Dialyzing a Patient with Human Immunodeficiency Virus Infection: What a Nephrologist Needs to Know

Sreedhar Mandayam Tejinder S. Ahuja

Department of Medicine, Division of Nephrology, University of Texas Medical Branch, Galveston, Tex., USA

Key Words

Human immunodeficiency virus · Dialysis · Chronic kidney disease · Anemia · Vaccination

Abstract

The percentage of dialysis centers that have reported dialyzing human immunodeficiency virus (HIV)-infected patients increased from 11% in 1985 to 37% in 2000. Being primary care physicians for the dialysis patients, nephrologists are frequently confronted with the management of HIV-infected dialysis patients especially in urban centers. The aims of the present review are to discuss issues that are unique to HIV infection and end-stage renal disease, and to provide dialysis caretakers with sufficient information to help them optimize care and improve outcomes of these patients. Issues related to the choice of renal replacement therapy, vascular access, management of anemia, vaccination, and antiretroviral therapies are discussed in detail.

Copyright © 2004 S. Karger AG, Basel

Introduction

After the first recognition in 1984 of a distinct form of focal segmental glomerulosclerosis termed human immunodeficiency virus (HIV)-associated nephropathy (HIVAN) that develops predominantly in HIV-infected blacks and progresses rapidly to end-stage renal disease (ESRD), the prevalence of HIV-infected patients receiving dialysis in the USA rose at an alarming rate until 1995, when over 900 new patients with HIVAN started dialysis in the USA. Since then, the number of patients with HIVAN starting dialysis has reached a plateau, although over 800 patients with HIVAN start dialysis each year in the USA [1–4]. This is consistent with accumulating reports that use of highly active antiretroviral therapy (HAART) (available since 1996) slows down or can cause remission of the rapidly progressive course of HIVAN [5–10]. Figure 1 shows the incident dialysis patients with HIVAN starting dialysis in the USA from 1984 until October 2000. Although the epidemic of HIV infection has reached a plateau in the USA, recent Centers for Disease Control data suggests that the epidemic in the population at risk for HIVAN (blacks) is still increasing. Also with increasing prevalence of drug-resistant strains of HIV, the incidence of HIVAN may not change even in the HAART era [11]. In addition, the prevalence which

KARGER

Fax +41 61 306 12 34
E-Mail karger@karger.ch
www.karger.com

© 2004 S. Karger AG, Basel
0250-8095/04/0245-0511\$21.00/0

Accessible online at:
www.karger.com/ajn

Tejinder S. Ahuja MBBS, Assoc. Prof.
4.200 John Sealy Annex
301 University Boulevard
Galveston, TX 77058 (USA)
Tel. +1 409 772 7407, Fax +1 409 772 5451, E-Mail tahuja@utmb.edu

Fig. 1. Number of new patients with HIV-AN starting dialysis in the USA (derived from USRDS Database Standard Analysis Files using PDIS codes 0429A).

depends not only on incidence but also on survival may not change or may increase with improving survival of HIV-infected dialysis patients [3]. Therefore, we believe that in the coming decade, despite the impact of HAART on the incidence of HIVAN and ESRD, nephrologists in the urban centers are going to be confronted with providing optimal care to HIV-infected ESRD patients. This review is aimed at providing nephrologists with important advancements in the treatment of HIV infection and suggesting management strategies to optimize care of these patients on dialysis.

Epidemiology

The estimates of HIV-infected patients in the dialysis patients in the USA are available from surveillance of dialysis associated diseases conducted by the Centers for Disease Control and Prevention (CDC) and from information available through the United States Renal System Database (USRDS). As dialysis patients are not routinely screened for HIV infection in the USA, the true incidence and prevalence is probably higher than reported by either the CDC or the USRDS.

Since 1976, the CDC initiated a cooperative program with Health Care Finance Administration that provided a questionnaire from the CDC to be included in CFA's annual facility survey. The questionnaire includes information on incidence and prevalence of hepatitis B surface

antigen, antibody to hepatitis C virus and HIV infection. The report of the last survey, for the calendar year 2000, represented 3,683 dialysis facilities and 241,113 patients. Since 1999, the prevalence of HIV infection has been reported as the percentage of patients with HIV infection who were present during a 1-week period in December divided by the total number of patients who were present during the same 1-week period in December. In 2000, 1.5% (range among networks 0.3–3.4%) of patients were reported to have HIV infection and 0.4% (range among networks 0–1.0%) to have AIDS. During 1985–2000, the percentage of centers that reported providing dialysis for patients with HIV infection increased from 11 to 37% [4]. A similar incidence and prevalence of HIV-infected patients with ESRD has been reported by studies utilizing the USRDS database [3, 12, 13]. The number of incident HIVAN patients starting dialysis each year increased until 1995 when 939 patients with HIVAN started dialysis. Since then, the number of HIVAN patients starting dialysis has reached a plateau around 800 per year. This salutary effect on the incidence is probably from the change in natural course of HIVAN due to the use of HAART. The incidence of HIV-associated renal diseases from 1995 to 1999 for black men aged 25–44 years fell from 8.5 to 6.8%. Despite this, the number of prevalent cases increased from 1,346 to 3,058 (0.4–0.8%) as 1-year survival rate improved from 52 to 69% [12]. ESRD Network 2 (N.Y.) reported that 820 (5.5%) of 15,000 new ESRD patients between 1992 and 1996 had renal failure

attributed to HIVAN. Another 354 ESRD patients had AIDS but renal failure was attributed to other causes. Subsequently, the incidence of ESRD from HIVAN declined to 2.5% (155 of 6,291) during 1999 and 2% (130 of 6,563) during 2000 [14, 15]. Although ESRD in HIV-infected patients is largely attributed to HIVAN, the number of patients that had the diagnosis confirmed by renal biopsies is unavailable either from the CDC or the USRDS database.

Several other countries have reported the prevalence of HIV infection in dialysis patients. In a survey of 260 dialysis facilities in France representing 22,707, a prevalence of 0.36% was found [16]. In an Italian survey corresponding to 27,000 patients, the prevalence of HIV infection was 0.13% [17]. The prevalence reported from Japan and Egypt in the pre-HAART era was low but Brazil reported a high prevalence (14%) of HIV infection in dialysis patients [18–20].

Renal Replacement Therapy

In the pre-HAART era several studies suggested that survival of HIV-infected patients was dismal to a point that it was an ethical dilemma whether chronic dialysis should be offered to these patients. However, with the use of HAART the survival of HIV-infected patients on dialysis has improved considerably [3, 21]. The theoretical possibility that hemodialysis may actually increase the morbidity of HIV-infected ESRD patients by enhancing viral replication through activation of white blood cells and release of cytokines such as tumor necrosis factor- α , interleukin-1 and interleukin-6 that enhance HIV replication remains unstudied [22–26]. Winston et al. [27] reported faster early decay rate of HIV after starting antiretroviral therapy in dialysis patients consistent with this hypothesis. We in contrast did not find any day-to-day increase in plasma viral load with hemodialysis in our previous study. However we did not rule out the possibility of a delayed increase in viral load [28]. Potent antiretroviral activity of the newer HIV drugs has made the concern regarding activation of HIV virus due to hemodialysis mute but with increasing prevalence of resistant strains of HIV this could become an important issue again.

