

## Perspective

# Renal Disease and Toxicities: Issues for HIV Care Providers

*The prevalence of renal disease is increasing in the HIV-infected population, likely reflecting increases in renal disease in the general population due to hypertension and diabetes, clustering of HIV cases in black Americans (who have a higher frequency of renal risk factors), and toxicities of antiretroviral and other drugs taken by HIV-infected patients. Screening for renal function and regular follow up are recommended for all HIV-infected individuals starting at the time of HIV diagnosis. Elements of screening include quantitative risk-factor assessment and screening tests, such as urine protein quantitation and estimation of creatinine clearance and glomerular filtration rate. Diagnosis of renal dysfunction includes consideration of causative factors common in the general population as well as HIV-specific factors. This article summarizes a presentation on renal impairment in HIV disease made by Derek M. Fine, MD, at the 9th Annual Ryan White CARE Act Clinical Update in Washington, DC, in August 2006. The original presentation is available as a Webcast at [www.iasusa.org](http://www.iasusa.org).*

The prevalence of kidney disease is increasing in the US HIV-infected population, even though the incidence of end stage renal disease (ESRD) attributed to HIV-associated nephropathy (HIVAN) has remained constant since the mid-1990s. Although the incidence of ESRD attributed to AIDS nephropathy—which may or may not represent HIVAN—reached a plateau after 1996, there is little information about the incidence of earlier stages of HIVAN in the potent antiretroviral therapy era. It is currently estimated that renal function is abnormal in up to 30% of HIV-infected patients (Gupta et al, *Clin Infect Dis*, 2005), and abnormal renal function is an independent predictor of mortality in this population (Szczec et al, *Clin Infect Dis*, 2004). Renal dysfunction, unless in advanced stages, is usually asymptomatic. Since it poses serious risks, including risks of drug toxicities, HIV-infected patients should have renal function assessed at the time of HIV diagnosis and at regular intervals thereafter, depending on renal function and risk factors.

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## Risk Factors

Risk factors for kidney disease in the HIV-infected population include hypertension, diabetes, black race and other genetic factors, family history, and hepatitis C virus infection, which are also risk factors in the general population, as well as HIV-specific factors such as lower CD4+ cell count and higher HIV viral load. There have been marked increases in rates of ESRD due to hypertension and diabetes in the general population over the past 20 years. These causes now account for 70% or more of ESRD, and these increases are likely occurring in the HIV-infected population. Part of the increase in renal disease in the HIV-infected population is also likely associated with clustering of HIV cases in black Americans and the high frequency of

hypertension and diabetes in this racial group. Centers for Disease Control and Prevention (CDC) data from 2003 indicate that 48% of US AIDS cases are in black individuals, who constitute only 13% of the US population. Black Americans are 1.8 times as likely to have diabetes as age-adjusted white Americans, and it has been estimated that more than 30% of black individuals aged 18 years and older have hypertension.

Hypertension, which is estimated to be present in 12% to 21% of the HIV-infected population, is an independent risk factor for mortality in patients beginning antiretroviral therapy. Independent risk factors for mortality include measures of renal function (elevated serum creatinine, proteinuria) and hypertension in HIV-infected women (Table 1; Szczec et al, *Clin Infect Dis*, 2004). Some antiretroviral therapies may increase risk of hypertension, and thus risk of renal dysfunction, in HIV-infected patients (Crane et al, *AIDS*, 2006).

