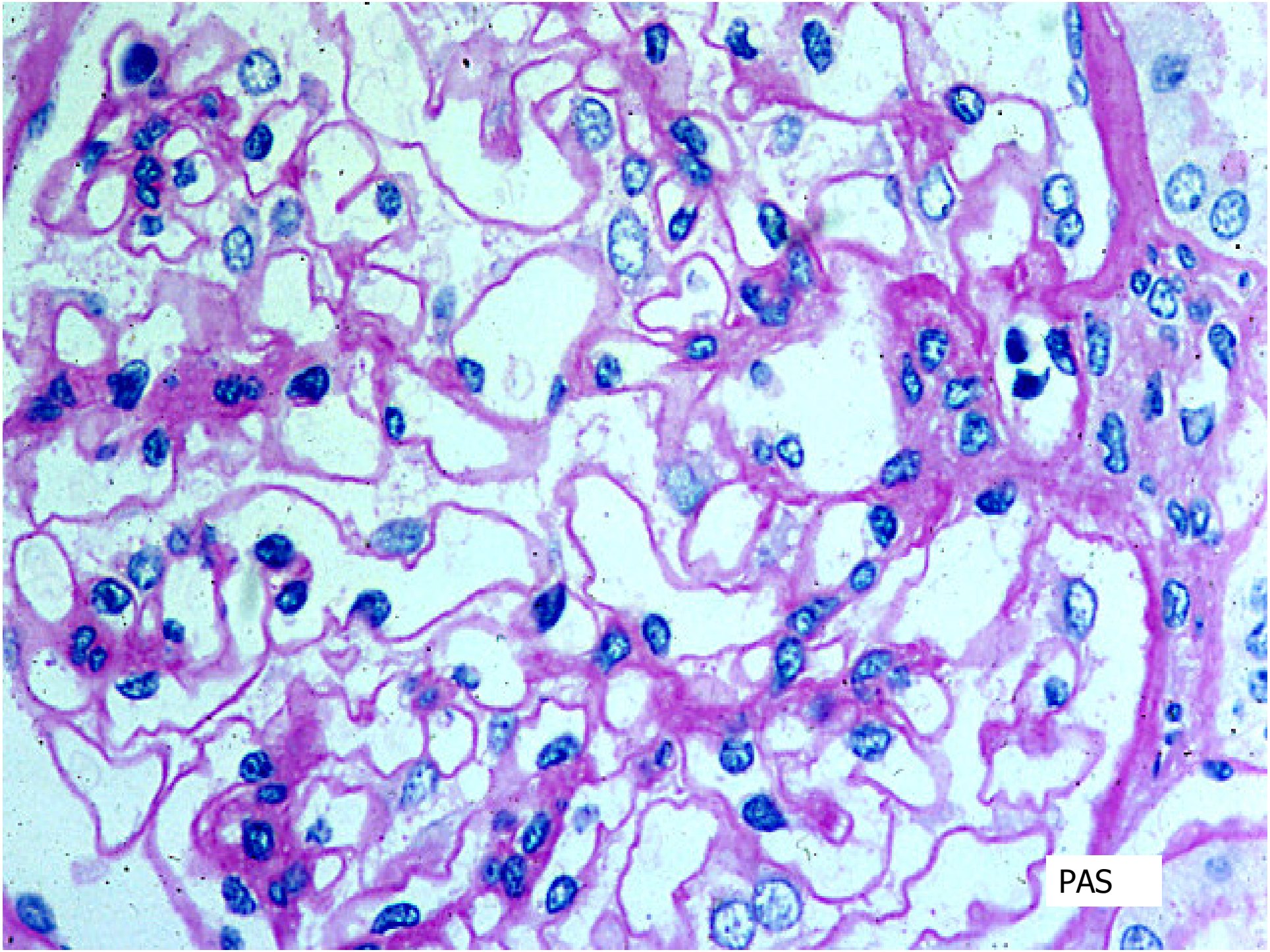
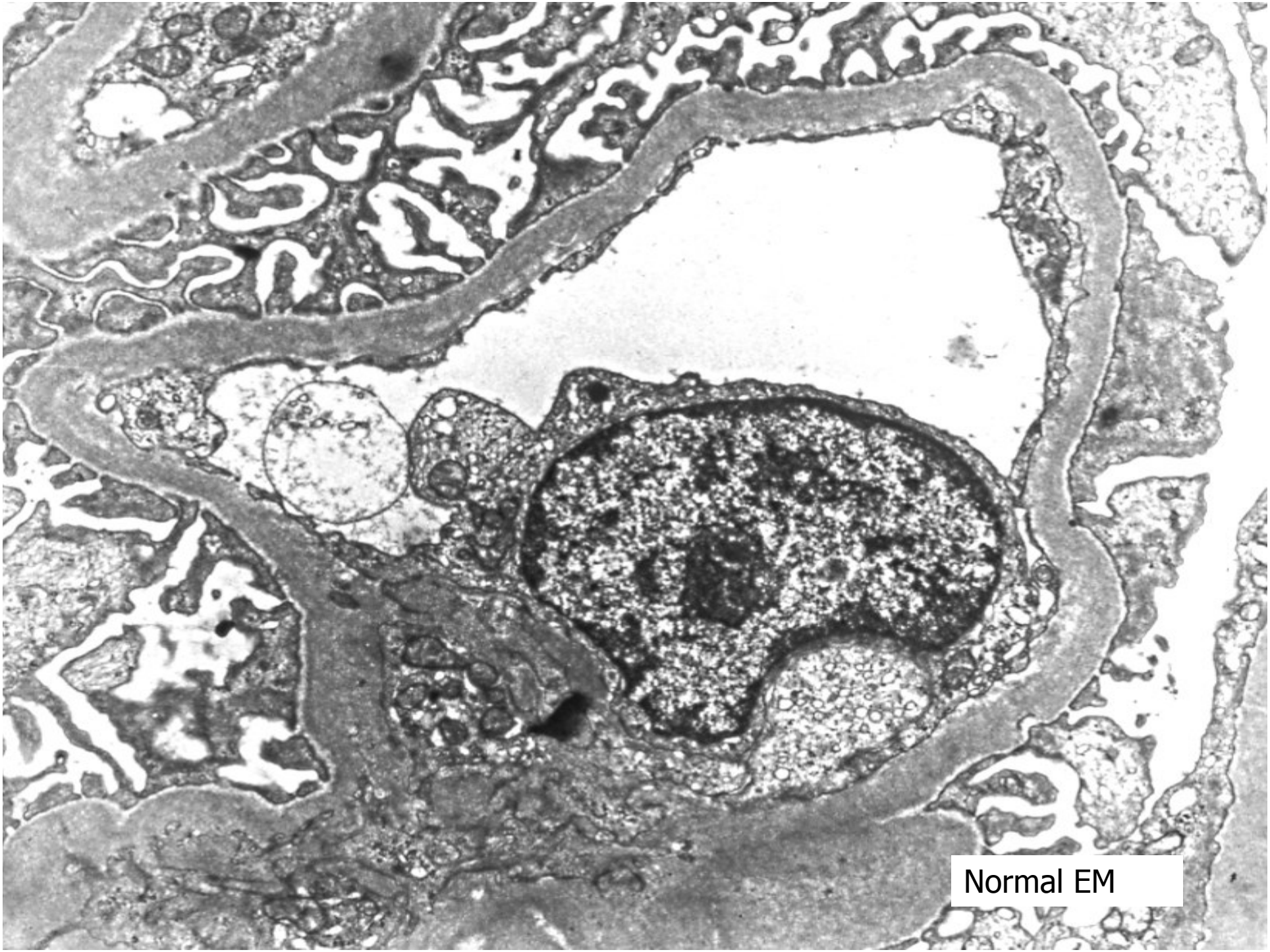
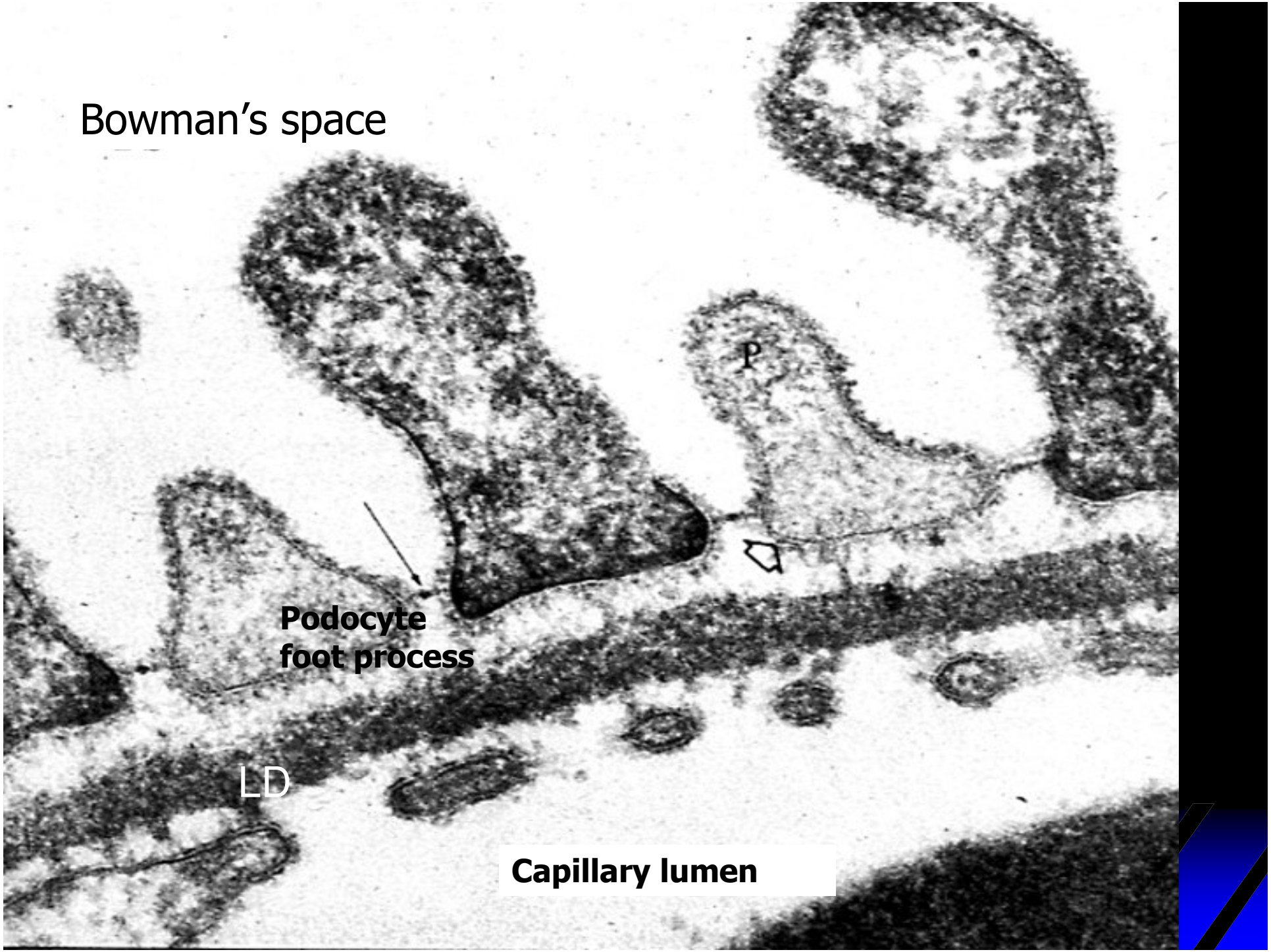
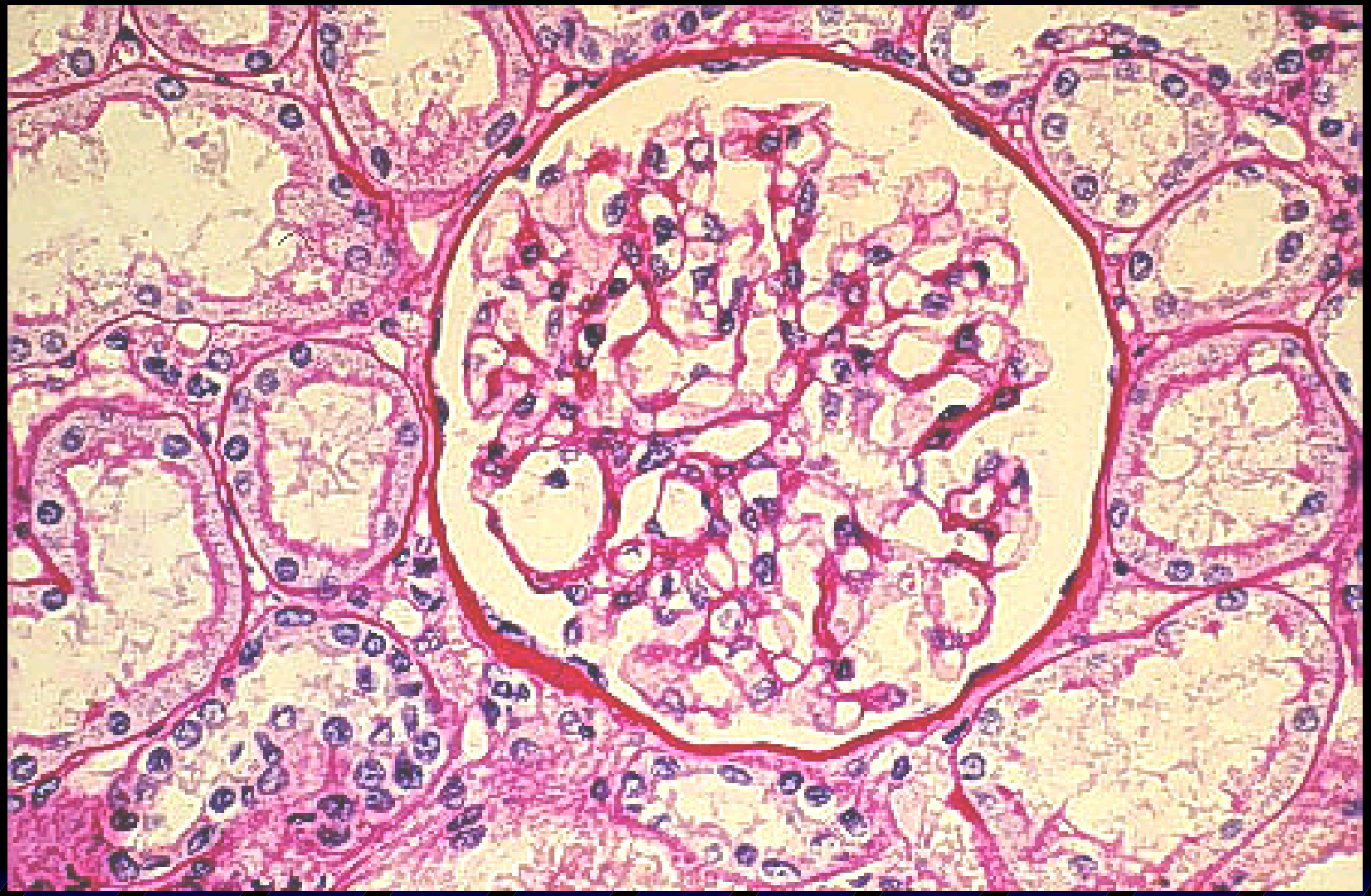

