

# Fatigue Symptom Management in People Living With Human Immunodeficiency Virus

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Fatigue is a subjective, unpleasant, potentially disabling symptom rooted in physiological, psychological, and behavioral causes. People living with human immunodeficiency virus (HIV) are a population highly affected by fatigue because of risk factors associated with HIV infection, treatment, and psychosocial disease burden. People with HIV are living longer and are facing the challenge of a longer disease trajectory. Palliative nurses with expertise in symptom management can play a crucial role in helping people with HIV to engage in health behaviors that prevent or mitigate fatigue. In this article, the authors present a definition and overview of fatigue, describe the problem of fatigue in people living with HIV, and present a case study that illustrates the role of the palliative nurse in helping a person with HIV to cope with fatigue.

Key Implications for Palliative Care Nurses:

- People living with HIV are at high risk for fatigue because of cardiovascular and metabolic changes that occur as a result of HIV infection and treatment.
- Fatigue is a multidimensional symptom that includes physical sensation changes and changes in thought processes and awareness, and it can affect behavioral and social function.
- Palliative care nurses with expertise in symptom management can advocate for people living with HIV by facilitating necessary clinical assessments and referrals and can help people with HIV address

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physiological, psychological, and behavioral factors that cause fatigue through holistic care planning with patients.

### **KEY WORDS:**

fatigue, HIV, palliative, symptom management

#### **FATIGUE**

Fatigue is a subjective, unpleasant, potentially disabling symptom characterized by physical and/or psychological exhaustion, experienced both acutely and chronically, that results to impaired function. In states of fatigue, individuals experience an imbalance between their available physical and psychological resources and the resources required for optimal functioning. Fatigue has been associated with depression, chronic disease states, prolonged exertion, stress, sleep disturbance, and inactivity. Although fatigue is often discussed in the context of physical weakness and sleepiness, it is a multidimensional symptom that also affects judgment, decision making, motivation, and awareness.

# FATIGUE IN PEOPLE LIVING WITH HUMAN IMMUNODEFICIENCY VIRUS

Fatigue affects nearly 90% of people living with human immunodeficiency virus (PLWH)<sup>3</sup> and has been reported as one of the most persistent and troubling symptoms they experience. Although a direct link between HIV and fatigue remains elusive,<sup>3</sup> PLWH have an elevated risk of fatigue related to hematologic and metabolic changes that are direct results of HIV infection and treatment, as well as psychological and psychosocial stressors that have been linked with high fatigue symptom burden<sup>2,4,5</sup> (Figure).

Physiological factors: Anemia (generally defined as hemoglobin <13 in men and <12 in women) is common in PLWH, affecting more than 70% of individuals with HIV. <sup>4,6</sup> Anemia in PLWH is multifactorial and can be caused by chronic inflammation, medication side effects, opportunistic infections, and disrupted red blood cell production in the bone marrow. <sup>6,7</sup> Anemia decreases the body's ability to deliver oxygen to the tissues and results in physical weakness,



