

Perspective

Update on Cardiovascular Complications in HIV Infection

HIV-infected patients are at increased risk of cardiovascular disease (CVD), reflecting interaction of risk associated with host, virus, and antiretroviral therapy factors. Although traditional risk factors appear to increase risk to a similar degree in HIV-infected and HIV-uninfected persons, some risk factors (eg, smoking) may be more common in HIV-infected persons. HIV infection per se may further increase CVD risk via proatherosclerotic effects on smooth muscle cells and macrophages or by increasing inflammation. Some drugs in the protease inhibitor class are associated with increased risk, at least partly in association with adverse lipid effects. The magnitude and mechanisms of risk reported to be associated with recent use of abacavir remain undefined. This article summarizes a presentation on cardiovascular complications in HIV infection made by Judith S. Currier, MD, at an International AIDS Society–USA continuing medical education course in Los Angeles in February 2009. The original presentation is available as a Webcast at www.iasusa.org.

Epidemiology of Cardiovascular Disease in HIV-Infected Persons

In the context of declining rates of HIV-related death, proportions of HIV-infected patients dying of other causes have increased. For example, a death certificate study in New York City showed that the proportion of deaths among HIV-infected patients due to non-HIV-related causes increased from 19.8% to 26.3% between 1999 and 2006, reflecting mortality resulting from cardiovascular disease (CVD), substance abuse, and non-AIDS-defining cancers (Sackoff et al, *Ann Intern Med*, 2006). Among individuals aged 55 years or older, CVD was the leading cause of death.

Numerous studies have indicated increased risk of myocardial infarction (MI) in HIV populations, with HIV infection considered at least a partial CVD risk factor in these studies. Klein and colleagues reported hospital-admission rates for coronary heart disease (CHD) in HIV-infected versus HIV-uninfected populations of 6.5 versus 3.8 per 1000 person-years (Klein et al, *JAIDS*, 2002) and 4.5 versus 2.9 per

1000 person-years in updated analyses with further follow-up time (Klein et al, *CROI*, 2007), respectively. Currier and colleagues found a higher risk of coronary artery disease (CAD) admissions among younger HIV-infected than among HIV-uninfected patients (Currier et al, *JAIDS*, 2003); Triant and colleagues found a 75% increase in risk of MI admissions in HIV-infected patients (Triant et al, *J Clin Endocrinol Metab*, 2007); and Obel and colleagues found a 39% to 112% increased risk of CAD admissions in HIV-infected patients (Obel et al, *Clin Infect Dis*, 2007).

The study by Triant and colleagues was performed using data from a Massachusetts administrative hospital da-

tabase including 3851 HIV-infected patients and more than 1 million HIV-uninfected patients from 1996 to 2004. The mean MI rates were 11.13 versus 6.98 per 1000 person-years, respectively. MI rates were higher in HIV-infected patients in all age groups, with very high rates in older patients (Figure 1). These investigators have also reported that levels of the acute-phase reactant C-reactive protein (CRP) were predictive of risk of MI in HIV-infected patients, despite the fact that CRP levels generally are nonspecifically elevated in HIV infection (Triant et al, *JAIDS*, 2009).

These findings underscore the need to determine why the rates of CVD are higher in HIV-infected than -uninfected individuals. Understanding the relative contributions of host, virus, and antiretroviral therapy to risk of CVD in HIV infection will help inform development of strategies for prevention and treatment.

