Depression in the Aging HIV Infected Population

- Depression is a common co-morbidity in older patients infected with HIV
- Depression is associated with increased risk taking behavior
- Cognitive impairment may coexist with depression compounding the difficulty in diagnosis
- Screening for depression using the Geriatric Depression Scale or the Montreal Cognitive Assessment should be done
- SSRI drugs are the mainstay of treating depression in this population
- Community support services are important in the treatment strategy

An estimated 50% of HIV infected individuals in the United States are over 50 years of age, with 15-25% of new infections diagnosed after the age of 50 [1, 2]. Since 1993, the CDC has designated as “older” HIV patients > 50 years old as a statistical definition, as HIV accentuates the aging process due to the increased medical comorbidities and decreases in physical and mental functional capacity [3, 4].

Sexual activity and substance use increase the risk for acquiring HIV. Depressed mood and cognitive impairment are associated with increased risk taking behavior. Depression may also mediate the effectiveness of interventions to decrease secondary transmission [5]. Denial about the older population being sexually active or using substances often leads to lack of counseling or screening for HIV. Older men and women may not recognize the risk for getting infected [6], especially as HIV has no longer been perceived as a lethal illness and is not as apparent in the press or publications accessed by older people.

Among MSMs even moderate levels of depression increase the risk for acquiring HIV [7]. MSMs continue to be the largest subgroup of HIV infected people in the US, even over age 50. In particular, white men who have sex with men constitute the largest demographic group of older HIV infected persons, although this may change as younger men of color age, particularly Black and Hispanic men, who are disproportionately represented among younger people with HIV. Intravenous drug users make up about 15% of older HIV infected people. Women who have sex with HIV infected men constitute the largest group of older women with HIV [8].

Depression is the most common of mental health disorders in all people infected with HIV, with some studies suggesting that older HIV patients have increased risk for both depression and cognitive impairment [9]. With age comes increased medical comorbidity that may present with depressive like symptoms such as decreased energy, libido and appetite, sleep disruption, and decreased mentation [10]. Older people are also more vulnerable to the inflammatory changes in the CNS, and side effects of antiretroviral therapies (ART) may precipitate or worsen cognition, mood and daily functioning [11-13]. ART in the older population may overlap with neuropsychiatric effects of HIV itself in the CNS [9, 14, 15]. Older patients are at risk for increased rates of toxicities due to ART such as lipodystrophy, dyslipidemia, peripheral neuropathy, metabolic syndrome, and endocrine and pancreatic dysfunction. Older patients with HIV are more likely to report symptoms characteristic of somatization, increased life stress HIV burden, decreased access to care, as well as depression [16].

With the advent of ART many older people infected with HIV in the pre-ART era (who
survived long enough to benefit from multidrug treatment) have been living with HIV for a two decades or more. They may have established social support networks and/or be engaged in HIV community based organizations while others may be socially isolated, abandoned by friends and family, and affected by ageism. Health care access continues to be significantly problematic in ethnic and racial minorities. One study reported that Hispanics with HIV had higher levels of declining health and increased depression attributable to discrimination. Health care disparities for Hispanics with HIV were five times more prevalent than for non-Hispanic whites.

Those who were infected before the advent of ART may have not expected to survive, and may be unable to work, with limited income, dramatically changing their social status and future orientation, having waited to die only to be “resurrected” after years of illness with AIDS. Many have watched the inexorable decline in significant others or friends who did not survive long enough to benefit from treatment. Repeated losses and unremitting grief increase the risk for acute and chronic depression.

There may be significant differences in the psychosocial supports for older men and women. Gay men who have lived within the gay community in urban areas may have more supports than straight men and women who did not develop social supports early on in community based organizations. Furthermore, women with children may have hidden their HIV infection from family.

Newly infected people over 50 may represent different psychological profiles. Some were diagnosed with HIV (or AIDS) having not expected to be at risk. With the absence of regular HIV screening in the older population, the discovery of HIV infection may be due to illnesses secondary to immunological decline. Others may have weathered the earlier years of the AIDS epidemic by shutting down sexually and isolating, only to get infected in later years, fatigued by years of safer sex behavior. Many newly infected remain quite unaware of HIV network resources and isolated due to the stigma associated with sex and/or substance use in the older population. Some are diagnosed late in the illness and may be overwhelmed with the medical issues associated with low CD4 count such as opportunistic infections or neoplasms. A new diagnosis of HIV in older patients may complicate already existing medical and psychiatric conditions that mediate depressed mood. Untreated depression increases non-adherence to ART and HIV treatment, increasing morbidity and mortality [5, 17-19]. Of people triply diagnosed with HIV, substance use, and psychiatric disorders 72.9% have been shown to meet criteria for major depressive disorder [20].

Cognitive Impairment
Confounding the diagnosis of depression in the older HIV infected population is the increased prevalence of cognitive impairment compared to the non-HIV infected population. The risk for cognitive impairment increases with age in the general population. Elevated rates of cognitive impairment have been shown in the HIV infected population independent of age, pre- and post-ART [21, 22]. The impact of cognitive impairment may be initially subtle, affecting adherence to medications and treatment, and may be confused with other aspects of normal aging, such as forgetfulness. Cognitive impairment due to HIV in the CNS can present with changes in personality, lethargy, affect dysregulation, and depressive symptoms. Depression may also affect neurocognitive assessment [23]. Increased mood disturbance is significantly related to poorer cognitive functioning, particularly in the domains of reasoning, speed of processing, psychomotor speed and visuomotor coordination [24]. Self-reports of cognitive difficulties may be more indicative of depression than cognitive impairment due to HIV in the CNS.

