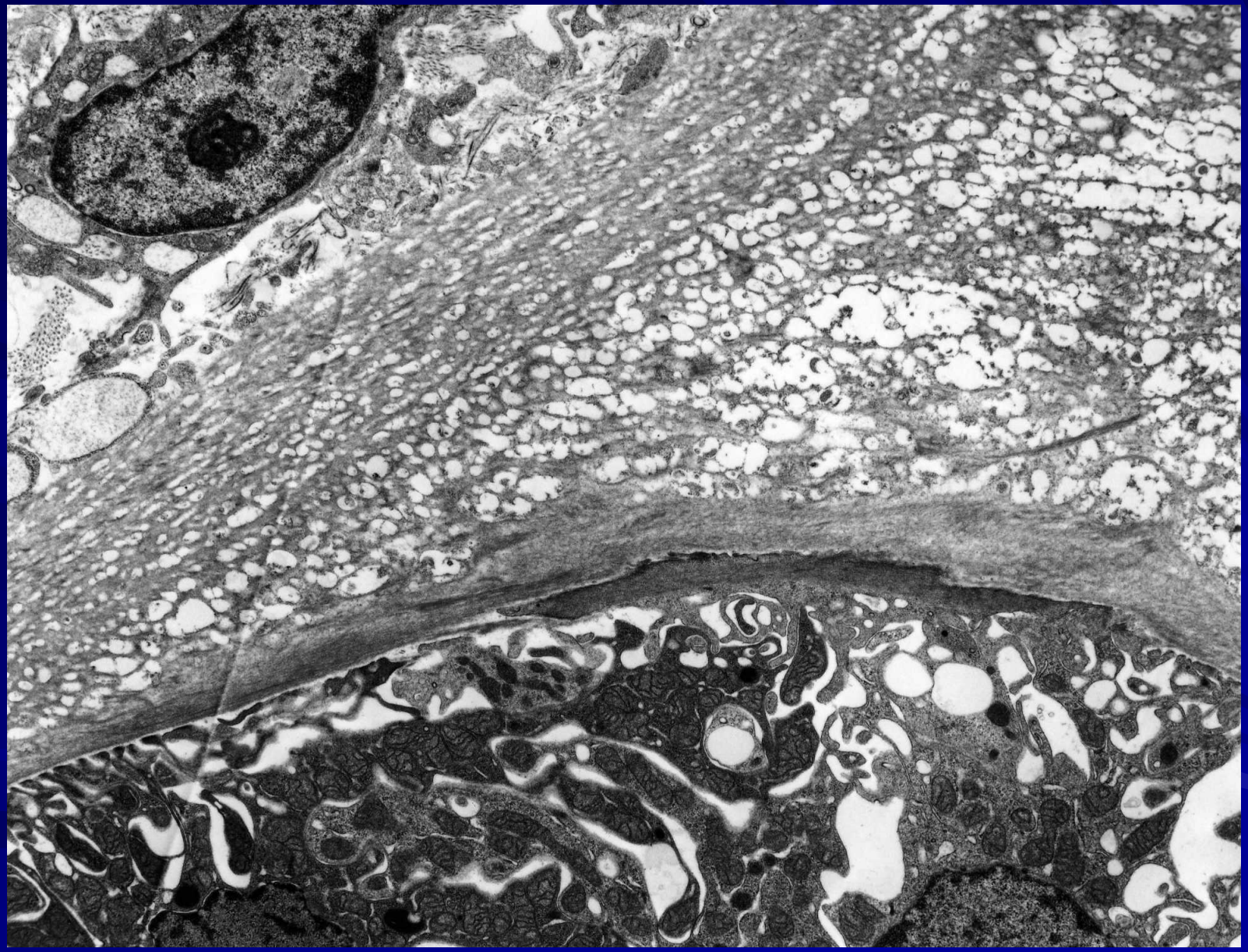


Fibrous collagen within capsular drop

Entrapped epithelial cell



Expanded tubular basement membrane

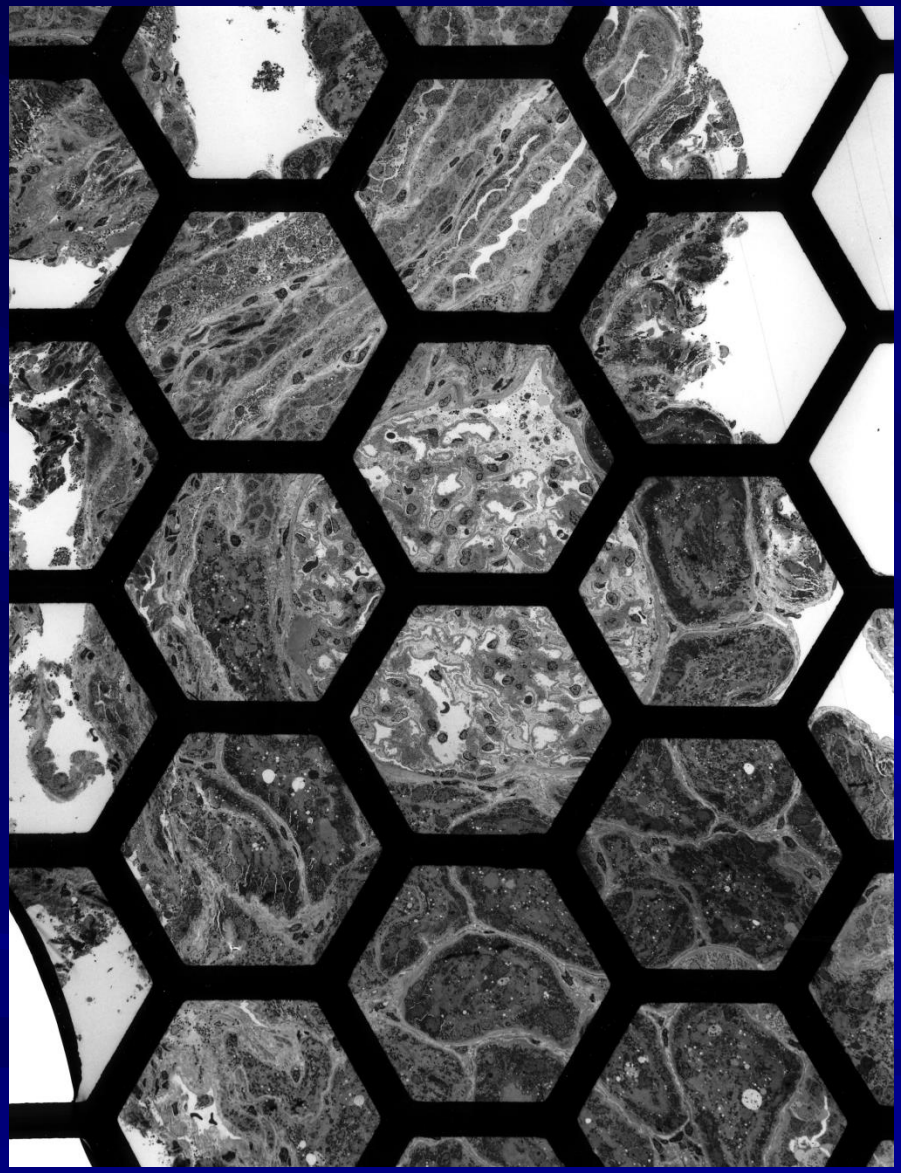


Tubular basement membrane vacuolation

