Clinical Concerns in HIV/AIDS

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Objectives

By the end of this educational encounter, the clinician will be able to identify at risk populations for HIV/AIDS.

Clinician will demonstrate comprehension of new testing recommendations for HIV

Clinician will be able to recognize new health concerns in HIV patients

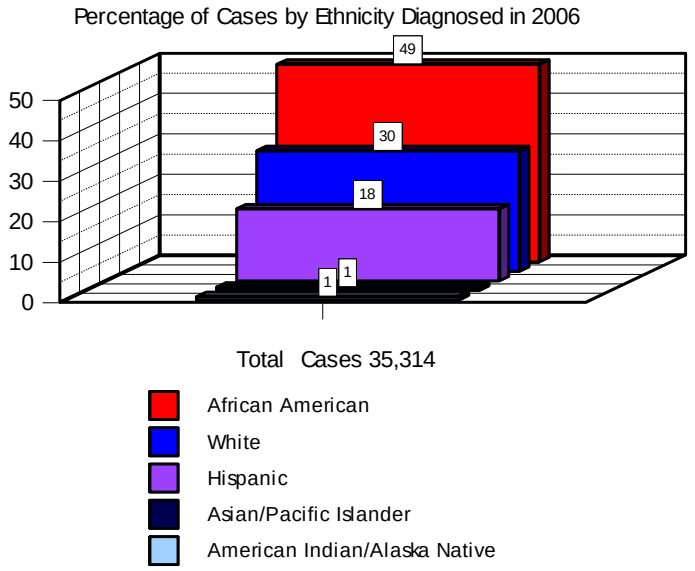
Introduction

The history of AIDS in the United States goes back to approximately 1969, when it was thought that the disease was introduced to the US by a Haitian immigrant. In the early part of the 1980's, larger city doctors began seeing a type of cancer in young men that usually is restricted to older men of Mediterranean origin. What is now known as Karposi's sarcoma was then coined as 'Gay Cancer' and added to the stigma of Homosexuality in the United States. However, cases in young children, women, and person's having blood transfusions began to occur and the symptoms were not limited to skin cancers, but also included specific types of pneumonia. In 1982, the CDC renamed the syndrome AIDS.

With the advanced strides made in medical treatment, persons with HIV are living longer. In New York City, where an estimated 100,000 persons are estimated to be living with the virus, over 30 percent of those are over fifty years of age. With medical advances that allow HIV patients to live longer, comes another set of realities as these patients are presented with compounding diagnoses never before encountered in this patient population and physicians are presented with the overwhelming task of attempting to manage the increased pathological burden in these patients.

While fewer people are dying of HIV, the numbers of infected persons are reaching epidemic proportions. In 2003, and estimated 1,039,000 to 1,185,000 persons in the United States were estimated to be living with HIV/AIDS and 24-27% of these persons were **totally unaware** that they were infected with the disease. This means that almost one fourth of over one million persons remain untreated and undiagnosed; and potentially are unknowingly spreading the disease to others.

Men still account for the greater number of HIV/AIDS cases present in the United States. In 2006, men accounted for three fourths of all cases diagnosed in the 33 states having confidential name based reporting.



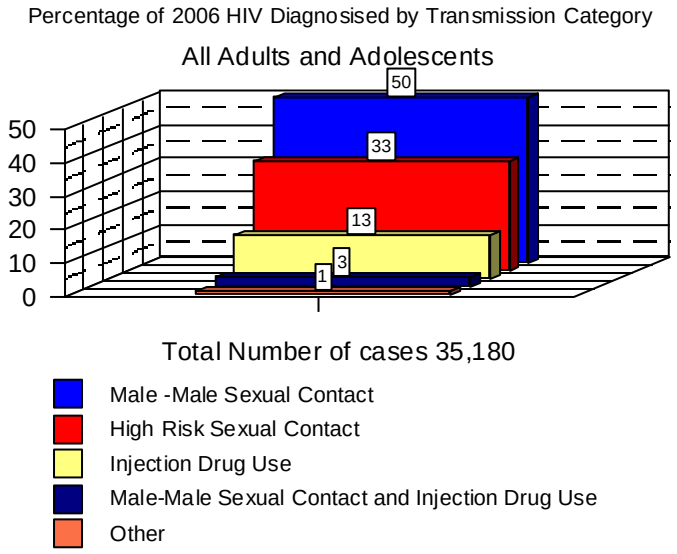
Data Based on the 33 states having confidential name based reporting

In 2006, the number of new HIV/Aids diagnoses is highest in the transmission category of men having sex with men (MSM). However, the rate of heterosexual high risk transmission among all groups is rapidly growing and is the most important factor in women being infected with the disease, even when IV drug use is present. These results were obtained after a 10-year study by the National Institute on Drug Abuse. The CDC categorizes the heterosexual transmission of HIV into two groups: primary and secondary. Primary transmission is defined as sexual contact with a partner with known risk factors for HIV transmission. Secondary transmission is contact with an HIV positive partner not known to be at risk for HIV. In 2001, more men reported sexual contact with a partner with risk factors for primary transmission for HIV while persons reporting secondary transmission were more likely to be women. Since 1988, the number of heterosexual mediated HIV/AIDS cases has continued to increase, changing the face of AIDS from a primarily high-risk behavior disease

to an increasingly generalized sexually transmitted entity. This is of particular concern in the medical community, because many heterosexual persons are still having a false sense of security about HIV/AIDS transmission and are engaging in unprotected sexual activity with very little knowledge about their risk.

