Advancing Kidney Health
Through Optimal Medication Management

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Glomerulonephritis: A primer on the detection, diagnosis, and an appreciation for the patient experience

What We're Going to Cover

- Understand the role of GN in CKD
- Describe screening tests (eGFR, UACR, hematuria)
- Describe the pathophysiology of GN
- Differentiate the major types of GN and their clinical presentations
- Describe the burden that GN places on patients

Glossary of Terms: Abbreviations

- **AKI** = acute kidney injury
- **CKD** = chronic kidney disease
- **ESRD** = end stage renal disease
- **GFR** = glomerular filtration rate, either estimated (e) or measured (m)
- **GN** = Glomerulonephritis
- **MEST-C** = Mesangial hypercellularity, Endocapillary hypercellularity, Segmental glomerulosclerosis, Tubular atrophy/interstitial fibrosis, and Crescents
- **UACR** = urine albumin-to-creatinine ratio
- **UPCR** = urine protein to creatinine ratio

Glossary of Terms: Definitions

- **Glomerulus** = capillary loop with basement membrane which allows passage of specific molecules into the nephron
- **GN** = inflammation/damage of the glomerular basement membrane resulting in altered function.

Glossary of Terms: Definitions (continued - 2)

GN can present as:

- **Nephrotic syndrome:** a clinical syndrome defined by proteinuria (greater than 3.5 g/day), hypoalbuminemia (less than 3.0 mg/L), with resulting hyperlipidemia, edema, and various complications
- **Nephritic syndrome:** characterized by inflammation of the glomeruli, leading to hematuria (blood in the urine), proteinuria (protein in the urine), hypertension (high blood pressure), and decreased urine output

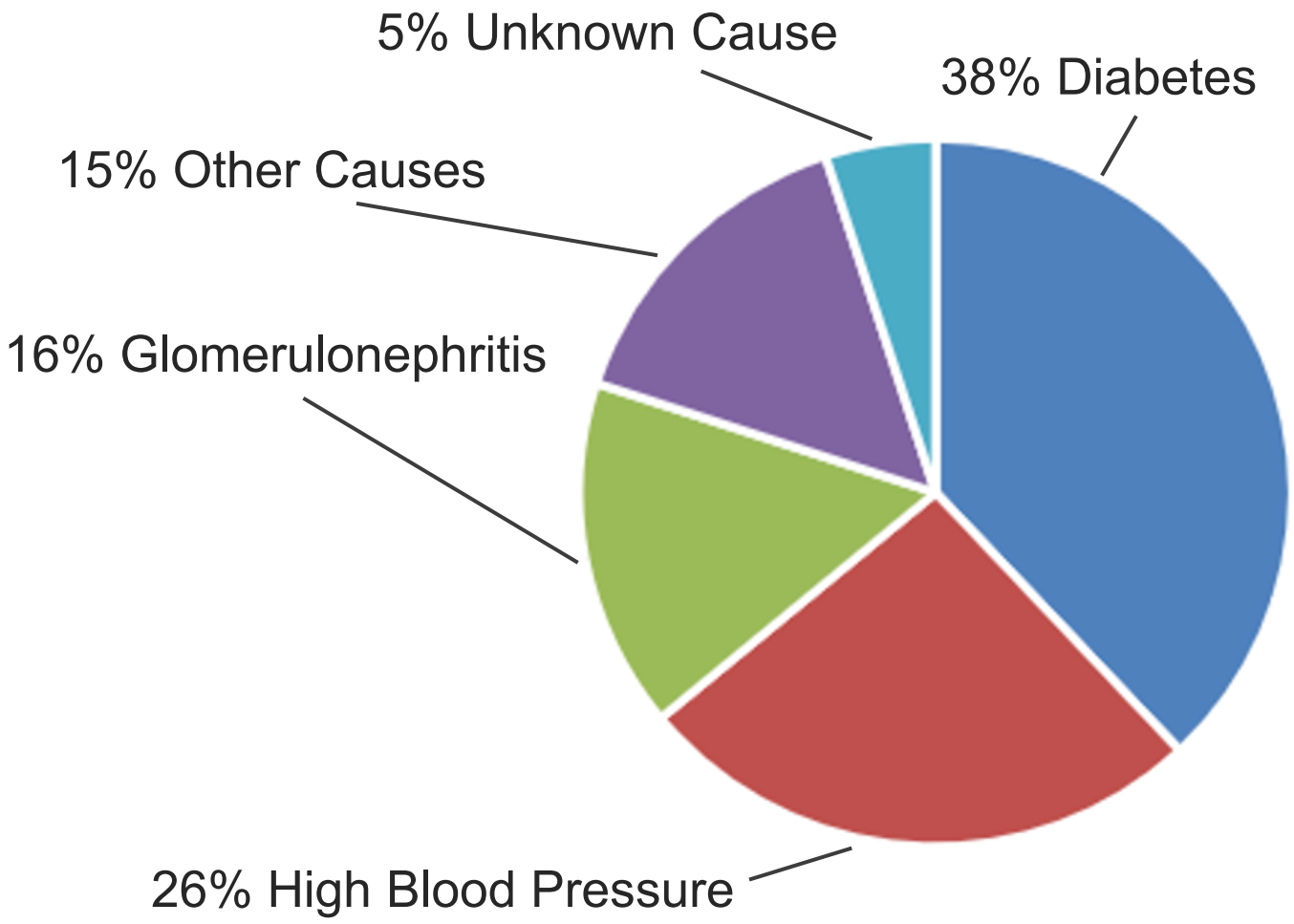
Glossary of Terms: Definitions (continued - 3)

- **ANCA** = Antineutrophil Cytoplasmic Antibody associated vasculitis is an autoimmune condition that causes inflammation of blood vessels with various manifestations.
- **FSGS** = Focal Segmental Glomerulosclerosis is a disease in which scar tissue develops on the glomeruli due to idiopathic, genetic, secondary or unknown causes
- **LN** = Lupus Nephritis is an inflammation of the kidneys caused by systemic lupus erythematosus
- **SLE** = Systemic Lupus Erythematosus is an autoimmune disease with multisystem involvement

Glossary of Terms: Definitions (continued – 4)

- **RPGN** = Rapidly Progressive Glomerulonephritis is characterized by a rapid decline in kidney function and an accelerated loss of renal function over a short period, classified based on the histopathology of immune complex (IC) deposition, linear antibody deposition, granular immune complex deposition disorders, and pauci-immune disorders.
- **MCD** = Minimal Change Disease is a disease that is characterized by an increased renal membrane permeability and loss of protein due to damage to the glomerular basement membrane
- **antiGBM** = anti Glomerular Basement Membrane disease is a rare autoimmune disorder, formerly known as Goodpasture syndrome where circulating antibodies are directed against the alpha-3 chain of type IV collagen normally present in the GBM and alveolar basement membrane

GN's Role in Chronic Kidney Disease

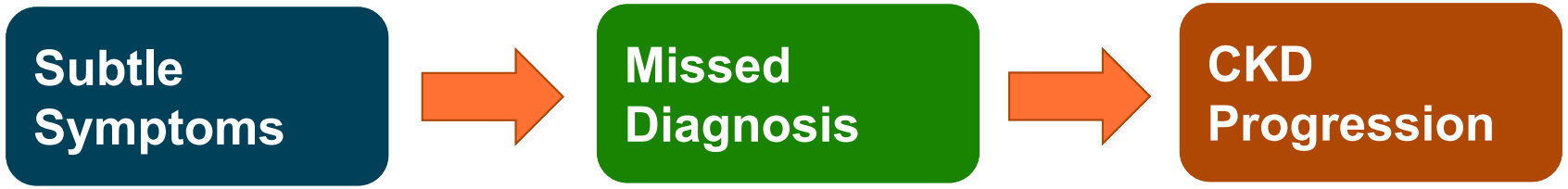


- GN accounts for ~10–15% of CKD in the US
- GN is a leading cause of CKD worldwide
- In some regions, GN is the second most common cause of end-stage kidney disease after diabetes/hypertension
- Early detection is critical to reduce progression to ESRD

National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK). NIH, 2021. Available at: https://www.niddk.nih.gov/health-information/kidney-disease/high-blood-pressure

Missed Diagnosis & Session Goals

- GN often presents with nonspecific findings:
  - Hematuria
  - Proteinuria
  - Edema
- Many cases are overlooked in primary care until advanced disease develops



Hricik DE, Chung-Park M, Sedor JR. Glomerulonephritis. *N Engl J Med*. 1998 Sep 24;339(13):888–899. doi: 10.1056/NEJM199809243391306

Glomerular Diseases in the US

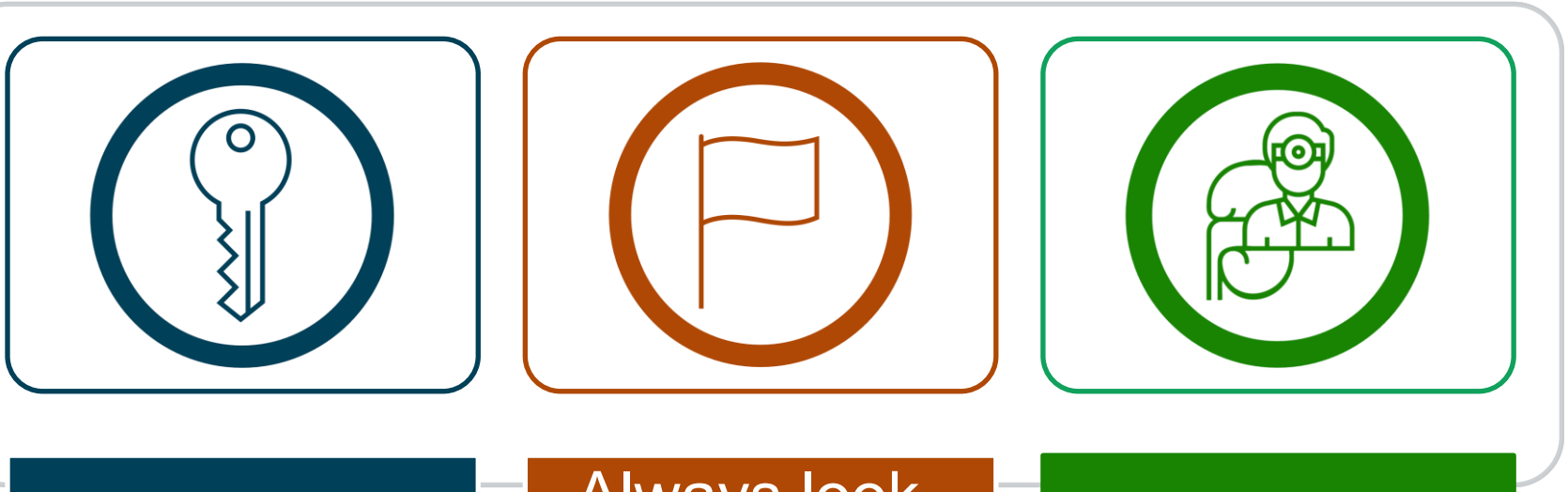
Glomerular diseases accounted for 51% of ESRD reported to the U.S. Renal Data System

115,938 cases of diabetic nephropathy (37.9%)

41,333 cases of nondiabetic glomerular disease (13.5%)

