

MODULE ONE

HIV Virology, Clinical Course, Medical Treatments, Epidemiology & Antibody Testing

A. Basic Facts About the Virology of HIV

1. History

- Between 1983 and 1984, the virus that causes the acquired immune deficiency syndrome (AIDS) was discovered by three laboratories (i.e., Luc Montagnier of the Pasteur Institute of France; Robert Gallo at the National Cancer Institute; and, Jay Levy of the Cancer Research Institute of the University of California at San Francisco) and given three different names. Because the three labs actually discovered variants of the same virus, all three variants were named the human immunodeficiency virus (HIV) type-1 in 1986. HIV-1 accounts for the majority of AIDS cases in the world.
- A second AIDS-causing virus, HIV-2, was discovered in 1986 in West Africa. There are few differences in the clinical symptomatology of HIV-1 and HIV-2. HIV-2 has not spread across populations to cause disease at nearly the same magnitude of HIV-1 and remains relatively contained in West Africa. Concerns about potential increases in North American HIV-2 have led to screening in the national blood supply for both HIV-1 and HIV-2 antibodies.

Possible Topics for Discussion:

Some people believe that HIV was developed by the defense department as a mechanism for genocide on the African-American population. Others believe that it arose from an experiment that went bad like Tuskegee. What do you believe? How do you respond to clients who have beliefs different than your own? How would these beliefs impact a client relationship with his or her medical provider?

2. Basic processes of the virus

- The various subtypes of HIV have different geographic distributions and many differ in their transmission properties. Variations within infected individuals make HIV particularly difficult for the immune system to manage. Rates of HIV replication and mutation translate to several thousands of generations of virus particles over a 10-year period.
- HIV is a retrovirus belonging to a group of cytopathic lentiviruses. Lentiviruses integrate their genetic material with a cell's genetic material through a complicated process called reverse transcription. The ability of retroviral

ribonucleic acid (RNA) to transcribe itself into a deoxyribonucleic acid (DNA) copy and integrate with the host cell DNA is the hallmark of a retrovirus.

3. Targets of the Virus

- HIV is transmitted through close intimate contacts where blood, semen, or vaginal fluids are exchanged. Upon entry into the bloodstream of an infected person, HIV becomes attached to the membrane of a target cell. HIV is highly selective in its binding properties, only targeting cells that express a surface molecule designated cluster determinant (CD4). After binding with the cell membrane, HIV enters the host cell by means of the same CD4 surface molecule involved in viral attachment.
- T-helper cell lymphocytes are one type of cell that expresses the surface molecule CD4. T-helper cell lymphocytes typically coordinate immune responses to foreign agents. T-helper lymphocytes are targeted by HIV and thus become host cells for HIV. T-helper lymphocytes are destroyed when HIV erupts, or buds, from host cells. T-helper lymphocytes are also destroyed through a number of additional mechanisms. On average, healthy individuals have 800-1200 T-helper lymphocytes cells/ml of blood; opportunistic infections develop for individuals at points below 500 cells/ml and especially below 200 cells/ml.
- Another type of cell that expresses the surface molecule CD4 is the monocyte macrophage. Monocyte macrophages typically engulf and destroy infectious agents. However, HIV-infected macrophages are unable to attack and destroy other microorganisms. HIV that is harbored inside of host macrophage cells is protected from immunologic responses and may be disseminated throughout the body.
- The depletion of T-helper cells, the infection of macrophages, and the accompanying cell disturbances result in profound immune suppression that causes AIDS. At 200 cells/ml, a person is diagnosed as having AIDS.

4. Viral Replication & Viral Load Testing

- When not replicating, HIV hides within host cells in a latent phase. HIV can exist in latent form in T-helper lymphocytes, as well as in other infected cells, for long periods of time. Latent HIV infection occurs while the viral genetic material is integrated within the host cell system. Viral latency should not be confused with clinically asymptomatic periods. Although there is an absence of clinical symptoms during viral latency, viral replication is occurring in host cells during asymptomatic periods. Thus, HIV can be latent during periods of symptomatic illness and can actively replicate during asymptomatic periods.
- Activation of dormant HIV in T-helper lymphocytes occurs from genetic regulation as well as the interaction between HIV, its host cell, and networks of

modulating cofactors. Infectious agents likely to facilitate HIV activation include re-infection with a new strain of HIV, herpes simplex virus type-2, Epstein-Barr virus, and hepatitis B virus.

- The amount of HIV detected in blood and other body systems varies over the course of infection. Quantities of HIV (also referred to as viral load, viral burden, and viremia) rapidly escalate during the onset of HIV infection. Later, viral load is first reduced as a result of immune responses to HIV infection and then at later stages of infection viral load once again increases. Viral replication occurs during all phases of infection, and viral load appears stable through untreated asymptomatic periods.
- Tests for viral load that measure HIV RNA include polymerase chain reaction (PCR) and branched DNA (bDNA) analyses. Monitoring viral load is critical to assessing the health of people with HIV disease.
- Viral load testing is now able to detect as few as 25 copies HIV virus/ml of blood. When no virus is evidenced in the blood work, one is said to have an undetectable viral load. Unfortunately, individuals mistake having undetectable viral loads with not being infectious. Having no evidence of virus in the blood does not mean that the virus is completely eradicated from the body. In fact, HIV continues to be present in genital fluids and lymph nodes, and elsewhere.
- Viral load, measured as the plasma HIV-1 RNA or DNA depending on the test used, is a strong predictor of disease progression independent of CD4+ T-cell count (Mellors, et al., 1996) and is useful in the prediction of future clinical response to therapy.

Possible Topics for Discussion:

Many patients now look to viral load testing as an indicator as to whether to practice safer sex. How would you respond to a patient who is monitoring viral load for this purpose? What issues would you discuss with your client? Similarly, how do you discuss undetectable or very low viral load without instilling false hope for a cure?

B. Clinical Course and Manifestations

1. Acute Infection

- In response to the introduction of HIV, the body may react with a brief period of acute infection symptoms. The usual time that elapses between exposure and acute illness is about 2 to 4 weeks, with the duration of symptoms lasting only 1 to 2 weeks. Acute HIV symptom illness, or primary HIV infection, may present with persistent fever, lethargy, malaise, muscle weakness, headache, pain in or around the eyes, sensitivity to bright light, sore throat, diarrhea, nausea, and skin rashes. Not all people with HIV develop symptoms of primary infection. Many

who did, upon reflection, attributed their illness to the flu and treated it accordingly.

- Following acute symptoms of HIV infection, antibodies are produced against HIV. Establishing HIV antibodies, or seroconversion to HIV, results after reaching a threshold of HIV antibody replication. On average, HIV antibodies are detectable through serological testing slightly more than 2 months after viral transmission, and 95% of HIV-infected people develop antibodies within three months of becoming infected. However, the incubation period for HIV may last longer than three months, and in rare cases may last 2 to 3 years.
- It is of note that from a public health standpoint, identifying and counseling persons who may be in the process of seroconverting (during the acute symptom phase, based on identified risk) is of great importance as viral load is peaking during seroconversion (before the body has mounted a full complement of antibodies to respond) and the individual may be considered hyper-infectious. Even before a positive HIV test.
- It is during the earliest days of acute infection that anti-HIV drugs may avert infection. Zidovudine (AZT), for example, administered to individuals exposed to HIV can reduce infection rates and otherwise reduce viral load, which can in turn have a positive effect on prognosis.

2. Asymptomatic Period

- During most of the HIV disease process individuals appear and feel otherwise healthy. Although an individual may be clinically asymptomatic, HIV, unless treated, is always actively replicating. In fact, HIV is quite productive in lymph nodes of symptom free patients. The virus is actively depleting T-helper lymphocytes during clinically asymptomatic phases, and HIV is transmittable to others during this time.
- Over time, untreated HIV infection continues to destroy the functioning of the immune system, largely through the destruction of T-helper lymphocytes. Vulnerability to diseases increases as the immune system loses T-helper cells. Although immune system suppression does not necessarily mean symptomatic illness, an HIV-related illness is clearly more likely.
- T-helper cell counts are a major marker of disease progression, but they are limited by extreme fluctuations due to a number of factors, including variability in laboratory procedures and changes in cell concentrations over diurnal cycles. Despite their limitations, T-helper cell lymphocyte counts often help guide decisions about initiating medications that suppress HIV replication, and decisions about when to initiate prophylaxis against opportunistic infections.

