Mental Health Comorbidity and HIV/AIDS

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Introduction

New data on the incidence and prevalence of HIV both in the United States and throughout the world underscore the continuing magnitude of the AIDS epidemic clearly. There are now an estimated 1.2 million people in the United States and 34 million people in the world living with HIV, with 2.7 million new infections in the world in 2010, including an estimated 390,000 among children (UNAIDS, 2011). The UNAIDS report urgently calls for accelerated responses from countries in efforts to completely halt the spread of the disease and highlights the declining incidence and death rate from the disease. However, there are still no current cures or available vaccines. Although medications which are available to manage HIV have been helpful in decreasing the ravages of the disease and prolonging life, each has drawbacks. We in health care must be prepared to manage HIV and AIDS for decades to come.

Psychiatric comorbidity in persons living with HIV is relatively high, specifically for psychiatric diagnoses such as depression and substance use disorders, as well as certain anxiety disorders, psychotic disorders, and cognitive disorders. The reverse relationship also seems to be true, namely that in general psychiatric populations, the rates of HIV infection are elevated. Furthermore, persons living with HIV are specifically at risk for increased symptoms related to psychiatric disorders. In some of these conditions the relationship is bidirectional; for example, persons with substance use disorders have a higher likelihood of also having HIV. In this chapter, we discuss the relationships between mental health and HIV, including the role of mental health in HIV transmission and treatment, the role of HIV in psychiatric illness and its course, and current recommendations for assessment and treatment of mental health in persons living with HIV.

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S. Loue (ed.), *Mental Health Practitioner's Guide to HIV/AIDS*,
DOI 10.1007/978-1-4614-5283-6_2,

Sample Clinical Treatment Scenario

The following composite case from a clinical practice setting demonstrates some of the relevant issues for consideration in assessment and treatment of people with mental health and HIV comorbidity.

A 45-year-old man presented to a community mental health center for treatment of depression and difficulty with attention. He reported that his mood symptoms had been severe since his mid-20s, including persistent low mood and thoughts of death. Although he indicated that he had also had low moods and poor attention in childhood, these had not been severely disabling and he had obtained some higher education and was a talented musician. He had used street drugs heavily at times, most notably having developed a methamphetamine addiction which peaked in his 20s and 30s. However, he states he has not used methamphetamines in 10 years. He is not sure when he acquired HIV, but feels it was likely in his late 20s from sexual contact with men. He is being treated for HIV with several medications. He admits that the symptoms of depression and inattention have interfered with his ability to take his HIV medications; at times when he is particularly depressed, he may spend an entire day in bed and fail to eat or take medications. At other times, he may simply forget to take a dose. Because of the increased recent depressive symptoms, decreased levels of movement and activity, and general physical debility, he is no longer able to continue his work in music at the same level as he had previously.

His treatment course has been difficult due to refractory depression and complex comorbidities of attentional difficulties and substance abuse. On presentation to the community mental health center, he was being prescribed two antidepressants with different actions, a benzodiazepine, and a stimulant by his clinician with whom he had worked with for several years; cross-referencing through the state-wide pharmacy repository confirmed that he did not have multiple providers. Chart review and conference with the previous provider confirmed that the medications had been added individually to address symptoms, and attempts to wean him off of any of the medication classes had been unsuccessful. In fact, as all of the diseases progressed, and he developed tolerance to certain medications, he seemed to need higher doses. He had particular difficulty with fatigue, low motivation versus a lack of interest, and poor appetite. He has not recently been able to access individual or group therapy other than supportive therapy per his psychiatrist and social work support at the clinic that manages his HIV. However, he is agreeable to these, as well as medication management.

Relationship Between Mental Illness and HIV Transmission

Several clinically relevant relationships exist between mental illness and HIV status. Having a preexisting mental illness may influence the likelihood of both contracting HIV as well as progression to AIDS. Conversely, it also seems that having HIV or AIDS increases the likelihood of developing certain mental illnesses

or disorders, as well as symptoms of mental illness that, although extremely troublesome to patients, may not reach the level of a disorder. Although more needs to be done, some research has begun to identify both illness and psychosocial factors that may be important in modulating these relationships. While it is important to keep in mind that many things about HIV may be changing (in particular, its prevalence in different demographics and associated psychosocial stressors, available treatments, prognosis), and care must be taken not to overgeneralize studies, we must rely on what may be available to understand the relationships between HIV and mental health.

Studies of persons who have mental illness or substitute measures that suggest mental illness, such as having an inpatient psychiatric hospitalization, have found that this population has had a higher rate of HIV infection in comparison with the general population. Studies done two decades ago found that the prevalence of HIV in a population of psychiatrically hospitalized patients was several times higher than that of the general population (Cournos, Horwath, Guido, McKinnon, & Hopkins, 1994; Gewirtz, Horwath, Cournos, & Empfield, 1988; Sacks, Dermatis, Looser-Ott, & Perry, 1992), particularly among patients who had multiple sexual partners, had traded sex for money or drugs, or had used injection drugs (Kalichman, Kelly, Johnson, & Bulto, 1994). Later studies have again shown that patients with a psychiatric diagnosis have a much higher rate of HIV, which has been estimated to be seven to eight times higher than control groups (Otto-Salaj, Heckman, Stevenson, & Kelly, 1998; Rosenberg et al., 2001; Vanable, Carey, Carey, & Maisto, 2007).