Hricik DE, Chung-Park M, Sedor JR. *Glomerulonephritis*. N Engl J Med. 1998 Sep 24;339(13):888–899. doi: 10.1056/NEJM199809243391306

Screening & Detection Essentials



eGFR trend + UACR persistence are key to early recognition

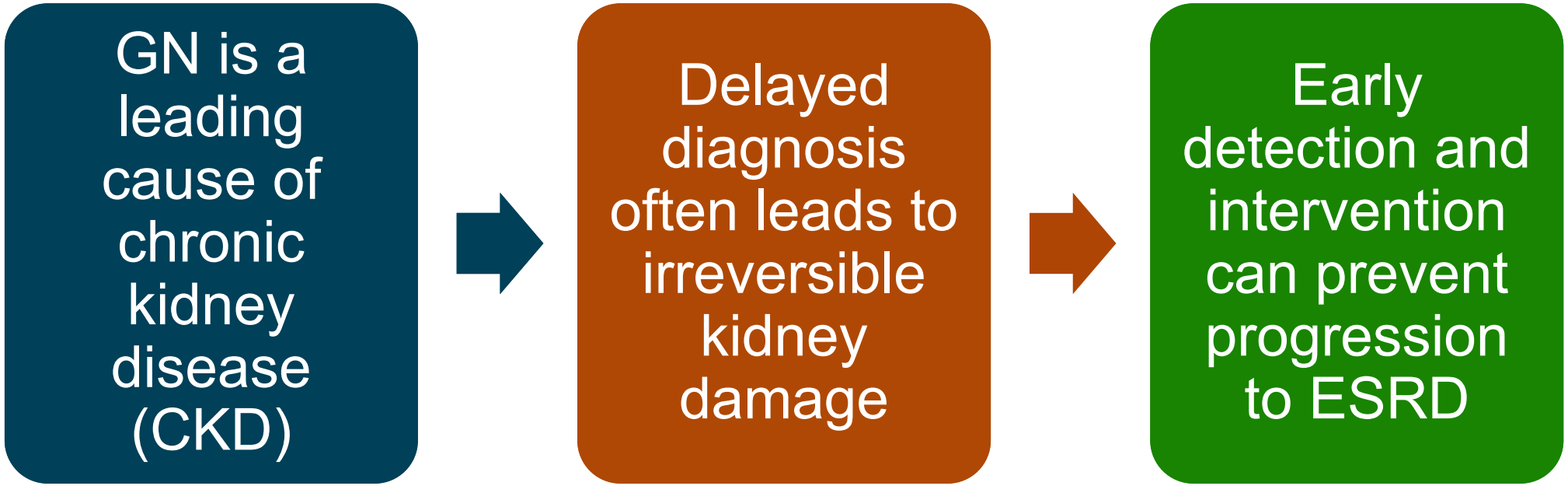
Always look for red flags:

- Hematuria
- Rapid progression
- Nephrotic syndrome
- Nephritic syndrome

Distinguish GN from other CKD to prevent delay in referral

KDIGO 2022 CKD Guidelines; *NEJM* 1998 review.

Why Early Detection of Glomerulonephritis Matters



When It's More than Diabetes or Hypertension

Hematuria

- Microscopic or gross

Rapid progression of kidney decline

- Drop >3 mL/min/m2/yr

Nephrotic syndrome

- Proteinuria >3.5 g/day + edema + hypoalbuminemia (usually < 3.0 mg/dL

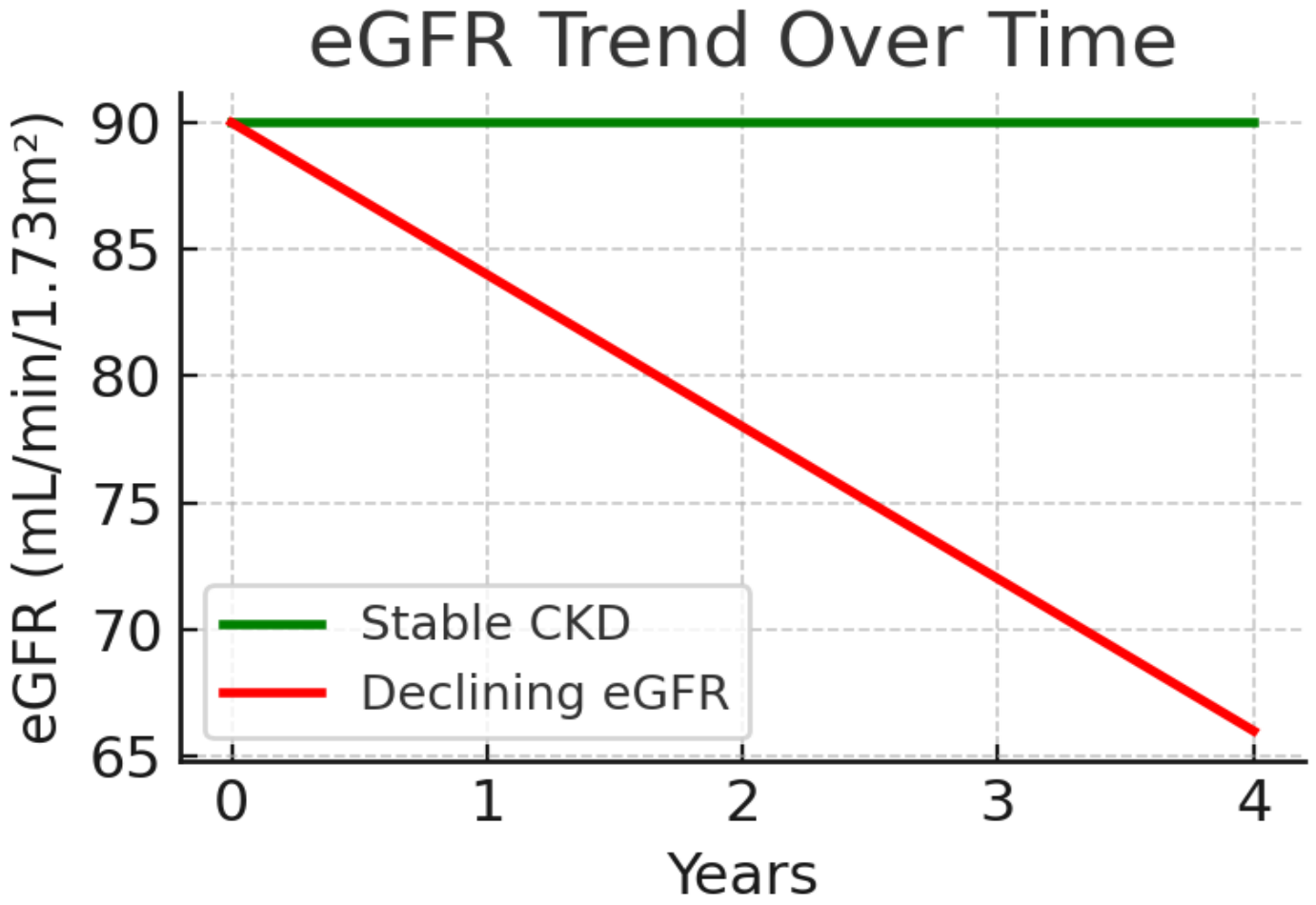
Atypical Patient Presentation

- No microvascular complications (neuropathy/ retinopathy)
- Other systemic signs of inflammation

Hricik DE, Chung-Park M, Sedor JR. Glomerulonephritis. *N Engl J Med*. 1998;339:888–899.

Estimated GFR (eGFR): Why It Matters

- Reflects kidney filtration capacity
- Calculated from serum creatinine, age, sex
- Declining trend is more important than one isolated value.



Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612.

UACR: Why It Matters

- Detects early glomerular damage be
- Persistent UACR >30 mg/g = abnorr severe risk
- Independent predictor of CKD progr cardiovascular outcomes

- Low risk, If no other markers of kidney disease, no CKD
- Moderately increased risk
- High risk
- Very high risk

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-300 mg/g 3-30 mg/mmol	>300 mg/g >30 mg/mmol
	G1	Normal or high	≥90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

KDIGO: Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl*. 2013;3:1-150. Copyright 2013

Summary of Relative Risks: Mortality

Charts: Summary of relative risks from categorical meta-analysis (dipstick included)(–, ±, +, ⩾++)

All-cause mortality

	ACR <10	ACR 10–29	ACR 30–299	ACR ⩾300
eGFR > 105	1.1	1.5	2.2	5.0
eGFR 90–105	Ref	1.4	1.5	3.1
eGFR 75–90	1.0	1.3	1.7	2.3
eGFR 60–75	1.0	1.4	1.8	2.7
eGFR 45–60	1.3	1.7	2.2	3.6
eGFR 30–45	1.9	2.3	3.3	4.9
eGFR 15–30	5.3	3.6	4.7	6.6

Cardiovascular mortality

	ACR <10	ACR 10–29	ACR 30–299	ACR ⩾300
eGFR > 105	0.9	1.3	2.3	2.1
eGFR 90–105	Ref	1.5	1.7	3.7
eGFR 75–90	1.0	1.3	1.6	3.7
eGFR 60–75	1.1	1.4	2.0	4.1
eGFR 45–60	1.5	2.2	2.8	4.3
eGFR 30–45	2.2	2.7	3.4	5.2
eGFR 15–30	14	7.9	4.8	8.1

Levey, Andrew S. et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. *Kidney International*, 2002;80(1):17–28.

Summary of Relative Risks: ESRD, AKI, & CKD

Kidney failure (ESRD)

	ACR <10	ACR 10–29	ACR 30–299	ACR ⩾300
eGFR > 105	Ref	Ref	7.8	18
eGFR 90–105	Ref	Ref	11	20
eGFR 75–90	Ref	Ref	3.8	48
eGFR 60–75	Ref	Ref	7.4	67
eGFR 45–60	5.2	22	40	147
eGFR 30–45	56	74	294	763
eGFR 15–30	433	1044	1056	2286

Acute kidney injury (AKI)

	ACR <10	ACR 10–29	ACR 30–299	ACR ⩾300
eGFR > 105	Ref	Ref	2.7	8.4
eGFR 90–105	Ref	Ref	2.4	5.8
eGFR 75–90	Ref	Ref	2.5	4.1
eGFR 60–75	Ref	Ref	3.3	6.4
eGFR 45–60	2.2	4.9	6.4	5.9
eGFR 30–45	7.3	10	12	20
eGFR 15–30	17	17	21	29

