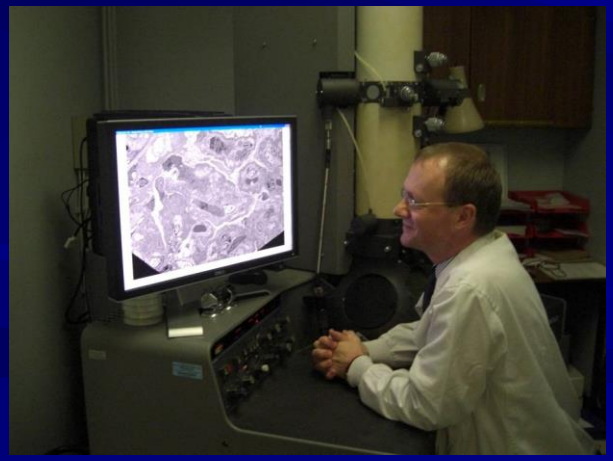
Basic Renal EM workshop

Southampton

September 30th 2011

Renal Ultrastructural Pathology
Lecture 2 F - Ma



Bart E Wagner
BSc CSc FIBMS Dip Ult Path
Chief Biomedical Scientist
Electron Microscopy Section
Histopathology Department
Northern General Hospital
Sheffield
South Yorkshire
UK
S5 7AU
bart.wagner@sth.nhs.uk
Tel+44(0)114-27 14154

Renal ultrastructural pathology
Lecture 2 - Topics

1. Fabry's disease
2. Focal Segmental Glomerulo Sclerosis FSGS
3. IgA disease
4. Immunotactoid and Fibrillary Glomeropathy
5. Micro Angiopathic Haemolytic Anaemia MAHA

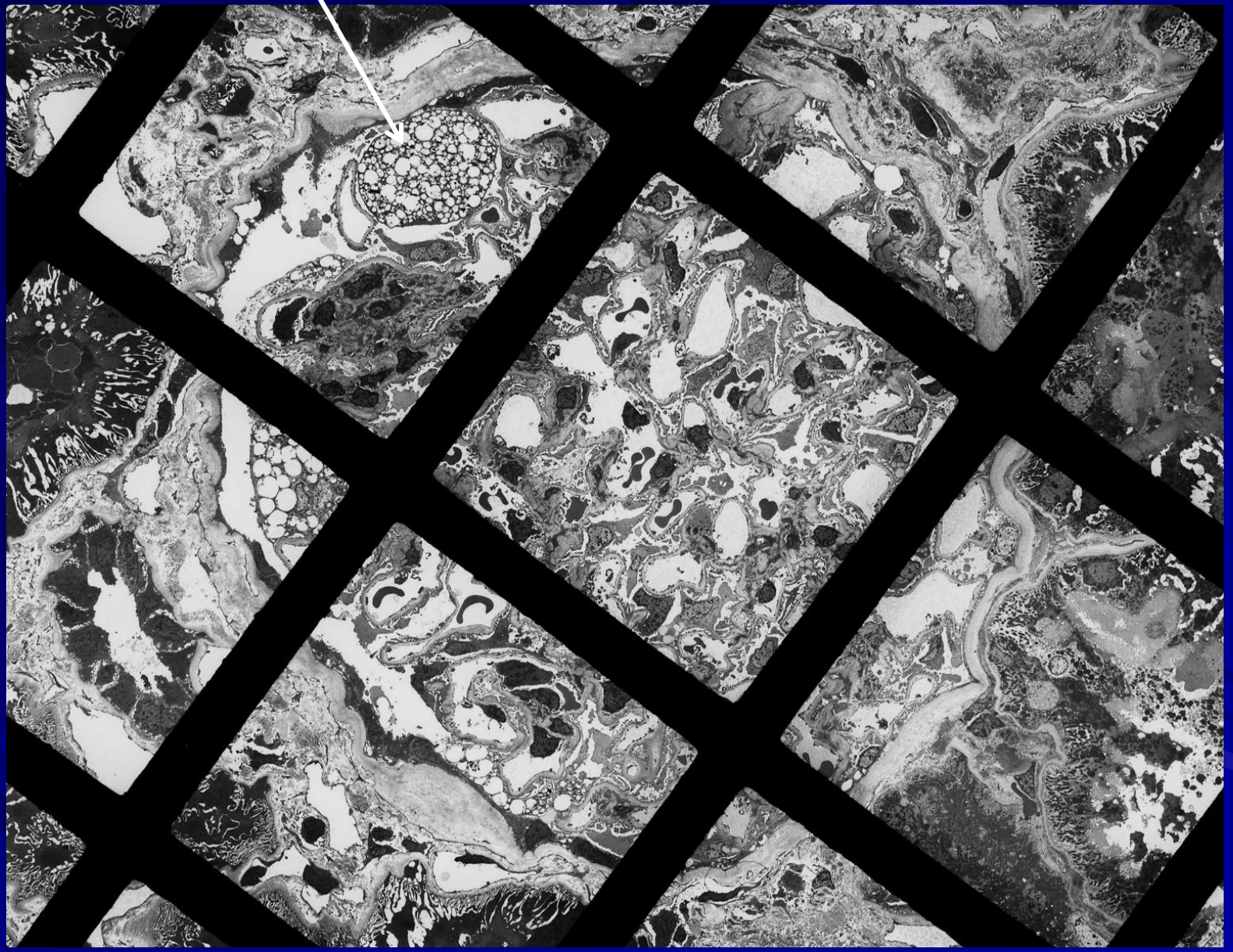
Fabry’s disease

Fabry's disease

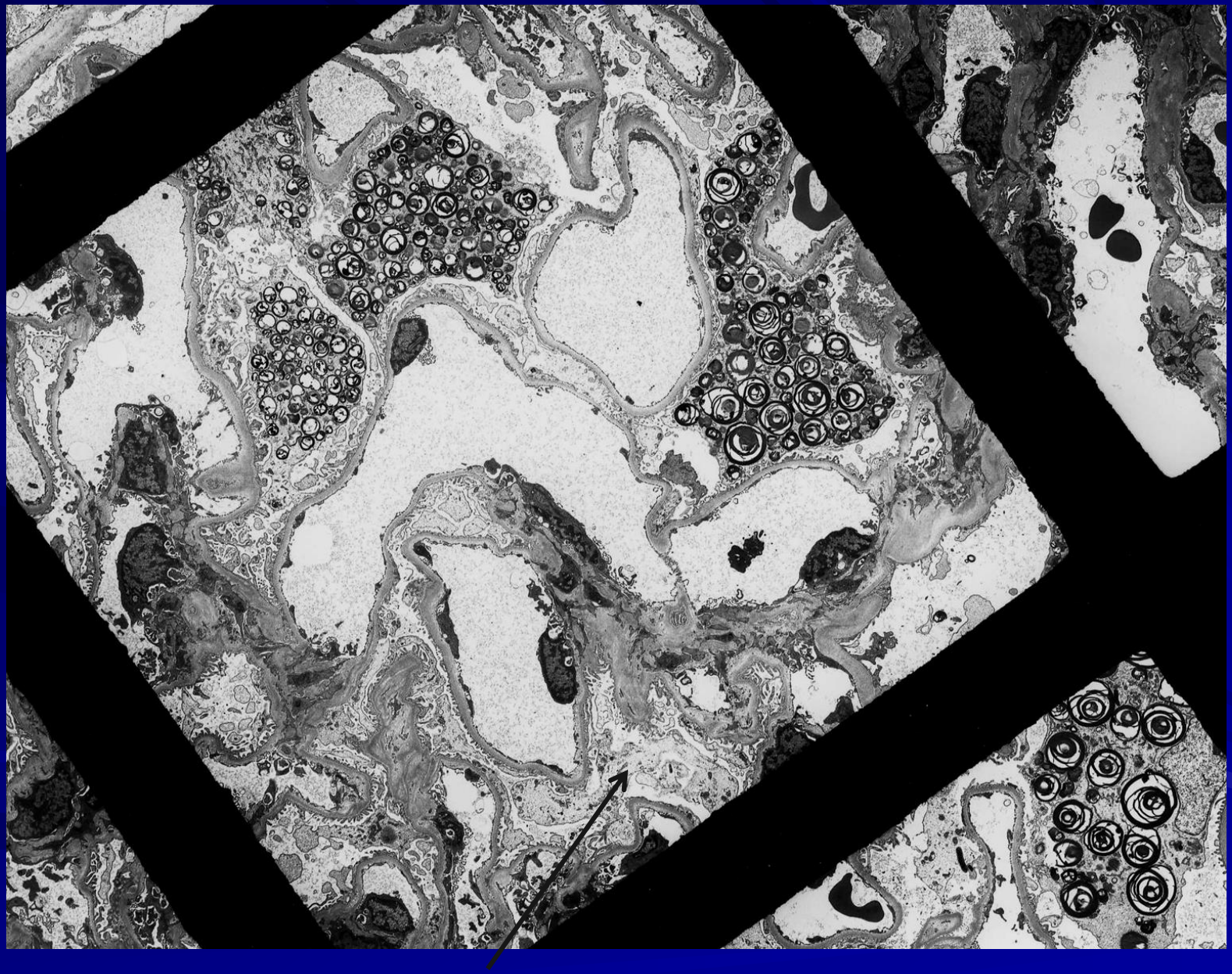
- Alpha galactosidase A deficiency
- X-linked inheritance
- Lyonization of X chromosome leads to variable expression
- One of the few treatable lysosomal storage disorders

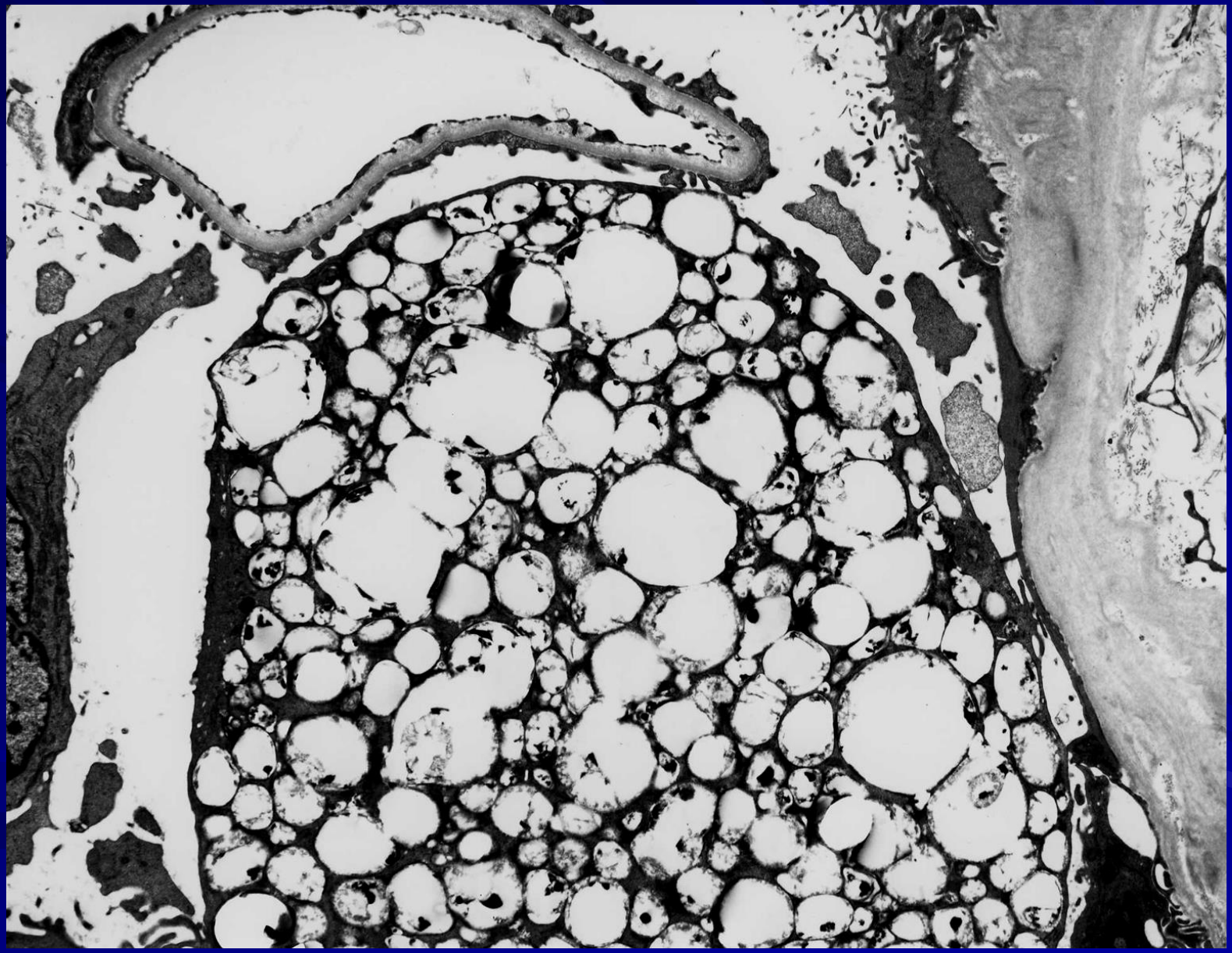
Persistent proteinuria following delivery

- Case from Royal Free Hospital, London


Occasional vacuolated podocyte

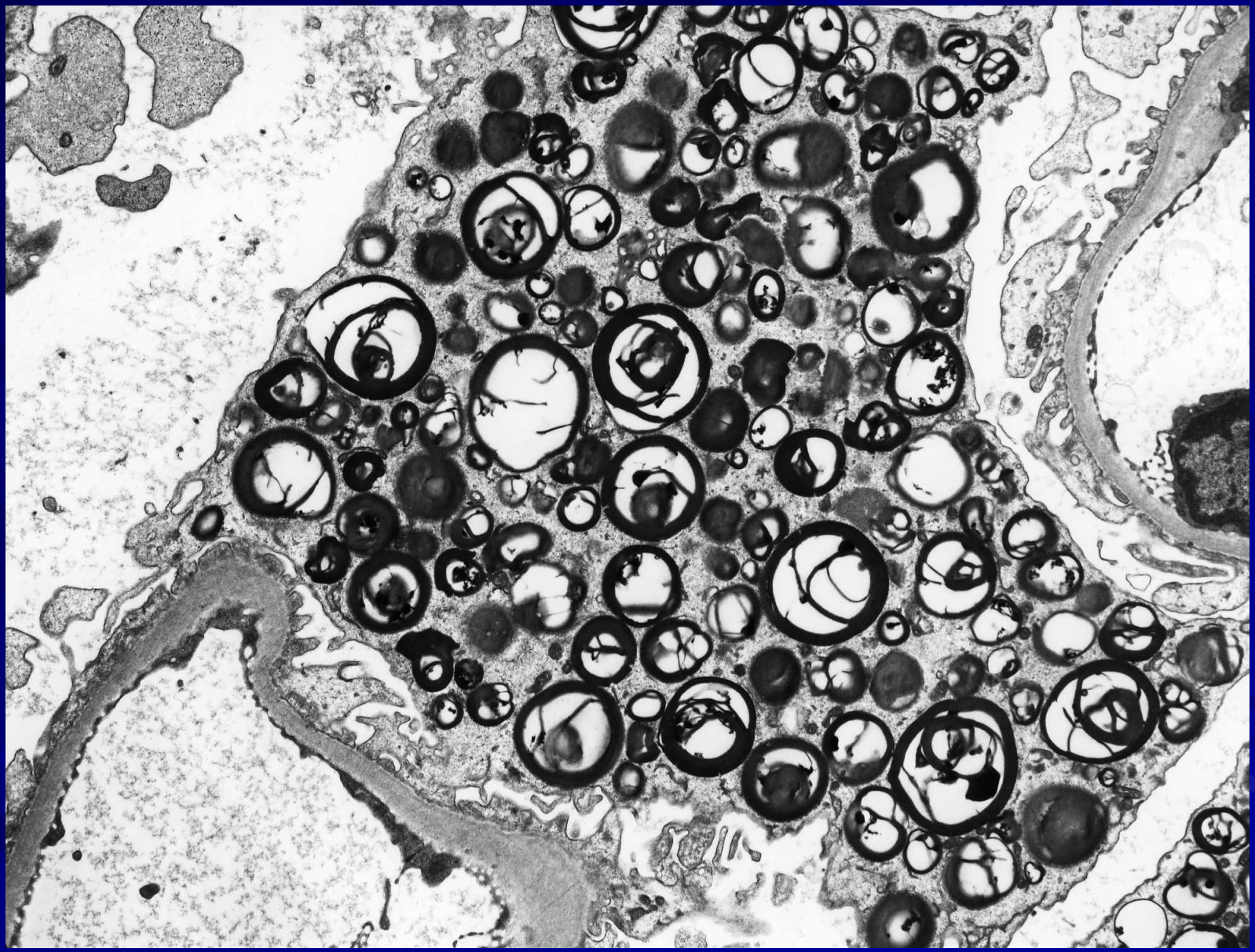
Same biopsy – different glomerulus





Podocyte lysosomes with electron lucent contents

Podocyte lysosomes with myelinoid contents



Higher magnification of previous slide

Myelinoid lysosomal contents

Pseudo Fabry's

Affects just one podocyte - stored material slightly different structure to Fabry's