Although peritoneal dialysis may cause less immune activation and cytokine alterations, these benefits may be nullified by increased protein losses with peritoneal dialysis [29]. Kimmel et al. [30] in the pre-HAART era in a small number of patients did not find dialysis modality as a factor in survival of HIV-infected dialysis patients. Using the

USRDS, we recently reported that dialysis modality was not a factor in survival of patients with HIVAN after comparing survival between 5,299 patients who received hemodialysis and 716 patients who received peritoneal dialysis in the USA (hazard ratio: peritoneal dialysis vs. center hemodialysis, 1.04, 95% CI, 0.96–1.13) [31]. However, the study was limited by the unavailability of information on plasma viral load and CD4 count. Until further studies controlling for the stage of HIV infection and other co-morbidities are conducted, criteria for selecting dialysis modality for HIV-infected patients should be similar to other patients with ESRD.

The arguments in favor of transplantation of HIV-infected patients have gained a new impetus with improvement in survival of these patients with HAART. The issue of transplantation in dialysis patients has been discussed in three recent reviews [32–34]. Long-term survival was not an uncommon occurrence in HIV-infected patients even in the pre-HAART era [35, 36]. It has been well known that immunosuppressive agents such as cyclosporine and tacrolimus may retard replication of HIV virus [37]. Starzl et al. [36] in the pre-HAART era reported that HIV-infected transplant recipients who were on cyclosporine-based immunosuppressive regimen had a better survival. Recent reports have suggested that even mycophenolate mofetil, another common drug used after transplantation, may potentiate the antiretroviral effect of commonly used HIV drugs [38, 39]. Although the concern about potential interactions between protease inhibitors and calcineurin inhibitor is real, this can be resolved by monitoring drug levels and pharmacokinetic studies [40]. Murphy et al. [41] have recently reported a short-term outcome of 23 HIV-infected patients who received kidney transplantation at different centers in the USA. The patient and the graft survival was comparable to United Network for Organ Sharing (UNOS) at 1 year. There was no evidence of progression of HIV, as HIV RNA remained undetectable in 21 of the 23 patients [41, 42]. Therefore, several centers have started offering solid organ transplantation to HIV-infected patients. Consequently, we believe that asymptomatic HIV-infected patients with ESRD should be referred to these transplant centers. The information regarding these centers and the referral form is available at the following website <http://spitfire.emmes.com/study/hiv-k/>.

Vascular Access

The complication rate of arteriovenous graft (AVG) in HIV-infected dialysis patients is reported to be higher [43]. In one study, the 12- and 24-month patency rates of prosthetic grafts in HIV-infected ESRD patients was lower, as compared with HIV-negative patients (49 and 21% vs. 77 and 45%) and infection rate was higher, 30 vs. 7%, respectively. The patency and infection rate in patients with autologous AVFs with or without HIV infection did not differ [44]. Some other studies validated a higher infection rate of the AVG in asymptomatic HIV-infected patients and patients with AIDS compared with control patients (36, 45 and 15%, respectively) [45]. The risk of infection associated with dialysis catheters has also been reported in HIV-infected patients. Mokrzycki et al. [46] compared tunnel-cuffed catheter-related bacteremia in 40 HIV-infected patients with 41 control patients. Although, the tunnel-cuffed catheter-related bacteremia was not different in HIV-infected patients compared with controls (2.23 vs. 2.53 per 100 tunnel-cuffed catheter days), HIV-infected patients had a fivefold increased risk of gram-negative rod bacteremia and sevenfold increased risk of fungal isolate. Therefore, arteriovenous fistula (AVF) should be created early if progression of renal failure in patients with HIVAN is rapid despite all therapies. Although HAART and use of angiotensin-converting enzyme inhibitors and steroids has decreased the rate of progression of renal failure, the majority would still progress over a period of time to ESRD [7–10, 47, 48]. If the renal failure is progressing slowly or patients have renal disease other than HIVAN, the Dialysis Outcome Quality Initiative (DOQI) guidelines should be used in timing placement of vascular access, i.e. AVF should be placed when creatinine clearance is <25 ml/min and if the patient cannot get AVF, dialysis AVG should be placed 3–6 weeks prior to the anticipated need for dialysis.

Prevention of Transmission of HIV in Dialysis Units

Routine testing of dialysis patients for HIV infection has not been recommended by the CDC [49, 50]. However, every patient starting dialysis should be evaluated for risk factors for HIV infections and if present should be tested. Practice guidelines do not exist for those patients who refuse to be tested for HIV. If infected, these patients can receive appropriate medical care, including education and counseling to prevent transmission of the virus. Stan-

dard infection control practices are adequate to prevent HIV transmission between patients and HIV-infected patients do not have to be isolated from other patients or dialyzed separately on separate machines. HIV is not transmitted efficiently through occupational exposures and reprocessing dialyzers from HIV-positive patients should not place staff members at increased risk of infection if necessary sterile precautions are undertaken. The CDC does not prohibit participation of HIV-infected patients in dialyzer reuse programs [50]. However, a break in proper infection control practices could lead to transmission from patient to patient in a dialysis unit; therefore it is extremely important to conform to the standard infection-control practice guidelines in dialysis centers [51–52].

Although the risk is small, transmission of HIV infection after a percutaneous (0.3%) and after a mucous membrane exposure (0.09%) can occur [53]. Dialysis care providers who get exposed should start post-exposure prophylaxis (PEP) as soon as possible. PEP utilized remains largely empiric, however treatment for 4 weeks comprising of two reverse transcriptase inhibitors (ZDV and lamivudine, stavudine and lamivudine, or stavudine and didanosine) for minor exposures, and an expanded regimen that includes addition of a third drug (usually a protease inhibitor) for more significant HIV exposures that pose an increased risk for transmission, is recommended [53]. As the prevalence of HIV drug resistance in untreated patients appears to be increasing, the regimen chosen should include drugs to which the virus is unlikely to be resistant [54, 55]. The regimens should be chosen after consultation with experts and antiretrovirals based on local knowledge and experience in treating HIV infection and disease and known drug resistance in the source should be given consideration. Initiation of PEP should not be delayed in order to obtain drug resistance testing in the source, however changes in the PEP can be made after it has been started and drug-resistant testing on the source. Post-exposure testing should be performed at 6 weeks, 12 weeks and 6 months, and persons exposed should be monitored for drug toxicity.

In the pre-HAART era studies showed potentially viable and infectious HIV-1 from the peritoneal dialysis effluent and peritoneal dialysis exchange tubing in HIV-infected patients [56, 57], therefore peritoneal dialysis effluents should be discarded in a toilet and disinfected and viricidal agents such as of Aukin or 10% household bleach should be poured and should be left for at least 30 min after disposal. Every precaution should be taken to avoid splashing, and gloves, aprons and face shields

should be used while disposing spent dialysate. Tubing and peritoneal dialysis bags should be discarded carefully in bags marked as highly contagious. Caretakers of HIV-infected peritoneal dialysis patients should also be educated regarding infection control practices to be followed at home.

