SECTION 1

Introduction to Kidney Pathology

J. Charles Jennette

1.1 Kidney Pathology History and Kidney Biopsy Methods

J. Charles Jennette, Vivette D. D'Agati, M. Barry Stokes, Agnes B. Fogo, and Volker Nickeleit

KIDNEY PATHOLOGY HISTORY

Noteworthy elucidation of the clinical and gross pathologic manifestations of kidney disease began during the 19th century with the studies of Bright, Rayer, Rokitansky, von Frerichs, and others.[1] Beginning in the second half of the 19th century and extending into the 20th century, Ellis, Fahr, and Klebs made major advances in the pathologic classification of kidney disease using light microscopy (LM) on postmortem specimens. Pioneered by Alwall, Brun, Iverson, and Kark in the 1950s, the kidney biopsy allowed access to the early stages of kidney diseases and provided an opportunity to make a pathologic diagnosis that could inform clinical care. By the 1960s, the first modern kidney pathologists, including Bergstrand, Churg, Germuth, Habib, McCluskey, and Spargo, were utilizing the newly available techniques of electron microscopy (EM), immunofluorescence microscopy (IF), and immunohistochemistry (IHC) to make major strides in elucidating native kidney diseases. Proteomic studies by mass spectrometry and genomic studies are used more and more for specific disease indications, such as mass spectrometry to identify the specific molecular composition of abnormal deposits (eg, amyloid) and genetic sequencing to identify a podocyte gene abnormality causing focal segmental glomerulosclerosis (FSGS).

In the 1960s, as kidney pathology was becoming a specialized subspecialty of pathology, kidney transplantation was gaining momentum,[2] which necessitated advances in kidney transplant pathology. Multiple strategies for classifying and diagnosing kidney rejection and other rejection-associated diseases coalesced in 1993 into the Banff working classification of kidney transplant pathology.[3] The most recent iteration of the Banff system is used in Section 8 on Transplant Pathology.[4]

Pathology classification and diagnosis of kidney neoplasms have been advanced and standardized for decades by sequentially updated World Health Organization (WHO) Classification of Tumors series of publications. The 8th edition of Heptinstall's Pathology of the Kidney primarily uses the 2016 WHO Classification of Kidney Neoplasms[5] supplemented by new information from the recently released 2022 version.[6]

Cystic kidney diseases and other congenital diseases of the kidneys have been recognized for centuries.[7] Although initial observations were based on gross examination of the kidneys, Section 3 on kidney congenital anomalies and cystic diseases illustrates that classification and diagnoses of these diseases have evolved from gross and microscopic examination to the level of molecular diagnosis based on genetic abnormalities and disturbed molecular pathways that control cell and tissue development, structure, and function.[8]

These and other advances in kidney pathology are chronicled in the 8th edition of this textbook on pathology of the kidney, first published by Robert Heptinstall in 1966.[9]

KIDNEY PATHOLOGY APPLICATIONS

Major pathology settings for applying kidney pathology knowledge and skills are autopsy pathology, uropathology (urologic pathology), and nephropathology (renal pathology). However, in-depth knowledge of kidney pathology also is essential for clinicians who must act on pathology results to care for patients with kidney disease, including but not limited to nephrologists, urologists, kidney transplant surgeons, and radiologists who perform and evaluate kidney imaging studies. In addition, research scientists who investigate pathophysiologic mechanisms of kidney disease must have in-depth knowledge of specific aspects of nephropathology that relate to their research. The goal of this comprehensive textbook on kidney pathology is to cover the full breadth of kidney pathology so that all branches of medicine that deal with kidney disease will be served.

