ACP Board Review: Nephrology

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Learning Objectives

1) Differentiate between nephrotic and nephritic syndromes
2) Recognize the clinical presentations of various causes of AKI
3) Identify polycystic kidney disease and its associated complications
4) Apply treatments to slow progression of CKD

Glomerular Diseases

53-year-old woman presents with severe lower extremity edema of two months duration. She was recently diagnosed with Stage 3 lung cancer and has not yet started chemotherapy. She denies rashes, joint pain, fevers, dyspnea, or NSAID use.

Physical Exam

T 37.2 HR 73 BP 121/74 RR 16

Anasarca with periorbital edema
Lungs clear
No JVD, NS1S2, no r/g/m
Abdomen soft, NTND
No rashes

Basic Labs

Creatinine 1.7 mg/dl
Albumin 1.4 g/dl
Ca 8.7 mg/dL

Specialty Labs

ANA (-)
SPEP and FLC wnl
Hepatitis panel (-)

Spin the urine

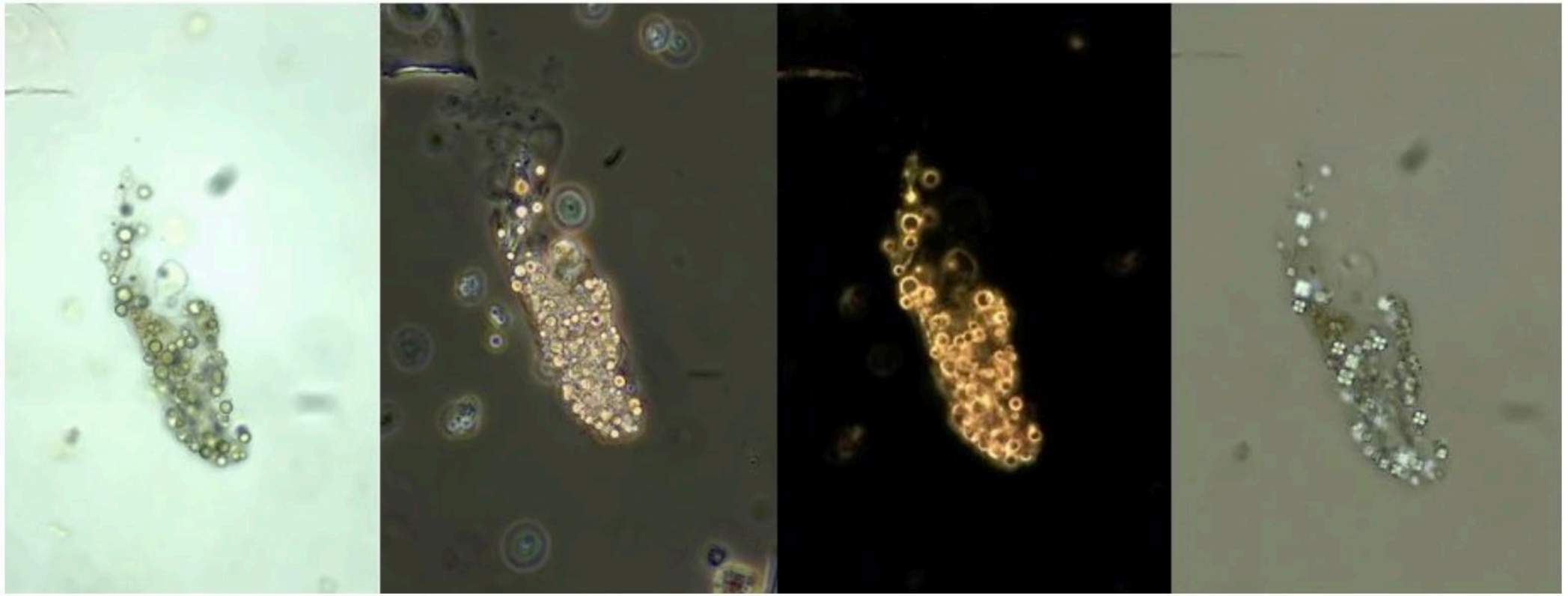


Figure 6. Lipid Casts in (Left to right) brightfield, phase contrast, darkfield, polarized light

@jrseltzer on

What would be the most likely finding on kidney biopsy?

A) Minimal Change Disease
B) Membranous Nephropathy
C) FSGS
D) MPGN
E) Amyloidosis

Hallmark features of Nephrotic Syndrome

Proteinuria >3.5 g/24h

Hypoalbuminemia < 3g/d

Edema

Hyperlipidemia

Lipiduria

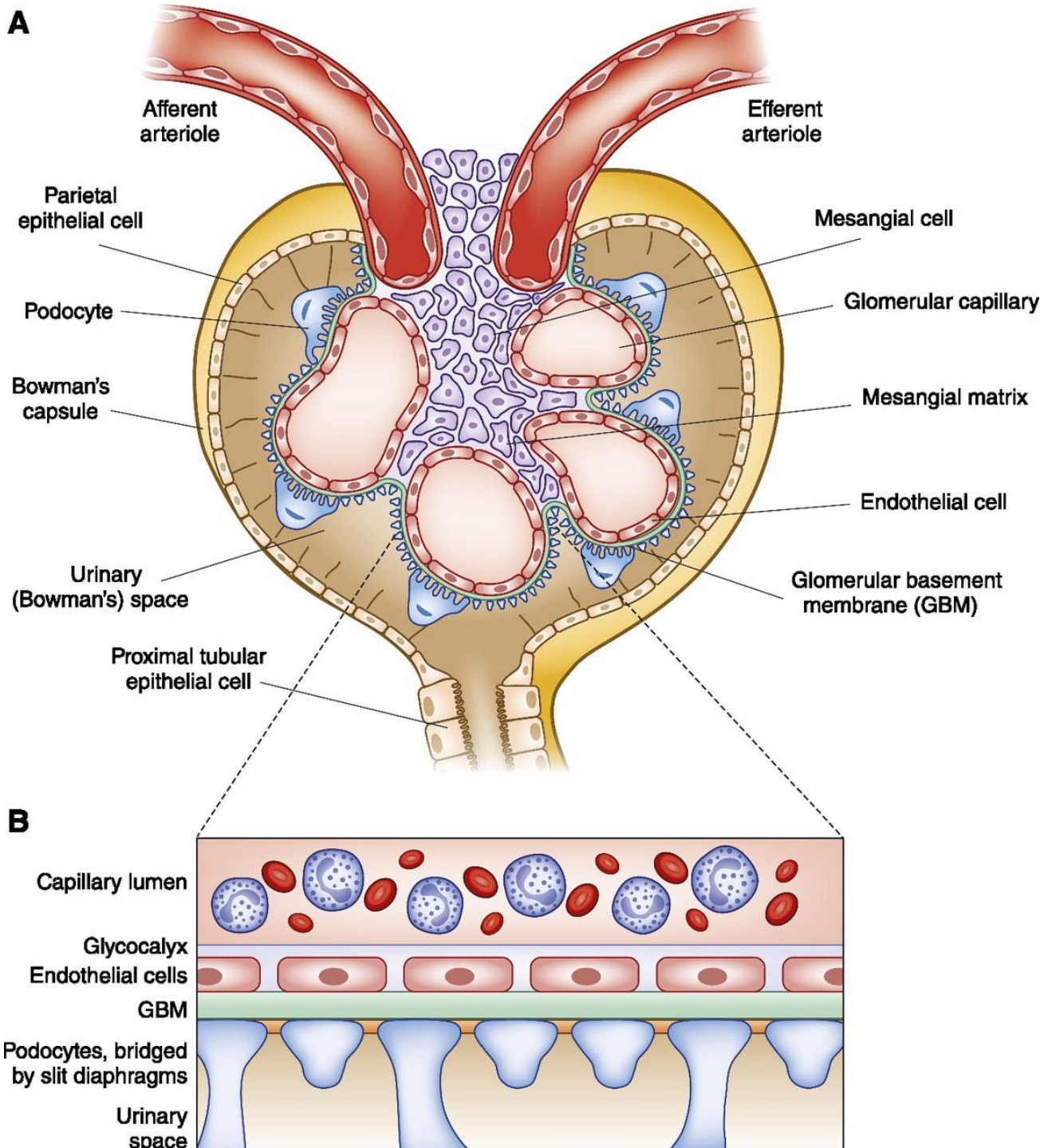
Common Causes of Nephrotic Range Proteinuria

