

## Perspective

# Chronic Pain in Patients With HIV Infection: What Clinicians Need To Know

*Chronic pain is common in individuals with HIV infection. The primary goal of treatment of chronic pain is not only to improve pain but also to improve physical and emotional function. Patients with chronic pain should be assessed for concurrent psychiatric and substance use disorders, as these conditions often coexist. Treatment of chronic pain may have limited success in the absence of treatment of psychiatric disorders. Treatments for chronic pain include nonopioid pharmacologic therapies and nonpharmacologic therapies (eg, cognitive and behavioral therapy, physical therapy), and the latter option is often the most effective for improving patient function. Care must be taken when initiating or continuing treatment with opioids, and the risks and benefits of treatment with opioids should be regularly assessed. This article summarizes a presentation by Jessica S. Merlin, MD, MBA, at the IAS–USA continuing education program held in New York, New York, in March 2015.*

**Keywords:** HIV, chronic pain, functional impairment, opioid treatment, nonopioid treatment

Chronic pain is pain that persists for longer than 3 months, beyond the period of normal tissue healing. Musculoskeletal pain (eg, lower back, knee, or shoulder pain), fibromyalgia, and neuropathy are some examples of chronic pain. There is a great deal of basic science literature that describes the pathophysiologic underpinnings of chronic pain. From this literature, 2 key etiologies of chronic pain are peripheral sensitization and central sensitization (Figure 1). In peripheral sensitization, peripheral nervous system receptors are hypersensitized by local tissue inflammation (eg, from an inflammatory disease such as rheumatoid arthritis) or damage (eg, from physical trauma), causing pain to remain even after the inflammation or injury is no longer present. During central sensitization, there is no inflammation in the periphery, but the brain receives a strong signal of pain. A prime example of this is fibromyalgia. The pathways that control central sensitization are associated with conditions such as mood disorders and addiction, and as a result, these conditions commonly occur together. Chronic pain may also be caused by ongoing active inflammation, such as that seen in rheumatoid arthritis. However, even in this circumstance, it is important to consider the potential role central sensitization might play. For example, an individual with rheumatoid arthritis and depression may continue to have severe chronic pain if their depression is not adequately treated.

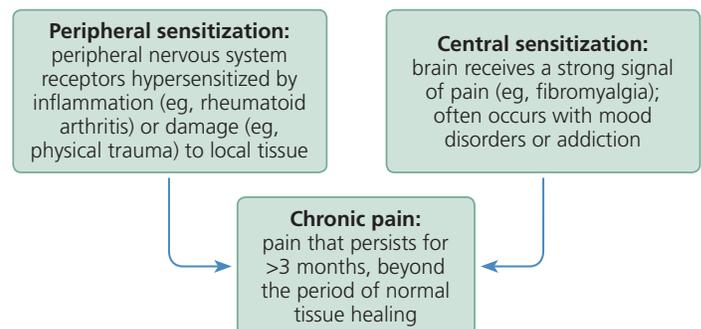
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Chronic pain can lead to substantial functional impairment, including difficulty across several domains of function: physical function (eg, work and household chores, ability to participate in leisure activities), social function (eg, close personal relationships), socioeconomic status (eg, health-care costs, disability), and emotional function (eg, anxiety and depression). As a result, over the past few years, chronic pain itself has been increasingly regarded as a chronic condition.<sup>1</sup>

## HIV Infection and Chronic Pain

In the current HIV treatment era, an estimated 39% to 85% of individuals with HIV infection also suffer from chronic pain compared with only 20% to 30% of the general population. Chronic pain in HIV-infected individuals is often musculoskeletal, although pain associated with peripheral neuropathy is observed in approximately 20% to 30% of individuals. Chronic pain in HIV-infected individuals often but not always coexists with mood disorders and addiction. Based on a cross-sectional study in a cohort of HIV-infected individuals, those with HIV infection and chronic pain are up to 10 times more likely to have functional impairment. Additionally, individuals with HIV infection and chronic pain who also report recent substance use are more likely to be retained in care, whereas individuals with HIV infection and chronic pain who do not report recent substance use are less likely to be retained in care. As a result of these factors and the minimal training most practitioners receive in this area, caring for individuals with chronic pain can be a substantial challenge for HIV practitioners.<sup>2-7</sup>

The reason for the high prevalence of chronic pain in individuals with HIV infection is unclear. Adverse effects associated with nucleoside analogue reverse transcriptase inhibitors (eg, peripheral neuropathy), with opportunistic infections (eg, herpes zoster virus infection), or with treatments