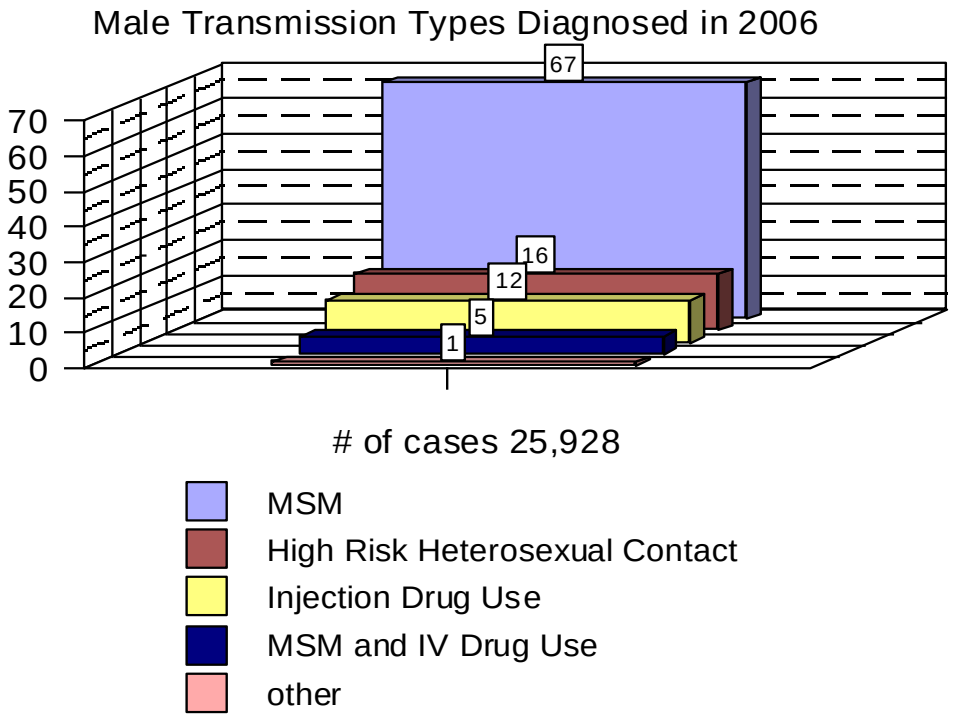
When the country was first introduced to HIV/AIDS, it was bombarded with information on the nightly news and in the media, leading to almost paranoia about the disease. However, in recent years media attention to the problem has diminished, leaving education about the disease largely in the hands on the medical and scientific community. This is bad news for persons not receiving routine health care services. This factor enhances the false sense of security in the heterosexual community regarding the risk of acquiring HIV. Additionally, it has been over 20 years since the public began receiving the reports of HIV/AIDS and a new generation is now in their late teens and early twenties and is engaging in sexual activity without the benefit of the early knowledge of HIV/AIDS that came with the initial media onslaught.

This data is backed up by the 2006 CDC report on HIV diagnoses by transmission category. Roughly, 83% of all cases diagnosed in 2006 were due to Heterosexual and MSM sexual contact. Total cases linked to injection drug abuse made up only 16% of all diagnosed HIV cases.



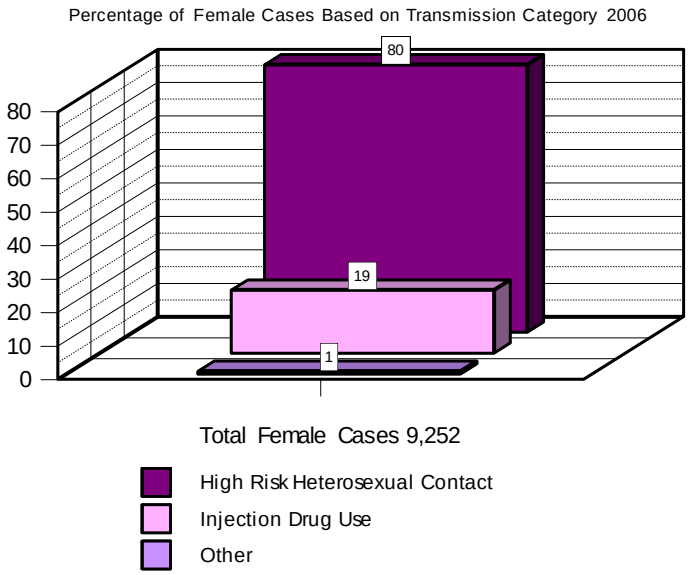
The rates of sexually acquired HIV/AIDS accounts for the majority of diagnosed cases in males in 2006. Male sexually acquired HIV diagnosis in 2006 accounted for 83% of all male cases compared to 80% of all female cases. When looking at actual case count figures, male sexual behaviors account for 3 times more diagnoses of HIV/AIDS than do female sexual behaviors. Males were slightly more likely to have an HIV diagnosis related to IV drug use (17%), than females were in 2006 (19%). These figures look deceptive at first; but when