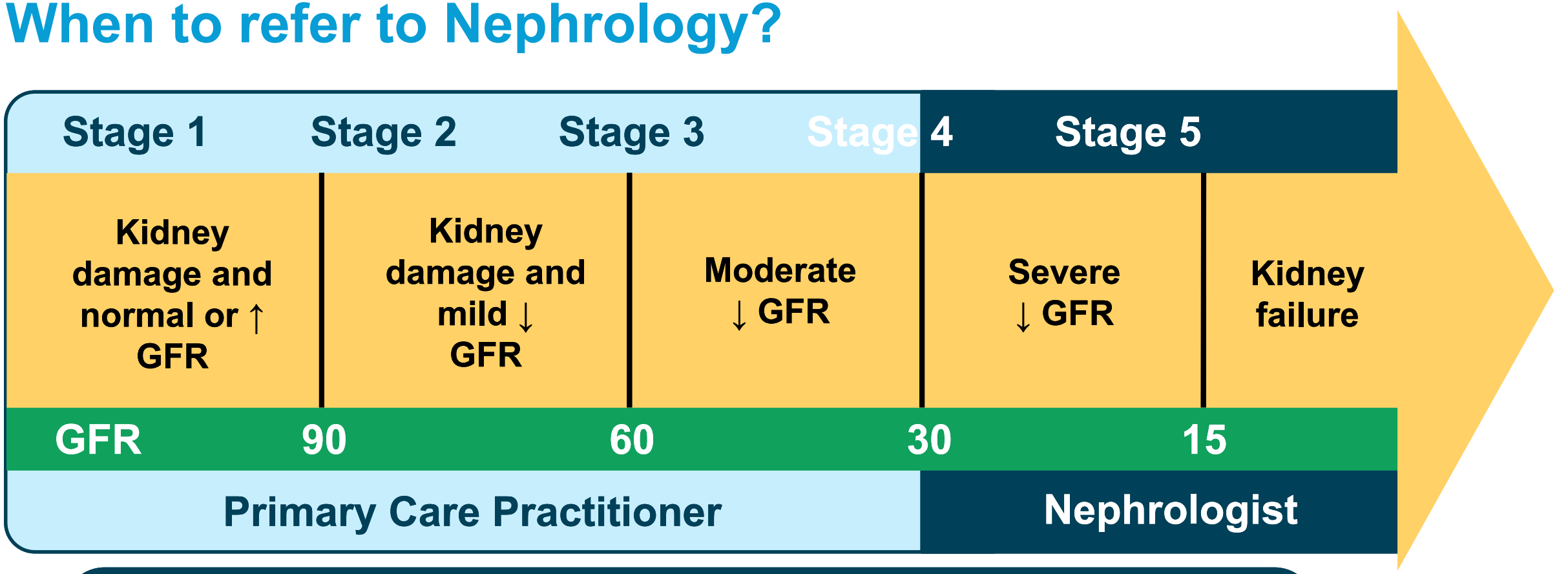
Progressive CKD

	ACR <10	ACR 10–29	ACR 30–299	ACR ⩾300
eGFR > 105	Ref	Ref	0.4	3.0
eGFR 90–105	Ref	Ref	0.9	3.3
eGFR 75–90	Ref	Ref	1.9	5.0
eGFR 60–75	Ref	Ref	3.2	8.1
eGFR 45–60	3.1	4.0	9.4	57
eGFR 30–45	3.0	19	15	22
eGFR 15–30	4.0	12	21	7.7

Charts: Summary of relative risks from categorical meta-analysis (dipstick included)(–, ±, +, ⩾++)

Levey, Andrew S. et al. The definition, classification, and prognosis of chronic kidney disease: a KDIGO Controversies Conference report. *Kidney International*, 2002;80(1):17–28.

When to refer to Nephrology?



Risk enhancing factors for Nephrologist referral:

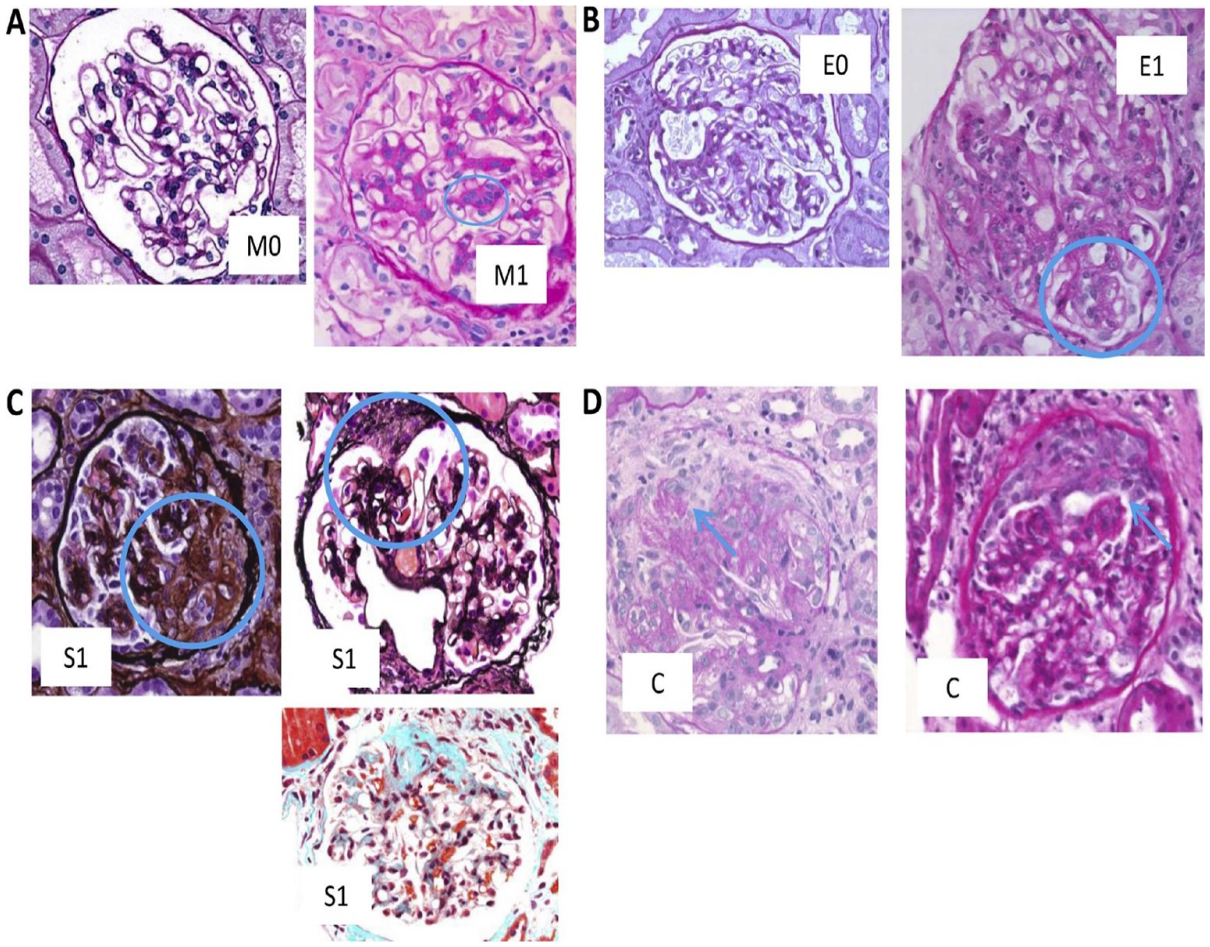
- Persistent albuminuria > 100mg/g
- Hematuria
- Rapid GFR decline (>3ml/min/1.73m2/year)

Patient Case

Patient
29 yo. WM, diagnosed with IgAN in 2020

PMH
Kidney stones
Factor V Leiden
Gallbladder disease

Baseline values	2020
Blood pressure	127/73
Hematuria	Yes, 10-20 rbc/hpf
Proteinuria (UPCR, g/d)	>3.8 g/day
eGFR (mL/min/1.73 m^2)	56
CKD disease stage	3
MEST-C score	M1 E0 S1 T1 C0



Pattrapornpisut, Prapa et al. IgA Nephropathy: Core Curriculum *American Journal of Kidney Diseases*, 2021;78(3)429–441.

IgAN Treatment History: 2021-2/23

2021-2022

Medications
prednisone (steroid dependent, 40 mg/day)
ARB/losartan

Objectives	Pertinent Findings
Blood pressure	<140/90
Hematuria	intermittent, 11-30 rbc/hpf
Proteinuria (UPCR, g/d)	<0.3 g/day
eGFR (mL/min/1.73 m^2)	42-51

10/2022

Medications
ARB/losartan
dapagliflozin
Started targeted release budesonide

Objectives	Pertinent Findings
Blood pressure	101/78
Hematuria	3-10 rbc/hpf
Proteinuria (UPCR, g/d)	0.6 g/day
eGFR (mL/min/1.73 m^2)	43

6/2022

Medications
prednisone (steroid dependent, 40 mg/day)
ARB/losartan
dapagliflozin

Objectives	Pertinent Findings
Blood pressure	116/72
Hematuria	3-10 rbc/hpf
Proteinuria (UPCR, g/d)	0.25 g/day
eGFR (mL/min/1.73 m^2)	46

2/2023

Medications
ARB/losartan
dapagliflozin
Targeted release budesonide

Objectives	Pertinent Findings
Blood pressure	118/80
Hematuria	3-10 rbc/hpf
Proteinuria (UPCR, g/d)	1.1g/day
eGFR (mL/min/1.73 m^2)	50

IgAN Treatment History: 6/23-3/25

Medications
dapagliflozin
sparsentan

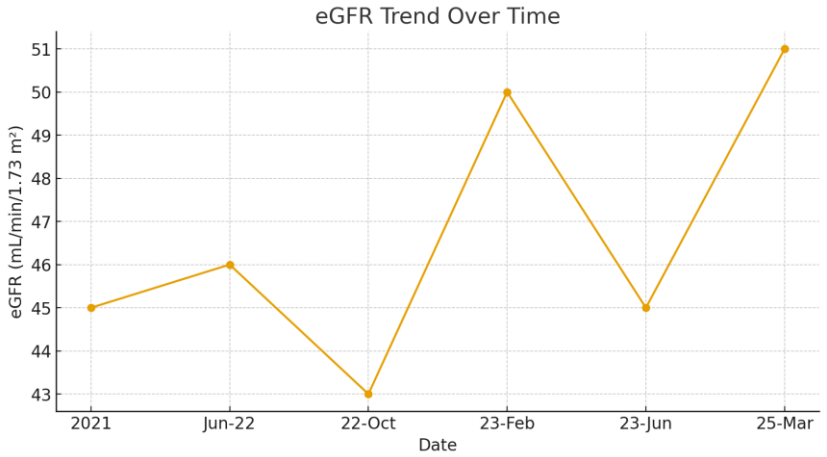
6/2023

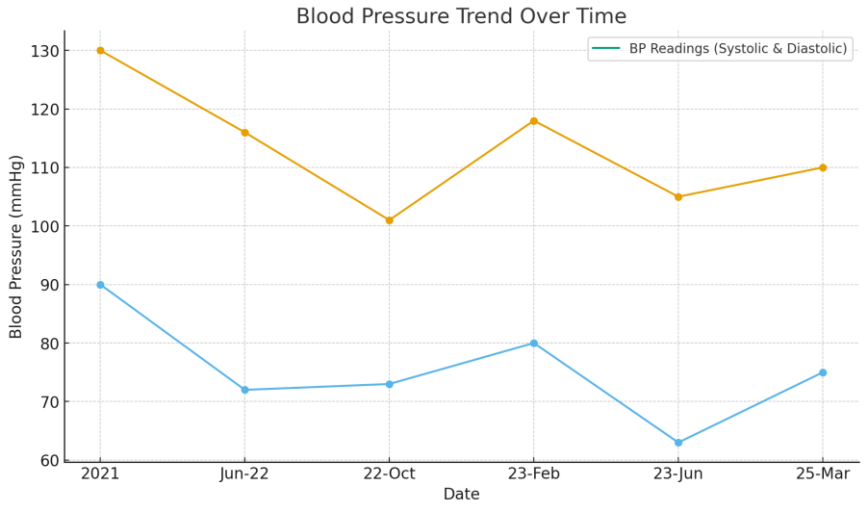
Objectives	Pertinent Findings
Blood pressure	105/68
Hematuria	0-2 rbc/hpf
Proteinuria (UPCR, g/d)	<0.2g/day
eGFR (mL/min/1.73 m^2)	45

