Psychiatric Aspects of HIV Spectrum Disease

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Abstract: The HIV/AIDS epidemic is not considered "under control" in the United States. An unacceptably high incident case rate has been sustained over the past decade. CDC now advocates for routine HIV antibody testing to be offered in all health care settings. The psychiatrist can play an important role in identifying HIV high risk behaviors, in presenting the option for HIV antibody testing, and in providing follow-up with counseling. The high risk for HIV infection among the severely mentally ill also directly involves the psychiatrist today in HIV/AIDS care. Anxiety, depressive spectrum, neurocognitive, and psychotic disorders present with symptom profiles and in settings that are specific to HIV infection and require the need for individually tailored psychiatric care. Guidelines for the psychiatrist treating HIV infected patients are available. It is incumbent upon the practicing psychiatrist to maintain familiarity with these guidelines and offer the capacity to treat the psychiatric disorders that occur in this patient population.

The number of persons with HIV-1 infection in the United States has continued to rise, consistently increasing at an estimated 56,000 per year for the past decade. Thus, the HIV/AIDS epidemic cannot be considered "under control" at this time. Since the introduction of highly active antiretroviral therapy (HAART) combination regimens in late 1995, great gains have been made in decreasing the morbidity and mortality of the disease. Nevertheless, replication of HIV-1 is known to continue at a very low level despite "nondetectable" levels of HIV-1 RNA in the peripheral blood (1). It has also been shown that HIV-1 replicates at a relatively higher level in the CSF than in the plasma in patients with a diagnosis of HIV-associated dementia (HAD) as opposed to those with no neurological disease (2). These results are supported by other studies showing that independent HIV-1 replication in the CNS predominates in advanced disease and is contributed to by CNS-derived virus. Hence, the CNS has been designated as a "reservoir" maintained by HIV-1 in the face of currently effective systemic treatment. As a result, increasing concern has been directed to the neuropsychiatric outcomes of HIV-1 infection: HIV-1-associated asymptomatic neurocognitive impairment, mild neurocognitive disorder (MND) [formerly minor cognitive-motor disorder (MCMD) (3)], and HAD [formerly AIDS dementia complex (ADC)] (4). After a brief background on HIV/AIDS, this article will focus on the information psychiatrists need to know today for 1) the evaluation of risk for HIV-1 infection, 2) HIV-1 antibody testing and related counseling, 3) the secondary prevention of HIV-1 disease progression, and 4) the diagnosis and treatment of neuropsychiatric disorders in HIV-1 infected persons. (Hereafter, I will refer to "HIV-1" as "HIV" for general usage, as the prevalence of HIV-2 is very low in the United States.)

Brief background on HIV/AIDS

The Centers for Disease Control and Prevention (CDC) began tracking cases of AIDS in 1981. Human T cell lymphotropic virus type III (HTLV-III, later to be called "HIV") was isolated in 1983 (5). The dementia associated with HIV infection was first characterized as caused by HIV itself in 1986 (6, 7). In the revised CDC case definition of AIDS of 1987, "HIV encephalopathy" was included as an AIDS-defining event (8). The CDC staging system and the AIDS case definition were both revised in 1993 (9). The CDC staging system was revised to be defined by three clinical stages (A = asymptomatic, B = early symptomatic, and C = late symptomatic/AIDS). In addition, immunological dis-

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ease staging was added to this staging system and defined by the number of $CD4^+$ T "helper" lymphocytes, which are directly invaded and killed by HIV: 1) CD4 cell count $\geq$500 cells/mm^3, 2) CD4 cell count of 200–499 cells/mm^3), and 3) CD4 cell count of <200 cells/mm^3. In the 1993 revision of the CDC AIDS case definition, the major change was that any patient with a CD4 cell count <200 cells/mm^3 would be defined as having AIDS, regardless of whether any symptoms referable to HIV infection had been experienced. In addition, the AIDS case definition was expanded to include invasive cervical cancer (as part of recognizing gender-specific complications), pulmonary tuberculosis, and recurrent bacterial pneumonia as AIDS-defining conditions.