Several factors may explain why certain mental illnesses increase the risk of contracting HIV. Patients with serious mental illnesses such as schizophrenia, recurrent major depression, and certain anxiety disorders such as posttraumatic stress disorder (PTSD) may have increased risk-taking behavior or lowered use of risk-reduction strategies in regard to sexual contacts and/or drug abuse during exacerbations; they may have lower knowledge about how to protect themselves from becoming infected; and they may also have other sexually transmitted or blood-borne infections that may increase the likelihood of HIV infection (Blumberg & Dickey, 2003). Studies examining the correlation between mental illness and higher rates of HIV transmission to others have not found this to be true. However, there is likely a link between depression and unprotected sex in HIV-negative men who have sex with men that may increase the likelihood of contracting the virus; a link was not found between depression and unprotected sex in HIV-positive men who have sex with men (Houston, Sandfort, Dolezal, & Carballo-Dieguez, 2012).

Mental illnesses and symptoms of mental illnesses also likely have an effect on HIV treatment success, which may be mediated by treatment adherence, biological factors, or other factors. Patients who have both HIV and a mental illness are likely to have worse outcomes, including higher likelihood of progression to AIDS and death (Evans et al., 1997; Rothbard, Miller, Lee, & Blank, 2009). Patients with symptoms associated with depression, even without meeting full criteria for depression, have been shown to have higher rates of poor HIV-related outcomes, such as higher rates of treatment failure and death (Leserman, 2008). A recent study has

similarly found that patients with HIV and co-occurring schizophrenia, bipolar disorder, and substance use disorders have higher rates of mortality, and that progression to AIDS was more likely in patients with substance use disorders (Nurutdinova et al., 2012).

Having HIV or AIDS also increases the likelihood of developing mental illness or sub-threshold symptoms of these disorders, or exacerbating preexisting mental illness.

Biology of HIV and Psychiatric Illness

The biological relationship between mental illness and HIV has received increasing attention in the past two decades. Knowing the common biological links between HIV and mental illness can inform clinical treatment decisions.

Depression may contribute to the progression of HIV by several direct and indirect mechanisms. The neurotransmitter serotonin has been studied as a direct mediator of the process, as it plays a role in both depression and immunity. In immune cells, serotonin is felt to regulate the cell's production of additional receptors and signaling molecules and enhance the body's production of the types of immune cells responsible for effectively containing the infection by killing infected cells. Serotonin has been found to decrease HIV replication within the infected cell (Fauci, Mavilio, & Kottilil, 2005). Recent research has found that medications used to alleviate depression by blocking reuptake and subsequent degradation of this neurotransmitter may also enhance the body's ability to suppress HIV through actions on key immune cells (Benton et al., 2010).

According to a recent review of the topic by Schuster and colleagues, direct mechanisms also involve depression-related increases in cortisol and other stress-related hormones, in turn causing poor immune function by blunting and dysregulating the response of immune cells and their infection-fighting products, as well as enhancing HIV replication (Schuster, Bornovalova, & Hunt, 2012). Additionally, biopsychosocial factors, including increased hopelessness, increased substance abuse, decreased social support, decreased medication adherence, and increased risk taking behaviors with likelihood of contracting additional sexually transmitted diseases, play an important role through some of the same central mediators. The resultant load of contributing factors, each triggering biologic pathways that affect the immune system, leads to measurably worse outcomes for patients, in particular increased disability, faster progression to AIDS, and decreased lifespan. It is important for the mental health provider to assess for these contributing factors, as each of them represents an area where intervention may be needed to achieve better immune outcome. Of note, it has been shown that improvement in depressive symptoms can improve not only cell counts and decrease viral load but also improve immune cell function (Cruess et al., 2005).

The relationship between psychosis and HIV likely has completely different biological mechanisms, although some mediators are likely shared. Studies of patients with HIV and new onset psychosis including hallucinations and delusions have suggested HIV encephalopathy (inflammation of the central nervous system), or the direct infection of the brain with HIV, with resultant changes in the brain due to the infection, as the cause (Sewell et al., 1994).

HIV and Mental Illness Comorbidity

Depression, Anxiety, and HIV

A 2001 meta-analysis of ten studies concluded that patients with HIV are at two-fold higher risk of depression than those without HIV; this effect appears to be independent of disease stage or sexual orientation (Ciesla & Roberts, 2001). The presence of depressive disorders has been estimated to approach 40% of patients with HIV (Bing et al., 2001). A substantial percentage of patients with a depressive disorder remain undiagnosed, and increased efforts should be made to improve detection. Differences in biological sex in this regard have also been studied in a large, prospective, cross-sectional study by Lopes et al. (2012). When compared with HIV-negative men, HIV-positive men were significantly more likely to have a mood disorder, major depressive disorder or dysthymia having the highest prevalence, followed by any anxiety disorder, and lastly any personality disorder. In contrast, HIV-positive women were not found to have an elevated prevalence of psychiatric disorders in general or in specific (Lopes et al., 2012). Of note, different studies of various demographic populations have also correlated female sex with depression or depressive symptoms as well. HIV has also been found to increase sub-threshold symptoms of depression and anxiety. The role that HIV plays in increasing depression may be partly mediated by the effects of social support and family functioning (Dyer, Stein, Rice, & Rotheram-Borus, 2012).

Certain aspects of mental health are particularly important to emphasize. In a study of patients who had attempted suicide after recent diagnosis of HIV, researchers found that HIV diagnosis increased the risk of suicide by approximately 16%, and that patients endorsed many comorbid stressors related to HIV as being present, particularly fear of negative impact on psychological, social, economic and health statuses due to HIV, lack of psychosocial and health support, and fear of being ostracized or victimized (Schlebusch & Vawda, 2010). The study also supported earlier findings that factors such as younger age, female sex, and mental health diagnoses further increased the risk of suicide.