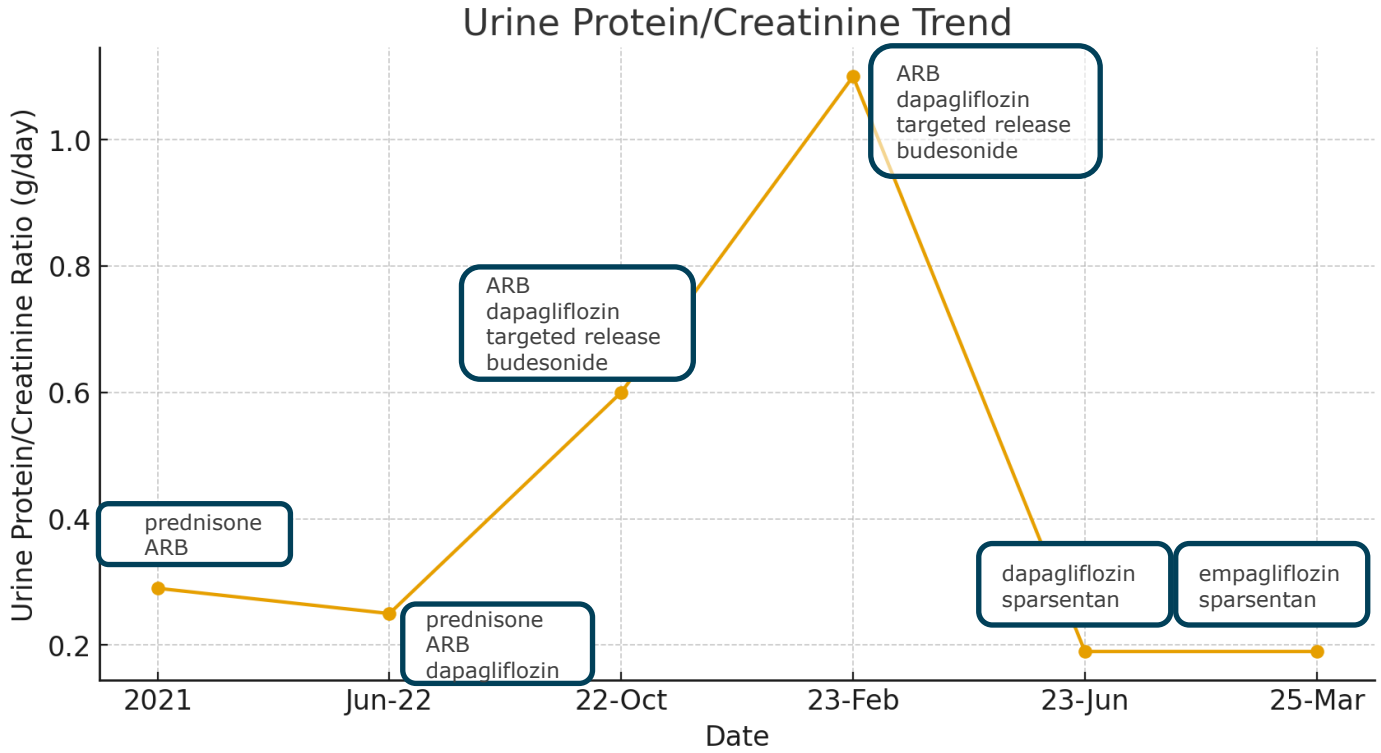
Medications
empagliflozin
sparsentan

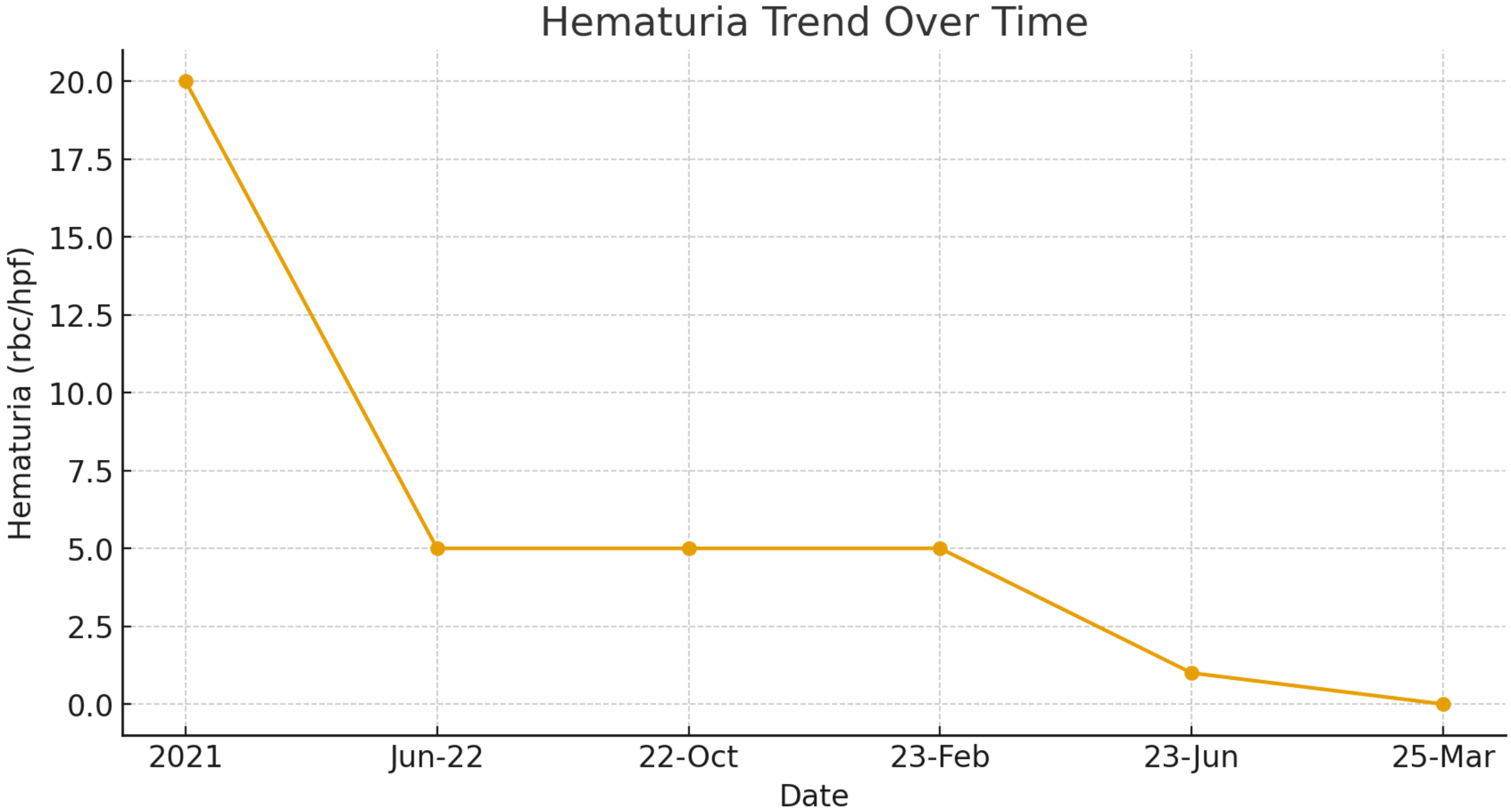
2/2025

Objectives	Pertinent Findings
Blood pressure	110/76
Hematuria	none
Proteinuria (UPCR, g/d)	<0.2g/day
eGFR (mL/min/1.73 m^2)	51


eGFR Trend Over Time
eGFR (mL/min/1.73 m²)
51
50
49
48
47
46
45
44
43
2021
Jun-22
22-Oct
23-Feb
23-Jun
25-Mar
Date


Blood Pressure Trend Over Time
BP Readings (Systolic & Diastolic)
Blood Pressure (mmHg)
130
120
110
100
90
80
70
60
2021
Jun-22
22-Oct
23-Feb
23-Jun
25-Mar
Date


Urine Protein/Creatinine Trend
Urine Protein/Creatinine Ratio (g/day)
1.0
0.8
0.6
0.4
0.2
prednisone
ARB
prednisone
ARB
dapagliflozin
ARB
dapagliflozin
targeted release
budesonide
ARB
dapagliflozin
targeted release
budesonide
dapagliflozin
sparsentan
empagliflozin
sparsentan
2021
Jun-22
22-Oct
23-Feb
23-Jun
25-Mar
Date


Hematuria Trend Over Time
Hematuria (rbc/hpf)
20.0
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
2021
Jun-22
22-Oct
23-Feb
23-Jun
25-Mar
Date

Pathophysiology of GN

Major Categories of Glomerulonephritis (GN)

Immune Complex GN	Pauci-immune GN	Anti-GBM Disease:	Podocytopathies:	Membranous Nephropathy:
IgA nephropathy, lupus nephritis, post-infectious GN	ANCA-associated vasculitis	Goodpasture syndrome	FSGS, minimal change disease	Immune complex deposition in a podocytopathy

Immune Complex GN

IgA nephropathy

- Recurrent hematuria
- Mesangial deposition
- Heterogenous patient distribution

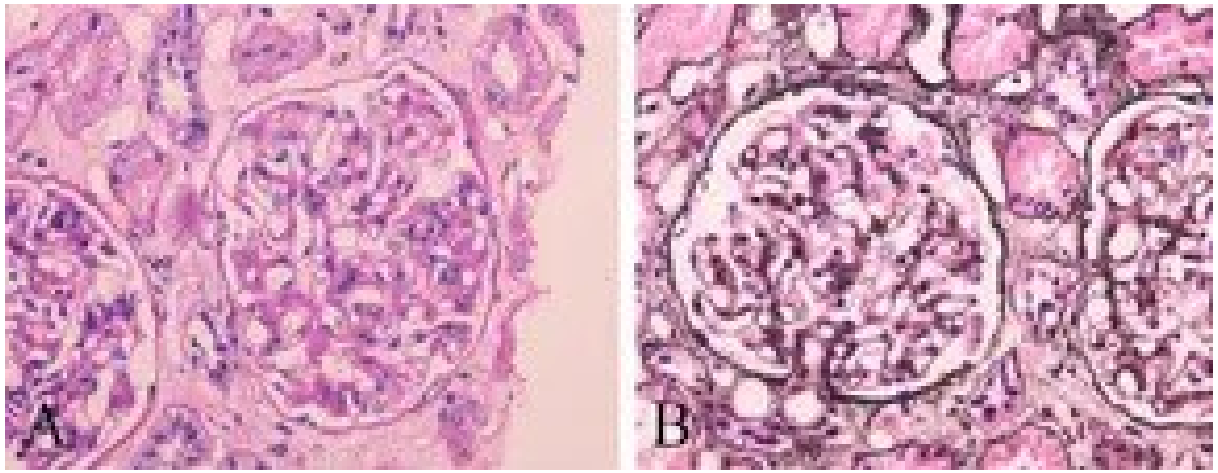
Typical Presentations

- Gross hematuria (~40-50%):
  - 'coca-cola colored' urine post-URI
- Asymptomatic microscopic hematuria with proteinuria
- RPGN or acute kidney injury

D'Agati VD, Fogo AB. *N Engl J Med*. 2021;384:1437–1452.
Rout P, Limaiem F, Hashmi MF. IgA Nephropathy (Berger Disease). StatPearls [Internet]. Accessed September 22, 2025.

