Glomerular disease

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Clinical manifestation of glomerular disease

Decreased eGFR

- ✓Azotemia
- ✓Oliguria
- ✓Salt/water retention (edema, HT)

Loss of barrier

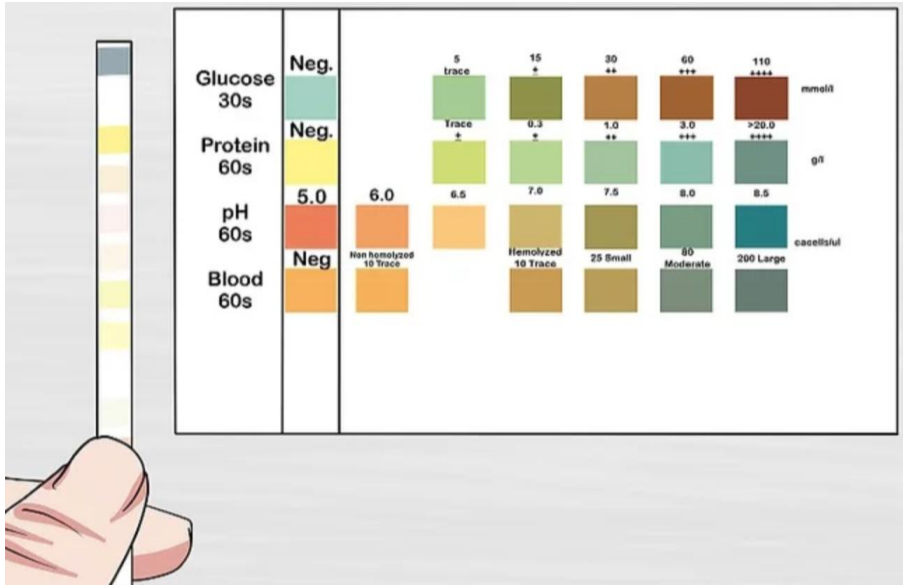
- ✓Proteinuria
- ✓Hematuria

Proteinuria

Abnormal
> 150 mg/day

- Semiquantitative measurement
  - Urine protein dipstick: albumin
  - Sulfosalicylic acid test: albumin, Ig, lysozyme
- Quantitative measurement
  - UPCR, 24-hour urine for total protein and Cr (normal urine Cr = 15-25 mg/kg/day)

Measurement	Normal to Mildly Increased (A1)	Moderately Increased (A2)	Severely Increased (A3)
AER, mg/24 h	<30	30–300	>300
PER, mg/24 h	<150	150–500	>500
ACR			
mg/mmol	<3	3–30	>30
mg/g	<30	30–300	>300
PCR			
mg/mmol	<15	15–50	>50
mg/g	<150	150–500	>500
Protein reagent strip	Negative or trace	Trace to 1+	1+ or greater



Negative	0 mg/dL
trace	15-30 mg/dL
1+	30-100 mg/dL
2+	100-300 mg/dL
3+	300-1000 mg/dL
4+	> 1000 mg/dL

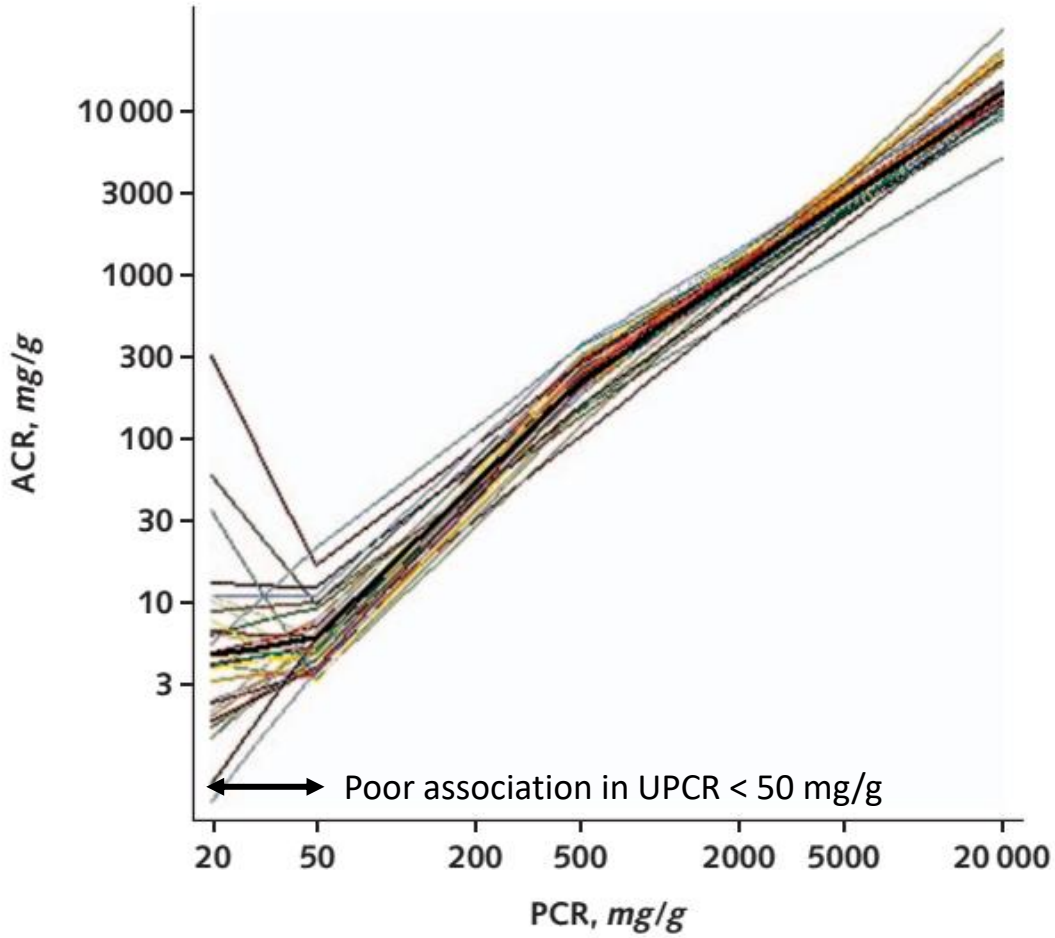
Gehrke, et al. “How to Use a Urine Dipstick Test”. December 12, 2019
Sana Waheed. “Evaluation of proteinuria”. BMJ Best Practice. BMJ 2018. July

ORIGINAL RESEARCH

Annals of Internal Medicine

Conversion of Urine Protein–Creatinine Ratio or Urine Dipstick Protein to Urine Albumin–Creatinine Ratio for Use in Chronic Kidney Disease Screening and Prognosis

An Individual Participant-Based Meta-analysis



Detect only albuminuria

Dipstick protein	UPCR (mg/g)	UACR (mg/g)
Negative	< 0.1	< 10
Trace	0.1-0.15	10-30
1+	0.15	30
2+	**0.5**	300
	1.0	500
3+	**2.0**	1000-1100
	3.5	2200
4+	> **5.0**	> 2800-3000

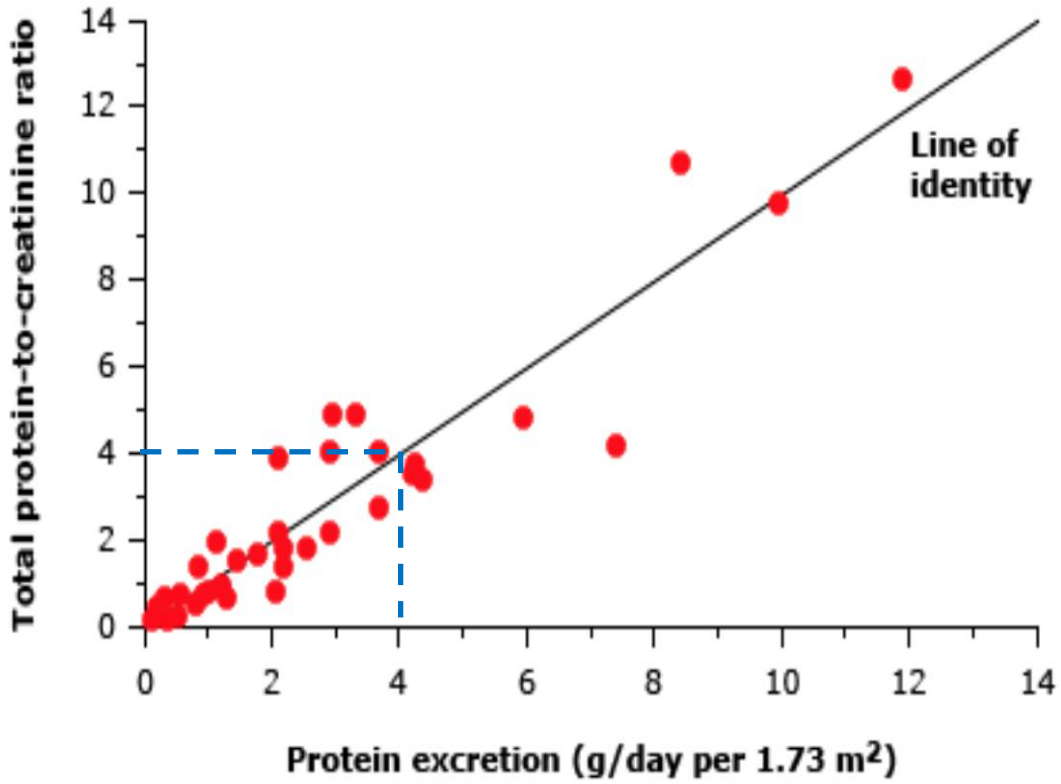
1. Cyriac J, et al. Arch Dis Child Educ Pract Ed. 2017 Jun;102(3):148-154. 2. Sana Waheed, et al. BMJ 2018. July 3. Sumida K, et al. Ann Intern Med. 2020 Sep 15;173(6):426-435.

Ginsberg JM, et al. N Engl J Med. 1983

Proteinuria

Abnormal
> 150 mg/day

- Semiquantitative measurement
  - Urine protein dipstick: albumin
  - Sulfosalicylic acid test: albumin, Ig, lysozyme
- Quantitative measurement
  - UPCR
  - 24-hour urine collection for total protein and Cr



UPCR > 4-5 g/day may **not accurately** equal to 24-hr urine protein

Ginsberg JM, et al. N Engl J Med. 1983

Proteinuria

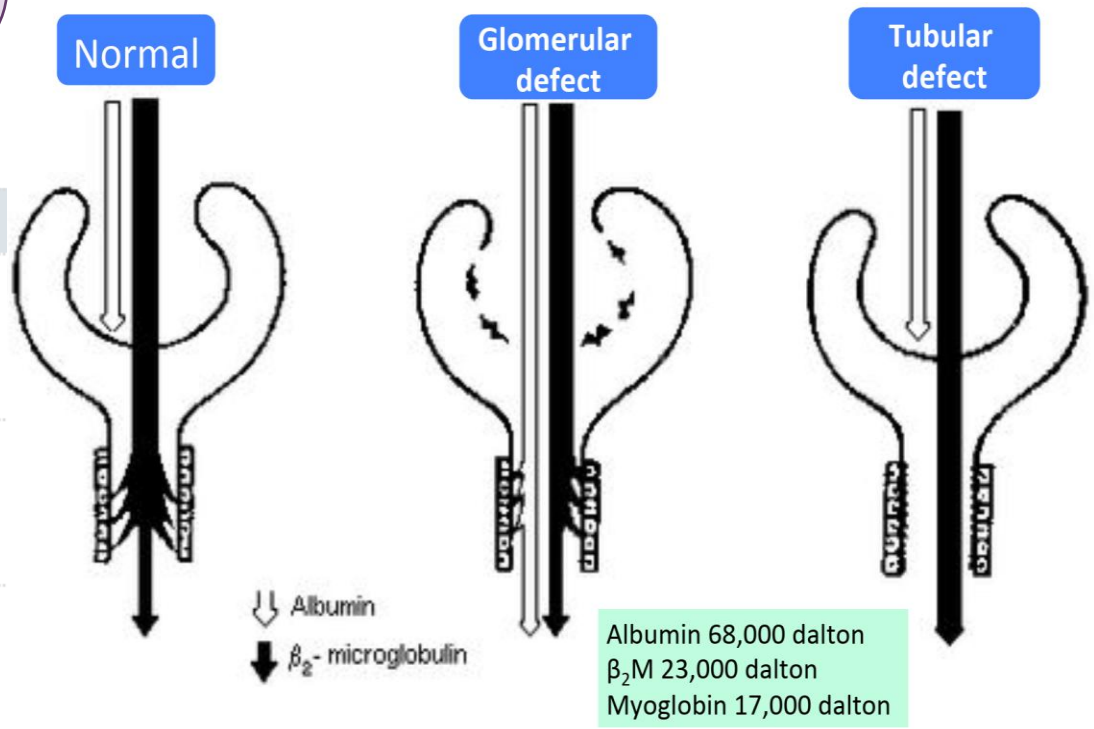
Funtional: fever, exercise, sepsis, high output HF, menstruation
Orthostatic: split urine test (overnight 8-hr urine pro < 50 mg)

Transient proteinuria → Functional, Orthostatic
Persistent proteinuria
Glomerular > 2 g/day → Glomerular disease
Tubular < 2 g/day → ATIN, CTIN
Overflow Any → Upro dipstick ≠ 24hr-Upro

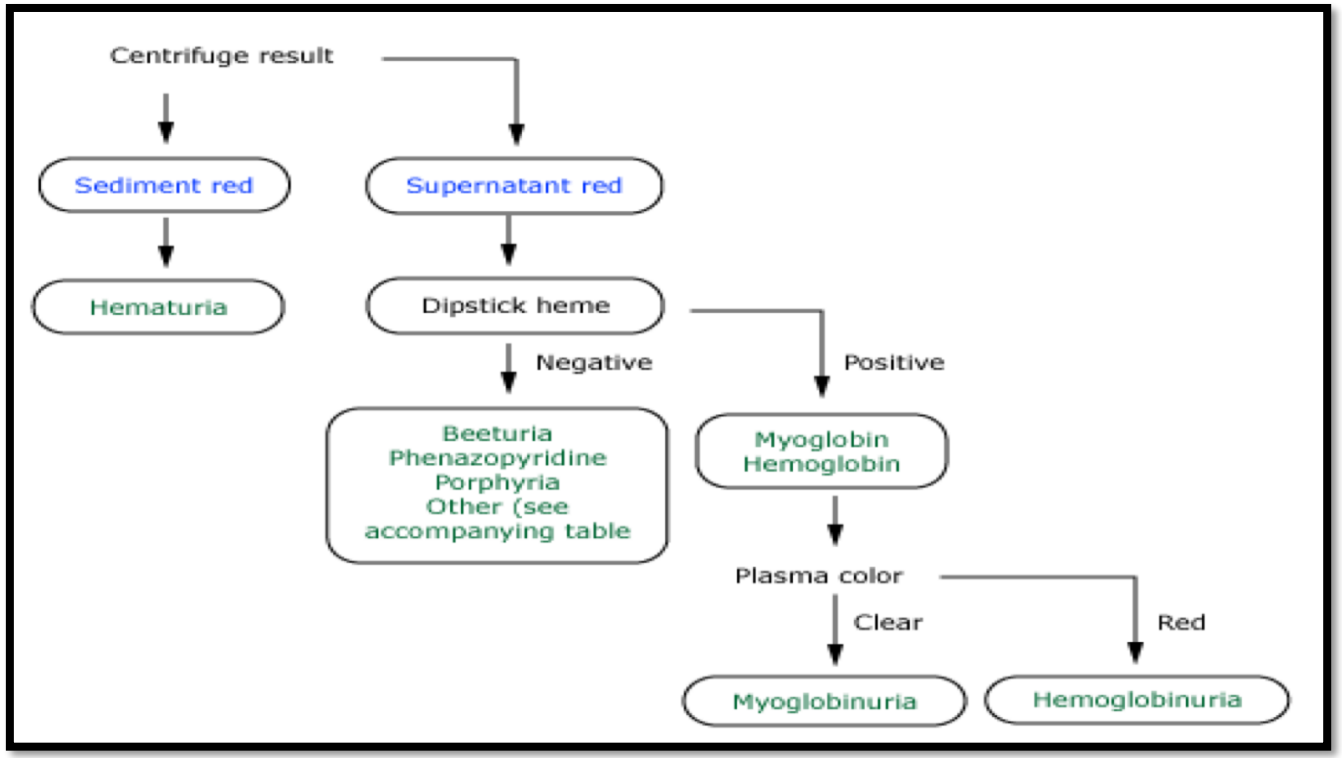
MM (light chain)
Rhabdomyolysis (Myoglobin)
Hemolysis (Hemoglobin)
AML (Lysozyme)

Classification of Proteinuria

TYPE	PATHOPHYSIOLOGIC FEATURES	CAUSE
Glomerular	Increased glomerular capillary permeability to protein	Primary or secondary glomerulopathy
Tubular	Decreased tubular reabsorption of proteins in glomerular filtrate	Tubular or interstitial disease
Overflow	Increased production of low-molecular-weight proteins	Monoclonal gammopathy, leukemia



Hematuria



Color: smoky brown, cola
No clots
Proteiuria > 500 mg/day
Dysmorphic RBC/RBC cast