Host Factors

Traditional CVD risk factors, as well as HIV infection and its treatment, contribute to the risk of CVD in HIV-infected individuals. The risk of MI in both HIV-infected and -uninfected populations is increased in a similar manner by the risk factors of increasing age, male sex, diabetes, smoking, and hy-

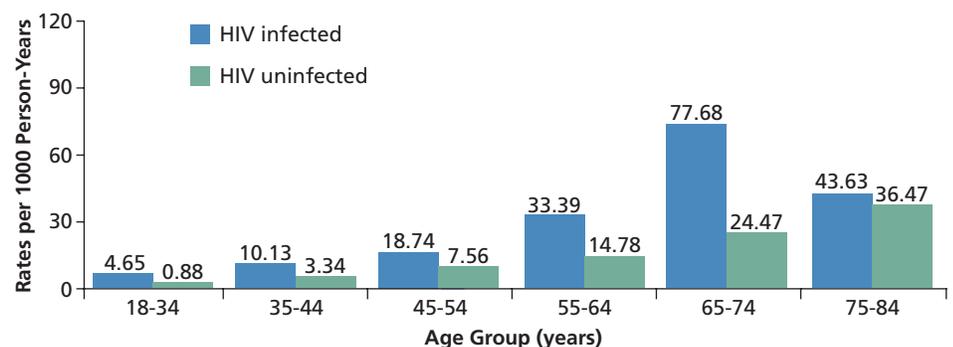


Figure 1. Myocardial infarction rates in HIV-infected (n = 3851) versus HIV-uninfected (n = 1,044,589) patients in a Massachusetts administrative hospital database, for 1996-2004. Adapted from Triant et al, *J Clin Endocrinol Metab*, 2007.

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Table 1. Contribution of Traditional Risk Factors to Risk of Myocardial Infarction in HIV-Infected and HIV-Uninfected Populations

Risk Factor	Unit	HIV-Infected		HIV-Uninfected (No. of studies)
		lloeje et al, <i>HIV Med</i> , 2005	Friis-Moller et al, <i>N Engl J Med</i> , 2003	
Age	Year increase	9%	6%	6%-9% (7)
Sex	Male vs female	--	110%	110%-160% (2)
Diabetes	Yes vs no	260%	90%	140%-252% (3)
Smoking	Yes vs no	140%	290%	70%-290% (3)
Hypertension	Yes vs no	30%	80%	80%-90% (3)

Adapted from Currier et al, *Circulation*, 2008, and Sabin and Worm, *Curr Opin HIV AIDS*, 2008.

pertension (Table 1) (Currier et al, *Circulation*, 2008; Sabin and Worm, *Curr Opin HIV AIDS*, 2008). The prevalence of some risk factors may be higher in HIV-infected populations, however. In the D:A:D (Data Collection on Adverse Events of Anti-HIV Drugs) study in 23,468 HIV-infected persons, at baseline 11.4% had a family history of coronary disease, 1.4% had a prior history of coronary disease, 51.5% were current smokers, 3.5% had a body mass index greater than 30 kg/m², 8.5% had hypertension, 2.5% had diabetes, 22.2% had elevated levels of total cholesterol, and 33.8% had elevated triglyceride levels (Friis-Moller et al, *AIDS*, 2003). A recent analysis of modifiable risk factors and death in the D:A:D study showed that smoking (rate ratio, 1.20), hypertension (rate ratio, 1.53), and diabetes (rate ratio, 1.83) were independently associated with risk of death during treatment for HIV infection (Smith et al, CROI, 2009). Smoking is common in many HIV-infected populations, and programs aimed at cessation have thus far been largely unsuccessful (Tashima et al, CROI, 2009). Greater attention needs to be given to smoking and other modifiable CVD risk factors in HIV-infected patients.

Increased carotid artery intima-media thickness (IMT), a marker for subclinical atherosclerosis, is associated with increased risk of MI. An analysis from the FRAM (Fat Redistribution and Metabolism) study showed that HIV

infection was associated with statistically significant increases in internal carotid (0.15 mm; $P < .001$) and common carotid (0.033 mm; $P < .01$) IMT compared with IMT values for a large population of HIV-uninfected persons (Grunfeld et al, CROI, 2009; Grunfeld et al, *AIDS*, 2009). Because most HIV-infected patients in the FRAM study were receiving antiretroviral therapy, any potential effect of antiretroviral therapy on this finding is uncertain. Other traditional risk factors associated with increased IMT in the FRAM patients were male sex, current and past smoking, diabetes, age per 10-year increase, systolic blood pressure increase, and total cholesterol level increase, with high-density lipoprotein (HDL) cholesterol level increase associated with a statistically significant reduction in IMT.