3. AIDS Diagnosis in Adults

- Most AIDS-defining conditions result after damage to the immune system. These include cancers and opportunistic infections that would otherwise be kept in check by a healthy immune system. As HIV infection progresses, disease-causing agents that are usually either completely suppressed or easily managed become potentially lethal.
- The first formal diagnostic criteria for AIDS were established in 1982 as a result of early clinical experiences with men who contracted HIV infection through homosexual activity. The diagnosis was updated in 1985, again in 1987, and once again in 1993 to include additional indicator diseases that characterized the diversity of HIV-infected individuals.
- The 1993 revised case definition addresses several criticisms of previous diagnostic criteria such as failure to include manifestations of HIV common in women. The revised definition includes the 23 original conditions and adds three new illnesses: pulmonary tuberculosis, recurrent pneumonia, and invasive cervical cancer.
- The most significant change in the 1993 AIDS case definition was the inclusion of immune diagnostic criteria. The 1993 definition specifies that individuals who are HIV infected and asymptomatic but who receive a T-helper lymphocyte count below 200 cells per cubic mm meet the criteria for AIDS. This change in 1993 resulted in a substantial adjustment/increase in the number of AIDS cases.
- The diagnostic criteria for AIDS are important in part because if one has an AIDS diagnosis then one is eligible for disability benefits.
- Each AIDS-defining condition entails its own disease processes and prognosis. The signs, symptoms, and complications of each condition pose substantially different challenges for people living with AIDS. A brief description of the AIDS case-defining conditions and other diseases that commonly confront people living with HIV infection can be found at the following Web site - http://www.hopkins-aids.edu/publications/book/ch1_table1_4.html#t14 and in the Resource Section for this module.
- In untreated adults, the average length of time between infection and developing AIDS is 7 to 10 years for those who have contracted HIV through sexual activity. It is considerably shorter for adults who contracted HIV through blood transfusion and for adults who contracted HIV through sharing drug injection equipment. The interval between infection and illness, however, is lengthening as a result of advances in medical treatments.
- As a result of effective combinations of anti-HIV medications, an AIDS diagnosis is no longer the marker for an irreversible decline that it once was. It is now common for combination therapies to rebound T-helper cells in conjunction with decreasing viral load, and these changes can remain stable for some time.

People with an AIDS diagnosis who may even be disabled can find themselves with elevated T-helper cells and improved health. Although the clinical diagnosis of AIDS is unlikely to be removed in such cases, the personal and social experience of AIDS will undoubtedly change.

- People with asymptomatic late stage HIV infection will become increasingly more common, suggesting a redefinition of the meaning of AIDS and its course. Many people with AIDS may become re-employed, go back to school, and restart their lives in other ways. The psychological aspects of reversing the course of AIDS, as well as the likely setbacks and cycles between reversals and setbacks as of yet are unknown.

4. Pediatric HIV Disease

- Infants born to HIV-seropositive women will test seropositive on standard antibody tests because the mother's antibodies pass through the placental barrier. Infants are therefore tested using virus cultures and PCR techniques to provide direct evidence for infection. These tests are repeated several times during the first 2 years of life to confirm the child's HIV infection status (most truly negative infants will test HIV antibody negative by 18 months) however, with PCR testing now much more widely available, a definitive HIV testing result can be achieved before the 18th month.
- Untreated HIV infection generally progresses more rapidly in children than in adults and HIV manifests differently in children compared with adults. Lymphoid interstitial pneumonitis (a slow progressing condition caused by a buildup of cells in the lungs) and recurrent bacterial infections are more common in children with AIDS. Children with AIDS are particularly susceptible to disorders of the central nervous system (CNS). HIV-related CNS disease may progress rapidly and can cause the loss of developmental milestones. Children can experience any number of opportunistic illnesses of the CNS and peripheral nervous system. In some cases, cortical atrophy and calcification with diffuse and/or focal lesions can occur.
- Recent years have seen significant advances in preventing mother to fetus or infant HIV transmission. Administering zidovudine (AZT) to mothers during pregnancy and infants decreases transmission risks dramatically. Without antiretroviral drugs during pregnancy, mother-to-child transmission has ranged from 16%–25% in North America and Europe. The perinatal transmission rate in the U.S. was 21% in 1994 before ZDV recommendations in pregnancy. In 1995, the transmission rate was 11% after the adoption of the “076” AZT regimen into practice (Simonds, 1996). Observational studies have confirmed the effectiveness of AZT in decreasing perinatal HIV transmission to as low as 5% (Lindegren, et al, 2000). However, long-term outcomes for those children born to mothers with HIV infection and exposed to AZT therapy are not known.

- HIVNET 012 study findings from a joint Uganda-US study show that a single oral dose of the NNRTI Nevirapine to the newborn (cost \$4) during delivery can cut vertical transmission rates. Interim results from 618 antiretroviral naïve mothers, 310 of whom received Nevirapine, 308 of whom received AZT, found that Nevirapine was markedly more effective. At 14 to 16 weeks of age, 13.1% of infants in the Nevirapine arm of the study were HIV-infected and 25.1 % of infants in the AZT arm were infected. This constitutes a 47% reduction compared with short-course AZT.
- Currently in the U.S., if an expectant HIV-positive woman is already on a successful combination therapy, continuing that antiretroviral treatment regimen throughout the pregnancy is the standard of care.

4. Hepatitis C and HIV

- Hepatitis C (HCV) is the most common chronic blood-borne infection in the US. Approximately 35,000 new cases are reported to the Centers for Disease Control (CDC) each year. Since the majority of those who are infected don't know they have the disease, this number is likely an underestimate of infections. Currently, it is estimated that more than 4 million Americans are infected, most between 30-49 years of age. In the U.S., infection rates are higher among ethnic minorities (3.2% of African Americans, 2.1% of Hispanics) than Caucasians (1.5%) and among identified risk groups, especially hemophiliacs (60-85%) and intravenous drug users (60-90%). While infection rates remain low among men who have sex with men (4-8%), they are still 4 times the national average.
- The prevalence of HCV among those with HIV is 40-50%. Individuals in the 40-49 year age group have the highest rate of co-infection (50%). The most common route of transmission is intravenous drug use. Spread of disease in this population is rapid, with many addicts seroconverting within one month of initiating IV drug use. Addicts who have been injecting for more than 2 years are 3.12 times as likely to test HCV seropositive. Although individuals who engage in risky sexual behavior have higher rates of infection, sexual transmission of the HCV virus is low (<3%) and difficult to confirm. Sexual transmission is facilitated by concurrent HIV infection.
- The course of the HCV is protracted, with 1 in 3 patients developing cirrhosis over 20 or more years. Patients with cirrhosis are, unfortunately, at increased risk for hepatocellular carcinoma (HCC). The most common physical complaint among asymptomatic patients is fatigue. Because the disease is frequently sub-clinical, patients often have symptoms of advanced liver disease before they come to the attention of medical professionals. These include variceal bleeding, ascites, coagulopathy (difficulty with blood clotting) and encephalopathy (cognitive dysfunction). Rates of morbidity and mortality are high 10-30 years post-infection. Although disease progression is variable, the average time from infection to clinical manifestation of disease is 10-18 years, while the average

time to cirrhosis is 21 years, and the average time to diagnosis of cancer is 28 years.

- Patients who are co-infected with HIV are less likely to resolve HCV infection. In addition, progression of liver disease is accelerated among co-infected individuals, especially those with advanced immunodeficiency. Rapid progression is manifested as a shorter time to development of cirrhosis and cancer, with some individuals developing HCV-related liver disease in less than 10 years.
- The goals of treatment include eliminating the virus or converting it to an “inactive” state, slowing disease progression, and reducing the risk for development of cancer. Treatments for HCV infection are limited. The most prominent involves use of alpha interferon alpha.
- Historically, HIV and HCV have been treated by physicians in different medical specialties. However, the complexities of both diseases demand that infectious disease physicians and hepatologists work together to treat those who are co-infected. The consensus appears to be that the infectious disease specialist should take the lead with regard to primary care, with the hepatologist providing input on management of liver disease. However, treatment must be provided in an integrated manner. Clinics, jointly managed by an HIV specialist and hepatologist and supported by substance abuse and other mental health providers make the most sense. Within the multi-disciplinary setting, each specialist will have the benefit of learning from the others.
- Today, many HIV seropositive patients who have undetectable viral loads and high CD4 counts are dying from liver disease and liver cancer. They have managed to get one virus under control, only to learn that another virus will probably kill them. Indeed, liver related problems are thought to be the number one cause of death among co-infected individuals, being responsible for half of all deaths. From the patient’s perspective, coping with one fatal illness can be emotionally challenging. Dealing with two can be overwhelming.
- Upon being diagnosed with liver disease, many co-infected patients experience increased anxiety, fear, and hopelessness. Co-diagnosis is clearly a “double whammy”. It is not uncommon for patients to become discouraged and feel like giving up. This “adjustment reaction” is similar to that observed in patients newly diagnosed with HIV. One concern is that negative emotions may undermine self-efficacy, resulting in decreased coping. Of course, there are others who enact denial as a defense against hearing this information, thereby protecting themselves emotionally. Unfortunately, this may result in failure to seek treatment. In some clinical settings, HCV infection is “downplayed” due to ignorance about the disease, its treatability, poor access to treatment resources, or the belief that other issues (such as HIV or active drug use) are more pressing.

- The efficiency of transmission of HCV is 10 times that of HIV and prevention efforts are key to containing the virus. Primary, secondary, and tertiary strategies are needed. The public needs to be educated about the disease in the same way they were educated about HIV. Educational efforts should be incorporated into primary health care settings, drug abuse clinics, and the schools. In many cases, HCV prevention messages could be delivered jointly with HIV prevention messages. Testing and counseling should be widely available to those with risk factors. For those who test positive, counseling regarding transmission risk, the impact of alcohol use on progression of liver disease, and treatment options are indicated.
- The socio-political issues pertaining to co-infection exceed mere lack of awareness. Both HCV and HIV disproportionately effect individuals who engage in behavior that is disapproved of by society, including illicit drug use. These behaviors are often seen as self-inflicted or as personality flaws. This pejorative view of drug use may influence current treatment practices which often involve denial of HCV treatment until abstinence is maintained for 6 months. Those who adhere to this treatment practice treat HCV differently from other chronic diseases. For example, it is uncommon to deny treatment to individuals with lung cancer who continue to smoke, or to diabetics who fail to follow a prescribed diet.