Pro-inflammatory cytokines have been studied in the pathophysiology of affective disorders [25]. Studies have shown the impact
of neuroinflammation in HIV related disorders. This is of particular importance in depression, as neuroinflammation has been documented in depression with or without HIV [26]. Depression may affect and /or be affected by the elaboration of pro-inflammatory cytokines influencing diverse processes for regulation of mood [27, 28]. Hypothalamic-pituitary-adrenal activation, also involved with depressed mood, has been documented in the non- HIV infected person [29] and may be present in HIV infected people who are at risk for higher prevalence rates of endocrine disorders. Many of the comorbid conditions of the older population such as coronary disease, or diabetes, are associated with inflammatory processes and increased prevalence of depression. Importantly, increased neuro-inflammation appears to be part of the mechanism for neurocognitive impairment in the HIV infected person, even in persons with suppressed peripheral viral load.

**Assessment of the Older Person with HIV**

Symptoms of low mood, or depressed feelings are seen in the older person with HIV, and may represent psychological, social, and/or biological disorders. Symptoms must be assessed in the overall context of a person’s social, cultural, economic, psychological and biological conditions [Table 1]. Depression in

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<td>Major depression</td>
<td>Dysthymia</td>
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<td>Addison’s Disease</td>
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<td>Addictive disorders</td>
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<td>Diabetes Mellitus</td>
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<td>Neurotoxicities of medications or adjunctive treatments</td>
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the older person may be difficult to distinguish from the somatic symptoms of HIV disease itself, which may delay the diagnosis of depression and increase the risk for the transmission of HIV due to inadequate adherence to ART as well as increase the functional impact of any cognitive impairment that may be present [30]. An appropriate standard measure for depression, such as the Geriatric Depression

Table 2: Treatment for HIV Related Depression

Goals of treatment:

- Decrease social isolation
  - Encourage engagement in HIV community support services where available
  - Connect over the internet with HIV support services
- Identify psychological issues potentiating depressed mood:
  - Attending to loss of function and social supports
  - Treatment for grief and bereavement
  - Shame of acquiring HIV in older years
  - “safer sex” fatigue
- Increasing physical activity [increases BDNF that increase neurotransmitter activity]
- Pharmacological interventions
  - Use of antidepressants that minimally affect the CYP 450
- Combination of Cognitive Behavioral Therapy and medication [most evidence based treatment]
- Use of family therapy to reconnect older people with support systems

Support maintenance of cognitive reserve:

- Reduce alcohol and substance use (illicit or prescribed)
- Improving nutrition
- Attention to treatment of co-morbidities
- Increasing social contact and engagement of cognitively stimulating activities
- Applying cognitive remediation therapies
- Using psychopharmacological interventions [e.g. psychostimulants]
Scale, that minimizes the impact of somatic depressive symptoms should be used in assessing the older person infected with HIV. Assessing daily function, and cognition as well as social factors allows for a truly biopsychosocial treatment plan.

While there are screening tools available that may provide some indications of cognitive impairment such as the HIV Dementia Scale, International Dementia Scale, or the Montreal Cognitive Assessment (MoCA), only a complete neurocognitive battery can demonstrate the more subtle changes over time. One study reported the MoCA as a useful screening tool in the older HIV infected population, as it examines both cortical and subcortical domains of function [31]. Assessment of real world function is important to determine the level of activity and impairment that is present in the older patient with HIV [32-34].

Treatment of the Older Person with HIV

A comprehensive approach is essential in treating the older person who is depressed and HIV positive (Table 2). All HIV infected patients should be screened for depression, as it is an independent factor affecting morbidity and mortality. In the older population especially, depression and mild to moderate cognitive impairment are often difficult to differentiate, and providers should develop a standard screening protocol that examines both mood and cognition. Since both depression and cognitive impairments may decrease medication and treatment adherence, a multimodal approach is essential. Particular attention should be paid to the psychosocial context, as older patients are more likely to be isolated, even from family, because of the stigma of HIV. Important psychosocial and economic issues should be considered in the older patient with limited resources include the impact of food and housing insecurity, increasing risks for depression and anxiety.

The most studied approach to the treatment of depression generally is a combination of antidepressant medication and cognitive behavioral therapy. There are few randomized controlled studies of most antidepressants, although there is clear support for the use of medication in HIV related depression. Antidepressants that minimally affect the CYP 450 isozyme system are preferable by reducing the risk for drug interactions that reduce viral suppression. Psychostimulants have been used in patients with depressed mood and mild cognitive impairment. Although effective for the treatment of depression in HIV as in the general population, caution must be used with tricyclic antidepressants due to side effects and drug interactions, which are more significant in the older population. Antipsychotic medications should be avoided in the absence of psychosis in order to reduce the risks for metabolic syndrome. Drug-drug interactions may be more common in older patients due to decreased renal and hepatic clearance, especially in co-occurring HCV and/or HBV infection. Benzodiazepines should be used with great caution in the older patient with HIV. SSRI’s are often effective in managing anxiety, especially in the context of co-occurring depressive symptoms. Some recent studies have suggested that SSRI’s may be protective of inflammation [35].

In addition to the medical management of depression, community support services, psychotherapy, individually or in groups can decrease shame and isolation, and increase adherence to care. Problem solving therapeutic interventions may help older patients identify both emotional and functional needs. Although more research is needed, there is growing evidence that exercise throughout the life cycle may increase brain derived neurotropic factor (BDNF) and confer some cognitive protection [36]. In addition to the medical management of depression, community support services, psychotherapy, individually or in groups can decrease shame and isolation, and increase adherence to care. Problem solving therapeutic interventions may help older patients identify both emotional and functional needs. Although
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