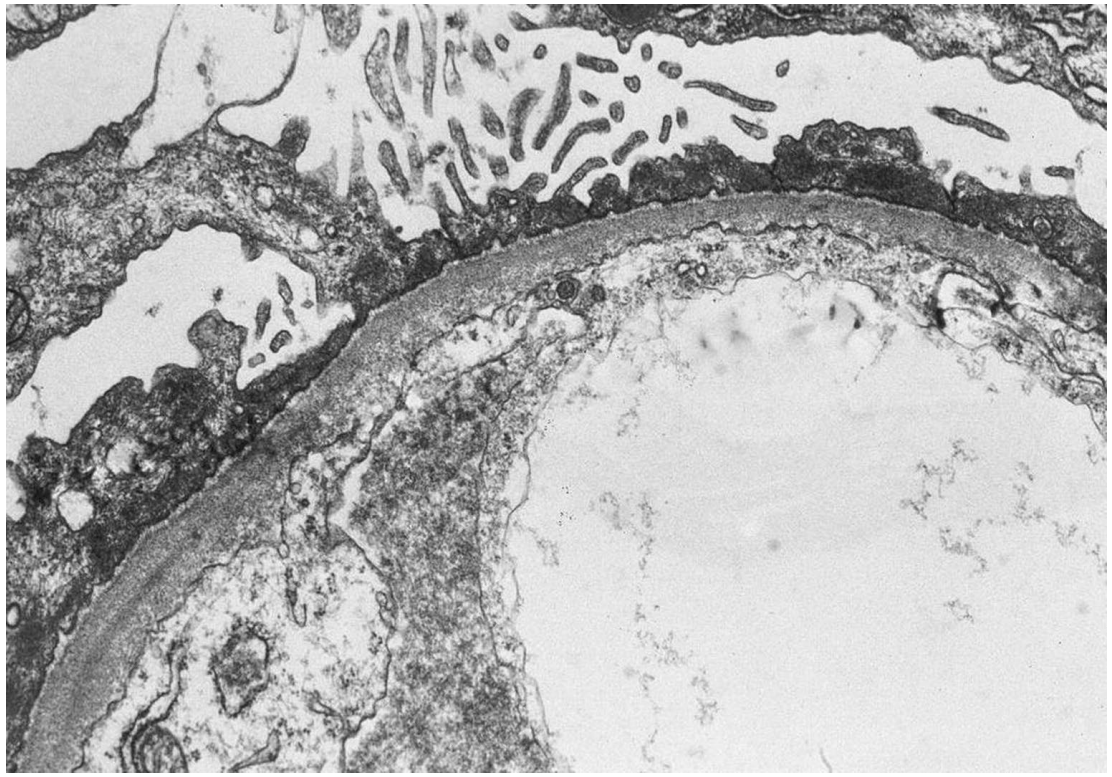
Kidney- limited

- Minimal change
- FSGS
- Membranous nephropathy
- Membranoproliferative GN

Systemic

- Diabetes
- Amyloidosis
- Systemic Lupus Erythematosus





Kitching et al. CJASN 2016

Atlas of Renal Pathology AJKD 2015

Secondary Causes by Pathology

	Minimal Change Disease	Membranous	MPGN	FSGS
Secondary Causes	Lymphoma NSAIDs, lithium	Solid cancers SLE NSAIDs, gold Hep B, Syphilis	Hepatitis C Cryoglobulinemia Complement Disorders	HIV Obesity Single kidney
Biopsy findings	Podocyte effacement ONLY	Subendothelial deposits	Subepithelial deposits	Segmental sclerosis

Nephrotic syndrome: Work-up

Urinalysis

Hepatitis and HIV testing

SPEP/free light chains

ANA, C3, C4

RPR

Anti-PLA2R - new antibody specific for membranous nephropathy

21-year-old woman with a recent diagnosis of minimal change disease began prednisone three weeks ago. She presents to the ED with exertional dyspnea, pleuritic chest pain, and cough.

Physical Exam

T 37.5 BP 153/83 HR 108 RR 20 O_2 sat 89%

HEENT: Unremarkable
Lungs: CTAB
Heart: Tachy, regular rhythm, no JVD
Abdomen: soft, NTND
Ext: 2+ edema

Labs:
BUN 23 mg/dl
Creatinine 1.1mg/dl
Albumin 1.2 g/dl
WBC 7 x 10^9/L

CXR: Normal heart size, no infiltrate

What is the most likely cause for this patient's presentation?

