Multiple cohort studies involving untreated HIV-infected persons have established that older persons have a more rapid progression to AIDS and shortened survival when compared with younger persons (Phillips et al. 2008; Balslev et al. 1997; Rezza 1998; Egger et al. 2002). For HIV-infected persons older than 50, sparse data exist from randomized, controlled antiretroviral therapy clinical trials, as most randomized therapy trials have excluded persons older than 50 or 60. A retrospective analysis of 253 patients 50 years of age or older found antiretroviral therapy substantially improved survival rates (Perez & Moore 2003). Several large retrospective studies have clearly shown delayed and diminished CD4 cell recovery after starting antiretroviral therapy in older HIV-infected patients when compared with younger age groups (Khanna et al. 2008; Silverberg et al. 2007; Althoff et al. 2010; Cohere 2008).

Studies have shown conflicting results with respect to virologic responses in older versus younger (Silverberg et al. 2007; Paredes et al. 2000; Manfredi et al. 2003; Lampe et al. 2006), with the most comprehensive study showing no significant difference in virologic responses based in older versus younger adults (Althoff et al. 2010).

The major antiretroviral therapy guidelines that most influence clinical practice in the United States—the Department of Health and Human Services (DHHS) Panel guidelines (Panel DHHS - 2013)—now recommends initiating antiretroviral therapy in all persons infected with HIV. The recommendation to use antiretroviral therapy in all HIV-infected persons is based on reducing the risk of disease progression and decreasing the risk of HIV transmission. Data from several large cohort studies have strongly suggested a survival advantage with initiation of antiretroviral therapy earlier in the course of HIV disease (Kitahata et al. 2009; Sterne et al. 2009). In addition, growing evidence suggests that uncontrolled HIV

When to Initiate Antiretroviral Therapy in HIV and Aging

- Antiretroviral therapy should be initiated in all patients older than 50 who have a CD4 count less than 500 cells/mm$^3$

- Antiretroviral therapy should be initiated in all patients older than 50, regardless of CD4 cell count, with the following conditions: AIDS-defining illness, HIV-associated nephropathy, or chronic hepatitis B virus infection

- For patients over age 50 who have a CD4 count greater than 500 cells/mm$^3$, antiretroviral therapy should be considered. Factors favoring initiating therapy include plasma HIV RNA levels greater than 50,000 copies/ml, greater than 100-point decline in CD4 count in prior 12 months, or risk factors for cardiovascular disease.

- For patients who have diabetes or hyperinsulinemia (and no baseline antiretroviral drug resistance), an initial ritonavir-boosted protease inhibitor-based regimen should be avoided, if possible
infection produces a “chronic inflammatory state” associated with an increased risk of developing cardiovascular disease (Phillips et al. 2008) and non-AIDS malignancies (Bruyand et al. 2009), and CD4 counts below 500 are associated with higher cardiovascular risk (Lichtenstein et al. 2010), and risk for non-AIDS malignancies (Guiguet et al. 2009). The rationale for recommending antiretroviral therapy for the prevention of HIV transmission is based on several recent studies, most notably the landmark HPTN 052 trial that showed a greater than 95% reduction in HIV transmission in HIV serodiscordant couples when the HIV-infected partner received antiretroviral therapy (Cohen 2011).

The 2013 DHHS Antiretroviral Therapy guidelines specifically addressed the use of antiretroviral therapy for persons 50 and older, recommending initiating antiretroviral therapy in all persons older than 50 years of age regardless of CD4 cell count, primarily because, when compared with younger patients, these older HIV-infected individuals have increased risk for non-AIDS related complications and they have diminished CD4 cell count recovery in response to antiretroviral therapy (Panel DHHS - 2013). Further, the DHHS guidelines emphasized that older individuals potentially have increased risk for HIV transmission or acquisition, for several reasons, including (1) alterations reduced mucosal and immunologic defenses may occur with post-menopausal atrophic vaginitis, (2) older individuals have less incentive to use of condoms given the lack of need for pregnancy prevention, and (3) persons older than 50 have lower frequency of HIV screening given their perceived low risk for HIV infection (Adekeye OA 2012).

The use of antiretroviral therapy in older HIV-infected patients presents several challenges, predominantly due to the increased prevalence of non-HIV-related comorbid medical conditions, such as hyperlipidemia, hypertension, diabetes, and coronary artery disease (Skiest et al. 1996). In addition, older patients may have age-related changes in body composition that can alter medication volume of distribution and influence drug pharmacokinetics. Compared with younger patients, older patients are more likely to be taking multiple medications not related to HIV and thus increasing the likelihood for drug-drug interactions. Further, several studies have shown older HIV-infected patients have increased risk for developing drug-related toxicity, including hyperglycemia, elevated creatinine, and unfavorable alterations in lipid profile (Silverberg et al. 2007).

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