Anemia

Prevalence of anemia is higher in HIV-infected patients with renal disease as anemia is the commonest hematological abnormality in HIV-infected patients and occurs in 3.2% of patients without clinical or immunologic AIDS but in 36.9% of patients with AIDS defining illness and 12.1% with immunologic AIDS [58–60]. Shrivastava et al. [61] found that the mean baseline hematocrit of HIV-infected ESRD patients was 22% compared with 26% in HIV-negative, diabetic and non-diabetic ESRD patients. Similarly, Abbott et al. [62] using data from Dialysis Morbidity and Mortality Wave 2 study found that mean hematocrit levels in patients with HIVAN ($n = 37$) were significantly lower compared with all other patients with ESRD starting dialysis ($Hct\ 26.2 \pm 6.5$ vs. 30.5 ± 6.1 , $p < 0.05$), respectively. HIV infections could exacerbate the severity of anemia in patients with kidney disease by direct effects of HIV infection on erythropoiesis, opportunistic infections, antiretroviral drugs or other drugs administered to treat infection or malignancies and from other rare mechanisms such as thrombotic microangiopathies [63]. As the presence of anemia is independently of other factors associated with shorter survival, it is imperative that it should be managed aggressively in patients with HIV infection and chronic kidney disease (CKD) [59, 64–65].

The National Kidney Foundation-Dialysis Outcomes Quality Initiative (NKF-DOQI) recommends that anemia work-up should be initiated in patients with CKD when the hemoglobin level is <11 g/dl ($Hct <33\%$) in premenopausal females and pre-pubertal patients and hemoglobin <12 g/dl ($Hct <37\%$) in adult males [66]. Some studies have recommended that in HIV-infected patients other etiologies of anemia should be ruled out once hemoglobin <1 g/dl below the lower limit of normal range. The same guidelines for starting work-up for anemia could be followed with HIV-infected patients with ESRD due to a higher chance of conditions (infections, drugs, etc.) other than renal failure to be associated with anemia in HIV-infected patients. In addition, more extensive work-up with special attention to infections and drug toxicity is

required for anemia work in HIV-infected patients with ESRD than recommended by NKF-DOQI guidelines. Recombinant human erythropoietin therapy or darbepoetin is an appropriate treatment option for patients with symptomatic mild anemia or moderate anemia (hemoglobin level = 2 g/dl below the lower limit of normal range). The target range for hemoglobin (hematocrit) recommended for patients with CKD is hemoglobin 11–12 g/dl. Unless more information becomes available, the same target hemoglobin levels should be aimed for in HIV-infected patients with CKD [67–69]. The response to erythropoietin in HIV-infected patients appears to be similar to HIV-negative patients and in a small study of HIV-infected ESRD patients, Shrivastava et al. [61] found that after 8 weeks of 100 U/kg body weight erythropoietin three times weekly the mean increase in hematocrit in these patients was similar to HIV-negative patients (5.8 vs. 6.7% in HIV-negative patients, respectively). Darbepoetin- α given once a week intravenously was found to have a similar response to erythropoietin in 12 HIV-positive hemodialysis patients. Ten of the 12 patients had hemoglobin ≥ 11 g/dl at monthly assessment through to the end of the study [70].

Although rare, parvovirus B19 infection should be suspected if anemia in HIV-infected patients does not respond to erythropoietin and other causes are ruled out. The patients have intense reticulocytopenia; serum PCR for parvovirus viremia and parvovirus IgM antibodies will establish the diagnosis in the majority of patients. Bone marrow is hypoplastic and giant pronormoblasts are commonly seen [71, 72].

Iron is essential for hemoglobin formation as is erythropoietin. NKF-DOQI recommends that iron status be monitored by the percent transferrin saturation (TSA) and serum ferritin levels and sufficient iron should be administered to maintain $TSAT \geq 20\%$ and a serum ferritin level of ≥ 100 ng/ml, which requires administration of intravenous iron in the majority of dialysis patients [66]. Not only are measurements of iron indices complicated in HIV-infected patients, but ferritin, which is an acute phase protein, is often elevated in patients with HIV infection, and high iron stores may also adversely influence the outcome of HIV-infected patients. Studies have shown that oxidative stress and iron may be important in activation of HIV-1. Induction of nuclear factor- κB expression, which regulates proviral transcription, can be influenced by iron through the production of reactive oxygen species [73–75]. Therefore, the safety of intravenous administration of iron needs to be studied in HIV-infected dialysis patients [76–80]. Until further studies

addressing the safety and effect of intravenous iron on HIV become available, we would suggest closely monitoring HIV disease progression in patients receiving intravenous iron by measuring plasma viral loads and CD4 counts.

Blood transfusions in HIV-infected patients with CKD should be avoided as some but not all studies have shown an increased activation of HIV-1 after transfusion, which could potentially accelerate HIV disease [81, 82].

Bone Disease

Osteopenia and osteoporosis are common in HIV-infected patients. Although an underlying mechanism triggering bone loss in HIV-infected patients is unknown, antiretroviral drugs, increased production of pro-inflammatory cytokines such as tumor necrosis factor and interleukin-6 may have a role in osteoclast activation and resorption [83, 84]. Some studies have shown that HIV-infected patients have low basal and maximal secretion of parathyroid hormone (PTH) and 1,25-dihydroxyvitamin D₃ levels [85, 86]. Parathyroid cells have been found to express proteins recognized by antibodies directed against CD4, the HIV-1 receptor, suggesting that the parathyroid cells may be infected with HIV directly leading to impaired PTH release. Abbott et al. [62] found that the mean PTH level was lower in patients with HIVAN and ESRD compared to patients with other causes of ESRD; the difference however was not statistically significant (239 ± 225 vs. 308 ± 319 pg/l, respectively). Although information on bone disease in patients with CKD and HIV infection is not available, HIV-infected patients with CKD develop complications of altered calcium and phosphate metabolism similar to HIV-negative patients [88]. Based on these observations and with the previous knowledge that vitamin D₃ enhances immune response, we suggest treating all HIV-infected ESRD patients with hyperparathyroidism with 1,25-dihydroxyvitamin D₃ or its analogues (using the same laboratory parameters for calcium, phosphate and PTH levels as HIV-negative ESRD patients) [89]. Recently, NKF-DOQI has published clinical practice guidelines for bone metabolism and disease in CKD. However, whether vitamin D and phosphate binders are equally effective in preventing bone disease in HIV-infected patients with CKD needs to be studied in controlled trials [90].

Vaccination

Two important issues related to vaccination of HIV-infected patients with CKD are its efficacy and effect on plasma viral load. The immunosuppression as a result of HIV infection and uremia is likely to lead to suboptimal response to vaccination in these patients. The development of protective antibodies and the duration of the protection is likely to be short due to decline in the levels of these protective antibodies as shown with anti-pneumococcal antibodies, which decrease to non-protective levels rapidly following pneumococcal vaccination in HIV-infected patients [91–93]. Initial observations that influenza vaccination increases replication of HIV replication has not been substantiated in more recent studies conducted in the era of HAART [94–101].