Glomerular hematuria

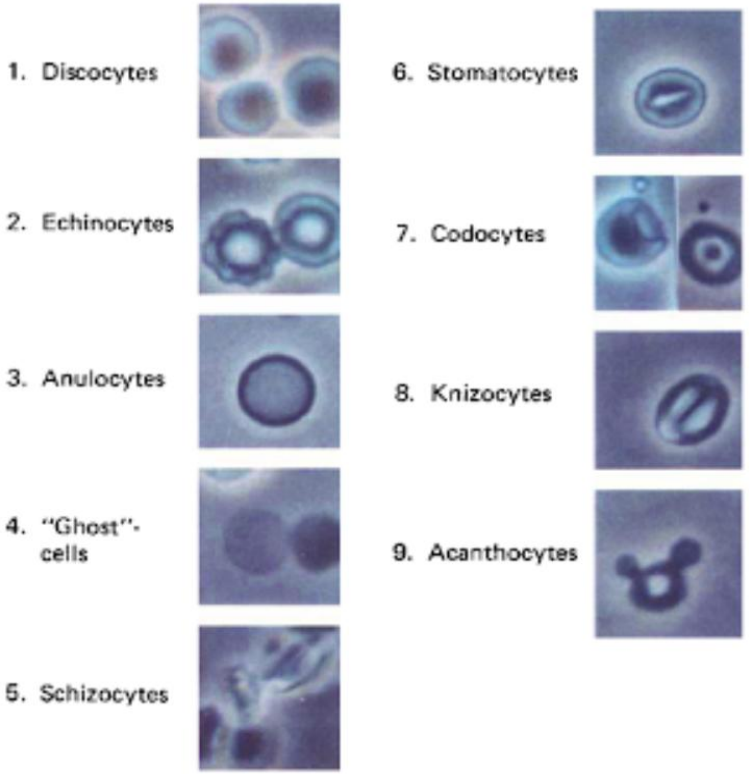
- ✓ IgAN/PSGN > ANCA >> LN
- ✓ Alport's syndrome (X-linked recessive 85%)

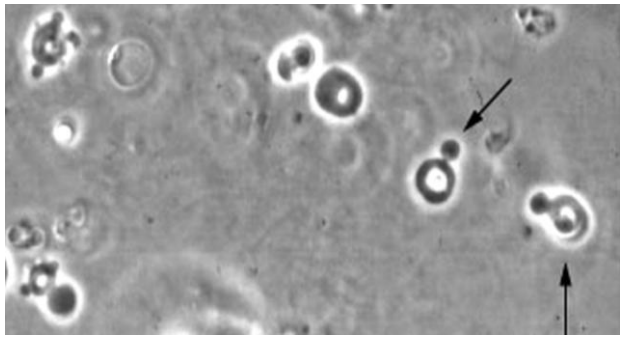
Non-glomerular hematuria

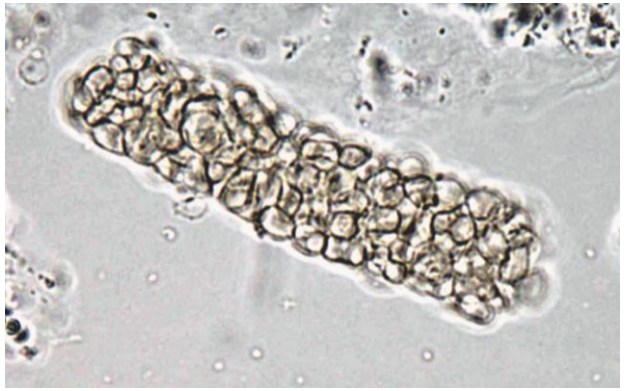
Color: red/pink + Clots
Proteinuria < 500 mg/day
No dysmorphic RBC/RBC cast

- ✓ Tumor: CA bladder, RCC, AML
- ✓ Stone
- ✓ Infection: hemorrhagic cystitis, pyelonephritis
- ✓ Cystic kidney: ADPKD
- ✓ Papillary necrosis
- ✓ Vascular: RVT > Renal infarction, coagulopathy

Hematuria







Glomerular RBC: ≥ 3/HPF

1. RBC cast ≥ 1/HPF
2. Dysmorphic RBC

- > 50% distorted microcytic RBC
- > 5% of acanthocyte

Glomerular hematuria

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Non-glomerular hematuria

Color: red/pink + Clots
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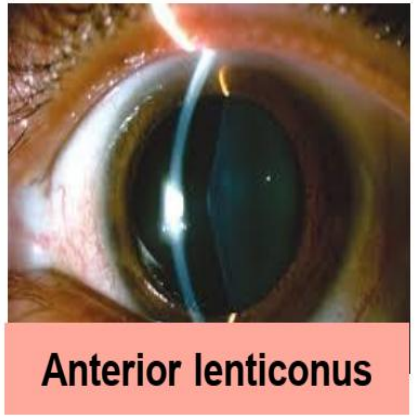
- ✓ Cystic kidney: ADPKD
- ✓ Papillary necrosis
- ✓ Vascular: RVT > Renal infarction, coagulopathy

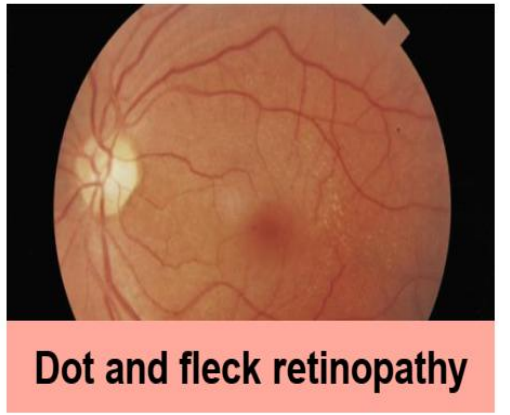
Clinical syndrome of glomerular disease

Proteinuria 0.3-3.0 g/day
Hematuria ≥ 3 RBC/HPF in spun urine

- ✓ Macroscopic hematuria
- ✓ Asymptomatic microscopic hematuria
- ✓ Nephrotic syndrome
- ✓ Nephritic syndrome
- ✓ Rapidly progressive glomerulonephritis
- ✓ Chronic glomerulonephritis

Asymptomatic hematuria


Anterior lenticonus


Dot and fleck retinopathy

Thin basement membrane disease

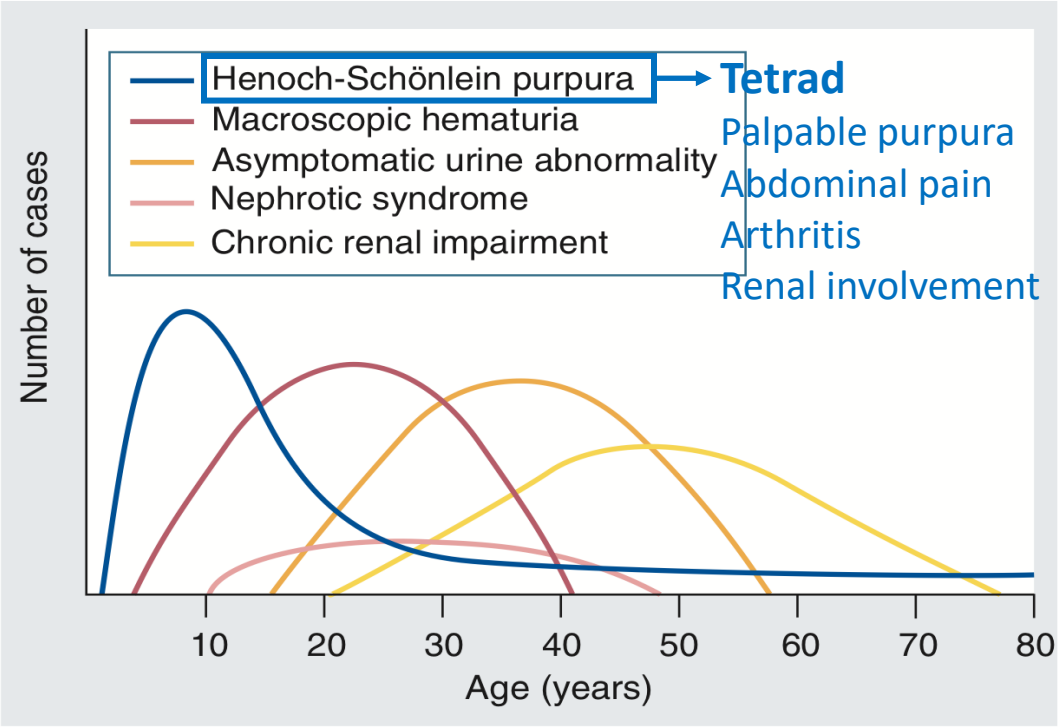
- ✓ AD, mostly thought to be carrier of Alport's
- ✓ Micro hematuria (with loin pain), less renal insufficiency, UPCR < 1.5 g/day
- ✓ **Bx:** GBM thickness < 250 nm

Alport's syndrome

- ✓ X-link recessive > AR/AD, COL4A5
- ✓ Recurrent gross hematuria, ESKD at age 16-35 yr
- ✓ SNHL, ant lenticonus > dot & fleck retinopathy

IgA nephropathy

- ✓ Macro hematuria 40-50% with recurrent
- ✓ Micro hematuria 30-40% with synpharyngitis
- ✓ NS 5-10%
- ✓ **Secondary:** Cirrhosis, AS, RA, Reiter, IBD, HIV/HBV, MM (IgA), CA lung, RCC, Dermatitis herpetiformis



Treatment of IgA nephropathy

Cautions of steroid

- eGFR <30 ml/min/1.73 m² *
- Diabetes
- Obesity (BMI >30 kg/m²)†
- Latent infections (e.g., viral hepatitis, TB)
- Secondary disease (e.g., cirrhosis)
- Active peptic ulceration
- Uncontrolled psychiatric illness
- Severe osteoporosis

Not applicable to variant forms of IgA:
- IgA deposition with minimal change disease
- IgAN with acute kidney injury
- IgAN with a rapidly progressive glomerulonephritis

Proteinuria >1 g/d despite at least 3 months of optimized supportive care:
- BP management
- Maximally tolerated dose of ACEi/ARB
- Lifestyle modification
- Address cardiovascular risk

Keep SBP < 120 mmHg
RAAS blockage 3 months

Not applicable to:
- IgA vasculitis
- IgA nephropathy secondary to:
  - Viral (HIV, hepatitis)
  - Inflammatory bowel disease
  - Autoimmune disease
  - Cirrhosis
- IgA-dominant postinfectious GN

Consider enrollment in a clinical trial

eGFR <30 ml/min/1.73 m²

Consider maximal supportive care

eGFR ≥ 30 ml/min/1.73 m²

Toxicity risk stratification:
- Advanced age
- Metabolic syndrome
- Obesity
- Latent infection (TB, HIV, HBV, HCV)

Risk/benefit profile of glucocorticoids should be individually discussed†

Specific populations:
- Japanese – consider tonsillectomy
- Chinese – consider mycophenolate mofetil as a glucocorticoid-sparing agent

Steroid x 6 months

A 36-year-old man check up, PE: normal. UA: protein 2+, RBC 10-20/HPF.
24-hr urine protein 0.3 g, normal CrCl. What is your initial management?

A. ANA
B. Repeat urine examination
C. Kidney biopsy
D. Consult UroSx for cystoscopy
E. IVP

Microscopic hematuria
Urine protein > 0.5 g/day: Biopsy

A 20-year-old man who has been in good general health underwent a routine physical examination and was found to have protein 2+ on a dipstick urinalysis. The urine sediment was normal and pH 5.0. Physical examination was normal. 24-hour urine collection demonstrated 500 mg of protein and creatinine clearance was normal.

Which is the **MOST** appropriate management?

A. Urine protein electrophoresis
B. Kidney biopsy
C. Intravenous pyelogram
D. ANA
E. Repeat urine examination

Isolated proteinuria
Urine protein > 1 g/day: Biopsy

Step Mx in asymptomatic glomerular disease
✓ Record 24-hr urine protein, Cr (repeat urine examination)

A 49-year-old man wanted to check-up. He had a history of HT, DLP, and cigarette smoking. Six months ago, a routine preoperative for cataract extraction revealed blood 2+ in urinalysis without proteinuria, his previous urinalysis were normal. PE: WNL, BUN/Cr 12/1.1 mg/dL,
UA: pH 5.0, pro neg, 2+ blood, and RBC 5-10/HPF.
Abdominal CT: 2.5 cm of simple cyst in upper pole of right kidney

What is the appropriate next step management?

A. ANCA study
B. Repeat urine examination
C. Kidney biopsy
D. Cystoscopy
E. Give ciprofloxacin

Box 61-1
Common Risk Factors for Urinary Tract Malignancy in Patients with Microhematuria

Risk factors for malignancy in patients with microhematuria.

- Male gender
- Age (>35 years)
- Past or current smoking
- Occupational or other exposure to chemicals or dyes (benzenes or aromatic amines)
- Analgesic abuse
- History of gross hematuria
- History of urologic disorder or disease
- History of irritative voiding symptoms
- History of pelvic irradiation
- History of chronic urinary tract infection
- History of exposure to known carcinogenic agents or chemotherapy such as alkylating agents
- History of chronic indwelling foreign body

A 55-year-old woman with T2DM and IgA nephropathy (Cr 1.5 mg/dL (GFR 41), 1 month ago) came to OPD for F/U. Current medications: glipizide 5 mg, enalapril 5 mg. PE: BP 110/70 mmHg

LAB: BUN/Cr 15/1.8 mg/dL (eGFR 33), K 4.8, HbA1c 6.7%,
UA- protein 2+, RBC 5-10/HPF, UPCI 1.4

What should you do to slow CKD progression?

A. Start prednisolone
B. Increase dose of enalapril
C. Decrease dose of enalapril
D. Continue same dose of enalapril
E. Control BS with low protein diet (TP = 0.8 g/kg/day)

A 24-year-old woman with IgAN came to ED due to generalized edema for 3 days. Two years ago, she had same symptom and was well-treated with steroid. PE: BP 140/80 mmHg

LAB: BUN/Cr 12/0.8 mg/dL, alb 1.8 g/dL, chol 248 mg/dL,

UA: protein 4+, WBC 3-5/HPF, RBC 5-10/HPF, UPCI 10

What's your proper management?

A. Prednisolone
B. Prednisolone + Aza
C. Prednisolone + Cyclosporin A
D. Prednisolone + MMF
E. Prednisolone + CY

A 26-year-old man with IgAN had intermittent gross hematuria and proteinuria 2 g/day. He was treated with enalapril 40 mg/day for 6 months.
PE: BP 150/80 mmHg
LAB: BUN/Cr 17/1.2 mg/dL, serum albumin 3 g/dL, UPCI 1.5
What is your next management?

A. Observe, follow-up
B. Add losartan
C. Prednisolone
D. Restrict Na diet
E. Cyclophosphamide

Clinical syndrome of glomerular disease

- ✓ Macroscopic hematuria
- ✓ Asymptomatic microscopic hematuria
- ✓ Nephrotic syndrome
- ✓ Nephritic syndrome
- ✓ Rapidly progressive glomerulonephritis
- ✓ Chronic glomerulonephritis

Nephrotic VS Nephritic

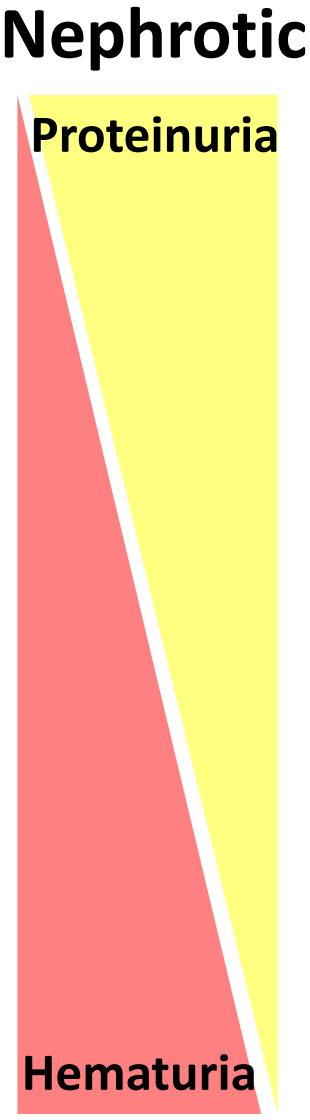
Nephrotic syndrome

Generalized edema
Urine protein > 3.5 g/day
Serum Alb < 3.5 g/dL
Hypercholesterolemia > 250 mg/dL
Lipiduria (oval fat body)

Nephritic syndrome

HT
Hematuria (glomerular)
Oliguria
Declined renal function
Edema

Nephrotic VS Nephritic



MCD
MN
FSGS

Amyloidosis
DN

SLE

MPGN

IgAN

PSGN
ANCA
Anti-GBM

Non-inflammatory injury (Podocytopathy)

- ✓ Glomerular permeability factors
- ✓ Complement membrane attack complex

Podocytopathy, mesangial expansion, sclerosis

Inflammatory injury (Glomerular inflammation)

- ✓ Complement and other humoral mediators
- ✓ Circulating inflammatory cells
- ✓ Activation and/or proliferation of glom cells

Proliferation, crescentic, GBM injury

ANCA: anti-neutrophil cytoplasmic antibody; DN: diabetic nephropathy; FSGS: focal segmental glomerulosclerosis; GBM: glomerular basement membrane; MCD: minimal change disease; MN: membranous nephropathy; MPGN: membranoproliferative GN; PSGN: post-streptococcal GN