Regarding treatment, before 1987, there was no medical treatment specifically for HIV infection itself. That year, azidothymidine (AZT) [now referred to as "zidovudine" (ZDV)] was approved by the Food and Drug Administration (FDA). ZDV acts by the inhibition of the reverse transcriptase enzyme of HIV. In late 1995, the FDA approved saquinavir, the first of the class of drugs known as the protease inhibitors. The additional clinical impact of the introduction of this class of antiretroviral medications was recognized by the use of the term "HAART." Next was the development of a class of drugs acting at a different site of the reverse transcriptase enzyme (the non-nucleoside reverse transcriptase inhibitors). This class includes efavirenz, a drug with a greater than 50% rate of CNS side effects, although these side effects seem to be mild-to-moderate, relatively short-lived (up to 200 days) to resolve spontaneously, and to not generally require switching of the antiretroviral regimen (10, 11). Subsequently, the fusion/entry inhibitors (with enfuvirtide and then maraviroc) and an integrase inhibitor (raltegravir) were introduced.

Screening for HIV risk behaviors

The current high-risk behaviors of major concern for contracting HIV infection are unprotected sexual intercourse and injection substance use. Unprotected sexual intercourse by the rectal route is particularly high-risk, because the friability of the rectal mucosa is greater than that of the vaginal mucosa. As a result, HIV is more likely to be introduced into the blood. Hence, men who have sex with men (MSMs) may be at particularly high risk; heterosexuals regularly practicing unprotected rectal intercourse are also at higher risk than the general population. It should be noted that high-risk sexual behavior characterizes the risk level of an individual patient, not membership in a "high-risk category."

Injecting psychoactive substances with shared needles or unsterilized paraphernalia places a patient at high risk also because of the direct introduction of HIV into the peripheral blood, although, interestingly, black tar heroin has recently been demonstrated to be associated with a lower risk than white powder heroin (12). As discussed above for MSMs and heterosexuals who engage in high-risk sexual behavior, injecting drug users are also at high risk when they continue to inject psychoactive substances directly into their blood and when they use unsterilized equipment, rather than by their membership in the category of "injecting drug users." Of note, behavioral modifications to reduce the high-risk behavior for unprotected sexual intercourse and for injecting psychoactive substance users have been proven to be efficacious. The psychiatrist interviewing a new patient should routinely screen for HIV risk factors when taking a sexual and substance use history. It should be noted that this need is not reduced by the assumption of a lack of multiple sexual partners, by marriage, or by the patient's own presumption that he or she is not at risk for HIV infection. In addition, HIV screening should be conducted through the life span of sexual activity to include patients older than 50 years of age. Recently, the incidence of HIV infection in this group has been noted to be significantly increasing. In addition, the prevalence of HIV infection at an older age has risen because of the long-term salutary effects of HAART. Alcohol and non-injection substance use also exposes a patient to high risk for HIV infection owing to decreased decision-making capacity as a result of increased frontal lobe disinhibition at the time of sexual activity. The HIV-seronegative patient exposes himself or herself to HIV and other infections and their associated illnesses, whereas the HIV-seropositive patient exposes himself or herself to reinoculation with HIV itself and an increased HIV load as well as to other infections. It should be recalled that follow-up counseling with HIV-seropositive and HIV-seronegative individuals about high-risk activity is, therefore, part of comprehensive clinical care for the patient as well as a public health mandate.

In the HAART era, young, minority MSMs in particular are at high risk. In addition, those who have recently been incarcerated have been targeted as a high-risk group of special concern. Women of color who are disempowered due to histories of physical and/or sexual abuse and low socioeconomic status are, likewise, at high risk. Further, and perhaps most concerning, is the fact that there is a growing complacency regarding becoming HIV-

infected in the general population due to an overestimation of the effects of HAART. To be successful, intervention strategies must target behavioral change, not solely attitude change and knowledge acquisition. The ongoing stigma of HIV infection, AIDS phobia, and homophobia all operate against HIV risk recognition and testing. Although older persons have now been recognized to be at increased risk for HIV infection related to increased sexual activity with use of the cGMP-dependent phosphodiesterase inhibitors (e.g., sildenafil, vardenafil, and tadalafil), there is a lack of specific prevention messages for this population. Finally, people with severe mental illness are also at increased risk for HIV infection (from 4.0% to 22.9%) (13), bringing the message directly into the purview of the practicing psychiatrist today.

