

# HAART to Heart

## *HIV-Related Cardiomyopathy and Other Cardiovascular Complications*

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■ More than one million Americans have been diagnosed with human immunodeficiency virus (HIV). Advances in prevention and treatment of HIV have led to an increased life expectancy for patients with HIV infection. Due to their increased life span, HIV+ patients are now presenting to hospitals with an increased number of diverse late-stage complications, such as cardiomyopathy and other cardiovascular conditions. These complications are as a direct or indirect result of HIV disease, HIV treatment modalities, comorbid conditions, dietary and lifestyle factors, and unknown etiologies. Cardiac complications, particularly HIV-related dilated cardiomyopathy, are potentially life-threatening diagnoses, with symptoms that may be minimized with appropriate cardiac-specific assessments and treatments, patient teaching, and collaboration among nurses caring for the HIV-positive client with cardiac disease. (KEYWORDS: collaboration, dilated cardiomyopathy, HIV-related cardiac complications)

### □ Case Presentation

The authors, as part of an HIV prevention and education team, were facilitating a group in a crowded room in a residential drug treatment program, when a man who appeared to be in some mild respiratory distress caught the attention of our team. After the completion of the group session and while other participants were individually being tested for HIV infection, we approached him to ask if he would agree to further nursing assessments.

L, a 45-year-old African American man with a 22-year history of active injection drug use (IDU), was short of breath at rest with a respiratory rate of 22, an irregular apical heart rate of 90, presence of S3 and S4 low-frequency heart sounds, and a blood pressure of 180/90. He had 2+ pitting edema in his lower extremities. Auscultation of his lungs was positive for pulmonary crackles. L reported fatigue with minimal exertion and a smoking history of 25 pack-a-day years. L told us that he had never been tested for

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HIV infection but had known many people from “the street” who had died from the “virus.” The HIV team facilitated L’s enrollment in healthcare entitlement programs and arranged an appointment for medical assessment at a community health center urgent care clinic later that day.

At that visit, ECG showed nonspecific ST-T wave and Q wave changes. L’s ejection fraction was determined to be 28%. A chest X-ray was positive for cardiomegaly with prominent vasculature of the upper lung fields. Echocardiography also revealed significantly abnormal left ventricle (LV) systolic function consistent with a diagnosis of dilated cardiomyopathy (DCM). L was referred to a cardiologist for consultation and further medical evaluation. He was also encouraged to be tested for HIV due to his reported risks of needle-sharing and unprotected sex. L was informed 1 week later that he was HIV positive.

Further laboratory studies indicated that L had an absolute CD4 cell count of 180 (normal range 500–1500 in HIV negative individuals) and HIV RNA of 170,000 copies/mL; thus, he now had a diagnosis of AIDS. L thought that he could “live with HIV for years” and was more immediately concerned about the management of his heart disease.

L’s initial needs included accessing home oxygen and a hospital bed for his use at the drug treatment program to improve his shortness of breath. Other self-identified needs were assistance with obtaining nutritional supplements and taxi vouchers for transportation to his cardiology appointments. The HIV team arranged referrals to address these needs. However, L still refused referral to HIV specialty care even though it was available at the agency where his cardiologist practiced. He said, “My heart doctor can help me with that problem. She does everything else.”

During the HIV nurse’s next encounter with L 3 weeks later, she learned that he had been prescribed many cardiac medications to manage the symptoms of his dilated cardiomyopathy; however, his cardiologist had also started him on suboptimal highly active antiretroviral treatment (HAART) to which he was non-adherent. A referral was made for HIV specialized home-based nursing care to assist him with medication teaching and ad-

herence. The HIV home care nurse also advocated with the cardiologist to consult with an HIV specialist so that L would receive a standardized regimen of antiretroviral therapy and arranged for a pharmacological assessment from an HIV pharmacist to notify the cardiologist about the many drug interactions among L’s present regimen of cardiac medications and HAART.

Almost 8 months later, L contacted the HIV team to say that he was now willing to accept a referral to HIV specialty care since his cardiologist was relocating to another city. He stated that he “believed that his heart condition was under control” and he could “now deal with that other issue.”

