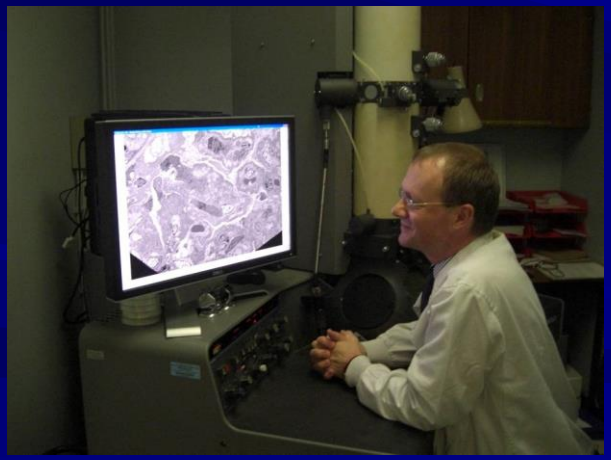
Basic Renal EM workshop

Southampton

September 30th 2011

Renal Ultrastructural Pathology
Lecture 3 T - V



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Renal ultrastructural pathology Lecture 3 - Topics

1. Transplant – Hyperacute rejection
2. Transplant – Acute cellular rejection
3. Transplant – Chronic Humoral rejection
4. Transplant – Calcineurin inhibitor (CNI) toxicity
5. Vasculopathy
6. Viral infection

Transplant

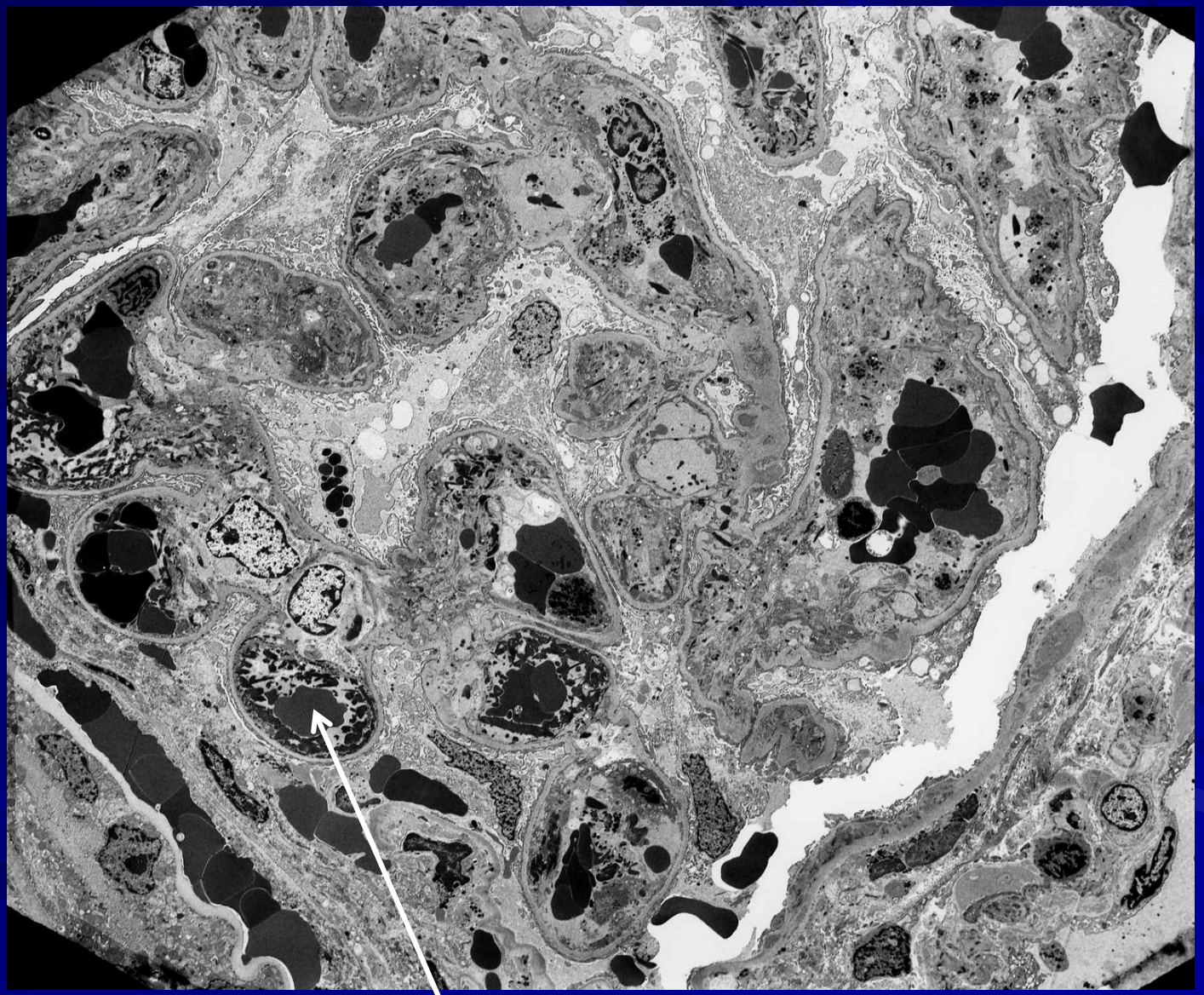
Hyperacute rejection

Transplant

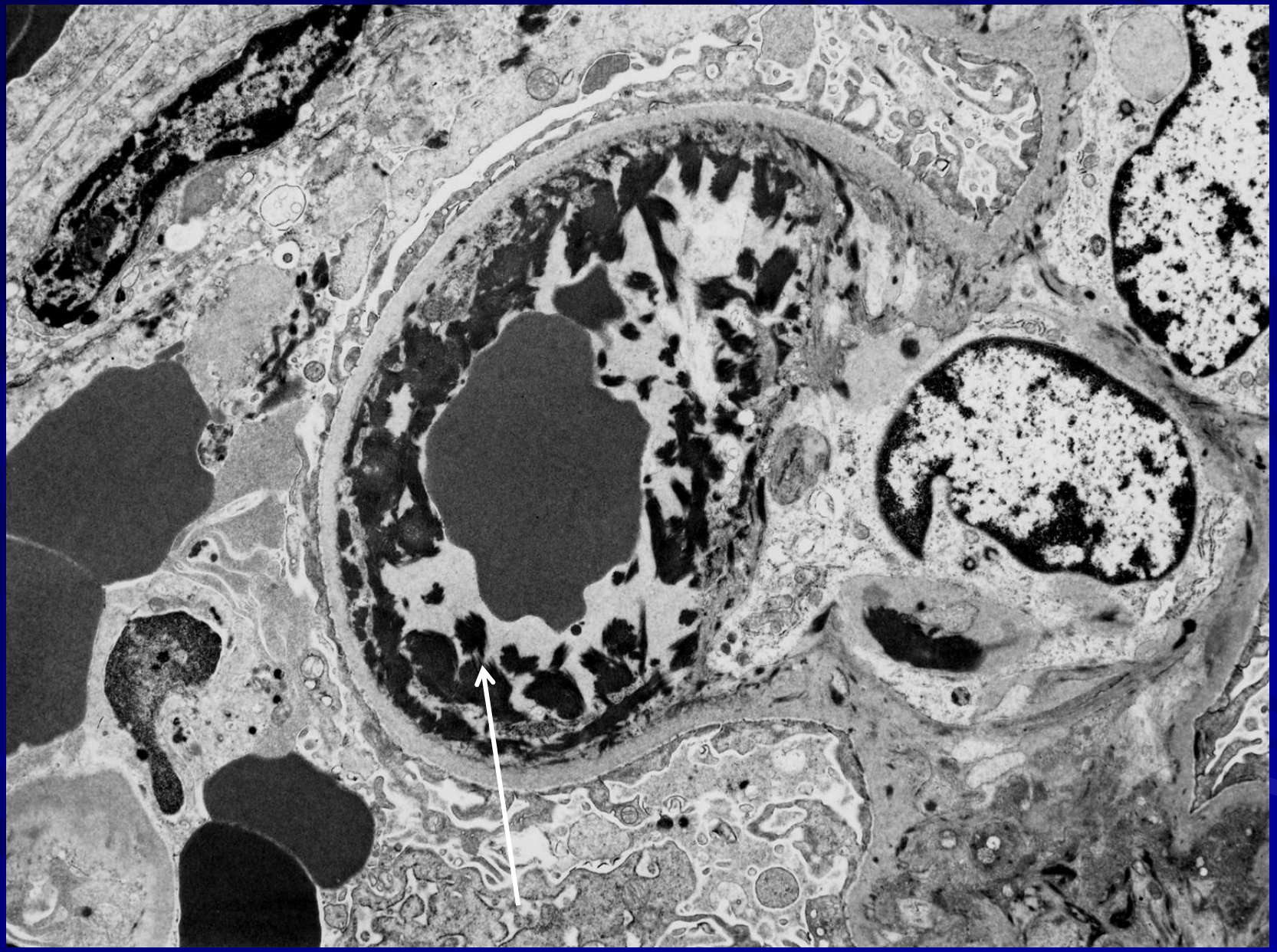
Hyperacute rejection

- Caused by putting a kidney into a person with high titre preformed antibodies, such as acquired following a previously rejected kidney
- Biopsy taken 30 minutes post vascular anastamosis
- Appearance similar to disseminated intravascular coagulation (DIC)
- Numerous intraglomerular platelet and fibrin thrombi
- Haemorrhagic infarcted kidney removed next day