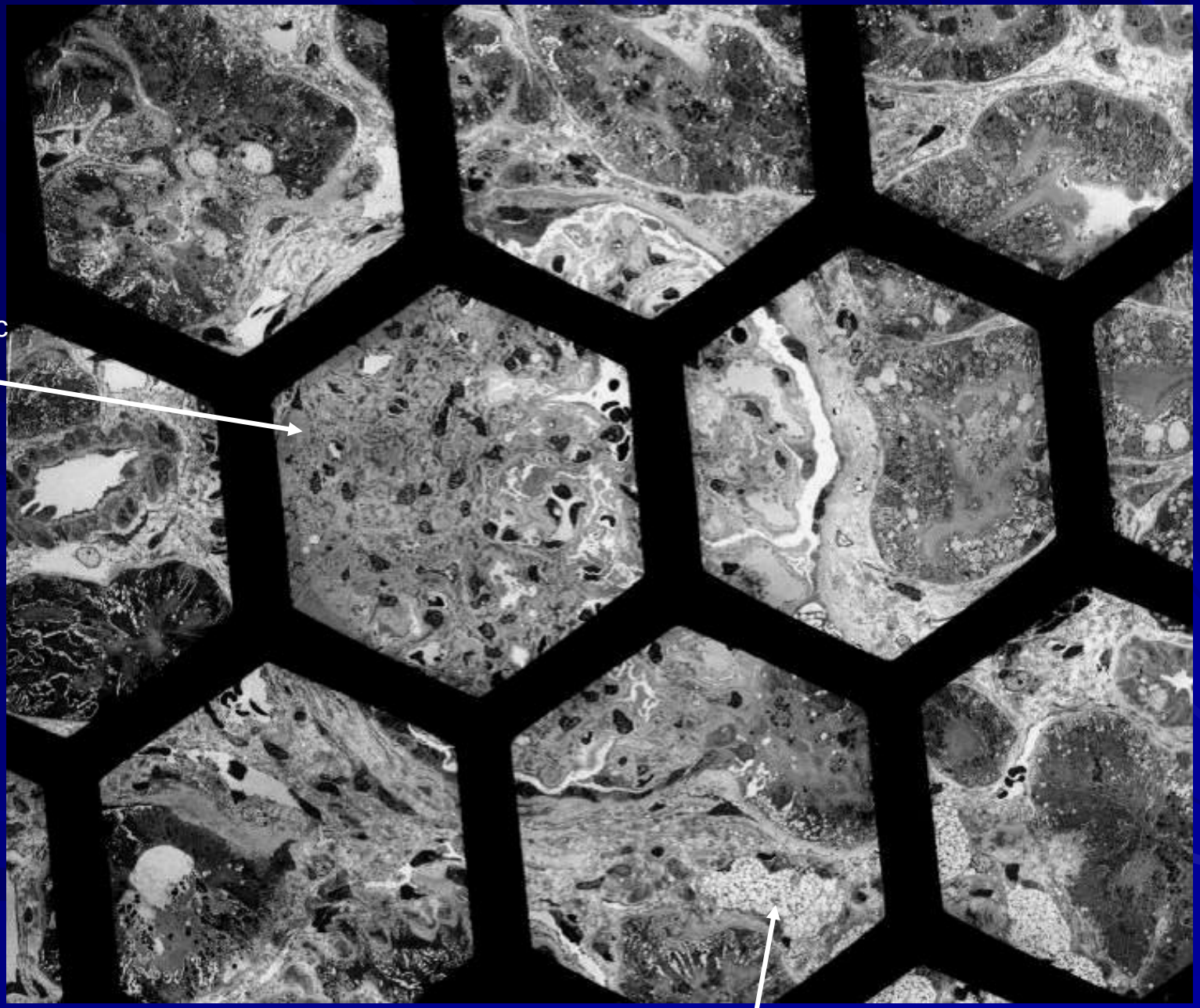
Focal Segmental Glomerulosclerosis

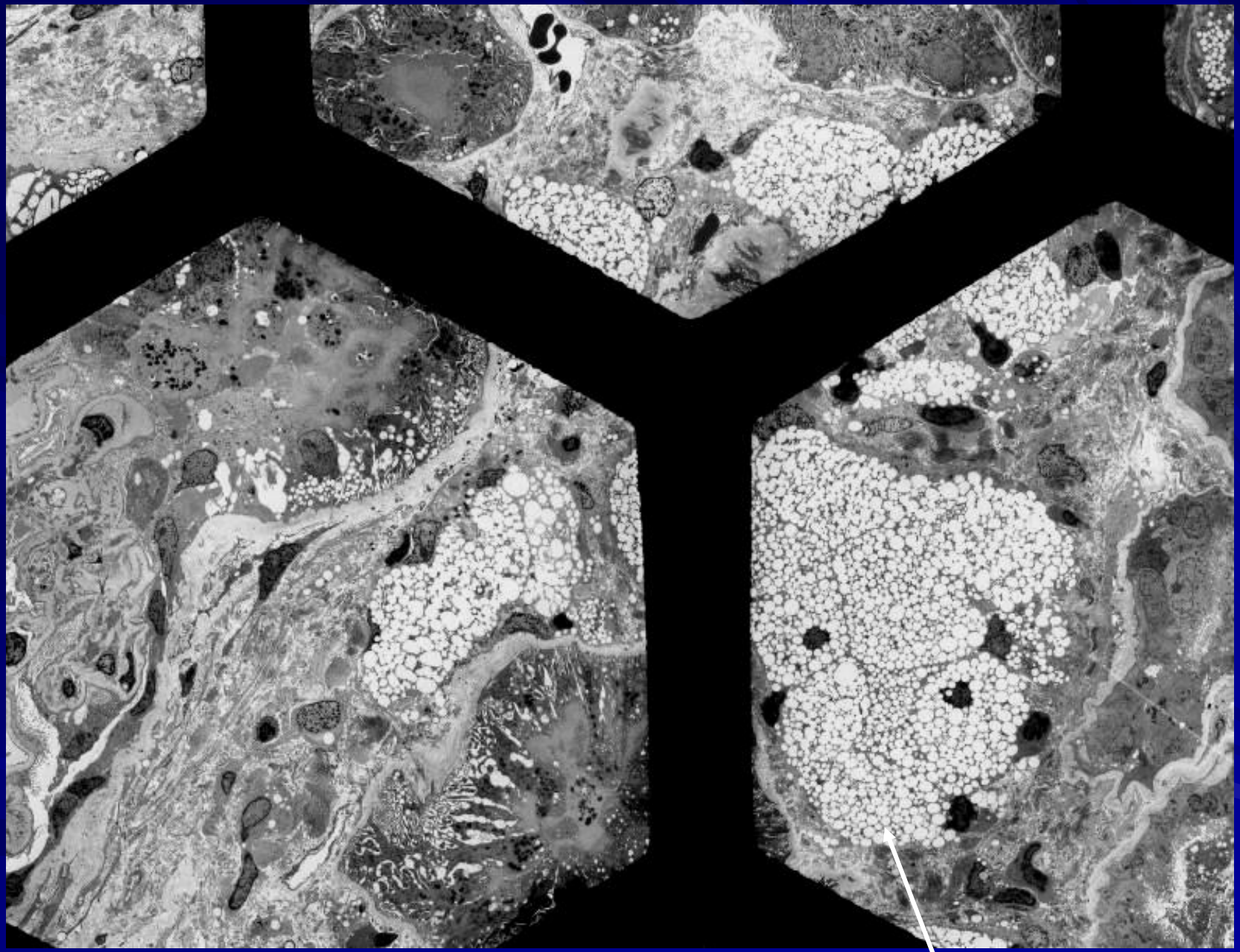
F S G S

Focal Segmental Glomerulosclerosis

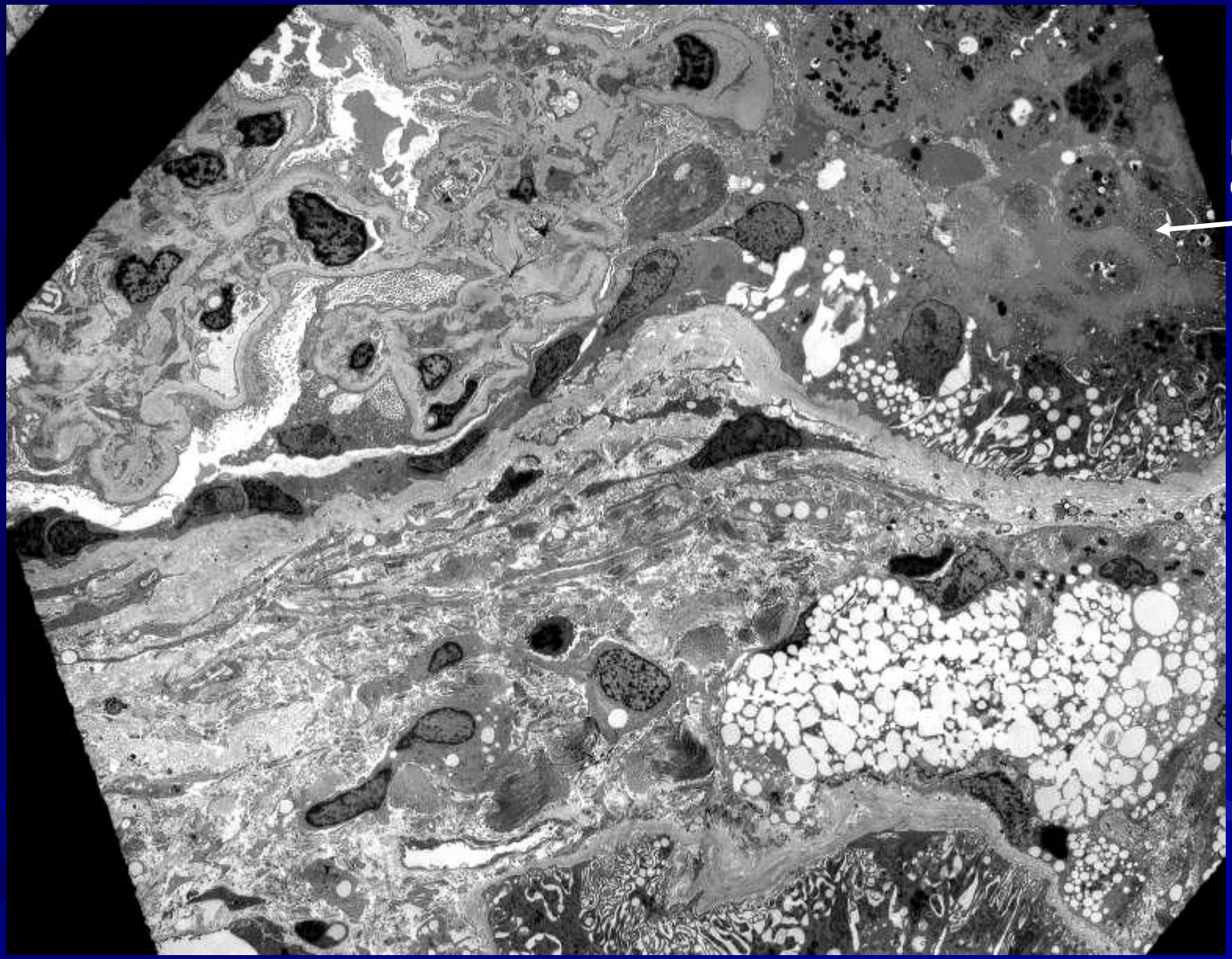
F S G S

- Primary and secondary FSGS
- The list of secondary FSGS expands constantly
- Steroid unresponsive nephrotic syndrome which has the appearance of minimal change may evolve into FSGS or be found to be early FSGS if a large enough sample of glomeruli are made
- Mildly enlarged glomeruli are seen more commonly in FSGS than minimal change.
- Juxtamedullary glomeruli are more often affected in early FSGS