HIV ANTIBODY TESTING AND RELATED COUNSELING

To ensure a provider-patient relationship conducive to optimal clinical and preventive care, the CDC now recommends that diagnostic HIV testing should be a part of routine clinical care in all health care settings, similar to screening for other treatable medical conditions, and also that the patient's option to decline HIV testing be preserved (14). In populations with a prevalence of undiagnosed HIV infection of ≥0.1%, HIV screening is as cost-effective as the screening programs for other chronic diseases. HIV antibody testing is specifically indicated for a patient confirmed to be at high risk who is willing to undergo the procedure after it has been completely explained. The rationale should be presented as a direct referent to the HIV risk factor under which the patient qualifies as "high." Once high risk is established, the test itself should be fully explained to the patient, and consent should be sought (note that there are rare exceptions to the need for informed consent, defined by state law). Currently, there are a wide variety of tests available, including tests of blood (used with the first FDA-approved HIV antibody test in 1985) as well as of urine and saliva. The rapid test now provides results within 24 hours. It should be pointed out that HIV antibody tests in the United States now identify not only HIV type 1, which is endemic in the Unites States, but also HIV type 2, which is not. Since 1992, all U.S. blood donations have been tested with a combination HIV-1/HIV-2 test sensitive to antibodies to both viruses.

For testing done in a clinical setting, the next step in HIV antibody test counseling is transmission of the test results. Provision of formal feedback to an HIV-seropositive person to prevent new HIV infections (i.e., secondary prevention) is of clear-cut efficacy. However, this benefit is less clear for such feedback when provided to an HIV-seronegative person (i.e., primary prevention) immediately after the seronegative test results.

From the psychiatric point of view, it is expected that the distress due to an HIV-seropositive result would resolve over approximately 6 weeks. If not, a mental health referral should be considered; otherwise, a psychiatric disorder may ensue. The most common form of disorder is an adjustment reaction with various types of mood disturbance (particularly anxious mood), reactions with disturbances of conduct, and reactions with mixed disturbances. Only a minority of 20% will have chronic anxiety in the asymptomatic stage (when the aim is to define serostatus) (15). This subgroup changes over time in longitudinal studies, suggesting that a smaller percentage may develop an anxiety disorder. Other disorders seen in this situation include major depressive disorder and recidivism of alcohol and substance use disorders. Treatment is guided by DSM-IV-TR diagnosis and by APA HIV/AIDS treatment guidelines (16, 17); most commonly, patients with adjustment disorder will respond to supportive therapy without psychopharmacotherapy.

SECONDARY PREVENTION OF HIV DISEASE PROGRESSION

Secondary prevention of the progression of HIV infection refers to the prevention of HIV-associated immunosuppression as well as clinical disease progression, e.g., to AIDS-defining conditions such as HAD, cryptococcal meningitis, CNS toxoplasmosis, primary CNS lymphoma, invasive cervical cancer, Kaposi's sarcoma, *Pneumocystis carinii* pneumonia, tuberculosis, and *Mycobacterium avium* complex infection, among others. A major approach to the prevention of HIV disease progression is the optimization of adherence to antiretroviral regimens, which require 95% adherence to achieve and maintain nondetectable levels of HIV load in plasma (i.e., <50 HIV-1 RNA copies/ml). In addition, a number of life style factors are relevant to the secondary prevention of disease progression. These include maintaining a normal total lean body weight, optimizing nutritional status, limiting alcohol and substance use (including caffeine intake), discontinuation of cigarette smoking, maximizing sleep quality, and maintaining a regular exercise (preferable aerobic) regimen (18). For example, related to weight control, dronabinol, which is closely related to tetrahydrocannabinol (THC), may be used to maintain body weight but should be used with caution, as THC is associated

