

Review

The Role of Palliative Care in the Current HIV Treatment Era in Developed Countries CME

Jessica S. Merlin, MD, MBA, Rodney O. Tucker, MD, MMM, Michael S. Saag, MD, Peter A. Selwyn, MD, MPH

The goal of palliative care is to minimize and prevent suffering and maximize physical function and quality of life in patients with serious illness. In the early years of the AIDS epidemic in developed countries, prognosis was poor and palliative care was often inseparable from HIV care. Despite the advent of effective antiretroviral therapy and its availability in developed countries, patients with HIV disease still present many palliative care challenges and opportunities. The cases of 3 HIV-infected patients who embody these challenges will be presented in this article: an older patient with numerous medical comorbidities, chronic pain, and severely impaired physical function; a patient with psychiatric illness and substance abuse, difficulties with adherence to antiretroviral therapy and retention in HIV primary care, and cryptococcal meningitis; and a patient with stable HIV disease and hepatitis C virus–related liver failure. These cases are being presented to stimulate a discussion between HIV and palliative care practitioners about potential areas of clinical and research collaboration.

The goal of palliative care is to alleviate and prevent suffering in patients with serious illness. Early in the AIDS epidemic in developed countries, prognosis was universally poor. HIV care and palliative care were seen as one and the same, and HIV practitioners, by necessity, became experts in palliative care. Patients dying with AIDS needed palliative care to help ease their suffering at the end of life; suffering related to pain and other symptoms experienced during the dying process, and eventually, suffering related to toxic antiretroviral medications used in the early treatment era. This era, the pre-potent antiretroviral therapy era, is an era that the field of HIV medicine was glad to leave behind.

The AIDS epidemic has changed dramatically over the past 20 years.

With the introduction of effective antiretroviral therapy and its widespread uptake in developed countries, the epidemic has matured. By 2015, 50% of patients with HIV disease in the United States will be older than 50 years.^{1,2} In addition, patients with HIV disease often have numerous comorbidities, such as cardiovascular, renal, or liver disease, and non-AIDS-defining malignancies. This has been described as a process of “accelerated aging.”³ The combination of a “graying” epidemic and multimorbidity likely contributes to the high prevalence of pain and symptoms still seen in patients with HIV disease. Estimates of pain occurrence in the current HIV treatment era in studies from the United States range from 39% to 55%.⁴⁻¹³ Physical symp-

toms such as nausea and fatigue and psychological symptoms such as depressed mood and anxiety are also common.^{7,9-11,13-16} Data from the pre-potent antiretroviral treatment era suggest that pain is underrecognized and undertreated.¹⁷⁻¹⁹ Adding to this complexity, psychiatric illness and substance abuse are common in HIV-infected patients.²⁰⁻²² All of this is compounded by an aging population, in which the complications of HIV as a chronic disease now intersect with the added challenges of geriatric care. These myriad issues lead to growing clinical complexity and impaired quality of life for HIV-infected patients.

Despite advances in therapeutics, patients with HIV infection still die, even in settings in which antiretroviral therapy is widely available. Deaths attributable to AIDS in an era of antiretroviral therapy have shifted “from fate to tragedy,” often relating to late diagnosis or failures in adherence to antiretroviral therapy or retention in HIV primary care.²³ Today, AIDS-related deaths account for less than half of all deaths in patients with HIV disease; the remainder are primarily due to other comorbidities such as liver disease and non-AIDS-defining malignancies.²⁴ Many HIV-infected patients are now being cared for by a generation of physicians who did not experience the epidemic of suffering, dying, and death in the pre-potent treatment era, and who may not be

Dr Merlin is an Assistant Professor in the Division of Infectious Diseases and Division of Gerontology, Geriatrics, and Palliative Care in the Department of Medicine at the University of Alabama at Birmingham. Dr Tucker is an Associate Professor in the Division of Gerontology, Geriatrics, and Palliative Care in the Department of Medicine at the University of Alabama at Birmingham. Dr Saag is Professor of Medicine, Jim Straley Chair in AIDS Research, and Director of the Center for AIDS Research at the University of Alabama at Birmingham; he is also a member of the IAS–USA Board of Directors and the Viral Hepatitis Advisory Board. Dr Selwyn is a Professor and Chairman of the Department of Family and Social Medicine at the Montefiore Medical Center, Albert Einstein College of Medicine, in the Bronx, New York. Send correspondence to Jessica S. Merlin, MD, MBA, Department of Medicine, University of Alabama at Birmingham, BBRB 220a, 1530 3rd Avenue S, Birmingham, AL 35294-2170. Received on January 8, 2013; accepted on February 14, 2013.

as attuned to the palliative aspects of HIV disease.

Palliative care as a medical specialty has also evolved over the past 20 years. It emerged from the hospice movement and is often employed near the end of life. However, palliative care has been increasingly understood as an approach to minimize and prevent suffering while maximizing physical function in the face of serious illness, irrespective of stage of illness or prognosis (Figure).^{25,26} Palliative care has been successfully integrated in the early stages of illness in patients with complex diseases such as heart failure, chronic obstructive pulmonary disease (COPD), and cancer.²⁷⁻³⁰

goals of care include functional improvement, comfort, and caregiver support and are considered an essential part of discussions with patients with serious illness.³¹

Palliative care is, by definition, interdisciplinary in nature. Physicians, nurses, psychologists, social workers, chaplains, physical and massage therapists, and counselors with special expertise and training in palliative care work together with patients' primary practitioners to help patients who are suffering achieve their care goals. When appropriate, palliative care can also help patients whose health is rapidly declining, or who are nearing the end of life.

is to stimulate a dialogue between HIV and palliative care practitioners and researchers and to challenge us to consider novel ways to reduce patient suffering while improving their physical function and quality of life.

