Running head: MOTHER-TO-CHILD TRANSMISSION

Prevention of Mother-to-child Transmission (PMTCT) of HIV in the Sub-Saharan Africa Region with a Focus on Uganda

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Abstract

With the rise of the HIV/AIDS epidemic in the past thirty years, people of all ages, infants to elderly alike, all over the world, suffer from its adverse effects. Even an unborn baby in-utero can contract this virulent infection by means of mother-to-child transmission (MTCT) (Sweeney, 2005). Infants and children diseased in this way comprise 90% of the estimated 800,000 new cases of HIV in children seen each year, but the region hit hardest, however, is Sub-Saharan Africa, with the country of Uganda historically having the highest incident rate for a time (Stringer, E.M., et al. 2008). Therefore, the purpose of this paper is to learn more about the prevention of MTCT in order to attain a better understanding of what is being done in this arena to impede HIV progression, to discover gaps in HIV/AIDS research and application, and to discern new and appropriate avenues in which a broader spectrum of people could contribute to the prevention of MTCT.

Prevention of Mother-to-child Transmission (PMTCT) of HIV in the Sub-Saharan Africa Region with a Focus on Uganda

No region of the world is exempt from the ravenous effects that the human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS) inflicts upon people of all ages at one level or another. It is an epidemic brought on by personal human behavior (UNAIDS, 2004). Unlike some diseases that have been around for centuries, HIV/AIDS is a more recent reality. In the year 1981, clinicians identified it as a new immunodeficiency syndrome found in homosexual men referred to as "gay-related immunodeficiency syndrome" or GRIDS (Sweeney, 2005). The incidence of this syndrome was steadily increasing, and it was eventually termed AIDS (Sweeney). It did not take long for people to realize that this disease could also be heterosexually transmitted when the virus was found passed to women as well (Gross, 2004).

Although a debatable issue, Kasensero, located in Uganda's Rakai district, is considered by some to be the site of the AIDS origination (Shoumatoff, 1988). The people of Uganda do not regard this disease as their own (Shoumatoff). However, evidence of AIDS in Uganda traces back to 1972 in the northwestern region, the homeland of Idi Amin in the Nile Province (Shoumatoff). Robert Gallo, who was a renowned AIDS researcher in America, noted that, "All the scientific signposts point to an origin in Africa, somewhere around the region of Lake Victoria" (cited in Shoumatoff, p. 132).

As knowledge of this fatal condition has increased in the last three or four decades, so have the number of people who have been infected with the virus. Despite the fact that the entire world experiences the effects of HIV, the region of Sub-Saharan

Africa has been more negatively affected by the virus than any other location (Sweeney, 2005). There has been a shift from men to women in the percentages of those infected with HIV. The Global Program of the World Health Organization's executive director announced it to the world back in 1993 that 50% of the new infections consisted of women and that most of the cases in Sub-Saharan Africa involved women (Gross, 2004).

More than a decade ago, in-depth scientific research was published in the *Journal of Virology* on HIV-1 infection of tissues and cells found on the upper and lower female reproductive tracts (Howell et al. 1997). From the Howell et al. research study, it was discovered that the tissues and cells of the female reproductive tract are vulnerable to being infected with HIV, and once those cells have been exposed to the virus, it only takes a minimum of 60 minutes for the infection to take hold (Howell, et al. 1997). The research also supported that varying levels of hormones may play a role in the production of the virus and its ability to infect the body because an increase in the recovery of the virus was observed in cervical ectopy, while using oral contraceptives, and pregnancy (Howell, et al. 1997). Even though these findings are from years ago, they have helped to set a framework for preventing transmission of HIV (Howell, et al. 1997).

As further research was performed and HIV/AIDS transmission was understood more, it was found that one of the three main modes of acquiring this virus is through perinatal transmission from the mother-to-child (MTCT) (Sweeney, 2005). In order to prevent the further spread of this virus, much work and research is still required so that the unborn babies of mothers who are inflicted with HIV may be protected.

The issue of MTCT is of great concern and demands attention because more recent records from 2006 show that approximately 2.3 million children under the age of

15 suffered from transfer of HIV, and of the 39.5 million people living with HIV around the world, approximately 17.7 million of them were women (Guidance, 2007). A study performed in Nigeria on leaders' perceptions of mother-to-child transmission prevention alleged that over half of a million children every year acquire the virus, but it is through mother-to-child transmission in which 90% of those children get it (Arulogun, Adewole, Olayinka-Alli, & Adesine, 2007). This means over 1400 young children and teenagers not yet 15 years old from impoverished areas are afflicted with this virus daily (Guidance). Updates from the World Health Organization (WHO) continue to support that most of these cases are found in Sub-Saharan Africa due to the fact that among pregnant women living in those countries there is a high prevalence for HIV, and it is a region in which the health-care infrastructure is under resourced (Stringer, E.M., et al. 2008). Without effective prevention measures, a large number of these infants and children, more than 50%, will not live to see the day they turn two years old (Guidance).

Of the 90% or more of the new cases seen in infants and young children that occur through mother-to-child transmission, there are three areas or routes by which these children are at risk of contracting the virus. According to researchers that make up the Interagency Task Team (IATT) on Prevention of Mother-to-Child Transmission (PMTCT), these include the following: during the antenatal time, or pregnancy, during the birth, or through breastfeeding (Guidance, 2007). An even more recent piece of literature from the *Bulletin of the World Health Organization* discussing the effectiveness of MTCT prevention in countries of low income identified from a plethora of studies some significant reoccurring risk factors. The following have been referred to as the most important when regarding perinatal transmission: vaginal birth, breastfeeding, a low

count of CD4+ lymphocyte cells in the mother, and a high HIV viral load in the mother's plasma (Stringer, E.M., et al. 2008). Whatever the causes may be, if nothing is done to prevent this infestation, then anywhere between 20% and 45% of those children born to HIV-diseased mothers could contract the virus (Guidance). Research gathered by the IATT estimates that breastfeeding could be responsible for 5-20%, labor and delivery 10-20%, and the time during the pregnancy, 5-10%, of transmitting HIV (Guidance). Earlier research from a decade ago suggested that breastfeeding was responsible for half of the mother-to-child transmissions, while pregnancy and birth caused the other half of transmissions (Weinreich, 2003).

Overview of the Disease Process

With all of these alarming statistics and specific terms being thrown around, terms such as "viral load" or "CD4 levels," a basic overview of the disease and why it is such a virulent infection is necessitated. This human immunodeficiency virus (HIV) can eventually develop into what has been termed AIDS which stands for "acquired immunodeficiency syndrome," as noted above. The passing of the virus has four main modes of transfer, two of which are horizontal modes and two that are vertical (Hockenberry, 2005). The former two include exposure to blood and sexual contact, the latter, childbirth and breastfeeding (Gallant, 2009). The term *vertical* refers to the passing of HIV perinatally from the mother to the infant (Hockenberry). Transmission through mosquitoes or other insects is not a mode of transfer (Sweeney, 2005). Also, the occurrence of viral spread from infected individuals to uninfected individuals by means of casual contact has not been supported by evidence (Hockenberry).