Some sections and chapters of this book have greater relevance to particular subspecialty areas of clinical medicine and pathology than others. For example, the kidney pathology covered in Section 3 on congenital kidney disease and Section 9 on kidney neoplasms are more relevant for urologists and uropathologists in the setting of nephrectomies and imaging studies and, to a lesser degree, kidney biopsies. However, kidney disease addressed in most sections is more often evaluated in kidney biopsy specimens, thus methods for performing and evaluating kidney biopsies will be reviewed in depth in this introductory section. Most of these methods apply also to evaluating kidney disease in surgical wedge biopsies, nephrectomies, and autopsies.

KIDNEY BIOPSY

The traditional approach to kidney biopsy analysis is to identify the pathology by systematically examining the different histologic compartments (glomeruli, tubules, interstitium, and blood vessels). Once the site and nature of the lesions are determined, the pathologist makes a final diagnosis by integrating the LM histopathology with IF and EM findings, and IHC if required, and with clinical information including relevant laboratory data. This chapter serves as a guide to kidney biopsy evaluation by focusing on each kidney compartment and its pathology in turn, and it refers the reader to detailed discussions of the specific diseases in other sections and chapters of the book.

Several factors make evaluation of kidney pathology challenging, especially in kidney biopsy specimens. There are a limited number of stereotypic kidney responses to injury. In other words, diverse pathogenetic mechanisms may produce a similar morphologic response. As a corollary, only a few findings are pathognomonic in kidney pathology, such as the reaction of the Congo red stain for amyloid (see Chapter 4.5), the linear staining for monoclonal immunoglobulin in glomerular and tubular basement membranes (TBMs) in monoclonal immunoglobulin deposition disease (see Chapter 4.6), and the unique intramembranous dense deposits seen by EM in dense-deposit disease (DDD) (see Chapter 5.7). Even the venerable Kimmelstiel-Wilson lesion of diabetic glomerulosclerosis (see Chapter 4.8) and the fibrils of amyloid seen by EM (see Chapters 4.5) are now subject to differential diagnoses.

The second major problem is the small size of the biopsy, although the amount of tissue that is sufficient for a specific diagnosis is influenced by the disease that is present. For example, one glomerulus with amyloid identified by light or IF is adequate for a diagnosis of amyloidosis and one glomerulus with the pathognomonic features of DDD by EM is sufficient for diagnosis. On the other hand, failure to detect glomerular lesions in a small sample with only a few glomeruli does not allow ruling out diseases with focal glomerular lesions, such as FSGS and focal pauci-immune focal necrotizing glomerulonephritis. Small sample size also impairs the assessment of the overall severity, activity, and chronicity of the disease, which can be as important in prognostication and therapeutic decisions as the specific disease diagnosis.

Another problem is that it is not always easy to identify the primary lesion because more than one compartment may be involved by the primary process, secondary processes may intervene, and diagnostic findings may be subtle. Finally, progression of many forms of kidney injury toward end-stage disease results in nonspecific chronic changes that obscure the nature of the original pathologic process. As Simeon Burt Wolbach, former Chairman of Pathology at Harvard, noted, "It is often difficult to ascertain the nature of the edifice that has burnt down from a study of the ashes" [quoted in Ref.[10]]. In spite of these problems, the pathologic interpretation of a kidney biopsy specimen remains an important guide for the clinician in the diagnosis, prognosis, and therapy of kidney disease.

The kidney biopsy has been used to identify pathogenetic mechanisms and to establish clinicopathologic correlations between pathologic findings and clinical symptoms. The kidney biopsy is frequently necessary to distinguish among diseases with similar clinical presentations. For example, the many diseases that cause nephrotic syndrome, nephritic syndrome, or acute kidney injury (AKI) have vastly different prognostic and therapeutic implications, exemplifying the importance of the kidney biopsy in differential diagnosis.

Traditionally, nonneoplastic kidney diseases that are managed primarily by nephrologists (ie, medical kidney diseases) are diagnosed by examination of kidney biopsies by nephropathologists (nephropathologists), whereas neoplastic kidney diseases and diseases of the urinary tract that are managed primarily by urologists and may lead to partial or complete nephrectomy without prior biopsy are evaluated by urologic pathologists.

