Aerobic Exercise Dysfunction in Human Immunodeficiency Virus: A Potential Link to Physical Disability

Approximately 282,000 adults, adolescents, and children are currently living with human immunodeficiency virus (HIV) infection or acquired immunodeficiency syndrome (AIDS) in the United States as of the year 2002. With the advent of highly active antiretroviral therapy (HAART), the life span of these individuals has dramatically increased, and HIV infection is now considered a chronic illness with accompanying episodes of exacerbations and remissions of symptoms. Numerous conditions such as lipodystrophy syndrome and skeletal myopathy have been associated with HIV and its medical management, many of which may result in physical disability and diminished quality of life. Due to the chronic nature of this condition, physical therapists will continue to manage many of these conditions in increased numbers of people who are living with HIV. Although guidelines for physical therapy evaluation and management of this potentially disabling condition have not been established, it appears that aerobic exercise training may have a beneficial effect on the cardiorespiratory health of people who are living with HIV. Thus, an understanding of the factors that limit the oxidative metabolic response to physical activity is paramount in developing effective exercise training programs for people with this virus. The focus of this Update is to examine the biological factors that might limit the oxidative metabolic response to physical activity in people with HIV.


Key Words: Antiretroviral therapy, Disability, Physical activity.

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Features of Fatigue and Physical Disability

HIV-related disability has been associated with fatigue and decreased physical functioning\textsuperscript{10–13} as well as other factors that may limit people’s ability to carry out necessary life activities.\textsuperscript{12,14,15} Fatigue in adults with HIV has been identified using patient self-reports of physical and functional limitations while performing activities of daily living such as housework, climbing stairs, and walking\textsuperscript{15} and activities required for employment.\textsuperscript{10,11} Asymptomatic HIV infection is defined as having no symptoms or as having symptoms related only to acute primary HIV infection, such as persistent generalized lymphadenopathy (swollen and firm lymph glands).\textsuperscript{11} Thirty-one percent of men and 53% of women with asymptomatic HIV infection have reported at least one limitation to physical activity as a result of fatigue.\textsuperscript{11} Among those with symptomatic HIV infection, defined as having a condition such as thrush (a fungal infection of the mouth, throat, and tongue) or having diarrhea or a fever longer than 1 month, who reported fatigue, 52.6% of men and 62.3% of women reported at least one or more limitations to physical activity resulting from fatigue.\textsuperscript{11} Seventy percent of men and 80% of women with AIDS reporting fatigue also were found to have at least one functional limitation resulting from fatigue.\textsuperscript{11} Moreover, approximately half the adults with HIV who reported fatigue in this particular study also reported a chronic inability to participate in other life activities, such as attending school or working at a job.\textsuperscript{11} Recreational activities that involve strenuous activity such as running, cycling, or hiking\textsuperscript{16} have been thought to be further limited in this population.\textsuperscript{17,18}

Exercise and Activity Intolerance

The aerobic or oxidative system provides energy (adenosine triphosphate [ATP]) to working muscles during physical activity through the oxidation of glucose, fatty acids, and amino acids in the mitochondria.\textsuperscript{19} According to the Fick equation, the total volume of oxygen consumed ($V_o_2$), the primary measure of oxidative capacity, equals the product of oxygen delivery to the working muscles (cardiac output) and the ability of the muscle to extract and utilize the oxygen to produce energy (arteriovenous oxygen difference).\textsuperscript{19} Disruption of any part of the pathway—from pulmonary extraction of atmospheric oxygen to mitochondrial uptake and utilization, including inhalation into the lungs, diffusion from the alveoli to the lung capillaries, blood transport by the heart and circulatory system to the working muscles, diffusion across the capillaries into the muscle cell, and movement across the cell and into the mitochondria—would impair oxidative metabolism.