C. Medical Treatments

1. History of HIV Treatment

- The use of antiretroviral medications to treat HIV infected individuals began in 1986 with the US Food and Drug Administration's (FDA's) approval of the first antiretroviral drug AZT (Zidovudine). AZT was used to prevent HIV replication in the blood by inhibiting the activity of the reverse transcriptase enzyme (the enzyme by which HIV turns its RNA into a cells DNA).
- While the use of AZT as an antiretroviral drug to treat HIV was promising at first, its benefits were short lived, as individuals developed different side effects and the virus soon became resistant to the drug's intended beneficial effects. AZT's lack of effectiveness lead to the production of a class of medications known as NRTIs (nucleoside reverse transcriptase inhibitors), such as Videx (Didanosine), Zerit (Stavudine), Hivid (Zalcitabine) and Epivir (Lamivudine). However, these drugs began to be seen as offshoots of AZT, as they worked on inhibiting the same enzyme. As such, it did not take long for the virus to become resistant to this class of drugs and once again to continue to mutate and multiply.
- For much of the decade between 1986-1996, the standard in HIV prescribed drug treatments remained a "monotherapeutic" approach, of using a solo NRTI to treat HIV. This approach was eventually found to be of limited effectiveness, as HIV

is a virus that has the potential to quickly develop a resistance to any one-antiretroviral medication (Shernoff & Smith, 2001).

- The first class of new antiretrovirals called NNRTIs (non-nucleoside reverse transcriptase inhibitors) was placed on the market in 1996. This class of antiretrovirals, which include Viramune (Nevirapine), Sustiva (Efavirenz), and Rescriptor (Delavirdine), are similar to NRTIs as they inhibit the same enzyme, but are chemically different and are more powerful.
- The second class of HIV medications to be released that same year was called protease inhibitors (PIs). Examples of this class of antiretrovirals include Norvir (Ritonavir), Crixivan (Indinavir), Viracept (Nelfinavir), and Fortovase (Saquinavir). PIs work by inhibiting the enzyme-protease. When protease is blocked, HIV is unable to make copies of the virus and therefore can't infect new cells. It was therefore thought that PIs might be agents that could possibly eradicate HIV from the body. While this was later found not to be the case, studies have in fact shown that PIs do have the capability of reducing the amount of the virus in the blood stream and increasing CD4⁺ T cell counts (New Mexico AIDS Infonet, 2000).
- Even though these new classes of HIV medications were more potent than their predecessors, when used alone, the virus becomes resistant to the drugs as it does when using solo NRTI therapy. However, due to the increase in the number of different classes of antiretroviral medications, a shift from "monotherapy" to "combination therapy" became possible in which drugs from two or more classes could be utilized simultaneously (Shernoff & Smith, 2001).
- The combinations that became (and continue to be) the "standard" in antiretroviral therapy consisted of some combination of the three classes of antiretroviral medications used in conjunction with one another. Popular types of "combination therapies" include a) 2 NRTIs and 1 PI, b) 2 NRTIs and 2 PIs, or c) 1 NRTI, 1 NNRTI, and 1 PI. These combinations are called Highly Active Antiretroviral Therapy or HAART.
- With the advent of HAART being prescribed to treat HIV infected individuals, the number of deaths due to HIV disease decreased for the first time since the outbreak of the virus. Due to these promising clinical results, medical researchers and practitioners began to theorize that by prescribing HAART, a complete suppression of the virus might be possible. The theory was based on the belief that if HIV could be completely inhibited, it would not be able to reproduce or mutate and would not become resistant to antiretroviral medications. This led to the late 90s approach to HIV-related antiretroviral treatment, "hit early, hit hard", whereby medical practitioners hoped that by placing their patients on a HAART regimen during the early stages of contraction of the virus, the virus could be controlled (Bartlett & Finkbeiner, 2001).

- Unfortunately, it appears that though HAART may be able to suppress the virus, it is not able to eradicate the virus, in most documented cases. For even with the aid of a HAART regimen, the body's immune system is unable to prevent mutations of the virus and it therefore persists in the body. Secondly, though HAART regimens increase the number of possible drug combinations, many of the drugs cannot be used together and resistance to any one drug can confer resistance to other drugs. Furthermore, while switching regimens is possible, the number of times a change is possible is limited. In fact, the first regimen that one is placed on is the one that is most likely to succeed. Subsequent treatments are much less likely to be as effective (Barlett & Finkbeiner, 2001).

2. Current Treatment Approaches

- Although there is widespread agreement that HAART is the standard of care for treating HIV positive individuals, the issue of when to initiate this therapy and the issue of appropriate criteria for determining when to change a specific HAART regimen, remains somewhat controversial on the front lines of medical care. Some medical practitioners believe that HAART should be implemented as soon as HIV infection is detected; as close as possible to the time of seroconversion; others suggest that treatment be initiated only at such a time when the individuals demonstrate a continuous and steady decrease in overall health as indicated by laboratory markers. Some practitioners believe that regimens should be changed with any significant increases in viral load or declines in T-helper lymphocyte counts, while other practitioners wait for a more sustained downturn in laboratory markers.
- It is important to note that the specific combinations most commonly used vary from provider to provider and decisions about what combination to use is often based upon the individual's medication history and success rates with other medications. A physician's decisions about treatment initiation and treatment switching may also be influenced by his or her belief in future drug options. Some physicians may "hold off" as long as possible in case drug options might "run out".
- The Panel on Clinical Practices for Treatment of HIV Infection (2002) issued revised *Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents* in February of 2002. The Panel now advises "caution and delay" in initiating highly active antiretroviral therapy (HAART), since such treatment, in and of itself, cannot completely eradicate the virus. This recommendation supersedes the "hit early, hit hard" approach advocated since 1996 and reflects concerns related to serious side effects and viral resistance associated with HAART. Current treatment guidelines may be viewed at <http://www.hivatis.org/trtgdlns.html>.
- Under the new guidelines, HAART is recommended only when CD4 cell counts fall below 350 cells/mm³ or viral load increases to > 30,000 copies/mL (as

measured by branched DNA) or > 55,000 copies/mL (as measured by RT-PCR testing); the previous markers were 500 cells/mm³ and a viral load of 10,000 copies/mL (on branched DNA) or 20,000 copies/mL (on RT-PCR).

- More recent studies (Hogg et al., 2001; Phillips et al., 2001), however, suggest that *some* individuals living with HIV may safely delay the initiation of antiretrovirals until their CD4 cell count falls to not < 200 cells/mm³. Others even suggest that guidelines for initiating HAART among those who are asymptomatic should place greater emphasis on CD4 cell counts than on viral load, since the former have been found to be more predictive of disease progression than the latter (Sterling, Chaisson, & Moore, 2001).
- Munoz, et al (2002) presented further evidence at that 14th International Conference on AIDS that treatment may be delayed till CD4 counts drop to a level close to 200 cells/mm³ and that that delay may be only marginally riskier than beginning treatment while the count is over 350. Their results showed that it was unwise to delay treatment until CD4 counts dipped below 200, but that there was only a negligible difference in outcome between people who started treatment with CD4 counts between 201-350 and those with CD4 counts between 351-500.
- Recent studies of the efficacy of once-daily dosing therapy suggest that the field of antiretroviral medication usage to treat HIV is ready to evolve in yet another way. Early results of studies such as those conducted by Claxton, Cramer, and Pierce (2001) and Dybul, Yoder, Belson, et al. (2000), suggest that a once-daily dosing regimen not only increases adherence to HAART regimens, but may well improve the quality of life of these individuals, as the time demands imposed by these regimens may be considerably reduced (Moyle, 2002).
- Combination treatments do not work for everyone. HAART may work best for individuals who do not have a long history of taking HIV antiretrovirals; such individuals are referred to as the “drug naïve”. Poor response to combination therapies may also be due to the fact that individuals sometimes fail to stick to the prescribed regimens; in other words they fail to adhere.

Possible Topics for Discussion:

Some patients watch their viral load very closely and their moods and hopes swing up and down with fluctuations in their laboratory findings. Others don't want to be obsessed with the numbers. Physicians' responses to fluctuations in viral loads vary as well. Some want to change treatments quickly if viral loads go up. Others are more cautious about switching regimens. Patients often wonder how much to attend to the numbers and what to do in response to changes in their viral load. Is it appropriate to assist them in their decision-making and if so, how?