A) Prednisone use

B) Low plasma oncotic pressure

C) Reduction in eGFR

D) Loss of Anti-thrombin III in the urine

E) Loss of immunoglobulins in the urine

Nephrotic Syndrome Complications

Venous thromboembolism
- Loss of more anticoagulant than procoagulant factors (ATIII)
- As high as 10% VTE risk in first 6 months
- Renal vein thrombosis
- Risk factors: hypoalbuminemia, Membranous nephropathy

Infection
- Loss of IgG and complement components, immunosuppression

34-year-old man presents for evaluation of painless hematuria. He describes a recent sore throat that was followed the next morning by gross blood in the urine. He states that a similar episode occurred after a gastroenteritis the prior winter.

PE: BP 143/95 Trace edema

Labs: Creatinine 1.5 mg/dl

ANA negative C3,C4 nl

RBC cast

Case 3

What is the most likely diagnosis?

A) IgA Nephropathy

B) Post-streptococcal glomerulonephritis

C) Cryoglobulinemia

D) Goodpasture’s syndrome

E) Bacterial endocarditis

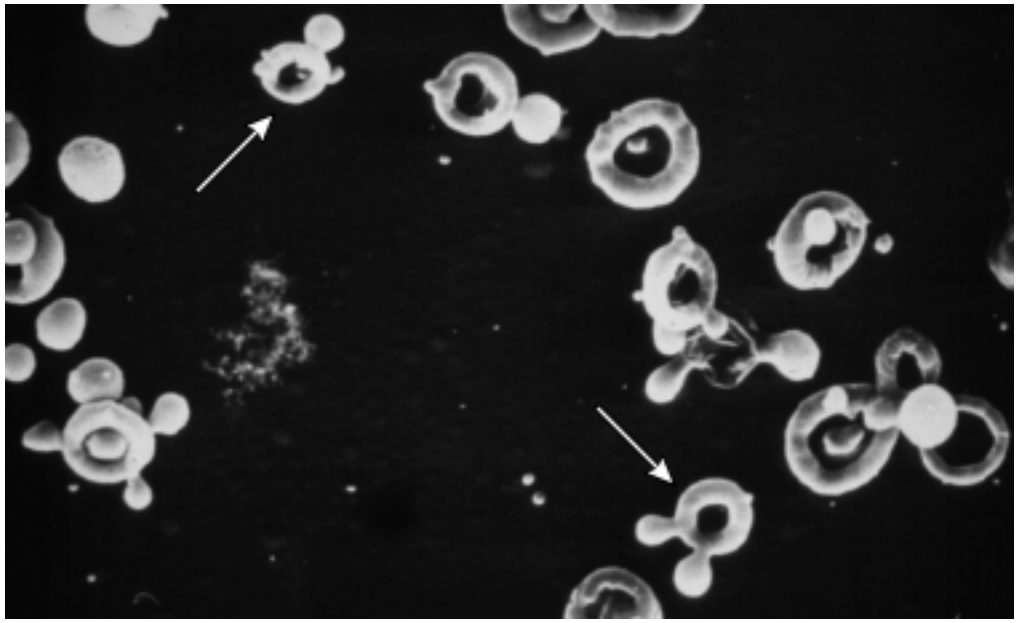
Features of Nephritic Syndrome

Hematuria/RBC casts ☑

Proteinuria < 3g/24h ?

Hypertension ☑

Reduced eGFR ☑



Common Causes of Nephritic Syndrome

Kidney- limited	Systemic
IgA Nephropathy	IgA vasculitis
Poststreptococcal GN	Cryoglobulinemia
Anti-GBM disease	Goodpasture’s disease
	ANCA-associated vasculitis
	SLE

Nephritic Syndrome following a respiratory infection

IgA nephropathy

2-3 days post URI

- Gross hematuria
- C3 normal
- Anti-streptolysin (-)
- +IgA deposits on renal biopsy
- Often recurrent

Post-streptococcal GN

2-4 weeks post infection

- Coca-cola urine
- C3 low
- Anti-streptolysin (+)
- Subepithelial humps on renal biopsy

IgA Nephropathy: Clinical Presentations

Macroscopic hematuria: **40-50%**

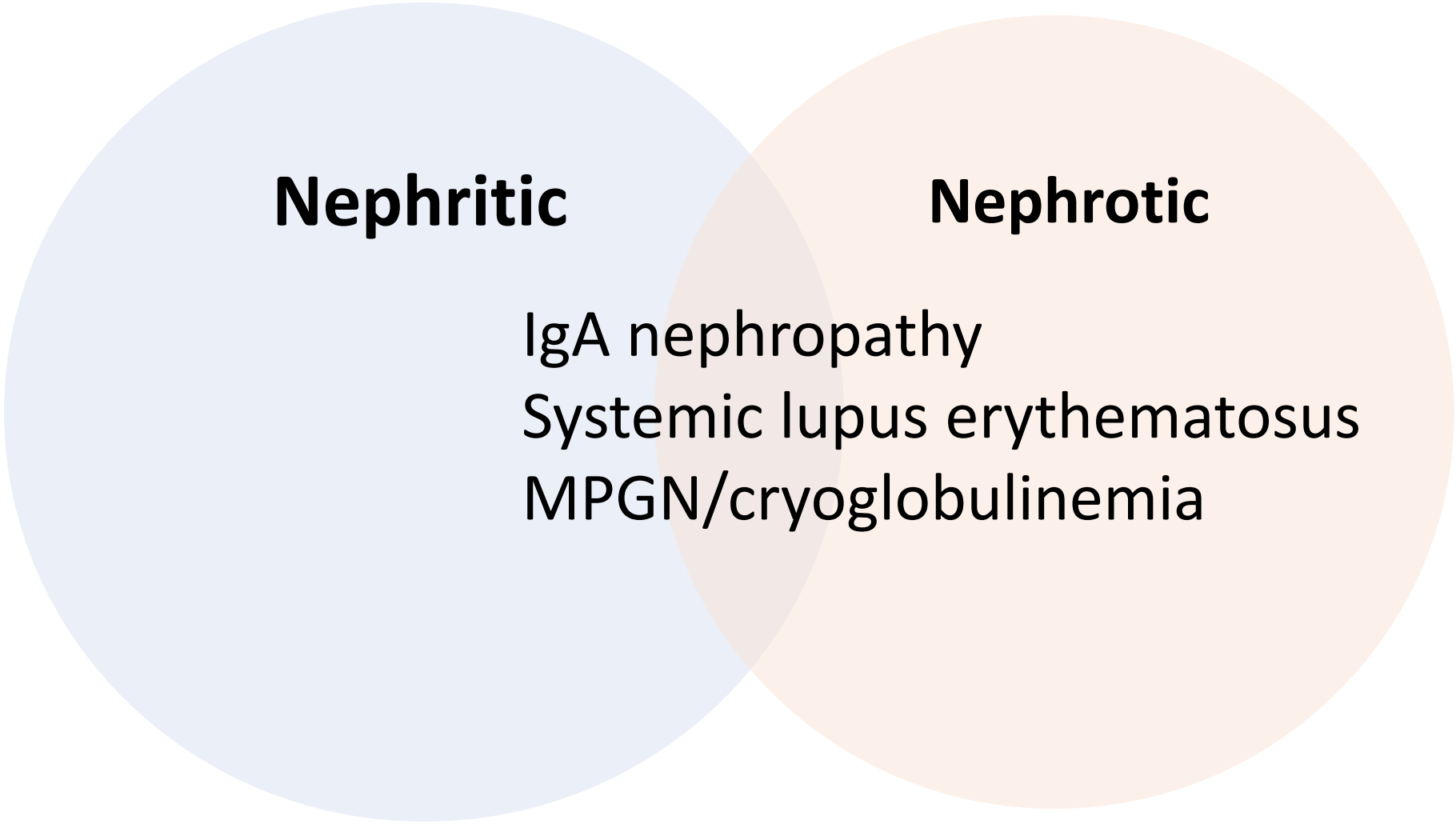
(*commonly follows a mucosal infection*)