Instrumental activities of daily living include tasks such as housework, meal preparation, grocery shopping, and light lawn work; these activities have energy requirements of between 3 and 5 metabolic equivalents (METs).\textsuperscript{20} One MET equals the average resting metabolic rate in the general population: 3.5 mL of oxygen consumed per kilogram of body weight per minute. Physical activity lasting over a minute requires the presence and use of oxygen, or aerobic respiration, to liberate energy.\textsuperscript{21} When activity is sustained at a high oxygen demand, the slow responsiveness of the oxidative system requires that the source of energy must be supplemented by a metabolic pathway that does not require oxygen: the glycolytic pathway. While the non-oxidative glycolytic pathway provides a small amount of energy supplement rapidly, among its by-products are hydrogen ions and lactic acid. These by-products tend to lower intracellular pH, and higher concentrations of these substances are associated with fatigue.\textsuperscript{22} Thus, in order for an individual to tolerate a particular intensity of physical activity without becoming fatigued, the effectiveness of the oxidative metabolic pathway must be high enough to meet the energy demand with minimal nonoxidative supplementation. Aerobic insufficiency, defined as aerobic capacity that is insufficient for meeting required energy demands, results in physical activity intolerance\textsuperscript{23} and may result in functional limitations placed on performance of daily activities and in physical disability. Age normative values for peak aerobic capacity, measured by indirect calorimetry during exercise...
testing, for sedentary men and women with no known pathology or impairments in the 50th percentile ranges\(^1^6\) are reported in the Table.

Diminished aerobic capacity in both adolescents and adults with HIV appears to be one mechanism of fatigue and physical disability.\(^1^7\) Diminished peak \(\dot{V}O_2\) has been identified among adults with HIV\(^2^5\) and ranges approximately 15% to 40% below that predicted for sedentary age-matched controls without HIV.\(^1^7\) Functional aerobic impairment, defined as peak \(\dot{V}O_2\) of \(\geq 27\%\) below predicted values for age, sex, and physical activity level, was found in both adolescents\(^1^7\) and adults\(^2^4\) who had asymptomatic to mildly symptomatic HIV infection.

Ventilatory threshold, a physiological marker of the onset of fatigue, was found to occur earlier during maximal exercise tests\(^2^5,2^7\) in people with HIV than in people without HIV.\(^2^1\) Ventilatory threshold occurs at a point during a progressive physical activity load where expired carbon dioxide (V\(CO_2\)) and minute ventilation begins to increase more rapidly than \(\dot{V}O_2\).\(^2^9\) This increase in expired V\(CO_2\) has been associated with increases in blood lactate and hydrogen ions and results from pulmonary buffering of these metabolites due to an increased need for glycolytic metabolic supplementation.\(^2^1\) If the oxidative system is inadequate (ie, during pathology) to meet the energy requirements of a particular activity, the glycolytic system will increase its contribution in order to meet the energy needs and the ventilatory threshold, and thus the onset of fatigue will occur at a lower intensity of activity. Ventilatory threshold has been shown to occur during the energy requirements associated with light instrumental activities of daily living (3.0–4.0 METs [10.5–14.0 mL·kg\(^{-1}\)·min\(^{-1}\)]) in adolescents with HIV.\(^1^7\) In combination with the finding of low peak \(\dot{V}O_2\), this report suggested that adolescents with HIV may not have had the ability to sustain some activities of daily living or to perform recreational or occupational activities at even slightly higher energy requirements.\(^1^7\) Indexes of aerobic impairment and oxidative metabolic dysfunction might provide quantitative evidence for fatigue-related disability in adolescents and adults with HIV.