Virus Factors

The SMART (Strategies for Management of Antiretroviral Therapy) study examined the potential for reducing antiretroviral therapy toxicity by limiting time on treatment, with 5472 patients with CD4+ counts higher than 350 cells/ μ L randomly assigned to a treatment-interruption plan (termed drug-conservation strategy) or to continuous treatment (viral-suppression strategy). The drug-conservation strategy increased risk over the viral-suppression strategy of opportunis-

tic disease or death (rates, 3.4% vs 1.3%, respectively; hazard ratio [HR], 2.6) and of CVD, renal, or liver events (rates, 1.8% vs 1.1%, respectively; HR, 1.7) (El-Sadr et al, *N Engl J Med*, 2006). The study brought into focus the importance of serious non-AIDS-related events among patients without viral suppression on antiretroviral therapy. Subsequent analysis did not find an association between viral load and risk of CVD but confirmed increased risk of CVD among patients who discontinued antiretroviral therapy.

A number of mechanisms have been proposed to explain how HIV infection might contribute to atherosclerosis. HIV has been reported to infect smooth muscle cells in vitro and in vivo and increases secretion of a monocyte chemoattractant (CCL2, or MCP-1), which facilitates development of foam cells (Eugenin et al, *Am J Pathol*, 2008). Macrophages, which play a pivotal role in atherosclerosis, are also hosts for HIV. The HIV Nef protein impairs the adenosine triphosphate binding cassette (ABCA-1) transporter in macrophages, which is important to reverse cholesterol transport. This inhibition may lead to conversion of macrophages into foam cells and initiate plaque formation in vessel walls (Mujawar et al, *PLoS Biol*, 2006). This effect of Nef inhibition of the ABCA-1 transporter has been demonstrated in simian immunodeficiency virus (SIV)-infected macaques (Bukrinsky et al, CROI, 2009).

HIV may also directly impair HDL metabolism, thus enhancing transfer of HDL to atherogenic apolipoprotein B lipoproteins (Rose et al, *Atherosclerosis*, 2008). This potential mechanism is consistent with findings in the recent SMART trial analysis indicating an association of total HDL particles with risk of CVD in patients in the drug-conservation group (Duprez et al, CROI, 2009). In particular, risk was elevated in patients with declining HDL cholesterol levels after stopping nonnucleoside reverse transcriptase inhibitor (NNRTI) treatment. Collectively, these findings suggest that untreated HIV infection could contribute to the development of atherosclerosis,

although the magnitude of the effects remains unclear. Strategies to increase HDL cholesterol levels in HIV-infected individuals should be investigated.

Another mechanism by which HIV infection itself may contribute to CVD risk is inflammation. CRP is a marker of inflammation that independently predicts risk of CVD in adults in the general population. In HIV infection, elevated CRP levels predict HIV disease progression and mortality in untreated women after adjustment for viral load and CD4+ count. Uncontrolled HIV infection is associated with elevated markers of inflammation, including CRP. Levels of these markers decline with treatment but not to normal levels. Little is known about how different antiretroviral drugs affect CRP levels during successful antiretroviral therapy. Recent data from ACTG (AIDS Clinical Trials Group) study 5095 demonstrated that CRP levels did not improve during 96 weeks of treatment with efavirenz; in fact, among women CRP levels rose (Shikuma et al, CROI, 2009). Elevated baseline levels of the inflammatory marker interleukin-6 (IL-6) and the coagulation marker D-dimer were associated with all-cause mortality (not specifically with CVD events) in the SMART trial, and levels of these markers rose after treatment interruption (Kuller et al, CROI, 2008).

