Published in final edited form as:

Curr Opin HIV AIDS. 2011 July ; 6(4): 285–289. doi:10.1097/COH.0b013e3283476bc3.

Renal disease in HIV infected Individuals

John Phair and

Emeritus Professor of Medicine, Feinberg School of Medicine, Northwestern University

Frank Palella

Professor of Medicine, Feinberg School of Medicine, Northwestern University

Abstract

Purpose of Review—Highly Active Antiretroviral Therapy (HAART) has resulted in a marked decrease in AIDS-related conditions and death. With improved survival, cardiovascular disease (CVD), hepatic, renal disease and non-AIDS related cancers represent an increasing burden for HIV infected individuals.

Recent Findings—HIV Associated Nephropathy (HIVAN), acute renal injury, HAART, and co-morbid conditions such as Hepatitis C, hypertension and diabetes are among the multiple causes of renal disease. In HIVAN there is incomplete understanding of the interaction of the virus with renal cells and the host genetics leading to susceptibility to this form of renal dysfunction. There is agreement that a baseline estimate of glomerular filtration (eGFR) should be obtained and that renal function should be monitored during antiretroviral therapy. There is, however no agreement as to the most accurate method of estimating GFR. Renal transplantation has emerged as a feasible and successful modality of management of end stage renal disease (ESRD) in HIV infected individuals.

Summary—Kidney disease represents an increasing concern in the care of HIV infected persons although there are questions remaining regarding the pathophysiology of HIVAN. Transplantation, however, can be carried out safely in infected persons with ESRD.

Key words/phrases

HIV Associated Nephropathy; Estimates of Glomerular filtration; Renal transplantation of HIV infected patients with end stage renal disease; Effects of antiretroviral drugs upon renal function

Introduction

Suppression of HIV replication and partial restoration of immune competence following administration of effective antiretroviral therapy has resulted in prolongation of survival of HIV infected individuals. In addition, HIVAN has diminished as a cause of renal dysfunction in areas of the world with adequate medical resources. Recipients of HAART, however, are subject to diseases associated with aging such as diabetes, hypertension, and chronic kidney disease (CKD). Furthermore, specific antiretroviral agents are associated with diminished renal function

Increasing Renal Disease in HIV infected Individuals

Adih et al have examined causes of death listed on death certificates of HIV infected persons in the HAART era [1*]. Their analysis documented declines of death due to Acquired Immunodeficiency Syndrome (AIDS) in the United States. Non-AIDS deaths have in part replace AIDS as a cause of death and renal disease was listed as the primary cause on 1682 of 13,750 (12.2%) of death certificates. A similar pattern of an increasing proportion of deaths due to non-AIDS conditions has been reported from Latin America [2] and by the D:A:D study [3], however, fewer deaths than reported by Adih were attributed to renal disease. A community based investigation in Rakai, Uganda, noted that 8% of infected persons initiating HAART had mildly reduced estimated glomerular filtration (eGFR) or moderately reduced eGFR. This frequency of moderate reduction in eGFR was lower than that seen in HIV infected African-Americans (AA) in Baltimore Md. The investigators speculated that modification of diet in renal disease (MDRD) equation which they used to estimate GFR does not incorporate weight and would overestimate eGFR in lighter individuals who eat a diet lower in protein than that eaten by persons in industrialized countries where the MDRD was developed [4*].

Multiple publications have linked kidney function to morbidity and mortality [5*]. Hemmelgarn et al reported that all cause mortality, myocardial infarction and progressive renal failure are increased in non-HIV infected in a community based cohort study in Alberta [6*]. Acute renal injury greatly increases the risk of CVD, ESRD and mortality in HIV infected individuals [7*]. Choi et al also report data from a study of HIV infected persons noting a 48 % mortality in persons with eGFR of less than 60 and albuminuria and 23% mortality in those eGFR <60 alone and 20% mortality in those with albuminuria alone [8*]. Estrella et al using data from the Women's Interagency HIV Study reported that kidney function at HAART initiation remained a determinant of mortality after adjusting for age, race, Hepatitis C, AIDS and CD4+T cell count. Adjustment for hypertension and diabetes did not completely attenuate this risk [9*]. Specifically renal dysfunction as determined by eGFR and proteinuria were noted by George et al to be associated with cardiovascular events in 63 patients compared to 252 matched controls without CVD in the Johns Hopkins HIV Clinic [10*].

