SPECIAL ARTICLE www.jasn.org

Mayo Clinic/Renal Pathology Society Consensus Report on Pathologic Classification, Diagnosis, and Reporting of GN

Sanjeev Sethi, Mark Haas, Glen S. Markowitz, Vivette D. D'Agati, Helmut G. Rennke, J. Charles Jennette, Ingeborg M. Bajema, Charles E. Alpers, Anthony Chang, Lynn D. Cornell, Fernando G. Cosio, Agnes B. Fogo, Richard J. Glassock, Sundaram Hariharan, Neeraja Kambham, Donna J. Lager, Nelson Leung, Michael Mengel, Karl A. Nath, Ian S. Roberts, Brad H. Rovin, Surya V. Seshan, Richard J.H. Smith, Patrick D. Walker, Christopher G. Winearls, Gerald B. Appel, Mariam P. Alexander, Daniel C. Cattran, Carmen Avila Casado, H. Terence Cook, An S. De Vriese, Jai Radhakrishnan, Lorraine C. Racusen, Pierre Ronco, and Fernando C. Fervenza

*Mayo Clinic, Rochester, Minnesota

ABSTRACT

Renal pathologists and nephrologists met on February 20, 2015 to establish an etiology/pathogenesis-based system for classification and diagnosis of GN, with a major aim of standardizing the kidney biopsy report of GN. On the basis of etiology/pathogenesis, GN is classified into the following five pathogenic types, each with specific disease entities: immune-complex GN, pauci-immune GN, antiglomerular basement membrane GN, monoclonal Ig GN, and C3 glomerulopathy. The pathogenesis-based classification forms the basis of the kidney biopsy report. To standardize the report, the diagnosis consists of a primary diagnosis and a secondary diagnosis. The primary diagnosis should include the disease entity/pathogenic type (if disease entity is not known) followed in order by pattern of injury (mixed patterns may be present); score/grade/class for disease entities, such as IgA nephropathy, lupus nephritis, and ANCA GN; and additional features as detailed herein. A pattern diagnosis as the sole primary diagnosis is not recommended. Secondary diagnoses should be reported separately and include coexisting lesions that do not form the primary diagnosis. Guidelines for the report format, light microscopy, immunofluorescence microscopy, electron microscopy, and ancillary studies are also provided. In summary, this consensus report emphasizes a pathogenesis-based classification of GN and provides guidelines for the standardized reporting of GN.

J Am Soc Nephrol 27: 1278–1287, 2016. doi: 10.1681/ASN.2015060612

A group of renal pathologists and nephrologists met at the Mayo Clinic (Rochester, MN) on February 20, 2015 to reach a consensus on the standardized classification and reporting of GN. The meeting was organized by S.S. and F.C.F. of the Mayo Clinic, endorsed by the Renal Pathology Society, and funded by an independent educational grant from the Fulk Foundation. The meeting opened with the identification of a major need for standardization of kidney pathology reporting in GN. Currently, the classification and reporting of GN are not standardized, which is disadvantageous for patient care, limits the ability to compare data between institutions, and hampers multicenter clinical and basic research. The focal point of the meeting was to recommend an etiology/pathogenesis-based classification of GN and standardize pathology reporting of GN. This manuscript describes the recommendations resulting from this meeting. The manuscript does not extend to other forms of glomerular diseases, such as membranous nephropathy, podocytopathies, and thrombotic microangiopathy.

GUIDELINES ON CLASSIFICATION OF GN

GN includes diseases characterized by increased glomerular cellularity caused by proliferation of indigenous cells and/or leukocyte infiltration. On the basis of pathogenesis/pathogenic type, there are five classes of GN: immune-complex GN,

Published online ahead of print. Publication date available at www.jasn.org.

Correspondence: Dr. Sanjeev Sethi and Dr. Fernando Fervenza, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905. Email: sethi.sanjeev@mayo.edu or fervenza.fernando@mayo.edu

pauci-immune GN, antiglomerular basement membrane antibody (anti-GBM) GN, monoclonal Ig GN, and C3 glomerulopathy (Table 1). The classification is primarily on the basis of the findings by immunofluorescence microscopy (IF) or less commonly, immunohistochemistry (IHC) integrated with light microscopy (LM) and electron microscopy (EM).

Immune-complex GN is characterized by granular deposits of polyclonal Ig on IF or IHC. Complement is often codeposited along with the Ig. The type and location of the immune deposits often point to the underlying etiology. Immune-complex GN includes specific disease entities, such as IgA nephropathy, lupus nephritis, and fibrillary GN,[1–4] with the understanding that fibrillary GN may not represent true immune–complex GN in the sense of antigen-antibody complexes. Immune-complex GN also includes GN resulting from infections and autoimmune diseases other than SLE.[5–14] Indeed, infections are an important cause of immune-complex GN in both developing and developed countries.[15–20] The pattern of glomerular injury is variable, and depending, in part, on the etiology, there may be no lesion by LM, mesangial proliferative, endocapillary proliferative, exudative, membranoproliferative, necrotizing and crescentic, sclerosing, or a combination of these patterns. Some forms of GN (*e.g.*, lupus nephritis) may have mixed membranous and proliferative patterns.

Pauci–immune necrotizing and crescentic GN is characterized by negative or few Ig deposits on IF or IHC[21,22]; 80%–90% of patients have serologic evidence of ANCA, and as such, this category has been referred to as ANCA-associated GN (ANCA GN) whereas the remaining patients are termed ANCA-negative GN.[23,24] The principal antigens targeted by ANCA include myeloperoxidase (MPO) and proteinase 3 (PR3). On the basis of the clinicopathologic findings ANCA GN is classified according to the Chapel Hill Consensus as microscopic polyangiitis, granulomatosis with polyangiitis, or eosinophilic granulomatosis with polyangiitis.[25] The diagnosis of ANCA GN should include both the clinicopathologic phenotype and the ANCA specificity (*e.g.*, MPO-ANCA microscopic polyangiitis).[25] Cellular, fibrocellular, and fibrous crescents may be present depending on the stage of the disease process.

