คู่มือคำจำกัดความพยาธิวิทยาทางไตและโรคโกลเมอรูลัส

Terminology in Renal pathology and Glomerular Disease

คณะผู้จัดทำ

1. ผศ. พญ.รัตนา ชวนะสุนทรพจน์ สาขาวิชาวักกะวิทยา ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล
2. รศ.นพ. บุณยฤทธิ์ ชื่นสุชน ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์ศิริราชพยาบาล
3. รศ.นพ.มล.ชาครีย์ กิติยากร สาขาวิชาโรคไต ภาควิชา อายุรศาสตร์ คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี
4. ผศ.นพ.สุชิน วรวิชชวงษ์ ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์โรงพยาบาลรามาธิบดี
5. พญ. นพนิต พัฒนชัยวิทย์ กองอายุรกรรม โรงพยาบาลภูมิพลอดุลยเดช
6. พ.ต.บัญชา สถิระพจน์ กองอายุรกรรม วิทยาลัยแพทยศาสตร์พระมงกุฎเกล้า
7. พ.ท.สุเมธ เติมมธุรพจน์ ภาควิชาพยาธิวิทยา วิทยาลัยแพทยศาสตร์พระมงกุฎเกล้า
8. พญ.วรางคณา พิชัยวงศ์ กลุ่มงานอายุรศาสตร์ โรงพยาบาลราชวิถี
9. พญ.ภานินี ถาวรังกูร สถาบันพยาธิวิทยา
10. รศ.พญ.สิริภา ช้างศิริกุลชัย สาขาวิชาโรคไต ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์มหาวิทยาลัยศรีนครินทรวิโรฒ
11. พญ.พรรณธิพา ต้นสวรรค์ สาขาวิชาโรคไต ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์โรงพยาบาลศรีนครินทร์ ม.ขอนแก่น
12. ผศ.นพ.อนุชา พัวไพโรจน์ ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์โรงพยาบาลศรีนครินทร์ ม.ขอนแก่น
13. ผศ.พญ.พรเพ็ญ แสงถวัลย์ สาขาวิชาโรคไต ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์มหาวิทยาลัยสงขลานครินทร์
14. ศ.นพ.วิญญู มิตรานันท์ ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์มหาวิทยาลัยสงขลานครินทร์
15. พญ.มนัสนันท์ รวีสุนทรเกียรติ ภาควิชาพยาธิวิทยา คณะแพทยศาสตร์มหาวิทยาลัยศรีนครินทรวิโรฒ
16. นพ.ภัทรวิน ภัทรนิธิมา สาขาวิชาโรคไต ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์มหาวิทยาลัยธรรมศาสตร์
17. ศ.นพ.ชัยรัตน์ ฉายากุล สาขาวิชาวักกะวิทยา ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์ศิริราชพยาบาล
18. รศ. นพ.ทวี ศิริวงศ์ สาขาวิชาโรคไต ภาควิชาอายุรศาสตร์ คณะแพทยศาสตร์โรงพยาบาลศรีนครินทร์ ม.ขอนแก่น

คำย่อ (Abbreviations)