### Potential Mechanisms for Exercise and Physical Activity Intolerance

#### Muscle Dysfunction

Several possible mechanisms for exercise and activity dysfunction in people with HIV have been reported. Structural and inflammatory muscle abnormalities in people with HIV, which may impair the muscle’s ability to extract or utilize oxygen during exercise, have been widely reported. HIV infection-mediated myopathy, as identified by the presence of necrosis (cell death), nemaline rod bodies (rod-shaped inclusion bodies consisting of alpha-actinin and desmin), inflammation, and vasculitis (inflammation of microvasculature) were found in 26% of individuals infected with HIV who either had never taken antiretroviral therapy or had a low lifetime dose, indicating a deleterious effect of HIV infection on skeletal muscle.\(^3^0\) Mitochondrial abnormalities also were found in people with HIV who had never taken HAART, including abnormal size, shape, and cristae (inner and outer mitochondrial membrane) structure.\(^3^1\) Cytokine expression (ie, interleukin-1 and tumor necrosis factor-\(\alpha\)) and macrophages were detected in muscle, indicating proteolysis and inflammation, in 5 individuals with HIV and known polymyositis or wasting syndrome.\(^3^2\) Although there has not been strong evidence for direct HIV infection of skeletal muscle, antigens have been identified in macrophages invading the muscle, implicating inflammation\(^3^3,3^4\) as a potential mediator of muscle tissue infection by the virus. Clinical manifestations of HIV-associated myopathy have been reported to include proximal weakness, myalgia, abnormal electromyographic activity, elevated creatine kinase, and diminished physical functioning of the muscle.\(^7,9\)

Medical management of HIV includes a combination of antiretroviral drugs aimed at stopping the replication of the virus and restoring and preserving immune function. Initial therapy recommendations for both people with asymptomatic HIV infection and those with advanced HIV disease include at least one nucleoside analog reverse transcriptase inhibitor (ie, stavudine, didanosine), a protease inhibitor (ie, ritonovir, indinavir), or a non-nucleoside reverse transcriptase inhibitor (ie, efavirenz). Intervention considerations include the quantity of the plasma viral burden, immunological function (ie, CD4 count), known antiretroviral drug resistance genotypes, adherence, and potential drug toxicities.\(^3^5\) Nucleoside analogs were first introduced in the late 1980s, followed by the introduction of other components of HAART (non-nucleoside reverse transcriptase

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### Table

Fiftieth Percentile Age Normative Values for Peak Aerobic Capacity\(^1^6\)

<table>
<thead>
<tr>
<th>Age Range (y)</th>
<th>20–29</th>
<th>30–39</th>
<th>40–49</th>
<th>50–59</th>
</tr>
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<tbody>
<tr>
<td>(\dot{V}O_2)(^{\text{peak}}) (mL·kg(^{-1})·min(^{-1}))</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Men</td>
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<td>41.0</td>
<td>38.0</td>
<td>35.0</td>
</tr>
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<td>34.0</td>
<td>31.0</td>
<td>28.0</td>
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<tr>
<td>METs(^b)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
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<td>12.9</td>
<td>11.7</td>
<td>10.9</td>
<td>10.0</td>
</tr>
<tr>
<td>Women</td>
<td>12.3</td>
<td>9.7</td>
<td>8.9</td>
<td>8.0</td>
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</tbody>
</table>

\(^a\)\(\dot{V}O_2\)\(^{\text{peak}}\)=peak volume of oxygen consumed.

\(^b\)METs=metabolic equivalents (1 MET=3.5 mL·O\(_2\)·kg\(^{-1}\)·min\(^{-1}\)).
inhibitors and protease inhibitors) in the 1990s. Therefore, physiological complications associated with HIV and their interventions appear to have changed since the initial advent of the disease.

