Overzicht van relevante classificatiesystemen in de nefropathologie

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Overzicht

- IgA nefropathie
- SLE
- Diabetische nefropathie
- ANCA-gerelateerde glomerulonefritis
- Proliferatieve glomerulonefritis

- Chroniciteitsgradering (bij alle diagnoses van toepassing)

Ig A nephropathy

- Oxford/MEST-C score

Table 1 MEST-C criteria in the updated Oxford Classification of IgA Nephropathy

Table 1 | **MEST-C criteria in the updated Oxford Classification of IgA Nephropathy**[3]

Histological variable	Definition	Score
Mesangial hypercellularity	More than four mesangial cells in any mesangial area of a glomerulus	• M0: <50% of glomeruli showing mesangial hypercellularity • M1: >50% of glomeruli showing mesangial hypercellularity
Endocapillary hypercellularity	Hypercellularity due to an increased number of cells within glomerular capillary lumina	• E0: no endocapillary hypercellularity • E1: any glomeruli showing endocapillary hypercellularity
Segmental glomerulosclerosis	Adhesion or sclerosis (obliteration of capillary lumina by matrix) in part but not the whole glomerular tuft	• S0: absent • S1: present in any glomeruli
Tubular atrophy/ interstitial fibrosis	Estimated percentage of cortical area showing tubular atrophy or interstitial fibrosis, whichever is greater	• T0: 0–25% of cortical area • T1: 26–50% of cortical area • T2: >50% of cortical area
Cellular or fibrocellular crescents	Percentage of glomeruli with cellular or fibrocellular crescents	• C0: absent • C1: 0–25% of glomeruli • C2: ≥25% of glomeruli

M, mesangial hypercellularity; C, crescents; E, endocapillary hypercellularity; S, segmental glomerulosclerosis; T, tubular atrophy/interstitial fibrosis. Modified with permission from Macmillan Publishers Limited © Roberts, I. S. D. *Nat. Rev. Neph.* **8**, 445–454 (2014).

Markowitz, G. (2017) Updated Oxford Classification of IgA nephropathy: a new MEST-C score
Nat. Rev. Nephrol. doi:10.1038/nrneph.2017.67

Verdere ontwikkelingen

- **Onderverdelen van S1-lesies**:

-S1 lesions with podocyte hypertrophy and/or tip lesions

-S1 lesions without podocyte hypertrophy and/or tip lesions

- Dit is nog geen verplicht item, nog niet onafhankelijk gevalideerd. (Mag maar hoeft dus niet)

- A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society*: Ian S D Roberts[1] et al. The Oxford classification of IgA nephropathy: pathology definitions, correlations, and reproducibility. *Kidney International* (2009) **76,** 546–556.
- A Working Group of the International IgA Nephropathy Network and the Renal Pathology Society*: Daniel C Cattran [et] al. The Oxford classification of IgA nephropathy: rationale, clinicopathological correlations, and classification. *Kidney International* (2009) **76,** 534–545

- IgAN Classification Working Group: Oxford Classification of IgA nephropathy 2016:

an update from the IgA Nephropathy Classification Working Group. Kidney International (2017) 91, 1014–1021

- Bellur et al. Evidence from the Oxford Classification cohort supports the clinical value of subclassification of focal segmental glomerulosclerosis in IgA nephropathy

SLE

- ISN/RPS

Table 3. International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification of lupus nephritis