## Assessment

The Infectious Diseases Society of America (IDSA) guidelines for screening for renal disease in HIV-infected patients are summarized in Figure 1 (Gupta et al, *Clin Infect Dis*, 2005). Risk-factor assessment and screening should begin at the first provider contact at which HIV infection is documented. History of nephrotoxic-medication use should include ask-

**Table 1.** Multivariable Independent Predictors of Mortality After Initiation of Antiretroviral Therapy in Women

Variable as Predictor of Death	Hazard Ratio (95% CI)	P-value
Proteinuria (presence vs. absence)	2.21 (1.33–3.67)	.002
History of hypertension	2.25 (1.37–3.68)	.001
CD4+ count (per 100 cells/ $\mu$ L decrease)	1.36 (1.15–1.60)	.0003
Hepatitis C virus infection	2.13 (1.34–3.39)	.001
Albumin level (per 1 mg/dL decrease)	2.04 (1.26–3.29)	.004
Prior history of AIDS-defining illness	1.81 (1.09–3.01)	.02

Adapted with permission from Szczec et al, *Clin Infect Dis*, 2004. CI indicates confidence interval.

**Kidney Disease Risk: Qualitative Assessment**

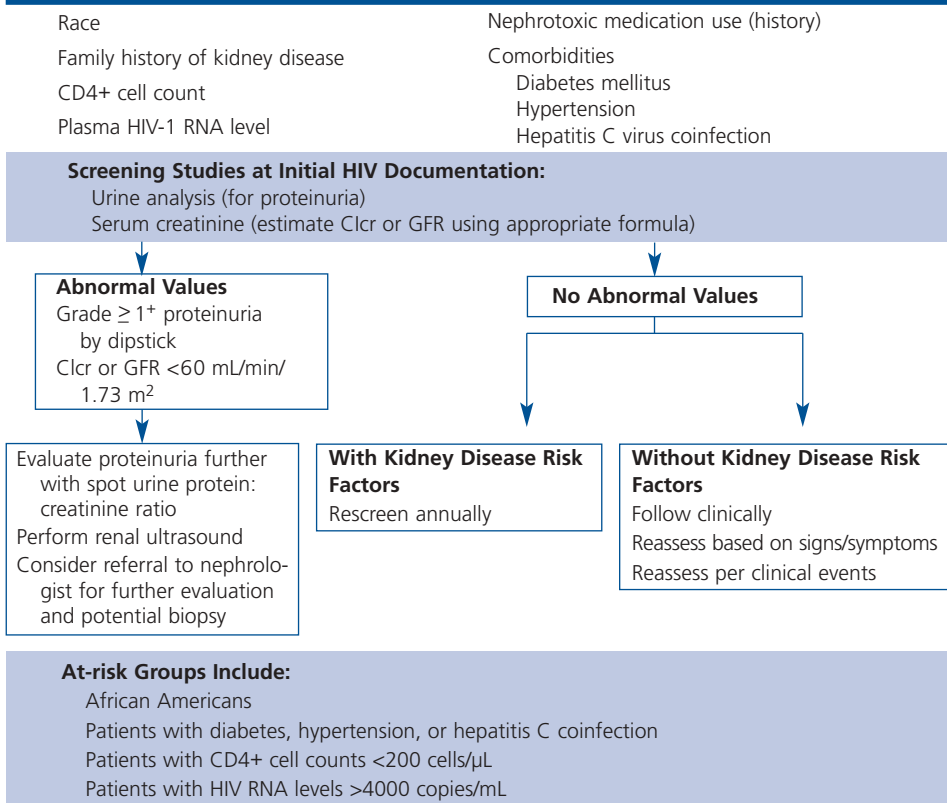


Figure 1. Infectious Diseases Society of America (IDSA) guidelines: Screening Algorithm for HIV-related Renal Diseases. Clcr indicates creatinine clearance; GFR, glomerular filtration rate. Adapted with permission from Gupta et al, *Clin Infect Dis*, 2005.

ing if the patient is using over-the-counter nonsteroidal anti-inflammatory drugs (NSAIDs). These are frequently omitted from consideration in terms of risk for renal dysfunction. The IDSA

guidelines recommend screening tests, including urinalysis for proteinuria and serum creatinine level for calculation of creatinine clearance or glomerular filtration rate (GFR)—proteinuria of grade

1+ or higher on dipstick and an estimated GFR below 60 mL/min/ $1.73$  m<sup>2</sup> are the abnormal thresholds that should prompt additional work-up.