Segmental glomerulosclerotic lesion
Interstitial foam cells

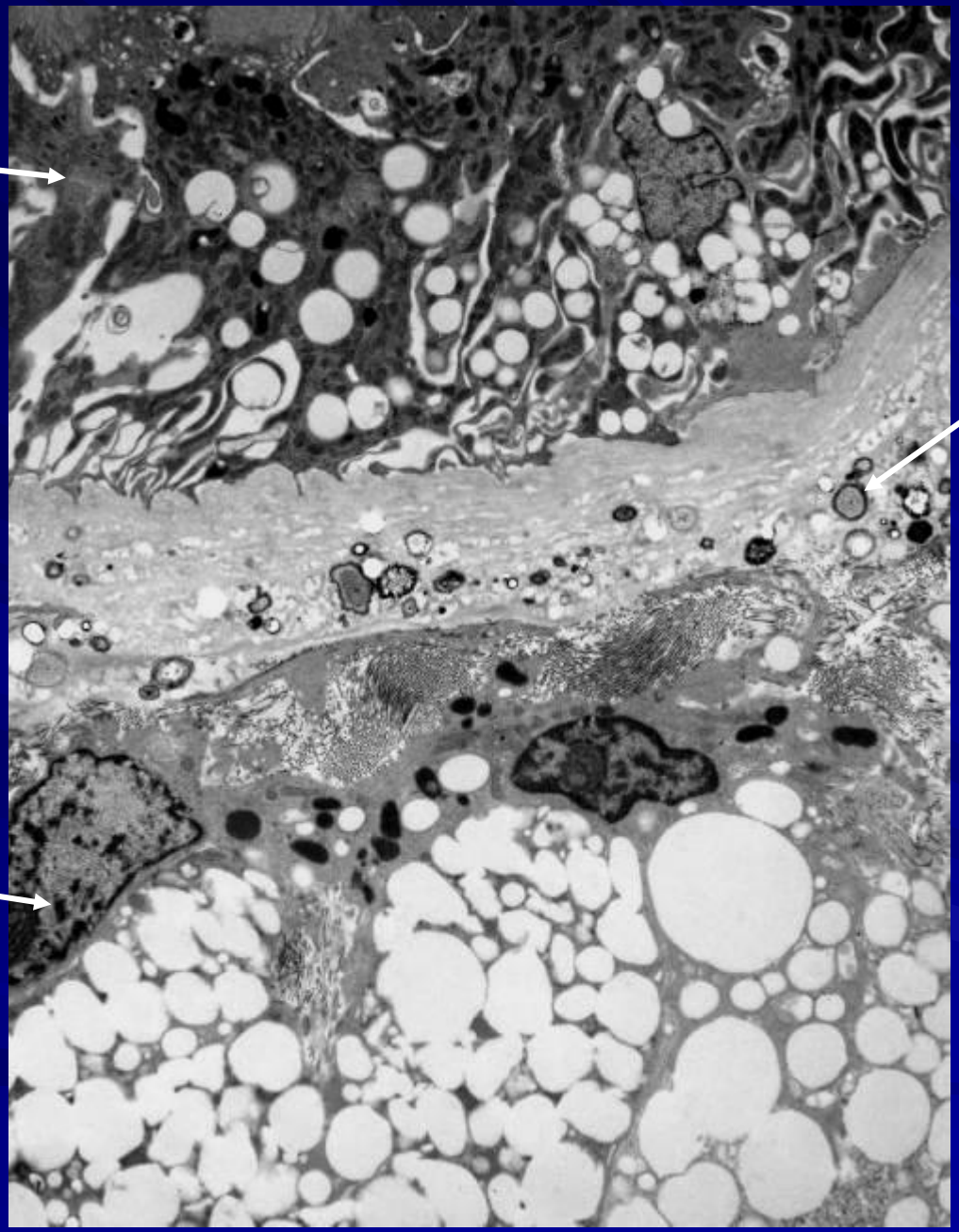


Higher magnification of previous



Higher magnification
of previous

Proximal convoluted tubular cells with numerous basal lipid droplets

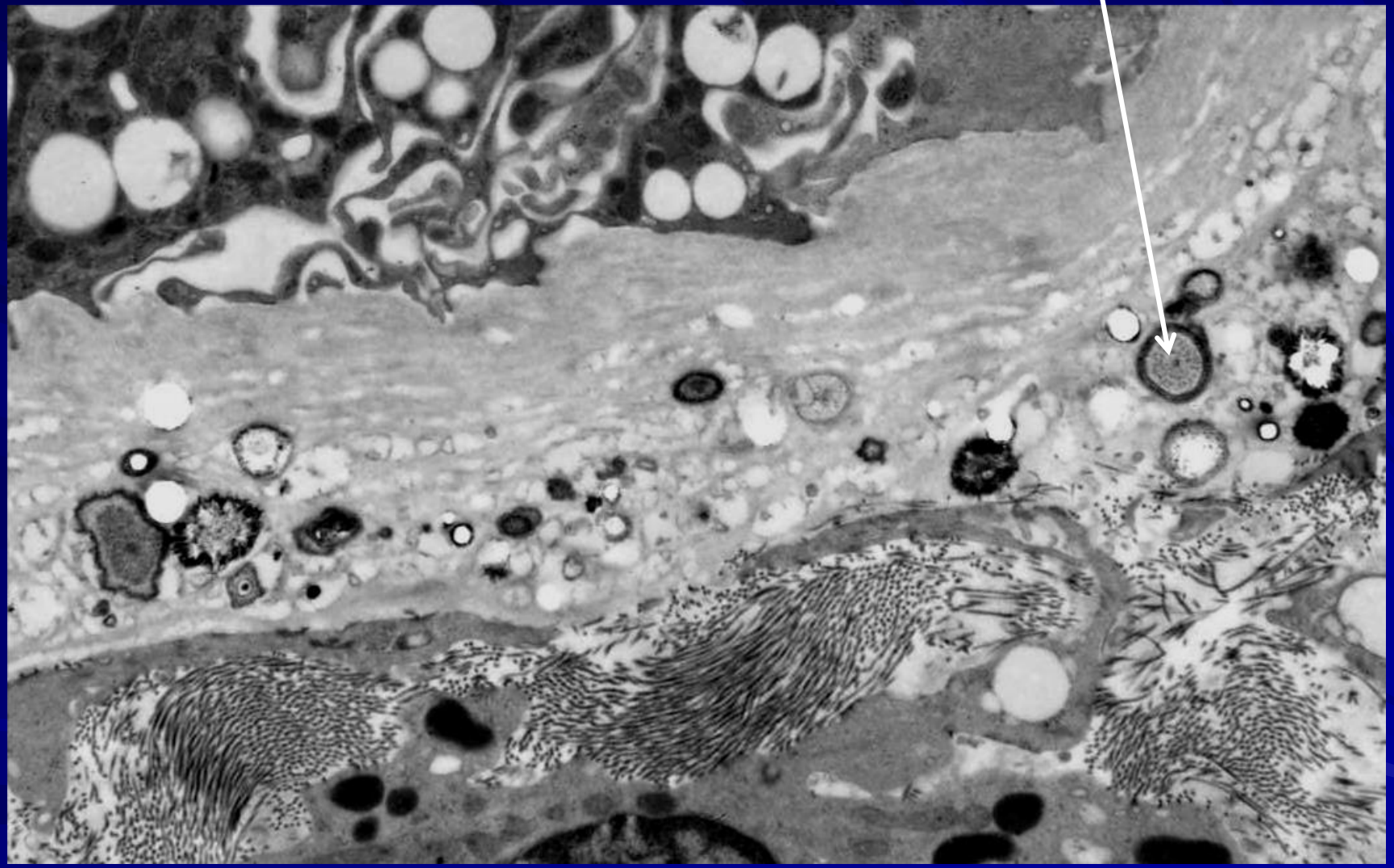


Tubular basement membrane with calcfic bodies

Interstitial foam cells

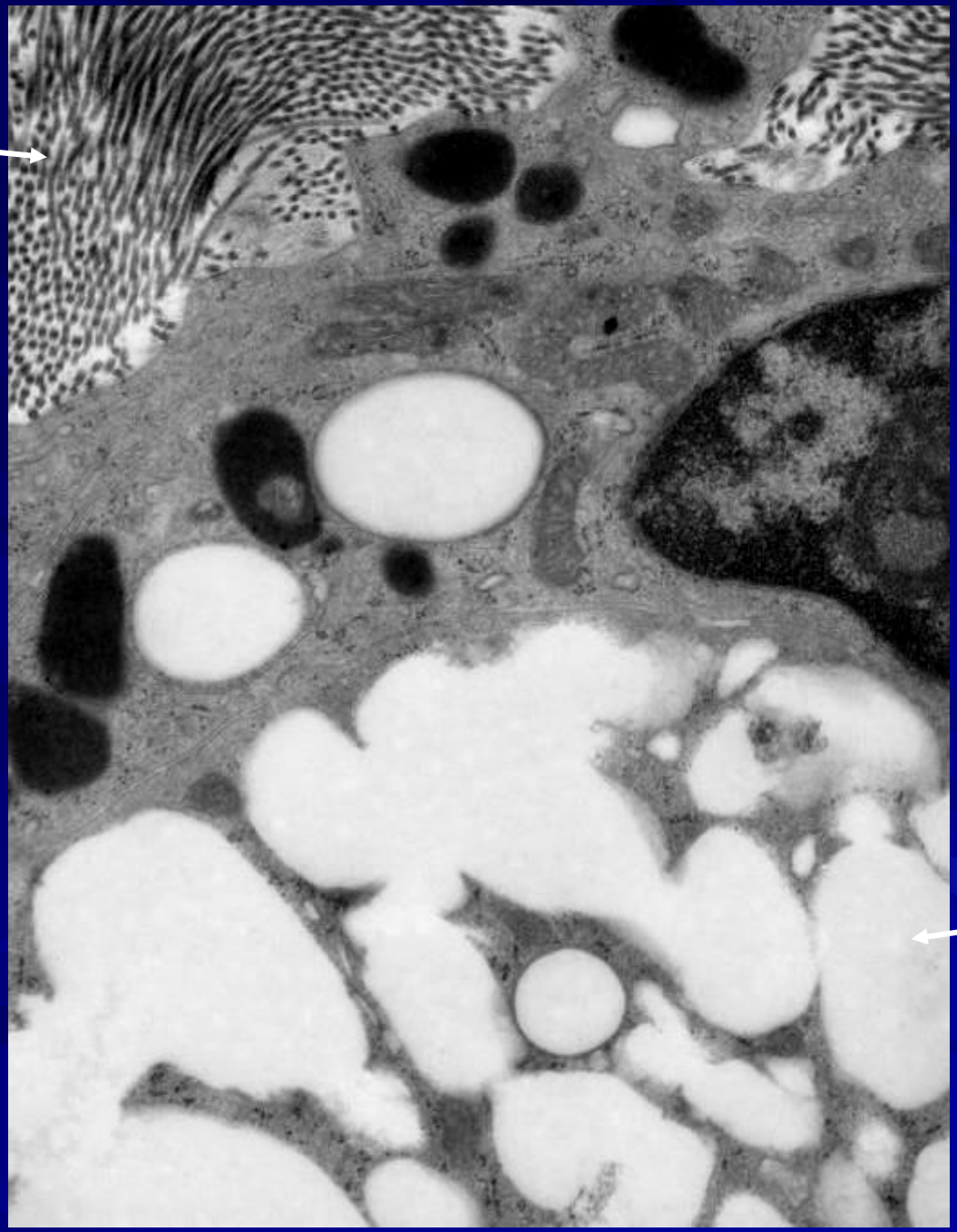
Higher magnification of previous

Early calcification of lipid moving across tubular basement membrane



Higher magnification of previous slide

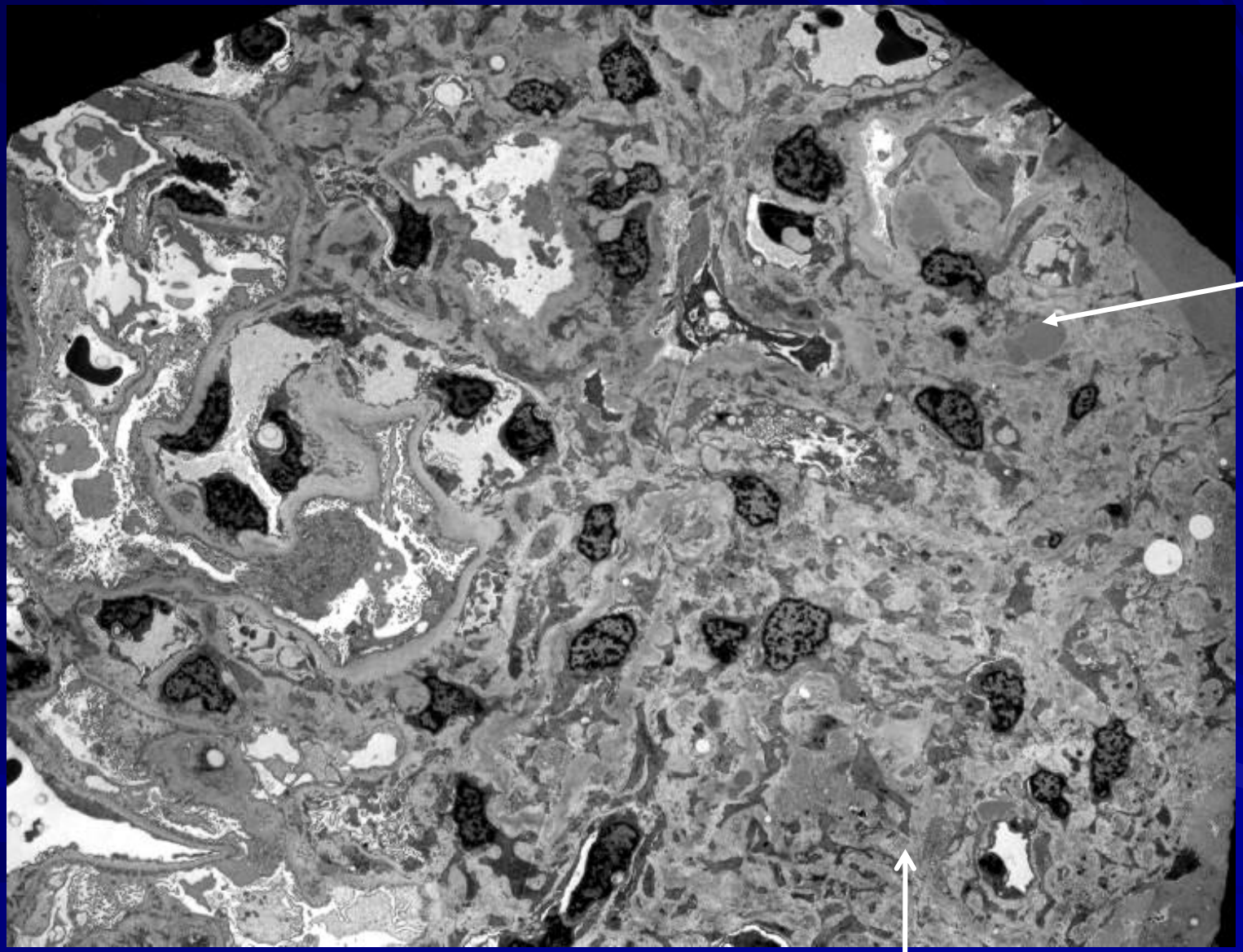
Fibrous collagen



Lipid laden interstitial foam cell

Mostly saturated lipid

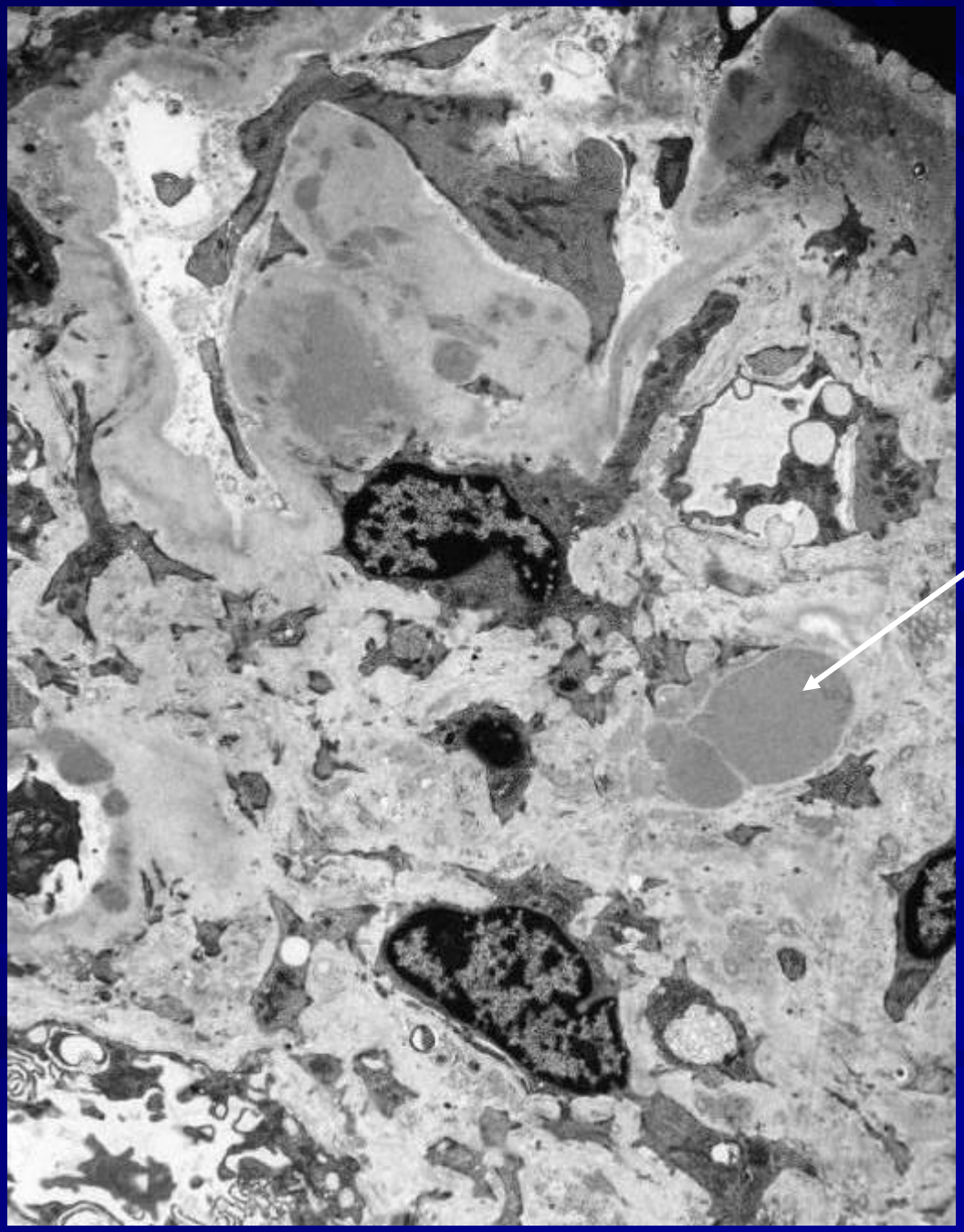
Higher magnification of previous



Hyalinotic deposits within sclerotic mesangium

IgM & C3

Segmental sclerosis

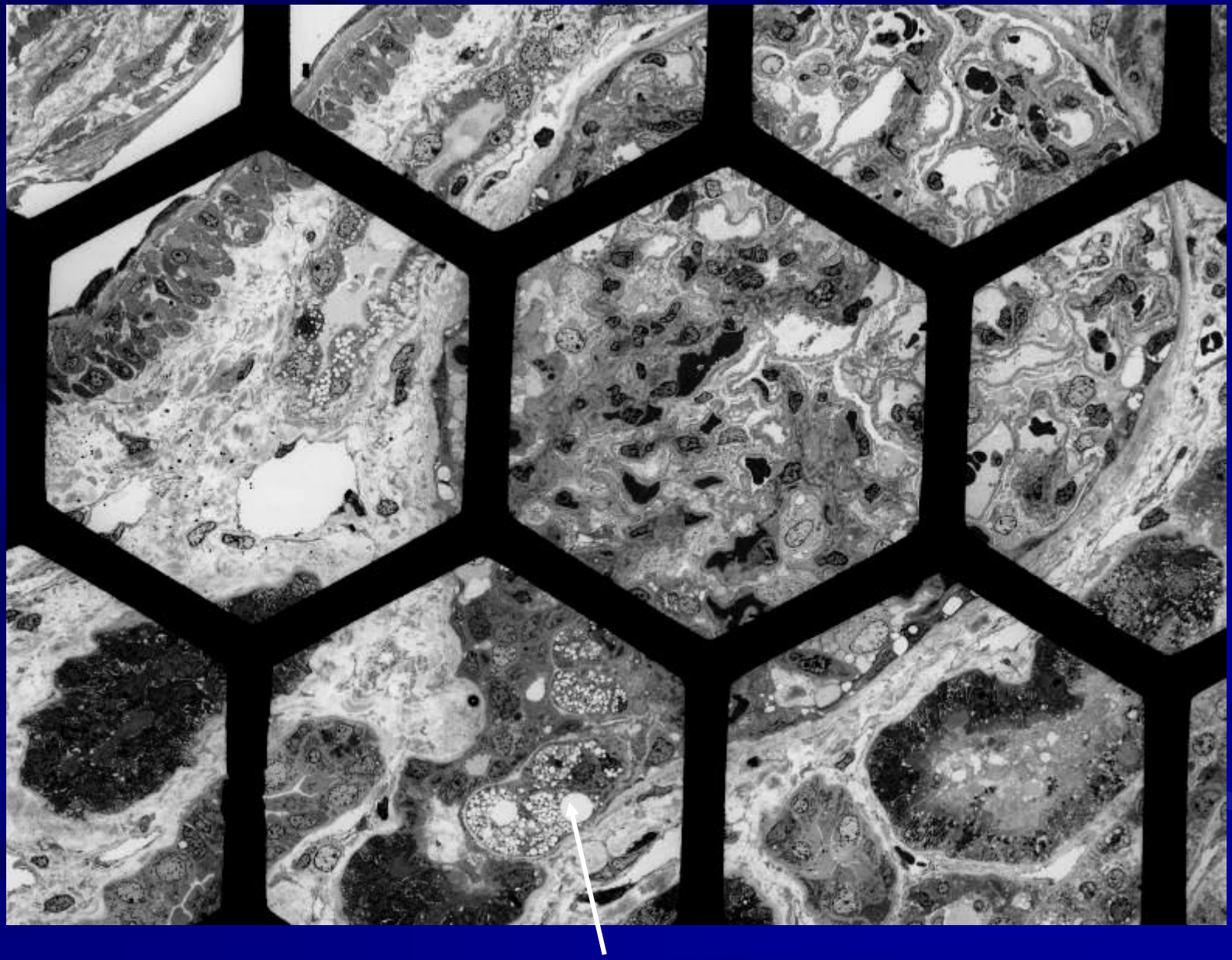


Sclerotic mesangium

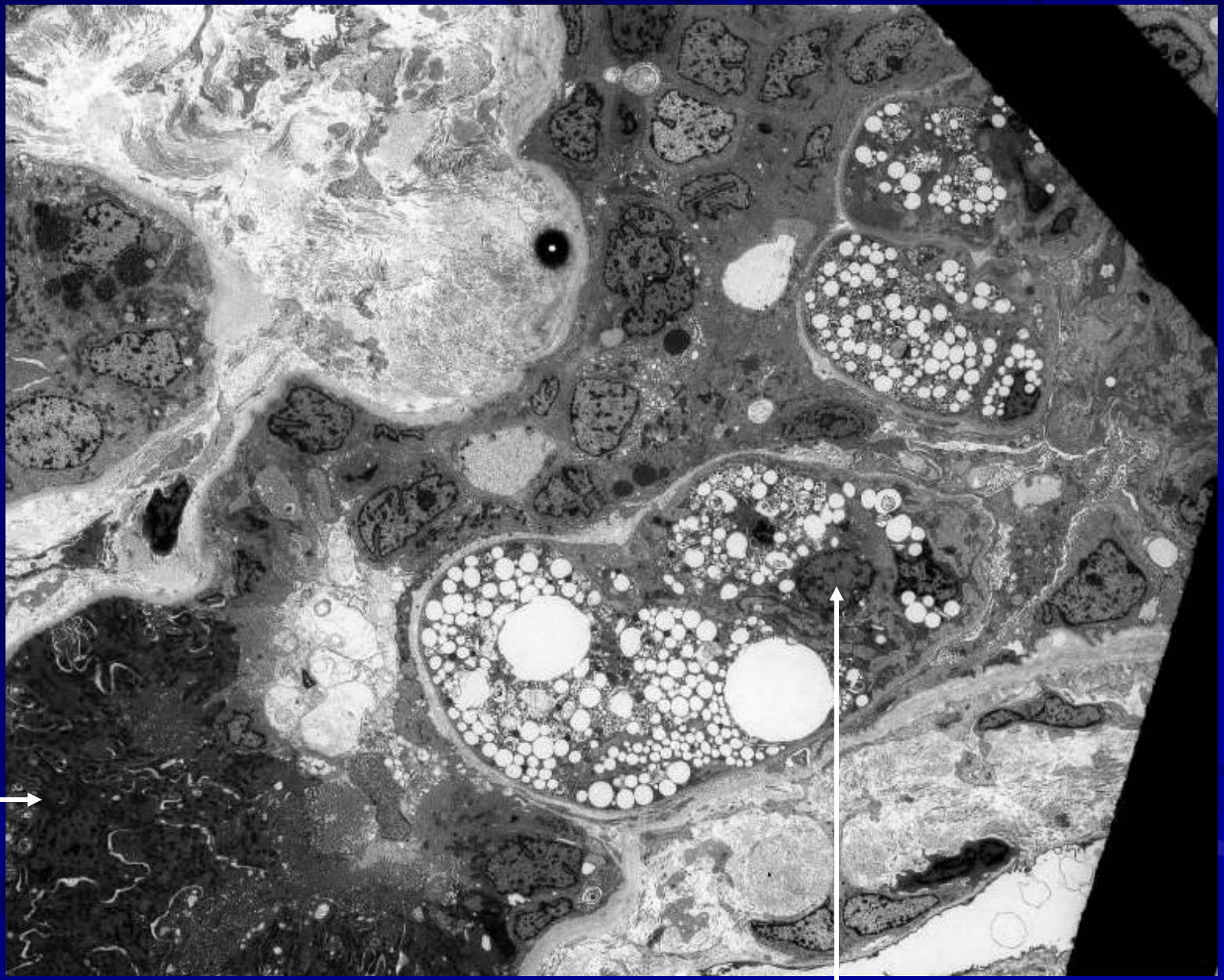
Hyalinotic deposits within the mesangium

IgM & C3

Higher magnification of previous slide



Glomerular Tip lesion



Proximal convoluted tubule

Higher magnification of previous slide

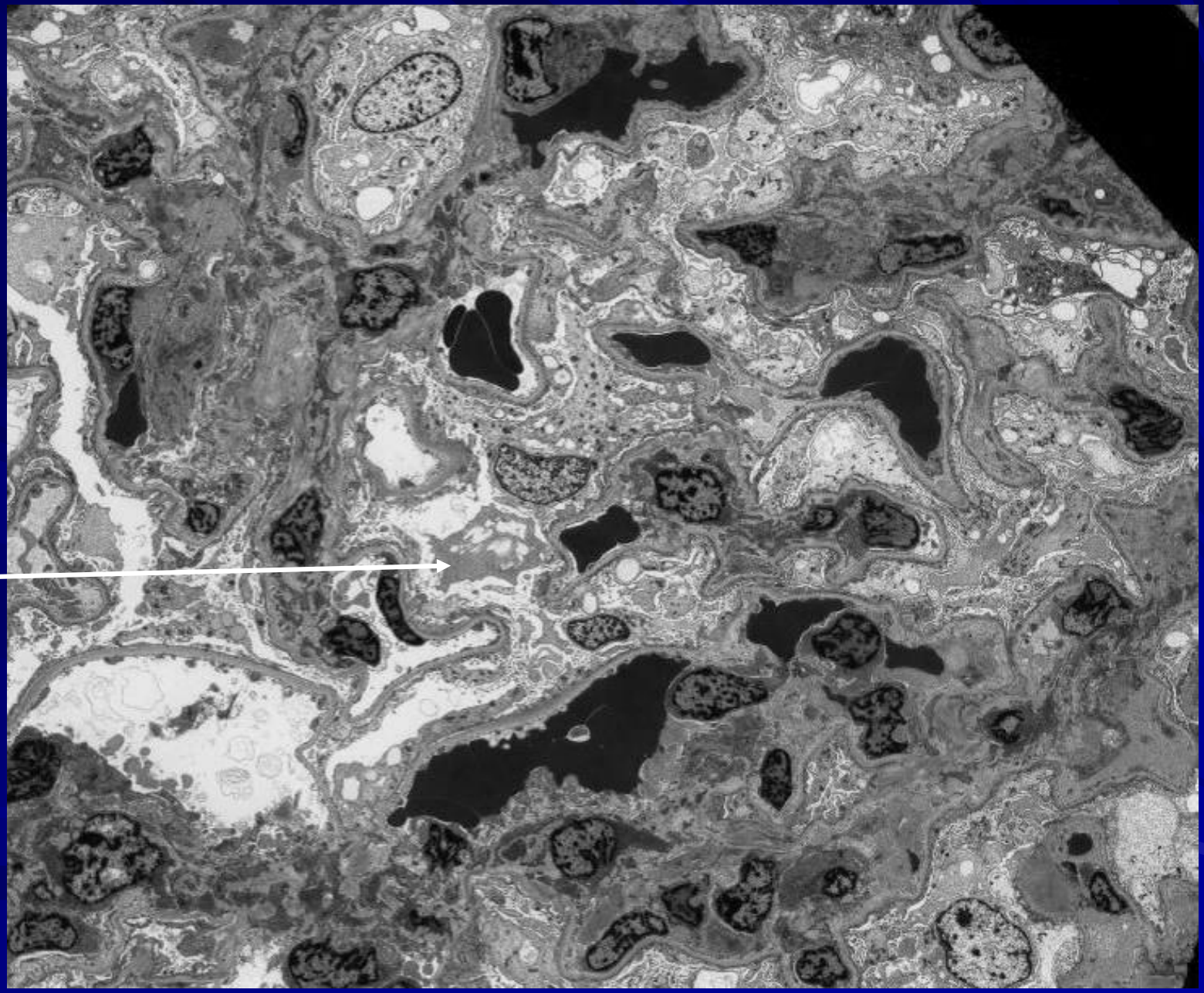
Segmental glomerulosclerosis with mesangial foam cells