AAV	Antineutrophil cytoplasmic antibody-associated vasculitis
ACEI	Angiotensin Converting Enzyme Inhibitor
AIN	Acute interstitial nephritis
AKI	Acute kidney injury
ANA	Antinuclear Antibody
ANCA	Antineutrophil cytoplasmic antibody
Anti-DNase B	Anti-Deoxyribonuclease B antibody
Anti-dsDNA	Anti-double stranded DNA
Anti-GBM	Anti-glomerular basement membrane
APS	Antiphospholipid syndrome
ARB	Angiotensin receptor blocker
ASO	Antistreptolysin antibody
ATIN	Acute tubulointerstitial nephritis
ATN	Acute tubular necrosis
AZA	Azathioprine
BP	Blood pressure
BM	Basement membrane
BMI	Body mass index
C1q	Complement C1q
C3	Complement C3
C4	Complement C4
C3G	C3 glomerulopathy
CGN	Chronic glomerulonephritis
CKD	Chronic kidney disease
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration
CNI	Calcineurin inhibitor
Cr	Creatinine
CrCl	Creatinine clearance
CTIN	Chronic tubulointerstitial nephritis
CYC	Cyclophosphamide
DIC	Disseminated intravascular hemolysis
DDD	Dense deposit disease
DM	Diabetes mellitus
DN	Diabetic nephropathy
eGFR	Estimated glomerular filtration rate
EDD	Electron dense deposit
EGPA	Eosinophilic granulomatosis with polyangiitis
EM	Electron microscopy
ESRD	End-stage renal failure
EULAR	European League Against Rheumatism
FSGS	Focal segmental glomerulosclerosis
GBM	Glomerular basement membrane
GN	Glomerulonephritis
GPA	Granulomatosis with polyangiitis
H&E	Hematoxylin and Eosin
HBV	Hepatitis B virus
HCDD	Heavy chain deposit disease
HCV	Hepatitis C virus
HIVAN	HIV-associated nephropathy
HPF	High power field
HSP	Henoch-Schönlein purpura
HT	Hypertension
IF	Immunofluorescence
IgA	Immunoglobulin A
IgAN	Immunoglobulin A nephropathy
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IgMN	Immunoglobulin M nephropathy
IMN	Idiopathic membranous nephropathy
IV	Intravenous
IVIG	Intravenous immunoglobulin
KDIGO	Kidney Disease/Improving Global Outcomes
KW	Kimmelstiel-Wilson
LCDD	Light chain deposit disease
LN I	Lupus nephritis class I
LN II	Lupus nephritis class II
LN III	Lupus nephritis class III
LN III+V	Lupus nephritis class III+V
LN IV	Lupus nephritis class IV
LN IV+V	Lupus nephritis class IV+V
LN V	Lupus nephritis class V

LN VI	Lupus nephritis class VI
LM	Light microscopy
LPM	Low power field
NS	Nephrotic syndrome
MCD	Minimal change disease
MM	Multiple myeloma
MMF	Mycofenolate mofietil
MN	Membranous nephropathy
MPA	Microscopic polyangiitis
MPGN	Membranoproliferative glomerulonephritis
MPGN type I	Membranoproliferative glomerulonephritis type I
MPGN type II	Membranoproliferative glomerulonephritis type II
MPGN type III	Membranoproliferative glomerulonephritis type III
NA	Not available
NOS	Not otherwise specified
PAN	Polyangiitis nodosa
PAS	Periodic acid-Schiff
PASM	Periodic Schiff-Methenamine Silver
PO	Per oral
PR3	Anti-proteinase-3
RBC	Red blood cell
RF	Rheumatic fever
RPGN	Rapidly progressive glomerulonephritis
SCr	Serum creatinine
SDNS	Steroid-dependent nephrotic syndrome
SLE	Systemic lupus erythematosus
SRNS	Steroid-resistant nephrotic syndrome
TBM	Thin basement membrane
TEM	Transmission electron microscope
TMA	Thrombotic microangiopathy
TTP	Thrombotic thrombocytopenic purpura
UPCR	Urine protein creatinine ratio

Terminology in renal pathology and glomerular diseases

Acute kidney injury (AKI):

- Increase in serum creatinine by ≥ 0.3 mg/dL within 48 hours; OR
- Increase in serum creatinine to ≥ 1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; OR
- Urine output < 0.5 ml/kg/hour for 6 hours

Alport syndrome: Genetic disease that results from mutation in alpha chain of type IV collagen. No specific lesion on light microscopy and negative IF studies. Discontinuation or absence of alpha chains staining along GBM. Ultrastructural examination shows thin and multiplication or basket weave appearance of the GBM.

Amyloidosis: Accumulation of amyloid proteins, characterized by apple-green birefringence after Congo red stain.

ANCA associated glomerulonephritis/Pauci-immune glomerulonephritis: Crescentic glomerulonephritis with no evidence of anti-GBM antibodies or deposited immune complex. The disease can be systemic vasculitis or renal limited vasculitis (ANCA associated GN).