PAS


Normal EM

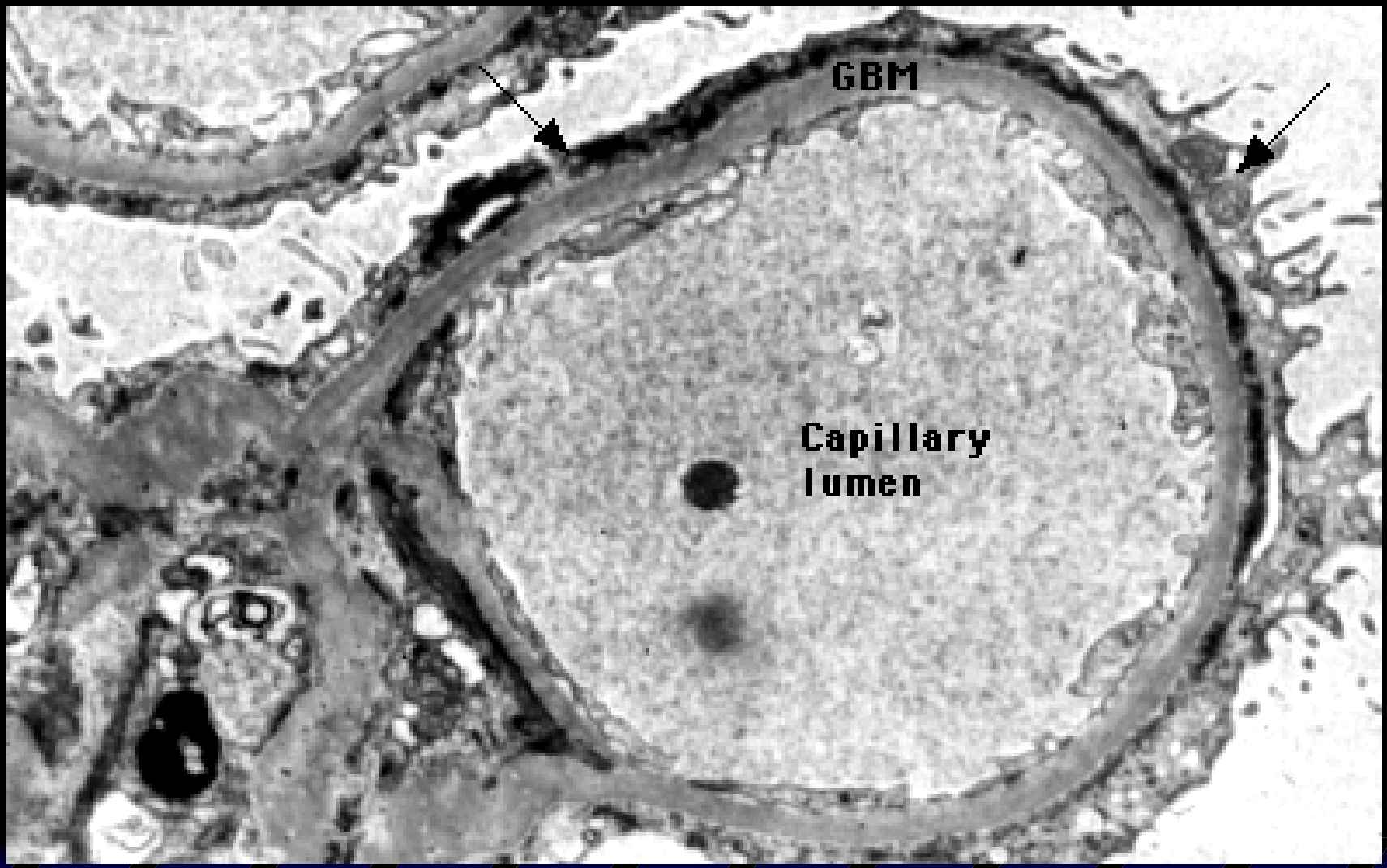

Bowman's space
P
Podocyte
foot process
LD
Capillary lumen

- A 24 yr old man had been taking indomethacin for back pain. He noted sudden edema. BP was 140/96, urinalysis 3+ proteinuria, creatinine 80 umol/L. What is the likely diagnosis?
  - Minimal Change Nephropathy
  - Interstitial nephritis
  - Membranous GN
  - SLE
  - Diabetes

Normal glomerulus



Minimal change nephropathy



Minimal change

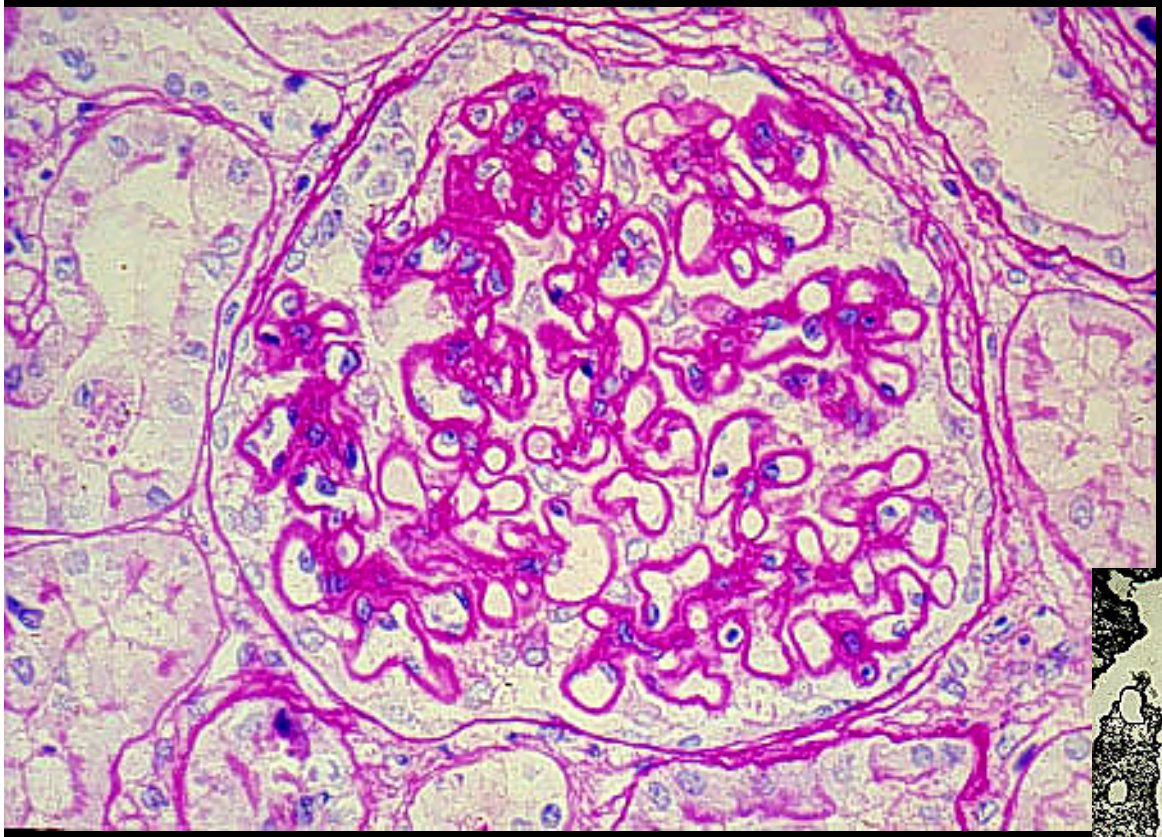
- Nephrotic syndrome , mostly children
- T-cell disorder
- some FGS are misdiagnosed
  - ? TGFB1 gene expression useful here
- causes
  - NSAIDs, rifampicin,ampicillin,interferon
  - Hodgkins
  - gold, lithium, tiopronin (rare)

