GLOMERULONEPHRITIS

CLINICAL APPROACH TO GLOMERULAR DISEASE

ACOI 2019

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:

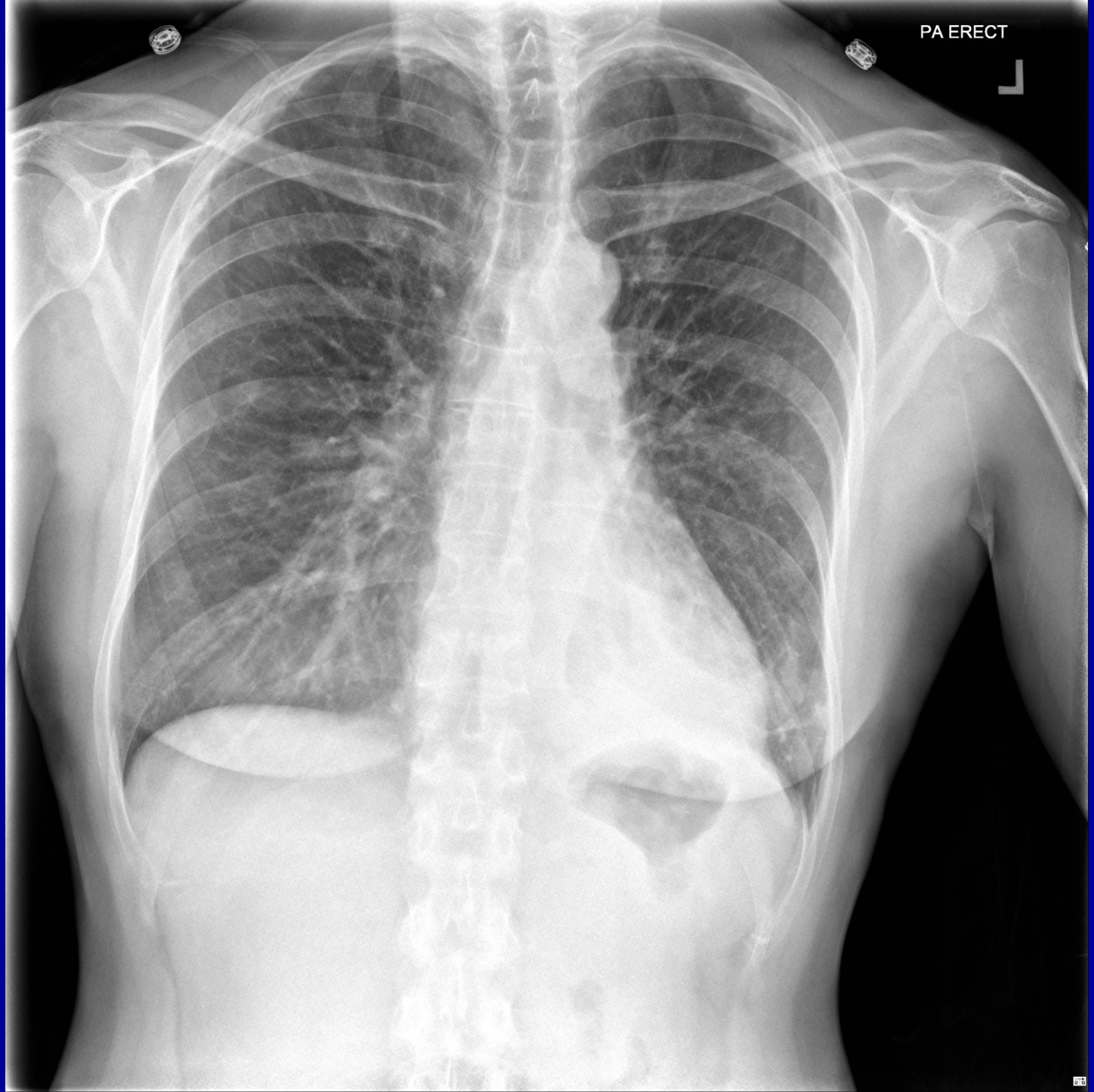
BUN 61 Creatinine 3.8 Lytes OK

WBC 11.08 diff – 15 eosinophils

UA - +4 protein 10-20 RBCs 5 WBCs

Microscopic UPC 4 UAC 3300

CXR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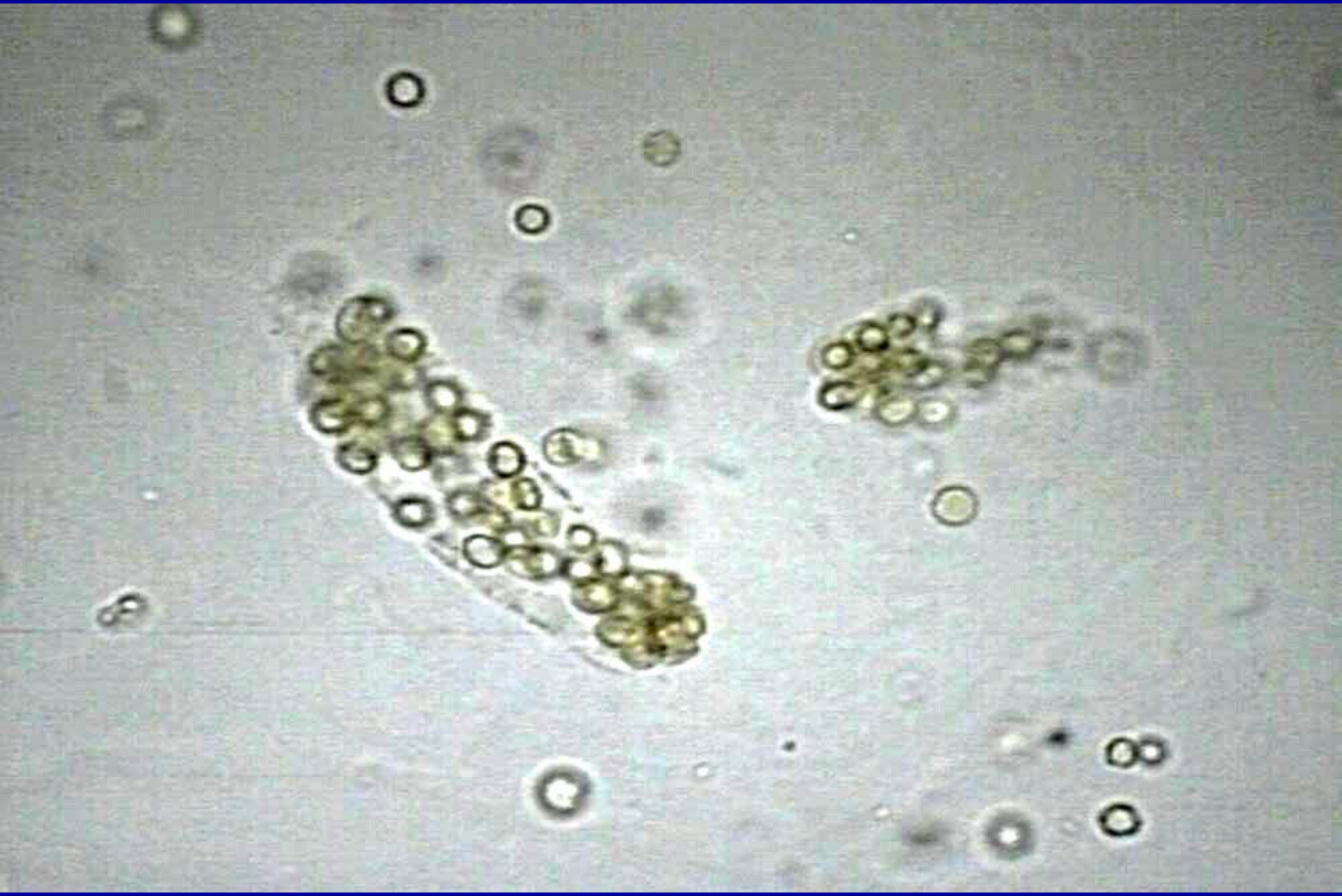
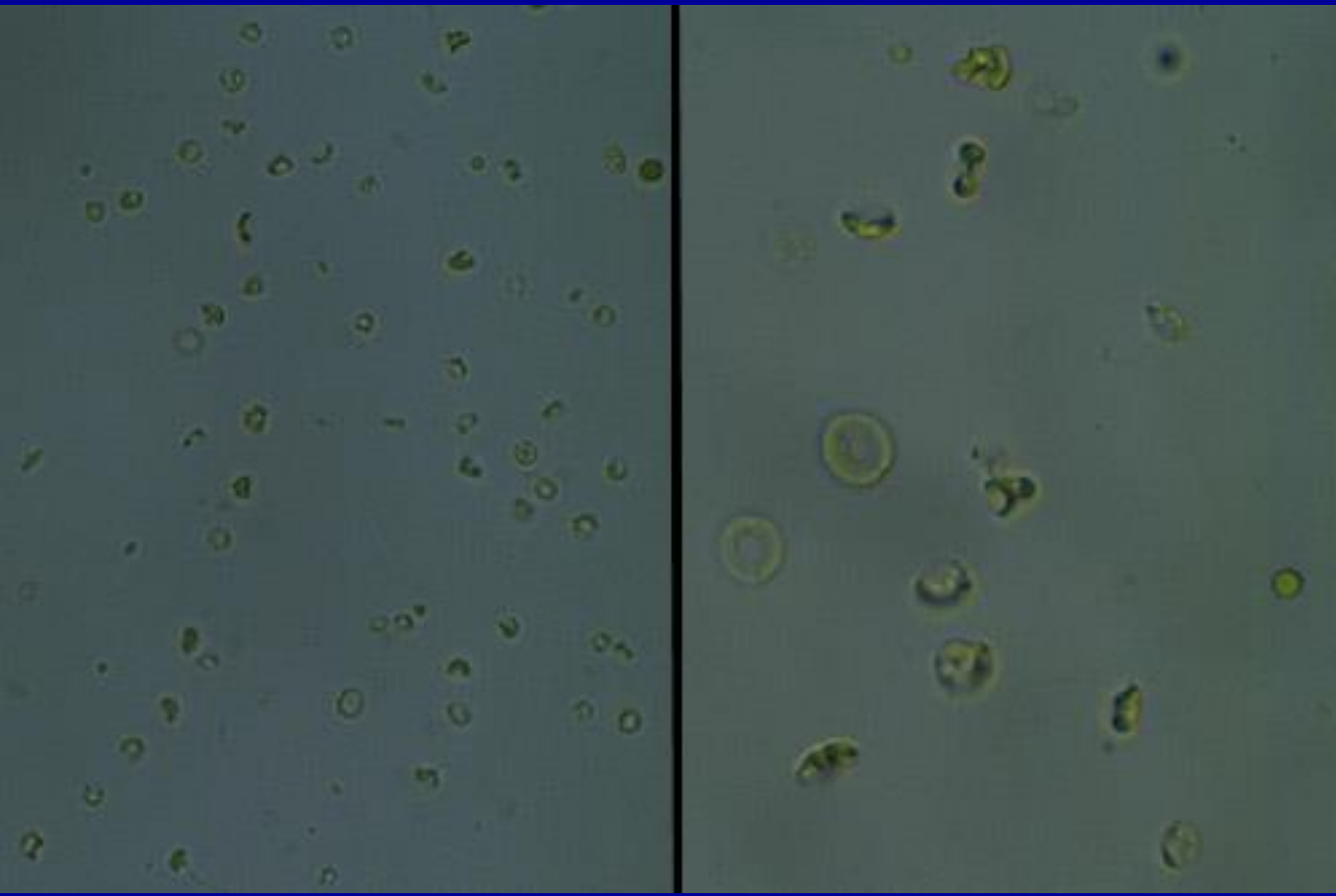
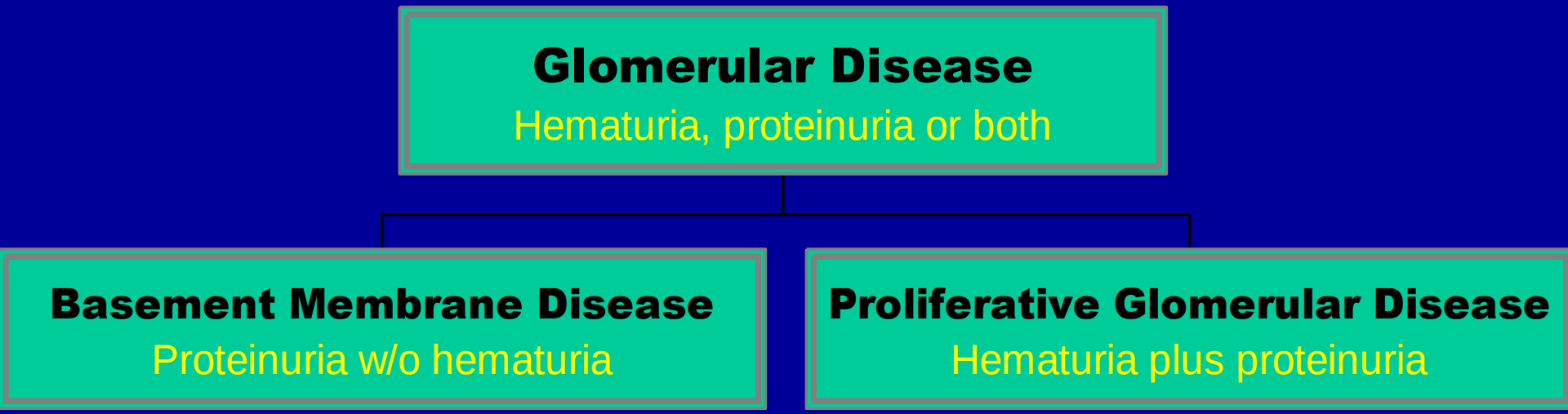