Protocol post-perfusion biopsy



Numerous thrombosed capillary loops

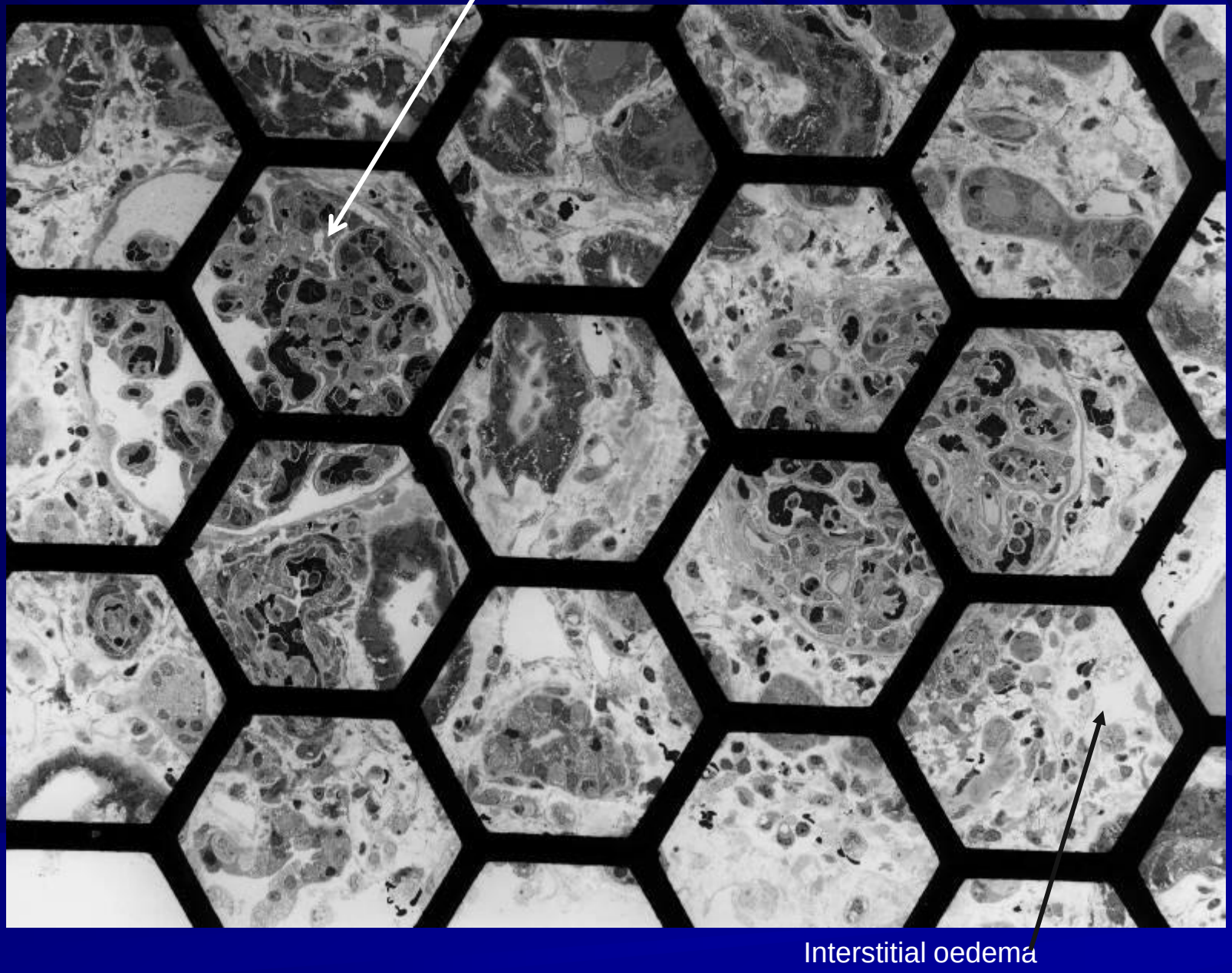


Filled with fibrin tactoids

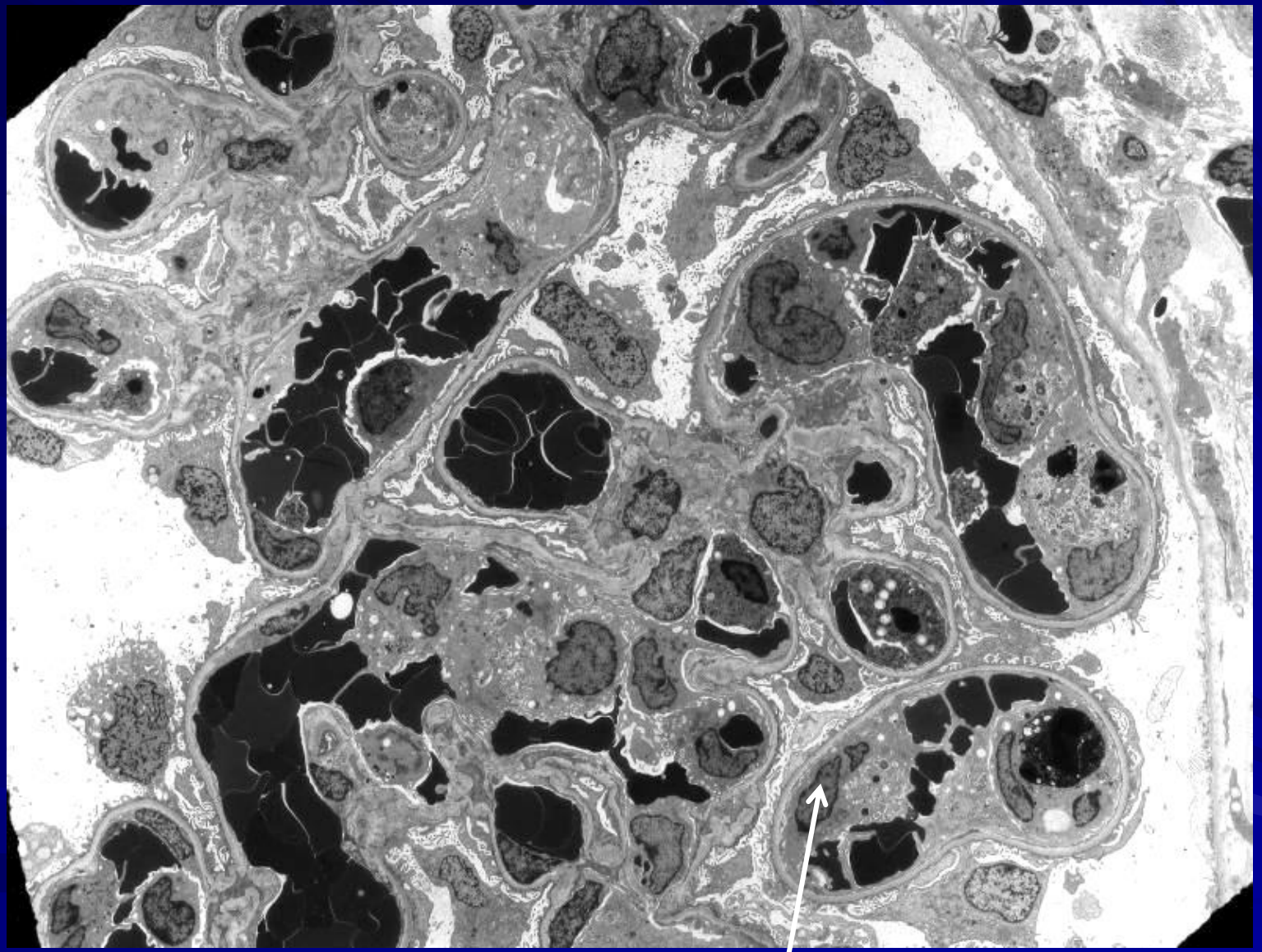

Necrotic endothelial cell nucleus
Aggregate of degranulated and non-degranulated platelets

Transplant

Acute cellular rejection


Glomerulitis
Interstitial oedema

Glomerulitis or intraglomerular endothelialitis



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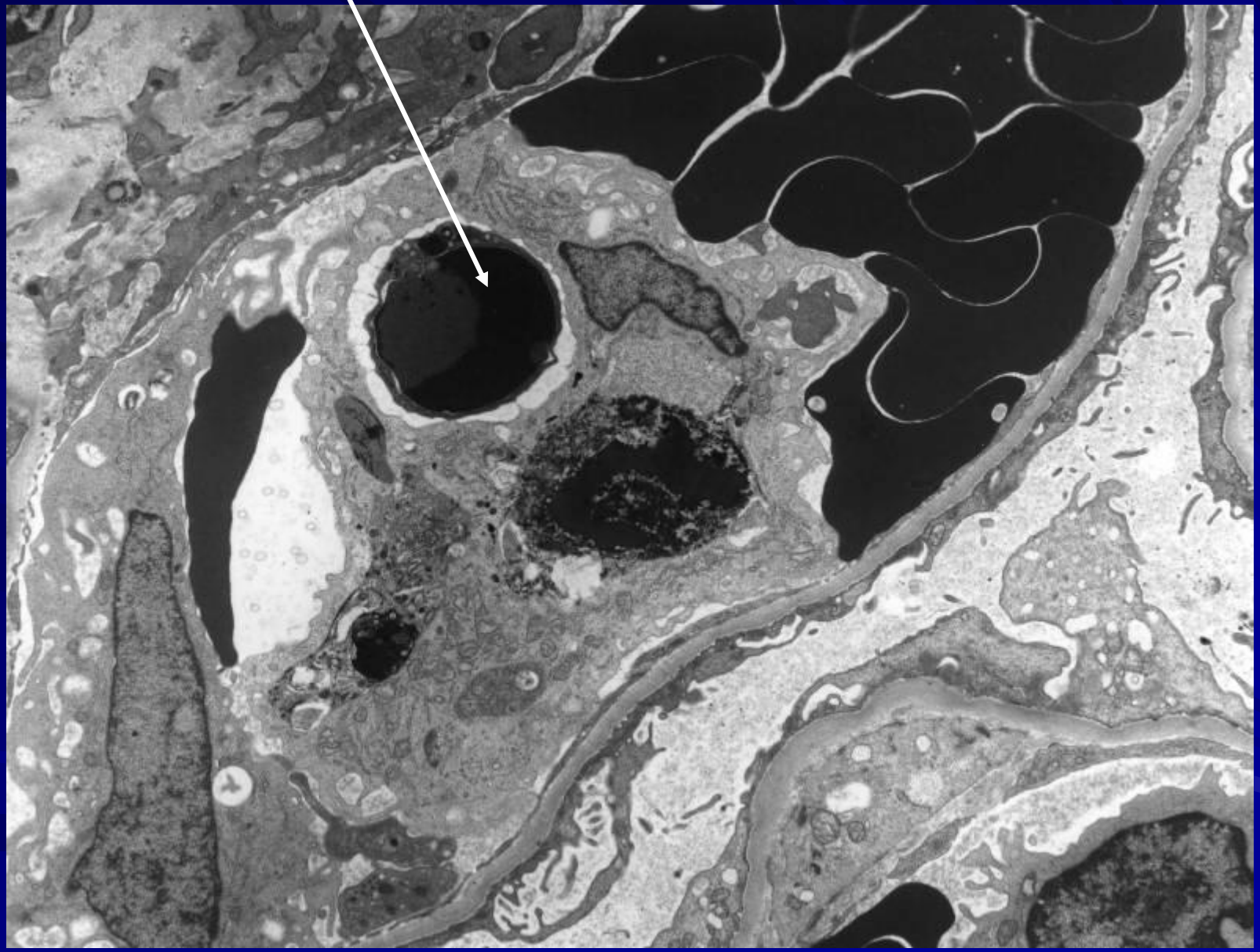
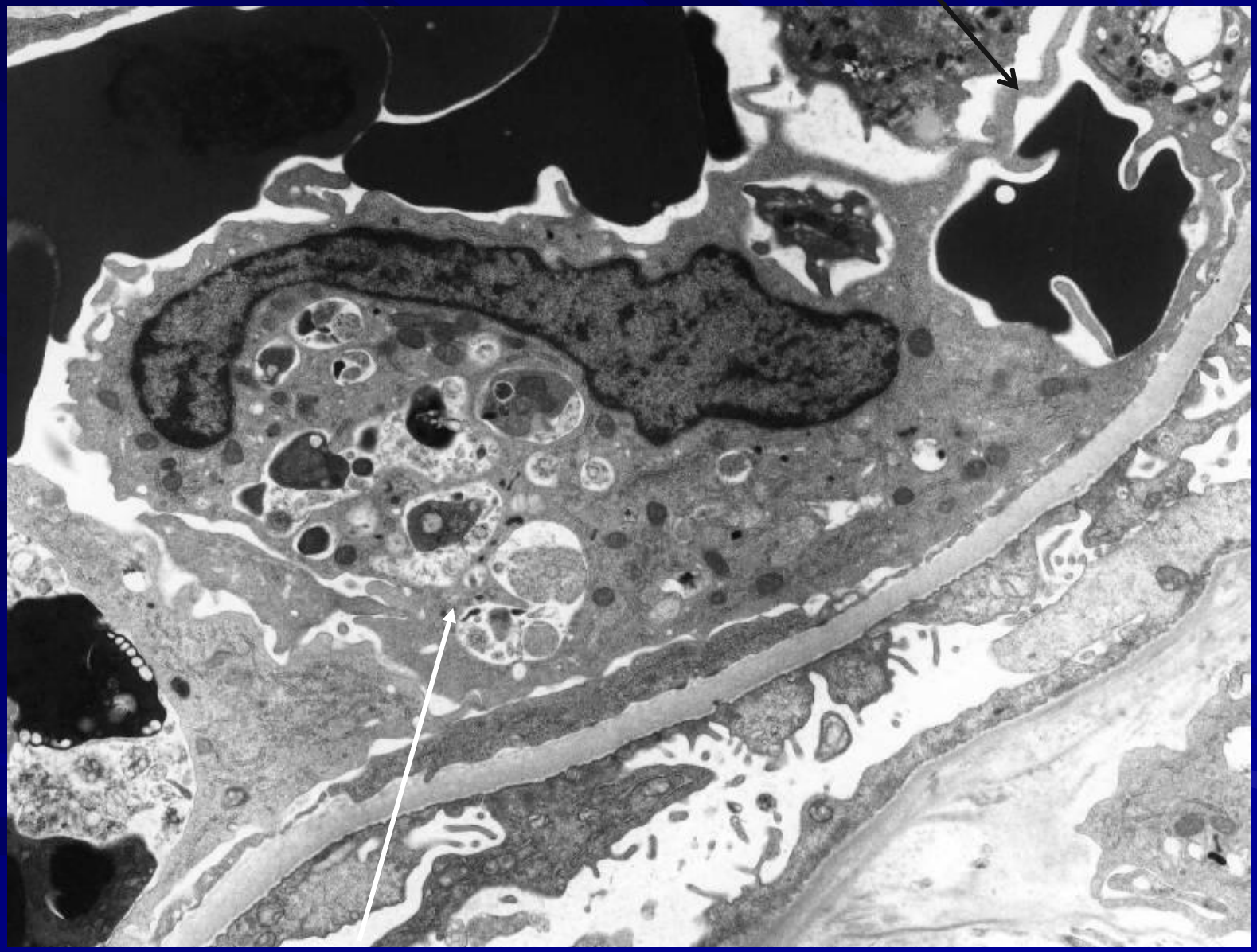
Numerous intracapillary mononuclear cells