you divide the percentages by actual number of cases, male IV drug use accounts for almost 3 times more HIV cases than females. For men, homosexual contact remains the primary risk behavior associated with HIV/AIDS diagnosis in the United States. The prevalence of unprotected anal sex among homosexual males has been shown to be more of a risk than vaginal intercourse. In fact, among heterosexual individual who practice unprotected anal sex on at least an occasional basis have higher percentages of HIV/AIDS than do heterosexuals who practice unprotected vaginal intercourse.



Several studies have been conducted to determine why men seem to be more at risk for HIV infection than women. One study of uncircumcised men found that the cells on the inner side of the foreskin contained high numbers of cells that are targeted by HIV. Men also tend to have more sexual partners than women do and are more likely to engage is risky sexual behaviors. Social pressures of masculine ideals may play a roll as well by overtly discouraging condom use and having discussions about sexual risk with their partner before engaging in intercourse.

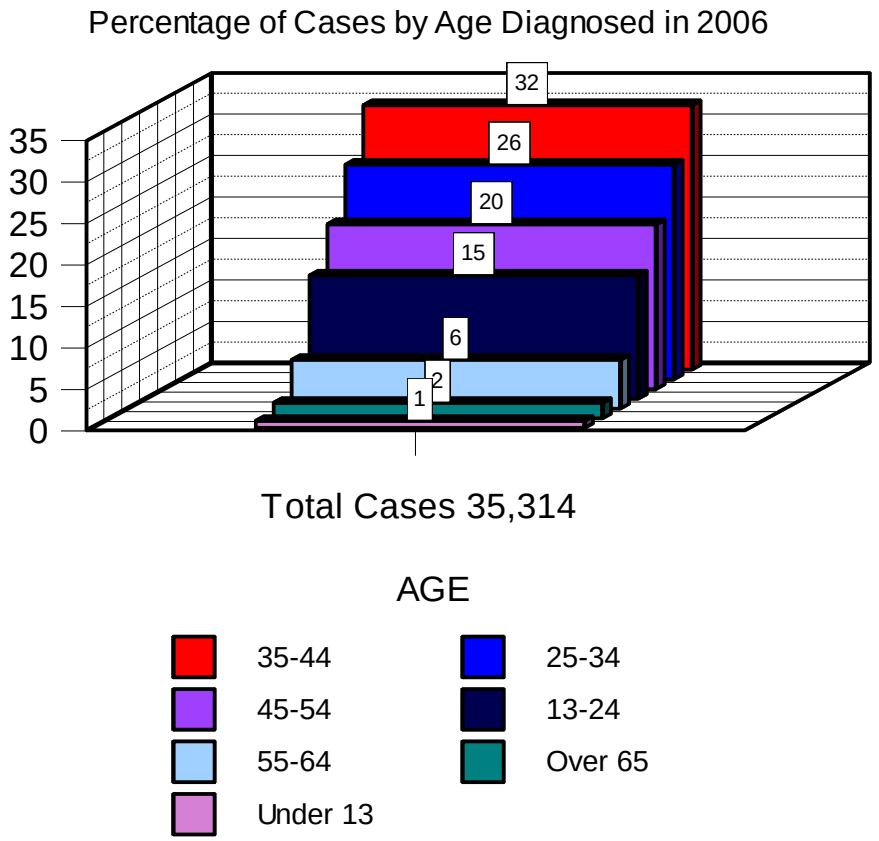
Researchers are also finding out that genetic differences may play a role in why some people are more susceptible to HIV. A protein called CCL3L1, which blocks the AIDS virus, is found in varying amounts in individuals. Persons with more copies than average of this protein have been found to be less susceptible to HIV, while persons with fewer copies have been found to be more susceptible.



In women, factors for susceptibility have been found to be related biology. The vaginal tissue gives a greater surface area for exposure to the HIV virus from sexual fluids. Diminished vaginal lubrication, which can lead to breaks in the vaginal mucosa during intercourse, can also be a factor. In addition, cervical ectopy can increase the risk of contracting chlamydia, which can increase the risk of acquiring HIV infection. Cervical ectopy is a common condition and occurs when the regular squamous cells of the cervix become replaced by more fragile, thinner tissue in the cervical tract.