Class I	**Minimal mesangial lupus nephritis** Normal glomeruli by light microscopy, but mesangial immune deposits by immunofluorescence
Class II	**Mesangial proliferative lupus nephritis** Purely mesangial hypercellularity of any degree or mesangial matrix expansion by light microscopy, with mesangial immune deposits May be a few isolated subepithelial or subendothelial deposits visible by immunofluorescence or electron microscopy, but not by light microscopy
Class III	**Focal lupus nephritis**[a] 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
Class III (A)	Active lesions: focal proliferative lupus nephritis
Class III (A/C)	Active and chronic lesions: focal proliferative and sclerosing lupus nephritis
Class III (C)	Chronic inactive lesions with glomerular scars: focal sclerosing lupus nephritis
Class IV	**Diffuse lupus nephritis**[b] Active or inactive diffuse, 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(IV-S) lupus nephritis when ≥50% of the involved glomeruli have segmental lesions, and diffuse global (IV-G) lupus nephritis when ≥50% of the involved glomeruli have global lesions. Segmental is defined as a glomerular lesion that involves less than half of the glomerular tuft. This class includes cases with diffuse wire loop deposits but with little or no glomerular proliferation
Class IV-S (A)	Active lesions: diffuse segmental proliferative lupus nephritis
Class IV-G (A)	Active lesions: diffuse global proliferative lupus nephritis
Class IV-S (A/C)	Active and chronic lesions: diffuse segmental proliferative and sclerosing lupus nephritis Active and chronic lesions: diffuse global proliferative and sclerosing lupus nephritis
Class IV-S (C)	Chronic inactive lesions with scars: diffuse segmental sclerosing lupus nephritis
Class IV-G (C)	Chronic inactive lesions with scars: diffuse global sclerosing lupus nephritis
Class V	**Membranous lupus nephritis** Global or segmental subepithelial immune deposits or their morphologic sequelae by light microscopy and by immunofluorescence or electron microscopy, with or without mesangial alterations Class V lupus nephritis may occur in combination with class III or IV in which case both will be diagnosed Class V lupus nephritis show advanced sclerosis
Class VI	**Advanced sclerosis lupus nephritis** ≥90% of glomeruli globally sclerosed without residual activity

[a] Indicate the proportion of glomeruli with active and with sclerotic lesions.
[b] Indicate the proportion of glomeruli with fibrinoid necrosis and/or cellular crescents.
Indicate and grade (mild, moderate, severe) tubular atrophy, interstitial inflammation and fibrosis, severity of arteriosclerosis or other vascular lesions.

vermelden van A/C (activiteit en chroniciteit) niet meer vereist

- Jan J. Weening et al. ON BEHALF OF THE INTERNATIONAL SOCIETY OF NEPHROLOGY and RENAL PATHOLOGY SOCIETY WORKING GROUP ON THE CLASSIFICATION OF LUPUS NEPHRITIS. The Classification of Glomerulonephritis in Systemic Lupus Erythematosus Revisited. J Am Soc Nephrol 2004;15: 241–250
- Ingeborg Bajema et al. Revision of the THE INTERNATIONAL SOCIETY OF NEPHROLOGY/ RENAL PATHOLOGY SOCIETY CLASSIFICATION OF LUPUS NEPHRITIS: clarification of definitions, and modified National Instituses of Health activity and chronicity indices. Kidney Int 2018; 93:789-796

Table 2 | Proposed modified NIH lupus nephritis activity and chronicity scoring system

Modified NIH activity index	Definition	Score
Endocapillary hypercellularity	Endocapillary hypercellularity in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Neutrophils/karyorrhexis	Neutrophils and/or karyorrhexis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Fibrinoid necrosis	Fibrinoid necrosis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	(0–3) × 2
Hyaline deposits	Wire loop lesions and/or hyaline thrombi in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Cellular/fibrocellular crescents	Cellular and/or fibrocellular crescents in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	(0–3) × 2
Interstitial Inflammation	Interstitial leukocytes in <25% (1+), 25%–50% (2+), or >50% (3+) in the cortex	0–3
Total		***0–24***
Modified NIH chronicity index	**Definition**	**Score**
Total glomerulosclerosis score	Global and/or segmental sclerosis in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Fibrous crescents	Fibrous crescents in <25% (1+), 25%–50% (2+), or >50% (3+) of glomeruli	0–3
Tubular atrophy	Tubular atrophy in <25% (1+), 25%–50% (2+), or >50% (3+) of the cortical tubules	0–3
Interstitial fibrosis	Interstitial fibrosis in <25% (1+), 25%–50% (2+), or >50% (3+) in the cortex	0–3
Total		***0–12***

NIH, National Institutes of Health.

Optioneel voor FCGG, niet vereist

Bajema et al. Kidney Int 2018

Diabetic nephropathy

- Cohen Tervaert

Table 1. Glomerular classification of DN

Class	Description	Inclusion Criteria
I	Mild or nonspecific LM changes and EM-proven GBM thickening	Biopsy does not meet any of the criteria mentioned below for class II, III, or IV GBM > 395 nm in female and >430 nm in male individuals 9 years of age and older[a]
IIa	Mild mesangial expansion	Biopsy does not meet criteria for class III or IV Mild mesangial expansion in >25% of the observed mesangium
IIb	Severe mesangial expansion	Biopsy does not meet criteria for class III or IV Severe mesangial expansion in >25% of the observed mesangium
III	Nodular sclerosis (Kimmelstiel–Wilson lesion)	Biopsy does not meet criteria for class IV At least one convincing Kimmelstiel–Wilson lesion
IV	Advanced diabetic glomerulosclerosis	Global glomerular sclerosis in >50% of glomeruli Lesions from classes I through III

LM, light microscopy.