Microscopic hematuria +/- proteinuria: **20-30%**

Nephrotic syndrome: **<10%**

Rapidly progressive/Crescentic GN: **<5%**

	Nephrotic	Nephritic
Proteinuria	> 3.5 g/24h	< 3g/24h
Clinical presentation	Edema	Hypertension
Urinalysis	Lipid casts	RBCs, RBC casts
Serum labs	Hypoalbuminemia, hyperlipidemia	Elevated creatinine
Complications	Hypercoagulability, infection	Worsening kidney function


Nephritic
Nephrotic
IgA nephropathy
Systemic lupus erythematosus
MPGN/cryoglobulinemia

A 27-year-old man with a 15-year smoking history presents to the ER with hemoptysis

Physical Exam

Tachypneic, uncomfortable
BP 168/110 P 93 R 22 T 36.9 SpO2 91%
HEENT: O/P clear
Lungs: coarse crackles B
Heart: RRR, No edema
Skin: No rashes

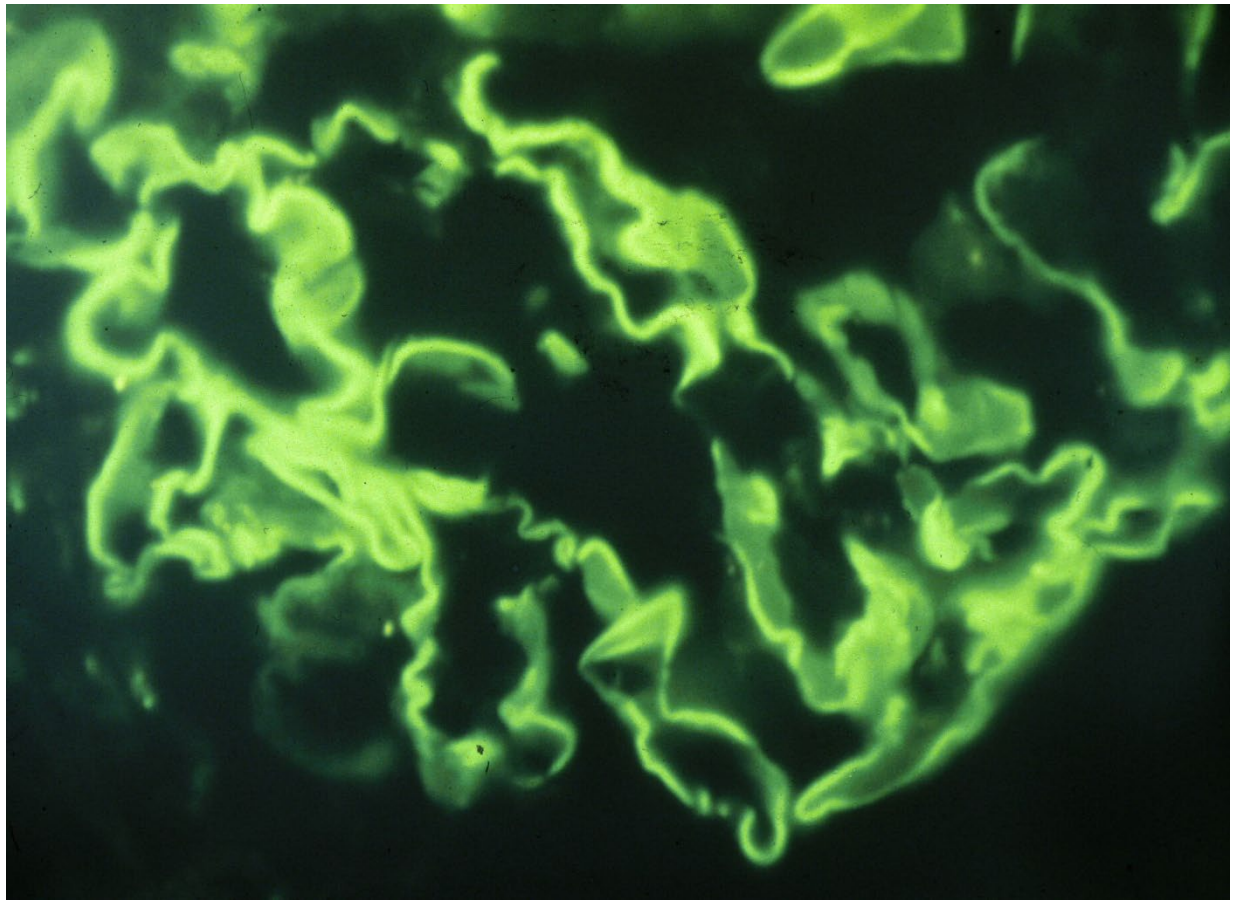
Labs

Creatinine: 2.8 mg/dl (no prior)
Urinalysis: 2+ protein, 3+ blood, many RBCs

CXR: Diffuse infiltrates bilaterally

A renal biopsy is obtained…

Immunofluorescence stain for IgG



Which serology would most likely be positive?