Mesangial foam cell

Mesangial hyalinotic deposits

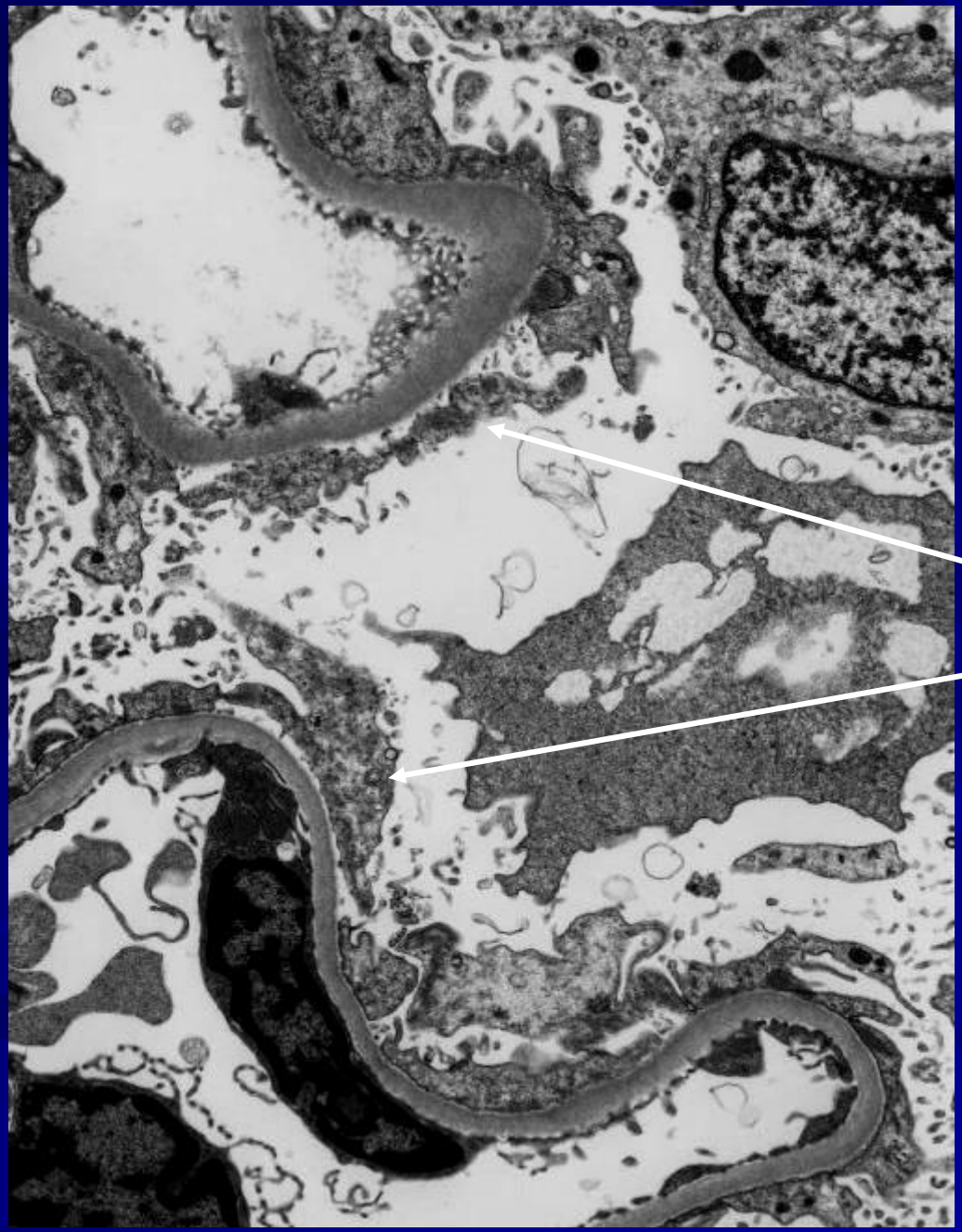
Higher magnification of previous image

Higher magnification of degenerate podocyte to follow



Severe (very widespread) foot process effacement

Higher magnification of 3 slides before this one



Degenerate podocyte which would lead to capsular adhesion if next to Bowman's capsular parietal epithelial cell

Ig A Disease

Ig A Disease Histological Classification

Haas M Am J Kid Dis 1997;29;829

Class1: Minimal histological lesion	21%
Class 2: FSGS-like	6%
Class 3: Focal proliferative GN	35%
Class 4: Diffuse proliferative GN	19%
Class 5: Advanced chronic GN	19%

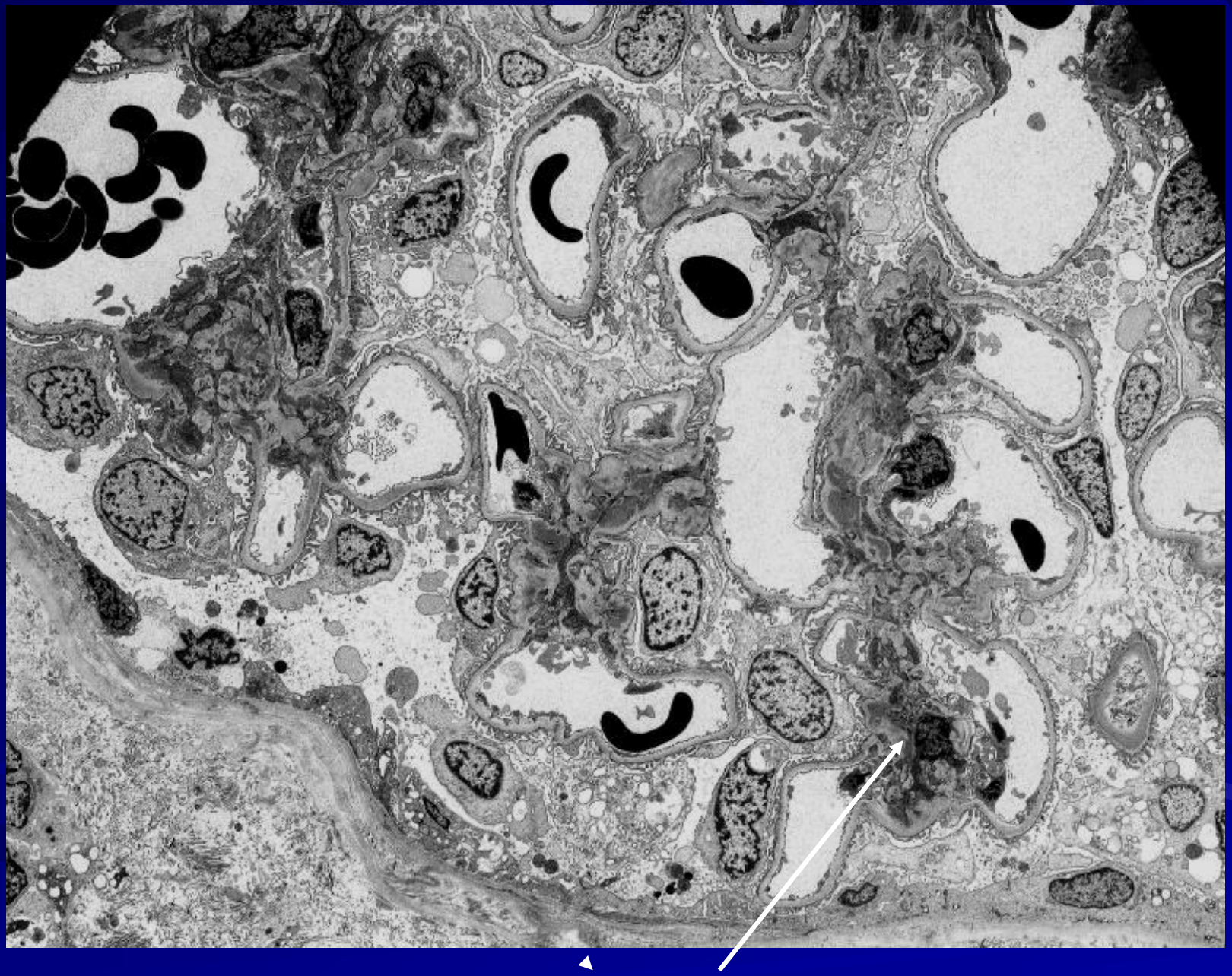
IgA disease

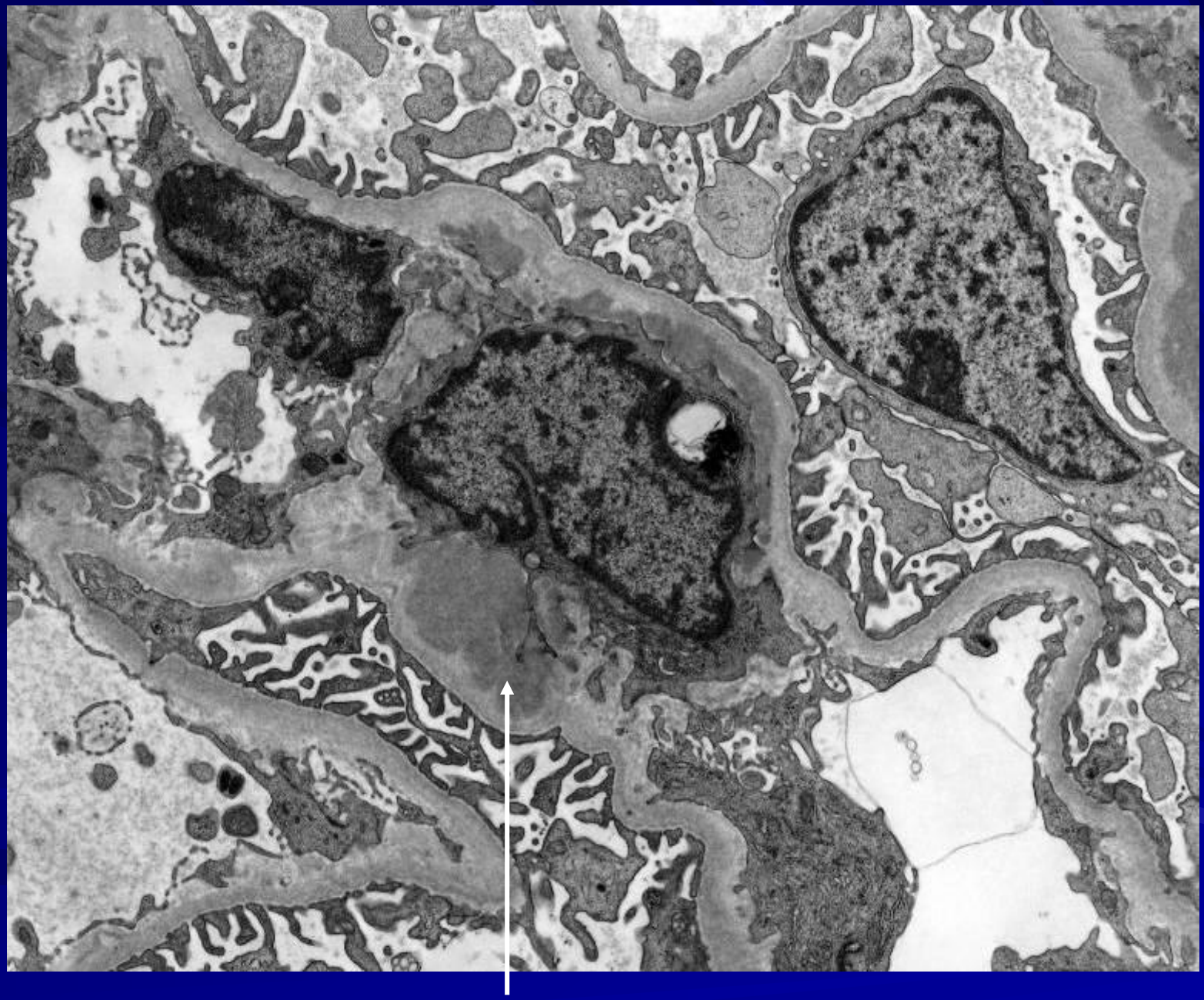
- Common disease and therefore can be found co-incidentally with other forms of renal disease.
- Eg Diabetes, minimal change, ANCA positive GN, etc etc
- Within IgA disease any pattern of glomerulopathy can found including no change, mild mesangial proliferative (4 mesangial cells or more), segmental necrosis, crescents, segmental sclerosis, mesangiocapillary patern.

IgA disease

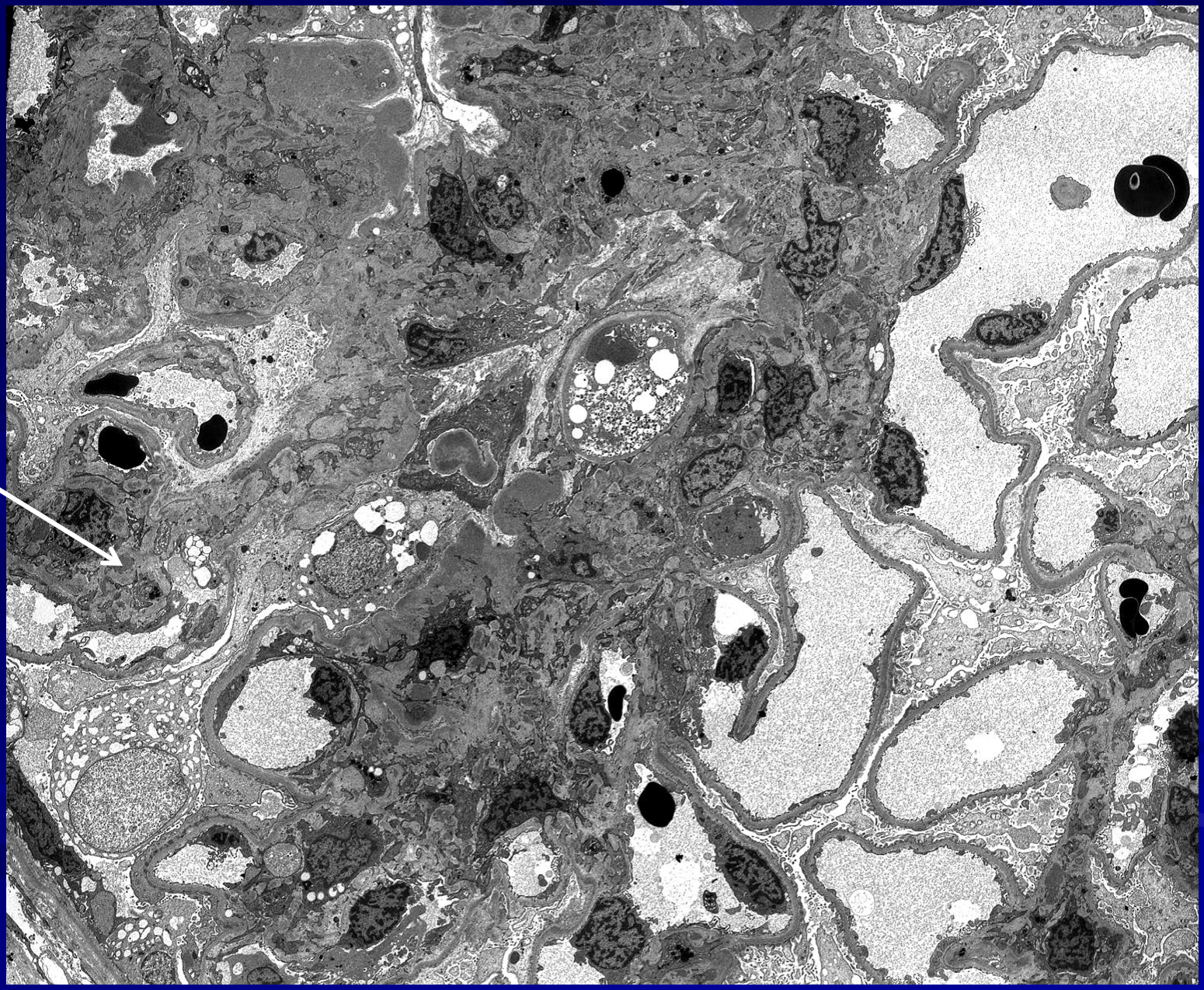
- With EM or LM alone it is impossible to diagnose IgA disease – can only say ‘the features are consistent with, and in view of it’s high frequency, it is likely to be IgA disease’.

- Rarely can see EM of glomeruli with mesangial deposits alone which on IF were demonstrated to be IgM disease.
- Rarely can see EM of glomeruli with mesangial deposits alone which on IF were demonstrated to be C3 alone – often this associated with malignancy.
- Rarely can see EM of glomeruli with mesangial deposits alone which on IF were demonstrated to be C1q nephropathy.