- Complete remission: Absence of systemic vasculitis; AND absence of microscopic hematuria; AND 24-hour urine protein < 0.3 g/day or UPCR < 0.3 g/g.Cr; AND stable SCr (± 25% SCr)
- Partial remission: Improvement of systemic vasculitis; AND absence of microscopic hematuria; AND 24-hour urine protein < 3.5 g/day or UPCR < 3.5 g/g.Cr; AND UPCR decrease ≥ 50% from peak values x 2 times ≥ 1 week apart; AND stable SCr (± 25% SCr)
- Resistant GN: Persistence of active GN or systemic vasculitis after initial immunosuppressive regimen (high dose)

Relapse: Increase disease activity after a period of remission (partial or complete)

Anti-GBM disease: Severe acute glomerulonephritis caused by circulating antibody that binds to collagen type IV in GBM. Light microscopy shows necrotizing and crescentic glomerulonephritis. IF shows strong linear IgG staining along GBM.

Antiphospholipid syndrome: An autoimmune/hypercoagulable state due to antiphospholipid antibodies causing thrombosis in venous or arterial sites. Glomerular lesions are similar to thrombotic microangiopathy.

Arteritis: Presence of an inflammatory infiltrate within arterial wall.

Asymptomatic hematuria:

- Urine RBC > 3 cells/HPF at least two of three midstream clean-catch voiding; AND
- eGFR (CKD-EPI) > 90 ml/min/1.73 m^2; AND
- BP < 140/90 mmHg; AND
- No edema; AND
- No oliguria (urine $\geq$ 400 ml/day); AND
- 24-hr urine protein < 150 mg/day, or UPCR < 0.15 g/g.Cr

Asymptomatic proteinuria:

- RBC < 3 cells/HPF at least two of three midstream clean-catch voiding ; AND
- eGFR (CKD-EPI) > 90 ml/min/1.73 m^2; AND
- BP < 140/90 mmHg; AND
- No edema; AND
- No oliguria (urine $\geq$ 400 ml/day); AND
- 24-hr urine protein 150 - 3,500 mg/day, or UPCR 0.15 - 3.5 g/g.Cr

Asymptomatic proteinuria and hematuria:

- RBC > 3 cells/HPF at least two of three midstream clean-catch voiding; AND
- eGFR (CKD-EPI) > 90 ml/min/1.73 m^2; AND
- BP < 140/90 mmHg; AND
- No edema; AND
- No oliguria (urine $\geq$ 400 ml/day); AND
- 24-hr urine protein $\geq$ 150 mg/day, or UPCR $\geq$ 0.15 g/g.Cr

Benign nephrosclerosis: Renal changes associated with benign hypertension characterized by intimal fibrosis in arteries and hyalinosis in arterioles.

C1q nephropathy: Idiopathic glomerular disease characterized by dominant or codominant C1q staining ($\geq$ 2+ intensity) primarily in mesangium in patients with no evidence of systemic lupus erythematosus (SLE), membranoproliferative glomerulonephritis (MPGN), or infection

C3 glomerulopathy: Any glomerular disease pattern with isolated C3 deposits related to abnormalities in alternative complement pathway, including dense deposit disease (DDD)

Capillary adhesion: Abnormal attachment of glomerular tuft to Bowman capsule.

Capillary collapsed: Collapse of glomerular capillaries with overlying podocyte hypercellularity.

Cast: Various coagulated proteins and formed elements in the tubular lumens.

Cholesterol emboli: Empty, needle-like clefts within vascular space in association with fibrin and organizing thrombi. The clefts represent cholesterol crystals which are dissolved out of the tissue during tissue processing and staining.

Chronic glomerulonephritis (CGN): CKD G3-5; and nephritic syndrome, or nephrotic syndrome, or nephrotic nephritic syndrome

Chronic kidney disease (CKD): Defined as abnormal kidney structure or function, present for > 3 months.

