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On the Potential Insurability of HIV

John F. White III, MD, MBA

For the past two years, a group of medical directors representing a wide variety of companies with a concentration in life insurance has reviewed literature pertinent to the mortality studies on Human Immunodeficiency Virus (HIV) and has had discussions with experts in the field. We did so as a result of our commitment to studying this disease process with an eye toward applying our findings to enhance individual companies' analysis of the potential insurability of people currently living with HIV. This is something that to our knowledge has not been done in a similar form in this country in the recent past. Through this process, we discovered many interesting facts that we thought all active medical directors should know. And, I think it is likely that the differing risk appetites of life insurers is such that a large number of individuals living with HIV might be found to be insurable for coverage at this time.

In this brief paper, I hope to refresh your memories of the virus responsible for HIV, review its current epidemiology and give some historical perspective to the virus, its treatment, and life insurers' responses to this infection.

Address for correspondence: American National Insurance Company, One Moody Plaza, 4th Floor, Galveston, TX 77550; John.white@anico.com

Correspondent: John F. White III, MD, MBA; SVP and Medical Director.

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HIV DEFINED

HIV is a retrovirus that infects humans via transmission through intimate contact (generally sexual intercourse), exposure to infected blood, and through the birthing process. The most common means of transmission worldwide is through heterosexual vaginal intercourse[1] but in North America is more commonly transmitted via men having sex with men (MSM), followed by heterosexual intercourse and intravenous drug use (IDU).[2]

Once an individual is infected by the HIV retrovirus, viral replication begins. The extent to which it replicates is heavily dependent on the interplay of various immune functions. HIV infects the CD4 (T helper) cells and takes over their cellular mechanisms for replication purposes, thereby depleting functional CD4 numbers. CD8 cells (Cytotoxic T cells) increase in number to fight the infection, and antibodies from B lymphocytes are formed to the retroviral particles to also help fight the infection in addition to the other proteins and molecules produced as part of the reaction to inflammation and infection. If left untreated, the vast majority of people infected with HIV will progress to Acquired Immune Deficiency Syndrome (AIDS), although about 5% of people infected with HIV have the immune capacity to maintain an asymptomatic state, so-called HIV controllers.

It is important to understand the difference between HIV infection and AIDS. According to the Centers for Disease Control (CDC) case definition, the diagnosis of HIV infection requires either a positive result on a multi-test algorithm (at least two distinct antibody/antigen tests positive) or a positive HIV virologic

Table 1. AIDS Defining Conditions as Adapted from UpToDate®

- Bacterial infections, multiple or recurrent*
- Candidiasis of bronchi, trachea, or lungs
- Candidiasis of esophagus†
- Cervical cancer, invasive‡
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, disseminated or extrapulmonary
- Cryptosporidiosis, chronic intestinal (>1 month's duration)
- Cytomegalovirus disease (other than liver, spleen or nodes), onset at age >1 month
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV related
- Herpes simplex: chronic ulcers (>1 month's duration) or bronchitis, pneumonitis, or esophagitis (onset at age >1 month)
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (> 1 month's duration)
- Kaposi sarcoma†
- Lymphoid interstitial pneumonia or pulmonary lymphoid hyperplasia complex*†
- Lymphoma, Burkitt (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- Mycobacterium avium complex or Mycobacterium kansasii, disseminated or extrapulmonary†
- Mycobacterium tuberculosis of any site, pulmonary, 1, 3 disseminated or extrapulmonary†
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary†
- Pneumocystis jirovecii pneumonia†
- Pneumonia, recurrent†‡
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain, onset at age >1 month†
- Wasting syndrome attributed to HIV

* Only among children aged <13 year
† Condition that might be diagnosed presumptively
‡ Only among adults and adolescents aged >13 years

test. AIDS, however, is defined as chronic HIV infection that has resulted in CD4 cell depletion to a level <200 cells/microliter or having an AIDS defining condition regardless of CD4 cell count. See Table 1 for a list of AIDS defining conditions.[3]

EPIDEMIOLOGY

HIV has been a persistent pandemic for over 30 years. In the course of that time, AIDS has accounted for up to 40 million deaths. According to the most recent UNAIDS data, in 2013 there were approximately 35 million people living with HIV infection the vast majority of whom live in Sub-Saharan Africa (~24.7 million). There has been a steady decline in the number of new infections since 2001, but there were still 2.1 million new infections worldwide in 2013 and approximately 1.5 million deaths from AIDS that year.[4]

Closer to home, the numbers are far less staggering. According to the CDC in 2011, the most recent year for which firm data is available, approximately 1.2 million people were living with HIV in the United States, a figure that includes an estimated 168,000 that were as yet undiagnosed. On average, there are about 50,000 newly diagnosed infections in the United States per annum. The most common ages for which a new diagnosis is made is early adulthood to middle age (20-49); and the 3 most common means of transmission include: MSM (67%), heterosexual contact (25%), and IDU (10%).[5]

HISTORICAL PERSPECTIVES ON HIV INFECTION

Since HIV's earliest recognition in 1981, the understanding of this infection and its treatment has made tremendous strides. Additionally, the mortality associated with it has changed dramatically. The response from life insurers has not changed dramatically but is undergoing slow transition.