Mild mesangial expansion

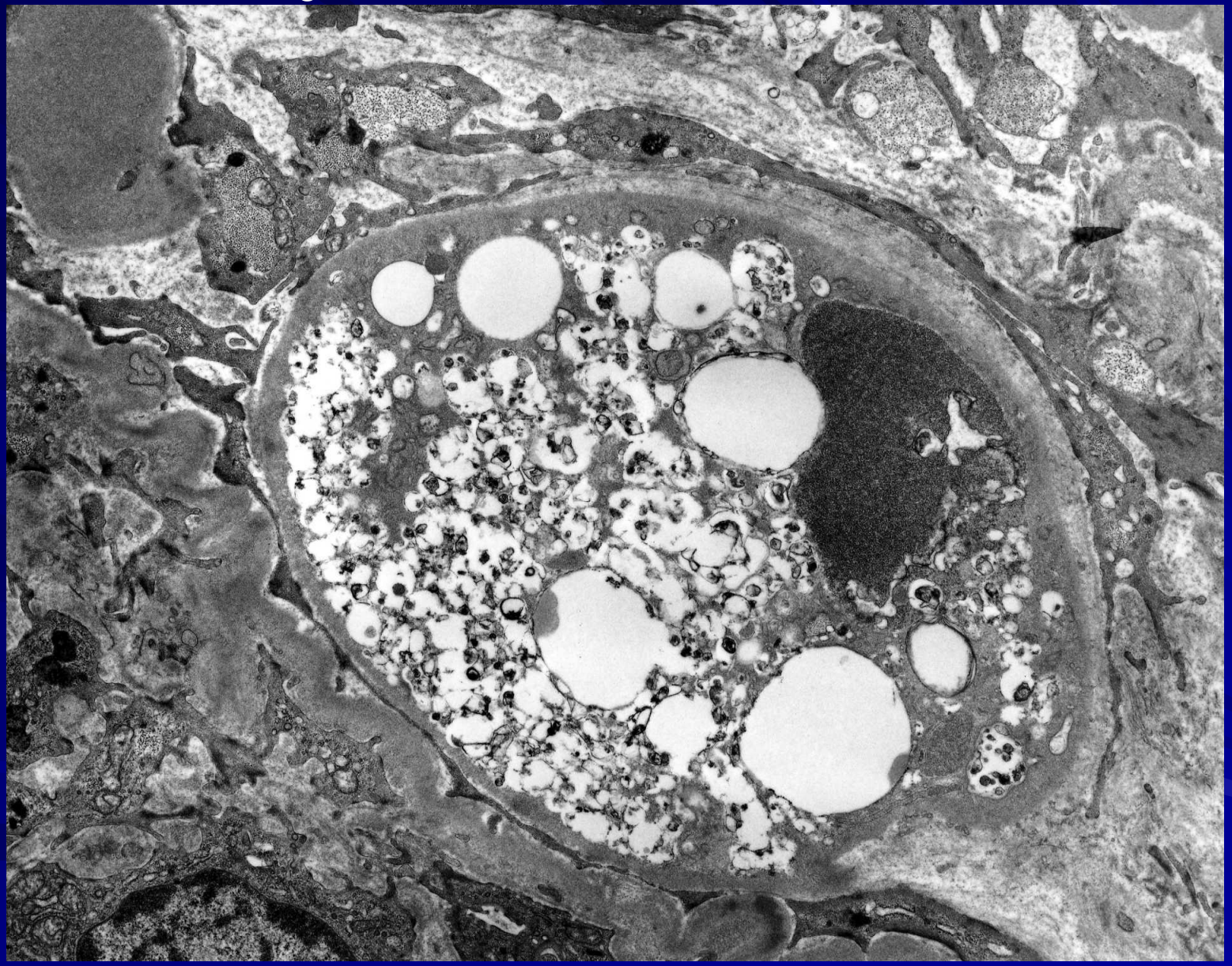


Mesangial deposit



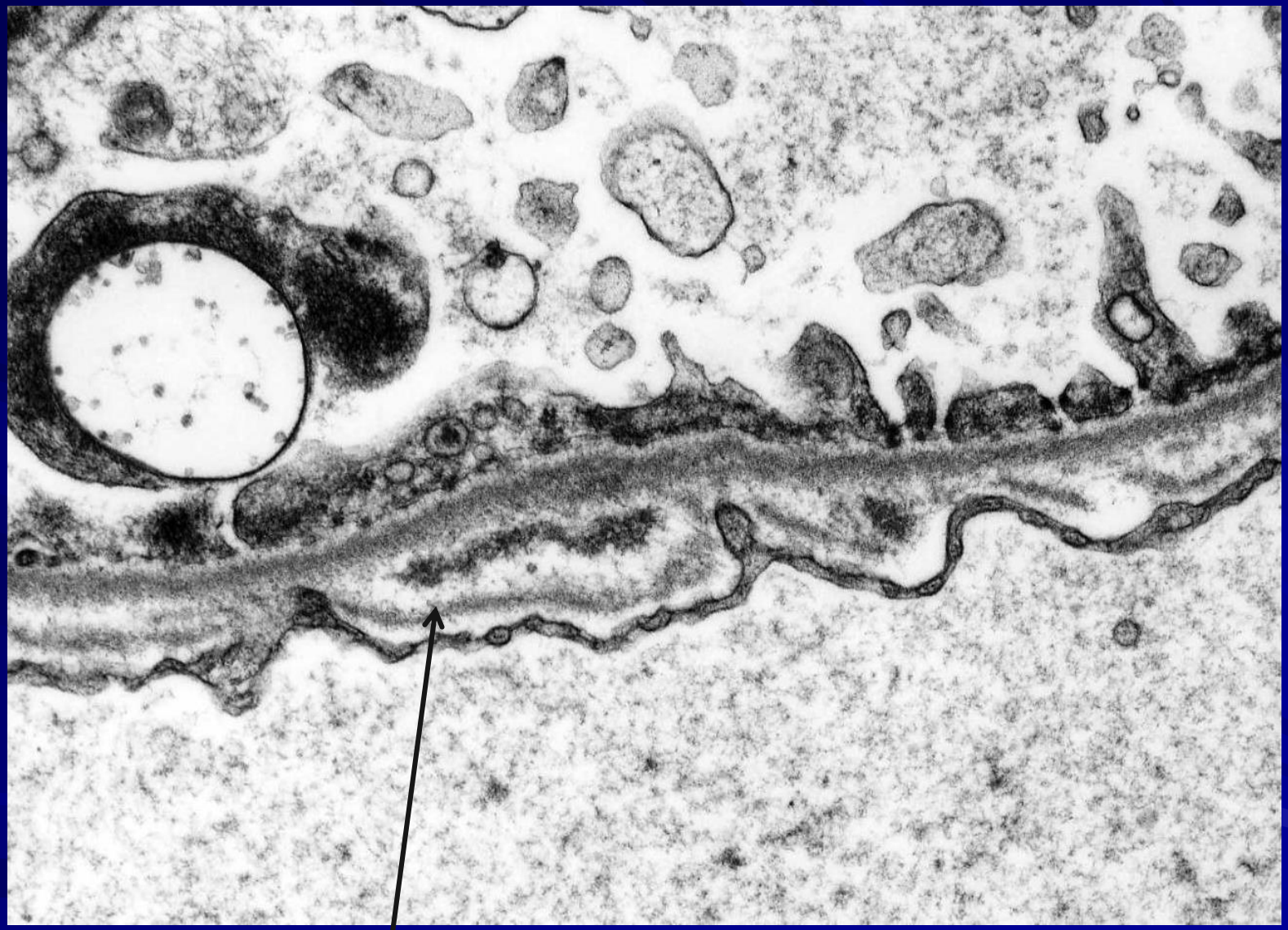
Segmental necrosis

Segmental necrosis

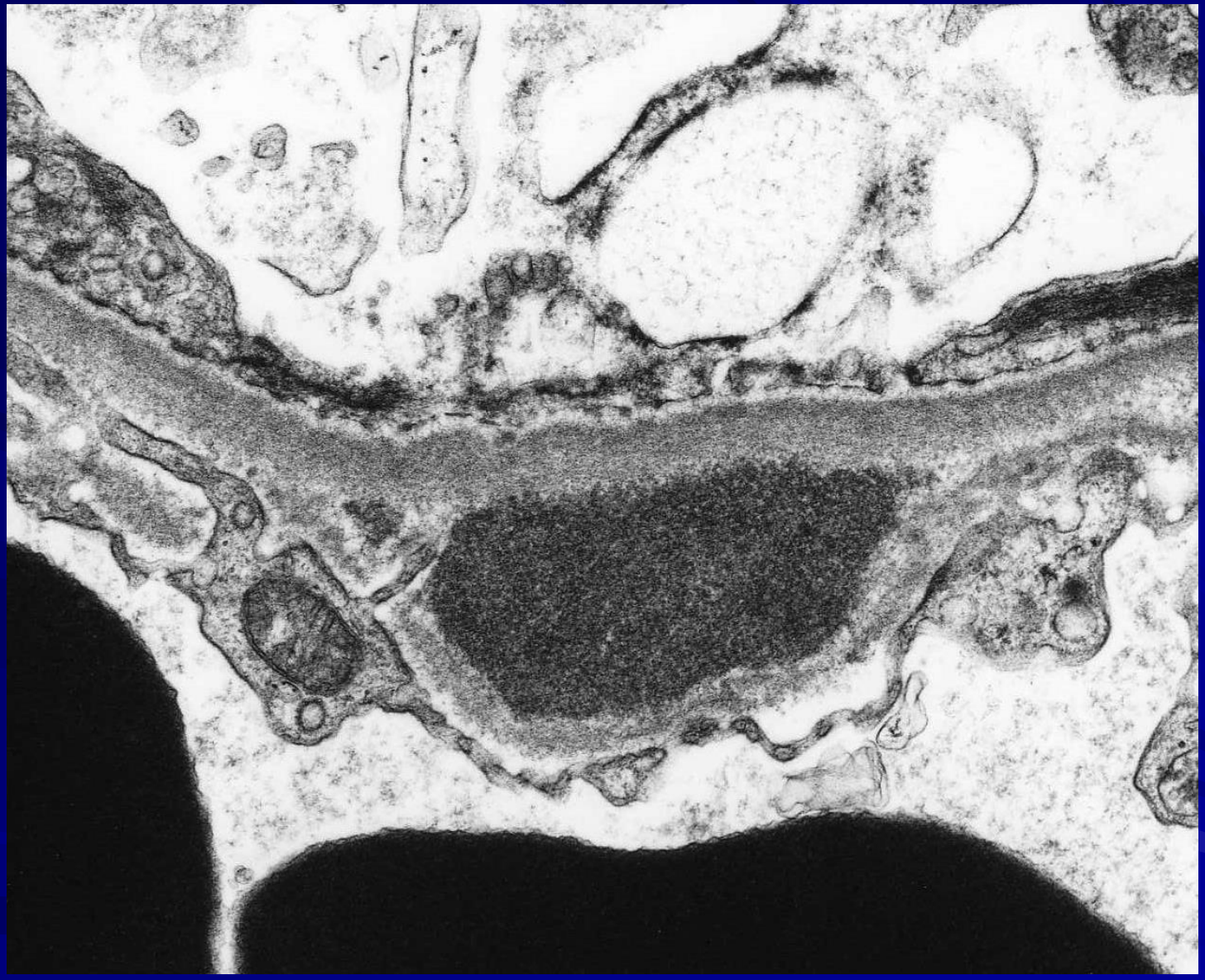


Higher magnification of previous slide


Subendothelial deposits

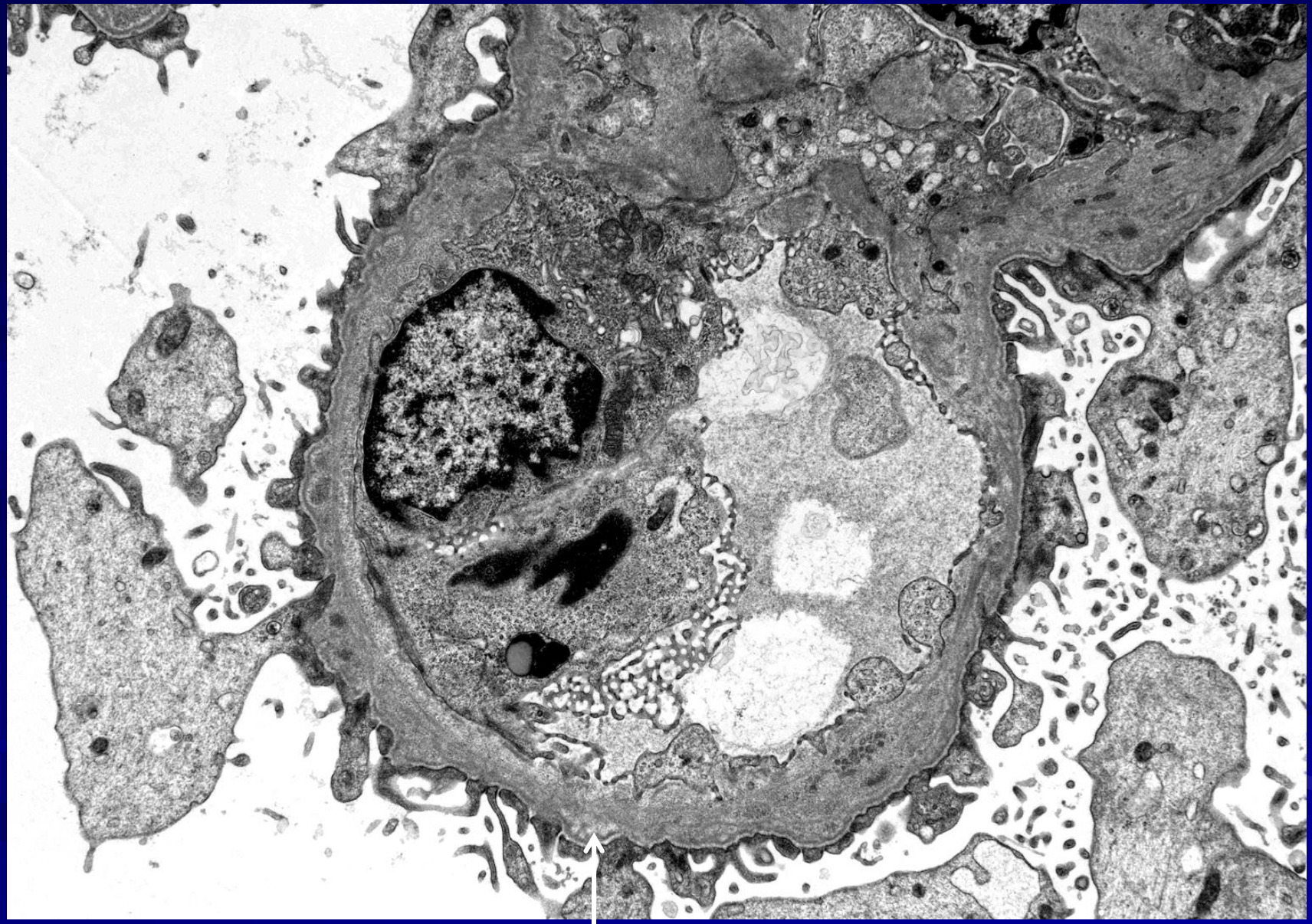


New basement membrane (produced by endothelial cell) around small subendothelial deposits