[a]On the basis of direct measurement of GBM width by EM, these individual cutoff levels may be considered indicative when other GBM measurements are used.

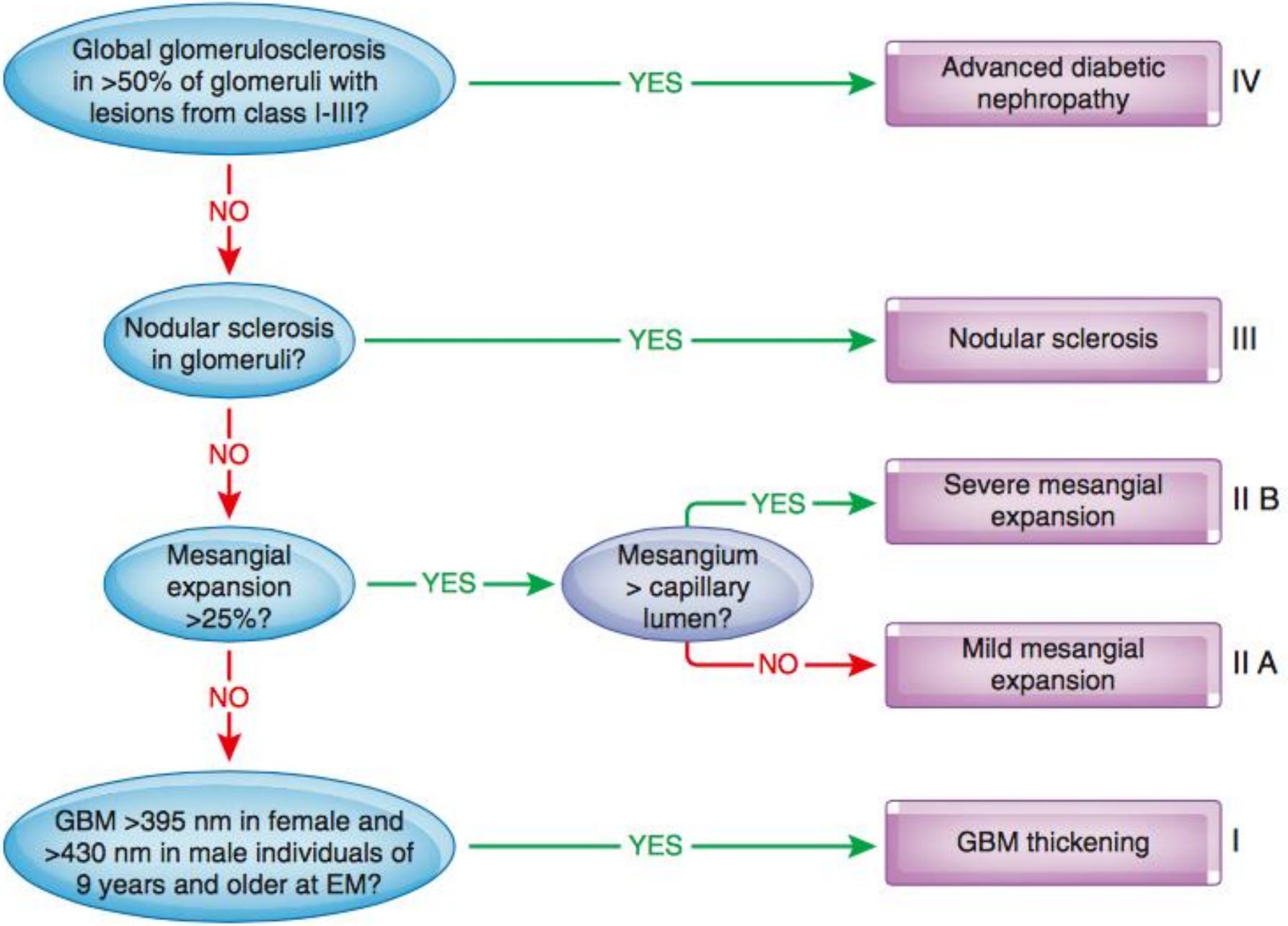


Figure 2. Flow chart for classifying DN.