Hepatitis B remains a significant risk to patients receiving chronic hemodialysis. Compared to adults with normal immune status, the proportion of hemodialysis patients who develop a protective antibody response after vaccination (with higher dosages) is lower, for those who receive the three-dose schedule, the median is 64% (range 34–88%) [102–104]. Immunization for hepatitis B in HIV-infected CKD patients is more important because not only does HBV infection occur more frequently with HIV infection for behavioral reasons, but also because the pre-HAART studies suggested that these patients are more likely to develop chronic infection [105]. However, several reports have suggested that antibody response to hepatitis vaccination is impaired in HIV-infected patients [106–108]. Although hepatitis vaccination may increase plasma viral load, the effect is minimal and transient and is unlikely to be of clinical relevance [109, 110]. We have recently reviewed hepatitis vaccination information on 348 HIV-infected patients who received dialysis in Gambro Inc. dialysis units in the USA from 1994 to 2003. Complete information was available in 116 patients who received three doses of 40 µg of subcutaneous Recombivax HBTM (Merck & Co. Inc.). Of these 116 patients, 63 (54.3%) developed protective antibody anti-HBs titers >10 IU/l [unpubl. data]. Hepatitis vaccination should therefore be offered to HIV-positive ESRD patients. Hepatitis B surface antibody levels should be checked and a booster should be attempted if antibody levels become undetectable, although the response to a booster dose is not known. Table 1 lists the vaccinations that HIV-infected patients with CKD should be offered [111], however the protection that vaccines may offer in HIV-infected ESRD patients is likely to be inadequate or transient and this underscores the importance that other

Table 1. Immunizations recommended for adult HIV-infected dialysis patients (adapted from USPHS guidelines [111], dosages have been changed to dosages appropriate for patients on dialysis)

<i>Streptococcus pneumoniae</i>	Pneumovax ^{®1} or PNU-IMUNE ^{®2} 23 0.5 ml, subcutaneously or i.m. × 1 if CD4 count >200/μl repeat vaccination for patients initially immunized at a CD4 count <200/μl whose CD4 count increases to >200/μl (vaccinate preferably prior to development of ESRD). Revaccinate after 5 years				
Influenza virus	All patients annually				
Hepatitis A	Anti-HAV negative, patients at increased risk for HAV infection (e.g. illicit drug users, men who have sex with men) chronic liver disease including chronic hepatitis B or hepatitis C				
Hepatitis B virus	Recombivax HB ^{TM1}		Engerix-B ^{®3}		Monitoring: Check anti-HBs 1–2 months after the last primary vaccine dose (adequate response ≥ 10 mIU/ml) Revaccinate with three doses in patients who do not respond For responders, follow anti-HBs semiannually if levels < 10 mIU/ml, administer a booster dose
	dose (i.m.)	schedule	dose (i.m.)	schedule	
Patients aged ≥ 20 years					
Predialysis	10 μg	0, 1, 6 months	20 μg	0, 1, 6 months	
Dialysis dependent	40 μg	0, 1, 6 months	40 μg	0, 1, 2, 6 months	
Patients aged < 20 years	5 μg	0, 1, 6 months	10 μg	0, 1, 6 months	

¹ Merck & Co. Inc., West Point, Pa.

² Lederle.

³ SmithKline Beecham Biologicals, Philadelphia, Pa.

infection control strategies should be simultaneously implemented in addition to vaccination. Further studies are required in the HAART era to determine safety and efficacy of vaccinations in HIV-infected patients.

Highly Active Antiretroviral Therapy

In the recent years, use of HAART, improved prophylaxis, and treatment of opportunistic infections have led to dramatic improvement in survival of HIV-infected patients [112, 113]. Despite the benefits of HAART in patients with HIV infection and ESRD, two recent reports have showed underutilization of HAART in HIV-infected dialysis patients [114, 115]. In addition, the dose of antiretroviral drugs administered was inconsistent with current treatment guidelines [115].

A recent review by Izzedine et al. [116] has summarized the pharmacokinetics of antiretroviral drugs in HIV-infected patients on hemodialysis. There are three main groups of antiretroviral drugs, nucleoside and non-nucleoside reverse transcriptase inhibitors (NRTI and NNRTI) and protease inhibitors (PI). In most patients, a combination of either two NRTI with a PI or two NRTI plus one NNRTI are used. NRTI used in HIV therapy are primarily excreted by the kidneys, therefore the dose administered is 30–50% of the normal dose for various drugs. In addition, on dialysis days the NRTIs should be dosed after dialysis. Abacavir is the only NRTI whose absorption, elimination and distribution phases are not altered by renal insufficiency and does not need dose

adjustment in patients with ESRD. Since the liver mainly metabolizes it, the fraction removed during dialysis is not clinically significant; hence it can be administered at any time on dialysis days [117]. Tenofovir, the first nucleotide RTI, is administered as a 300-mg tablet once daily, has rare and mild side effects, and is active against NRTI-resistant strains. As tenofovir is primarily eliminated by the kidneys, it can be given once a week after dialysis [118]. NNRTI and PI are mainly metabolized by the liver by cytochrome P₄₅₀ isoenzymes, and do not need dose adjustments in patients with ESRD. NNRTI should be administered after hemodialysis to minimize loss during dialysis. In contrast, PI could be administered regardless of the dialysis schedule. The dosages of antiretroviral drugs in dialysis patients and their side effects have been summarized in table 2.

Several antiretroviral drugs (PI and NNRTI) are potent inhibitors of cytochrome P₄₅₀ isoenzymes (CYP3A4). Therefore, concomitant administration of other drugs metabolized by these isoenzymes may lead to an increase in their blood levels and side effects. An HIV specialist should be consulted if other drugs metabolized by these isoenzymes need to be prescribed to them. The nephrologist taking care of HIV-infected dialysis patients should work closely with the HIV specialist and should monitor response to therapy by following plasma viral load and CD4⁺ lymphocyte counts at least every 3 months. We suggest following the same guidelines for the treatment of HIV-infected HD patients as with other HIV-infected patients [119]; the guidelines with recent updates are available on the World Wide Web at <http://www>.

Table 2. Dosage of antiretroviral drugs for patients with ESRD

Drug	Dose for dialysis patients	Normal dose
<i>NRTI</i>		
Zidovudine	100 mg three times/day	200 mg three times/day or
Didanosine		300 mg twice/day
BW >60 kg	100 mg once/day	200 mg twice/day
BW ≤ 60 kg	50 mg once/day	125 mg twice/day
Zalcitabine	0.75 mg once/day	0.75 mg three times/day
Stavudine		
BWB ≥ 360 kg	20 mg once/day	40 mg once/day
BW ≤ 60 kg	15 mg once/day	30 mg once/day
Lamivudine	150 one dose followed by 25–50 mg once/day	150 mg twice/day
Abacavir	300 mg twice/day	Same dose
<i>NNRTI</i>		
Nevirapine	Normal dosage	200 mg once/day for 14 days thereafter 200 mg twice
Delavirdine	Data not available	400 mg three times/day
Efavirenz	Normal dose	600 mg once/day
<i>Protease Inhibitors</i>		
Indinavir	Normal dosage	800 three times/day
Ritonavir		600 mg twice/day
Nelfinavir		750 mg three times/day
Saquinavir/invirase		400 mg twice/day
Amprenavir		1,200 mg twice/day
Tenofovir	300 mg once a week	300 mg once/day

NRTI = Nucleoside reverse transcriptase inhibitors; NNRTI = non-nucleoside reverse transcriptase inhibitors.

cdcnac.org and <http://www.hivatis.org>. Nephrologists should also ensure that HIV-infected dialysis patients with low CD4 count should be receiving prophylaxis against opportunistic infections. In 1995, the USPHS/IDSA suggested guidelines for prophylaxis against opportunistic infections in HIV-infected patients. These guidelines have recently been revised and updated. These guidelines have suggested that it may be safe to stop primary or secondary prophylaxis for some pathogens if

HAART leads to an increase in CD4 lymphocyte counts above specified levels [119].