Serum creatinine measurement alone does not provide sufficient information on renal function. The left section of Figure 2 shows that a substantial proportion of individuals with abnormal renal function based on measured actual inulin clearance (GFR) has serum creatinine levels that would be considered within the normal range. There is not a good correlation between change in serum creatinine and change in GFR.

The Cockcroft-Gault formula and the Modified Diet in Renal Disease (MDRD) formula are used to calculate GFR from serum creatinine, but it is important to note that neither is perfect. The Cockcroft-Gault formula has the advantage of including body weight as a variable, which accounts for the significant weight changes that can occur in HIV-infected patients and patients with renal disease. The MDRD formula, which does not include body weight, has been widely adopted in the 4-variable form. The middle and right sections of Figure 2 show the correlations between creatinine clearance predicted by the Cockcroft-Gault equation and GFR predicted by the MDRD formula and actual GFR. The correspondence between predicted and actual values is fairly tight at GFR below 60 mL/min/ $1.73$  m<sup>2</sup>. Both equations can

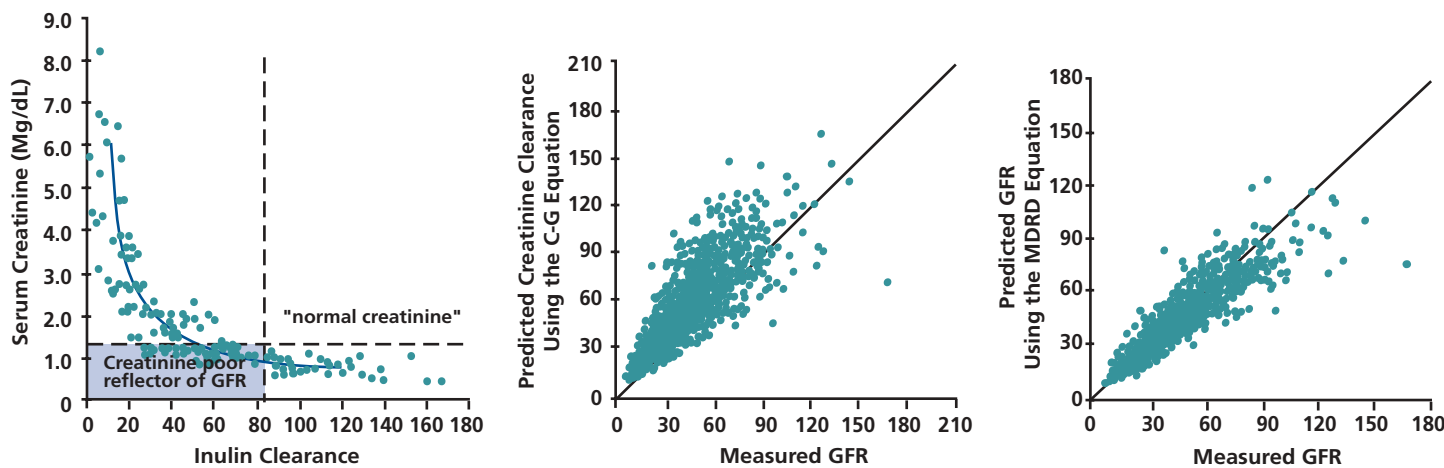


Figure 2. Left: relationship of serum creatinine level and inulin clearance rate (mL/min/ $1.73$ m<sup>2</sup>) estimated by using the Cockcroft-Gault (C-G) equation; middle: correlation of creatinine (cr) clearance rate (mL/min/ $1.73$ m<sup>2</sup>) predicted by C-G equation with measured glomerular filtration rate (GFR; mL/min/ $1.73$ m<sup>2</sup>); and right: correlation of GFR predicted by the 6-variable (cr, blood urea nitrogen, age, race, sex, albumin) Modified Diet in Renal Disease (MDRD) equation with measured GFR. Left section adapted with permission from Johnson et al, *Comprehensive Clinical Nephrology*, 2000. Middle and right sections adapted with permission from Levey et al, *Ann Intern Med*, 1999.