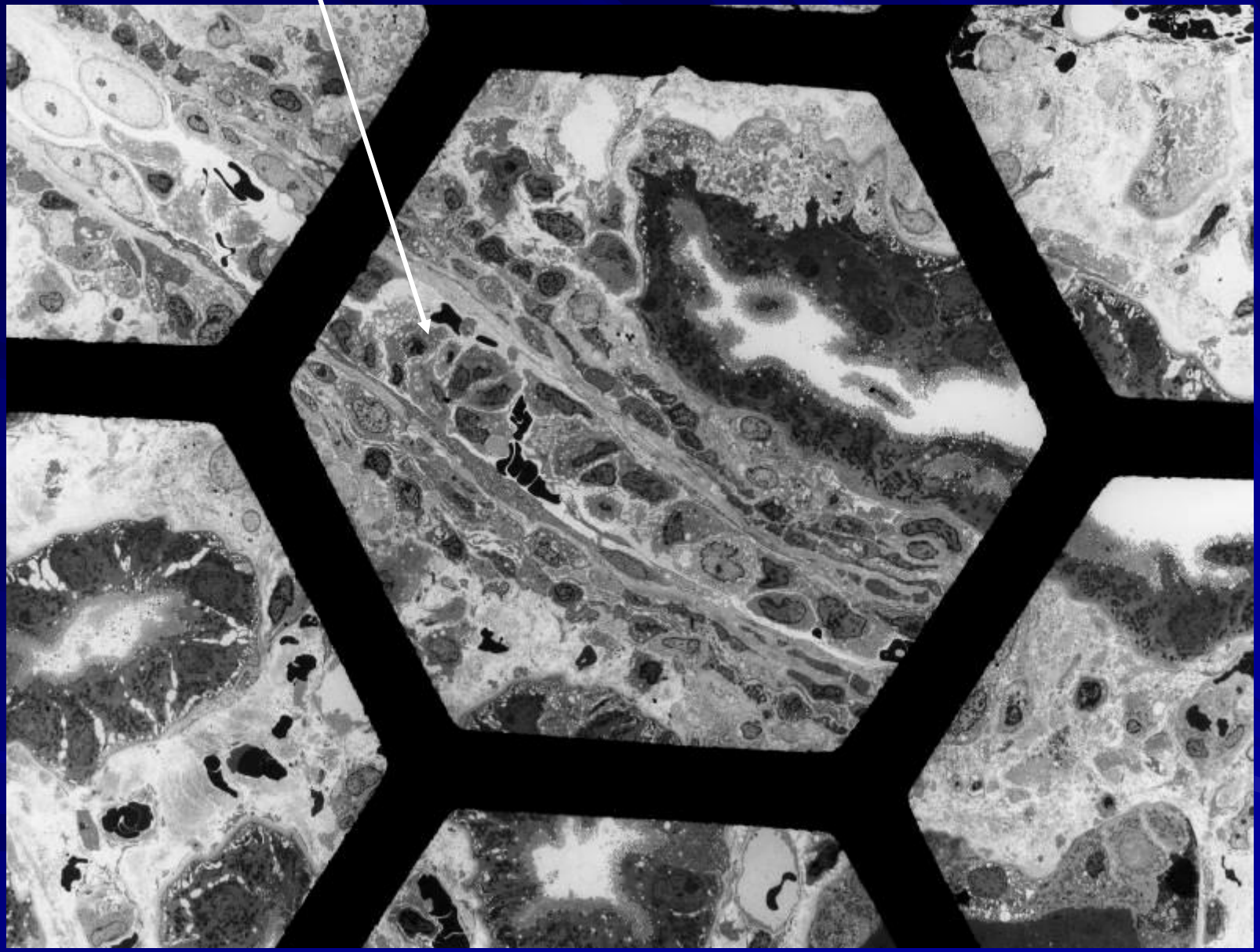
Apoptotic lymphocyte



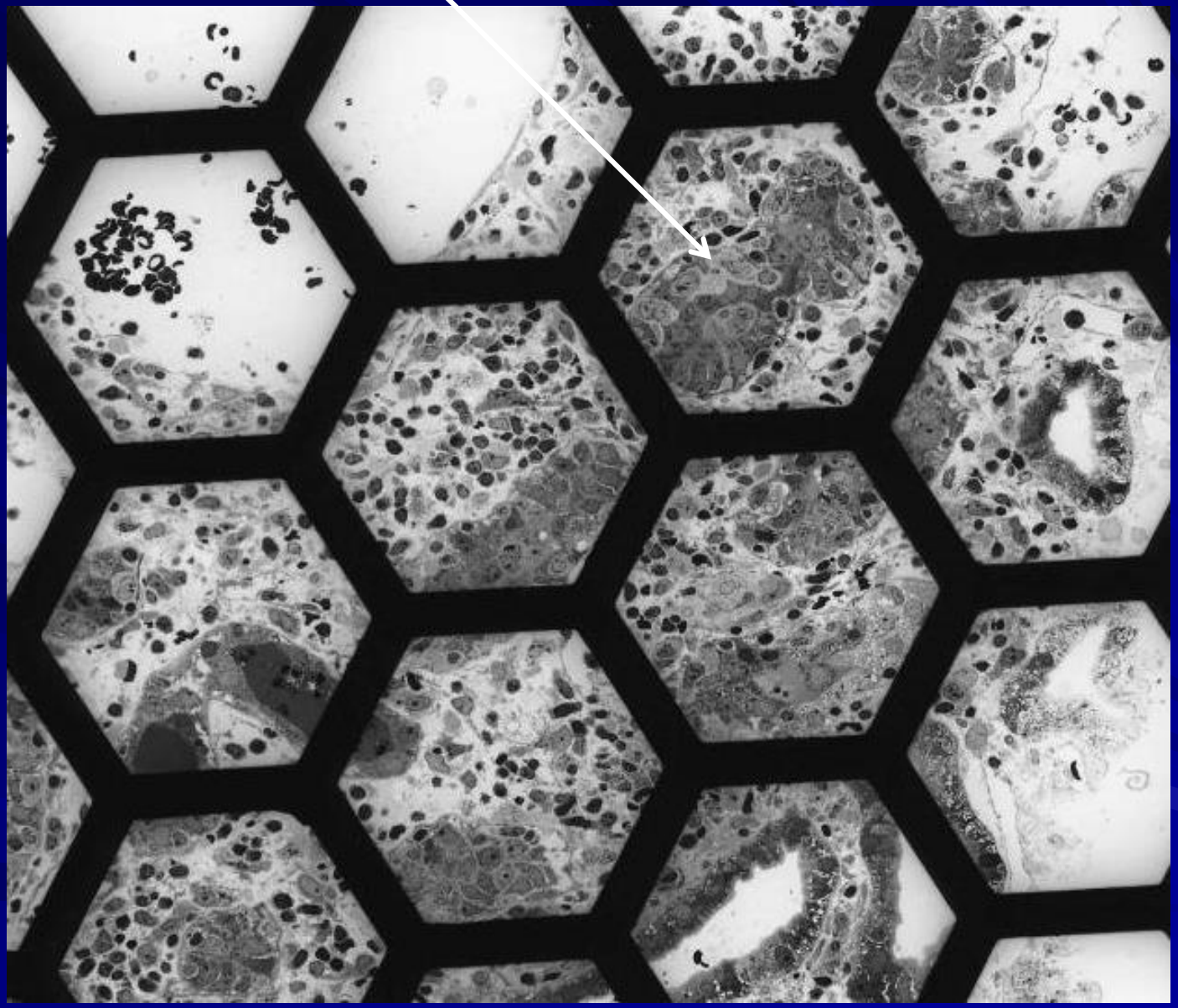

Filopodia
Dendritic cell

Antigen in exosomes (endosomal vesicles)

Endothelialitis of peritubular capillary (PTC)



Tubulitis



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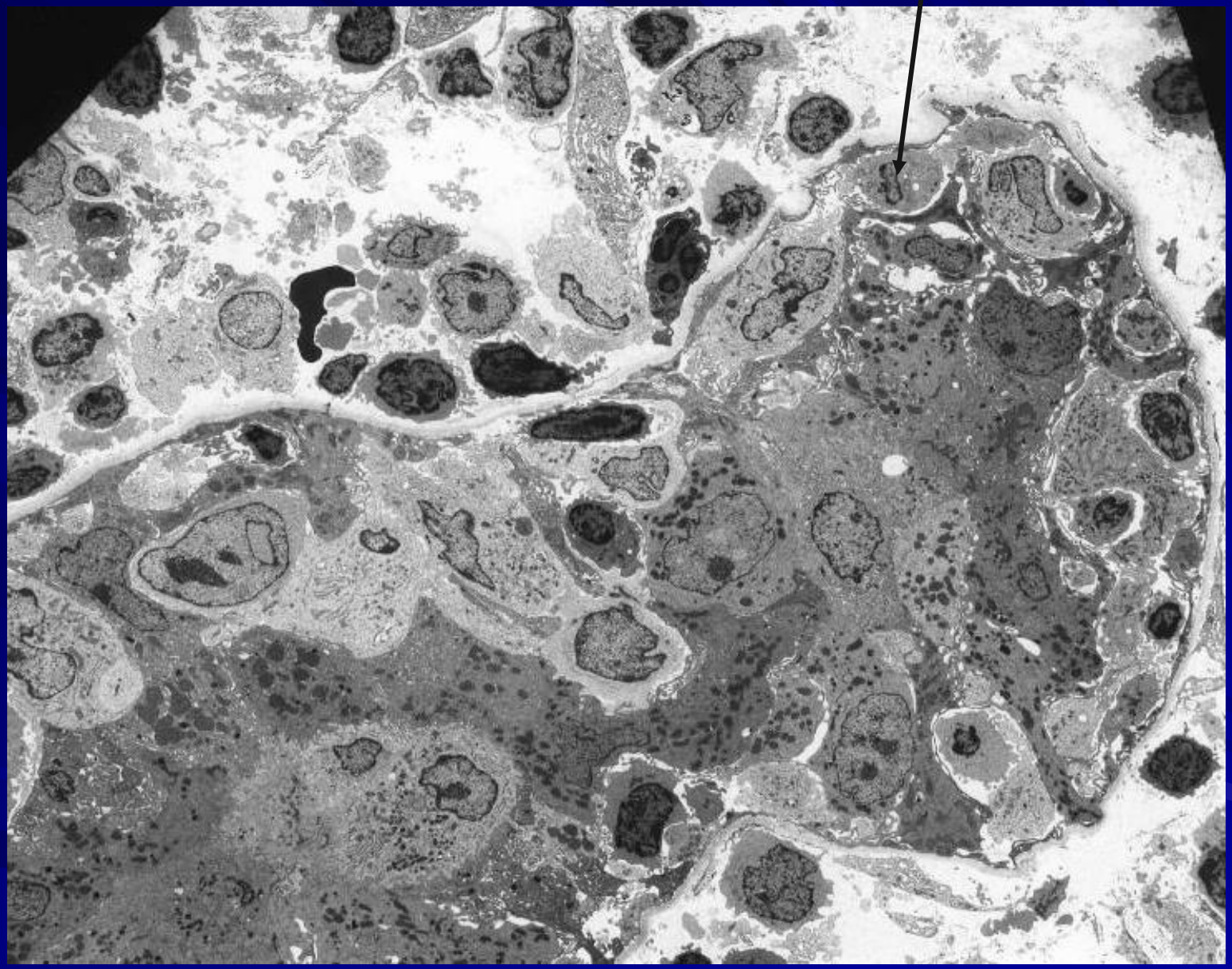
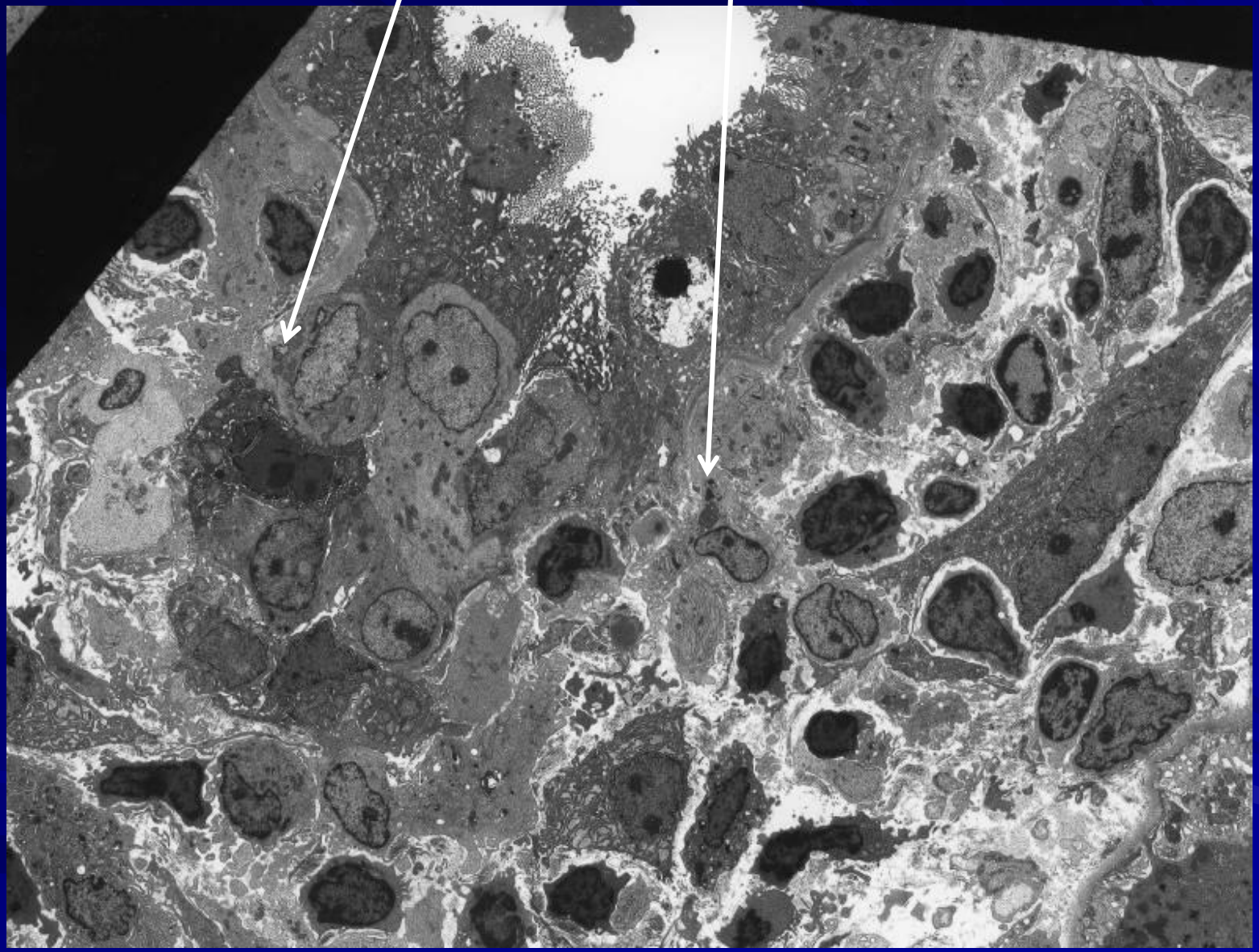


Disruption of tubular basement membrane



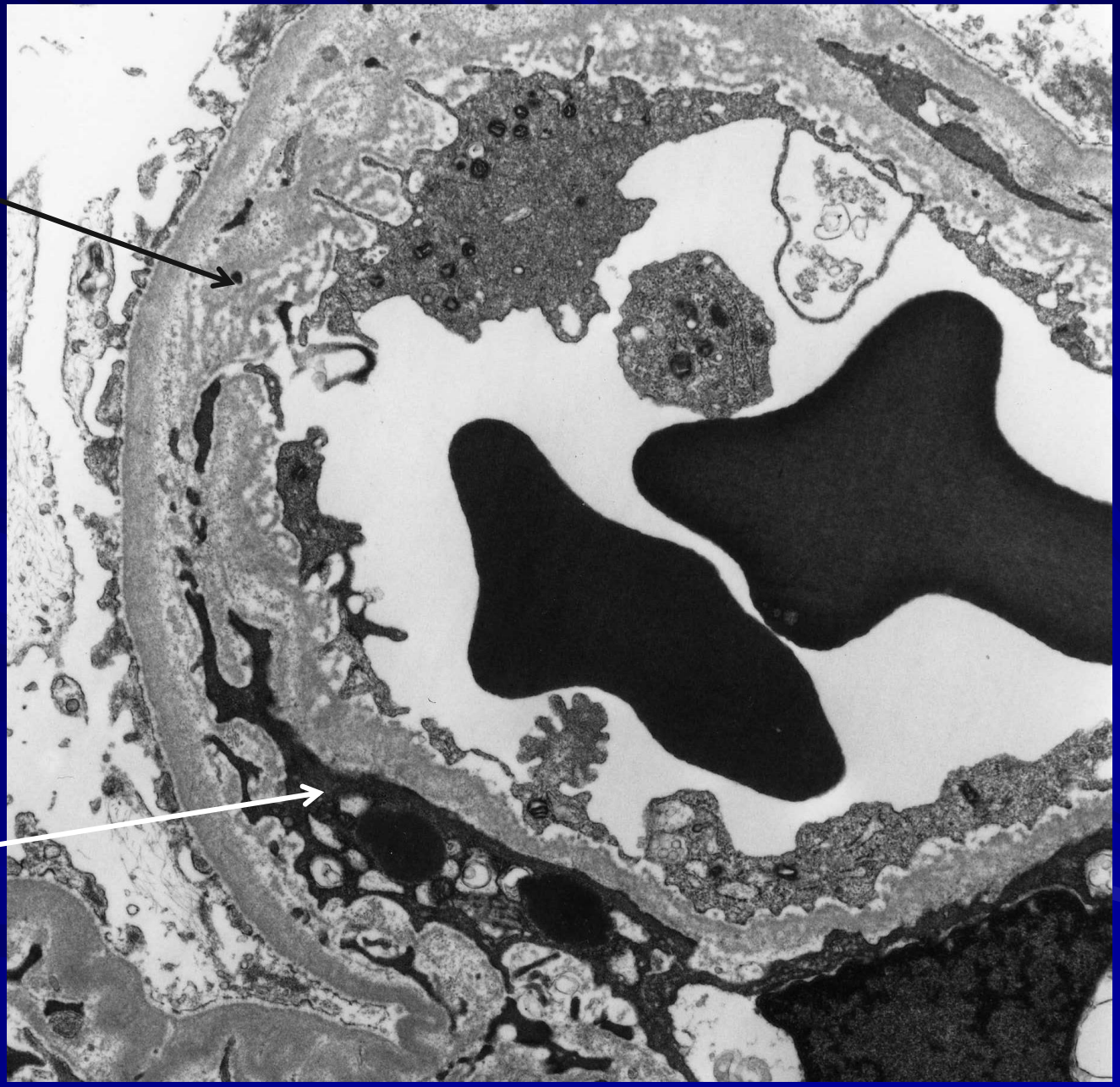
Transplant

Chronic humoral rejection (CHR)