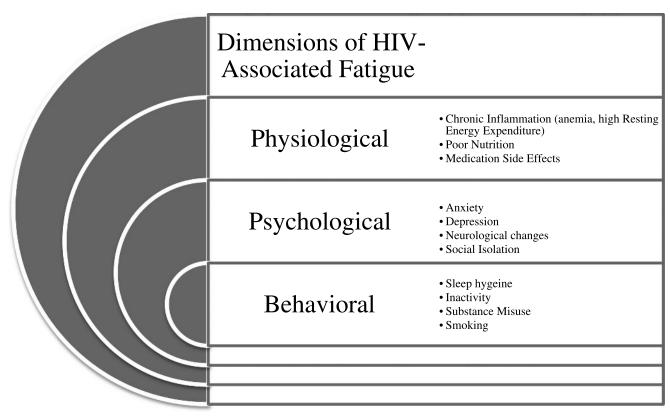


FIGURE. Dimensions of HIV-associated fatigue. 1,3,8-10,14,15,17,18,20,27

exhaustion, and fatigue<sup>4,8</sup> (eg, muscle weakness, exhaustion). Nutritional deficiencies in PLWH have been associated with fatigue and are caused by multiple factors including high resting energy expenditure, poor absorption of nutrients, and structural challenges related to food access. Resting energy expenditure (aka resting metabolic rate) is the amount of energy (kilocalories) expended by the body while at rest. PLWH live with chronic inflammation, which causes their bodies to expend a greater amount of energy than someone who does not have HIV. 9 When energy expenditure is high, the body demands a corresponding increase in nutrients to carry out its normal function and to maintain a healthy weight. When these increased demands are not met, a person can experience profound weight loss, wasting, weakness, and fatigue. <sup>9</sup> The problem of adequate nutrition is further exacerbated by a decreased ability to absorb nutrients due to compromised gut integrity because of intestinal inflammation. 10 Furthermore, PLWH are at high risk for food insecurity, a structural challenge that can lead to an inability to access and subsequently take in adequate nutrition. <sup>11</sup> Another physiological mechanism of fatigue is related to endocrine dysfunction, including adrenal, gonadal, and thyroid dysfunctions. 1,3 Although exact mechanisms that connect HIV to endocrine dysfunction are not well understood, current theories suggest a multifactorial cause including direct effects of HIV infection on endocrine organs and indirect effects of inflammation.<sup>12</sup> Hormone imbalances disproportionately affect PLWH and cause fatigue through decreased production of testosterone (hypogonadism, particularly in men), adrenal insufficiency, and hypothyroidism.<sup>13,14</sup> Fatigue has also been linked to certain HIV medications (most commonly efavirenz [Sustiva]) that cause poor sleep quality because of vivid dreams or insomnia.<sup>1,15</sup> Finally, fatigue in PLWH may be the result of co-occurring illness including opportunistic infections or comorbid conditions, particularly those that require additional pharmacological treatment.<sup>3</sup>

Psychological factors: Anxiety and depression are common in PLWH, with anxiety affecting more than  $30\%^{16}$  of PLWH. PLWH have an elevated risk for anxiety disorders due to social stigma, uncertainty regarding their disease, and issues of disclosure, and social isolation may contribute to fatigue. <sup>17</sup> First, anxiety has been associated with higher levels of sleep disturbance among PLWH, predisposing them to fatigue due to inability to get adequate rest. <sup>17</sup> Furthermore, medications used to treat anxiety (eg, benzodiazepines) may induce fatigue by activating  $\gamma$ -aminobutyric (GABA) receptors resulting in a sedative effect that causes drowsiness and somnolence. <sup>18</sup>

Depression is arguably the most-well-documented link between HIV and fatigue, affecting up to 80% of PLWH. <sup>16</sup> Depression and depressive symptoms have been associated with low quality of life and poor adherence to HIV treatment. <sup>16,19</sup> Depression among PLWH is rooted in



biological mechanisms (decreased monoaminergic function, HIV-associated neurotoxicity) and psychosocial stressors (long-term disease burden, stigma). 16,20 A cyclical relationship between depression and fatigue is set in motion when these biological and/or psychosocial sources of depression form a pathway to fatigue (eg, decreased motivation and activity, 16,19 excessive or deficient sleep<sup>19</sup>), which in turn exacerbate depressive symptoms that lead to further fatigue.<sup>21</sup> Compounding this problem are disparities in depression treatment among PLWH, particularly among highly-affected racial/ethnic minority groups. 16 Without access to treatment, depression and its associated symptoms (including fatigue) persist 16 and can disrupt an individual's ability to achieve viral suppression and a stable immune system. 19 Fatigue is also seen in PLWH who are receiving treatment for both HIV and depression because sleep disturbance and insomnia are side effects of antiretrovirals 15 and antidepressants. 18