- Thijs W. Cohen Tervaert et al. on behalf of the Renal Pathology Society. Pathologic Classification of Diabetic Nephropathy. J Am Soc Nephrol 21: 556–563, 2010

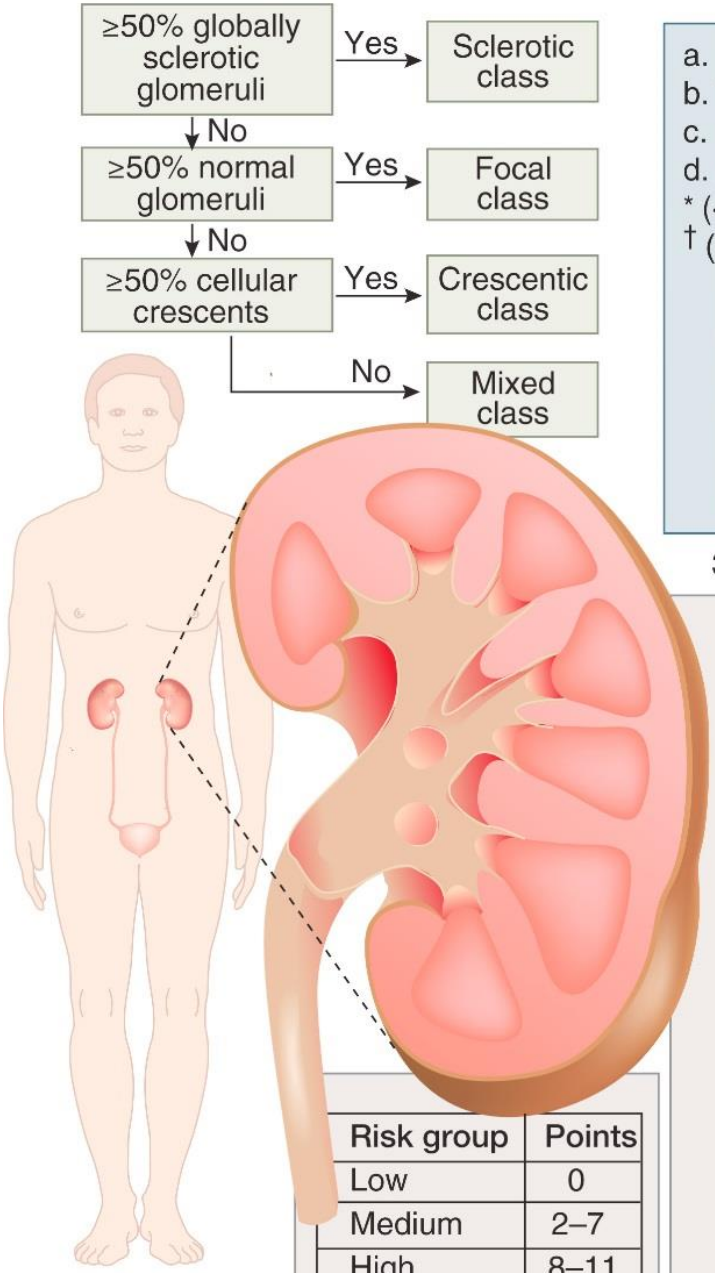
ANCA-associated glomerulonephritis

- EUVAS/Berden

of

- Brix renal risk score

1. Berden classification



Risk group	Points
Low	0
Medium	2–7
High	8–11

2. Mayo Clinic/Renal Pathology Society Chronicity Score (CS)

a. Global and segmental glomerulosclerosis*
b. Tubular atrophy*
c. Interstitial fibrosis*
d. Arteriosclerosis†

* (<10% = 0, 10%–25% = 1, 26%–50% = 2, ≥50% = 3)
† (intimal thickening ≥ media thickness = 1)

Score	Points
Minimal	0–1
Mild	2–4
Moderate	5–7
Severe	≥8

3. ANCA renal risk score (ARRS)

Percentage of normal glomeruli	Points
N_0 (>25%)	0
N_1 (10%–25%)	4
N_2 (<10%)	6

Tubular atrophy and interstitial fibrosis	
T_0 (≤25%)	0
T_1 (>25%)	2

Renal function at the time of diagnosis (GFR)	
G_0 (>15 ml/min per 1.73 m^2)	0
G_1 (≤15 ml/min per 1.73 m^2)	3