Anti-GBM GN is characterized by linear deposits of Ig, most often IgG, and frequently, C3 along the GBM on IF or IHC, and it is confirmed by detection of circulating anti–GBM antibodies. The linear Ig staining characterizes this form of GN and contrasts with the granular deposits usually seen in immune-complex GN or smudgy deposits seen in fibrillary GN. Most active anti–GBM GN is characterized by a severe necrotizing and crescentic pattern; ≤25% of patients with anti-GBM GN also have circulating ANCA.[26–28]

Monoclonal Ig GN is characterized by monotypic Ig deposits in the glomeruli and/or along tubular basement membranes on IF or IHC.[29–31] Monoclonal Ig GN is associated with an underlying monoclonal gammopathy/paraproteinemia in many but not all patients.[32] Specific disease entities in this category that have diagnostic features by IF/IHC and EM include proliferative forms of monoclonal Ig deposition disease, immunotactoid GN, and rare patients of fibrillary GN with monoclonal Ig deposits.[3,4,33,34] In the absence of these distinct patterns, GN with monotypic Ig glomerular deposits on IF/IHC and mesangial/capillary wall deposits on EM is labeled as proliferative GN with monoclonal Ig deposits.[29–31,35] Although a membranoproliferative pattern is most common, other patterns, including mesangial proliferative, diffuse proliferative, necrotizing and crescentic, or sclerosing, may be present.

C3 glomerulopathy is characterized by the presence of dominant C3 deposits in the glomeruli with minimal or no Ig

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).

deposits on IF or IHC.[36–40] C3 glomerulopathy is associated with abnormalities in regulation of the alternative pathway of complement. C3 glomerulopathy is further categorized as dense deposit disease or C3 GN on the basis of EM findings. The pattern of glomerular injury in C3 glomerulopathy is variable and can be mesangial proliferative, diffuse endocapillary proliferative, membranoproliferative, necrotizing and crescentic, or sclerosing GN.[38,39]

GUIDELINES FOR BASIC STRUCTURE OF THE KIDNEY BIOPSY REPORT

The basic report structure should include the following reporting fields: specimen type, diagnosis (which includes a primary diagnosis and secondary diagnoses if present), comment, clinical data, gross description, LM description, IF findings, EM description, and addendum for special studies (Table 2). The main sections of the kidney biopsy report are discussed in the following paragraphs.

GUIDELINES FOR NOMENCLATURE FOR THE PRIMARY DIAGNOSIS

The primary diagnosis (examples are shown in Table 3) is composed of three or four components in the following order: (*1*) disease entity or pathogenesis/pathogenic type (when specific disease entity is not known), (*2*) pattern of glomerular injury, (*3*) scores and/or class of the disease entity where appropriate, and (*4*) additional disease–related features. In some instances, when two distinct processes are contributing to the patient's renal dysfunction, more than one primary diagnosis may be listed in order (*e.g.*, ANCA GN and IgA nephropathy).

First, the disease entity or pathogenesis/pathogenic type should be written. If the disease entity is known, it takes precedence over the pathogenesis/pathogenic type.

Second, the pattern of injury should be listed. The GN may be focal or diffuse and segmental or global. The basic patterns of injury include no lesion by LM, mesangial proliferative, exudative, endocapillary proliferative, membranoproliferative, crescentic, necrotizing, and sclerosing GN. The percentage of glomeruli with crescents should be mentioned. Multiple patterns may be present, and in such patients, the different patterns should be listed. A pattern diagnosis as the sole primary diagnosis is not recommended. The definitions of glomerular lesions and patterns are given in Table 4.

Third, standardized scores and/or classes of the GN should be added as part of the primary diagnosis as applicable. Thus, Oxford/MEST (mesangial hypercellularity, endocapillary hypercellularity, segmental sclerosis, interstitial fibrosis/tubular atrophy) score, International Society of Nephrology/Renal Pathology Society class for lupus nephritis, and prognostic (Berden/European vasculitis study group) class for ANCA GN should be part of the primary diagnosis.[1,2,41]

Fourth, additional features, including clinical modifiers (where appropriate), that suggest the underlying etiology may be stated here. For example, an infection-related GN that is IgA dominant on IF suggests an underlying staphylococcal infection, and if known, pathogen and the site of infection may be stated here (*e.g.*, associated with *Staphylococcus aureus* cellulitis).[9,11,42] In patients with anti-GBM nephritis with both anti-GBM antibody and positive ANCA serology, the clinical modifier anti-GBM antibody and ANCA-associated/clinical should be added. An immune-complex GN with a membranoproliferative pattern of injury and polyclonal IgM/IgG on IF suggesting an infectious etiology may require a clinical modifier such as associated with hepatitis C/clinical if the infectious agent is known or associated with cryoglobulinemia and hepatitis C/clinical if both cryoglobulins and hepatitis C are known to be present. In the setting of monoclonal Ig GN, the presence of cryoglobulin-like deposits on LM and IgMκ on IF may require a modifier (Waldenström macroglobulinemia/clinical) if the patient is known to have Waldenström macroglobulinemia. A clinical modifier to indicate that a

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.

Table 3. Some examples of GN diagnoses

(*1*) IgA nephropathy
- Primary diagnosis: IgA nephropathy
- Pattern of injury: diffuse mesangial and focal segmental endocapillary proliferative and sclerosing GN
- Score/grade: Oxford classification: M1 E1 S1 T1
- Additional features: focal global glomerulosclerosis (20%), moderate tubular atrophy and interstitial fibrosis (30%), mild arteriosclerosis and hyaline arteriolosclerosis
- Secondary diagnoses: diabetic nephropathy, mild

(*2*) Lupus nephritis
- Primary diagnosis: (*1*) lupus nephritis and (*2*) thrombotic microangiopathy
- Pattern of injury: diffuse proliferative and sclerosing GN with focal (10%) cellular crescents
- Score/grade: ISN/RPS class IV-G (A/C)
- Additional features: thrombotic microangiopathy associated with antiphospholipid antibodies/clinical, focal global glomerulosclerosis (10%), mild tubular atrophy and interstitial fibrosis (10%), moderate arteriosclerosis, and moderate hyaline arteriolosclerosis

(*3*) Hepatitis C–associated immune–complex GN
- Primary diagnosis: immune-complex GN
- Pattern of injury: membranoproliferative GN
- Additional features: with features of cryoglobulinemic GN (hepatitis C/clinical), focal global glomerulosclerosis (20%), moderate tubular atrophy and interstitial fibrosis (30%), moderate arteriosclerosis, and moderate hyaline arteriolosclerosis

(*4*) Infection-related GN
- Primary diagnosis: IgA–dominant infection–related GN
- Pattern of injury: diffuse exudative GN
- Additional features: associated with *S. aureus* cellulitis infection/clinical, focal global glomerulosclerosis (30%), moderate tubular atrophy and interstitial fibrosis (30%), moderate arteriosclerosis, and moderate hyaline arteriolosclerosis
- Secondary diagnoses: diabetic nephropathy, moderate