### □ Scope and Nature of the Problem

Like L in this case presentation, about 1.1 million people living in the United States are HIV+, and nearly half of these cases are African Americans. In addition, an estimated 25% of HIV+ individuals are unaware of their status.<sup>1</sup> These statistics also reflect the growing number of HIV/AIDS patients who are living longer due to the advances of highly active antiretroviral therapy (HAART). With extended life expectancy, the natural history of HIV progression and the multi-organ, systemic effects of this chronic disease become more complex when superimposed on changes associated with the aging process. Nurses in acute care settings who care for HIV+ individuals must be informed about the presentation of cardiomyopathy and other cardiovascular complications, as well as the challenges and barriers associated with the implementation of nursing care for this unique population.

### □ HIV-Related Dilated Cardiomyopathy

Cardiomyopathy has been identified in 10% to 20% of individuals with HIV infection and has been recognized as the cause of death in 4 times as many HIV+ patients with dilated cardiomyopathy as patients with idiopathic cardiomyopathy.<sup>2</sup> Estimates for the worldwide prevalence of HIV is 120 million

people,<sup>3</sup> which equates to 12 million cases of cardiomyopathy annually.

Cardiomyopathy is a disease associated with myocardial dysfunction. Symptoms of cardiomyopathy include exertional dyspnea, chest pain, pulmonary edema, peripheral edema, dysrhythmias, jugular venous distension (JVD), and hepatomegaly. Diagnostic tests performed and findings that confirm a diagnosis of cardiomyopathy include: (1) chest x-ray, which reveals cardiac hypertrophy and pulmonary congestion, (2) electrocardiogram (ECG), which may indicate left ventricular hypertrophy (diffuse ST-segment abnormalities, left bundle branch block or intraventricular conduction delay, atrial fibrillation, and abnormal P waves) and dysrhythmias, and (3) echocardiogram, which demonstrates cardiac structural abnormalities and dysfunction of the ventricles, as well as an ejection fraction <40%.<sup>4</sup>

Dilated cardiomyopathy (DCM), the type most frequently seen in HIV+ individuals, may be defined as an ejection fraction <40% in the presence of increased left ventricular dimensions (left ventricular end-diastolic size >115% of that calculated for age and body surface area) frequently resulting in heart failure.<sup>4</sup> Research has supported the theory that myocarditis, HIV-1 myocardial infection, and cardiac-specific autoantibodies are possible precursors, if not causes, of HIV-related cardiomyopathy, along with a low CD4 count (<200/mm<sup>3</sup>).<sup>2,5,6</sup> Additionally, dysfunction of the left ventricle has been singled out as an independent predictor of death in HIV+ individuals.<sup>7</sup>

The pathophysiology of the left ventricular dysfunction associated with HIV/AIDS remains undetermined. The fact that myocardial cells do not have CD4 receptors contradicts the theory that HIV has a direct action on myocardial cells.<sup>8</sup> HIV-1 infection of the myocardium seems to occur in a patchy distribution without any definite association between HIV-1 and cardiac myocyte dysfunction.<sup>6</sup> Coinfection with coxsackie group B virus, Epstein Barr virus, and cytomegalovirus (CMV) has been observed in some HIV+ patients, and these viruses may be implicated in the pathogenesis of cardiomyopathy.<sup>9</sup> CMV, a frequently occurring comorbidity in patients with HIV, has also been diagnosed in 17% of non-HIV in-

tensive care unit patients.<sup>10</sup> Although there is no definitive proof that CMV is a precursor to HIV-related cardiomyopathy, it is now thought that CMV in HIV+ patients may trigger an autoimmune reaction eventually resulting in cardiomyopathy.<sup>5</sup> Additionally, a significant relationship has been identified between encephalopathy and HIV-related cardiomyopathy. Patients who were diagnosed with HIV and encephalopathy were 3 times more likely to die from complications of congestive heart failure than those patients without encephalopathy.<sup>6</sup> It has been postulated that HIV-1 reservoir cells may remain in myocardial tissue and the cerebral cortex even after antiretroviral treatment since reservoir cells are not susceptible to the effects of antiretroviral medications. Finally, left ventricular hypertrophy and DCM have been identified as myocardial manifestations of chronic cocaine abuse in both human and animal studies. However, the complicated pathogenic mechanisms involved in the development of DCM associated with cocaine abuse have not been elucidated.<sup>11</sup>

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#### □ Other Cardiac Complications of HIV

In addition to dilated cardiomyopathy, a wide spectrum of HIV-related cardiac pathology exists with multiple etiologies associated with their development (Table 1). Infective endocarditis is a serious complication for injection drug users (IDUs), especially if they also have HIV infection and is responsible for 5% to 10% of the deaths of HIV+ IDUs.<sup>12</sup> Furthermore, in the late stages of HIV infection, a significantly increased mortality rate of 30% has been reported.<sup>13</sup> Infective endocarditis in HIV+ patients is usually located on the right side of the heart, primarily affecting the tricuspid valve with vegetation from *Staphylococcus aureus* as the offending organism.<sup>12,14,15</sup> Cases of infective fungal endocarditis have also been reported with *Candida* identified as the causative agent.<sup>2,15,16</sup> It is hypothesized that mucosal *Candida* may be disseminated throughout the body, particularly to the heart, thus leading to fungal endocarditis.