Cases

Case 1: Aging With HIV

Mr A, a 65-year-old white man, was diagnosed with HIV infection in 1996 during an episode of *Pneumocystis jiroveci* pneumonia. Mr A has a history of good adherence to antiretroviral therapy and retention in HIV primary care. He is currently taking a regimen of emtricitabine, tenofovir, and ritonavir-boosted darunavir, his CD4+ count is 350 cells/ μ L, and his viral load is undetectable. Over the past 10 years, Mr A has developed several comorbidities. He has diabetes, requiring oral hypoglycemic therapy and insulin. Although he is not overweight, he has central adiposity, and his total cholesterol and triglycerides are elevated. He also has peripheral neuropathy, which may be secondary to a combination of early treatment with stavudine, diabetes, and HIV itself. His neuropathy improved somewhat after initiation of gabapentin but still affects his quality of life. Last year, he began to have hip pain and was diagnosed with bilateral severe hip osteonecrosis. The pain has severely limited Mr A's mobility and he is unable to participate in activities that he previously enjoyed, such as working in his garden or playing with his nieces. While undergoing an evaluation for a bilateral total hip replacement, he had an episode of chest pain and a positive stress test, resulting in a cardiac catheterization and stent placement. Over the past few years, Mr A has also begun to appear more frail; he is thinner, has less muscle mass, has a slow gait, and has begun to show signs of cognitive decline.

Mr A lives with his 85-year-old mother and has become increasingly dependent on her for some activities of daily living, such as grocery

Therefore, palliative care is a natural fit to address suffering and maximize function and quality of life for patients living with HIV disease, and for patients with HIV disease who are nearing the end of life.³² Unfortunately, palliative care for patients with HIV disease in the current treatment era in developed countries has received little attention in the HIV literature or at national and international HIV conferences. This is a missed opportunity. Inpatient and ambulatory palliative care programs are growing rapidly, with more

than 60% of US hospitals now providing a palliative care team.³³ HIV clinicians have the opportunity to collaborate with and learn from their palliative care colleagues, to integrate palliative care with disease-specific care for patients with HIV in order to improve their quality of life and HIV-related clinical outcomes. Three cases are presented that illustrate opportunities for integration of palliative care with disease-specific care for patients with HIV throughout the course of their illness. The intent

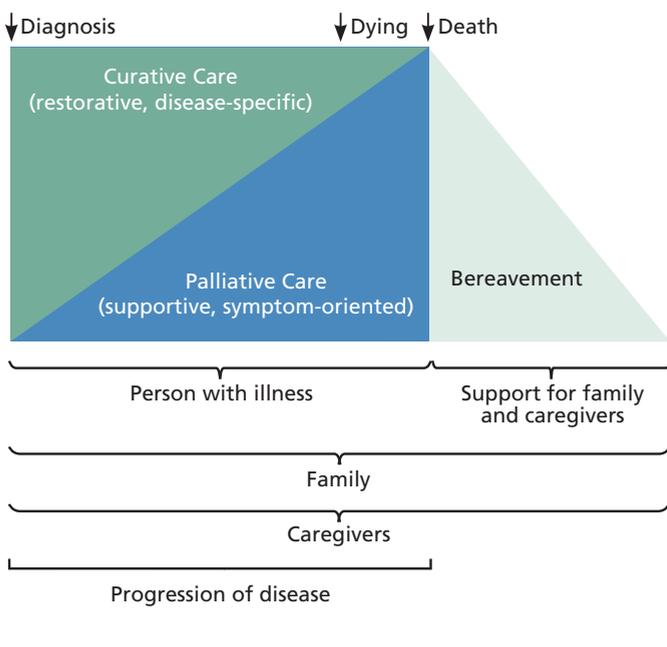


Figure. Palliative care's place in the course of illness. Adapted from World Health Organization.⁵³

Palliative care has recently been recognized as a medical specialty in the United States, requiring fellowship training and board certification for physicians who practice in this area. The palliative care skill set includes pain and symptom management and communication about physical, emotional, psychosocial, and spiritual suffering in the context of serious illness. In particular, palliative care specialists have specific expertise in communicating about goals of care. Common

shopping and other errands. She has cardiovascular disease and suffers from arthritis, which impairs her mobility. Mr A notes that his mother's health has been declining over the past year, and notably, they share many of the same comorbidities.

Commentary

This case illustrates the numerous challenges that may be faced when caring for aging HIV “survivors.” At this point in Mr A's illness trajectory, diabetes and cardiovascular disease have surpassed HIV infection itself as drivers of functional impairment. An HIV practitioner, seeing this patient in a 15- to 30-minute office visit, is likely to focus on the biggest threats to Mr A's health: his cardiovascular risk factors and glycemic control. However, there are other pressing issues that must be addressed, including Mr A's disabling pain, his increasingly challenging family environment, his cognitive decline, and possibly his mood.

Research on the impact of chronic pain in patients with HIV disease and the approaches to its management in the current treatment era is limited. There is some evidence that pain impacts retention, adherence, virologic suppression, and physical function in HIV-infected patients.^{10,12,34,35} The goal of successful chronic pain management is to restore physical function. This involves a combination of pharmacologic management and the use of psychologic-based therapeutic techniques. In this case, Mr A's peripheral neuropathy is only somewhat improved with gabapentin. Numerous other pharmacologic agents (Table 1), in addition to cognitive behavioral therapy and supportive psychotherapy,³⁶ are effective in the treatment of this painful disorder. In addition, although not a factor in this case, psychiatric illnesses such as mood disorders and substance abuse must be addressed when present, as these often impact the patient's pain and response to therapy.³⁷

Mr A's chronic pain and declining health impact his relationship with his mother, who is also ailing. Mr A may

Table 1. Agents Used in the Treatment of Peripheral Neuropathy in HIV-Infected Patients