(*5*) ANCA GN
- Primary diagnosis: proteinase 3-ANCA GN[a]
- Pattern of injury: necrotizing and crescentic GN
- Prognostic class: focal (≥50% normal glomeruli)
- Additional features: clinicopathologic features of granulomatosis with polyangiitis (proteinase 3 and cytoplasmic ANCA/clinical), focal global glomerulosclerosis (10%), mild tubular atrophy and interstitial fibrosis (10%), mild arteriosclerosis, and moderate hyaline arteriolosclerosis

(*6*) Anti-GBM GN
- Primary diagnosis: anti-GBM GN
- Pattern of injury: necrotizing and crescentic GN, severe
- Additional features: clinicopathologic features of Goodpasture syndrome (anti-GBM antibody/clinical), focal global glomerulosclerosis (40%), moderate tubular atrophy and interstitial fibrosis (40%), mild arteriosclerosis, and moderate hyaline arteriolosclerosis

(*7*) Monoclonal Ig GN
- Primary diagnosis: monoclonal Ig GN
- Pattern of injury: membranoproliferative GN with intracapillary hyaline thrombi (pseudothrombi)
- Additional features: IgM κ-staining of glomerular intracapillary deposits consistent with type 1 cryoglobulins (Waldenström macroglobulinemia/type 1 cryoglobulins/clinical), focal global glomerulosclerosis (30%), moderate tubular atrophy and interstitial fibrosis (40%), moderate arteriosclerosis, and moderate hyaline arteriolosclerosis

(*8*) C3 glomerulopathy
- Primary diagnosis: C3 GN
- Pattern of injury: membranoproliferative GN
- Additional features: focal global glomerulosclerosis (20%), mild tubular atrophy and interstitial fibrosis (20%), mild arteriosclerosis, and moderate hyaline arteriolosclerosis

ISN/RPS, International Society of Nephrology/Renal Pathology Society; A/C, active/chronic.
[a]If MPO/PR3 titers are not known, it is acceptable to label as ANCA GN.

thrombotic microangiopathy is associated with antiphospholipid antibodies in lupus nephritis should be included here if it is felt that these reflect a component of the primary disease.

Additional features also include the proportion of globally sclerotic glomeruli, extent of interstitial fibrosis and tubular atrophy (IFTA), and severity of vascular changes, including arterial intimal sclerosis (arteriosclerosis) and arteriolar thickening and hyalinization (arteriolosclerosis). The severity of vascular sclerosis may be reported as mild, moderate, or severe.

Although the report deals with GN, chronic changes may result from additional lesions present on the biopsy. In such patients, the contribution of the separate lesions to the chronic changes may be mentioned in the comment section.

The distinct advantage of this format of reporting is that it is etiology and pathogenesis oriented.[43–45] The report is adaptable to include new diseases, it is suitable to fit databases, and it is standardized and most importantly, patient centered by providing relevant information for targeted, mechanism–based treatment approaches.

GUIDELINES ON SECONDARY DIAGNOSES

Secondary diagnoses include coexisting lesions that do not form the primary diagnosis. These include underlying glomerular diseases, such as diabetic glomerulosclerosis and thin GBM nephropathy. Similarly, tubulointerstitial or vascular findings unrelated to the primary diagnosis, such as drug–induced interstitial nephritis, acute tubular injury, atheroembolic disease, *etc.*, should also be listed as secondary diagnoses. However, glomerular findings etiologically related to the primary diagnosis, such as thrombotic microangiopathy in lupus nephritis, should be included within the primary diagnosis with a clinical modifier, such as lupus anticoagulant/clinical or anticardiolipin antibody/clinical if these are known (Table 3, example 2). Tubulointerstitial

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.

inflammation or acute tubular injury that is a component of the primary disease may be listed with the primary diagnosis or simply described in the LM report (*e.g.*, mild to moderate inflammation that often accompanies crescentic and other severe forms of GN). This is at the discretion of the renal pathologist and should relate to the severity of the tubulointerstitial process and its perceived contribution to the patient's clinical presentation.

Also note that, although the main focus of the report is on GN, a nonproliferative glomerular, tubulointerstitial, or vascular lesion may be the primary diagnosis in light of the clinical indications of the biopsy, and the GN may be the secondary diagnosis; also, there may be more than one primary diagnosis if the pathologist feels that they are of similar clinical importance (Table 3, example 2).

GUIDELINES ON COMMENT

The comment should summarize the biopsy findings and discuss their implications and how they relate to the clinical presentation. If required, a differential diagnosis of the findings may be included with a discussion of why one diagnosis might be favored and the evidence supporting or opposing each potential diagnosis. If pertinent, the comment should explain the score/grade, prognosis of the disease, and risk of recurrence in renal allografts. Key literature references may be added in this section.

GUIDELINES ON CLINICAL DATA

A brief overview of the clinical data should be included in the report. These data must be provided by the nephrologist who submits the specimen for pathologic evaluation. These consist of the patient's age, sex, ethnicity, acute kidney disease versus CKD, and indication for the kidney biopsy (*e.g.*, hematuria, proteinuria, elevated creatinine, or others [for example, biopsy for prognostic purposes]). Pertinent clinical findings, such as fatigue, edema, shortness of breath, hemoptysis, rash, infection, *etc.*, should be included. Coexisting diseases, such as diabetes, hypertension, and lymphoproliferative disorders, and a brief drug history (including pertinent past exposures) should be mentioned as well as any relevant family history. Laboratory findings to be included are serum creatinine, urinalysis and proteinuria per 24 hours or urine protein-to-creatinine ratio, serum complement levels (C3 and C4), protein electrophoresis, and serologic findings, such as antinuclear antibody and anti-double stranded DNA titers, ANCA (anti-MPO and anti-PR3), hepatitis serologies, and cryoglobulin titers as appropriate. Any pertinent microbiology results should be stated.

GUIDELINES ON GROSS DESCRIPTION

The number, size of cores, and fixative(s) in which the tissue is received for LM, IF, and EM should be stated. Poorly preserved tissue (*e.g.*, dry tissue with no fixative or leaking fixative) should be documented. Documentation should be made if tissue from a single (*e.g.*, formalin) vial is allocated for EM as well as LM.