Crescent: Represent accumulation of cells and extracellular material in the urinary space. Crescents are the result of severe capillary wall damage with disruptions in continuity and spillage of fibrin from inside the damaged capillaries into the urinary space. This is associated with proliferation of mainly parietal and perhaps visceral epithelial cells and accumulation of monocytes and other blood cells in the urinary space. Crescent characteristics;

- Segmental: Crescent that involve less than half of glomerular tufts.
- Circumferential: Crescent that involves all segments of the glomerular tufts.
- Cellular: Crescent that compose of only cells in the urinary space.
- Fibrocellular: Crescent that compose an admixture of cells and collagen in the urinary space.
- Fibrous: Crescent that compose of only collagen in the urinary space.

Cryoglobulinemic glomerulonephritis: Glomerular lesion characterized with MPGN pattern on LM, strongly PAS-positive cryo-“plugs” (hyaline thrombi) in capillary lumina, predominant IgM deposits by IF. The cryoplugs typically show vague, short, curved, fibrillary substructure by EM. There may also be vasculitis involving medium-sized arteries.

Dense deposit disease (DDD): A variant of C3 glomerulonephritis manifested by broad, linear, extremely electron-dense deposits with C3 within GBM, mesangium, Bowman capsule, and TBM. Formerly known as MPGN type II.

Diabetic nephropathy (DN): Changing of the kidney in DM type I or II, involving all renal compartments including the glomeruli, tubules, interstitium and vasculature such as thickened

GBM and/or TBM, increased mesangial matrix, mesangial KW nodules etc. IF shows weak linear IgG staining on GBM, Bowman's capsule, and TBM.

Disseminated intravascular coagulation (DIC): Thrombi formation within the glomerular capillaries and small arteries is present. There is widening of the subintimal regions of arterioles with extravasated red blood cells, resulting in narrowed vascular lumina. The majority of the intra-glomerular thrombi were identified by PTAH staining. The fibrinogen immunostaining revealed that most of the thrombi consisted of fibrin strands.

Electron microscopy findings:

- Electron dense: Hyperdensity area under transmission electron microscope (TEM).
- Electron lucent: Hypodensity area under TEM.
- Fibril: A threadlike fiber or filament.
- Humps deposit: Large electron dense deposit in subepithelium.
- Intra-membrane deposits: Electron dense deposit in glomerular basement membrane.
- Mesangial deposits: Electron dense deposit in mesangium.
- Powdery deposits: Fine granular electron dense deposit.
- Subendothelial deposits: Electron dense deposit in subendothelium.
- Subendothelial widening: Widening of subendothelial area without electron dense deposit.
- Subepithelial/epi-membranous deposits: Electron dense deposit in sub-epithelium/ epi-membranous.
- Tubuloreticular inclusion/body: Subcellular organelles characterized by small clusters of anastomosing tubule-like structures within cisternae of endoplasmic reticulum.

Endocapillary proliferation: Increased number of intracapillary cells causing narrowing or occlusion of glomerular capillary lumens.

Endothelial swelling: Increased volume of endothelial cell cytoplasm

Fibrillary GN: Glomerular disease characterized by non-amyloid, non-periodic fibrillar deposits of immunoglobulin, 10-30 nm in diameter.

Fibrinoid necrosis: Area of necrosis that stains brick red with eosin due to denatured proteins and fibrin.

Fibrin thrombi: Thrombi formed by repeated deposits of fibrin from the circulating blood.

Fibrointimal thickening/intimal fibrosis: Concentric collagen deposition in the intima.

Focal segmental glomerulosclerosis (FSGS): A group of glomerular diseases characterized by at least one glomerulus containing sclerosis or adhesion in at least a portion but not the entire of glomerular tufts accompanying with lack of significant evidence of immune complexes in both immunofluorescence and electron microscopy.