Substantial evidence for the mediating role of nucleoside analog therapy with respect to mitochondrial dysfunction has been presented. Nucleoside analog-mediated inhibition of HIV replication occurs by substitution of the phosphorylated drug into the DNA in place of deoxythymidine triphosphate (dTTP). This alteration results in termination of the elongating DNA chain, which, in turn, blocks reverse transcription. A similar action of nucleoside analogs on the mitochondrial transcription enzyme, DNA polymerase γ, and mitochondrial DNA (mtDNA) chain terminators has been proposed as a mechanism of mitochondrial dysfunction. Mitochondrial abnormalities secondary to the effects of nucleoside analog therapy have been found in both human and animal studies. The mitochondrial enzyme, cytochrome-c oxidase, which is essential in ATP production via oxidative phosphorylation, has been found to be deficient in both in vitro and in vivo muscle treated with a nucleoside analog. Numerous other nucleoside analog-induced mitochondrial alterations also have been identified, including oxidative damage to and decreases in mtDNA; decreased mitochondrial RNA (mtRNA); ultrastructural damage to mitochondria (eg, swelling, cristae disruption, inclusion-body presence); presence of mitochondrial-bound interleukin-1α in zidovudine-treated muscle fibers; inhibition of both NADH-linked respiration and NADH-reductase activity; and a diminished aerobic training response of cytochrome-c oxidase by means of chronic electrical stimulation. These abnormalities were further evidenced by the presence of lactic acidosis, which has frequently been found in people with HIV who were receiving nucleoside analog therapy. Other reported nucleoside analog-mediated muscle abnormalities have included diminished muscle cell and myoblast (somite cells, which will develop into muscle cells) proliferation; increased amounts of intramuscular lipid, glycogen, and lipofuscin (the pigment remaining after the breakdown and digestion of damaged blood cells); and ragged red and necrotic fibers (histological features that are associated with myopathy).

Deleterious effects of nucleoside analog therapy may be seen during in vivo metabolism as well. A delayed recovery and larger depletion of phosphocreatine following muscular exercise were reported in a group that received nucleoside analog therapy as compared with a group that did not receive nucleoside analog therapy. A recent study further demonstrated decreased arteriovenous oxygen difference during peak treadmill exercise in a group of individuals with HIV who received HAART compared with a group of individuals with HIV who did not receive HAART and with a non–HIV-infected control group, indicating a deleterious effect of HAART on peak peripheral muscle oxygen extraction and utilization during exercise. This decrease in peripheral muscle extraction and utilization during exercise appears to reduce peak exercise capacity and would likely limit participation in many recreational activities for individuals with HIV who are receiving HAART. However, it also appears that HIV infection alone, apart from the effects of HAART, independently impairs oxygen on-kinetics (the speed with which the muscle is able to extract and utilize oxygen to create energy upon the initiation or change in the intensity of activity) during exercise intensities above the ventilatory threshold in both those receiving and not receiving HAART. How impaired oxygen on-kinetics affect activity tolerance is not yet clear, but early indications are that people with HIV appear to have a reduced ability to quickly obtain a steady state of oxidative metabolism for certain activities above the ventilatory threshold.

The effect of protease inhibitors on muscle function is unclear, but it appears that at least one protease inhibitor, indinavir, has a direct effect on glucose uptake. Indinavir has been shown to be inhibitory to the skeletal muscle glucose transporter, GLUT-4, in rats. If this inhibition also occurs in humans, it could potentially impair plasma glucose uptake and limit the amount of plasma glucose used for glycolysis and subsequent oxidation. This inhibition could potentially limit the amount of fuel that could be used for energy production during activity. An impairment of glucose transport also might reduce the amount of glycogen that could be stored in the skeletal muscle, thereby further limiting a potential substrate for energy production. The combination of these impairments would most likely be seen during higher-intensity activities such as sports and other recreational activities.

**Cardiovascular Abnormalities**

The prevalence of cardiac abnormalities in adults with HIV and AIDS has been reported to range between 28% and 73%. Greater longevity in patients with HIV and AIDS due to improved intervention has increased manifestations of late-stage cardiac disease. Cardiac diseases seen in people with HIV infection have included myocarditis, pericardial effusion, dilated cardiomyopathy, endocarditis, coronary artery disease, pulmonary hypertension, neoplasms, drug-related cardiomyopathy, and vascular lesions. Abnormalities have often been associated with infectious organisms such as Toxoplasma gondii, Mycobacterium tuberculosis, Cryptococcus neoformans, and Candida albicans and the resulting inflammatory response. Autoantibodies to the myocardium as well...
as direct infection of cardiac muscle by HIV also have been reported in people with HIV. When compared with people with idiopathic cardiomyopathy, individuals with HIV-related cardiomyopathy had a lower likelihood of survival, indicating an independent relationship among HIV infection, cardiomyopathy, and greater mortality.

