

GLOMERULONEPHRITIS

CLINICAL APPROACH TO GLOMERULAR
DISEASE

ACOI 2017

Disclosures

Nothing to declare

Case 1

44 yo Caucasian woman admitted from PCP
with dyspnea and HTN

Has not felt well for 3-4 months with
recurrent episodes of “bronchitis” with
wheezing

No PMH or PSH + seasonal allergies

No significant family or social history

Case 1

PE – BP 160/ 100 HR 112 Afebrile
pale, wheezing, with few crackles

Case 1

Labs:

BUN 61 Creatinine 3.8 Lytes OK

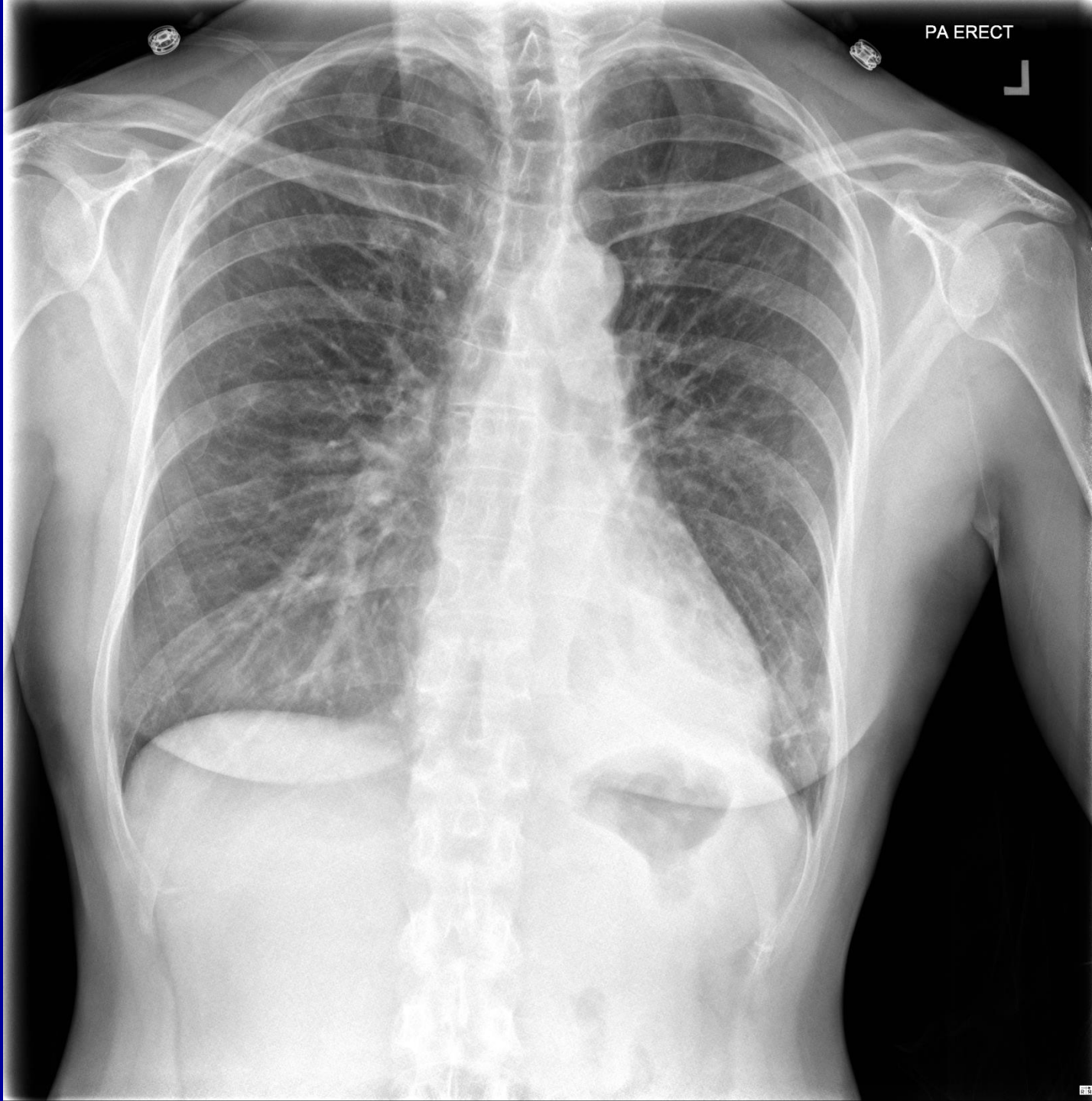
WBC 11.08 diff – 15 eosinophils

UA - +4 protein 10-20 RBCs 5 WBCs

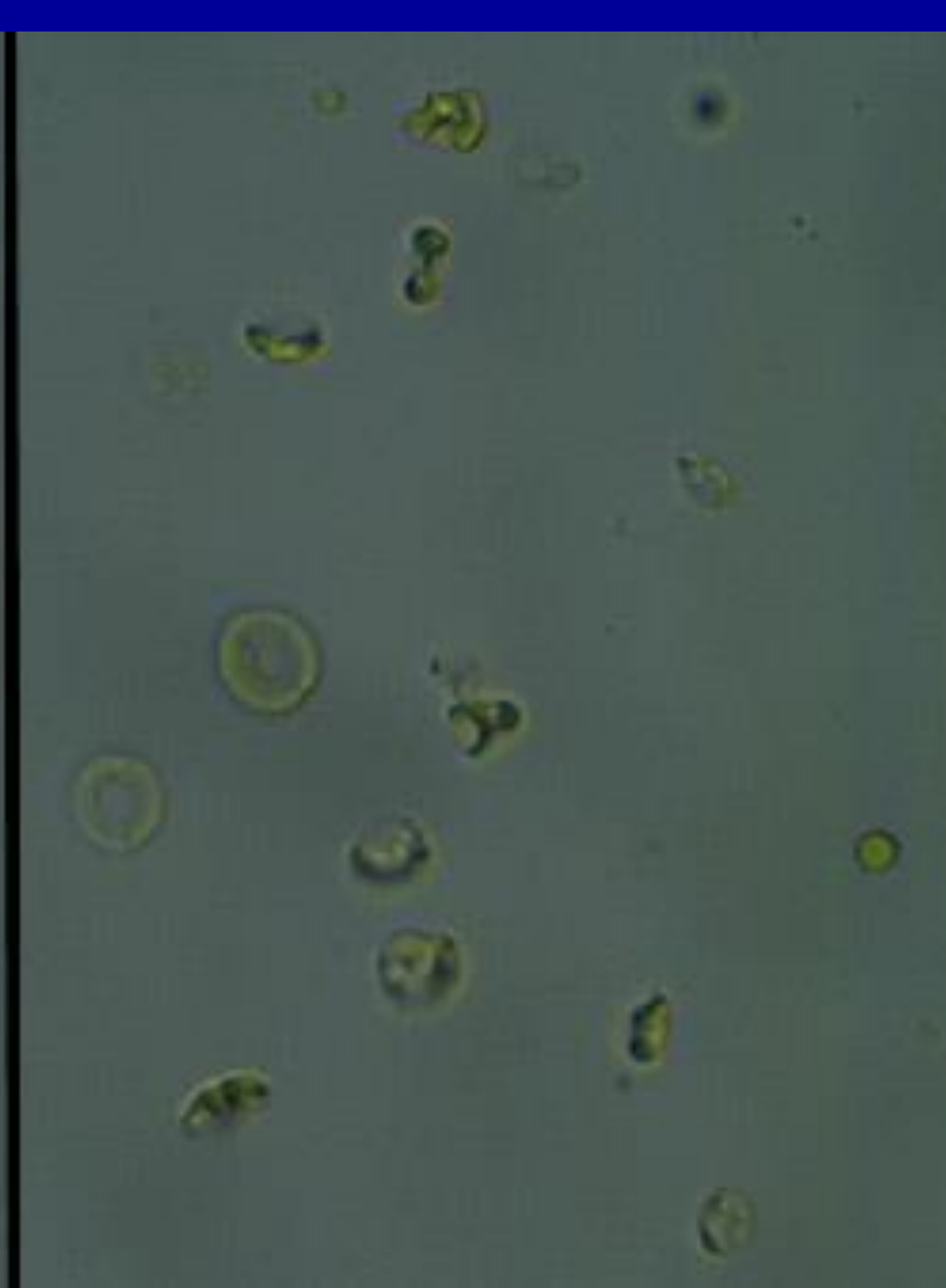
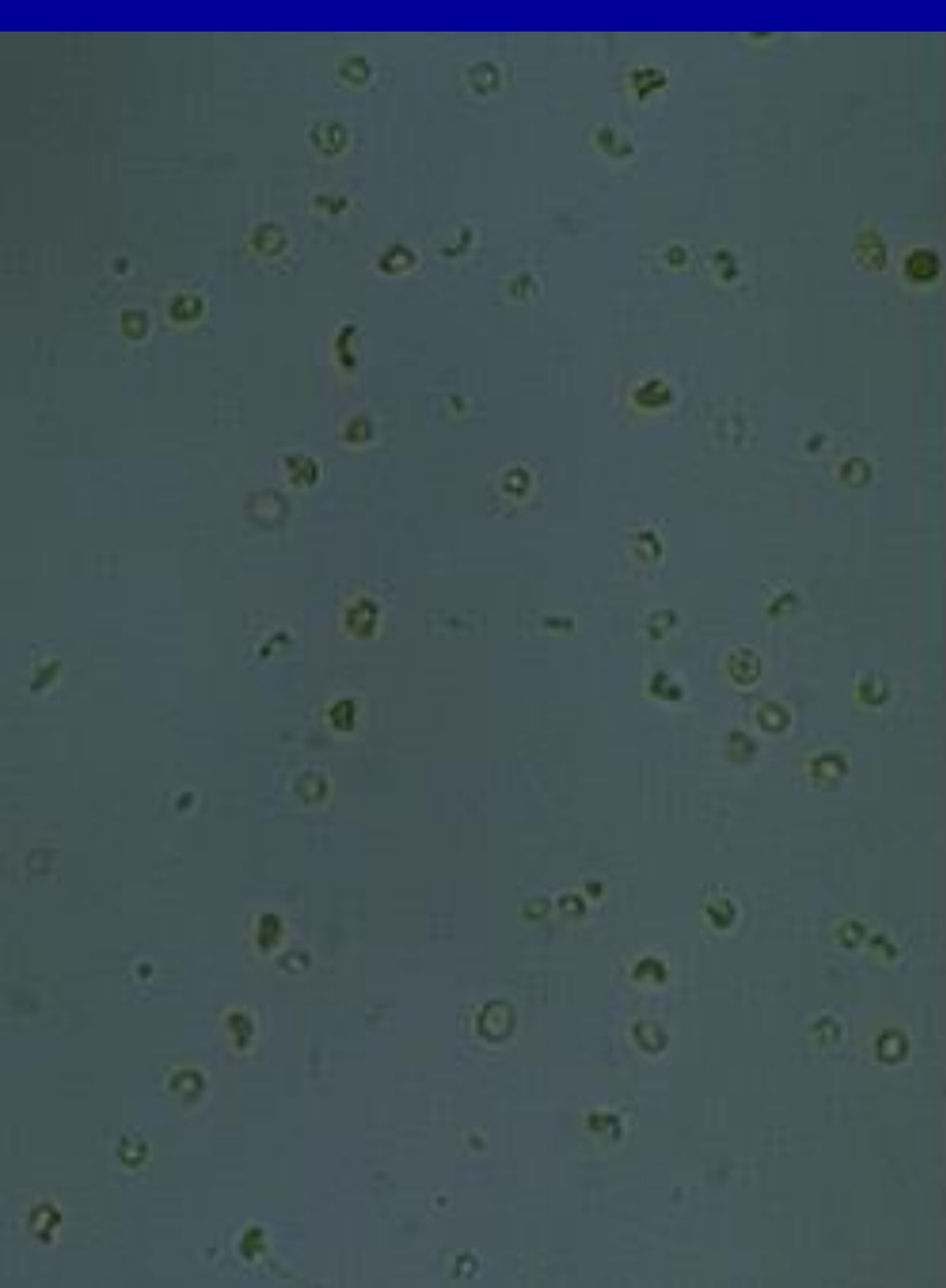
Microscopic UPC 4 UAC 3300

CXR

PA ERECT







What is her diagnosis?

1. SLE
2. HSP
3. Churg-Strauss - Eosinophilic granulomatous polyangiitis (EGPA)
4. Granulomatosis polyangiitis (GPA)
5. Microscopic polyangiitis (MPA)