In 1981, an unusual cluster of cases of previously healthy men with *Pneumocystis carinii* pneumonia and Kaposi's sarcoma was identified. A common link was their practice of having sex with other men, and a common finding was depletion of T helper cells. A viral pathogen was identified that was thought to be the etiology behind these unusual cases and was called HTLV-III (Human T-Lymphotrophic

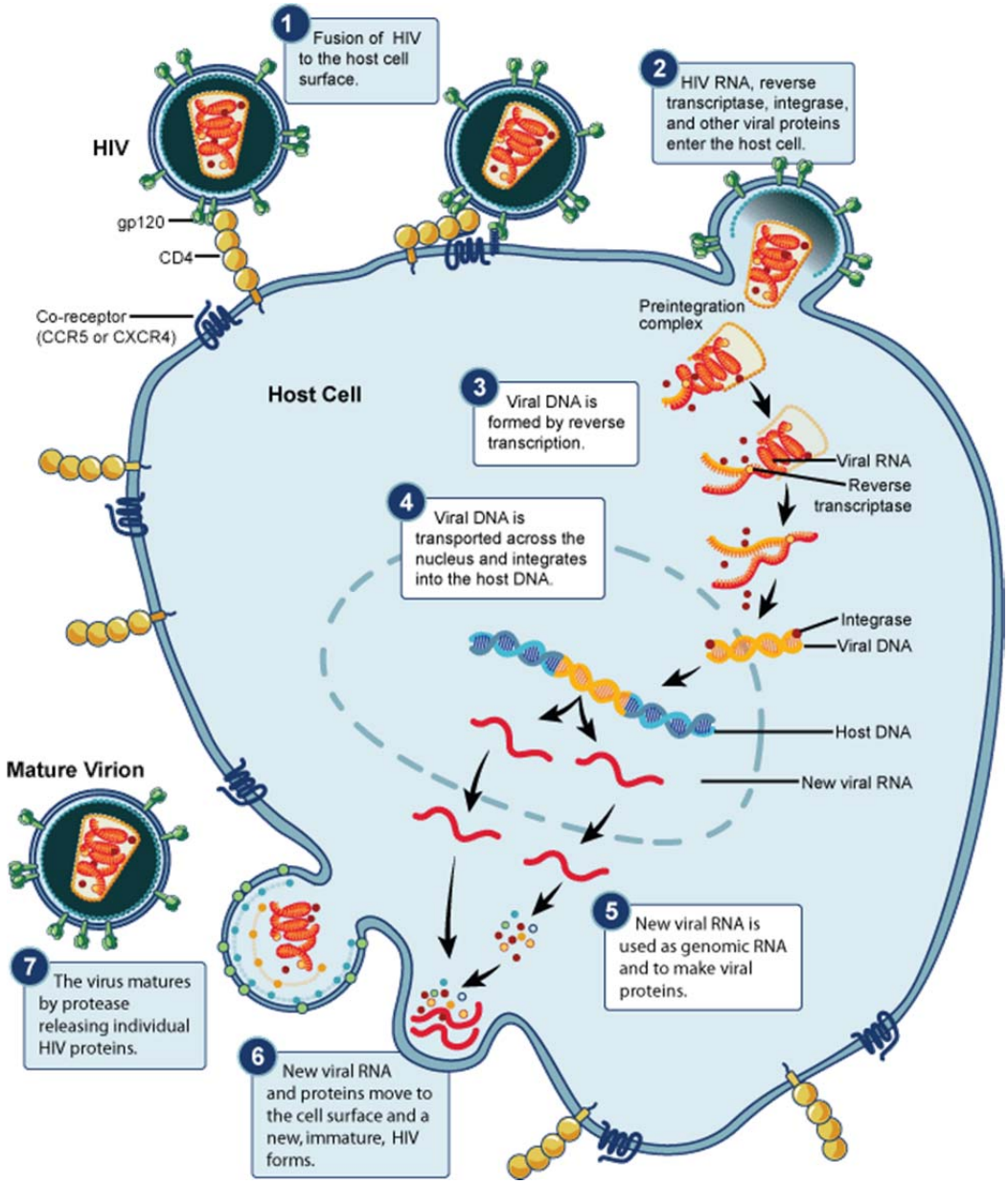

Figure. *Lifecycle of the HIV virus, with permission from the National Institute of Allergy and Infectious Diseases.*

Virus). With further investigation, HIV was isolated and definitively linked to the epidemic of AIDS.