What is her diagnosis?

1. SLE
2. IgA Vasculitis
3. Eosinophilic granulomatous polyangiitis (EGPA)
4. Mixed cryoglobulimemia
5. Microscopic polyangiitis (MPA)

Glomerulonephritis



GLOMERULONEPHRITITS 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

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	**Normal Complement**
SLE	Goodpasture's
Mixed Cryoglobinemia	GPA
Postinfectious	IgA, MPA, EGPA
Post Strep	IgA, Misc. IC Dx
MPGN	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 ABSCESSES, 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

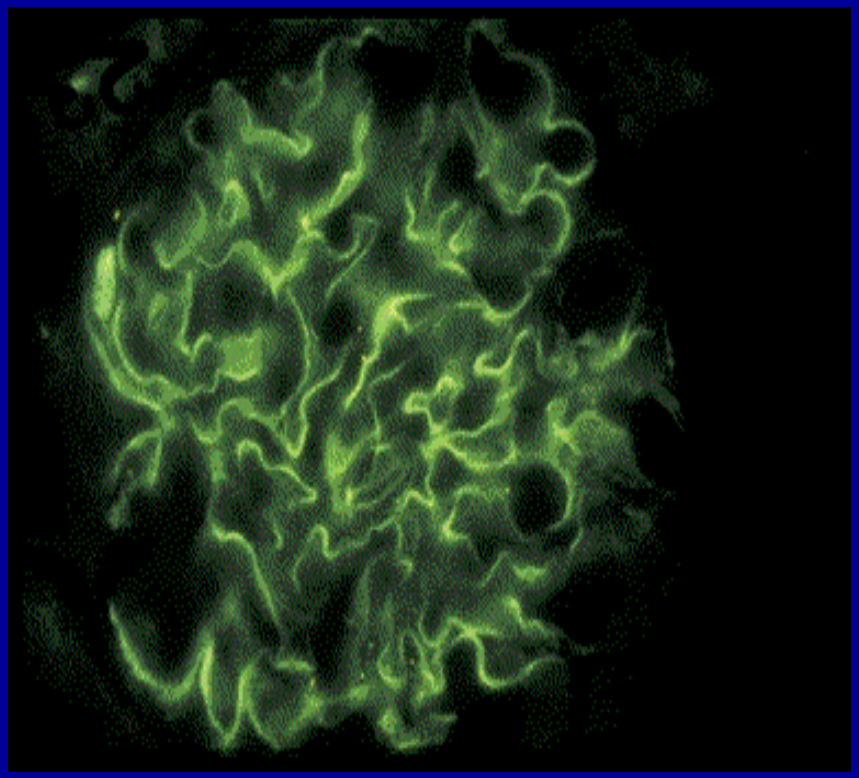
EOSINOPHILIC GRANULOMATOUS POLYANGIITIS

IGA VASCULITIS

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 VACULITITIS (SMALL VESSEL)
- EXAMPLES - GPA, MPA, IGA, 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)

IGA VASCULITIS

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

NO DIAGNOSTIC SEROLOGY

POST STAPH

FORMERLY HENOCH SCHONLEIN PURPURA

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)
- FORMERLY CHURG STRAUS

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

Case 2 Hematuria

25 yo woman presents with respiratory tract infection associated with dark urine

UA + 3 blood. + 3 protein 20-30 dysmorphic RBCs. UPC 2500 UAC 1400

GFR 45. C3 and C4 normal

Case 2 Hematuria

What is the most likely diagnosis?

1. Post Strep GN
2. IgA GN

Case 2 Hematuria

What is the most likely diagnosis?