Glomerulonephritis

Glomerular Disease

Hematuria, proteinuria or both

Basement Membrane Disease

Proteinuria w/o hematuria

Proliferative Glomerular Disease

Hematuria plus proteinuria

GLOMERULONEPHRITIS

PROLIFERATIVE

PROLIFERATION DENOTES CELLULAR INFILTRATION OF THE GLOMERULUS

IMMUNE CELLS ARE ATTRACTED BY CYTOKINES, COMPLEMENT, AND IMMUNE COMPLEXES

INFLAMMATORY RESPONSE LEADS TO HOLES PUNCHED IN THE BM LARGE ENOUGH TO PASS RBCS

MILD DX IS MESANGIAL AND PROGRESSES TO SEVERE DISEASE OR CRESCENTIC

GLOMERULONEPHRITIS PROLIFERATIVE GN

PATTERNS OF INJURY

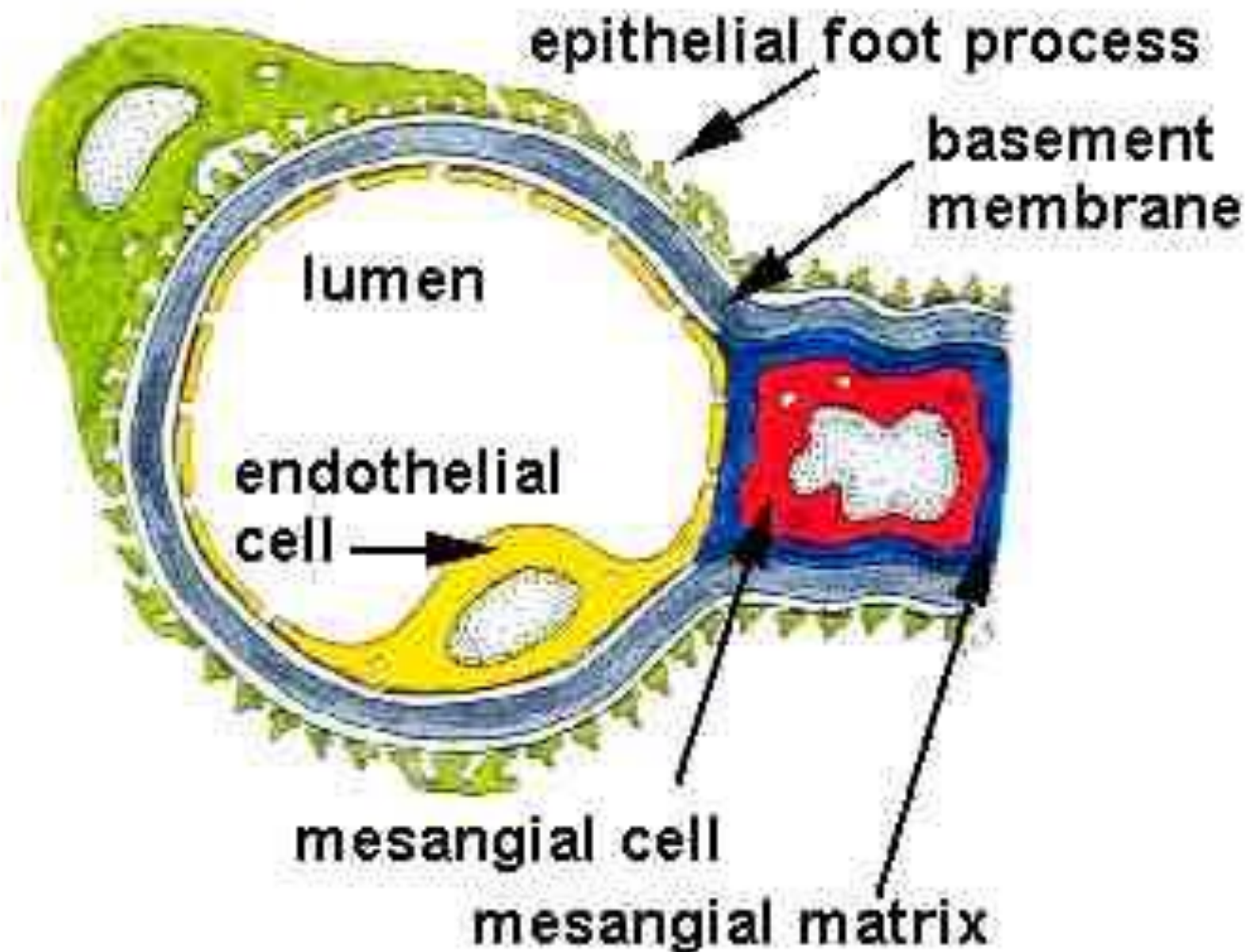
MESANGIAL – SUPPORT STRUCTURE

FOCAL AND SEGMENTAL – SOME PARTS OF
SOME ENDOTHELIA

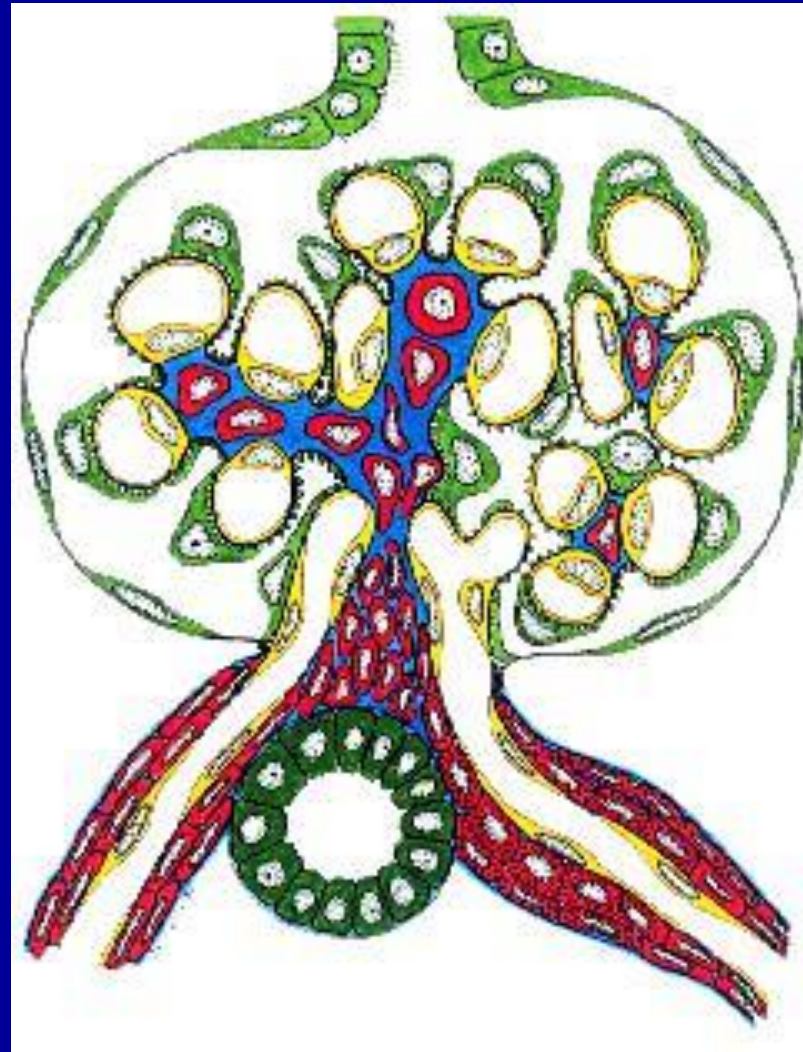
DIFFUSE – ALL ENDOTHELIA

CRESCENTIC - EPITHELIAL

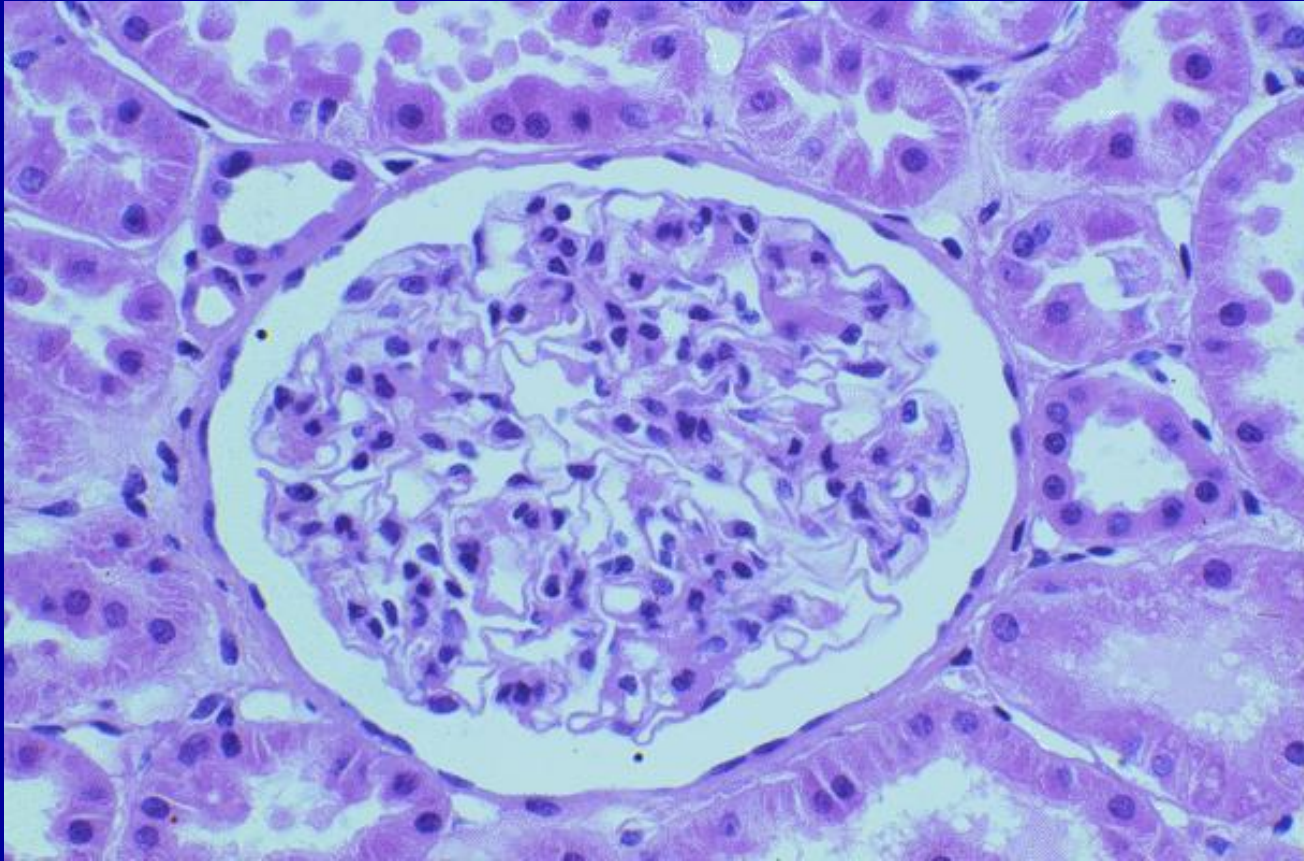
Normal Glomerular Capillary



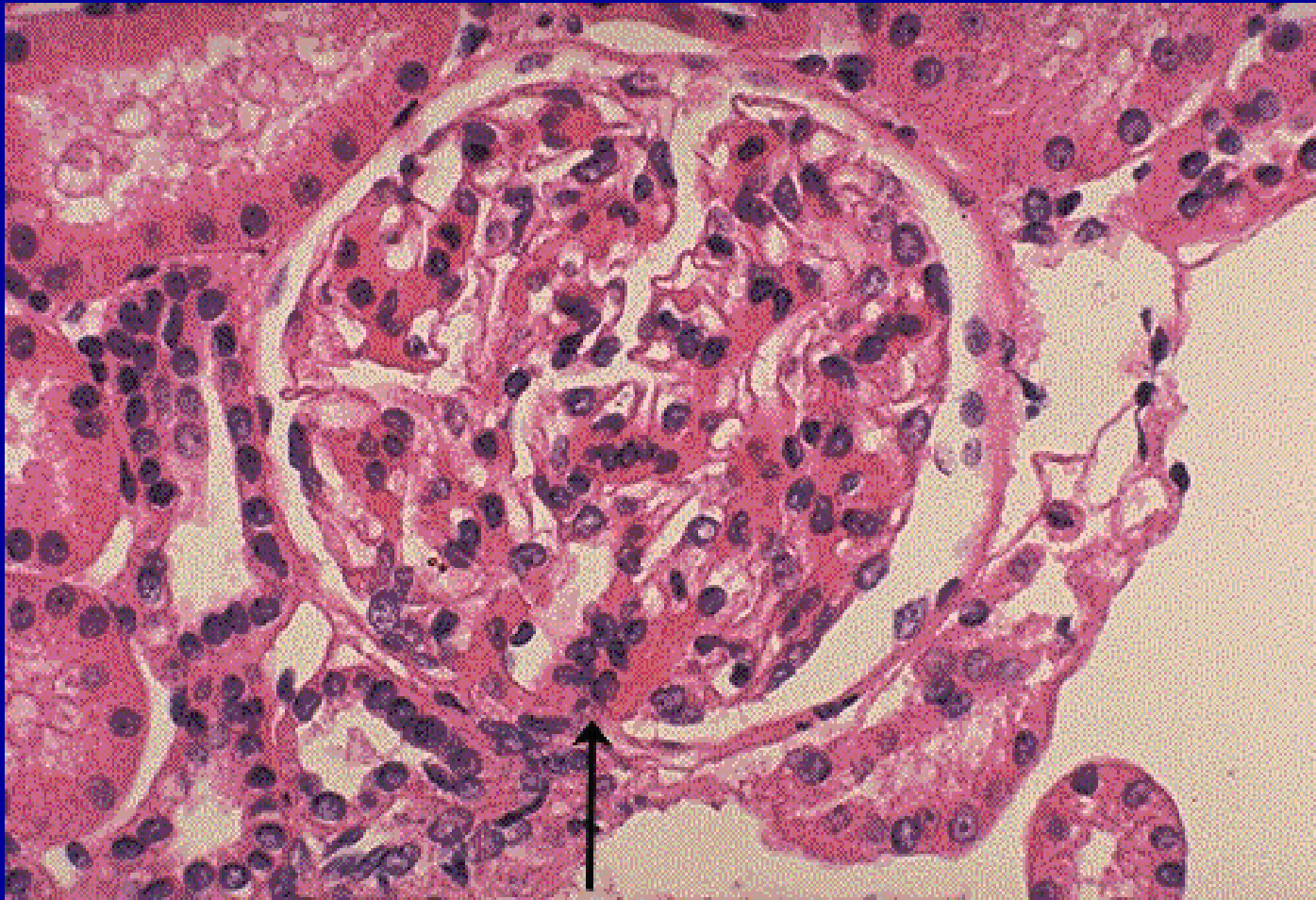
Normal Glomerulus



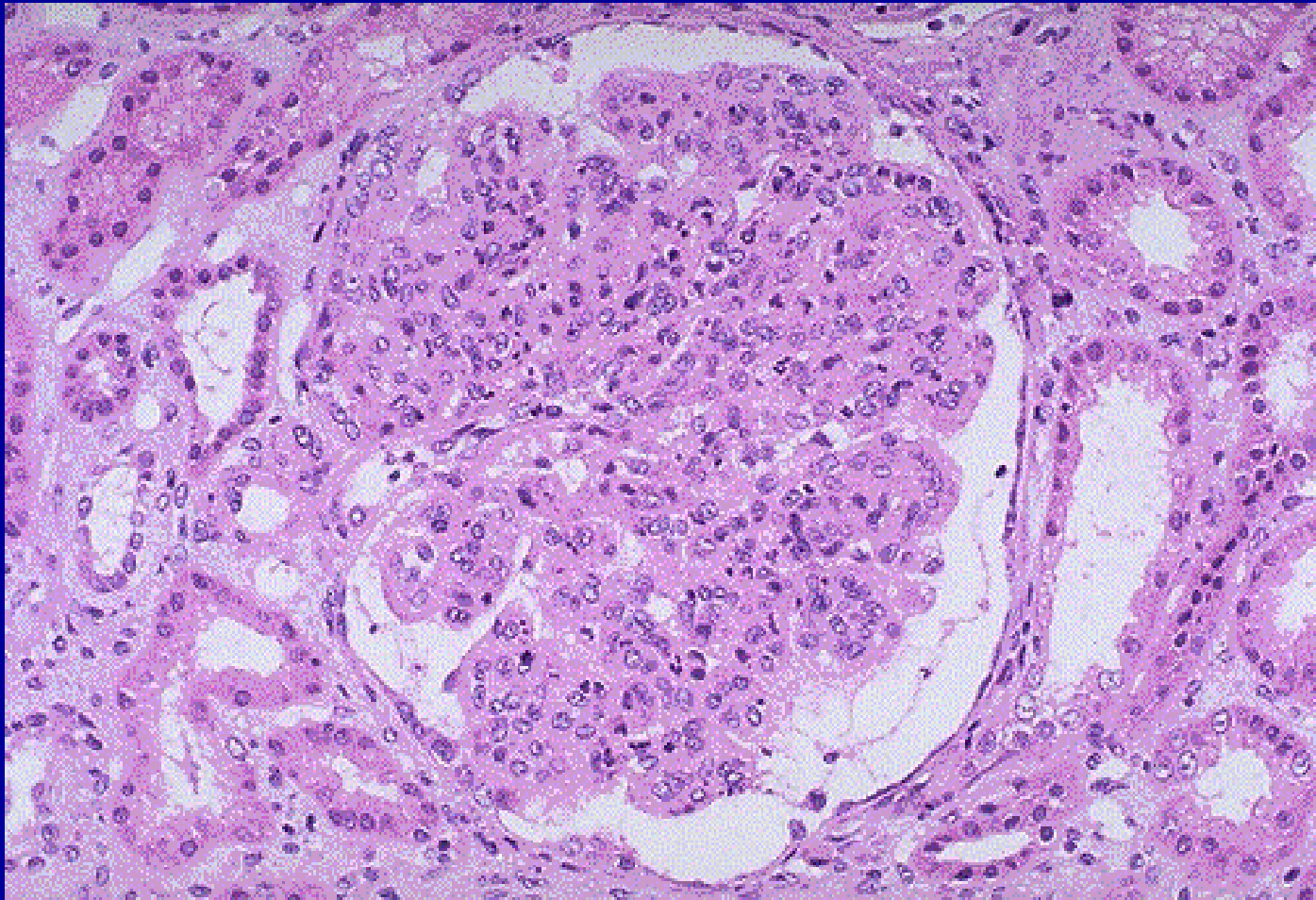
Normal Glomerulus



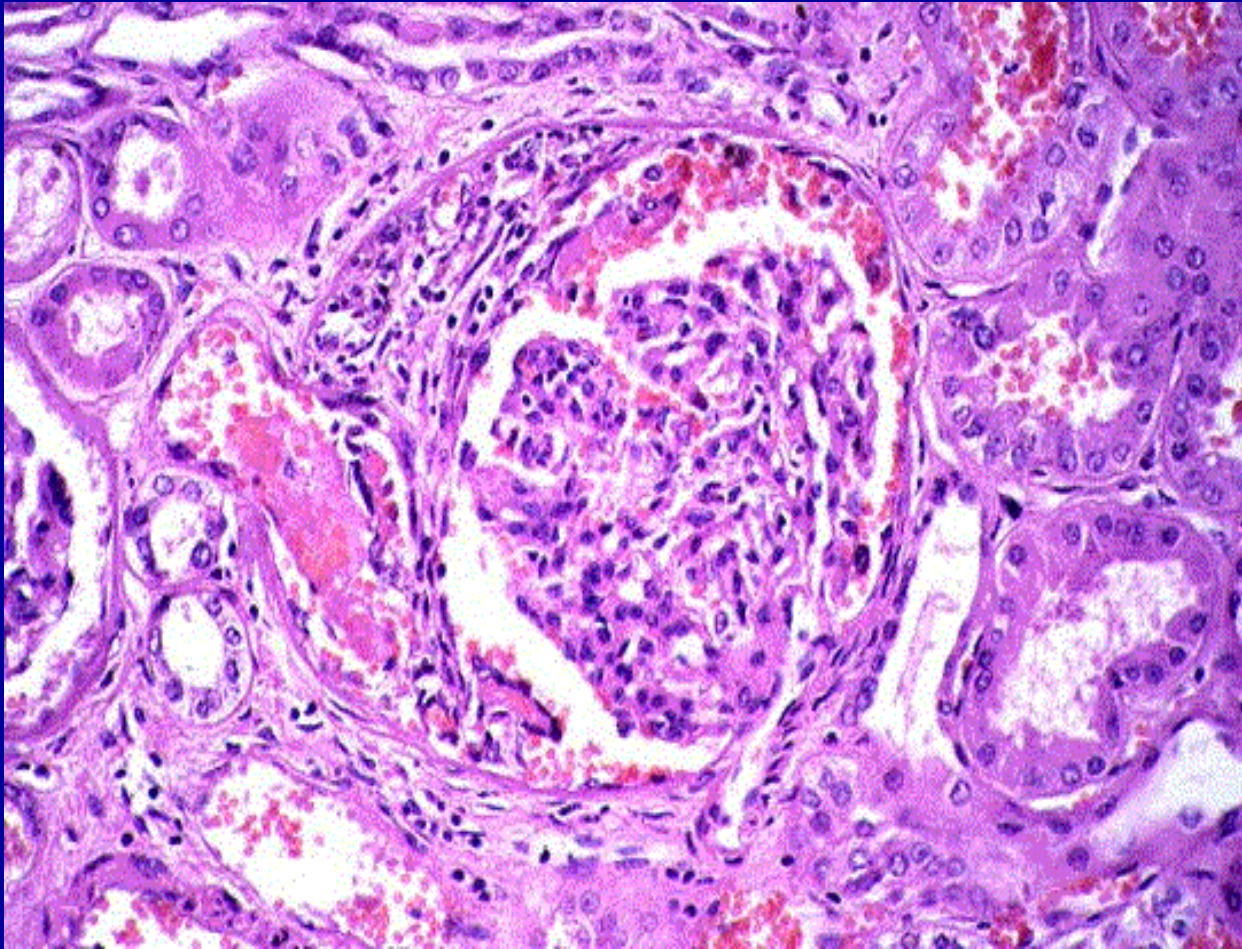
IGA GN - Mesangial

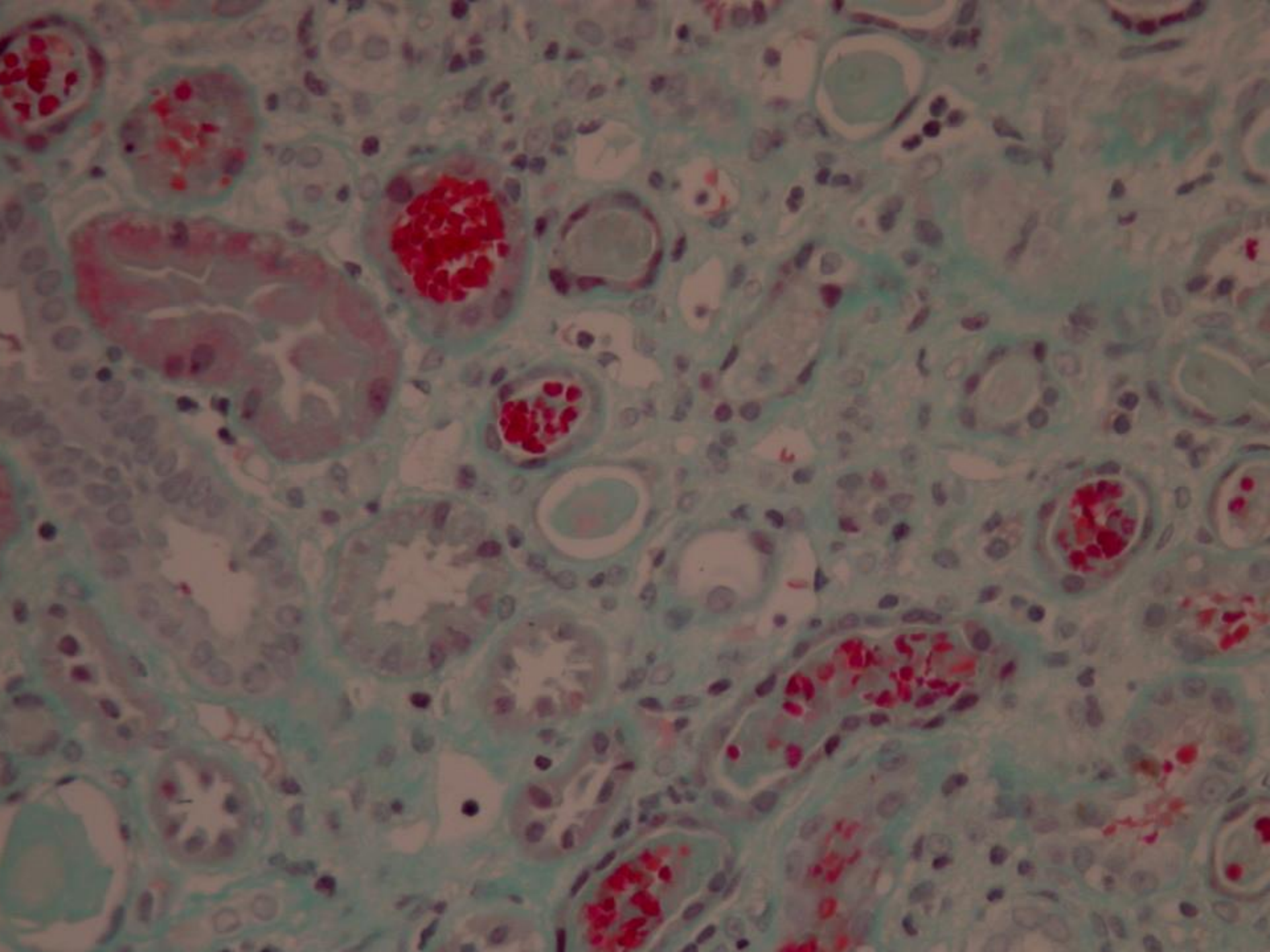


Post Strep GN - Diffuse



Crescentic Glomerulonephritis RPGN





GLOMERULONEPHRITIS PROLIFERATIVE

CLINICAL APPROACH TO PROLIFERATIVE

GN IS BASED ON TWO CRITERIA

1.H&P - SYSTEMIC OR RENAL

2.COMPLEMENT - LOW OR NL

AFTER CATEGORIZING ACCORDING
TO ABOVE, SELECTED LABS AND
HISTOLOGY WILL LEAD TO THE
DIAGNOSIS

Glomerulonephritis - Proliferative

Low Complement

SLE

Mixed Cryoglobulinemia

Postinfectious



Post Strep

MPGN

Normal Complement

Goodpasture's

GPA

HSP, MPA, C-S



IgA, Misc. IC Dx

Anti GBM

Renal Vasculitis

LOW COMPLEMENT SYSTEMIC DISEASE

SLE

MIXED CRYOGLOBULINEMIA

POST INFECTIOUS GLOMERULONEPHRITIS

SYSTEMIC LUPUS ERYTHEMATOSIS

PROTOTYPE IMMUNE COMPLEX DX

DEPOSITION OF IMMUNE COMPLEXES
OF ALL TYPES FROM THE MESANGIUM
THROUGH THE ENDOTHELIUM INTO
THE EPITHELIUM

MAY ALSO CAUSE MEMBRANOUS AND
AIN

LABS - ANA, DSDNA, ANTI SMITH

MORE SEVERE AND COMMON IN HISPANICS AND