Pericarditis is one of the most frequent cardiac conditions in HIV+ patients. It may

**TABLE 1 ■ Spectrum of HIV-Related Cardiovascular Abnormalities.** Adapted with permission from Fisher SD, Lipshultz SE. Epidemiology of cardiovascular involvement in HIV disease and AIDS. *Ann NY Acad Sci.* 2001;946:13–22.

Type	Possible Etiologies and Associations	Incidence
Dilated cardiomyopathy	Infectious: HIV, toxoplasma, coxsackievirus group B, Epstein-Barr virus, cytomegalovirus, adenovirus, Autoimmune response to infection Drug-related: cocaine, possibly AZT, IL-2, doxorubicin, interferon Metabolic/Endocrine: nutritional deficiency/wasting (selenium, B12, carnitine), thyroid hormone, growth hormone, adrenal insufficiency, hyperinsulinemia Cytokines: TNF-alpha, nitric oxide, TGF-beta, endothelin-1 Immunodeficiency	Estimated 15.9 patients/1,000 asymptomatic HIV-infected persons <sup>9</sup>
Pericardial effusion	Bacterial: Staphylococcus, Streptococcus, Proteus, Nocardia, Pseudomonas, Klebsiella, Enterococcus, Listeria Mycobacteria Viral Pathogens: cryptococcus, toxoplasma, histoplasma Malignancy Capillary leak/wasting/malnutrition Hypothyroidism Prolonged acquired immunodeficiency	11%/year; <sup>19</sup> Spontaneous resolution in up to 42% of affected patients (Blanchard DG, Hagendhoff C, Chow LC, et al. 1991; Heidenrich PA, et al. 1995)
Infective endocarditis	Autoimmune response to infection Bacterial: <i>Staphylococcus aureus</i> or <i>epidermidis</i> , <i>Salmonella</i> species, <i>Streptococcus</i> species (Enterococcus), <i>Hemophilus parainfluenza</i> , <i>Pseudalleschira boydii</i> Fungal/yeast: <i>Aspergillus fumigatus</i> , <i>Candida</i> species, <i>Cryptococcus neoformans</i>	Up to 6% incidence (Currie PF, Jacob AJ, Foreman AR, et al. 1994)
Nonbacterial Thrombotic endocarditis (generally tricuspid valve)	Underlying valvular endothelial damage, Vitamin C deficiency, disseminated intravascular coagulation, hypercoagulable state, malnutrition, wasting, prolonged acquired immunodeficiency	Rare incidence (Currie PF, et al. 1994; Lopez JA, Ross RS, Fishbein MC, & Siegel RJ 1987)
Malignancy (Kaposi's sarcoma, non-Hodgkin's lymphoma, Leiomyosarcoma)	Prolonged immunodeficiency, low CD4 count Viral associations: human herpes virus-8, Epstein-Barr virus	1% incidence (3/440) (Jenson HB & Pollock BH 1998)
Right centricular and pulmonary disease	Recurrent bronchopulmonary infections, pulmonary arteritis, microvascular pulmonary emboli due to thrombus or drug injection	0.5% incidence (Himelman RB, Dohrmann M, Goodman P, et al. 1989)
Primary pulmonary hypertension	Plexogenic pulmonary arteriopathy Mediator release from endothelium	0.5% incidence (Himelman RB, et al. 1989)
Vasculitis (all types)	Drug therapy (antibiotic and anti-retroviral)	Case reports
Accelerated atherosclerosis	Protease inhibitor therapy, atherogenesis by virus-infected macrophages, chronic inflammation	Up to 8% prevalence by autopsy and case reports (Tabib A, Leroux C, Mornex JF, & Loire R 2000; Constans J, Marchand JM, Conri C, et al. 1995)
Autonomic dysfunction	Associated nervous system disease Drug therapy side effects Prolonged immunodeficiency Malnutrition	Common in late-stage disease (Freeman R, Roberts LS, Friedman, et al. 1990)
Arrhythmias	Drug therapy, Pentamidine, Autonomic dysfunction	Unknown