Measures of renal function

The critical issue of the method used to determine eGFR in the absence of a direct measure of GFR was discussed by Post et al. Serum creatinine-based estimates of GFR all have limitations [11**]. The Cockcroft-Gault equation adjusts for muscle mass and gender but not for tubular reabsorption of creatinine. The MDRD, also using serum creatinine, again does not account for tubular reabsorption of creatinine. Derived from both men and women the MDRD was compared to a direct measure of GFR, iothalamate clearance. The CKD Epidemiology Collaboration (CKD-EPI) also based upon serum creatinine combined data from more 8000 persons in 10 different studies and was validated in an external sample. The CKD-EPI is more accurate than the Cockcroft-Gault or MDRD equations in persons with normal renal function. However, only small studies of renal function have been conducted in HIV infected persons. Cystatin C has been proposed as an alternate to creatinine as it is not influenced by muscle mass and tubular secretion. Post et al conclude that until creatinine and cystatin C based eGFR are compared to a gold standard the best estimate of renal function in HIV infected persons remains unclear. Post et al also noted that routine measurement of urinary bio-markers of tubular function in clinical practice is not indicated [11**].

Determination of urinary protein or albumin can contribute to estimates of renal dysfunction. A comparison of the urinary albumin-creatinine ratio (ACR), urinary total protein-creatinine

ratio (PCR), 24 hour urinary albumin or total protein demonstrated that ACR and PCR were as effective as 24 hour urinary albumin or protein in predicting renal outcomes. Spot urine for either ACR or PCR moreover, are more convenient for patients, clinicians and laboratories. Tonelli et al used total proteinuria measured by dipstick or ACR plus the MDRD equation to classify the risk of all cause mortality and a composite renal outcome of failure or doubling of serum creatinine in a large sample of uninfected persons.[12**] An accompanying editorial in the Annals of Internal Medicine discussed revision of the definition of CKD to include ACR and clinical diagnoses as well as eGFR to determine risk categories for progression to CKD [13].

HIVAN

HIVAN is the most common cause of CKD in HIV infected persons of African descent who are not receiving HAART. HIV mediates dysregulation of glomerular podocytes, the epithelial cells which maintain the glomerular basement membrane, and apoptosis of renal tubular cells. The resulting lesion of HIVAN is a focal glomerulosclerosis (FGS) and microcytic dilation of tubules [14**][15].

It appears that HIVAN occurs in the setting of specific host genes and it has been widely accepted that the gene encoding a non-myosin A heavy chain (MYH9) is associated with FGS, HIVAN and end stage kidney disease due to hypertension in persons of African descent [16,17]. Recently, however, Genovese and co-workers have reported that genome wide association analysis in AA and European Americans (EA) with FGS identified a 60kb region on chromosome 22 which contains MYH9 and a gene which transcribes a trypanolytic APOL1 variant protein which lyses *Trypanosoma brucei*. This variant was found in AA but not in EA and was presumably selected because of exposure to Trypanosome in Africa. Genovese et al state that this 60kb region spans disequilibrium blocks which includes the gene encoding MYH9. This and a later publication from this group noted that APOL1 variants are absent in Europeans [18,19**]. Other investigators have confirmed the association of the APOL1 variant and FGS in AA [20*].

The interaction of HIV with renal cells has not been clarified. Renal cells lack the classic receptors for HIV, CD4 and the chemokine receptors CCR5 and CXCR4. However, HIV mRNA has been detected in renal epithelial cells and HAART slows progression of HIVAN to renal failure [21]. Non-conventional receptors on renal cells such as C-type lectins including DC-Sign and lipid rafts have been suggested as portals of entry of HIV into renal cells. [22*]. Renal cell infection by HIV, however, is non-productive [23]. Host factors such as activation of the renin-angiotension-aldosterone system have also been implicated in the pathogenesis of HIVAN) and blocking production of Angiotensin II slows progression of HIVAN [15]. Finally, Sharma et al suggest that the NOTCH signaling pathway is activated by HIV proteins that leads to cellular dysregulation of podocytes and dedifferentiation of these cells [24]. Of interest is a recent report that in AA men HIVAN with low PBMC proviral DNA. Conversely, AA men with undetectable plasma HIV RNA but high proviral DNA were at risk for HIVAN as documented by renal biopsy [25*].