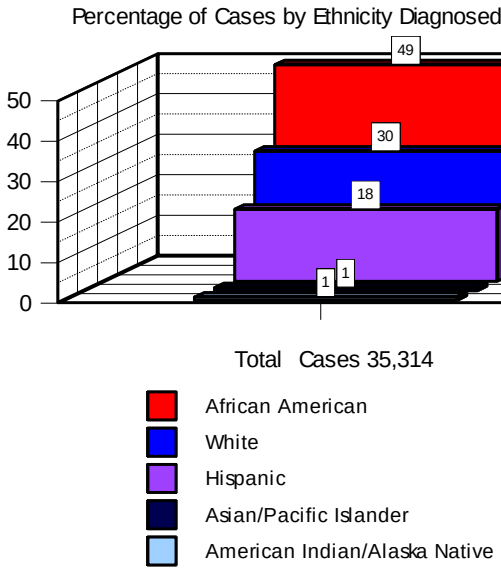
For women, the largest transmission category is high-risk heterosexual contact, which accounts for 80% of all the female cases of HIV diagnosed among the areas with confidential name based reporting in 2006. Injection drug use still carries approximately one fifth of the case diagnoses and remains a significant number among females.

Persons aged 25 to 54 account for 75% of all the cases of HIV diagnosed in 2006. Persons over fifty that are living with HIV/AIDS has steadily been increasing in recent years, and account for approximately 25% of persons that were living with the disease in 2005 and 15% of all the new diagnoses for that year. The largest age group within this category were persons aged 35 to 44 who accounted for 32 percent of all the diagnosed cases. Surprisingly the age group 13 to 24 accounted for only 15% of the cases that were diagnosed in 2006, by numbers that amounts to almost 5,300 cases.



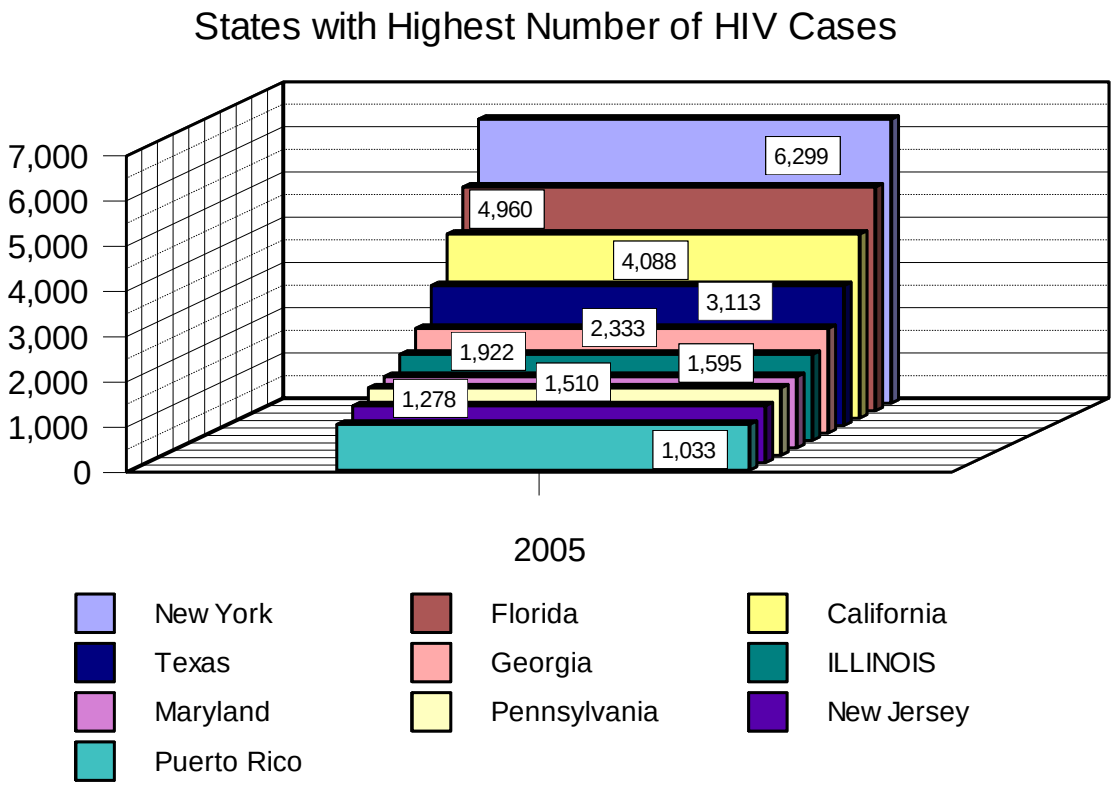
HIV/AIDS is now becoming a growing concern for mature adults; however, they may think themselves immune to the risk. Risk factors for this age group are the same as for any other. A recent survey of sexual behavior among older adults showed that 73% of persons aged 57–64 had had sex during the past year, as had 53% of those aged 65–74 and 26% of those aged 75–85. The numbers of mature adults is expected to continue to climb well into the next decades, meaning that the numbers of mature adults with HIV/AIDS will also increase.