with decrements in several immune functions and may also cause mental confusion. As another example, the prevalence of cigarette smoking is estimated to be 50%–70% among HIV-seropositive persons, compared with 20.8% overall in the general population. In the HAART era, smoking cessation has become a more important target than ever before, given its better recognized association with decrements in immune measures (CD4 cell count and mucosal immunoglobulin levels); an increased incidence of AIDS-defining conditions; the associated occurrence of pneumonia, myocardial infarction, and malignancy; and the increased mortality risk, compared with that in HIV-seropositive nonsmokers. Of note, varenicline, an $\alpha_4\beta_2$ nicotinic acetylcholine receptor partial agonist, may have advantages over bupropion SR for smoking cessation in HIV infection.

DIAGNOSIS AND TREATMENT OF PSYCHIATRIC DISORDERS IN HIV-INFECTED INDIVIDUALS

HIV INFECTION AND ANXIETY DISORDERS

As noted above, adjustment disorder is frequently seen after serostatus notification and is the most common psychiatric disorder manifesting with anxiety. Nevertheless, the HIV-seropositive patient referred for anxiety warrants careful diagnostic evaluation. General medical causes of anxiety have been noted, such as early symptoms of pneumonia presenting with anxiety and agitation related to hypoxemia. For those patients with anxiety of longer than 6 months duration and unrealistic worries, generalized anxiety disorder is diagnosed and has been noted in 15.8% of HIV-seropositive persons versus 2.1% of the general population (19). Panic disorder, known to be associated with viral infections, cocaine use disorder, and major depressive disorder, has been noted in 10.5% of HIV-seropositive persons versus 2.5% of the general population and has been associated with an elevated pain level in HIV-infected persons (20). Posttraumatic stress disorder has likewise been reported at an elevated rate among HIV-infected persons (21), which may, at least in part, be related to a history or trauma as well as physical and sexual abuse. Such a history could, in turn, lead to a decreased sense of empowerment and a decreased likelihood of negotiating HIV precautions in high-risk situations. Psychopharmacotherapy for these conditions should be avoided, if at all possible. Nevertheless, at least initially, it may be useful to use psychopharmacotherapy to support the patient's sense of control and autonomy. The most common anxiolytic therapies used, the benzodiazepines, are sedating, interact with alcohol, foster dependence, and are associated with drug interactions on the cytochrome P450 (CYP) 3A4 isoenzyme system particularly, which is strongly inhibited by the protease inhibitors. As noted, the anxiety disorders may respond to supportive therapy, cognitive behavior therapy, progressive muscular relaxation training, self-hypnosis, cognitive imagery, and biofeedback without anxiolytic therapy. When pharmacologic treatment is deemed necessary, selective serotonin reuptake inhibitors (SSRIs) (along with venlafaxine, which has a low potential for drug interactions), are generally preferred to the benzodiazepines. However, short- to intermediate-acting benzodiazepines with no active metabolites, such as lorazepam and oxazepam, are also frequently chosen. Buspirone, which is nonsedating, safe in overdose, and has no abuse potential is an option to consider, but its delay of onset is significant. Randomized controlled trial evidence in the general population has been reported to support the use of pregabalin, specifically for generalized anxiety disorder (22). Pregabalin has the advantages of not being protein bound and not being associated with drug interactions on the CYP isoenzyme system.