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be self-limiting or occur with effusion. Patients are most often asymptomatic, and the diagnosis of pericardial disease is frequently made at autopsy. Patients that are symptomatic of pericarditis present with chest pain and sometimes with hypotension, tachycardia, shortness of breath, jugular venous distention, and ECG changes.<sup>2,17</sup> Auscultation usually reveals a pericardial friction rub. ECG tracings may reveal elevated ST-segments, depression of PR segments, or inverted T waves. Echocardiography is useful in diagnosing pericarditis where a pericardial effusion is present but may remain normal if the patient has fibrous acute pericarditis.<sup>17</sup>

Pericardial effusion is often idiopathic in origin and has a variable presentation. It is estimated that it occurred in approximately 11% to 20% of asymptomatic HIV+ patients before the inclusion of HAART therapy in HIV treatment regimens.<sup>6,17</sup> Patients with a CD4 cell count of <500/mm<sup>3</sup> have a higher incidence of pericardial effusion and mitral regurgitation.<sup>8</sup> Other comorbid conditions that contribute to the development of pericardial effusion in HIV+ patients may be opportunistic infections or malignant conditions such as Kaposi's sarcoma and non-Hodgkin's lymphoma.<sup>18</sup> Usually, pericardial effusions involve a small amount of fluid and resolve without intervention. If the effusion is large, it may lead to cardiac tamponade and therefore may require a pericardiocentesis or pericardiostomy. Research has demonstrated that HIV+ patients who have a history of pericardial effusion, even when the effusion was resolved, have a significantly shorter life span (36% living at 6 months) than HIV+ patients without effusions (93% living at 6 months).<sup>19</sup>

The incidence of HIV-related primary pulmonary hypertension has been estimated as 1/200, which is considerably higher than 1/200,000 in the general population.<sup>6</sup> HIV, along with chronic Hepatitis B and C, have been identified as risk factors for the development of pulmonary hypertension, and it is speculated that cytokines play a role in the development and progression of this chronic disease.

Patients in the later stages of AIDS can be affected by malignant disease. Cardiac malignancy is typically related to metastatic spread. During the pre-HAART era, Kaposi's sarcoma affected up to 35% of AIDS patients, with an

incidence inversely related to CD4 counts.<sup>20,21</sup> Primary cardiac malignancy associated with HIV infection is generally due to cardiac lymphoma. Non-Hodgkin's lymphomas are 25 to 60 times more common in HIV+ individuals and were the first reported manifestations of AIDS in up to 45 of new cases in the pre-HAART era.<sup>3</sup>

The incidence of acute myocardial infarction in HIV+ patients has been reported at 5 to 5.5 per 1,000 persons per year, a 3-fold increase compared to non-HIV-infected patients (1.52 per 1,000 persons per year).<sup>22</sup> Following hospital discharge, after acute myocardial infarction, HIV-infected patients have a higher incidence of reinfarction, restenosis, and stent thrombosis.<sup>23</sup>

In summary, with the increased effectiveness of HIV treatment therapies, the lifespans of HIV+ patients has increased. Concomitantly, cardiac complications (ie, cardiomyopathy) have also increased in prevalence. Cardiac involvement may be related to the extended time periods of immunosuppression, opportunistic infections, viral infections (i.e., viral myocardial infection), autoimmune responses (i.e., formation of cardiac autoantibodies), dietary deficiencies (i.e. selenium), and cardiotoxicity of drugs used to treat HIV.<sup>24</sup>

#### □ Cardiovascular Effects of AIDS-related Medications

HAART is a multiple drug therapy approach to treatment that combines different classes of drugs to limit HIV replication. Nucleoside reverse transcriptase inhibitors (NRTI) drugs, particularly zidovudine (AZT), have been studied as contributors to the development of dilated cardiomyopathy. It is thought that NRTI cardiotoxicity is related to detrimental effects on cardiac mitochondrial function.<sup>11</sup> A major side effect of zidovudine (AZT) is bone marrow toxicity resulting in anemia and/or granulocytopenia. A study with a sample of 758 HIV+ patients identified anemia in 30.3% of the patients and further showed that anemia was statistically linked with zidovudine use.<sup>25</sup> However, additional studies with large samples of adults and infants have not demonstrated a significant relationship between zidovudine and cardiac dysfunction.