A) Antibodies to myeloperoxidase (P-ANCA)

B) Antibodies to PR-3 (C-ANCA)

C) Antibodies to dsDNA

D) Antibodies to glomerular basement membrane antigens

E) Antibodies to Human Immunodeficiency Virus

Anti-GBM Disease: Clinical Presentation

Extremely rare: 1 per million persons

Nephritic syndrome with rapid onset of renal failure

Renal manifestations alone in 30-50% of patients

Smoking is a risk factor for kidney-lung syndrome: Goodpasture’ s disease

Rapidly Progressive Glomerulonephritis

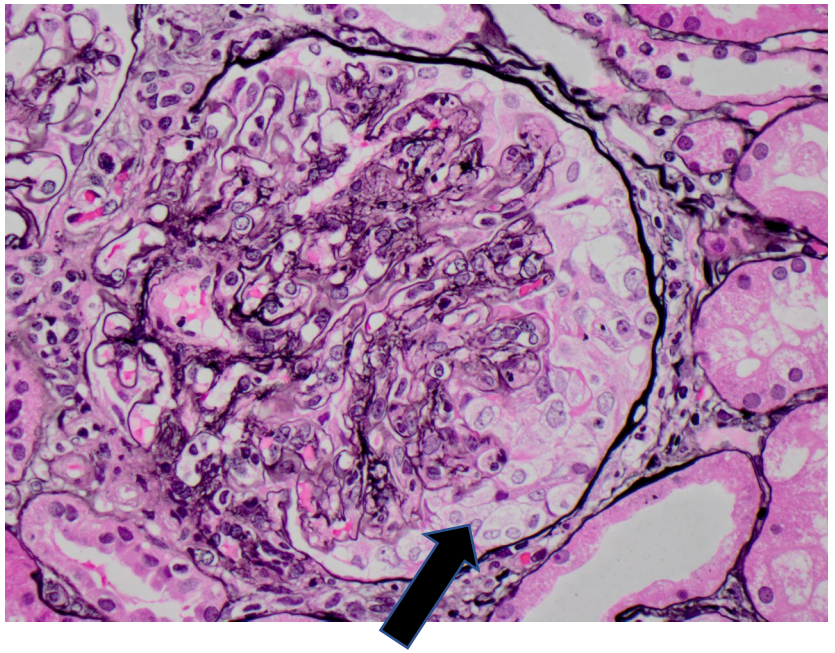
Significant creatinine rise within 3 months

Renal biopsy reveals ***crescents***

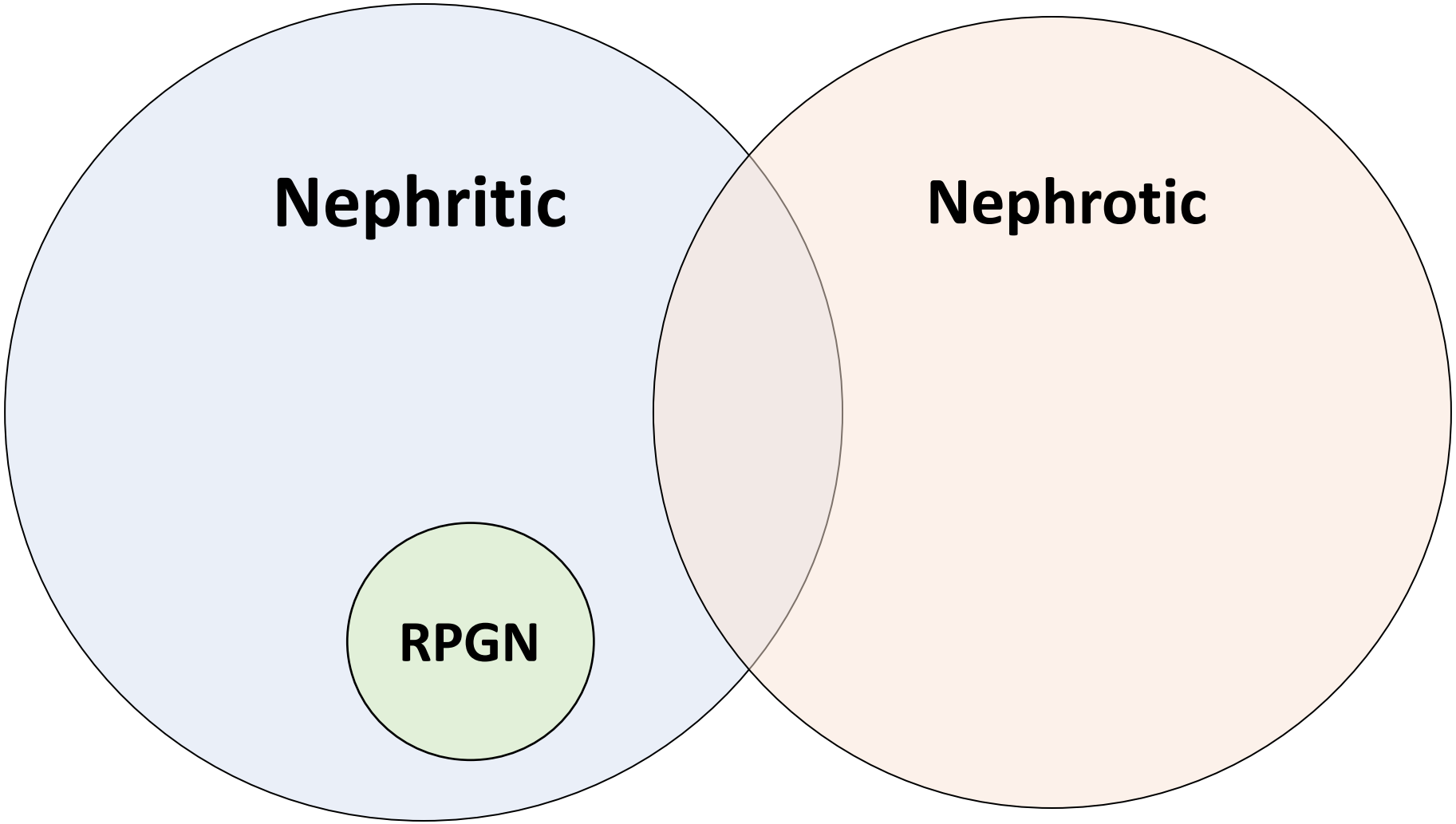
Often systemically ill

Nephritic presentation

RPGN is a subset for nephritis syndrome



Crescent


Nephritic
Nephrotic
RPGN

Common Causes of Nephritic Syndrome

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	ANCA-associated vasculitis
	SLE

Anti-GBM disease: Treatment

Pulse steroids 500 mg to 1 g solumedrol for inflammation

Cyclophosphamide to decrease antibody production

General agreement that **plasmapheresis** is indicated, although there are no prospective trials

Acute Kidney Injury

47-year-old man is brought to the ED after being found poorly responsive and sleeping under a tree. A foley catheter is placed and drains 30 ml of dark brown urine

Physical Exam:

BP 116/62 P 97 RR 10

General: thin, but muscular

HEENT: small pupils, reactive

Lungs: CTAB

Heart: RRR, NS1S2, no r/g/m

Abdomen: soft

Extremities: no edema

Skin: no rashes

Labs:

K 5.5 meq/l

Creatinine 5.4 mg/dl

UA: 1+ protein, 3+ blood

Sediment: 1-3 RBCs, 10-20 WBCs, scattered hyaline and granular casts

What would a kidney biopsy from this patient most closely resemble?