HIV INFECTION AND DEPRESSIVE SPECTRUM DISORDERS

Disorders associated with depressed mood have been estimated to occur in a majority of HIV-infected patients over the course of their infection. When an HIV-infected patient is confronted by the first symptoms referable to HIV, which are frequently not AIDS-defining symptoms, the patient's shell of optimism that she or he will never have a symptom is cracked. The resulting future uncertainty spawns an increased frequency of depressive spectrum disorders, including adjustment disorder, major depressive disorder, and dysthymic disorder. Recently, a prospective study confirmed a relationship between the history of symptomatic HIV infection and subsequent major depressive disorder in HIV-infected patients (23). Physical and psychological symptoms are also associated with an elevated level of suicidal ideation, which remains a concern in the HAART era (24). Further, elevated physical symptom burden is associated with psychoactive substance use and an elevated pain level (25). Thus, the patient must learn a way to adjust to the increased level of uncertainty that is associated with an elevated physical symptom burden. Of note, persons with the triple diagnosis of a

psychiatric disorder, a substance use disorder, and HIV/AIDS are particularly disposed to major depressive disorder, with 72.9% of this group qualifying for this diagnosis in one recent study (26). In the differential diagnosis of depressive disorders in HIV infection, one must include disorders due to HIV infection itself (including HIV wasting syndrome and early HAD) as well as toxicities of medications prescribed to control HIV infection or its associated conditions (e.g., interferon-α for concomitant hepatitis C virus infection). Concomitant medications may also show salutary effects for depressive spectrum disorders, such as testosterone treatment in the setting of testosterone deficiency (which also treats fatigue). Likewise, ketoconazole, an antiglucocorticoid drug used for control of candidiasis, has been associated with decreases in major depressive disorder (27), as has dehydroepiandrosterone, another glucocorticoid antagonist, specifically in subsyndromal major depressive disorder in HIV-infected persons (28). Early HAD, presenting with apathy, lethargy, and social withdrawal, may be confused with major depressive disorder. However, the cognitive symptoms of helplessness, hopelessness, and low self-worth are generally absent, as are the primary affective symptoms. Regarding the impact on HIV disease itself, major depressive disorder may be treated with the same medications that would be indicated outside of HIV infection. However, important considerations are side effect profiles, the potential for drug interactions, and the neuroinflammatory impact of major depressive disorder itself. Regarding side effect profiles, in the patient manifesting with psychomotor retardation, activating antidepressants without effects on the CYP isoenzyme system in the liver, such as venlafaxine, may be preferred. Of the SSRIs, paroxetine has been favored as well as citalopram. Fluoxetine should be avoided because of its long half-life and its metabolism by both CYP 2D6 and 3A4 isoenzymes, which are also used by the protease inhibitors and the non-nucleoside reverse transcriptase inhibitors, potentially leading to drug interactions. Bupropion should be avoided because of its seizure diathesis combined with the potential that HIV-infected patients may manifest this diathesis at a low dose, given that HAD, for example, is associated with an increased frequency of seizures. The psychostimulants may be useful as a second-line option for the treatment of depressive disorders, particularly if there is concomitant neurocognitive impairment. In addition, testosterone deficiency should be assessed and treated in the setting of depressive disorders among HIV-infected persons. Finally, the relief of major depressive disorder itself may be expected to be associated with a reduction in proinflammatory cytokines in the brain (e.g., tumor necrosis factor-α, interleukin-1, and interleukin-6) (29). This neuroinflammatory impact of major depressive disorder could contribute to HIV-associated neurocognitive disorder pathogenesis, which may be alleviated by the successful treatment of major depressive disorder.

HIV-ASSOCIATED NEUROCOGNITIVE DISORDERS (HAND)