Nephrotic VS Nephritic

Differentiation Between Nephrotic Syndrome and Nephritic Syndrome

Typical Features	Nephrotic	Nephritic
Onset	Insidious	Abrupt
Edema	++++	++
Blood pressure	Normal	Raised
Jugular venous pressure	Normal/low	Raised
Proteinuria	++++	++
Hematuria	May/may not occur	+++
Red blood cell casts	Absent	Present
Serum albumin	Low	Normal/slightly reduced

	Nephrotic Features	Nephritic Features
Minimal change disease	++++	–
Membranous nephropathy	++++	+
Focal segmental glomerulosclerosis	+++	++
Fibrillary glomerulonephritis	+++	++
Mesangioproliferative glomerulopathy*	++	++
Membranoproliferative glomerulonephritis†	++	+++
Proliferative glomerulonephritis*	++	+++
Acute diffuse proliferative glomerulonephritis‡	+	++++
Crescentic glomerulonephritis§	+	++++

Johnson, R. Comprehensive Clinical Nephrology, 5th edition. 2015

Classification of glomerular disease

Primary (idiopathic) glomerular disease

Renal limited

- MCD, IgMN, FSGS, MN, MPGN, IgAN

Secondary glomerular disease

Systemic disease

- 2º MCD, 2º FSGS, 2º MN, 2º MPGN, 2º IgAN, DN, LN, amyloid, cryoglobulin, HSP, TMA, vasculitis, APS

Secondary cause of glomerular disease

- ✓ **Infection:** HBV/HCV/HIV, SY, Malaria, Strep, Staph
- ✓ **Autoimmune/Vasculitis:** SLE, RA, AS, MCTD, Small vessel
- ✓ **Malignancy/Paraproteinemia:** Solid tumor, Hematologic dz
- ✓ **Allergy/Toxin:** Bee sting, snake venom
- ✓ **Drugs:** NSAIDs, Pamidronate, Lithium
- ✓ **Metabolic:** Morbid obesity, DM

Genetic

Secondary glomerular disease

Pathology	Cause
MCD	Allergy, NSAIDs **(combined with AIN)**, Li, IFN, Thymoma, Hodgkin's lymphoma, Strongyloidiasis, Bee sting
MN	Gold, D-Penicillamine, NSAIDs, LN Class V, solid organ tumor, HBV > HCV, HIV, SY, P. Falciparum, filariasis
FSGS	Obesity, Black, HIV, IVDU (Heroin), Li, Pamidronate, IFN, ParvovirusB19, VUR, Atheroemboli, single kidney, DM/HT, cyanotic heart disease
MPGN	HCV > HBV, HIV, TMA, IE, solid organ tumor, LN class III/IV, Sjogren, PIGN, Cryoglobulinemia, LCDD
IgAN	Liver cirrhosis, HBV, HIV, RA/AS/Reiter's, IBD, Celiac disease, NHL

Nephrotic VS Nephritic

Nephrotic syndrome

MCD **MN** **FSGS**

DN **Amyloidosis**

Nephritic syndrome

IC
- Classical: LN, Cryoglobulinemia
- Alternative: IRGN, C3GN, IgAN
- Lectin: IgAN

Anti-GBM

Pauci-immune (ANCA +,-)

Nephrotic syndrome

	Onset	Hematuria
MCD	Abrupt (1°), insidious (2°)	+/-
FSGS	Abrupt (1°), insidious (2°)	+++ (> 50%)
MN	Abrupt (2°), insidious (1°)	++ (30-50%)
DN	Insidious	+/- from ruptured microaneurysm
Amyloidosis	Insidious, Age > 50 yr	+/-

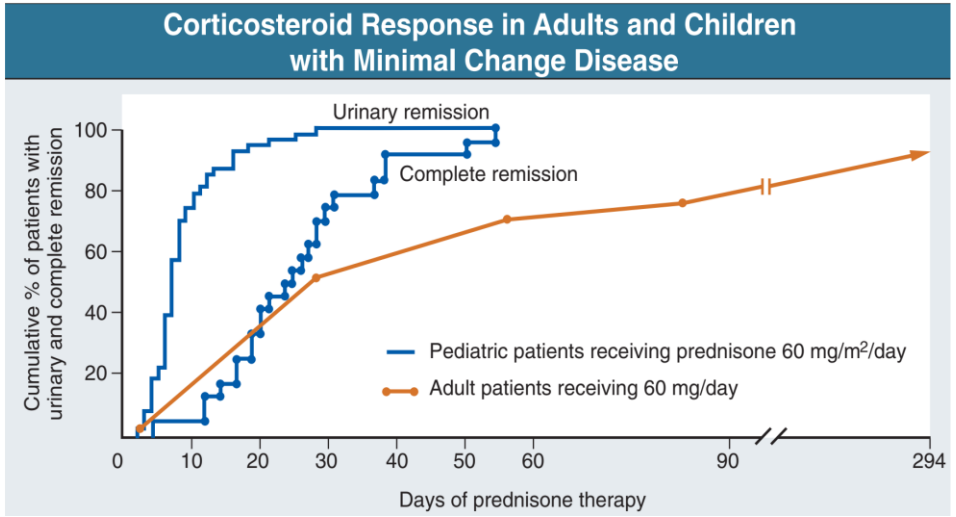
MCD

Bi-modal age

<u>Abrupt onset</u> in 1° (day-week)

<u>Insidious onset</u> in 2° (week-month)

100% NS



FSGS

Age 10-40 yr

<u>Abrupt onset</u> in 1°

<u>Insidious onset</u> in 2°

70-100% NS

50% Micro hematuria

20% HT

25-50% Cr rising

Treatment

Prednisolone 1 MKD upto 80 mg OD or 2 MKD upto 120 mg AD for 4-16 wks then taper off upto 6 mo

(Contraindication: Uncontrolled DM, Psychi, severe osteoporosis)

Frequent relapse, resistant: CY, CNI, MMF, Ritux

Pattern of response to steroid (MCD/FSGS)

- ✓ **CR:** UPCI < 0.3 g/d, stable Cr, Serum Alb > 3.5 g/dL
- ✓ **PR:** UPCI 0.3-3.5 g/d + decrease > 50% baseline
- ✓ **Relapse:** UPCI > 3.5 g/d after CR
- ✓ **Steroid-resistant:** Persist proteinuria (UPCI > 3.5 g/d + < 50% reduction from baseline) with pred 1 MKD > 16 weeks
- ✓ **Steroid-dependent:** Relapse during or within 2 weeks of completing steroid therapy
- ✓ **Frequent relapse:** ≥ 2 relapses in 6 months

CR: complete remission; PR: partial remission

Nephrotic syndrome

	Onset	Hematuria
MCD	Abrupt (1°), insidious (2°)	+/-
FSGS	Abrupt (1°), insidious (2°)	+++ (> 50%)
MN	**Abrupt (2°), insidious (1°)**	**++ (30-50%)**
DN	**Insidious**	**+/-** **from ruptured microaneurysm**
Amyloidosis	Insidious, Age > 50 yr	+/-

Membranous nephropathy

Pathogenesis

AutoAb to podocyte Ag: PLA2R, THSD7A, NELL-1
Planted Ag: HBeAg, tumor, drug, cBSA
Circulating IC: autoimmune disease

Clinical

Age > 40 yr, 2nd m/c in adults
Insidious onset in 1° (wk-mo)
Acute onset in 2°
80% NS, 30-50% microscopic hematuria, 30% Cr rising

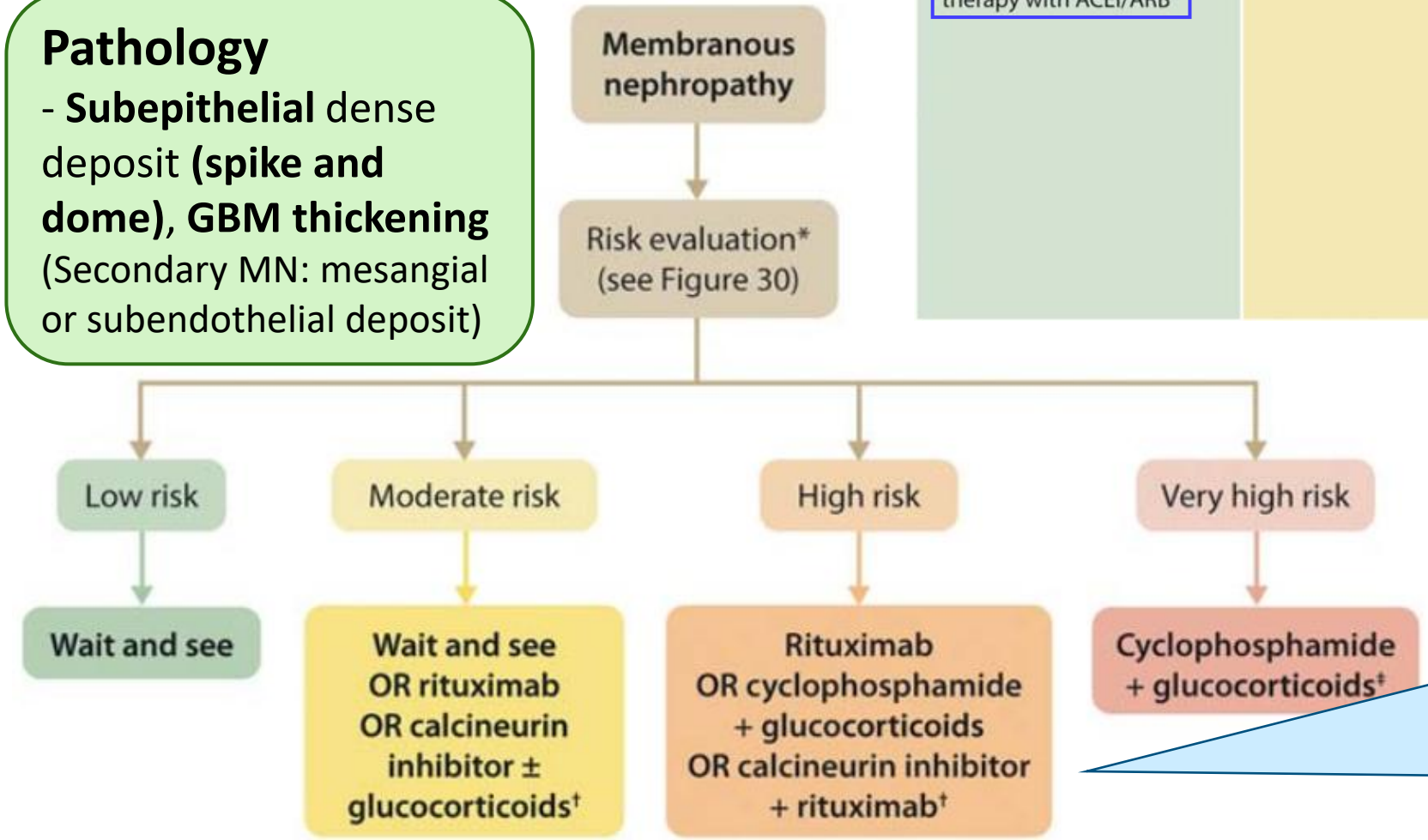
1/3 → Spont improved
1/3 → Stable Cr
1/3 → Progress to ESKD

Secondary

Autoimmune: LN class V > RA, autoimmune thyroid
Infection: HBV > HCV, HIV, SY, malaria, filariasis
Malig: Solid tumor, NHL, CLL
Drug: Gold, penicillamine, NSAIDs

Membranous nephropathy

Pathology
- **Subepithelial** dense deposit **(spike and dome)**, **GBM thickening**
(Secondary MN: mesangial or subendothelial deposit)



Low risk	Moderate risk	High risk	Very high risk
• Normal eGFR, **eGFR > 60** proteinuria <3.5 g/d and serum albumin >30 g/l OR • Normal eGFR, proteinuria <3.5 g/d or a decrease >50% after 6 months of conservative therapy with ACEi/ARB	• Normal eGFR, proteinuria >3.5 g/d and no decrease >50% after 6 months of conservative therapy with ACEi/ARB AND • Not fulfilling high-risk criteria	• eGFR <60 ml/min/1.73 m²* and/or proteinuria >8 g/d for >6 months OR • Normal eGFR, proteinuria >3.5 g/d and no decrease >50% after 6 months of conservative therapy with ACEi/ARB AND at least one of the following: • Serum albumin <25 g/l† • PLA2Rab >50 RU/ml‡ • Urinary α_1-microglobulin >40 µg/min • Urinary IgG >1 µg/min • Urinary β_2-microglobulin >250 mg/d • Selectivity index >0.20§	• Life-threatening nephrotic syndrome OR • Rapid deterioration of kidney function not otherwise explained **AKI** **Infection** **Thromboembolism**

Modified Ponticelli
- POCY at month 2,4,6
- IVMP 1 g/d x 3 d then pred 0.5 MKD x 27 days at month 1,3,5

CNI 6-12 months
Rituximab 2-4 weeks

Less likely to be DKD

1) Absence of diabetic retinopathy
2) Rapidly increasing proteinuria or nephrotic syndrome
3) Low or rapidly decreasing GFR
4) Refractory hypertension
5) Presence of active urinary sediment
6) Signs or symptoms of other systemic disease
7) > 30% reduction in GFR within 2-3 months after initiation of ACEI or ARB

Diabetic retinopathy
- DM type I: DR 90-95% (PDR 60%)
- DM type II: DR 56 %

DDx
- Ruptured microaneurysm
- Pre-existing disease: TBM dz
- Other glomerular disease

NKF KDOQI Guidelines for Diabetes and Chronic Kidney Disease 2007.

Nephrotic syndrome

	Onset	Hematuria
MCD	Abrupt (1°), insidious (2°)	+/-
FSGS	Abrupt (1°), insidious (2°)	+++ (> 50%)
MN	Abrupt (2°), insidious (1°)	++ (30-50%)
DN	Insidious	+/- from ruptured microaneurysm
Amyloidosis	**Insidious, Age > 50 yr MM, hematologic malignancy**	**+/-**

MM and The Kidney

Renal disease	Manifestation
Myeloma cast nephropathy (40-63%) (LC cast nephropathy or Myeloma Kidney) Light chain + Uromodulin (THP) deposit at distal tubule ไตวายมากกก albuminuria น้อย **LM:** Eosinophilic fractured cast (pale stain PAS) + giant cell reaction, interstitial inflammation, flat tubule **IF:** Kappa or Lambda restriction	- AKI 50%, NS 10% - **<u>Upro dipstick ≠ Upro 24 hr</u> (overflow)** - HyperCa in renal failure + hyperPO_4 - Unexplained progressive AKD/CKD - Disproportion of anemia and renal failure - **Bone pain, osteolytic lesion <u>BUT</u> ALP ↔** - Low anion gap (IgG myeloma) - SFLC (K:λ) > 500 mg/L
Light chain proximal tubulopathy (40%)	- pRTA ± Fanconi syndrome ± AKI/CKD

MM and The Kidney

Renal disease	Manifestation
Myeloma cast nephropathy (40-63%) (LC cast nephropathy or Myeloma Kidney) Light chain + Uromodulin (THP) deposit at distal tubule ไตวายมากกก albuminuria น้อย **LM:** Eosinophilic fractured cast (pale stain PAS) + giant cell reaction, interstitial inflammation, flat tubule **IF:** Kappa or Lambda restriction	- AKI 50%, NS 10% - **Upro dipstick ≠ Upro 24 hr (overflow)** - HyperCa in renal failure + hyperPO_4 - Unexplained progressive AKD/CKD - Disproportion of anemia and renal failure - **Bone pain, osteolytic lesion BUT ALP ↔** - Low anion gap (IgG myeloma) - SFLC (K:λ) > 500 mg/L
Light chain proximal tubulopathy (40%)	- pRTA ± Fanconi syndrome ± AKI/CKD
Amyloidosis (7-30%) AL, AH type LC (94%; lambda:kappa=3:1), HC ไตไม่ค่อยวาย Proteinuria เยอะมากกก **Pathology:** apple-green birefringent by congo red	- **NS 60-70%**, AKI 3% - **Extra-renal:** fatigue, wt loss, purpura, hepatomegaly, macroglossia, shoulder pad sign, autonomic neuropathy, HFpEF (restrictive cardiomyopathy)
Monoclonal Ig deposition disease (MIDD) (20%) (kappa 75%) LCDD 70%, HCDD 20%, LHCDD 10%	- **AKI 56%, (CKD 44%)**, GN, NS 20-40% - Proteinuria 1.8-2.4 g/day - **Extra-renal:** cardiomegaly, hepatomegaly
Cryoglobulinemia (< 1%)	- AKI 20-50%, NS20 %

Nephrotic syndrome

****Combined NS + Nephritic****

1. IgAN c MCD
2. MPGN (LN, Cryo, PSGN)
3. FSGS
4. MIDD

	Onset	Hematuria
MCD	Abrupt (1°), insidious (2°)	+/-
FSGS	Abrupt (1°), insidious (2°)	+++ (> 50%)
MN	Abrupt (2°), insidious (1°)	++ (30-50%)
DN	Insidious	+/- from ruptured microaneurysm
Amyloidosis	Insidious, Age > 50 yr MM, hematologic malignancy	+/-

A 20-year-old man had generalized edema for 1 week.

BP 120/80 mmHg, BUN/Cr 25/0.8 mg/dL, Alb 2 g/dL, Chol 570 mg/dL, UA: pro 4+, RBC 1-2/HPF, WBC 0-1/HPF, UPCl 8.

He had been treated with prednisolone 1 MKD.

At 4 weeks F/U, His leg edema slightly decreases and urinalysis still shows protein 4+.

Which is the appropriate management at this step?