Increased attention needs to be aimed at this age group by the medical community when assessing HIV/AIDS risk. This age group often is not comfortable discussing preventative measures if they are engaging in sexual activity after a long-term relationship has ended. In addition, we must overcome our own stereotypes in thinking that the elderly are not sexually active. The healthcare community must take a proactive approach in initiating discussions about healthy sexual activity with mature adults; they are not likely to be the ones to take the first steps. There is great opportunity for health care workers to apprise these adults of risks and make them aware of the need for HIV/AIDS prevention.

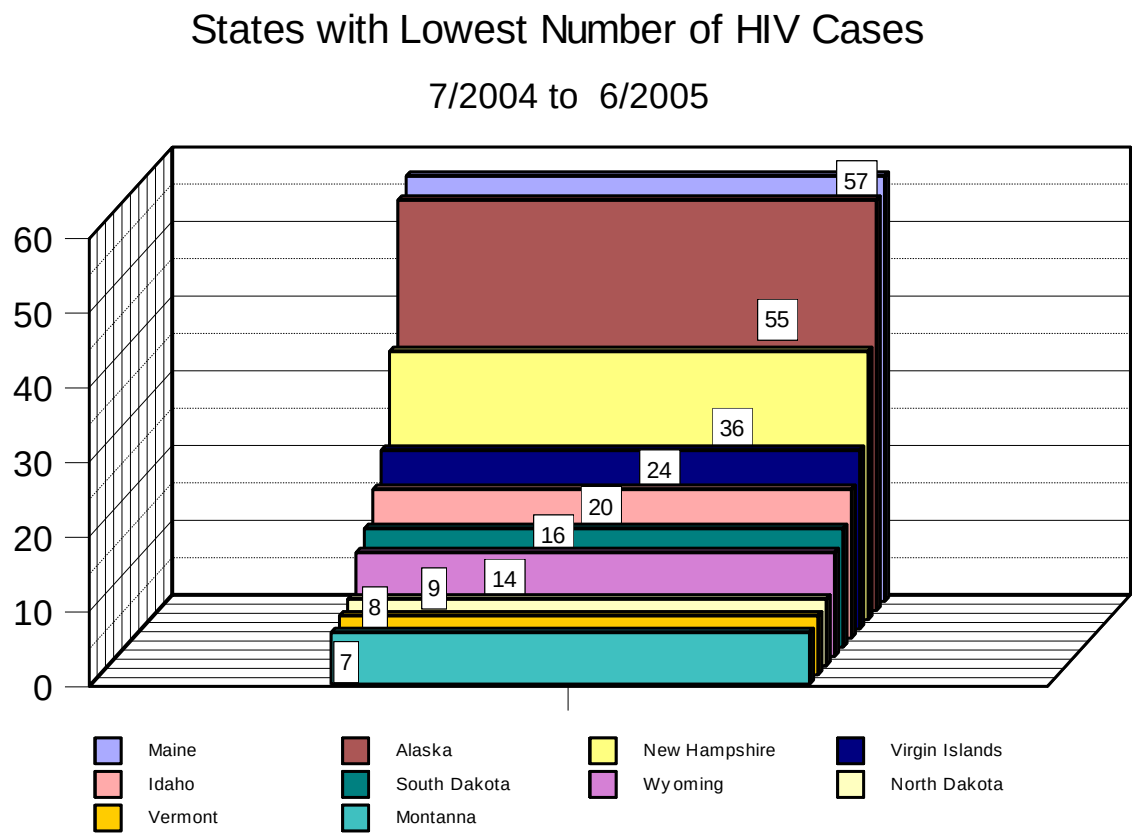


HIV is growing among ethnic populations at an alarming rate. Almost fifty percent of the HIV cases diagnosed in 2006 were to African Americans and the number of cases among Latinos/Hispanics is growing in alarming numbers. Ethnic groups are hit harder not because of their ethnicity, but because of the barriers that they face. The barriers can be poverty, STD's and social stigmas. Ethnic groups also face more limited access to health care and may also be less educated, leading then to difficulties in understanding the limited amounts of accurate HIV information that they come in contact with. For ethnic groups, the risk factors for HIV are the same as other groups, and having any type of STD increases the chances of contracting HIV. In the Latino/Hispanic ethnic group, HIV is the fourth leading cause of death. Since these groups may not encounter health professionals on a regular basis, risk factors need to be assessed at any medical encounter, which the patient has and educational information or referral resources be provided.

Regional differences can also exist in how risk is perceived by the patient. In areas where HIV is more prevalent, patients and healthcare worker are more likely to be aware of the potential for infection. Patients may also harbor false perceptions of the prevalence of HIV in their area, increasing a false sense of security regarding their risk of contracting the disease. Areas that have shown to have the highest high numbers of HIV cases are New York, Florida, California, Texas, Georgia, Illinois, Maryland, Pennsylvania, New Jersey, and Puerto Rico.