A key concept about this virus is that HIV is a retrovirus (Sweeney, 2005). Such is the nature of all viruses HIV cannot duplicate if it is not inside of a living cell (Bradley-Springer, Shaw, & Lewis, 2007). A retrovirus produces enzymes that allow RNA to manufacture DNA through a reverse transcription process. RNA is the retrovirus' own genetic material that has the capability of becoming DNA. Normally, DNA turns into RNA through the process of transcription, but HIV is called a retrovirus because it does just the opposite (Gallant, 2009). Once the virus has infected the body, it uses reverse transcriptase, the enzyme, to convert the RNA into the DNA. This new DNA, which used to be RNA, is now able to enter human cell DNA (Gallant). This entry allows for more virus to be formed and more healthy cells to potentially be affected. It is as if the virus is disguised in human DNA but now wears an ominous mask. It can also lie quiet for years, in a latent phase, like a dangerous reservoir or volcano waiting to erupt (Gallant). A reservoir cell can survive as long as a human while it houses the infection, which allows the virus to be latent (Gallant). An example of a reservoir would be a long-lasting resting CD4 cell. The inside of the cell is a nest for viral DNA. Because replication cannot occur, antiretroviral therapy will prove ineffective for this sick cell (Gallant). The phrase "viral load" refers to the quantity of HIV components found within the blood plasma (Bradley-Springer, et al.).

The significance of this retrovirus attacking the CD4+ cells is that the CD4+ cell is a kind of T lymphocyte, more specifically a T lymphocyte sub-category (Hockenberry, 2005). It is the job of the lymphocytes to take charge over the response of the immune system when infection invades the body (Sweeney, 2005). The lymphocytes are what help to keep a normally functioning healthy body from illness. When HIV strikes

however, these crucial lymphocytes are now becoming poisoned, so to speak, with the virus and cannot effectively perform their life-sustaining responsibilities. This is because the virus hijacks CD4+ lymphocyte's mechanics so that viral duplication can occur. This leaves the CD4+ cell unable to function properly (Hockenberry). It is a vicious cycle, for when the RNA of HIV has used reverse transcriptase to become DNA, the virus proliferates (Sweeney). As the virus continues to spread, the levels of healthy CD4+ T lymphocytes significantly decline, and as a result, the immune system deteriorates. The body, under normal circumstances, has approximately 800-1000 CD4 cells/uL. An HIV-infected person transitions into having AIDS when their CD4+ T lymphocyte count falls below 200 cells/uL (Hockenberry). This is why people with HIV acquire other forms of infection, such as *pneumocystis carinii*, which is a type of pneumonia that is hallmark in a patient with HIV. Susceptibility to *Kaposi sarcoma*, a form of malignant skin cancer that negatively impacts the endothelial cells of blood vessels is also prevalent (Sweeney). It is fascinating that this type of sarcoma has been noted as mainly a cancer of Africa that was seldom seen in the West (Shoumatoff, 1988). It was apparently *Kaposi sarcoma* that was a significant cause of death in some of the earlier AIDS incidents seen in Europeans and Americans; they were vexed by the seemingly "African" pattern of the disease process (Shoumatoff).

These conditions, along with a long list of others, are referred to as opportunistic infections. Because the immune system is so compromised due to the sick CD4 cells, the body is incapable of controlling and battling off these non-rapacious diseases (Sweeney, 2005). The Centers for Disease Control (CDC) established a defining classification grid for people with the infection that became effective in 1993 on January first. Three

categories were designed based on the levels of CD4 cells per microliter (ul) of blood (Sweeney). Category 1: >500 cells/uL, category 2: 200-400 cells/uL, and category 3: <200 cells/uL (Sweeney, p. 431). See Table 1 below.

Table 1: CD4+ Cell Categories	**Clinical Categories**		
Key to abbreviations: **CDC** = *U.S. Centers for Disease Control and Prevention* **PGL** = *persistent generalized lymphadenopathy.*	**A** Asymptomatic, Acute HIV, or PGL	**B** Symptomatic Conditions, not A or C	**C** AIDS-Indicator Conditions
(1) ≥500 cells/µL	A1	B1	C1
(2) 200-499 cells/µL	A2	B2	C2
(3) <200 cells/µL	A3	B3	C3
Category B Symptomatic Conditions parameters are identified in **Table 2** Category C AIDS-Indicator Conditions parameters are identified in **Table 3**			

Note: Re-designed from the CDC "1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults," by K.G. Castro & J.W. Curran, 1992, *MMWR* and (HIV Classification: CDC & WHO Staging Systems, (2006) *AETC National Resource Center, 2009)*

Table 2: Symptomatic Conditions included in Category B: CDC Classification System in Adolescents and Adults

- Bacillary angiomatosis
- Candidiasis, oropharyngeal (thrush)
- Candidiasis, vulvovaginal; persistent, frequent, or poorly responsive to therapy
- Cervical dysplasia (moderate or severe)/cervical carcinoma in situ
- Constitutional symptoms, such as fever (38.5 C) or diarrhea lasting greater than 1 month
- Hairy leukoplakia, oral
- Herpes zoster (shingles), involving at least two distinct episodes or more than one dermatome
- Idiopathic thrombocytopenic purpura
- Listeriosis
- Pelvic inflammatory disease, particularly if complicated by tubo-ovarian abscess
- Peripheral neuropathy

Note: Table 2 & 3 Re-created from "1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults," by K.G. Castro & J.W. Curran, 1992, *MMWR* Copyright 1993 Centers for Disease Control

Table 3: Conditions included in the 1993 AIDS surveillance case definition

- Candidiasis of bronchi, trachea, or lungs
- Candidiasis, esophageal
- Cervical cancer, invasive *
- Coccidioidomycosis, disseminated or extrapulmonary
- Cryptococcosis, extrapulmonary
- Cryptosporidiosis, chronic intestinal (greater than 1 month's duration)
- Cytomegalovirus disease (other than liver, spleen, or nodes)
- Cytomegalovirus retinitis (with loss of vision)
- Encephalopathy, HIV-related
- Herpes simplex: chronic ulcer(s) (greater than 1 month's duration); or bronchitis, pneumonitis, or esophagitis
- Histoplasmosis, disseminated or extrapulmonary
- Isosporiasis, chronic intestinal (greater than 1 month's duration)
- Kaposi's sarcoma
- Lymphoma, Burkitt's (or equivalent term)
- Lymphoma, immunoblastic (or equivalent term)
- Lymphoma, primary, of brain
- Mycobacterium avium complex or M. kansasii, disseminated or extrapulmonary
- Mycobacterium tuberculosis, any site (pulmonary * or extrapulmonary)
- Mycobacterium, other species or unidentified species, disseminated or extrapulmonary
- Pneumocystis carinii pneumonia
- Pneumonia, recurrent *
- Progressive multifocal leukoencephalopathy
- Salmonella septicemia, recurrent
- Toxoplasmosis of brain
- Wasting syndrome due to HIV
- Added in the 1993 expansion of the AIDS surveillance case definition.