We conclude that nephrologists taking care of HIV-infected ESRD patients need to take care of the special issues relevant to HIV-infected patients with ESRD and should participate actively with HIV specialists to improve the outcome and quality of life of this group of patients.

References

- 1 Rao TK, Friedman EA, Nicastri AD: The types of renal disease in the acquired immunodeficiency syndrome. *N Engl J Med* 1987;316:1062–1068.
- 2 US Renal Data System, USRDS 2001 Annual Data Report: Atlas of End-Stage. Renal Disease in the United States. Bethesda, NIH, National Institute of Diabetes and Digestive and Kidney Diseases, 2001.
- 3 Ahuja TS, Grady J, Khan S: Changing trends in the survival of dialysis patients with human immunodeficiency virus in the United States. *J Am Soc Nephrol* 2002;13:1889–1993.
- 4 Tokars JJ, Frank M, Alter MJ, Arduino MJ: National surveillance of dialysis-associated diseases in the United States, 2000. *Semin Dial* 2002;15:N162–N171.
- 5 Wali RK, Drachenberg CI, Papadimitriou JC, Keay S, Ramos E: HIV-1-associated nephropathy and response to highly-active antiretroviral therapy. *Lancet* 1998;352:783–784.
- 6 Winston JA, Bruggeman LA, Ross MD, et al: Nephropathy and establishment of a renal reservoir of HIV type I during primary infection. *N Engl J Med* 2001;344:1979–1984.

- 7 Kirschner JT: Resolution of renal failure after initiation of HAART: Three cases and a discussion of the literature. *AIDS Read* 2002;12:103–105.
- 8 Cosgrove CJ, Abu-Alfa AK, Perazella MA: Observations on HIV-associated renal disease in the era of highly active antiretroviral therapy. *Am J Med Sci* 2002;102–106.
- 9 Pugach Z, Ahuja TS: Prevalence of HIV-associated nephropathy has not changed in the era of highly active antiretroviral therapy (abstract). *J Am Soc Nephrol* 2001;12:A0639.
- 10 Szczech LA, Edwards LJ, Sanders LL, van der Horst C, Barlett JA, Heald AE, Svetkey LP: Protease inhibitors are associated with slowed progression of HIV-related renal diseases. *Clin Nephrol* 2002;57:336–341.
- 11 Little SJ, Holte S, Routy JP, Daar ES, Markowitz M, Collier AC, Koup RA, Mellors JW, Connick E, Conway B, Kilby M, Wang L, Whitcomb JM, Hellmann NS, Richman DD: Antiretroviral drug resistance among patients recently infected with HIV. *N Engl J Med* 2002;347:385–394.
- 12 Eggers PW, Kimmel PL: Is there an epidemic of HIV-associated nephropathy in the ESRD program? (abstract) *J Am Soc Nephrol* 2002;13:SA-FC184, 38A.
- 13 Abbott KC, Hypolite I, Welch PG, Agodoa LY: Human immunodeficiency virus/acquired immunodeficiency syndrome-associated nephropathy at end-stage renal disease in the United States: Patient characteristics and survival in the pre-highly active antiretroviral therapy era. *J Nephrol* 2001;14:377–383.
- 14 Neff MS, Hogson ME, Rasmussen G, Waring S: HIV-infected dialysis patients in New York State. 1996 Annual Report. New York, ESRD Network of New York, 1996.
- 15 Rao TK: Human immunodeficiency virus infection in end-stage renal disease patients. *Semin Dial* 2003;16:233–244.
- 16 Poignet JL, Desassis JF, Chanton N, Litchinko MB, Zins B, Kolko A, Patte R, Sobel A: Prevalence of HIV infection in dialysis patients: Results of a national multicenter study. *Nephrologie* 1999;20:159–163.
- 17 Barbiano di Belgiojoso G, Trezzi M, Scorza D, et al: HIV infection in dialysis centers in Italy: A nationwide multicenter study. *J Nephrol* 1998;11:249–254.
- 18 Morikawa K, Kuroda M, Tofuku Y, Uehara H, Koshikawa S: Prevalence of HTLV and HIV among hemodialysis patients in Japan. *Nephron* 1988;50:77–78.
- 19 Hassan NF, el Ghoran NM, Abdel Rahim MS, Sharkawy El, El Sayed NM, Emara K, Solant Y, Sanad M, Hibbs RG, Arthur RR: HIV infection in renal dialysis patients in Egypt. *AIDS* 1994;8:853.
- 20 Falcao HA, Rebelo M: Anti-HIV Antibodies in population of 132 patients in hemodialysis (abstract). Xth International Congress of Nephrology, London, Aug 1987.
- 21 Ahuja TS, Borucki M, Grady J: Highly active antiretroviral therapy improves survival of HIV-infected hemodialysis patients. *Am J Kidney Dis* 2000;36:574–580.
- 22 Bingel M, Lonnemann G, Koch KM, Dinarello CA, Shalton S: Plasma interleukin-1 activity during hemodialysis: The influence of dialysis membrane. *Nephron* 1988;50:273–276.
- 23 Herbelin A, Nguyen AT, Zingraff J, Urena P, Descamps-Latscha B: Influence of uremia and hemodialysis on circulating interleukin-1 and tumor necrosis factor. *Kidney Int* 1990;37:116–125.
- 24 Osborn L, Kunkel S, Nabel GJ: Tumor necrosis factor- α and interleukin-1 stimulate the human immunodeficiency virus enhancer by activation of the nuclear factor- κ B. *Proc Natl Acad Sci USA* 1989;86:2336–2340.