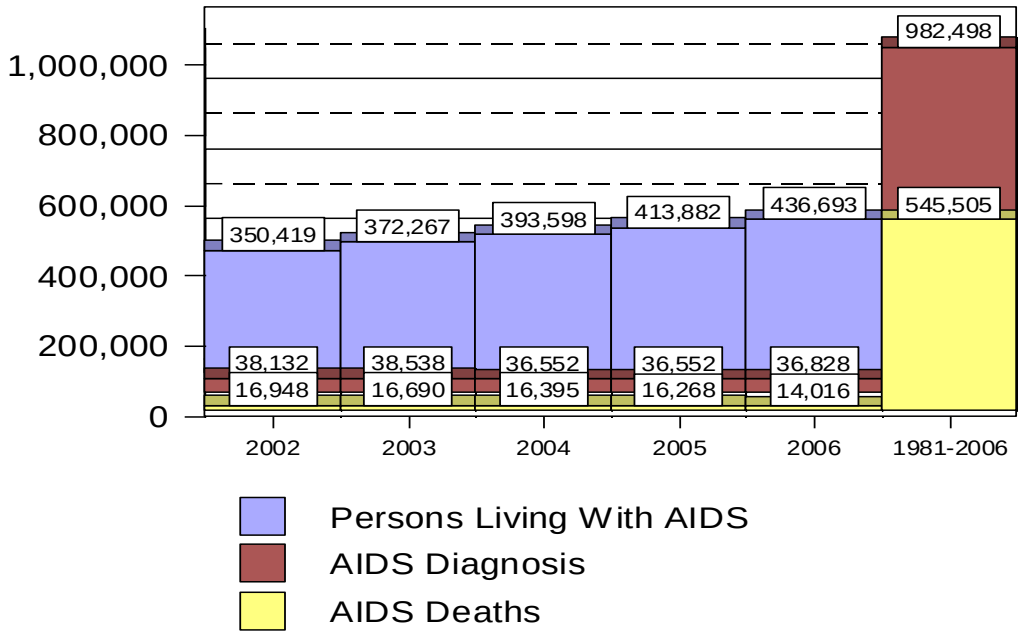


States having the fewest number of HIV cases in descending order are: Maine, Alaska, New Hampshire, Virgin Islands, Idaho, South Dakota, Wyoming, North Dakota, Vermont, and Montana. The differences in the highest and lowest numbers most likely are relevant to the population concentration in the individual areas. States having the highest number of cases tend to have the highest concentration of metropolitan areas with major US cities, while the areas with fewer cases tend to be less populated and more rural in nature. Patients may not know that they live in a high risk are and are more likely to come into contact with the HIV virus than their more isolated and rural counterparts, and there fore do not perceive the level of danger associated with their risky sexual behaviors.



As the numbers of AIDS diagnoses yearly continue to climb, the number of deaths per year stayed at a steady rate between the years 2002-2005 and dropped slightly in 2006. Not enough data is available yet to determine if this trend is going to continue, but it does reflect the achievements that have been made in treating the disease. Persons are now living longer, more viable lives with the diagnosis of HIV. AIDS has already claimed over one-half million lives since 1981. The battle does not lie in treating the disease, but detecting it and especially detecting it in the early stages of the illness, before the ravages of the disease have destroyed the body. The routine screening of blood donors has virtually eliminated blood transfusions as a means of transmission of HIV. Perinatal transmission has decreased to around 2% due to routine HIV testing during pregnancy combined with management practices for HIV positive mothers. The institution of these procedures proved the value of the screening process in the fight against HIV. However, routine screening to prevent sexual transmission had not been undertaken. This fact, in part, has lead to new recommendations by the Centers for Disease Control regarding HIV testing.

Number of AIDS Diagnoses, Deaths, and People Living with Aids 2002-2006



New Recommendations for HIV Testing

The CDC has recommended the routine screening of all patients aged 13-64 years in all healthcare settings unless their infection rate has been documented to be less than 0.1 percent. If no prevalence data is available, the institution should initiate routine testing until data yields determine positive results of less than 1 case per 1,000 cases screened. At this level of prevalence, routine screening is no longer warranted.

All patients beginning treatment for TB should be routinely screened for HIV infection.

Patients that seek treatment for STD, including treatment at STD clinics, should be routinely screened at each new patient complaint visit regardless of known or suspected risk status.

Guidelines for repeat screenings include the screening on all high-risk individuals on an annual basis. High risk individuals include: MSM or heterosexual persons who themselves or whose sex partners have had more than one sex partner since their most recent HIV test, injection-drug users and their sex partners, persons who exchange sex for money or drugs, and sex partners of HIV-infected persons. Health care personnel should encourage all patients and their partners to be tested before forming a new sexual relationship. Repeat screening for individuals not at high risk should be at the discretion of the clinician. If any occupational blood or body fluid exposure occurs and HIV test results are not

readily available, then the patient should be informed and testing should be completed at the time of the exposure. Under the new guidelines, a separate consent is not required for HIV testing. The consent is incorporated into the general consent for medical care. Patients should be informed orally or in writing that testing will be performed unless they opt out. The patient should be afforded the opportunity to decline testing and information should be provided about the meaning of positive and negative test results as well as information about HIV infection. Informational materials that are written in the patient's native language should be provided and the materials should be written as to be readily understood. Persons should be available to assist with translation services as necessary. If a patient declines testing, the decision should be documented in the medical record. Patients should not be tested without their knowledge, and testing must be voluntary and without coercion. The recommendations have not changed regarding testing in non-clinical settings such as community based centers or mobile testing facilities.