Antiretroviral therapy, particularly the use of protease inhibitors, has been associated with abnormal lipid metabolism, including hyperglycemia, hypertriglyceridemia, hypercholesterolemia, glucose intolerance, insulin resistance, and abnormal fat distribution (ie, visceral adiposity and peripheral lipoatrophy). All of these conditions are known to increase the risk of cardiovascular disease. However, marked increased triglycerides in those with HIV also have been independently linked to HIV infection alone, indicating that HAART does not account for all of the risk. Protease inhibitors also have been associated with cardiac dysfunction via impaired diastolic function, myocardial infarction, and an increased risk of coronary artery disease through endothelial dysfunction.

The effect of nucleoside analog medications on cardiac function among people with HIV also has been examined. It has been demonstrated that a child taking zidovudine was 8.4 times more likely to develop cardiomyopathy than a child who was not taking the medication. Rats treated with zidovudine showed marked and widespread cardiac mitochondrial swelling with fractured and disrupted cristae and decreased mitochondrial cytochrome-b mRNA expression when compared with control animals. Overall, these cardiac abnormalities may impair left ventricular function, lower oxygen delivery to working musculature, and diminish exercise and activity tolerance. This reduction in cardiac pump function may lead to physical inactivity and peripheral muscle atrophy, potentially further limiting exercise and activity tolerance.

Although the majority of HIV-related cardiac dysfunction has been reported in patients with AIDS, recent reports have indicated that cardiac dysfunction may be seen subclinically (absence of overt clinical symptoms) in patients with asymptomatic and mildly symptomatic HIV infection. Subclinical findings suggest that the onset of cardiac abnormalities during the initial stages of HIV infection progresses with the disease and with susceptibility to opportunistic infections, as well as the potential cumulative effects of HAART. Subclinical cardiac abnormalities might combine with other complications of HIV infection, exacerabating fatigue and physical activity intolerance and resulting in functional limitations and physical disability.

The exercise dysfunction that accompanies HIV infection appears to have several characteristics in common with those seen in people with congestive heart failure. Individuals with congestive heart failure also demonstrate ventricular dysfunction and profound muscle dysfunction, specifically mitochondrial deficits, atrophy, and weakness, but further demonstrate respiratory muscle weakness and increased vascular resistance. Physical disability in people with congestive heart failure is well described and may provide insight into evaluation and management of physical function limitations in people with HIV.

Anemia

The Centers for Disease Control and Prevention reported the 1-year incidence of anemia (hemoglobin <10 g/dL) to be 3.2% in adults with non-AIDS HIV infection, 12.1% in those with immunologic AIDS (CD4 <200 cells/mm³ or CD4 % <14), and 36.9% in those with late-stage AIDS. Anemia may be caused by an array of mechanisms, including medical therapy such as the use of zidovudine, ganciclovir (a nucleoside analog used in management of cytomegalovirus), and trimethoprim-sulfamethoxazole (Bactrim, an antibiotic); an alteration of hematopoesis via changes in cytokine production; opportunistic infections such as parvovirus B-19 and Mycobacterium avium-intracellulare; vitamin B₁₂ deficiency; and autoimmunity to erythrocytes. Severe anemia has been reported to lower exercise capacity by reducing the oxygen-carrying content and arterial partial pressure of oxygen of the blood, thus lowering peakVO₂, especially in people with heart failure. Increases in cardiac output at a given workload appear to compensate for the reduction in blood oxygen. However, the influence of anemia on VO₂, and therefore peak exercise capacity, in both people with and without HIV, is, as of yet, not well understood.