The primary role of the kidney biopsy is to provide a diagnosis and information about disease activity and chronicity that allow the clinician to make an informed prognosis and choose the optimal therapy. In some instances, a specific cause of the kidney injury may be identified by pathologic examination or suggested by the pathologic findings and subsequently confirmed clinically. This may lead to elimination of the cause and resolution of the disease. Determination of the relative amount of acute, potentially reversible injury vs irreversible scarring, which may not be apparent from the clinical findings, is equally important. In cases with advanced chronic injury, the decision not to treat lesions that are deemed to be too advanced to respond to therapy may be based on the kidney biopsy findings. Furthermore, kidney biopsy is the only way to recognize and describe some new kidney diseases, for example, the adverse effects of new drugs. Finally, kidney biopsy is required in clinical trials to ensure that the disease process and the disease severity are comparable among the study groups and to serve as a baseline for evaluating therapeutic efficacy.

Kidney Biopsy Technical Considerations

The clinician must balance the information to be gained and its impact on patient care against the risks associated with a kidney biopsy; however, kidney biopsy using the spring-loaded biopsy instrument with ultrasound guidance is a very safe procedure.[11,12] Following a biopsy procedure, microscopic hematuria occurs in about 35% of patients, but gross hematuria is seen in <0.5%. A perirenal hematoma is identified in ~65% of patients, depending upon the diligence of the search. Transfusion is required as a consequence of <1% of biopsies and nephrectomy in <0.1%. Mortality is extremely rare. To obtain optimal tissue for pathologic evaluation without increased morbidity, 14- or 16-gauge needles are recommended for kidney biopsies in adults and 16- or 18-gauge needles in children younger than 8 years old.[13] Examination of needle biopsy cores should be performed at the site of biopsy with dissecting microscope or other magnifying device to confirm that cortical tissue is included in the specimen and to facilitate triaging the specimen for LM, IF, and EM.[14]

Pathologic Evaluation

Tissue sections for routine surgical pathology and autopsy pathology often are 6 μm thick for LM examination. Kidney biopsy specimens for LM evaluation are routinely cut at 2-3 μm, for more precise evaluation. For routine nephropathology evaluation, multiple kidney biopsy sections are cut and typically stained with hematoxylin and eosin (H&E), methenamine silver-periodic acid (Jones stain), Masson trichrome, and periodic acid Schiff (PAS).[14] Congo red to detect amyloid may be used routinely or only when amyloidosis is suspected based

on clinical or pathologic findings. An immunohistology technique (either IF or IHC) to demonstrate deposits of immunoglobulins (IgG, IgM, IgA, kappa, and lambda light chains), complement components (C3 and C1q), and fibrin is required for adequate pathologic evaluation of glomerular disease.[14]

Electron microscopy is required for some pathologic diagnoses, such as minimal change disease (MCD), DDD, fibrillary glomerulonephritis, thin glomerular basement membrane lesions associated with collagen IV nephropathies, immunotactoid glomerulopathy, collagenofibrotic glomerulopathy, Fabry disease, etc. Once these diseases are identified by EM, they often can be confirmed by special LM, IF, or IHC examinations. EM also helps confirm diagnoses made by LM and IF and narrows the differential diagnosis for some conditions (eg, primary FSGS vs other causes of FSGS).

Multiple special techniques can be used when specific disease processes are suspected from the routine examination, for example, IHC for infectious pathogens (eg, polyomavirus) and immune cell types (eg, B vs T lymphocytes), and ultrastructural morphometric techniques to measure glomerular basement membrane thickness and the diameter of fibrils or microtubules. Kidney biopsies should be processed only in laboratories that are proficient in the performance and interpretation of these tests.[14]

Specimen Adequacy for Diagnosis

How much kidney tissue is adequate for a confident pathologic diagnosis is a complex question, and the answer depends in part on the indication for biopsy. If the differential diagnosis includes diseases that require immunohistology or ultrastructure for definitive diagnosis, tissue must be processed for these studies as well as for LM. A single glomerulus may be sufficient for the diagnosis of diffusely distributed glomerular disease with specific pathologic features, such as amyloidosis or membranous nephropathy. However, most diseases require that more than one glomerulus is examined, due to the possibility of focal glomerular involvement and the need to confidently decide how much disease activity vs disease chronicity is present.

