Pain is recognized as a significant disability in HIV-infected persons. Pain related to HIV/AIDS is a considerable clinical challenge that is associated with increased psychological distress, negative impact on health-related quality of life (HRQOL), and greater impairment of functional ability. This article, the continuation of a previously published review, looks at the current literature on psychiatric issues of HIV/AIDS-related pain with a focus on comorbid psychiatric disorders and psychotherapeutic interventions.

The first section below discusses the assessment and treatment of mood and anxiety disorders in patients with HIV/AIDS-related pain. This is followed by a review of issues relating to substance use disorders, with a focus on the problem of opioid use. The third section highlights patient, provider, and system barriers to effective treatment. The final sections discuss principles of pain management and psychotherapeutic interventions in the setting of comprehensive HIV/AIDS-related pain management.

MOOD AND ANXIETY DISORDERS
Recognizing and treating comorbid psychiatric disorders is of vital importance in HIV/AIDS care. This may be especially true for patients with chronic pain, given the association of psychiatric disorders with poor adherence to treatment, decline in psychosocial functioning, faster progression of disease, and higher mortality. The lifetime prevalence of major depressive disorder in the HIV population ranges from 5% to 45%. A brief review of the assessment and management of depression and anxiety disorders is presented below. A more thorough discussion can be found in recent reviews by Basu and colleagues and Colibazzi and colleagues.

Depression
The overlap in the symptoms of HIV/AIDS, chronic pain, and depression (ie, somatic symptoms, sleep difficulties, decreased libido, and fatigue) greatly complicates the detection of depression. Routinely incorporating screening tools for depression into patient assessments can facilitate the diagnosis. One screening tool that has been used specifically for persons with HIV/AIDS living with chronic pain is the Beck Depression Inventory-Fast Screen (BDI-FS). The BDI-FS has been modified for use in primary care settings, where patients frequently have somatic symptoms that confound the diagnosis of depression. This tool evaluates 7 depressive symptoms for the "past 2 weeks, including today" on a 4-point scale. In this comorbid population in whom the rates of depression are expected to be high, Krefetz and associates found that the BDI-FS has a specificity of 90% and a sensitivity of 74% with a cutoff score of 4. A score on the BDI-FS greater than 4 may indicate depression and should prompt a more detailed clinical interview.

Patients whose symptoms have not improved after 2 trials of different antidepressants or those in need of more intensive treatment should be referred to a psychiatrist. Psychotherapy should be
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considered as an adjunctive or alternative treatment of depression for persons with HIV/AIDS. Referral to a psychotherapist may be warranted, especially for those who refuse to be treated with antidepressant medications.5 A growing body of evidence supports exercise as an alternative therapy to enhance the quality of life for HIV-infected patients and to diminish depressive symptoms; however, further research is needed to determine the impact and generalizability of these findings (as reviewed by Nixon and colleagues10). The effectiveness of exercise in the HIV/AIDS population with chronic pain is unknown at this time.

Few studies have investigated the relationships among HIV/AIDS-related pain, psychiatric illness, and suicide. Studies have failed to show a direct correlation between suicidal ideation and the presence or severity of pain; however, suicidal ideation may be influenced by other factors,11,12 and more research is needed to elucidate the nature of suicide risk in this population. Including a suicide risk assessment as part of a complete psychosocial evaluation is valuable. The assessment should include personal and family psychiatric history, previous suicidal ideation and attempts, family/friend suicide history, social support, plans for the future, and specific suicidal thoughts and plans.

**Anxiety Disorders**

Anxiety disorders, such as generalized anxiety disorder, posttraumatic stress disorder (PTSD), and panic disorder, are also prevalent in HIV-positive persons, with rates of more than 20% reported.13 It is widely recognized that emotionality can influence the subjective experience of pain, which raises the question of how the presence of pathological anxiety might affect the illness burden of a person with chronic pain.

**Posttraumatic stress disorder.** Two recent studies have examined the influence of PTSD and panic disorder in persons with HIV/AIDS and chronic pain. Smith and colleagues14 found that PTSD predicted increased pain intensity and functional interference in mood and daily activities, consistent with the correlation found in other trauma victims (eg, burn survivors, motor vehicle accident survivors, combat veterans). It has been argued that persons living with HIV/AIDS encounter a number of traumatic stressors that can precipitate PTSD, such as receiving the diagnosis of HIV infection, abrupt drops in their CD4 count, and the loss of family and friends to AIDS and AIDS-related complications.14 In addition, a considerable portion of the HIV-positive population has a history of trauma secondary to childhood abuse, rape, homelessness, and substance abuse.