**Figure 1.** The 2 key etiologies of chronic pain: peripheral sensitization and central sensitization.

for opportunistic infections (eg, isoniazid-related polyneuropathy) contribute to chronic pain in individuals with HIV infection. However, these effects do not account for many cases of chronic pain, including cases of musculoskeletal pain, seen in many of these individuals. Some have hypothesized that even in the setting of virologic suppression, chronic pain may develop from persistent inflammation caused by HIV infection. To date, there is no evidence to support this, and this is an actively ongoing area of investigation. Another explanation might be that mental illness and addiction are commonly associated with chronic pain and with HIV infection. Therefore, individuals infected with HIV may represent a population that is saturated with individuals with chronic pain. Further research in this area is needed.

## Evaluation

The experience of pain is highly subjective, which can be challenging for practitioners. The optimal approach is to assume that all patients who report having chronic pain suffer from chronic pain. When reviewing a patient's history of chronic pain, the practitioner should note the effect chronic pain has on the patient's function, mood, and sleep.<sup>8</sup> Practitioners may be reluctant to ask patients about the relationship between pain and mood for fear of implying that the patient's pain is purely psychological in nature or "all in their head." One approach may be to tell a patient with depression that some patients with depression indicate that when their mood is down their pain is worse, and that when their pain is more intense it worsens their mood, creating a cycle and making it difficult to tell which came first. The practitioner can then ask if this is something the patient has experienced themselves. Practitioners should also note the level of pain a patient is experiencing on a standardized scale (eg, from 0 to 10). However, the impact of pain on a patient's ability to function is as important if not more important than their level of pain. For example, a patient who reports severe pain and who works a full-time job is different than one who reports severe pain and is confined to their house or their bed.

Other key elements to consider when reviewing a patient's history of chronic pain are the patient's employment status and history of disability. Regardless of whether a patient is employed outside the home or is working inside the home (eg, caring for children or an elderly parent), they should be asked how they spend their time. It is helpful to have the patient describe their level of function before and after they began experiencing symptoms of chronic pain. It may also be useful to ask patients what they would ideally like to be doing. This can help the practitioner identify a patient's skills and interests (eg, Are they social? Do they enjoy jobs that involve physical activity?), information which can eventually be used to help set functional goals for chronic pain treatment. A history of the patient's psychiatric conditions and substance use should be elicited, as both are common and can be missed if no direct query is made. During the interview, it is also important to note the behaviors a patient exhibits during moments of pain.

**Table 1.** Risk Factors for Disability Associated With Chronic Pain

– Anxiety	– Fear avoidance
– Catastrophizing	– High level of initial pain
– Compensation dependency	– Increasing age
– Decreased function	– Poor health
– Depression	

Practitioners should be aware of several known risk factors for disability, including fear avoidance (avoiding physical activity in order to avoid pain; eg, a patient will not leave bed for fear it will aggravate lower back pain), catastrophizing (eg, worry that a condition such as fibromyalgia will result in confinement to a wheelchair), depression, anxiety, decreased function, high levels of initial pain, increasing age, poor general health, and compensation dependency (Table 1). Noting such risk factors and discussing them with patients while a therapeutic relationship is built is an important part of chronic pain treatment.

When assessing etiology, the practitioner should attempt to determine if the patient's chronic pain is neuropathic (eg, sciatica, postherpetic neuralgia, or alcohol- or diabetes-related neuropathy), musculoskeletal (eg, myofascial pain syndrome), inflammatory (eg, arthritis, tendonitis, or chronic infection), or mechanical or compressive (eg, pain related to tumors, cysts, or fractures). This can be done with a thorough initial medical history, a physical examination, and appropriate diagnostic testing. However, many patients with chronic pain do not fit neatly into one of these categories and may have a less well-defined musculoskeletal chronic pain syndrome. If this is the case, practitioners should not be discouraged, and patients should not be told that their symptoms cannot be explained or that their medical condition will be difficult to treat.

Additionally, a judicious, evidence-based approach to diagnostic testing for chronic pain is important. Chronic pain often does not have a radiographically identifiable cause, presenting a challenge to patients and practitioners who are both looking for a clear explanation. Patients in whom workups with blood testing or magnetic resonance imaging have revealed no explanation for chronic pain should be informed that their test results do not reveal a life-threatening condition or that their symptoms do not require a serious intervention such as surgery. Rather, they should be informed that they have chronic pain, which can be treated.