**Table 2.** Differential Diagnosis of Acute Renal Failure in HIV Disease

HIV-related Causes	Other Causes
HIV-associated nephropathy	Usual causes in general population: pre-renal, etc.
Thrombotic microangiopathy	Acute interstitial nephritis: multiple medication exposures
Membranoproliferative glomerulonephritis (MPGN)	Hepatitis B virus- and hepatitis C virus-related disease
Immune complex glomerulonephritis (MPGN or lupus-like)	Rhabdomyolysis: statins and protease inhibitors
Medication	
Indinavir, tenofovir, sulfadiazine, pentamidine, sulfamethoxazole, and trimethoprim	

be used to provide a “ballpark” estimate of GFR, although the MDRD is considered the more accurate of the two. Neither formula, however, has been validated in the HIV population.

Determination of urine protein via dipstick, as recommended in current guidelines, is unreliable. In 52 HIV-infected patients in The Johns Hopkins HIV Nephrology Clinic with proteinuria of 500 to 1000 mg, dipstick results were “none” or “trace” in 19%, and within each dipstick grade there was a wide variation of amount of protein (unpublished data). The newer automated dipsticks are highly sensitive, resulting in a large proportion of false-positives among grade 1+ results. The 24-hour urine collection is the gold standard for measuring protein but is highly impractical, since a large number of patients will not complete the test. A practical and reliable method for quantitation of urine protein in initial work-up is the random urine protein:creatinine ratio, which divides protein concentration by creatinine concentration in a random urine sample. This method has shown a good correlation with 24-hour protein measurement. Although it may be inconvenient or too expensive to use this method at every contact, it is very useful for providing an initial quantitative assessment that will more accurately reflect whether or not the patient has renal dysfunction and requires further work-up.

## Diagnoses

Differential diagnosis of acute renal failure in HIV-infected patients includes HIV-related conditions (eg, HIVAN and drug-related renal failure) and other conditions that may affect HIV-infected

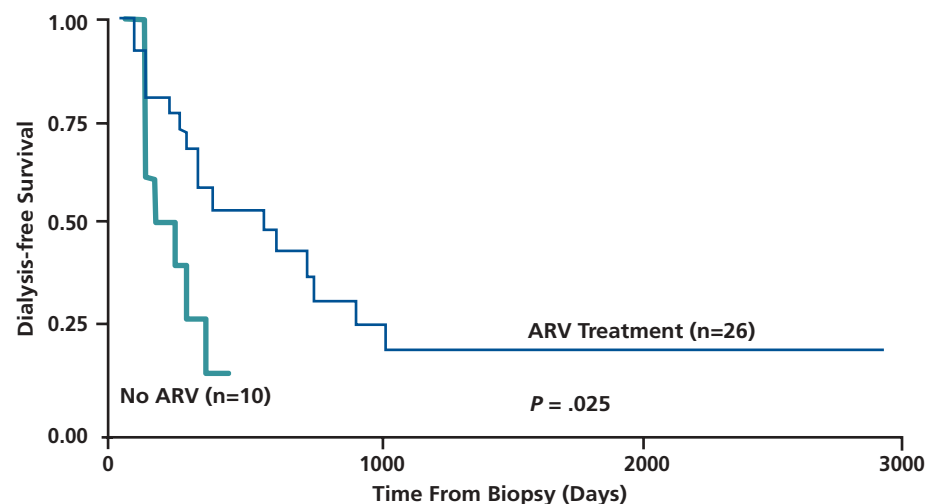
and noninfected individuals (see Table 2). After consideration of non-HIV-related causes, HIVAN should be ruled out first, due to its poor prognosis if untreated. Drug-related problems that have occurred with some frequency in the HIV-infected population include acute tubular necrosis and tubular disorders (eg, with tenofovir), acute interstitial nephritis (eg, with trimethoprim/sulfamethoxazole, indinavir, or a variety of other drugs), and crystalluria or renal stones (eg, with indinavir, acyclovir, sulfadiazine). There should also be heightened suspicion for hepatitis C virus-related membranoproliferative glomerulonephritis and rhabdomyolysis in HIV-infected patients.