Agent	Comments
Gabapentin ^a	In a randomized controlled trial of gabapentin vs placebo in 26 HIV-infected patients, 44% of subjects reported improvement in neuropathic pain and 48% reported improvement in sleep in the gabapentin group, and no improvements were reported in the placebo group. ⁴⁴
Pregabalin	A randomized controlled trial of pregabalin vs placebo in 302 HIV-infected patients showed lack of superiority of pregabalin. ⁴⁵ However, based on its similarity to gabapentin, and its ease of administration and superior tolerability, it is often prescribed for the treatment of peripheral neuropathy.
Amitriptyline	Randomized trials of amitriptyline, mexiletine, or placebo ⁴⁶ and a 2 x 2 factorial design of amitriptyline and acupuncture ⁴⁷ found no difference between amitriptyline and placebo. However, due to its efficacy in other populations (eg, diabetic neuropathy), amitriptyline and other tricyclic antidepressants are often used to treat neuropathy in HIV-infected patients.
Capsaicin ^a	Two similarly designed randomized controlled trials in which high-dose capsaicin (8%) was compared with a low-dose control (0.04%) demonstrated efficacy. Analysis of combined data from both trials showed an improvement of 27% with the high dose vs 16% with the low dose (n = 239 and n = 100, respectively). ⁴⁸
Lidocaine	A randomized, controlled, crossover study of topical lidocaine in 64 participants found it to be no more effective than placebo in HIV-infected patients with peripheral neuropathy. ⁴⁹
Opioids	There are no studies of opioids in HIV-infected patients with peripheral neuropathy. However, opioids are commonly used in the treatment of chronic nonmalignant pain and, in particular, have been shown to have at least some efficacy in the treatment of neuropathic pain in non-HIV-infected patients. ⁵⁰ They are sometimes used in the management of peripheral neuropathy in HIV-infected patients.

Based on the literature for diabetic neuropathy, duloxetine or valproic acid may be considered for second-line management of peripheral neuropathy in HIV-infected patients.

^aProven efficacy for HIV peripheral neuropathy in at least 1 randomized controlled trial. Compiled from Hahn et al,⁴⁴ Simpson et al,⁴⁵ Kiebertz et al,⁴⁶ Shlay et al,⁴⁷ Brown et al,⁴⁸ Estanislao et al,⁴⁹ and Eisenberg et al.⁵⁰

wonder what will happen if his mother can no longer take care of him, or of herself. Mr A's mother may be experiencing a high degree of caregiver burden from caring for an adult child who is declining.

Consultation with a palliative care specialist could assist Mr A with the activities and issues that are most important to him. It is becoming more common for palliative care providers to see patients with chronic pain in the ambulatory setting.³⁸ A palliative care approach to this patient's chronic pain could include pharmacologic management, including opioids and drugs specifically targeted at peripheral neuropathy (ie, gabapentin, pregabalin, or other anticonvulsants); setting realistic

functional goals with the patient; using advanced therapeutic techniques such as cognitive behavioral therapy and motivational interviewing to help him achieve his goals; assessing the patient for cognitive decline and mood disorders such as depression and anxiety; and testing for hypogonadism, given the patient's frailty and declining muscle mass. Addressing the patient's declining health, planning for the future, treating his comorbidities and increasing frailty, and anticipating advanced care planning for an ailing parent are all part of the palliative care skill set.

Additionally, palliative care is provided in the context of an interdisciplinary approach, which includes nurs-

es, social workers, and chaplains with palliative care training or expertise. The focus of the palliative care team's efforts is not only on the patient but on the patient's entire family or support system. In the case of Mr A, team members could be involved in a variety of ways, including emotional and spiritual support to him and his mother, which is an often neglected but important part of decision making for patients with life-threatening illness,³⁹ and identifying community resources such as meal preparation programs or caregiver support.

Case 2: Retention and Adherence

Ms B is a 22-year-old African American woman who was diagnosed with HIV infection during a pregnancy 5 years ago and placed on antiretroviral therapy. She gave birth to a healthy, HIV-seronegative girl. Her CD4+ count at antiretroviral therapy initiation was 200 cells/mL and was 300 cells/mL with an undetectable viral load at the time she gave birth. She was encouraged to continue on antiretroviral therapy and was connected to a Ryan White HIV/AIDS Program clinic to receive ongoing HIV care. Ms B has suffered from addiction to cocaine since the age of 16 years. During her pregnancy, she lived in a recovery house and was able to deliver her baby cocaine-free. However, after giving birth, she suffered from depression and relapsed. Her daughter was removed from her care by social services and taken to live with the patient's parents. Despite numerous calls from the clinic social workers and other staff trying to locate her, Ms B disappeared from the clinic. When she reappeared a year later, it was at a dual diagnosis unit where she was hospitalized for depression and cocaine relapse. After discharge, she was referred back to the Ryan White clinic. Laboratory samples were drawn, and a 1-month follow-up visit to discuss reinitiation of antiretroviral therapy was scheduled. Ms B missed that visit and clinic staff were later notified that she was in the hospital again. She had been found unresponsive in a local park; her urine tested positive for cocaine, and a

lumbar puncture revealed an opening pressure of 30 cm and a white blood cell count of 100/ μ L. Her cerebrospinal fluid tested positive for cryptococcal antigen and an India ink stain showed yeast forms. She was hospitalized for 2 weeks, during which time she suffered from severe headaches, nausea, and vomiting. She received therapy with liposomal amphotericin and flucytosine and daily lumbar punctures. She was discharged with a prescription for fluconazole and an appointment to see her HIV care practitioner in 1 month to initiate antiretroviral therapy. She was readmitted after only 2 weeks, once again with a urine drug screen that tested positive for cocaine, a full bottle of fluconazole in her pocket, and a relapse of cryptococcal meningitis.

Commentary

This is an all too common scenario and is likely to cause distress not only for the patient and her family but for the medical team involved in the patient's care. This patient is young and has

the potential to be relatively healthy. Unfortunately, this patient has experienced a high burden of illness secondary to depression and substance abuse, which have impacted key health behaviors: retention in HIV primary care and adherence to antiretroviral therapy. She now has cryptococcal meningitis, which if not treated properly is universally fatal. Her prognosis could be excellent, but given her psychiatric and substance abuse comorbidities is likely poor.