Other infections and renal disease

The major co-infection associated with renal disease in the presence of HIV infection is Hepatitis C (HCV). As reviewed by Operskalski and Kovacs, patients with HIV/HCV demonstrate proteinuria, acute interstitial nephritis and acute tubular necrosis although the mechanism underlying the pathogenesis of these conditions is unknown. In contrast, membranoproliferative glomerulonephritis secondary to B-cell stimulation, increased cryoglobulin production and deposition in the renal vasculature has been well documented [26**]. CKD in HIV/HCV infected persons is associated with reduced survival as reported

from a large study from the Veterans Administration [27**] Smaller studies have documented that co-infection increases the risk death as compared to HCV or HIV mono infections [28]. Finally, in Cape Town South Africa where tuberculosis is endemic, granulomatous tubercular interstitial nephritis has been recognized as a cause of proteinuric CKD in children [29].

Antiretroviral drugs and renal disease

Several large investigations have reported that renal impairment is associated with administration receipt of tenofovir or indinavir[30–33*]. In the EuroSida study the incidence rate ratio of developing CKD for cumulative exposure to tenofovir was 1.16 (95% CI 1.06–1.25), indinavir 1.12 (95% CI 1.06–1.18), atazanavir 1.12 (95% CI 1.09–1.35) and lopinavir/ritonavir 1.08 (95% CI 1.01–1.16) all significant increases. [34*]. Rodriguez et al noted that although tenofovir has clinically unimportant effects upon eGFR, high plasma trough levels are associated with renal tubular dysfunction[35]. Specific polymorphisms in genes coding transport proteins have been associated with tubular damage with tenofovir administration. Labarga et al have also reported tubular damage in patients with little or no loss of creatinine clearance [36]. In multivariate analysis comparing 154 patients receiving tenofovir, 49 on other HAART regimens and 81 untreated HIV patients the odds ratios predicting tubular dysfunction was 21.6 (95% CI 4.1–113) [35]. Post et al also noted that routine measurement of urinary bio-markers of tubular function in clinical practice is not indicated[11]. Several reports in children have also emphasized the use of tenofovir in association with tubular dysfunction in the absence of changes in eGFR. Judd et al notes that tubular dysfunction is associated with prolonged use of the tenofovir and is generally reversible with withdrawal of the drug [37].

Raltegravir has been reported to be associated with rhabdomyolysis and renal dysfunction in three cases [38]. The fact that raltegravir has a low molecular weight and is highly soluble in water suggests that it would be removed by hemodialysis. In two patients with ESRD, however, hemodialysis minimally removed raltegravir [39]. The pharmacokinetics of the as yet unreleased CCR5 antagonist, vicriviroc, are not altered in patients with ESKD and the plasma concentration post dialysis was similar to predialysis levels[40].

Treatment of renal disease in HIV infected persons

Reducing the prevalence of renal disease in HIV infected persons will have an impact upon non-AIDS morbidity and mortality. Szezech has pointed out that although HAART slows progression of HIVAN it is likely that the prevalence of CKD will increase with prolongation of survival and the probable increase of hypertension and diabetes in HAART treated HIV persons. Furthermore, biopsy data is rare which prevents developing rationale treatment of other forms of renal disease [21*]. Arendes et al have noted in Cape Town that acute tubular necrosis, nephrotoxic drug exposure or hypovolemic shock were diagnosed in 58% of hospitalized HIV patients requiring renal support. Renal biopsies demonstrated HIVAN in 20% and 10% had other renal pathology. HIVAN was most commonly seen in late stages of HIV infection and it has not been established when institution of HAART is no longer effective in slowing or reversing HIVAN [41]. The experience in Cape Town illustrates also that immune complex nephritis alone or in combination with HIVAN was found in a large number by biopsy and that the treatment of immune complex nephritis has not been established.

Szczech et al noted that microalbuminuria predicts proteinuria in HIV infected individuals and studies have linked proteinuria to CVD and mortality. She suggests that treatment strategies such as angiotensin receptor blockers and HAART need to be evaluated to determine if management of microalbuminuria can prevent these outcomes [42*].