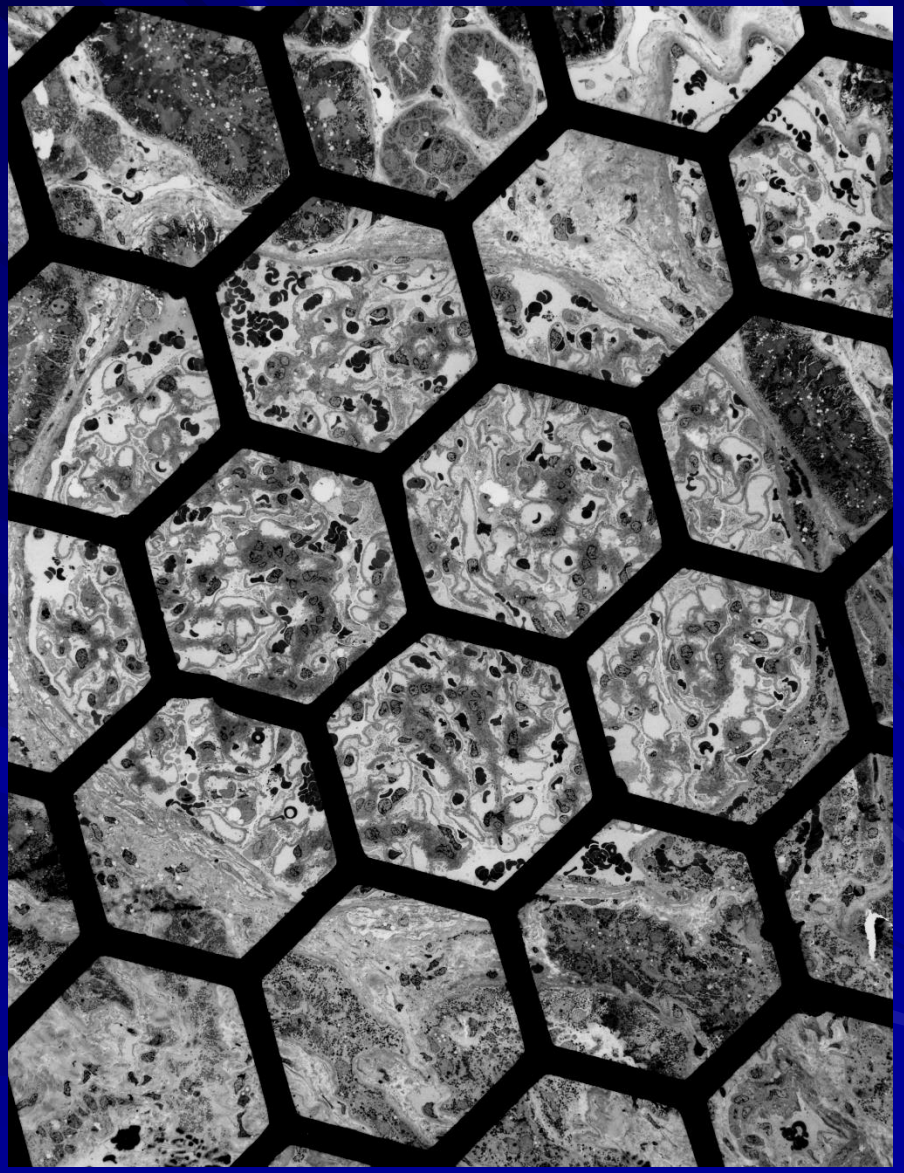
Morbid obesity study

- No microalbumenuria in any patient consenting for biopsy during gastric banding operation
- Pre-type II diabetic glomerulopathy in some patients
- Glomerulomegaly
- Early histological changes in the kidney of people with **morbid obesity**. Goumenos DS, Kawar B, El Nahas M, Conti S, **Wagner** B E, Spyropoulos C, Vlachojannis JG, Benigni A, Kalfarentzos F. Nephrol Dial Transplant. 2009 Dec;24(12):3732-8. Epub 2009 Jul 13