**Panic disorder.** Tsao and coworkers15 investigated the interaction between panic disorder and pain in HIV-infected patients. In a nationally representative sample from the HIV Cost and Services Utilization Study, these investigators found that panic disorder was a stronger predictor of pain than depression or PTSD. The hallmark of panic disorder is the tendency to interpret harmless physical symptoms of anxiety as catastrophic events (eg, "impending doom"). Tsao and associates15 hypothesized that the panic disorder–pain interaction is related to the tendency of persons with panic disorder to "catastrophize" physical symptoms and bodily sensations, which could intensify pain as well as increase panic and anxiety. Other studies have confirmed that catastrophizing is linked with HIV infection and chronic pain. In a study of coping strategies of HIV-infected patients with peripheral neuropathy, catastrophization was the only strategy that predicted distress and impaired function.16 Clinicians should screen for and be attentive to anxiety symptoms, which may play a key role in how pain is experienced for many HIV-infected patients.

Appropriate treatment interventions need to be identified and implemented in a timely fashion. The SSRIs and the serotonin norepinephrine reuptake inhibitors (SNRIs) are currently the first-line treatments for panic disorder; benzodiazepines help control panic symptoms over the first 2 to 4 weeks until the SSRI or SNRI becomes therapeutic.

Initiating discussions with patients regarding their coping strategies and thoughts about pain can help you determine which of your patients may benefit from psychotherapy, such as cognitive therapy, that targets negative cognitions as part of a comprehensive pain treatment program.

**SUBSTANCE USE DISORDERS**

Transmission of HIV infection via injection drug use accounts for more than a third of HIV cases in the United States, with higher rates seen for adolescents and women.17 HIV-positive persons who are active users of illicit substances experience increased pain and a greater illness burden,15,18 and current drug use has a stronger association with pain compared with past use.19 In addition, physical pain is independently associated with poorer adherence to antiretroviral therapy by HIV-infected current and former drug users in substance abuse treatment.20 Screening tools for quick, reliable detection of alcohol and drug abuse/dependence have been well established. These include the CAGE questionnaire and the Michigan Alcohol Screening Test.21,22
Clinicians should not let their fear of addicting their patients to pain medications hinder effective pain management. Iatrogenic addiction to opiates in patients without a history of substance use is exceedingly rare, reportedly less than 1%. However, fear of opiate addiction by both patients and physicians remains a substantial barrier to effective pain management. This factor creates unique dilemmas that affect a clinician's treatment of HIV-positive patients with pain and a patient's own perceptions and management of his or her chronic illness.

Patients with chronic pain and a history of substance use are likely to be more difficult to manage and should be monitored for aberrant drug-taking behaviors. However, additional monitoring need not interfere with providing adequate pain relief. The patient with chronic pain and a substance use history deserves to have pain relief just as much as those without previous substance abuse. The occurrence of aberrant drug-taking behaviors (eg, "ER-hopping" or "doctor-shopping," buying opioids without a prescription, stealing opioids, increasing the dosage without physician recommendation) should generate a differential diagnosis that includes true addiction, pseudoaddiction, psychiatric disorder, criminal intent, and family dysfunction (eg, family members using the patient's medications).

Pseudoaddiction is the phenomenon by which patients with uncontrolled pain will undertake seemingly "addictive" behaviors (eg, aggressive complaining about pain, drug hoarding, "clock watching") in an effort to achieve better pain control. These behaviors are often mistaken for true addiction in clinical practice. Clinicians must continually assess drug-related behaviors and make conclusions based on a person's clinical presentation, history, and pattern of drug-seeking behaviors over time. In the case of pseudoaddiction, such behavior will cease when adequate pain control is achieved. Treatment of pseudoaddiction may involve an increase in drug dosage, a change in frequency, or a change of medication.