Unlike anxiety disorders (frequently seen in the asymptomatic stage and just after diagnosis of HIV seroconversion) and depressive spectrum disorders (frequently seen with the appearance of the first symptoms related to HIV infection and in early symptomatic HIV disease), the neurocognitive disorders are most commonly seen in the late symptomatic stage of HIV disease, i.e., "full-blown" AIDS. The recently promulgated Frascati Conference revision of the American Academy of Neurology (3) criteria recognizes two clinical neurocognitive disorders: MND and HAD (4). For a diagnosis of MND, there must be mild neurocognitive impairment in at least two domains of cognitive performance and, at most, a minor functional impairment in daily living, insufficient severity for a diagnosis of HAD, and no other known etiology for the symptoms. For a diagnosis of HAD, there must be severe cognitive impairment in two or more domains, at least a moderate level of functional status impairment due to the cognitive symptoms, a lack of clouding of consciousness (i.e., delirium), and no support for another etiology accounting for these symptoms. It should be noted that it is preferred that deficits in neurocognitive domains are established by formal neuropsychological testing. However, under many circumstances in clinical practice, it may not be feasible to obtain formal neuropsychological testing; thus, broad, screening tests, although less definitive, may be used to establish neurocognitive deficits in such patients, as noted in the Frascati Conference criteria. HAD is an AIDS-defining diagnosis and may be the first symptom of AIDS in 10%–25% of patients. Both MND and HAD have been reported to have declined in incidence by as much as 50% since the introduction of HAART. This decline results in an estimate of 7%–10% of patients with AIDS who will have HAD and 12%–15% of early symptomatic patients as well as 25% of late symptomatic patients who will have MND. The Frascati Conference also coined the condition "asymptomatic neurocognitive impairment" (ANI) (or subclinical neurocognitive impairment) (4). This condition occurs when there is significant cognitive decline in two or

more domains of neuropsychological performance but no significant decline in functional status. It is important to note that ANI is a "condition," not a "disorder." It is estimated that ANI, as opposed to MND and HAD, has not significantly declined in prevalence in the HAART era. In fact, ANI may constitute the substrate for an eventual recrudescence of HAND in the future, should resistance to antiretroviral medications become widespread.

The Mini-Mental State Examination is used widely as a screening test for dementia. It has been used in the specific context of HIV-associated neurocognitive impairment and is cited as an alternative to formal neuropsychological testing by the Frascati Conference criteria (4). Nevertheless, it is suboptimal as a broad screening test for HAD, in contrast to the HIV Dementia Scale (HDS) (30). The HDS was specifically developed to screen for subcortical dementia caused by HIV. In addition, the International HIV Dementia Scale (IHDS) (31) may be justified and used when necessary as a more culture-fair screening device than the HDS. When such broad neurocognitive screening tests are themselves not feasible to administer, score, and interpret, it is worth noting that large groups of patients may be simultaneously screened with a self-report measure known as the Medical Outcomes Study-HIV cognitive functioning subscale. This four-item subscale has been shown to have a significant relationship to performance on formal neuropsychological tests (32).

The diagnosis of a neurocognitive disorder due to HIV presumes that results of a workup for other disorders are negative. Such a workup should include computed tomography or magnetic resonance imaging of the head to rule out CNS toxoplasmosis and primary CNS lymphoma, among other illnesses. A lumbar puncture should be done to rule out cryptococcal meningitis as well as neurosyphilis and polymerase chain reaction testing should be used to rule out other diseases (such as cytomegalovirus encephalopathy and progressive multifocal leukoencephalopathy caused by JC virus). The workup should also include screening for metabolic causes (such as hepatic and renal encephalopathy) and for psychoneurotoxicity of prescribed medications (such as the antiretroviral efavirenz and interferon-α for hepatitis C virus coinfection) as well as psychoactive substance use (e.g., cocaine and methamphetamine). Symptoms of systemic HIV disease progression that might be associated with neurocognitive impairment, such as fatigue and wasting, should also be ruled out. Finally, primary psychiatric disorders manifesting with symptoms related to neurocognitive dysfunction, such as major depressive disorder, must also be considered in the differential diagnosis. Only after this extensive workup has been conducted and results documented to be negative can a diagnosis of HAND be justified. Regarding treatment, HAD has been better studied than either MND or ANI. The CSF-penetrating antiretroviral medications have received the greatest attention; yet to date results to support specific agents are limited to the use of zidovudine and, to a lesser extent, abacavir, nevirapine, and indinavir. The recently approved agents acting by novel mechanisms, maraviroc and raltegravir, are of current interest. Anti-inflammatory agents active in the CNS (e.g., *N*-acetylcysteine) have been investigated to a limited extent without clear-cut benefits. Neurotransmitter manipulation is also of treatment relevance. Although results with *N*-methyl-D-aspartate receptor antagonists (e.g., memantine), decreasing glutamatergic activity, have been disappointing to date, agents increasing dopaminergic transmission, including the psychostimulants (33) (which also treat concomitant fatigue) and dopaminergic agonists (34) have garnered some support over time. The combination of a short-acting form of methylphenidate with a long-acting form may be particularly useful. The short-acting form may be used to establish the effective total daily dose, followed by a switch to the long-acting agent on a milligram-per-milligram basis, which, in turn, is followed by supplementation with the short-acting agent as needed. However, it must be cautioned that empirical data supporting this specific dosing strategy are lacking, and this treatment is palliative rather than pathophysiologically based.