3. Adherence

- Since the widespread implementation of HAART, both physical and mental health professionals have been concerned with the issue of medication adherence. Adherence, also known as compliance, refers to the extent to which a person's behavior (in terms of taking medications, following diets, or executing lifestyle changes) coincides with medical or health advice (Sackett, Haynes, & Taylor, 1979).
- Since HAART often consists of two, three, or four different medications taken in combination, each with different dosing requirements, adherence to these treatments often represents a complex and demanding set of challenges. And while newer formulations of antiretrovirals often require both fewer pills and less dosing times, the behavior can still be a demanding one in light of the other medical, psychological, sociological, and economic burdens an HIV seropositive individual faces.
- Adherence rates to HIV antiretroviral medications among diverse populations of HIV+ persons have been found to be highly variable (Chesney et al., 2000; Geletko et al., 1996; Ickovics & Meisler, 1996; Kalichman, Catz, & Ramachandran, 1999a; Melbourne et al., 1999; Weidle et al., 1999). Rates of adherence have been shown to differ substantially based on measurement period (e.g., missed doses in past month, past week, past day) and measurement format (e.g., interview, anonymous self-report, pill counts, electronic measurement) (Chesney et al., 2000). Recent studies have identified rates of adherence to HIV medications ranging from 56% to 77% (Arnsten et al., 2000; Chesney et al., 2000; Demas et al., 1998; Eldred, Wu, Chaisson, & Moore, 1998; Weidle et al., 1999).
- For those on HAART, the reduction of virus is achieved when an effective regimen is provided continuously, offering the virus little chance to grow in the presence of the combination of drugs. Recent work has shown adherence rates of 95% or greater are necessary for HAART to be most effective (Low-Beer et al., 2000; Montaner et al., 1998; Paterson et al., 2000) and that a 10% decline in adherence results in a 16% increase in AIDS-related mortality (Hogg et al., 2000) and a doubling of HIV-1 RNA blood levels (Bangsberg et al., 2000). Patients who miss even a few doses of their medications demonstrate increases of 100,000 copies or more of the virus per milliliter of blood (Ho et al., 1995; Kastrissios et al., 1998).

4. Drug Resistance

- The failure to maintain strict adherence to HAART can result in the proliferation of virus that is drug resistant (Flexner, 1998; Hecht et al., 1998a; Vanhove, Schapiro, Winters, Merigan, & Blaschke, 1996). Resistance to antiretrovirals and a reversal of viral suppression have been identified among HIV+ persons reporting even slight disruptions to their medication regimen (Shafer, Winters,

Palmer, & Merigan, 1998). As a consequence, HIV seropositive persons who are unable to adhere to their regimens may experience greater progression of HIV related medical complications (Andrade et al., 2000; Hogg, Yip, Chan, O'Shaughnessy, & Montaner, 2000), as well as the potential transmission of drug resistant strains to others (Hecht et al., 1998b; Routy et al., 2000; Wainberg & Friedland, 1998).

- While drug resistance may occur for a variety of reasons, the most common reason appears to be nonadherence. Drug resistance as a result of nonadherence to combination therapy has been well-documented (Friedland & Williams, 1999; Mayers, 1998; Richman, 1996; Vanhove et al., 1996). Provided the individual is on highly potent HAART and maintains perfect adherence, viral replication is shut off and resistant mutations do not develop. HIV mutates rapidly in the absence of medications and in the presence of subtherapeutic treatment. Studies indicate that viral mutations can confer cross resistance—resistance to one protease inhibitor can cause one to become resistant to other protease inhibitors (Boucher, 1996; Condra et al., 1995; Markowitz & Ho, 1996; Mellors, 1997; Roland, 1998; Schmidt, Ruiz, & Clotet, 1996; Shafer, Winters, Palmer, & Merigan, 1998; Tisdale et al., 1995).
- According to Susan Little and her colleagues (2002), the number of people newly infected with a strain of HIV that is already resistant to at least one antiretroviral drug more than tripled between 1995 and 2000. The researchers found that between 1995 and 1998, 3.4% of the patients they tested had a strain of HIV that was already resistant to at least one drug. By 2000, the frequency had risen to 12.4%. The overall frequency of multidrug resistance rose from 1.1% to 6.2% over the same time period and was most commonly found in men who have sex with men. According to the researchers, the figures represent a "conservative" estimate because they used the most "stringent" standards when defining drug resistance. Under more relaxed guidelines, up to 20% of newly infected patients may have drug-resistant HIV.

5. Drug Resistance Testing

- It is generally recommended that doctors test patients for drug resistance before initiating antiretroviral therapy. Although such tests are costly -- ranging in price from \$300 to \$1,000 -- they will eventually save money, as physicians will be able to eliminate ineffective drug options earlier.
- Drug resistance can be measured using either genotypic or phenotypic assays. Genotypic assays detect mutations that cause drug resistance. Phenotypic assays are drug susceptibility assays in which HIV is cultured in the presence of serial dilutions of an inhibitory drug. Current commercially available genotypic and phenotypic assays both test HIV extracted from plasma.

- Genotypic testing is used more commonly than phenotypic testing because of its lower cost, wider availability, and shorter turnaround time. Genotypic testing provides early evidence of drug resistance within a virus population. Genotypic assays detect mutations present as mixtures even if the mutation is present at a level too low to affect susceptibility in a phenotypic assay, and detect transitional mutations that do not cause drug resistance by themselves but indicate the presence of selective drug pressure.
- HIV drug resistance is rarely an all-or-none phenomenon. Clinicians treating infected patients usually need the answers to the following two questions: 1) Does the result suggest that the patient will respond to a drug in a manner comparable to a patient with a wild-type isolate?, and 2) Does the result suggest that the patient will obtain any antiviral benefit from the drug? To answer both these questions it is necessary to grade the extent of inferred resistance relative to wild type (eg, low-level, intermediate, high-level).
- The clinical significance of both genotypic and phenotypic data have been difficult to establish for the following reasons: 1) all antiretroviral drugs are used in combinations, many of which are synergistic (reduced susceptibility to a drug may not interfere with the drug's beneficial effect on the antiretroviral activity of another drug used in the same regimen); 2) a drug may have some benefit even in the setting of resistance, because many drug-resistant variants are less fit than drug-susceptible variants; and 3) the serum levels of some drugs, particularly the PIs, can be highly variable. Low levels of PI resistance may be overcome in some cases if higher serum PI levels can be obtained.
- Genotypic assays frequently do not identify enough fully active non-cross-resistant drugs to completely block HIV replication, and many patients changing regimens because of virologic failure will have to use a regimen containing drugs that are partially compromised at the start of therapy. Nonetheless, by providing prognostic data and helping to avoid unnecessary drugs, resistance testing can have a role even in heavily treated patients. When fully active drugs are not available, salvage therapy in heavily treated patients may include drug combinations that exploit antagonistic mutational interactions.

6. Structured Intermittent Therapy

- Research continues on structured intermittent therapy (STI), which may be of benefit to those who initiate antiretrovirals shortly after HIV infection (Lori et al., 2000; Rosenberg et al., 2000). Researchers believe that early and intermittent treatment protects CD4 cells from destruction, allowing them to continue to summon killer T-cells to destroy HIV-infected cells, thereby suppressing viral load and, in essence, "teaching" the immune system to fight HIV without the continual use of medications.

- In one recent preliminary study (Dybul et al., 2001), investigators followed a small group of individuals on daily HAART with low viral loads and high CD4 counts and had them begin cycling their HAART regimen in a seven days on/seven days off pattern over a period of up to 68 weeks. Virus levels not only remained suppressed on this short-cycle intermittent treatment schedule, but cholesterol levels dropped by 22% on average, and triglyceride levels by 51%. Should these findings bear out in larger studies, the toxicity of these medications might be lowered and the cost of treatment could be cut in half for many people living with HIV.
- While it is still too early to know if people living with HIV will be able to discontinue taking pills daily to fight HIV as a result of these experiments, and "drug holidays" are extremely risky since they do result in viral rebound and potential viral resistance to previously effective medications (and should not be attempted without close medical supervision), the findings are encouraging.

7. Long-Term Adverse Effects of Medication

- There is increasing concern about the long-term adverse effects of medications (i.e., fat redistribution; elevated triglycerides, cholesterol, and glucose; liver and heart disease; osteonecrosis of the hip [a bone disorder that reduces blood supply and results in bone death, potentially requiring total hip replacement]; and, decreases in sexual interest and erectile dysfunction).
- A prospective Swiss cohort study (Fellay et al., 2001) found that 47% of participants experienced adverse, treatment-related side effects and 9% of these effects were rated as "serious" or "severe".
- The antiretroviral efavirenz (Sustiva® or EFV) has been associated with a variety of neuropsychiatric side effects (e.g., feelings of "disengagement" and nightmares; to a lesser extent, increases in the severity of previously-diagnosed depression, apathy, agitation, emotional lability, euphoria, hallucinations, and psychosis). Clinicians should screen for mental status, physical and psychological distress, and quality of life before initiating treatment with EFV (Blanch et al., 2001).

8. Alternative Medicine

- Complementary and alternative medicine (CAM) approaches utilized by people living with HIV include: aerobic exercise, prayer, massage, needle acupuncture, meditation, support groups, visualization and imagery, breathing exercises, and spiritual activities. In most cases, CAM has been found to improve the mental health of the individual, and some, such as aerobics, also enhance physiological well-being (Greene et al., 1999).

- Use of CAM may increase perceptions of control in managing HIV disease and may represent an adaptive response to illness. Notably, use of *some* CAM has been associated with better psychological adjustment and greater life satisfaction than non-use or extensive use of CAM (Suarez & Reese, 2000)
- Among gay men living with HIV, Dutch researchers (Knippels & Weiss, 2000) found typical CAM users had symptomatic HIV disease, experienced little or no pain, coped actively with disease-specific problems, and expressed feelings about these problems. If prescribed HAART, they were also more adherent than those not utilizing alternative approaches.