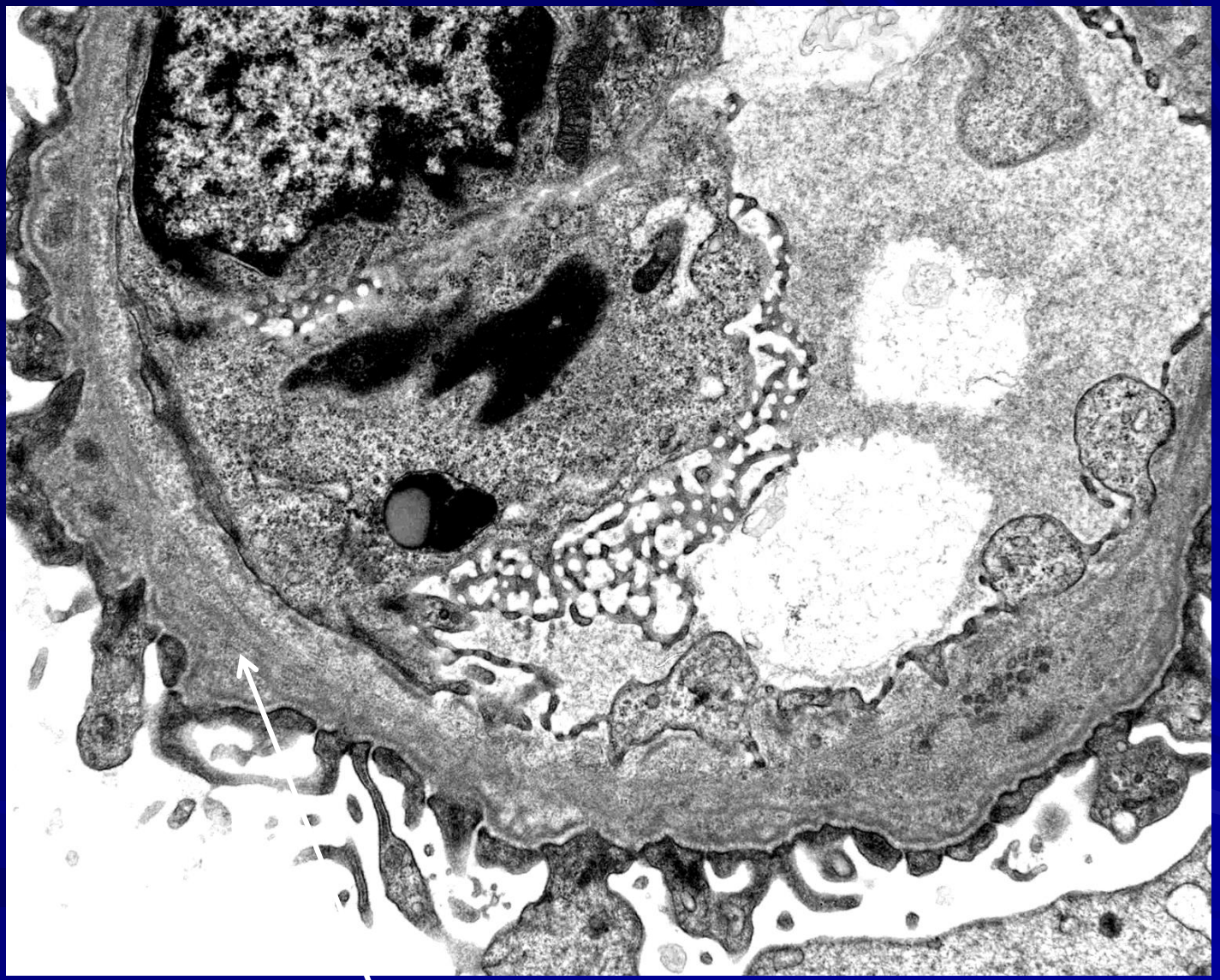
Medium sized subendothelial deposit

Multiple subendothelial deposits, some of which are partially lysed

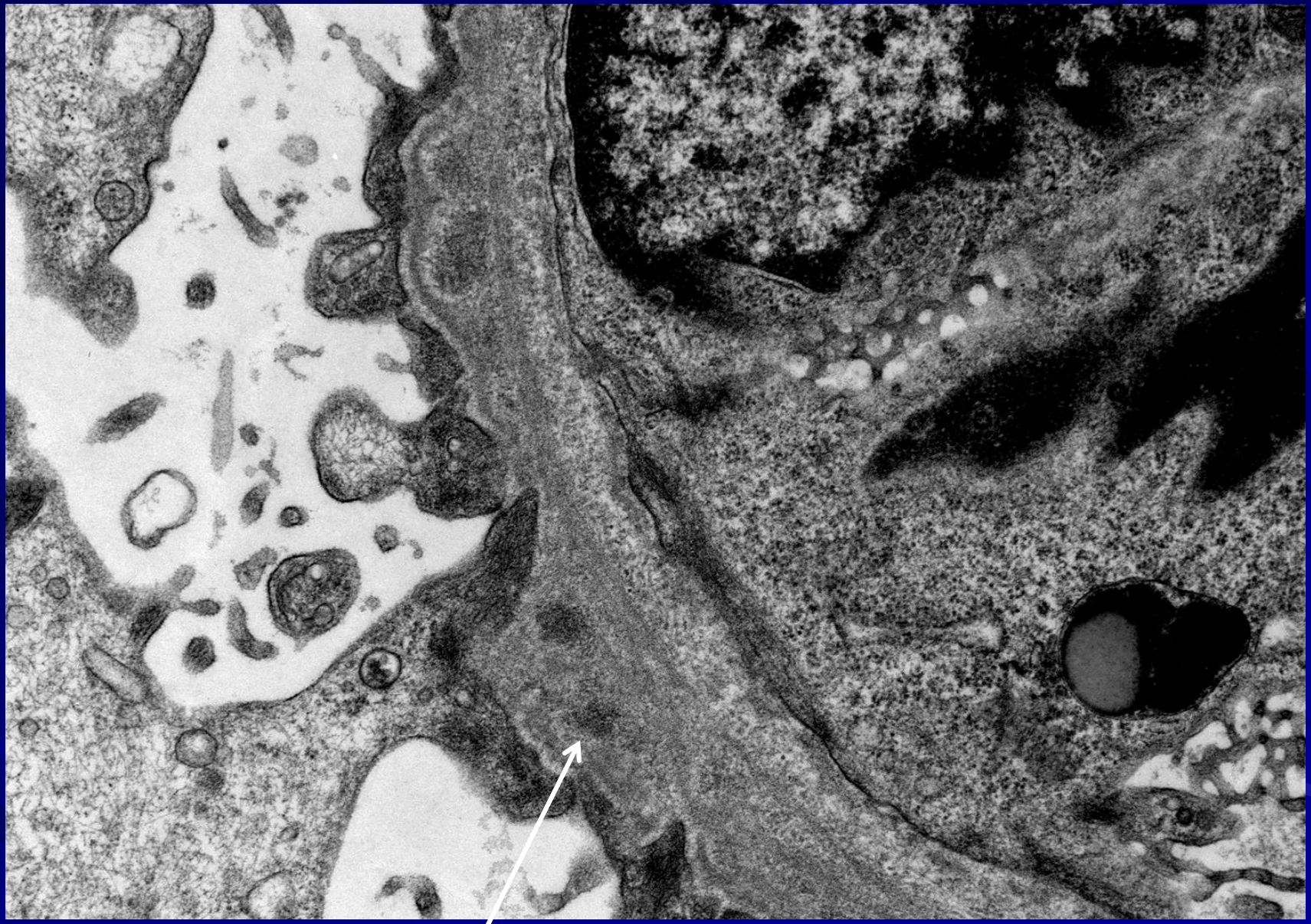


Subendothelial deposits incorporated and in places lysed

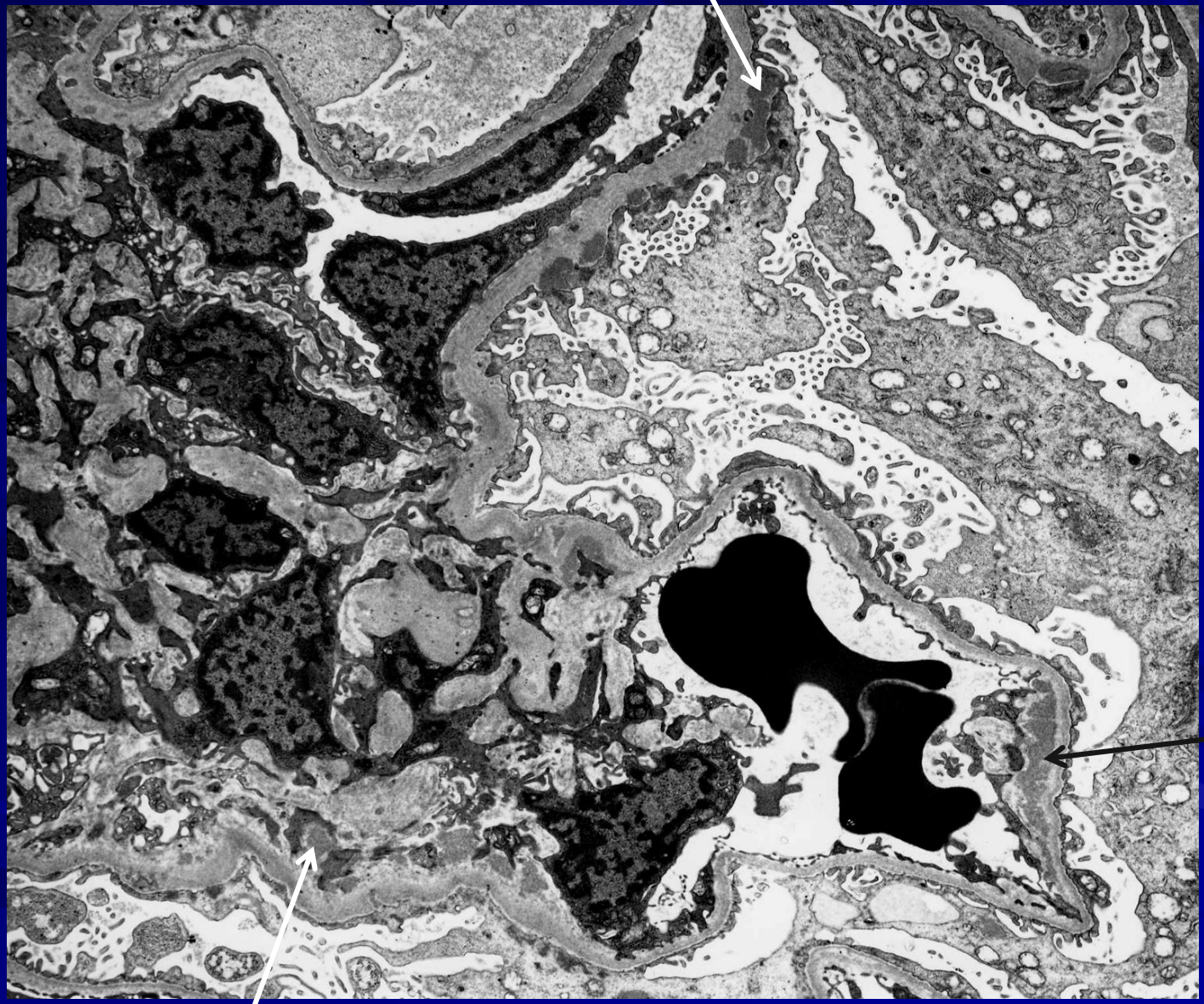
Chronic Henochoid IgA disease



Can look similar to Alport's

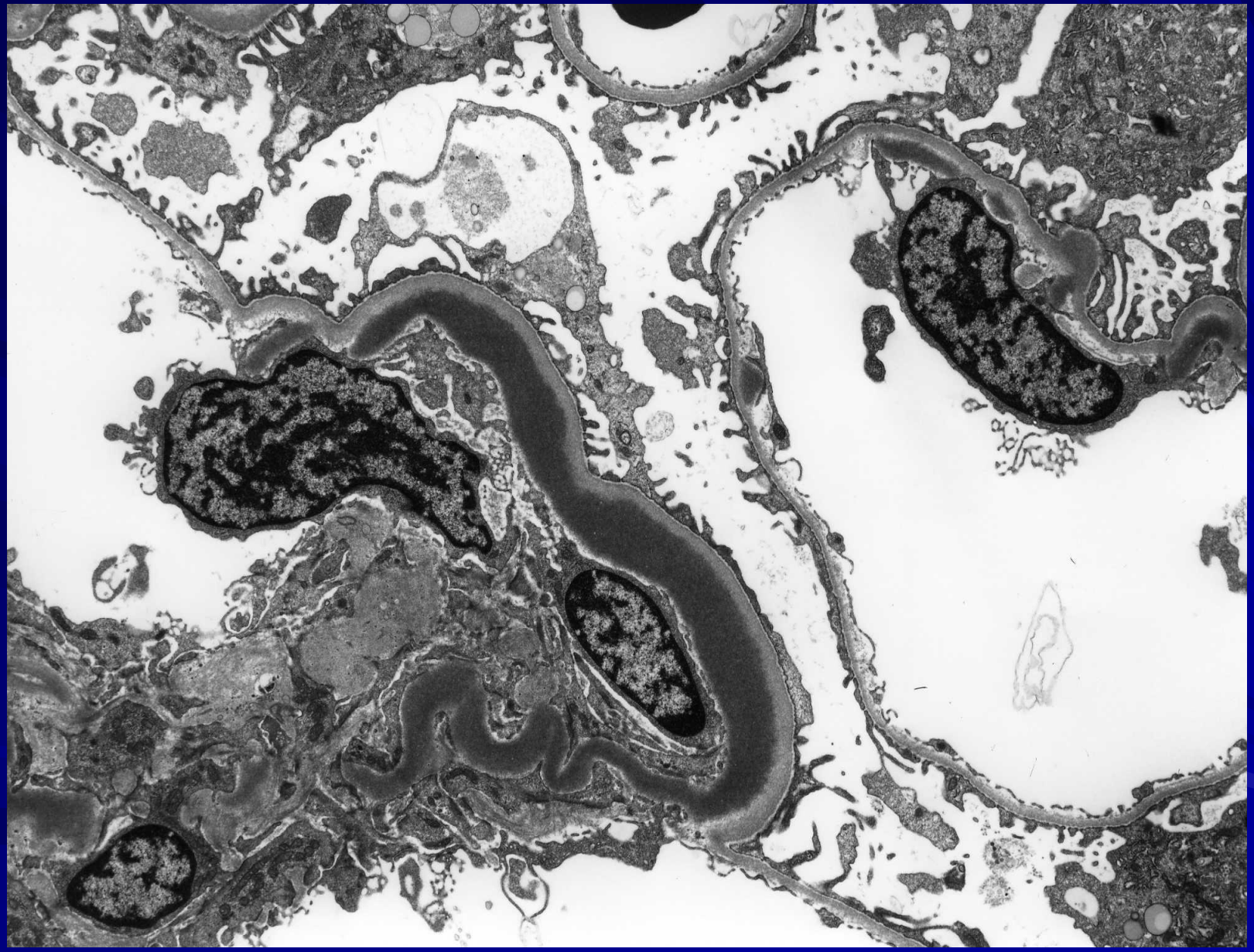

Incorporated subendothelial deposits

Occasional subepithelial deposits



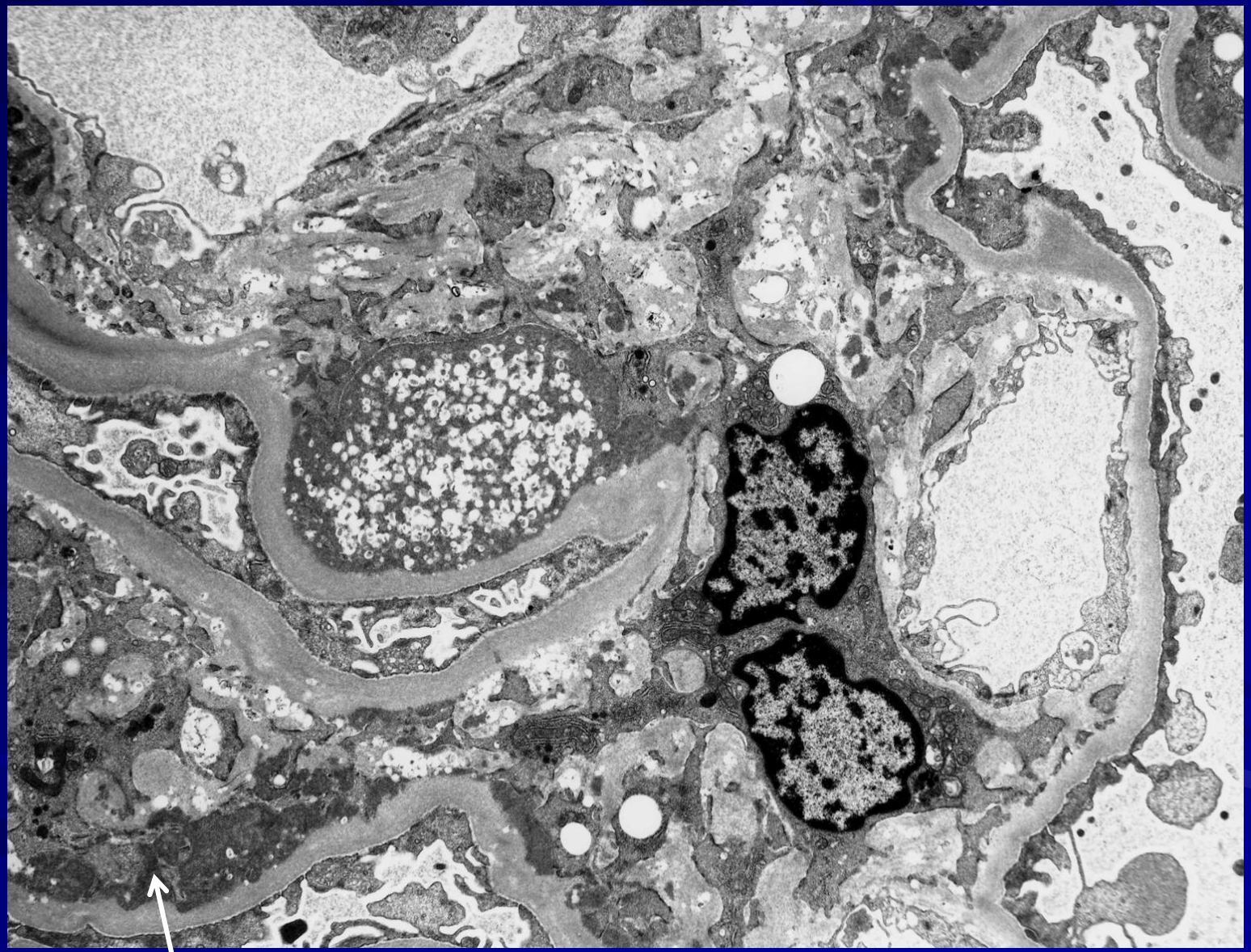
Subendothelial deposits

Mesangial deposits



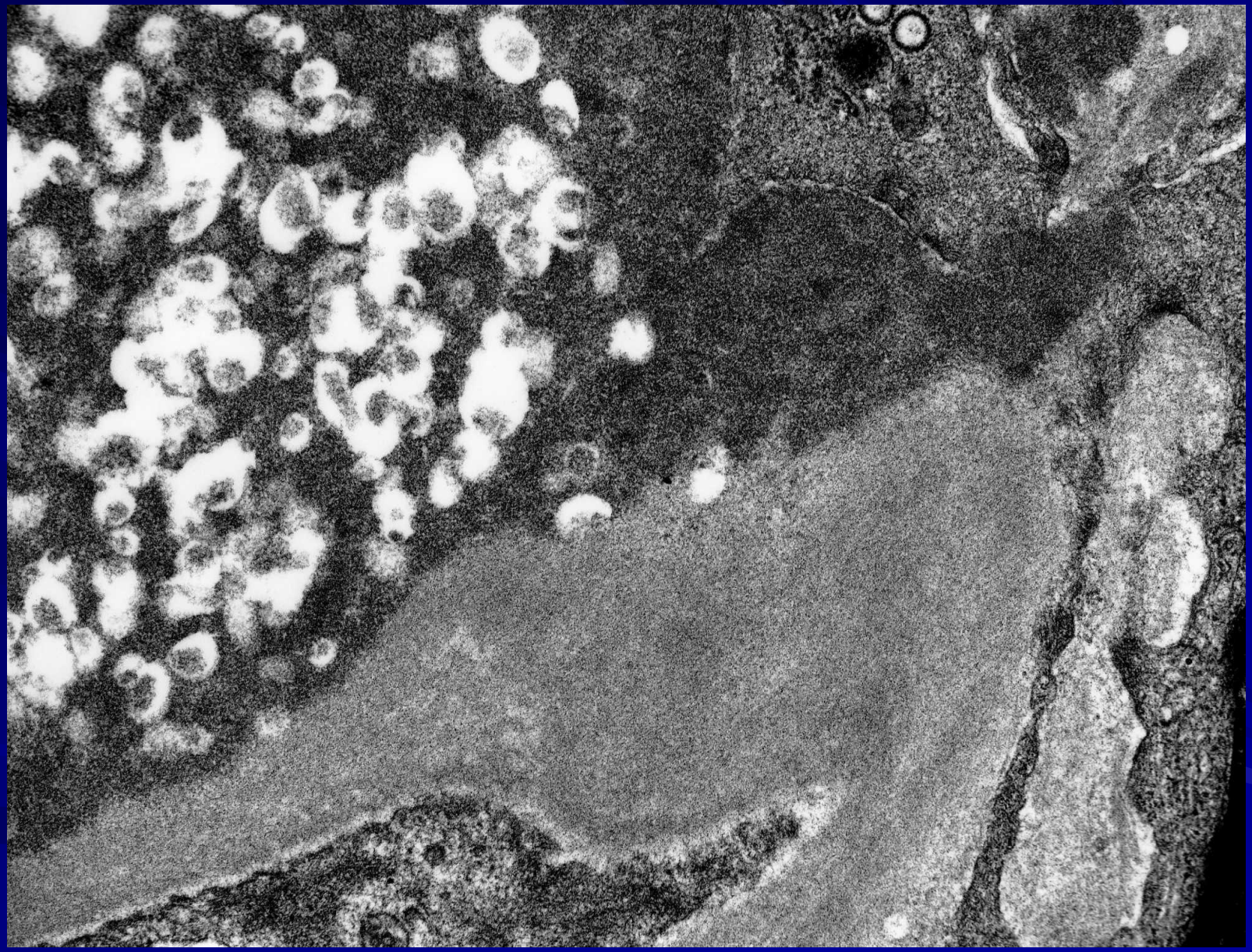
IgA deposited in a pattern reminiscent of linear dense deposit disease, but without interposition

Cadaveric donor kidney biopsy. Cocaine addict.



IgA deposits

Higher magnification of previous slide



Foamy mesangial deposits

Immunotactoid Glomerulopathy (ITG)

Fibrillary Glomerulonephritis

Immunotactoid Glomerulopathy (ITG)

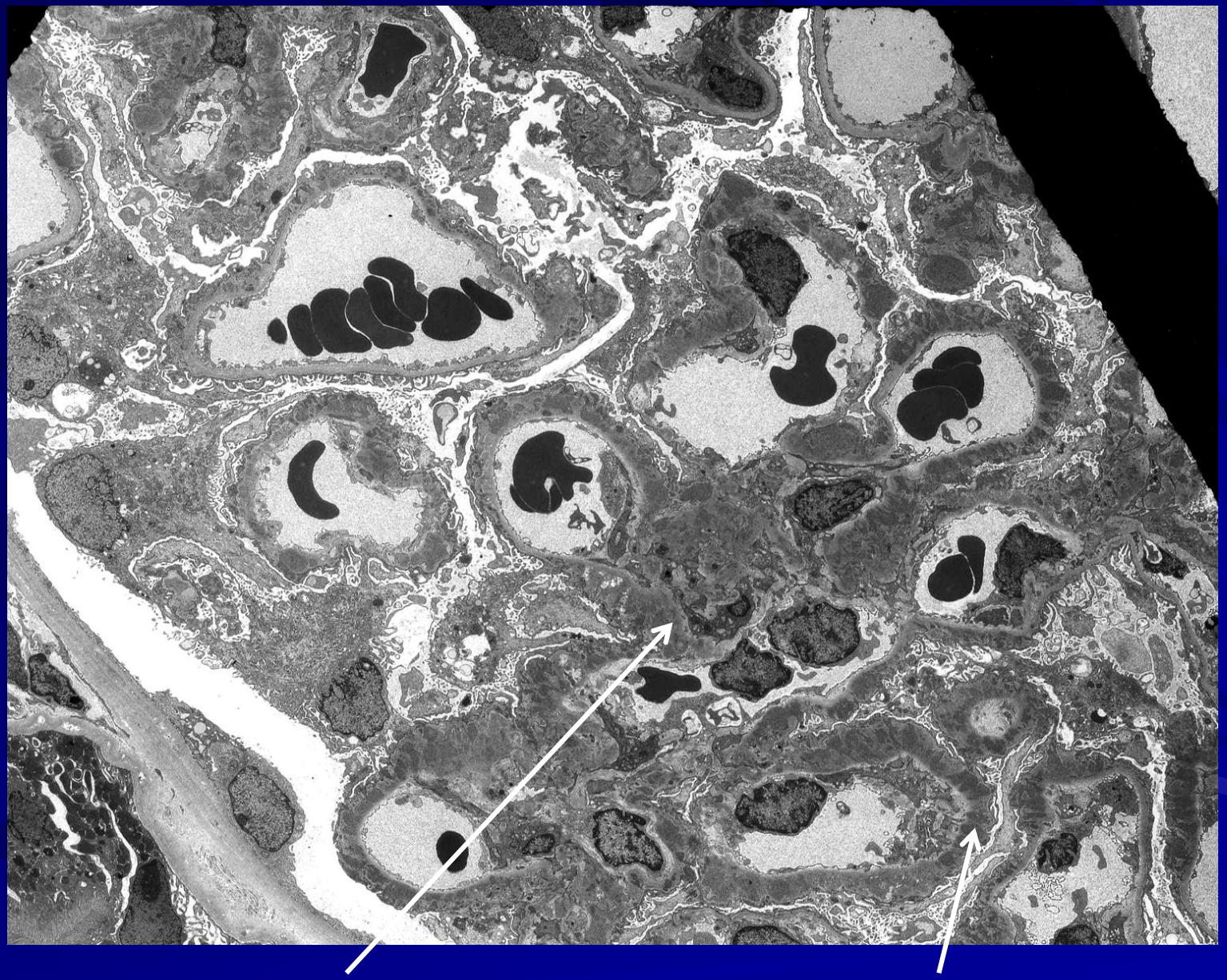
Fibrillary Glomerulonephritis

Both typically positive for IgG and C3 by IF

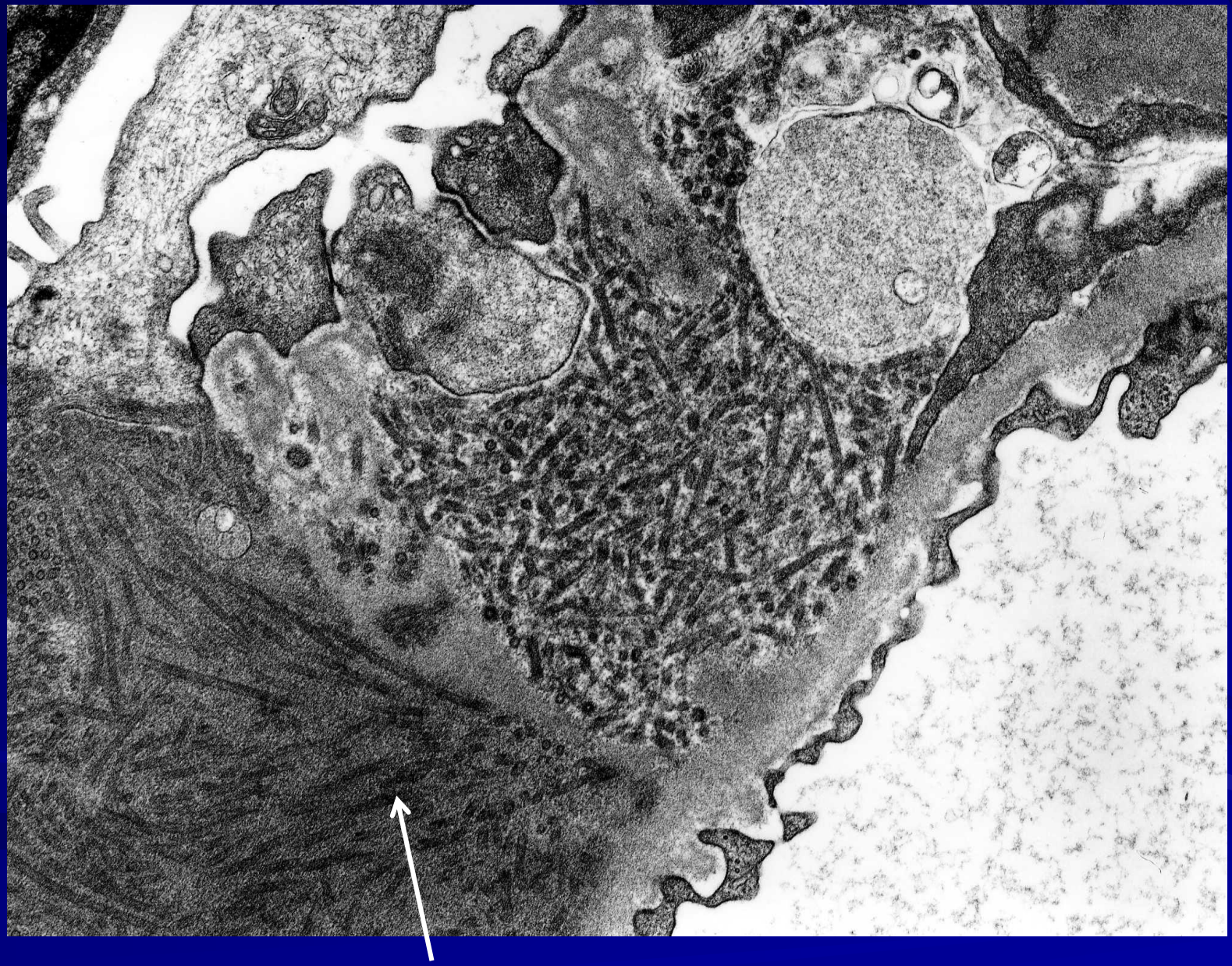
Negative for Sirius/Congo Red.