1. Post Strep GN
2. IgA GN

Case 3 Hematuria

35 yo man present with dark urine and rash

UA 20-30 dysmorphic RBCs , UPC 1800 UAC 1200

GFR 30, Hg 8, PLT 40 K

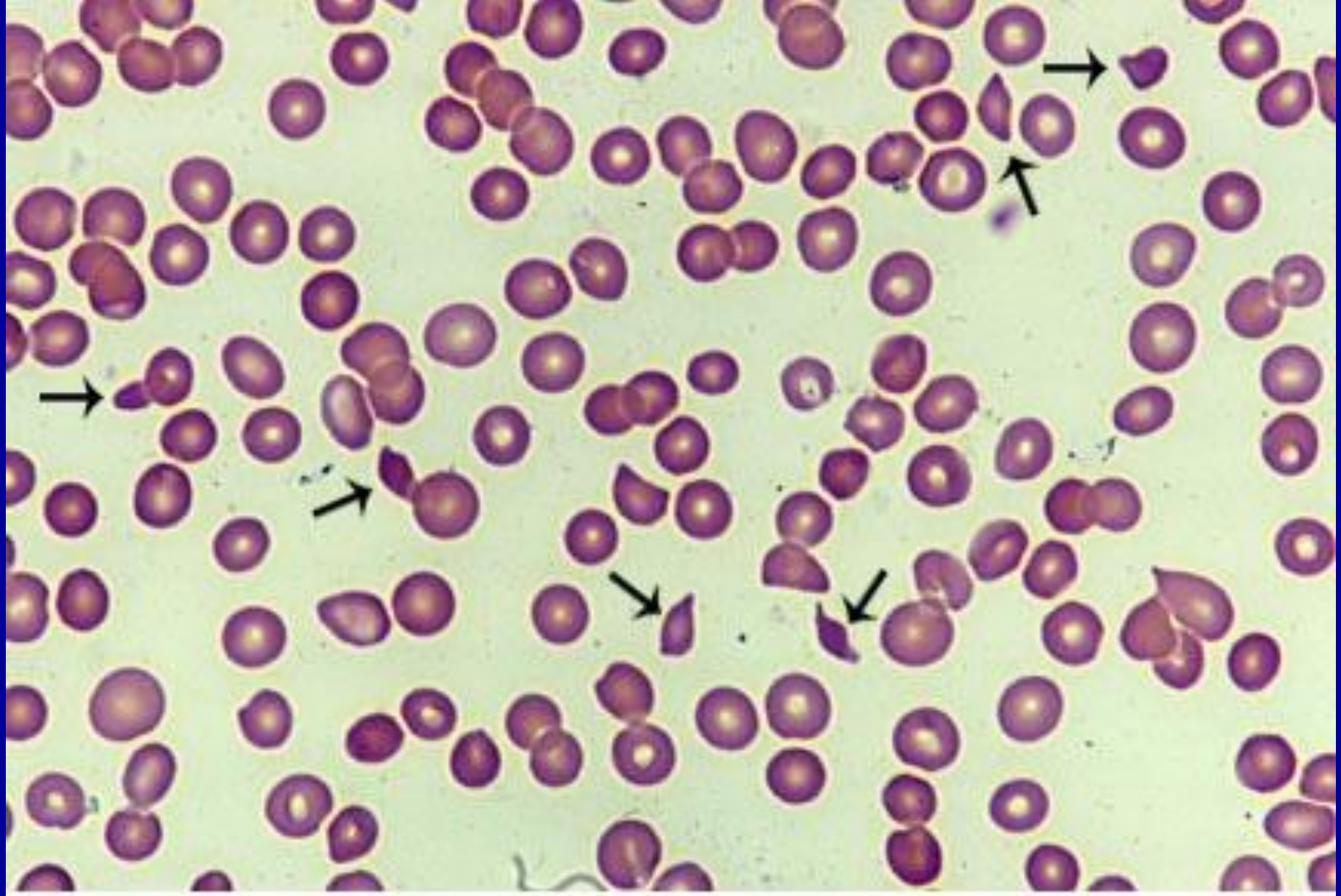
ALT and LDH > 1000

PE - purpura

Case 3 Hematuria

What is the most appropriate next test?

1. C3 C4
2. Peripheral smear
3. ANA
4. ANCA
5. Hep C



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

Case 3 Hematuria

What is the most appropriate next test?

1. C3 C4
2. Peripheral smear
3. ANA
4. ANCA
5. Hep C

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

Case 4 Hematuria

55 yo woman presents with 3 month hx of painless hematuria. GFR NL, UAC and UPC NL

PMH negative, + tobacco (quit)BP NL,

Renal US – normal without mass, stones or hydronephrosis

Urine culture negative

Case 4 Hematuria

What is the appropriate next test?

1. Renal biopsy
2. C3 and C4
3. Genetic testing for Alport's syndrome
4. Urine cytology
5. Cystoscopy

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

Case 4 Hematuria

What is the appropriate next test?

1. Renal biopsy
2. C3 and C4
3. Genetic testing for Alport's syndrome
4. Urine cytology
5. Cystoscopy

Case 5 Hematuria

60 yo man presents with progressive renal failure. Hx of GERD dxed 4 months ago and started on PPI. No rash. + fever

Baseline GFR 80. Current GFR 22

UA – 10-20 dysmorphic RBCs, few WBCs. On eosinophils. UPC 500 UAC 150

Case 5 Hematuria

The most likely diagnosis here?

1. IgA GN
2. Allergic interstitial nephritis
3. Post Strep GN
4. TMA
5. SLE

AIN vs. AGN Differentiation

AIN - Rash – 15 percent

Fever – 27 percent

Eosinophilia – 23 percent

Triad of rash, fever, and eosinophilia – 10 percent

UPC < 1000

GN – more proteinuria, HTN and edema

Case 5 Hematuria

The most likely diagnosis here?

1. IgA GN
2. Allergic interstitial nephritis
3. Post Strep GN
4. TMA
5. SLE

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 +)

