such as M-type phospholipase A2 receptor (PLA2R), thrombospondin type-1 domain-containing 7A (THSD7A), DnaJ homolog subfamily B member 9 (DNAJB9—seen in fibrillary GN), fibronectin, lipoproteins, collagen III, collagen IV α3 and α5 chains, and specific amyloid species. Antigen retrieval methods, such as protease digestion of paraffin-embedded tissue, can be helpful diagnostically.

Ideally, all kidney biopsies should be assessed by light microscopy, immune-histology, and electron microscopy. Due to cost and equipment limitations, it is recognized that electron microscopy may not be available everywhere. Electron microscopy defines the location, extent, and specific characteristics, including organized substructure, of the immune or monoclonal deposits, the extent of foot process effacement, structural glomerular basement membrane (GBM) alterations, and glycoprotein or lipid deposition. Some diagnoses, including minimal change disease (MCD) and immunotactoid deposition disease, are dependent on electron microscopy. In others, electron microscopy contributes significant descriptive and semi-quantitative information about podocytes and GBM, adding to diagnostic certainty. In centers where electron microscopy is not available, consideration should be given to the development of consultative relationships to obtain microscopy assessment in such instances.

"Active" lesions are acute and potentially responsive to specific therapy. "Chronic" lesions are usually not reversible or treatable. Glomerular scarring is associated with downstream tubular atrophy and interstitial fibrosis. The degree of chronic irreversible damage is most easily assessed from the amount of interstitial fibrosis and tubular atrophy. The assessment of chronic damage from the biopsy must always be interpreted together with the clinical data to avoid misinterpretation if the biopsy is taken (by chance) from a focal cortical scar. The amount of information derived from kidney pathology varies substantially in the different types of glomerular diseases; when of particular relevance, this issue is addressed specifically within the appropriate Chapters.

Clinicians should pay attention to the contents and detailed descriptions of active or chronic histopathologic features, and not just the diagnosis, in the biopsy report. Internationally validated scoring systems have been developed for some entities (e.g., MEST-C—mesangial (M) and endocapillary (E) hypercellularity, segmental sclerosis (S); interstitial fibrosis/tubular atrophy (T), and crescents (C) scoring in IgA nephropathy [IgAN; International Society of Nephrology and the Renal Pathology Society [ISN/RPS] classes in lupus nephritis [LN]), which should also be taken into account when discussing treatment.

Practice Point 1.1.3: Repeat kidney biopsy should be performed if the information will potentially alter the therapeutic plan or contribute to the estimation of prognosis.

Repeat kidney biopsy may be needed when the initial biopsy is inadequate to arrive at a diagnosis. Occasionally, sufficient uncertainty regarding the response to management or the progression of kidney disease may be present to warrant a repeat biopsy, even in patients with a well-established diagnosis.

Repeat kidney biopsies are often considered in diseases that have a tendency for a relapsing course or transformations to other histopathologic forms, such as MCD/FSGS. However, there is no evidence that repeat kidney biopsy in SSNS with an initial kidney biopsy showing MCD or FSGS has any material benefit for management (Chapters 5 and 6). A repeat kidney biopsy might be considered, even when the original biopsy was adequate for diagnosis, in the following circumstances:

- when evaluation of a cause for an unexpected deterioration in kidney function is not compatible with the known natural history;
- when the response to treatment is unsatisfactory, especially when a change of therapy is considered;
- in evaluating changes in clinical or laboratory parameters that suggest a change of injury pattern within the same diagnosis (e.g., conversion of membranous to diffuse proliferative LN[6]);
- in reaffirming the morphologic diagnosis and re-evaluating the relative contributions of disease activity and chronicity, to determine whether to intensify, maintain, reduce, or otherwise modify therapy; or
- when defining a "point of no return/therapeutic futility."

Given the invasive nature of the procedure, repeat kidney biopsies should be used when the information expected cannot be obtained from the synthesis of the available clinical information, and when the result is likely to change therapy. Local cost–benefit analysis applied to the clinical decision-making for the care of individual patients may be necessary. There are no RCTs to support recommendations for when or how often a repeat biopsy is necessary.

Research recommendation

- Determine whether proteomics, mass spectroscopy, and/or RNA sequencing analyses on kidney biopsy material can supplement or replace therapeutic decision-making based on morphologic characterizations alone.

1.2 Assessment of kidney function

Key measures for the diagnosis, evaluation of prognosis, and management decision in patients with glomerular disease include assessment of kidney function, particularly measurement (or estimation) of proteinuria and glomerular filtration rate (GFR).

Proteinuria

Assessment of urine total protein excretion rate (PER) using timed urine collections is the preferred method for patients with glomerular disease, particularly when marked proteinuria is present on qualitative testing.[7] It averages the variation of proteinuria due to the circadian rhythm, physical activity, and posture, and avoids the errors introduced by using a random "spot" protein–creatinine ratio (PCR). However, 24-hour urine collection can also be subject to error due to overcollection or undercollection. Simultaneous measurement of urine creatinine and protein in an aliquot of an intended 12–24-hour urine collection is a good compromise