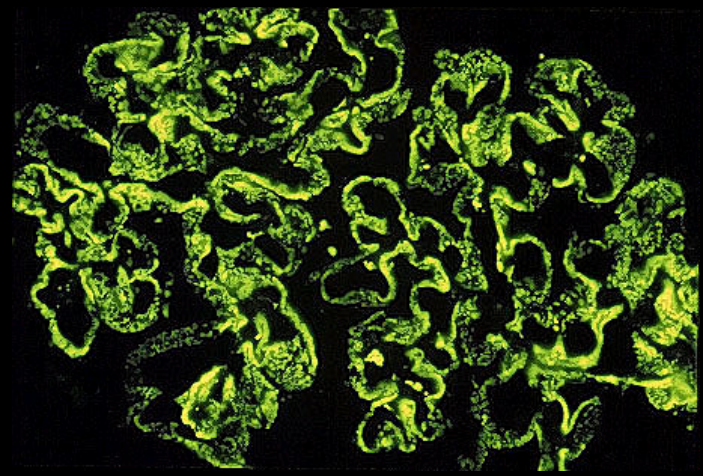
Treatment of adult MCN

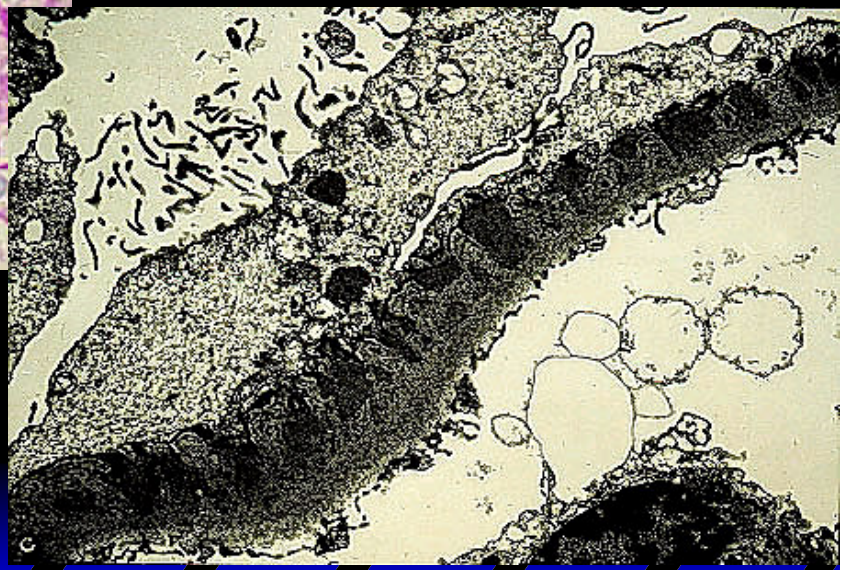
- Steroids 2-4 months or until 1 week post remission, then taper 1-2 months
  - 90% response
- 30-50% relapse within 1 year
- frequent relapsers or steroid dependence
  - cyclophosphamide
  - Cyclosporin

- A 40 yr old man develops edema. Urinalysis shows 3+ protein and urine protein is 3.1g/day. Serum albumin is 30 and creatinine 90 umol/L. Renal biopsy shows membranous GN. Which of the following is correct?
  - He is likely to have renal vein thrombosis
  - He should receive steroids alone
  - He should receive ACEI but no immunosuppression unless his condition worsens
  - He has a 25% risk of underlying Cancer
  - He has a 25% risk of underlying SLE

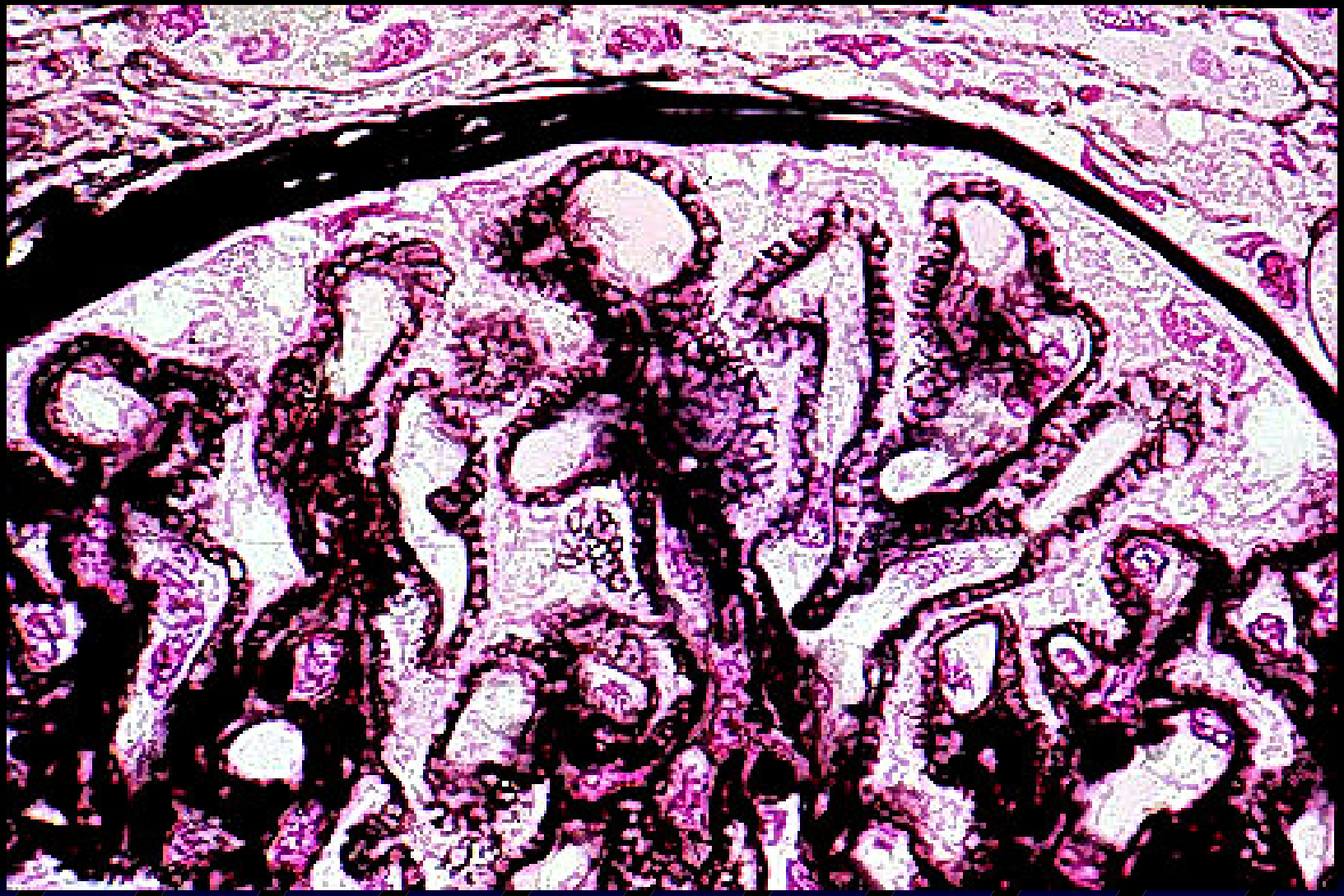
Membranous GN







Membranous GN

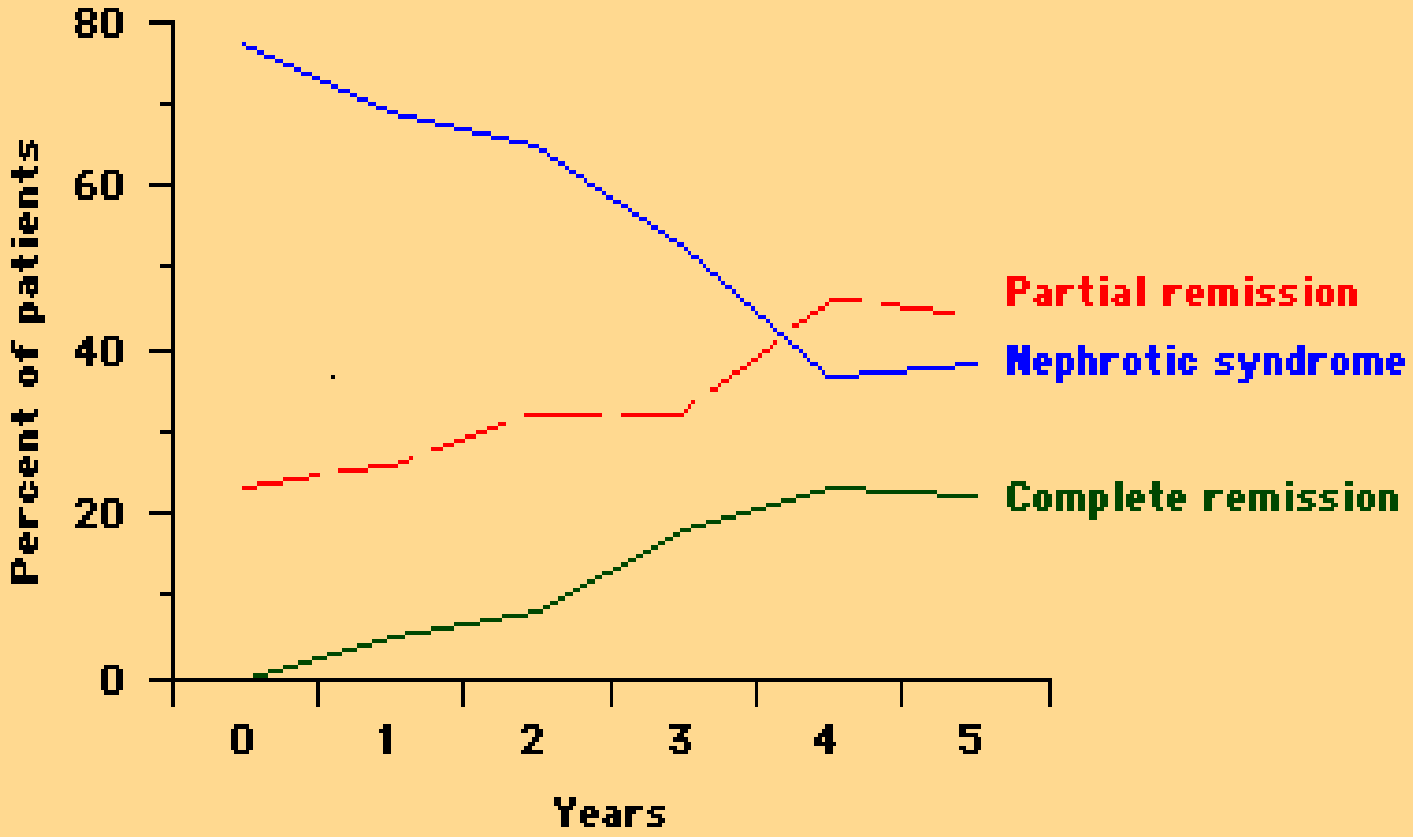


Membranous GN

- **Causes**
  - malignancy
  - drugs
  - SLE / RA / other CTs
  - Hep B / C
  - schistosomiasis
  - syphilis
  - Sarcoid

- podocyte-expressed M-type secretory phospholipase A2 receptor (PLA2R) is the target of autoantibodies in MGN