Diagnosis of diseases involving only a proportion of the glomeruli (focal) requires demonstration of only one diagnostic abnormal glomerulus, and the relevant question is how many normal glomeruli are needed to confidently exclude focal pathology. Assuming that the disease is randomly distributed among the glomeruli, the glomeruli are independently affected, and the glomerular sample is random, the probability of finding any number of abnormal glomeruli in the kidney biopsy can be represented by the binomial equation.[15] The number of abnormal glomeruli in the biopsy is a function of the sample size (specifically the amount of cortex) and the proportion of abnormal glomeruli in the kidney.[15] In a kidney with 10% glomerular involvement, a biopsy containing 10 glomeruli will have a 35% chance of having no abnormal glomeruli, but when glomerular involvement is 35%, the chance of finding no abnormal glomeruli in a biopsy with 10 glomeruli is <5%. Thus, a biopsy with few glomeruli cannot confidently exclude focal disease with a low proportion of glomerular involvement, and the minimal sample needed to exclude focal disease present in fewer than 10% of the glomeruli with >90% confidence is at least 20 glomeruli. However, the true proportion of glomerular involvement in human kidney diseases is impossible to determine from a biopsy specimen.

Complicating the issue of adequate sampling is the possibility of segmental involvement of an individual glomerulus, defined as involvement of only a portion of the glomerular tuft area. Evaluation of multiple levels of section is particularly important in such diseases as FSGS, focal lupus nephritis, and focal pauci-immune necrotizing and crescentic glomerulonephritis, where careful serial sectioning of the biopsy increases the diagnostic yield. Most nephropathologists section each biopsy with multiple serial sections to maximize the likelihood of identifying focal and segmental glomerular lesions.

Specimen Adequacy for Assessing Activity and Chronicity

Semiquantitative scoring of abnormal glomeruli in a biopsy specimen for predicting outcome or for assignment to research cohorts is a more complex problem. For example, the distribution of abnormal glomeruli found in biopsies from patients with systemic lupus erythematosus (SLE) with mild focal (<20%), moderate focal (20%-50%), and diffuse (50% or more) glomerular involvement can be calculated from the binomial equation.[15] Small differences between groups (eg, 10%) require more than 100 glomeruli to achieve statistical significance, and a minimum of 20-25 glomeruli is necessary to detect relatively large differences (25%-40%).

In study design, the limitations of morphologic stratification must be appreciated or incorrectly classified patients will dilute the study outcomes. The inclusion of patients from a good prognosis group in a bad prognosis group will improve the outcome in both groups without changing the overall incidence of bad outcomes. Attention to statistical rules will lead to results that are internally consistent within groups and reliably different between groups. A final caveat is that observations made on the even more limited samples studied by EM should be extrapolated to the whole kidney cautiously. Because of the need for integration of information from all three modalities of biopsy workup, it is important for the same pathologist to evaluate the findings by LM, IF, and EM.