- 25 Takahashi T, Kubota M, Nakamura T, Ebihara I, Koide H: Interleukin-6 gene expression in peripheral blood mononuclear cells from patients undergoing hemodialysis or continuous ambulatory peritoneal dialysis. *Ren Fail* 2000;22:345–354.
- 26 Poli G, Bressler P, Kinter A, et al: Interleukin-6 induces human immunodeficiency virus expression in infected monocytic cells alone and in synergy with tumor necrosis factor- α by transcription and post-transcriptional mechanisms. *J Exp Med* 1990;172:151–158.
- 27 Schwartz EJ, Fierer DS, Neumann AU, et al: HIV-1 dynamic in hemodialysis patients. *AIDS* 2002;16:1301–1302.
- 28 Ahuja TS, Niaz N, Velasco A, Watts B, Paar D: Effect of hemodialysis and antiretroviral therapy on plasma viral load in HIV-1-infected hemodialysis patients. *Clin Nephrol* 1999;51:40–44.
- 29 Tebben JA, Rigsby MO, Selwyn PA, Brennan PA, Kliger A, Finkelstein FO: Outcome of HIV-infected patients on continuous ambulatory peritoneal dialysis. *Kidney Int* 1993;44:191–198.
- 30 Kimmel PL, Umana WO, Simmens SJ, Watson J, Bosch JP: Continuous ambulatory peritoneal dialysis and survival of HIV-infected patients with end-stage renal disease. *Kidney Int* 1993;44:373–378.
- 31 Ahuja TS, Grady J, Khan S: Is dialysis modality a factor in survival of patients with ESRD an HIV-associated nephropathy? *Am J Kidney Dis* 2003;41:1060–1064.
- 32 Fishman JA, Rubin RH: Solid organ transplantation in HIV-infected individuals: Obstacles and opportunities. *Transplant Proc* 2001;33:1310–1314.
- 33 Kuo PC, Stock PG: Transplantation in the HIV+ patient. *Am J Transplant* 2001;1:13–17.
- 34 Halpern SD, Ubel PA, Caplan AL: Solid-organ transplantation in HIV-infected patients. *N Engl J Med* 2002;347:284–286.
- 35 Ahuja TS, Zingman B, Glicklich D: Long-term survival in HIV-infected renal transplant recipient. *Am J Nephrol* 1997;17:480–482.
- 36 Tzakis AG, Cooper MH, Dummer JS, Ragni M, Ward JW, Starzl TE: Transplantation in HIV+ patients. *Transplantation* 1990;49:354–358.
- 37 Schwarz A, Offermann G, Keller F: The effect of cyclosporine on the progression of human immunodeficiency virus type 1 infection transmitted by transplantation – Data on four cases and review of the literature. *Transplantation* 1993;55:95–103.
- 38 Margolis D, Heredia A, Gaywee J, Oldach D, Drusano G, Redfield R: Abacavir and mycophenolic acid, an inhibitor of inosine monophosphate dehydrogenase, have profound and synergistic anti-HIV activity. *J Acquir Immune Defic Syndr* 1999;21:362–370.
- 39 Heredia A, Margolis D, Oldach D, Hazen R, Le N, Redfield R: Abacavir in combination with the inosine monophosphate dehydrogenase inhibitor mycophenolic acid is active against multidrug-resistant HIV-1. *J Acquir Immune Defic Syndr* 1999;22:406–407.
- 40 Izzedine H, Launay-Vacher V, Baumelou A, Deray G: Antiretroviral and immunosuppressive drug-drug interactions: An update. *Kidney Intl* 2004;66:532–534.
- 41 Murphy B, Carlson L, Rohal S, et al: Renal transplantation in HIV-infected recipients twenty-three cases in the HAART era (abstract). *J Am Soc Nephrol* 2002;13:F-FC501, 11A.
- 42 Stock PG, Roland ME, Carlson L, Freise CE, Roberts JP, Hirose R, Terrault NA, Frassetto LA, Palefsky JM, Tomlanovich SJ, Ascher NL: Kidney and liver transplantation in human immunodeficiency virus-infected patients: A pilot safety and efficacy study. *Transplantation* 2003;76:370–375.
- 43 Gorski TF, Gorski YC: Complication of hemodialysis access in HIV-positive patients. *Am Surg* 2002;68:1104–1106.
- 44 Curi MA, Pappas PJ, Silva MB Jr, et al: Hemodialysis access: Influence of the human immunodeficiency virus on patency and infection rates. *J Vasc Surg* 1999;29:608–616.
- 45 Brock JS, Sussman M, Wamsley M, Mintzer R, Baumann FG, Riles TS: The influence of human-immunodeficiency virus infection and intravenous drug abuse on complications of hemodialysis access surgery. HIV- and HD-related vascular access. *J Vasc Surg* 1992;16:904–910.
- 46 Mokrzycki MH, Schröppel B, Gersdorff GV, Rush H, Zdunek MP, Feingold R: Tunneled-cuffed catheter-associated infections in hemodialysis patients who are seropositive for the human immunodeficiency virus. *J Am Soc Nephrol* 2000;11:2122–2127.
- 47 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;64:1462–1471.
- 48 Eustace JA, Nuermberger E, Choi M, Scheel PJ Jr, Moore R, Briggs WA: Cohort study of the treatment of severe HIV-associated nephropathy with corticosteroids. *Kidney Int* 2000;58:1253–1260.
- 49 CDC: Revised guidelines for HIV counseling, testing and referral. *MMWR Morb Mortal Wkly Rep* 2001;50(No RR 19):1–58.