Histopathological Characteristics of IgA Nephropathy

- Baseline Labs & Characteristics
- Hypertension common
  - ~34% nephrotic-range proteinuria
- Variable eGFR at baseline despite chronicity in histology
- Male predominance (M:F = 2.4:1)

A  B

Images A and B: Light microscopy shows a glomerulus with mild-to-moderate mesangial hypercellularity and endocapillary hypercellularity.

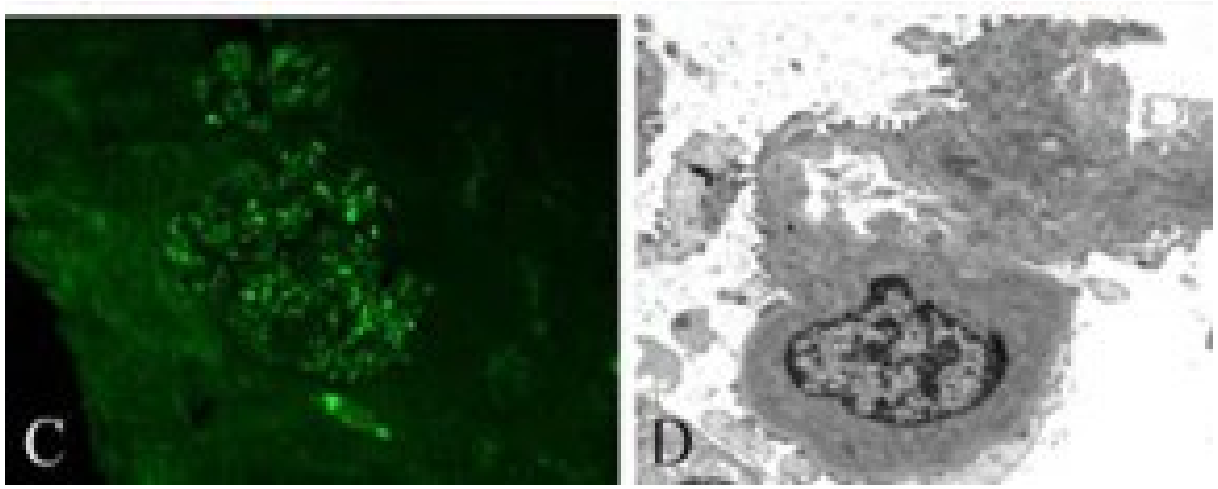
C  D

Image C: Immunofluorescence image reveals IgA deposits along the glomerular mesangial area
Image D: Electron microscopy image shows deposits along the mesangium and matrix.

D'Agati VD, Fogo AB. *N Engl J Med*. 2021;384:1437–1452.
Rout P, Limaiem F, Hashmi MF. IgA Nephropathy (Berger Disease). StatPearls [Internet]. Accessed September 22, 2025.

Histology Images

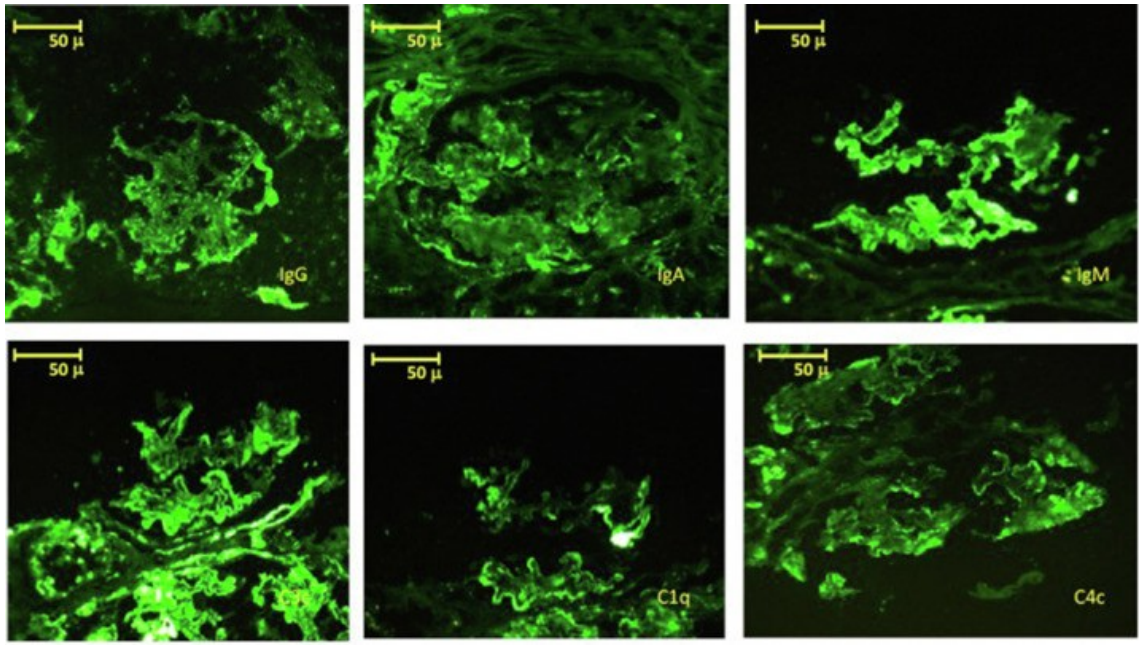


Image: Panels show direct immunofluorescence staining with granular positivity in the mesangium and in some segments of the capillary loops for all immunoglobulins and for complement, characteristic of the “full house” pattern.

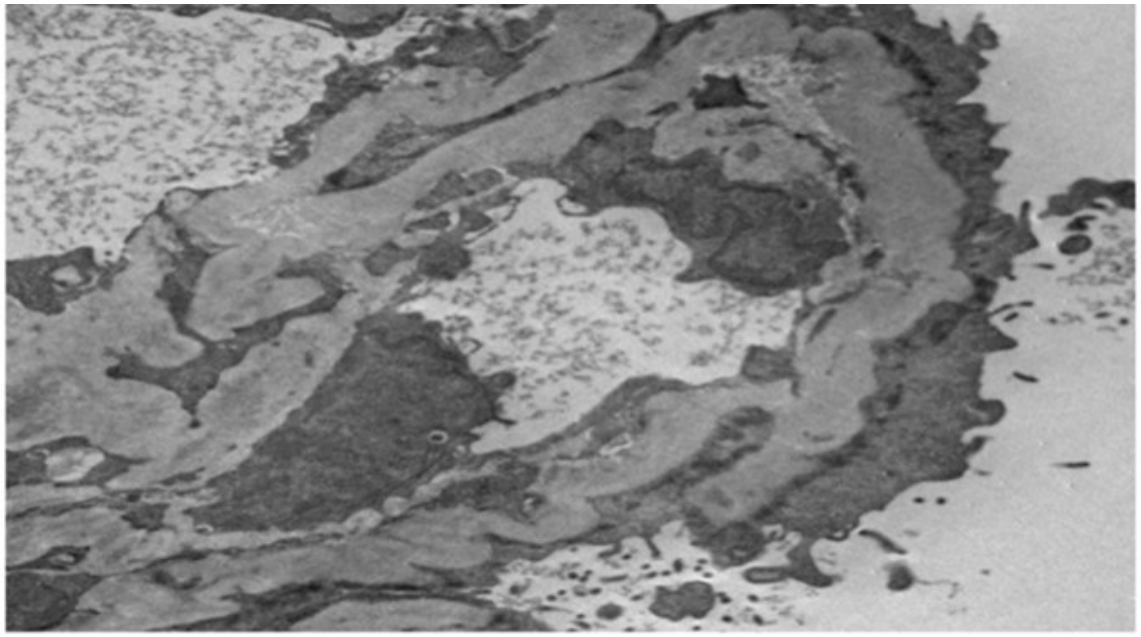


Image: Electron microscopy (original magnification ×10,000) showing the presence of subendothelial and intramembranous electron dense deposits.

Orozco-Guillén AO, Abraham VS, Moguel Gonzalez B, et al. Kidney-Limited Full-House Lupus-like Membranous Nephropathy and Membranoproliferative Glomerulonephritis in Pregnancy. *Kidney Int Rep*. 2023;8(4):932-938. doi:10.1016/j.ekir.2023.01.006

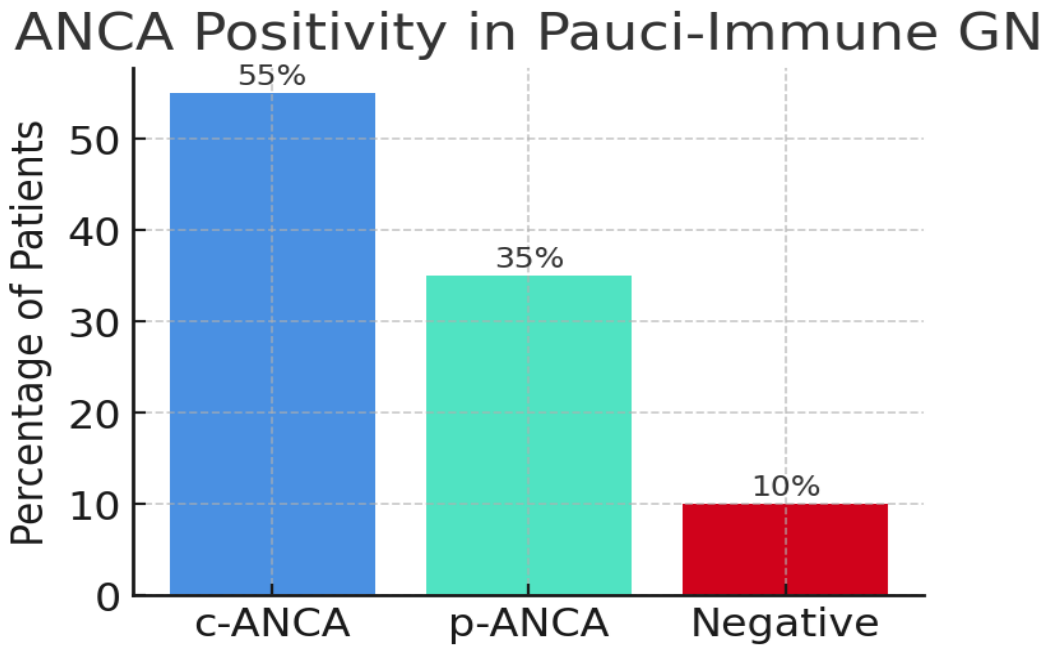
Immune Complex GN Types

Lupus Nephritis	General SLE Features	Renal-specific Signs	Occurrence Rate	Class IV (diffuse proliferative)	LN patients
Systemic autoimmunity, full-house IF	• Malar rash • Arthritis • Serositis • Oral ulcers • Fatigue • Fever	• Hypertension • Edema • Nephritic or nephrotic presentation • RBC casts	• ~40% of SLE patients • Usually within 5 years of diagnosis	• Most common • Worst prognosis • 10–30% to ESRD in 10 years	• Younger age at SLE diagnosis, • More hypertension, serositis, anti-dsDNA positivity