Most chronic pain research has involved cancer patients, but this research may be limited in its applicability to persons with HIV/AIDS. One reason is that the HIV-infected population is a remarkably disparate population regarding demographics, disease progression, treatment, and stigma. In addition, in contrast to the HIV-infected population as a whole, substance abuse disorders are considerably less prevalent in persons with cancer. A pilot study compared the attitudes and behaviors of persons with HIV/AIDS regarding pain treatment, substance use, and addiction with the attitudes and behaviors of those with cancer. A potential physician barrier to an assessment of addictive behaviors is the commonly held belief that patients will find a discussion on addiction offensive or intrusive. However, the study's results showed that few patients from either study group found the questions on addictive behavior offensive or intrusive and that many patients from both groups believed that addiction was common among their peers. These findings highlight the importance of initiating open discussions about drug misuse and of providing education to patients and their families regarding addiction. It is critical that health care providers have a clear understanding of addiction, drug abuse, dependence, tolerance, withdrawal, and pseudoaddiction to facilitate such discussions and to make appropriate decisions regarding pain management.

No reliable and validated assessment tool exists for identifying aberrant drug-taking behavior in medically ill populations. Indicators of aberrant drug use in patients with chronic pain may include a pattern of early refills, multiple administrative issues with clinical staff, prescription problems, and use of supplemental sources of opioids. Recently, Webster and Webster created and performed a preliminary validation of a self-report Opioid Risk Tool (Table 1). It stratifies risk of developing opioid addiction based on weighted risk factors, such as personal/family history of substance abuse, age, history of childhood sexual trauma, and psychological disease. In a study of 185 consecutively enrolled patients, the Opioid Risk Tool was both highly sensitive and highly specific in predicting which patients would exhibit aberrant drug-related behaviors.
This screening tool can be easily administered in the clinic or physician's office to recognize the patient's potential for abuse even before starting a therapeutic regimen of opioids. Those patients who are at high risk may require additional monitoring and, possibly, referral to a specialized treatment setting. Additional studies are needed to validate this tool in larger and more varied populations to determine its wider applicability.

**BARRIERS TO TREATMENT**

Both patients and practitioners contribute to the undertreatment of HIV/AIDS-related pain. The barriers to pain treatment most frequently reported by patients are those concerning the addiction potential of pain medications and the physical discomfort and adverse effects associated with opioid treatment. Studies that have examined patient barriers to proper pain management have used the Barriers Questionnaire. These studies have demonstrated a positive correlation of the Barriers score with the number of physical symptoms as well as with measures of psychological distress. Moreover, a study by Breitbart and colleagues showed that patients are afraid to report their distress because of concerns that their underlying conditions will not be treated adequately. A patient may also be extremely afraid of becoming addicted or of relapsing if he or she is currently in recovery. Lack of awareness by health care providers to address these barriers can lead to inadequate pain management and can have a negative impact on the patient's overall quality of life. Limited data exist on clinician-related barriers to pain management in patients with HIV/AIDS. The most frequently endorsed barriers are a lack of knowledge about pain management or limited access to pain management experts; concerns regarding potential substance abuse and addiction; and inadequate psychological support and drug treatment services. These data indicate that treating clinicians need to learn to recognize "red flag" behaviors that reflect pain medication misuse or addiction potential and to address their own concerns and misconceptions about treatment approaches.

One recent study compared 2 groups of patients with AIDS-related pain—one group with previous substance use and the other without—following short-term treatment with sustained-release morphine. In this study, patients with a history of drug use were treated successfully for AIDS-related pain. The 2 groups (N = 43) did not differ significantly on quality of life, baseline pain ratings, causes of pain, and pain intensity at study end. Not surprisingly, the group with a history of drug use required considerably higher doses of an opioid for an equivalent analgesic effect.

**Table 1. Opioid Risk Tool**

<table>
<thead>
<tr>
<th>Item</th>
<th>Risk score*</th>
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<tbody>
<tr>
<td></td>
<td>Women</td>
</tr>
<tr>
<td>Family history of substance abuse</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>1</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>2</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>4</td>
</tr>
<tr>
<td>Personal history of substance abuse</td>
<td></td>
</tr>
<tr>
<td>Alcohol</td>
<td>3</td>
</tr>
<tr>
<td>Illegal drugs</td>
<td>4</td>
</tr>
<tr>
<td>Prescription drugs</td>
<td>5</td>
</tr>
<tr>
<td>Ages 16 - 45</td>
<td>1</td>
</tr>
<tr>
<td>History of preadolescent substance abuse</td>
<td>3</td>
</tr>
<tr>
<td>Psychological disease</td>
<td></td>
</tr>
<tr>
<td>Attention-deficit/hyperactivity disorder, obsessive-compulsive disorder, bipolar disorder, or schizophrenia</td>
<td>2</td>
</tr>
<tr>
<td>Depression</td>
<td>1</td>
</tr>
</tbody>
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*Total score risk category: low risk, 0 - 3; moderate risk, 4 - 7; high risk, ≥ 8.
Adapted from Webster LR, Webster RM. Pain Med. 2006.
In addition to patient and clinician barriers, there are various system barriers that interfere with the provision of adequate pain assessment and treatment. These barriers include a lack of an interdisciplinary approach among health care professionals, access to care, and treatment resources. Comprehensive interventions addressing all types of barriers must be implemented to overcome undertreatment of pain in this population.