Both biopsies from patients with morbid obesity

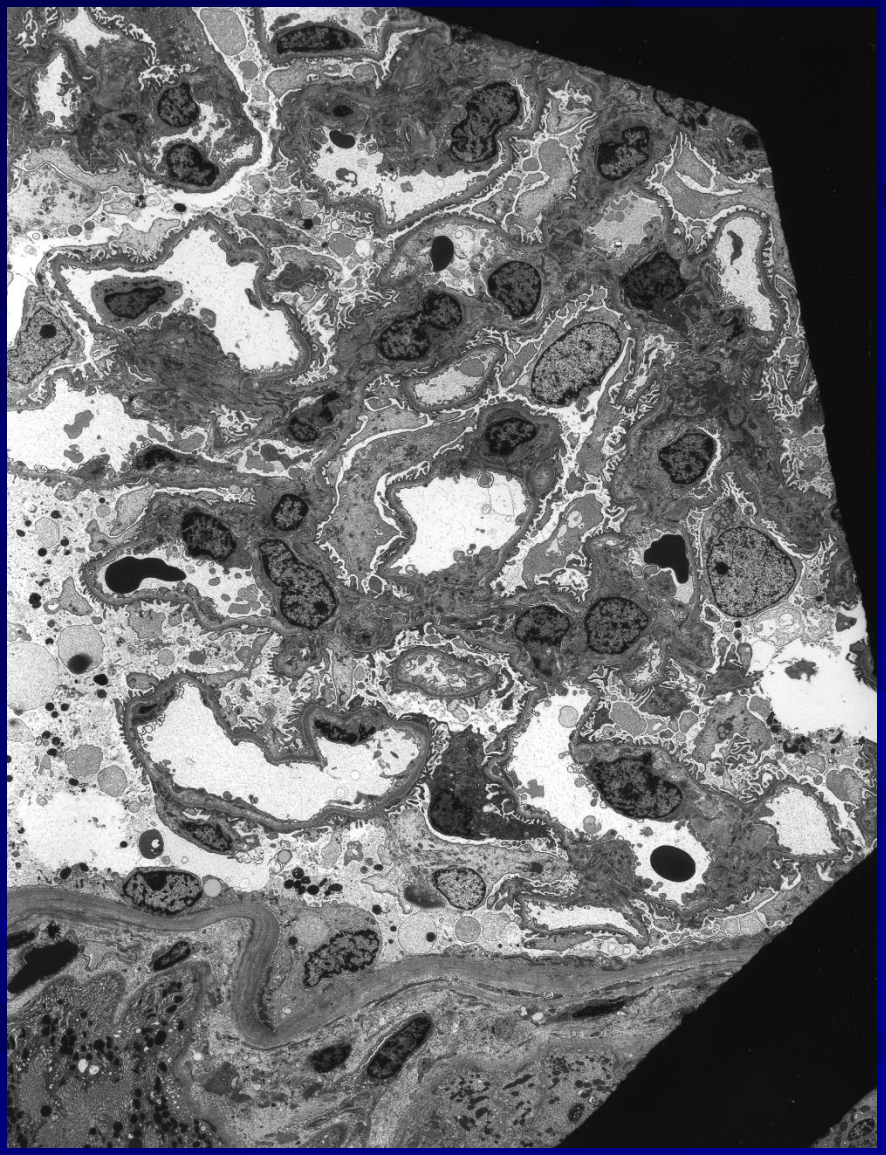


Same magnification – different grid bar thickness