Findings from studies to explore HAART as a causative agent in the development of cardiomyopathy have been inconclusive. However, recent research has indicated that protease inhibitors (PIs) may play a role in the development of coronary artery disease. Class-specific metabolic side effects of PIs, such as dyslipidemia and insulin resistance, add to preexisting cardiovascular risk factors and contribute to premature arteriosclerosis.<sup>26</sup> No correlation has been found between the development and progression of coronary artery disease and patients' CD4 counts or HIV-related opportunistic infections.<sup>27</sup> It has also been suggested that non-nucleoside reverse transcriptase inhibitors (NNRTIs) may increase the levels of high-density lipoprotein (HDL) cholesterol; therefore, it would be expected that these drugs would be associated with decreased incidence of coronary artery disease.<sup>22</sup> Therefore, choosing a HAART regimen that includes NNRTIs may be beneficial in patients who are at high risk of coronary artery disease.

HIV+ patients are prescribed many other medications for prophylaxis and treatment of opportunistic infections. Some of these medications have been associated with serious cardiac complications (eg, pentamidine, foscarnet, and trimethoprim sulfamethoxazole, among other anti-infective drugs) (Table 2). These medications may also initiate a serious ventricular arrhythmia, torsades de pointes. Torsade de pointes can result in sudden arrhythmic death due to the action of these drugs: delay of cardiac repolarization, lengthening the QT interval, and prominent U waves (Figure 1).<sup>28,29</sup> Torsade de pointes is a useless or nonperfusing rhythm. Episodes of torsades lasting longer than 10 seconds usually cause unconsciousness. If the episode is shorter than 10 seconds, the patient may report feeling lightheaded, dizzy, a sensation of rapid heart rate (palpitations), shortness of breath, or difficulty breathing for a split second.<sup>29</sup> If the episode persists without intervention, it can lead to sudden cardiac death.

Thus, while HAART and other medications have extended the life expectancy of persons living with HIV/AIDS, they are also associated with a range of cardiac manifestations that require further investigation and clinical consideration.

## □ Clinical Considerations: Cardiac Assessment

As with all patients, HIV+ individuals should be assessed for risk factors of cardiovascular disease, such as age (increased prevalence with age), gender (increased prevalence in males), increased systolic or diastolic blood pressure, tobacco use, elevated total cholesterol, HDL and LDL-C levels, alcohol abuse, sedentary lifestyle, obesity, family history of atherosclerosis/coronary artery disease, and dietary habits. Additionally, HIV+ patients should be screened for comorbid conditions that contribute to the development of cardiovascular disease including diabetes, renal impairment, thyroid disorders, and liver disease. It is widely accepted that smoking is a risk factor for the development of coronary artery disease. Cigarette smoking lowers the cardioprotective levels of HDL in addition to increasing the levels of nicotine and carbon monoxide in the blood.<sup>30</sup> These 3 actions cause endothelial damage, possibly leading to the development of atherosclerotic plaque. Research has identified that >70% of HIV+ patients smoke and that >80% of these patients had not considered smoking cessation.<sup>31</sup> Today, there are multiple options when assisting patients to quit smoking, such as the nicotine patch, nicotine gum, nicotine lozenges, nicotine nasal spray, nicotine oral inhaler, and bupropion SR (Wellbutrin).

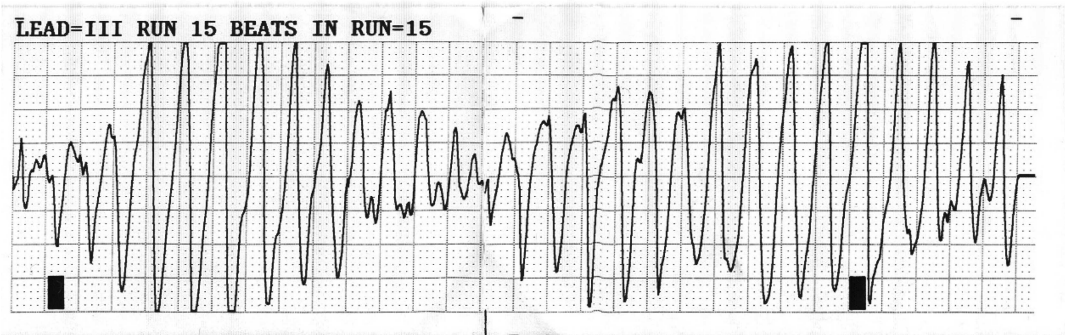
Patients with HIV-related cardiomyopathy and other cardiac illnesses often become symptomatic of these diagnoses late in the HIV disease process.<sup>3,32,33</sup> Additionally, the presenting signs/symptoms are nonspecific to cardiac disease and may be mistaken for indicators of advanced HIV or pulmonary disease.<sup>7,32</sup> HIV+ patients, similar to patients who are HIV-, may not exhibit overt signs or symptoms of cardiac disease, which may only be detected with further diagnostic evaluation.