Transplant
Chronic Humoral Rejection

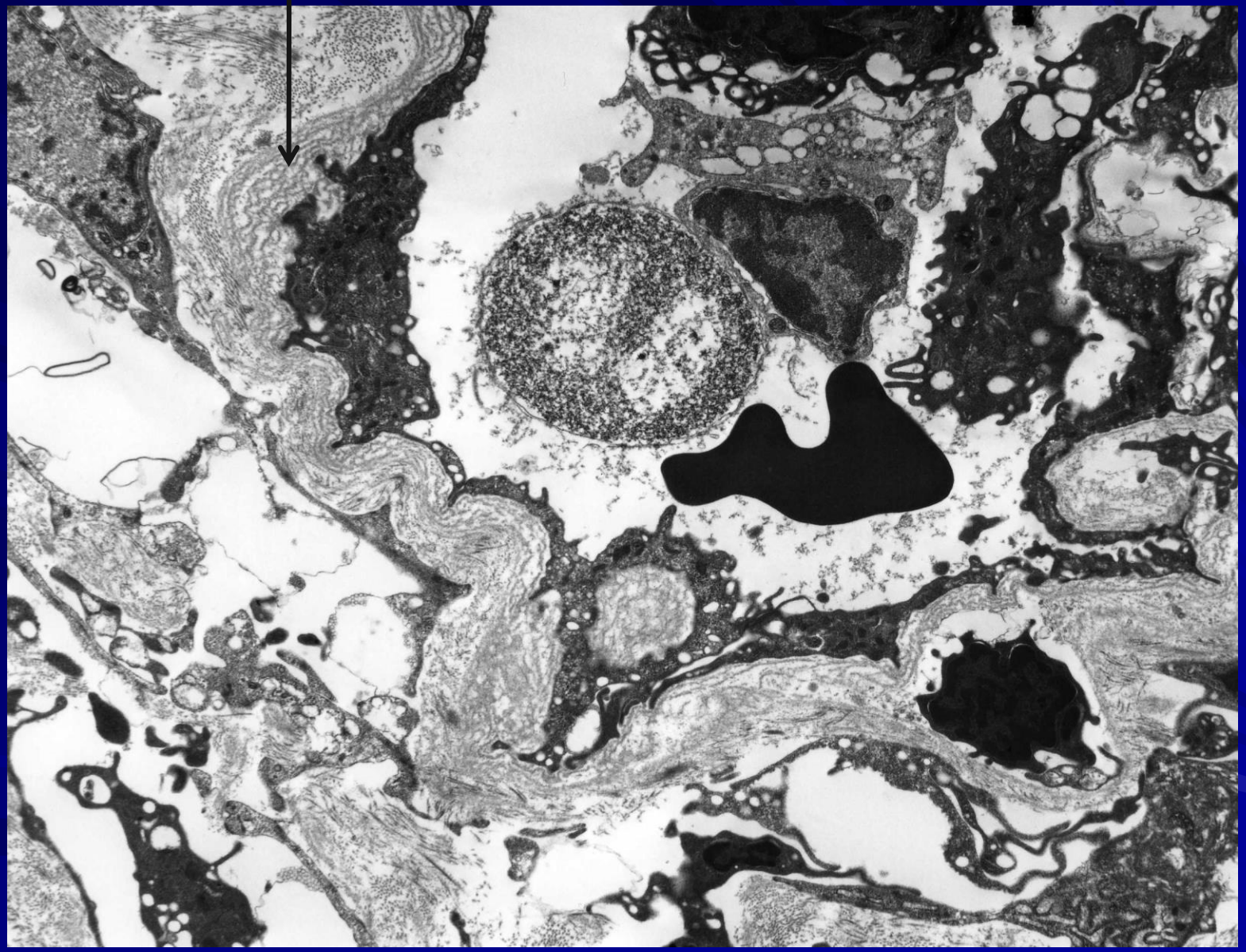
- C4D staining of vessel walls by immunoperoxidase or fluorescence
- Basement membrane multilayering in glomerular subendothelial zone by endothelial cells producing multiple new basement membranes
- In excess of 6 layers of new basement membrane around peritubular capillaries