A. Continue prednisolone at the same dose
B. Increase dose of prednisolone to 1.5 MKD
C. Kidney biopsy
D. Add cyclophosphamide
E. Add cyclosporin A

A 50-year-old man came with frothy urine for 2 months.

BP 120/80 mmHg, no edema. LAB: BUN/Cr 12/0.8 mg/dL,

UA: pro 2+, WBC 0-1, RBC 2-3/HPF, UPCI 2.5

Kidney biopsy: Membranous nephropathy

What's your proper management?

A. Prednisolone
B. Prednisolone + CY
C. Prednisolone + MMF
D. Enalapril
E. Observe and close follow up

A 59-year-old woman developed progressive generalized edema for 2 weeks. She had a history of chronic smoking for 40 years and chronic cough for 6 months. PE: generalized edema with clubbing fingers.

LAB: UA – pro 4+, RBC 1-2, WBC 0-1/HPF, Cr 0.9 mg/dL.

CXR: lung nodule 2 cm in the right middle lung field with hilar adenopathy

What is the **MOST** likely renal pathology in this patient?

A. Minimal change lesion
B. Membranous nephropathy
C. Focal segmental glomerulosclerosis
D. IgM nephropathy
E. Amyloidosis

A 55-year-old man came with fatigue, low back pain for 2 months.

BP 150/90 mmHg. LAB: CBC – Hb 9 g/dL (MCV 85), WBC 9600,

BUN/Cr 40/3.8 mg/dL, Ca 11, uric 10 mg/dL, Alb 3.8, Glob 6.2 g/dL

UA: pro 1+, WBC 0-1, RBC 3-5/HPF, 24hr-Upro 2.9 g.

U/S KUB: mild renal parenchymatous change

What's the most likely cause of AKI?

A. Acute uric acid nephropathy
B. Myeloma cast nephropathy
C. Renal amyloidosis
D. Hypercalcemia
E. Light chain deposition disease

A 65-year-old woman presented with weight loss, dizziness when standing. PE: BP 100/60 mmHg, moderately pale, pitting edema 3+ both legs.

LAB: UA- pro 4+, WBC 2-3, RBC 0-1/HPF, Hct 20%, WBC 5,400, BUN/Cr 26/1.3 mg/dL, alb 2.4, glob 5.5 g/dL, UPCI 8

What's the most likely cause of renal abnormalities?

A. Lupus nephritis

B. Membranous nephropathy

C. Focal segmental glomerulosclerosis

D. Renal amyloidosis

E. Myeloma cast nephropathy

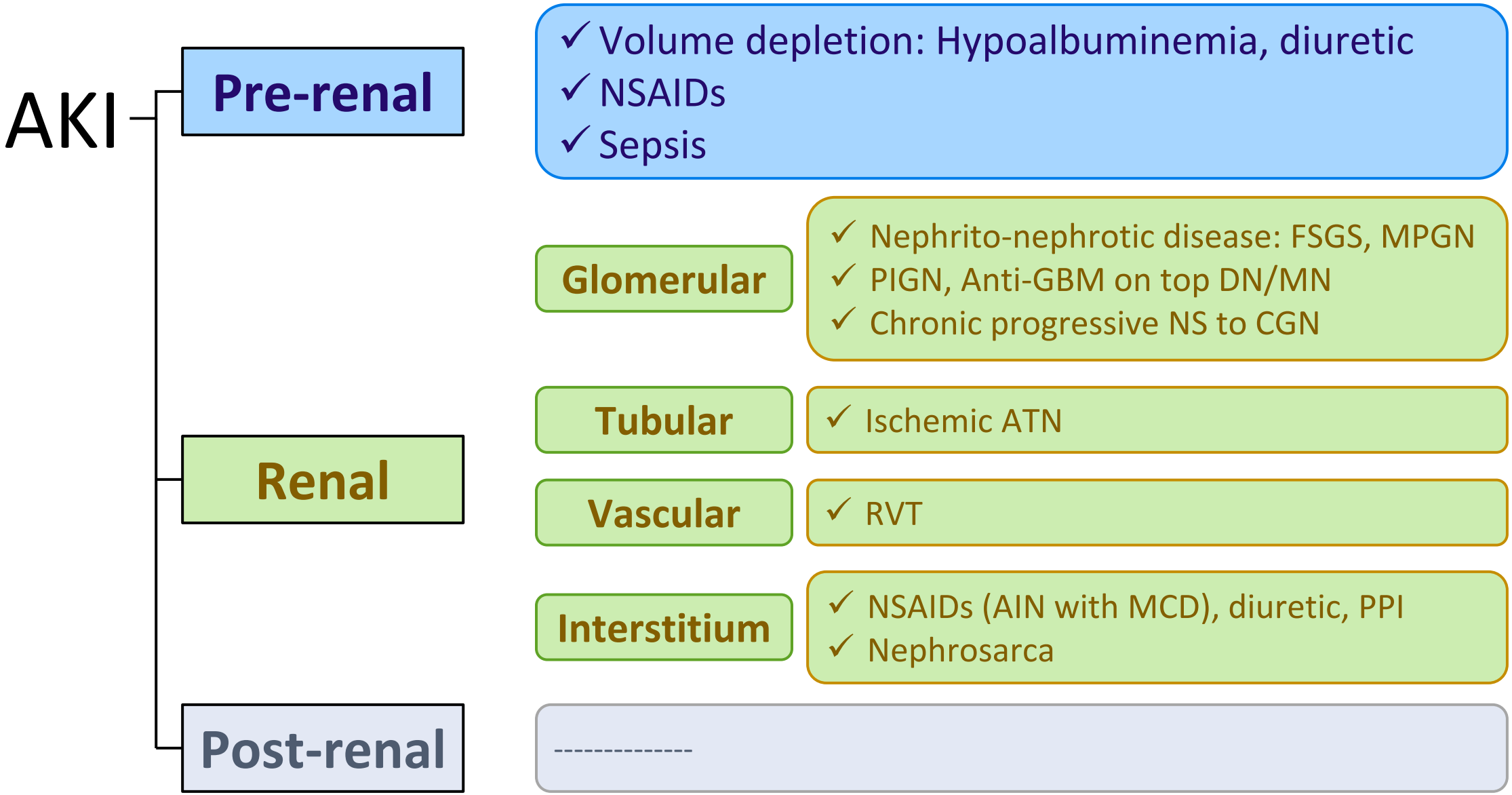
Complications in nephrotic syndrome

AKI

Hypercoagulable state

Hyperlipidemia

Complications in nephrotic syndrome

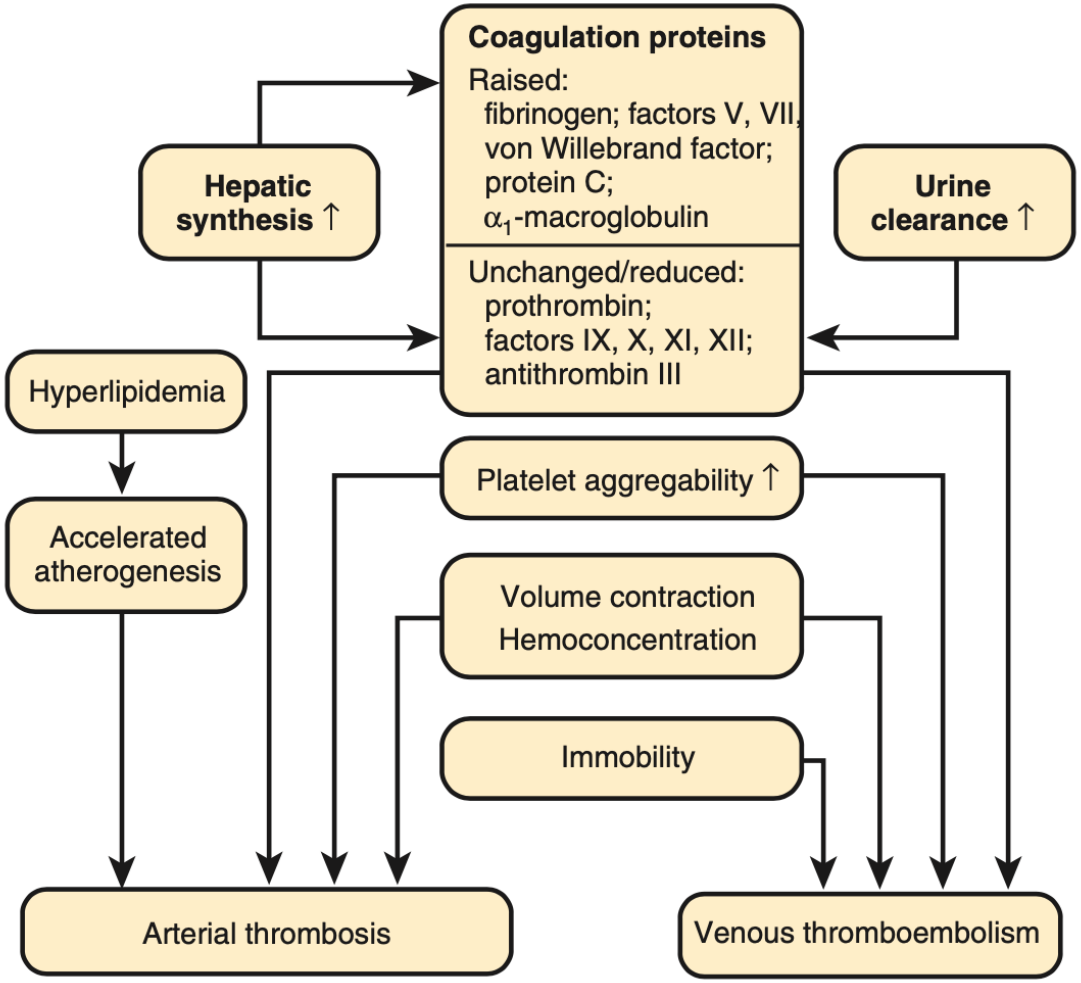


Complications in nephrotic syndrome

AKI

Hypercoagulable state

Hyperlipidemia



Johnson, R. Comprehensive Clinical Nephrology, 5th edition. 2015

Renal vein thrombosis

Cause

- ✓ Loss of anticoagulation protein: NS, SLE
- ✓ Tumor thrombus: RCC, lymphoma
- ✓ Renal sepsis (thrombophlebitis)

Cardinal features

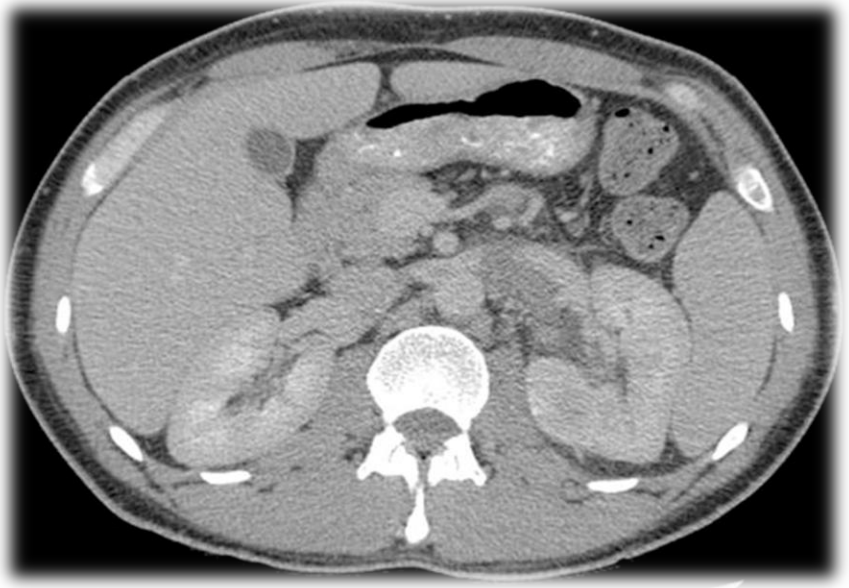
- ✓ **Triad:** flank pain + hematuria + renal failure

Complication: PE, renal atrophy, renal papillary necrosis

Screening: doppler U/S

Gold standard Ix for dx: CT venography

Treatment: anticoagulant and underlying disease



Risk of hypercoagulable state

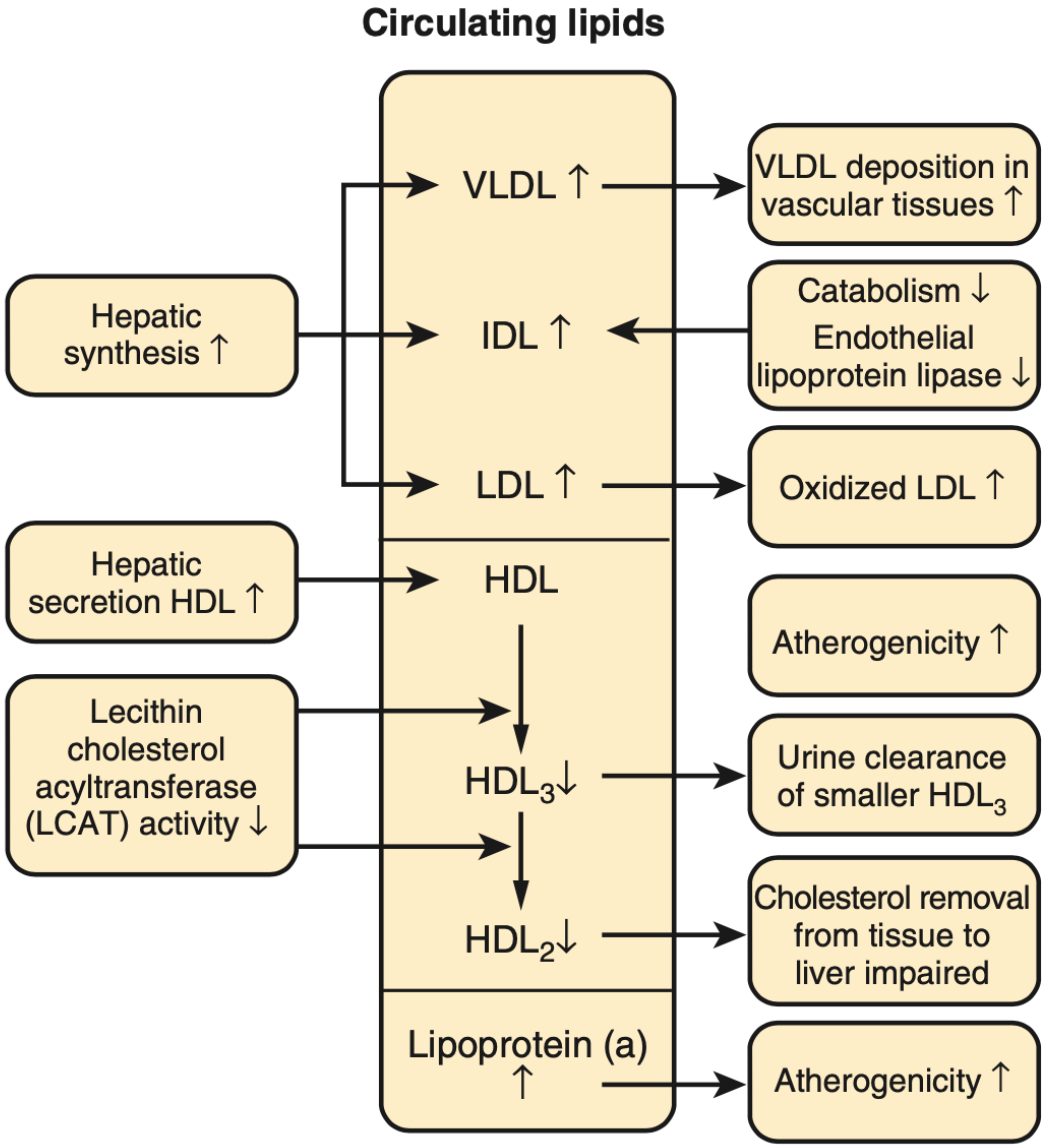
- ✓ Serum Alb < 2-2.5 g/dL
- \+ BISCUIT/Family Hx

Complications in nephrotic syndrome

AKI

Hypercoagulable state

Hyperlipidemia



Johnson, R. Comprehensive Clinical Nephrology, 5th edition. 2015

A 56-year-old woman presented with flank pain and oliguria for 2 days. She was diagnosed of advanced CA cervix requiring CMT for 6 months. PE: BP 140/80 mmHg, edema 2+.
LAB: BUN/Cr 74/5 mg/dL, UA- protein 2+, numerous RBC.
Non-contrast CT KUB: no evidence of renal stone or hydronephrosis
What is the MOST appropriate next step management?

A. Anti-PLA2R antibody
B. ANCA titer
C. Kidney biopsy
D. Doppler renal ultrasound
E. MRI abdomen

A 76-year-old woman with history of lumbar fracture for 2 months presented with foamy urine for 2 weeks. Two months ago, she took counter medication for relieve back pain.

PE: BP 130/90 mmHg, mild pale, pitting edema 2+

LAB: UA- pro 4+, WBC 15-20, RBC 0-1/HPF, UPCR 6 g/day, Hct 30%, BUN/Cr 66/3.2 mg/dL, alb 2.9, glob 4.5 g/dL.

What's the most likely cause of renal abnormalities?