D. Epidemiology of HIV and AIDS in the United States

1. Overview

- The first cases of what would later become known as AIDS were reported in the United States in June of 1981. Since that time, approximately 800,000 cases of AIDS have been reported in the U.S. Advances in the treatment of HIV disease have substantially reduced AIDS-related mortality and extended the lives of many people living with HIV, although there continues to be a steady number of new HIV infections each year (i.e., approximately 40,000).
- These trends have resulted in more Americans living with AIDS today than ever before. New treatments, however, are not a cure, have numerous side effects, and do not benefit all people with HIV. In addition, it is estimated that 42% to 59% of people living with HIV/AIDS are not in regular HIV care. As many as one-third of those living with HIV/AIDS do not know they are HIV positive.
- Over 793,000 cases of AIDS have been reported in the U.S. since 1981, including 40,894 cases reported between July 2000 and June 2001.
- To date, there have been 457,667 AIDS-related deaths.
- An estimated 850,000 to 950,000 Americans are living with HIV/AIDS, including more than 300,000 living with AIDS, the most advanced stage of HIV disease.
- AIDS cases have been concentrated largely in urban areas and 10 U.S. metropolitan areas (with 500,000 or more population) account for 43% of all cases.
- The Southern region of the country has the greatest estimated numbers of people living with AIDS and AIDS cases diagnosed in 2000, followed by the Northeast, West, and Midwest. Between July 2000 and June 2001, 7 of the 10 states/territories with the highest AIDS case rates per 100,000 (a measure of the epidemic's impact standardized to population size) were in the South.

- Treatment advances have led to dramatic declines in AIDS-related deaths, including a decline of more than 40% between 1996 and 1997. However, the rate of decline is slowing, and was 11% between 1999 and 2000. HIV is now the 5th leading cause of death among Americans ages 25 to 44, down from #1 in 1995.
- Treatment advances have also delayed the progression of HIV to AIDS, leading to a decrease in new AIDS cases. These declines are also slowing. In addition, the estimated number of new AIDS diagnoses among women and those infected through heterosexual sex has increased.
- Sexual transmission and injection drug use (IDU) are the primary modes of HIV transmission. Almost half (46%) of all reported adult/adolescent AIDS cases have been linked to sex between men and 25% to injection drug use. Eleven percent have been linked to heterosexual sex, and 6% to men who have sex with men and inject drugs. Injection drug use also indirectly accounts for HIV transmission among the partners and children of injection drug users.
- Estimates of new HIV infections indicate that one-third (33%) are attributable to heterosexual sex and 42% to sex between men. One-quarter are due directly to injection drug use.

2. Impact on Racial and Ethnic Minority Americans

- Racial and ethnic minorities have been disproportionately affected by HIV/AIDS since the beginning of the epidemic, and minority Americans now represent both the majority of new AIDS cases and the greatest number Americans living with AIDS in the U.S.
- Although African Americans and Latinos represent 12% and 14% of the U.S. population respectively, they accounted for 47% and 19% of newly reported AIDS cases in 2000. The majority of new HIV infections are among African Americans (54%); 19% are among Latinos.
- HIV is the leading cause of death among African Americans between the ages of 25 and 44 and the 3rd leading cause of death for Latinos in this age group, compared to the 5th for whites.

3. Impact on Women and Young People

- Women account for a growing proportion of new AIDS cases, rising from 7% in 1986 to one quarter (25%) of new AIDS cases reported in the most recent period. Women are estimated to account for 30% of new HIV infections.

- New HIV infections among women are primarily due to heterosexual sex (75%), followed by IDU (25%).
- Women of color are particularly affected. African American women account for 64% of new AIDS cases reported among women and Latinas account for 17%.
- Young adults and teens also continue to be at risk. At least one-half of all new HIV infections are estimated to be among those under the age of 25. Most young people are infected through sex.
- Among young people, young women and young minority Americans have been particularly affected. Teen girls now represent more than half (54%) of new AIDS cases among those aged 13-19. Young African Americans represent 64% of new AIDS cases among 13-19 years olds and Latinos represent 20% in this age group.
- Due to the availability of treatments that dramatically reduce the risk of transmission during pregnancy, the perinatal transmission rate in the U.S. has significantly declined.

4. Impact on Men Who Have Sex with Men

- Despite declines in HIV infection rates among men who have sex with men (MSM) since the early years of the epidemic, they continue to be at high risk for infection, accounting for an estimated 42% of all new HIV infections. Recent data indicate increases in sexual risk taking among MSM in a growing number of cities, and that MSM are at significantly greater risk than other groups in the U.S.
- Younger MSM and MSM of color are at particularly high risk and minority MSM now account for a majority of AIDS cases reported among MSMs.

5. The U.S. Response to the Epidemic

- In FY 2002, U.S. federal spending on HIV/AIDS is expected to total \$14.7 billion. Of this total, 18% will go to research, 7% to prevention, 59% to care (health care and support services), 11% to cash and housing assistance, and 6% to combating the international epidemic.
- Some of the key programs that provide health insurance coverage, care, and support to people with HIV/AIDS in the U.S. are Medicaid, Medicare, and the Ryan White CARE Act. A variety of federally and state-supported prevention services are provided by state and local health departments and community planning groups.

The foregoing statistics were taken from the Henry J. Kaiser Family Foundation HIV/AIDS Policy Fact Sheet entitled, The HIV/AIDS Epidemic in the United States (July 2002). This fact sheet can be found at the following website: <http://www.kff.org/docs/AIDSat20/>. References for the statistics cited above can be found on the website and are listed below:

- 1 CDC, "Pneumocystis Pneumonia – Los Angeles," *MMWR*, Vol.30, June 1981.
- 2 CDC, *HIV/AIDS Surveillance Report, Mid-Year Edition*, Vol. 13, No.1., 2002.
- 3 CDC, *A Glance at the HIV Epidemic*, 2002.
- 4 Fleming, P., et.al., *HIV Prevalence in the United States, 2000*, 9th Conference on Retroviruses and Opportunistic Infections, February 2002.
- 5 Metropolitan areas with 500,000 or more population; includes the greater Washington DC metro area.
- 6 NCHS, *National Vital Statistics Report*, Vol.49: No. 11; October 12, 2001.
- 7 NCHS, *Press Release: AIDS falls from Top Ten Causes of Death; Teen Births, Infant Mortality, Homicide All Decline*, October 7,1998.
- 8 CDC, Fact Sheet, *Drug-Associated HIV Transmission Continues in the United States*, 2002.
- 9 CDC, *HIV/AIDS Surveillance by Race/Ethnicity*, L238 Slide Series (through 2000).
- 10 U.S. Bureau of the Census, 2002. Includes Puerto Rico. With the exception of the category "multiracial", percentages represent people who reported only one racial group in the 2000 Census. All persons who report Latino or Hispanic ancestry are identified as Latino regardless of race.
- 11 CDC, *HIV/AIDS Surveillance Report*, 1986.
- 12 CDC, *Fact Sheet: Young People at Risk – HIV/AIDS Among America's Youth*, 2002.
- 13 CDC, *HIV/AIDS Surveillance in Adolescents*, L265 Slide Series (through 2000).
- 14 CDC, *HIV Prevention Strategic Plan Through 2005*, January 2001.
- 15 CDC, *No Turning Back: Addressing the HIV Crisis Among Men Who Have Sex with Men*, November 2001.
- 16 CDC, *HIV/AIDS Among Racial/Ethnic Minority Men Who Have Sex with Men - United States, 1989-1998*, *MMWR*, Vol. 49, No.1, 2000.
- 17 Alagiri, P., Summers, T., Kates, J. *Trends in U.S. Spending on HIV/AIDS*, Kaiser Family Foundation, July 2002.
- 18 Kates, J., Sorian, R., *Financing HIV/AIDS Care: A Quilt with Many Holes*, Kaiser Family Foundation, October 2000.

Please Note: Powerpoint slides that graphically depict a wide range of HIV/AIDS statistics can be found at: <http://www.cdc.gov/hiv/graphics.htm>

6. HIV Case Surveillance

- HIV infection is not yet reportable in every state or territory. Because AIDS incidence trends do not reflect HIV incidence trends (due to effective antiretroviral therapy delaying progression of HIV infection to AIDS), HIV data are needed to meet federal, state, and local needs for monitoring trends and

planning. As of June 2001, 37 areas have implemented confidential, name-based case surveillance. Oregon and Connecticut have implemented HIV case surveillance for pediatric cases only. Several states have implemented non-name-based HIV surveillance systems and others were considering different HIV reporting systems (See figure 3) (Centers for Disease Control and Prevention, 2002).