**MANAGEMENT OF PAIN**

HIV/AIDS-related pain may be best conceptualized as chronic pain because of the following:

- The epidemiology of HIV is changing.
- Recent advances have extended the life span of persons with HIV/AIDS.
- HIV/AIDS-related pain is associated with functional limitations, psychological distress, and reduced HRQOL.
- Pain in HIV/AIDS is surrounded by complex psychosocial issues.

When HIV/AIDS-related pain is viewed as chronic, it becomes clear that approaches to management of pain need to be integrated throughout the course of HIV disease. The chronic pain models for assessment and treatment, however, may only be appropriate in situations in which the patient’s multidimensional experience of pain requires long-term management. A biopsychosocial framework allows the clinician to fully recognize the complex biological, psychosocial, and interpersonal dimensions and to implement flexible treatment strategies.

Treatment of HIV/AIDS-related pain should have multiple goals and targets. A multidisciplinary team approach is needed to provide primary care, psychosocial interventions, medication management, physical therapy, and interventional procedures. Coordinating efforts to meet the patient’s short- and long-term pain management needs is crucial to the success of treatment (Tables 2 and 3).

<table>
<thead>
<tr>
<th>Table 2. Principles of Effective HIV/AIDS-Related Pain Management in Patients With Comorbid Addiction and Applications to Clinical Care</th>
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<tr>
<td><strong>Conduct ongoing comprehensive assessments</strong> Use tools for periodic pain assessment; evaluate for mood and anxiety disorders; monitor and address patient barriers to care</td>
</tr>
<tr>
<td><strong>Assess substance use disorder</strong> Differentiate between past and current use, on replacement therapy (methadone or buprenorphine) or in recovery; identify biological and environmental susceptibilities; distinguish between aberrant drug-taking attitudes and behaviors and unmet pain needs; use screening tools to identify patients at risk for opioid-related aberrant behaviors</td>
</tr>
<tr>
<td><strong>Always maintain a patient-centered nonjudgmental and empathic approach</strong> Assess the level of readiness to make a change (for both substance use and pain) and “meet the patients where they are”</td>
</tr>
<tr>
<td><strong>Individualize the treatment plan</strong> Set clear goals and expectations in collaboration with patient; discuss the patient’s responsibilities for treatment</td>
</tr>
<tr>
<td><strong>Use the principles of pain management outlined in the World Health Organization’s analgesic ladder</strong> Target pharmacotherapy to pain needs, escalating from nonopioid analgesics to progressively stronger opioids</td>
</tr>
<tr>
<td><strong>Optimize nonopioid and nonbenzodiazepine treatment methods</strong> Encourage exercise, biofeedback, relaxation training; use adjuvant medications for sleep, pain, anxiety, and depression</td>
</tr>
<tr>
<td><strong>Integrate pain management and recovery-focused substance use treatment within an interdisciplinary team approach</strong> Initiate regular communication with other physicians, nurses, therapists, and social workers and address provider barriers to care</td>
</tr>
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The mainstay of analgesic intervention for HIV/AIDS-related pain of moderate to severe intensity continues to be the appropriate use of opioid analgesics based on the World Health Organization's analgesic ladder.\(^3\) (A detailed discussion of analgesic use for the management of HIV/AIDS-related pain is beyond the scope of this article and can be found elsewhere.\(^36\)) There is, however, a growing appreciation and evidence for the role of adjuvant analgesics, such as anticonvulsants, tricyclic antidepressants, specific SSRIs, anxiolytics, and psychostimulants, particularly in the treatment of neuropathic pain.\(^37\) Dronabinol, a cannabinoid, can provide anxiolytic effects that are palliative for some patients with chronic pain.\(^38\) Some evidence has also suggested that cannabinoids might improve such symptoms as pain and nausea.\(^39\) Psychotherapeutic approaches to patients in pain vary depending on whether the patient is experiencing acute, continuous, or chronic pain (Table 4). Severe pain can interfere with the patient's ability to use psychosocial interventions and should be addressed aggressively with somatic therapies. Nonpharmacological techniques should complement adequate pharmacological
analgesic relief.