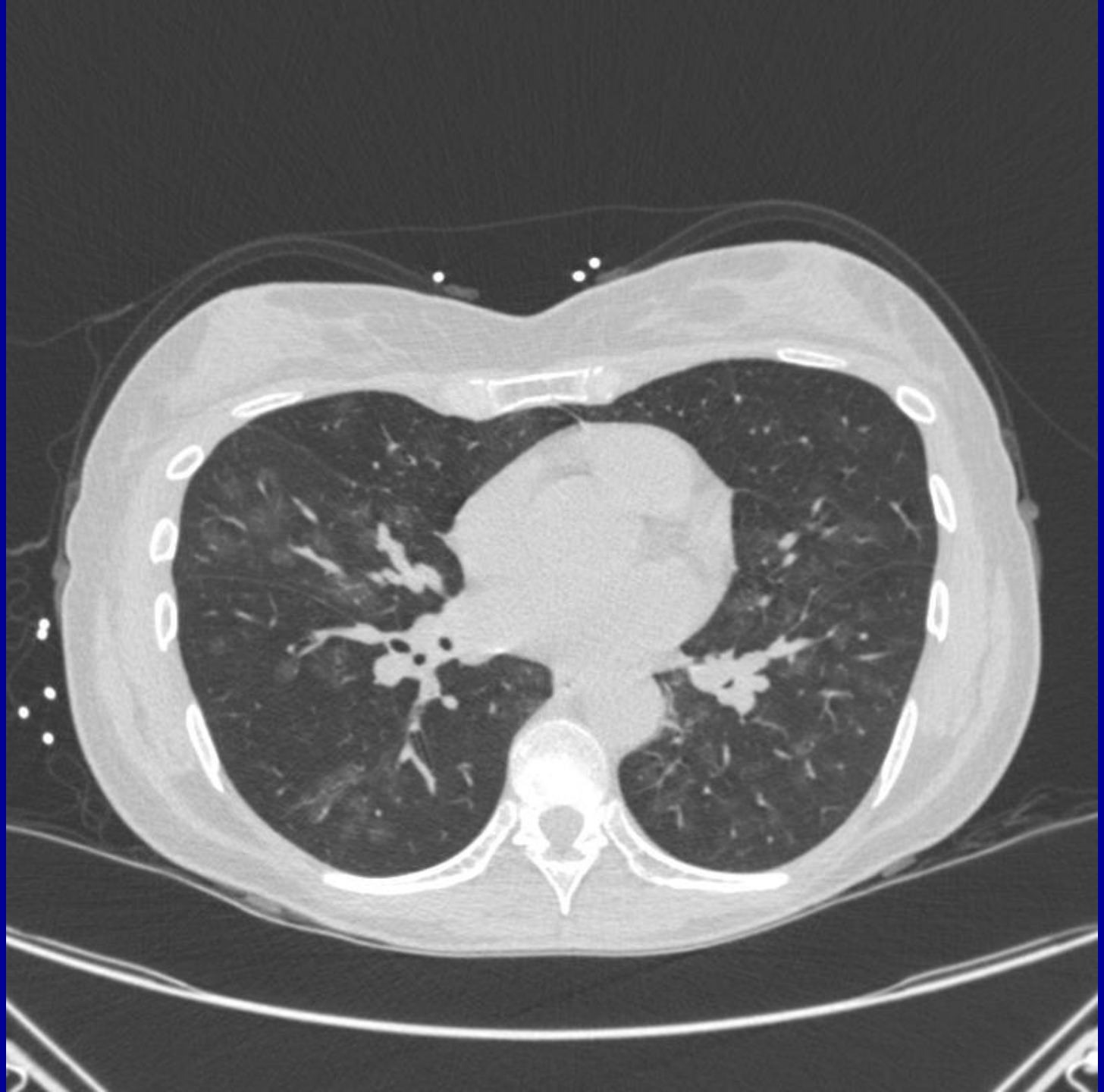
Case 1

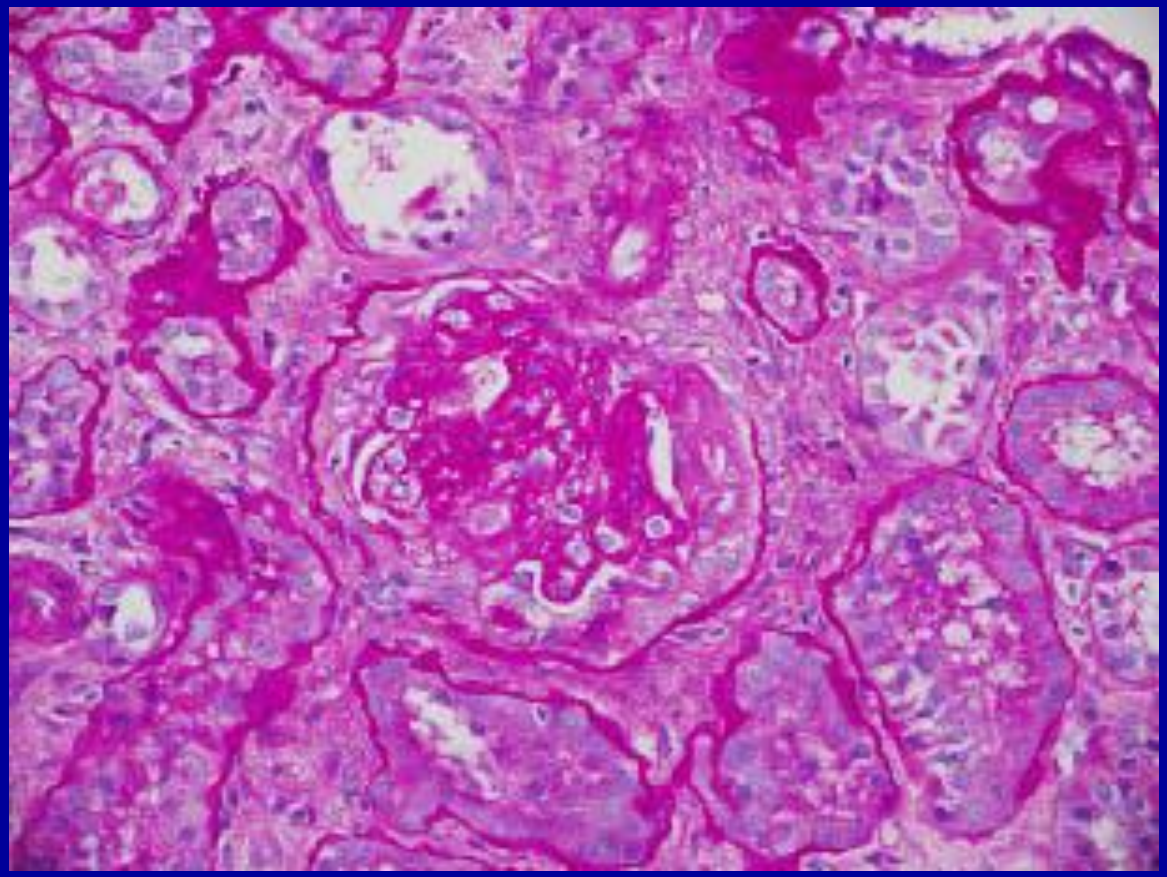
BM bx – negative for myeloma

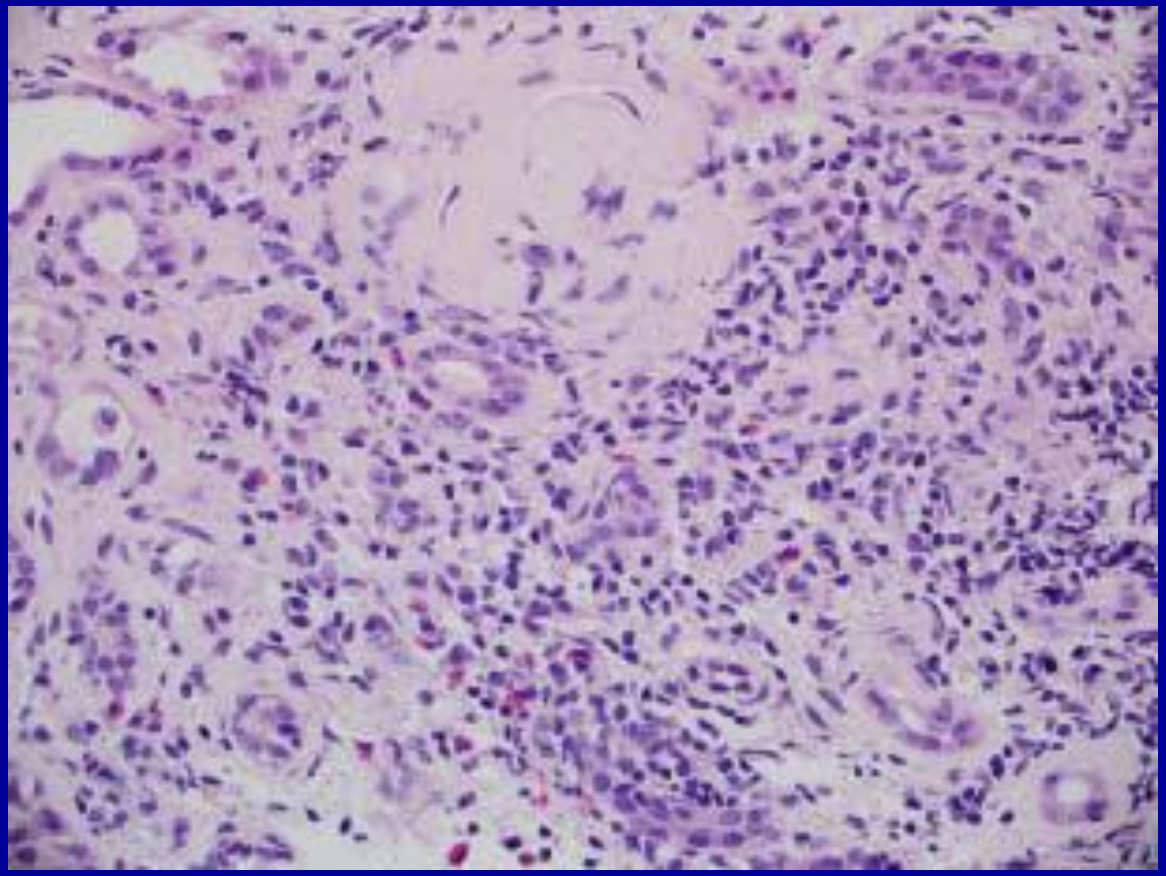
CT chest

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

Renal biopsy







Glomerulonephritis - proliferative

Low Complement	**Normal Complement**
SLE	Goodpasture's
Mixed Cryoglobinemia	GPA
Postinfectious	IGA, MPA, EGPA
Post Strep	IgA, Misc. Im Complex
MPGN	Anti GBM
	Renal Vasculitis

What is her diagnosis?

1. SLE
2. IgA Vasculitis
3. Eosinophilic granulomatous polyangiitis (EGPA)
4. Mixed cryoglobulimemia
5. Microscopic polyangiitis (MPA)

Case 6

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

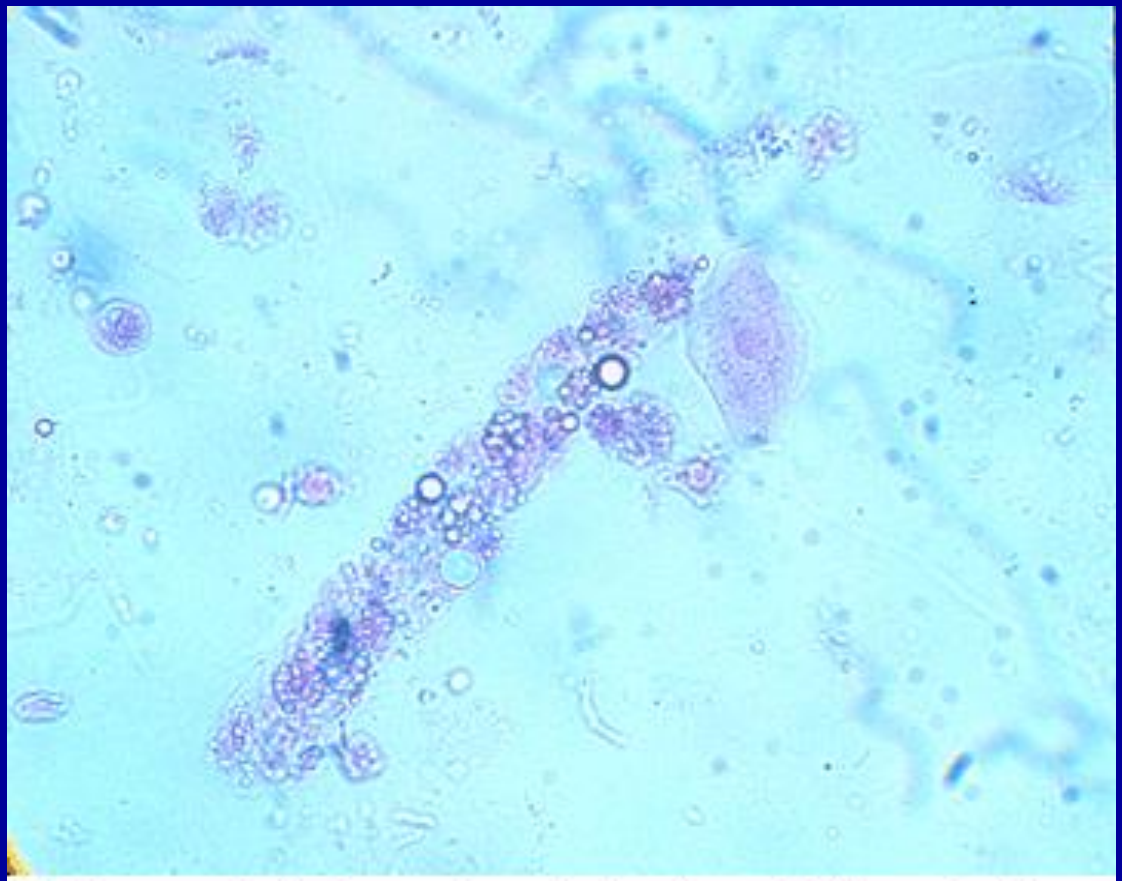
Urine albumin to protein ratio (UAPR)