Classification:

- Tip: At least one glomerulus with sclerotic lesion involving only the tubular pole of the glomerulus in the absence of collapsing lesion and perihilar lesion of any glomerulus.
- Perihilar: At least one glomerulus with perihilar sclerosis and hyalinosis involving > 50 % of the involved glomerulus with exclusion of collapsing lesion, tip lesion and cellular lesion.
- Cellular: At least one glomerulus with endocapillary proliferation involving at least 25% of the tuft and occluding the lumen with exclusion of collapsing lesion and tip lesion of any glomerulus.
- Collapsing: At least one glomerulus with segmental or globally glomerular tuft collapse and overlying podocyte hyperplasia and hypertrophy. At least one glomerulus with segmental or globally glomerular tuft collapse and overlying podocyte hyperplasia and hypertrophy.
- NOS: Segmental lesions that do not fit in to any of the specific types.

Clinical FSGS/MCD/IgMN;

- Complete remission: 24-hr urine proteinuria < 0.3 g/day or UPCR < 0.3 g/g.Cr; AND normal SCr; AND normal serum albumin
- Partial remission: 24-hr urine proteinuria 0.3-3.5 g/day or UPCR 0.3-3.5 g/g.Cr; AND UPCR decrease > 50% from baseline; AND stable SCr ($\pm$ 25% SCr)
- Relapse: 24-hr urine proteinuria > 3.5 g/day or UPCR > 3.5 g/g.Cr after complete remission
- Frequent relapse: Not defined in adults
- Steroid dependent: 2 relapses during or within 2 weeks of completing steroid therapy
- Steroid resistant: Persistent of proteinuria despite prednisolone 1 mg/kg/day or 2 mg/kg every other day for > 4 months

Foot process effacement: By electron microscopy, the visceral epithelial cells (podocytes) change shapes; the foot process (pedicles) retract and swell, resulting in loss of individual foot processes and a near solid mass of cytoplasm covering the glomerular basement membrane. Characteristics;

- Focal: The change involves a part of glomerular tufts.
- Partial: The change which has partial response to therapy.
- Diffuse: The change involves all segments of glomerular tufts.

Global sclerosis: Obliteration of capillary lumens by increased extracellular matrix involving all segments of a glomerulus.

Glomerular basement membrane (GBM):

- Bubble appearance: Clear vacuolated appearance of the basement membrane on silver staining.
- Duplicated BM/Tram track: Double contour appearance of the glomerular basement membrane by light microscopy
- Ruptured BM: Discontinuation of the GBM or fragmented GBM
- Thick basement membrane: GBM thicker than 400 nm. by EM
- Thin basement membrane: GBM thinner than 200 nm. by EM
- Spike: Perpendicular protrusion of the GBM caused by subepithelial immune complex deposit

Heavy chain deposit disease: Deposition of abnormal heavy chain protein along glomerular and tubular basement membrane. The deposits are characterized by linear GBM and TBM staining by IF and finely granular by EM.

Henoch-Schönlein purpura nephritis: IgAN with extrarenal symptoms caused by small vessels vasculitis.

Hematuria: Urine RBC > 3 cells/HPF

HIV-associated nephropathy (HIVAN): The secondary FSGS associated with HIV infection. It is characterized by collapsing of glomerular turf, and severe tubular injury including cystic dilatation, out of proportion to the FSGS. EM demonstrates numerous tubuloreticular aggregates in endothelial cells.

Hyaline thrombi: Translucent colorless plug, partly or wholly filling a capillary.

Hyalinosis: Acellular material (by light microscopy) consisting of glycoproteins and sometimes incorporating lipids, staining positive with eosin and PAS and red with Trichrome. Not staining with PASM and Jones.

IgA nephropathy: Variable changes in glomeruli on LM with granular IgA deposits in mesangium under IF. EM shows electron dense deposits in mesangium.

IgM nephropathy: Proteinuria/nephrotic syndrome with mesangial proliferation on LM. IF shows dominant IgM deposit in mesangium (>2+) and electron dense deposits in mesangium on EM.

Immunotactoid glomerulopathy: Congo red negative microtubular deposits typically >30 nm in diameter and arranged in parallel arrays.

Immunofluorescent staining:

- Granular pattern: Granular staining by FITC under fluorescent microscope.
- Linear pattern: Linear staining by FITC under fluorescent microscope
- Positive: Presence of granular or linear staining by FITC under fluorescent microscope (1+, 2+, 3+)
- Negative: Absence of granular or linear staining by FITC under fluorescent microscope (0)
- Trace: Presence of granular or linear staining by FITC under fluorescent microscope (between 0 to 1+)

Interstitial edema: Widening/expansion of interstitium without cellular infiltration or collagen.