## Communication

Communicating with patients about chronic pain is not always easy, for several reasons. First, patients might bring negative expectations to a meeting with a new practitioner based on previous experience. A patient may have been previously accused of drug seeking, may have been questioned about the existence of their pain, or may have received an inconclusive diagnosis. Encounters with previous patients

may influence a practitioner's attitude toward a current patient. Additionally, pain is often referred to as the fifth vital sign and is often viewed by patients and practitioners as indicative of an emergency. Although it may be reasonable for acute pain, it is not appropriate to treat chronic pain as an emergency. As with other chronic conditions, improvement of chronic pain takes time. The focus of treatment of chronic pain should not be immediate pain relief, but rather, improvement in function over time. Communication about medications can also be difficult because some medications (eg, opioids) carry risks. Some patients may have an active psychiatric illness, substance use disorder, or personality type that influences the way they communicate with practitioners.

Initial discussions with patients with chronic pain should include education about chronic pain. Practitioners may refer to chronic pain as a medical condition with a known biologic basis and known treatments. Patience, partnership, and collaboration should be emphasized. Practitioners and patients should acknowledge that evaluation and management of chronic pain will take time, and practitioners should explain that pharmacologic and nonpharmacologic strategies to manage chronic pain exist and that they are best used together. Motivational interviewing can be useful for promoting partnership and a true understanding of patient concerns, and for discussing behavioral changes that might help a patient's pain (eg, weight loss, improving physical activity, or reducing dependence on opioids for pain relief).

## Management

Management of chronic pain should focus on evidence-based therapies. Procedures, surgeries, and medications that are not evidence based should be avoided. Concrete goals and timelines should be set, and therapies that do not work should be discontinued. If possible, practitioners should treat any psychiatric illness first, as chronic pain is most likely to improve in the context of well-controlled psychiatric symptoms.

### Nonopioid-Based Pharmacologic Therapy

Nonopioid-based pharmacologic therapy includes acetaminophen (mostly studied in the context of osteoarthritis) given at under 3 g per day. It is important to remember that hepatitis C virus infection and alcohol use are relative contraindications for the use of acetaminophen. Nonsteroidal antiinflammatory drugs can be used to treat chronic back pain, but consideration should be given to potential risks for cardiovascular, gastrointestinal, and renal adverse events. Although they are frequently used, benzodiazepines carry risks, and no evidence exists that supports the use of these drugs for the treatment of chronic pain. Other agents include anticonvulsants, anti-depressants, and topical agents; lidocaine is used to treat post-herpetic neuralgia, capsaicin is used to treat postherpetic distal sensory polyneuropathy, and diclofenac is used to treat osteoarthritis.

## Opioids

There is growing consensus that long-term opioid therapy is not an appropriate initial treatment for chronic pain. Opioids may be effective in treating chronic pain in some patients, but data on the benefit of opioids as a long-term treatment are limited. There is increasing awareness of the potential harms associated with opioid use. Currently, the United States is experiencing an epidemic of opioid overdoses. There is evidence of increased mortality risk for individuals who receive opioid doses greater than the equivalent dose of 50 mg to 200 mg of morphine per day, depending on the threshold used in the study, and mortality risk is greater for individuals who combine use of opioids with use of benzodiazepines.<sup>6,9-15</sup>

To mitigate risk, practitioners and patients should jointly review an opioid treatment agreement. The term agreement is preferred to contract, as agreement implies that both the patient and practitioner have responsibilities with regard to patient safety. An agreement should be written at a low literacy level, should include information about safe prescribing, should limit the patient to 1 prescribing physician and 1 pharmacy, should note the need to store medication safely, and should state that opioid prescription may be reconsidered if the patient is not able to adhere to these guidelines. Ideally, such documents also contain information about informed consent that explains the risks of, benefits of, and alternatives to opioid treatment. Strategies for monitoring individuals taking long-term opioid therapy should include routine checks of prescription drug databases and urine drug testing. Based on the consensus opinions of numerous groups, routine use of these strategies become the standard of care for individuals taking long-term opioid therapy. Official guidance regarding strategies for risk mitigation differs among states, and practitioners should be familiar with their state's policies.