The primary care and infectious disease settings are the ports of entry for most patients seeking medical attention for pain. The patient's readiness to accept and adopt a self-management approach is therefore a key issue in the consultation. For this reason, a central task for clinicians is to understand and motivate patients to self-manage pain and adhere to other therapeutic strategies, such as cognitive-behavioral therapy. A patient-centered approach has multiple goals, such as to assess and address patients' worries and concerns, to enhance a collaborative relationship, to provide information that patients can understand, to change the focus of the visit from treatment recommendations to supporting and enhancing patient self-care practices, and to foster greater patient control of decision making and responsibility for self-care. There is significant evidence showing the effectiveness of this approach (as reviewed by Douaihy and colleagues). Such an approach for patients with HIV/AIDS-related pain can substantially reduce some of the patient barriers to effective pain management. Strategies that health care providers can use to increase patient understanding and self-confidence focus on empowering patients to address their concerns, to consider the pros and cons of changing self-care behaviors, and to create their own pain management agenda. Psychoeducation allows patients to be more knowledgeable about their pain condition and treatments. Education sessions should encourage patients to be active participants. Important topics include discussions on physiology of pain, purposes of medications, the role of exercise in pain control, strategies to manage stress and sleep disturbances, weight management and nutrition, sexual activities, and healthy lifestyle behaviors. These interventions can be provided in individual or group settings. Supportive therapy serves to reassure patients that someone "is in their corner" and that they are not suffering alone. Patients may take great comfort from offers of reassurance, the opportunity to express their fears and concerns in a nonjudgmental atmosphere, and the chance to discuss concrete strategies. Disengagement from family can lead to more patient isolation and potentially greater disability. Therefore, active involvement of family and significant others helps optimize management of pain. Operant-behavioral therapy emphasizes the potential role that the patient's family can play in contributing inadvertently to pain behavior. In this therapy, families are taught to ignore pain behavior, such as by retreating to the bedroom, and to strongly reinforce every small step toward increased functioning. Negative, inappropriate, and catastrophic thoughts related to pain can be associated with greater pain intensity, emotional distress, and disability among patients with HIV/AIDS. Such thought patterns are often noted in patients with pain disorder, anxiety, or depression. Cognitive-behavioral therapy focuses on restructuring this negative cognitive schema into a more realistic appraisal of the patient's current condition. When a realistic perspective regarding the past, present, and future can be achieved, patients may be better able to cope with their pain. Homework assignments, relaxation techniques, physical activity, coping skills (including positive affirmation and relapse prevention techniques) can be incorporated into the therapy. Cognitive-behavioral therapy can also be used for the HIV-infected population for insomnia; when effective, this approach can indirectly improve medical and psychological end points. In addition,
cognitive-behavioral therapy can reduce pain and suffering in some patients with HIV/AIDS-related neuropathic pain.\textsuperscript{43} Biofeedback, self-hypnosis/hypnosis, and meditation are other possible tools used to alleviate pain in HIV-infected persons.\textsuperscript{34,44} Patients with HIV/AIDS-related pain are often hesitant to accept a referral for psychotherapy. They may resent any implication that there is an emotional overlay to their struggle with pain. Health care professionals should avoid suggesting to patients that the pain is "in their head" and work collaboratively to help patients understand the importance of simultaneously addressing pain and coexisting depression and anxiety.

CONCLUSIONS AND FUTURE RESEARCH

Pain in persons with HIV/AIDS remains a considerable problem despite the recent improvements in treatment modalities. Pain is often not adequately treated by health care providers. Furthermore, pain has a major impact on HRQOL. A multidisciplinary team approach to pain control is the most appropriate strategy, allowing for adequate assessment of pain, evaluation of possible underlying causes, and recognition of the attentional, cognitive, affective, and social components of the patient's pain experience. Ideally, such a team would include a primary care physician; infectious disease specialist; and specialists in pain management, psychiatry, and addiction medicine. Additional research should examine the interrelationships among pain, psychological disorders, drug use, and health outcomes. Future studies allowing a better understanding of the role of health care providers in preventing and treating pain could have the additional benefit of leading to an improvement in HRQOL for persons living with HIV/AIDS. Further research should also examine whether adequate treatment of pain among drug-dependent persons could lead to improved health outcomes.

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