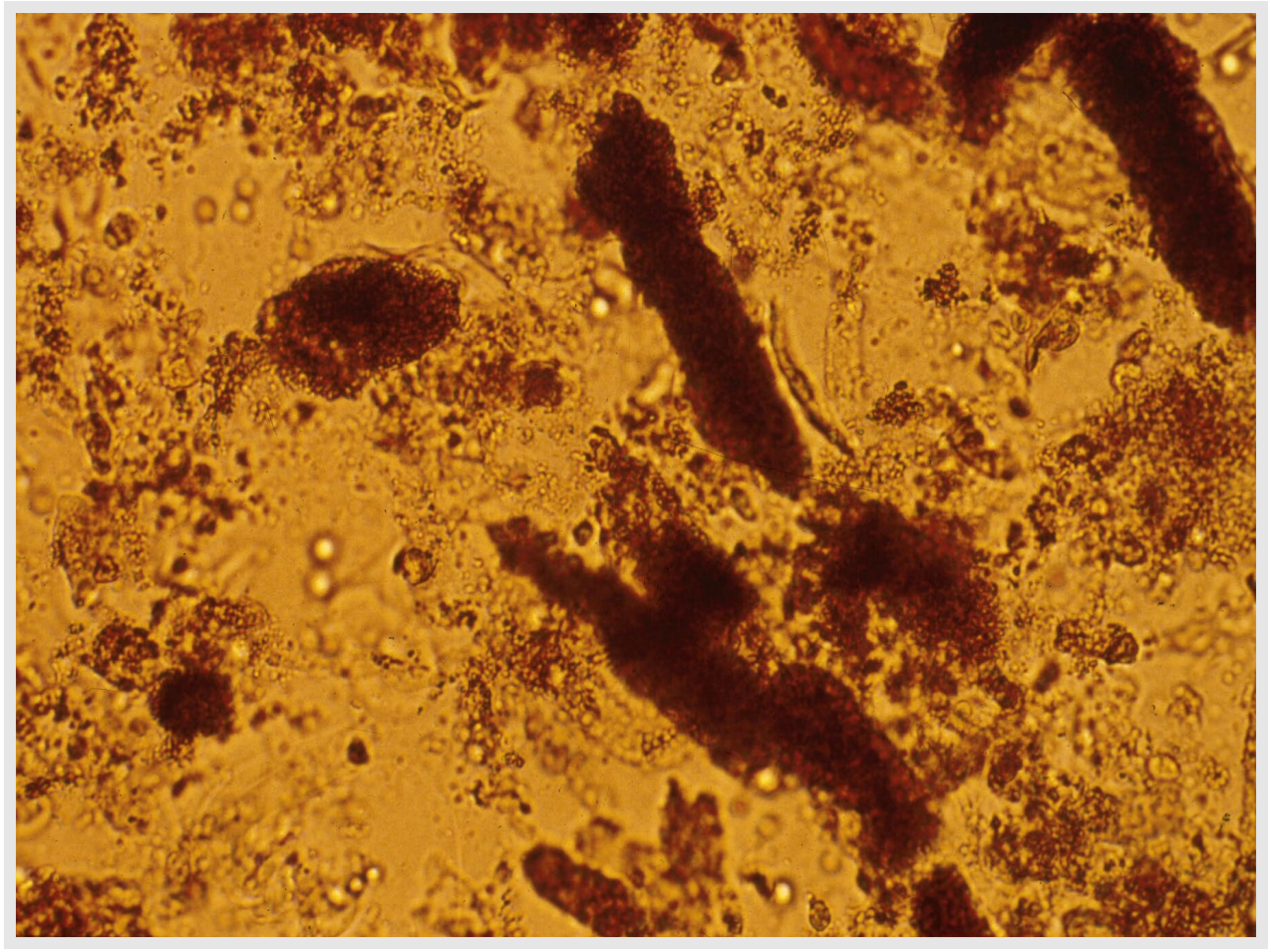
A) 67-year-old man with sinus disease, proteinuria, and + ANCA

B) A 45-year-old HIV positive man with nephrotic syndrome

C) A 56-year-old woman with AKI following exposure to gentamicin

D) A 33-year-old woman with rash and AKI following oxacillin use

Granular casts in acute tubular necrosis (ATN)



Etiology of ATN

Ischemic ATN

- Hemorrhage
- Hypotension

Nephrotoxic

- Aminoglycosides
- Amphotericin
- Tenofovir
- Cisplatin

Pigment induced

- Myoglobin
- Hemoglobin

Rhabdomyolysis features

Dark urine

Cause for muscle injury

Dipstick positive blood with few *RBCs*

Hyperkalemia, hyperphosphatemia, hypocalcemia

Rhabdomyolysis: Etiology

- Trauma, compression (found down), exertion
- Viruses, snake bites
- Meds: Statins, fibrates, colchicine
- Drugs: Cocaine, amphetamines, ecstasy
- Malignant hyperthermia
- Metabolic disease: McArdle's disease (myophosphorylase deficiency)
- Electrolyte disorders: Hypophosphatemia

A 78-year-old woman with type 2 diabetes and CKD has an NSTEMI. She undergoes urgent LHC and stenting of her RCA. Fifteen days later, she returns with nausea, vomiting, and SOB.

Physical Exam:

BP 170/108 P 105 T 37.1

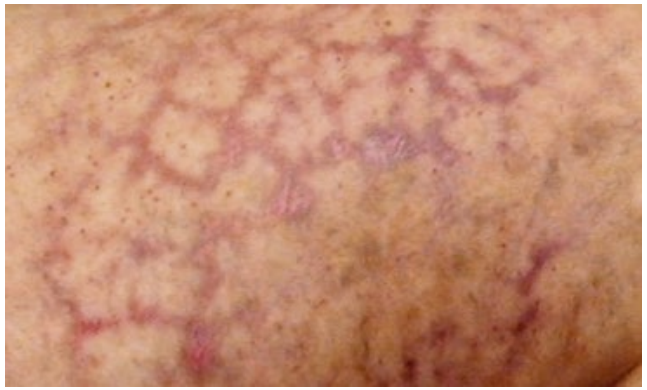
Lungs: crackles

Heart: (+) JVD, tachycardic, no murmurs

Abdomen: soft

Extremities: 1+ edema

Skin:



Labs:

EKG unchanged

Troponins normal

BUN 84 mg/dl Creatinine 5.1 mg/d

Which of the following studies would be most informative at this time?