Deconditioning

Physiological deconditioning also may play a role in activity intolerance in people with HIV. Researchers in a number of aerobic exercise training studies of people with HIV have suggested that a training effect was achievable, reporting an increase in peak VO₂ and ventilatory threshold and a decrease in resting submaximal heart rate. One interpretation of these findings was that aerobic impairment in people with HIV may be due only to deconditioning. However, the finding of functional aerobic impairment in adolescents and adults with HIV indicated that aerobic capacity was limited far below that occurring as a result of physiologic deconditioning alone. Some authors concluded that it was likely that deconditioning played a part in aerobic insufficiency and activity intolerance in

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HIV infection, but that deconditioning alone could not have fully accounted for the severity of the limitation or the fatigue-mediated functional limitations associated with HIV infection. Numerous reports,\(^{64–71,73}\) of cardiac dysfunction in individuals with HIV, especially those with symptomatic infection,\(^{64}\) make it unlikely that deconditioning alone accounts for the decreases in aerobic function. Furthermore, results from recent studies\(^{24,61}\) suggest that the exercising musculature’s ability to extract and utilize oxygen accounts for peak aerobic exercise dysfunction in individuals with asymptomatic HIV infection and that HAART, rather than deconditioning alone, appears to limit peak aerobic capacity.

**Smoking**

Smoking may add to exercise and activity limitation by increasing carboxyhemoglobin content and subsequently reducing the oxygen-carrying content capacity in the blood. Carbon monoxide has been reported to compete with oxygen for binding sites on the hemoglobin molecule, thus reducing the amount of bound oxygen and subsequently the amount of oxygen delivered to the working muscles.\(^{101}\) Smoking has been reported to have a small, but significant, effect on peak \(\text{VO}_2\),\(^{103}\) but not all evidence supports smoking-mediated decreases in aerobic capacity.\(^{104}\) The percentages of smokers in exercise studies involving subjects with HIV ranged from 27% to 59%.\(^{25,26,28}\) Smoking may account for a small decrease in exercise capacity due to the high prevalence of smokers in previous studies but it is not likely to have caused the large decreases in aerobic capacity seen in individuals with HIV.

**Pulmonary Ventilation Limitations**

Decreased total lung capacity, vital capacity, and other lung volumes have been seen in some subjects with AIDS and various pulmonary disorders, including *Pneumocystis carinii* pneumonia, Kaposi sarcoma, cytomegalovirus, and nonspecific pneumonia.\(^{105,106}\) There have been mixed findings in airflow rates (forced expiratory volume in 1 second [FEV\(_1\)] and forced vital capacity [FVC]) in people with AIDS.\(^{107–109}\) Diffusion capacity also has been reported to be lower in some people with HIV.\(^{106,110}\) In a study by Smith et al,\(^{111}\) severe exercise hypoxemia was found in 15 of 16 individuals with AIDS, with an average of 79% oxygen saturation as measured by pulse oximetry. Diminished gas transfer was further seen in subjects with HIV who had no history of respiratory disease when compared with controls.\(^{27}\) In contrast, Stringer\(^{101}\) found no evidence for ventilation/perfusion mismatching in 34 subjects with asymptomatic HIV infection. Furthermore, other investigators\(^{25,27}\) found resting FEV\(_1\) and FVC to have been within 95% to 100% of predicted values in subjects with HIV who had no history or current evidence of pulmonary disease. Although no study to date has associated pulmonary ventilation limitations with reduced exercise capacity and activity intolerance in people with HIV, this association has been reported in other pathologies.\(^{112}\) Therefore, in people with HIV with acute or chronic respiratory disease, pulmonary limitations might contribute to exercise and activity intolerance; however, the majority of exercise dysfunction in people with HIV is most likely associated with other factors.