AFRICAN AMERICANS

MIXED CRYOGLOBULINEMIA

THREE TYPES BASED ON THE PRESENCE OR TYPE OF MONOCLONAL PROTEIN –MONOCLONAL, MONOCLONAL/POLYCLONAL, POLYCLONAL

MAY BE ESSENTIAL (IDIOPATHIC) OR SECONDARY (CA, HEPB, INFECTION, SBE ETC) **HEP C - MOST COMMON**

HYPERSENSITIVITY (SMALL VESSEL) VASCULITIS
USUALLY ACRAL DISTRIBUTION, SEASONAL AND SYSTEMIC INVOLVEMENT

LABS - CRYOGLOBINS, SPEP, HEPBSAg,
RHEUMATOID FACTOR, HEPC ANTIGEN PCR

POST INFECTIOUS

MANY TYPES OF INFECTIONS LEAD
TO IC FORMATION WHICH CAN
DEPOSIT IN THE KIDNEY

VP SHUNT, SBE, STAPH, VISCERAL
ABSCESSSES, MALARIA, AND MULTIPLE
OTHER CAUSES

LABS - CULTURES AND SEROLOGY

LOW C3, NORMAL C4

POST STAPH IGA

LOW COMPLEMENT RENAL DISEASE

POST STREPTOCOCCAL GN

MEMBRANOPROLIFERATIVE GN

POST STREPTOCOCCAL

FORMATION OF IC OF IG AND
STREPTOCOCCAL ANTIGENS DEP-
OSIT IN THE KIDNEY

SKIN INFX OR PHARYNGITIS

OCCURS **2-3 WEEKS** AFTER INFEC-
TION WITH GRP A STREP

LAB - ASO(PHAR) AND ANTI DNASE
(SKIN) (NON SPECIFIC)(LOW C3)

MEMBRANOPROLIFERATIVE

NEW CLASSIFICATION BASED ON Ig AND
COMPLEMENT ON BX

Ig + C+ - MONOCLONAL OR POLYCLONAL (HEP C,
SLE, GAMMOPATHIES

Ig- C+ - C3 NEPHRITIC FACTOR. DYSREGULATED
COMPLEMENT

Ig- C- - THROMBOTIC MICROOANGIOPATHIES,
TRANSPLANT REJECTION

MACULAR DEGENERATION

NORMAL COMPLEMENT SYSTEMIC DISEASE

GOODPASTURES SYNDROME

GRANULOMATOUS POLYANGIITIS

MICROSCOPIC POLYANGIITIS

EOSINOPHILIC GRANULOMATOUS
POLYANGIITIS

HENOCH-SCHONLEIN PURPURA

GOODPASTURE'S

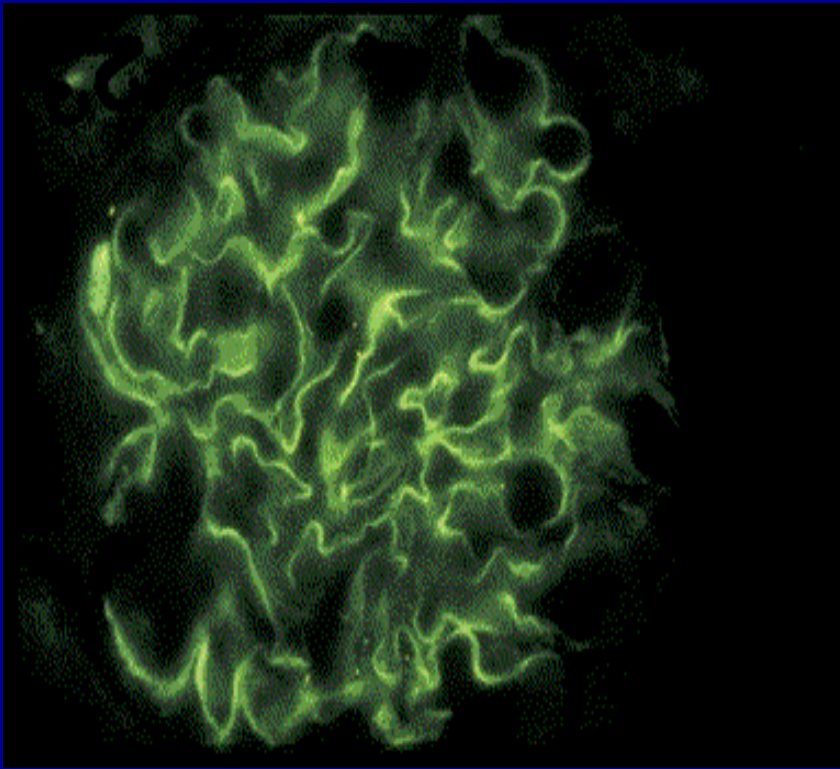
ANTIBODIES TO NC1 REGION OF
COLLAGEN IN THE GLOMERULAR
AND ALVEOLAR BM

ALPORT'S SYNDROME IS THE
CONGENITAL LACK OF THIS
ANTIGEN COL4A3-5 Type 4 Collagen

PULMONARY, RENAL, OR PULM-
ONARY/RENAL INVOLVEMENT

LABS - ANTI GBM, 30% ANCA+

Goodpasture's Syndrome



linear deposits of IgG
associated with
pulmonary
hemorrhage
circulating anti-GBM

SYSTEMIC VASCULITIS

GLOMERULUS IS A BLOOD VESSEL
AND MAY BE INVOLVED IN ANY
TYPE OF SYSTEMIC OR LIMITED
VASCULITIS (SMALL VESSEL)