## □ Diagnostic Evaluation

Echocardiography is a relatively inexpensive and non-invasive evaluation of cardiac function in HIV+ patients. A baseline echocardiogram should be obtained at the time

**TABLE 2 ■ Cardiovascular Actions/Interactions of Common HIV Therapies. Adapted with permission from Barbaro G. Cardiovascular manifestations of HIV infection. *Circ J Am Heart Assoc.* 2002;106:1424.**

Class	Drugs	Cardiac Drug Interactions	Cardiac Side Effects
Anti-retroviral Nucleoside Reverse Transcriptase Inhibitors	Abacavir (Ziagen), zidovudine (AZT, Retrovir)	Dipyridamole	Lactic acidosis (rare), hypotension, skeletal muscle myopathy, (mitochondrial dysfunction hypothesized but not seen)
Nonnucleoside Reverse transcriptase inhibitors	Delavirdine (Rescriptor), efavirenz (Sustiva), nevirapine (Viramune)	Warfarin (class interaction), Ca <sup>++</sup> channel blockers, $\beta$ blockers, nifedipine, quinidine, steroids, theophylline	Delavirdine can cause serious toxic effects if given with antiarrhythmic drugs and MI if given with vasoconstrictors
Protease inhibitors	Amprenavir (Agenerase), indinavir (Crixivan), nelfinavir (Viracept), ritonavir (Norvir), Saquinavir (Invirase, Fortovase)	All are metabolized by cytochrome p-450 and interact with: sildenafil, amiodarone, lidocaine, quinidine, warfarin, statins. Calcium channel blockers, $\beta$ blocker levels (1.5–3x increase), prednisone, quinine, theophylline (decrease concentration)	Implicated in premature atherosclerosis, dyslipidemia, insulin resistance, fat wasting & redistribution (lipodystrophy)
Anti-infective antibiotics	Erythromycin Rifampicin Trimethoprim/sulfamethoxazole (Bactrim)	Cytochrome p-450 metabolism and drug interactions Reduces therapeutic effect of digoxin Increases warfarin effects	Orthostatic hypotension, ventricular tachycardia, bradycardia, torsades (drug interactions) Orthostatic hypotension, anaphylaxis, QT prolongation
Antifungal agents	Amphotericin B Ketoconazole, itraconazole (Sporanox)	Digoxin toxicity Cytochrome p-450 metabolism & drug interactions- increases levels of sildenafil, warfarin, statins, nifedipine, digoxin	Hypertension, arrhythmia, renal failure, hypokalemia, thrombophlebitis, bradycardia, angioedema, DCM
Antiviral agents	Foscarnet, ganciclovir	Zidovudine	Reversible cardiac failure, electrolyte abnormalities, vtach, hypotension
Anti-parasitic	Pentamidine (IV)		Hypotension, arrhythmias (torsades, VT), hyperglycemia, hypoglycemia, sudden death. Note: Contraindicated if baseline QTc > 0.48
Chemotherapy agents	Vincristine, doxorubicin Interferon IL-2	Decreases digoxin level	Arrhythmia, MI, DCM Hypertension, hypotension, DCM, ventricular and supraventricular arrhythmias, A-V block Hypotension, arrhythmia, MI, cardiac failure, capillary leak, thyroid alterations



**Figure 1.** ECG tracing of Torsade de pointes. Reprinted with permission from Geiter, H, Jr, Knowledge is Power Web site. Available at: <http://www.Nurse411.com/Case%20Study/ECGCase6.asp>. Palm Harbor, Florida, © 2004.

of HIV diagnosis and then repeated at intervals of 6 months to 1 year.<sup>16,28</sup> Undiagnosed dilated cardiomyopathy may be identified through the use of echocardiography since information about ventricle wall thickness, movement, and ejection fraction can be determined.