## HIVAN

HIVAN *must* be diagnosed when present, given its extremely rapid progression to ESRD over the course of weeks

to months. HIVAN occurs almost exclusively in patients of African descent. Patients have a rapidly rising creatinine level, proteinuria that is usually in the nephrotic range (>3 g), and, almost invariably, a detectable viral load. Definitive diagnosis can be made only by biopsy. Although biopsy carries some risk, the benefit of immediate diagnosis of HIVAN (and ruling out the numerous other diseases that may be present) outweighs such risk.

Antiretroviral therapy can treat and prevent HIVAN, and should be immediately initiated in patients with HIV infection and HIVAN. A 12-year study in a Johns Hopkins HIV clinic cohort showed that rates of presumed HIVAN (based on clinical diagnosis) among HIV-infected patients without AIDS were 0% in those on highly active antiretroviral therapy, 5.0% in those receiving only nucleoside reverse transcriptase inhibitor (nRTI) therapy, and 2.6% in those receiving no antiretroviral treatment. In patients with AIDS, rates were 6.8% in those receiving antiretroviral therapy, 14.4% in those receiving nRTI therapy, and 26.3% in those receiving no antiretroviral treatment ( $P < .001$  for trend; Lucas, *AIDS*, 2004). Among 56 patients with HIVAN followed up in The Johns Hopkins HIV Nephrology Clinic, 20 were on dialysis within 1 month of diagnosis; dialysis-free survival was significantly pro-



**Figure 3.** Dialysis-free survival estimate in patients with HIV-associated nephropathy in The Johns Hopkins Nephrology HIV Cohort according to treatment with antiretroviral therapy (ARV). Adapted with permission from Atta et al, *Nephrol Dial Transplant*, 2006.

longed among the remaining 26 who received antiretroviral therapy compared with the 10 who did not (with the 1 patient in the latter group who did not require dialysis disappearing from treatment with a creatinine of 6 mg/dL; see Figure 3; Atta et al, *Nephrol Dial Transplant*, 2006).

Other treatments that may be attempted include glucocorticoids (Eustace et al, *Kidney Int*, 2000; Smith et al, *Am J Med*, 1996) and angiotensin converting enzyme (ACE) inhibitors (Kimmel et al, *Am J Kidney Dis*, 1996; Wei et al, *Kidney Int*, 2003) or angiotensin-II receptor blockers (ARBs), though none of these treatments have been tested in a randomized clinical trial. Due to the aggressive nature of HIVAN, initiation of such potentially useful agents should be considered in all cases if tolerated by the patient.

### Tenofovir-associated Renal Dysfunction

Tenofovir is closely related to adefovir, a known nephrotoxic agent that was removed from the HIV treatment market due to its causing acute renal failure and Fanconi syndrome; this toxicity has not been observed with adefovir at currently-used hepatitis B treatment doses. No significant nephrotoxicity with tenofovir was reported in clinical trials of the agent, although a small but statistically significant decline in GFR was observed in patients receiving tenofovir over 48 weeks in an observational cohort (Gallant et al, *Clin Infect Dis*, 2005). In this study, a greater than 50% reduction in creatinine clearance occurred in 4.4% of patients receiving tenofovir compared with 1.9% of those receiving other nRTIs, and a decline of 25% to 50% occurred in 13.4% and 10.8%, respectively. These data suggest that some patients may be experiencing significant renal impairment on tenofovir.