EXAMPLES - GPA, MPA, HSP,
EGPA, AND HYPERSENSITIVITY

DX MADE BY HISTOLOGY, CLINICAL
INVOLVEMENT, AND LABS

GRANULOMATOSIS POLYANGIITIS (GPA)

GRANULOMATOUS SMALL VESSEL
VASCULITIS AFFECTING THE KIDNEY,
UPPER RESPIRATORY TRACT, AND LOWER
RESPIRATORY TRACT

C-ANCA -ANTI Proteinase 3 (PR3) IS A
MARKER AND INVOLVED IN THE
PATHOGENESIS OF THE DISEASE

Formerly Wegener's

MICROSCOPIC POLYANGIITIS

DIFFUSE SMALL VESSEL VASCULITIS
AFFECTING THE CAPILLARIES OF ANY
ORGAN SYSTEM (UNLIKE CLASSIC
POLYARTERITIS NODOSA)

COCAINE VASCULITIS DUE TO LEVAMISOLE
CONTAMINATION

P-ANCA (ANTI MYELOPEROXIDASE)

HENOCH-SCHOENLEIN PURPURA

IGA SMALL VESSEL VASULITIS INVOLVING
THE SKIN, JOINTS , GI TRACT AND KIDNEY

NO DIAGNOSTIC SEROLOGY

POST STAPH

EOSINOPHILIC GRANULOMATOUS POLYANGIITIS

EOSINOPHILIC SMALL VESSEL VASCULITIS
INVOLVING THE LUNG AND RARELY THE
KIDNEY

OCCURS WITH ASTHMA, EOSINOPHILIA, AND
LEUKOTRIENE INHIBITORS, SKIN and PNS
50% ANCA + (IF + ACTS LIKE MPA)

NORMAL COMPLEMENT RENAL DISEASE

IgA

IMMUNE COMPLEX GN

ANTI GBM

RENAL VASCULITIS

GLOMERULONEPHRITIS

IGA NEPHRITIS

RESPIRATORY OR GI INFECTION

SETS OFF IMMEDIATE PRODUCTION
OF IgA IC WHICH DEPOSIT IN THE

KIDNEY (CONCURRENT). GALACTOSE DEFICIENT
IgA

MOST COMMON GN IN THE WORLD

**GROSS OR MICRO HEMATURIA CONCURRENT WITH
INFECTION**

CKD, PROTEINURIA, AND HTN

LABS – NONE POST STAPH

Benign Hematuria

Benign hematuria is hematuria and the absence of HTN, proteinuria, systemic disease and azotemia.

Age < 50 - caused by IGA, thin basement membrane, hypercalcuria, hereditary nephritis and hyperuricosuria

Risk of ESRD and RRT low but not absent and needs followup

Benign Hematuria Workup

Work up: 24 hr urines, spot urine protein-albumin, US of Kidneys, IgA, + bx if present for > 6 months

Age > 50 (>40 in a smoker) - cystoscopy

Imaging of the urinary tract (CTU)(US) to R/O malignancy for all

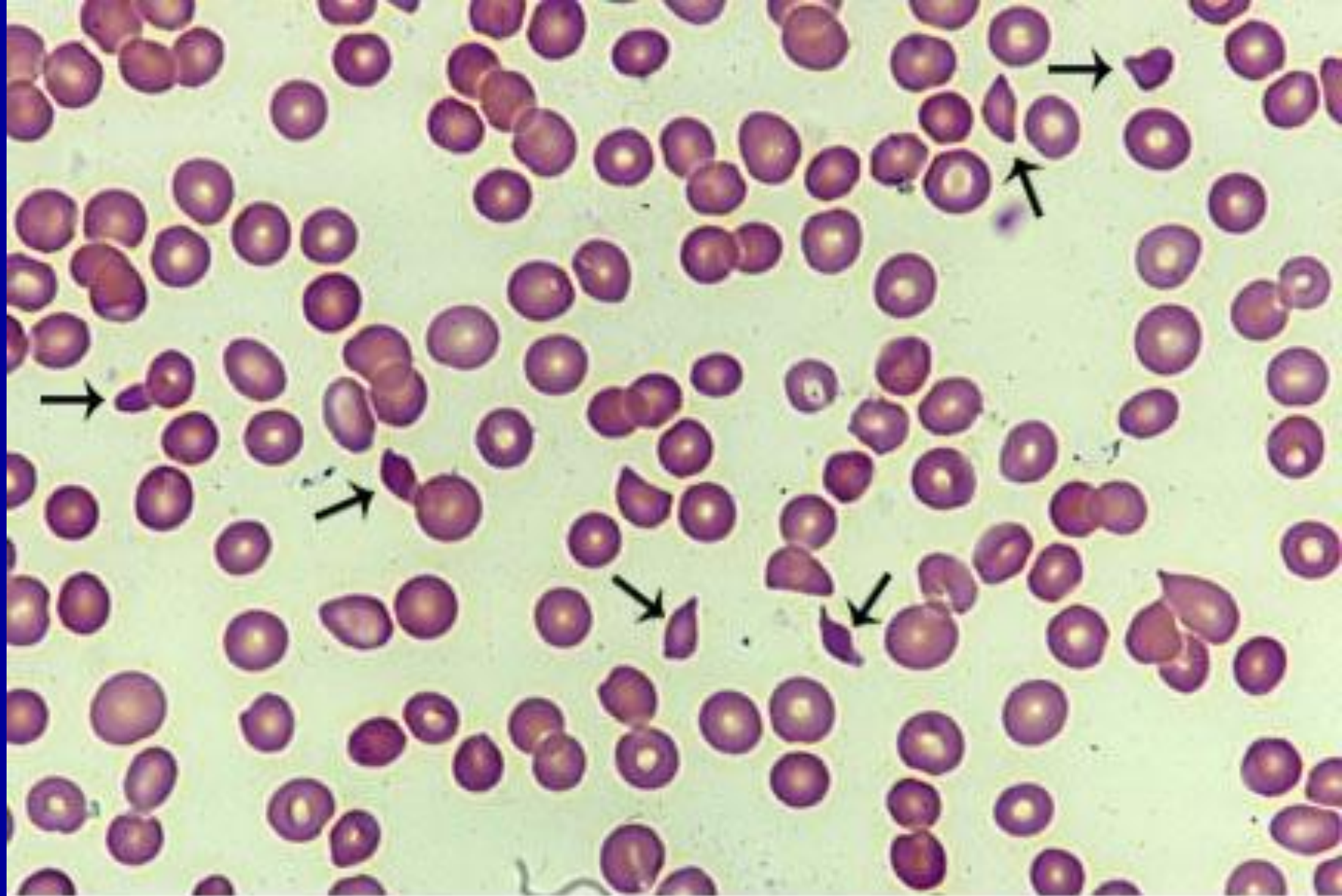
TTP -HUS

Deficiencies of ADAMTS 13 or antibodies to this enzyme lead to widespread intravascular thrombosis

Diagnosis – MAHA + Thrombocytopenia (>2 schistocytes/hpf)

Therapy replaces ADAMTS 13, removes antibodies and decreases production of these antibodies

STEC –HUS and aHUS



Source: Lichtman MA, Shafer MS, Felgar RE, Wang N:
Lichtman's Atlas of Hematology: <http://www.accessmedicine.com>

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AIN vs. AGN

Differentiation

AIN - classically presents with rash, **hematuria**, eosinophilia, eosinophiluria. Proteinuria is usually < 1000 mg. HTN and edema are absent.

AGN - usually presents with **hematuria**, proteinuria, HTN, and edema.

Case 1

A workup was pursued because of systemic disease and proliferative GN

C3 and C4 normal

SPEP and UPEP – monoclonal lambda

ANA -, RF -, C-ANCA -, P-ANCA suspicious
(MPO +)