Ms B's suffering is multifaceted. In palliative care, this is often conceptualized as "total pain," which includes suffering that is not only physical but also psychological, social, emotional, and spiritual.⁴⁰ She has a high burden of physical pain and nausea, which, regardless of their cause or the fact that they could have been prevented, can be treated with careful selection of analgesics and antiemetics (Table 2). The assessment and management of symptoms in a patient with altered mental status may be particularly complex but can be achieved. The patient's

Table 2. Mechanisms and Locations of Action of Common Antiemetic Therapies

Etiology	Pathophysiology	Therapy
Brain metastases, meningeal irritation	Increased intracranial pressure	Steroids
Movement	Vestibular stimulation	Anti-acetylcholine (scopolamine)
Anxiety	Cortical	Anxiolytics (benzodiazepines)
Medications (chemotherapy, opioids)	CTZ, vestibular stimulation	Antidopaminergics (haloperidol, metoclopramide), antihistamines (diphenhydramine, meclizine), serotonin antagonists (ondansetron), anti-acetylcholine
Motility (opioids, ileus, other medications)	Gastrointestinal	Prokinetic agents (metoclopramide), stimulant laxatives (sennosides)
Mechanical obstruction	Constipation, tumor, stricture	Manage constipation, surgery when appropriate, steroids, inhibit secretions with octreotide
Metabolic (hypercalcemia, hyponatremia, hepatic or renal failure)	CTZ	Antidopaminergics, antihistamines, fluids, steroids

CTZ indicates chemoreceptor trigger zone (medulla). Adapted from Glare et al⁵¹ and International Palliative Care Resource Center.⁵²

psychiatric illness and substance abuse are also likely to be contributing to her suffering and must be directly addressed; given the barriers to accessing mental health services in the United States, it is often difficult to address these issues. Ms B and her family may also experience a high degree of emotional and existential suffering, and even grief, over how their lives have been changed so dramatically by Ms B's illness.

These are complex issues that may be difficult to address in the context of an inpatient hospital stay. Two central themes of the palliative care approach are identifying the patient's and the family's goals of care, and identifying and treating their suffering, not only physical but spiritual, emotional, and psychosocial. This approach is especially well-suited to situations like Ms B's, which are both medically and socially complex. Communicating with patients about goals of care and suffering under such complex circumstances is often challenging; palliative care interdisciplinary team members must be highly skilled communicators. By understanding the patient's and family's goals, the palliative care team can help guide the patient, family, and other clinicians through complex medical decision making.

It is often necessary to call on psychiatric and addiction specialist colleagues to collaborate in cases when mental illness itself has become a barrier to effective HIV treatment. Regardless of the patient's goals of care, treatment of psychiatric illness and addiction as core causes of suffering is essential and must not be overlooked.

Case 3: Liver Failure in an HIV-Infected Patient

Mr D is a 55-year-old white man who was infected with HIV in his 30s when he injected heroin. He was diagnosed with HIV in 2002 and had a CD4+ count of 600 cells/ μ L. His hepatitis C virus (HCV) antibody test was also positive, with a viral load of 1 million IU/mL. Because of bouts of depression and alcohol abuse, he was deemed to be a poor candidate for HCV treatment

with peginterferon alfa and ribavirin and was not started on antiretroviral therapy owing to concerns about adherence. He was observed off antiretroviral therapy until 2009, when his CD4+ cell count was 300/ μ L, and his HCV viral load was 2 million IU/mL. His laboratory test results were unremarkable, except for a platelet count of 90/ μ L and an albumin level of 3 g/dL. At that time, he also had a liver ultrasound, which showed results consistent with cirrhosis. Mr D was started on antiretroviral therapy with emtricitabine, tenofovir, and efavirenz for his HIV infection, but due to his advanced liver disease, no HCV therapy was initiated. Over the subsequent 3 years, Mr D developed decompensated cirrhosis. Most troubling was the detection of large-volume ascites that caused the patient abdominal pain and shortness of breath, and hepatic encephalopathy, resulting in numerous hospital admissions and difficulty with his activities of daily living. Mr D also admits to drinking alcohol up until 3 months before his most recent visit and therefore is not a candidate for liver transplant. Mr D is estranged from his wife, whom clinic staff have tried unsuccessfully to locate. He has no other family and does not have a health care proxy.

Commentary

Cirrhosis leading to liver failure is the second most common cause of non-AIDS-related comorbidity and death in patients infected with HIV.^{41,42} This patient is not a transplant candidate, because of his alcohol use, and his decompensated cirrhosis and poor functional status make survival to the point of transplantation unlikely. This patient's prognosis is likely a life expectancy of only a few months. As with many patients in this type of situation, Mr D's HIV infection is well controlled, whereas his HCV infection is the primary driver of morbidity and ultimately mortality.

Palliative care involvement, during one of Mr D's many hospital admissions or in the outpatient setting, could be beneficial in several ways. Mr D's

symptom burden is high. The use of pharmacologic approaches to relieve his shortness of breath, such as low-dose opioids or benzodiazepines, is challenging for patients with liver disease but achievable with close monitoring. The addition of nonpharmacologic measures, such as forced oxygen treatment or a fan, yoga to help the patient with positioning, relaxation therapy, cognitive behavioral therapies, and paracentesis or peritoneal drain placement, may prove helpful. Addressing his symptoms may help the patient to focus on the things he wants to do during the last stage of his life, such as saying goodbye to the people who are close to him, addressing any outstanding financial issues, and achieving existential or spiritual closure.