New basement membrane laid down by endothelial cells

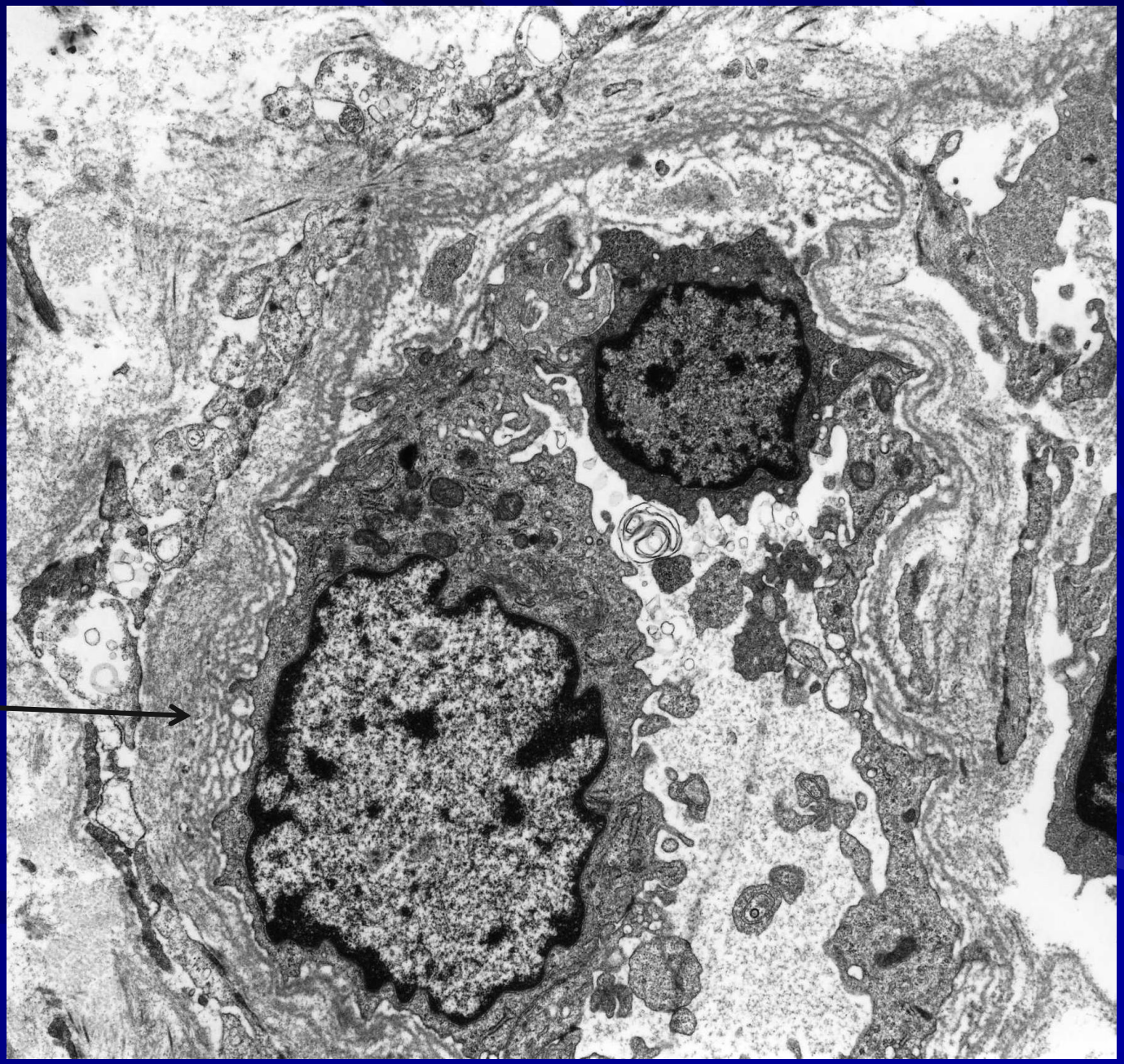


Mesangial cell interpositioning

Peritubular capillary (PTC) basement membrane multilayering



Peritubular capillary basement membrane multilayering

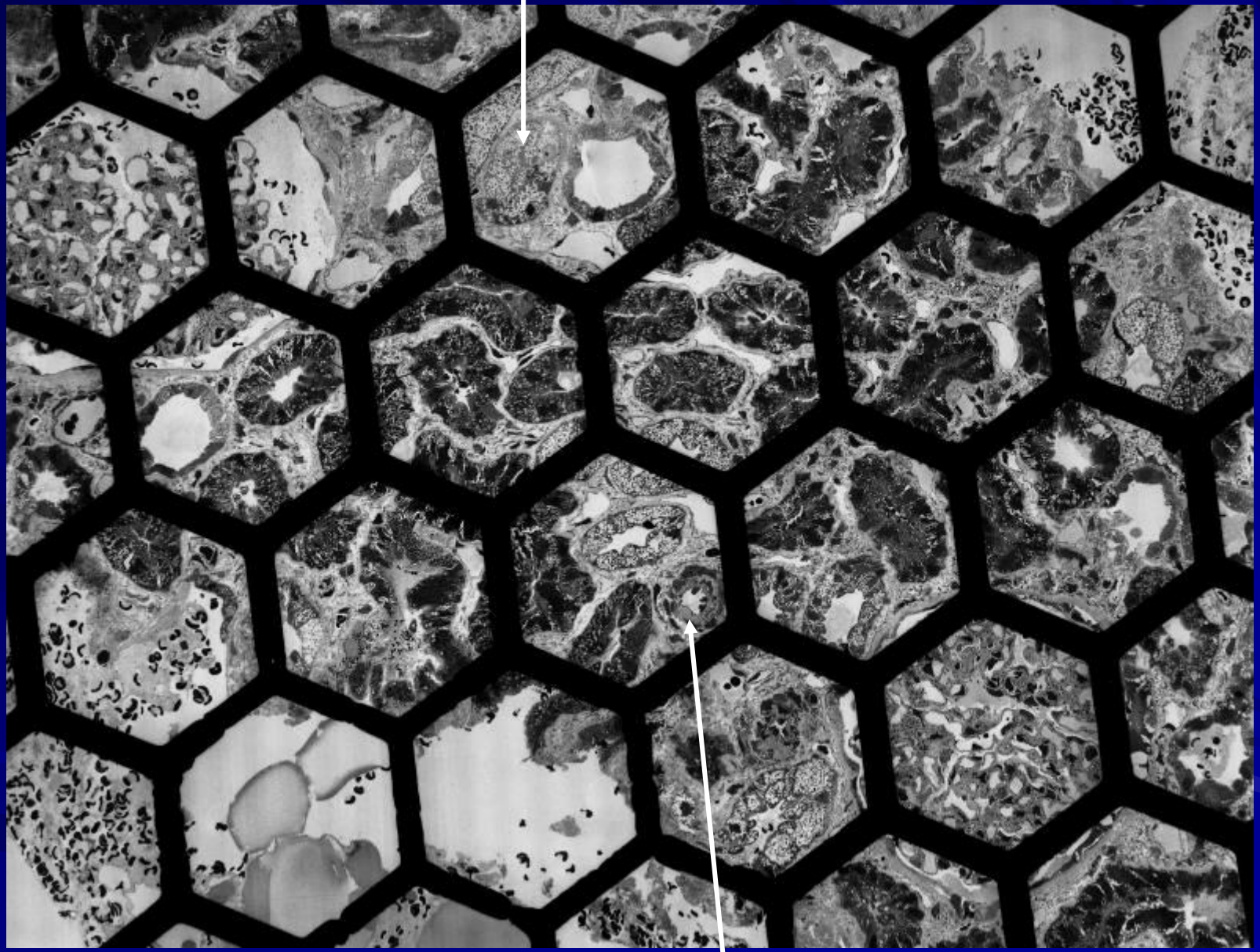


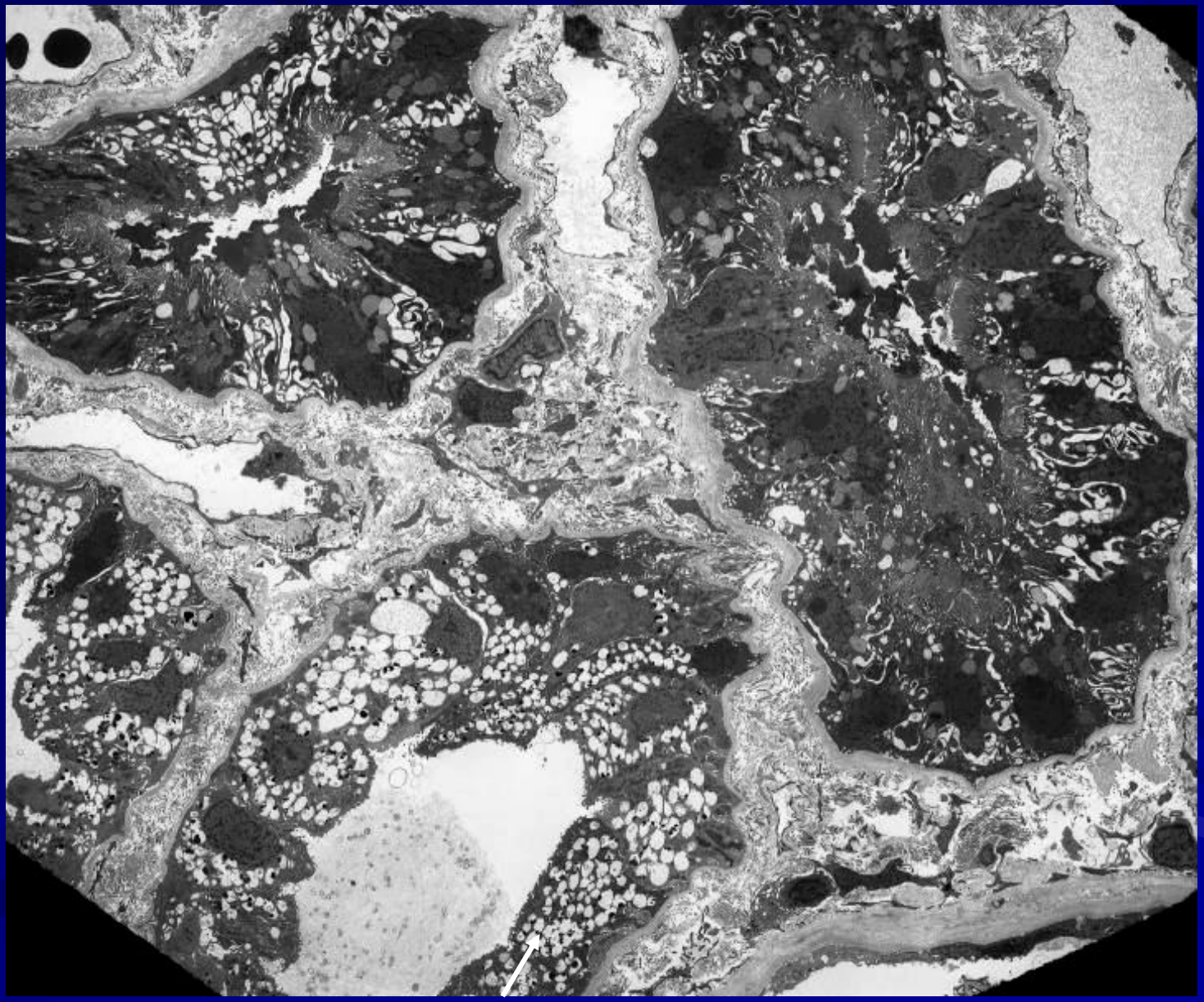
Transplant cyclosporine toxicity

Lung transplant patient

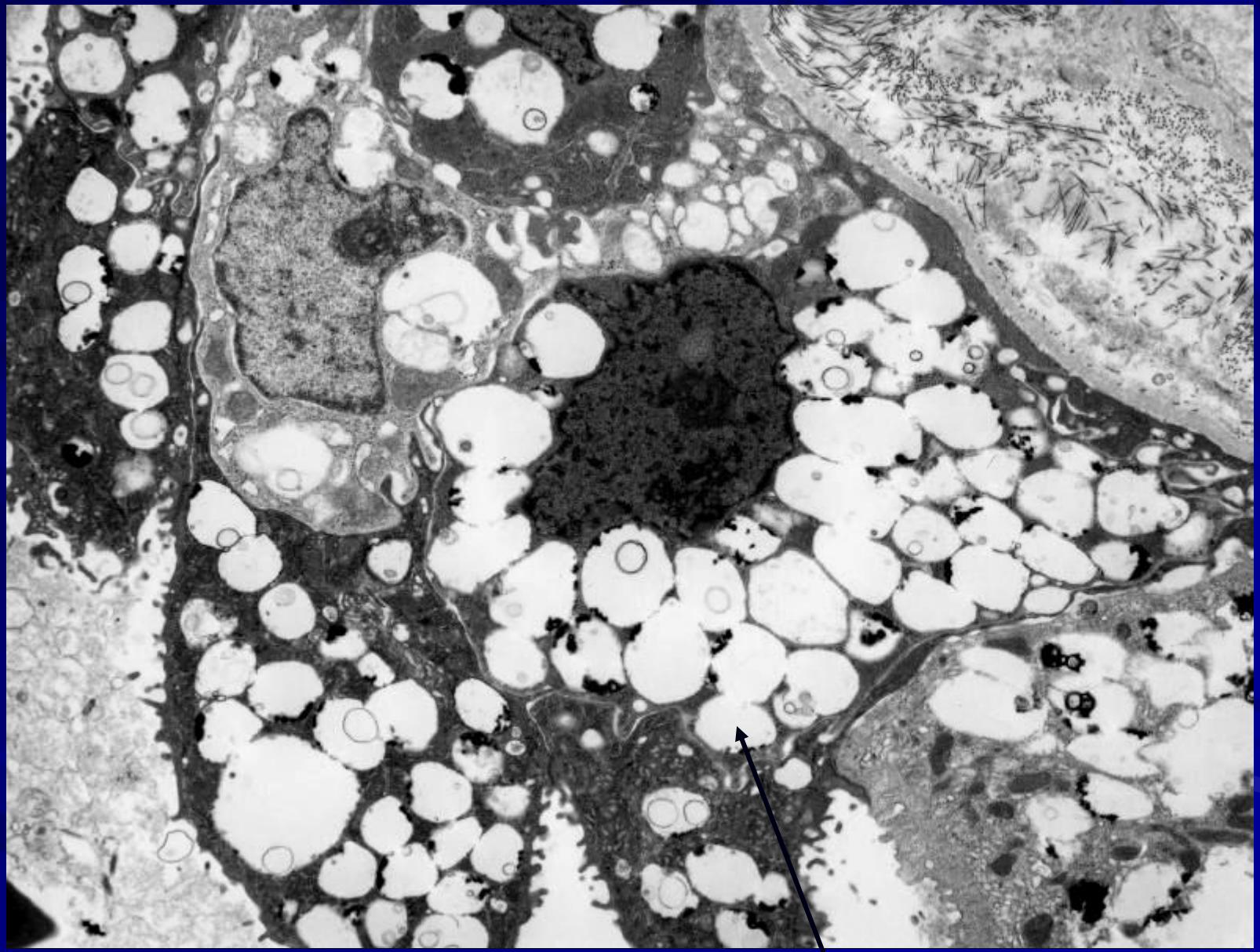
Transplant
Cyclosporine A toxicity

- Lung transplant patient
- Iatrogenic acute renal failure
- Biopsied for prognostic reasons
- Calcineurin inhibitor (CNI) toxicity


Fine isometric vacuolation
Arteriolar hyalinosis



Swollen lysosomes in distal convoluted tubule



Fine isometric vacuolation distal convoluted tubular cells

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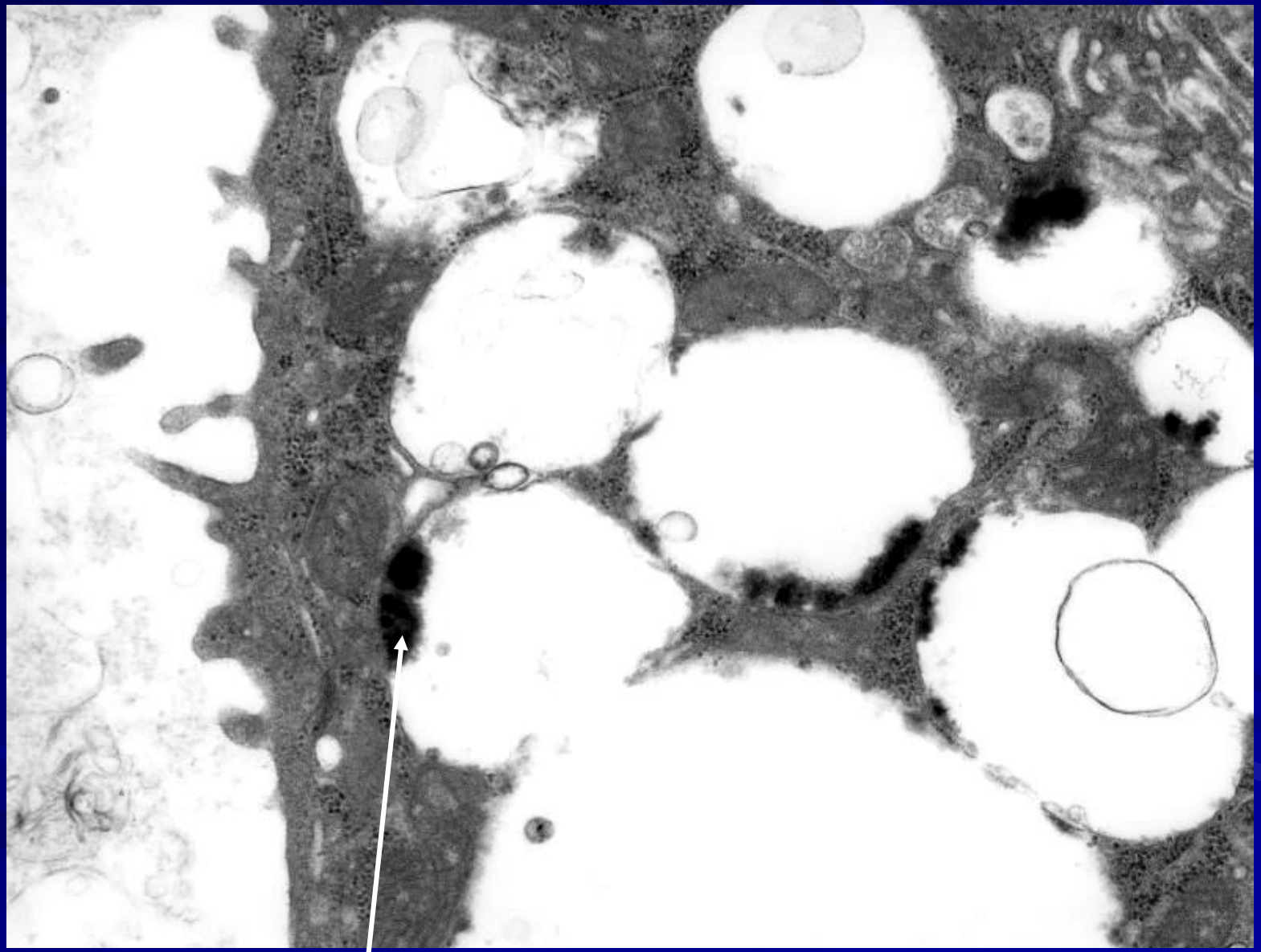
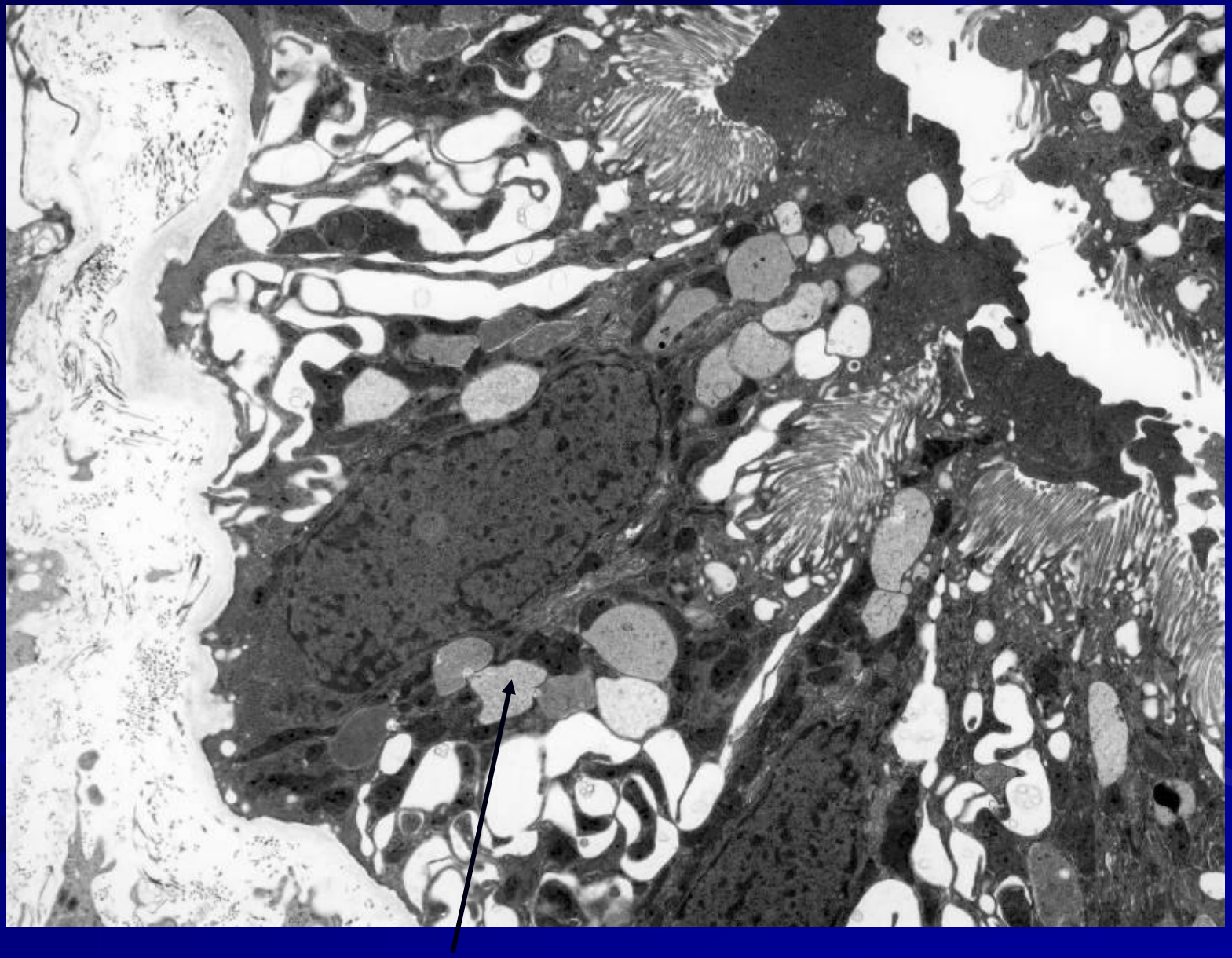