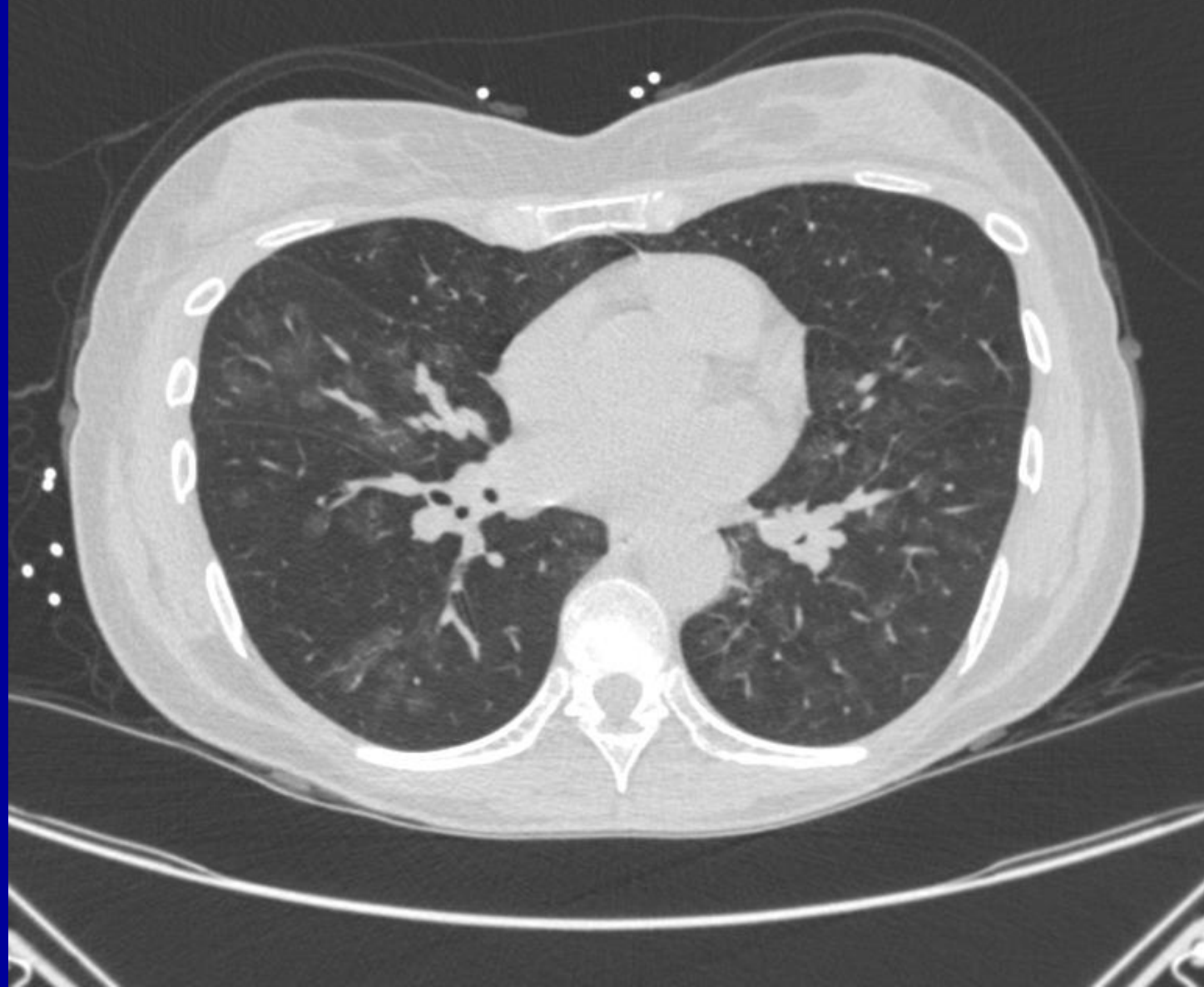
Case 1

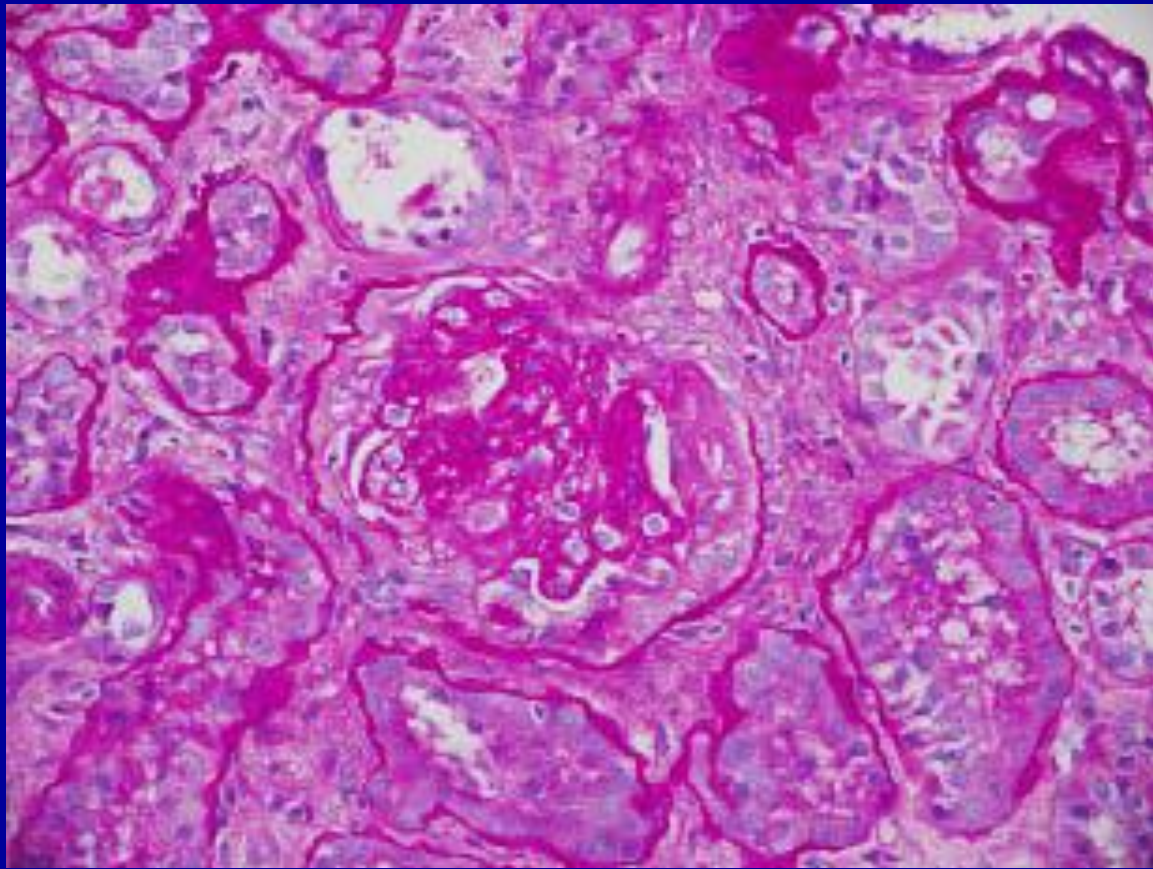
BM bx – negative for myeloma

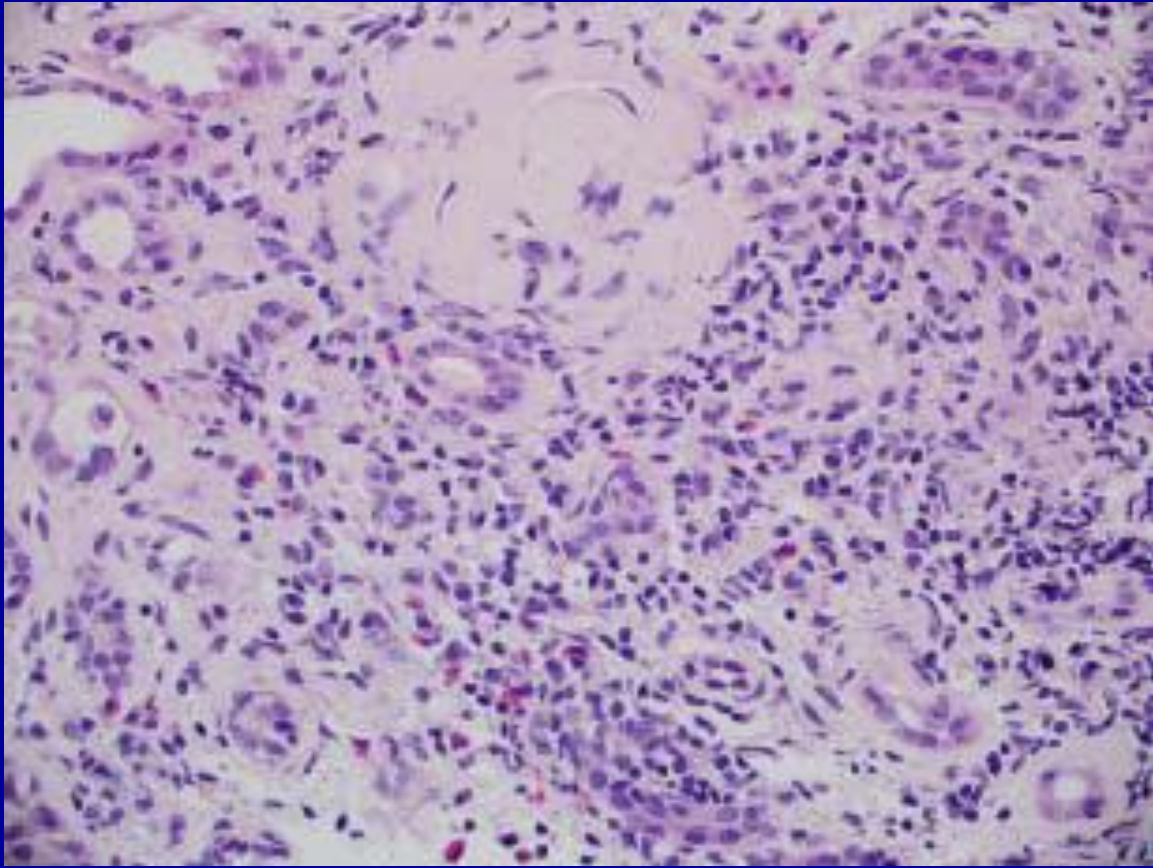
CT chest

PFT – FVC 2.47 (63), FEV1 1.86 (60),
decreased diffusion capacity

Renal biopsy







Glomerulonephritis - proliferative

Low Complement

SLE

Mixed Cryoglobulinemia

Postinfectious

=====

Post Strep

MPGN

Normal Complement

Goodpasture's

GPA

HSP, MPA, C-S

=====

IgA, Misc. Im Complx

Anti GBM

Renal Vasculitis

What is her diagnosis?

1. SLE
2. HSP
3. Eosinophilic granulomatous polyangiitis (EGPA)
4. Granulomatosis polyangiitis (GPA)
5. Microscopic Polyangiitis (MPA)

Case 2

60 yo AA man presents with worsening edema of 3 months duration

PMH – DM II X 2 yrs, HTN X 2yrs, morbid obesity, sleep apnea

ROS – distal polyneuropathy

PE – mild proliferative retinopathy

UA U P/C ratio 6.6 +4 protein dipstick
UAC 4200 UAPR > 50% Creatinine 1.2

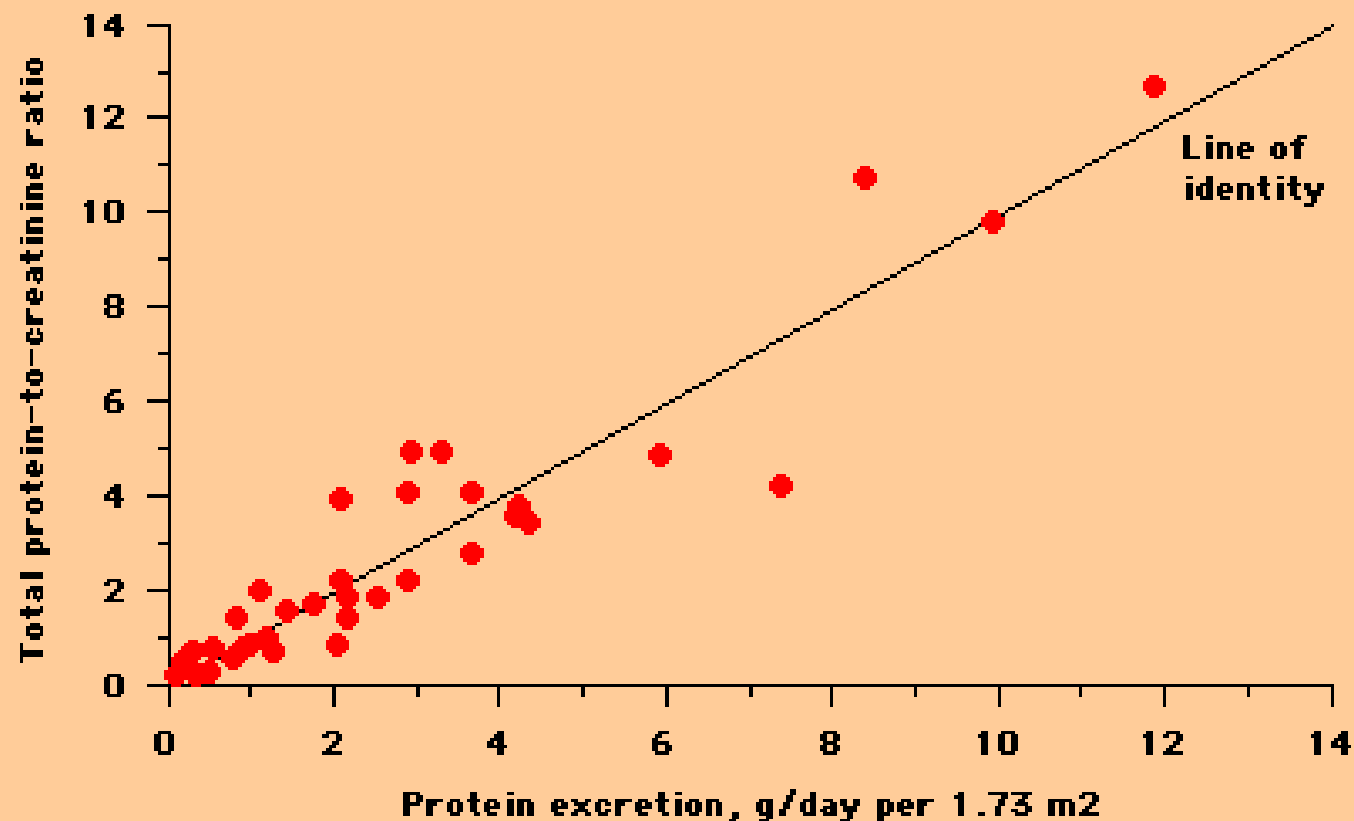
What glomerular disease does this patient have?

1. Focal segmental glomerulosclerosis
2. Amyloidosis
3. Diabetic glomerulosclerosis
4. Minimal change
5. Membranous

GLOMERULONEPHRITIS

PROTEINURIA – spot urine

UPC MG/MG/DL	DIAGNOSIS
<0.2	NRML OR VASCULAR DX
0.2- 0.5	VASC/INTERSTIT/GN
0.5 – 1.0	INTERSTIT/GN
> 1.0	GN/INTERSTIT



Protein-creatinine ratio to estimate protein excretion The relation between total daily protein excretion and the total protein-to-creatinine ratio (mg/mg) determined on a random urine specimen. (Data from Ginsberg, JM, Chang, BS, Matarese, RA, Garella, S, N Engl J Med 1983; 309:1543.)

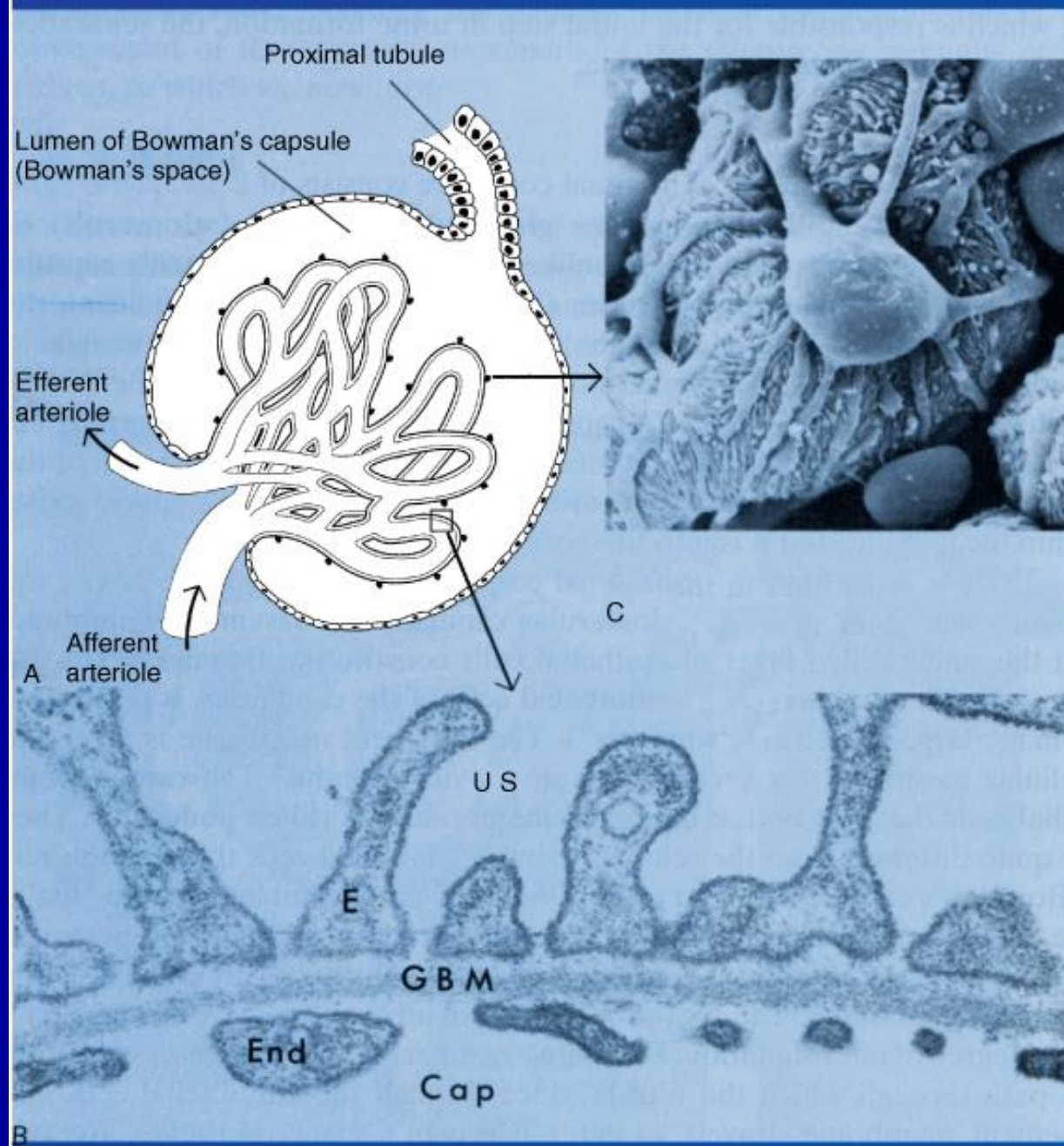
Urine albumin to protein ratio (UAPR)

The ratio of UAC to UPC can be helpful in
localizing kidney disease

UAPR > 50% - glomerular

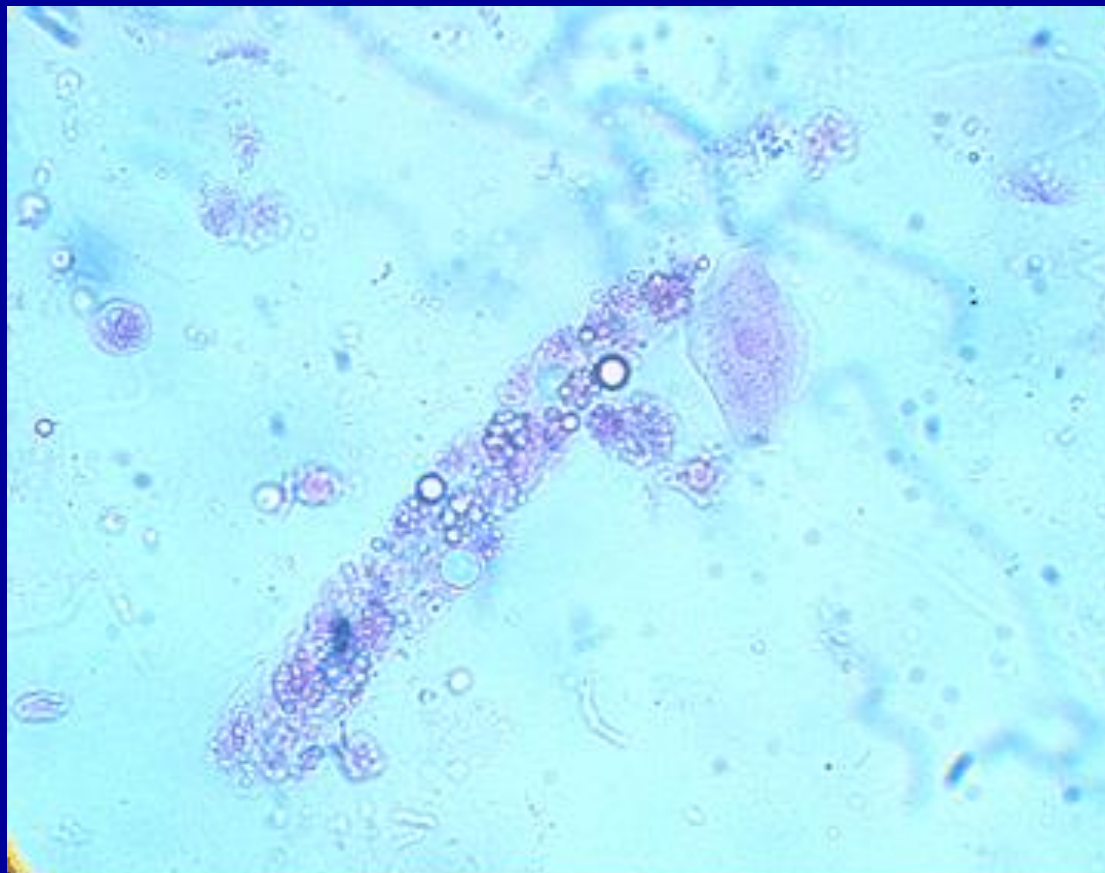
UAPR < 40% - tubular

UAPR < 25% - myeloma cast



Source: Eaton DC, Pooler JP: *Vander's Renal Physiology, 7th Edition*; <http://www.accessmedicine.com>

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Fatty cast Urine sediment showing a fatty cast. The fat droplets (or globules) can be distinguished from red cells (which also have a round appearance) by their variable size (from much smaller to much larger than a red cell), dark outline, and "Maltese cross" appearance under polarized light. Courtesy of Frances Andrus, BA, Victoria Hospital, London, Ontario.