Note: Table 2 & 3 Created From "1993 Revised Classification System for HIV Infection and Expanded Surveillance Case Definition for AIDS Among Adolescents and Adults," by K.G. Castro & J.W. Curran, 1992, *MMWR* Copyright 1993 Centers for Disease Control

The three divided phases of this infection are also significant to note. It takes about 8-12 years for these phases to run their course (Sweeney, 2005). These include the following: the primary infection phase, chronic asymptomatic or latency phase, and the overt AIDS phase (Sweeney). In the primary infection phase, a victim of the virus may experience symptoms such as fever and rash, the two most commonly seen, two to four weeks after they have been exposed (Sweeney). The symptoms could last for a few days to a couple of weeks (Sweeney). Other symptoms of this acute phase include the following: fatigue, myalgias, sore throat, night sweats, gastrointestinal complications,

lymphadenopathy, maculopapular rash, and headache. This phase resembles a mononucleosis-like syndrome (Sweeney). It is in this first phase when patients should receive treatment so as to decrease the existing CD4+ memory cells that have been infested by the virus (Sweeney). From the primary phase, the course of the disease goes into the latent phase, in which the virus may stay quiet and demonstrate no symptoms or signs of disease. The average latent period is ten years (Sweeney). Despite its illusive existence, the CD4 levels have then plummeted to 200u/L or lower, and once these levels hit 200, the patient is deemed to be in the third phase of HIV, which then becomes "overt AIDS," and signs and symptoms seen through these opportunistic infections become more and more apparent, to the point where they are quite distinguishable and unavoidable (Sweeney). Death is impending in two to three years if left untreated by anti-retroviral therapy (Sweeney).

Interventions Overview

The goal of reviewing literature pertaining to the prevention of MTCT is to research methods or practices that are effective in making the PMTCT successful. It is important to assess the gaps or loopholes that do not allow for prevention to take effect. If the virus is transmitted through breastfeeding, pregnancy, and labor and delivery, then reviewing research that focuses on how the transmission occurs in those areas is important, as well as interventions that have shown to either be helpful or ineffective.

The *Weekly Epidemiological Record* suggested that there has been an increase in interventions to halt vertical transmission from happening between the mother and child (May, 2007). The Record supports the belief that if these interventions are implented between the mother and child, then a significant number of infants birthed from mothers

who have HIV will not end up contracting the virus perinatally (Weekly, 2007). If safe delivery practices are utilized and antiretroviral therapy is incorporated to prevent the mother from transmitting the virus to the baby, and diagnosing the mother with HIV early on so prevention can be attempted, then these infants have a chance of escaping this deadly virus (Weekly). For a pregnant mother who carries her child to term, the risk of passing the virus to the infant can be reduced to approximately two percent if the child is delivered via cesarean section, and she is on medication that will lower the circulating virus in her blood (Bartlett & Finkbeiner, 2001).

Advances in such implementations are crucial because if proper preventative measures are not taken infants could end up struggling to live life HIV-infected from birth. Because of the body's phenomenal design and natural protection set in place, the placenta prevents the passage of the virus to the fetus. Nevertheless, this is not fully guaranteed because the placenta is vulnerable to failure if the following three conditions occur: the mother during the antenatal period acquires a parasitic, bacterial, or viral infection in the placenta, she herself gets the virus while pregnant, her viral load is high, or she is extremely immune compromised because her current case of AIDS is quite advanced (Campbell, 2005). The fetus is in a potential danger zone and not just during the antenatal time; the birthing process jeopardizes the infant's safety. It has been noted that, if nothing is done to keep the infant from acquiring the virus via birth, then as many as 10 to 20 percent will get the infection (Campbell). As gruesome as it sounds, the child may access the virus during the delivery process by aspirating the mother's HIV contaminated blood or secretions or through imbibing or sucking (Campbell). At least two other conditions have also been correlated with an increased risk of transmitting the

virus to the infant because exposure to maternal blood escalates. These would include acute chorioamnionitis and membrane rupture time interval. The former is the result of sexually transmitted infections as well as other forms of infections that were left untreated. The latter procedure is done to initiate or enhance labor. Finally, delivery tactics that are invasive and that heighten the infant's interaction with maternal blood can also increase HIV transmission (Campbell). In light of cases such as these, a Caesarean section performed at 38 weeks is highly encouraged and preferable. However, in certain regions where HIV is rampant and healthcare interventions and resources are basically nonexistent, a C-section is asking too much. This is where intervention programs incorporating volunteer testing, transportation, funds, planning, availability of antiretroviral drugs, safe antenatal care, delivery, replacement feeding, and postnatal care campaigns are vital to infant survival for some of these families, as well as their mothers (Campbell).

Since HIV can also be secreted in breast milk, practicing safe infant feeding methods is critical. Evidence-based research supports transmission of HIV through breastfeeding, particularly in the early weeks of life of the infant (Ross & Labbock, 2004). When discussing how to avoid transmitting the virus, some experts strongly counsel against breastfeeding in a situation in which the mother is infected with HIV (Bartlett & Finkbeiner, 2001). The risk of HIV being transmitted through breast milk over a six to twelve month period is between 15% & 25%. Anti-retrovirals administered to both mother or child will likely reduce transmission; the exact reduction is not defined (Bartlett & Finkbeiner, 2001). Alternatives to breastfeeding might include infant formula,

utilizing the services of a lactating HIV negative woman within the community, or acquiring breast milk from a milk bank or a local co-op.

In the United States breast milk is available through a plethora of banking and co-op services. In these organizations, healthy women donate their milk to help care for children whose nutritional statues is hindered by the mother's inability to breast-feed. The most exacting of these services is the National Milk Bank that requires certification for their milk product. To date, they are the strictest of the milk banks to ensure safety. For example, all of their donors are screened for HIV and hepatitis B and C and are DNA finger-printed to ensure that the donation matches the screened donor (National, 2008).

While Bartlett & Finkbeiner (2001) are steadfast on their opposition to breastfeeding when HIV positive, clearly the expense and practicality of milk bank services in a developing nation setting would preclude this as an option. Even the expense of formula is beyond the means of most families in under-developed areas. Therefore, other authorities are more open to the breastfeeding option for HIV positive mothers.

Ross & Labbok (2004) offer an important additional argument in consideration of breastfeeding versus artificial feeding. Infants depending entirely on artificial feeding may receive nutrition, but are deprived of the natural antibodies. Without the benefit of maternal antibodies the child's risk of death is compounded. The risk-to-benefit ratio of acquiring HIV must be weighed to determine the value of artificial feedings versus breastfeeding. In their study of a region of high HIV prevalence, they concluded that an infant should not be given artificial feeding prior to six months of age (Ross & Labbok). During those early months, the feeding of natural breast milk should be initiated because

HIV-free survival increases by over three percent (Ross & Labbok). Their findings invalidate earlier studies (Miotti, et el., 1999; Taha, et al., 1998) alleging the risk of MTCT through breastfeeding is at its highest during those earlier months. The transmission risk continues as breastfeeding continues; some studies supported an increased risk of transfer with a longer duration of breastfeeding (Miotti, et el., 1999; Taha, et al., 1998). Increased parity greater than four and increased maternal age decreased the risk of transmission among HIV positive women (Miotti, et el., 1999). These findings are contradicted by a South African study, which found that exclusive breastfeeding might protect children from HIV infection while maintaining the benefits of breastfeeding (Coutsoudis, Pillay, Spooner, Kuhn, & Coovadia, 1999). Further study from South Africa found no excess risk of HIV infection for infants that were exclusively breastfed for three or more months (Coutsoudis, A. et al., 2001). Recent research from Tanzania found that the risk of MTCT in breast milk might be reduced if concentrations of n-6 polyunsaturated fatty acids including arachidonic acid were increased in breast milk. (Villamor, et al. 2007). Readily available maternal food sources for these compounds include fish, eggs, meat, and peanut oils may increase these essential fatty acids in breast milk (Calder, 2007).