Along with identification and naming of the retrovirus responsible for this infection came a better understanding of its mechanism of infection, replication and ability to cause disease and ultimately death. Additionally, the ability of clinicians to test for the retrovirus early after infection has progressed such that early testing after exposure accompanied by rapid results is comparable to other similar infectious diseases. See Figure for a pictorial representation of the lifecycle of the HIV retrovirus.

TREATMENT

Early in the course of this epidemic, treatment was aimed at the complications associated with infection to include surgery and radiation for Kaposi's sarcoma and medications to treat the infectious complications. Unfortunately, early treatments were minimally effective and upwards of 95% of infected individuals would succumb to AIDS.

As science progressed, administration of 3-azido-3-deoxythymidine (AZT) in very high doses along with pentamidine to those with AIDS to directly affect viral replication and prevent infection with *Pneumocystis carinii*, respectively, was attempted with some success. As understanding of the life cycle of the HIV virus grew, so did the number and type of medications used to treat it, as did the timing for institution of therapy. We are currently in the era of Antiretroviral Therapy or ART, formerly known as HAART (Highly Active Antiretroviral Therapy), which is described below.

ART consists of two potent nucleoside reverse transcriptase inhibitors along with a third drug with a different mechanism of action. The third drug is generally a protease inhibitor, non-nucleoside reverse transcriptase inhibitor, integrase strand transfer inhibitor or a CCR5 antagonist. See Table 2 for a list of medications currently available. Early on, treatment was begun only after AIDS was established. With the understanding of the viral life cycle and development of better and less toxic drugs, treatment is now often started at the time of initial diagnosis of HIV with the goals of maintaining CD4 counts, decreasing viral load, improving morbidity and mortality associated with infection, and decreasing the risk of transmission of the infections to others.[6]

Table 2. Current Medications for Treatment of HIV as Adapted from UpToDate®, 2014

Generic Name (Abbreviation)	Brand Name
Nucleoside and nucleotide reverse transcriptase inhibitors (NRTIs)	
Abacavir (ABC)	Ziagen
Didanosine (ddI)	Videx, Videx EC
Emtricitabine (FTC)	Emtriva
Lamivudine (3TC)	Epivir
Stavudine (d4T)	Zerit
Tenofovir (TDF)	Viread*
Zalcitabine (ddC) (no longer marketed in most countries)	Hivid
Zidovudine (ZDV, AZT)	Retrovir
Non-nucleoside reverse transcriptase inhibitors (NNRTIs)	
Delavirdine (DLV)	Rescriptor
Efavirenz (EFV)	Sustiva
Etravirine (ETR)	Intelence
Nevirapine (NVP)	Viramune, Viramune XR
Rilpivirine (RPV)	Edurant
Protease Inhibitors (PIs)	
Amprenavir (APV) (no longer marketed in most countries)	Agenerase
Atazanavir (ATV)	Reyataz
Darunavir (DRV)	Prezista
Fosamprenavir (FPV)	Lexiva
Indinavir (IDV)	Crixivan
Lopinavir/ritonavir boosting (LPV/r)	Kaletra
Nelfinavir (NFV)	Viracept
Ritonavir (RTV) (used as a pharmacokinetic boosting agent)	Norvir
Saquinavir (SQV)	Invirase
Tipranavir (TPV)	Aptivus
Fusion Inhibitor	
Enfuvirtide (T-20)	Fuzeon
Integrase Inhibitors	
Elvitegravir (EVG)	Vitekta
Raltegravir (RAL)	Isentress
Dolutegravir (DTG)	Tivicay
CCR5 Antagonist	
Maraviroc (MVC)	Selzentry

LIFE INSURANCE RESPONSE

As much as clinical medicine and HIV have changed over the past 30 odd years, attitudes and treatment by life insurers in this country have not necessarily kept up. Soon after the epidemic began and viatical companies swooped in to buy the policies of those with HIV and AIDS, a sea change in life insurance began. Generalized laboratory testing of applicants to include testing for HIV infection was begun. At the advice of the Society of Actuaries (SOA), very large reserves were set aside for claims. And, anyone with HIV was (and for the most part still is) declined for life insurance coverage. The 1987 SOA AIDS Task Force Summary predicted in excess of $30 billion in claims by the end of the 20th century based on a projection that large numbers would become infected and die within a short period of time and that "the outlook for developing a treatment to reverse the infection is not promising." For those applying with HIV, excess mortality

charges were estimated to be 5000% of standard with a cost of insurance of $500/1000.[7]

To my knowledge, there has not been another formal study by the SOA since 1987. There has been some change in consideration for issuing life insurance, however, primarily outside the borders of North America. As much as the science that has led to a better understanding of HIV has changed; and, as significantly as treatment, and its side effects, has improved; I believe it is time that North American life insurance companies, in particular the medical directors, reconsider the mortality characteristics of this disease with an eye toward potential insurability.

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