Not cryogobulin

Immunotactoid Glomerulopathy



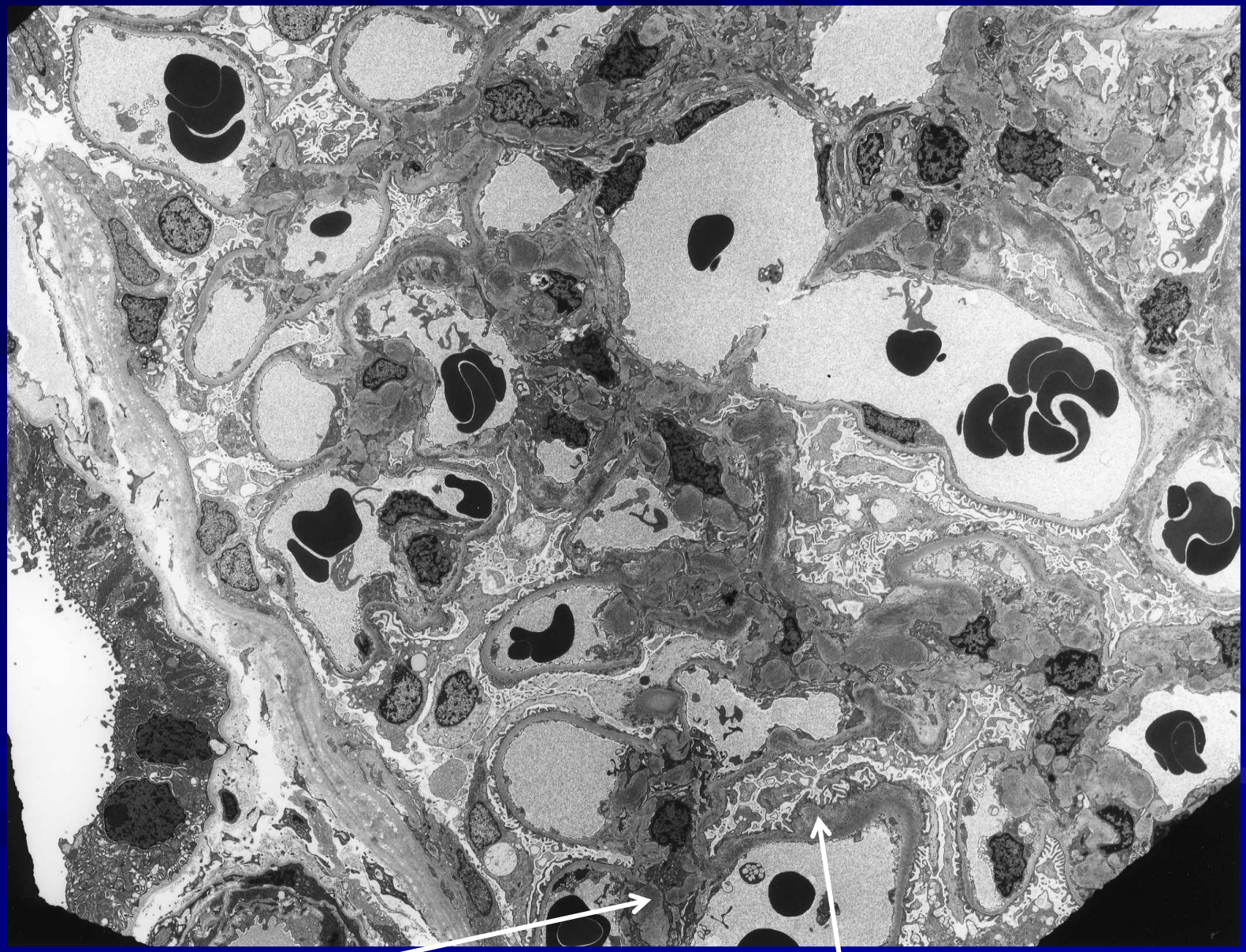
Immunotactoid glomerulopathy



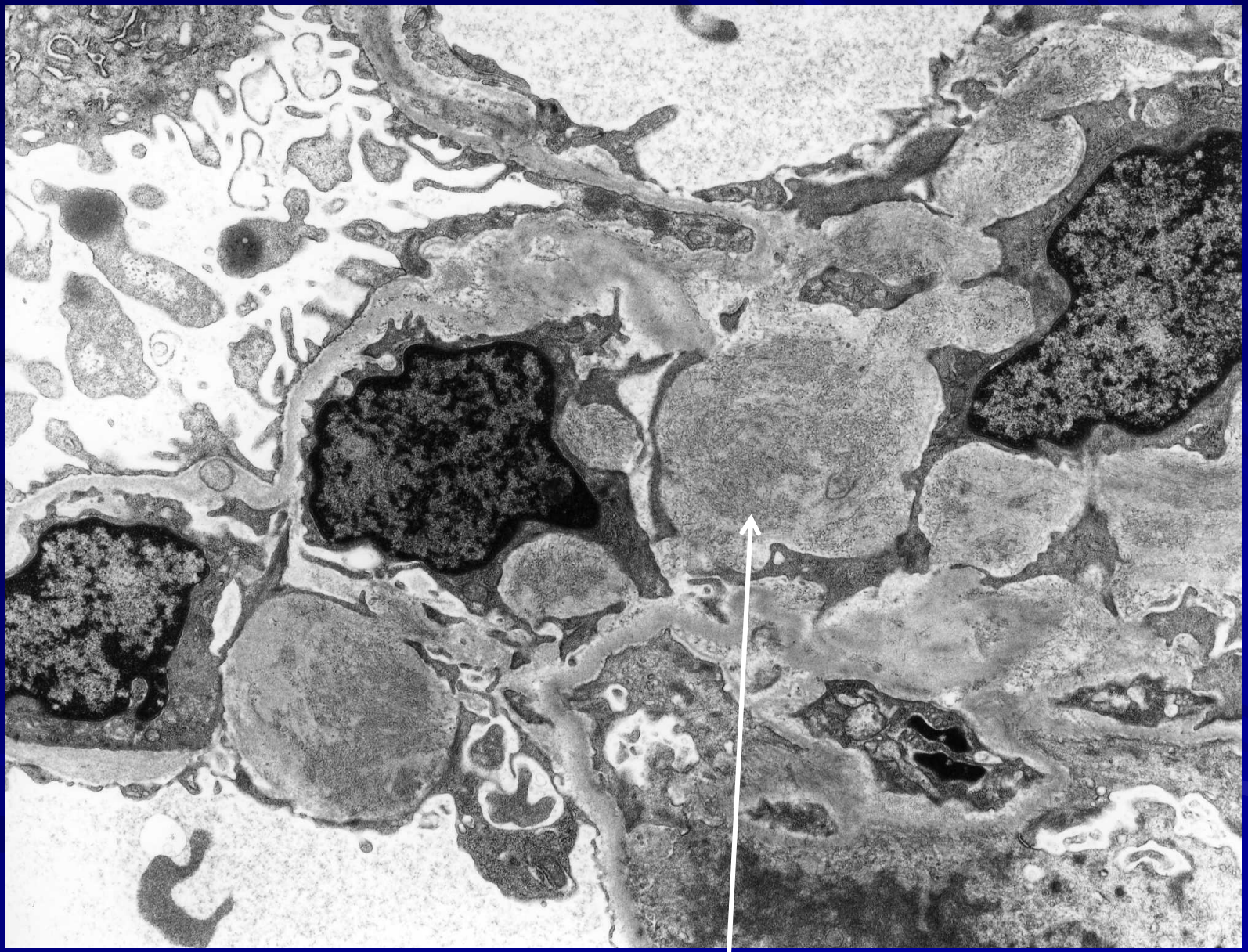
Subepithelial deposits with tubular substructure

Higher magnification of previous slide

Fibrillary Glomerulonephritis

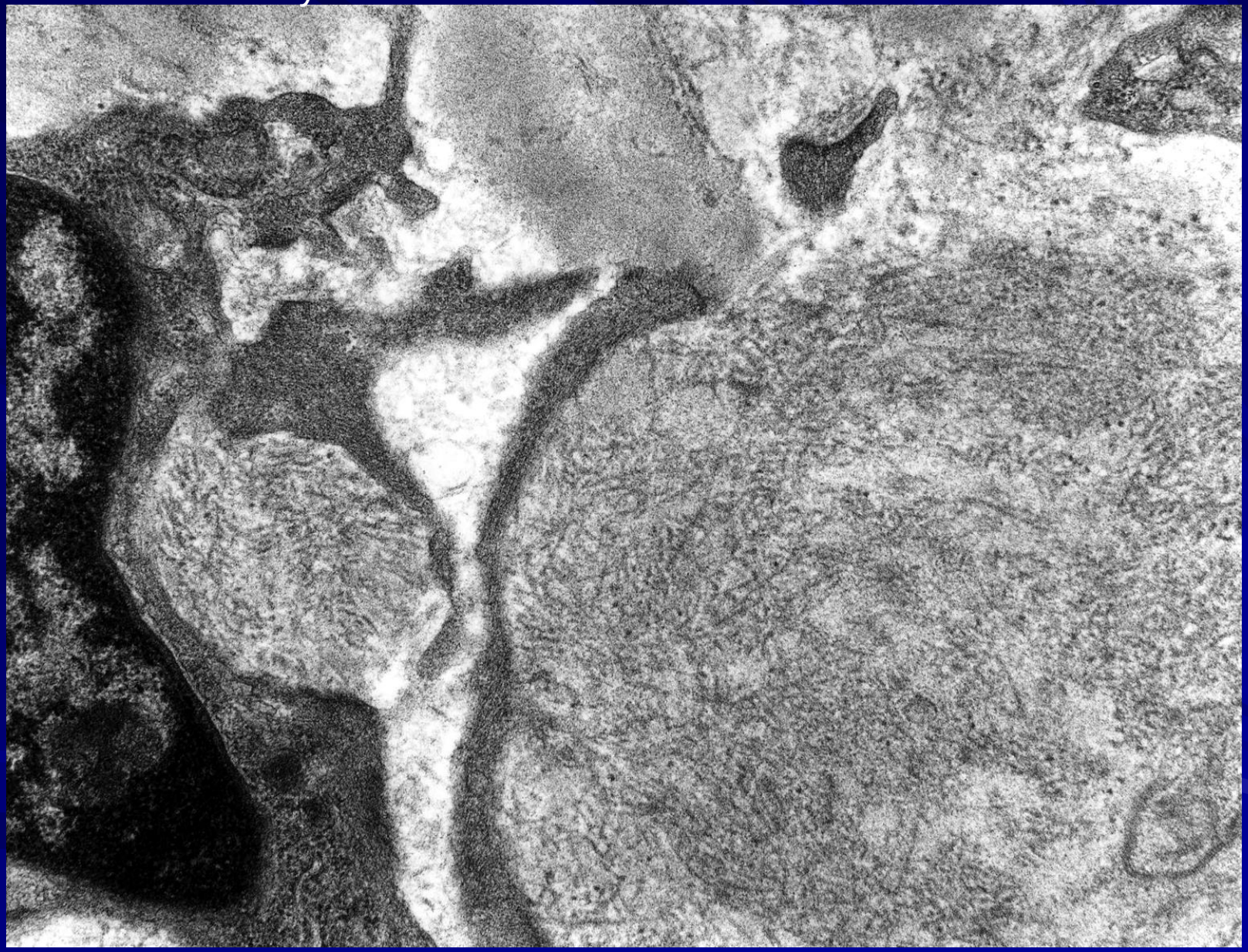


Fibrillary GN



Higher magnification of previous slide

Fibrillary GN



Deposits with amyloid-like structure

Higher magnification of previous slide

Fibrillary GN

Higher magnification of 3 slides back

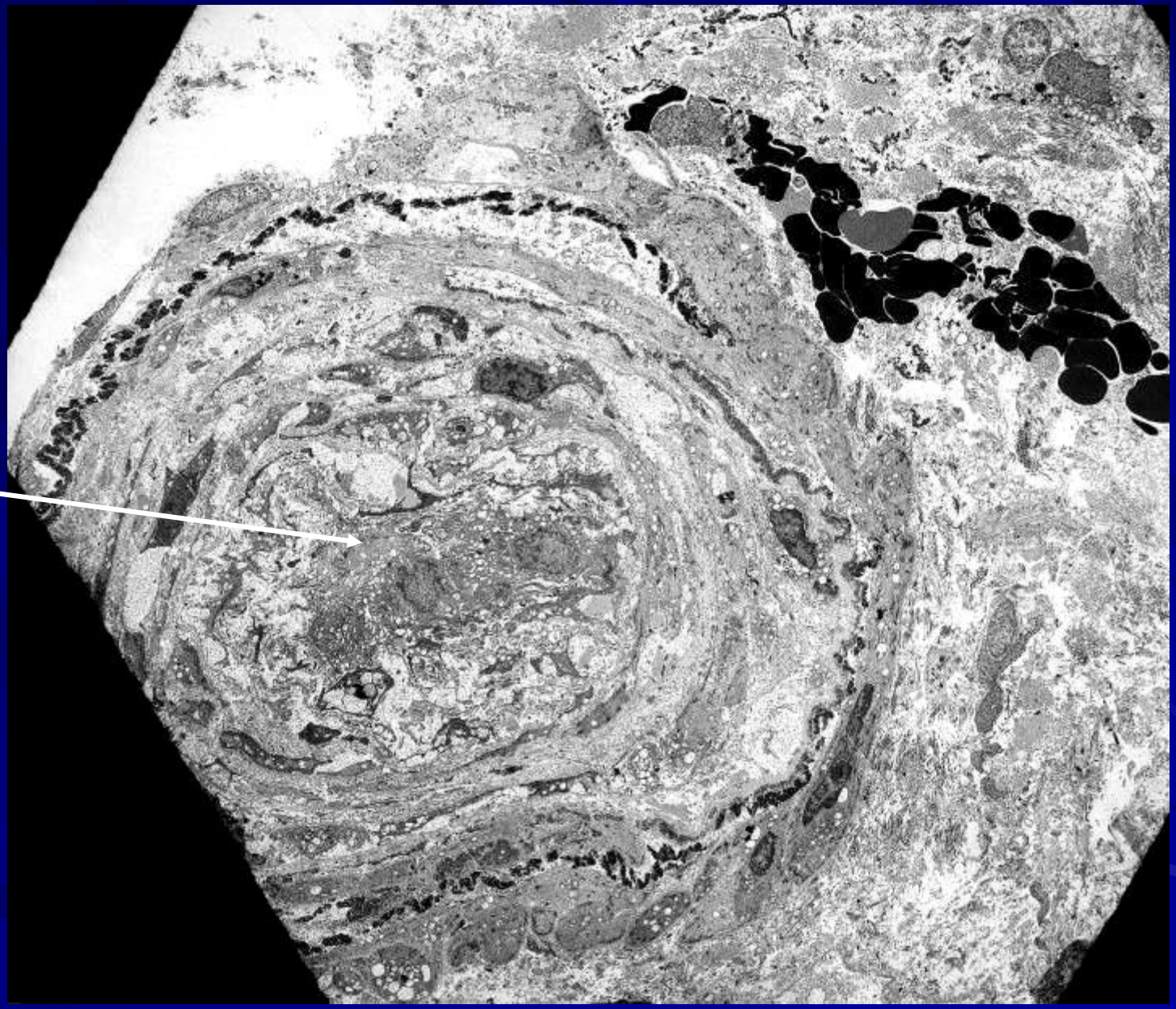
Subepithelial amyloid like fibrils. Note: they are thicker than intermediate filaments in podocyte

Microangiopathic Haemolytic Anaemia (M A H A)

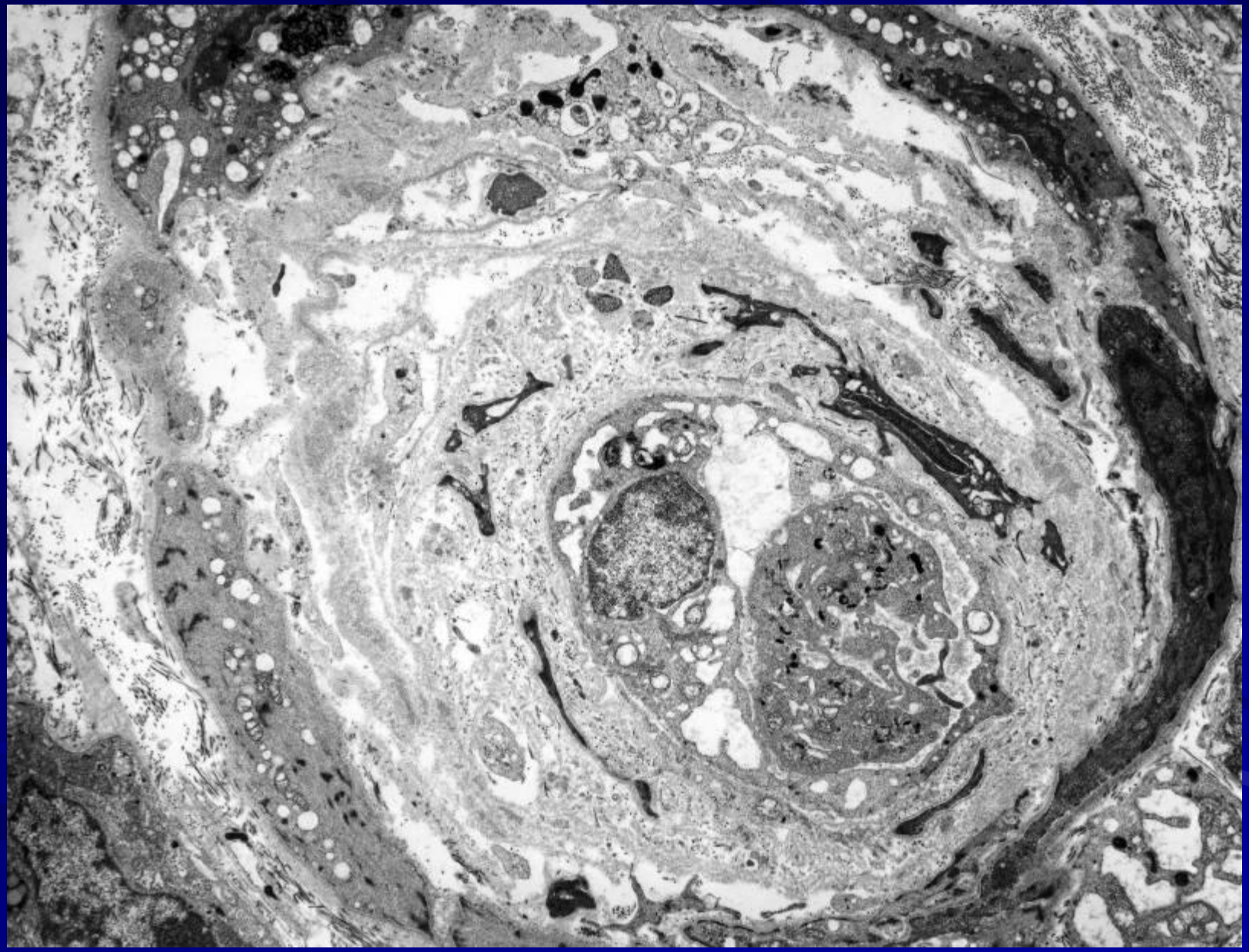
Microangiopathic Haemolytic Anaemia (M A H A)

- Haemolytic Uraemic Syndrome (HUS)
- Thrombotic microangiopathy (TMA)
- Most commonly E. coli 0157 infection – not biopsied