**Miscellaneous**

Other possible mechanisms that might be related to fatigue and associated physical limitations include decreased immunological function as indicated by decreases in CD4 counts,\(^{113}\) magnesium deficiencies,\(^{114}\) autoantibodies to acetylcholine receptors at the neuromuscular junction,\(^{115}\) low testosterone levels,\(^{116}\) nutritional deficiencies,\(^{116}\) cortisol abnormalities,\(^{117}\) depression,\(^{118}\) and sleep abnormalities, including increased levels of TNF-\(\alpha\) at night, increased slow-wave sleep,\(^{10}\) altered delta-frequency sleep electroencephalogram patterns, and altered growth hormone secretion relationships.\(^{56}\)

**Implications for Rehabilitation**

Exercise and activity intolerance in people with HIV has been manifested as decreased peak aerobic capacity, ventilatory threshold occurring during MET levels associated with instrumental activities of daily living, and prolonged oxygen on-kinetics. Decreased peak aerobic capacity in people with HIV indicates an impaired ability to participate in recreational activities that are associated with a high-energy requirement. A reduced ventilatory threshold in these individuals indicates that early anaerobic energy supplementation and the onset of fatigue may occur during activities of daily living such as housework, lawn care, and employment activities. These impairments may have important implications for physical disability in this population. Moreover, these impairments provide an opportunity for rehabilitation clinicians and researchers to address mechanisms and interventions for these limitations. Evidence for an achievable aerobic training effect has been documented in the literature,\(^{26,28,102,119–122}\) suggesting a potential role for physical therapy in the management of this disorder. Increases in aerobic capacity have been reported as increased time on the treadmill during a maximal exercise test,\(^{119–121}\) increased peak \(\text{VO}_2\) (13%–24%),\(^{26,28,102,120}\) and increased ventilatory threshold (13%).\(^{26}\) Other beneficial effects of aerobic exercise training may include decreased body mass index, subcutaneous fat, and abdominal girth\(^{120}\) and reports of improved quality of life.\(^{26}\) Although reports of the effect of aerobic exercise on immune function in people with HIV are equivocal,\(^{26,28,119–122}\) it appears that aerobic exercise training does not adversely affect immunological function in people with HIV and is safe.\(^{122}\)
These physiological adaptations to aerobic exercise training may improve fatigue, decrease functional limitations, and reduce physical disability resulting from HIV infection. It appears that performing constant or interval aerobic exercise for at least 20 minutes, at least 3 times per week for 4 weeks, may lead to improved cardiopulmonary fitness and improved psychological status, with an accompanying maintenance of immunological function.123 Among people with HIV who have known cardiovascular disease, pulmonary limitations, or muscle dysfunction, exercise prescription should be tailored to address the limitation, and the referring physician should determine any contraindications for exercise participation. Furthermore, as in people without HIV or AIDS, regular resistance training may improve muscle force and maintain lean body mass, especially in those with muscle wasting and unintended weight loss.124

Conclusions and Limitations
Aerobic exercise and activity dysfunction in individuals with HIV appears to be multifactorial, including detrimental inflammatory effects of the HIV virus as well as the pharmacological toxicity in skeletal and cardiac muscle. This oxidative dysfunction in HIV may be manifested as fatigue and physical functional limitations, and therefore physical disability, in both people with asymptomatic and symptomatic HIV infection. Impairments from HIV infection may now occur to a lesser extent from a better-controlled viral burden since the advent of HAART in the mid-1990s. However, the prevalence of impairments resulting from HAART itself may be increasing due to additions of the newer medications (ie, protease inhibitors). Moreover, people who have HIV infection are living longer, so the normal effects of aging also may result in physical disability in those with HIV. A limitation of this Update includes the lack of direct evidence for the link between physiological alterations and exercise and physical activity limitations in people with HIV. The complex nature of HIV disease also may influence interpretation of the pathophysiological and exercise limitation data in this population. Physical therapists can play an important role in diagnosis and management of aerobic insufficiency and the related physical dysfunction in people with HIV. Further studies are warranted on the specific role of aerobic dysfunction and disability in people with HIV infection.

References