Stock et al [43**] have reported the experience of a multicenter investigation of renal transplantation in HIV infected persons with ESRD receiving HAART. Eligibility depended upon control of HIV infection and a CD4+ T cell count greater than 200/mm³. In persons with evidence of viral hepatitis a liver biopsy was obtained to rule out cirrhosis. Prophylaxis for opportunistic pathogens was utilized as clinically indicated. The recipients were followed for a median of 1.7 years. Both living and deceased donors were utilized. Survival at one and three years was 94.6 and 88.2% and graft survival was 90.4% and 73.7% respectively. These results were equivalent to those seen in non-HIV infected graft recipients older than 65 years of age. Few recipients showed progression of HIV infection; however, the cumulative incidence of rejection was 31% (95% CI 24–40) at one year and 41% (95% CI 32–52) at three years, which is higher than seen in non-HIV infected graft recipients. The authors, in summary, state that renal transplantation is feasible in appropriately selected HIV infected patients. Strategies to lower graft rejection are needed.

Other investigators have evaluated whether or not HIV infected persons with ESRD would accept a kidney from an HIV infected donor. A majority, under specific circumstances would consider acceptance of a graft from an infected donor [44]. A companion paper raised the issue of whether it was ethical to inform a living donor that the recipient was HIV infected. The authors concluded that the privacy of the recipient was paramount and that the donor should be told only that the potential recipient required a renal transplant [45].

Conclusion

Renal disease represents an increasing cause of morbidity and mortality in HIV infected individuals who are surviving longer due to effective antiretroviral therapy. Longitudinal studies of renal disease in HIV infected persons receiving or not receiving HAART, however, are not yet available. Effective treatment when initiated early. GFR in HIV infected persons has not been clearly established. Clinically management of HIV infection includes monitoring of serum creatinine and urinary albumin or protein as well as treatment of hypertension and diabetes. Successful renal transplantation of selected HIV infected persons represents a major breakthrough in the management of this condition.

Summary

Enhanced survival of treated HIV infected persons will result in an increased number with renal disease. The pathogenesis of HIVAN in persons of African descent is related to host genetics.

Both glomerular and tubular dysfunction can be related to exposure to specific antiretroviral agents. Renal transplantation is feasible for HIV infected patients with end stage renal disease.

Acknowledgments

Dr. Phair is supported by NIH grants U01AIO35039, RO1AG0348522 and UO1 AI034041

Dr. Palella is supported by NIH grants 1RO1HL095129, 1520//RO1AG034853 and CDC 200-2006-18797

References

- 1*. Adih WK, Selik RM, Hu X. Trends in Diseases Reported on US Death Certificates That Mentioned HIV Infection, 1996–2006. J Int Assoc Physicians AIDS Care (Chic Ill). 2010 Multiple-cause mortality was determined from review of death certificates mentioning HIV. Liver disease, renal disease and heart disease were prominent non-AIDS causes of death.