Despite the potential association of inflammation with increased CVD risk, a number of small studies have not found a strong association between higher levels of high-sensitivity CRP (hsCRP) and IMT. Hsue and colleagues found no association of hsCRP or immune activation (CD38+, CD4+, CD8+ cell responses) with IMT, but they reported an association between IMT and cytomegalovirus-specific T-cell responses, suggesting that response to latent or persistent viral infection might be driving a proatherosclerotic response (Hsue et al, *AIDS*, 2006). Other findings include improved endothelial function (measured by brachial artery reactivity) after 24 weeks of antiretroviral therapy in treatment-naive patients but no significant change in hsCRP level. In a pilot study in patients with untreated HIV infection, 8 weeks

of treatment with the tumor necrosis factor inhibitor pentoxifylline resulted in improvements in the endothelial activation marker VCAM-1 and brachial artery flow-mediated dilation (Gupta et al, CROI, 2008). The effects of such an approach to reducing inflammation in antiretroviral therapy-treated patients with viral suppression are being investigated.

Antiretroviral Therapy Factors

Numerous studies have been performed in the effort to sort out the potential effects of antiretroviral therapy on risk of CVD. Obtaining more definitive information in this regard would likely require additional randomized trials to control for potential confounding factors.

Although there are differences between individual drugs in the protease inhibitor (PI) class with respect to lipid-altering effects, several studies have described how PI treatment is associated with adverse effects on lipids, and numerous studies have reported an adverse effect on CVD risk. Among 10 studies of the effects of PI treatment (conducted before the availability of newer PIs) considered in a recent review including randomized, controlled trials, prospective observational cohort studies, retrospective reviews, and administrative database studies, 6 found an effect of PIs, 2 found an effect of antiretroviral therapy, and 2 found no effect of PIs on risk of CVD, MI, or CAD hospital admissions (Currier et al, *Circulation*, 2008). With regard to risk associated with particular PIs, the D:A:D study investigators found that lopinavir/ritonavir and indinavir were associated with increased risk of MI; there was no association between risk and ritonavir-boosted PIs as a group; and there was insufficient information to assess risk associated with atazanavir use. Data from the French Hospital Database indicate increased risk of MI with use of lopinavir/ritonavir and ritonavir-boosted fosamprenavir (Lang et al, CROI, 2009).

The general conclusion with regard to the effect of PIs on CVD risk is that it is cumulative and at least partly medi-

ated by lipid changes. Data on the effects of newer PIs on cardiovascular events are limited, however. Future research needs to focus on the effects of individual drugs rather than on drug classes, given the heterogeneity of metabolic effects of drugs within the PI class.

More recently, attention has focused on the effects of nucleoside analogue reverse transcriptase inhibitors (nRTIs) on CVD risk. The D:A:D study included a preplanned analysis of CVD risk associated with thymidine analogue nRTIs, which have known effects on lipid levels. No association between zidovudine or stavudine use and risk of MI was found in the initial report (D:A:D Study Group et al, *Lancet*, 2008), and subsequently no association for tenofovir was observed (Lundgren et al, CROI, 2009). However, recent exposure to abacavir and didanosine were each associated with increased risk of MI.

Several analyses have been performed in an attempt to better understand the association between abacavir and to a lesser extent didanosine and CVD events. A retrospective analysis of the abacavir clinical trials database involving 1570 abacavir-treated patients and 1692 patients not receiving abacavir with 24 weeks to 48 weeks of follow-up showed no association of abacavir treatment with risk of any or acute MI (relative risk [RR], 0.863; 95% confidence interval [CI], 0.40-1.86) or risk of any ischemic CAD or disorder (RR, 0.593; 95% CI, 0.35-1.01) (Cutrell et al, IAC, 2008). Similarly, an analysis of 119 CVD events in the HOPS (HIV Outpatient Study) cohort showed no association with abacavir treatment (Lichtenstein et al, IAC, 2008). Analysis of data from the observational group in the SMART study showed higher levels of hsCRP (27% increase; $P = .02$) and IL-6 (16% increase; $P = .02$) in patients receiving abacavir without didanosine than in those receiving other nRTIs (Lundgren et al, IAC, 2008).