Preventing the transmission of this virus to the child is so essential because these babies do not respond in the same way immunologically as adults do to the attack of the HIV infection (Bartlett & Finkbeiner, 2001). As children grow, their bodies build up their immune systems to be able to attack foreign invaders or pathogens and produce antibodies to fight them off when they return, but if a child is born with an immunodeficiency virus and cannot be breastfed, then HIV will be hindering an immune

system that is not even fully developed, causing the infant to be in a weakened state that will lead to an impending death if interventions do not come to the aid of the child. The child is born with immunity, but a mother's endogenous breast milk steeped with antibodies allows the infant to gain the essential natural passive immunity from the mother (Porth, 2005).

The agencies collaborating on global improvement of the PMTCT of HIV note that decreasing the percentages that HIV is transmitted to the baby through breastfeeding, pregnancy, labor and delivery can be done by implementing an evidence-based interventions package (Guidance, 2007). In the majority of countries that have a higher income, this package serves as the standard (Guidance). This literature published six years after Bartlett and Finkbeiner's alleges that the risk factor of PMTCT is now less than two percent. In areas where the package is implemented, the results show very few new HIV cases in children (Guidance). The concern that the WHO has for developing countries such as those in Sub-Saharan Africa is that the resources are limited (Stringer, E.M., et al. 2008). The transmission risks do not change, but the implementation of effective prophylaxis is universally lacking including availability of preliminary antenatal care, Caesarean-sections that are elective, anti-retroviral (ARV) regimens, and finally substantial substitutes to breastfeeding (Stringer, E.M., et al. 2008). Despite this pessimistic fact, data from the World Health Organization recorded from the years 2003-2007 demonstrates in Chart 1 below an example in which global intervention has not been in vain as antiretroviral coverage in the Sub-Saharan region has clearly gone in the right direction.

Chart 1. Map Displaying ART Treatment in the sub-Saharan Region in the years 2003-07

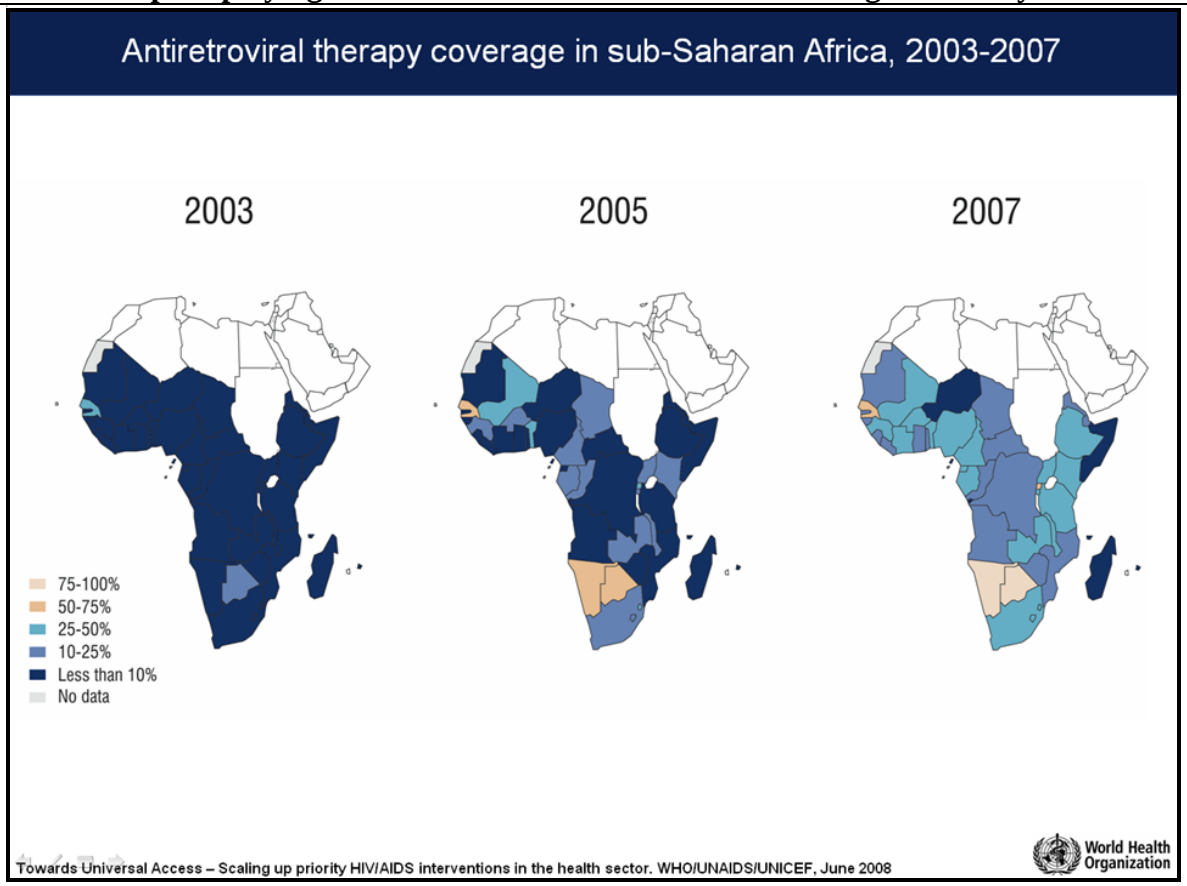

Chart 1. Note: From HIV/AIDS Data and statistics. *World Health Organization*. Copyright WHO 2009

Incorporating interventions by means of family planning and primary prevention offer more hope (Weinreich, 2003). Primary prevention means that women in their reproductive years should attempt to prevent themselves from getting the HIV infection in the first place, but that uncovers a whole other set of issues and complications (Weinreich). Family planning for women already infected with HIV can take advantage of contraceptive methods and seek counseling since they are already aware of their condition (Weinreich). There is still hope for prevention; all is not yet lost.

Table 4: Six Categories of HIV Antiretroviral Drugs

Since the arrival of the first drug used to treat HIV in 1987, a number of classes and drug types have been produced and are to be taken in combination with each other to counteract the many effects that this virus has on the body (Hockenberry, 2005). With these therapy regimens, the desired effect is to see a decline in the viral load, an incline in the healthy CD4+ T lymphocytes, and finally to impede the progression of opportunistic disorders and accompanying symptoms that are notorious of the HIV infection (Bradley-Springer, et al., 2007).

There are six categories of antiretroviral drugs. Table four below may be referred to for a clear depiction of what the job of each class is and examples of each category.