A. Disseminated TB

B. Renal amyloidosis

C. Drug-induced interstitial nephritis

D. Acute tubular necrosis

E. Myeloma cast nephropathy

Approach to glomerular disease

Nephrotic syndrome

- Primary
  - MCD/IgM
  - MN
  - FSGS
- Secondary
  - DN
  - Amyloid
  - LN

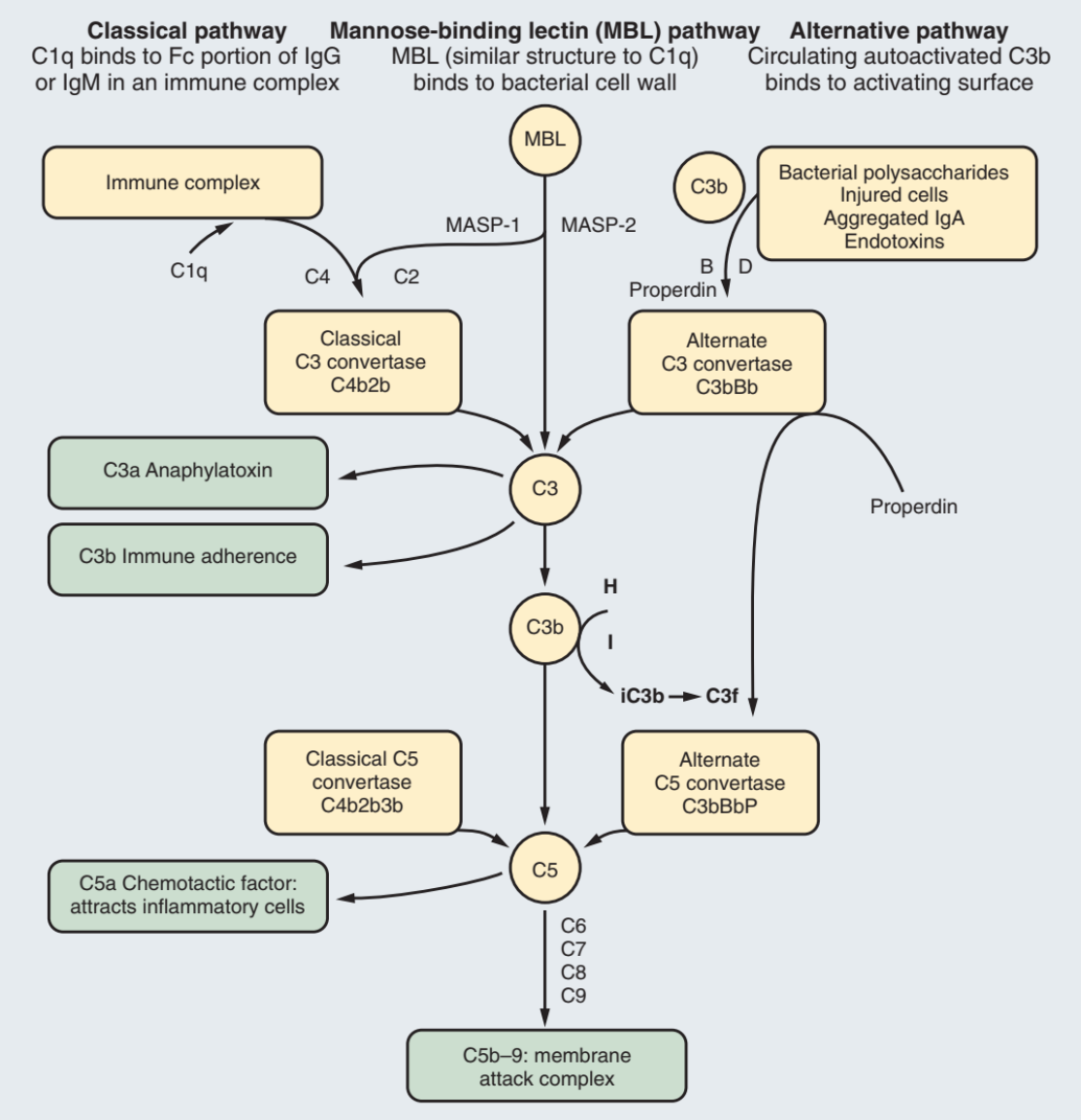
Onset & Hematuria

Nephritic syndrome

complement level

- Low
  - C3
    - **PIGN**
    - Shunt nephritis
    - Endocarditis
    - MPGN II
  - C3,C4
    - **Cryoglob**
    - **LN**
    - MPGN I
- Normal
  - **IgAN**
  - **ANCA**
  - **Anti-GBM**
  - PAN
  - TMA
  - Alport's
  - Monoclonal gammopathy

Glomerular disease



MCD MN FSGS

DN Deposition dz

IC

Classical: LN, Cryoglobulinemia

Alternative: PIGN, C3GN, IgAN

Lectin: IgAN

Anti-GBM

Pauci-immune (ANCA +,-)

Nephritic syndrome

Immune complex

Classical

LN

Age 15-45 yr
Class III/IV: Nephritis, Class V: NS
ANA 90-95%, dsDNA 75%, Sm 25-30%

Cryoglob

Associated with **HCV** > HBV, IE, CNT, CLL, lymphoma, solid organ tumor

PIGN

Alternative

IgAN

C3 glomerulopathy

Pauci-immune

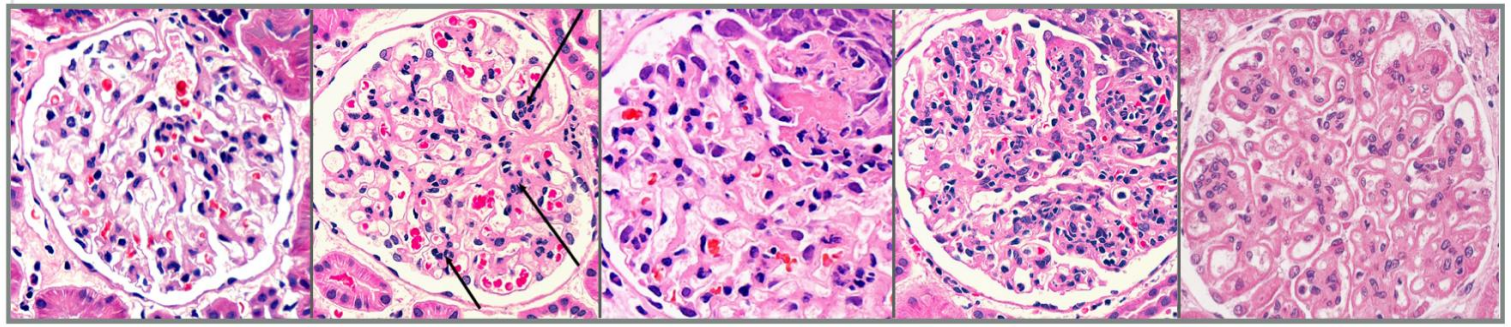
ANCA positive or negative

Anti-GBM

or Goodpasture syndrome

ISN/RPS Classification 2004

Class	Pathology	Clinical
I	Minimal mesangial	Minimal renal S&S, normal SCr
II	Mesangial proliferative	
III	Focal proliferative (< 50% of glomeruli)	HT, active sediment, nephrotic UPCI 25-33%, ↑Cr 25%
IV	Diffuse proliferative (≥ 50% of glomeruli)	HT, active sediment, nephrotic UPCI 50%, ↑Cr > 25%, low C3/C4, dsDNA Ab
V	Membranous	Nephrotic, UPCI 60%, ↑Cr < 25%, uncommon HT, normal-low C3/C4
VI	Sclerosis	Chronic ↑Cr

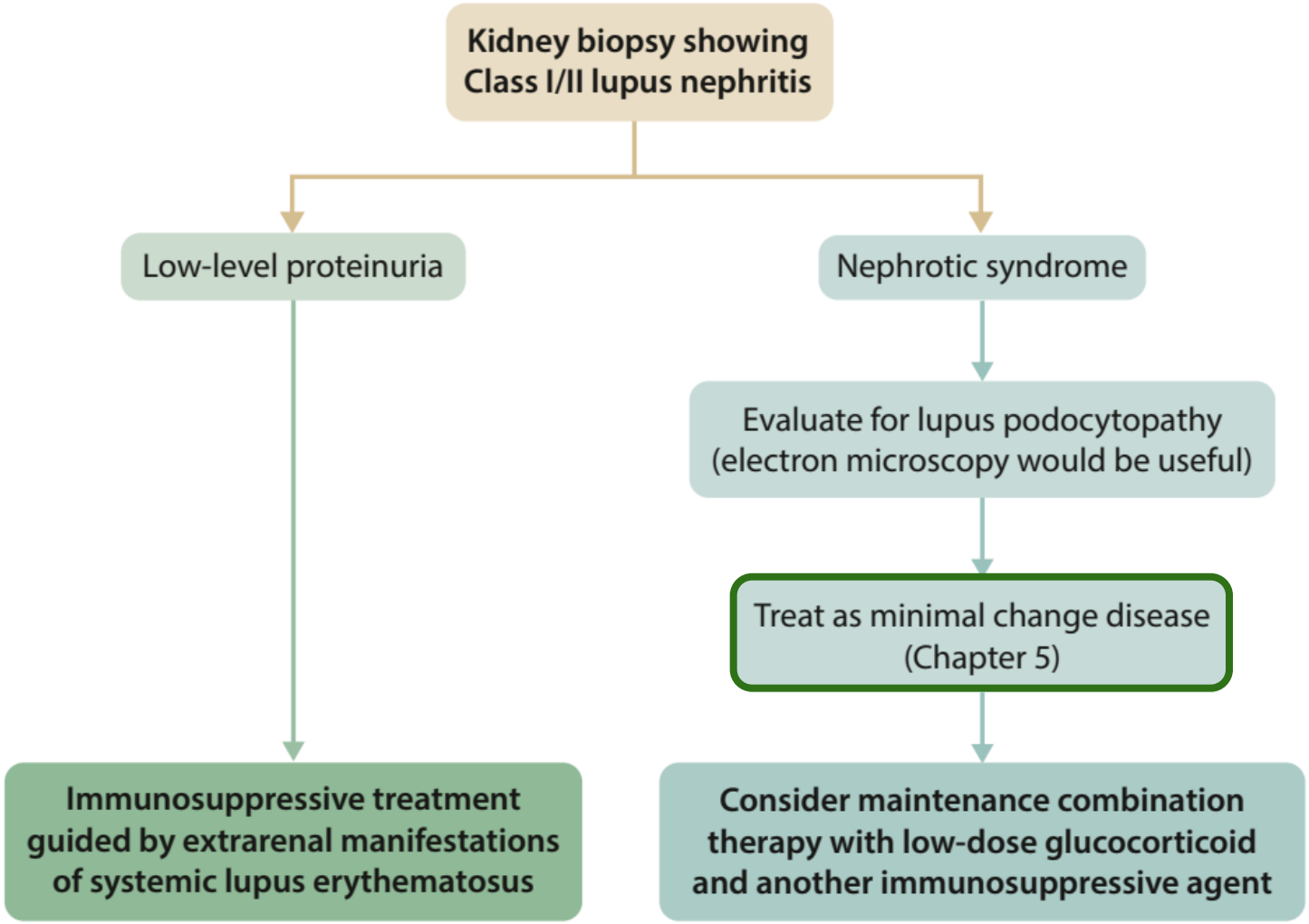


LN I LN II LN III LN IV LN V

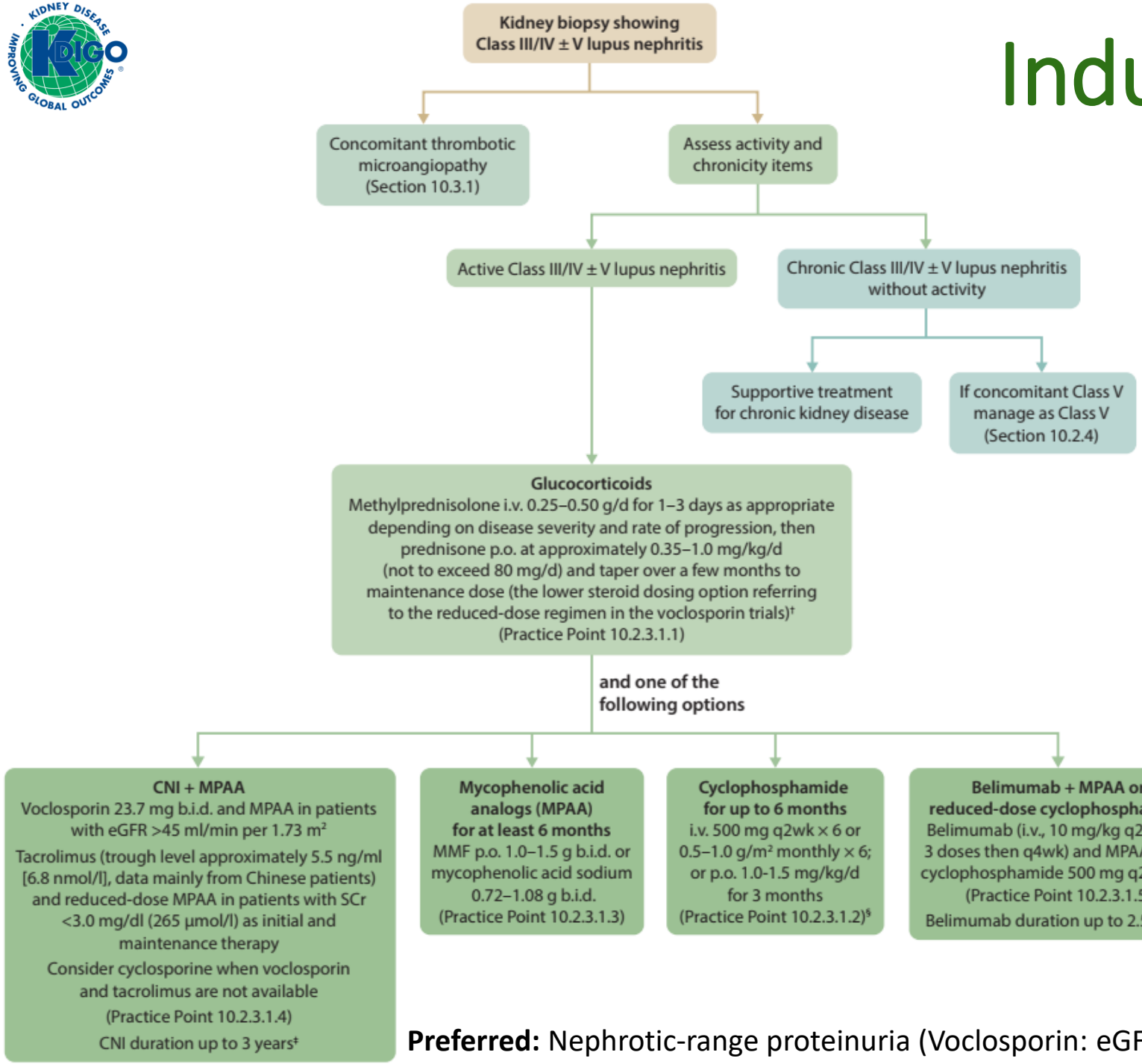
IF: Full house

IgM, IgG, IgA, C1q, C3

Treatment of LN Class I/II



Induction Rx of LN III/IV



Recommendation 10.2.3.1.1: We recommend that patients with active Class III or IV LN, with or without a membranous component, be treated initially with glucocorticoids plus any *one* of the following:

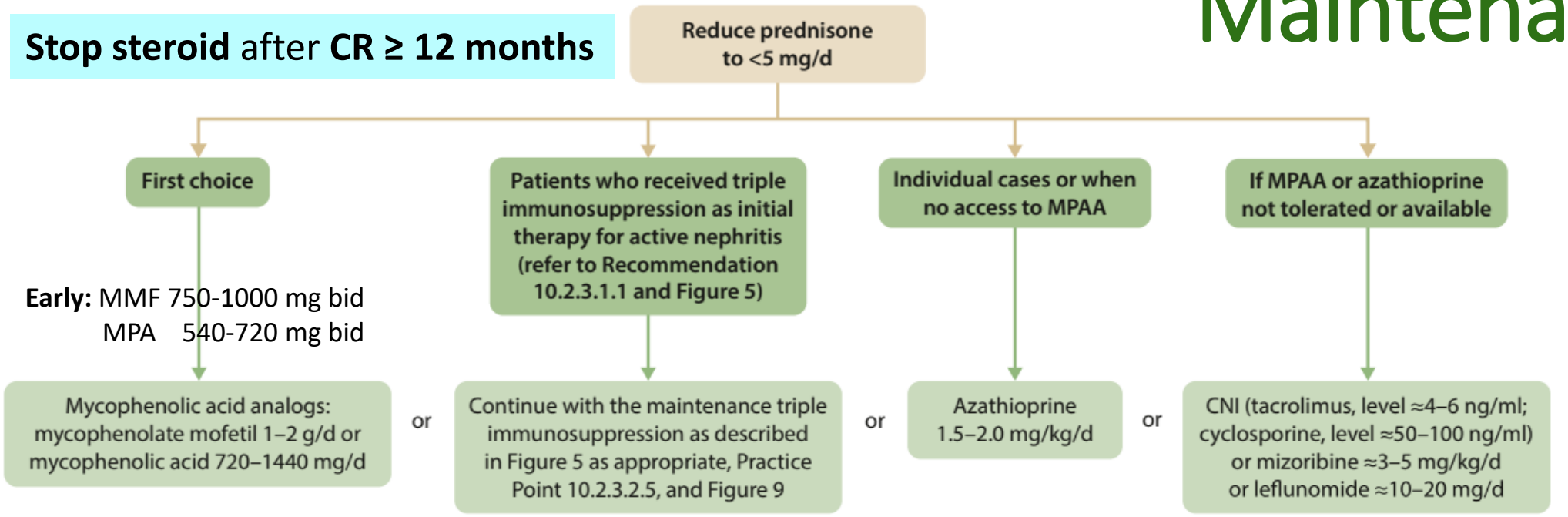
i. **mycophenolic acid analogs (MPAAs) *(1B)*; or**
ii. **low-dose intravenous cyclophosphamide *(1B)*; or**
iii. **belimumab and either MPAA or low-dose intravenous cyclophosphamide *(1B)*; or**
iv. **MPAA and a calcineurin inhibitor (CNI) when kidney function is not severely impaired (i.e., estimated glomerular filtration rate [eGFR] ≤45 ml/min per 1.73 m^2) *(1B)*.**