Table 5. Guidelines for LM

Glomeruli
No. of glomeruli, including no. of globally and segmentally sclerosed and ischemic glomeruli
Focal versus diffuse and segmental versus global findings
Hypercellularity: mesangial, endocapillary, or exudative
Crescents: no./percentage, type (cellular, fibrocellular, or fibrous), and size (segmental or circumferential)
Fibrinoid necrosis and karyorrhexis
Wire loops, pseudo-(hyaline) microthrombi, and fibrin thrombi
Mesangial matrix expansion and presence of mesangiolysis
GBM thickening/thinning, double-contour formation, and other GBM abnormalities (*e.g.*, spikes)
Disruption of GBM
Disruption of Bowman's capsule
Tubules and interstitium
Interstitial inflammation: type of infiltrate and location
Casts, crystals, and cysts
Acute tubular injury
Tubular basement abnormalities
IFTA: absent, mild, moderate, or severe
Vessels
Arteritis, emboli, and thrombosis
Arteriosclerosis and arteriolosclerosis: absent, mild, moderate, or severe

GUIDELINES ON LM REPORT

General guidelines for LM examination of medical renal biopsies have been described by Chang *et al.*,[46] and essential information to be included in the biopsy report is summarized in Table 5; we will focus here on those aspects most specific to evaluation of GN. The pattern of injury should be described, including whether the lesion is focal or diffuse and segmental or global. Key features include mesangial and endocapillary hypercellularity; infiltration of capillary tufts by leukocytes and whether these are mononuclear cells, neutrophils, or both; presence of necrosis; karyorrhexis and/or crescents; and rupture of GBMs and/or Bowman's capsule. Crescents may be cellular, fibrocellular, or fibrous, and they may be segmental or circumferential (or nearly so). The percentage of glomeruli involved by crescents should be mentioned. Lobular accentuation of the glomerular tufts may be present. Mesangial expansion and capillary wall thickening should be mentioned. Intracapillary fibrin thrombi, hyaline thrombi (pseudothrombi), and wire loops should be noted. The presence of GBM changes, such as vacuoles/pinholes, spikes, or double contours, should be described.

Next, the tubular and interstitial pathology should be described. This includes interstitial inflammation, characteristics of the infiltrate, and presence or absence of granulomas. The location of the infiltrates (*i.e.*, in preserved areas or areas of IFTA) should be mentioned. To indicate the severity of IFTA, which is a key prognostic indicator in many if not all forms of GN, the estimated percentage of IFTA in the cortical area should be given (rounded off to the nearest 5% or 10%). Grades of IFTA scored as mild (10%–25%), moderate (26%–50%), and severe (>50%) are an acceptable form of reporting, with the percentages mentioned in parentheses after the grade. If the amount of interstitial (mononuclear cell) infiltrate is concordant with the amount of IFTA and limited exclusively or mainly to areas of IFTA, it should not be described as a chronic interstitial nephritis to avoid the misinterpretation that a separate or superimposed interstitial nephritis is present. If it seems evident that an interstitial nephritis is present and distinct from the chronic fibrotic changes, this should be described here but also, listed as a secondary diagnosis, with its differential diagnosis given in the comment.

Finally, vascular lesions should be described. Lesions most pertinent to GN include arteritis, thrombotic microangiopathy, and arterio- and arteriolosclerosis caused by hypertension associated with the GN. The severity of vascular sclerosis may be reported as mild, moderate, or severe.

GUIDELINES ON IF REPORT

Again, we will focus on those aspects most specific to evaluation of GN; for general guidelines, refer to the work by Chang *et al.*[46] and Table 6, which summarize essential information to be included in the biopsy report. The optimum panel of stains includes IgG, IgM, IgA, C3, C1q, fibrinogen, albumin, and κ- and λ-light chains, and the report should separately address findings in glomeruli, tubules, interstitium, and blood vessels. The results can be reported in paragraph or tabular form at the discretion of the renal pathologist.

Table 6. Guidelines for IF

No. of glomeruli, including no. of globally sclerosed glomeruli or with other evident lesions
Intensity of staining: negative, ±, 1+, 2+, and 3+
Staining pattern: granular, linear, semilinear, smudgy, and linear accentuation
Location: focal or diffuse; segmental or global; and mesangial, glomerular capillary wall, or both
Interstitial and tubular basement membrane staining: if present
Segmental trapping of C3 and IgM is common in areas of segmental sclerosis or scarring: segmental glomerular tuft or coarse segmental staining
Internal controls: albumin along TBM and GBM, C3 in vessels, and polyclonal IgA casts in tubules

TBM, tubular basement membrane.

For glomerular staining, the report should clearly state whether staining for each immune reactant is seen in some or all glomeruli, whether this is segmental or global, and the location(s) of staining within glomeruli: mesangial, capillary wall, or both. The results should also specify the type of staining. Potential descriptors include (*1*) granular, (*2*) semilinear (*e.g.*, for conditions associated with subendothelial deposits, including immune-complex GN with a membranoproliferative pattern and diffuse proliferative lupus nephritis), (*3*) coarsely granular (*e.g.*, infection-related GN), (*4*) linear (*e.g.*, anti-GBM GN and monoclonal Ig deposition disease), and (*5*) smudgy (*e.g.*, fibrillary GN). Importantly, segmental staining for IgM, C3, and occasionally, C1q is common in areas of segmental sclerosis; this finding should not be described with any of the descriptors provided above. One

possible terminology is segmental glomerular tuft, avoiding the need to specify as mesangial or glomerular capillary wall. The overwhelming majority of biopsies will exhibit at least mild staining for C3 in blood vessels, and tubular casts nearly always will stain for κ- and λ-IgA. It is important to maintain awareness of these as internal positive controls.

KEY DISEASE–SPECIFIC COMMENTS

The type, relative intensity, and pattern of distribution of the various immune reactants are critical to properly diagnose the type of immune-complex GN. Thus, IgA nephropathy is characterized by the presence of mesangial dominant or codominant IgA; lupus nephritis is characterized by presence of mesangial and/or capillary wall deposits of multiple classes of Ig, including IgG, IgA, IgM, and Sjögren syndrome by IgM/IgG; and infection-related GN is usually associated with capillary wall deposits of IgG/IgM in many bacterial infections, dominant IgA in staphylococcal infections, and IgM/IgG in viral infections. C3 is often present and less commonly, C1q along with the Ig in most patients of immune-complex GN.

In pauci-immune GN, the intensity of staining for Ig and complement is typically in the range of negative to 1+ but can reach 2+ in areas of necrosis. Greater intensity of staining or staining for IgA or IgG in areas not involved by necrosis should raise the possibility of the overlap of two separate disease processes (*e.g.*, ANCA GN and IgA nephropathy or ANCA GN and membranous glomerulopathy). Fibrinogen may be present in the distribution of glomerular necrotizing lesions and/or crescents.

Anti-GBM GN is defined by intense and diffuse linear staining for IgG along the GBM. There is linear GBM staining for κ- and λ-light chains with similar intensity. Rarely, linear staining for monoclonal IgG occurs,[47] or linear IgA rather than IgG may be present, indicating an IgA class of anti-GBM antibodies.[48] C3 is often present in a semilinear or granular pattern along the glomerular capillary walls. To avoid confusion with anti-GBM GN, the linear staining seen in diabetic glomerulosclerosis can be called linear accentuation, which is commonly observed for IgG and albumin.