Anti-retroviral Drug Classes	Description of Action	Drug Examples
Group 1: Non-nucleoside reverse transcriptase inhibitors *NNRTI*	These drugs, in combination with the reverse transcriptase enzyme, basically prevent the process necessary for the conversion of HIV RNA to HIV DNA to take place	• Nevirapine (Viramune) • Delavirdine (Rescriptor) • Efavirenz (Sustiva)
Group 2: Nucleoside reverse transcriptase inhibitors *NRTI*	This class of drugs interleaves a portion of DNA into the HIV DNA chain that is in the process of developing. The newly placed DNA halts the progression of the HIV DNA, rendering it an unfinished chain	• Zidovudine (AZT, ZDV, Retrovir • Stavudine (d4T, Zerit) • Lamivudine (3TC, Epivir), Abacavir (Ziagen)
Group 3: Nucleotide reverse transcriptase inhibitors *NtRI*	These drugs prohibit the activity of reverse transcriptase	• Tenofovir DF (Viread) • Truvada (tenofovir and emtricitabine combination)
Group 4: Protease Inhibitors *PI*	The PIs thwart the work of the protease enzyme so that it cannot compartmentalize the HIV proteins into appropriate sections necessary for the workable virions to amass and sprout out from the membrane of the cell	• Saquinavir (Fortovase, Invirase) • Indinavir(Crixivan) • Ritonavir (Norvir) • Nelfinavir (Viracept) • Amprenavir (Agenerase)
Group 5: Entry Inhibitor	This drug type is given to not allow passage of HIV into the cells by halting the binding of the virus to the desired CD4+ receptor site. By stopping this entry, internal duplication within the cell is prevented	• Enfuvirtide (Fuzeon)
Group 6: Integrase Inhibitors	These drugs inhibit the process known as integration that has to occur for HIV's DNA to become part of the CD4 cell's DNA (aidsmeds.com)	• Raltegravir • Elvitegravir

Note. [Material used to create table from] *Medical-Surgical Nursing: Assessment and Management Clinical Problems* (7th ed.). (p. 257), by L. Bradley-Springer, C.A., Shaw, & S.L. Lewis, 2007, St. Louis, MO: Mosby, Inc.

The first group is the nonnucleoside reverse transcriptase inhibitors (NNRTIs). These drugs, in combination with the reverse transcriptase enzyme, basically prevent the process necessary for the conversion of HIV RNA to HIV DNA to take place. (Bradley-

Springer, Shaw, & Lewis, 2007). The second group known as the nucleoside reverse transcriptase inhibitors (NRTIs), interleaves a portion of DNA into the HIV DNA chain that is in the process of developing. The newly placed DNA halts the progression of the HIV DNA, rendering it an unfinished chain (Bradley-Springer, et al.). The nucleotide reverse transcriptase inhibitors (NtRI) prohibit the activity of reverse transcriptase (Bradley-Springer, et al.). Despite their individual specific modes of interference, these three classes together halt the action of reverse transcriptase. The next group, the protease inhibitors (PIs) interrupt the work of the protease enzyme. More specifically, the PIs thwart the work of the protease enzyme so that it cannot compartmentalize the HIV proteins into appropriate sections necessary for the workable virions to amass and sprout out from the membrane of the cell (Bradley-Springer, et al.). The entry inhibitor drug is given to not allow passage of HIV into the cells by halting the binding of the virus to the desired CD4+ receptor site. By stopping this entry, internal duplication within the cell is prevented (Bradley-Springer, et al.). Finally, the integrase inhibitor drugs attempt to halt the process known as integration that has to occur for HIV's DNA to become part of the CD4 cell's DNA (Integrase, 2007). It is crucial that these anti-retrovirals are taken in combination with each other, such as an HIV drug cocktail, to impede viral progression as well as prevent potential viral mutations that can occur with not following an ART regimen. Also, the virus can become resistant and unresponsive to treatment (Bradley-Springer, et al.). In other words, one region of a country may not respond to a certain drug due to the corresponding resistance that has arisen in the virus in that particular area. Sensitivity data must be researched and considered to determine the most affective drug treatment combinations.

Study trials performed in countries such as Thailand and Cote d'Ivoire using short-course zidovudine (ZDV) and in Uganda using single-dose nevirapine showed hopeful results that simple, short course ARV regimens work. It also showed though that the more suppressive regimens that are used for a longer time period do work better (Stringer, E.M., et al. 2008). Even for countries that are resource-constrained, it is encouraging that simple, short-course zidovudine coupled with single-dose nevirapine used prophylactically (a cheaper antiretroviral regimen), has shown to be effective in significantly decreasing the risk of transmission to a fetus in utero and intra-partum (Guidance, 2007).

Even though this regimen is less expensive than others, for some countries drug cost is still an issue. Records from Uganda show that in the year 2004, it took US $-180.00 per person for the year as the average cost coverage for the first-line regimen, laboratory tests, and training. The first-line regimen included the zidovudine (stavudine), lamivudine, and nevirapine (or efavirenz) (Uganda, 2005). Even though that is a small sum for a year for high-income countries, there is a shortage of human resources as well as low salaries, a ban on hiring, and decreased incentive in the public sector (Uganda). The district and sub-district levels are at a disadvantage because accessibility to antiretroviral therapy is quite limited (Uganda).

Donations of Nevirapine by the Boehringer/Ingelheim manufacturer have been given at no charge since 2001 to developing countries, which effectively decreases MTCT (Weinreich, 2003). A study done in Uganda with the use of Nevirapine displayed a reduction in vertical transmission by 50%; both the mother and child received the drug, the mother during delivery and the infant after birth (Weinreich). Also, the children that

received nevirapine (NVP) over zidovudine (AZT) were at a much lower risk of acquiring the infection (Weinreich). An attempt made by the Division of HIV/AIDS Prevention to decrease MTCT by the use of zidovudine therapy in the nineties was written up in the Morbidity and Mortality Weekly Report (MMWR) seven years ago, stating that ZDV was effective in lowering MTCT and was eagerly accepted in clinical practice (Wortley, Lindegren, & Fleming, 2001). More recent evidence-based findings support that nevirapine has shown to be more efficacious than zidovudine in certain circumstances, and the literature does support NVP as a more favorable drug in some areas than ZDV. This observation though is based on reviewed literature from a limited number of studies and research that has previously been performed.

There has been concern over the issue of nevirapine toxicity due to extensive use of this drug. The Stringer, J.S., Sinkala, Rouse, Goldenberg, & Vermund research study aspired to weigh drug toxicity versus benefit. This uneasiness had halted the use of nevirapine as prophylactic therapy for perinatal HIV transmission because of it (2002). Results of this study also supported NVP as a more effective drug than ZDV in that it showed NVP would prevent more deaths than ZDV would, and they concluded that there should not be a delay in the utilization of NVP on the field, despite the arisen qualms regarding its toxicity (Stringer, J.S., et al. 2002). However, field implementation also showed that NVP resistance is a problem due to viral strains (Stringer, J.S., et al. 2002). It is widely used as a first-line drug, thus some kind of intervention is necessary, and it needs to be done quickly (Weinreich, 2003). The World Health Organization (WHO) Technical Consultation supports the conclusion from the Stringer, J.S., et al. 2002 study in noting that the benefit that drugs such as ZDV, NVP, and lamivudine (3TC) have on

decreasing MTCT of HIV significantly countervails for any of the possible consequences that exposure to these drugs would have on the individuals (Technical, 2000).

