CHAPTER **54**

VIRAL LOAD: Podiatric Surgical Implications

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INTRODUCTION

Acquired immunodeficiency syndrome (AIDS) has killed more than 25 million people since 1981, roughly half as many deaths as World War II. According to the Centers for Disease Control and Prevention, in the US the estimated number of people with human immunodeficiency syndrome (HIV)/AIDS is approximately 1,185,000 with approximately 25% of the patients unaware of their infection. The estimated number of new cases of HIV is 42,000 each year. Currently, these 1.1 million Americans are among the 33 million people now living with HIV, the virus that causes AIDS, which represents an increase of 11% from 2003. Today, of this 33 million people, only 3 million are receiving treatment. That is less than one-third of those who need immediate treatment. Combine this with the number of individuals who are unaware of their HIV status and the numbers are staggering. It is imperative then, that the podiatric physician is aware of these statistics that suggest many of the patients presenting to offices are unaware of their HIV status at the time of treatment.

So, how does this affect the podiatric practitioner? First, a solid understanding of what HIV/AIDS is, and how it is transmitted is critical. This knowledge will assist in providing the best possible care to patients in both a clinical and surgical setting. As health care providers, utilizing universal precautions consistently is of obvious importance. Second, as a podiatric surgeon, it is imperative to recognize when a patient's immune system may not be adequate to protect against the possible risks associated with surgical injury as well as the opportunistic infections that are considered at most, a minimal threat to the otherwise healthy individual. The podiatric physician therefore has an obligation to utilize the resources available and have an understanding of their relevance to aid in patient selection, especially when it concerns performing elective surgery. In this article, current laboratory tests will be explained along with their implications as they pertain to the status of the HIV positive patient. This knowledge will aid in insuring the best possible post surgical outcome.

HIV/AIDS: DEFINITION AND DIAGNOSIS

HIV is a lentivirus, which is part of a larger group of viruses known as retroviruses that attack the immune system. The name lentivirus literally means "slow virus" as the virus takes a very long time before it produces adverse effects in the body. A 2008 study by Worobey et al dated the origin of HIV to between 1884 and 1924. Today, the most common, cost-effective, and accurate method of diagnosing HIV is via a blood test. An enzyme-linked immunosorbent assay, (ELISA), looks for antibodies to HIV. A positive ELISA requires a second test, a Western Blot, be done to confirm the presence of HIV. A Western Blot detects antibodies to several specific components of a virus such as HIV. More rapid methods (Rapid EIA) use blood, saliva, or urine, are 99.5% accurate and are also approved by the Food and Drug Administration (FDA) with results available in 20 minutes. A positive Rapid EIA, is considered a preliminarily positive and must be confirmed with an ELISA and Western Blot.

Secondarily, a polymerase chain reaction (PCR) test, also known as a viral load test is used to measure the small amount of HIV that escapes the lymph nodes. This test measures HIV RNA (HIV genetic material), and may detect infection about a week after an exposure. Therefore, the PCR test is used by researchers and health-care providers to identify infections during the window period (Figure 1).

As a point of interest, the risk of transmission from a hepatitis B-, hepatitis C- and HIV-positive patient can be estimated using the rule of 3s (hepatitis B = 30%, hepatitis C = 3%, HIV = 0.3%.) In the event of an accidental needle stick with an HIV-infected person it is advisable to take the following precautionary measures:

Bleed and wash. Squeeze as much blood out of the injury site as possible and wash with chlorhexidine solution.

Get blood for testing. Test the patient and yourself for HIV markers (HIV DNA/RNA.)