Behavioral factors: Behavioral factors that contribute to fatigue in PLWH often contain both physiological and psychosocial components. Physical activity is a widely recommended health behavior that has demonstrated potential to combat fatigue in PLWH. <sup>22</sup> Webel et al<sup>22</sup> found that PLWH who engage in higher levels of physical activity reported 17% less fatigue than those who were more sedentary. <sup>22</sup> Paradoxically, increasing physical activity may offer a solution to lower the severity of fatigue for PLWH, but fatigue symptom experience (psychological dimension) may diminish an individual's perceived ability to be physically active. <sup>23</sup> Researchers continue to seek out solutions to this problem through interventions designed to change behaviors that promote increased physical activity in PLWH. <sup>24-26</sup>

One of the most prominent behavioral factors contributing to fatigue is poor sleep hygiene. 27,28 Sleep disturbances are common in PLWH, affecting between 30% and 100% of PLWH, <sup>28</sup> and can manifest in a lack or poor quality of sleep. 5,28,29 Inability to sleep results from physiological factors including the effect of HIV on the central nervous system, <sup>28</sup> medication side effects (eg, vivid dreams, neuropathy), 15,29 and effects of stimulant intake (eg, nicotine, caffeine, amphetamines)<sup>28,29</sup> or from psychological factors that impede restful sleep (eg, anxiety and stress). 17,30 In addition to inability to sleep, the aforementioned factors can diminish the quality of sleep resulting in experiences of physical and mental fatigue, depression, and excessive daytime sleepiness. 5,28,29 Finally, PLWH may turn to the use of substances or caffeine intake to help them sleep or to cope with fatigue or psychological symptoms,<sup>2</sup> but studies have found that such actions often exacerbate sleep disturbances thus perpetuating fatigue rather than eliminating it.

### ASSESSMENT OF FATIGUE

Fatigue assessment is a crucial component of an HIV care plan that allows clinicians to understand patient-specific circumstances and conditions that lead to fatigue symptom experiences. As explained in a review by Barroso and Voss, <sup>1</sup> accurate assessments of fatigue are challenging because of limitations in how fatigue is measured. Measures may be unidimensional, only assessing certain aspects of fatigue (eg, frequency, intensity, or functionality). For example, the widely used Fatigue Severity Scale<sup>31</sup> primarily addresses the effect of fatigue on functionality without regard to intensity (despite its name). Furthermore, scales may have primarily been tested and may have validated some populations (eg, cancer patients) but may not capture specific aspects of people living with other illnesses. Even though patients may primarily be focused on the physical dimension of fatigue, failure to assess fatigue as a multidimensional symptom results in a limited ability to adequately address fatigue. Barroso and Lynn<sup>32</sup> addressed these limitations by creating the HIV-related fatigue scale, a validated fatigue measure for the assessment of the intensity of fatigue, responsiveness to fatigue circumstances, and fatigue-related functional impairment in PLWH. The scale is ideal for determining how fatigue is affecting the activities of daily living and mental and social functioning.

Proactive patient involvement in fatigue assessment through daily recording (eg, journaling) can provide invaluable information for clinician understanding of symptoms, including fatigue. Mobile health technology has made it possible for people to record their symptoms in real time through smartphone applications and short message service. Although much of the mobile health research in PLWH has been focused on medication adherence, it may prove to be an innovative and useful way to track and manage symptoms, and research into the uses of mobile technology in PLWH is ongoing.

### MANAGEMENT OF FATIGUE

Once clinicians have been able to assess and measure fatigue, they are faced with the challenge of determining the best course of action to treat and help patients manage fatigue. Clinical and pharmacological options include supplements to address hormone imbalances and anemia (when blood loss is not indicated) and to improve nutritional deficiencies that cause fatigue and stimulant medications to directly treat fatigue symptoms. 1 Although these measures have been effective in alleviating fatigue symptoms in PLWH, little is known about how effective they are long term. 1 Nonpharmacological interventions, particularly engagement in health behaviors (stress reduction, exercise), 22 have also been effective in alleviating fatigue symptoms and have strong potential to be effective long-term solutions for addressing fatigue in chronic illness. Furthermore, Webel et al<sup>27</sup> found that a diet and an exercise self-management intervention resulted in improved sleep hygiene in PLWH. Palliative nurses can play a pivotal role, as healthcare team members



and directly with patients to recommend supplementation and nutritional consultation, educate patients on how to integrate health behaviors that will decrease inflammation, promote daytime energy through activity, and encourage rest planning and healthy sleep patterns, ultimately improving fatigue symptoms.