Semiquantitative Scoring of Pathologic Findings

Pirani et al.[13] pioneered the use of semiquantitative kidney pathologic assessment "to force the pathologist to look at all elements of renal histology" in a systematic fashion. For example, a given pattern of injury can be assessed as absent, mild, moderate, moderately severe, or severe or with a numerical designation 0-4+. This approach was used in the context of lupus glomerulonephritis to develop indices of disease activity and chronicity based on semiquantitative observations[16] and was most recently updated in 2018.[17] Additional examples of systematic semiquantitative evaluation in kidney pathology are the Banff classification for kidney allograft pathology,[4] the Oxford classification for IgA nephropathy,[18] the Berden classification of ANCA glomerulonephritis,[19] the van Daalen classification of anti-GBM glomerulonephritis,[20] the Renal Pathology Society classification of diabetic nephropathy,[21] and the Columbia classification for FSGS.[22] Although most of these semiquantitative scoring systems are essentially heuristic, and not based on empirical data, certain quantitative and semiquantitative data should be included in every nonneoplastic kidney biopsy report. Table 1.1.1 lists essential elements and pathologic parameters that should be reported for every kidney biopsy specimen based on a Renal Pathology Society position paper.[23] This content should be modified based on the diseases process to include additional observations and in some instances semiquantitative scoring, for example, for diseases that have

Table 1.1.1 Requirements for Optimum Kidney Biopsy Results

Complete relevant clinical history
Adequate specimen obtained by kidney biopsy
Technically well-prepared specimen for all methods of evaluation
Pathologist who is knowledgeable and experienced in nephropathology
Accurate and informative report and diagnosis
Nephrologist who understands the report and how it should influence the patient's management

widely used scoring or classification systems.[4,18-22] These and other classification and scoring systems evolve, and hopefully improve, over time and thus the reported observations in kidney biopsy reports change over time as well.

Digital Nephropathology

Digital pathology using whole slide images (WSIs), also called virtual microscopy, is rapidly gaining applications not only in research and education but also in clinical practice.[24-26] Glass slides with histologic preparations are digitized (scanned) into WSI and viewed at a computer workstation similarly to the routine views of radiology images that already is standard practice. Many nephropathologists already examine only digital electron micrographs taken from the EM specimen by a laboratory person, rather than directly viewing the entire stained ultrathin sections with an electron microscope.

Evaluation of WSIs simulates evaluation of a glass slide with a microscope. Most current scanners produce WSIs at 40× magnification, although 100× is possible. Once the slide is accessed using WSI slide viewing software, the image can be viewed by zooming over a range from 2× to 40× (or 100×). Figure 1.1.1 shows snapshots of a kidney biopsy WSI as the image was zoomed from lowest to highest magnification. The Masson trichrome stained section is from a biopsy of a patient with active necrotizing and crescentic ANCA glomerulonephritis that has segmental fibrinoid necrosis and cellular crescent formation. In addition to semiquantitative scoring of lesions, WSI images can be used for numerous morphometric and machine learning applications.[26] Of note, polarization is not possible from WSI, so some crystals may be overlooked.

Multiple research consortia funded by NIH NIDDK (eg, Kidney Precision Medicine Program (KPMP), CureGlomerulonephropathy (CureGN), and Nephrotic Syndrome Study Network (NEPTUNE)) already are using digital pathology repositories containing thousands of WSIs of kidney biopsy specimens that are being evaluated by expert nephropathologists to generate data for research protocols. These studies are also validating the value of various histopathologic lesions for predicting clinical outcomes and correlating these lesions with molecular data to elucidate pathogenic mechanisms that ultimately could identify effective molecular targets for therapy.

Diagnostic virtual histopathology using WSIs already is entering clinical practice as acceptable validation of reproducibility and accuracy are accruing, and regulatory oversight is being established.[27] This will revolutionize how pathologic lesions are viewed, but the knowledge required to make an accurate and precise diagnosis will remain the same whether the images and the histopathologic patterns are evaluated on glass slides or on a digital image viewing device.

REPORTING KIDNEY BIOPSY RESULTS

Several factors contribute to an optimal kidney biopsy and these are listed in Table 1.1.1.