Interstitial fibrosis: Accumulation of collagen (fibrous) in interstitium.

Interstitial hemorrhage: Extravasated erythrocytes in interstitium.

Interstitial infiltration/inflammation: Presence of leukocytes in interstitium

Light chain deposit disease (LCDD): Deposition of abnormal light chain protein along glomerular and tubular basement membrane. The deposits are characterized by linear GBM and TBM staining by IF and finely granular by EM.

Lupus nephritis (LN): Renal involvement by Systemic Lupus Erythematous (SLE). Classification of Lupus nephritis (ISN/RPS) 2003 shows as following;

LN class I: Minimal Mesangial LN; normal glomeruli by light microscopy, but mesangial immune deposits by IF, and/or EM

LN class II: Mesangial proliferative LN; purely mesangial hypercellularity of any degree or mesangial matrix expansion by LM, with mesangial immune deposits; may be a few isolated subepithelial and/or subendothelial deposits by IF and/or EM, but not visible by LM.

LN class III: Focal LN; active or inactive focal, segmental or global endo - or extracapillary glomerulonephritis involving < 50% of all glomeruli, typically with focal subendothelial immune deposits, with or without mesangial alterations.

- III (A) Active lesions: focal proliferative LN
- III (A/C) Active and chronic lesions: focal proliferative and sclerosing LN
- III (C) chronic inactive lesions with glomerular scars: focal sclerosing LN

LN class IV: Diffuse LN; active or inactive focal, segmental or global endo- or extracapillary glomerulonephritis involving ≥ 50% of all glomeruli, typically with diffuse subendothelial immune deposits, with or without mesangial alterations. This class is divided into diffuse segmental LN (IV-S) LN when ≥ 50% of the involved glomeruli have segmental lesions, and diffuse global (IV-G) LN when ≥ 50% of the involved glomeruli have global lesions. Segmental is defined as glomerular lesion that involves less than half of the glomerular turf. This class includes cases with diffuse wire loop deposits but with little or no glomerular proliferation.

- IV-S (A) Active lesions: diffuse segmental proliferative LN
- IV-G (A) Active lesions: diffuse global proliferative LN
- IV-S (A/C) Active and chronic lesions: diffuse segmental proliferative and sclerosing LN
- IV-G (A/C) Active and chronic lesions: diffuse global proliferative and sclerosing LN
- IV-S (C) Chronic inactive lesions with scars: diffuse segmental sclerosing LN
- IV-G (C) Chronic inactive lesions with scars: diffuse global sclerosing LN

LN class V: Membranous LN; global or segmental subepithelial immune deposits or their morphologic sequelae by LM and by IF or EM, with or without mesangial alterations. LN class V may occur in combination with class III or IV, in which case both will be diagnosed. LN class V may show advanced sclerosis.

LN class VI: Advanced sclerosing LN; more than 90% of glomeruli globally sclerosed without residual activity.

Clinical LN:

- Complete response:
  - SCr to previous baseline (SCr < 1.2 mg/dL) and UPCR < 0.5 g/g.Cr
- Partial response:
  - Stable SCr (+/- 25% from baseline) or improve SCr but not normal (SCr < 1.2 mg/dL), and UPCR decrease ≥ 50%. If UPCR > 3 g/gCr, UPCR decrease ≥ 50% and < 3 g/g.Cr
- Non response:
  - Persist 25% SCr rising or SCr > 1.2 mg/dL, UPCR > 3 g/g.Cr or decrease < 50% after initial therapy
- Flare/Relapse after response:
  - Mild: Increase urine RBC from 5 to 15/HPF, with ≥ 2 acanthocytes/HPF, AND/OR ≥ 1 RBC cast, WBC cast, or both
  - Moderate: Increase SCr 0.2-1 mg/dL if baseline < 2 mg/dL, 0.4-1.5 mg/dL if baseline ≥ 2 mg/dL, AND/OR
    - Increase UPCR ≥ 1 g/g.Cr if baseline UPCR < 0.5 g/g.Cr
    - Increase UPCR to 2-5 g/g.Cr if baseline UPCR 0.5-1 g/g.Cr
    - Increase UPCR ≥ 2-fold but < 5 g/g.Cr if base UPCR > 1 g/g.Cr
  - Severe: Increase SCr > 1 mg/dL if baseline < 2 mg/dL, > 1.5 mg/dL if baseline ≥ 2 mg/dL, AND/OR UPCR > 5 g/g.Cr
- Refractory/Resistant: Worsening of SCr and proteinuria after initial therapy