Mr D has had bouts of depression and, until very recently, was actively drinking alcohol. Mood disorders and addiction are often ongoing sources of suffering for patients and their families near the end of life. Therefore, it is important to assess these issues, recognizing that the way they should be addressed may be different for patients who have a life-limiting illness than for those who do not; eg, engaging in recovery may not be feasible given the severity of illness; if life expectancy is very short, then a selective serotonin reuptake inhibitor may not be practical; and stimulants like methylphenidate may be used.⁴³ The interdisciplinary palliative care team, in collaboration with psychiatric and addiction specialists when appropriate, can help address the sources of suffering during the last phase of Mr D's life.

Identifying a health care proxy for patients with serious medical illness is extremely important, especially for patients where no "natural proxy" (ie, easily identifiable next of kin such as a spouse or partner) exists. Mr D should discuss with his proxy his medical condition and what his wishes might be should his condition worsen. The question of artificial nutrition and hydration (eg, a feeding tube) may arise, since Mr D's worsening condition will likely lead to an inability to swallow medications, including lactulose, or eat. The risks and benefits of such

interventions in dying patients must be carefully considered. The medical team should explore whether Mr D would like a team member to be present for his conversation with his health care proxy to assist with communication about these difficult issues. Many patients at the end of life also wish to communicate final thoughts with their families, such as “please forgive me,” “I forgive you,” “thank you,” “I love you,” and sometimes, “goodbye” (see <http://www.thefourthings.org>).

Finally, the question of if and when to stop antiretroviral therapy in patients like Mr D who are dying of a comorbidity, or in patients dying with AIDS, is a challenging one. Many factors must be taken into consideration, including pill burden, cost (especially if hospice care is being considered, as some hospices cannot afford to continue providing antiretroviral drugs), patient and family preference, adverse effects, and whether there are any remaining potential benefits of the medications.

Summary

Palliative care is a specialty that may be applied to the practice of HIV medicine in the current treatment era. Challenges faced by patients and practitioners, such as aging, multimorbidity, complex decision making for seriously ill patients with AIDS, and caring for patients with HIV infection who are dying of causes other than HIV, may be aided by a palliative care approach. These cases are meant to prompt discussion between HIV and palliative care practitioners about potential areas of clinical and research collaboration.

Acknowledgements

We thank Sarah Goodlin, MD, Associate Professor and Chief of Geriatrics, Portland VA Medical Center, Portland, Oregon, for her help in developing the concept for this paper and her review of an earlier version of the manuscript. □

Financial Affiliations: Dr Merlin has no relevant financial affiliations to disclose (Updated 3/5/13). Dr Tucker has no relevant financial affiliations to disclose (Updated 3/5/13).

Dr Saag has received research support from and has been a scientific advisor to Bristol-Myers Squibb, Gilead Sciences, Inc, Janssen Therapeutics, Merck & Co, Inc, and Viiv Healthcare. He has served as a scientific advisor and consultant for Vertex Pharmaceuticals and has received additional research support from Boehringer Ingelheim Pharmaceuticals, Inc, and GlaxoSmithKline (Updated 3/5/13). Dr Selwyn has no relevant financial affiliations to disclose (Updated 3/5/13).

References

- Centers for Disease Control and Prevention (CDC). HIV/AIDS among persons aged 50 and older. <http://www.cdc.gov/hiv/topics/over50/resources/factsheets/over50.htm>. Accessed February 5, 2013.
- Saag MS. HIV now firmly established in the Middle Ages. *Clin Infect Dis*. 2011;53(11):1140-1142.
- Deeks SG. Immune dysfunction, inflammation, and accelerated aging in patients on antiretroviral therapy. *Top HIV Med*. 2009;17(4):118-123.
- Breitbart W, McDonald M, Rosenfeld B, et al. Pain in ambulatory AIDS patients. I: Pain characteristics and medical correlates. *Pain*. 1996;68(2-3):315-321.
- Dobalian A, Tsao JC, Duncan RP. Pain and the use of outpatient services among persons with HIV: results from a nationally representative survey. *Med Care*. 2004;42(2):129-138.
- Harding R, Easterbrook P, Dinat N, Higginson IJ. Pain and symptom control in HIV disease: under-researched and poorly managed. *Clin Infect Dis*. 2005;40(5):491-492.
- 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;38:882-895.
- Tsao JC, Soto T. Pain in persons living with HIV and comorbid psychologic and substance use disorders. *Clin J Pain*. 2009;25(4):307-312.
- Aouizerat BE, Miaskowski CA, Gay C, et al. Risk factors and symptoms associated with pain in HIV-infected adults. *J Assoc Nurses AIDS Care*. 2010;21(2):125-133.
- Harding R, Lampe FC, Norwood S, et al. Symptoms are highly prevalent among HIV outpatients and associated with poor adherence and unprotected sexual intercourse. *Sex Transm Infect*. 2010;86(7):520-524.
- 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(5):638-645.
- 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.
- Newshan G, Bennett J, Holman S. Pain and other symptoms in ambulatory HIV patients in the age of highly active antiretroviral therapy. *J Assoc Nurses AIDS Care*. 2002;13:78-83.
- Ickovics JR, Hamburger ME, Vlahov D, et al. Mortality, CD4 cell count decline, and depressive symptoms among HIV-seropositive women: longitudinal analysis from the HIV Epidemiology Research Study. *JAMA*. 2001;285(11):1466-1474.
- Justice AC, Chang CH, Rabeneck L, Zackin R. Clinical importance of provider-reported HIV symptoms compared with patient-report. *Med Care*. 2001;39(4):397-408.
- Silverberg MJ, Jacobson LP, French AL, Witt MD, Gange SJ. Age and racial/ethnic differences in the prevalence of reported symptoms in human immunodeficiency virus-infected persons on antiretroviral therapy. *J Pain Symptom Manage*. 2009;38(2):197-207.
- Breitbart W, Rosenfeld BD, Passik SD, McDonald MV, Thaler H, Portenoy RK. The undertreatment of pain in ambulatory AIDS patients. *Pain*. 1996;65:243-249.
- Larue F, Fontaine A, Colleau SM. Underestimation and undertreatment of pain in HIV disease: multicentre study. *BMJ*. 1997;314:23-28.
- Breitbart W, Passik S, McDonald MV, et al. Patient-related barriers to pain management in ambulatory AIDS patients. *Pain*. 1998;76(1-2):9-16.
- Galvan FH, Burnam MA, Bing EG. Co-occurring psychiatric symptoms and drug dependence or heavy drinking among HIV-positive people. *J Psychoactive Drugs*. 2003;35(Suppl 1):153-160.
- Pence BW, Miller WC, Whetten K, Eron JJ, Gaynes BN. Prevalence of DSM-IV-defined mood, anxiety, and substance use disorders in an HIV clinic in the Southeastern United States. *JAIDS*. 2006;42(3):298-306.
- Gaynes BN, Pence BW, Eron JJ Jr, Miller WC. Prevalence and comorbidity of psychiatric diagnoses based on reference standard in an HIV+ patient population. *Psychosom Med*. 2008;70(4):505-511.
- Selwyn PA, Arnold R. From fate to tragedy: the changing meanings of life, death, and AIDS. *Ann Intern Med*. 1998;129(11):899-902.
- Antiretroviral Therapy Cohort Collaboration. Causes of death in HIV-1-infected patients treated with antiretroviral therapy, 1996-2006: collaborative analysis of 13 HIV cohort studies. *Clin Infect Dis*. 2010;50(10):1387-1396.
- Morrison RS, Meier DE. Clinical practice. Palliative care. *N Engl J Med*. 2004;350:2582-2590.
- Center to Advance Palliative Care. Defining palliative care. <http://www.capc.org/building-a-hospital-based-palliative-care-program/case/definingppl>. Accessed February 5, 2013.
- Rabow MW, Petersen J, Schanche K, Dibble SL, McPhee SJ. The comprehensive care team: a description of a controlled trial of care at the beginning of the end of life. *J Palliat Med*. 2003;6(3):489-499.
- Rabow MW, Dibble SL, Pantilat SZ, McPhee SJ. The comprehensive care team: a controlled trial of outpatient palliative medicine consultation. *Arch Intern Med*. 2004;164(1):83-91.
- Bekelman DB, Nowels CT, Allen LA, Shaker S, Kutner JS, Matlock DD. Outpatient palliative care for chronic heart failure: a