- 50 CDC: Recommendations for preventing transmission of infections among chronic hemodialysis patients. *MMWR Morb Mortal Wkly Rep* 2001;50(No RR 05):1-43.
- 51 El Sayed NM, Gomatos PJ, Beck-Sague CM, et al: Epidemic transmission of human immunodeficiency virus in renal dialysis center in Egypt. *J Infect Dis* 2000;181:91-97.
- 52 Velandia M, Fridkin SK, Cardenas V, et al: Transmission of HIV in dialysis center. *Lancet* 1995;345:1417-1422.
- 53 CDC: Updated US Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. *MMWR Morb Mortal Wkly Rep* 2001;50(No RR 11):1-52.
- 54 Little SJ, Daar ES, D'Aquila RT, et al: Reduced antiretroviral drug susceptibility among patients with primary HIV infection. *JAMA* 1999;282:1177-1179.
- 55 D'Aquila RT, Johnson VA, Welles SL, et al: Zidovudine resistance and HIV-1 disease progression during antiretroviral therapy. *AIDS Clinical Trials Group Protocol 116 B/117 Team and Virology Committee Resistance Working Group. Ann Intern Med* 1995;122:401-408.
- 56 Scheel PJ Jr, Farzadegan H, Ford D, Malan M, Watson A: Recovery of human immunodeficiency virus from peritoneal dialysis effluent. *J Am Soc Nephrol* 1995;5:1926-1929.
- 57 Farzadegan H, Ford D, Malan M, Maters B, Scheel PJ Jr: HIV survival kinetics in peritoneal dialysis effluent. *Kidney Int* 1996;50:1659-1662.
- 58 Sullivan PS, Hanson DL, Chu SY, Jones JL, Ward JW: Epidemiology of anemia in HIV-infected persons: Results from the multistate adult and adolescent spectrum of HIV disease surveillance project. *Blood* 1998;91:301-308.
- 59 Semba RD, Gray GE: Pathogenesis of anemia during human immunodeficiency virus infection. *J Invest Med* 2001;49:225-239.
- 60 Moore RD: Anemia and human immunodeficiency virus disease in the era of highly active antiretroviral therapy. *Semin Hematol* 2000;37:18-23.
- 61 Shrivastava D, Rao TKS, Sinert R, Khurana E, Lundin AP, Friedman EA: The efficacy of erythropoietin in human immunodeficiency virus-infected end-stage renal disease patients treated by maintenance hemodialysis. *Am J Kidney Dis* 1995;25:904-909.
- 62 Abbott KC, Trespalacios F, Agodoa LY, Ahuja TS: HIVAN and medication use in chronic dialysis patients in the United States: Analysis of the USRDS DMMS Wave 2 Study. *BMC Nephrol* 2003;4:5.
- 63 Barbara BJ: Pathogenesis and pathophysiology of anemia in HIV infection. *Curr Opin Hematol* 1999;6:89.
- 64 Lowrie EG, Ling J, Lew NL, Yiu Y: The relative contribution of measured variables to death risk among hemodialysis patients; in Friedman EA (ed): *Death on Hemodialysis: Preventable or Inevitable?* Boston, Kluwer, 1994, chapt 13, pp 121-141.
- 65 Moore RD, Keruly JC, Chaisson RE: Anemia and survival in HIV infection. *J Acquir Immune Defic Syndr Hum Retrovirol* 1998;19:29-33.
- 66 National Kidney Foundation K/DOQI: Clinical practice guidelines for anemia of chronic kidney disease. *Am J Kidney Dis* 1998;37(suppl 1):182-238.
- 67 Volberding P: Consensus Statement: Anemia in HIV infection-current trends, treatment options, and practice strategies. *Anemia in HIV Working Group. Clin Ther* 2000;22:1004-1020.
- 68 Ferri RS, Adinolfi A, Orsi AJ, Sterken DJ, Keruly JC, Davis S, MacIntyre RC: Treatment of anemia in patients with HIV infection. 1. The need for adequate guidelines. *J Assoc Nurses AIDS Care* 2001;12:39-51.
- 69 Ferri RS, Adinolfi A, Orsi AJ, Sterken DJ, Keruly JC, Davis S, MacIntyre RC: Nursing guidelines committee for anemia in patients with HIV infection. Treatment of anemia in patients with HIV infection. 2. Guidelines for management of anemia. *J Assoc Nurses AIDS care* 2002;13:50-59.
- 70 Lucas Carlos, Carrera F, Jorge C, Boquinhas H, Paris MJ: Once-weekly Aranesp (darbepoetin- α) successfully maintains haemoglobin in haemodialysis patients who are positive for the human immunodeficiency virus: A 6-month observational assessment (abstract). *ERA-EDTA, Lisbon 2004*, p 322, MP270.
- 71 Abkowitz JL, Brown KE, Wood RW, Kovach NL, Green SW, Young NS: Clinical relevance of parvovirus B19 as a cause of anemia in patients with human immunodeficiency virus infection. *J Infect Dis* 1997;176:269-273.
- 72 Frickhofen N, Abkowitz JL, Safford M, Berry M, Antunex-de-Mayolo J, Astrow A, Cohen R, Halperin I, King L, Mintzer D: Persistent B19 parvovirus infection in patients infected with human immunodeficiency virus type 1: A treatable cause of anemia in AIDS. *Ann Intern Med* 1990;113:926-933.
- 73 Savarino A, Pescarmona GP, Boelaert JR: Iron metabolism and HIV infection: Reciprocal interactions with consequences? *Cell Biochem Funct* 1999;17:27987.
- 74 Geogiou NA, van der Bruggen T, Oudshoorn M, Nottet HS, Marx JJ, van Asbeck BS: Inhibition of human immunodeficiency virus type 1 replication in human mononuclear blood cells by the iron chelators deferoxamine, deferiprone, and bleomycin. *J Infect Dis* 2000;181:484-490.
- 75 Gordeuk VR, Delanghe JR, Langlois MR, Boelaert JR: Iron status and the outcome of HIV infection: An overview. *J Clin Virol* 2001;20:111-115.
- 76 Costagliola DG, de Montalembert M, Lefree JJ, et al: Dose of desferrioxamine and evolution of HIV infection in thalassemic patients. *Br J Haematol* 1994;87:849-852.
- 77 Weinberg GA: Iron overload as a mechanism for the lowered survival in AIDS patients receiving dapsone-iron protoxalate for secondary prophylaxis of *Pneumocystis carinii* pneumonia. *J Infect Dis* 1996;174:241-242.
- 78 Delanghe JR, Langlois MR, Boelaert JR, et al: Haptoglobin polymorphism, iron metabolism and mortality in HIV infection. *AIDS* 1998;12:1027-1032.
- 79 De Monye C, Karcher DS, Boelaert JR, et al: Bone marrow macrophage iron grade and survival of HIV-seropositive patients. *AIDS* 1999;13:375-380.
- 80 Ahuja TS, O'Brien WA: Special issues in the management of patients with ESRD and HIV infection. *Am J Kidney Dis* 2003;41:279-291.
- 81 Mudido PM, Georges D, Dorazio D, Yen-Lieberman B, Bae S, O'Brien WA, Spritzler J, Lederman MM: Human immunodeficiency virus type 1 activation after blood transfusion. *Transfusion* 1996;36:860-865.
- 82 Collier AC, Kalish LA, Busch MP, Gernsheimer T, Assmann SF, Lane TA, Asmuth DM, Lederman MM, Murphy EL, Kumar P, Kelley M, Flanigan TP, McMahon DK, Sacks HS, Kennedy MS, Holland PV: Leukocyte-reduced red blood cell transfusions in patients with anemia and human immunodeficiency virus infection. The Viral Activation Transfusion Study: A randomized controlled trial. *JAMA* 2001;285:1592-1601.
- 83 Thomas J, Doherty SM: HIV infection - A risk factor for osteoporosis. *J Acquir Immune Defic Syndr* 2003;33:281-291.
- 84 Teichmann J, Stephan E, Discher T, Lange U, Federlin K, Stracke H, Frieser J, Lohmeyer J, Bretzel RG: Changes in calcitropic hormones and biochemical markers of bone metabolism in patients with human immunodeficiency virus infection. *Metabolism* 2000;49:1134-1139.
- 85 Hellman P, Albert J, Gidlund M, Klareskog L, Rastad J, Akerstrom G, Juhlin C: Impaired parathyroid hormone release in human immunodeficiency virus infection. *AIDS Res Hum Retroviruses* 1994;10:391-394.
- 86 Haug CJ, Aukrust P, Haug E, Morkid L, Muller F, Froland SS: Severe deficiency of 1,25-dihydroxyvitamin D₃ in human immunodeficiency virus infection: Association with immunological hyperactivity and only minor changes in calcium homeostasis. *J Clin Endocrinol Metab* 1998;83:383-388.
- 87 Jaeger P, Otto S, Speck RF, Villiger L, Horber FF, Casez JP, Takkinen R: Altered parathyroid gland functions in severely immunocompromised patients infected with human immunodeficiency virus. *J Clin Endocrinol Metab* 1994;79:1701-1705.
- 88 Cockerell CJ, Dolan ET: Widespread cutaneous and systemic calcification (calciophylaxis) in patients with acquired immunodeficiency syndrome and renal disease. *J Am Acad Dermatol* 1993;28:135-136.
- 89 Amento EP: Vitamin D and immune system. *Steroids* 1987;49:55-72.
- 90 National Kidney Foundation K/DOQI: Clinical practice guidelines for bone metabolism and disease in chronic kidney disease. *Am J Kidney Dis* 2003;42:S1-S202.