A) ANCA
B) Serum electrophoresis
C) Serum complements
D) Blood cultures
E) Echocardiogram

Atheroembolic Disease

AAA, angiography, warfarin are risks

Livedo reticularis

Presentation days to WEEKS after procedure

Eosinophilia

Low C3

Skin biopsy and kidney biopsy helpful

A 25-year-old woman is transferred from a community hospital for management of severe hypertension. She was recently evaluated by her PCP for trouble swallowing and her hands “turning blue” in the cold.

Physical Exam:

Thin, uncomfortable
BP 190/115 P 96 R 18
Lungs: scattered crackles
Heart: RRR S4S1S2 1-2/6 SM
Abd: Soft, no organomegaly
Skin: Slight tightening of skin over the fingers bilaterally

Labs:

Hct 29% with schistocytes on smear
Plts 95,000
Creatinine 2.1 mg/dl

Urine sediment: 2+ protein, otherwise bland

What is the most appropriate treatment at this time?

A) Plasmapheresis

B) Amlodipine

C) Steroids

D) Labetalol

E) Captopril

Scleroderma Renal Crisis

- Life-threatening complication of systemic sclerosis
- Look for rapid onset moderate to severe HTN with AKI and thrombotic microangiopathy
- Risk highest in pts with rapid onset of diffuse skin involvement
- Often occurs soon after disease diagnosis
- ACE inhibitors reduce risk for ESRD and markedly reduce mortality

Beware of TTP Mimics

Scleroderma Renal Crisis

Malignant HTN

Atypical HUS

*All of these can present with a thrombotic microangiopathy. Look for more severe hypertension or renal involvement and less severe hematologic disease compared to classic TTP

A 54-year-old man presents with low grade fever and nausea. He saw his PCP three weeks prior and was begun on a PPI for presumed GERD.

Physical Exam

T 38.2

Fatigued

1+ edema

Erythematous rash over trunk

Labs

BUN 68 mg/dl

Cr 3.8 mg/dl

Urine dipstick:

1+ protein, 1+ LE, trace blood

Urine microscopy:

Few WBCs, rare WBC cast

What would a renal biopsy be most likely to show?

A) Acute tubular necrosis

D) Acute glomerulonephritis

C) Acute interstitial nephritis

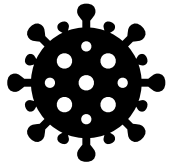
D) Obstructive uropathy

E) Urate nephropathy

Acute Interstitial Nephritis: Common Causes

Drugs

Beta lactams
NSAIDs
PPIs
Sulfa
PD-1 inhibitors



Infection

Leptospirosis
Legionella
Viruses

Autoimmune

SLE
Sjögren's
Sarcoidosis
IgG4 disease

AIN Features

- Immune-mediated: occurs in a small percentage of patients taking a given drug
- Not dose-dependent
- Extrarenal manifestations of hypersensitivity occur in 10-20%
- Recurs after re-exposure to the drug

AIN: key points

- Classic triad of fever, rash, eosinophilia is RARE (only 10%)
- Most important management is to STOP the offending agent
- Steroid use common but has not been studied in randomized trials

A 31-year-old woman sees her PCP for gross hematuria. She denies abdominal pain or history of kidney stones. She was adopted. CT A/P is obtained.

BP 168/110.

Labs: Cr 0.9mg/dl

UA: 1+ protein, TNTC RBCs.

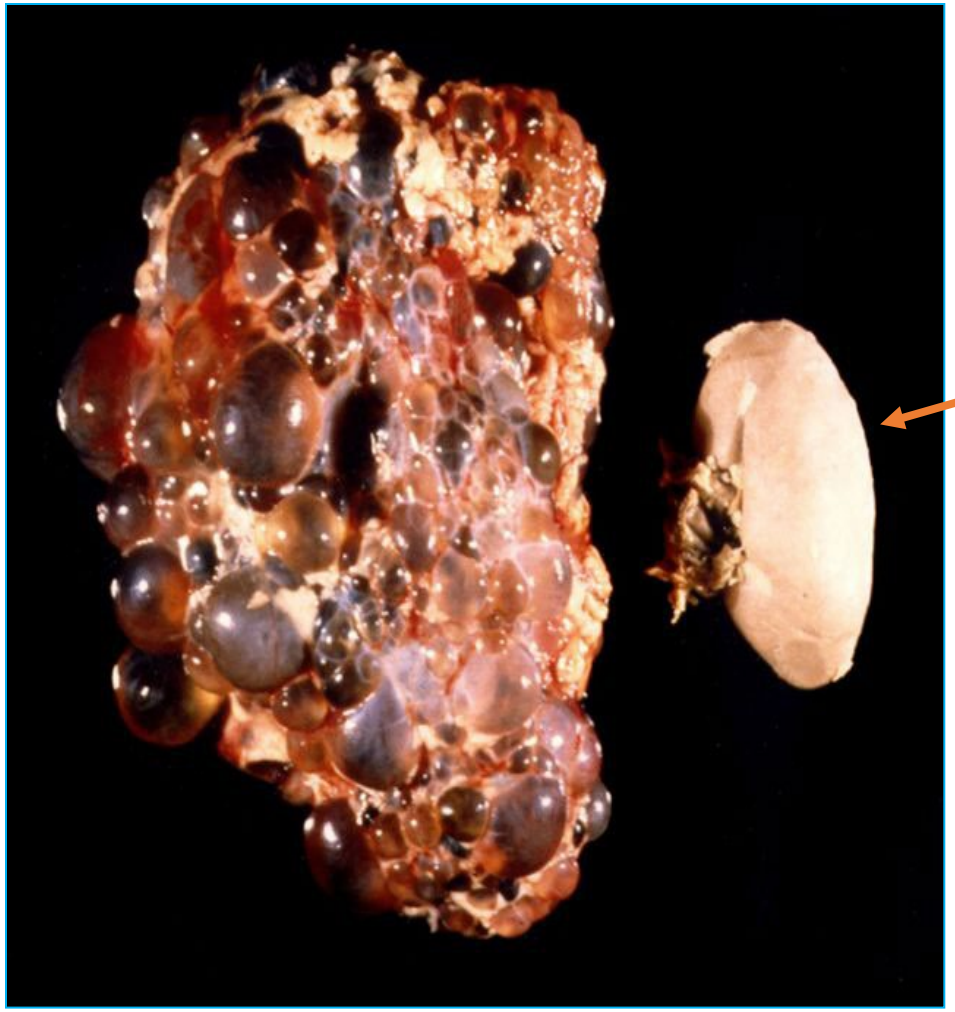
No casts

Case 9

Which of the following is a complication of this disease?