The decision to initiate or continue opioid treatment is guided by assessment of risks and benefits to the patient at regular intervals. Risk factors for misuse and abuse of opioids include personal or family history of substance use, younger age, history of sexual abuse, and history of depression. Evidence of benefit in patients taking opioids includes improvements in physical and emotional function as well as a reduction in pain. Evidence of harm in patients taking opioids includes adverse events such as falls, fractures, and poor physical or emotional function, and the development of depression, hypogonadism, or hyperalgesia.

Concerning behaviors, also referred to as aberrant behaviors, may also arise in individuals taking long-term opioid therapy. Such behaviors include unsanctioned dose escalation, reporting lost or stolen prescriptions, obtaining opioids from more than 1 prescriber, unwillingness to adhere to nonopioid-based aspects of the treatment plan, concurrent use of nonprescription substances including illicit substances, and aggressive behavior. These behaviors each represent a substantial clinical challenge to HIV primary care. When such behaviors arise, the practitioner should promptly discuss the

behavior with the patient and carefully consider the differential diagnosis of the behavior. Depending on the findings, strategies for addressing such behaviors include reeducating the patient on the appropriate use of and risks associated with opioids, closer monitoring (eg, smaller supplies of medication, more-frequent clinic visits to reassess clinical condition and further assess behavior), and involvement of pain, psychology, and substance use professionals. If behaviors are serious or if they persist over time and do not resolve with these strategies, tapering of opioid treatment should be considered. As patients are further evaluated during repeated office visits or by specialist colleagues, it may become apparent that they meet the criteria for addiction in individuals taking long-term opioid therapy, which include the 4 Cs: loss of control, compulsive use, craving, and continued use despite harm.

Regular office visits (eg, every 3-6 months) during which the above monitoring and risk-benefit assessments are conducted are becoming the standard of care during treatment of chronic pain with opioids. An important factor to consider during treatment and management of chronic pain is the lack of evidence that long-acting opioids are safer than short-acting drugs; some evidence indicates that long-acting drugs may be associated with greater risk of overdose. Repeated dose escalation should be avoided; high doses are not typically more efficacious than lower ones, but recent evidence suggests they are more dangerous.

It is important to remember that urine drug tests may be difficult to interpret. Initial urine drug tests are screening tests and may have false-positive or false-negative results (eg, use of quinolones causing a false-positive result for opiates, or a lack of detectable opioid levels in a patient who is taking them and who has a low urine concentration). Following up a urine drug test with a confirmatory test, usually a gas chromatography/mass spectrometry test or a liquid chromatography/mass spectrometry test, may be useful.

Additionally, knowledge of pathways of drug metabolism (eg, that hydrocodone is metabolized into hydromorphone and therefore may appear on a urine drug test as hydromorphone) is important. Documentation of the risk-benefit analysis of opioid treatment for an individual patient, as well as of the monitoring strategy employed and of any adverse events or concerning behaviors, is crucial.

Practitioners sometimes “inherit” patients who are taking long-term opioid therapy from outside clinics or colleagues. This transition of care provides an ideal opportunity to reassess a patient’s opioid therapy. The practitioner should take the steps described above, providing patients with basic pain education and basic monitoring. Keeping decisions regarding continuation of long-term opioid therapy within a risk-benefit framework is important and useful. If there is no evidence of harm, if the risk is judged to be low, and if the patient is benefitting from it, opioid therapy may be continued with standard monitoring as described above. However, concerning behaviors or active substance use disorders should be addressed promptly.

## Nonpharmacologic Approaches

Cognitive-behavioral therapy and physical therapy are 2 important evidence-based nonpharmacologic approaches to treatment of chronic pain. These are often the most effective treatment options for improving function in patients with chronic pain. Other options include exercise, complementary or alternative therapies such as acupuncture, and surgery for specific indications.<sup>8,16-22</sup>

## Summary

Chronic pain is common in patients with HIV infection and may cause substantial functional impairment. Therapies for chronic pain include many options in addition to opioids. Careful attention must be paid to psychiatric symptoms in patients with chronic pain, and psychiatric conditions should also be treated if treatment of chronic pain is to be effective. ☐

*Presented by Dr Merlin in March 2015. First draft prepared from transcripts by Matthew Stenger. Reviewed and edited by Dr Merlin in September 2015.*