2. Belloso WH, Orellana LC, Grinsztejn B, et al. Analysis of serious non-AIDS events among HIV-infected adults at Latin American sites. *HIV Med.* 2010; 11(9):554–64. [PubMed: 20345879]
3. Smith C, Sabin CA, Lundgren JD, et al. Factors associated with specific causes of death amongst HIV-positive individuals in the D:A:D Study. *AIDS.* 2010; 24(10):1537–48. [PubMed: 20453631]
- 4*. Lucas GM, Clarke W, Kagaayi J, et al. Decreased kidney function in a community-based cohort of HIV-Infected and HIV-negative individuals in Rakai, Uganda. *J Acquir Immune Defic Syndr.* 2010; 55(4):491–4. Estimated GFR was determined among HIV-infected and uninfected individuals in a cohort in Rakai, before anti retroviral therapy was started. The HIV infected were twice as likely to have evidence of mild or moderate reduction in GFR although moderately impaired renal function was uncommon as measured by the MDRD equation. [PubMed: 20613548]
- 5*. Stenvinkel P. Chronic kidney disease: a public health priority and harbinger of premature cardiovascular disease. *J Intern Med.* 2010; 268(5):456–67. Kidney disease is a silent epidemic. The global increase in hypertension, obesity, and diabetes requires that effective strategies be developed to control CKD and reduce cardiovascular risk. [PubMed: 20809922]
- 6*. Hemmelgarn BR, Manns BJ, Lloyd A, et al. Relation between kidney function, proteinuria, and adverse outcomes. *JAMA.* 2010; 303(5):423–9. All cause mortality was increased in an analysis of outcomes among close to a million uninfected individuals in Alberta, Canada. Mortality was higher in those with lower eGFR and/or proteinuria. [PubMed: 20124537]
- 7*. Choi AI, Li Y, Parikh C, et al. Long-term clinical consequences of acute kidney injury in the HIV-infected. *Kidney Int.* 2010; 78(5):478–85. Acute kidney injury in HIV-infected individuals was associated with progression of renal disease and death but not CVD. [PubMed: 20520594]
- 8**. Choi A, Scherzer R, Bacchetti P, et al. Cystatin C, albuminuria, and 5-year all-cause mortality in HIV-infected persons. *Am J Kidney Dis.* 2010; 56(5):872–82. A large study using cystatin c to determine eGFR which demonstrated that reduced GFR and/or albuminuria was associated with increased mortality. The five year follow up adds to the relevance of this study. [PubMed: 20709438]
- 9**. Estrella MM, Parekh RS, Abraham A, et al. The impact of kidney function at highly active antiretroviral therapy initiation on mortality in HIV-infected women. *J Acquir Immune Defic Syndr.* 2010; 55(2):217–220. In the Women's Interagency HIV Study, a large prospective cohort investigation, renal function at initiation of HAART was an independent predictor of death, especially in women with AIDS. [PubMed: 20581688]
- 10*. George E, Lucas GM, Nadkarni GN, et al. Kidney function and the risk of cardiovascular events in HIV-1-infected patients. *AIDS.* 2010; 24(3):387–94. Investigators at the Hopkins HIV clinic determined that decreased renal function was associated with CVD as compared to HIV infected without evidence of CVD. Reduced renal function was an independent determinant of CVD after controlling for traditional risk factors for CVD. [PubMed: 20019575]
- 11**. Post FA, Wyatt CM, Mocroft A. Biomarkers of impaired renal function. *Curr Opin HIV AIDS.* 2010; 5(6):524–30. The authors thoroughly reviewed the literature discussing indirect and direct measures on GFR and tubular function in HIV infected individuals. They concluded that further studies are needed to determine the best method of detecting and monitoring renal disease in this population. [PubMed: 20978396]
- 12**. Tonelli M, Muntner P, Lloyd A, et al. Using proteinuria and estimated glomerular filtration rate to classify risk in patients with chronic kidney disease: a cohort study. *Ann Intern Med.* 2011; 154(1):12–21. A major analysis of the value of adding measures of albuminuria or proteinuria to eGFR in order to determine risk of progression to CKD among close to 500,000 non-HIV infected persons in Alberta. Two independent validation cohorts were used to compare the five-category risk system. Higher risk of progression of renal disease was associated with lower eGFR or increase proteinuria. [PubMed: 21200034]
13. Levey AS, Tangri N, Stevens LA. Classification of chronic kidney disease: a step forward. *Ann Intern Med.* 2011; 154(1):65–7. [PubMed: 21200043]
- 14**. Gopalakrishnan I, Iskandar SS, Daeihagh P, et al. Coincident idiopathic focal segmental glomerulosclerosis collapsing variant and diabetic nephropathy in an African American homozygous for MYH9 risk variants. *Hum Pathol.* 2011; 42(2):291–4. This is a comprehensive review of the interaction of HIV and renal cells. The authors emphasize African descent, the

MYH9 susceptible allele and activation of the renin-angiotensin-aldosterone system as the important factors in the development of HIVAN. The authors review renal biopsy studies from patients with HIVAN and the potential portals of entry of HIV in to renal cells. [PubMed: 21074826]