Lysosomal enzymes displaced peripherally

These changes can be seen in fibroblast lysosomes in renal transplant biopsies

Proximal convoluted tubular cells



Isometric vaculation

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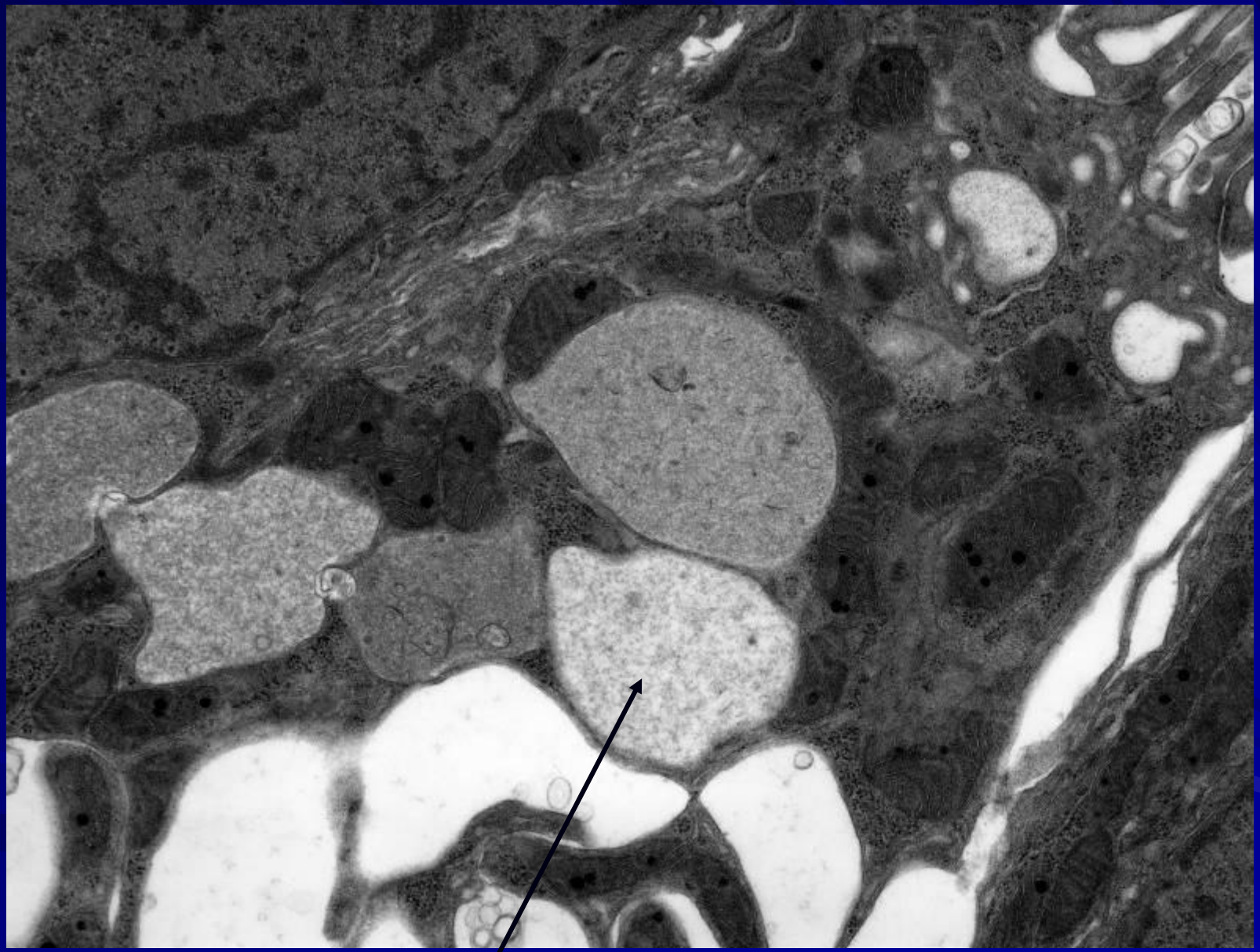


Diffusely swollen lysosomes

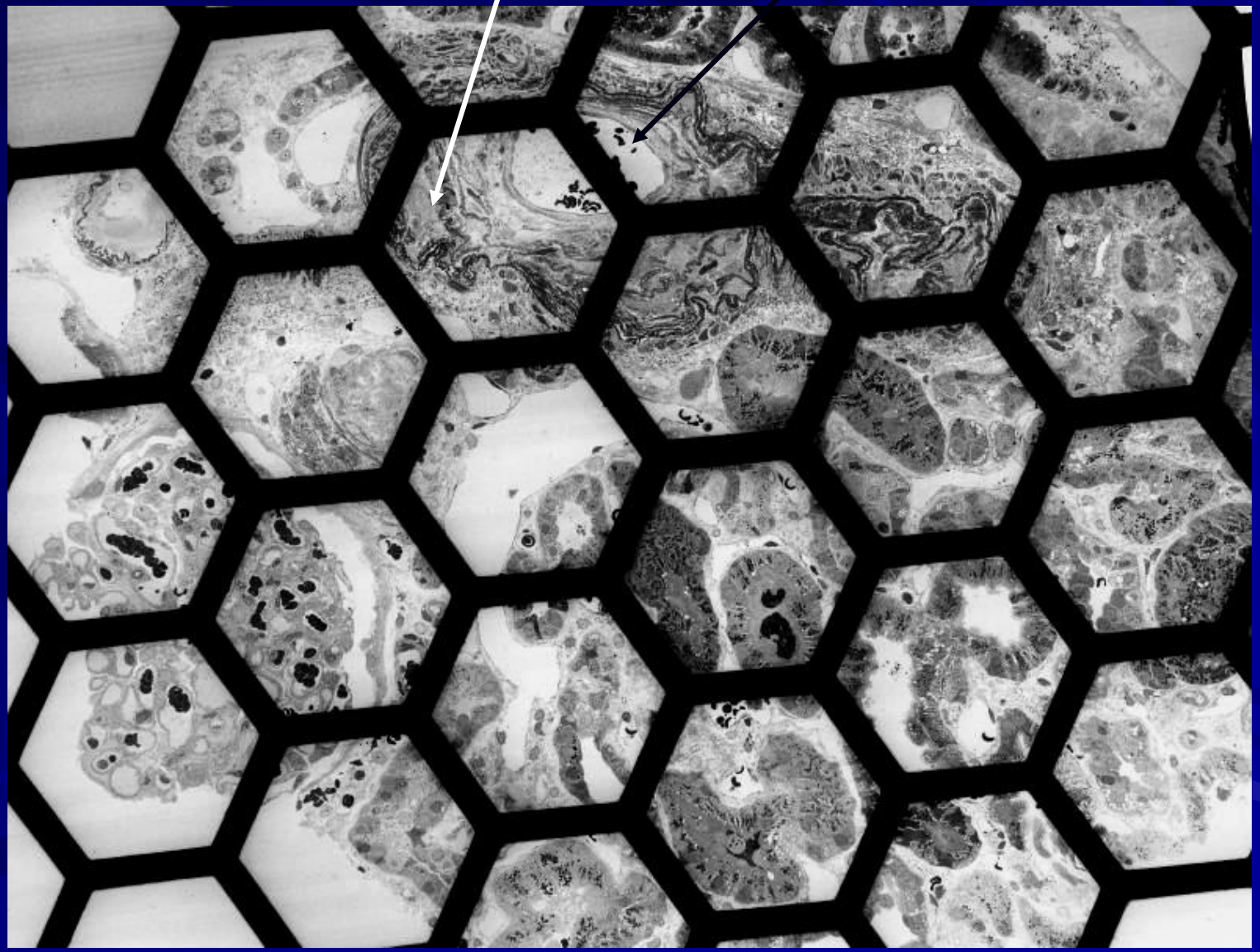
Hydropically swollen lysosomes have also been seen in:

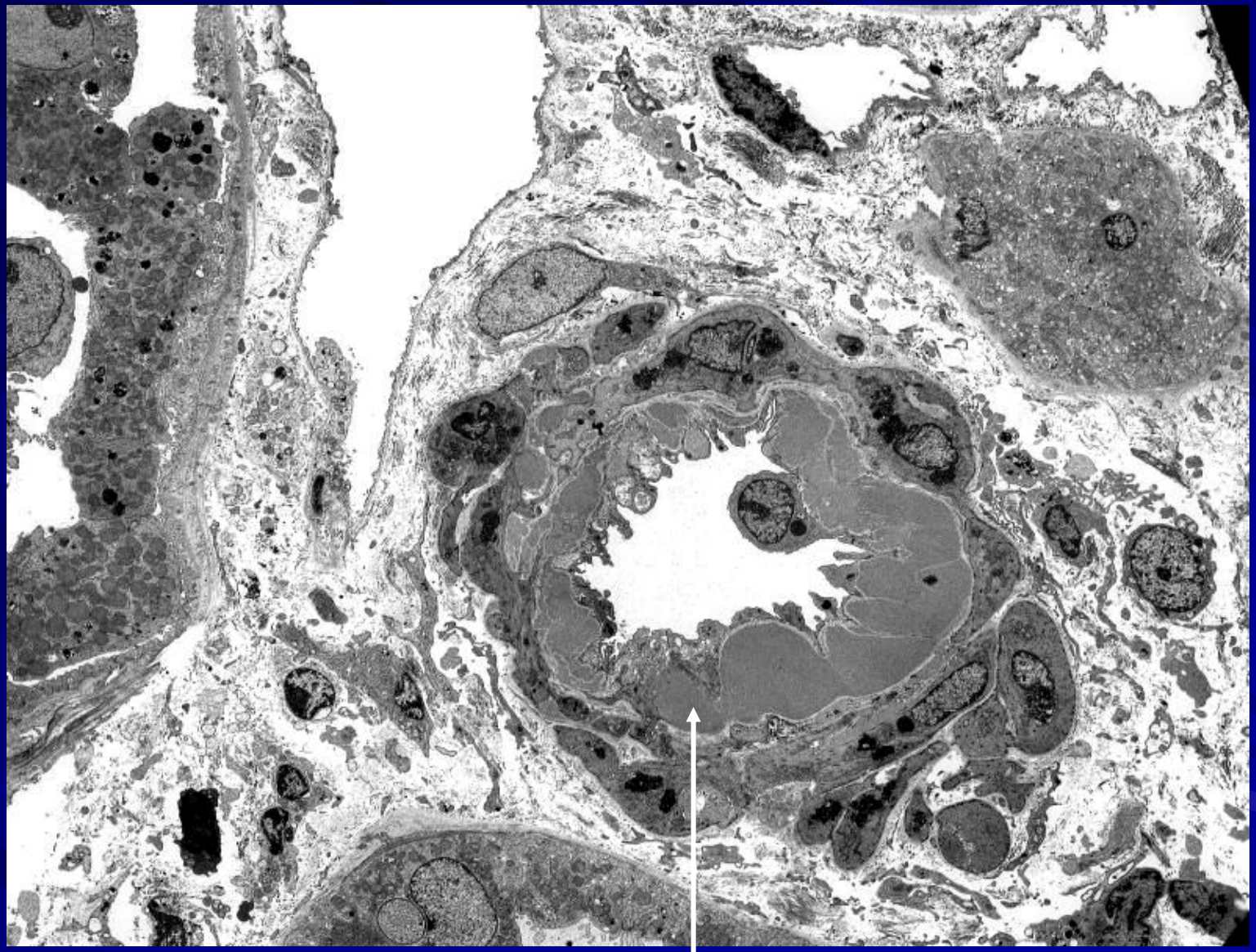
- Muscle biopsy in patient given colloid.
  J Hepatol 1986;3:223-227
- Skin biopsy in patient given amphipathic antibiotics.
  Personal observation G Mierau, Denver.
- Skin biopsy pre-treated with topical local anaesthetic. J
  Inherit Metab 27 (2004) 507-511

- On seeing the expanded lysosomes, I initially thought they might be cases of unsuspected lysosomal storage disorder.
- i.e. Pseudo lysosomal storage.

Vasculopathy

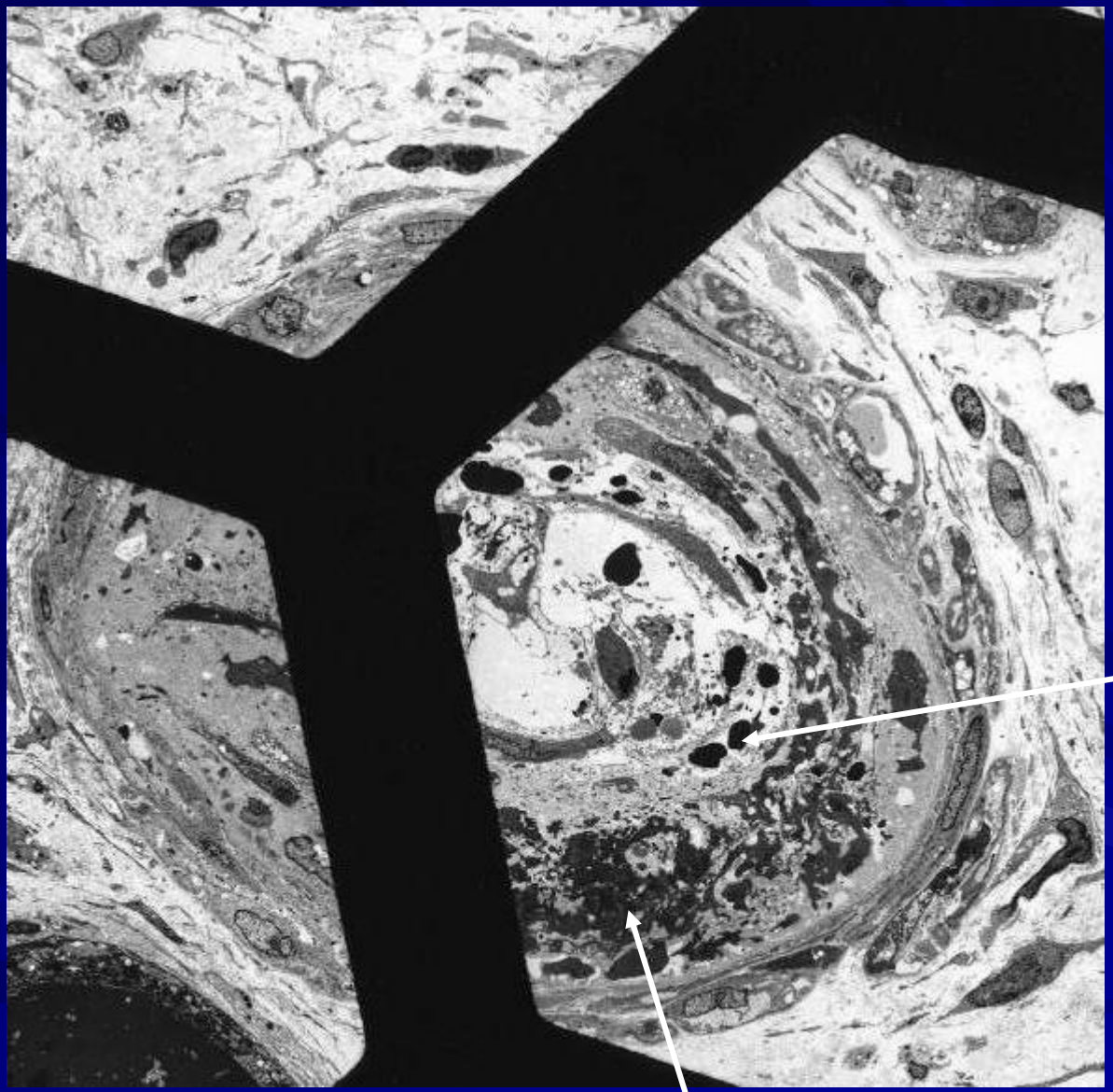
Chronic hypertensive elastic reduplication and lumen narrowing