- In the year 2000, the latest date for which figures are available, 21,704 individuals were reported as HIV-diagnosed in these 37 areas. (See figure 4)
- Until the mid-1990s, AIDS case surveillance was the best measure of the magnitude and direction of the HIV epidemic because the time between infection with HIV and the development of AIDS was believed to be relatively consistent. However, since the introduction of new medical treatments that can delay the progression of HIV disease, AIDS case surveillance has not been as representative of HIV epidemiology. Because the characteristics of this delayed progression are variable, AIDS case reporting is much less useful in estimating HIV incidence or monitoring trends in the epidemic.
- The limitations of AIDS case surveillance have increased the need for accurate estimates of HIV incidence. Recently developed technology that can distinguish recent HIV infections from longstanding infections with the use of a single specimen has led to the ability to conduct cross-sectional serosurveys of HIV incidence. Because incidence is indicative of recent infection, it is an important epidemiologic measure for allocating resources and evaluating prevention programs.
- The HIV epidemic has slowed from a period of rapid growth (approximately 150,000 new infections per year) during the mid-1980s to late 1980s to a more stable epidemic (estimated at approximately 40,000 new infections per year) since the mid-1990s.
- When anonymous unlinked HIV serosurveys were initiated by CDC in 1988 to document the extent of the epidemic in the United States, information about HIV epidemiology was limited. Unlinked surveys use residual sera from blood specimens originally collected for routine clinical purposes. There is no contact between persons whose specimens are included in the surveys and the investigators conducting the surveys. Before the specimens are tested for HIV, demographic and risk information is abstracted from routine medical records and intake forms, and then linked to the residual specimens through a unique study number. After the permanent removal of all personal identifiers, residual specimens, which otherwise would be discarded, are anonymously tested for antibodies to HIV. Neither the HIV test results nor the information obtained from medical records and intake forms can be linked to specific persons.

- The most recent CDC report on sero-surveillance (*HIV Prevalence Trends in Selected Populations in the United States: Results from National Serosurveillance, 1993-1997*; see - <http://www.cdc.gov/hiv/pubs.htm>) includes summaries of data from January 1993 through December 1997 from anonymous, unlinked prevalence surveys conducted in selected STD clinics, drug treatment centers (DTCs), and adolescent medicine clinics, as well as data from routine HIV screening programs for entrants to the Job Corps, applicants for military service, and first-time blood donors. High-risk populations include men who have sex with men (MSM) and heterosexual patients at STD clinics and injection drug users (IDUs) entering DTCs. Youth populations include patients at adolescent medicine clinics and Job Corps entrants. Low-risk populations include military applicants and blood donors.
- The overall patterns of HIV seroprevalence data from 1993–1997 suggest that HIV prevalence continues to decrease or to remain stable in the populations included in the report. Overall prevalence did not increase in any sentinel population. Despite these encouraging findings, prevalence remained high among MSM and IDUs and was substantially higher among blacks than among whites in all populations included in the report.
- Patterns in the HIV epidemic among adults in the United States are primarily influenced by three interrelated subepidemics among groups at risk for HIV infection: MSM, IDUs, and heterosexual persons. STD clinic surveys provide information about HIV infection among MSM. Overall HIV prevalence was higher among MSM at STD clinics (26%) than among any of the other survey populations. Prevalence for these MSM was high in all metropolitan areas, ranging from 8% in Seattle to 39% in Atlanta. However, overall prevalence among MSM decreased steadily from 1993–1997. Although prevalence was lower among younger MSM, the 1997 standardized prevalence rate of 11% among those in the youngest age group (< 25 years) indicates that new infections continue to occur. This is consistent with the results of other recent studies showing high numbers of new infections among young MSM.
- Overall seroprevalence among IDUs entering treatment programs (19%) was the second highest of the populations in the surveys. In contrast to prevalence among MSM, prevalence among these IDUs differed greatly by region, ranging from 2% or less in Denver and Los Angeles to 37% in New York City. During the survey period, prevalence decreased or remained relatively stable among most subgroups of IDUs. A notable exception to the pattern of decreasing prevalence was white IDUs in the South, among whom prevalence increased more than threefold, from 3.2% in 1993 to 11.1% in 1997.
- The HIV epidemic among heterosexual men and women is influenced by persons who inject drugs or who have heterosexual contact with IDUs, MSM, or other persons at high risk of HIV infection. HIV prevalence among heterosexual men and women at the STD clinics was substantially lower than that among MSM and

IDUs at the STD clinics and IDUs entering drug treatment programs. Among high-risk heterosexual patients at STD clinics who reported no male same-sex contact and no injection drug use, overall prevalence for the 5-year period was 2.3%.

- Overall prevalence rates among youth attending adolescent medicine clinics and those entering the Job Corps remained low (0.4% or less). However, considering the young ages of these populations, prevalence was high, especially among young disadvantaged women entering the Job Corps. These women, particularly those who were black, were infected with HIV at younger ages and at higher rates than men. The high prevalence rates among these women could be due to several factors, including lack of knowledge or lack of skills in negotiating condom use and early sexual intercourse with older men who are more likely than young men to be infected with HIV.
- Strong geographic heterogeneity in HIV prevalence rates was observed among heterosexual patients at STD clinics, IDUs entering DTCs, Job Corps entrants, and military applicants. Although the reasons for this geographic diversity are not clear, HIV prevalence has been higher among all of these populations in the Northeast and the South since CDC began the serosurveillance system in 1988. These regional variations reflect the large differences in the effect of the HIV epidemic in different areas of the United States.
- One of the most striking observations from these surveys is the marked race/ethnicity differences in HIV prevalence. In nearly all of the populations, prevalence was substantially higher among blacks than among whites. Although data from Hispanics were less consistent, prevalence among Hispanics was lower than among blacks and slightly higher than among whites in most populations. The exception was among IDUs in the Midwest and South, where prevalence was almost always higher for Hispanics than for blacks. The marked disparities by race and ethnicity suggest that social mixing patterns within racial and ethnic groups are important determinants of HIV transmission risk.

Possible Topics for Discussion:

Many people hold strong feelings about HIV reporting, some believe that it poses a health threat and may in fact result in serious problems such as preventing people from seeking testing (and therefore early detection and the opportunity for treatment) or further discrimination and stigma. Others maintain that HIV should be treated like any other disease and point to states' records of monitoring TB and many sexually transmitted diseases. Those who support HIV reporting assert that the real threat is *not* reporting in that it prevents epidemiologists from ever getting a true picture of the disease (funding for research and treatment issues) and further perpetuates the attitude of HIV/AIDS as "other" thereby also perpetuating social stigma and fear.

Both sides make very convincing arguments. Which side makes more sense to you? How might this issue impact testing and treatment in your view? How does your opinion change if you consider “names” reporting versus reporting using an anonymous unique identifier? How comfortable would you feel about discussing this issue with a client?

Are you aware of the racial and ethnic makeup of your community? Has there been a similar shift in AIDS demographics where you practice or *in* your practice? How has that shift manifested itself in your community? Are there different providers for the different groups? Are there providers that serve, or organizations for, gay men of color in your community? Have provider organizations changed the way they work/look or have new providers surfaced and taken the lead in service provision? How might rising AIDS prevalence rates be seen by the communities affected? What impact might changing attitudes and demographics have on your organization or practice? How do you see your professional peers reacting to demographic and attitude shifts?

In many communities, women and families are the hardest hit by AIDS. Widowed or otherwise single mothers are left to support families where they might not be the only one living with HIV or AIDS. Has the number of women with HIV or AIDS increased in your community? What services are in place in your community to assist women and families living with AIDS? Who are the women who seek these services? Are you seeing women with HIV/AIDS in your practice? How are their needs different from those of males with HIV/AIDS?

Women’s dependence on male partners for protection and reluctance to use barrier methods is a problem of considerable note. What cultural differences come into play here?

Have you ever had a discussion of HIV/AIDS with a female client? Did she bring it up or did you? How have you approached a discussion of HIV/AIDS with a female client? If it is something you consider or do regularly, are there certain women with whom you would *more likely* or *always* bring up the topic? Why? Have you ever heard colleagues express a philosophy on discussing HIV/AIDS with clients?

Of how many cases of pediatric AIDS are you aware in your community? Have you any direct experience with pediatric AIDS? (Odds are, not unless you live in one of the harder hit areas.) What issues does the topic of pediatric AIDS bring up for you or your professional peers? *For the community*? How might these issues affect provision of care? What are the family issues you associate with pediatric AIDS?

How many young people do you see in your practice setting or perhaps volunteer work? Do you have your own children who have talked to you about sexuality and drug issues in terms of their friends’ behaviors?

How does your community view sexual or drug-using activity among its young people? Is there a perceived problem? How does the viewpoint of your community's youth differ from the adult population? Do different socioeconomic and/or racial and ethnic groups view these issues differently? Have church or school groups risen to address these issues? What actions have they taken? How have youth responded?

What does the science say; what does your state or local department of health say? What are the youth pregnancy rates? What are the STD rates among youth in your state or community? What is the HIV seroprevalence in your area in general? Are there reproductive health or other service organizations that address the issues of sexuality or drug use either anonymously or confidentially? Where do youth go for information in your community? Are there support groups for young people with HIV or even support groups for HIV negative youth with an eye on prevention? Are there safe places for gay teens to gather for support? Are there places where gay youth are known to meet socially? Is this area also frequented by adults?

Is there a college campus in your area? What is its part in the community? Are there programs for youth on campus? Are they ever open to outside youth?

E. HIV Antibody Testing

1. Overview of HIV Antibody Tests

- According to the CDC, more than one-third of the 2.2 million Americans tested every year at public health clinics do not return to receive their test results. At least 11,000 individuals who test and then HIV antibody positive do not return for their results. Moreover, it is estimated that one-fourth of the approximately 900,000 individuals living with HIV may not know of their status.
- The "HIV Test" of common parlance (introduced in 1985) is no longer a single testing process involving the ELISA and Western Blot Tests (see below) as it once was. There are now several ways of determining one's HIV status and results may take anywhere from a few minutes to several weeks depending on the particular testing method used, the laboratory location, and the number of tests being processed by the laboratory.