Preferred:
UPCR < 3, repeated renal flare, eGFR > 30

Preferred: Nephrotic-range proteinuria (Voclosporin: eGFR > 45, Tacrolimus: Cr < 3)

Maintenance Rx of LN III/IV

Stop steroid after **CR ≥ 12 months**

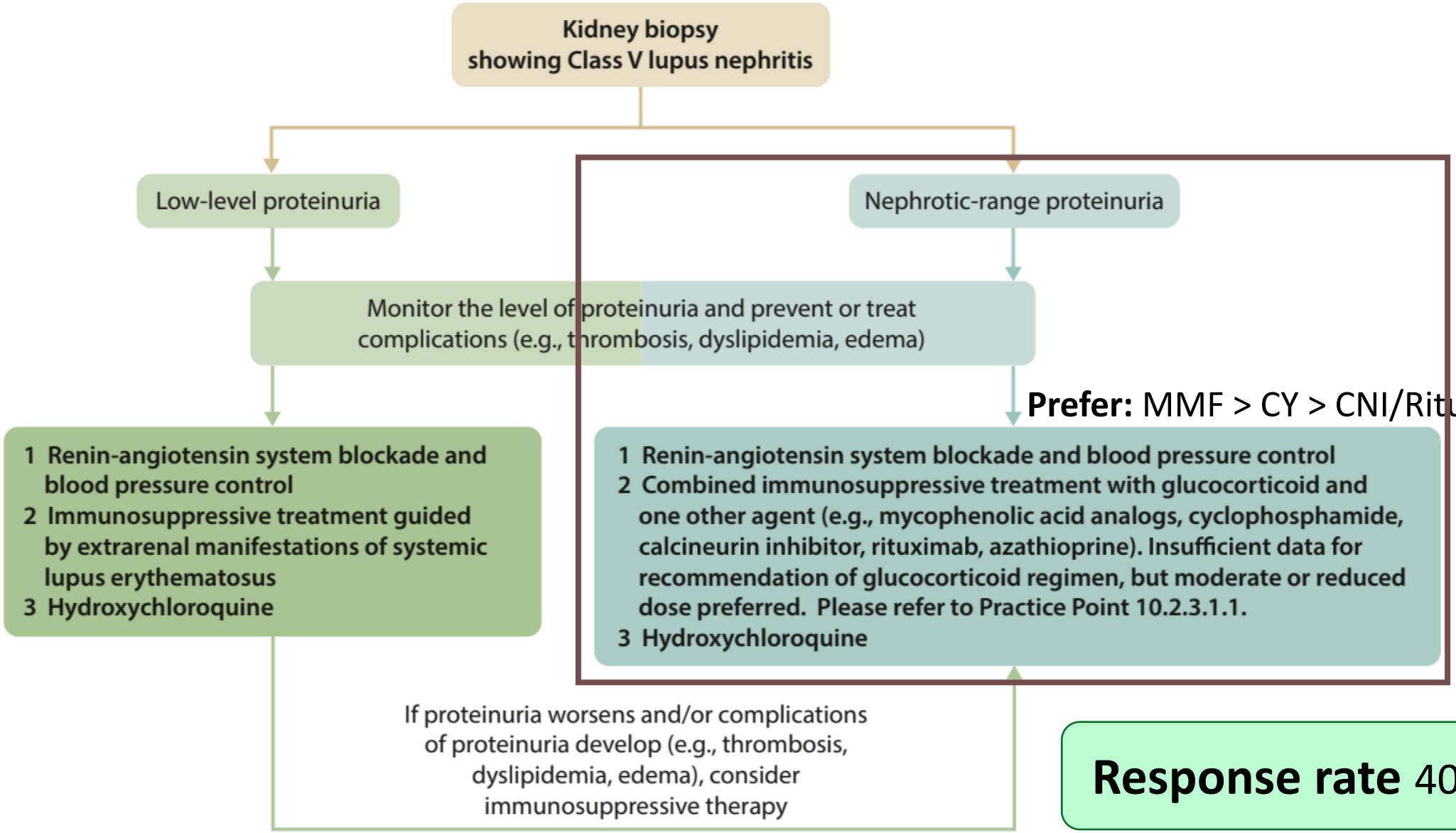


Maintenance immuno-suppressive regimens	Low-dose glucocorticoids AND					
	Mycophenolic acid analogs	Azathioprine	Belimumab and mycophenolic acid analogs or azathioprine	CNI and mycophenolic acid analogs	CNI (such as voclosporin, tacrolimus or cyclosporine)	Mizoribine
Comments	Preferred treatment based on high-certainty evidence; lower flare rate than azathioprine maintenance	Low medication cost; safe in pregnancy	Efficacy and safety of belimumab demonstrated in BLISS-LN (104-wk) and open-label extension trials (28-wk) [Practice Point 10.2.3.2.5]	Efficacy and safety of voclosporin demonstrated in AURORA 1 (52-wk) and AURORA 2 continuation trials (2-yr); efficacy and safety of tacrolimus demonstrated in 'Multitarget Therapy' trial in Chinese patients in which tacrolimus and reduced-dose MPAA were given for 24 months [Practice Point 10.2.3.2.5]	Tacrolimus and cyclosporine safe in pregnancy; insufficient pregnancy data on voclosporin	Experience mostly in Japanese patients

Duration

Induction + Maintenance should be **≥ 36 months**

Treatment of LN Class V



Prefer: MMF > CY > CNI/Ritux/Aza

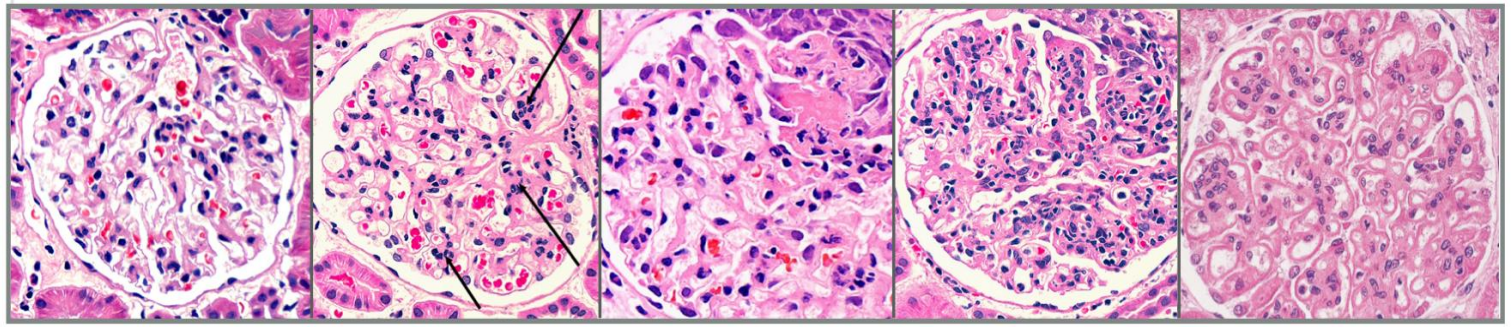
Response rate 40-60%

Toxic dosage of CY

- ✓ **> 25 g:** Hemorrhagic cystitis
- ✓ **> 36 g:** CA bladder
- ✓ **> 80 g:** Myelofibrosis
- ✓ **> 360 mg/kg:** solid organ, hematologic malignancy
- ✓ **Ovarian failure** depend on age
  (20 g: 20 yr; 9 g: 30 yr; 5 g: 40 yr)

Relapse: same initial Rx
Refractory: Switch to MMF/CY or CNI

IV	Diffuse proliferative (≥ 50% of glomeruli)	HT, active sediment, nephrotic UPCI 50%, ↑Cr > 25%, low C3/C4, dsDNA Ab
V	Membranous	Nephrotic, UPCI 60%, ↑Cr < 25%, uncommon HT, normal-low C3/C4
VI	Sclerosis	Chronic ↑Cr



LN I LN II LN III LN IV LN V

Class I, II

Non-NS → Extra-renal
NS → Pred 1 MKD/CNI as MCD

Class III, IV

Induction → Maintenance
(IVCY, MMF, CNI, Belimumab)

Class V

Non-NS → RAASi + Extra-renal
NS → ISD + Pred 0.5 MKD

Class VI

Supportive Rx

Nephritic syndrome

Immune complex

Classical

LN

Age 15-45 yr
Class III/IV: Nephritis, Class V: NS
ANA 90-95%, dsDNA 75%, Sm 25-30%

Cryoglob

Associated with **HCV** > HBV, IE, CNT, CLL, lymphoma, solid organ tumor

PIGN

Alternative

IgAN

C3 glomerulopathy

Pauci-immune

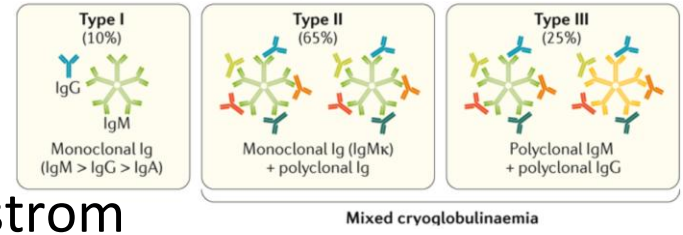
ANCA positive or negative

Anti-GBM

or Goodpasture syndrome

Cryoglobulin: protein that precipitated from serum or plasma on cold exposure

Cryoglobulinemia



Type

- ✓ **Type I (Monoclonal IgM/IgG, 10-15%):** MM, CLL, Waldenstrom
- ✓ **Type II (Monoclonal IgM + Polyclonal IgG, 50-60%):** HCV > HBV, Sjogren, B-lymphoma, solid organ tumor
- ✓ **Type III (Polyclonal IgM and IgG, 25-30%):** Infect (IE, HCV,HBV,HIV), SLE, RA

Clinical

Melzer's triad (purpura, arthralgia, weakness) 25-30%

- Palpable purpura (75-95%), RP (20-30%), distal ulcer/necrosis (10-25%), migratory arthralgia (40-80%), peripheral neuropathy (20-75%), Nephritonephrotic feature (25-50%)
- Type I: hyperviscosity, thrombosis, Type II/III: asymptom (not assoc with cold)

LAB

- ✓ Cryoglobulin > 0.05 g/L, Cryocrit > 1-2 %
- ✓ Rheumatoid factor positive, Low C3 (50%), **C4 (75%)**
- ✓ Abnormal LFT with hepatosplenomegaly (5-70%)

Treat

For HCV + Mixed Cryoglob + NS (or renal fail or acute flare cryoglob)

- Anti-viral + IVMP + Plasma exchange (or Rituximab or POCY)

Nephritic syndrome

Immune complex

Classical

LN

Age 15-45 yr
Class III/IV: Nephritis, Class V: NS
ANA 90-95%, dsDNA 75%, Sm 25-30%

Cryoglob

Associated with **HCV** > HBV, IE, CNT, CLL, lymphoma, solid organ tumor

Alternative

PIGN

Within 1-3 wks after URI/GI infection

IgAN

Within 3-5 days after URI/GI infection
May be still fever
Recurrent episode

C3 glomerulopathy

Pauci-immune

ANCA positive or negative

Anti-GBM

or Goodpasture syndrome

Post-infectious GN

✓ Pathogenesis

- Strep pyrogenic exotoxin-B (SpeB)
- Nephritis-associated strep plasmin receptor (NaPlr)

✓ Clinical

- Pharyngitis 7-21 d, Skin infect 14-30 d
- Hematuria 100% (70% microscopic, 30-50% gross hematuria)
- **Abrupt onset of edema** (nephrotic-range 5-20%), HT 50-90%
- Oliguria (50%), Cr >2 (20%, 60% in age > 55 yr), RPGN < 5%

Resolution

- ✓ HT/Edema: 2wk
- ✓ Low C3: 6-8 wk
- ✓ Hematuria: 6-12 mo
- ✓ Proteinuria: years

✓ LAB

- Low C3 (> 90%), normal or mild low C4, RTA type IV (renin deficiency)
- ASO in URI (30%), Anti-DNAse B in skin infect (70%), RF 30-40%, MPO-ANCA 10%
- Patho: MPGN (Lobular pattern), IF (Starry sky, Garland, Mesangial)

✓ Treatment

- **BP control:** Diuretics
- **UPCI > 1 g/day x > 6 mo:** ACEI/ARB
- **Concomittant with Strep infect:** Penicillin, Erythromycin for prevent spread nephritogenic Ag to others
- **Crescentic RPGN:** IVMP 0.5-1 g/day then prednisolone 0.5 MKD tape in 2-6 months

A 24-year-old woman with LN III, being treated with prednisolone 10 mg and MMF 2 g/day, came to OPD for follow-up schedule. She was well and no abnormal sign on physical examination.

From her BP diary, the range of BP were 130-140/80-90 mmHg.
Her 24-hour urine protein was 1.2 g/day and urinary analysis showed no active sediment.

Which of the followings is the MOST appropriate management?

A. Add anti-hypertensive drug

B. Increased prednisolone to 30 mg/day

C. Increased MMF to 3 gm/day

D. Switch treatment from MMF to cyclophosphamide

E. Observed clinical without change medication

A 23-year-old woman with LN, presents with acute left flank pain and elevated SCr from 1.0 to 2.1 mg/dL within 2 weeks. BP is 120/70 mmHg. LAB: UA- protein 4+, 5-10 dysmorphic RBC/HPF.

6 months ago, she was started on monthly IVCY.

3 months later, her urinalysis showed protein 1+. She received the sixth cycle of cyclophosphamide for 4 weeks ago.

Current medications: prednisolone 10 mg, hydroxychloroquine 200 mg and enalapril 10 mg, MMF 2 g

What is the **MOST** appropriate investigation?

A. Renal biopsy
B. Renal angiogram
C. Renal doppler ultrasound
D. Intravenous pyelography
E. CT abdomen with contrast

LN with TMA

PLASMIC SCORE

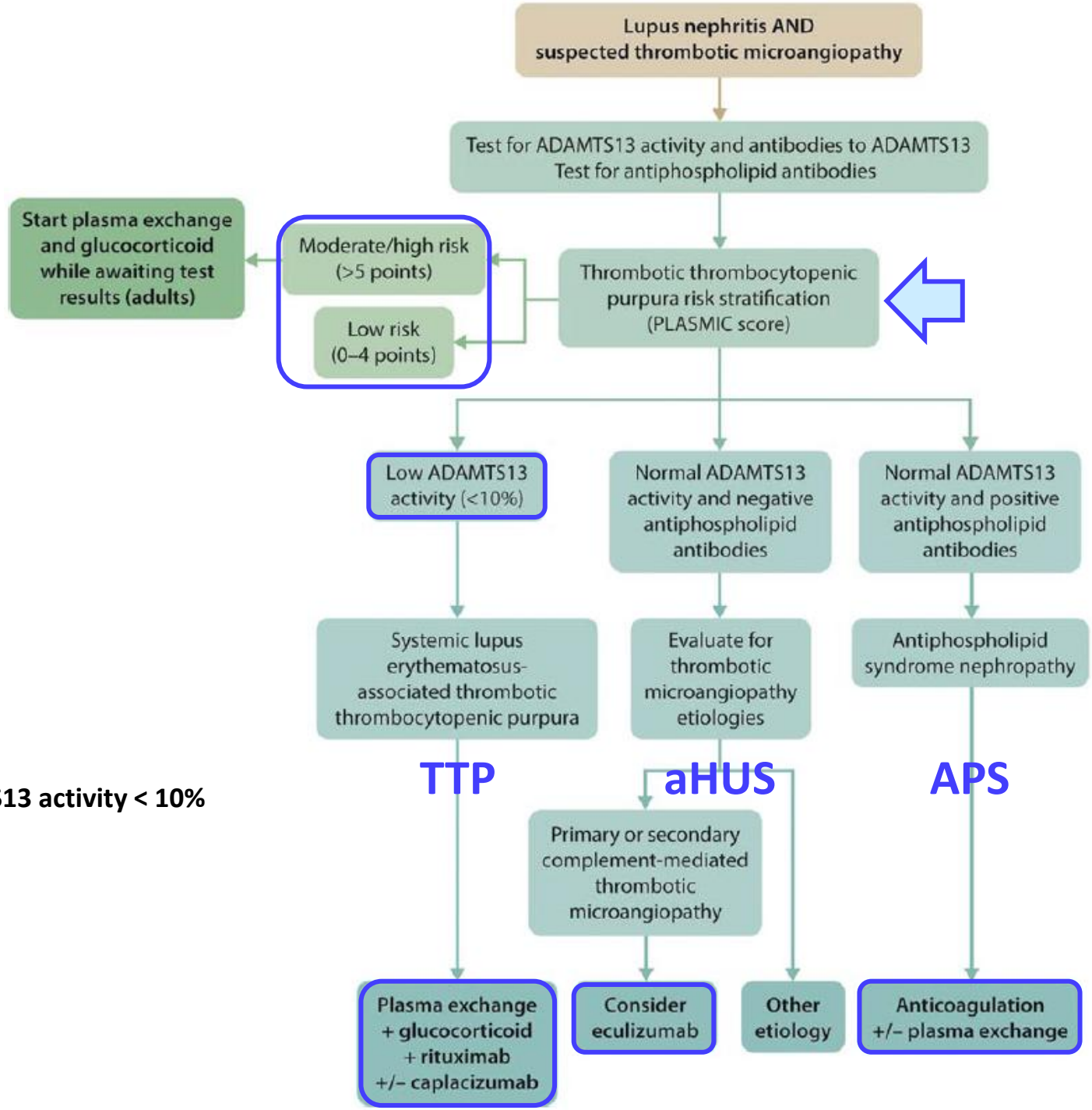
Points	
Platelet count <30 × 10^9 per L	1
Haemolysis variable *	1
No active cancer	1
No history of solid-organ or stem-cell transplant	1
MCV <90 fL	1
INR <1·5	1
Creatinine <2·0 mg/dL	1

Score 0–4: low risk
Score 5: intermediate risk
Score 6 or 7: high risk.