- case series. *J Palliat Med.* 2011;14(7):815-821.
30. Temel JS, Greer JA, Muzikansky A, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *N Engl J Med.* 2010;363(8):733-742.
 31. Kaldjian LC, Curtis AE, Shinkunas LA, Cannon KT. Goals of care toward the end of life: a structured literature review. *Am J Hosp Palliat Care.* 2008;25(6):501-511.
 32. Simms V, Higginson IJ, Harding R. Integration of palliative care throughout HIV disease. *Lancet Infect Dis.* 2012;12(7):571-575.
 33. Center to Advance Palliative Care. A state-by-state report card on access to palliative care in our nation's hospitals. <http://www.capc.org/reportcard/summary>. Accessed February 5, 2012.
 34. Merlin JS, Westfall AO, Raper JL, et al. Chronic pain, psychiatric, and substance abuse comorbidities: implications for adherence to HIV care, ART, and virologic suppression. International Workshop on HIV Observational Database. March 29-31, 2012; Athens, Greece.
 35. Lampe FC, Harding R, Smith CJ, Phillips AN, Johnson M, Sherr L. Physical and psychological symptoms and risk of virologic rebound among patients with virologic suppression on antiretroviral therapy. *JAIDS.* 2010;54(5):500-505.
 36. Evans S, Fishman B, Spielman L, Haley A. Randomized trial of cognitive behavior therapy versus supportive psychotherapy for HIV-related peripheral neuropathic pain. *Psychosomatics.* 2003;44(1):44-50.
 37. Chou R, Fanciullo GJ, Fine PG, et al. Clinical guidelines for the use of chronic opioid therapy in chronic noncancer pain. *J Pain.* 2009;10:113-130.
 38. Merlin JS, Childers J, Arnold RM. Chronic pain in the outpatient palliative care clinic. *Am J Hosp Palliat Care.* 2012;doi:10.1177/1049909112443587
 39. Kaldjian LC, Jekel JF, Friedland G. End-of-life decisions in HIV-positive patients: the role of spiritual beliefs. *AIDS.* 1998;12(1):103-107.
 40. Clark D. 'Total pain', disciplinary power and the body in the work of Cicely Saunders, 1958-1967. *Soc Sci Med.* 1999;49(6):727-736.
 41. Joshi D, O'Grady J, Dieterich D, Gazzard B, Agarwal K. Increasing burden of liver disease in patients with HIV infection. *Lancet.* 2011;377(9772):1198-1209.
 42. Weber R, Sabin CA, Friis-Møller N, et al. Liver-related deaths in persons infected with the D:A:D study. *Arch Intern Med.* 2006;166(15):1632-1641.
 43. Passik SD, Theobald DE. Managing addiction in advanced cancer patients: why bother? *J Pain Symptom Manage.* 2000;19(3):229-234.
 44. Hahn K, Arendt G, Braun JS, et al. A placebo-controlled trial of gabapentin for painful HIV-associated sensory neuropathies. *J Neurol.* 2004;251:1260-1266.
 45. Simpson DM, Schifitto G, Clifford DB, et al. Pregabalin for painful HIV neuropathy: a randomized, double-blind, placebo-controlled trial. *Neurology.* 2010;74:413-420.
 46. Kieburts K, Simpson D, Yiannoutsos C, et al. A randomized trial of amitriptyline and mexiletine for painful neuropathy in HIV infection. *Neurology.* 1998;51(6):1682-1688.
 47. Shlay JC, Chaloner K, Max MB, et al. Acupuncture and amitriptyline for pain due to HIV-related peripheral neuropathy: a randomized controlled trial. *JAMA.* 1998;280(18):1590-1595.
 48. Brown S, Simpson DM, Moyle G, et al. NGX-4010, a capsaicin 8% patch, for the treatment of painful HIV-associated distal sensory polyneuropathy: integrated analysis of two phase III, randomized, controlled trials. *AIDS Res Ther.* 2013;10(1):5.
 49. Estanislao L, Carter K, McArthur J, Olney R, Simpson D. A randomized controlled trial of 5% lidocaine gel for HIV-associated distal symmetric polyneuropathy. *J Acquir Immune Defic Syndr.* 2004;37:1584-1586.
 50. Eisenberg E, McNicol E, Carr DB. Opioids for neuropathic pain. *Cochrane Database Syst Rev.* 2006;3:CD006146.
 51. Glare P, Miller J, Nikolova T, Tickoo R. Treating nausea and vomiting in palliative care: a review. *Clin Interv Aging.* 2011;6:243-259.
 52. International Palliative Care Resource Center. Education in palliative and end-of-life care for oncology module. Available at: <http://www.ipcrc.net/who-education-epec-oncology.php>.
 53. World Health Organization. Cancer pain relief and palliative care. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser.* 1990;804:1-75..01