Treatment of depression has been shown to improve not only the depressive symptoms, but also improve measures of the HIV infection, such as viral load and cell counts (Coleman, Blashill, Gandhi, Safren, & Freudenreich, 2012). Assessment of depression and anxiety at the primary point of contact for patients who have HIV

can facilitate correct treatment referral, act to destigmatize mental illnesses for the patient, and serve to support the patient even if he or she does not meet criteria for a psychiatric disorder. Rating tools can be used to quickly screen for many disorders, and can be used by a broad array of clinical providers. Tools that have been studied specifically with patients who have HIV include the Zung rating scale (Lombardi, Mizuno, & Thornberry, 2010), the Beck Depressive Inventory (Levine, Aaron, & Criniti, 2008), the PHQ-2 and the PHQ9 (Monahan et al., 2009). Other scales may also be useful in clinical practice as well. Continued research is needed to determine the optimal rating scale. Diagnosis should then be made based on clinical interview that will be able to rule out conditions that may mimic depression or anxiety. Of particular importance in this regard is HIV-associated dementia, which shares many symptoms of depression and anxiety, bipolar spectrum disorders, medication-related mood disorders, substance use disorders, and various medical illnesses, all of which will affect treatment decisions.

Treatments that appear to have at least some evidence base for people with HIV and depression include psychotherapies and antidepressant medications (Kelly et al., 1993; Olatunji, Mimiaga, O'Cleirigh, & Safren, 2006; Psaros, Israel, O'Cleirigh, Bedoya, & Safren, 2011). Medication treatment choices for treatment of depression and anxiety in the HIV patient should take into account medication interactions and particularly bothersome versus clinically useful side effects. A recent review of medication treatment for psychiatric disorders in patients with HIV and AIDS notes that there is a relative lack of research done since the advent of currently used antiretroviral regimens; however, antidepressants and anxiolytics are widely used (Repetto & Petitto, 2008). As in the general population with depression, use of antidepressant medications side effect profile that minimizes possible exacerbation of physical complaints such as fatigue or insomnia should be considered before medication initiation. It is reported that antidepressant medications that may be useful in treating depression in people with HIV include imipramine, desipramine, nortriptyline, amitriptyline, fluoxetine, sertraline, paroxetine, citalopram, escitalopram, fluvoxamine, venlafaxaine, nefazodone, trazodone, bupropion, and mirtazapine (Mainie, McGurk, McClintock, & Robinson, 2001). Double-blind trials have been conducted with imipramine, fluoxetine, sertraline, and paroxetine (Ferrando, 2005). No single antidepressant drug appears to have evidence of superior efficacy (Yanofski & Croarkin, 2008).

Psychotherapeutic approaches that appear to be helpful include cognitive behavioral therapy and interpersonal therapy (Psaros et al., 2011). Important elements of psychotherapy for people with HIV/AIDS may include dealing with stigma, discrimination, punishment beliefs and addressing barriers to illness self-management for both HIV and for depression such as adherence with antiretroviral medication. One report noted that patients with HIV who are treated for depression with antidepressants appear to benefit from improved levels of adherence to their antiretroviral therapy as well (Dalessandro et al., 2007).

Psychosis and HIV

Psychotic disorders are characterized by delusions, hallucinations and impaired insight. HIV-infected individuals presenting with psychosis require a thorough clinical assessment to determine the underlying etiology of the psychotic state.

An increased risk of psychosis in HIV infected individuals has been found to be associated with a history of psychiatric illness (de Ronchi et al., 2000; Dew et al., 1997), psychosis caused by physical illness such as opportunistic infections of the central nervous system (Johannessen & Wilson, 1988; Sewell, 1996), a high lifetime prevalence of stimulant and sedative/hypnotic abuse (Sewell et al., 1994), as well as lower cognitive abilities (de Ronchi et al., 2000) and stressful life events (Sewell, 1996).

A psychiatric history to evaluate for a preexisting (primary) psychotic disorder such as schizophrenia or bipolar disorder should be obtained. Schizophrenia is more prevalent (approximately 5%) in individuals with HIV than in the general populations (about 1%) (Walkup, Crystal, & Sambamoorthi, 1999). Despite this, a study of people with schizophrenia in an inpatient population showed that only 17% had been tested for HIV within the last month (Walkup, McAlpine, Olfson, Boyer, & Hansell, 2000), suggesting that screening for HIV in this population could be improved. Individuals with schizophrenia may be at an increased risk of contracting HIV due to symptoms or effects of schizophrenia including poor impulse control, delusions (Psaros et al., 2011), impaired judgment, substance abuse including intravenous drug use, a high risk of trading sex for money or drugs (Cournos, Guido, et al., 1994; Kalichman et al., 1994; Kelly et al., 1992; McKinnon, Cournos, Sugden, Guido, & Herman, 1996), and lack of effective HIV education (Gottesman & Groome, 1997; Sewell, 1996). Despite being at high risk for contracting HIV, individuals with psychotic disorders are less likely to be tested for HIV than those with other severe mental illnesses or substance abuse, possibly due to cognitive or social deficits, lack of patient education, and lack of clinician knowledge about risk behaviors in this population (Meade & Sikkema, 2005). However, timely diagnosis and treatment is critical since people with comorbid schizophrenia and HIV are at a greater risk of morbidity and mortality due to impaired ability to comply with medical care, difficulty explaining symptoms to medical personnel, and possibly receiving less attention than those without psychosis as it relates to physical complaints (Sewell, 1996; Sewell et al., 1994).