Natural history of membranous GN



Membranous GN

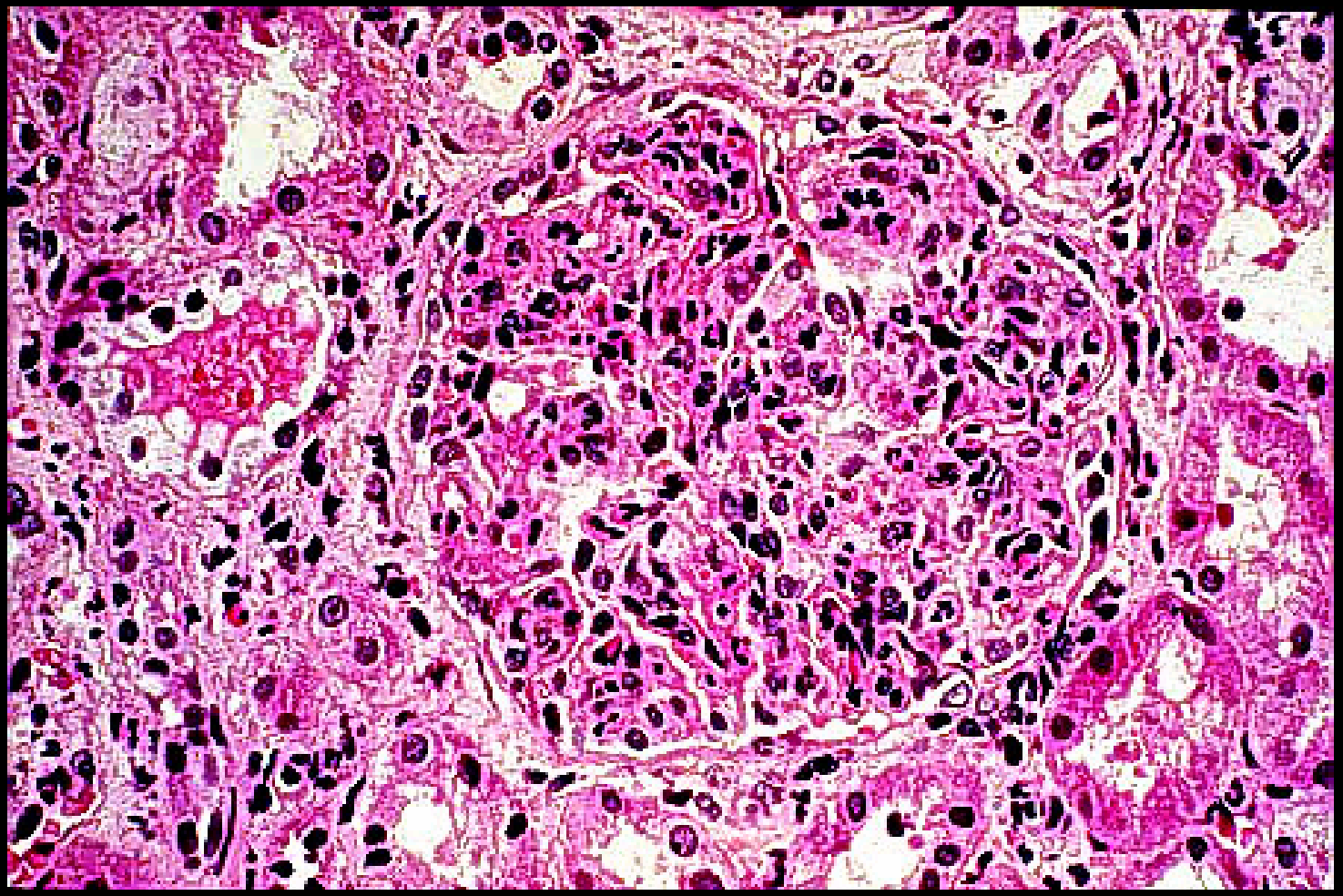
- **Highest risk**
  - males > 50 yrs
  - proteinuria > 10g/d
  - raised creatinine at presentation
- **Best prognosis**
  - women, young adults
  - non-nephrotic
  - drug induced

Treatment of membranous GN

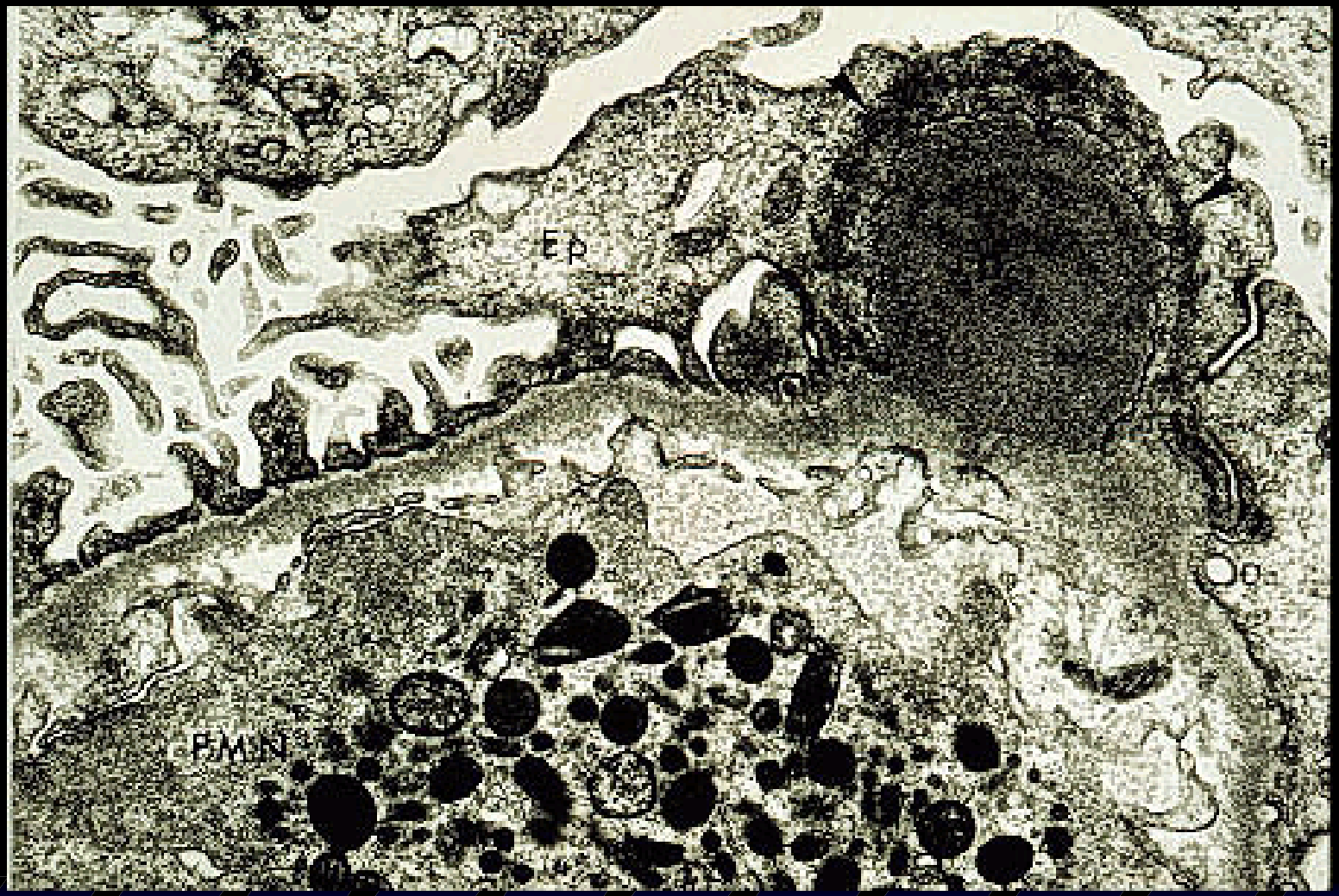
- **Non- nephrotic normal GFR**
  - observe 6 months for remission or progression
- **High risk for progression or thrombi**
  - steroids alone inadequate
  - chlorambucil / steroids for 6 months
  - cyclophosphamide / steroids 6 months
- other options
  - Cyclosporin / NSAIDs / ACEI

- A 20 yr old woman went swimming in a public pool in Fiji. She returned to Australia almost 3 weeks later feeling generally unwell with numerous impetigo-like skin lesions. Soon after she developed oliguria. Creatinine rose to 1000 umol/L and urine showed rbc casts and 2+ proteinuria. The most likely diagnosis is:
  - Post streptococcal GN
  - SLE
  - Leptospirosis
  - Adult Henoch Schonlein purpura
  - Dengue fever

Post - infectious GN



Subepithelial ‘hump’ in PSGN



PSGN

- Almost all recover completely
  - hematuria lasts 3-6 months
  - proteinuria in 15% at 3 yrs
  - 1% ESRF
- steroids not of benefit
- some develop late (10 - 40 yrs)
  - proteinuria
  - hypertension
  - renal insufficiency

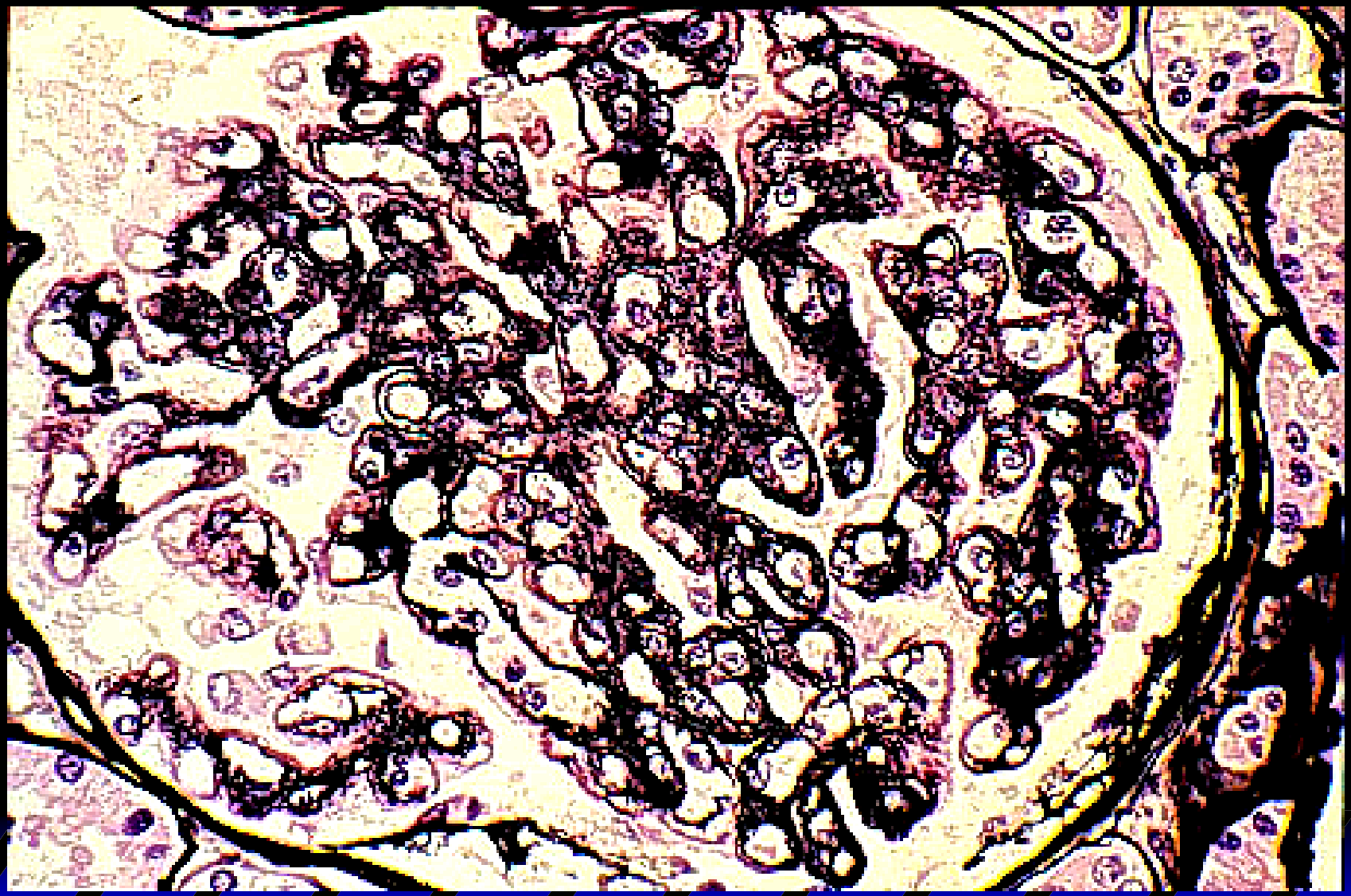
MCGN

- Type 1
  - mesangial & subendothelial deposits
- Type 2
  - dense deposits BM, tubule membrane
- Type 3
  - subepithelial deposits predominant
  - large lucent areas in BM