Monoclonal Ig GN is characterized by monotypic Ig deposits in the glomeruli. In the setting of proliferative GN with monoclonal Ig, the deposits frequently stain for a heavy chain (most commonly, IgG, less commonly, IgM, and rarely, IgA) and one of the light chains, either κ and λ.[29–31,49] In some instances, the monotypic deposits may be composed of either a heavy or light chain only. One caveat is that λ-staining may significantly exceed κ-staining in IgA nephropathy. Granular C3 is often present along the monoclonal Ig.

If the intensity of staining for C3 exceeds the intensity of staining for all other immune reactants by two orders of magnitude (*i.e.*, 3+ versus 1+ and 2+ versus ±), the most likely diagnosis is C3 glomerulopathy or an infection-related GN if an obvious history of infection is present.

Awareness of situations in which positive staining may be incorrectly interpreted as signifying immune-complex GN is essential. Examples include (*1*) C3 and IgM in areas of segmental scarring or segmental sclerosis, (*2*) IgG in areas of fibrinoid necrosis in ANCA GN, and (*3*) IgG and/or IgA in protein droplets within podocytes in proteinuric states.

Ischemic and sclerosed glomeruli may be negative for Ig in immune-complex GN.

GUIDELINES ON EM REPORT

EM is a crucial diagnostic tool for glomerular diseases. Data indicate that 20% of renal biopsies cannot be accurately diagnosed without EM, and nearly all of these are glomerular diseases.[50] Processing a sample of renal cortex for EM is recommended for all native renal biopsies. Although there is a small subset of glomerular diseases for which, when diagnostically well established by LM and IF or IHC, elective deferment of EM might be considered, this is done at a risk of missing possible underlying pathology (*e.g.*, early changes of diabetic nephropathy). Examination of stained 1-μm-thick sections of tissue processed for EM should be considered as part of the histologic examination of the biopsy and should be done by the pathologist and not by a technologist. Glomeruli selected for EM study should be representative of the LM findings, and glomeruli showing global or extensive segmental sclerosis or ischemic changes should be avoided. If the EM sample contains no glomeruli or only sclerotic/ischemic glomeruli, paraffin-embedded tissue should be reprocessed for EM when possible. Exceptions to this would be in patients with a diagnosis that is well established by LM and IF/IHC; EM on deparaffinized tissue with its inherent limitations (*e.g.*, accurate determination of GBM thickness[51]) is unlikely to add additional diagnostic information.

The EM portion of the biopsy report may be written in narrative or tabular form and should contain the number of blocks processed, the number of blocks cut, the total number of glomeruli on 1-μm sections cut from these blocks, the number of globally and segmentally sclerotic glomeruli, the number(s) of glomeruli with other lesions (*e.g.*, crescents), and tubulointerstitial and vascular lesions if present. EM findings pertinent to GN to be included in the biopsy report are summarized in Table 7.

Table 7. Guidelines for EM

No. of glomeruli studied by EM, including no. globally sclerosed or with other evident lesions
Glomerular deposits: location, type, quantity, size, and substructure
GBM: architecture, thin/thick, duplication, ischemic changes, and rupture
Endothelium: fenestrations, swelling, and presence of tubuloreticular inclusions
Mesangial matrix: normal/increased and mesangiolysis
Mesangial cellularity: normal/increased
Podocytes: preserved or effaced (%), protein reabsorption granules, and microvillus change
Leukocytes/platelets/fibrin in capillary lumen/Bowman's space
Tubular epithelial and basement membrane abnormalities when present

KEY DISEASE–SPECIFIC COMMENTS

EM studies are helpful in confirming the electron dense deposits of immune-complex GN, monoclonal Ig GN, and C3 glomerulopathy.

Immune-complex GN is characterized by mesangial and/or capillary wall electron dense deposits. Endocapillary proliferative and membranoproliferative patterns of injury are associated with capillary wall deposits, usually subendothelial and in some patients, intramembranous and subepithelial. However, a mesangial proliferative pattern of injury is usually associated with mesangial deposits. Subepithelial humps are typically seen in infection-related GN but may be present in C3 glomerulopathy as well.[9,11,39,52,53] Fibrillary GN is characterized by deposits of nonbranching, randomly oriented fibrils with a diameter typically exceeding that of amyloid fibrils (generally 15–24 nm).[3,4] Tubular substructures may be present indicating cryoglobulins, and other substructures, such as fingerprints, suggest an autoimmune disease along with tubuloreticular inclusions (IFN signature) in endothelial cells.

ANCA GN and anti-GBM GN show few or no electron dense deposits but may show crescents/fibrinoid necrosis with fibrin in the glomerular tufts/Bowman's space.

EM findings are variable in monoclonal Ig GN.[54] Mesangial and mostly, subendothelial and less commonly, subepithelial electron dense deposits are present in proliferative GN with monoclonal Ig deposits.[29,30] Punctate, finely granular deposits in the mesangium along the inner (subendothelial) aspect of GBMs and in tubular basement membranes are present in monoclonal Ig deposition disease. However, microtubules measuring 20–60 nm, often in parallel arrays, are present in immunotactoid glomerulopathy. Substructures may also be present in deposits in monoclonal Ig GN, particularly when cryoglobulins are present.

For C3 glomerulopathy, dense deposit disease is characterized by highly osmiophilic intramembranous, continuous, or interrupted band–like deposits involving large segments of the GBM.[39] The deposits are also found as rounded deposits in the mesangium and in many patients, Bowman's capsule and tubular basement membranes. However, C3 GN is characterized by mostly mesangial and subendothelial and sometimes, intramembranous and subepithelial deposits. In some patients, there may be multiple layers of electron dense deposits and basement membrane material, resulting in thickening and fraying of the GBMs. The deposits appear less discrete, more ill-defined, and confluent compared with the electron dense deposits of immune-complex GN.

GUIDELINES ON USE OF ANCILLARY STUDIES

These include IF on pronase–digested paraffin material (or possible IHC on paraffin material), IgG subclass determination by IF, C4d staining in GN, and mass spectrometry to determine the composition of deposits.[29,55–61] The recommendations for ancillary studies are strong (A; established as contributory to diagnosis or prognosis), moderate (B; probably contributory to diagnosis or prognosis), possibly contributory to diagnosis or prognosis (C), and insufficient data (U).

When frozen tissue is not available for IF, salvage techniques should be available. These include IF after pronase digestion using formalin–fixed, paraffin–embedded tissue or immunoperoxidase staining on paraffin-embedded material. Recommendation: A.