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

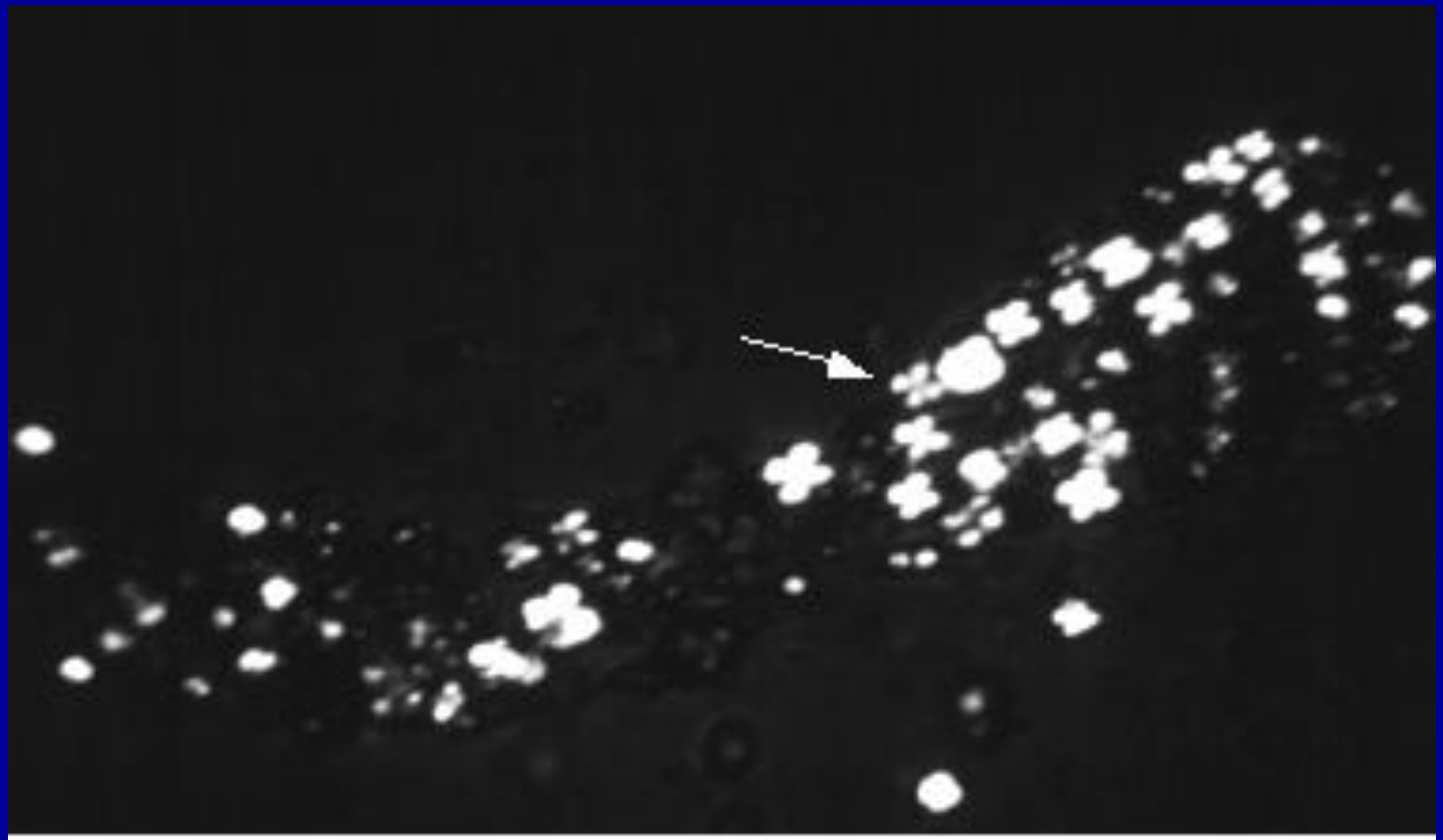
UAPR > 50% - glomerular

UAPR < 40% - tubular

UAPR < 25% - myeloma cast



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 polzarized 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

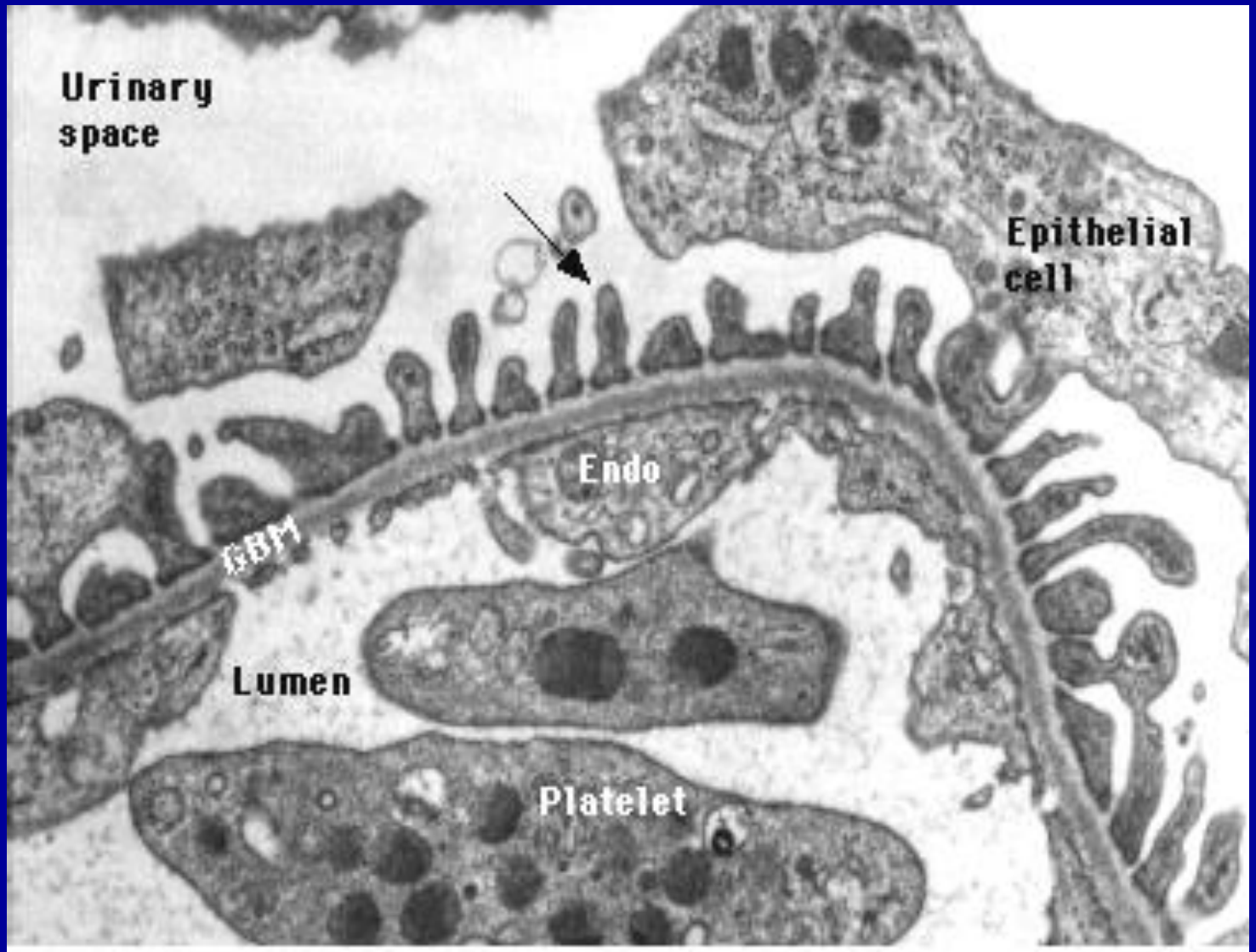
MINIMAL CHANGE

ALTERATION OF CHARGE OF BASEMENT MEMBRANE PORE ALLOWS ALBUMIN TO LEAK INTO URINARY SPACE

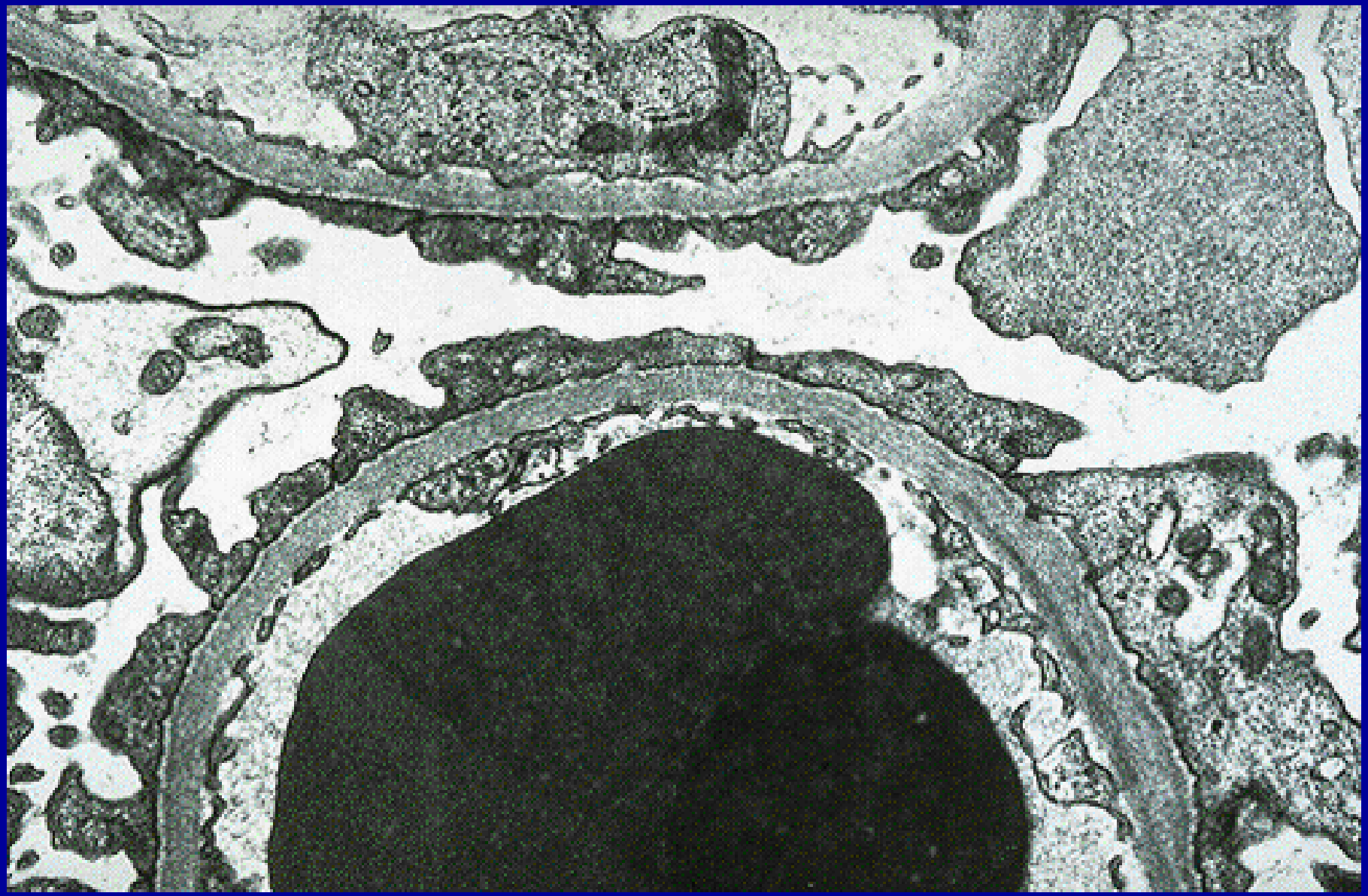
NO CHANGE IN KIDNEY FUNCTION AND ABSCENCE OF HTN (ATN IN ADULTS)