Predictive of ADAMTS13 activity < 10%

*Hemolysis variable: Retic count > 2.5% or Haptoglobin or indirect bilirubin > 2 mg/dL

Sen 90%, Spec 92%, PPV 72%, NPV 98%



Lancet Haematol. 2017 Apr;4(4):e157-164.

An 18-year-old man came with edema and oliguria for 1 week. 10 days ago, he had URI symptom and improved with amoxicillin for 5 days. PE: BP 150/100 mmHg, puffy eyelid, pitting edema 1+.

LAB: Cr 1.4 mg/dL, UA: protein 1+, WBC 2-5, RBC 15-20/HPF with dysmorphic RBC

What is the most proper management?

1. Furosemide
2. Enalapril
3. Prednisolone
4. MMF
5. Observe

A 35-year-old man with HCV infection presented with generalized edema and decreased urine output for 10 days. He had intermittent headache without neuro deficit.

PE: BP 150/90 mmHg, pitting edema 2+

LAB: BUN/Cr 40/2.1 mg/dL, low C3, normal C4, UA - protein 3+, RBC 20-30/HPF,

ASO titer 800 IU/mL, UPCI 4 g/day

He did not undergo kidney biopsy. He was treated with RAAS blocker.

After 8 weeks, he came to F/U and he still had UPCI 3 g/day, Cr 1.4 mg/dL

What is the most appropriate management?

A. Repeat C3 level
B. Repeat C3 level; if level is still low, kidney biopsy is advised
C. Repeat ASO titer; if level is still high, ATB is given
D. Adjust dosage of RAAS blocker to reduce proteinuria
E. Reassure the patient and arrange for another F/U at 3 months

Clinical syndrome of glomerular disease

- ✓ Macroscopic hematuria
- ✓ Asymptomatic microscopic hematuria
- ✓ Nephrotic syndrome
- ✓ Nephritic syndrome
- ✓ Rapidly progressive glomerulonephritis
- ✓ Chronic glomerulonephritis

RPGN

- ✓ Age: 50-60 yrs (10-30), M:F = 2:1
- ✓ Prodromal illness: URI, flu-like
- ✓ Decline of eGFR > 50% in weeks to 3 months + Crescent > 50%

Clinical

Non-specific: malaise, lethargy	> 90 %
Edema	60-70 %
HT	10-20 %
Oliguria	> 60 %
Macroscopic hematuria	20-30 %
Nephrotic syndrome	10-30 %
Acute nephritic syndrome	10-20 %

LAB

Microscopic hematuria	100 %
Proteinuria	100 % (> 3 g: 10-30 %)
Renal failure	100 % (eGFR < 20: 30 %)
Immune complex	10-15 %
ANCA	80 %
Anti-GBM Ab	30 %

Pseudo-RPGN

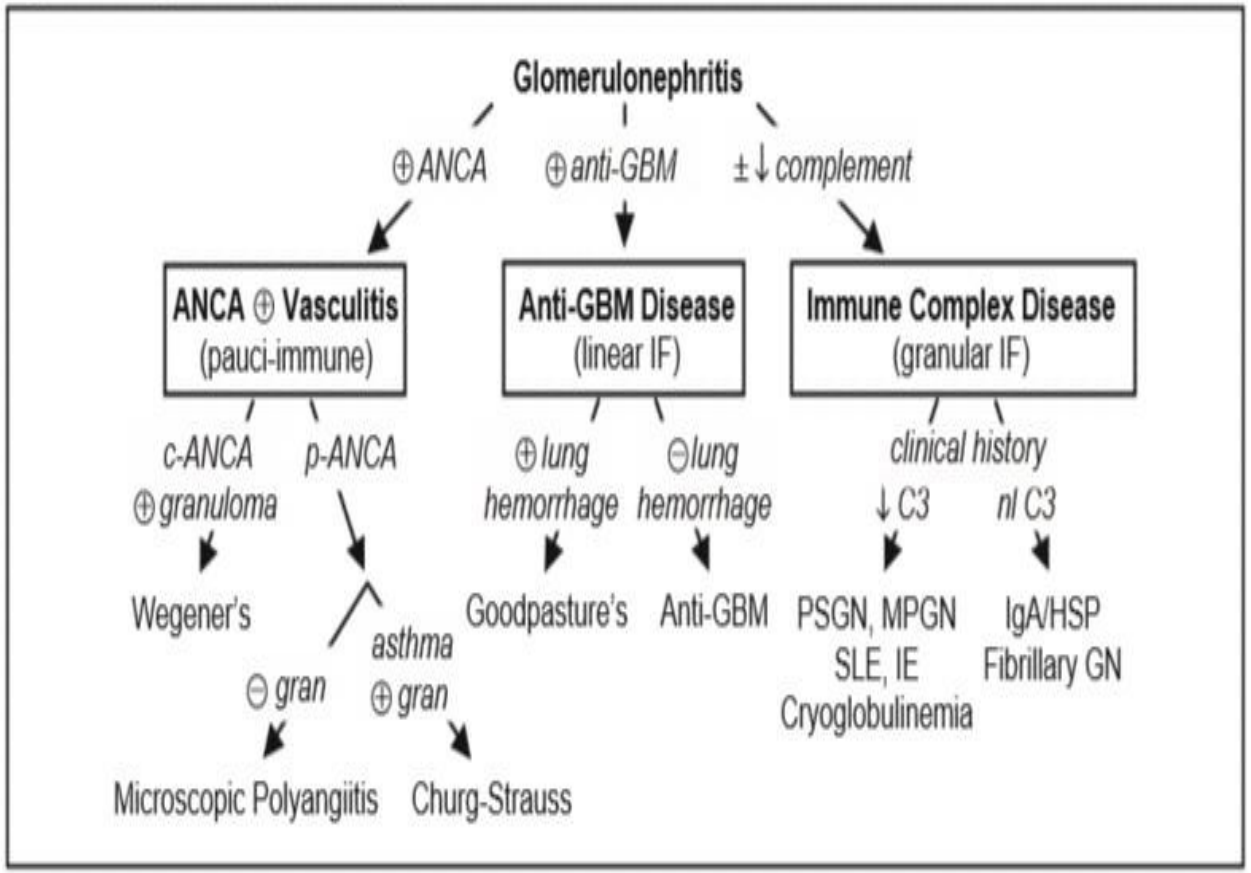
1. ATN
2. AIN
3. TTP/HUS
4. Malignant HT
5. Scleroderma renal crisis
6. Renal artery stenosis
7. Renal vein thrombosis
8. Atheroembolic renal disease
9. Light chain nephropathy
10. UTO, Papillary necrosis
11. Chronic GN

RPGN

Clinical

Non-specific: malaise, lethargy	> 90 %
Edema	60-70 %
HT	10-20 %
Oliguria	> 60 %
Macroscopic hematuria	20-30 %
Nephrotic syndrome	10-30 %
Acute nephritic syndrome	10-20 %

Figure 4-8 Approach to glomerulonephritis



LAB

Microscopic hematuria	100 %
Proteinuria	100 % (> 3 g: 10-30 %)
Renal failure	100 % (eGFR < 20: 30 %)
Immune complex	10-15 %
ANCA	80 %
Anti-GBM Ab	30 %

Types of RPGN

Type I: Anti-GBM antibody
(< 15%)

Anti-GBM disease, Goodpasture's syn, Post-KT (Alport's)

Type II: Immune complex
(40-45%)

Normal complement: IgAN/HSP
Low complement: LN, Cryoglob, PIGN, MPGN I

Type III: ANCA
(40-45%)

ANCA-pos: GPA, EGPA, MPA, renal-limited
ANCA-neg GN

Type IV: Double Ab

Anti-GBM + ANCA

Comprehensive Clinical Nephrology, 5th ed.
Clin J Am Soc Nephrol. 2017;12:1162

Type I: Anti-GBM antibody

Pathogenesis

- AutoAb to non-collagenous (NC1) domain of α3 chain of type IV collagen

Clinical

- Bimodal age; age 20-30 yr: more lung hemorrhage, age 60-70: renal-limited)
- Triggers (flu, smoking, hydrocarbon, endogenous oxidants)

LAB

- Anti-GBM Ab positive 95%
- MPO-ANCA positive 10-15% → Better prognosis

IF: linear IgG staining

Anti-GBM Disease (linear staining) <15% of total (CJASN 2017;12:1162)			
Disease	Glomerulonephritis	Pulm Hemorrhage	Anti-GBM
Goodpasture's	⊕	⊕	⊕
Anti-GBM disease	⊕	—	⊕

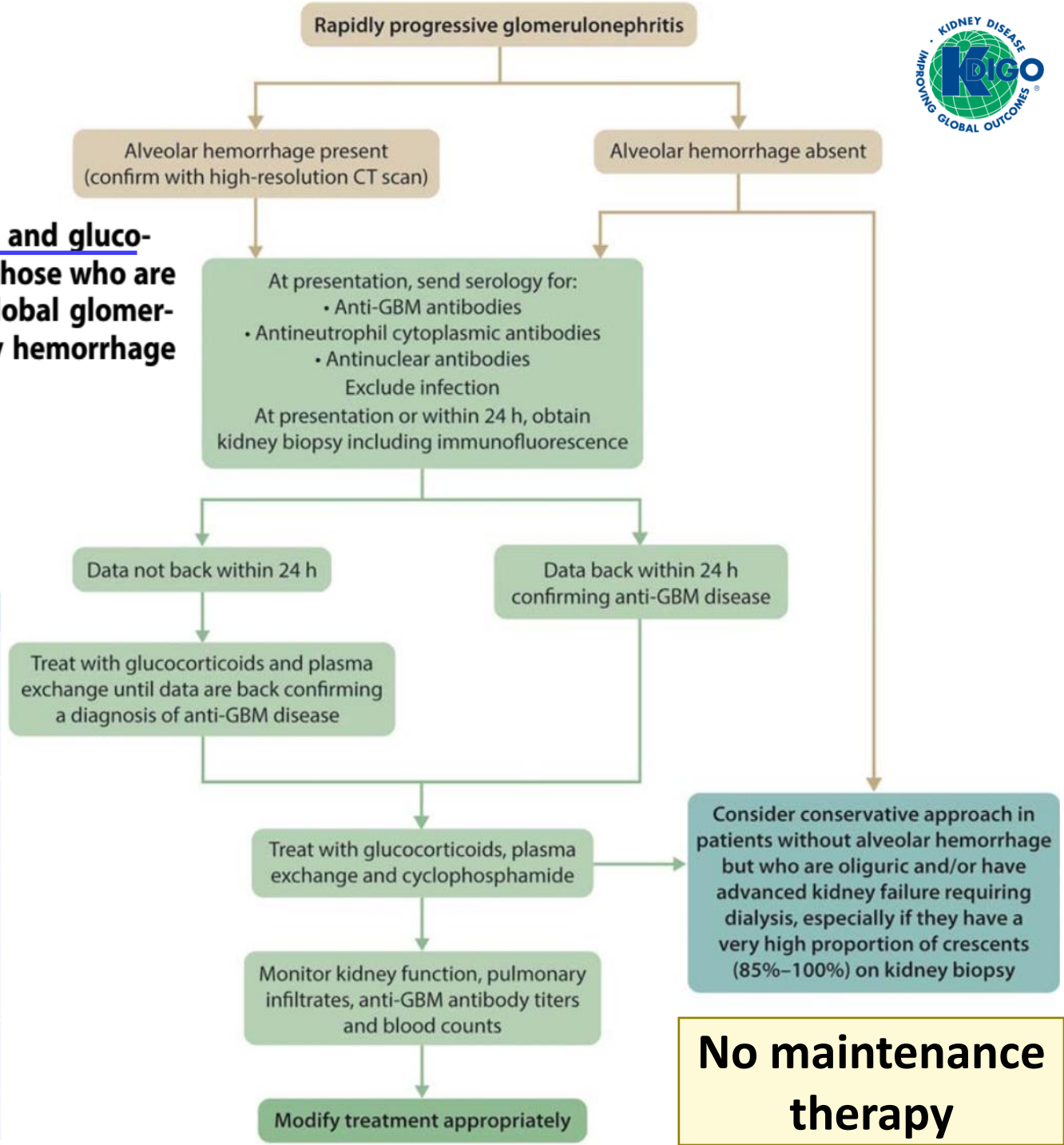
Renal survival	60%
Patient survival	85%

Type I: Anti-GBM

We recommend initiating immunosuppression with cyclophosphamide and glucocorticoids plus plasmapheresis in all patients with anti-GBM GN except those who are treated with dialysis at presentation, have 100% crescents or >50% global glomerulosclerosis in an adequate biopsy sample, and do not have pulmonary hemorrhage *(1C)*.

Contraindication for treatment
Dialysis dependent, 100% crescent,
> 50% GS, No lung hemorrhage

Intervention	Dosing	Duration of treatment
Plasma exchange	• 40–50 ml/kg ideal body weight exchange daily against 5% albumin • Add fresh frozen plasma at the end of plasma exchange in patients with alveolar hemorrhage and/or after kidney biopsy	Until circulating anti-GBM antibodies can no longer be detected; usually 14 days
Cyclophosphamide **POCY**	• 2–3 mg/kg orally (reduce to 2 mg/kg in patients >55 years); experience with pulse intravenous cyclophosphamide is limited and efficacy is uncertain • Cyclophosphamide dosing should be reduced (or treatment interrupted) in cases of leukopenia • In patients not tolerating (or not responding to) cyclophosphamide, rituximab or mycophenolate mofetil may be tried but experience is limited and efficacy uncertain	3 months
Glucocorticoids	• Pulse methylprednisolone may be given initially up to 1000 mg/d on 3 consecutive days • Prednisone 1 mg/kg orally • Reduce to 20 mg/d by 6 weeks	6 months



No maintenance therapy

Comprehensive Clinical Nephrology, 5th ed.
Clin J Am Soc Nephrol. 2017;12:1680

Type III: ANCA

IF: negative

Disease	Pulmonary	Renal	Granuloma	Key points
Granulomatosis with polyangiitis (GPA = Wegener's)	90% (+ENT)	80%	+	Young-middle age pts Upper Resp: nasal crust, saddle nose, recurrent sinusitis Lung nodule/infiltrate/cavity
Microscopic polyangiitis (MPA)	50%	90%	-	Age 50-60 yrs Non-granuloma, less neuro S&S
Eosinophilic granulomatosis with polyangiitis (EGPA = Churg-Strauss)	70%	45%	+	Age 30-40 yrs, Eo > 500-1000 Late-onset asthma More mononeuritis multiplex More cardiac: coronary arteritis, myocarditis