A study was published in 2007 that judged the operational effectiveness of single-dose nevirapine in preventing mother-to-child transmission of HIV presented with similar results, concluding that in the operational setting, early transmission of HIV can be reduced when single-dose nevirapine is administered to both the infant and the mother (Colvin, et al., 2007). Even though nevirapine has shown to be effective, the study was aimed at evaluating the effectiveness of the program, which was intended to prevent mother-to-child transmission. The researchers noted that in order for MTCT of HIV to be lowered, many important steps must be incorporated. For example, a care continuum must be present so that the acceptance and availability of pre-test counseling and HIV testing is monitored, women revisit in order to review the results, and follow-up care after the child is born is accessible (Colvin, et al., 2007). From the study, however, there was a deficit in a number of these critical factors seen in multiple African countries. This is attributed to the fact that PMTCT programs like this are being offered to health systems that are, as Colvin, et al., 2007 describes, “overburdened” (p. 466). This makes programs with good intentions ineffective to floundering health systems (Colvin et al., 2007). Therefore, the study concluded that there is a need for scaling-up antiretroviral regimens (Colvin et al., 2007). Similar to the study done in Uganda, nevirapine also showed to be more efficacious than zidovudine in the Colvin et al. research when looking at the percentage of infants found to be HIV positive at age 5-8 weeks (2007). The results of zidovudine therapy revealed 20.0% of infected infants, but the infection rate using nevirapine was only11.8% (Colvin et al., 2007). Finally, it was noted for this particular

study that a high viral load of HIV-1 RNA in the mother was the most significant risk factor for transmission; this fact is supported by numerous multivariate analyses in women not receiving prophylaxis through antiretroviral therapy or in those taking antiretrovirals (Colvin et al., 2007). Analysis has repeatedly displayed that maternal HIV-1 RNA levels represent the leading predictor of newly transmitted HIV or the risk of acquisition during labor and delivery for their infants (Colvin et al., 2007). It is quite logical that this is the case.

The Arvold et al. research study on maternal HIV-1 DNA load and MTCT found the same to be true in that it notes the maternal HIV-1 RNA viral load (RNA-VL) was repeatedly shown to be the main risk factor. They mention that this includes antiretroviral prophylaxis when used for PMTCT (2007). The ART used in this study was zidovudine prophylaxis in the antenatal period, as well as for the infants after they were born (Arvold et al., 2007). The following chart provides another detailed visual that compares percentages of pregnant women who were getting drug therapy in Sub-Sahara Africa with other regions of the world from 2004-2007.

Chart 2. Percentage of Seropositive Pregnant Women Covered by ART Therapy

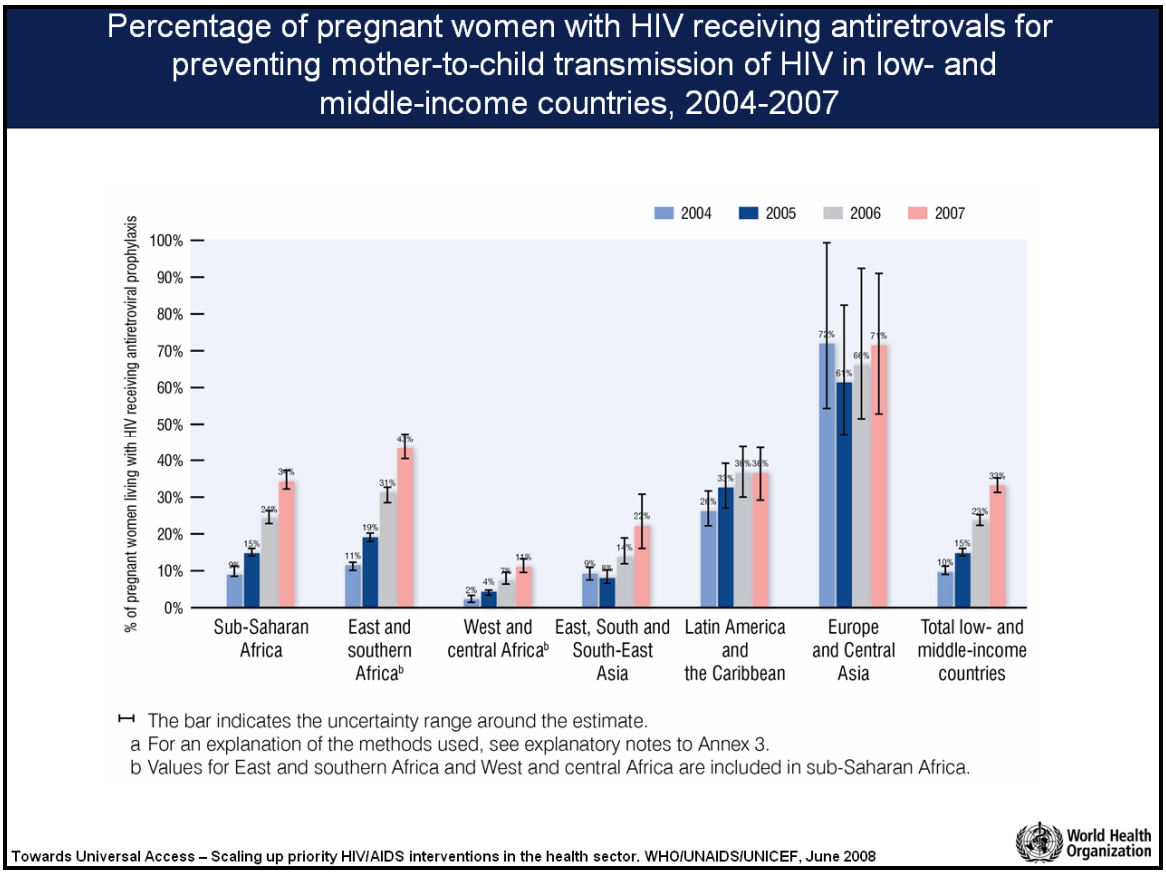

Chart 2. Note: From HIV/AIDS Data and statistics. *World Health Organization*. Copyright WHO 2009

Interventions and Gaps to Successful Prevention

Antiretroviral regimens have shown to be a beneficial mode of slowing the HIV/AIDS epidemic, along with safer delivery practices, education on prevention, programs in PMTCT, and alternative feeding strategies, but HIV testing and volunteer counseling and testing (VCT) is another important venue used to decrease this MTCT. As helpful as antiretroviral therapy is, however, and manufacturers like Boehringer/Ingelheim have donated drugs to pregnant Ugandan women, it strongly necessitates further testing that many countries cannot afford (Weinreich, 2003). In light of this dilemma, only 1% of all pregnant African women receive VCT (Weinrich). Literature from the *American Journal of Public Health* supports this by noting that the necessary bridge to providing antiretroviral drug therapy will be through testing for HIV

during antenatal care (Bassett, 2002). The article agrees that African clinicians are unable to extend much help to those infected with HIV (Bassett). It mentions though that Uganda accepts its AIDS condition and has made strides in setting up voluntary testing centers for HIV (Bassett). It is important that a pregnant woman is aware of her infection status and that antenatal care can be given to both mothers and babies so they can not only survive, but be able to live healthy lives (Bassett).

From a law and ethics perspective, an individual's right to privacy and informed consent is certainly violated when HIV testing is something required (Davis & Cohen, 1994). However, mandatory screening is a debatable issue. But the flip side is when an infant could be spared the infection if the mother's status is revealed. A child can contract the virus during childbirth and through breastfeeding. If the proper preventative measures are taken, that child's life has the potential to be free from HIV for life, despite its mother's seropositive status (Post, 2003). Though they are not specifically mentioned, newborn HIV testing is a requirement in two states so far, based on material recorded from 2003 (Post). This clearly overrules the informed consent parameter because if the child is positive then the mother's HIV condition is circuitously broadcasted (Post). No human individual wants to confront that he or she has been infected with AIDS. In many countries, if not the entire globe, there is a stigma attached to those who carry the sticker across their foreheads, and no one wants to be marginalized or judged based on their condition. Knowing whether one is positive for HIV or not is obviously a better option for everyone involved. It would not be an easy thing to face, but if screening were mandatory, especially if it impacted another being so closely, would not the benefit of preventing an infant from contracting the virus outweigh the shame that may accompany

accepting one's state that can only be improved if properly acknowledged? Granted, as mentioned earlier, there are countries unlike the United States that do not look as kindly on or treat women with AIDS as they may do here. That fact is not to be belittled. Even in that case, if a woman were to conceive a child who was HIV positive and no interventions were acted upon, then eventually both could perish with no escape. It is a crisis that requires hope, a stigma change, and mostly prevention. With intervention such as screening, progress can be made.