Fatty cast Urine sediment showing fatty cast under polarized light. The fat droplets have a characteristic "Maltese cross" appearance (arrow). Courtesy of Harvard Medical School.

GLOMERULAR DISEASE BASEMENT MEMBRANE DX

PATTERNS OF INJURY – PODOCYTE DX

MINIMAL CHANGE DISEASE

MEMBRANOUS NEPHROPATHY

FOCAL SEGMENTAL GS

DIABETIC GLOMERULOSCLEROSIS

PROTEIN DEPOSITION DX

AMYLOIDOSIS/LDD/FIBRILLAR

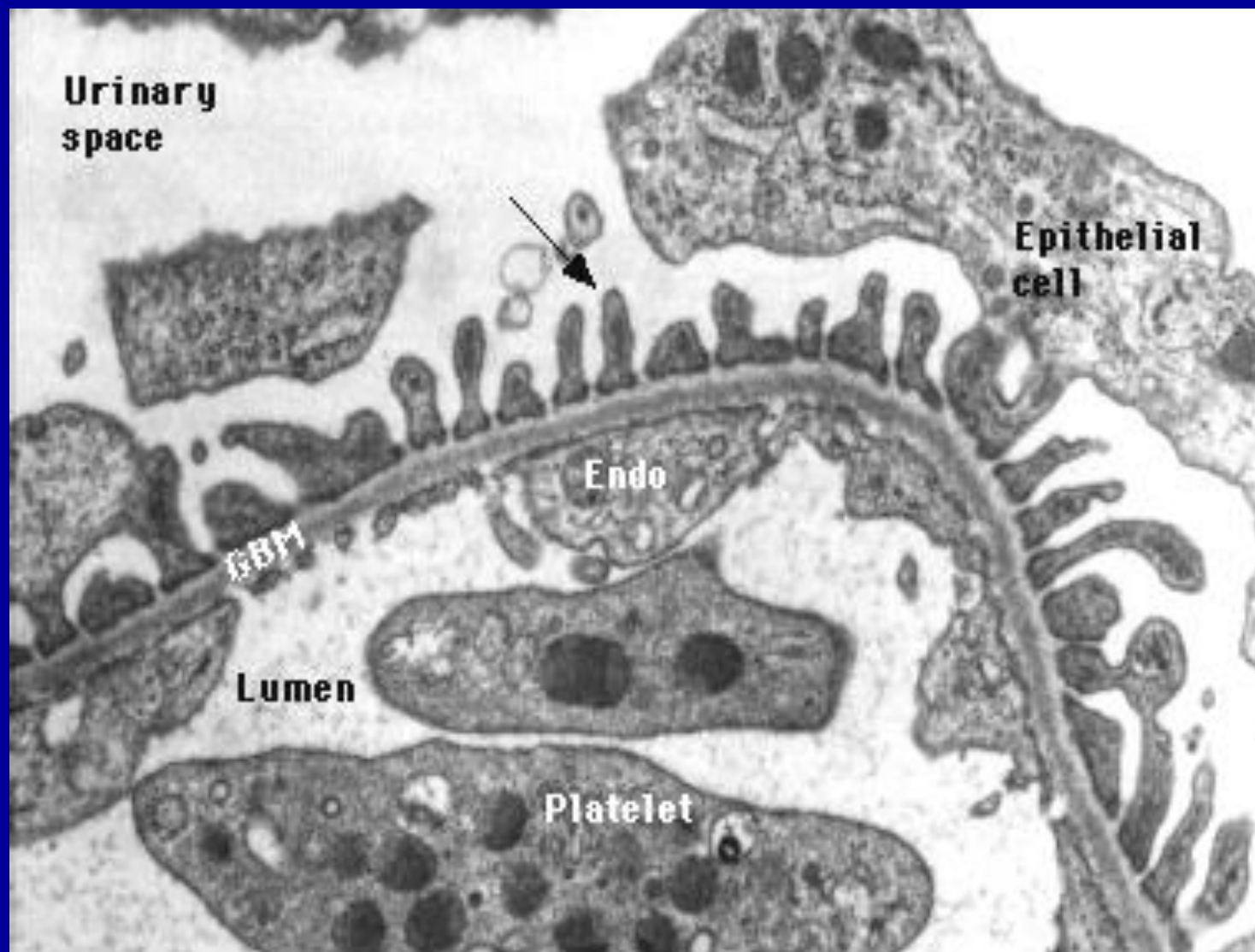
MINIMAL CHANGE

ALTERATION OF CHARGE OF BASE-
MENT MEMBRANE PORE ALLOWS ALBUMIN TO
LEAK INTO URINARY SPACE

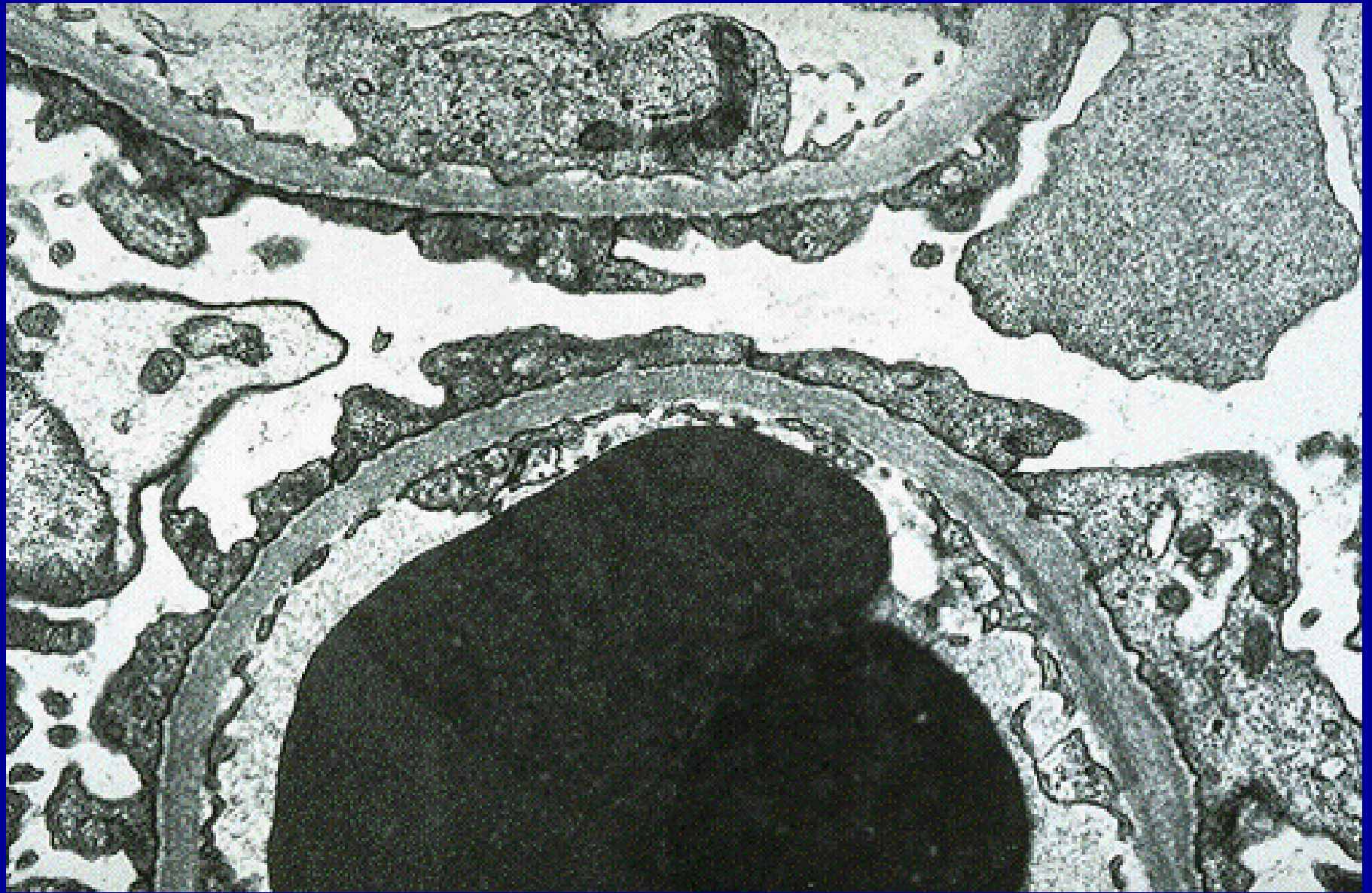
NO CHANGE IN KIDNEY FUNCTION AND
ABSCENCE OF HTN (ATN IN ADULTS)

SEEN IN CHILDREN, LYMPHOPROLIFER-
ATIVE DX, NSAIDS, IDIOPATHIC

PRODUCTION OF CYTOKINES MAY ALTER
NEGATIVE CHARGE OF PORE GLYCOPROTEINS



Normal glomerulus Electron micrograph of a normal glomerular capillary loop showing the fenestrated endothelial cell (Endo), the glomerular basement membrane (GBM), and the epithelial cells with its



MEMBRANOUS GN

PRESENCE OF IC IN BASEMENT
MEMBRANE LEADS TO ALTERATION
IN STRUCTURE AND PROTEIN PERM

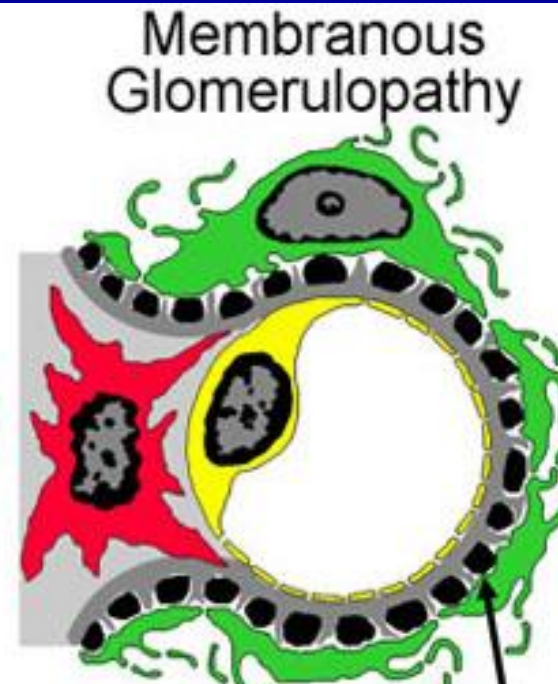
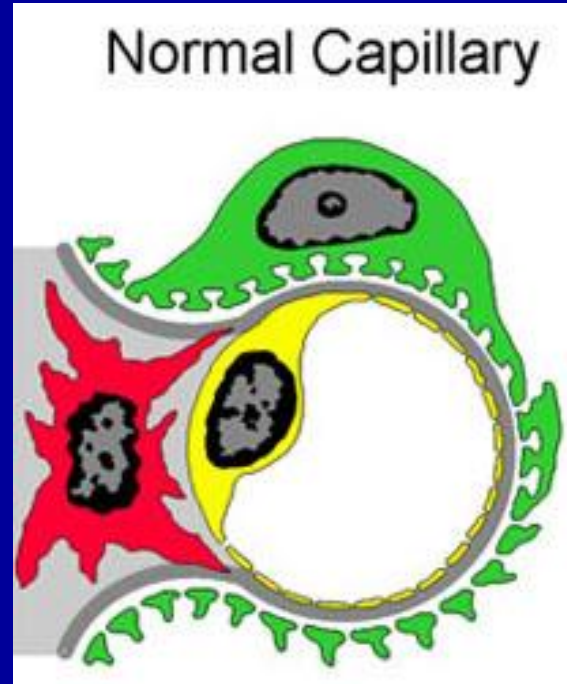
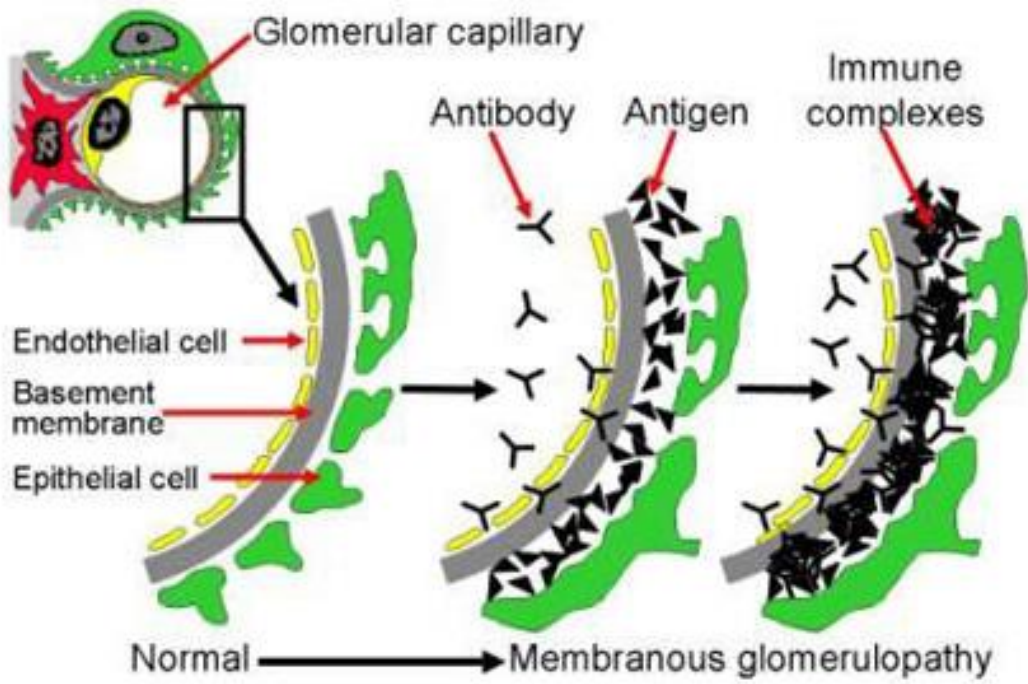
MAY HAVE CKD AND HTN