15. Mikulak J, Singhal PC. HIV-1 and kidney cells: better understanding of viral interaction. *Nephron Exp Nephrol*. 2010; 115(2):e15–21. [PubMed: 20407278]
16. Nelson GW, Freedman BI, Bowden DW, et al. Dense mapping of MYH9 localizes the strongest kidney disease associations to the region of introns 13 to 15. *Hum Mol Genet*. 2010; 19(9):1805–15. [PubMed: 20124285]
17. Murea M, Freedman BI. Essential hypertension and risk of nephropathy: a reappraisal. *Curr Opin Nephrol Hypertens*. 2010; 19(3):235–41. [PubMed: 20051853]
- 18**. Genovese G, Friedman DJ, Ross MD, et al. Association of trypanolytic ApoL1 variants with kidney disease in African Americans. *Science*. 2010; 329(5993):841–5. The authors have identified that focal segmental glomerulosclerosis and hypertension in African-Americans are associated with a variant of genes encoding a serum factor, apolipoprotein L-1 that lyses trypanosomes. Only serum from persons with the kidney associated variant lyse *Trypanosoma brucei*. This study provides a plausible biologic rationale for the selection of this genotype in persons of African descent and an explanation for the occurrence of HIVAN in persons of African descent. [PubMed: 20647424]
- 19**. Genovese G, Tonna SJ, Knob AU, et al. A risk allele for focal segmental glomerulosclerosis in African Americans is located within a region containing APOL1 and MYH9. *Kidney Int*. 2010; 78(7):698–704. A further analysis demonstrating that variants within a 60kb region of chromosome 22 contained both APOL1 and MYH9 genes associated with glomerulosclerosis in African-Americans. [PubMed: 20668430]
- 20*. Tzur S, Rosset S, Shemer R, et al. Missense mutations in the APOL1 gene are highly associated with end stage kidney disease risk previously attributed to the MYH9 gene. *Hum Genet*. 2010; 128(3):345–50. Another study that identifies two west African-specific missense mutations in the neighboring APOL1 gene that are more strongly associated with end stage renal diseases than the MYH9 gene. [PubMed: 20635188]
- 21*. Szczech LA. Tackling the unknowns in HIV-related kidney diseases. *N Engl J Med*. 2010; 363(21):2058–9. An editorial which concisely reviews the status of our knowledge of renal disease in HIV infected persons. [PubMed: 21083392]
- 22*. Mikulak J, Teichberg S, Arora S, et al. DC-specific ICAM-3-grabbing nonintegrin mediates internalization of HIV-1 into human podocytes. *Am J Physiol Renal Physiol*. 2010; 299(3):F664–73. An important investigation which examines the possible mechanisms of the interaction of HIV with renal cells. [PubMed: 20630938]
23. Khatua AK, Taylor HE, Hildreth JE, et al. Non-productive HIV-1 infection of human glomerular and urinary podocytes. *Virology*. 2010; 408(1):119–27. [PubMed: 20937511]
24. Sharma M, Callen S, Zhang D, et al. Activation of Notch signaling pathway in HIV-associated nephropathy. *AIDS*. 2010; 24(14):2161–70. [PubMed: 20706108]
- 25*. Izzedine H, Acharya V, Wirden M, et al. Role of HIV-1 DNA levels as clinical marker of HIV-1-associated nephropathies. *Nephrol Dial Transplant*. 2011; 26(2):580–3. The authors note that HIV-1 DNA determines the occurrence of HIVAN. [PubMed: 20624771]
- 26**. Operskalski EA, Kovacs A. HIV/HCV Co-infection: Pathogenesis, Clinical Complications, Treatment, and New Therapeutic Technologies. *Curr HIV/AIDS Rep*. 2011; 8(1):12–22. A thorough evaluation of the clinical problems associated with HIV/HCV coinfection. [PubMed: 21221855]
- 27**. Fischer MJ, Wyatt CM, Gordon K, et al. Hepatitis C and the risk of kidney disease and mortality in veterans with HIV. *J Acquir Immune Defic Syndr*. 2010; 53(2):222–6. The impact of HIV/HCV co-infection upon the development of CKD in a large cohort of veterans is reviewed. The study documents the increased risk of CVD and mortality in persons with CKD associated with HIV/HCV infection. [PubMed: 20104121]
28. Izzedine H, Sene D, Cacoub P, et al. Kidney diseases in HIV/HCV-co-infected patients. *AIDS*. 2009; 23(10):1219–26. [PubMed: 19440143]