SEEN IN CHILDREN, LYMPHOPROLIFERATIVE DX, NSAIDS, IDIOPATHIC

PRODUCTION OF CYTOKINES MAY ALTER NEGATIVE CHARGE OF PORE GLYCOPROTEINS

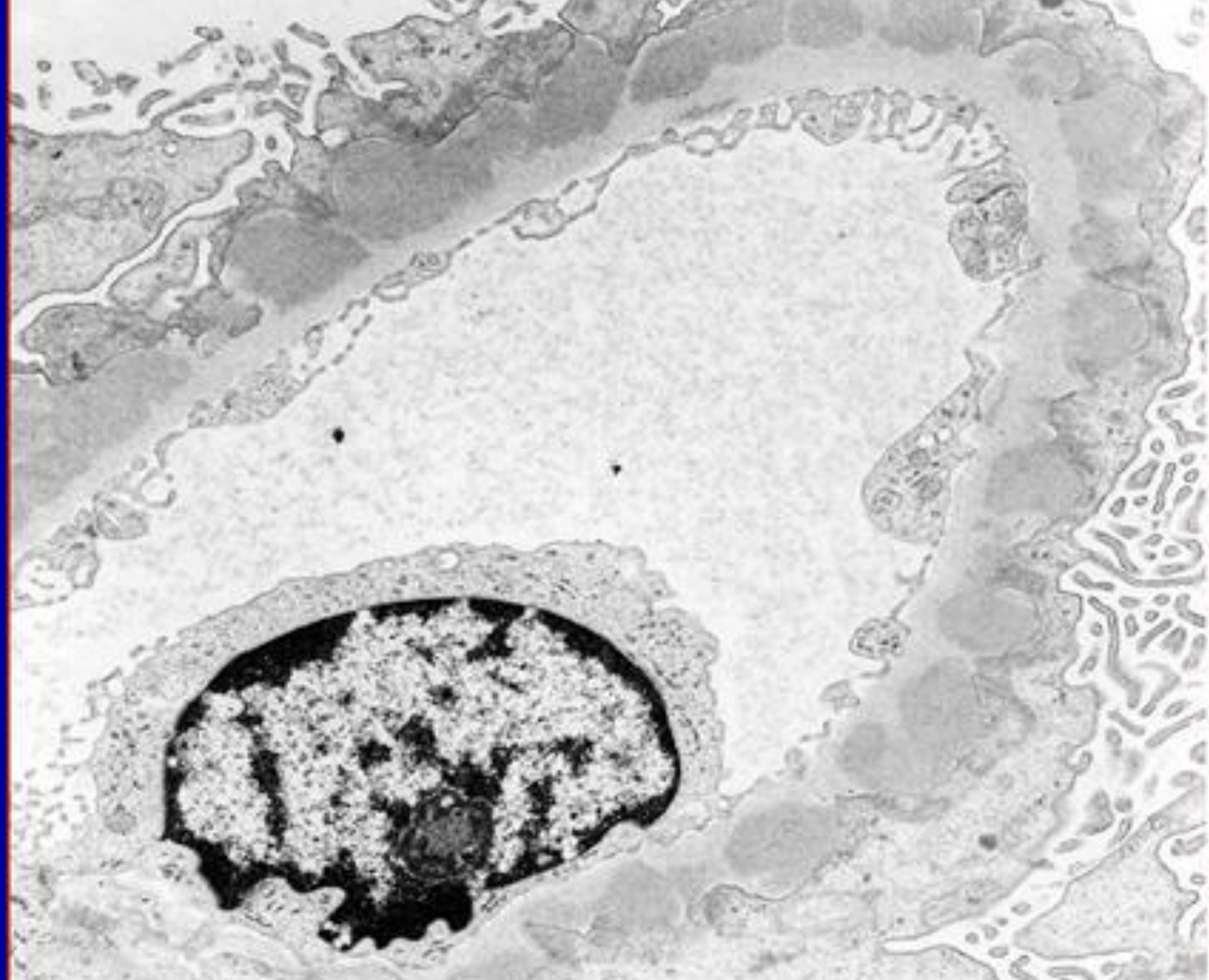


Normal glomerulus Electron micrograph of a normal glomerular capillar loop showing the fenestrated endothelial cell (Endo), the glomerular basement membrane (GBM), and the epithelial cells with its



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 SECONDARY 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