Seek medical attention. If the patient is HIV-positive (especially HIV acute seroconversion syndrome), get therapy as soon as possible, preferably a combination therapy and/or

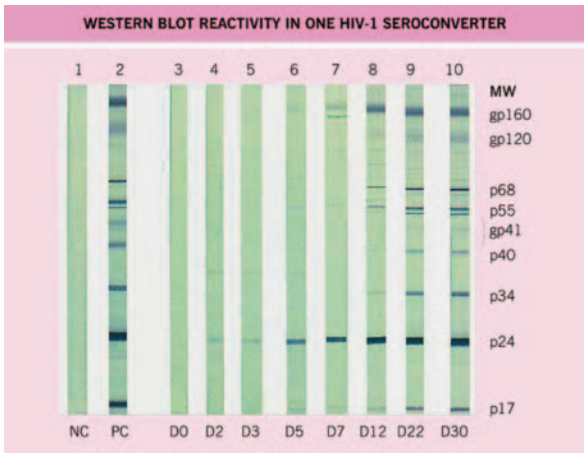

Figure 1. Western Blot test illustrates the window period. Left: two columns to be used as points of comparison. NC = HIV-negative test result, PC = HIV-positive test result. Columns 3 to 10 show a series of tests on one individual who became infected with HIV to illustrate how an HIV test result can change during the window period from HIV-negative to HIV-positive. Each column is one Western Blot test. Tests were performed on a single person beginning the day first infected with HIV (Column 3, Day 0) to when the person had a conclusive HIV infection (Column 10, Day 30). Each black or dark grey horizontal stripe is representative of the presence of a different antibody against a protein found in HIV. To be conclusive (HIV-positive), a Western Blot must have 5 horizontal stripes. Source: http://www.hivinfosource.org.

immunoglobulin within 2 hours post-exposure. Next, determine the HIV status code of the patient, and determine if the exposure is low titer or high titer. Low-titer exposures are asymptomatic patients with high CD4 counts; these are HIV status code 1. High-titer exposures are patients with primary HIV infection, high or increasing viral load or low CD4 counts, or advanced AIDS; these are HIV status code 2. The exposure code is matched with HIV status code to determine if any post-exposure prophylaxis is indicated. The basic regimen is 4 weeks of zidovudine (600 mg/day in 2-3 divided doses) and lamivudine (150 mg twice daily). The expanded regimen is the basic regimen plus either indinavir (800 mg q 8 hours) or nelfinavir (750 mg 3 times/day). Interferon ribavirin prophylaxis decreases risk by 40%. Exposed workers should be counseled on the risks of disease transmission based upon their specific exposure.

Follow-up blood tests. ELISA for anti-HIV antibodies should be performed at 6 weeks then again at 3 months, by which time it is rare not to have seroconverted. If positive, a confirmatory Western Blot test for protein bands is performed. However, it can take up to 1 year. After 1 year, if tests have all been negative, one is given the all-clear.

MEASURING THE PROGRESSION OF THE DISEASE

On average, without treatment, progression from infection with HIV to AIDS is about 7 to 10 years with the average time from infection to death being 10-12 years. In general, the rate of progression is higher for those infected via blood contact, rather than sexual contact.

HIV infection can generally be broken down into four distinct stages. Primary stage 1 infection lasts a few weeks and is often accompanied by a mild, short flu-like illness that can often go undiagnosed. Infected persons may experience flu-like symptoms, fever, fatigue, sore throat, joint pains, and/or lymphadenopathy. These symptoms resolve untreated, soon after onset and this marks the end of the window period. During this period large amounts of HIV are seen in the peripheral blood, and the immune system begins to respond by producing HIV antibodies and cytotoxic lymphocytes. This is known as the seroconversion or the window period. HIV antibody tests done before seroconversion is complete may not be positive.

Stage 2, the clinically asymptomatic period lasts on average ten years and is free from major symptoms, although swollen glands may be present. Levels of HIV in the peripheral blood are very low, yet people remain infectious. HIV antibodies are detectable in the blood and antibody tests will be positive.

Stage 3, the symptomatic HIV infection period is mainly caused by the emergence of opportunistic infections and cancers that the immune system would normally prevent. Unless HIV itself can be slowed down, the symptoms of immune suppression will continue to worsen.

Stage 4, progession from HIV TO AIDS. As the immune system becomes more and more damaged, the illnesses that occur become more and more severe. In the US, a diagnosis of AIDS may be a very low count of T-helper cells in the blood.