Subtyping of IgG (*i.e.*, IgG1, IgG2, IgG3, and IgG4) should be performed in patients with monoclonal IgG GN. Recommendation: A.

The salvage technique of pronase digestion may also be used in some instances where masked monotypic Ig deposits are suspected in setting of monoclonal gammopathy and when routine IF studies are negative but EM studies show electron dense deposits. Recommendation: C.

C4d stain to distinguish immune-complex GN versus C3 glomerulopathy. Recommendation: C.

C4d as a prognostic marker for IgA nephropathy. Recommendation: C.

Mass spectrometry to determine the composition of deposits. Recommendation: U.

SUMMARY

This manuscript provides guidelines for classification, diagnosis, and reporting of GN. The main conclusion of the consensus meeting was that the kidney biopsy report should be etiology and pathogenesis driven. The kidney biopsy diagnosis should consist of a primary diagnosis that includes the disease entity or pathogenic type (if disease entity is not known) followed by pattern of injury, a score/grade of the disease if appropriate, and additional findings directly related to the primary disease entity. The diagnosis should also include separate secondary diagnoses if present. Guidelines for LM, IF, and EM and ancillary studies are also provided. This should be regarded as a working document, much like the Banff classification for renal allograft pathology,[62] subject to modification at future meetings and as new data evolve regarding the pathogenesis of and relationships between different glomerular diseases. The flexibility of the Banff schema has been one of its greatest strengths; whereas the initial version of that classification, like this document, was on the basis of consensus opinions of experts in the field rather than actual data, later iterations of Banff have been more data driven.[63]

ACKNOWLEDGMENTS

We thank Julie Ray for the arrangements with the consensus meeting.

This study was supported by the Fulk Foundation.

DISCLOSURES

None.