Orozco-Guillén AO, Abraham VS, Moguel Gonzalez B, et al. Kidney-Limited Full-House Lupus-like Membranous Nephropathy and Membranoproliferative Glomerulonephritis in Pregnancy. *Kidney Int Rep*. 2023;8(4):932-938. Published 2023 Jan 16. doi:10.1016/j.ekir.2023.01.006

Pauci-Immune GN (ANCA-Associated)

- Presents with rapidly progressive GN (RPGN) and acute kidney injury
- ANCA-positive (c-ANCA or p-ANCA) in 80–95% of cases
- Rare ANCA-negative cases with similar prognosis
- Labs:
  - hematuria, nephritic range proteinuria
  - elevated creatinine
  - Anemia
  - ↑ESR/CRP
- 20–25% progress to ESRD within a few years despite therapy



AJKD Core Curriculum (2020); BMC Nephrol 2013 (IWGRP); Xiao et al. Front Med 2022; PMC open-access cohort studies.
Jennette JC, Nachman PH. ANCA Glomerulonephritis and Vasculitis. *Clin J Am Soc Nephrol.* 2017;12:1680–91. doi: 10.2215/CJN.02500317

Pauci-Immune GN (ANCA-Associated) - continued

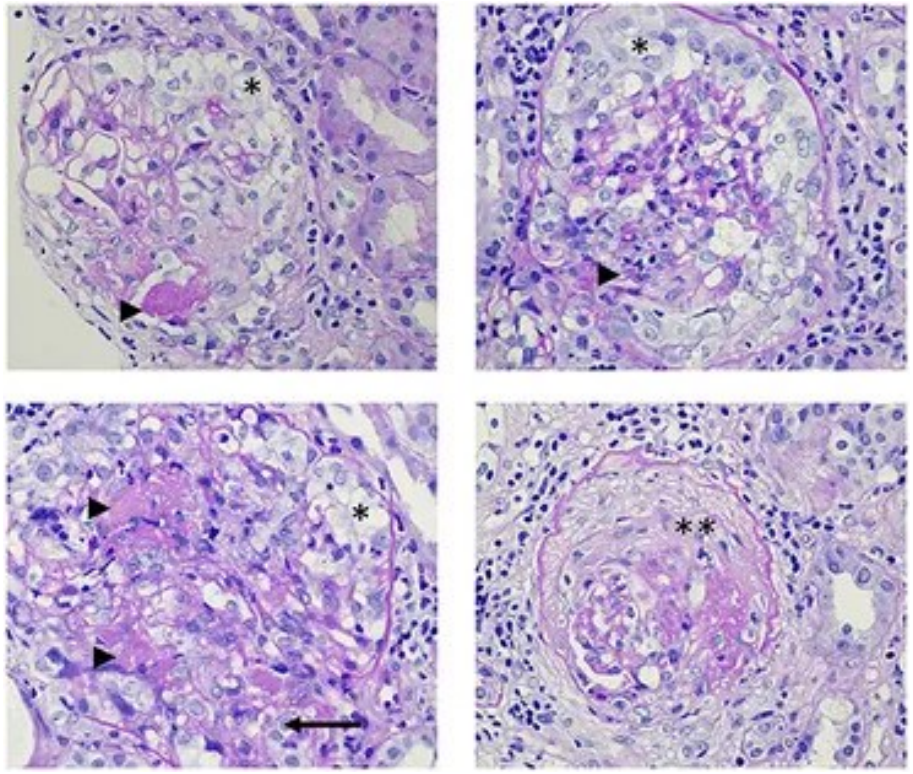


Image 1: Histopathology images from the renal biopsy of a patient with ANCA-associated glomerulonephritis. The patient has renal limited vasculitis with anti-myeloperoxidase positivity, causing rapidly progressive glomerulonephritis syndrome. Arrowheads: fibrin; *: cellular crescents; **: sclerotic crescent; arrow: rupture of the Bowman's capsule. Light microscopy, Periodic Acid-Schiff (PAS) staining, magnification: 600x.

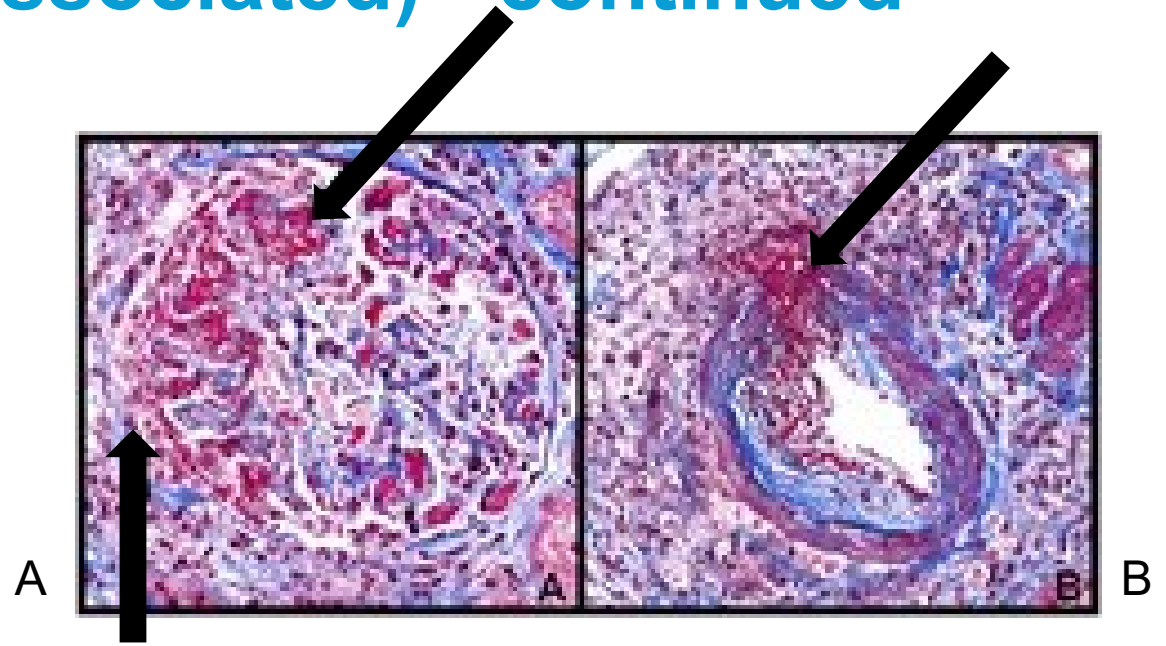


Image 2. Photomicrographs of a kidney biopsy specimen from a patient with ANCA vasculitis showing segmental fibrinoid necrosis. In a glomerulus (A) and an interlobular artery (B) (short arrows). The glomerulus has a small cellular crescent (long arrow), and a break in Bowman's capsule in the upper left corner. (Masson trichrome stain.)

AJKD Core Curriculum (2020); BMC Nephrol 2013 (IWGRP); Xiao et al. Front Med 2022; PMC open-access cohort studies.

Jennette JC, Nachman PH. ANCA Glomerulonephritis and Vasculitis. *Clin J Am Soc Nephrol.* 2017;12:1680–91. doi: 10.2215/CJN.02500317

Anti-GBM Disease

Linear IgG along GBM

Pulmonary hemorrhage + renal failure

SYMPTOMS:
Hematuria
Oliguria
Edema
Hemoptysis

SEROLOGY:
Anti-GBM antibodies positive in ~90%
Overlap with ANCA

LABS:
Hematuria
RBC casts Proteinuria
↑creatinine
Anemia

RARE:
Incidence ~1 per million/year

BIMODAL:
Young males (~20s)
Older females (~60s-70s)

High mortality if untreated

With therapy 5-yr survival ~80-90%

POOR RENAL SURVIVAL IF:
Cr >6-7 mg/dL OR dialysis-dependent at presentation

KDIGO GN Guideline 2021 PMC case series on Anti-GBM disease immunofluorescence.
Bharati J, Yang Y, Sharma P, Jhaveri KD, Atypical Anti-Glomerular Basement Membrane Disease. *Kidney International Reports*. 2023;8(6):1151-1161.