However, analysis of inflammation biomarkers in the randomized HEAT (Head-to-Head Epzicom and Truvada) trial showed reduced hsCRP and IL-6 levels after 48 weeks and 96 weeks, both in treatment-naive patients receiving abacavir/lamivudine and in

patients receiving tenofovir/emtricitabine (Smith et al, IAC, 2008). A case-control study in the French Hospital Database (MI cases, $n = 289$; controls, $n = 884$) indicated an increased risk of MI (odds ratio, 1.97) among patients receiving abacavir for less than 1 year or who had stopped abacavir within 6 months, but no association of abacavir with MI risk in those exposed for more than 1 year or who had stopped for more than 6 months. In the STEAL (Switching to Tenofovir/Emtricitabine or Abacavir/Lamivudine) trial, 360 virologically suppressed patients were randomly assigned to receive abacavir/lamivudine or tenofovir/emtricitabine; 7 CVD events occurred in the abacavir/lamivudine group versus 1 in the tenofovir/emtricitabine group. An analysis in the ALLRT (AIDS Clinical Trials Group Longitudinal Linked Randomized Trials) study involving 3205 patients on randomized antiretroviral therapy showed no statistically significantly increased risk of MI with recent abacavir use (RR, 1.2; 95% CI, 0.5-3.1).

Where does this leave us with regard to potential CVD risk associated with abacavir use? Observational studies with control for known confounders have suggested an association of recent abacavir use with MI risk; however, this risk has not been confirmed in randomized trials. In addition, the risk does not appear to accumulate over time and appears to fade after the drug has been stopped. This suggests a mechanism of action that is triggered soon after the drug is started and that resolves when the drug is stopped. The increased risk with abacavir treatment has been observed to be heightened in patients with conventional risk factors and possibly in virologically suppressed patients for whom abacavir is substituted (Reiss, CROI, 2009).

Thus, for the present, any potential risk associated with abacavir use needs to be interpreted in the context of the overall benefits of antiretroviral treatment and the presence of modifiable risk factors. To date, any potential interaction between risk posed by PI use and that associated with abacavir remains unclear and should be evalu-

ated. The potential mechanisms for abacavir-associated risk also remain undefined. One small study thus far has suggested an effect of the drug on platelet function.

For the present, Dr Currier's opinion is to consider an individualized approach to the management of a patient on a stable abacavir-containing regimen. In a patient with 5 cardiovascular risk factors who has alternative antiretroviral therapy options, a switch can be considered. Because successful treatment of HIV is the priority, switching is far less attractive if there are limited antiretroviral therapy options. Switching likely does not need to be considered in patients without cardiovascular risk factors. Control of traditional risk factors is essential; for example, smoking cessation should be a higher priority than changing the nRTI component of antiretroviral therapy. Although the populations are too small to reach definitive conclusions regarding MI risk, data from ongoing randomized trials comparing abacavir and tenofovir in treatment-naïve patients should provide additional information on potential abacavir-related CVD risk.

Summary

CVD risk in HIV infection is likely a product of host, virus, and antiretroviral therapy factors (Figure 2). The benefits of antiretroviral therapy outweigh CVD

risks. Delaying antiretroviral therapy is not the answer to reducing these risks. Indeed, because HIV infection that is not suppressed may be accelerating atherosclerosis, earlier treatment may be of benefit in reducing CVD risk; the potential impact of such a strategy currently is being studied. Understanding the differences between antiretroviral drugs with regard to CVD risk is crucial when planning treatment that is to be maintained for decades, and more work needs to be done in this area. The ability to tailor antiretroviral therapy based on individual patient CVD risk profile also awaits further information. Finally, much work remains to be done in understanding the mechanisms of risk posed by antiretroviral therapy and by HIV infection itself. The prospective assessment of inflammatory markers in cohorts and controlled trials with patients at comparable stages of disease provide a beginning to this process.