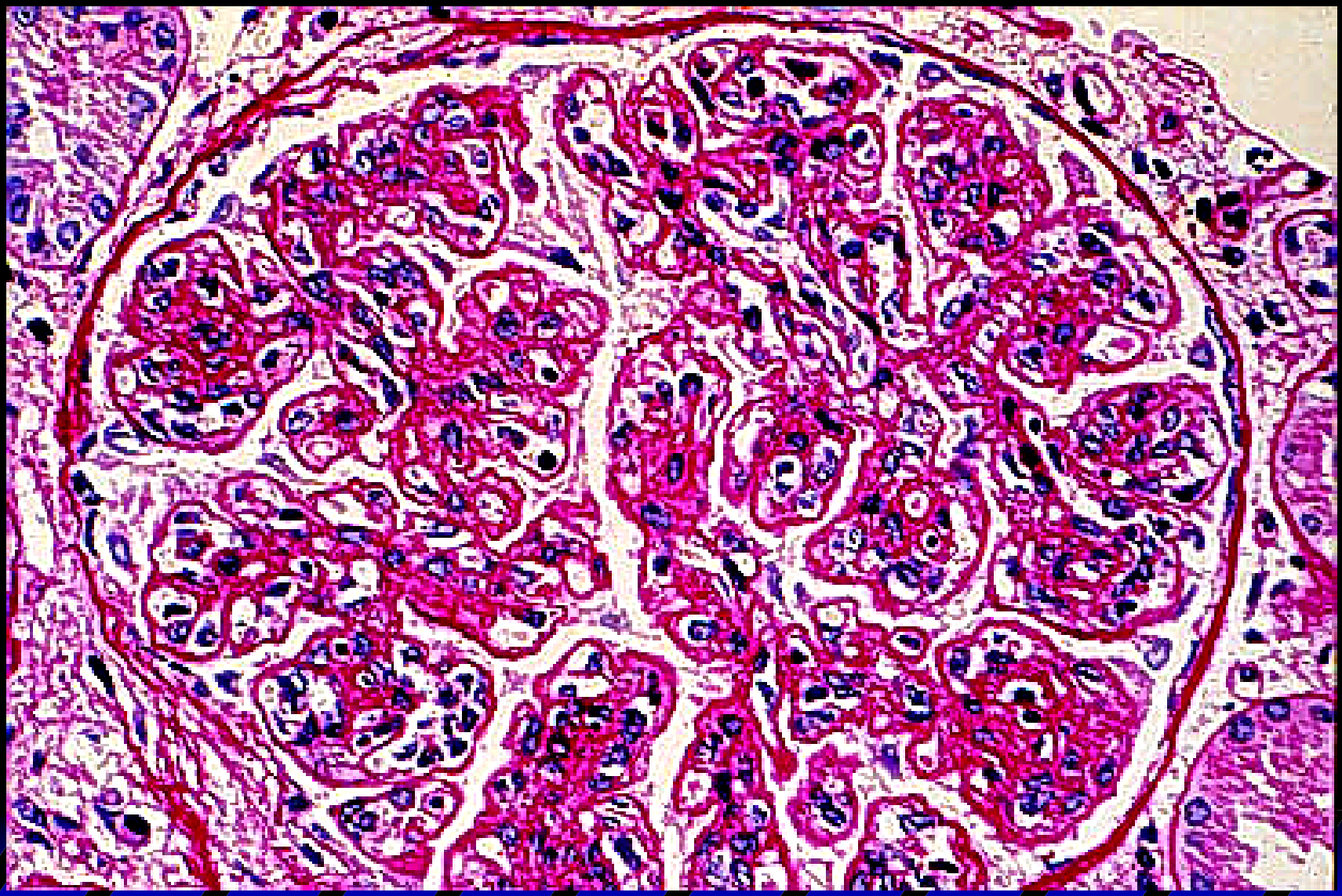
Mesangiocapillary GN

- **Type 1**
  - SLE / Sjogren's
  - Hep B / C
  - mixed cryoglobulinemia
  - IE / schistosomiasis / shunt nephritis
  - chronic visceral abscess
  - CLL / NHL / leukemias
  - a1 antitrypsin deficiency
- **Type 2**
  - dense deposit disease
  - C3 NeF / partial lipodystrophy
- **Type 3**