TESTS TO MONITOR IMMUNE STATUS

As previously mentioned, a PCR test measures the amount of the viral load that escapes the lymph nodes. This is a helpful test in determining when treatment may become necessary. In addition to measuring the viral load, CD4 levels may also be obtained. CD4 (cluster of differentiation 4) is a glycoprotein pressed on the surface of T-helper cells,

regulatory T cells, monocytes, macrophages, and dendritic cells. CD4 is the primary receptor used to gain entry into host T cells. HIV infection leads to a progressive reduction in the number of T cells possessing CD4 receptors. Therefore, the CD4 count guides the decision when to begin treatment.

The healthy individual has a CD4 count in excess of 1000µL-1. Early AIDS symptoms may appear when CD4 counts fall to levels ranging from 350-500µL-1, Intermediate symptoms at levels from 200-350µL-1, and advanced AIDS symptoms at CD4 counts below 200µL-1. Opportunistic infections will occur when CD4 counts are < 200µL-1 (Figure 2).

CLINICAL SIGNS AND SYMPTOMS TO MONITOR

In healthy adults, a T4 cell count of 1,000 or more per millimeter is normal. As CD4 levels drop to levels near 200-350µL-1 the following may begin to appear: thrush (oral/ vaginal), hairy leukoplakia, herpes simplex viruses (recurrent cold mouth sores), night sweats, unexplained fevers and/or shrinking of previously swollen glands. In addition, as CD4 counts continue to fall below 200µL-1 serious illness becomes more commonly seen in the forms of RTI – persistent cough, fever chest pains, GIT (ongoing diarrhea), cancers (Kaposi's sarcoma, lymphoma, squamous cell carcinoma, blindness/retinopathy, and or tissue wasting. Of those mentioned Kaposi's sarcoma may be of particular interest to the podiatrist as it often presents on the lower extremities and has also been reported on the feet (Figure 3).

When contemplating elective surgery on the HIV patient the most important laboratory values to be aware of are viral load and CD4 levels. A CD4 count at 350µL-1 or above should be stable enough for elective surgery as long as the patient is asymptomatic and not experiencing any opportunistic infections. As well, a patient with a viral load above 48 or CD4 T cell count below 200µL-1 (or 15%; normal range of CD4 being 30-50%) is not considered safe for elective surgery (Figure 2).

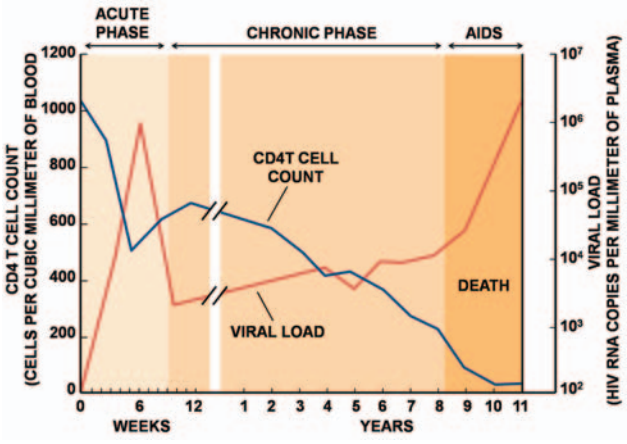

Figure 2. Diagram of the effects on CD4 T-cell counts and viral load during acute and chronic phases of HIV, and ultimate progression to AIDS over time.

CURRENT TREATMENTS AVAILABLE

In 1989, scientists discovered even before AIDS symptoms develop, HIV is replicating wildly in the blood. The goal of treatment was therefore aimed at keeping HIV at low levels. In 1996-1997, a treatment breakthrough was identified known as the AIDS drug cocktail more commonly known as a highly active anti-retroviral therapy (HAART.)