Anti-GBM Disease with linear IgG Deposition Images

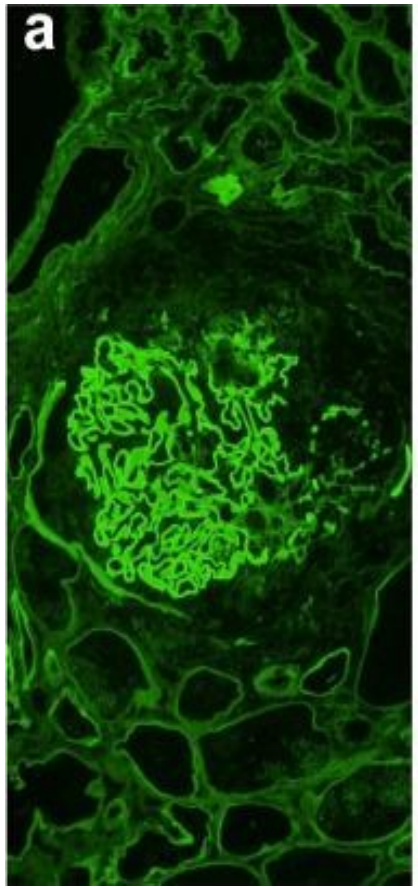


Image a: Classic anti-GBM disease with strong IgG staining along GBM

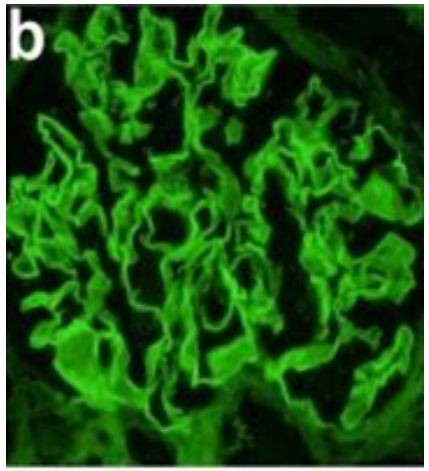


Image b: IgG reactivity along GBM in fibrillary glomerulopathy

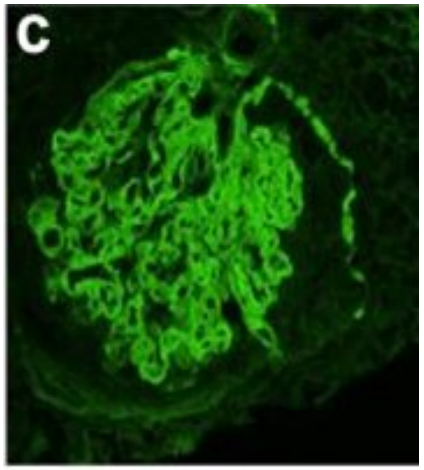


Image c: linear IgG staining along GBM in an atypical anti-GBM disease

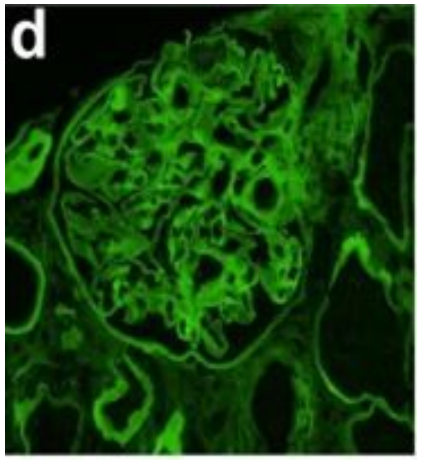


Image d: Faint linear IgG entrapment along GBM in diabetic nephropathy

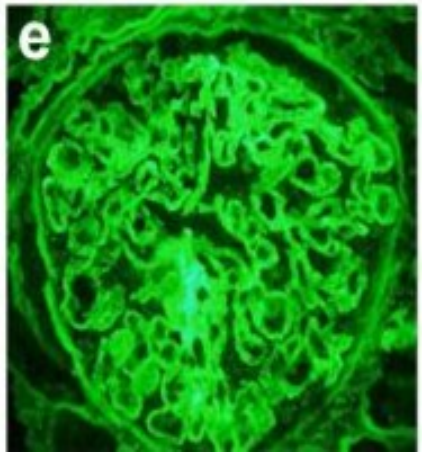


Image e: Strong IgG staining along GBM

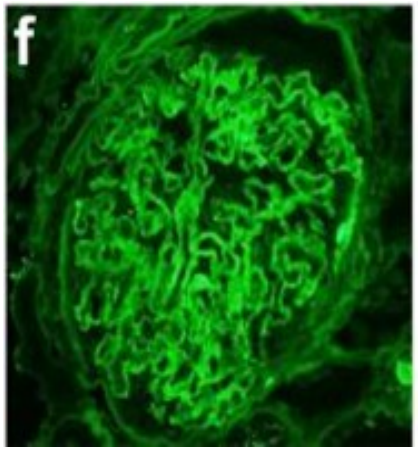


Image f: Strong kappa staining along GBM

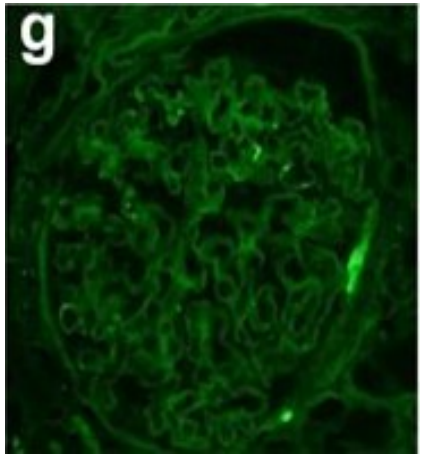


Image g: Negative lambda stain

Images e-g: IgG linear stain along GBM with kappa restriction.

KDIGO GN Guideline 2021
PMC case series on Anti-GBM disease immunofluorescence.
Bharati J, Yang Y, Sharma P, Jhaveri KD, Atypical Anti-Glomerular Basement Membrane Disease. *Kidney International Reports*. 2023;8(6):1151-1161.

Podocytopathies (FSGS & MCD): Clinical Presentation & Labs

FSGS

- Proteinuria, often nephrotic-range
- Hematuria, hypertension common
- May progress to CKD/ESRD despite therapy

Minimal Change Disease (MCD)

- Nephrotic syndrome:
- Microscopic hematuria uncommon
- More common in children; adults also affected
- Normal renal function in MCD; impaired renal function more frequent in FSGS

Diagnosis

- Biopsy required:
  - FSGS seen on LM
- MCD requires EM (podocyte effacement)

Rosenberg, AZ, Kopp, JB Focal. Segmental Glomerulosclerosis. *Clinical Journal of the American Society of Nephrology.* 2017:12(3):502-517. doi: 10.2215/CJN.05960616
KDIGO GN Guidelines (2021); Rosenberg & Kopp, CJASN 2017; NCBI Bookshelf: MCD (2023); StatPearls: FSGS (2024).

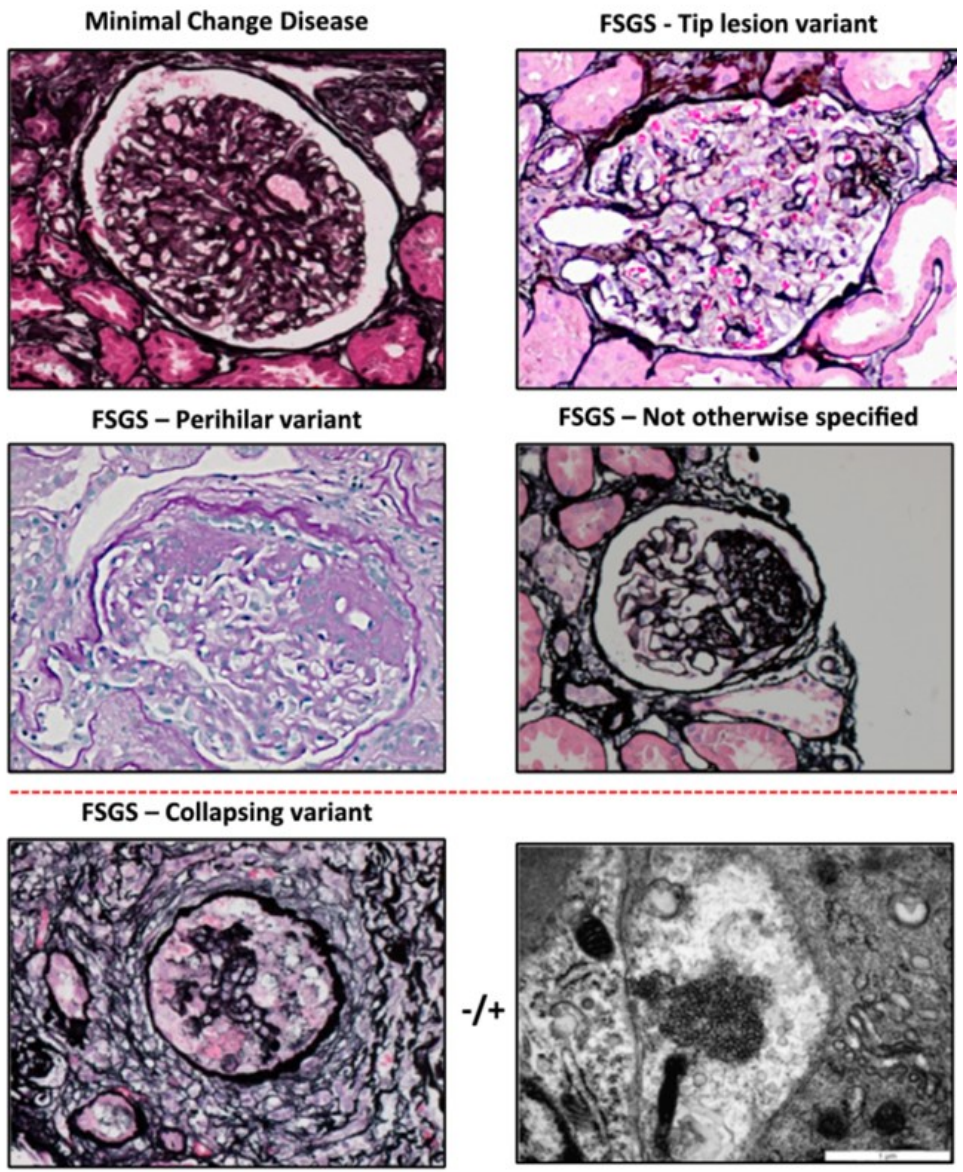
FSGS, an overview of clinical and pathologic features

Characteristic Features	Primary FSGS	FSGS	APOL1 FSGS	Genetic FSGS	Infection/ Inflammation Associated	Medication-Associated FSGS
Mechanism of Podocyte Injury	Circulating factor, possibly a cytokine	Mismatch between metabolic load and glomerular capacity	APOL1 variant–initiated inflammation	High-penetrance genetic variants (Mendelian or mitochondrial inheritance)	Postulated role of IFN and possible other cytokines	Presumed direct effect on podocytes
History	Acute onset of edema	Reduced renal mass: low birth weight, oligomeganephronia, ureteral reflux, morbid obesity; increased single-nephron GFR: cyanotic congenital heart disease, sickle cell anemia	Family history, may be unremarkable	Family history, may be unremarkable with recessive inheritance genes	HIV, CMV, possible: parvovirus B19, Still disease, natural killer cell leukemia	Bisphosphonate, lithium
Laboratory tests	Many have high-grade proteinuria and nephrotic syndrome	Any level of proteinuria, serum albumin may be normal	Any level of proteinuria	Any level of proteinuria	Any level of proteinuria	Any level of proteinuria
Renal pathology	Widespread foot process effacement	Large glomeruli, perihilar sclerosis variant most typical, partial foot process effacement	May resemble primary or adaptive forms	Variable	Variable	Variable
Treatment and response	May respond to IST	Responds well to RAAS antagonism, often with >50% proteinuria reduction	May respond to therapies used for primary and adaptive forms	High-penetrance genetic mutations: usually does not respond to IST	Treat the virus	Stop the medication
Recurrence after renal transplant	Possible	Unlikely	Possible	Unlikely	Possible if infection/ inflammation persists	Unlikely

Kopp JB: Focal segmental glomerulosclerosis and collapsing glomerulopathy syndromes. In: Essentials of Chronic Kidney Disease, edited by Fadem SZ, Hauppauge, Nova Science Publishers, 2015

Podocytopathies (FSGS & MCD): Images

Minimal Change Disease (MCD)	• Patent glomeruli in the absence of tubulointerstitial scarring
Tip Lesion	• Focal adhesion of the glomerular tuft to Bowman's capsule near the proximal tubule
Perihilar Variant	• Most common variant
Collapsing Variant	• Endothelial tubuloreticular inclusions • May be observed in high IFN states, including viral infection /exogenous IFN
MCD and Tip Lesion	• Most responsive and least progressive
Collapsing Glomerulopathy	• Therapy resistant and rapidly progressing



Rosenberg, AZ, Kopp, JB Focal. Segmental Glomerulosclerosis. *Clinical Journal of the American Society of Nephrology.* 2017:12(3):502-517. doi: 10.2215/CJN.05960616

Image: Histopathology of minimal change disease and focal segmental glomerulosclerosis.

Membranous Nephropathy

Most common cause of nephrotic syndrome in adults

SYMPTOMS:
Edema
Foamy urine
Fatigue
Rarely hematuria

Nephrotic-range proteinuria (>3.5 g/day)

Hypoalbuminemia, hyperlipidemia, ± normal creatinine

Anti-PLA2R antibodies positive in ~70–80% (primary MN)

ANA, hepatitis B/C, malignancy screen for secondary MN

PEAK AGE:
40–60 years; male predominance

30% spontaneous remission,
30% persistent proteinuria,
30% progress to ESRD at 10 yrs

POOR PROGNOSIS IF MALE:
Persistent nephrotic proteinuria OR high creatinine at baseline

KDIGO GN Guidelines (2021); Beck & Salant, NEJM 2014; Cattran & Brenchley, JASN 2017
Bharati J, Waguespack, D, Beck L. Membranous Nephropathy: Updates on Management. *Advances in Kidney Disease and Health*. 2024;31:299-308. doi:10.1053/j.akdh.2024.04.004.