The following case study illustrates the potential role of palliative care integration in helping an individual living with HIV and suffering from fatigue.

### **CASE STUDY**

Sam is a 41-year-old white man living with HIV who is receiving care at an urban university-based infectious disease clinic specializing in the care of PLWH. He received a diagnosis of HIV 1 year ago and presents to his regular clinic appointment with his brother whom he has lived with since HIV was diagnosed. He has attended all scheduled appointments and adhered to his antiretroviral medication regimen. His appearance is unkempt, and he is tearful, stating "I cannot keep going like this; I am so tired all the time, I can't do anything anymore." His brother adds that he "doesn't do anything anymore, he never eats—just snacks, drinks coffee, and smokes cigarettes" and "sleeps most of the day and is up all night on his computer." He denies alcohol use, is a 20-pack-year smoker and occasionally takes a psychostimulant medication (dextroamphetamine/ amphetamine, Adderall) that he buys from a friend to "get some energy to go out" but that this is rare. His laboratory test results indicate an undetectable HIV-1 RNA viral load and normal CD4+ T-lymphocyte count. All laboratory values including hemoglobin and hematocrit, basic metabolic panel, thyroid-stimulating hormone, and testosterone levels were within normal limits. Sam reports that he has not visited with his case manager because he "doesn't need her." His provider has requested a palliative care consultation for symptom management. On review, the palliative care nurse notes that he reported 8 of 10 on a basic fatigue assessment and a Beck Depression Inventory<sup>35</sup> score of 20 of a possible 63 at this visit. The Beck Depression Inventory asks 21 questions with answers ranging from "0" (not experiencing) to "3" (an extreme level of experience of symptom) to assess the intensity, severity, and depth of depressive symptoms (eg. sadness, hopelessness). Higher scores indicating more severe depression, with Sam's score indicating he is experiencing moderate depression at the time of this assessment.<sup>35</sup>

Sam's fatigue is likely because of multiple factors including, but not limited to, physiological factors such as HIV medication side effects and poor nutrition; psychological factors including depression and anxiety; and behavioral factors including substance misuse, poor sleep hygiene, smoking, inactivity, and excessive caffeine. The normal hemoglobin and hematocrit, testosterone, and thyroid-stimulating hormone levels rule out a hematologic or hormonal cause,

and the self-reported substance use (eg, marijuana, amphetamines, caffeine, nicotine) provide insight into Sam's difficulty in achieving restful sleep. The palliative care nurse wants to gather more information about Sam's fatigue that has not been captured from the basic rating scale. Sam completes the HIV-related fatigue scale which indicates poor responsiveness to fatigue circumstances, including high disruption to daily activities and high levels of social and mental functioning. Based on these findings, the palliative care nurse develops the following care plan.

### **Symptom Management Plan**

- Provide Sam with encouragement, emphasizing his strengths including his adherence to medication and achievement of an undetectable viral load; moreover, focus on reinforcing that there are potential solutions to the problem of fatigue.
- Educate Sam on the benefits of working with case management, emphasizing that case managers help to coordinate patient care, keep patients connected within the healthcare setting, and help patients solve unexpected problems. Ensure that Sam knows that having a case manager does not suggest that he is not independent, but that the case manager is someone he can work with on health-related matters including venues of care and healthcare financing.
- Educate Sam on sleep hygiene, emphasizing that rest periods are important, but sleeping throughout the day will make it difficult to sleep at night and perpetuates the cycle of fatigue. The palliative care nurse can provide the patient with educational and interactive resources from the American Sleep Association at https://www.sleepassociation.org.
- Sam has some high-risk behaviors that likely have a direct relationship to fatigue, particularly his use of amphetamines, nicotine, and caffeine. In a judgment-free manner, express understanding of his desire to take substances that make him feel energized, but remind him that although caffeine, nicotine, and amphetamines may appear to provide energy they actually drain the body's resources more quickly, interfere with sleep, and can contribute more to fatigue than they prevent. The palliative care nurse can suggest stopping all caffeine intakes after noon and encourage Sam to stop taking amphetamines because of their high addiction potential and adverse psychological effect when not taken as prescribed.
- Sam's diet, particularly the snacking behaviors and lack of intake of nutritious food, is of particular concern to his overall health and may be a major contributor to his fatigue. The palliative care nurse can provide Sam with resources such as the Veteran's Association Web site on nutrition for people with HIV/AIDS (www.hiv.va.gov/patient/daily/diet/index.asp) and review the information with him. The palliative care nurse should help Sam with meal planning emphasizing preparation of foods in