29. Nourse PJ, Cotton MF, Bates WD. Renal manifestations in children co-infected with HIV and disseminated tuberculosis. *Pediatr Nephrol*. 2010; 25(9):1759–63. [PubMed: 20422226]
- 30*. Cooper RD, Wiebe N, Smith N, et al. Systematic review and meta-analysis: renal safety of tenofovir disoproxil fumarate in HIV-infected patients. *Clin Infect Dis*. 2010; 51(5):496–505. This analysis concludes that although administration of tenofovir is followed by a decreased eGFR the clinical consequences are modest. [PubMed: 20673002]
- 31*. Deti EK, Thiebaut R, Bonnet F, et al. Prevalence and factors associated with renal impairment in HIV-infected patients, ANRS C03 Aquitaine Cohort, France. *HIV Med* 2. 2010; 11(5):308–17. The authors review the effect of tenofovir and other antiretroviral agents upon renal function in the large cohort of HIV infected French individuals.
- 32*. De Beaudrap P, Diallo MB, Landman R, et al. Changes in the renal function after tenofovir-containing antiretroviral therapy initiation in a Senegalese cohort (ANRS 1215). *AIDS Res Hum Retroviruses*. 2010; 26(11):1221–7. These authors noted a moderate decline in eGFR with tenofovir therapy. One year post discontinuation one third had persistence of the decreased GFR. [PubMed: 20854202]
- 33*. Wever K, van Agtmael MA, Carr A. Incomplete reversibility of tenofovir-related renal toxicity in HIV-infected men. *J Acquir Immune Defic Syndr*. 2010; 55(1):78–81. Another report of the failure of renal function to completely return to normal following discontinuation of tenofovir. [PubMed: 20173649]
- 34*. Mocroft A, Kirk O, Reiss P, et al. Estimated glomerular filtration rate, chronic kidney disease and antiretroviral drug use in HIV-positive patients. *AIDS*. 2010; 24(11):1667–78. The experience of the EuroSIDA cohort with CKD in association with the use of antiretroviral agents is reviewed in this publication. [PubMed: 20523203]
35. Rodriguez-Novoa S, Alvarez E, Labarga P, Soriano V. Renal toxicity associated with tenofovir use. *Expert Opin Drug Saf*. 2010; 9(4):545–59. [PubMed: 20384533]
36. Labarga P, Barreiro P, Martin-Carbonero L, et al. Kidney tubular abnormalities in the absence of impaired glomerular function in HIV patients treated with tenofovir. *AIDS*. 2009; 23(6):689–96. [PubMed: 19262355]
37. Judd A, Boyd KL, Stohr W, Dunn D, et al. Effect of tenofovir disoproxil fumarate on risk of renal abnormality in HIV-1-infected children on antiretroviral therapy: a nested case-control study. *AIDS*. 2010; 24(4):525–34. [PubMed: 20139752]
38. Masia M, Enriquez R, Sirvent A, Gutierrez F, et al. Severe acute renal failure associated with rhabdomyolysis during treatment with raltegravir. A call for caution. *J Infect*. 2010; 61(2):189–90. [PubMed: 20447415]
39. Molto J, Sanz-Moreno J, Valle M, et al. Minimal removal of raltegravir by hemodialysis in HIV-infected patients with end-stage renal disease. *Antimicrob Agents Chemother*. 2010; 54(7):3047–8. [PubMed: 20439608]
40. Kasserra C, Sansone-Parsons A, Keung A, et al. Renal insufficiency has no effect on the pharmacokinetics of vicriviroc in a ritonavir-containing regimen. *Clin Pharmacokinet*. 2010; 49(6):397–406. [PubMed: 20481650]
41. Arendse CG, Wearne N, Okpechi IG, Swanepoel CR. The acute, the chronic and the news of HIV-related renal disease in Africa. *Kidney Int*. 2010; 78(3):239–45. [PubMed: 20531456]
- 42*. Szczech LA, Menezes P, Byrd Quinliva E, et al. Microalbuminuria predicts overt proteinuria among patients with HIV infection. *HIV Med*. 2010; 11(7):419–26. The authors have documented that microalbuminuria progresses to proteinuria in HIV-infected individuals. This progression was associated with lower CD4T cell number and higher HIV RNA levels. [PubMed: 20059571]
- 43**. Stock PG, Barin B, Murphy B, et al. Outcomes of kidney transplantation in HIV-infected recipients. *N Engl J Med*. 2010; 363(21):2004–14. This important study documents the results of renal transplantation in selected HIV-infected individuals with ESRD. The authors compared results to transplantation in non HIV-infected persons over the age of 65. Mortality and graft survival were comparable in the recipients of renal grafts to historical controls but graft rejection occurred more commonly. [PubMed: 21083386]

44. Reese PP, Tehrani T, Lim MA, et al. Determinants of the decision to accept a kidney from a donor at increased risk for blood-borne viral infection. *Clin J Am Soc Nephrol*. 2010; 5(5):917–23. [PubMed: 20338966]
45. Formica RN Jr, Asch WS, Wagner KR, Kulkarni S. Kidney transplantation and HIV: does recipient privacy outweigh the donor's right to information? *Clin J Am Soc Nephrol*. 2010; 5(5): 924–8. [PubMed: 20203162]