Presented by Dr Currier in February 2009. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Currier in July 2009.

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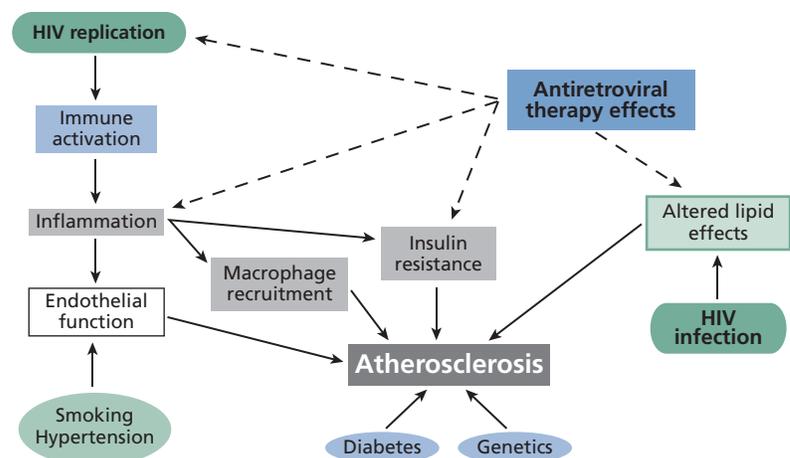


Figure 2. Interaction of host, virus, and antiretroviral therapy effects in cardiovascular disease risk.

and safety monitoring boards for Achillion Pharmaceuticals, Inc, and Koronis Pharmaceuticals.

Suggested Reading

Bukrinsky M, Asztalos B, Mujawar Z, et al. Nef-mediated suppression of ABCA1-dependent cholesterol efflux activity may contribute to primary dyslipidemia in SIV-infected macaques. [Abstract 147.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Currier JS, Lundgren JD, Carr A, et al. Epidemiological evidence for cardiovascular disease in HIV-infected patients and relationship to highly active antiretroviral therapy. *Circulation*. 2008;118:e29-e35.

Currier JS, Taylor A, Boyd F, et al. Coronary heart disease in HIV-infected individuals. *JAIDS*. 2003;33:506-512.

Cutrell A, Hernandez J, Yeo J, Brothers C, Burkle W, Spreen W. Is abacavir (ABC)-containing combination antiretroviral therapy (CART) associated with myocardial infarction (MI)? No association identified in pooled summary of 54 clinical trials. [Abstract WEAB0106.] 17th International AIDS Conference. August 3-8, 2008; Mexico City, Mexico.

D:A:D Study Group, Sabin CA, Worm SW, et al. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. *Lancet*. 2008;371:1417-1426.

Duprez D, INSIGHT/SMART Group. High-density lipoprotein particles but not low-density lipoprotein particles predict cardiovascular disease events in HIV patients: Strategies for Management of ART study. [Abstract 149.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

El-Sadr WM, Lundgren JD, Neaton JD, et al. CD4+ count-guided interruption of antiretroviral treatment. *N Engl J Med*. 2006;355:2283-2296.

Eugenin EA, Morgello S, Klotman ME, et al. Human immunodeficiency virus (HIV) infects human arterial smooth muscle cells in vivo and in vitro: implications for the pathogenesis of HIV-mediated vascular disease. *Am J Pathol*. 2008;172:1100-1111.

Friis-Moller N, Sabin CA, Weber R, et al. Combination antiretroviral therapy and the risk of myocardial infarction. *N Engl J Med*. 2003;349:1993-2003.

Friis-Moller N, Weber R, Reiss P, et al. Cardiovascular disease risk factors in HIV patients—association with antiretroviral therapy. Results from the DAD study. *AIDS*. 2003;17:1179-1193.