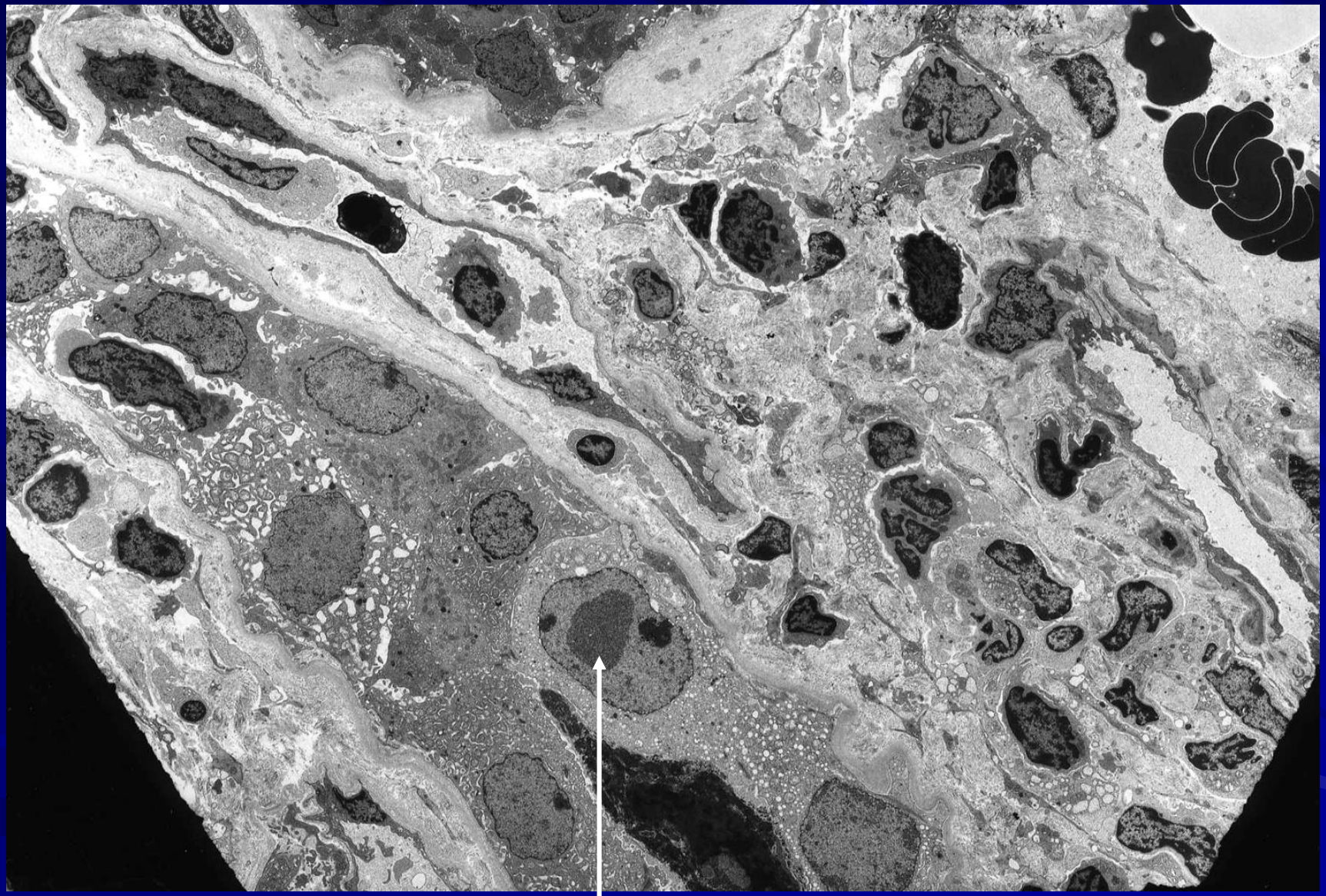


Hypertensive arteriolar hyalinosis

Malignant phase hypertension



Viral infection
BK polyoma



Distal convoluted tubule intranuclear inclusion

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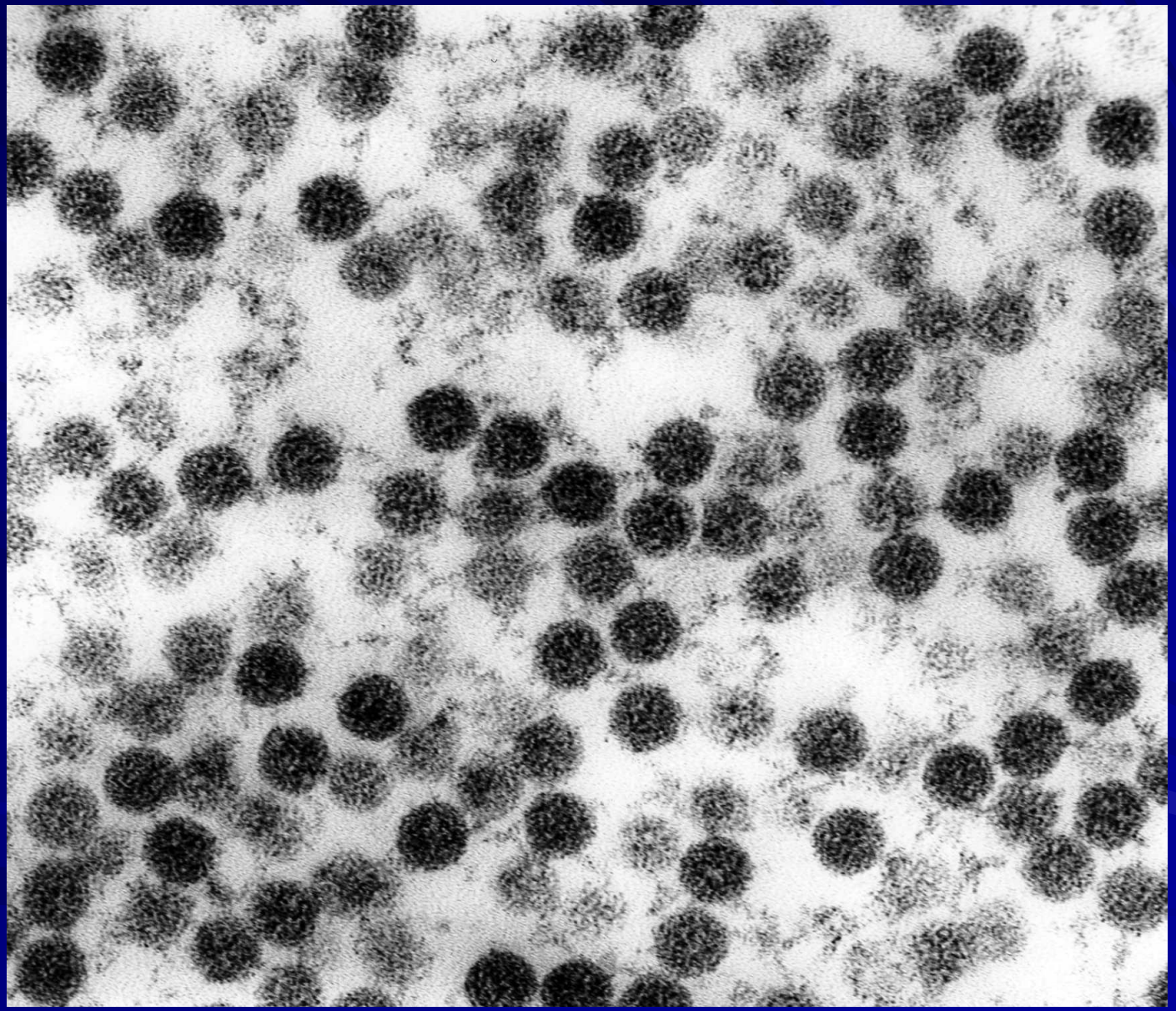
Intranuclear inclusion formed of numerous polyoma virus particles



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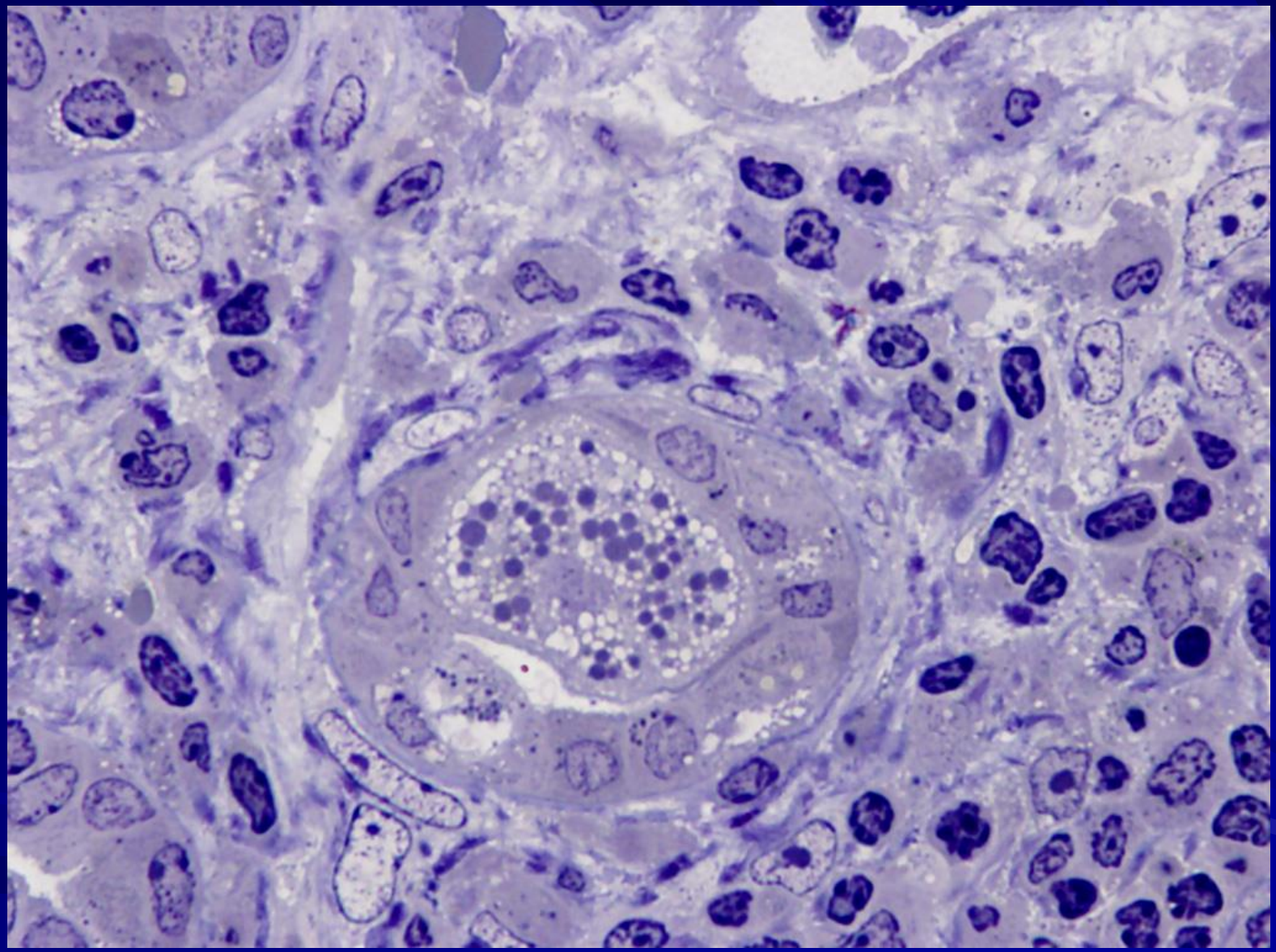
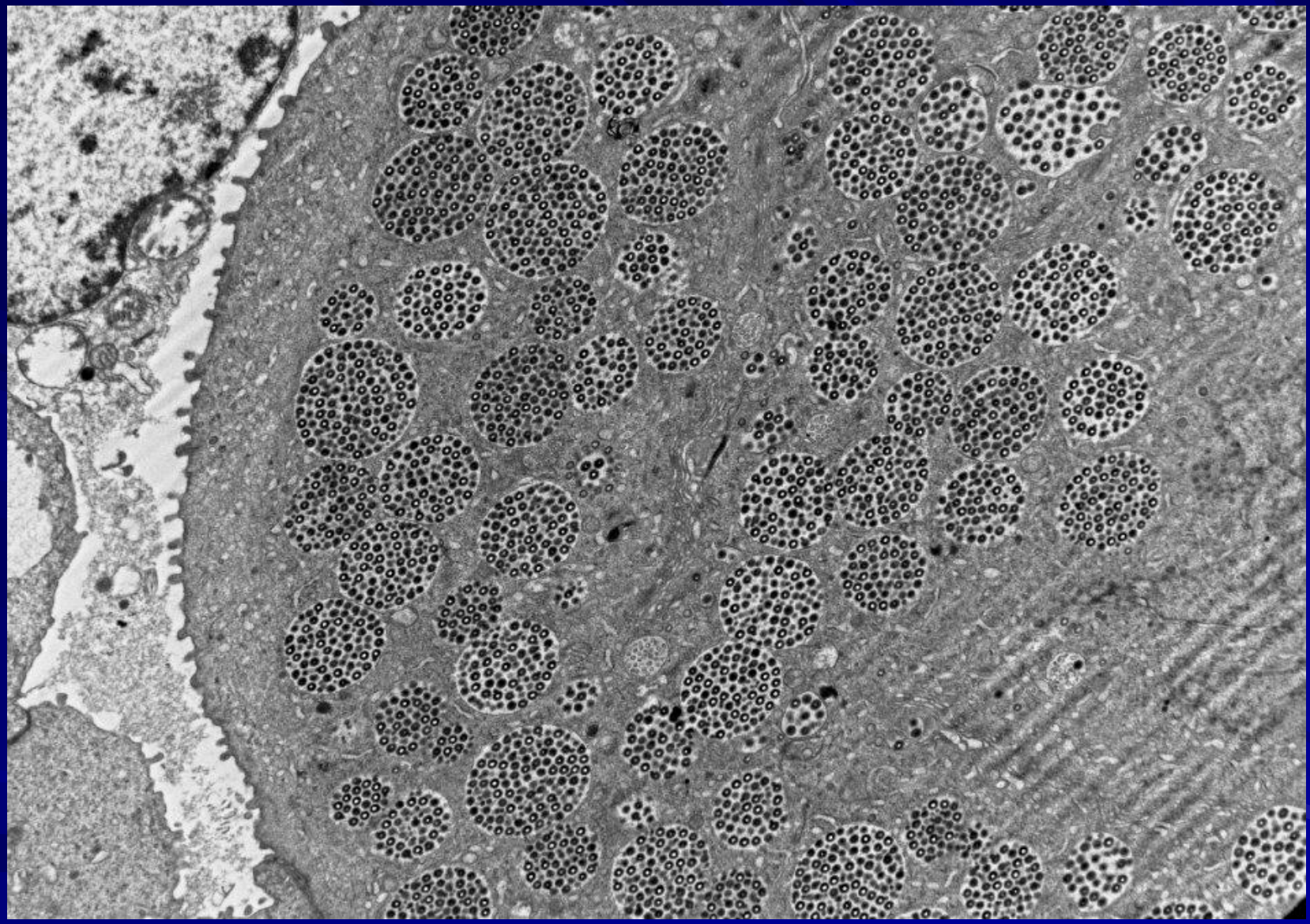
Cytomegalovirus
CMV

Transplant kidney



Case from Dr Michael Mengel, Greifswald, Germany. With permission.