FSGS

- Columbia

Table 3. Morphological Classification of FSGS

Variant	Inclusion Criteria	Exclusion Criteria
FSGS (NOS)	At least 1 glomerulus with segmental increase in matrix obliterating the capillary lumina There may be segmental glomerular capillary wall collapse without overlying podocyte hyperplasia	Exclude perihilar, cellular, tip, and collapsing variants
Perihilar variant	At least 1 glomerulus with perihilar hyalinosis, with or without sclerosis >50% of glomeruli with segmental lesions must have perihilar sclerosis and/or hyalinosis	Exclude cellular, tip, and collapsing variants
Cellular variant	At least 1 glomerulus with segmental endocapillary hypercellularity occluding lumina, with or without foam cells and karyorrhexis	Exclude tip and collapsing variants
Tip variant	At least 1 segmental lesion involving the tip domain (outer 25% of tuft next to origin of proximal tubule) The tubular pole must be identified in the defining lesion The lesion must have either an adhesion or confluence of podocytes with parietal or tubular cells at the tubular lumen or neck The tip lesion may be cellular or sclerosing	Exclude collapsing variant Exclude any perihilar sclerosis
Collapsing variant	At least 1 glomerulus with segmental or global collapse and overlying podocyte hypertrophy and hyperplasia	None

- Vivette D'Agati et al. Pathologic classification of focal segmental glomerulosclerosis: a working proposal. Am J Kidney Dis 2004;43:368-382.

Proliferative glomerulonephritis

- Sethi

Table 1. Classification of GN

Pathogenic Type	Specific Disease Entity	Pattern of Injury: Focal or Diffuse	Scores or Class
Immune-complex GN[a]	IgA nephropathy, IgA vasculitis, lupus nephritis, infection-related GN, fibrillary GN with polyclonal Ig deposits	Mesangial, endocapillary, exudative, membranoproliferative, necrotizing, crescentic, sclerosing, or multiple[b]	Oxford/MEST scores for IgA nephropathy ISN/RPS class for lupus nephritis
Pauci-immune GN	MPO-ANCA GN, proteinase 3-ANCA GN, ANCA-negative GN	Necrotizing, crescentic, sclerosing, or multiple[b]	Focal, crescentic, mixed, or sclerosing class (Berden/EUVAS class)
Anti-GBM GN	Anti-GBM GN	Necrotizing, crescentic, sclerosing, or mixed[b]	
Monoclonal Ig GN[a]	Monoclonal Ig deposition disease, proliferative GN with monoclonal Ig deposits, immunotactoid glomerulopathy, fibrillary GN with monoclonal Ig deposits	Mesangial, endocapillary, exudative, membranoproliferative, necrotizing, crescentic, sclerosing, or multiple[b]	
C3 glomerulopathy	C3 GN, dense deposit disease	Mesangial, endocapillary, exudative, membranoproliferative, necrotizing, crescentic, sclerosing, or multiple[b]	

MEST, mesangial hypercellularity, endocapillary hypercellularity, segmental sclerosis, interstitial fibrosis/tubular atrophy; ISN/RPS, International Society of Nephrology/Renal Pathology Society; EUVAS, European vasculitis study group.

[a]Some pathologists use the terms immune complex–mediated GN, monoclonal Ig–associated GN, *etc.* It is up to the discretion of the pathologist to use these terms.

[b]Multiple patterns include two or more patterns of injury. The patterns should be stated (*e.g.*, focal mesangial proliferative, crescentic, and sclerosing or diffuse necrotizing, crescentic, and sclerosing).

Table 4. Definitions of glomerular lesions derived from the Oxford classification of IgA nephropathy[1,64] and patterns of GN derived from the ISN/RPS lupus classification[22]

Glomerular lesions	
Mesangial hypercellularity	>3 Mesangial cells per mesangial area
Cellular crescent	Extracapillary cell proliferation of more than two cell layers with >50% of the lesion occupied by cells
Fibrocellular crescent	An extracapillary lesion comprising cells and extracellular matrix, with <50% cells and <90% matrix
Fibrous crescent	Extracapillary crescents with >90% matrix
Endocapillary hypercellularity	Hypercellularity caused by an increased no. of cells within glomerular capillary lumina, causing narrowing of the lumina
Fibrinoid necrosis	Disruption of the GBM with fibrin exudation
Sclerosis	Obliteration of the capillary lumen by increased extracellular matrix with or without hyalinosis or foam cells
Patterns of GN	
Minimal mesangial GN[a]	Normal glomeruli by LM but mesangial immune deposits by IF
Mesangial proliferative GN[a]	Purely mesangial hypercellularity
Active (proliferative) GN[a]	Any or all of the following glomerular lesions: endocapillary hypercellularity, karyorrhexis, fibrinoid necrosis, rupture of GBMs, cellular or fibrocellular crescents, subendothelial deposits identifiable by LM, and intraluminal immune aggregates
Necrotizing GN	Segmental or global fibrinoid necrosis
Crescentic GN	≥50% Glomeruli with cellular, fibrocellular, or fibrous crescents (with percentage of crescents always noted in the diagnostic line, even when <50%)[b]
Membranoproliferative GN	Mesangial and/or endocapillary hypercellularity and thickening of capillary walls caused by subendothelial Ig and/or complement factors
Exudative GN	Neutrophils accounting for >50% of glomerular hypercellularity
Sclerosing GN[a]	Any or all of the following glomerular lesions: glomerular sclerosis, fibrous adhesions, and fibrous crescents