The differential diagnosis of psychosis in HIV infected individuals also includes substance intoxication or withdrawal, HIV encephalopathy, delirium, dementia or side effects of medications (Table 1) (Brogan & Lux, 2009; Foster, Olajide, & Everall, 2003; Sewell et al., 1994). Between 0.2 and 15% of HIV-positive individuals have no prior history of a psychotic illness and experience secondary or new onset psychosis (Sewell, 1996). Psychosis in HIV-positive individuals may be clinically distinct from primary psychotic conditions with more paranoid, grandiose and somatic delusions than bizarre delusions, impairment in attention and concentration, more visual hallucinations, fewer affective symptoms and a greater

Table 1 Differential diagnosis of psychosis in individuals with HIV/AIDS

Primary psychotic disorders	Schizophrenia
	Bipolar disorder
	Other psychotic disorders, e.g., schizoaffective disorder, depression
Secondary psychotic disorders	HIV infection
	HIV-related infections/opportunistic infections
	HIV encephalopathy
	Secondary mania
	Substance intoxication or withdrawal
	Delirium
	HIV-associated dementia
	Medication side effects or interactions
	Medical disorders (i.e., electrolyte disturbances, sepsis, hypoglycemia)

likelihood of remission (De Ronchi et al., 2006; Harris, Jeste, Gleghorn, & Sewell, 1991).

A variety of drug interactions or side effects of medications may induce psychotic symptoms in HIV-infected individuals. Medications used to treat HIV and associated conditions have significant side effects and a medication list should be obtained, including an assessment of any temporal relationship between starting new medications and the onset of psychotic symptoms. In particular, psychosis has been observed in those treated with the HIV medication efavirenz (de la Garza, Paoletti-Duarte, Garcia-Martin, & Gutierrez-Casares, 2001; Lowenhaupt, Matson, Qureishi, Saitoh, & Pugatch, 2007) and another HIV medication, zidovudine, may induce mania (O'Dowd & McKegney, 1988). Other HIV medications including nevirapine (Wise, Mistry, & Reid, 2002) and abacavir (Foster et al., 2003) have also been implicated in causing transient psychosis. Other drugs, including ganciclovir and ethambutol, used in the treatment of HIV-related illnesses such as cytomegalovirus and mycobacterium avium complex have also been reported to cause psychosis (Hansen, Greenberg, & Richter, 1996; Martin & Bowden, 2007).

HIV and hepatitis C virus (HCV) have similar routes of transmission (i.e., intravenous drug use) and 30–50% of individuals with HIV are coinfected with HCV (Dodig & Tavill, 2001). Individuals infected with HIV alone or HIV and HCV together were found to have higher rates of bipolar disorder, schizophrenia and psychotic disorders than those without HIV (Baillargeon et al., 2008). Interferon alpha is a medication used in the treatment of HCV (Ferguson, 2011) that may cause psychiatric side effects including psychosis in HIV-positive individuals (Hoffman et al., 2003).

Adherence with treatment for both HIV antiretroviral drugs and antipsychotic medications may be adversely affected by psychosis (Bansil, Jamieson, Posner, & Kourtis, 2009), although one study suggested that adherence may be better in HIV-infected people with schizophrenia than HIV-infected people who do not have schizophrenia due to increased access to medical care (Walkup, Sambamoorthi, & Crystal, 2001). Since adherence with antiretrovirals may be an issue and since

psychotic individuals may present a risk of harm to themselves or others, it is critical to treat psychotic symptoms in HIV positive individuals.

Newer atypical antipsychotics such as quetipaine, risperidone, olanzapine, and aripiprazole can be used for psychosis and for mood stabilization and are generally preferred over the older, typical antipsychotics, such as haloperidol and thorazine. Typical antipsychotics are known to cause more extrapyramidal symptoms (EPS) such as abnormal movements, dystonia, or parkinsonism. However, atypical antipsychotics carry a greater risk for metabolic syndrome and those with the higher risk should generally be avoided or closely monitored. Increased appetite, obesity, and abnormal triglycerides and cholesterol as a result of antipsychotic medication can lead to diabetes and cardiovascular events and switching to an antipsychotic with lower metabolic risks may be considered (Stahl, Mignon, & Meyer, 2009).

A consensus survey conducted by Freudenreich et al. (2010) showed that the atypical antipsychotics quetiapine, risperidone, and aripiprazole were most often used for treatment of psychosis. Risperidone has been shown to be efficacious in the treatment of HIV-related psychosis (Singh, Golledge, & Catalan, 1997) but has higher rates of EPS than other atypical antipsychotics, especially at higher doses; individuals with HIV may be more likely to develop EPS due to loss of dopaminergic neurons (Hriso, Kuhn, Masdeu, & Grundman, 1991). Clozapine, another atypical antipsychotic, is generally not recommended for the treatment of psychosis in HIV-infected people due to concerns for agranulocytosis (a dangerous decrease in white blood cell count), toxicity, and drug interactions (Cournos, McKinnon, & Sullivan, 2005).

General recommendations for treating HIV-positive individuals with antipsychotic medications include starting at lower doses than in individuals without HIV, up-titrating doses slowly, and closely monitoring for side effects (Cournos et al., 2005). Discontinuing antiretroviral treatment until remission of the psychotic symptoms occurs should be considered (Arendt, de Nocker, von Giesen, & Nolting, 2007; Foster et al., 2003). Following stabilization of psychotic symptoms, individuals may benefit from psychotherapy, and psychosocial interventions for people with schizophrenia including skills training, cognitive therapies, education and HIV risk reduction programs. All of these approaches may improve self-care and overall functioning (Cournos et al., 2005; Heinssen, Liberman, & Kopelowicz, 2000).