Case from Dr Michael Mengel, Greifswald, Germany.



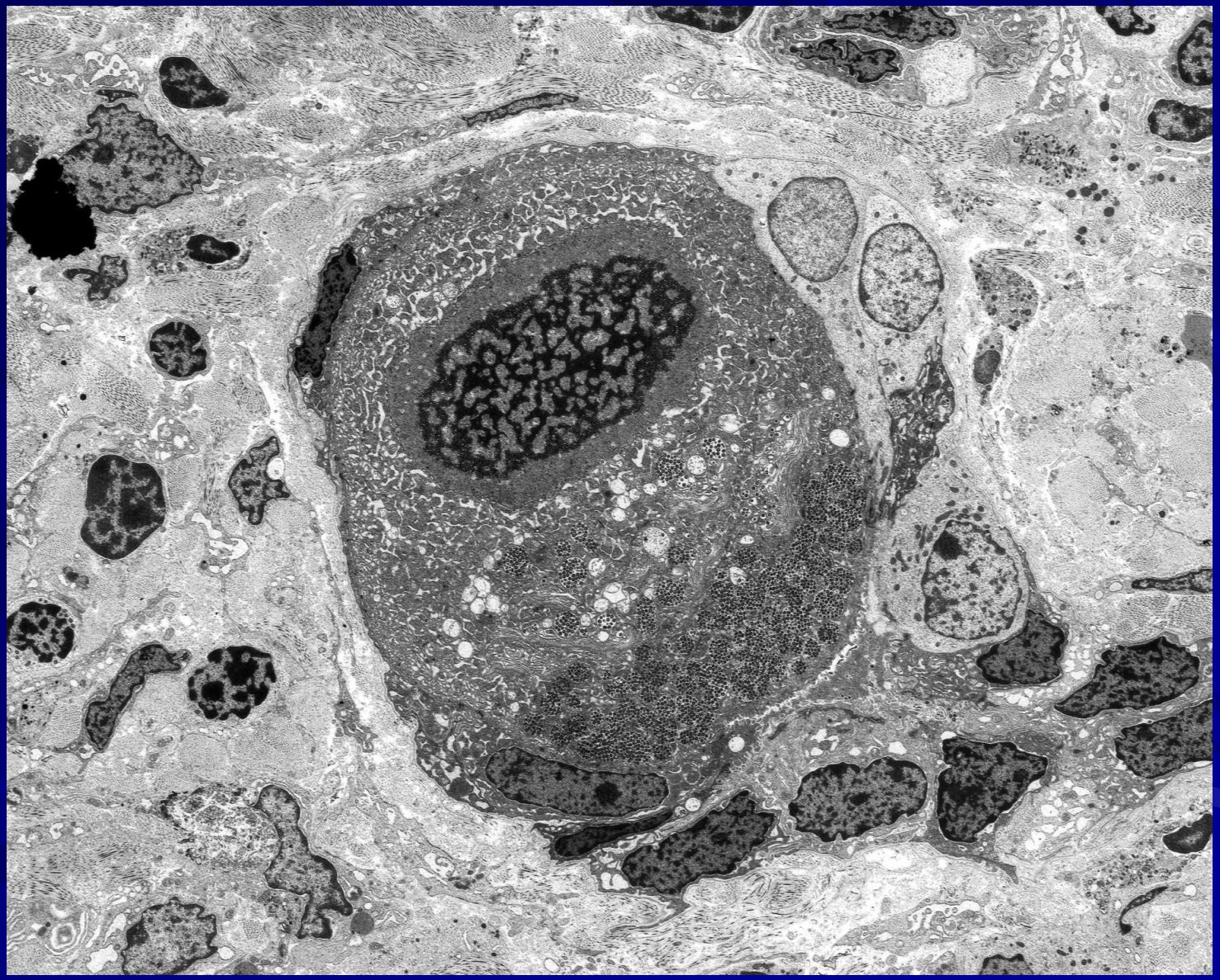
Nucleus not in plane of section

Intracytoplasmic vesicles filled with virions

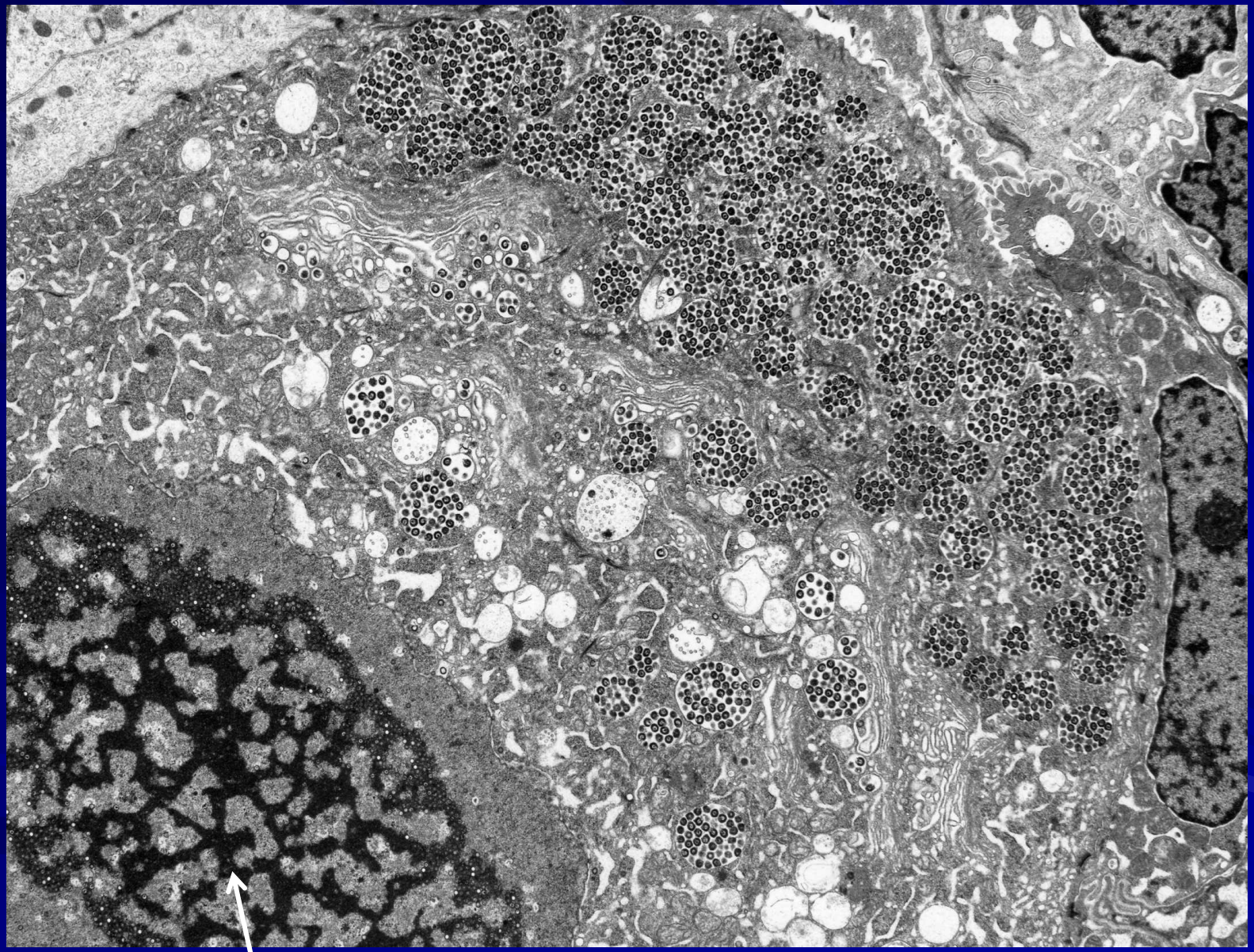
CMV

Liver biopsy

Liver biopsy. CMV in intraportal tract bile duct cholagiocyte



CMV in liver biopsy



‘Owls eye’ intranuclear inclusion

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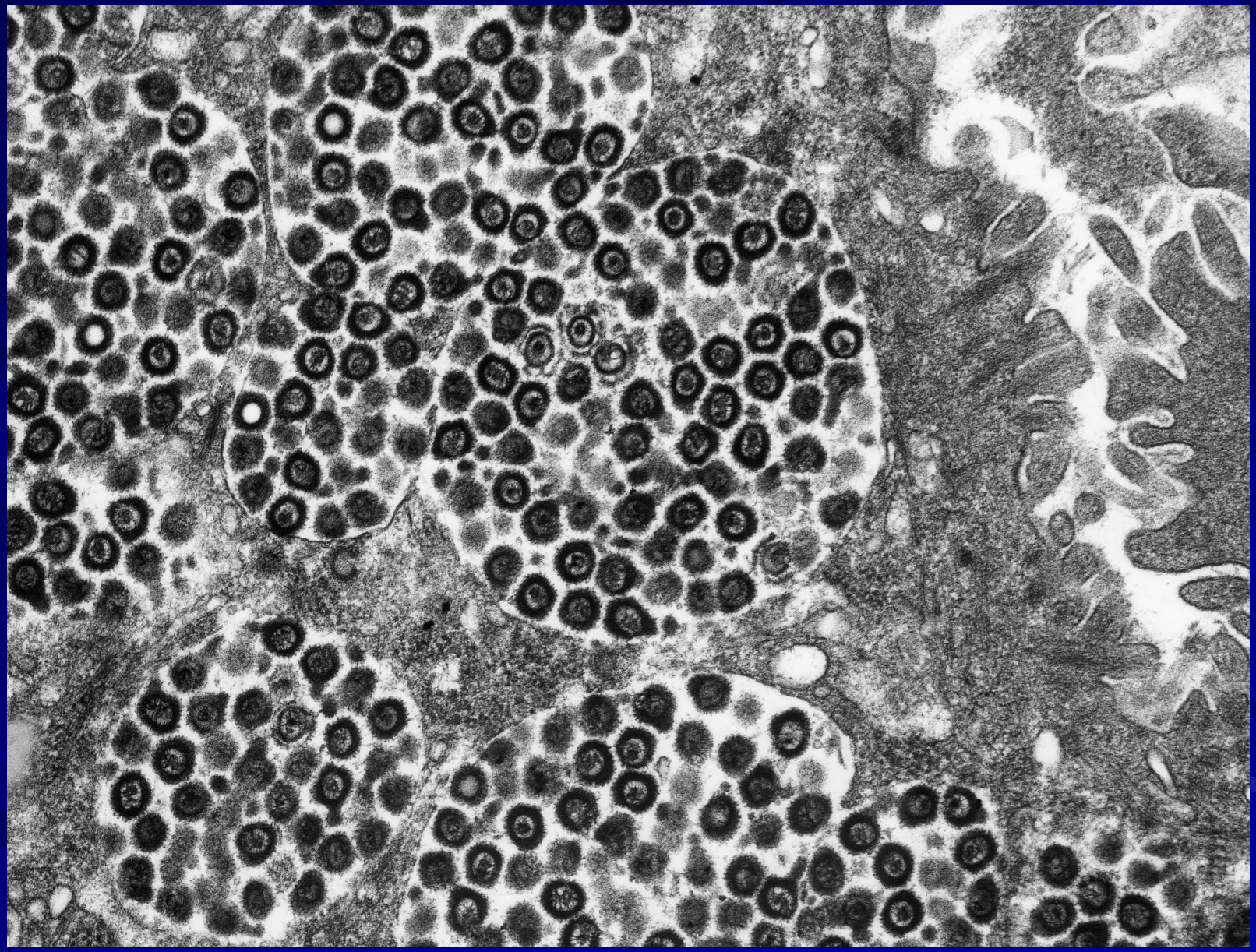

Intracytoplasmic vesicles filled with typical herpes group virions

Final comments

- Do toluidine blues on all biopsies and add description to light microscopy report.
- When choosing which block to cut thin sections off, choose the one with glomeruli that are neither completely normal nor sclerosed, and has the most glomeruli, but not one with GBM wrinkling.
- Either, do EM on all renal biopsies, in which case expect to be confirmatory in 50% of cases, and to change diagnosis partially in 25%, and completely in 25%.
- Or, if being selective as to which cases should do EM on, should be done on 60% of cases.
- As for which cases to choose: heavy proteinuria, uncertainly of diagnosis, unexpected findings on light microscopy immunofluorescence or resin sections, clinicopathological miss-match.
- If having difficulty in interpreting EM findings:
  HAVE A LOOK AT ANOTHER GLOMERULUS.
- If requesting a second opinion, send with clinical details, histology and IF report, and EM images in step magnifications.

I hope you enjoy these lectures.

You are more than welcome to use these images for your own lecture purposes, with acknowledgement – but I'd rather you didn't use them for publication, in print or on a web site, without checking with me first.
If you have any diagnostic EM related queries do contact me on bart.wagner@sth.nhs.uk
and I'd be happy to try to help you out.

Bart Wagner

Don’t forget the group photo!

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