Along with echocardiography, an ECG should be performed at the time of HIV diagnosis to provide a baseline for comparison and should be periodically repeated throughout the course of the patient's lifetime. ECG can identify conduction and rhythm abnormalities that indicate the need for further clinical and diagnostic testing.

Stress testing may be particularly useful in making the diagnosis of dilated cardiomyopathy due to left ventricular malfunction. Measurements of cardiac reserve and exertion-induced ischemia along with subjective, self-report data about patient's symptoms during exercise can be obtained. Stress testing provides an estimate of the patient's cardiac output during exercise, thereby providing indicators of the prognosis of patients with heart failure. Maximal oxygen uptake ( $VO_2$  max) is measured and if  $<14\text{ml/kg/m}^2$ , life expectancy has been found to be significantly reduced to 1 year with medical therapy regardless of the measurements of resting cardiac output, pulmonary artery wedge pressure (PAWP), or pulmonary pressures.<sup>28</sup>

Several routine blood tests can provide indicators of HIV-related cardiomyopathy and, in some cases, the cause of the cardiomyopathy. The following should be considered routine when HIV+ patients are being screened for cardiac disease: complete blood count

(CBC), electrolytes, BUN, creatinine, albumin, triglycerides, cholesterol, and lipid profile. If chronic alcoholism is documented or suspected, serum tests should be performed for mean corpuscular volume (MCV), liver enzymes, gamma glutamyltransferase (GGT), aspartate aminotransferase (AST), alanine aminotransferase (ALT), and carbohydrate-deficient transferrin (CDT). Additional serum tests should be performed to detect deficiencies in selenium and carnitine, along with deficiencies in growth hormone, all of which are reversible causes of cardiomyopathy.<sup>28</sup> Additionally, the assessment of the B-type or brain natriuretic peptide (BNP) assay can support a new diagnosis of heart failure, as well as provide information about mortality or morbidity probabilities associated with left ventricular dysfunction.<sup>28,34</sup> The BNP is a quick and easy test that can be performed at the bedside with results in 15 minutes and can be invaluable toward initiation of rapid treatment for the newly diagnosed patient as well as acutely ill, unstable patients experiencing cardiac decompensation.

#### □ Clinical Considerations: Treatment

The main objective of treatment for HIV-related dilated cardiomyopathy is to target symptom management, decrease the effects of heart failure, and decrease the morbidity and mortality associated with heart failure. Primary medical management includes the administration of angiotensin-converting enzyme (ACE) inhibitors, beta-blockers, digoxin, and diuretics.<sup>28,35</sup> In the event

that a patient's condition is not sufficiently improved with the prescribed medications, a biventricular pacemaker may be inserted and eventually a cardiac transplant may be suggested.<sup>35</sup> Findings from outcome studies that have examined the efficacy of prophylactic treatment with an anticoagulant (warfarin) or antiplatelet therapy (aspirin or clopidogrel) have been incomplete, but preliminary results provide support for prescribing an anticoagulant (warfarin) versus an antiplatelet (aspirin or clopidogrel).<sup>36</sup> The warfarin/aspirin study in heart failure (WASH)<sup>36</sup> failed to find a significant difference in mortality between three groups of non-HIV<sup>+</sup> heart failure patients prescribed warfarin, aspirin, or no antithrombotic medication, but more patients in the aspirin group were hospitalized for heart failure than those in the warfarin group.<sup>37</sup> Subsequent to the WASH study, the warfarin and antiplatelet therapy in heart failure (WATCH) study<sup>37</sup> concluded that fewer patients on warfarin were admitted to the hospital for heart failure than patients in the aspirin group. There was no significant difference, however, between the different treatment groups (ie, warfarin, aspirin, clopidogrel) with respect to outcomes of death, myocardial infarction, or stroke. The overarching consideration when making the decision to prescribe anticoagulants for patients with HIV-related cardiomyopathy relates to the presence of comorbid conditions, particularly for patients with a history of thromboembolism, atrial fibrillation, or a left ventricular thrombus documented on echocardiogram. If these or other comorbid conditions that predispose the patient to the development of emboli are present, then administration of anticoagulants would be prudent.<sup>38</sup>