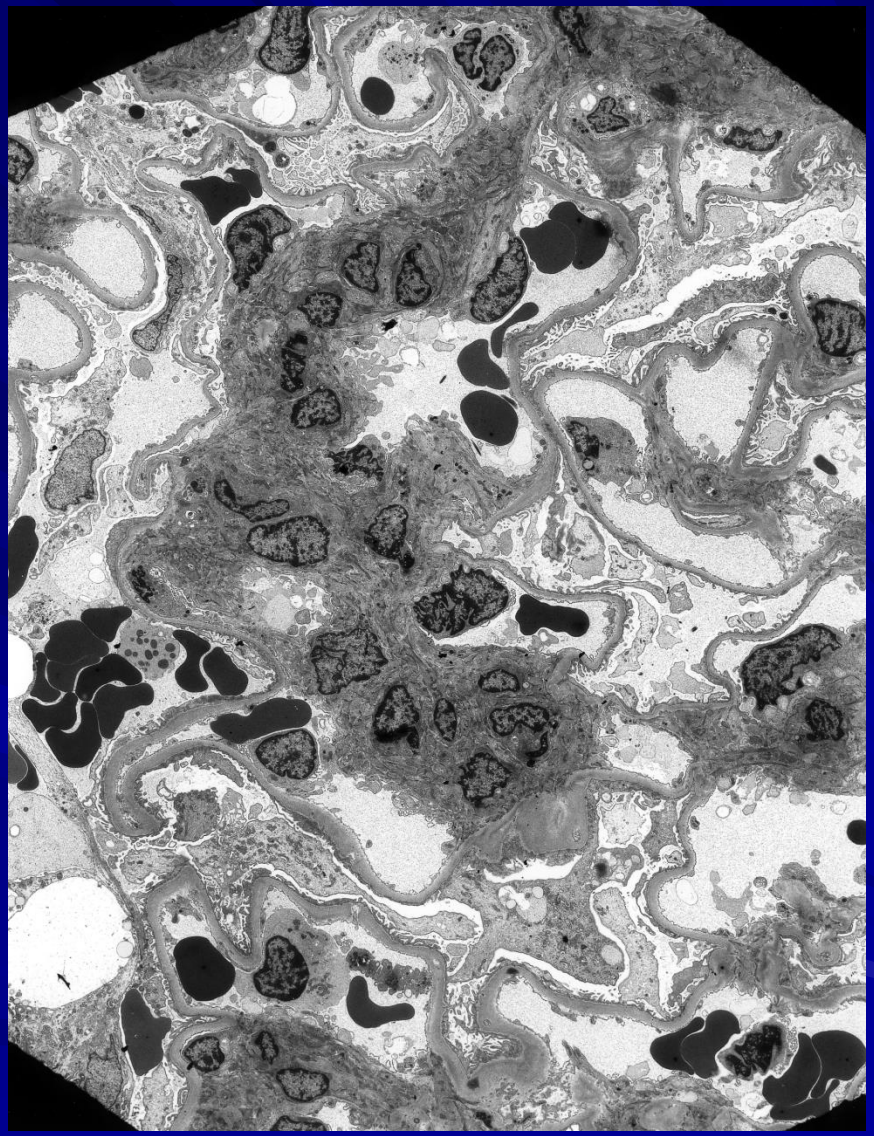


Glomerulomegaly

Morbid obesity study

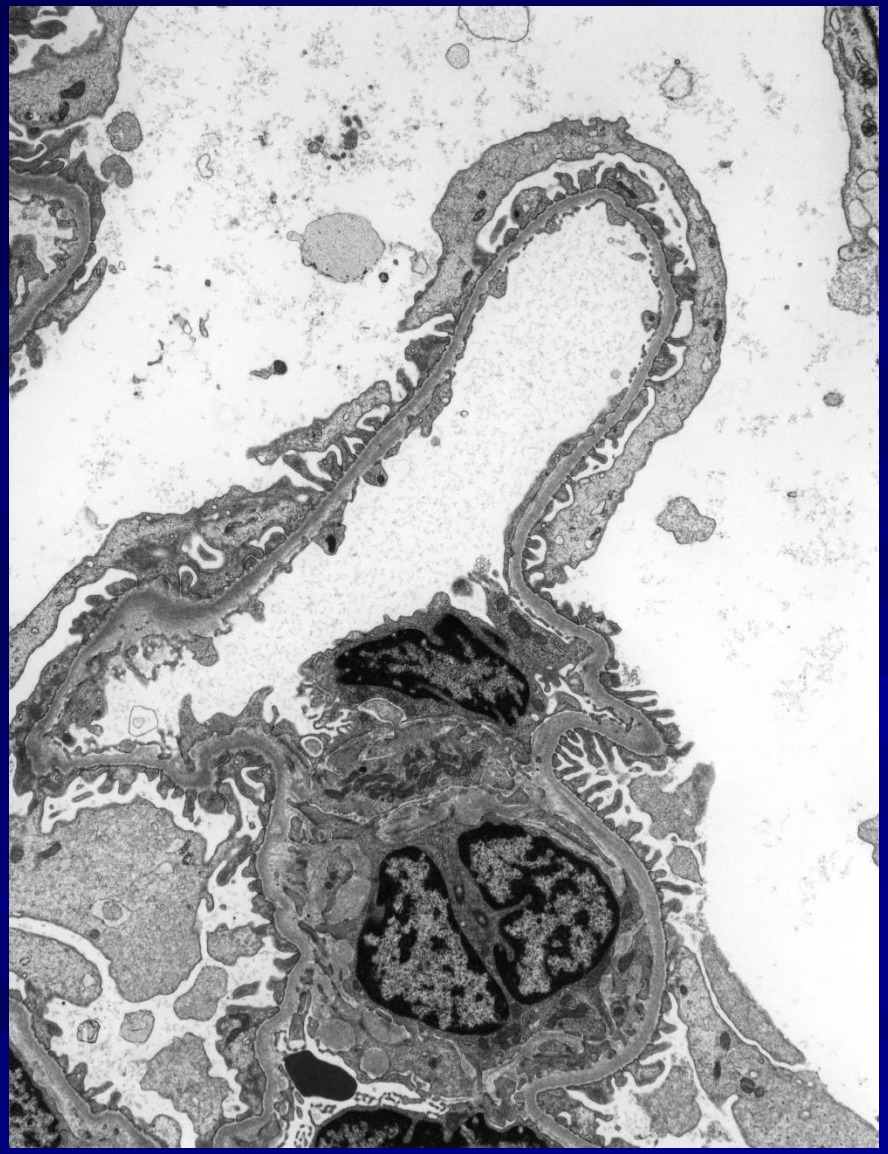


Higher magnification of previous slide