Malignant nephrosclerosis: Renal changes occurring in patients with malignant hypertension (blood pressure more than 200/120 mmHg. The lesions are characterized by small, pinpoint petechial hemorrhages on gross examination. By histology the arterioles show fibrinoid necrosis and interlobular arteries show proliferation of intimal cells producing an onion-skin appearance.

Medial hypertrophy: Thickened tunica media of vascular wall due to smooth muscle cell proliferation (smooth muscle hyperplasia in the tunica media).

Membranoproliferative glomerulonephritis (MPGN): A pattern of glomerular injury characterized by diffuse mesangial expansion due to endocapillary proliferation and increased mesangial

matrix, thickened capillary wall, often with a split “tram-track” appearance. Typically, IgG and IgM and C3 are present in an irregular capillary and mesangial distribution. By electron microscopy, MPGN type I shows numerous dense deposits in subendothelial and mesangial areas. Interposition of cytoplasmic processes of mononuclear cells between the endothelial cells and the basement membrane. Reduplication of new basement material is also present. MPGN type II is a variant of type I with prominent subepithelial or intramembranous deposits.

Membranous nephropathy: Diffuse Immune complex deposits in subepithelium/intra- membrane demonstrated by thickened capillary wall by H&E, spikes or bubbly appearance of the GBM by silver stain.

- Clinical risk:
    - Low risk: NS with proteinuria < 4 g/day and normal renal function
    - Intermediate risk: NS with proteinuria 4-8 g/day and normal renal function
    - High risk: NS with proteinuria > 8 g/day or impaired renal function without other specific causes
- Complete remission: 24-hour urine protein < 0.3 g/day or UPCR < 0.3 g/g.Cr x 2 times ≥ 1 week apart; AND normal serum albumin; AND stable creatinine (± 25% SCr)
- Partial remission: 24-hour urine protein < 3.5 g/day or UPCR < 3.5 g/g.Cr; AND decrease ≥ 50% from peak values x 2 times ≥ 1 week apart; AND improve serum albumin; AND stable creatinine (± 25% SCr)
- Resistant: Failure to achieve remission after initial therapy (6 months)
- Relapse:
    - Mild: Redevelop subnephrotic proteinuria after complete remission
    - NS: Redevelop NS after remission

Mesangium: The mesangium has two components. The extracellular one, mesangial matrix, has many structural, compositional, and, therefore, tinctorial properties similar to basement membrane. The cells of the mesangium are known as mesangial cells.

- Hyperplasia/proliferation: Increased in mesangial cell usually ≥ 3 cells per cluster/lobule.
- Expansion: Increase in mesangial matrix. This may be uniform and disuse pattern in all lobules or cause a nodular appearance to the mesangium.

- Sclerosis (glomerular scarring): Increased extracellular matrix and other material leading to obliteration of capillaries and solidification of all or part of the turfs. Sclerosis may be associated with obliteration of the urinary space by collagen along with increased extracellular matrix in the capillary tufts.
- Mesangiolysis: Dissolution or attenuation of mesangial matrix and degeneration of mesangial cells.

Minimal change disease: A glomerular disease characterized by structurally normal glomeruli in light microscopy from adequate biopsy and extensive foot process effacement in electron microscopy with lack of significant evidence of immune complexes in both immunofluorescent study and electron microscopy. Clinical response are shown in FSGS.