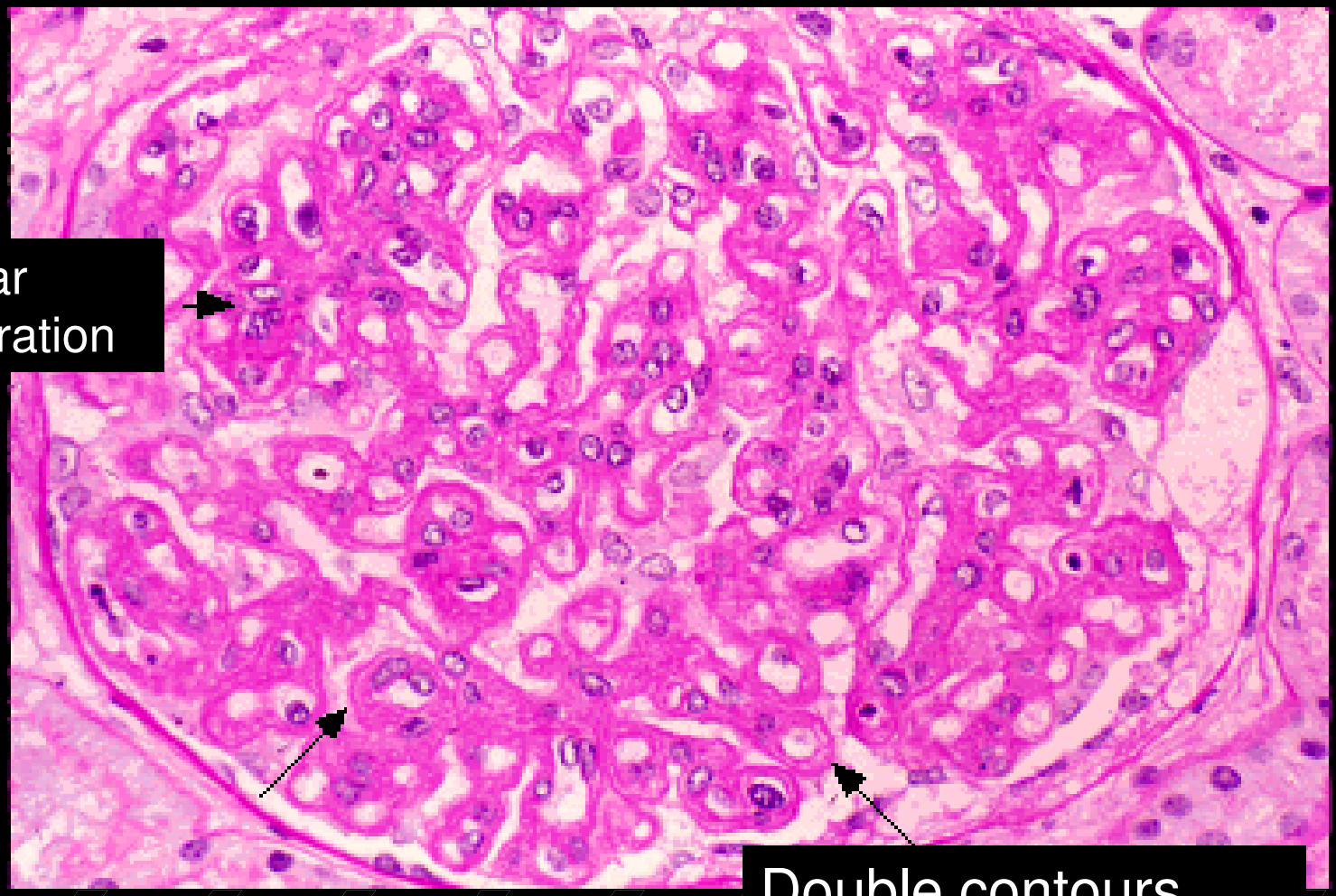
MCGN Type 1



MCGN Type 1



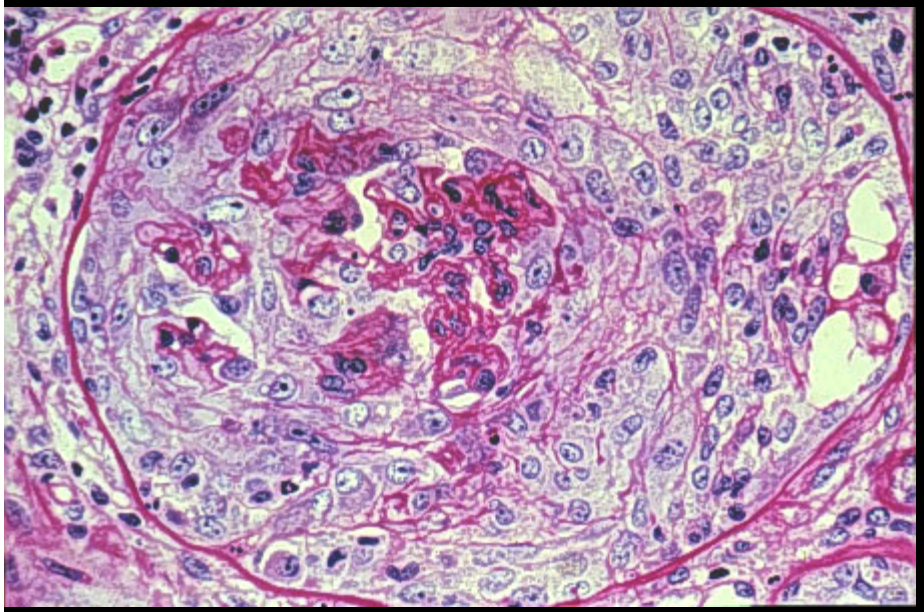
MCGN Type 1

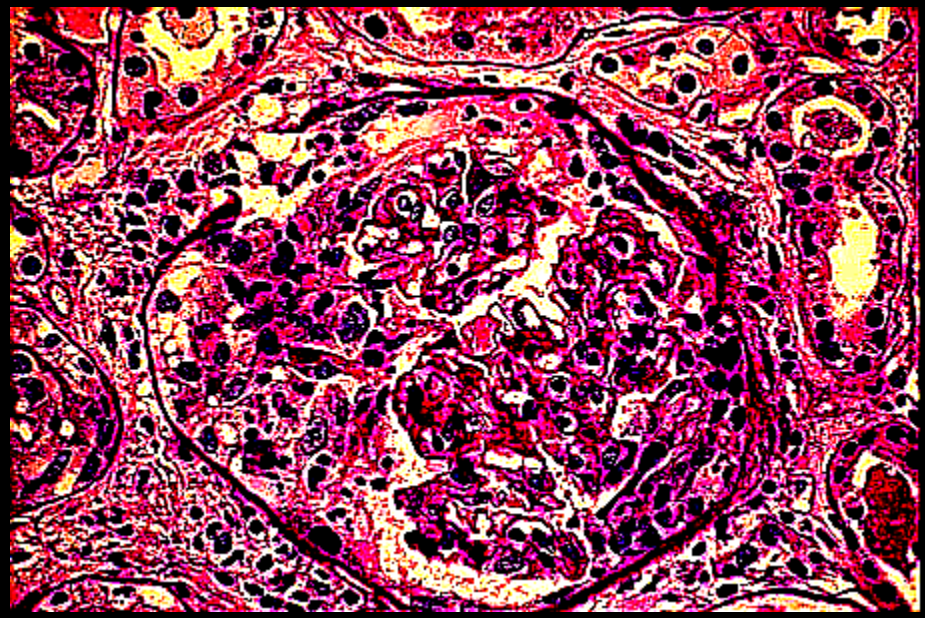


Mesangiocapillary GN

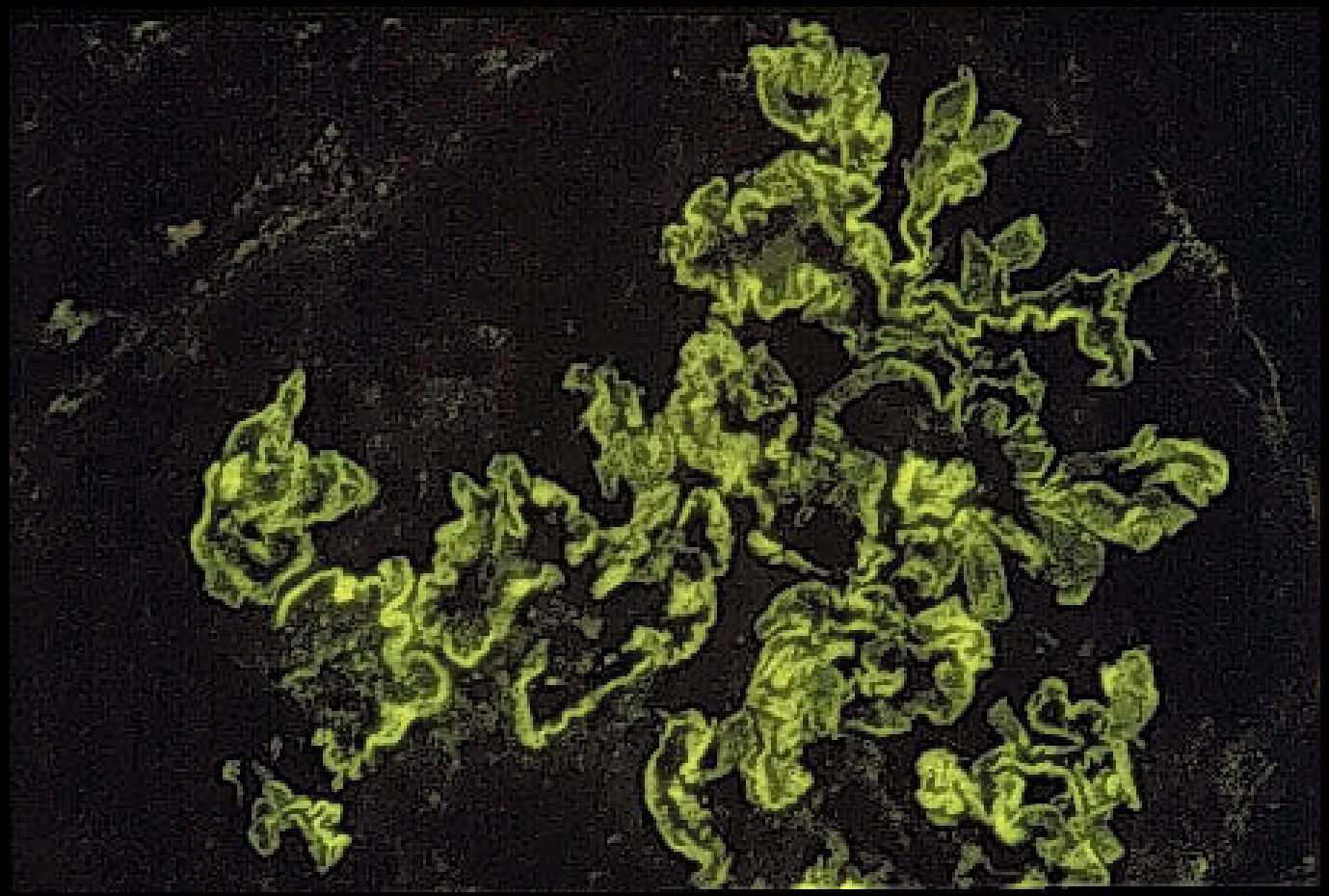
- **Outcome**
  - 10% spontaneous improvement
  - 30% unchanged
  - 60% ESKD 10-15 yrs
- **Treatments**
  - steroids – uncontrolled data
  - +/- aspirin, dipyridamole
- no treatment of proven benefit

Crescentic Glomerulonephritis + fibrinoid necrosis

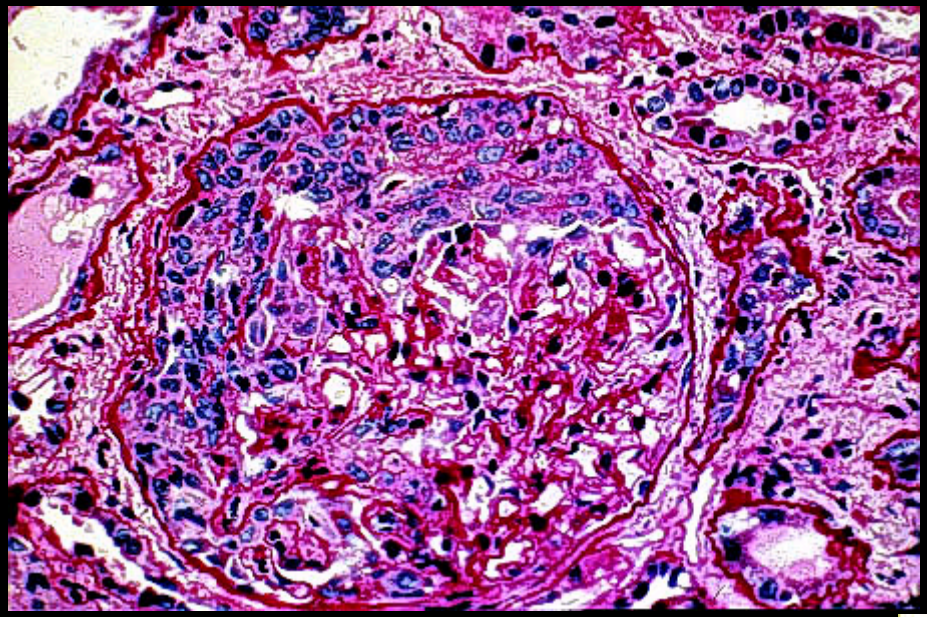




Anti - GBM disease

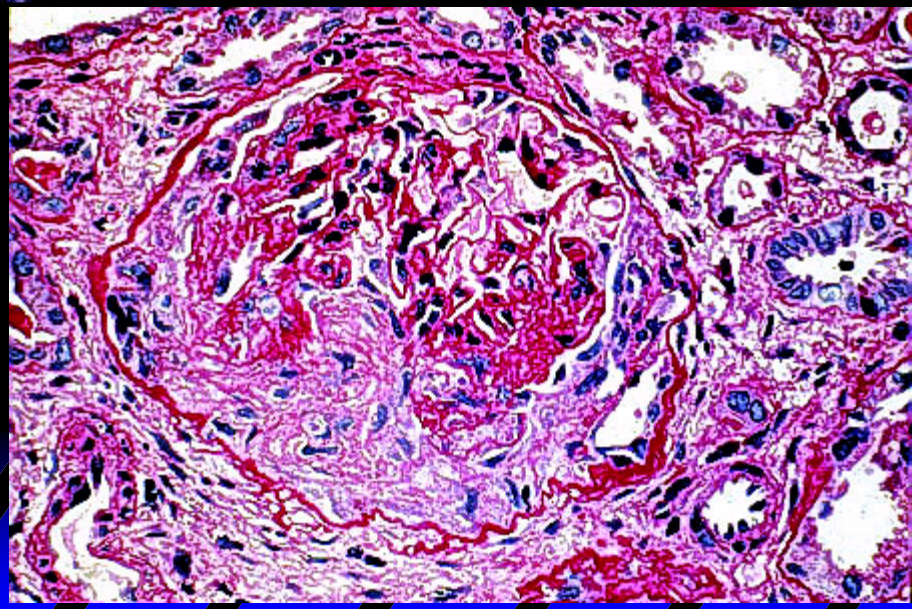


Crescentic GN



cellular

fibrosis



Crescentic GN

- **Type 1** (10%) - antiGBM Ab
  - Goodpasture's
- **Type 2** (45%) - immune complex
  - IgA / membranous / PIGN
  - HSP
  - SLE
  - cryoglobulinemia
  - IE
- **Type 3** (45%) - pauci-immune (ANCA)
- Type 4 : features of Type 1 and 3

Treatment of Crescentic GN

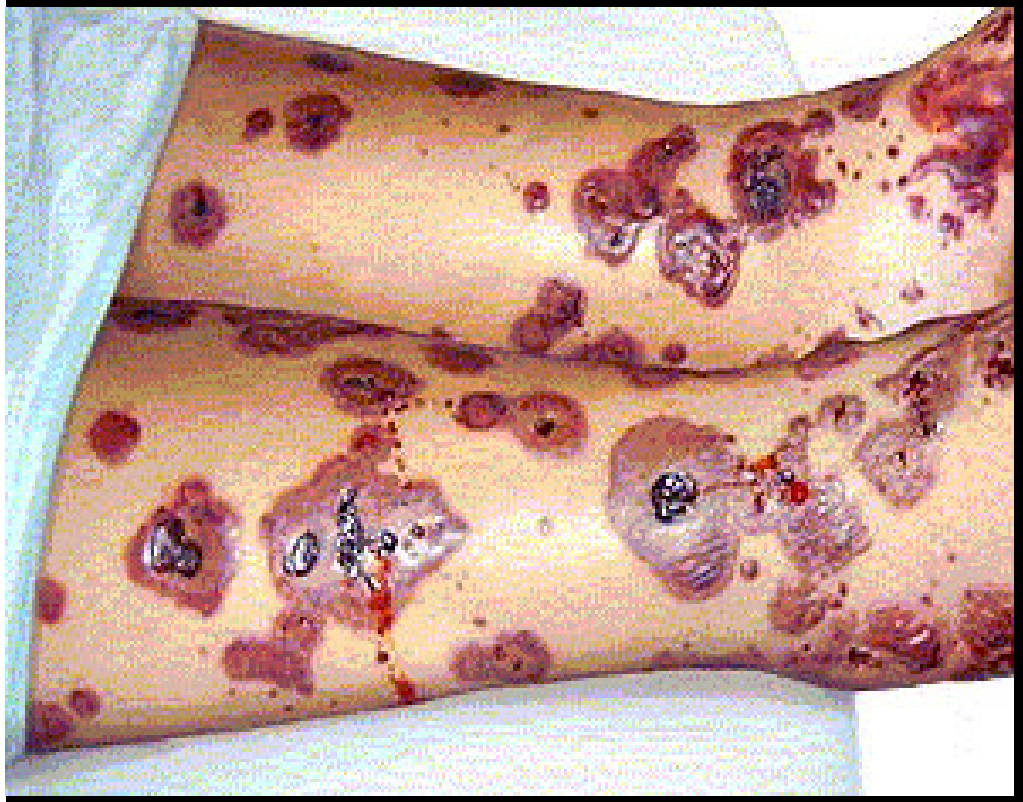
- **Type 1**
  - plasma exchange
  - steroids / cyclophosphamide
  - select if
    - pulmonary haemorrhage
    - creatinine < 600 umol/L
  - remainder worse with therapy