The drug is secreted by the renal tubule but is also filtered freely through the glomerulus. It is likely that renal impairment from other causes (whether pre-existing chronic kidney disease or new acute renal failure) results in reduced clearance of tenofovir, with the elevated tenofovir levels then con-

tributing to renal dysfunction. Table 3 shows independent risk factors for renal impairment from a CDC analysis of 9535 antiretroviral therapy-experienced patients with 17,357 person-years of follow up. Tenofovir use compared with use of other antiretroviral drugs was associated with a statistically significant 1.6-fold greater risk for renal impairment (Heffelfinger, 13th CROI, 2006)

There have been several case reports of renal toxicity, including Fanconi syndrome, associated with tenofovir. Fanconi syndrome is a loss of proximal tubular function that results in failure to reabsorb electrolytes and nutrients (eg, glucose, bicarbonate, phosphates, uric acid, potassium, sodium, amino acids), with subsequent elimination of these compounds in the urine. The syndrome is defined by a hypokalemic, metabolic acidosis with hypophosphatemia and glucosuria, however, the presence of any combination of these features can

occur when the proximal tubule is affected. The underlying risk factors cannot be determined on the basis of these reports; however, in some of these cases, there was an acute event leading to renal failure that did not resolve until tenofovir was discontinued. In a report of 27 cases of tenofovir-associated renal dysfunction, mean baseline creatinine was 0.9 mg/dL, peak creatinine was 3.9 mg/dL ( $P < .05$ ), and post-discontinuation creatinine was 1.2 mg/dL ( $P < .05$ ), with creatinine returning to baseline levels in 22 (81%) of patients. Proteinuria was present in 6 (35%) of 17 patients assessed. Fanconi syndrome was diagnosed in 16 (59%) of the patients, and 2 (7%) required dialysis (Zimmerman, *Clin Infect Dis*, 2006).

A summary of 25 reported cases of Fanconi syndrome in patients receiving tenofovir indicates that patients had a mean age of 45.5-years old (range, 34–60-years old) and mean time to diagnosis from the initiation of teno-

**Table 3. Independent Risk Factors for Acute Renal Failure in 9535 Antiretroviral Therapy-experienced Patients with 17,357 Person-years of Follow-up**

	Odds Ratio (95% Confidence Interval) for Renal Impairment			
	Any (GFR <90 vs ≥ 90)	Mild (GFR 60-89 vs ≥ 90)	Moderate (GFR 30-59 vs ≥ 90)	Severe (GFR 0-29 vs ≥ 90)
<b>CD4+ Count (Cells/μL): Vs 350 (Referent)</b>				
<50	1.5 (1.3–1.7)	1.3 (1.1–1.5)	3.0 (2.2–4.1)	3.5 (2.1–5.9)
50–199	1.3 (1.2–1.5)	1.3 (1.2–1.4)	1.7 (1.4–2.2)	2.2 (1.4–3.4)
200–349	1.1 (1.1–1.2)	1.1 (1.0–1.2)	1.2 (0.9–1.5)	1.5 (1.0–2.4)
<b>Hemoglobin (Mg/dL): Vs 10.5 (Referent)</b>				
<8.0	4.7 (3.9–5.7)	2.4 (1.9–3.0)	13.8 (10.1–18.8)	75.6 (47.5–120.3)
8.0–10.4	1.7 (1.5–1.9)	1.3 (1.2–1.5)	3.8 (2.9–4.9)	14.6 (9.3–22.9)
<b>Diabetes Yes vs no (referent)</b>	1.3 (1.1–1.5)	1.2 (1.0–1.4)	1.5 (1.1–2.0)	1.9 (1.2–3.0)
<b>Hypertension Yes vs no (referent)</b>	1.5 (1.4–1.7)	1.4 (1.3–1.6)	2.6 (2.1–3.2)	3.6 (2.5–5.0)
<b>Antiretroviral Therapy Prescribed Tenofovir vs other (referent)</b>	1.6 (1.4–1.7)	1.6 (1.4–1.7)	1.5 (1.2–1.9)	1.5 (1.0–2.2)

