



THE LATEST NEWS IN MEDICAL RENAL PATHOLOGY

By Carla L. Ellis, M.D., M.S.

HIV Associated Renal Disease

- Patients with HIV infection have a wide spectrum of renal diseases; some are thought to be the direct effect of the viral infection, while others are renal diseases that also occur in uninfected populations.

- Despite the advent of antiretroviral drugs, HIV associated nephropathy (HIVAN) is still relatively common. It is thought to be a virus related subtype of primary focal and segmental glomerulosclerosis (FSGS), characterized by collapse of the glomerular tuft with overlying podocyte hyperplasia. Electron microscopy shows tubuloreticular inclusions with podocyte foot process effacement (see Figures 1 and 2, [Semin Diagn Pathol 2017;34:377](#)). It is associated with mutations of the

apolipoprotein L1 (*APOL1*) gene.

- Other important kidney diseases include: (a) HIV associated immune complex kidney disease, characterized by immune complex deposition within glomeruli; (b) HIV associated thrombotic microangiopathy, which presents with hemolytic anemia, renal failure and thrombocytopenia and has very high mortality; and (c) nephrotoxicity due to the multitude of antimicrobial drugs used for treatment of HIV related infections.

- General awareness of the different histopathologic features of HIV associated and unassociated diseases is of paramount importance in the treatment and subsequent outcome of renal function in HIV infected patients.

C3 Glomerulopathy

- C3 glomerulopathy is a disorder of the alternative pathway of complement which includes dense deposit disease, as well as some previously diagnosed cases of membranoproliferative and post-infectious glomerulonephritis.

- Immunofluorescence shows glomerular staining with C3 that is higher in intensity by 2 or more

orders of magnitude than other reactants, but with little or no staining of immunoglobulin. The more specific diagnosis of dense deposit disease is made only when sausage shaped, intramembranous, electron dense deposition is seen. Otherwise, the pattern of dense deposits is variable.

- C3 glomerulopathy may be due to mutations of complement regulatory protein factor H, complement factor I, CD46 or other complement proteins.

- A detailed algorithm with recommendations for classifying biopsy findings and subsequent genetic testing can be found in [Kidney Int 2013;84:1079](#).

Mesoamerican Nephropathy

- Mesoamerican nephropathy is a newly described, endemic chronic kidney disease affecting rural inhabitants in Central America with severe occupational heat stress and volume and salt depletion. Patients typically present with elevated creatinine, but are normotensive with normal to non-nephrotic proteinuria. There is diffuse glomerulosclerosis, universal

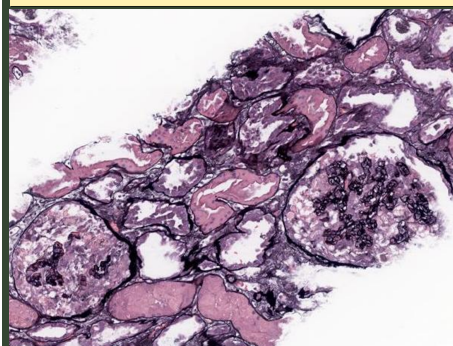
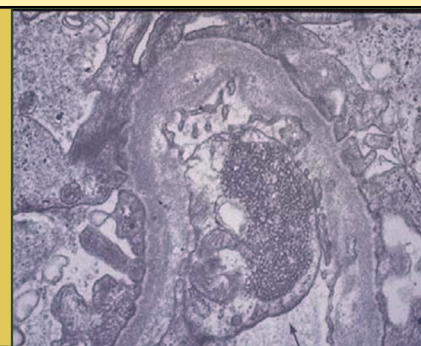


Figure 1 (Left): Jones Silver stain at 20x magnification showing two glomeruli with collapse of the glomerular tuft and overlying podocyte hyperplasia.

Figure 2 (Right): Ultrastructural image of a glomerular capillary loop. An endothelial cell shows a large tubuloreticular inclusion (TRI) within the cytoplasm (arrow). The podocyte foot process overlying the glomerular basement membrane show diffuse effacement as is seen in severe proteinuria.



glomerular hypertrophy in non-sclerotic glomeruli and the suggestion of chronic glomerular ischemia (thickening of Bowman's capsule and glomerular capillary wall wrinkling). There is also mild to moderate tubulointerstitial and vascular disease ([Am J Kidney Dis 2017;69:626](#)).

- Electron microscopy shows vacuolization and lipofuscin-like bodies involving podocyte cytoplasm, but no immune complex deposits.

Anti-PLA2R in Idiopathic Membranous Glomerulonephritis

• M-Type Phospholipase A2 Receptor (PLA2R) was recently identified as a target antigen in idiopathic membranous glomerulonephritis (MGN), a common etiology of nephrotic syndrome in adults ([N Engl J Med 2009;361:11](#)). As a result, there has been a marked increase in its use in renal biopsies, either by IHC or indirect immunofluorescence. It stains subepithelial deposits along the glomerular basement membrane in PLA2R positive cases of idiopathic MGN, with normal podocytes providing a positive internal control ([Clin Nephrol 2015;84:1](#)).

• Although occasional cases of anti-PLA2R negative primary MGN exist, most MGN cases can now be categorized, based on this antibody, as primary or secondary at diagnosis or onset of nephrotic syndrome, without the need to investigate possible secondary causes.

• In addition, PLA2R serum levels, which mirror disease activity, can be monitored to evaluate treatment induced remission and subsequent relapse, which is important because primary MGN has a variable clinical course and does not always respond to

immunosuppressive therapy.

Renal Allograft Biopsies (Transplantation): Recent Updates in Classification of the Banff Criteria:

• The biennial Banff meeting is the largest conference related to solid organ transplantation. Its goal is to produce an accurate, consensus based and organ specific reporting system for allograft rejection. The 2017 report is in press; however the most pertinent findings from the 2013 and 2015 kidney meetings are:

2013 ([Am J Transplant 2014;14:272](#))

• Establishing a diagnosis of antibody mediated rejection in the presence and absence of detectable C4d deposition.

• Developing consensus definitions for glomerulitis (g) and chronic glomerulopathy (cg) scores

• Determining whether isolated "v" lesions represent acute rejection in the presence of tubulointerstitial inflammation.

• Comparing different methodologies for evaluating interstitial fibrosis with regard to reproducibility and prediction of graft function.

• Defining clinically and prognostically significant morphologic criteria for subclassifying polyomavirus nephropathy.

2015 ([Am J Transplant 2017;17:28](#))

• Reviewing the clinical impact of C4d negative antibody mediated rejection from the 2013 meeting.

• Evaluating the relationships of

donor specific antibody testing (anti-HLA and non-HLA).

• Analyzing the use of transcriptome gene sets, their resultant diagnostic classifiers or common key genes to supplement the diagnosis and classification of rejection.

• Introduction of the i-IFTA score (interstitial inflammation in areas of interstitial fibrosis and tubular atrophy).

• Acceptance of transplant arteriopathy within the descriptors of chronic antibody mediated rejection.



MEET THE AUTHOR

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Dr. Ellis is the medical renal pathology editor for PathologyOutlines. She is also chair of the training committee for the Renal Pathology Society, an active USCAP ambassador and works passionately to promote diversity and inclusion in academic medicine.

She has received the Liliane Striker Young Investigator Award (RPS), the Excellence in Urologic Pathology Resident/Fellow Research Award (ISUP), multiple awards for excellence in clinical research from the Johns Hopkins Young Investigator Day ceremony and the Golden Apple teaching award from Emory residents.

She has authored over 40 original/review articles and has an active Twitter following at @theglasspusher.