Treatment of Crescentic GN

- **Types 2 / 3**
  - Plasma exchange if dialysis dependent or lung haemorrhage
  - steroids / cyclophosphamide
  - benefits may occur even if dialysis dependent eg. Wegner's

QUESTION 29

A week after a flu like illness, a 22-year-old presents with a haemorrhagic rash on the lower extremities (as shown in the figure below), and generalised arthralgia. The serum creatinine is elevated (125 μmol/L, [<110 μmol/L]) and there is blood and protein in the urine.



The most likely finding on renal biopsy is:

A. glomerular microangiopathy (haemolytic-uraemic syndrome).

B. mesangiocapillary glomerulonephritis.

C. Henoch-Schönlein nephropathy.

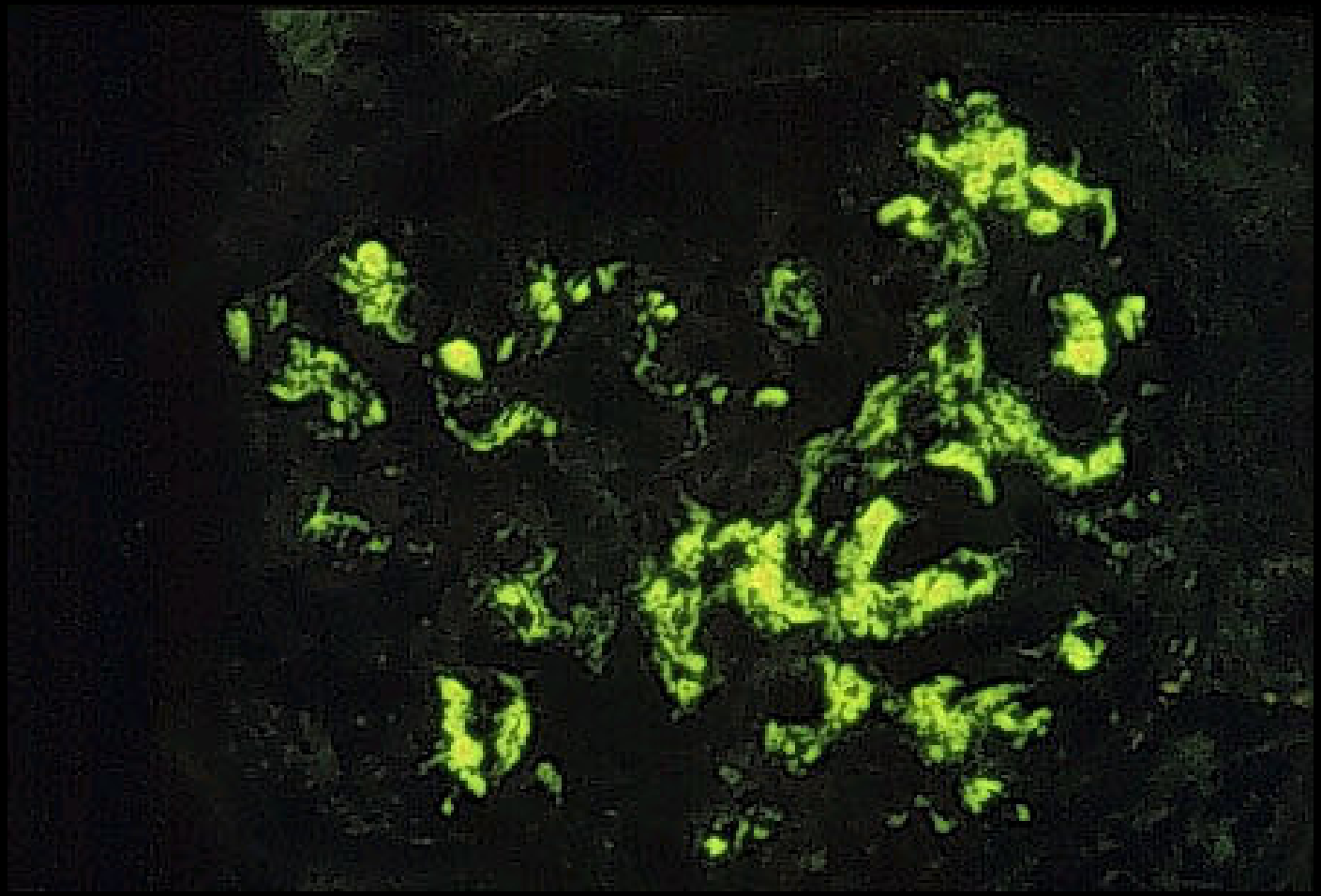
D. antineutrophil cytoplasmic antibody (ANCA) positive vasculitis.

E. lupus nephropathy.

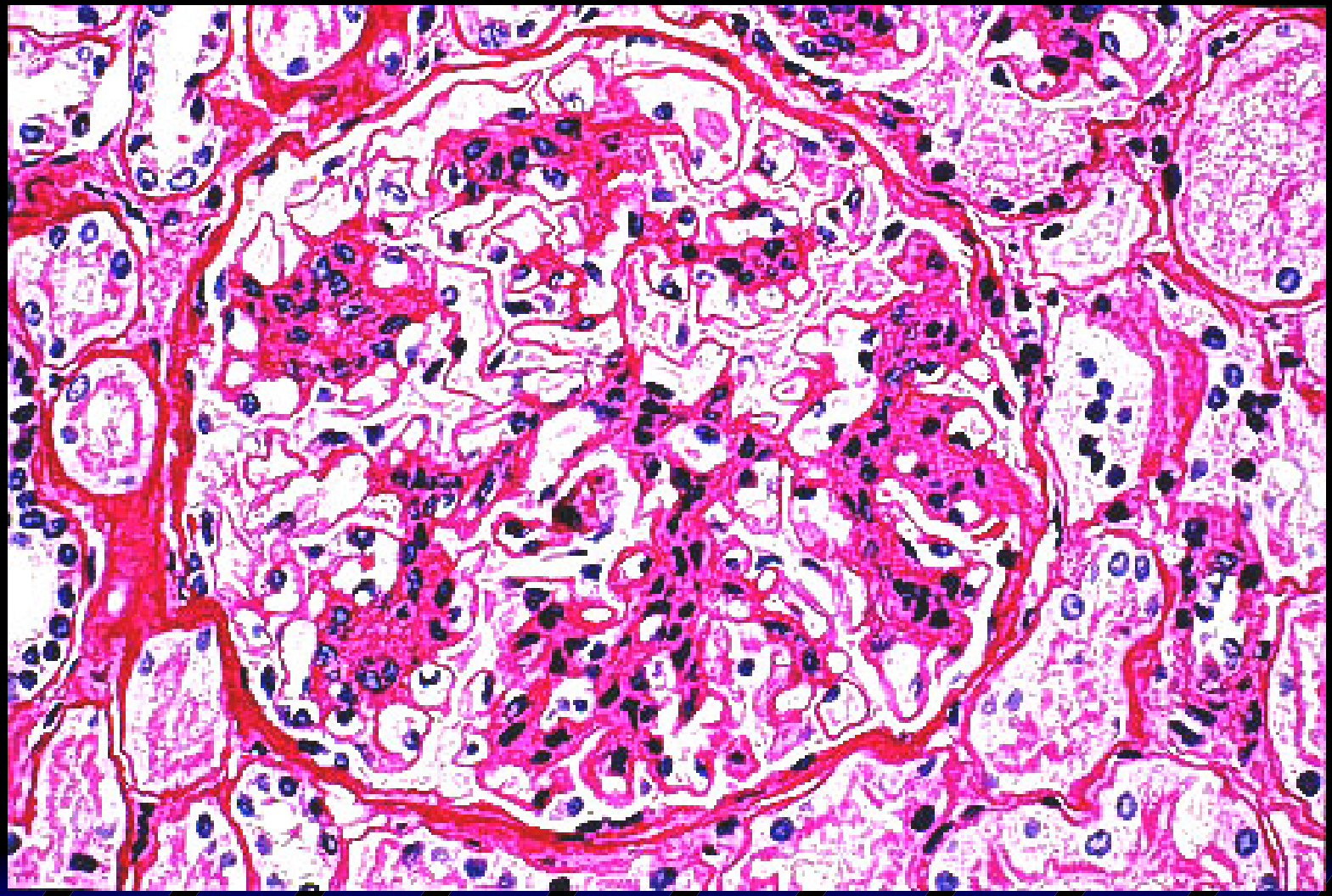
IgA nephropathy

- **Causes**
  - cirrhosis
  - coeliac disease
  - dermatitis herpetiformis
  - seronegative arthritis
  - HSP
  - HIV
  - mycosis fungoides
- **Course**
  - 15% CRF 10 yrs
  - 20% CRF 20 yrs
  - further 20% renal insufficiency at 20 yrs
  - **possibly underestimates**