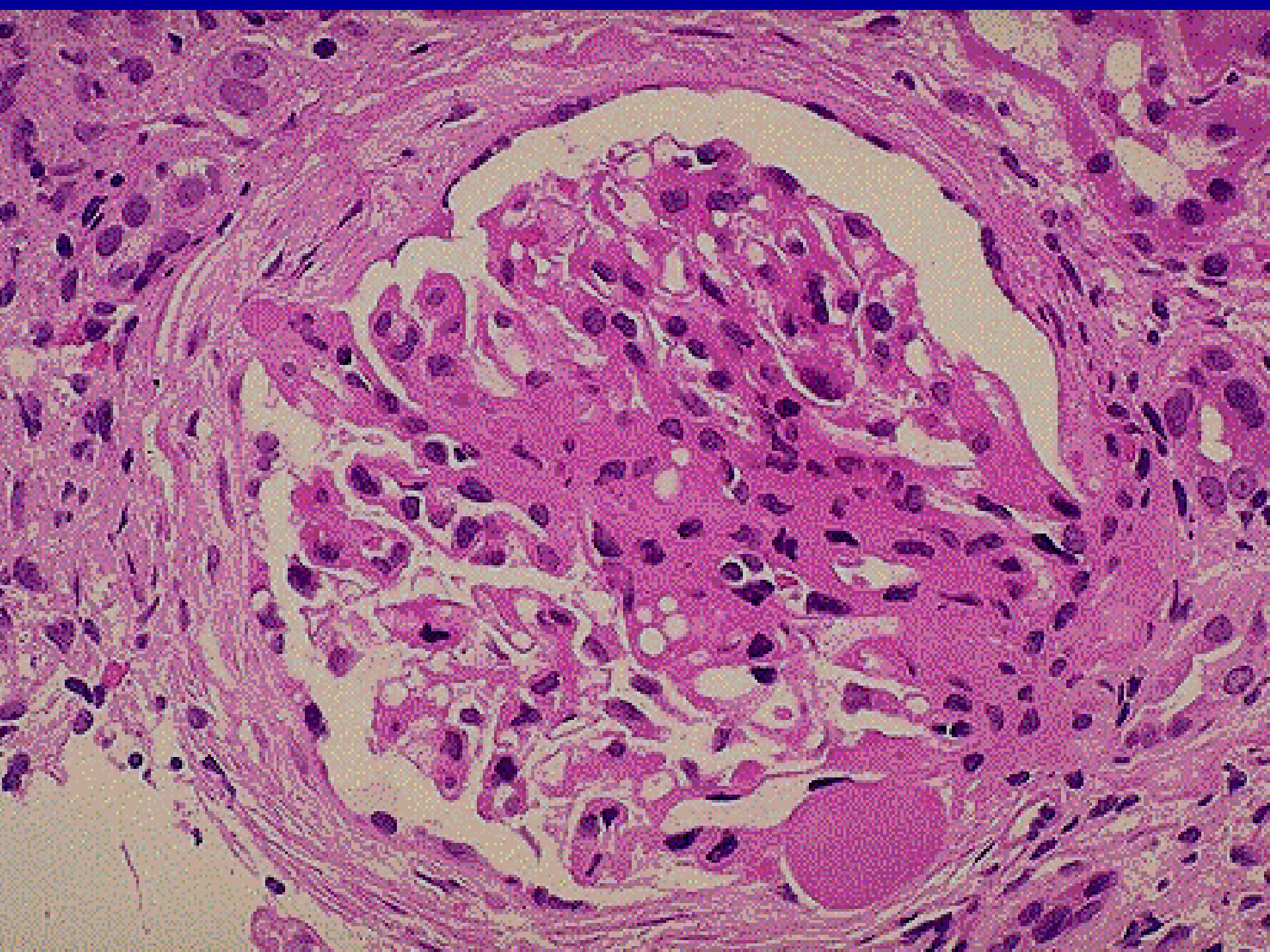
HTN AND CRF COMMON

(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



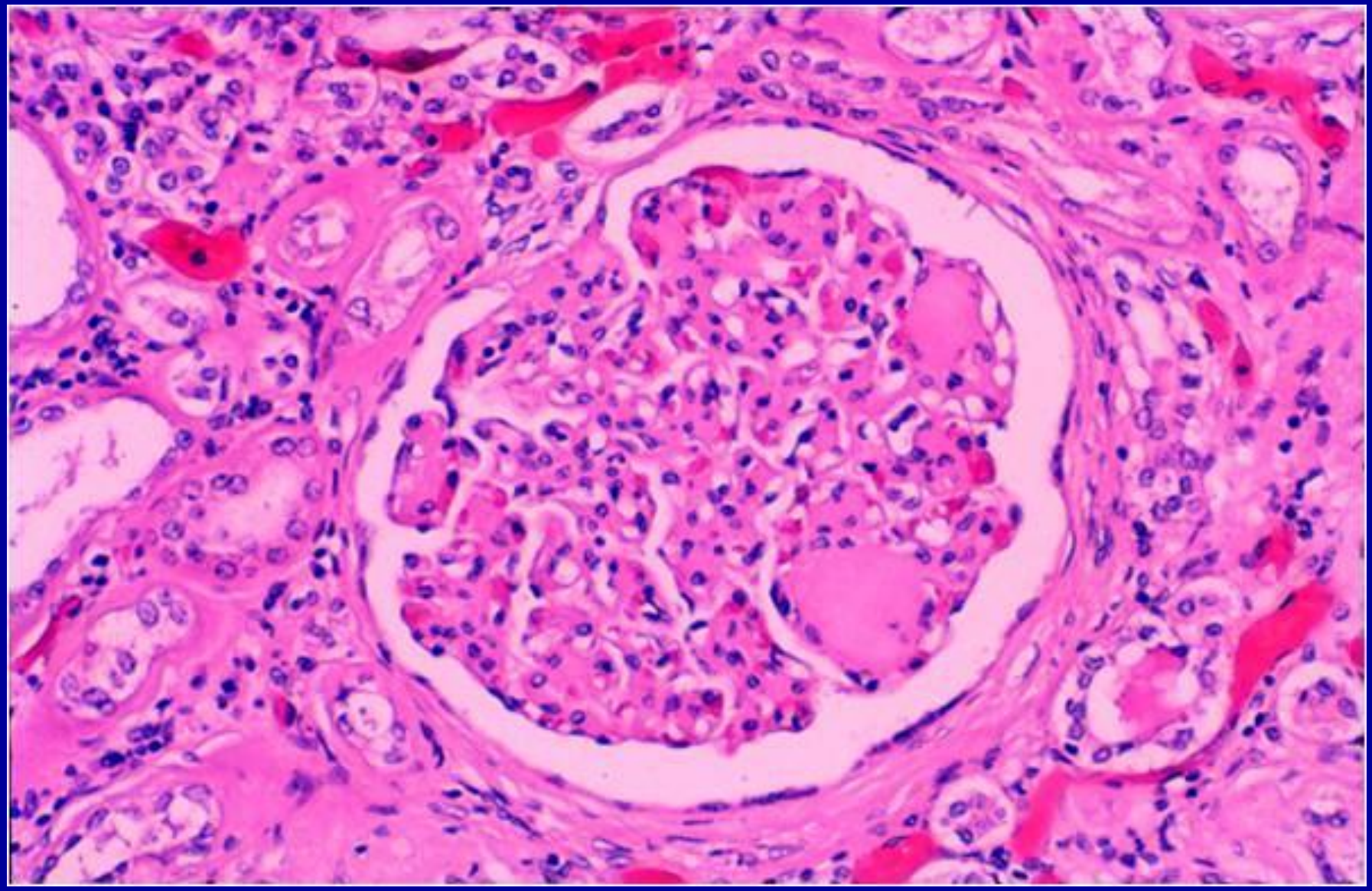
DIABETIC GLOMERULOSCLEROSIS

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

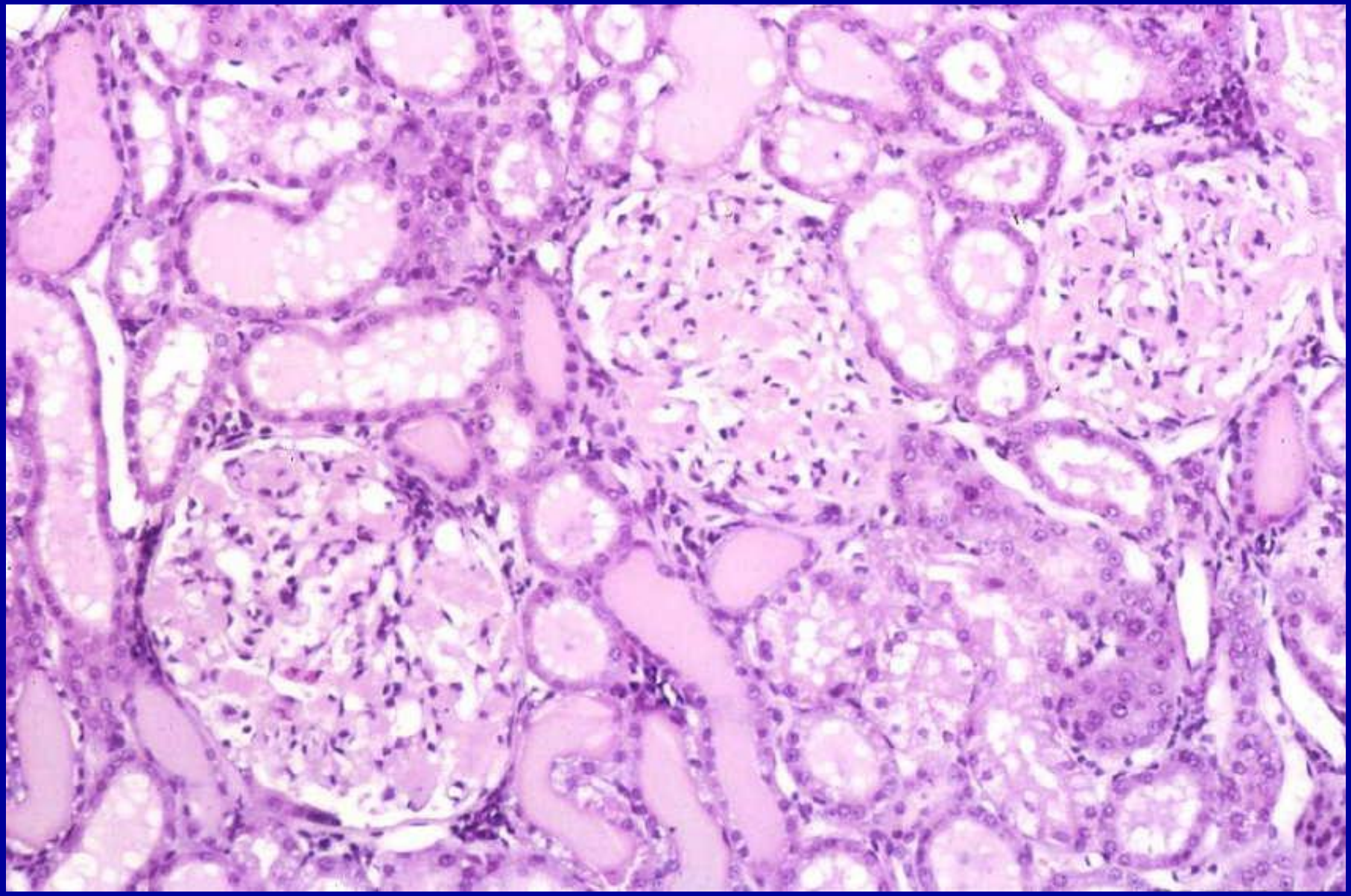
AMYLOIDOSIS/LDD

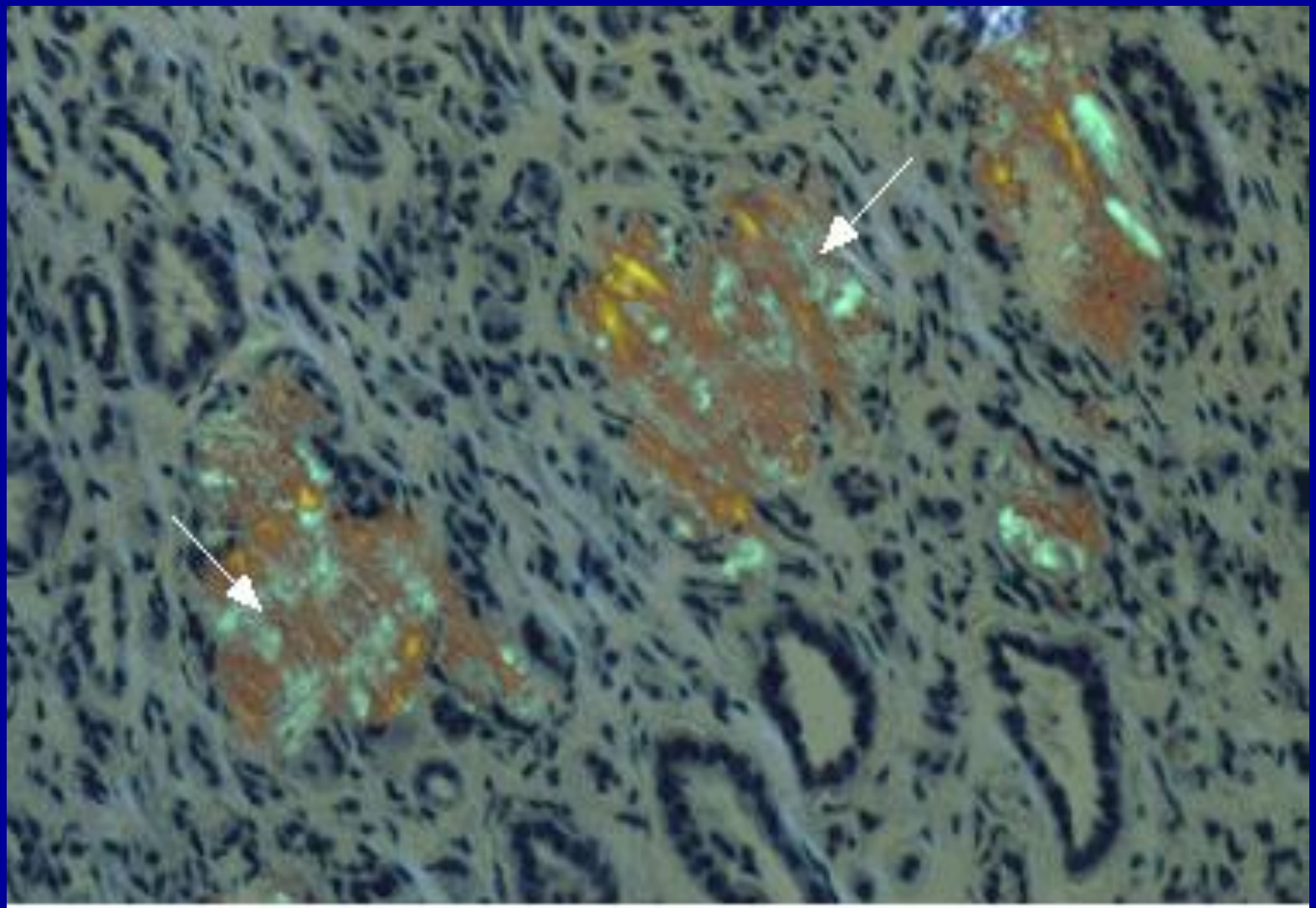
DEPOSITION OF ABNORMAL PROTEINS AROUND THE BASEMENT MEMBRANE ALTER THE PERMEABILITY AND FUNCTION