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## References

1. Institute of Medicine (US) Committee on Advancing Pain Research, Care, and Education. *Relieving pain in America: a blueprint for transforming prevention, care, education, and research*. Washington, DC: National Academies Press (US), 2011.
2. Lee KA, Gay C, Portillo CJ, et al. Symptom experience in HIV-infected adults: a function of demographic and clinical characteristics. *J Pain Symptom Manage*. 2009;38(6):882-893.
3. Cervia LD, McGowan JP, Weseley AJ. Clinical and demographic variables related to pain in HIV-infected individuals treated with effective, combination antiretroviral therapy (cART). *Pain Med*. 2010; 11(4):498-505.
4. Merlin JS, Cen L, Praestgaard A, et al. Pain and physical and psychological symptoms in ambulatory HIV patients in the current treatment era. *J Pain Symptom Manage*. 2012;43(3):638-645.
5. Merlin JS, Westfall AO, Raper JL, et al. Pain, mood, and substance abuse in HIV: implications for clinic visit utilization, antiretroviral therapy adherence, and virologic failure. *JAIDS*. 2012;61(2):164-170.
6. Lum PJ, Little S, Botsko M, et al. Opioid-prescribing practices and provider confidence recognizing opioid analgesic abuse in HIV primary care settings. *JAIDS*. 2011;56 Suppl 1:S91-S97.
7. Tsao JC, Stein JA, Ostrow D, Stall RD, Plankey MW. The mediating role of pain in substance use and depressive symptoms among Multicenter AIDS Cohort Study (MACS) participants. *Pain*. 2011;152(12):2757-2764.
8. Institute for Clinical Systems Improvement (ICSI). Assessment and management of chronic pain. [https://www.icsi.org/\\_asset/bw798b/ChronicPain.pdf](https://www.icsi.org/_asset/bw798b/ChronicPain.pdf). Accessed on August 31, 2015.
9. Bohnert AS, Valenstein M, Bair MJ, et al. Association between opioid prescribing patterns and opioid overdose-related deaths. *JAMA*. 2011;305(13):1315-1321.
10. Gomes T, Mamdani MM, Dhalla IA, Paterson JM, Juurlink DN. Opioid dose and drug-related mortality in patients with nonmalignant pain. *Arch Intern Med*. 2011;171(7):686-691.
11. Manchikanti L, Vallejo R, Manchikanti KN, Benyamin RM, Datta S, Christo PJ. Effectiveness of long-term opioid therapy for chronic non-cancer pain. *Pain Physician*. 2011;14(2):E153-E156.
12. Noble M, Treadwell JR, Tregear SJ, et al. Long-term opioid management for chronic noncancer pain. *Cochrane Database Syst Rev*. 2010;(1):CD006605.
13. Webster LR, Cochella S, Dasgupta N, et al. An analysis of the root causes for opioid-related overdose deaths in the United States. *Pain Med*. 2011;12 Suppl 2:S26-S35.

14. Chou R, Turner JA, Devine EB, et al. The effectiveness and risks of long-term opioid therapy for chronic pain: a systematic review for a national institutes of health pathways to prevention workshop. *Ann Intern Med.* 2015;162(4):276-86.
15. Weisberg DF, Gordon KS, Barry DT, et al. Long-term prescription of opioids and/or benzodiazepines and mortality among HIV-infected and uninfected patients. *J AIDS.* 2015;69(2):223-233.
16. Cucciare MA, Sorrell JT, Trafton JA. Predicting response to cognitive-behavioral therapy in a sample of HIV-positive patients with chronic pain. *J Behav Med.* 2009;32(4):340-348.
17. Hayden JA, van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non-specific low back pain. *Cochrane Database Syst Rev.* 2005;(3):CD000335.
18. Trafton JA, Sorrell JT, Holodniy M, et al. Outcomes associated with a cognitive-behavioral chronic pain management program implemented in three public HIV primary care clinics. *J Behav Health Serv Res.* 2012;39(2):158-173.
19. Turk DC, Wilson HD, Cahana A. Treatment of chronic non-cancer pain. *Lancet.* 2011;377(9784):2226-2235.
20. Vickers AJ, Cronin AM, Maschino AC, Lewith G, MacPherson H, Foster NE et al. Acupuncture for chronic pain: individual patient data meta-analysis. *Arch Intern Med.* 2012;172(19):1444-1453.
21. Mirza SK, Deyo RA. Systematic review of randomized trials comparing lumbar fusion surgery to nonoperative care for treatment of chronic back pain. *Spine (Phila Pa 1976).* 2007;32(7):816-823.
22. Cucciare MA, Sorrell JT, Trafton JA. Predicting response to cognitive-behavioral therapy in a sample of HIV-positive patients with chronic pain. *J Behav Med.* 2009;32(4):340-348.

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