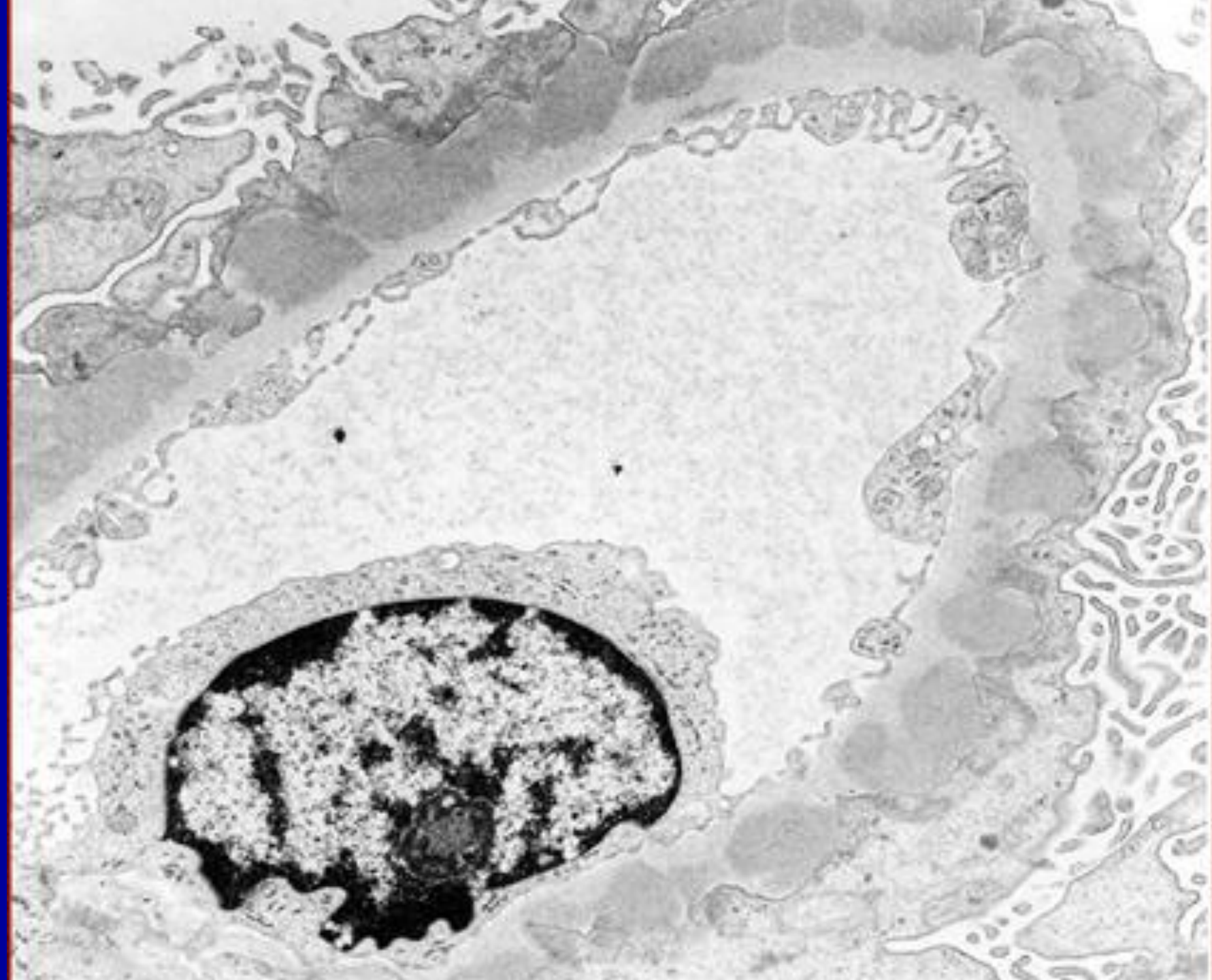
OCCURS AS IDIOPATHIC OR SECOND-
ARY TO HEPB, CA, GOLD, OR SLE

LABS - HEPBsAg, ANA, AND ROUTINE
AGE RELATED CA SCREENING

ANTIBODIES TO PLA2R (GBM PROTEIN)

High risk of VTE if UPC > 3, ALBUMIN < 2.5





FSGS

CAUSED BY REPLACEMENT OF BM
BY CONNECTIVE TISSUE WHICH LEADS
TO ALTERED PERMEABILITY AND FUNCTION

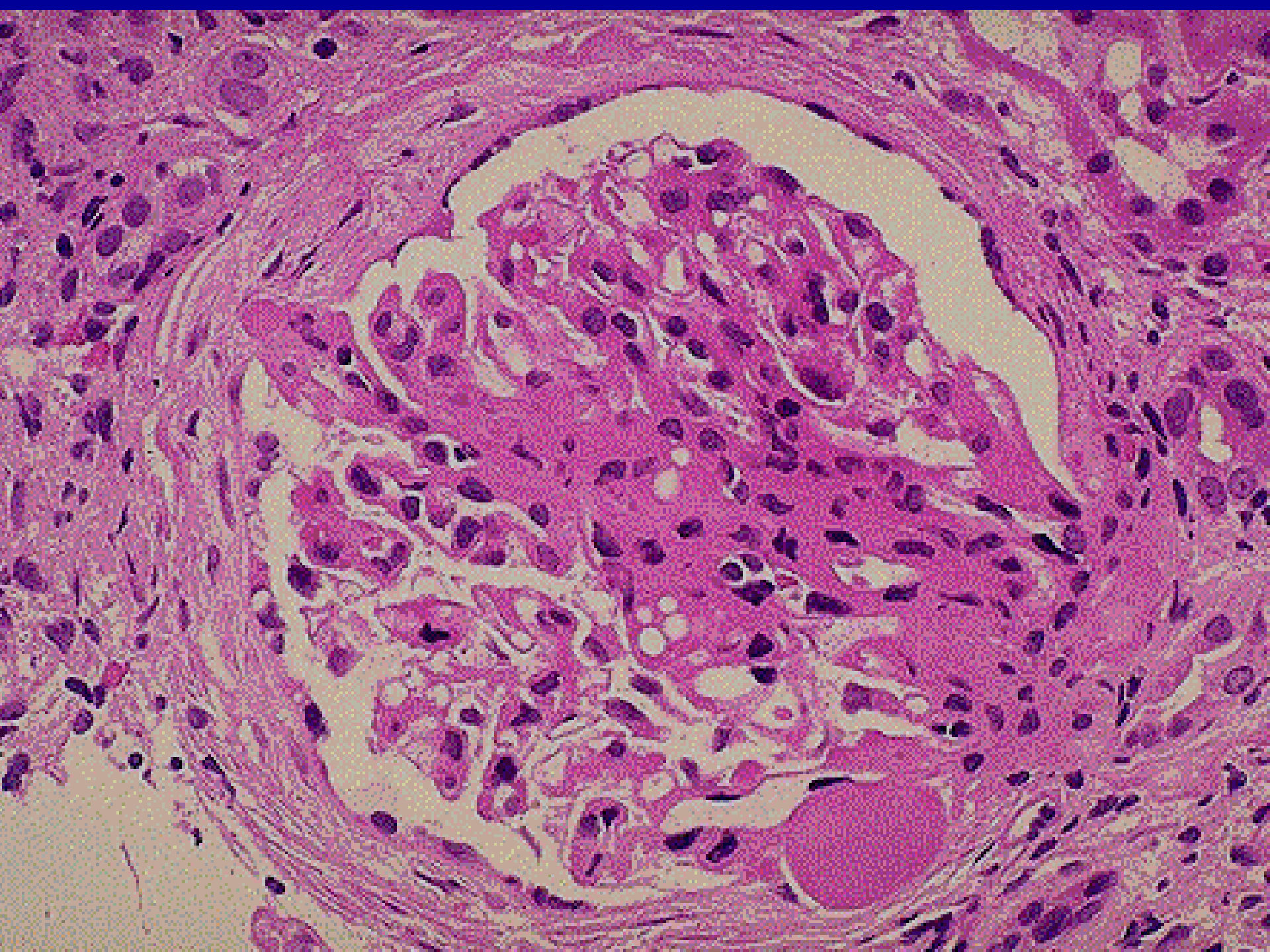
HTN AND CRF COMMON

(2nd most common primary gn)

MAY BE IDIOPATHIC AND FAMILIAL OR
SECONDARY TO HIV, HEROIN, SLEEP APNEA OBESITY,
PAMIDRONATE OR HYPERFILTRATION

LABS - HIV, DRUG SCREEN

APOL -1 IN AFRICAN AMERICANS – WORSE DX



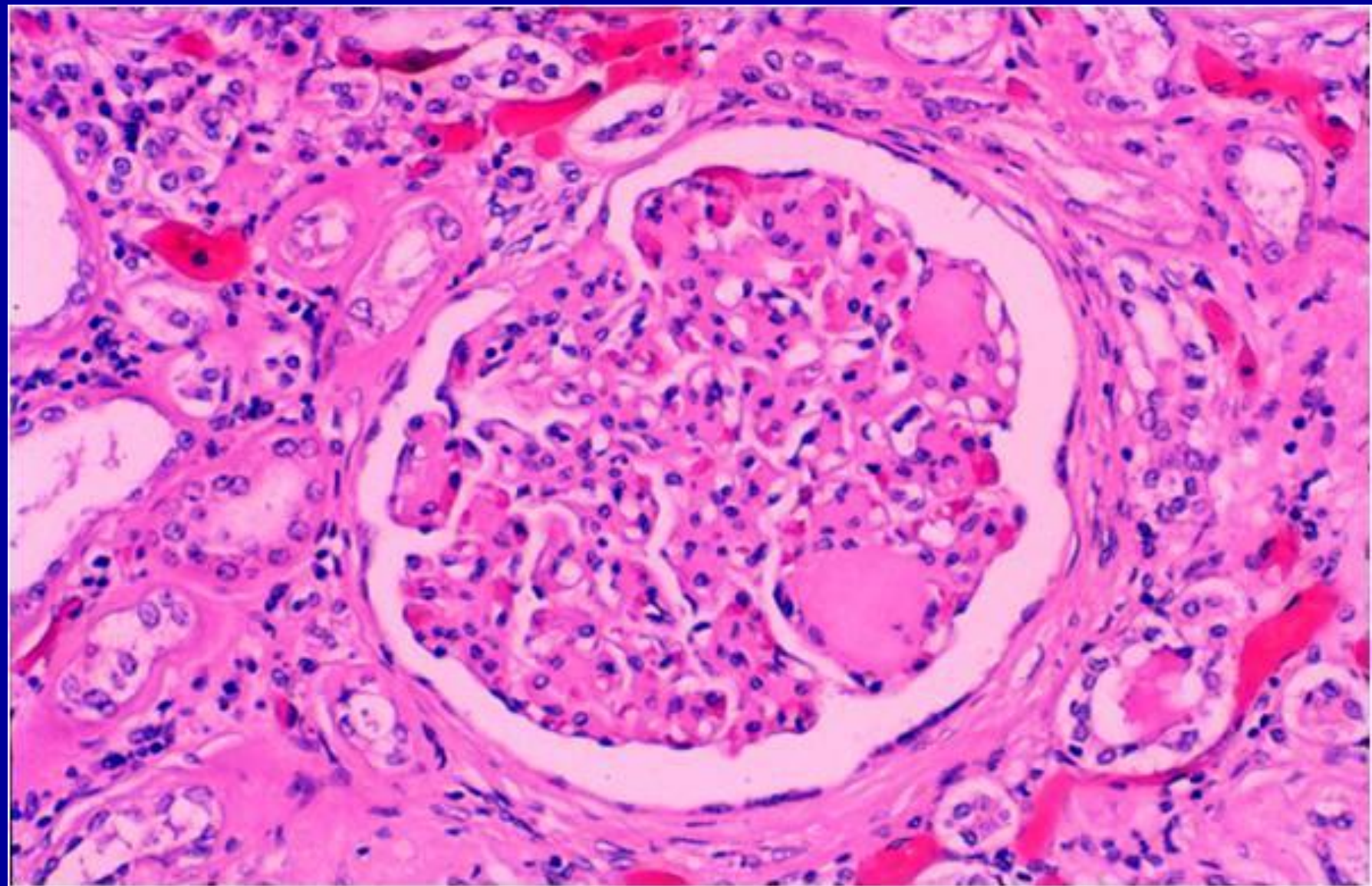
DIABETIC GLOMERULOSCLEROSIS

MODIFICATION OF GLYCOPROTEINS AND
HEMODYNAMIC FACTORS LEAD TO ALTER-
ATION OF PROTEIN PERMEABILITY AND
FUNCTION

CRF AND HTN ARE INEVITABLE (#1 cause of ESRD
US)