REFERENCES

1. Cattran DC, Coppo R, Cook HT, Feehally J, Roberts IS, Troyanov S, Alpers CE, Amore A, Barratt J, Berthoux F, Bonsib S, Bruijn JA, D'Agati V, D'Amico G, Emancipator S, Emma F, Ferrario F, Fervenza FC, Florquin S, Fogo A, Geddes CC, Groene HJ, Haas M, Herzenberg AM, Hill PA, Hogg RJ, Hsu SI, Jennette JC, Joh K, Julian BA, Kawamura T, Lai FM, Leung CB, Li LS, Li PK, Liu ZH, Mackinnon B, Mezzano S, Schena FP, Tomino Y, Walker PD, Wang H, Weening JJ, Yoshikawa N, Zhang H; Working Group of the International IgA Nephropathy Network and the Renal Pathology Society: The Oxford classification of IgA nephropathy: Rationale, clinicopathological correlations, and classification. *Kidney Int* 76: 534–545, 2009
2. Weening JJ, D'Agati VD, Schwartz MM, Seshan SV, Alpers CE, Appel GB, Balow JE, Bruijn JA, Cook T, Ferrario F, Fogo AB, Ginzler EM, Hebert L, Hill G, Hill P, Jennette JC, Kong NC, Lesavre P, Lockshin M, LooiL-M, Makino H, Moura LA, Nagata M: The classification of glomerulonephritis in systemic lupus erythematosus revisited. *J Am Soc Nephrol* 15: 241–250, 2004
3. Rosenstock JL, Markowitz GS, Valeri AM, Sacchi G, Appel GB, D'Agati VD: Fibrillary and immunotactoid glomerulonephritis: Distinct entities with different clinical and pathologic features. *Kidney Int* 63: 1450–1461, 2003
4. Alpers CE, Kowalewska J: Fibrillary glomerulonephritis and immunotactoid glomerulopathy. *J Am Soc Nephrol* 19: 34–37, 2008
5. Zand L, Fervenza FC, Nasr SH, Sethi S: Membranoproliferative glomerulonephritis associated with autoimmune diseases. *J Nephrol* 27: 165–171, 2014
6. Johnson RJ, Gretch DR, Yamabe H, Hart J, Bacchi CE, Hartwell P, Couser WG, Corey L, Wener MH, Alpers CE, Willson R: Membranoproliferative glomerulonephritis associated with hepatitis C virus infection. *N Engl J Med* 328: 465–470, 1993
7. Appel GB: Immune-complex glomerulonephritis–deposits plus interest. *N Engl J Med* 328: 505–506, 1993
8. Dathan JR, Heyworth MF: Glomerulonephritis associated with Coxiella burnetii endocarditis. *BMJ* 1: 376–377, 1975
9. Nadasdy T, Hebert LA: Infection-related glomerulonephritis: Understanding mechanisms. *Semin Nephrol* 31: 369–375, 2011
10. Nasr SH, Fidler ME, Valeri AM, Cornell LD, Sethi S, Zoller A, Stokes MB, Markowitz GS, D'Agati VD: Postinfectious glomerulonephritis in the elderly. *J Am Soc Nephrol* 22: 187–195, 2011
11. Nasr SH, Radhakrishnan J, D'Agati VD: Bacterial infection-related glomerulonephritis in adults. *Kidney Int* 83: 792–803, 2013
12. Haffner D, Schindera F, Aschoff A, Matthias S, Waldherr R, Schärer K: The clinical spectrum of shunt nephritis. *Nephrol Dial Transplant* 12: 1143–1148, 1997
13. Hulton SA, Risdon RA, Dillon MJ: Mesangiocapillary glomerulonephritis associated with meningococcal meningitis, C3 nephritic factor and persistently low complement C3 and C5. *Pediatr Nephrol* 6: 239–243, 1992
14. Jhaveri KD, D'Agati VD, Pursell R, Serur D: Coeliac sprue-associated membranoproliferative glomerulonephritis (MPGN). *Nephrol Dial Transplant* 24: 3545–3548, 2009
15. Kambham N: Postinfectious glomerulonephritis. *Adv Anat Pathol* 19: 338–347, 2012
16. Kanodia KV, Vanikar AV, Kute VB, Trivedi HL: Plasmodium vivax malaria associated with acute post infectious glomerulonephritis. *Ren Fail* 35: 1024–1026, 2013
17. Rincón B, Bernis C, Garcia A, Traver JA: Mesangiocapillary glomerulonephritis associated with hydatid disease. *Nephrol Dial Transplant* 8: 783–784, 1993
18. Martinelli R, Noblat AC, Brito E, Rocha H: Schistosoma mansoni-induced mesangiocapillary glomerulonephritis: Influence of therapy. *Kidney Int* 35: 1227–1233, 1989
19. Rodrigues VL, Otoni A, Voieta I, Antunes CM, Lambertucci JR: Glomerulonephritis in schistosomiasis mansoni: A time to reappraise. *Rev Soc Bras Med Trop* 43: 638–642, 2010
20. Pecchini F, Bufano G, Ghiringhelli P: Membranoproliferative glomerulonephritis secondary to tuberculosis. *Clin Nephrol* 47: 63–64, 1997
21. Jennette JC, Falk RJ: Pathogenesis of antineutrophil cytoplasmic autoantibody-mediated disease. *Nat Rev Rheumatol* 10: 463–473, 2014
22. Falk RJ, Nachman PH, Hogan SL, Jennette JC: ANCA glomerulonephritis and vasculitis: A Chapel Hill perspective. *Semin Nephrol* 20: 233–243, 2000
23. Eisenberger U, Fakhouri F, Vanhille P, Beaufils H, Mahr A, Guillevin L, Lesavre P, Noël L-H: ANCA-negative pauci-immune renal vasculitis: Histology and outcome. *Nephrol Dial Transplant* 20: 1392–1399, 2005
24. Chen M, Kallenberg CGM, Zhao M-H: ANCA-negative pauci-immune crescentic glomerulonephritis. *Nat Rev Nephrol* 5: 313–318, 2009
25. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, Flores-Suarez LF, Gross WL, Guillevin L, Hagen EC, Hoffman GS, Jayne DR, Kallenberg CGM, Lamprecht P, Langford CA, Luqmani RA, Mahr AD, Matteson EL, Merkel PA, Ozen S, Pusey CD, Rasmussen N, Rees AJ, Scott DGI, Specks U, Stone JH, Takahashi K, Watts RA: 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Arthritis Rheum* 65: 1–11, 2013
26. Levy JB, Hammad T, Coulthart A, Dougan T, Pusey CD: Clinical features and outcome of patients with both ANCA and anti-GBM antibodies. *Kidney Int* 66: 1535–1540, 2004
27. Rutgers A, Slot M, van Paassen P, van Breda Vriesman P, Heeringa P, Tervaert JWC: Coexistence of anti-glomerular basement membrane antibodies and myeloperoxidase-ANCAs in crescentic glomerulonephritis. *Am J Kidney Dis* 46: 253–262, 2005
28. Hellmark T, Niles JL, Collins AB, McCluskey RT, Brunmark C: Comparison of anti-GBM antibodies in sera with or without ANCA. *J Am Soc Nephrol* 8: 376–385, 1997
29. Nasr SH, Satoskar A, Markowitz GS, Valeri AM, Appel GB, Stokes MB, Nadasdy T, D'Agati VD: Proliferative glomerulonephritis with monoclonal IgG deposits. *J Am Soc Nephrol* 20: 2055–2064, 2009
30. Sethi S, Zand L, Leung N, Smith RJH, Jevremonic D, Herrmann SS, Fervenza FC: Membranoproliferative glomerulonephritis secondary to monoclonal gammopathy. *Clin J Am Soc Nephrol* 5: 770–782, 2010
31. Sethi S, Rajkumar SV: Monoclonal gammopathy-associated proliferative glomerulonephritis. *Mayo Clin Proc* 88: 1284–1293, 2013
32. Bhutani G, Nasr SH, Said SM, Sethi S, Fervenza FC, Morice WG, Kurtin PJ, Buadi FK, Dingli D, Dispenzieri A, Gertz MA, Lacy MQ, Kapoor P, Kumar S, Kyle RA, Rajkumar SV, Leung N: Hematologic characteristics of proliferative glomerulonephritides with nonorganized monoclonal immunoglobulin deposits. *Mayo Clin Proc* 90: 587–596, 2015
33. Lin J, Markowitz GS, Valeri AM, Kambham N, Sherman WH, Appel GB, D'Agati VD: Renal monoclonal immunoglobulin deposition disease: The disease spectrum. *J Am Soc Nephrol* 12: 1482–1492, 2001
34. Fogo A, Qureshi N, Horn RG: Morphologic and clinical features of fibrillary glomerulonephritis versus immunotactoid glomerulopathy. *Am J Kidney Dis* 22: 367–377, 1993
35. Nasr SH, Markowitz GS, Stokes MB, Seshan SV, Valderrama E, Appel GB, Aucouturier P, D'Agati VD: Proliferative glomerulonephritis with monoclonal IgG deposits: A distinct entity mimicking immune-complex glomerulonephritis. *Kidney Int* 65: 85–96, 2004
36. Servais A, Frémeaux-Bacchi V, Lequintrec M, Salomon R, Blouin J, Knebelmann B, Grünfeld J-P, Lesavre P, Noël LH, Fakhouri F: Primary glomerulonephritis with isolated C3 deposits: A new entity which shares common genetic risk factors with haemolytic uraemic syndrome. *J Med Genet* 44: 193–199, 2007
37. Sethi S, Fervenza FC, Zhang Y, Nasr SH, Leung N, Vrana J, Cramer C, Nester CM, Smith RJH: Proliferative glomerulonephritis secondary to dysfunction of the alternative pathway of complement. *Clin J Am Soc Nephrol* 6: 1009–1017, 2011
38. Sethi S, Fervenza FC, Zhang Y, Zand L, Vrana JA, Nasr SH, Theis JD, Dogan A, Smith RJH: C3 glomerulonephritis: Clinicopathological