There is no universally adopted format for kidney biopsy reports; however, a number of recommendations have been made by consensus groups, and most kidney biopsy reports are in line with these recommendations. Certain quantitative and semiquantitative data should be included in every nonneoplastic kidney biopsy report. Table 1.1.2 lists pathologic parameters and other data that should be reported for every kidney biopsy specimen based on a Renal Pathology Society position paper on standardizing the nonneoplastic kidney biopsy report.[23] This content should be modified based on the diseases process to include additional observations and in some instances semiquantitative scoring mentioned earlier, for example, lupus nephritis,[19] IgA nephropathy,[20] ANCA glomerulonephritis,[21] anti-GBM glomerulonephritis,[22] diabetic glomerulosclerosis,[23] FSGS,[24] and kidney transplants.[4]

Table 1.1.3 shows two different approaches for organizing the content of a kidney biopsy report. The Renal Pathology Society (RPS) consensus group that made recommendation for reporting kidney biopsy pathology results on glomerulonephritis included both nephrologists and nephropathologists in the deliberations.[28] The consensus from this group was that there is

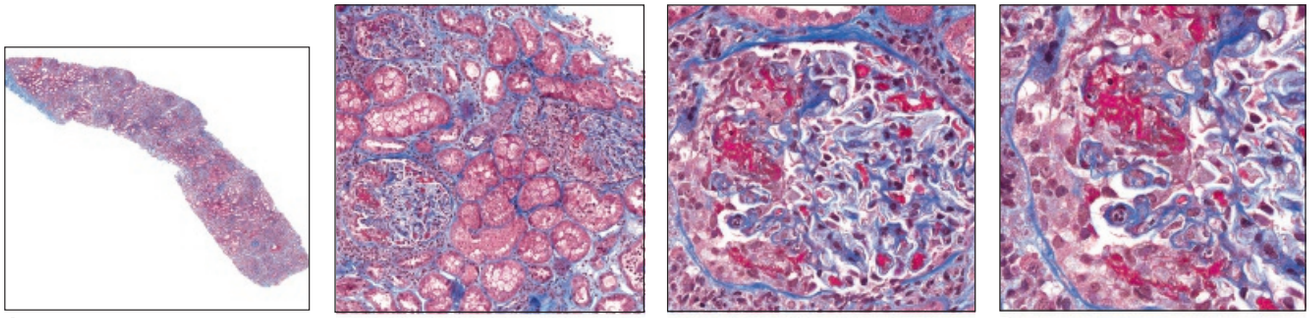

FIGURE 1.1.1 Snapshots of a kidney biopsy WSI taken as the viewer was zoomed from 2× **(A)**, to 10× **(B)**, to 20× **(C)**, and to 40× **(D)**.

Table 1.1.2 List of Content That Should Be Included in a Nonneoplastic Kidney Biopsy Report Based on a Renal Pathology Society Position Paper[23]

Clinical history/data
Brief summary of history provided by clinician or obtained from another authoritative source
Gross description
No. of tissue core(s) for light microscopy and core length(s)
No. of tissue core(s) for immunofluorescence microscopy and core length(s)
No. of tissue core(s) for electron microscopy and core length(s)
Microscopic description
Light microscopy
Histochemical stains (eg, periodic acid-Schiff, Jones methenamine silver, Masson trichrome, Congo red) or IHC performed
Presence of cortex/medulla/capsule/calyceal mucosa
Glomeruli
No. of glomeruli
No. of (%) global sclerosis (if present)
No. of (%) segmental sclerosis (if present)
No. of (%) crescents, cellular to fibrocellular (if present)
No. of (%) fibrinoid necrosis (if present)
Additional abnormalities (eg, hypercellularity, deposits, thrombosis, double contours, spikes)
Tubulointerstitium
Extent of interstitial fibrosis/tubular atrophy, at least semiquantitative
Interstitial inflammation, tubular injury, crystals
Arteries/arterioles
Intimal fibrosis (absent/present/severity)
Arteriolar hyalinosis (absent/present/severity)
Immunofluorescence microscopy
No. of glomeruli present
No. of globally sclerosed glomeruli
Staining intensity, location/pattern of staining for each antibody, and specify intensity scale (0-3+ or 0-4+)
Relative intensity of κ/λ staining of tubular casts
State when IF has been performed on paraffin sections
Electron microscopy
Absence or presence and location of electron dense deposits
GBM thickness (normal, thin, thick) and appearance (eg, layered)
If abnormal, state reference range of GBM thickness for age and sex
Additional abnormalities (eg, infiltrates, deposit substructure, fibrillary deposits, cellular interposition, tubuloreticular inclusions, fibrin tactoids)
Indicate tubulointerstitium was evaluated, specify if tubulointerstitial deposits present
Indicate peritubular capillary basement membrane was evaluated (for transplant biopsies), specify if multilayering present (focal vs diffuse)