Growing Health Concerns Amid HIV Infected Populations

Metabolic Syndrome

Combination antiretroviral therapy (ART) has significantly decreased the mortality and morbidity of HIV and led to improved quality of life for its victims. However, concerns are now being raised about some of the long-term effects of the drugs and potential toxicities. Metabolic Syndrome, which is defined by the National Cholesterol Education Program as the presence of three or more of the following: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, high blood pressure, and high fasting glucose, has become linked to the use of protease inhibitors, in particular stavudine and lopinavir/ritonavir when individual antiretroviral drugs were analyzed in HIV patients. This is of particular concern because of the increased risk of cardiovascular disease. A 2006 study by Massachusetts General Hospital found that exercise manages symptoms of metabolic syndrome. As many as 45 percent of HIV patients have this condition, which raises the risk of diabetes and heart disease. Metabolic syndrome is characterized as increased resistance to insulin, alterations in blood lipid levels, and increased blood pressure.

Also noted among patients with HIV and Metabolic syndrome are changes in the fat distribution within the body. Lipodystrophy is defined by the presence of peripheral lipoatrophy (diminished fat deposits in the face, arms, legs, buttocks, and prominent veins), central lipohypertrophy (increased fat deposits in the abdomen, breasts, dorsocervical region), and mixed lipodystrophy. "As detailed in the ATP III report, participants with three or more of the following criteria were defined as having the metabolic syndrome: waist circumference >102 cm in men and >88 cm in women; triglycerides ≥150 mg/dl (1.69 mmol/l); HDL cholesterol <40 mg/dl (1.04 mmol/l) in men and <50 mg/dl (1.29 mmol/l) in women; blood

pressure ≥130/85 mmHg; and fasting glucose ≥110 mg/dl (6.1 mmol/l). Individuals met criteria for high blood pressure or high fasting glucose concentration if they were currently on antihypertensive or oral hypoglycemic therapies, respectively." (Jerico, et. Al, 2005). The association of metabolic syndrome with protease inhibitors indicates that increased clinical diligence is necessary to prevent diabetes and heart disease as virtually all the components of metabolic syndrome consist of modifiable risk factors.

Hyperlactatemia and Lactic Acidosis

Nucleoside reverse transcriptase inhibitors (NRTIs) have had a long association with hyperlactemia and lactic acidosis. Lactic academia refers to the increased presence of plasma lactate without changes in blood pH, where lactic acidosis consists of increased plasma lactate with metabolic acidosis. The spectrum of lactic acidosis is quite variable with minimal symptoms including symptomatic hyperlactatemia with hepatic steatosis (fatty liver), to intermittent or chronic low-grade hyperlactatemia without acidosis, steatosis, or symptoms to fulminant multiorgan dysfunction characterized by severe acidosis and hemodynamic instability. Patients with lactate levels above 90mg/dl have an overall mortality rate of 80%. Generally, the first line treatment is to withhold antivirals until they can safely be reintroduced. It is desirable to withdraw therapy in all patients with lactic levels above 90 and in symptomatic persons with levels over 45. Other therapies are limited to those that are supportive in nature. All patients taking antiviral medication regimens need to be made aware of the potential and symptoms of lactic acidosis, especially after infection and to seek medical care at once if symptoms develop.

Bone Disease

Osteonecrosis, osteopenia, and osteoporosis

Osteonecrosis is the death of bone tissue as a result of diminished blood flow. The destruction of bone most often occurs near the joint and affects the hip and shoulder joints, the knee joint and bones of the hand and wrist. Osteonecrosis affects patients predominantly with advanced HIV, and males between the ages of 20 and 50 years. Most of the patients also have at least one risk factor present from the non-HIV infected populations including: use of systemic corticosteroids, alcohol abuse, hyperlipidemia (particularly hypertriglyceridemia), hypercoagulable states, hemoglobinopathies, autoimmune disorders, pancreatitis, pregnancy, bearing heavy weight, trauma, and osteomyelitis. While there is no evidence that Osteonecrosis is directly linked to ART therapy, many HIV infected patients do have to take steroid medications. These medications should be used in the lowest effective dose and for the shortest length of time

possible. Surgical intervention to replace the affected joint is the only viable treatment available.