- 91 Nielsen H, Kvinesdal B, Benfield TL, Lundgren JD, Konradsen HB: Rapid loss of specific antibodies after pneumococcal vaccination in patients with human immunodeficiency virus-1 infection. *Scand J Infect Dis* 1998;30:597-601.
- 92 Proavil M, Fires W, Matter L, Blazer J, Luthier R: Poor antibody response after tetanus and pneumococcal vaccination in immunocompromised HIV-infected patients. *Clin Exp Immunol* 1991;84:185-189.
- 93 Lineman CC Jr, First MR, Schiffman G: Revaccination of renal transplant and hemodialysis recipients with pneumococcal vaccine. *Arch Intern Med* 1986;146:1554-1556.
- 94 O'Brien WA, Grovit-Ferbas K, Namazi A, Ovchak-Dezic S, Park J, Yeramian C, Mao SH, Zack JA: HIV-1 replication can be increased in peripheral blood of seropositive patients after influenza immunization. *Blood* 1995;86:1082-1089.
- 95 Staprans SI, Hamilton BL, Follansbee SE, Elbeik T, Barbosa P, Grant RM, Feinberg MB: Activation of virus replication after vaccination of HIV-1-infected individuals. *J Exp Med* 1995;182:1727-1737.
- 96 Antonen JA, Hannula PM, Pyhala R, Saha HH, Ala-Houhala IO, Pasternack AI: Adequate seroresponse to influenza vaccination in dialysis patients. *Nephron* 2000;86:56-61.
- 97 Tasker SA, Treanor JJ, Paxton WB, Wallace MR: Efficacy of influenza vaccination in HIV-infected persons. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med* 1999;131:430-433.
- 98 Sullivan PS, Hanson DL, Dworkin MS, Jones JL, Ward JW: Effect of influenza vaccination on disease progression among HIV-infected persons. *AIDS* 2000;14:2781-2785.
- 99 King JC Jr, Treanor J, Fast J, Fast PE, Wolff M, Yan L, Iacuzio D, Readmond B, O'Brien D, Mallon K, Highsmith WE, Lambert JS, Belshe RB: Comparison of the safety, vaccine virus shedding, and immunogenicity of influenza virus vaccine, trivalent, types A and B, live cold-adapted, administered to HIV-infected and non-HIV-infected adults. *J Infect Dis* 2000;181:725-728.
- 100 Fuller JD, Craven DE, Steger KA, Cox N, Heeren TC, Chernoff D: Influenza vaccination of HIV-infected adults: Impact on plasma levels of HIV type 1 RNA and determinants of antibody response. *Clin Infect Dis* 1999;28:541-547.
- 101 Glesby MJ, Hoover DR, Farzadegan H, Margolick JB, Saah AJ: The effect of influenza vaccination on human immunodeficiency virus type 1 load: A randomized, double-blind, placebo-controlled study. *J Infect Dis* 1996;174:1332-1336.
- 102 Zanetti AR, Mannucci PM, Tanzi E, Moroni GA, DePaschale M, Morfini M, Carnelli V, Stevens CE, Alter HJ, Taylor PE, Zang EA, Harley EJ, Szmunness W: Hepatitis B vaccine in patients receiving hemodialysis immunogenicity and efficacy. *N Engl J Med* 1984;311:496-501.
- 103 Carletti P, Bibiano L, Boggi R, Bordoni E, Ricciatti AM, Della Bella S, Pauri P, Salvoni G, Mioli VA: HBV infection in hemodialysis patients: Monitoring and prevention. *Nephron* 1992;61:269-270.
- 104 Schwabek J, Mujais S: Vaccination in hemodialysis patients. *Int J Artif Organs* 1989;12:481-484.
- 105 Bodsworth NJ, Cooper DA, Donovan B: The influence of human immunodeficiency virus type 1 infection on the development of the hepatitis B virus carrier state. *J Infect Dis* 1991;163:1138-1140.
- 106 Tirindelli MC, DeBiasi R, Ciavarella N: Hepatitis B vaccination of 113 hemophiliacs: Lower antibody response in anti-LAV/HTLV-III-positive patients. *Am J Hematol* 1986;23:339-345.
- 107 Wong EK, Bodsworth NJ, Slade MA, Mulhall BP, Donovan B: Response to hepatitis B vaccination in a primary care setting: Influence of HIV infection, CD4⁺ lymphocyte count and vaccination schedule. *Int J STD AIDS* 1996;7:490-494.
- 108 Dukes CS, Street AC, Starling JF, Hamilton JD: Hepatitis B vaccination and booster in predialysis patients: A 4-year analysis. *Vaccine* 1993;11:1229-1232.
- 109 Rey D, Krantz V, Partisani M, Schmitt MP, Meyer P, Libbrecht E, Wendling MJ, Vetter D, Nicolle M, Kempf-Durepaire G, Lang JM: Increasing the number of hepatitis B vaccine injections augments anti-HBs response rate in HIV-infected patients. Effects on HIV-viral load. *Vaccine* 2000;18:116-125.
- 110 Cheeseman SH, Davaro RE, Ellison RT III: Hepatitis B vaccination and plasma HIV-1 RNA. *N Engl J Med* 1996;334:1272.
- 111 Recommendations of the US Public Health Service and the Infectious Disease Society of America: Guidelines for preventing opportunistic infections among HIV-infected persons. *MMWR Morb Mortal Wkly Rep* 2002;51(RR 08):1-46.
- 112 Palella FJ Jr, Delaney KM, Moorman AC, Loveless MO, Fuhrer J, Satten GA, Aschman DJ, Holmberg SD: Declining morbidity and human immunodeficiency virus infection. *N Engl J Med* 1998;338:853-860.
- 113 Detels R, Munoz A, McFarlane G, Kingsley LA, Margolick JB, Giorgi J, Schragar LK, Phair JP: Effectiveness of potent antiretroviral therapy on time to AIDS and death in men with known HIV infection duration. *JAMA* 1998;280:1497-1503.
- 114 Rodriguez RA, Mendelson M, O'Hare AM, Hsu LC, Schoenfeld P: Determinants of survival among HIV-infected chronic dialysis patients. *J Am Soc Nephrol* 2003;14:1307-1313.
- 115 Szczec LA, Kalayjian R, Rodriguez R, Gupta S, Coladonato J, Winston J: Adult AIDS Clinical Trial Group Renal Complications Committee. The clinical characteristics and antiretroviral dosing patterns of HIV-infected patients receiving dialysis. *Kidney Int* 2003;63:2295-2301.
- 116 Izzedine H, Launay-Vacher V, Baumelou A, Deray G: An appraisal of antiretroviral drugs in hemodialysis. *Kidney Int* 2001;60:821-830.
- 117 Izzedine H, Launay-Vacher V, Aymard G, Legrand M, Deray G: Pharmacokinetics of abacavir in HIV-1-infected patients with impaired renal function. *Nephron* 2001;89:62-67.
- 118 Izzedine H, Launay-Vacher V, Jullien V, Aymard G, Duvivier C, Deray G: Pharmacokinetics of tenofovir in haemodialysis. *Nephrol Dial Transplant* 2003;18:1931-1933.
- 119 CDC: Guidelines for using antiretroviral agents among HIV-infected adults and adolescents. *MMWR Morb Mortal Wkly Rep* 2002;51(No RR 07):1-53.