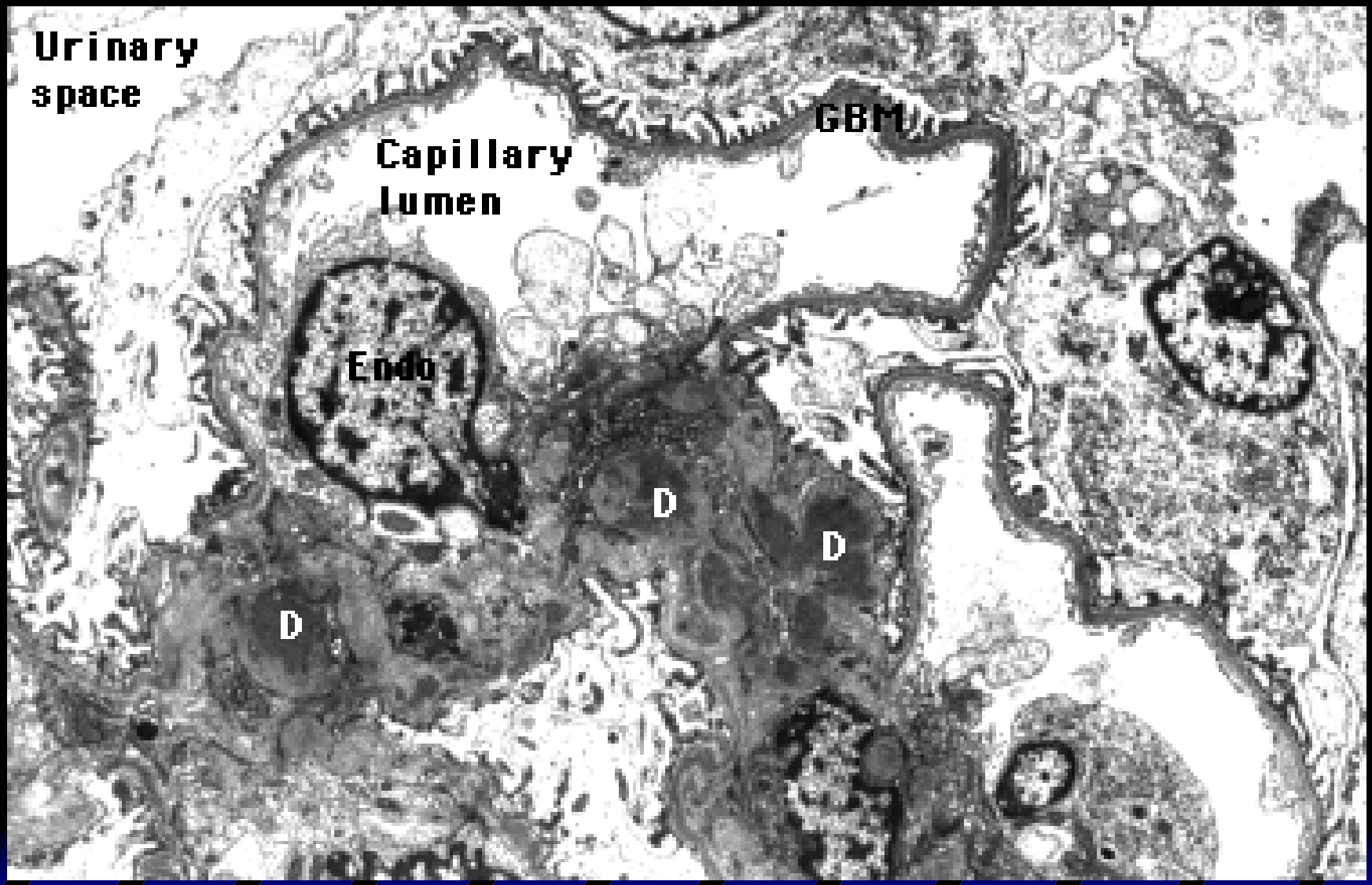
IgA nephropathy



IgA nephropathy



IgA nephropathy



IgA nephropathy

- **Predictors of progression**
  - impaired GFR at presentation
  - proteinuria > 1g / d
  - hypertension

  - glomerulosclerosis
  - interstitial fibrosis
  - crescents

IgA nephropathy

- **Treatments** (all unproven)
  - steroids
  - cyclophosphamide
  - fish oil
  - CyA
  - ivi immune globulin
  - ACEI

Trials of patients with proteinuric IgAN

Table 1 | Comparison of recent trials of patients with proteinuric IgAN[1,2]

Parameter	Manno *et al.*[1]		Lv *et al.*[2]	
	ACEI arm	Combination* arm	ACEI arm	Combination* arm
Number of participants	46	45	29	31
Mean baseline eGFR (ml/min/1.73m²)‡	98	100	102	101
Mean baseline proteinuria (g per day)‡	1.5	1.7	2.0	2.5
ACEI	Ramipril	Ramipril	Cilazapril	Cilazapril
Maximum daily ACEI dose (mg)	6.7	6.5	Unavailable (initial 2.5; target 5.0)	Unavailable (initial 2.5; target 5.0)
Prednisone treatment	NA	6 months; 1.0mg/kg per day for 2 months and then taper by 0.2mg/kg per day every month	NA	6–8 months; 0.8–1.0mg/kg per day for 8 weeks, then taper by 5–10mg every 2 weeks
Mean follow-up (months)	57	63	28	26
Mean blood pressure at end of follow-up (mmHg)	121/77	121/77	Unavailable	Unavailable
Patients reaching the study's primary outcome	27%§	4%§	24%‖	3%‖

*Therapy including administration of an ACEI and prednisone. ‡In the absence of ACEI therapy. §Doubling of baseline serum creatinine from baseline or end-stage renal disease. ‖50% increase in serum creatinine level from baseline. Abbreviations: ACEI, angiotensin-converting-enzyme inhibitor; eGFR, estimated glomerular filtration rate; NA, not applicable.

Recommendation:

Maximise ACEI/ARB & BP control first;

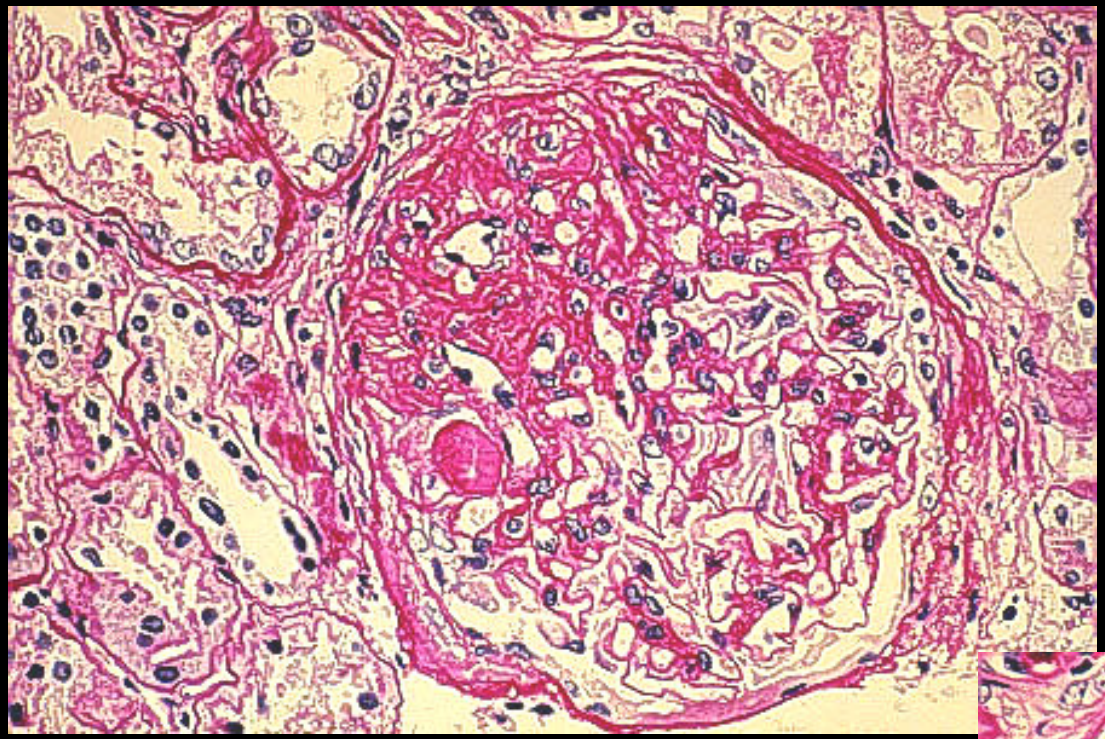
If proteinuria still > 1g/d trial 6 months PRD .

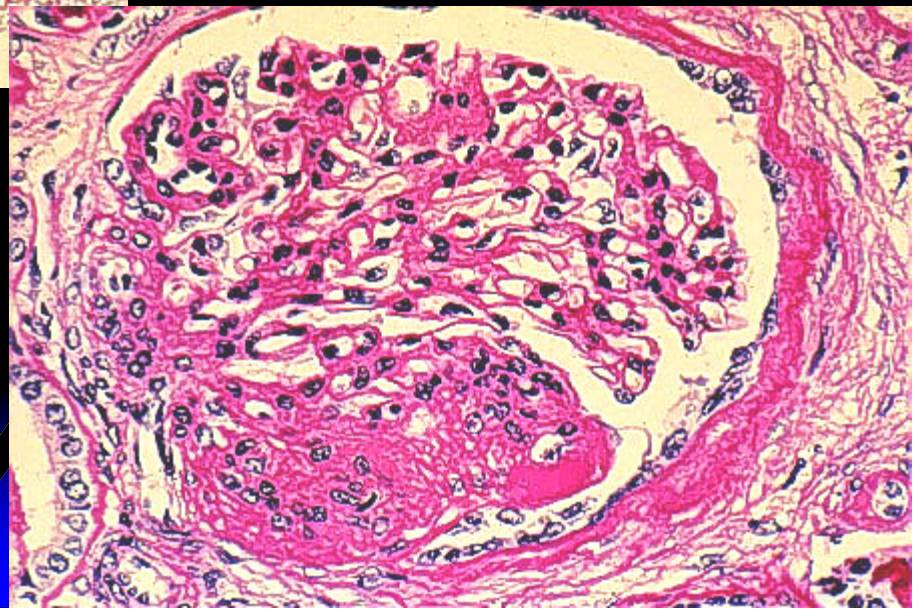
Frank Eitner and Jürgen Floege (2010) ACEIs with or without corticosteroids in IgA nephropathy? *Nat. Rev. Nephrol.* doi:10.1038/nrneph.2010.31

nature REVIEWS NEPHROLOGY

- A 50 yr old man presents with hypertension (170/100) and proteinuria 3g/day. Creatinine is 100umol/L. Renal biopsy shows FSGS. Which of the following are correct:
  - Rituximab is now considered the best treatment for this disorder
  - This may be secondary to poorly controlled hypertension
  - Most adults with FSGS will need dialysis within 5 years
  - HIV does not induce this lesion
  - This disorder is more common in children than adults

Focal Glomerulosclerosis





FGS - causes

- **Primary**
  - idiopathic
  - familial - autosomal dominant, Chr 19
    - gain of function mutation a-activin 4
    - linked to increase podocyte cytoskeleton
  - HIV
  - lithium (chronic toxicity)
  - Hodgkin's & NHL
  - heroin

FGS - causes

- Secondary
  - healing of prior glomerular disease
    - e.g.SLE, IgA, vasculitis
  - nephron loss
    - reflux, hypertension, ischaemia, ?nephrectomy
  - glomerular hypertension
    - diabetes, sickle cell, Type 1 GSD
  - obesity

Natural history of primary FGS

- **Nephrotic**
  - 40-70% ESRF at 10 yrs
- **Non - nephrotic**
  - 10-15% ESRF at 10yrs
- **‘responders’** to therapy
  - 10% ESRF at 10 yrs
- **‘non - responders’** to therapy
  - 60-80% ESRF at 10 yrs

Treatment of FGS

- Trial of steroids
  - up to 50% remission if treated 5-8 mths
  - all responders are within 9 months
  - steroid resistance likely if :
    - tubulointerstitial disease
    - secondary FGS
    - elevated creatinine
    - proteinuria > 10g/d
- CyA
- tacrolimus + steroids if dependent on CyA
- MMF used with success - no controlled trials
- NSAIDs / ACEI

FSGS

- Increasing frequency & new demographics
  - Age 50-70, no longer 20-30
- 10yr renal survival determined by response to treatment
  - 90% if complete remission
  - 80% if partial remission
  - 40% if no remission
- As pts now older, more obese, more co-morbidities
  - Use CyA 1st (1mg/kg bd)
    - No controlled data

Cattran ASN 2009

Classification of Glomerulonephritis

- **Diffuse**
  - minimal change
  - membranous
  - proliferative
    - PIGN / PSGN
    - MCGN
    - mesangial
    - crescentic
- **Focal**
  - IgA
  - FGS
  - Thin basement membrane disease