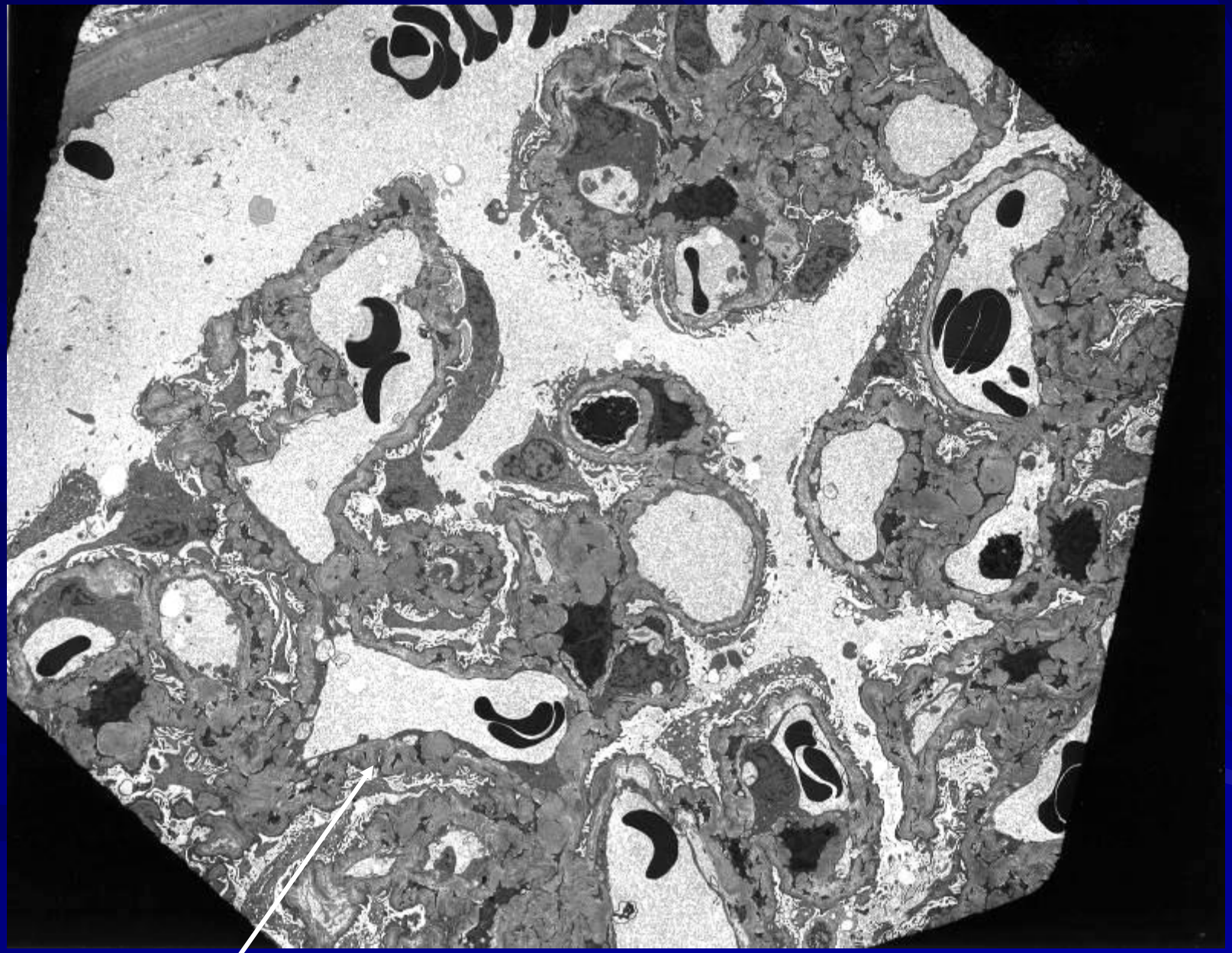
Stenotic lumen of arteriole/small artery



Systemic sclerosis

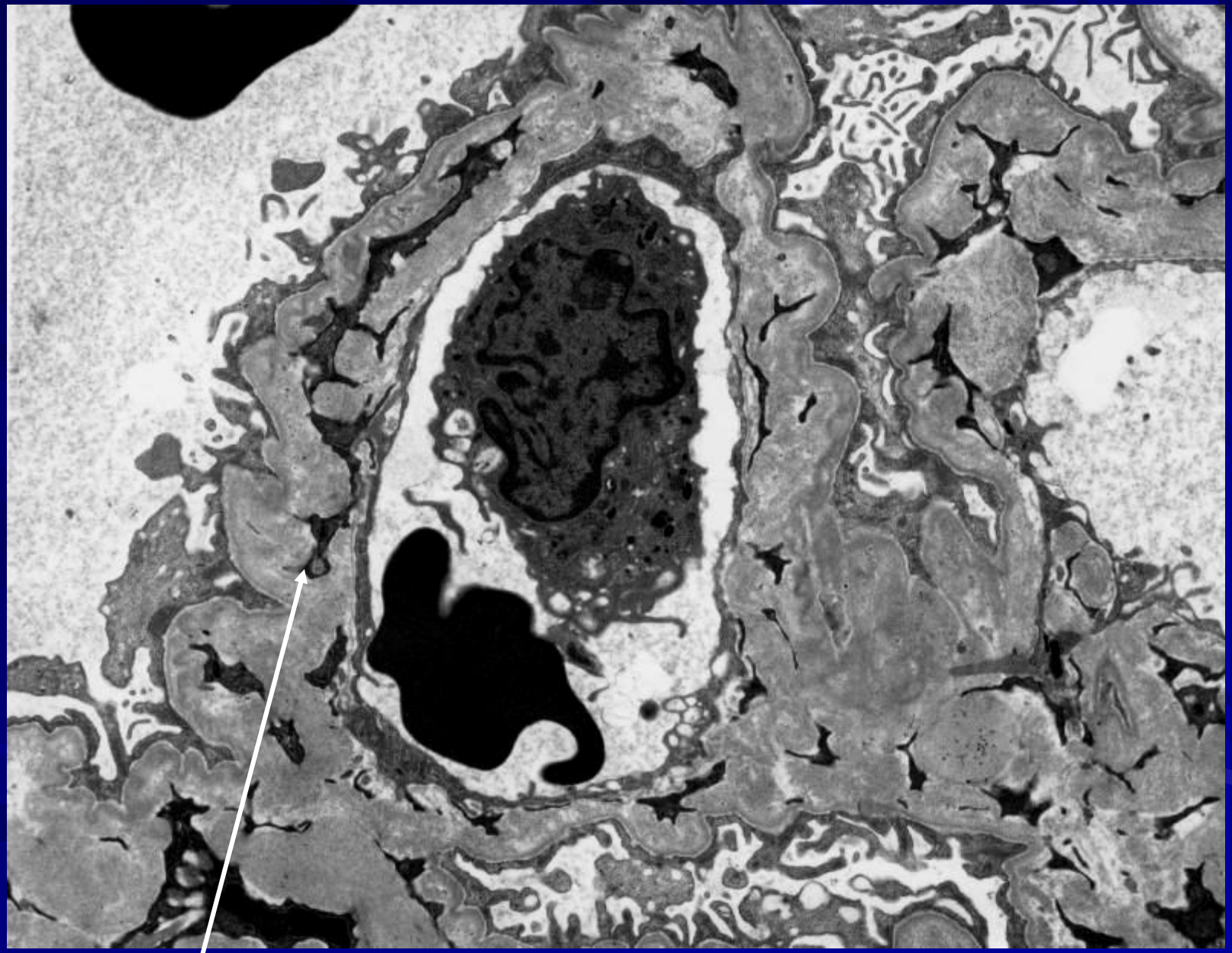


Narrow lumen of arteriole

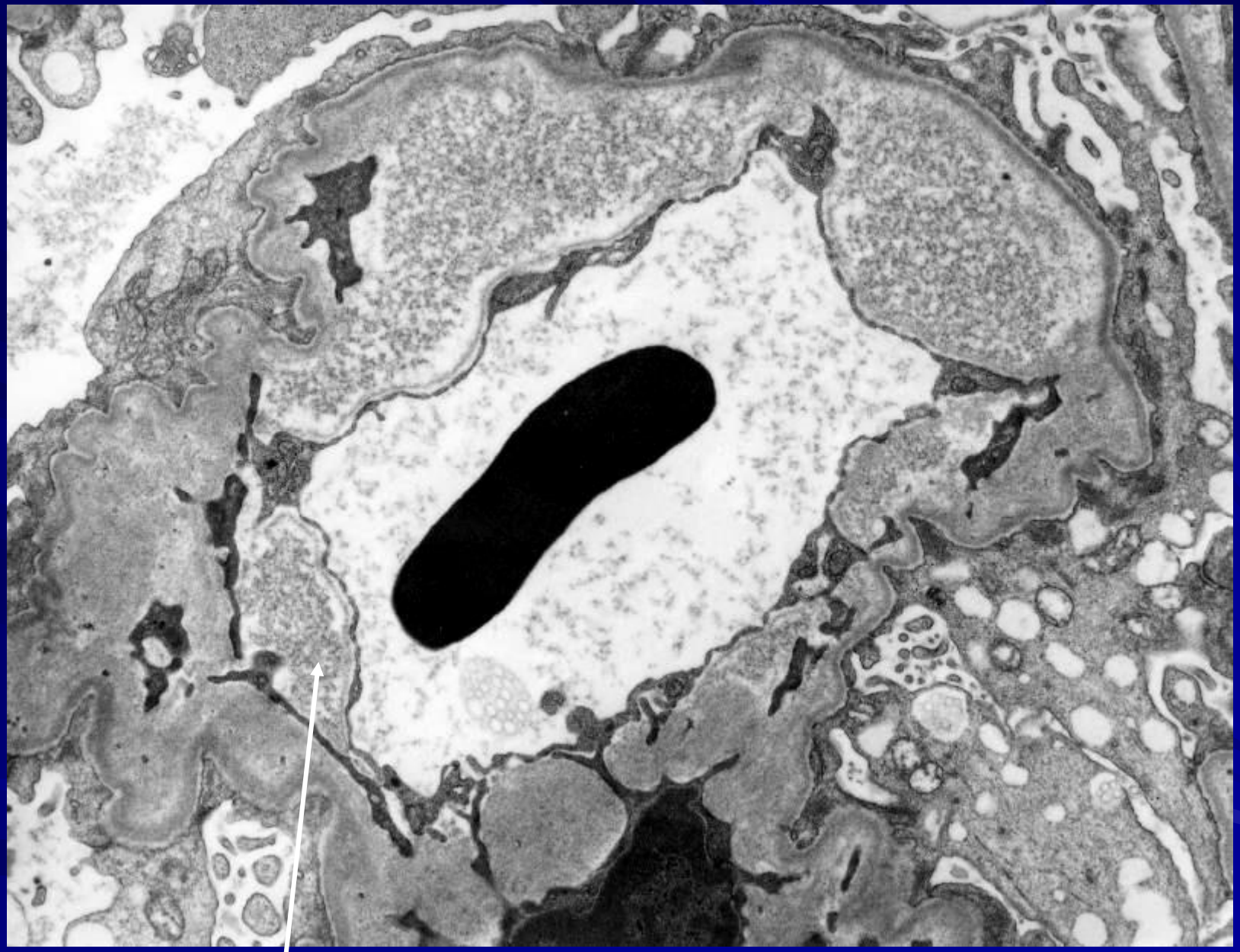


Marked GBM wrinkling cause by hypo-perfusion, also seen in chronic hypertension

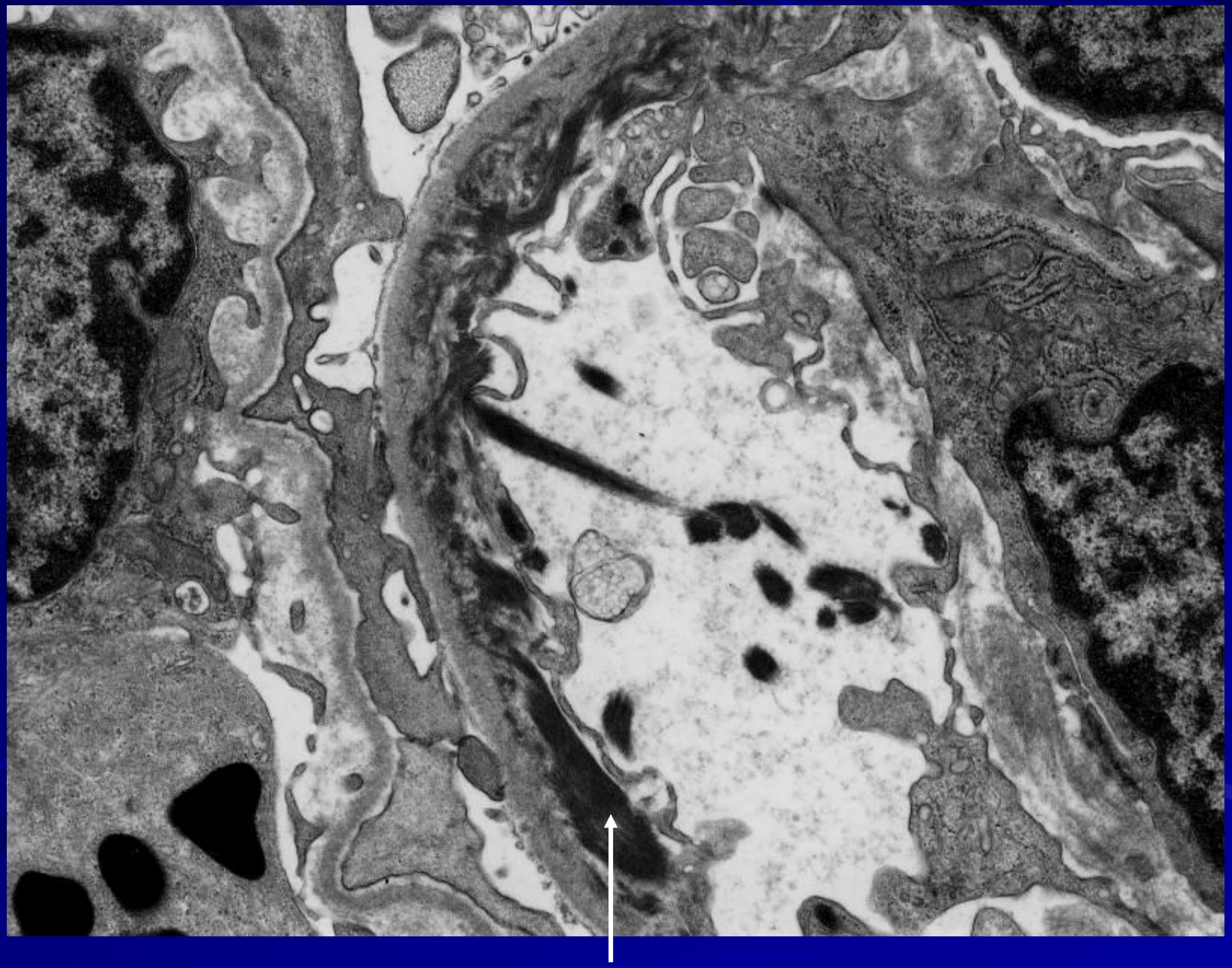
Higher magnification – same biopsy



GBM wrinkling, mesangial interposition

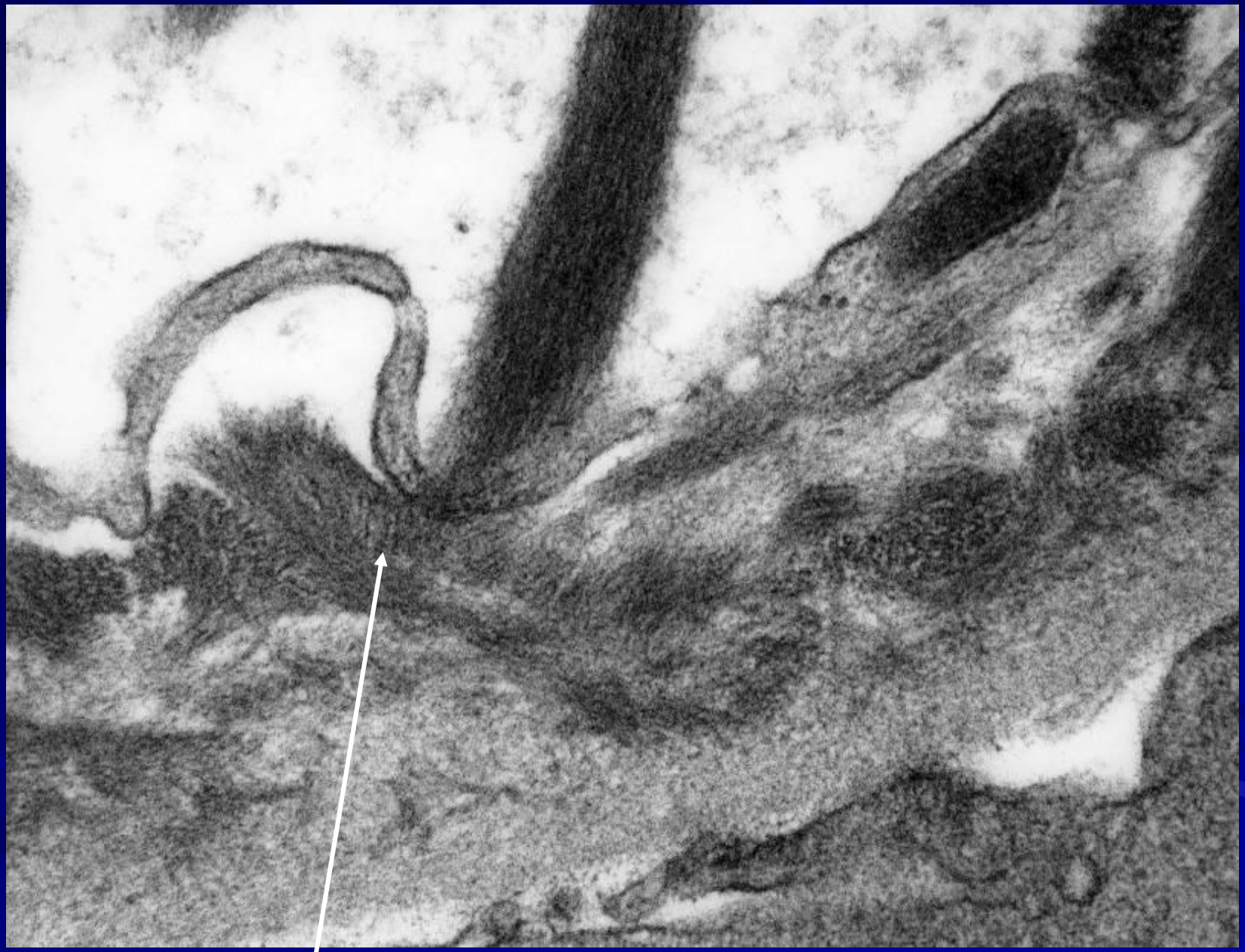


Marked subendothelial expansion - filled with plasmatic material



Transplant kidney biopsy

Intralumenal and subendothelial polymerised fibrin



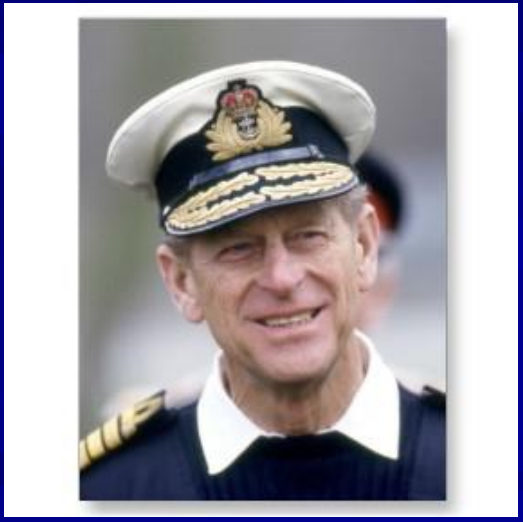
Subendothelial polymerized fibrin

HUS – proposed mechanism

- Bacterial toxin in circulation
- Endothelial damage
- Fibrin strand polymerisation straddling capillary lumen
- Red cell fragmentation following fibrin strand impact
- Release of haemoglobin
- Damage to endothelial cell
- Endothelial cell leakiness
- Plasma protein expanding subendothelial space

Time for a quick break?

‘The mind cannot absorb what the backside cannot endure’



Prince Philip ,The Duke of Edinburgh.