AL, AA, OR LIGHT CHAINS

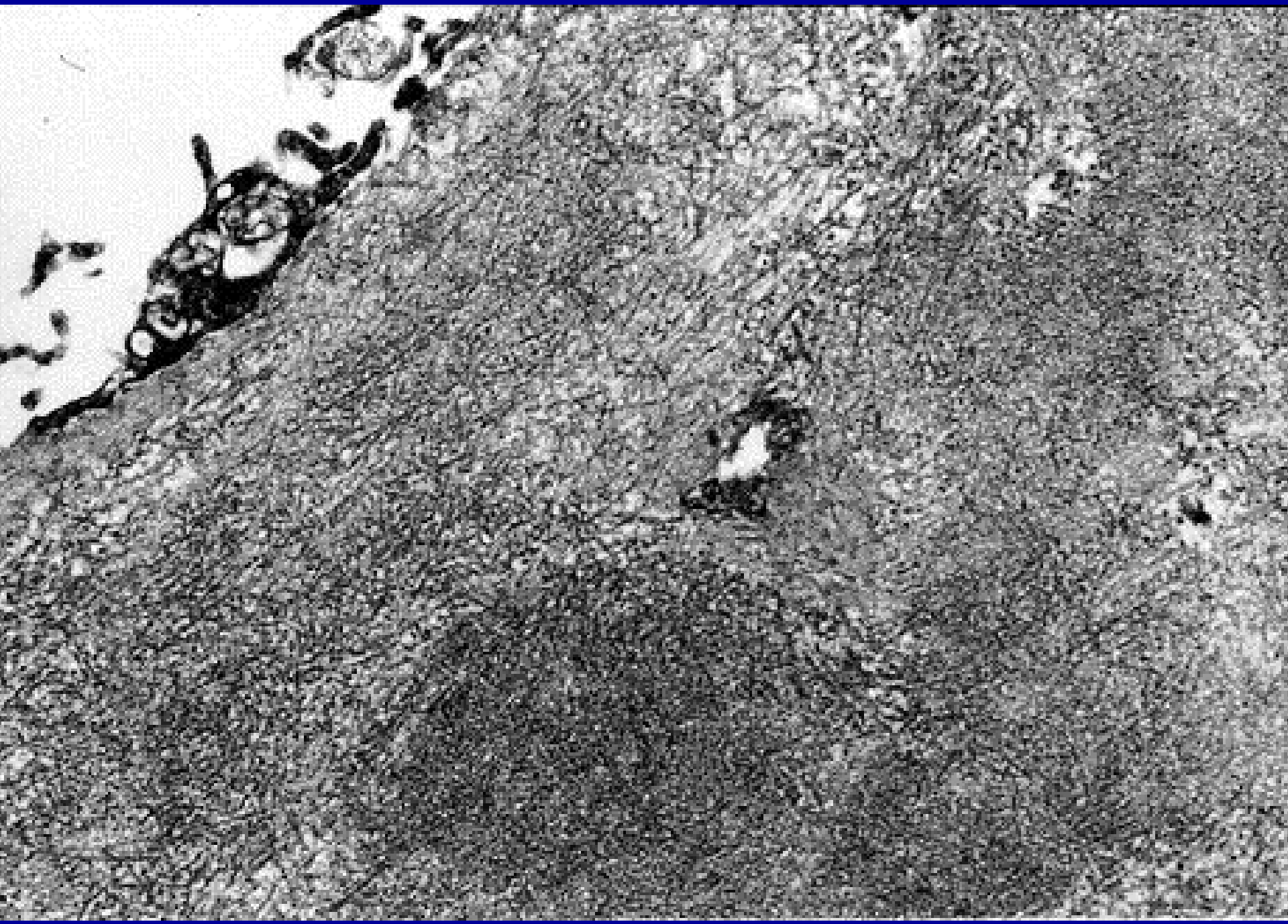
MAY BE PRIMARY (+ OR - MYELOMA) AL OR SECONDARY TO INFLAMMATORY DX AA

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



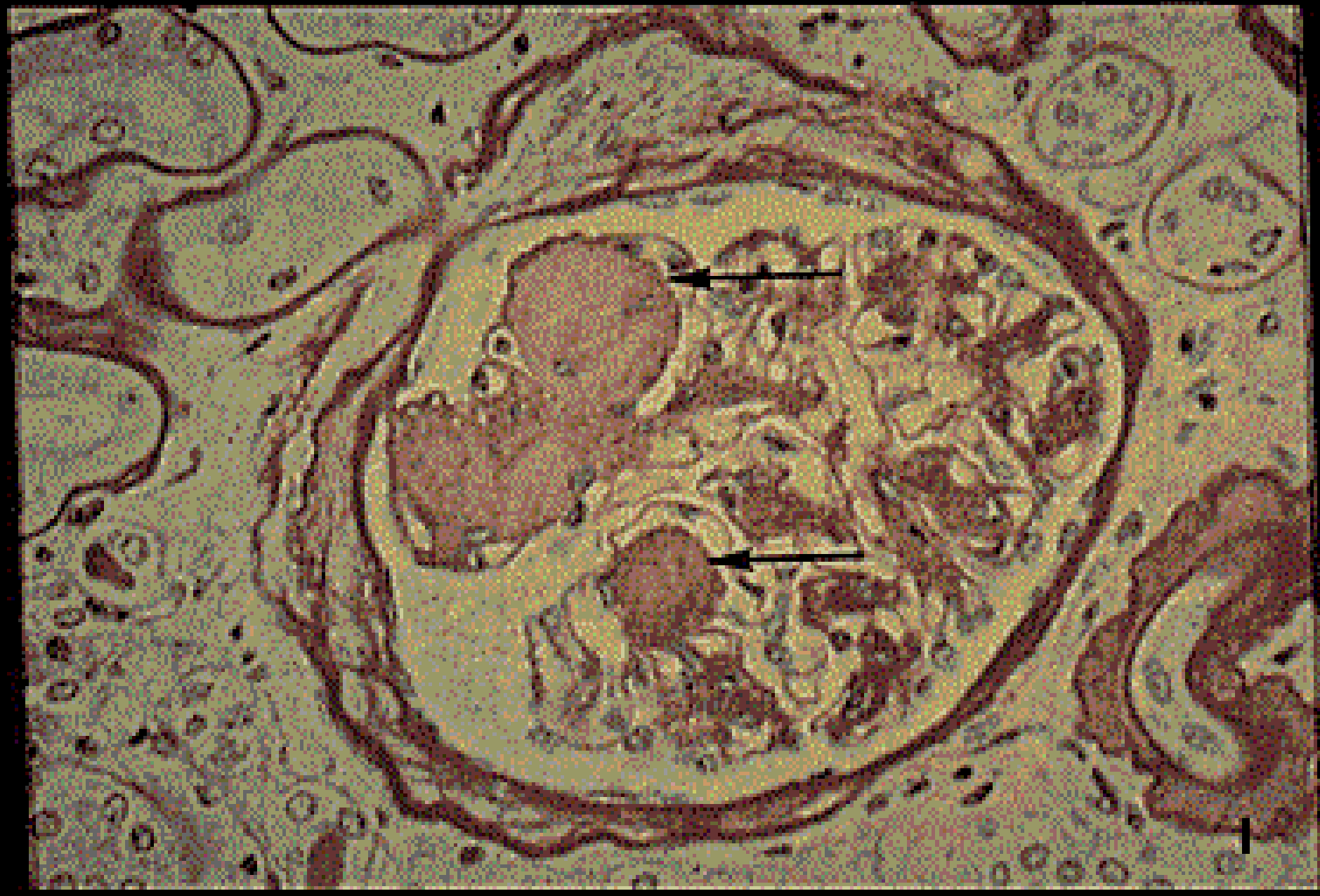


Congo red stain in amyloidosis Congo red stain viewed under polarized light of a renal biopsy from a patient with renal amyloidosis. Green birefringence (white arrows) of interstitial amyloid deposits can be



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



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GLOMERULONEPHRITIS

CLINICAL APPROACH TO GLOMERULAR DISEASE

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