PSYCHOSIS AND HIV INFECTION

Psychosis associated with HIV infection has been less frequently studied than the foregoing psychiatric disorders. There are many causes for psychotic symptoms in an HIV-seropositive patient. These include delirium, late-stage HIV-associated dementia, mania (which may be due to HIV infection itself), recurrence of premorbid psychotic illnesses (particularly in the severely mentally ill), psychoactive substance intoxication, antiretroviral medication toxicities (e.g., efavirenz, particularly in patients with the CYP2B6-G516T polymorphism) (35), and general medical conditions manifesting with psychotic symptoms (e.g., cryptococcal meningitis and neurosyphilis). Although less is known in this area, it is recognized that antipsychotic medications are effective in treating psychotic symptoms in this setting. With the established long-term efficacy of HAART and the general

association of psychotic symptoms with late-stage HIV disease manifestations (such as delirium and dementia), the overall prevalence of psychotic disorders among HIV-seropositive patients is expected to increase. Of note, with regard to the treatment of psychosis in this setting, there are special concerns associated with the choice of antipsychotic medications in HIV-infected persons (36, 37). Specifically, the high-potency typical drugs are associated with high rates of extrapyramidal reactions, to which HIV-infected patients are highly sensitive. Similarly, the low-potency typical drugs are associated with anticholinergic side effects, another area of high sensitivity in HIV-infected patients. Thus, the atypical drugs are generally considered to be preferred; however, these drugs present a distinct toxicity problem, that of metabolic syndrome, to the HIV-infected patient. The toxicity of metabolic syndrome is of special concern to an HIV-infected patient because this syndrome is also a toxicity of the antiretroviral medications themselves and has been associated with an increased risk for the occurrence of myocardial infarction and cerebrovascular accident (as well as HIV-associated neurocognitive impairment). Thus, the atypical antipsychotic agents less likely to be associated with the metabolic syndrome, ziprasidone and aripiprazole, might be considered the first-line choices, although data do not yet exist to support these specific choices and low-dose treatment with the typical antipsychotics, e.g., haloperidol, is also effective and may be well tolerated.

Summary

Complacency regarding the spread of the HIV pandemic is not justifiable, either worldwide or in the United States. Psychiatric disorders are relevant throughout the stages of HIV disease progression. Psychiatrists need to be aware of HIV risk factors and screen regularly for them in their patients. HIV antibody testing is now being promoted by the CDC as routine testing in clinical medical settings, including psychiatric settings. Psychiatrists can play an important role in reducing HIV transmission and in secondary prevention of HIV disease progression as well.

Anxiety disorders may occur in several forms, tend to occur soon after seroconversion, and may frequently be treated effectively without the use of pharmacotherapy. Depressive disorders tend to occur after the first symptoms of HIV infection or in association with a high overall symptom burden. These disorders may be effectively and safely treated with standard antidepressant therapy. Neurocognitive disorders show a predilection for late-stage HIV disease, require a thorough medical workup, and may be treated with a variety of agents (or combinations) including the psychostimulants, CSF-penetrating antiretroviral medications, and CNS anti-inflammatory medications. Psychosis in HIV infection has been studied least among the psychiatric disorders; it may exist premorbidly and occur as a result of HIV infection of the brain or its complications. The choice of antipsychotic medication, which must be tailored to the needs of the specific patient, generally is difficult in HIV-infected patients.

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