Immunoglobulins as a treatment for dilated cardiomyopathy and myocarditis have dominated cardiac research for the past few decades. A research study was conducted in which intravenous immunoglobulin (IVIG) was administered to HIV<sup>+</sup> children who did not have congestive heart failure (CHF). Echocardiograms and serum immunoglobulin measurements were performed throughout the study. Results indicated improved left ventricular structure and function, with a significant increase in wall thickness.<sup>39</sup> However, subsequent research has been un-

successful in establishing a significant relationship between the administration of IVIGs and improved cardiac function in adult CHF patients.<sup>40</sup> Researchers have indicated that they are still in the early phases of examining the effect of immunoglobulins on heart failure, as well as determining the specific instances when administration of IVIGs to patients will maximize improvement in cardiac function. Furthermore, it has been proposed that IVIG therapy may best be prescribed to patients with heart failure who have been diagnosed with an inflammatory process.<sup>40</sup>

#### □ Nursing Implications for Comprehensive Care of HIV+ Cardiac Patients

Studies and clinical observations have documented relationships between HIV/AIDS and the heart at various stages of the disease. Cardiac involvement is one of the most controversial topics in AIDS research and care due to the variance in underlying etiologies for the wide variety of structural, clinical, and echocardiographic abnormalities associated with HIV-related cardiac conditions. With the advent of HAART and the availability of effective prophylactic agents to suppress the development of opportunistic infections, nurses in acute and critical care environments will care for increasing numbers of HIV<sup>+</sup> patients with complex cardiac disease and potentially life-threatening comorbid conditions. Nurses will be challenged to thoroughly assess and monitor these complex patients for the development of signs and symptoms of HIV-related cardiomyopathy and other complications. It is important for critical care and acute care nurses to gather a thorough dietary history, a list of past and current medications for HIV and other conditions, and history of past and present comorbid conditions, as well as to monitor vital signs and conduct comprehensive cardiac assessments. Furthermore, nurses can help ensure that patients who have been receiving HAART medications receive a thorough cardiac screening to identify any cardiac complications early in their hospital stay.

However, as "L's" case illustrates, comprehensive care of complex HIV<sup>+</sup> patients with

HIV-related cardiomyopathy or other cardiac complications must extend beyond the monitor and medications in order to be effective in extending their life expectancies and improving the quality of their lives. For example, comprehensive assessment of HIV+ patients should not only include screening for cardiac risk factors and complications, but also include diagnostic tests and interviews to detect the presence of other comorbid conditions such as substance abuse, viral hepatitis, sexually transmitted infections, tuberculosis, chronic mental health problems, and homelessness.<sup>41</sup> Comprehensive management of HIV and cardiac drugs must not only include recognition of potential side effects and drug interactions, but also include accommodations for educational limitations, such as illiteracy as well as the host of other physical, psychosocial, and socioeconomic factors that affect medication adherence.<sup>42,43</sup> Additionally, comprehensive treatment of HIV+ individuals with cardiac complications should address lifestyle factors and include patient education regarding dietary modifications, along with micronutrient supplementation to correct dietary deficiencies, implementation of short-term measures to ease nicotine withdrawal and long-term smoking cessation strategies, and the provision of sophisticated pain management and detoxification regimens for drug and alcohol addiction. Since both HIV/AIDS and cardiac conditions disproportionately affect ethnic minorities,<sup>44,45</sup> it is particularly important that care of HIV+ patients, as with care of patients in general, take ethnic variations into account and be planned and delivered in a culturally competent manner. Prior to patient discharge, critical care and acute care nurses should make necessary referrals to assist patients in obtaining necessary home equipment and supplies to help compensate for patients' chronic fatigue, which may negatively impact on self assessment and care. Linkage of HIV+ patients with cardiac disease to other community-based resources may also be warranted. It is also important for critical care and acute care nurses to determine the availability of a social support network to help prevent a cycle of repeated hospital readmissions and promote adherence to components of a complex treatment plan.

Similar to HIV providers who may impose an "HIV-first" agenda on patients, families, and communities,<sup>41,46</sup> it would be expected that critical care and acute care nurses, as did "L" as a patient, may have a "cardiac-first" agenda in their care of patients with HIV-related cardiomyopathy or other cardiac complications. However, comprehensive care of these complex patients necessitates multidisciplinary collaboration between HIV teams and critical care and acute care teams. As the incidence of HIV/AIDS and cardiac complications continues to increase and new research findings and treatments rapidly emerge, nurses and other providers will need to come "HAART-to heart" toward a "patient-first" agenda that bridges specialties and settings.

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AQ1: Have added "a-day": Is that correct?

AQ2: Have added "tissue": okay?

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