Top Antivir Med. 2013;21(1):20-26

©2013, IAS–USA

Topics in Antiviral Medicine™

Continuing Medical Education

Continuing medical education (CME) enduring material in this issue: Merlin JS, Tucker RO, Saag MS, Selwyn PA. The Role of Palliative Care in the Current HIV Treatment Era in Developed Countries. *Top Antiviral Med.* 2013;21(1):20-26

Overview

- CME credits available: 1.25 *AMA PRA Category 1 Credits™*
- Release date: March 29, 2013
- Expiration date: March 29, 2014

This enduring material provides a review of the role of palliative care in the current HIV treatment era. To complete the activity, read the article, successfully complete the posttest, submit the evaluation, and complete and submit the CME claim form. To claim CME credit, submit the claim form online or, for paper copies, via fax or mail.

The IAS–USA offers this state-of-the-art activity as part of a nationwide CME effort for physicians on the evolving challenges of managing HIV disease.

Learning Objectives

On completion of this activity, the learner will be able to:

- Describe the role of palliative care in contemporary HIV care
- Recognize opportunities for integration of palliative care with disease-specific care for patients with HIV throughout the course of disease
- List opportunities for dialogue between HIV and palliative care clinicians and researchers about ways to reduce HIV-infected patients' suffering and improve their physical function and quality of life

Intended Audience

This enduring material is designed for physicians who are actively involved in the medical care of people with HIV infection, specifically those who:

- Have a solid, working knowledge of HIV disease management
- Provide comprehensive or specialty care for patients with HIV infection
- Are currently active in HIV research

This activity is also relevant for other practitioners, including nurse practitioners, nurses, physician assistants, pharmacists, and others.

CME Information

The International Antiviral Society–USA (IAS–USA) is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The IAS–USA designates this enduring material for a maximum of 1.25 *AMA PRA Category 1 Credits™*. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

This CME activity is offered from March 29, 2013 to March 29, 2014. Participants who successfully complete the activity posttest and submit the evaluation and registration forms are eligible to receive CME Credit. Physicians (MDs, DOs, and international equivalents) may receive CME credit for completing this activity. Other health care practitioners will receive a certificate of participation.

To take the test online, please go to:

<https://www.iasusa.org/content/tam-volume-21-issue-1-cme-posttest>

Disclosure of Financial Interests

In the interest of maintaining the independence of its CME activities, and in accordance with the policies of the Accreditation Council for Continuing Medical Education (ACCME), the IAS–USA requires all persons with control of content (ie, faculty, IAS–USA Board members, and program staff) to disclose any financial relationships that they (or their spouses or partners) have had with commercial companies within the past 12 months. Any real or apparent conflicts of interest of those parties are resolved prior to the continuing medical education activity being delivered. Individuals who refuse to disclose financial interests may not participate in an IAS–USA CME activity.

Financial Affiliations: Drs Merlin, Tucker, and Selwyn have no relevant financial affiliations to disclose (Updated 3/5/13). Dr Saag has received research support from and has been a scientific advisor to Bristol-Myers Squibb, Gilead Sciences, Inc, Janssen Therapeutics, Merck & Co, Inc, and ViiV Healthcare. He has served as a scientific advisor and consultant for Vertex Pharmaceuticals and has received additional research support from Boehringer Ingelheim Pharmaceuticals, Inc, and GlaxoSmithKline (Updated 3/5/13). Dr Richman has been a consultant to Biota, Bristol-Myers Squibb, Chimerix, Gen-Probe Inc, Gilead Sciences, Inc, Merck & Co, Inc, and Monogram Biosciences, Inc. He has held stock options for Chimerix (Updated 3/27/13). Dr Benson has no relevant financial affiliations to disclose (Updated 4/1/13). Dr Benson's spouse, Dr Robert T. Schooley, has served as a scientific advisory board member for Gilead Sciences, Inc, Monogram Biosciences, and Globelmmune, Inc. He has served as scientific collaborator for MBio Diagnostics. He has received grant support from Boehringer Ingelheim and Bristol-Myers Squibb. He has stock in Globelmmune, Inc. He has served as a consultant to Merck & Co, Inc, and Santaris Pharma A/S (Updated 3/27/13). Dr Hirsch has no relevant financial affiliations to disclose (Updated 3/27/13). Ms Jacobsen has no relevant financial affiliations to disclose (Updated 3/22/13).

Grant Support

This HIV activity is funded through independent, educational grants at a national level from commercial organizations that are committed to supporting high-quality continuing medical education (CME). We gratefully acknowledge the supporters of the 2013 *Improving the Management of HIV Disease* CME program.