DM I AND DM II 10-15 year history

LABS - FBS, 2HR PP, FUNDI



PROTEIN DEPOSITION DISEASE

DIFFERENT PROTEINS MAY BE DEPOSITED
IN THE GLOMERULUS

AMYLOID - AA OR AL

LDD - INTACT LIGHT CHAINS

FIBRILLAR/IMMUNOTACTOID - IgG

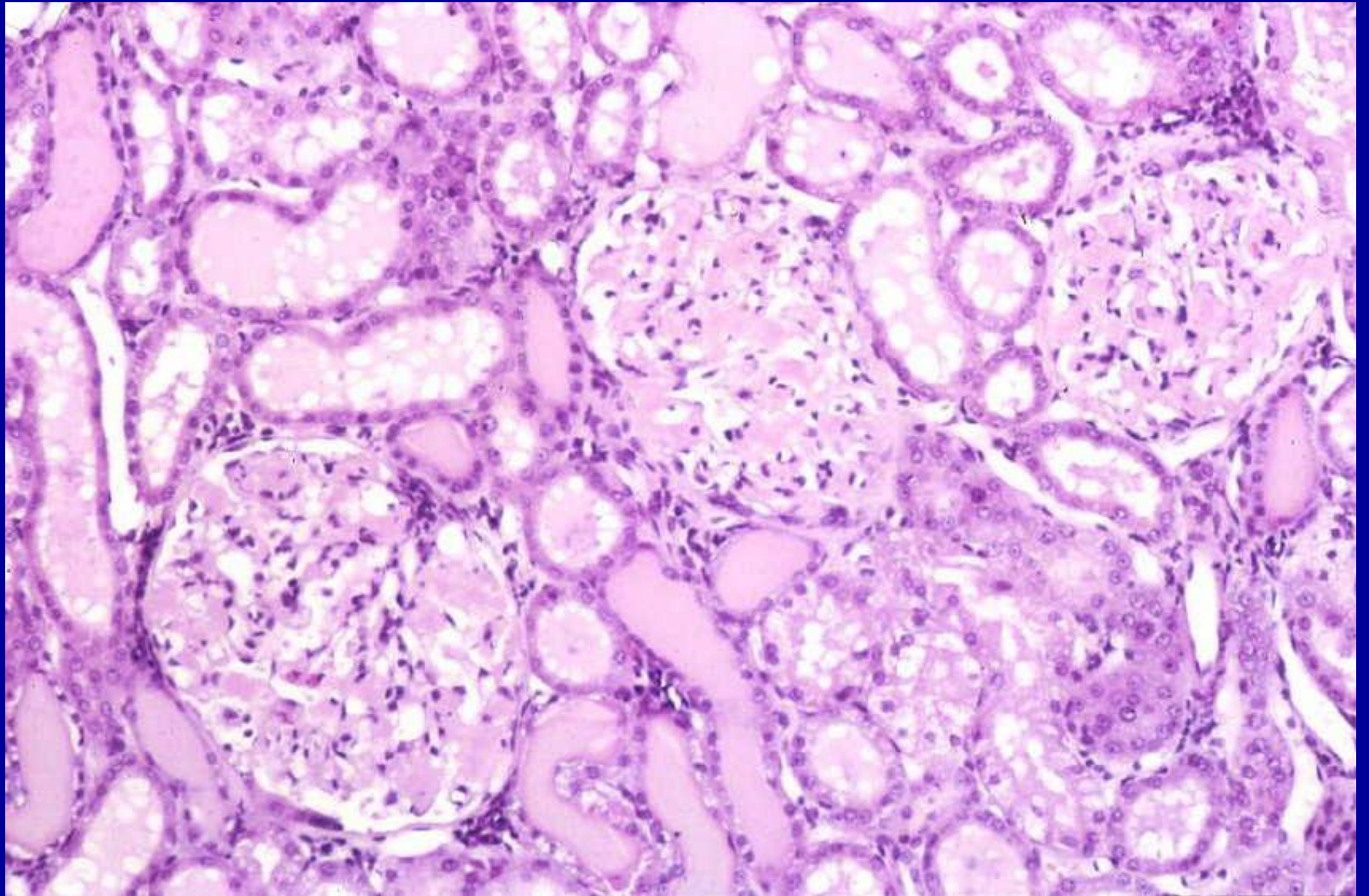
AMYLOIDOSIS/LDD

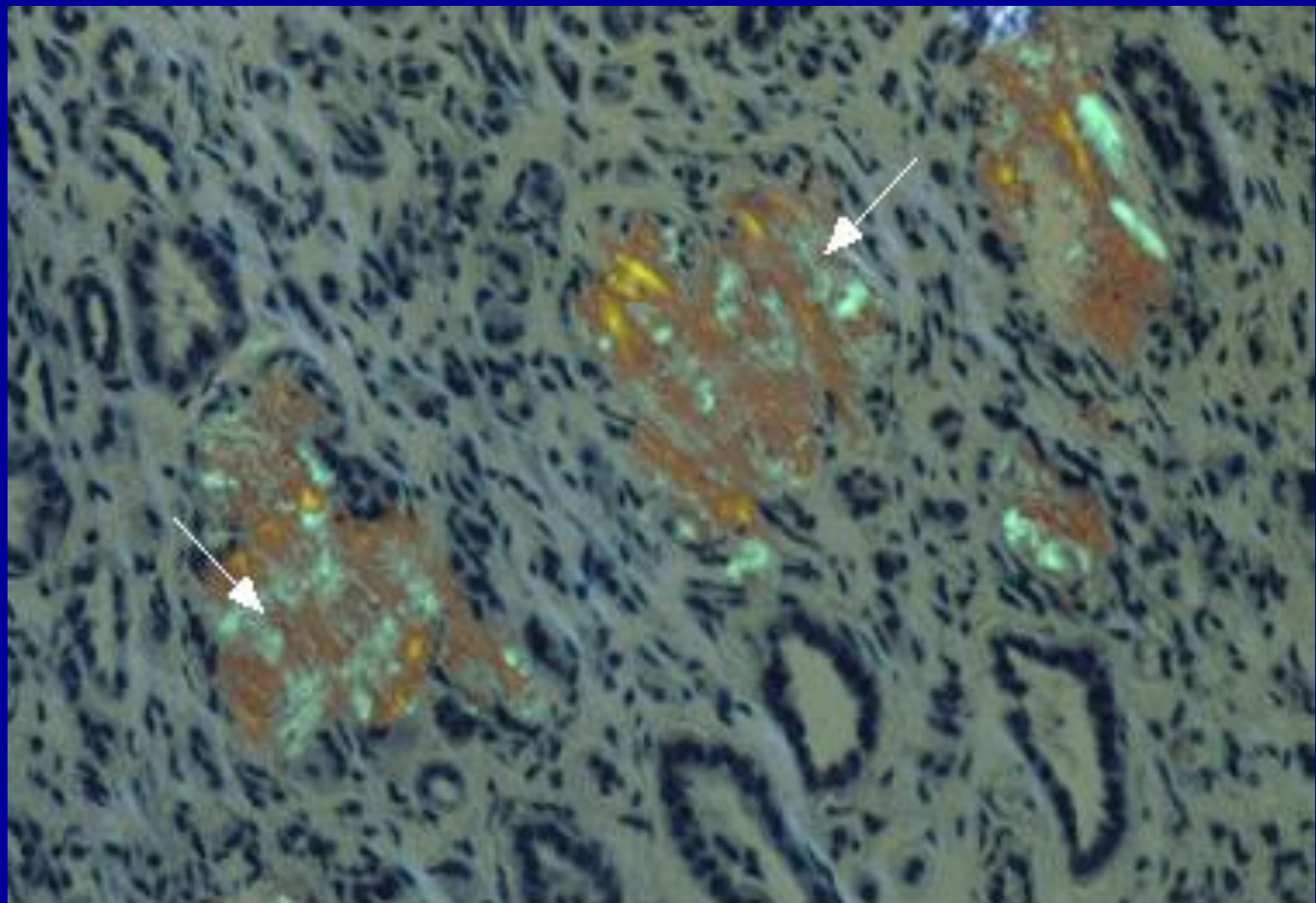
DEPOSITION OF ABNORMAL PROTEINS
AROUND THE BASEMENT MEMBRANE ALTER
THE PERMEABILITY AND FUNCTION

AL, AA, OR LIGHT CHAINS

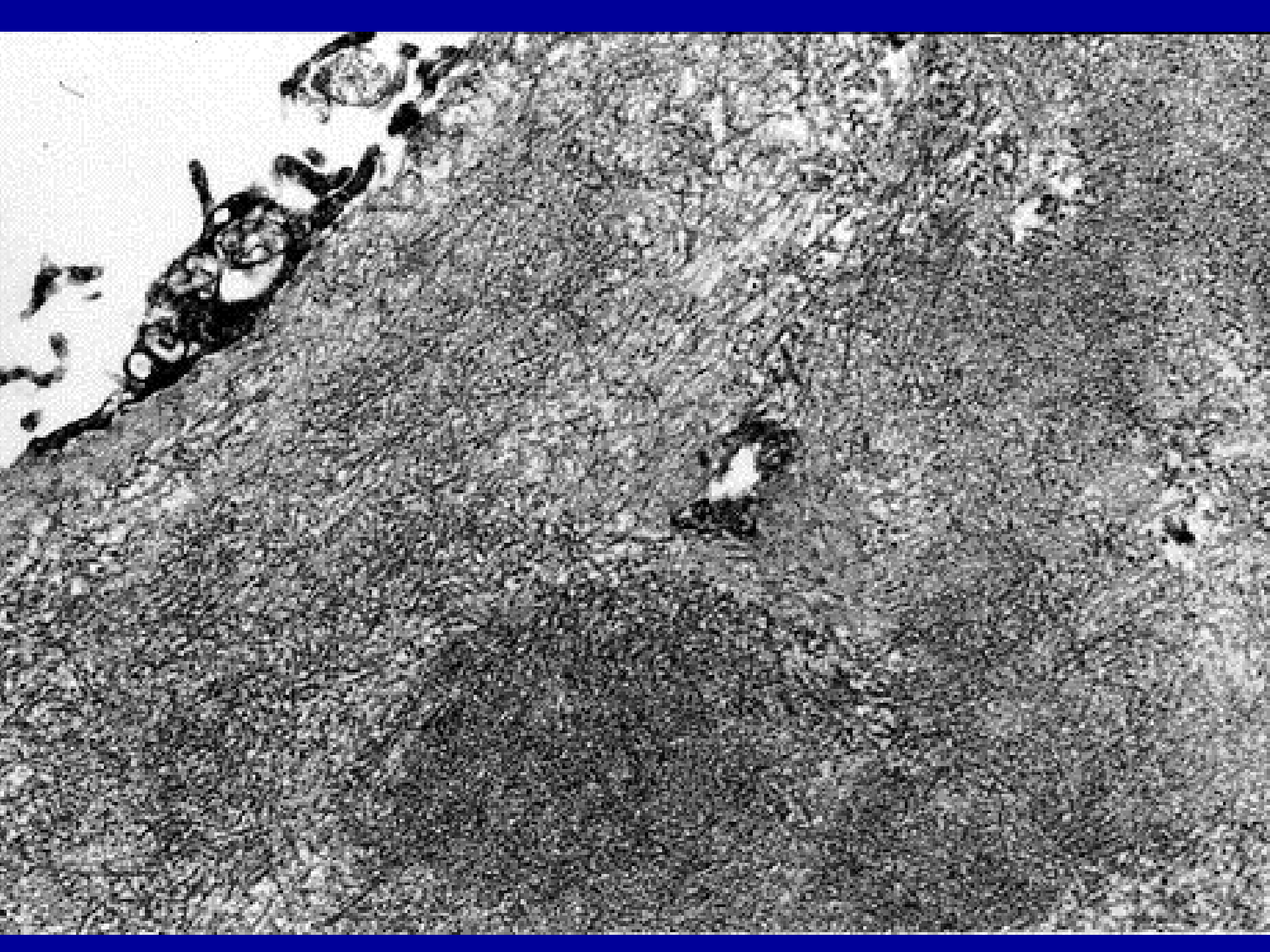
MAY BE PRIMARY (+ OR - MYELOMA) AL
OR SECONDARY TO INFLAMMATORY DX AA

LABS - SPEP, IEP, UPEP, BM BX, OR
BLIND BIOPSY (FAT PAD), SERUM FREE LIGHT
CHAINS





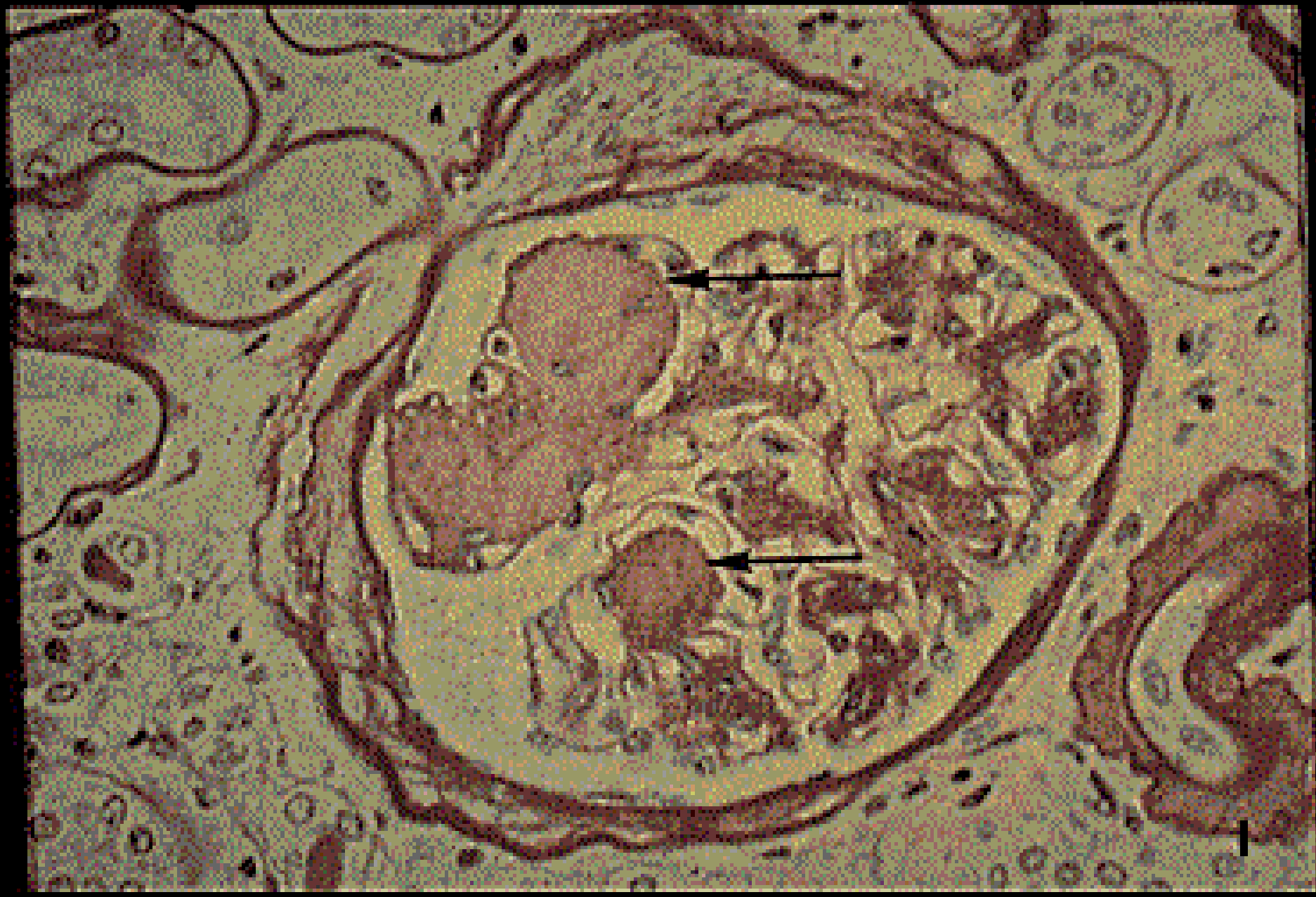
Congo red stain in amyloidosis Congo red stain viewed under polarized light of a renal biopsy from a patient with renal amyloidosis. Green birefringence (white arrows) of interstitial amyloid deposits can be seen. Courtesy of Helmut Bockler, MD.



Case 2

What glomerular disease does this patient have?

After a limited serologic workup (hepatitis, HIV, and ANA) was negative a kidney biopsy was performed



What glomerular disease does this patient have?

1. Focal segmental glomerulosclerosis
2. Amyloidosis
3. **Diabetic glomerulosclerosis**
4. Minimal change
5. Membranous

GLOMERULONEPHRITIS

CLINICAL APPROACH TO GLOMERULAR DISEASE

John Prior prior.jack@gmail.com

570-348-0360