Glomerular filtration rate (GFR) in mL/min/1.73 m<sup>2</sup>. Adapted with permission from Heffelfinger et al, 13th CROI, 2006.

fovir therapy of 9.6 months (range, 1–25 months). Concurrent antiretroviral drug use included ritonavir in 18 patients (72%), lopinavir in 15 (60%), lamivudine in 11 (44%), and abacavir in 11 (44%). As would be expected in a proximal tubule disorder in which glucose and phosphate are not being reabsorbed and are wasted in the urine, hypophosphatemia was found in 20 (100%) of 20 patients and glycosuria was found in 12 (89%) of 13. Urine protein was 1.7 mg/g creatinine in 14 patients. Two (8%) were diagnosed with diabetes insipidus. Tenofovir levels were elevated in patients in whom such levels were measured. Both the electrolyte abnormalities and glycosuria resolved with discontinuation of tenofovir treatment. Biopsies showed proximal acute tubular necrosis with no glomerular, vascular, or interstitial changes.

It appears likely that most patients experiencing tenofovir nephrotoxicity have some degree of renal impairment to begin with, or experience acute renal failure due to another cause that results in, and is exacerbated by, tenofovir toxicity. Nonetheless, the data indicate that patients receiving tenofovir should be monitored for renal function fairly closely, and the need for initial screening and monitoring of renal function in all patients should be emphasized. The IDSA guidelines suggest biannual monitoring in patients receiving tenofovir.

### Acute Interstitial Nephritis

For many years, the model of drug-related interstitial nephritis was that of methicillin-related interstitial nephritis, characterized by eosinophilia, pyuria, hematuria, and extrarenal symptoms including flank pain and rash. Although cases of drug-related interstitial nephritis may include many of these symptoms, it may also be present in the absence of these findings, and patients may have no symptoms other than a high or rising creatinine level. Acute interstitial nephritis should be considered in cases in which creatinine level is increasing after the introduction or reintroduction of any drug treatment in the absence of any other explanation for the renal dysfunction.

Diagnosis, if not apparent by clinical criteria, is made by biopsy, and early diagnosis is crucial for avoiding tubulointerstitial fibrosis and permanent renal insufficiency. The putative culprit medication should be withdrawn immediately. Corticosteroid treatment should be considered if renal function does not improve within 7 to 10 days.

### Conclusions

Dr Fine concluded with his personal recommendations regarding screening for renal impairment in HIV-infected patients: (1) Initial screening of patients should include urine protein quantification by spot-urine protein:creatinine ratio, rather than dipstick. The threshold for nephrologist referral on this test should be estimated proteinuria of above 500 mg (although one could consider a lower cut-off at 300 mg, the upper limit of normal). (2) Patients with no abnormal findings at baseline, who are nevertheless at high risk due to other factors (eg, CD4+ cell count below 200/ $\mu$ L, plasma HIV RNA level above 4000 copies/mL, diabetes, hepatitis C virus infection), should undergo screening every 6 months rather than annually. (3) Monitoring for renal function and urinary abnormalities should occur every 3 months, rather than every 6 months, in patients receiving tenofovir.