Osteopenia is the demineralization of bone and osteoporosis is the advancement osteopenia to the point that bone fractures have occurred or are likely to occur with minimal trauma or stress to the bone. Osteopenia and osteoporosis occur at higher rates in patients on ART therapy than in the general population. Patients on heavy ART regimens demonstrate high levels of alkaline phosphate and osteocalcin, and some patients on protease inhibitors may show diminished growth of new bone; but the definite role of ART therapy in osteopenia is not yet determined. Lifestyle modifications are at this point the best course of therapy and include increase in weight-bearing exercise, weight loss, and smoking cessation, Dietary modification to include calcium rich foods equivalent to 1,500mgs of calcium per day and Vitamin D 400-1,000 IU per day.

Tuberculosis

Tuberculosis, or TB, has in itself become a worldwide epidemic. In 2005, TB killed an estimated 1.6 million people. It is estimated that worldwide 195,000 of these individuals were infected with HIV. Why is TB some important among the HIV population? TB is the number one killer of persons infected with HIV and is the cause of death in one third of the individuals with fully involved AIDS. When someone becomes infected with the TB pathogen, it is much more likely that they will become ill with TB if they also are immunocompromised from HIV. Having HIV makes it much more likely that persons infected with TB will spread much more of the TB bacteria, resulting in more cases of latent TB and more TB cases in the general population. Being infected with TB and HIV at the same time results in a likelihood that is 800 times greater that the TB pathogen will become active within the body. Persons with HIV are at greater risk for infection and malignancy because of the weakened state of the immune system. TB in HIV infected persons is harder to diagnose and progresses at a faster rate than persons without TB. TB infection is much more likely to be fatal in persons with positive HIV status, and appears earlier in the course of HIV infection than other opportunistic infections. TB is the only HIV associated infection that poses a risk to HIV negative individuals. Since TB occurs so early in the course of HIV infection, it is also wise for the clinician to investigate cases of TB infection for HIV coinfection. The medication INH can be used to prevent TB infected individuals from progressing to active TB, and can be used to treat current TB infections. HIV infected persons who have latent TB should be treated with INH therapy.

Renal Failure

The renal manifestations of HIV disease are quite diverse and may include: HIV associated nephropathy (HIVAN), HIV immune complex disease, ART or antibiotic associated renal damage, renal disease associated with microthrombi, and renal damage associated with comorbid diagnoses such as diabetes or amyloidosis related to heroin use, and Hepatitis C related glomerular basement membrane disease.

Although renal biopsy is performed only in rare instances, it is the only way of confirming HIVAN. Any person with HIV who has significant urinary protein, hematuria, or diminished renal function, especially African Americans, should have a renal biopsy performed. Studies have shown that African Americans with HIV have the same risk of End Stage Renal Disease as the entire general diabetic population. Renal biopsy in HIV is essential to determining the cellular pathology of the disease and for use as a tool to guide the treatment regimen.

The typical presentation of renal disease in an HIV infected individual is marked by significant urinary protein, rapidly declining renal function with poorly controlled HIV infection, diminished CD4 counts and elevated HIV RNA. Significant edema and high blood pressure are typically absent. Enlargement of the kidneys is usually noted on abdominal ultrasound.

The presence of HIVAN is classified as an absolute indicator for ART therapy without regard to the CD4 count. The kidney is able to be a reservoir for the HIV virus even though serum viral loads remain undetectable. HIVAN can progress from renal insufficiency to fully involved renal failure with in a few weeks or months.

ART has been shown to cause dramatic reversal of HIVAN and is now a first line treatment in the course of the disease. ACE inhibitors and angiotensin II receptor blockade drugs have demonstrated the ability to delay the progression of renal insufficiency in the HIV population and are considered a sound medical choice in the treatment of HIVAN. For patients that are experiencing rapid decline in renal function despite the application of ART therapy, steroids may be used without significant increased risk of infection. The use of steroids has shown to diminish urinary protein excretion in patients afflicted with HIVAN and is considered a second line medical therapy.

When HIVAN ESRD first became recognized in the early 1980's the lifespan of these patients from the start of dialysis was three months. Since the arrival of ART the lifespan of HIVAN affected patients on dialysis approximates that of the general ESRD population. The patient should be referred for AV fistula creation if hemodialysis is chosen as a mode of therapy as problems associated with AV grafts, such as infection and thrombus, are magnified in the HIV population. Kidney transplant is a viable treatment option for HIVAN patients with well controlled HIV infection as long term renal graft survival rates differ little from the general population. However, there is a slightly higher rate of rejection episodes

in the post transplant period. HIV does not progress with the immunosupression that a renal transplant requires as might first be assumed. Referral to a transplant surgeon should be made when the glomerular filtration rate falls below 25ml/min.

Conclusion

Despite the fact that numbers of new HIV cases are climbing, patients are living longer with HIV/AIDS since the arrival of ART. This presents new challenges for clinicians as patients are living with more comorbid diseases. Clinicians will have to be more knowledgeable in managing the complex health problems in this patient population as well as more proactive with regard to prevention and patient teaching. Through early identification and intervention, many of the problems presented here can be drastically reduced.

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