Anti-retro virals (ARVs) slow down viral activities at various points of viral growth and viral replication. The different types of ARVs are protease inhibitors (PIs), nucleoside reductase inhibitors (NRIs), and non-nucleoside reductase inhibitors (NNRIs). PIs work by inhibiting division of viral nucleotide to short strands that form new HIV; whereas NRIs/NNRIs work by inhibiting the enzyme that causes the viral RNA to write itself out using host cell's DNA, thus slowing down the rate of viral self-replication and

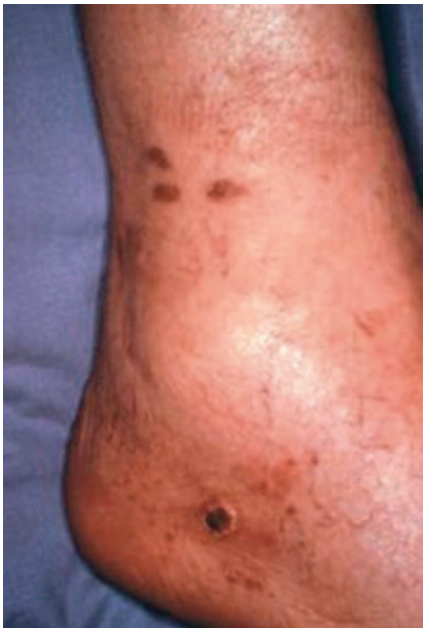

Figure 3. Image of cutaneous brown Kaposi's sarcoma (KS) lesions located over the medial left ankle and foot. (Source: CDC). KS is a rare cancer of vascular endothelial cells. Clinically present as brownish-red to blue colored skin lesions found most frequently on legs and feet. It is caused by human herpes virus 8, which causes endothelial cells to become cancerous in the setting of profound and prolonged immunosuppression.

rate of cellular resource depletion. It has become the standard of care to begin the discussion of starting HAART with patients whose CD4 counts are between 350-200μL-1.

Many benefits are associated with HAART including prolonging lives by delaying onset of symptoms, reducing rates of viral replication, reducing rates of CD4 nucleotide depletion, hence reducing the speed towards immune deficiency, and reducing the severity of opportunistic infections due to better resultant immunity. Adherence to therapy once started is also stressed as it has been found that intermittent treatment is not effective. The prevention of complications and preservation of good health is more effective than attempts to treat complications when they arise. Also, maintenance and/or restoration of the immune defenses require ongoing treatment. There are most notably specific characteristics of HIV/AIDS treatments that require near perfect adherence and lifetime commitment for success.

A study conducted by Patterson et al measured adherence via electronic monitors (MEMS caps). He found at 3 months, there was a significant association between adherence and viral suppression ($P < 0.001$). Adherence to HAART and the undetectable viral load were noted with the following correlations respectively: (>95%, 81%; 80-90%, 64%; 70-80%, 25%; <70%, 6%).

It is important to understand that once a patient begins HAART it can cut the HIV viral load to undetectable levels, but the CD4 count may or may not respond or it may increase. It is therefore considered safer to base decisions on the viral load rather than the CD4 count. The good news is, in many people, HAART successfully reduces viral load to undetectable levels (<50 virions/mm3). Yet on the contrary, viral load rebounds quickly if HAART is stopped.

WHERE WE ARE TODAY

Currently, HIV treatment is shown to extend life by 24 years, at a cost of $618,900. The high cost treatment unattainable for many patients, particularly in the developing world. HAART is however, not without serious side effects. The FDA has approved new classes of drugs that have made HIV treatment safer, easier, and more effective. Unfortunately, we are still without a cure for AIDS. Recently, Merck's AIDS vaccine was found to fail in clinical trials, this was the latest in a long line of vaccines through the development pipeline.

SUMMARY

Today, about 1,185,000 people are living with HIV/AIDS, and approximately 25% of those are unaware of their infection. As a podiatric physician, it is imperative to be aware of these statistics and make use of universal precautions a consistent practice. When considering elective surgery, be aware of laboratory tests available and their significance to aid in insuring the best postoperative outcome.

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