Manic episodes in HIV-infected individuals may be due to a preexisting (primary) bipolar disorder which can be characterized by elevated mood, grandiosity, impulsivity, a decreased need for sleep, and/or pressured speech (American Psychiatric Association, 2000). First-episode (secondary) mania which is directly related to HIV infection in the brain or HIV-related infections may present differently with greater irritability, aggression, disruptive behaviors, decreased need for sleep, higher rates of psychotic symptoms, visual and auditory hallucinations, and cognitive impairment (Nakimuli-Mpungu, Musisi, Mpungu, & Katabira, 2006). Secondary mania, in contrast to primary mania, has been shown to develop later in the course of HIV/AIDS (Kieburtz, Zettelmaier, Ketonen, Tuite, & Caine, 1991; Lyketsos, Schwartz, Fishman, & Treisman, 1997) with a rate of 1.2% in

HIV-positive individuals and 4.3–8% in those with AIDS (Ellen, Judd, Mijch, & Cockram, 1999; Lyketsos et al., 1993). There is a limited amount of evidence suggesting that antiretroviral drugs that strongly penetrate the cerebrospinal fluid may decrease the likelihood of secondary mania (Mijch, Judd, Lyketsos, Ellen, & Cockram, 1999).

Secondary manias are most often treated with quetiapine, valproic acid and risperidone (Freudenreich et al., 2010). While the mood stabilizing drugs lithium and valproic acid both may be used in the treatment of secondary mania, they must be used cautiously in those with HIV and AIDS. Kidney disease and altered levels of critical electrolytes such as sodium and potassium are common in individuals with AIDS and increase the risk for lithium toxicity which can manifest as nausea, confusion, gait disturbances, kidney failure, seizures and coma (Freudenreich et al., 2010). Valproic acid undergoes metabolism in the liver and use may be affected in those with HIV due to comorbid HCV infection or drug interactions (Freudenreich et al., 2010; Romanelli, Jennings, Nath, Ryan, & Berger, 2000). The mood stabilizing medication carbamazepine, which is sometimes used in the treatment of bipolar mania, induces liver enzyme activity (cytochrome P450 CYP3A) and thus may lead to decreased efficacy of HIV medications (Romanelli et al., 2000).

Substance Use Disorders and HIV

Injection drug use (IDU) and non-injection drug use (NIDU) are risk factors for contracting HIV/AIDS (Koblin et al., 2006; Lampinen, Mattheis, Chan, & Hogg, 2007; Ostrow et al., 2009). In 2009, 8% of diagnosed HIV infection in males and 15% in females were due to injection drug use (Centers for Disease Control and Prevention, 2011). The use of contaminated injection equipment is a significant risk factor for HIV transmission; however, drug use via methods other than injection can also increase the risk of HIV transmission or exposure due to increased sexual risk-taking, multiple partners, sex trade, and decreased condom use (Meade, 2006). In addition, mother-to-child transmission of HIV may be increased in women who use drugs during their pregnancy (Purohit, Rapaka, & Shurtleff, 2010).

Alcohol and stimulant use is associated with an increased risk of HIV transmission among heterosexuals and men who have sex with men (MSM) (Morin et al., 2007). For example, amphetamine use increases high risk sexual behavior, thereby increasing the risk of HIV transmission (Plankey et al., 2007). Substance use is likely to continue after seroconversion, with 40% of HIV-infected individuals using illicit drugs other than marijuana and 12.5% screening positive for substance dependence (Bing et al., 2001). Substance abuse disorders (either active or in remission) among those with HIV/AIDS have been reported to be as high as 75% (Treisman & Angelino, 2007). Unfortunately, diagnosis of HIV may occur later in injection drug users than in others (Grigoryan, Hall, Durant, & Wei, 2009) and this population is less likely to have ever received Highly Active Antiretroviral Therapy (HAART), a combination of medications used in the treatment of HIV (Malta et al.,

2009; McGowan et al., 2011; Tegger et al., 2008) or may experience delayed initiation of antiretroviral therapy (Rodriguez-Arenas et al., 2006).

Decreased adherence to HIV medications has been associated with substance use, including alcohol dependence (Azar, Springer, Meyer, & Altice, 2010; Hendershot, Stoner, Pantalone, & Simoni, 2009; Hinkin et al., 2007; Sandelowski, Voils, Chang, & Lee, 2009). Less than maximal adherence can increase the likelihood of developing resistance to HIV therapies, thereby limiting treatment options (Colfax et al., 2007). Markers of HIV disease progression such as HIV viral load may also be negatively impacted by decreased adherence (Arnsten et al., 2002; Carrico et al., 2007; Rodriguez-Arenas et al., 2006). Stimulant use has also been shown to decrease HAART adherence (Carrico et al., 2007; Hinkin et al., 2007) leading to drug resistance including resistance to non-nucleoside reverse transcriptase inhibitors, a specific class of antiretroviral drugs used to treat HIV infection (Colfax et al., 2007; Gorbach et al., 2008).

HAART therapy has improved outcomes for individuals with HIV; however, these benefits may be significantly decreased in those using intravenous drugs. Studies indicate that IDU increases the rate of progression to AIDS, increases the incidence of AIDS defining illnesses such as *Pneumocystis carinii* or Kaposi's sarcoma, and increases the mortality rate in this population (Baum et al., 2010; Malta et al., 2009; Porter et al., 2003; Rodriguez-Arenas et al., 2006). Three-year survival rates are lower for HIV patients with IDU than nonusers (Grigoryan et al., 2009).