ELISA (enzyme-linked immunosorbent assay) Test

- Historically, the ELISA was the first test often used to detect HIV antibodies because it is sensitive* to HIV and is a fairly inexpensive test for laboratories to run. The results of ELISA tests are read mechanically. ELISA tests can be either positive or negative. If the test is positive, the testing process is repeated. The protocol depends on the particular laboratory. Often labs repeat the test in duplicate using testing kits from different manufacturers. This is a quality assurance measure utilized to rule out error because of problems that may have occurred during the manufacturing process. If either of the second tests is positive,

a confirmatory test (the Western Blot) is then utilized -- preferably before patients are given HIV antibody test results.

Western Blot Confirmatory Test

- On specimens for which ELISA tests repeatedly demonstrate positive HIV antibody results, a confirmatory test is conducted. The most popular is the Western Blot which is used because it is more specific than ELISA tests. Unlike the ELISA test, the Western Blot is read by humans and the results are recorded manually.
- Results of Western Blot antibody tests can be either positive, negative, or indeterminate (reactive, non-reactive, or inconclusive). A positive result means someone is infected with HIV. A negative result means that someone is not infected with HIV or the person has been infected with HIV so recently that his/her body has not yet produced enough antibodies for the test to detect.

Oral Mucosal Transudate

- Another collection method, the Oral Mucosal Transudate (OMT) (FDA approved in 1996) involves the collection of a specimen from a client's mouth using a treated pad attached to a handle. The pad is placed between the client's lower cheek and gum for two minutes. It is important to note is that this **is not a saliva test**. The treated pad draws out the OMT fluid which contains high concentrations of HIV antibodies and is free of most of the contaminants in saliva. After two minutes, the pad is removed and placed in a special vial containing a preservative and sent to a lab for testing in the same way blood samples are tested. The test is marketed under the name Orasure and is a highly reliable alternative to blood testing.

Home Testing

- Home testing kits hit the market several years ago, despite outcry from many mental health professionals who felt that anyone considering to HIV testing should be afforded the opportunity for face-to-face counseling from a qualified prevention counseling specialist, a service unavailable to home test kit users.
- In June of 1999 the Federal Trade Commission (FTC) announced that anyone who had tested using a home testing kit purchased over the Internet may want to be retested because some home testing kits can give false information about HIV status. The FTC recently tested HIV kits advertised and sold over the Internet for self-diagnosis at home. In every case, the kits showed a negative result when used on a known HIV-positive sample. That is, when the test should have shown a positive result.
- The Food and Drug Administration (FDA) has approved only one home test collection kit, the Home Access Express HIV-1 Test System, manufactured by

Home Access Health Corporation. This system allows consumers to collect a sample in the privacy of their homes and then requires that the sample be sent to their lab for analysis. Consumers then call a designated phone number and provide their ID number (comes on the kit) to get the test results. Standard lab tests (ELISA and WB) are used as mentioned earlier.

Rapid HIV Antibody Testing Kit

- On November 7, 2002, Health and Human Services Administration (HHS) announced that the U.S. Food and Drug Administration (FDA) had approved a new rapid HIV diagnostic test kit that provides results with 99.6 percent accuracy (similar to more common laboratory HIV antibody testing specificity) in as little as 20 minutes.
- Using less than a drop of blood collected, this new test, OraQuick®, can quickly and reliably detect antibodies to HIV-1, the HIV virus that causes infection in most cases in the U.S. Unlike other antibody tests for HIV, this test can be stored at room temperature, requires no specialized equipment, and may soon be considered for use outside of traditional laboratory or clinical settings. The OraQuick® Rapid HIV-1 Antibody Test is manufactured by OraSure Technologies, Inc., Bethlehem, Pennsylvania.
- Testing is as simple as fingerstick sample of blood collected from an individual and transferred to a vial where it is mixed with a developing solution. The test device, which resembles a dipstick, is then inserted into the vial. Within as little as 20 minutes the test device will indicate if HIV-1 antibodies are present in the solution by displaying two reddish-purple lines in a small window on the device.
- Although the results of rapid screenings will be reported in point-of-care settings, as with all screening tests for HIV, if the OraQuick® test gives a reactive (i.e. positive indicating the presence of HIV antibodies) test result, that result must then be confirmed with an additional specific laboratory test. OraQuick® test has not been approved to screen blood donors.
- In February 2003, President Bush announced that HHS approved expanded availability for a "rapid" HIV test, allowing health care workers to use it in more than 100,000 doctors' offices and public health clinics across the country. Prior to that time, the FDA approved the test for use in only about 40,000 hospitals and clinics with laboratories. AIDS groups had advocated for making the test available at smaller outreach clinics and mobile testing sites in order to make the test more accessible to the general population.

2. Additional HIV Antibody Testing Information and Considerations

- It is now possible to test directly for the presence of the virus itself. Viral load, a quantifiable measurement of how many viral particles are present in a cubic millimeter (mm^3) of blood, can be determined by several different assays. Occasionally, viral load testing may be used as an *initial* testing method in place of standard antibody testing if a physician suspects a patient is in the acute viral infection phase and therefore unlikely to receive an accurate diagnosis using standard testing methods.
- If a person has HIV infection, he/she can transmit the virus to other people regardless of whether he/she tests positive, or tests negative because of a new infection.
- An indeterminate HIV antibody result is gut wrenching because the person is left not knowing much except that something, not necessarily HIV, has been detected.
- One cannot assume that an indeterminate result will eventually seroconvert. Many people who initially receive indeterminate test results will later seroconvert to negative results, some will eventually seroconvert to positive results, and still others have results that forever remain indeterminate.
- Often patients with repeatedly indeterminate HIV antibody test results want to be evaluated by a physician to try to ascertain what else, if not HIV, may be active in their bodies.
- Seroconversion refers to a change in the blood. With HIV, this term usually means, but is not limited to mean, a change from a negative or indeterminate test result to a positive result.

3. Counseling and Testing Guidelines

- There has been a long and acrimonious debate over the purpose and methods of counseling and testing - a debate that reflects the history of the entire AIDS epidemic. As treatments for HIV infection have become more effective, there has been increased emphasis on more widespread testing so that infected individuals can obtain early treatment.
- The earlier guidelines emerged from paradigm that *risk screening* as the primary goal of counseling and testing—a paradigm that emerged in the era of therapeutic impotence. Therefore, the emphasis was on risk screening to determine which individuals should be offered C&T, detailed informed consent procedures, and extensive pretest and posttest counseling. By 1999, however, the context of C&T had dramatically changed. The availability of new treatments for HIV infection, the availability of new testing technologies, such as rapid testing and home collection tests with results provided via telephone, forced a rethinking of the existing paradigm.

- The historical paradigm did not correspond to the substantial amount of relevant literature that had been accumulated in recent years indicating that:

Many individuals do not receive their test results when in-person visits to obtain counseling are required.

Individuals often do not seek or accept C&T under targeted approaches because of the need to disclose personal risks and the stigma associated with being “singled out.” Individuals may be more likely to accept C&T when presented as a routine part of care and when informed consent procedures are less extensive (e.g., “right of refusal” approach).

Primary care providers often do not provide counseling because of the time and expense required as well as discomfort and inadequate training. The result is that many health care providers do not offer C&T unless patients request it or they use ad hoc risk screening and provide limited counseling.

Targeted C&T may provide fewer societal benefits than universal, routine C&T by hindering efforts to reduce HIV stigmatization and by being more costly relative to the benefits.

Many HIV-positive individuals are missed under targeted C&T approaches because individuals do not disclose risk behaviors, health care providers do not use valid and reliable screening approaches, and targeting based on HIV prevalence is difficult due to the epidemic’s shifting epidemiology.

- In 2001, CDC issues revised guidelines for HIV counseling, testing, and referral (and) revised recommendations for HIV screening of pregnant women. The guidelines are available at the HIV Counseling, Testing, and Referral website at <<http://www.cdc.gov/hiv/ctr>>. Key elements of the guidelines are summarized below:

Primary goals:

To ensure that HIV-infected persons and persons at increased risk for HIV:

Have access to HIV testing to promote early knowledge of their HIV status.

Receive high-quality HIV prevention counseling to reduce their risk for transmitting or acquiring HIV.

Have access to appropriate medical, preventive, and psychosocial support services.

To promote early knowledge of HIV status through HIV testing and ensure that all persons recommended and/or receiving HIV testing are provided information regarding transmission, prevention, and the meaning of HIV test results.

Testing Strategies

HIV testing should be voluntary, preceded by informed consent, and provided in a way that ensures strict client confidentiality. HIV testing should be available in both confidential and anonymous formats.

Routine offering of voluntary testing is recommended for all clients in settings where the client population is at increased behavioral or clinical risk of acquiring or transmitting HIV infection, regardless of setting prevalence.

Routine offering of voluntary testing is recommended in settings where HIV prevalence is high (e.g., > 1%).

Targeted HIV testing based on risk screening is recommended in settings where both the HIV prevalence and the behavioral or clinical risk for HIV of the client population are low (e.g., health care settings). Any client requesting an HIV test should be provided one, regardless of his or her risk.

Routine offering of voluntary testing is recommended for clients with “prevention treatment potential” (i.e., pregnant women and clients with acute occupational or non-occupational exposure), given the existence of effective biomedical interventions to prevent HIV transmission.