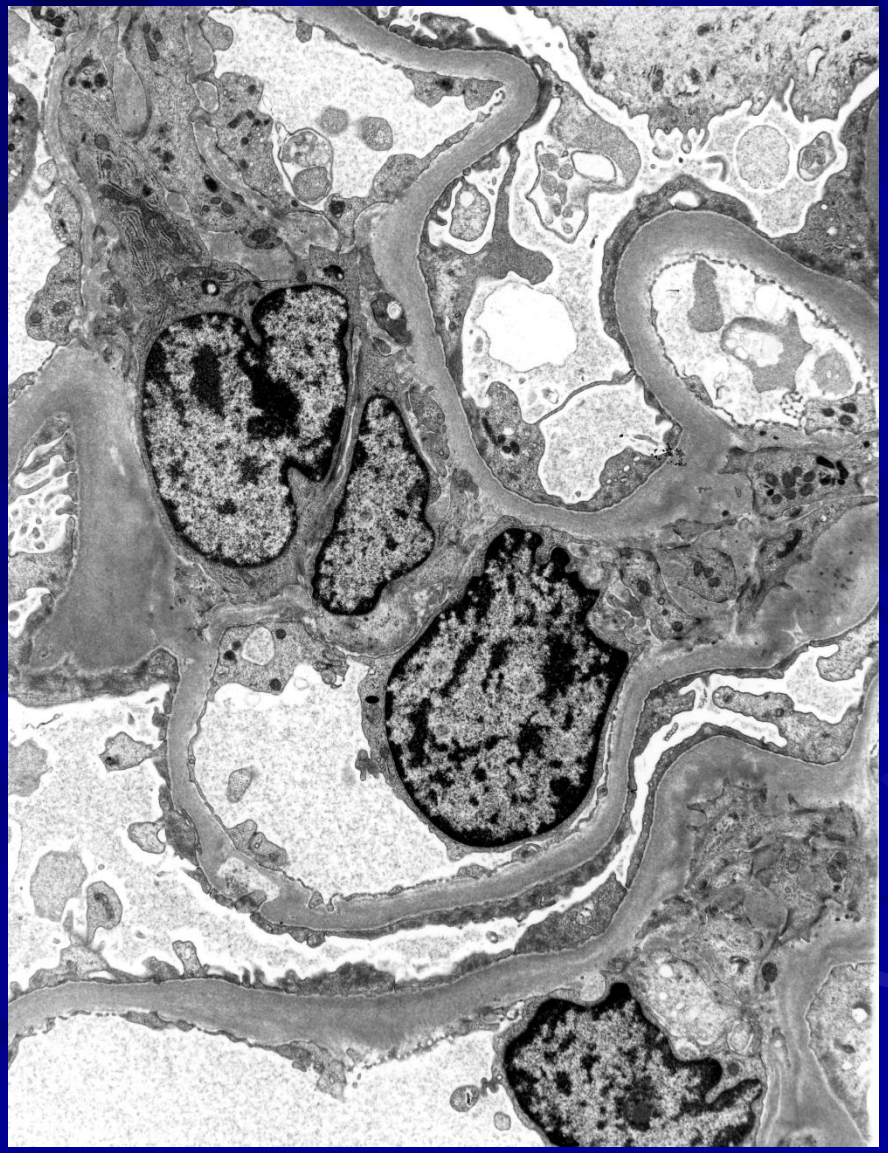


Mild mesangial matrix expansion and proliferation

Morbid obesity study



Higher magnification of previous slide



Thickened GBM