This activity is part of a national effort that includes this and other live CME courses, live course webcasts, *Cases on the Web*, and *Topics in Antiviral Medicine™*. In the interest of an objective, unbiased, balanced, and scientifically rigorous program, the IAS–USA seeks and pools funding from companies with competing products to support the program. These companies have no input into or control over the program content or the selection of faculty.

Supporters of the 2012 *Improving Management of HIV Disease* and *Management of Hepatitis C Virus in the New Era* national programs can be found at www.iasusa.org.

PLATINUM
AbbVie

Gold
ViiV Healthcare

Silver
Merck & Co, Inc
Janssen Therapeutics
Bristol-Myers Squibb
Gilead Sciences, Inc

Drug and Product Disclaimer

This activity may contain information about the investigational uses of drugs or products that are not approved by the US Food and Drug Administration. Please consult full prescribing information before using any medication or product mentioned in this activity.

The views and opinions expressed herein are those of the faculty and do not necessarily represent the opinions or recommendations of the IAS–USA.

Contact Information

If you have any questions about this activity, please contact the IAS–USA.

E-mail: journal@iasusa.org

Phone: 415-544-9400

Mail: IAS–USA

425 California Street, Suite 1450

San Francisco, CA 94104-2120

CME Posttest

This posttest and the associated CME credit claim form can be completed online at www.iasusa.org.

Readers who do not have internet access and need to take the test on paper (below) should check the box next to the correct answer to each question and complete the following evaluation form. To earn CME credit, readers must receive a passing score of 80% or higher.

1. Palliative care is best described as:
 - A. Care for patients in the end stages of a terminal illness
 - B. Synonymous with hospice care
 - C. Alleviating suffering while maximizing physical function
 - D. Only available in inpatient settings
2. In the context of an aging HIV-infected patient with multiple medical comorbidities, a palliative care consultant should provide input and guidance on all of the following except:
 - A. Physical and emotional symptoms
 - B. Advanced care planning
 - C. Interdisciplinary team support that includes nurses, social workers, and chaplains to assess and address the needs of the patient and family
 - D. Antiretroviral therapy selection
3. In the context of an HIV-infected patient who has struggled with adherence to antiretroviral therapy and is dying with AIDS, a palliative care consultant should provide input and guidance on all of the following except:
 - A. Antiretroviral therapy adherence
 - B. The patient's goals of care, and complex medical decision making
 - C. Physical, psychological, social, emotional, and spiritual aspects of suffering
 - D. Psychiatric illness and addiction, in collaboration with specialists in these areas
4. End-stage cirrhosis in HIV-infected patients is best described as:
 - A. An opportunity for palliative care consultation, to help with symptom burden and end-of-life care issues
 - B. An uncommon cause of morbidity and mortality
 - C. Not associated with symptoms such as pain or shortness of breath
 - D. A contraindication to prescribing opioids and benzodiazepines
5. End-of-life care issues in HIV-infected patients that merit attention include all of the following except:
 - A. Advanced care planning, including identifying a health care proxy
 - B. Mood disorders and addiction
 - C. Risks and benefits of procedures such as the insertion of a feeding tube
 - D. If and when to stop antiretroviral therapy
 - E. Counseling patients to continue taking antiretroviral therapy

To claim CME credit, please successfully complete the posttest and evaluation form, which will help us evaluate this activity and plan future activities. Your responses will not affect your CME credit. Fill out the test and the evaluation online at www.iasusa.org or mail or fax this page along with the completed test to: IAS–USA, 425 California Street, Suite 1450, San Francisco, CA 94104-2120; Fax: (415) 544-9401

Participant Information

Number of CME credit hours I am claiming (maximum 1.25): _____

Please indicate your academic degree or license:

MD DO PA RN NP PharmD other (specify) _____

First Name _____ MI _____ Last Name _____

Institution or Organization _____

Address (Please check one: Home Work) _____

Telephone (Home Work) _____ Fax _____

Address (2nd Line) _____

E-mail address to receive your CME certificate (Home Work) _____

City _____ State/Province _____

What is the setting of your current work? Select ONE:

Solo practice Hospital-based Managed care organization

Clinical research Group practice Clinics/sessional work

Laboratory research Commercial company Corrections

Community-based health center/clinic Government

Other (please specify): _____

Postal Code _____ Country _____

Evaluation

Please rate this activity in terms of meeting each of its stated objectives.

	Excellent	Very Good	Good	Fair	Poor
Describe the role of palliative care in contemporary HIV care	<input type="radio"/>				
Recognize opportunities for integration of palliative care with disease-specific care for patients with HIV throughout the course of disease	<input type="radio"/>				
List opportunities for dialogue between HIV and palliative care clinicians and researchers about ways to reduce HIV-infected patients' suffering and improve their physical function and quality of life	<input type="radio"/>				

How challenging was this activity? Highly challenging Sufficiently challenging Insufficiently challenging

Please rate this activity based on:

	Excellent	Very Good	Good	Fair	Poor
Quality of this activity overall	<input type="radio"/>				
Overall value of this activity to your practice or responsibility	<input type="radio"/>				
The extent to which the information presented was supported by the evidence	<input type="radio"/>				
Freedom from commercial bias	<input type="radio"/>				

Do you expect to make changes in your clinical practice based on the information presented in this activity? Yes No

If so, please list 3 measurable changes you expect to make:

- _____
- _____
- _____

Other comments (please feel free to comment on any aspect of this enduring material or *Topics in Antiviral Medicine*TM):

How many HIV-infected patients do you personally manage?

None 1–4 5–10 11–15 16–50 51–100 101–200 More than 200

How many HIV-infected patients are in your clinic overall?

None 1–4 5–10 11–15 16–50 51–100 101–200 More than 200

Please rate your expertise in treating HIV infection: 1 (novice) 2 3 4 5 (expert)