The long-term solution would be to have community education that would publicize and encourage volunteer counseling and testing, which would also incorporate men (Bassett, 2002). The use of VCT is necessary, but sometimes there are loopholes because women may not want to get tested, or if they do, they may not return for results. However, a short-term solution could involve offering the test with the right of the woman to "opt out" if she so desired (Bassett). This approach to testing supported by the Centers for Disease Control (CDC) is when a pregnant woman is informed that the HIV test is part of the group of standard prenatal tests provided to all women; she has the option to deter from having the test. If she does not request to decline from this HIV test, it will automatically be given (Reducing HIV, 2006). This way the woman does not feel forced into being tested by having the right to not take advantage of it.

A study performed in urban Zimbabwe was recently done to understand the influence that routine antenatal HIV testing, using this "opt-out" approach, had on the PMTCT (Chandisarewa, et al., 2007). As the other trials have shown, simple antiretroviral therapy has proven to be efficacious in Sub-Saharan countries, but the uptake of these kinds of prevention or treatment drugs has been low in the clinics in

Zimbabwe. This is due mostly to HIV antenatal testing rates that are poor, but they believe that early detection of HIV in pregnant mothers through VCT to PMTCT is of utmost importance (Chandisarewa, et al., 2007). The study discussion notes that women in urban Zimbabwe perceived this routine testing to be a good option and they would be accepting of it, and thus positive statistics for PMTCT were increasing (Chandisarewa, et al., 2007). The study concluded that this kind of routine testing should be performed and executed in all Zimbabwe sites so that the impact that it has on PMTCT can be maximized to its fullest potential in the public health realm (Chandisarewa, et al., 2007).

The "opt-out" approach has shown to be effective in the goal of PMTCT. Some support that mandatory HIV testing in areas where HIV is prominent has the possibility of decreasing MTCT as long as certain contingencies are in order. If so, then it is morally required for mandatory testing to be implemented (Schuklenk & Keinsmidt, 2007). This research advocates that pilot studies should be performed in certain areas of Africa to assess the ease at which it could be implemented as well as the potential ramifications, positive or negative, that mandatory testing might generate. The ethical and policy issues that accompany this approach make for a multifaceted debate (Schuklenk & Keinsmidt).

There is yet another loophole with the initiation and follow up of VCT. Hypothetically, when a woman chooses to be tested and does find that her serostatus is positive, she may not adhere to partaking in the sometimes-available antiretroviral therapy (Bassett, 2002). This is due to the fact that ART regimens can be extremely burdensome. A devout commitment to keeping up with the disease is crucial for survival. Some patients with HIV have to take two to twenty pills at a time. The dedication required to taking the medication at specific time frames is meticulous for the individual.

Additionally, the side effects are often unpleasant. Another key piece of information that the patient has to be aware of is that certain other drugs, some of which are even over-the-counter (OTC), taken in combination with HIV anti-retrovirals can produce some fatal side effects (Bradley-Springer, et al., 2007). These drawbacks discourage patients and put up barricades that keep them from being consistent with their treatment plans or successful in maintaining health and building immunity.

Literature regarding the transmission of HIV mentions that MTCT can also be referred to as parent-to-child transmission (PTCT) because often the father of the child is responsible for infecting the mother in the first place. By interchanging the use of the abbreviation PTCT with MTCT, the mother is prevented from being solely disgraced or blamed for infecting her infant (Weinreich, 2003). The issue of the male's role in this worldwide problem has so much to do with why these women become infected with HIV and then pass it on to their babies. The cycle just continues since it does not stop with the parents. Mother-to-child transmission could be significantly prevented if the males practiced morality and marital faithfulness to their spouses. There is a rampant inequality between the genders, and there has been for centuries in regards to female oppression, not in the feministic sense, but in relation to discrimination, lack of monetary resources, and forced sexual relations (Gross, 2004). The secretary-general of the United Nations, Kofi Annan, shared on International Women's Day in March of 2004 that, "All over the world, women are increasingly bearing the brunt of the epidemic…because society's inequalities put them at risk. There are many factors including poverty, abuse and violence, lack of information, coercion by older men, and men having several partners" (cited in Gross, p. 1079). In that same year, Stephen Lewis, a United Nations diplomatic agent for

HIV/AIDS in Africa, alleged that AIDS coupled with unjust female oppression can serve as a death sentence to women on a worldwide scale. He attributed it to the male sexual behavior, the culture, the violence, the power, and the patriarchy, factors that have played an influential role for centuries (Gross).

A study performed by Koenig, et al. discussed this issue of violence that happens during pregnancy to those women who may already have HIV or who are at risk for getting the virus. It supported that a number of factors influence an increase in the risk of violence particularly for women who are pregnant with HIV (2002). This could be attributed to location as well as dangerous behavior that can be associated with passing or acquiring HIV, which could include drug use, poor living or financial status, and sex bartering; all of which are factors that may welcome violence more easily (Koenig, et al., 2002). If a pregnant woman is unaware of her HIV status and gets screened for it during a prenatal visit, it could be difficult to keep her positive serostatus a secret, which is another possible factor that brings violence upon the woman, when others find out she has contracted HIV (Koenig, et al., 2002). The study concluded and suggested that hundreds of pregnant women who are infected yearly with HIV are also affected by violence, and should be provided with counseling and screening by prenatal clinics or offices (Koenig, et al., 2002).

A Focused Discussion on the Ugandan Experience

A country in Africa that has been ravaged by violence through war and other means and has experienced HIV/AIDS in large quantities and is yet attempting to implement prevention strategies would be Uganda (Westerhaus, Finnegan, Zabulon, & Mukherjee, 2007). Reported from 1993, in Africa and the world, AIDS cases in Uganda

were in the lead for having the highest rates per population with 2,314/1,000,000 population. One of the leading causes of death for Uganda has been HIV/AIDS with 2.4 million people having HIV (Uganda Health Profile, 2001). The population of Uganda noted in 2005 was 28,816,000 people (Uganda, 2007). The research performed by Westerhaus, et al. focuses more specifically on Northern Uganda, which has been traumatized by violence; "political repression, economic inequality, and gender-based discrimination" are the very factors that eventually cause infants to get infected with HIV (p. 1184). Prevention must reach far beyond methods of abstinence, condom prevention, and behavior change because the issues entangled in the corruption of Northern Uganda involve a brutal competition between the Ugandan government and an insurgent group referred to as the Lord's Resistance Army (LRA) (Westerhaus, et al.).