Informed Consent and Information

Written documentation of informed consent is recommended for HIV testing. Information about consent may be presented orally or written. State or local laws governing HIV testing should be followed.

When HIV testing is offered, information should be provided about the HIV test, risks of transmission, importance of obtaining test results, meaning of test results, and where to obtain further information and services. Information can be delivered in the form of a pamphlet, brochure, poster, or video.

Counseling

HIV prevention counseling should be conducted for all clients in settings where clients are at increased behavioral risk for HIV, regardless of HIV prevalence. Targeted prevention counseling based on risk screening is recommended in settings of high and low HIV prevalence, and for populations with low behavioral or clinical risk for HIV.

Prevention counseling should focus on the client’s own unique circumstances and risk through an in-depth, personalized risk assessment. Counseling should help the client set and reach an explicit behavior change goal through use of an interactive rather than informational approach.

PRENATAL GUIDELINES

Primary Goal

All pregnant women in the United States should be tested for HIV as a routine part of prenatal care because of the benefits of knowledge of HIV status for both women and their babies. HIV testing should be voluntary.

Informed Consent and Information

Written documentation of informed consent is recommended for HIV testing. Information about consent may be presented orally or written. State or local laws governing HIV testing should be followed.

When HIV testing is offered, information should be provided about HIV, risks of transmission, effective interventions, that testing is recommended for all pregnant women, services are available, and that women who decline testing will not be denied care. Although face-to-face counseling is ideal, other methods can be used.

Counseling

HIV prevention counseling, including education about HIV and assessment of risks or HIV infection, should be provided to all pregnant women as part of routine health education during pregnancy. Reluctance to provide HIV prevention counseling should never be a barrier to testing. Women found at increased behavioral risk for acquiring HIV or who want more intensive client-centered counseling should be provided with or referred to HIV risk reduction services.

4. Counseling Issues Associated with HIV Testing

- The decision to get tested involves four main counseling tasks: (1) helping clients overcome any ambivalence regarding taking the test; (2) reviewing options with clients and the consequences of receiving a positive or negative test result; (3) supporting clients while they wait for results by discussing and validating their fears; and (4) preparing clients for the results of the test.
- Acute distress in response to a positive HIV antibody test is nearly universal. People may experience many reactive psychological symptoms including depression, anxiety, and preoccupation with illness. These symptoms often take the form of transient and situational adjustment disorders. However, it is often observed that depression and other aspects of the initial shock of learning one is HIV infected decline over the first few weeks of adjustment. Emotional problems can remain relatively absent during the asymptomatic phases of HIV disease.
- People have a wide range of reactions to the receipt of positive results,

including:

1. numbness accompanied by an inability to take in the news that they are positive
 2. an immediate rational acceptance of their positive status without any exploration of possible emotional reactions;
 3. intense fatalism, a belief that they have only a short time left to live. Despite knowledge of promising new drug treatments, these people often hold onto the belief that the treatments will not work for them;
 4. guilt and remorse for past behaviors; Lynch & Palacios-Jimenez (1993) observed that many of their clients began taking inventory to determine what they did to deserve AIDS. This often results in feelings of self-blame as well as intense anger directed at the people believed to be responsible for transmission;
 5. people may receive a positive test result and go into denial for years until they become symptomatic;
 6. suicidal ideation. Rabkin, Remien & Wilson (1994) note that although many people believe they might choose suicide at some future point, when severe physical problems develop, they often discover new strengths and renegotiate the circumstances in which they would end their lives; and,
 7. hopefulness regarding new treatment options such as protease inhibitors.
- The tasks of psychologists working with patients who have recently received a positive diagnosis include:
 1. being alert to explicit and implicit messages that patients receive along with their results that patients may internalize, especially when they have received results with limited post-test counseling;
 2. helping patients adjust to the multiple tasks they immediately face upon testing positive such as forming a medical team, making treatment decisions, and disclosing their status;
 3. finding developmentally appropriate messages to convey information about HIV disease and to dispel fears, particularly in young patients;
 4. helping patients' understand and manage their emotional reactions to testing positive and to manage their symptoms. Counselors may use a crisis counseling model. Some patients may need psychotropic medications;

5. assessing patients' support networks and making referrals to community resources when necessary; and, managing the balance between a duty to protect confidentiality and a duty to warn HIV-positive clients' partners in the rare circumstance when a client's refusal to tell a partner of his/her HIV-positive status leaves the partner at risk.

Possible Topics for Discussion:

Considering HIV antibody testing and then following through can be one of the most difficult times in a person's life? What do you imagine may be some of the considerations people weigh before actual testing? What are some of the feelings individuals may present at the time of consideration? during the waiting period for results?

Have individuals shared their interest in antibody testing with you in your practice? What might the benefits be for choosing to test? What might the cost of testing be for an individual? If someone presents at the point of considering an antibody test, might there be a time when you would consider a recommendation or support a decision to postpone the test? Under what conditions?

The advent of home testing has raised some new challenges for mental health providers. What issues would you want to raise with a client considering using a home test?

5. Additional Findings Pertaining to Counseling Associated with HIV Testing

- In one study involving gay men (Conley, Taylor, Kemeny, Cole, & Visscher, 1999), HIV-negative men unaware of that fact suffered unnecessary worries and concerns, since those who kept themselves unaware of their serostatus had AIDS-related worries and concerns significantly higher than individuals aware that they were HIV-negative and equivalent to individuals aware that they were HIV-positive. At a later point, both HIV-positive and HIV-negative men who were initially unaware showed a decline in mood disturbance on learning their HIV status, suggesting that learning threatening information may be more psychologically beneficial than avoiding it.
- HIV testing might be encouraged by reframing testing messages to underscore benefits *lost* by not testing, including protection of one's partner and access to early medical intervention (Salt, Davidson, & Harvey, 2001).
- With drug-using women, playing up the importance of family concerns (e.g., benefits to an unborn child) may promote HIV testing while, with drug-using men, a more useful focus might be increasing control over one's life (e.g., obtaining relief from anxiety related to learning one's HIV status) (Riess, Kim, & Downing, 2001).

- Certain testing methods and procedures may sway some individuals considering testing. In one study (Peralta, Constantine, Deeds, Martin, & Ghalib, 2001), for example, teens voiced a clear preference for a noninvasive procedure (the collection of saliva) and a rapid result response time when submitting to HIV antibody testing.
- Setting is another key consideration. As an example, if results can be made available during treatment and HIV clinical care is also readily available, HIV testing is acceptable and even desirable among people receiving inpatient substance abuse treatment services (Pugatch et al., 2001a, 2001b).
- What has been the impact of HIV counseling and testing on sexual risk behavior? In a meta-analysis of 27 published studies (Weinhardt, Carey, Johnson, & Bickham, 1999), researchers found that HIV-infected individuals and HIV-serodiscordant couples decreased unprotected sex and increased condom use more than HIV-negative and untested individuals after counseling and testing. Individuals who were HIV-negative did not, however, change their sexual risk behavior more than participants who had not been tested, leading these researchers to conclude that counseling and testing does not appear to be an effective primary prevention method for uninfected individuals, although the strategy is effective as a secondary prevention for individuals who are already HIV-infected.
- While repeat HIV testing by HIV-negative individuals may reflect a normative shift in testing behavior and may be understood as one part of a risk-reduction strategy for repeaters, higher rates of repetitive testing may, in some cases, be viewed as an invitation to challenge risk-taking behaviors and to discuss additional strategies for risk reduction (Leaity et al., 2000).
- Motivational interviewing may promote increases in HIV repeat testing among substance abusers who decline an offer of HIV testing in the context of ongoing sex- and drug-related risk behavior (Pugatch et al., 2001b).
- Vernon, Mulia, Downing, Knight, & Reiss, (2001), investigators found that low-income drug users recruited from the street did not generally engage in repeat HIV testing behavior in connection with *current* risk behavior. Rather, these individuals:
 - Anticipated an eventual positive test result, regardless of past negative test results and an absence of current risk behavior;
 - Believed that there was a 10-year window period, during which time the virus remains undetectable;
 - Utilized repeated HIV testing as a routine form of healthcare; and
 - Viewed testing as a means of exercising control over HIV.

- Clearly, respondents were confusing the 10 years of infection preceding the emergence of HIV disease with the "window period" between infection and the development of HIV antibodies, and were therefore using HIV testing as a type of "screening procedure" associated with other types of chronic illness (e.g., hypertension, diabetes). While this misconception resulted in regular use of HIV testing services, it may also cause drug users to ignore current risk behavior, believing that current behavior is unrelated to risk for infection.
- The disassociation of behavior and risk dramatizes the challenge of personalizing risk for purposes of increasing the monitoring of health status among drug users (Brown, O'Grady, Farrell, Flechner, & Nurco, 2001). Clinicians working with drug users in communities hard-hit by HIV should:
 - Clarify confusion regarding "window periods";
 - Shift focus to current risk behavior;
 - Reinforce the understanding that one may remain uninfected despite known exposure to HIV and/or years of risky behavior, but that does not guarantee that one will remain uninfected; and
 - Capitalize on the use of HIV testing services as a form of self-care and employ testing as a linkage into other types of healthcare and social support (Vernon, Mulia, Downing, Knight, & Reiss, 2001).

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