While IDU is concerning, individuals with drug use by routes other than injection are at risk as well. Those individuals with NIDU (including those who use alcohol and nicotine), like those with IDU, progress more quickly to AIDS than non-drug users (Kapadia et al., 2005). In addition, those with NIDU have an increased risk of developing opportunistic infections due to their impaired immune system (Lucas, Griswold, et al., 2006), increased mortality (Cook et al., 2008; Lucas, Cheever, Chaisson, & Moore, 2001), and a negative impact on markers of HIV disease progression such as greater decline in white blood cell (CD4+) count and increased HIV viral load as compared to HIV-positive individuals who do not use drugs (Baum et al., 2010; Carrico et al., 2008; Cook et al., 2008; Lucas et al., 2001).

HIV progression in substance abusers may also be affected by homelessness (Gore-Felton & Koopman, 2008), and poor nutrition (McGowan et al., 2011), as well as comorbid infections including tuberculosis (Gore-Felton & Koopman, 2008), hepatitis C virus infection (Braitstein et al., 2006) and other sexually transmitted diseases (Wong, Chaw, Kent, & Klausner, 2005). In addition, HIV-infected individuals who use nicotine are more likely than nonsmokers to be hospitalized with the HIV-associated pneumonia, *P. carinii* or community acquired pneumonia (Miguez-Burbano et al., 2005). HIV-positive individuals who have substance use disorders are more likely to screen positive for comorbid psychiatric disorders than individuals who do not abuse substances (Bansil et al., 2009; Bing et al., 2001; Gaynes, Pence, Eron, & Miller, 2008; Tegger et al., 2008). Clearly,

substance abuse in patients with HIV is concerning and contributes to a variety of concerning issues.

Assessment of substance use should be included in any mental health evaluation and is a critical component of medical history taking when clinicians are assessing individuals presenting with HIV. A thorough clinical assessment includes a detailed history of drug use including age of first use, which substances have been or are being used (keeping in mind that polysubstance use is not uncommon), experience with alcohol or drug rehabilitation programs (including the 12-step program Alcoholics Anonymous (AA)), periods of abstinence or sobriety, history of withdrawal and associated problems such as delirium tremens or seizures, social support and social contact (i.e., other users), legal problems associated with drug use, and current use (Table 2). If a substance use disorder is suspected it is useful to determine the individual's stage of willingness to change through common behavioral treatments including motivational interviewing (Rollnick, Miller, & Butler, 2008).

Improvements in antiretroviral adherence and medical outcomes are improved when substance users stop using (Altice, Kamarulzaman, Soriano, Schechter, & Friedland, 2010; Lucas, Griswold, et al., 2006; Lucas, Mullen, et al., 2006). Appropriate individuals should be referred to substance abuse treatment programs including inpatient hospitalizations, day program, and/or AA/narcotics anonymous (Berg, Michelson, & Safren, 2007). In addition, needle exchange programs can decrease the risk of HIV seroconversion (Wodak & Cooney, 2006) and individuals should be educated regarding using sterile needles or disinfecting injection equipment with bleach. Behavioral interventions and talk therapy may also be beneficial. Suggesting and coordinating case management which can provide a single point of contact for social services, medical and psychiatric care, and substance abuse treatment (Samet, Walley, & Bridden, 2007) may be helpful for some people.

Medication assisted therapy for HIV-infected drug users may improve access and adherence to antiretroviral therapy (ART) and decrease risky behaviors (Spire, Lucas, & Carrieri, 2007). For example, methadone and buprenorphine are opioid replacement medication therapies that reduce cravings for narcotic drugs (opioids), block euphoric effects if individuals use opioids, and treat withdrawal symptoms (Samet et al., 2007). Methadone treatment has been shown to improve HIV medication adherence, HIV virus suppression, and CD4+ count maintenance (Palepu et al., 2006). There can be significant drug interactions between methadone or buprenorphine and HIV drugs and treating clinicians should be aware of these and closely monitor this treatment (Samet et al., 2007). Other medication assisted therapy options include naltrexone for opioid and alcohol dependence and acamprosate and disulfram for alcohol dependence.

The use of directly observed therapy programs may also increase adherence in individuals with HIV infection (Lucas, Mullen, et al., 2006; Mitty et al., 2005; Smith-Rohrberg, Mezger, Walton, Bruce, & Altice, 2006). Evidence suggests that access to appropriate support services can increase adherence to ART and therefore increase the likelihood of a good outcome for HIV-positive individuals who present with substance use problems (Malta, Strathdee, Magnanini, & Bastos, 2008).

Table 2 Elements of the clinical assessment of substance use

History of substance use	Age of first use
	Substances used
	Rehabilitation programs
	Periods of abstinence/sobriety
	History of withdrawal
	History of legal problems associated with substance use
Current substance use	Which substances? How much? How often?
	Social contacts (i.e., associating with other substance users)
	Social supports
	Insight into problem
	Stage of willingness/readiness to change

Issues Specific to Children, Adolescents, and Families

Assessment of children and adolescents with HIV should include developmental, environmental, social, and family factors including collateral information from school and family members. A psychiatric history including recent stressors should be taken (Benton, 2010). Multiple factors including effects of the HIV virus on the central nervous system (CNS), genetic factors, prenatal exposure to substances, and opportunistic infections can affect the presentation of psychiatric symptoms in this population (Benton et al., 2010; Donenberg & Pao, 2005; Lwin & Melvin, 2001).