A) Kidney stones
B) Albuminuria
C) Aortic valve disease
D) Anemia
E) Hypernatremia

Polycystic Kidney Disease



Polycystic Kidney Disease Complications

Renal

HTN

CKD (ESRD age 50s)

Cyst hemorrhage

Cyst infection

Kidney stones

UTIs

Chronic pain

Extra-renal

Cerebral aneurysm

Mitral valve prolapse

Liver cysts

Diverticular disease

Polycythemia

A 64-year-old previously healthy man comes to your office with 2 months of low back pain and fatigue

Physical Exam

T 37.6 BP 140/80 P 99

Lungs: Clear

Heart: RRR, (+) S4, 2/6 SM

Extremities 1+ edema

Labs

Hct 24%

Cr 3.7 mg/dl Glucose 73 mg/dl

Urine Dipstick: 1+ LE, (-) protein, 2+ glucose

24-hour urine protein = 5 grams

Which of the following tests would be most informative?

A) Lumbar spine films

B) Peripheral smear

C) ANCA panel

D) SPEP with free light chains

E) PTH level

Multiple Myeloma

CRAB

Calcium (high)

Renal failure

Anemia

Bone (lytic lesions)

Various presentations in multiple myeloma

	Presentation	Urine
AL amyloid	Nephrotic syndrome	Albuminuria
Light chain deposition disease	Nephrotic syndrome	Albuminuria
Cast Nephropathy	AKI	Proteinuria WITHOUT albuminuria
Type II RTA	Non-anion gap acidosis	Glucosuria

A 47-year-old woman with diabetes and CKD 3 presents for her 6-month visit. She takes lisinopril, metformin, and atorvastatin.

Physical:

BP 143/97 P 76 T 36.5

Lungs clear

Heart: RRR, NS1S2, no m/g/r

Ext: tr edema

Labs:

Na	137 meq/liter
K	5.1 meq/liter
HCO_3	22 meq/liter
BUN	42 mg/dl
Cr	1.8 mg/dl
Glu	180 mg/dl
UACR	350 mg/g

What other medication should you recommend at this time?

A) Losartan

B) Spironolactone

C) Semaglutide

D) Erythropoeitin

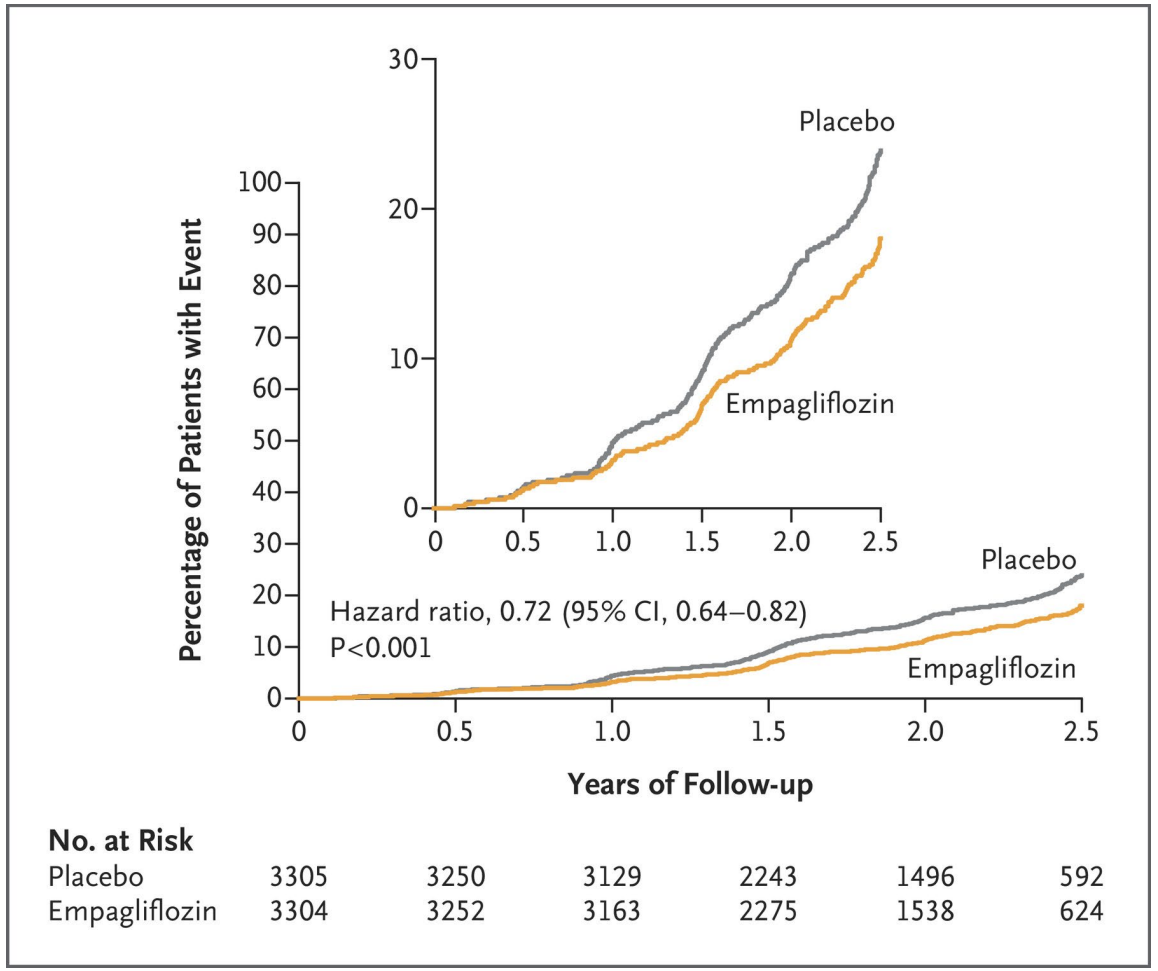
E) Empagliflozin

SGLT2 inhibitors in Chronic Kidney Disease

SGLT2 inhibitors improve outcomes in CKD when albuminuria > 200 mg/g

Can be started when eGFR > 20 ml/min

Major side effects are perineal infections, urinary frequency



EMPA-kidney NEJM 2023.

Good Luck!
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Answer Key

1. B
2. D
3. A
4. D
5. C
6. C
7. E
8. C
9. A
10. D
11. E