Representative Histopathology Images of Membranous Nephropathy

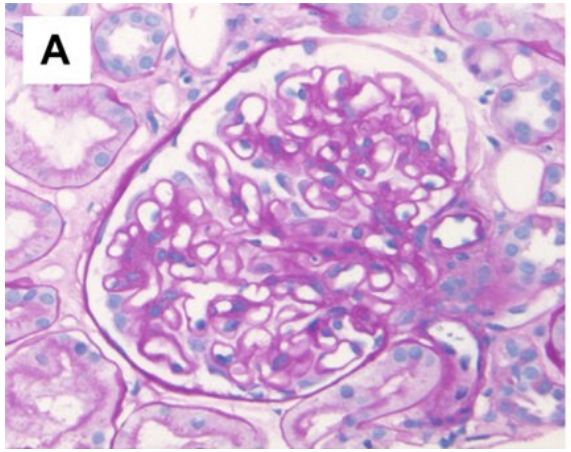


Image A: Light microscopy (PAS) demonstrating rigid, thickened capillary loops.

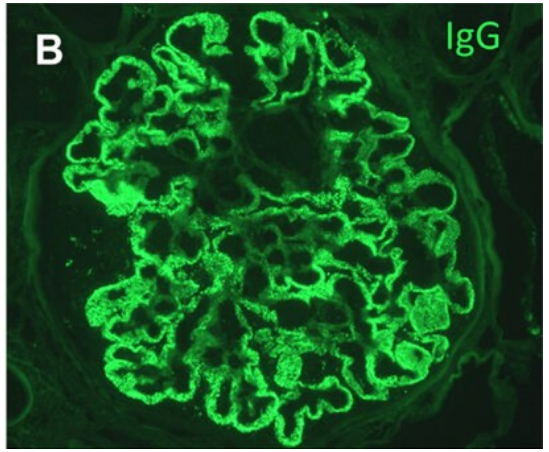


Image B: Light microscopy (PAS) demonstrating rigid, thickened capillary loops.

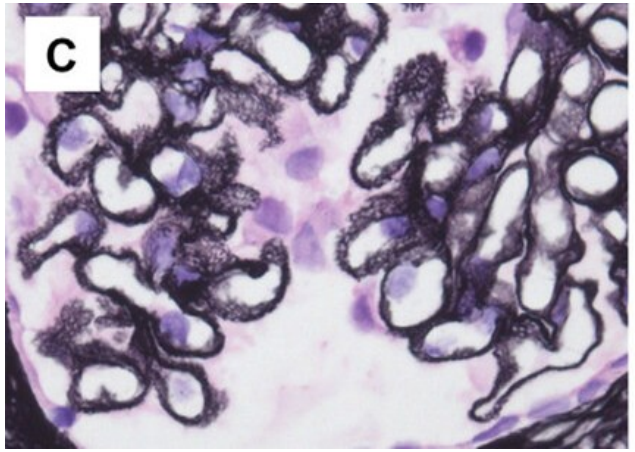


Image C: Silver stain of a portion of the glomerular tuft showing numerous open spaces (craters) reflecting the immune deposits, which remain unstained by this method

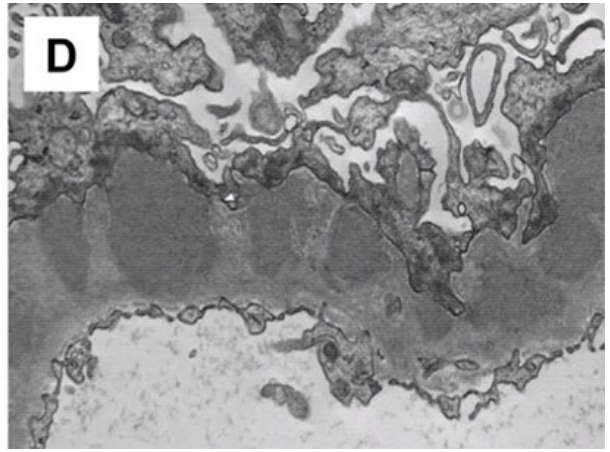


Image D: Electron micrograph showing large electron-dense subepithelial deposits with interspersed matrix material (stage 2).

KDIGO GN Guidelines (2021); Beck & Salant, NEJM 2014; Cattran & Brenchley, JASN 2017
Bharati J, Waguespack, D, Beck L. Membranous Nephropathy: Updates on Management. *Advances in Kidney Disease and Health*. 2024;31:299-308. doi:10.1053/j.akdh.2024.04.004.

To simplify : GN Mechanisms and Presentation

Category	Mechanism	Presentation
Immune Complex (IgA, Lupus)	Immune complex deposition	Hematuria, proteinuria
Pauci-Immune (ANCA associated vasculitis)	ANCA mediated vasculitis	RPGN, systemic vasculitis, crescents
Anti-GBM	Anti-GBM autoantibodies	RPGN + pulmonary hemorrhage
Podocytopathies (FSGS, MCD)	Podocyte injury	Nephrotic syndrome (MCD, FSGS) +/- hematuria
Membranous Nephropathy (MN)	Subepithelial immune complex deposition	Nephrotic syndrome, edema, proteinuria, hypoalbuminemia

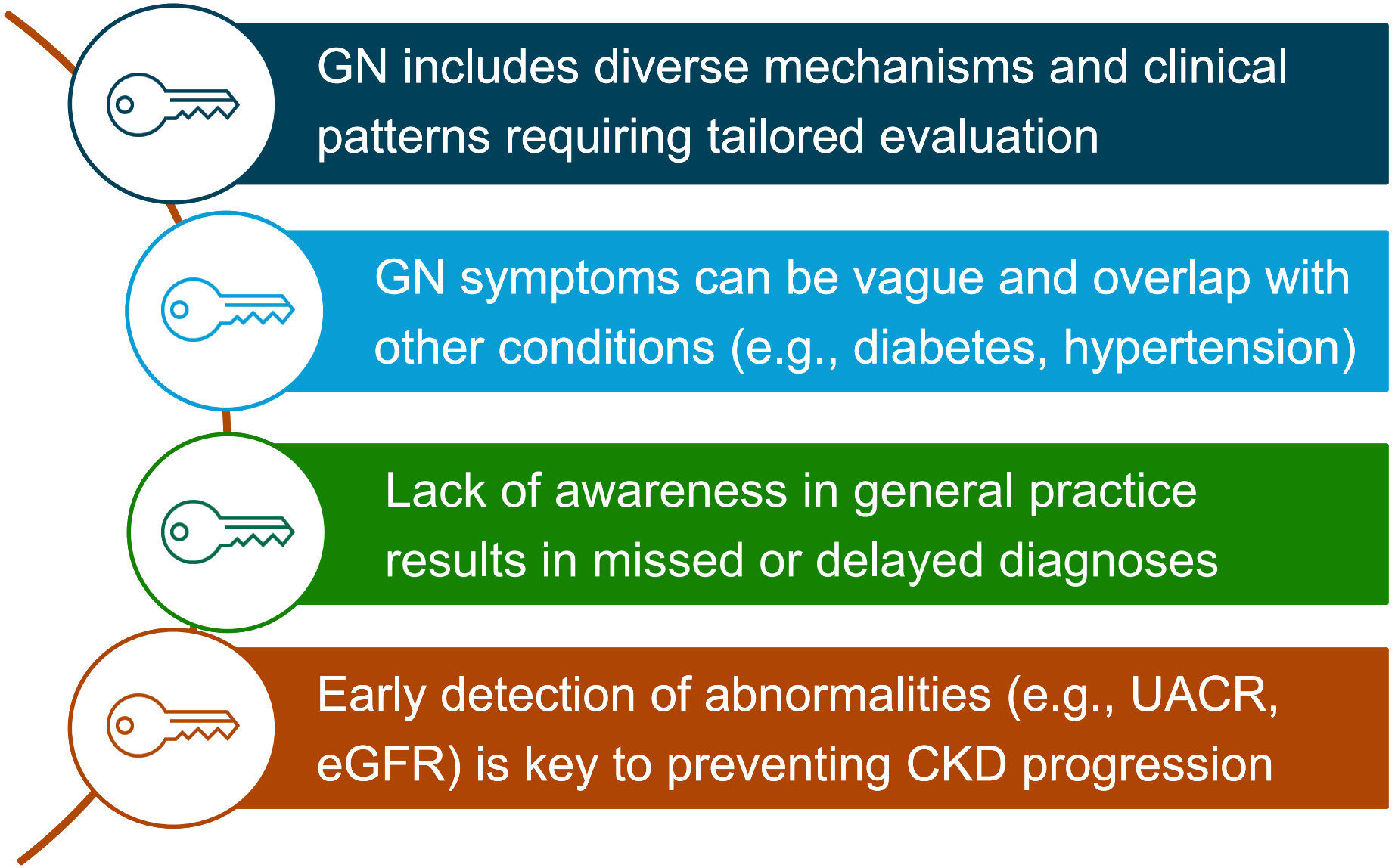
KDIGO GN Guidelines (2021); D'Agati & Fogo, NEJM 2021; Beck & Salant, NEJM 2014.

To simplify: Labs and Prognosis

Category	Labs	Prognosis
Immune Complex (IgA, Lupus)	IgA: maybe Gd-IgA ? LN: ANA/dsDNA, low C3	IgA: heterogeneous LN: can be severe
Pauci-Immune (ANCA associated vasculitis)	ANCA positive (80-90%) hematuria, ↑Cr	20-25% progress to ESRD
Anti-GBM	Anti-GBM autoantibodies	High mortality if untreated, poor renal survival
Podocytopathies (FSGS, MCD)	Proteinuria (> 3.5g/day), hypoalbuminemia, anti-nephrin antibodies	MCD excellent if steroid responsive, FSGS variable – collapsing has worst success of remission
Membranous Nephropathy (MN)	Proteinuria (> 3.5g/day), hypoalbuminemia, hyperlipidemia	30% remission spontaneous, 30% persistent, 30% progress to ESRD

KDIGO GN Guidelines (2021); D'Agati & Fogo, NEJM 2021; Beck & Salant, NEJM 2014.

Key Takeaways



Key Takeaways: Clinical Relevance

Recognizing GN subtype directs workup (serology, biopsy) and urgency of referral

Lack of awareness in general practice results in missed or delayed diagnoses:

Immune Complex GN	Pauci-Immune GN:	Anti-GBM Disease	Podocytopathies	Membranous Nephropathy

• IgA often indolent
• Lupus more severe with systemic features
	• Rapidly progressive
	• ANCA-associated
	• Histology guides prognosis
		• Pulmonary-renal syndrome
		• Linear IgG
		• Poor renal survival if late
			• MCD is steroid-responsive with good prognosis
			• FSGS often resistant and progressive
				• Leading cause of adult nephrotic syndrome:
				  • ~30% remit
				  • ~30% persist
				  • ~30% progress to ESKD
				• Recurrence possible post-transplant

Patient Perspective: What GN Feels Like

Advancing Kidney Health

Through Optimal Medication Management

Thank you!