Type III: ANCA

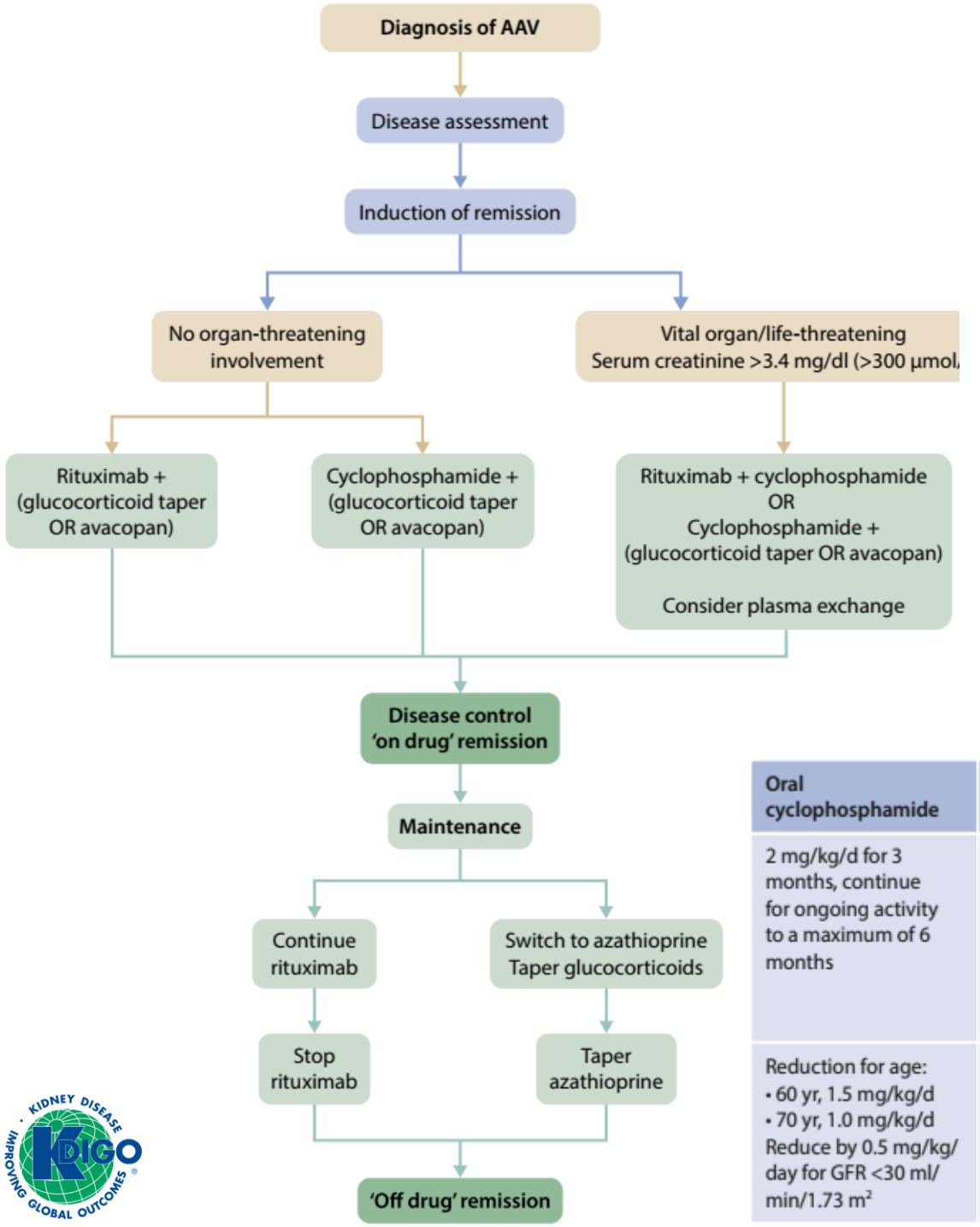
Drug-induced ANCA
- Cocaine (in levamisole), PTU, MMI, Hydralazine, Allopurinol, D-penicillamine, Sulfasalazine, Phenytoin
- p-ANCA 90%, c-ANCA 10%, high titer

Disease	Pulmonary	Renal	Granuloma	ANCA
Granulomatosis with polyangiitis (GPA = Wegener's)	90%			c-ANCA 75%, p-ANCA 20%, Neg-ANCA 5%
Microscopic polyangiitis (MPA)				c-ANCA 30%, p-ANCA 60%, Neg-ANCA 10%
Eosinophilic granulomatosis with polyangiitis (EGPA = Churg-Strauss)	70%	45%	+	c-ANCA 5%, p-ANCA 45%, Neg-ANCA 50%

c-ANCA = **PR3**-ANCA
p-ANCA = **MPO**-ANCA

Renal-limited vasculitis: p-ANCA 80%, c-ANCA 10%, Negative-ANCA 10%
ANCA negative GN (10-30%): age 40 yr, poor prognosis

Treatment of ANCA



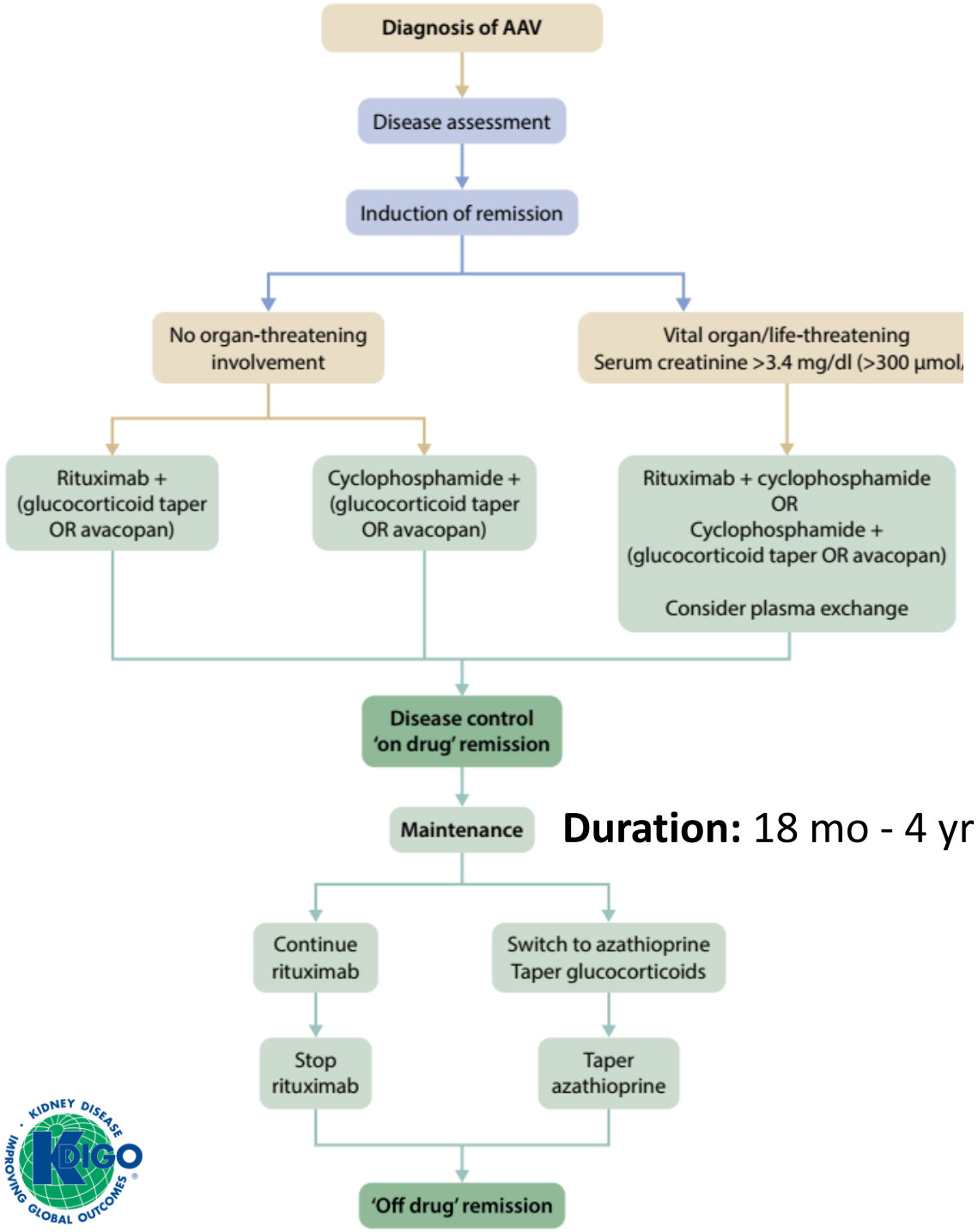
1. SCr > 3.4 mg/dL
2. Dialysis or rapidly increasing SCr
3. DAH with hypoxemia
4. Overlap with anti-GBM

Stop ISD

After 3 months in patients on **dialysis** and **do not have any extrarenal** manifestation

Oral cyclophosphamide	Intravenous cyclophosphamide	Rituximab	Rituximab and i.v. cyclophosphamide	MMF	Avacopan
2 mg/kg/d for 3 months, continue for ongoing activity to a maximum of 6 months	15 mg/kg at weeks 0, 2, 4, 7, 10, 13 (16, 19, 21, 24 if required)	375 mg/m²/week × 4 weeks OR 1 g at weeks 0 and 2	Rituximab 375 mg/m²/week × 4 weeks, with i.v. cyclophosphamide 15 mg/kg at weeks 0 and 2 OR Rituximab 1 g at 0 and 2 weeks with i.v. cyclophosphamide 500 mg/2 weeks × 6	2000 mg/d (divided doses), may be increased to 3000 mg/d for poor treatment response	30 mg twice daily as alternative to glucocorticoids, in combination with rituximab or cyclophosphamide induction
Reduction for age: • 60 yr, 1.5 mg/kg/d • 70 yr, 1.0 mg/kg/d Reduce by 0.5 mg/kg/day for GFR <30 ml/min/1.73 m²	Reduction for age: • 60 yr 12.5 mg/kg • 70 yr, 10 mg/kg Reduce by 2.5 mg/kg for GFR <30 ml/min/1.73 m²				

Treatment of ANCA



Duration: 18 mo - 4 yr

1. SCr > 3.4 mg/dL
2. Dialysis or rapidly increasing SCr
3. DAH with hypoxemia
4. Overlap with anti-GBM

Rituximab	Azathioprine	MMF
Scheduled dosing protocol: **1.** 500 mg × 2 at complete remission, and 500 mg at mo 6, 12, and 18 thereafter (MAINRITSAN scheme) OR **2.** 1000 mg infusion after induction of remission, and at mo 4, 8, 12, and 16 after the first infusion (RITAZAREM* scheme)	1.5–2 mg/kg/d at complete remission until 1 yr after diagnosis then decrease by 25 mg every 3 mo	2000 mg/d (divided doses) at complete remission for 2 yr
	Extend azathioprine at complete remission until 4 yr after diagnosis; start at 1.5–2 mg/kg/d for 18–24 mo, then decrease to a dose of 1 mg/kg/d until 4 yr after diagnosis, then taper by 25 mg every 3 mo. Glucocorticoids should also be continued at 5–7.5 mg/d for 2 yr and then slowly reduced by 1 mg every 2 mo	

A 65-year-old woman presented with edema and oliguria for 1 week. She denied hemoptysis or hematuria.

PE: BP 150/60 mmHg, crepitation at both lungs.

LAB: BUN/Cr 110/10 mg/dL, UA: RBC 30-50/HPF with dysmorphic RBC.

Kidney biopsy showed 50% fibrocellular crescent glomeruli.

IF staining is negative.

What is the most appropriate management?

A. Hemodialysis alone

B. Hemodialysis + IVCY

C. Hemodialysis + Plasmapheresis

D. Hemodialysis + Plasmapheresis + IVCY

E. Hemodialysis + Plasmapheresis + IVCY + IVMP

A 20-year-old woman presented with edema and oliguria for 1 week. She denied hemoptysis or hematuria.

PE: BP 150/60 mmHg, crepitation at both lungs.

LAB: BUN/Cr 110/10 mg/dL, UA: RBC 30-50/HPF with dysmorphic RBC.

Kidney biopsy showed 100% fibrocellular crescent glomeruli with linear IgG deposition.

What is the most appropriate management?

A. Hemodialysis alone

B. Hemodialysis + IVCY

C. Hemodialysis + Plasmapheresis

D. Hemodialysis + Plasmapheresis + IVCY

E. Hemodialysis + Plasmapheresis + IVCY + IVMP

DDx in glomerular disease

Age < 15 yr

1. MCD/IgM
2. FSGS
3. LN
4. PIGN/IgAN
5. Hereditary nephritis

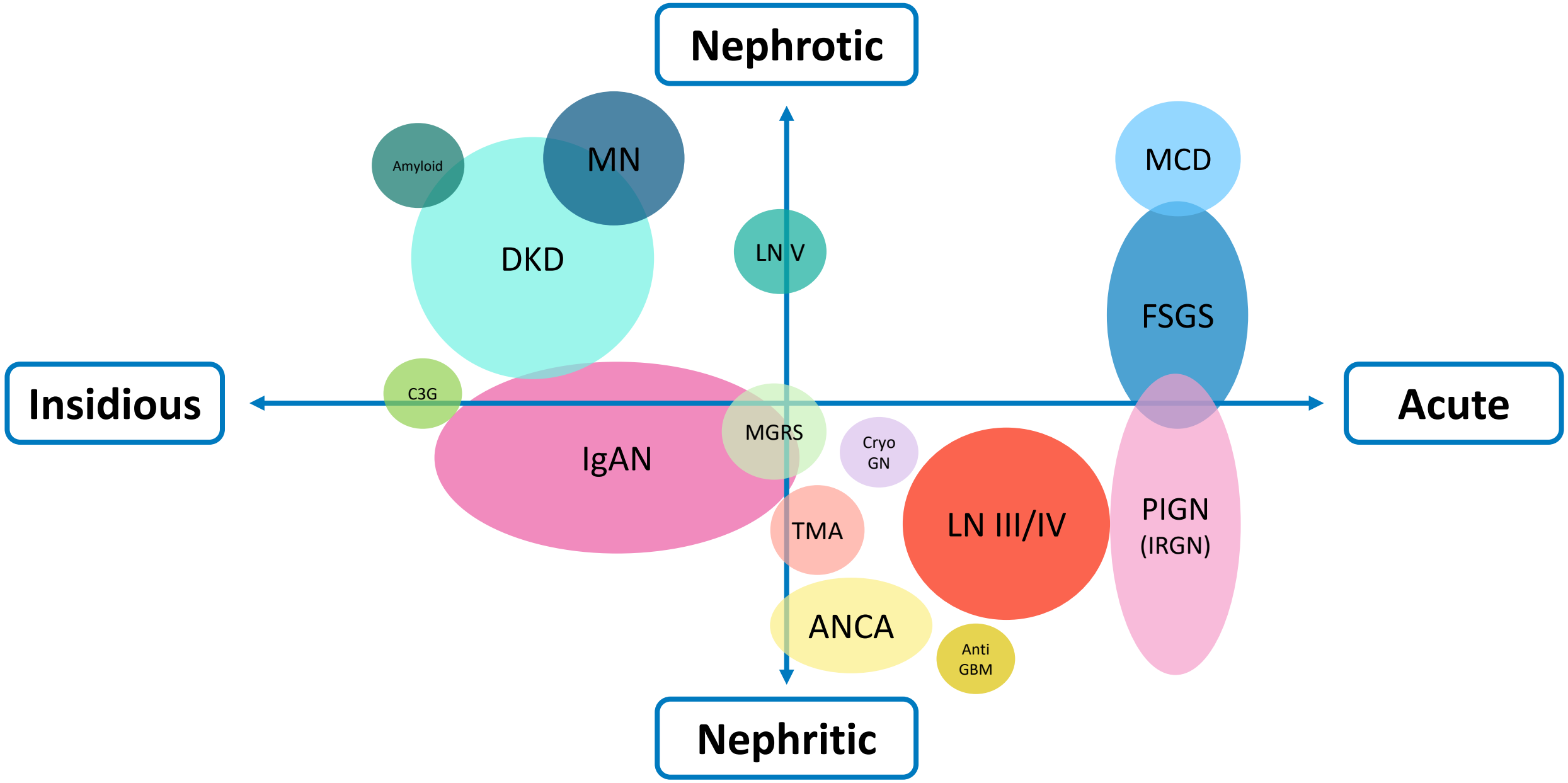
Age 15-40 yr

1. FSGS
2. MCD/IgM
3. LN
4. PIGN/IgAN
5. Hereditary nephritis
6. DN
7. MN

Age > 40 yr

1. MN
2. MCD/IgM
3. DN/2°FSGS
4. LN, ANCA
5. PIGN/IgAN
6. Amyloidosis
7. Malig-related GN

Infect: HBV, HCV, HIV, Strep



Adaptive FSGS: insidious onset of proteinuria (less likely NS)

C3G: G3 glomerulopathy; IRGN: infection-related GN; MGRS: monoclonal gammopathy of renal significance

This slide shows common presentation of glomerular disease

Adapted from Dr Ali Poyan Mehr

Supportive treatment for glomerular disease

1. Low salt diet (Na < 2 g/d)
2. TP 0.8-1.0 g/kg/d for nephrotic-range (+ add 1 g/g of pro loss: upto 5 g)
3. TC 35 kcal/kg/day (eGFR < 60: TC 30-35)
4. Keep SBP < 120 mmHg (THAI: SBP < 130 mmHg)
5. ACEI/ARB
6. Diuretic for volume overload
7. Statin depend on CV risk
8. Stop smoking
9. Pneumococcal/Influenza/Zoster vaccine
10. Risk of Hypercoagulable state: Alb < 2-2.5 g/dL + BISCUIT/Fam

Goal: UPCI < 1

UPCI < 0.5: prevent CKD progression

UPCI < 1-1.5: slow CKD progression

Supportive treatment for glomerular disease

If on Pred > 2.5 mg/day for > 3 mo
- $CaCO_3$ 1-1.2 g/day
- Vit D 600-800 IU/day

4. Keep SBP < 120 mmHg (THA
5. ACEI/ARB
6. Diuretic for volume overloa
7. Statin depend on CV risk
8. Stop smoking
9. Pneumococcal/Influenza/Zoster vaccine
10. Risk of Hypercoagulable state: Alb < 2-2.5 g/dL + <u>BISCUIT/Fam</u>

B: BMI > 35
I: Immobilization (prolonged)
S: Sx (recent abdo/ortho Sx)
C: CHF-NY Class III-IV
U: Upro > 10 g/day
I: ---
T: Thromboemobolism (history)
Fam: Family Hx of thromboembolism

Specific treatment for glomerular disease

MCD/FSGS	**Pred** 1 MKD at least 4-16 wk tape over 6 months → CY/CNI
MN	**Failed RAASi <u>> 6 mo</u>** (UPCI > 3.5 g or decrease < 50%) → **ISD:** steroid alternate with CY or CNI or Ritux
Amyloidosis	CMT +/- stem cell transplantation
IgAN	**Failed RAASi <u>≥ 3 mo</u>** + UPCI > 1 g + GFR > 30 → Pred 6 mo
PIGN	**Diuretic** for control BP, supportive care
LN	**Depend on classification of LN**
ANCA **Anti-GBM**	CY + steroid ± plasmapheresis

Thank you for your attention

Question is always welcome…