Because of the vicious conflict between these two groups, children are abducted or forced to become "night commuters" where they run without parents or guardians for attempted safety during the night to hospitals or shelters, but along the way they may experience sexual assault that can lead to HIV. The boys abducted by the LRA are often forced to rape others as a war weapon and many of the girls become sex slaves as "wives" to the men of the army resulting in young children with HIV (Westerhaus, et al., 2007). The probability of dying in Uganda under the age of five was recorded at 136 per 1,000 live births in 2005 (Uganda, 2007). It is important to understand cases like this in which prevention attempts must stretch beyond traditional behavior change and awareness, and involve on a much deeper scale the social, political, and, economic resources of the world into strategies to prevent HIV from spreading further (Westerhaus, et al.).

The trials and blockades in Uganda that counteract progress on preventing HIV transmission continue to pervade. While attempts are being made at halting the violence that keeps HIV prevalent in war-torn Northern Uganda and finding appropriate prevention methods for slowing the HIV pandemic in Uganda, ethnographic research has been done on southeastern Uganda which poses that it is the husbands sexual indulgences outside of the marriage committment that causes the greatest risk for their wives to acquire the HIV infection (Parikh, 2007). If the ABC approach that stands for **a**bstinence, **b**e faithful, and the use of **c**ondoms is not taken seriously, which it clearly has not been, then HIV will continue to thrive (Parihk). The once-revered marital relationship that upheld trust, safety, and support is in some couples a cesspool for dishonesty, unfaithfulness, and greed. Now there is global evidence demonstrating that many women are at risk for getting infected with HIV from having sexual relations with their very own spouses or significant partners due to interactions that their men are having outside of the marriage commitment (Parihk). Even the marriage bed is no longer safe. The men need to take a stand and a responsibility to halt the virulent spread of this deadly disease that many helped cause themselves. If something is not done, they will watch their own nation vanish before them if AIDS does not take their lives first.

Despite its alarming statistics, traumatic war experiences, and marital unfaithfulness, Uganda has been more recently recognized as a radical HIV success story in Africa in which HIV/AIDS cases have dramatically decreased (Parikh, 2007). What is ironic about this phenomena in Uganda is that people involved in assessing this case are facing great difficulty in answering the question “what worked” and having irrefutable evidence to demonstrate in the annals of Uganda where to attribute the success

(Parkhurst, 2008). They are having a hard time putting their finger on what has caused the decline. Thus, five components were instigated including *HIV prevalence, HIV incidence, behavior change, causes of behavior change, and responsible policies* in order to seek a viable explanation and foundational agreement for these more recent statistics (Parkhurst). These proponents of prevention represent a backwards cascade of cause and effect. For example, if the nation saw a change in behavior within the population, then what interventions or steps took place to reach that end result (Parkhurst)? Even so, there is a deficit in the data within the categories making it hard to establish where the country of Uganda succeeded and at what phase the most progress was made (Parkhurst). This information is extremely valuable as other nations are looking now to Uganda for answers so that they too can experience similar improvements within their country (Parkhurst). The following chart displays the numerical decline of HIV cases over the span of fourteen years in Uganda (Parkhurst). See Chart 3 below.

Chart 3. Estimate Percentages of HIV Prevalence Decline in Uganda 1991-2005

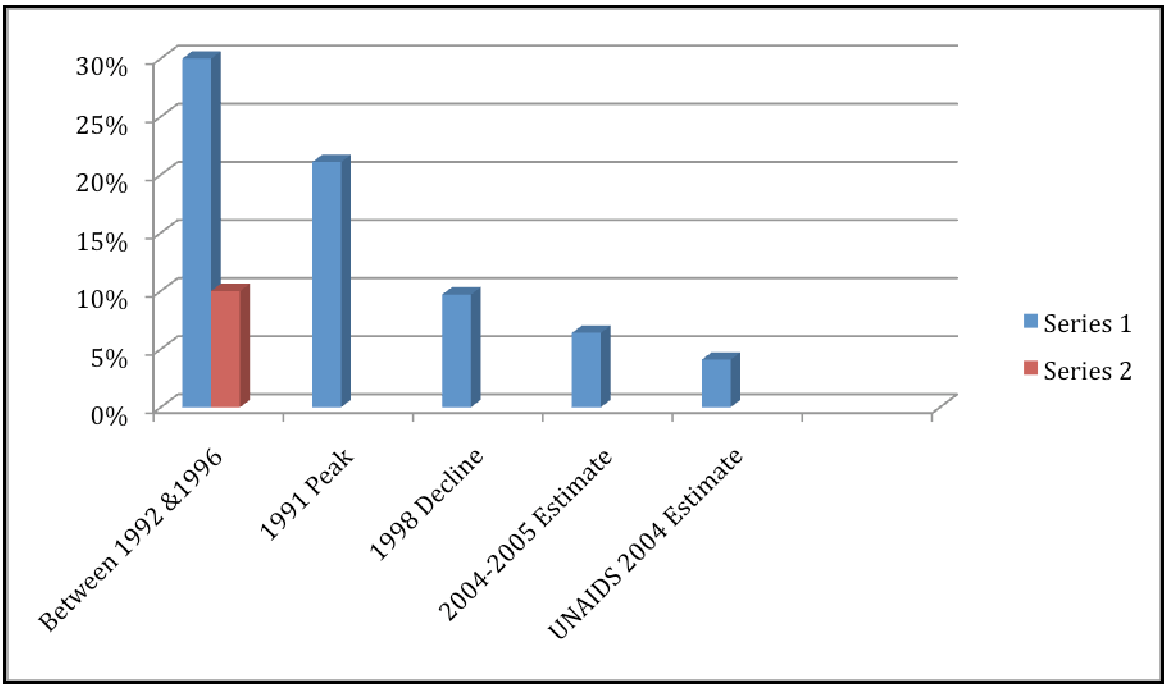

Chart 3. Note: Information gathered to create Chart 3: Cited from Parkhurst, J.O. (2008). "What worked?" The evidence challenges in determining the causes of HIV prevalence decline. *AIDS Education and Prevention, 20*(3), 275-283.

These statistics demonstrate from different sources that the research is somewhat incongruent. For example, the data obtained from research done, shown in the first column between the years of 1992 and 1996, was gathered from a limited number of prenatal sites (Parkhurst, 2002). Also, it was written in the *Science* journal that there was a percentage peak of expecting mothers with HIV in Uganda in the year 1991 as shown above: 21.1%, but it significantly decreased seven years later to 9.7% (Stoneburner & Low-Beer, 2004). The 2004-2005 estimate documented in the Uganda Ministry of Health from 2006 recorded a national percentage of 6.4 from the sero-survey done, but UNAIDS estimated in 2004 that it was a percentage of 4.1 (UNAIDS, 2004b). Granted these "estimates" do show some inconsistency. Nonetheless, wherever the data is coming from, the bottom line is that the Ugandan percentage, as demonstrated in the chart above, has clearly been decreasing.

There is a deficit in data, yes, but not only are people working towards researching this issue; the plain fact is that HIV/AIDS has declined. It is news such as this that will keep the fetus, the infant, and the child from having to experience a life with HIV and AIDS. In certain cases the solution to the problem is simple, prevention. This does not belittle or down play that even in its short history, the HIV/AIDS pandemic has clearly ravaged and taken the lives of many people from nations and countries all over the world. Because of its deleterious effects and the wake-up call that it has brought to the world, many have been responsive to the cry for global assistance. Much has been done to halt its progression, however, a cure is not yet found. Because HIV is transmitted to infants through breastfeeding, pregnancy, and labor and delivery, research and clinical trials and rescue intervention must continue to be performed so that MTCT can be prevented in every way possible.

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