Although congenitally acquired HIV is rare in the United States where highly active antiretroviral therapy (HAART) is readily available, 59 cases were reported to the Centers for Disease Control and Prevention (CDC) in 2003 (Centers for Disease Control and Prevention, 2007) and it is still a problem worldwide. Transmission of HIV from mother to child may occur during pregnancy, childbirth or breastfeeding. Routine, voluntary HIV screening for pregnant women (Branson et al., 2006) and the use of reverse transcriptase inhibitors (a class of antiretroviral drug used to treat HIV infection) during pregnancy and breast-feeding has decreased mother to child transmission of HIV (Benton, 2011). Infants presenting with HIV may have cognitive, language, motor, and behavioral impairments and, in severe forms, can exhibit a rapidly progressive course characterized by an acute encephalopathy leading to brain injury and loss of previously acquired skills with eventual loss of brain tissue (cortical atrophy) and learning disabilities (Burchett & Pizzo, 2003; Wolters & Brouwers, 2005).

Between 2006 and 2009 there was an estimated 21% increase in HIV incidence for people between the ages of 13 and 29 with the highest increase (48%) in African American young men who have sex with men (Centers for Disease Control and Prevention, 2011). Children living with HIV may have to deal with a myriad of emotional and physical issues including dealing with their medical illness, missing school and activities for appointments or hospitalizations, stigma when HIV status is known or disclosed, and blaming themselves for perinatally acquired HIV (Benton, 2011). Additional stressors may include poverty, an unstable home life,

family stress, parental mental illness or substance abuse, and limited social support (Donenberg & Pao, 2005; Gaughan et al., 2004). Fears associated with chronic disease and mortality, body image issues associated with delayed development, dermatologic issues, and lipodystrophy (a condition in which body fat is redistributed and can lead to changes in body shape) can also affect HIV-infected youth (Brown, Lourie, & Pao, 2000; DeLaMora, Aledort, & Stavola, 2006).

Psychiatric problems are often seen in this population (Chernoff et al., 2009; Mellins et al., 2009). Children with HIV/AIDS are at an increased risk of being psychiatrically hospitalized compared with children in the general population (Gaughan et al., 2004), although some studies suggest no difference in psychiatric or behavioral problems between HIV-infected youth and peers living in similar conditions (Gadow et al., 2010; Mellins et al., 2003). HIV-negative adolescents with psychiatric or substance use problems may be at a particularly high risk of seroconversion due to risky sexual behavior (Brown, Danovsky, Lourie, DiClemente, & Ponton, 1997; Lehrer, Shrier, Gortmaker, & Buka, 2006; Tubman, Gil, Wagner, & Artigues, 2003) including the use of drugs or alcohol (Donenberg & Pao, 2005).

Diagnosis of psychiatric disorders should be assessed taking into consideration medical status, antiretroviral drug adherence and/or resistance and recent stressors (Benton, 2010). Adherence to antiretroviral therapies (ART) presents a significant problem for adolescents with up to 24% nonadherence seen in 15–18-year olds (Williams et al., 2006). Decreased or nonadherence presents the risk of increased viral load (a marker of HIV disease progression), acquisition of viral drug resistance (which can limit drug treatment options), and an increased risk for central nervous system (CNS) disease (Benton, 2011; Van Dyke et al., 2002; Williams et al., 2006). A combination of nonadherence, high risk sexual behavior, mental health and substance abuse problems more often seen in patients with behaviorally acquired HIV may increase the risk of HIV transmission to sexual or drug partners as well as lead to poor medical and quality of life outcomes (Koenig et al., 2010; Mellins et al., 2011).

HIV-infected youth with depression or anxiety may have an increased risk of acquiring other sexually transmitted diseases or becoming pregnant due to increased high-risk sexual behaviors (Murphy, Durako, et al., 2001). High rates of depression, up to four times greater than that seen in the general adolescent population, have been noted in youth with HIV (Misdrahi et al., 2004; Pao et al., 2000; Scharko, 2006). Adolescent depression presents similarly to that in adults, and making a formal psychiatric diagnosis requires two weeks of depressive symptoms with impairment in functioning or significant distress (American Psychiatric Association, 2000). However, symptoms of the medical illness and side effects of HIV medications may be difficult to differentiate from biologically based depressive symptoms including loss of appetite or fatigue (Benton, 2011). Untreated depression can cause impairments in social functioning and increase the risk of suicide, and in HIV-infected individuals may contribute to negative effects on markers of HIV progression including CD4 counts and viral loads (DeLaMora et al., 2006). Anxiety disorders including phobias, separation anxiety,

agoraphobia, generalized anxiety disorder, panic disorder and obsessive compulsive disorder are not uncommon in HIV-infected children and adolescents (Mellins, Brackis-Cott, Dolezal, & Abrams, 2006). Providers working with HIV infected children and adolescents should routinely screen for depression and anxiety.

Pharmacotherapeutic treatment of depression and anxiety in children and adolescents is typically with specific serotonin reuptake inhibitors (SSRIs). All SSRIs carry an FDA (Food and Drug Administration) black box warning for risk of increased suicidality in children and adolescents; accordingly, adolescents started on SSRIs should be closely monitored. Tricyclic antidepressants drugs (TCAs), while FDA approved for the treatment of depression in adolescents, can be sedating and toxic in overdose and are rarely used in most clinical practice settings. In addition, the HIV drug ritonavir inhibits TCA's metabolism via interactions with liver enzymes, thereby increasing its potential for toxicity (De Maat et al., 2003). Depression has been associated with decreased adherence to ART (Murphy et al., 2005; Murphy, Wilson et al., 2001; Williams et al., 2006) and effectively treating depression may improve adherence and overall outcomes for HIV-infected youth. In treating any psychiatric disorder, the benefits must outweigh the risks from taking psychotropic medications.