Mucoid intimal hyperplasia: Thickening of the tunica intima of a blood vessel by translucent material deposit in H&E stain.

Nephritic syndrome:

- RBC > 3 cells/HPF, or RBC cast; AND
- 24-hour urine protein < 3.5 g/day, or UPCR < 3.5 g/g.Cr; AND
- BP $\geq$ 140/90 mmHg, or edema, or oliguria (urine < 400 ml/day), or eGFR (CKD-EPI) < 90 ml/min/1.73 m^2

Nephrotic syndrome (NS):

- 24-hour urine protein $\geq$ 3.5 g/day, or UPCR $\geq$ 3.5 g/g.Cr; AND
- Hypoalbuminemia < 3.5 g/dL

Nephrotic nephritic syndrome:

- RBC > 3 cells/HPF, or RBC cast; AND
- 24-hour urine protein $\geq$ 3.5 g/day, or UPCR $\geq$ 3.5 g/g.Cr; AND
- BP $\geq$ 140/90 mmHg, or edema, or oliguria (urine < 400 ml/day)

Nodular sclerosis: Rounded expansion of mesangial matrix and/or cells.

Onion-skin appearance/concentric intimal hyperplasia: Thickening of the tunica intima of a blood vessel by smooth muscle cells infiltration and collagen deposits.

Postinfectious glomerulonephritis: A kidney disease follows after an infection. It is characterized by diffuse global dilated capillary lumen, hypercellularity of endothelial and Mesangial cells

accompanied with influx of inflammatory cells especially neutrophilic granulocytes and monocytes. Immunofluorescence studies in biopsies taken during the first 2-3 weeks of the disease most often show diffuse, irregular, coarse granular deposits of IgG and C3 along the glomerular capillary walls. Electron microscopy showing large subepithelial electron dense deposits ("humps") with obliteration of visceral epithelial pedicles.

Pseudocrescent: Dedifferentiated podocytes hyperplasia/hypertrophy found in collapsing glomerulonephritis.

Rapidly progressive glomerulonephritis (RPGN):

- Progressive decline of eGFR within 3 months; AND
- RBC > 3 cells/HPF, or RBC cast; AND
- 24-hour urine protein > 500 mg/day, or UPCR 0.5 g/g.Cr
- Usually BP $\geq$ 140/90 mmHg, or edema, or oliguria (urine <400 ml/day)

Scleroderma renal disease: Renal morphological changes in systemic sclerosis, including scleroderma renal crisis ; abrupt renal vascular reaction resembling thrombotic microangiopathy (TMA)

Segmental sclerosis: Obliteration of capillary lumens by increased extracellular matrix involving part of a glomerulus.

Thin basement membrane: GBM thickness < 200 nm. No specific lesion on light microscopy. Negative standard IF studies.

Thrombotic microangiopathy (TMA): Fibrin (chunky eosinophilic material) and platelet thrombi primarily found in glomerular capillary best visualized on hematoxylin and eosin or silver stains. Lesions may extend to arterioles. Mesangiolysis occurs frequently but is focal seen. Mesangial areas seem to "unravel", resulting in very long, sausage-shape capillary loop due to the loss of mesangial integrity and coalescence of adjoining loop.

Tubular atrophy: Tubular change with light microscopic appearance including simplified tubular cells with reduction in cell size, luminal dilation with or without intratubular casts or narrow to absence of lumen and usually thickened basement membrane.

Tubular cytopathic change: Specific cellular change indicative of viral infection usually presents with dense nuclear and/or cytoplasmic inclusions.

Tubular injury/necrosis: Loss of brush border, flattening, sloughing, denudation or karyolysis of tubular epithelium.

Tubular regeneration: Tubular change with histologic indicators of cellular proliferation including mitoses, hyperchromatic nuclei and a high nuclear cytoplasmic ratio.

Tubular vacuolization: Vacuolization of tubular cytoplasm.

Tubulitis: Leukocytic infiltrate in tubules

Tubulointerstitial foam cell: Lipid-containing cells in interstitium and/or tubules.

Tubulorrhexis: Rupture of the tubular basement membrane.