Grunfeld C, Delaney J, Wanke C, et al. HIV infection is an independent risk factor for atherosclerosis similar in magnitude to traditional cardiovascular disease risk factors. [Abstract 146.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Grunfeld C, Delaney JA, Wanke C, et al. Pre-clinical atherosclerosis due to HIV infection: carotid intima-medial thickness measurements from the FRAM study [published online ahead of print May 18, 2009]. *AIDS*. 2009.

Gupta S, Johnson R, Saha C, et al. A pilot study of the TNF- α inhibitor pentoxifylline to improve HIV-related endothelial dysfunction. [Abstract 955.] 15th Conference on Retroviruses and Opportunistic Infections. February 3-6, 2008; Boston, MA.

Hsue PY, Hunt PW, Sinclair E, et al. Increased carotid intima-media thickness in HIV patients is associated with increased cytomegalovirus-specific T-cell responses. *AIDS*. 2006;20:2275-2283.

Iloeje UH, Yuan Y, Litalien G, et al. Protease inhibitor exposure and increased risk of cardiovascular disease in HIV-infected patients. *HIV Med*. 2005;6:37-44.

Klein D, Hurley L, Silverberg M, Horberg M, Quesenberry C, Sidney S. Surveillance data for myocardial infarction hospitalizations among HIV+ and HIV- Northern Californians: 1994-2006. [Abstract 807.] 14th Conference on Retroviruses and Opportunistic Infections. February 25-28, 2007; Los Angeles, CA.

Klein D, Hurley LB, Quesenberry CP, Jr., Sidney S. Do protease inhibitors increase the risk for coronary heart disease in patients with HIV-1 infection? *JAIDS*. 2002;30:471-477.

Kuller L, SMART Study Group. Elevated levels of interleukin-6 and D-dimer are associated with an increased risk of death in patients with HIV. [Abstract Oral 139.] 15th Conference on Retroviruses and Opportunistic Infections. February 3-6, 2008; Boston, MA.

Lang S, Mary-Krause M, Cotte L, et al. Impact of specific nRTI and PI exposure on the risk of myocardial infarction: a case-control study nested within FHDH ANRS CO4. [Abstract 43LB.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Lichtenstein K, Buckner K, Armon C, et al. Low CD4 count is an important risk factor for cardiovascular disease in the HIV outpatient

study (HOPS) in the US. [Abstract THPE0236.] 17th International AIDS Conference. August 3-8, 2008; Mexico City, Mexico.

Strategies for Management of Anti-Retroviral Therapy/INSIGHT, DAD Study Groups. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients. *AIDS*. 2008;22:F17-F24.

D:A:D Study Group, Sabin CA, Worm SW, et al. Use of nucleoside reverse transcriptase inhibitors and risk of myocardial infarction in HIV-infected patients enrolled in the D:A:D study: a multi-cohort collaboration. *Lancet*. 2008;371:1417-1426.

Lundgren J, Reiss P, Worm S, et al. Risk of myocardial infarction with exposure to specific ARV from the PI, NNRTI, and NRTI drug classes: the D:A:D study. [Abstract 44LB.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Mujawar Z, Rose H, Morrow MP, et al. Human immunodeficiency virus impairs reverse cholesterol transport from macrophages. *PLoS Biol*. 2006;4:e365.

Obel N, Thomsen HF, Kronborg G, et al. Ischemic heart disease in HIV-infected and HIV-uninfected individuals: a population-based cohort study. *Clin Infect Dis*. 2007;44:1625-1631.

Reiss P. Abacavir and cardiovascular risk. [Abstract 152.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Rose H, Hoy J, Woolley I, et al. HIV infection and high density lipoprotein metabolism. *Atherosclerosis*. 2008;199:79-86.

Sabin CA, Worm SW. Conventional cardiovascular risk factors in HIV infection: how conventional are they? *Curr Opin HIV AIDS*. 2008;3:214-219.

Sackoff JE, Hanna DB, Pfeiffer MR, Torian LV. Causes of death among persons with AIDS in the era of highly active antiretroviral therapy: New York City. *Ann Intern Med*. 2006;145:397-406.