Substance abuse is found in up to 59% of HIV-positive adolescents (Pao et al., 2000) and may contribute to high-risk sexual behaviors (Elkington, Bauermeister, Brackis-Cott, Dolezal, & Mellins, 2009). Considering that there is an association between lower levels of alcohol and drug use and improved adherence (Comulada, Swendeman, Rotheram-Borus, Mattes, & Weiss, 2003; Murphy et al., 2005), HIV-infected youth should be assessed for substance use disorders and treated as appropriate.

Other psychiatric disorders including bipolar disorder, attention deficit-hyperactivity disorder (ADHD), posttraumatic stress disorder (PTSD), conduct disorders and psychotic disorders are not as extensively studied in HIV-infected youth as in HIV-negative youth. Bipolar disorder in children has a presentation that is similar to that seen in adults with decreased need for sleep, grandiosity, racing thoughts and hypersexuality, but has not been examined in HIV-positive youth (Benton 2010; Geller et al., 2002). Treatment for bipolar disorder is generally with mood stabilizers. As with all psychiatric drugs, drug interactions, liver toxicity, and side effects should be monitored (Geller et al., 2002; Kowatch & DelBello, 2006).

Rates of ADHD, which is characterized by inattention, hyperactivity, and impulsivity, may be higher in HIV-infected children and adolescents than in their HIV-negative peers (American Psychiatric Association, 2000; Mellins et al., 2009; Scharko, 2006). Stimulant medications including amphetamine and methylphenidate are used in the treatment of ADHD in the same manner as used in non-HIV-infected children and have few drug interactions (Benton, 2010). Rates of conduct disorders, manifested by a persistent pattern of violating the basic rights of others or societal norms (American Psychiatric Association, 2000), have been found to be nearly 30% in HIV-positive adolescents (Pao et al., 2000), although this rate is similar to that found in HIV-negative individuals (Mellins et al., 2009).

Diagnosis of a life-threatening illness is considered a precipitating event for the diagnosis of PTSD in children, and youth with HIV may experience PTSD symptoms including avoidance, reexperiencing, and hyperarousal (American Psychiatric Association, 2000). It has been suggested that individuals with pediatric HIV who also exhibit symptoms of PTSD may have a greater risk of medication nonadherence than those without PTSD (Radcliffe et al., 2007). Appropriate screening and diagnosis should be done to ensure appropriate treatment for PTSD in this population. PTSD treatment includes adequate pain management, psychopharmacology, cognitive behavioral therapy and psychodynamic psychotherapy (Stuber & Shemesh, 2006). In addition, it is important to be aware that parents of children with life-threatening illness may also suffer from PTSD associated with their child's diagnosis and prognosis (Stuber & Shemesh, 2006) and appropriate support and treatment should be offered.

Up to 62% of parents of HIV-infected children have psychiatric disorders or hospitalizations, substance abuse issues or incarceration (thereby exposing the child to heritable factors, in utero risks, and stressful home environments) which increase the risk of children growing up in these homes having their own psychiatric and substance abuse problems (Pao et al., 2000). Simply living with a parent with HIV can lead to increased depressive symptoms, somatic complaints, distress, irritability and anger in adolescents (Rotheram-Borus, Weiss, Alber, & Lester, 2005). Separation from parents due to parental loss from death due to HIV or other causes is not uncommon (DeLaMora et al., 2006; Mellins et al., 2006).

The role of the family in HIV is important, complex and affects all members. Acceptance of a chronic and eventually fatal illness, caring for children while ill, adherence to complicated medical regimens, facing stigma, planning for death and care of children, living with chronically ill parents or children and dealing with comorbid mental health or substance abuse problems are just a few of the issues families must address (Benton, 2011).

Routine mental health screening should be incorporated into health care practices dealing with children and adolescents who are HIV-positive (Mellins et al., 2011) and coordinated care with psychiatric caregivers should be undertaken (Spiegel & Futterman, 2009). In addition, clinicians should be aware that children exposed to HIV in utero have been found to have higher rates of anxiety and depression than their nonexposed peers, but may not have their mental health care needs adequately addressed since they are not necessarily seen in the HIV care system (Esposito et al., 1999; Mellins et al., 2009). Support groups may improve quality of life for children and families (Spiegel & Futterman, 2009) and interventions that are family-focused and coping-skills oriented may benefit adolescents, especially with regard to decreasing substance use (Rotheram-Borus, Stein, & Lester, 2006). In addition, disclosure of information regarding HIV status and treatment should be undertaken at an appropriate level based on the child's age and be a combined effort of the medical caregiver, the parents and the family (Burchett & Pizzo, 2003). Adherence with both psychiatric and HIV treatments may be increased by case management services, education, reminder systems, directly observed therapy, simplifying regimes, parental support and incentives for adherence (Simoni et al., 2007).

Conclusion

Many individuals with HIV/AIDS experience comorbid mental conditions that need to be considered in the context of HIV or other medical status and treatments, individual preferences and needs, as well as the individual's social and cultural context. Mental disorder nearly always complicates illness management. However, there is strong evidence that appropriate and assessment of comorbid mental conditions can optimize overall health outcomes. While there has been some growth in the extant literature on the topic of how best to assess and treat comorbid mental illness in people with HIV/AIDS, more attention and research is clearly needed to better inform future interventions for this most vulnerable group of individuals.

Related Topics: Adherence, antiretroviral therapy, caregiving and caregivers, case management, children, cognitive impairment, coping, cytomegalovirus, harm reduction, HIV-related dementia, protease inhibitors, social support, stigma and stigmatization, suicide and suicidal ideation.

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