findings, complement abnormalities, glomerular proteomic profile, treatment, and follow-up. *Kidney Int* 82: 465–473, 2012
39. Pickering MC, D'Agati VD, Nester CM, Smith RJ, Haas M, Appel GB, Alpers CE, Bajema IM, Bedrosian C, Braun M, Doyle M, Fakhouri F, Fervenza FC, Fogo AB, Frémeaux-Bacchi V, Gale DP, Goicoechea de Jorge E, Griffin G, Harris CL, Holers VM, Johnson S, Lavin PJ, Medjeral-Thomas N, Paul Morgan B, Nast CC, Noel L-H, Peters DK, Rodríguez de Córdoba S, Servais A, Sethi S, Song W-C, Tamburini P, Thurman JM, Zavros M, Cook HT: C3 glomerulopathy: Consensus report. *Kidney Int* 84: 1079–1089, 2013
40. Hou J, Markowitz GS, Bomback AS, Appel GB, Herlitz LC, Barry Stokes M, D'Agati VD: Toward a working definition of C3 glomerulopathy by immunofluorescence. *Kidney Int* 85: 450–456, 2014
41. Berden AE, Ferrario F, Hagen EC, Jayne DR, Jennette JC, Joh K, Neumann I, Noël LH, Pusey CD, Waldherr R, Bruijn JA, Bajema IM: Histopathologic classification of ANCA-associated glomerulonephritis. *J Am Soc Nephrol* 21: 1628–1636, 2010
42. Glassock RJ, Alvarado A, Prosek J, Hebert C, Parikh S, Satoskar A, Nadasdy T, Forman J, Rovin B, Hebert LA: Staphylococcus-related glomerulonephritis and poststreptococcal glomerulonephritis: Why defining "post" is important in understanding and treating infection-related glomerulonephritis. *Am J Kidney Dis* 65: 826–832, 2015
43. Sethi S: Etiology-based diagnostic approach to proliferative glomerulonephritis. *Am J Kidney Dis* 63: 561–566, 2014
44. D'Agati VD, Mengel M: The rise of renal pathology in nephrology: Structure illuminates function. *Am J Kidney Dis* 61: 1016–1025, 2013
45. Sethi S, Fervenza FC: Membranoproliferative glomerulonephritis–a new look at an old entity. *N Engl J Med* 366: 1119–1131, 2012
46. Chang A, Gibson IW, Cohen AH, Weening JW, Jennette JC, Fogo AB; Renal Pathology Society: A position paper on standardizing the nonneoplastic kidney biopsy report. *Hum Pathol* 43: 1192–1196, 2012
47. Coley SM, Shirazian S, Radhakrishnan J, D'Agati VD: Monoclonal IgG1κ anti-glomerular basement membrane disease: A case report. *Am J Kidney Dis* 65: 322–326, 2015
48. Ho J, Gibson IW, Zacharias J, Fervenza F, Colon S, Borza D-B: Antigenic heterogeneity of IgA anti-GBM disease: New renal targets of IgA autoantibodies. *Am J Kidney Dis* 52: 761–765, 2008
49. Rajkumar SV, Kyle RA, Therneau TM, Melton LJ 3rd, Bradwell AR, Clark RJ, Larson DR, Plevak MF, Dispenzieri A, Katzmann JA: Serum free light chain ratio is an independent risk factor for progression in monoclonal gammopathy of undetermined significance. *Blood* 106: 812–817, 2005
50. Haas M: A reevaluation of routine electron microscopy in the examination of native renal biopsies. *J Am Soc Nephrol* 8: 70–76, 1997
51. Collar J, Cattell V: Paraffin-processed material is unsuitable for diagnosis of thin-membrane disease. *Nephron* 69: 187–188, 1995
52. Sethi S, Fervenza FC, Zhang Y, Zand L, Meyer NC, Borsa N, Nasr SH, Smith RJH: Atypical postinfectious glomerulonephritis is associated with abnormalities in the alternative pathway of complement. *Kidney Int* 83: 293–299, 2013
53. Nasr SH, Valeri AM, Appel GB, Sherwinter J, Stokes MB, Said SM, Markowitz GS, D'Agati VD: Dense deposit disease: Clinicopathologic study of 32 pediatric and adult patients. *Clin J Am Soc Nephrol* 4: 22–32, 2009
54. Bridoux F, Leung N, Hutchison CA, Touchard G, Sethi S, Fermand J-P, Picken MM, Herrera GA, Kastritis E, Merlini G, Roussel M, Fervenza FC, Dispenzieri A, Kyle RA, Nasr SH; International Kidney and Monoclonal Gammopathy Research Group: Diagnosis of monoclonal gammopathy of renal significance. *Kidney Int* 87: 698–711, 2015
55. Nasr SH, Galgano SJ, Markowitz GS, Stokes MB, D'Agati VD: Immunofluorescence on pronase-digested paraffin sections: A valuable salvage technique for renal biopsies. *Kidney Int* 70: 2148–2151, 2006
56. Sethi S, Vrana JA, Theis JD, Dogan A: Mass spectrometry based proteomics in the diagnosis of kidney disease. *Curr Opin Nephrol Hypertens* 22: 273–280, 2013
57. Larsen CP, Ambuzs JM, Bonsib SM, Boils CL, Nicholas Cossey L, Messias NC, Silva FG, Wang YH, Gokden N, Walker PD: Membranous-like glomerulopathy with masked IgG kappa deposits. *Kidney Int* 86: 154–161, 2014
58. Messias NC, Walker PD, Larsen CP: Paraffin immunofluorescence in the renal pathology laboratory: More than a salvage technique. *Mod Pathol* 28: 854–860, 2015
59. Jain D, Green JA, Bastacky S, Theis JD, Sethi S: Membranoproliferative glomerulonephritis: The role for laser microdissection and mass spectrometry. *Am J Kidney Dis* 63: 324–328, 2014
60. Espinosa M, Ortega R, Sánchez M, Segarra A, Salcedo MT, González F, Camacho R, Valdivia MA, Cabrera R, López K, Pinedo F, Gutierrez E, Valera A, Leon M, Cobo MA, Rodriguez R, Ballarín J, Arce Y, García B, Muñoz MD, Praga M; Spanish Group for Study of Glomerular Diseases (GLOSEN): Association of C4d deposition with clinical outcomes in IgA nephropathy. *Clin J Am Soc Nephrol* 9: 897–904, 2014
61. Sethi S, Nasr SH, De Vriese AS, Fervenza FC: C4d as a diagnostic tool in proliferative GN [published online ahead of print May 19, 2015]. *J Am Soc Nephrol* doi: ASN.2014040406
62. Solez K, Axelsen RA, Benediktsson H, Burdick JF, Cohen AH, Colvin RB, Croker BP, Droz D, Dunnill MS, Halloran PF: International standardization of criteria for the histologic diagnosis of renal allograft rejection: The Banff working classification of kidney transplant pathology. *Kidney Int* 44: 411–421, 1993
63. Solez K, Racusen LC: The Banff classification revisited. *Kidney Int* 83: 201–206, 2013
64. Roberts IS, Cook HT, Troyanov S, Alpers CE, Amore A, Barratt J, Berthoux F, Bonsib S, Bruijn JA, Cattran DC, Coppo R, D'Agati V, D'Amico G, Emancipator S, Emma F, Feehally J, Ferrario F, Fervenza FC, Florquin S, Fogo A, Geddes CC, Groene HJ, Haas M, Herzenberg AM, Hill PA, Hogg RJ, Hsu SI, Jennette JC, Joh K, Julian BA, Kawamura T, Lai FM, Li LS, Li PK, Liu ZH, Mackinnon B, Mezzano S, Schena FP, Tomino Y, Walker PD, Wang H, Weening JJ, Yoshikawa N, Zhang H; Working Group of the International IgA Nephropathy Network and the Renal Pathology Society: The Oxford classification of IgA nephropathy: Pathology definitions, correlations, and reproducibility. *Kidney Int* 76: 546–556, 2009

See related editorial, "A Systematic Method for Categorizing GN," on pages 1265–1266.