In addition to the recommendation for renal-function screening and follow up in all HIV-infected patients, certain elements of the IDSA guidelines need to be stressed. In patients with evidence of chronic kidney disease, blood pressure should be controlled to 125/75 mmHg. In those with proteinuria, initial use of ACE inhibitors or ARBs is preferred based on evidence of benefit in other proteinuric diseases. Diagnosis of HIVAN is crucial, and patients with HIVAN should have antiretroviral therapy started at confirmed diagnosis. Insufficient improvement with antiretroviral treatment warrants consideration of treatment with ACE inhibitors, ARBs, and prednisone (although, as stated earlier, the aggressive nature of this entity may support early initiation of both these agents). In patients with renal impair-

ment, dose-reduction is warranted for antiretroviral drugs that are primarily renally excreted. Likewise, in hemodialysis patients, attention must be given to providing additional post-dialysis doses of antiretroviral drugs that are readily removed in dialysis.

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### Suggested Reading

- Atta MG**, Gallant JE, Rahman MH, et al. Antiretroviral therapy in the treatment of HIV-associated nephropathy. *Nephrol Dial Transplant*. 2006;21:2809-2813.
- Crane HM**, Van Rompaey S, Kitahata MM. Antiretroviral medications associated with elevated blood pressure among patients receiving highly active antiretroviral therapy. *AIDS*. 2006;20:1019-1026.
- Eustace JA**, Nuermberger E, Choi M, Scheel PJ, Moore R, Briggs WA. Cohort study of the treatment of severe HIV-associated nephropathy with corticosteroids. *Kidney Int*. 2000;58:1253-1260.
- Gallant JE**, DeJesus E, Arribas JR, et al. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. *N Engl J Med*. 2006;354:251-260.
- Gallant JE**, Parish MA, Keruly JC, Moore RD. Changes in renal function associated with tenofovir disoproxil fumarate treatment, compared with nucleoside reverse-transcriptase inhibitor treatment. *Clin Infect Dis*. 2005;40:1194-1198.
- Gupta SK**, Eustace JA, Winston JA, et al. Guidelines for the management of chronic kidney disease in HIV-infected patients: recommendations of the HIV Medicine Association of the Infectious Diseases Society of America. *Clin Infect Dis*. 2005;40:1559-1585.
- Heffelfinger J**, Hanson D, Voetsch A, McNaghten A, Sullivan P. Renal impairment associated with the use of tenofovir. [Abstract 779.] 13th Conference on Retroviruses and Opportunistic Infections. February 5-8, 2006; Denver, Colorado.
- Johnson RJ** and Feehally J. *Comprehensive Clinical Nephrology*, St Louis: Mosby; 2000:2-33.
- Kimmel PL**, Mishkin GJ, Umana WO. Captopril and renal survival in patients with human immunodeficiency virus nephropathy. *Am J Kidney Dis*. 1996;28:202-208.

**Levey AS**, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med.* 1999;130:461-470.

**Lucas M**, Eustace JA, Sozio S, Mentari EK, Appiah KA, Moore RD. Highly active antiretroviral therapy and the incidence of HIV-1-associated nephropathy: a 12-year cohort study. *AIDS.* 2004;18:541-546.

**Ray AS**, Cihlar T, Robinson KL, et al. Mechanism of active renal tubular efflux of tenofovir. *Antimicrob Agents Chemother.* 2006;50:3297-3304.

**Smith MC**, Austen JL, Carey JT, et al. Prednisone improves renal function and proteinuria in human immunodeficiency virus-associated nephropathy. *Am J Med.* 1996;101:41-48.

**Szczzech LA**, Hoover DR, Feldman JG, et al. Association between renal disease and outcomes among HIV-infected women receiving or not receiving antiretroviral therapy. *Clin Infect Dis.* 2004;39:1199-1206.

**Wei A**, Burns GC, Williams BA, Mohammed NB, Visintainer P, Sivak SL. Long-term renal survival in HIV-associated nephropathy with angiotensin-converting enzyme inhibition. *Kidney Int.* 2003;65:1114-1115.

**Zimmermann AE**, Pizzoferrato T, Bedford J, Morris A, Hoffman R, Braden G. Tenofovir-associated acute and chronic kidney disease: a case of multiple drug interactions. *Clin Infect Dis.* 2006;42:283-290.

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