Shikuma C, Zheng E, Ribaudo H, et al. 96-week effects of suppressive efavirenz-containing ART, abacavir, and sex on high-sensitivity C-reactive protein: ACTG A5095. [Abstract 736.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Smith C, D:A:D Study Group. Association between modifiable and non-modifiable risk factors and specific causes of death in the HAART era: the Data Collection on Adverse Events of Anti-HIV Drugs study. [Abstract

145.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Smith KY, Fine DM, Patel P, et al. Similarity in efficacy and safety of abacavir/lamivudine (ABC/3TC) compared to tenofovir/emtricitabine (TDF/FTC) in combination with QD lopinavir/ritonavir (LPV/r) over 96 weeks in the HEAT Study. [Abstract LBPE1138.] 17th Annual International AIDS Conference. August 3-8, 2008; Mexico City, Mexico.

Tashima K, Niura R, Richardson E, Stanton C, De Dios M, Kojic M. Positive paths: a motivational intervention for smoking cessation among HIV+ smokers. [Abstract 148.] 16th Conference on Retroviruses and Opportunistic Infections. February 8-11, 2009; Montreal, Canada.

Triant VA, Lee H, Hadigan C, Grinspoon SK. Increased acute myocardial infarction rates and cardiovascular risk factors among patients with human immunodeficiency virus disease. *J Clin Endocrinol Metab.* 2007;92:2506-2512.

Triant VA, Meigs JB, Grinspoon SK. Association of C-reactive protein and HIV infection with acute myocardial infarction. *JAIDS.* 2009;51:268-273.

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The Use of Chemokine Receptor Antagonists in Antiretroviral Treatment Failure

by David M. Margolis, MD, FACP, and Gretchen Shaughnessy Arnoczy, MD

HIV engages in complex interactions with host cell-surface receptors to gain cellular entry and begin viral replication. The use of entry inhibitors such as chemokine receptor antagonists offers the potential for achieving virologic suppression in highly drug-experienced patients in whom this state was previously difficult to attain. This activity discusses the interpretation and the significance of certain HIV tropism assay results and the implementation of a chemokine receptor antagonist in a treatment-experienced patient with numerous treatment failures.

End-Stage Renal Disease in the HIV-Infected Patient

by Christina M. Wyatt, MD

HIV-infected patients are at heightened risk of kidney disease related to HIV and coinfections and to the direct toxicity of antiretroviral therapy and concomitant medications. This expertly developed activity discusses current recommendations for the screening and management of chronic kidney disease (CKD) and end-stage renal disease in HIV-infected patients. Issues unique to the diagnosis and management of CKD in the HIV-infected are discussed as are criteria for identifying HIV-infected patients with end-stage renal disease who may be eligible for kidney transplantation.

Pregnancy Planning and Preconception Health Care for HIV-Infected Individuals and Couples

by Erika Aaron, MSN, CRNP, and Shannon M. Criniti, MPH

Owing to effective antiretroviral therapy, many HIV-infected individuals and couples are choosing to have children. This activity discusses a comprehensive preconception plan of health care for HIV-infected women of child-bearing age, contraception choices, and promoting safer conception in HIV-infected women and serodiscordant couples who desire pregnancy. Learners will identify interactions between antiretroviral drugs and hormonal contraceptives and be able to explain assisted reproduction methods such as sperm washing that reduce the risk of HIV transmission to the noninfected partner.

Initiation and Maintenance of HIV Treatment in Adolescents

by Jaime Martinez, MD

Estimates of the number of HIV and AIDS cases continue to increase among adolescents in the United States despite advances in antiretroviral therapy and the development of targeted HIV prevention and testing programs. Adult HIV treatment settings are not wholly sufficient to meet the needs of HIV-infected adolescents, whose unique developmental and psychosocial needs complicate the provision of care. This activity describes features of adolescent development that should be considered when planning care for HIV-infected adolescent patients and considerations for initiating antiretroviral therapy in such patients.

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