Adapted from Chang A, Gibson I, Cohen A, et al.; Renal Pathology Society. A Position Paper on Standardizing the Nonneoplastic Kidney Biopsy Report. *Hum Pathol.* 2012;43(8):1192-1296, with permission from Elsevier.

Table 1.1.3 Sequence of Kidney Biopsy Report Information

From the Mayo Clinic/Renal Pathology Society Consensus Report on Pathologic Reporting of GN[28]	*From a Position Paper on Standardizing the Nonneoplastic Kidney Biopsy Report*[23]
Diagnosis	Clinical history/data
Comment	Gross description
Clinical history/data	Microscopic description
Gross description	Light microscopy
Microscopic description	Immunofluorescence microscopy
Light microscopy	Electron microscopy
Immunofluorescence microscopy	**Diagnosis**
Electron microscopy	**Comment**

value in having the diagnosis, and any comments about clinical or pathologic issues related to the biopsy findings, placed at the top of the kidney biopsy report, not at the end. We agree with this recommendation not only for glomerulonephritis but also for all kidney biopsy reports.

The Mayo Clinic/RPS consensus group also emphasized that a pattern-based diagnosis should always be paired with terminology indicating the etiology and pathogenesis whenever possible (eg, anti-GBM necrotizing and crescentic glomerulonephritis). This concept extends beyond the diagnosis of glomerulonephritis to all forms of kidney disease (eg, AL amyloidosis, myoglobin cast nephropathy, aristolochic acid nephropathy, succinate dehydrogenase-deficient renal cell carcinoma, uromodulin mutation medullary cystic disease, etc.).

The next chapter in the section (Chapter 1.2) will provide an overview of this approach to diagnosing kidney disease; all following sections and chapters will fill in the details.

