Monitoring of Serum Lipids and Cardiovascular Disease Screening in HIV and Aging

- There is insufficient evidence to alter current recommendations for management of dyslipidemia or CVD/cerebrovascular disease screening by specific age criteria. It is reasonable to recommend Framingham Risk Score (FRS) assessment in addition to aggressive primary prevention using standardized guidelines for cholesterol and blood pressure (JNC-8). Whether or not screening for CVD/cerebrovascular disease and treatment of hyperlipidemia in the setting of HIV should be modified for age and/or for HIV itself remains unknown and will require further study.

A growing body of evidence suggests cardiovascular disease is more frequent in HIV-infected subjects (Klein et al. 2002; Triant et al. 2007). In one study, HIV-infected individuals presenting with acute coronary syndromes were more than a decade younger compared to controls (Hsue et al. 2004). Some evidence suggests this may be associated with specific drugs used to treat HIV such as protease inhibitor therapy (Friis-Møller et al. 2007). However, the effect of antiretroviral therapy is clearly complicated as interruption of antiretroviral therapy was associated with an increased risk of cardiovascular events in untreated HIV patients and associated with treatment interruption (El-Sadr et al. 2006).

Age is a component of the Framingham Risk Score (FRS) (Wilson et al. 1998) and advanced age is a well-recognized cardiovascular (CVD) risk factor. Whether the “points” awarded in the FRS for age should be modified in HIV-infected patients remains unclear, but there are some data from surrogate marker studies that subclinical CVD occurs more frequently at younger ages when HIV-infection is present. It is unclear whether this is due to HIV itself, anti-retroviral therapy or traditional risk factors. One estimate from studies examining coronary artery calcium deposition (Guaraldi et al. 2009) and some studies examining carotid intima-media thickness (summarized in Maggi et al. 2009) is that average vascular age in HIV-infected patients is approximately 15 years “older” than expected for chronologic age. Taken together these findings may suggest the screening of CVD for HIV-infected individuals should occur at a younger age; however future studies will be needed to further evaluate this concept. Guidelines for screening of CVD in the setting of HIV infection are summarized in the literature and largely follow guidelines for individuals without HIV infection (Hsue et al. 2008).

Specific IDSA/HIVMA guidelines for evaluation and management of dyslipidemia (Figure 1) have not been updated since 2003 (Dubé et al. 2003) and largely follow the NCEP/ATPIII guidelines. Primary Care Guidelines for HIV-infected patients that included recommendations for CVD/cerebrovascular disease and lipid screening/management were published in 2009 (Aberg et al. 2009).

The following summarizes their recommendations:
Serum fasting lipid profile (FLP)  
Obtain FLP  
  o Obtain every 6-12 months in all HIV-infected patients  
  o Obtain FLP 4-6 months after starting anti-retroviral therapy  
  o “Consider” FLP within 1-3 months of changing anti-retroviral therapy  
  o Dyslipidemia should be managed per NCEP guidelines (www.nhlbi.nih.gov/guidelines/cholesterol/atp3full.pdf) that suggest target levels for dyslipidemia management for those with and without CAD equivalents (i.e. diabetes mellitus, aortic aneurysm, peripheral vascular disease, symptomatic CAD, transient ischemic attack or stroke, and 10-year risk for CAD > 20% by Framingham criteria).  

Other CVD risk factor screening  
  o Blood pressure check in all patients annually  

Whether or not HIV infection should be considered a risk equivalent similar to DM is not known but may be a possibility in the future which would imply lower BP guidelines and LDL cholesterol targets.

Managing Risk for Transient Ischemic Attack (TIA) and Cerebrovascular Accident (CVA)  
While an elevated but small CVA risk was noted prior to the era of effective ART, preventive management
of CVA currently has taken on a prominent focus for older HIV infected patients. Although uncommon (0.5–7%) prior to effective ART, CVA was nevertheless found at a higher-than-expected rate (10–25 per 100,000), controlling for age (Berger et al. 1990). Both small vessel disease, which would be consistent with HIV-associated neurocognitive impairment without focal neurological findings, and large vessel disease, which would be consistent with focal neurological findings as well as neurocognitive impairment, are involved. Both contribute to the vasculopathy associated with aging and HIV infection. In one population-based retrospective study of the pathogenic mechanisms of CVA among 82 HIV infected patients, cardioembolism accounted for 18%, as did small vessel disease, followed by large vessel disease (12%), vasculitis (13%) and hypercoagulability (9%) (Ortiz et al. 2007). The results on CVA risk have become increasingly notable over time and support the conception of HIV infection in the era of effective ART as an inflammatory disease that continues in the face of effective ART.

As with HIV-uninfected patients, cardiomyopathy represents an additional CVA risk factor. One 4-year observational study of 296 pts with a spectrum of HIV-associated illnesses before the initiation of effective ART found that 15% had a dilated cardiomyopathy with global left ventricular hypokinesis (Currie et al. 1994). The incidence was strongly associated with CD4 count of less than 100 cells/mm³. Atrial fibrillation and HIV-associated dilated cardiomyopathy were examined in one recent study of HIV and CVA but were found to be similarly frequent in a group with ischemic stroke (n = 17) and a group without stroke (n = 99) (Ekpebhegh et al. 2011) (Longo-Mbenza et al. 2011). Thus, while atrial fibrillation is common in HIV-associated dilated cardiomyopathy, the specific relationship of CVA to atrial fibrillation, while expected, remains unclear in HIV infection. Related to this issue, interactions between ARVs and oral anticoagulants represent an issue in the current treatment of thromboembolism in the HIV infected. To date, nine case reports documenting drug interactions between oral anticoagulants and ARVs have been reported (Goldstein 2008) conducted a retrospective analysis of these cases and found that, the median percentage of INR measurements of blood clotting time in the therapeutic range was 28.6%. Of those outside the range, 50.5% were sub-therapeutic and 21.2% were supra-therapeutic. It might be concluded that a heightened awareness of the potential difficulty in achieving adequate anti-coagulation in HIV infected patients on effective ART is warranted.

References
Ekpebhegh, C.O. et al. 2011. Advanced age, altered level of consciousness and a new diagnosis of diabetes are independently