advance and including food choices that Sam likes that contain adequate amounts of calories, protein, fruits, vegetables, and water.

- Work with Sam on a plan to increase physical activity, beginning with lower intensity activities (eg, walking), and encourage incremental increases in intensity (eg, calisthenics) as tolerated. Emphasize that engaging in any form of exercise is better than none.
- Present Sam with options for smoking cessation, being careful not to seem judgmental or intolerant of smoking behavior. The palliative care nurse should emphasize Sam's ability to take steps to reduce and eventually quit smoking, highlighting that each step he takes to cut back on smoking can improve energy levels and help him get restful sleep. Furthermore, the palliative care nurse can refer Sam to the AIDS.gov smoking cessation Web site, which offers help including social support (eg, via Internet and phone support groups), smartphone application recommendations, and smoking cessation information materials to PLWH to quit smoking.
- Refer Sam to a local support group for PLWH if available, which may help him to find others he relates to and prevent social isolation related to HIV and his symptoms. If no such support group exists in the area, Web-based resources such as Poz (www.poz.com) and The Body (www.thebody.com) contain informational and social support resources that Sam can explore to learn more about HIV and hear the stories of others living with HIV.
- Encourage Sam to keep a fatigue diary or use a symptom tracking smartphone application (eg, trakmyhealth [www.trakmyhealthapps.com]) that will help him identify time points and specific contexts associated with his fatigue, will be an invaluable resource in future clinical interactions, and will provide a tangible source from which Sam can identify improvements and setbacks with his health.
- Set up weekly phone calls for 1 month to provide Sam with support in the proposed changes.

### Three-Month Follow-up

At Sam's next appointment, his appearance is much improved. He has been in regular contact with a case manager who has connected him with a local HIV support group that meets 2 nights each week and does a group walk every weekend. In addition to support group meetings, he has started volunteering 3 days each week answering phones at the organization's central office. He reports that he and his brother have started cooking meals for the week each Sunday, and they are working together on eating healthy. His fatigue journal helped him realize that he was sleeping primarily during the midafternoon, often when he feels overwhelmed and frustrated by his current life situation. He states that although he often needs to rest he does something to busy himself so he does not fall asleep during

the day and so he can sleep through the night. His Beck Depression Inventory<sup>35</sup> and HIV-Related Fatigue Scale<sup>32</sup> scores have both decreased, and he states that he feels like he is doing something that helps himself and others by being involved with the support network. Finally, he states that he is working on not drinking caffeine after noon and is using the Web resources to help him cut down on cigarette smoking, learn more about how he can better his health, and connect with other people living with HIV.

### **SUMMARY**

In this article, the authors have provided an overview of fatigue in PLWH and have illustrated potential nursing interventions to help a person living with HIV who is experiencing fatigue. Sam's palliative care nurse addressed his fatigue holistically, providing interventions and referrals consistent with physiological, psychological, and behavioral factors that cause fatigue. Thorough assessment with validated measures and interventions designed to address the multiple dimensions of fatigue will yield the best results when helping patients to reduce fatigue. Scientists and clinicians are still learning about the implications of long-term infection with HIV; but in this article, the authors have demonstrated the potentially disabling effects of fatigue. Palliative care nurses will continue to play an increasingly pivotal role in the care of PLWH as this population ages. Expertise in symptom management will be crucial to helping PLWH to achieve high quality of life and optimal health as they age.

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