ISN/RPS, International Society of Nephrology/Renal Pathology Society.

[a]Except for the first two patterns, multiple patterns can occur together in a single specimen (derived from the ISN/RPS lupus classification[22]).

[b]The term crescentic GN is used when crescents are present in at least 50% of glomeruli, and applies to immune-complex GN/C3 glomerulopathy. This does not apply to ANCA GN and anti-GBM GN, where less than 50% of the glomeruli may be involved by crescents.

Table 2. Basic format of kidney biopsy report

(1) Specimen type: needle biopsy, wedge, *etc.*
(2) Diagnosis
  Primary diagnosis
    Disease process/pathogenic type (*e.g.*, IgA nephropathy, lupus GN, ANCA GN, C3 GN)
    Pattern of glomerular injury (*e.g.*, mesangial proliferative, membranoproliferative, necrotizing/crescentic, and focal and segmental sclerosing)
    Histologic scores or grade (*e.g.*, Oxford/MEST for IgA nephropathy and ISN/RPS for lupus nephritis)
    Additional features (*e.g.*, degree of global glomerulosclerosis, IFTA, vascular sclerosis, clinical modifiers, such as cryoglobulin/clinical HCV, bacterial endocarditis/clinical, staphylococcal cellulitis/clinical)
  Secondary diagnoses (list; *e.g.*, acute interstitial nephritis and diabetic glomerulosclerosis); these are not felt to be part of the primary disease
(3) Comment/narrative
  Can be used for summarizing/clarifying morphologic basis of primary and/or secondary diagnoses or clinicopathologic correlations, providing prognostic information, discussing differential diagnosis, and providing appropriate references
(4) Summary of clinical data
(5) Gross description
(6) LM description
(7) IF/IHC
(8) EM
(9) Addendum for special studies

MEST, mesangial hypercellularity, endocapillary hypercellularity, segmental sclerosis, interstitial fibrosis/tubular atrophy; ISN/RPS, International Society of Nephrology/Renal Pathology Society; EUVAS, European vasculitis study group; HCV, hepatitis C virus.

- Sanjeev Sethi et al. Mayo Clinic/Renal Pathology Society Consensus Report on Pathologic Classification, Diagnosis, and Reporting of GN. published ahead of print November 13, 2015, doi:10.1681/ASN.2015060612

Chroniciteitsgradering

Table 1 | Scoring of the chronic lesions in individual renal tissue compartments

Tissue compartment[a]	Score			
	0	1	2	3
Glomerulosclerosis (GS score)	<10%	10–25%	26%–50%	>50%
Interstitial fibrosis (IF score)	<10%	10–25%	26%–50%	>50%
Tubular atrophy (TA score)	<10%	10–25%	26%–50%	>50%
Arteriosclerosis (CV score)	Intimal thickening < thickness of media	Intimal thickening ≥ thickness of media		

[a]GS score includes the percentage of glomeruli with global and segmental sclerosis and ischemic glomeruli; IF and TA score includes the percentage of renal cortex involved by interstitial fibrosis and tubular atrophy, respectively; CV score includes the severity of arteriosclerosis determined by the extent of thickening of the intima.

Voor som: zie volgende slide

Chroniciteitsgradering

Table 2 | Grades of chronic changes based on total renal chronicity score (0–10)

Grade	Total renal chronicity score[a]
Minimal chronic changes	0–1
Mild chronic changes	2–4
Moderate chronic changes	5–7
Severe chronic changes	≥8

[a]Total chronicity score is the sum of individual chronicity scores for each renal tissue compartment as shown in Table 1.

- Sethi et al. A proposal for standardized grading of chronic changes in native kidney biopsy specimens. Kidney Int 2017; 91: 787-789