REFERENCES

1. Weening J, Jennette JC. Historical milestones in renal pathology. *Virchows Arch*. 2012;461:3.
2. Shackman R. The story of kidney transplantation. *Br Med J*. 1966;1(5500):1379-1383.
3. Solez K, Axelsen RA, Benediktsson H, et al. International standardization of criteria for the histologic diagnosis of renal allograft rejection: the Banff working classification of kidney transplant pathology. *Kidney Int*. 1993;44(2):411-422.
4. Loupy A, Mengel M, Haas M. Thirty years of the International Banff Classification for Allograft Pathology: the past, present, and future of kidney transplant diagnostics. *Kidney Int*. 2022;101(4):678-691.
5. Moch H, Humphrey PA, Ulbright TM, Reuter VE. *WHO Classification of Tumours of the Urinary System and Male Genital Organs*. 4th ed. International Agency for Research on Cancer (IARC) Press; 2016.
6. Moch H, Amin MB, Berney DM, et al. The 2022 World Health Organization Classification of Tumours of the Urinary System and Male Genital Organs-Part A: Renal, Penile, and Testicular Tumours. *Eur Urol*. 2022;82(5):458-468.
7. Balat A. Tear drops of kidney: a historical overview of Polycystic Kidney Disease. *G Ital Nefrol*. 2016;33(Suppl 66):33.S66.21.
8. Kagan M, Pleniceanu O, Vivante A. The genetic basis of congenital anomalies of the kidney and urinary tract. *Pediatr Nephrol*. 2022;37(10):2231-2243.
9. Heptinstall RH. *Pathology of the Kidney*. 1st ed. Little, Brown and Company; 1966.
10. Papper S. *Clinical Nephrology*. 2nd ed. Little, Brown and Company; 1978.
11. Walker PD. The renal biopsy. *Arch Pathol Lab Med*. 2009;133:181.
12. Montes D, Beamish C, Waheed S, et al. What happens after the kidney biopsy? The findings nephrologists should know. *BMC Nephrol*. 2022;23(1):265.
13. Pirani CL, Pollak VE, Schwartz FD. The reproducibility of semiquantitative analyses of renal histology. *Nephron*. 1964;29:230.
14. Walker PD, Cavallo T, Bonsib SM. Practice guidelines for the renal biopsy. *Mod Pathol*. 2004;17:1555.
15. Corwin HL, Schwartz MM, Lewis EJ. The importance of sample size in the interpretation of the renal biopsy. *Am J Nephrol*. 1988;8:85.
16. Austin HA III, Muenz LR, Joyce KM, et al. Diffuse proliferative lupus nephritis: identification of specific pathologic features affecting renal out- come. *Kidney Int*. 1984;25:689.
17. Bajema IM, Wilhelmus S, Alpers CE, et al. Revision of the International Society of Nephrology/Renal Pathology Society classification for lupus nephritis: clarification of definitions, and modified National Institutes of Health activity and chronicity indices. *Kidney Int*. 2018;93(4):789-796.
18. Working Group of the International IgA Nephropathy Network and the Renal Pathology Society; Roberts IS, Cook HT, et al. The Oxford classification of IgA nephropathy: pathology definitions, correlations, and reproducibility. *Kidney Int* 2009;76:546.
19. Berden AE, Ferrario F, Hagen EC, Jayne DR, Jennette JC, et al. Histopathologic classification of ANCA-associated glomerulonephritis. *J Am Soc Nephrol*. 2010;21(10):1628-1636.
20. van Daalen EE, Jennette JC, McAdoo SP, et al. Predicting outcome in patients with anti-GBM glomerulonephritis. *Clin J Am Soc Nephrol*. 2018;13(1):63-72.
21. Tervaert TW, Mooyaart AL, Amann K, et al. Renal Pathology Society. Pathologic classification of diabetic nephropathy. *J Am Soc Nephrol*. 2010;21(4):556-563.
22. D'Agati VD, Fogo AB, Bruijn JA, Jennette JC. Pathologic classification of focal segmental glomerulosclerosis: a working proposal. *Am J Kidney Dis*. 2004;43(2):368-382.
23. Chang A, Gibson I, Cohen A, et al.; Renal Pathology Society. A Position Paper on Standardizing the Nonneoplastic Kidney Biopsy Report. *Clin J Am Soc Nephrol*. 2012;7(8):1365-1368.
24. Barisoni L, Hodgin JB. Digital pathology in nephrology clinical trials, research, and pathology practice. *Curr Opin Nephrol Hypertens*. 2017;26(6):450-459.
25. Barisoni L, Gimpel C, Kain R, et al. Digital pathology imaging as a novel platform for standardization and globalization of quantitative nephropathology. *Clin Kidney J*. 2017;10(2):176-187.
26. Barisoni L, Lafata KJ, Hewitt SM, Madabhushi A, Balis UGJ. Digital pathology and computational image analysis in nephropathology. *Nat Rev Nephrol*. 2020;16(11):669-685.
27. Boyce BF. An update on the validation of whole slide imaging systems following FDA approval of a system for a routine pathology diagnostic service in the United States. *Biotech Histochem*. 2017;92(6):381-389.
28. Sethi A, Haas M, Markowitz G, et al. Mayo Clinic/Renal Pathology Society Consensus Report on Pathologic Classification, Diagnosis, and Reporting of GN. *Am Soc Nephrol*. 2016;27:1278-1287.