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A Guide to AIDS Research and Counseling

The State of the Science of HIV Treatment Approaches

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In resource-rich countries, the management of HIV has entered a new era. The dismal prognosis of death within six months of the diagnosis of an AIDS-defining condition such as pneumonia has dramatically improved.

It is estimated that 2.8 million years of life have been saved since 1989 in the United States alone due to HIV antiviral treatment.[1] Newly diagnosed individuals face a life expectancy that can be considered relatively normal. These lives, however, are encumbered by the necessity for life-long treatment and the complications of treatment. This article reviews the current menu of antiviral drugs and drug classes, current treatment timing and combination strategies, and medical complications that arise despite effective treatment.

New Drugs and New Drug Classes

HIV treatment still requires three or more medications and medications from two or more classes of drugs. Zidovudine (ZDV; AZT; Retrovir), the first licensed agent, was approved by the U.S. Food and Drug Administration in March 1987. This drug belongs to the nucleoside reverse transcriptase inhibitors (nRTI). The advances in this class include some new drugs that do not share some of the toxicity evident in early drugs, such as fat wasting associated with stavudine (Zerit), didanosine (Videx) and zidovudine or the peripheral neuropathy seen with some of these drugs.

Some nRTI drugs have been co-formulated to make administration easier. For example, abacavir (Ziagen) and lamivudine (Epivir) are co-formulated into a once-daily tablet, Epzicom. A new drug tenofovir (Viread) has been co-formulated with emtricabine (Emtriva) and recently with another drug from a second class, efavirenz (Sustiva), into Atripla. For some individuals, this single, once-daily tablet comprises a complete antiviral regimen.

The problem with the nRTI class of medications, in addition to their side effects, is that cross-resistance among these drugs is likely. Cross-resistance means that a strain of HIV that has mutated to become resistant to one drug may also be resistant to other drugs in that class, limiting the number of drugs that may be chosen for alternative regimens.

The non-nucleoside reverse transcriptase inhibitors (nnRTI) include efavirenz, nevirapine (Viramune), and delavirdine (Rescriptor). These drugs are potent, but associated with risk of liver toxicity. Efavirenz and nevirapine are potent inducers of cytochrome P450 enzyme system and, thus, can lead to many interactions with other drugs. In addition, a single gene mutation can render HIV resistant to these two medications. Depending on the geographic location, widespread use of these drugs has resulted in resistance to this class of drugs in up to 16 percent of newly infected individuals, rendering these medications useless in initial regimens.[2]

There are now eight protease inhibitors on the market. These drugs are generally potent, but use commonly leads to cross-resistance. To maximize potency, the majority of the protease inhibitors must be boosted with low dose of another protease inhibitor, ritonavir (Norvir.) Ritonavir is a potent inhibitor of the cytochrome P450 CYP 3A4 enzyme system. This inhibition not only improves the levels of other co-administered protease inhibitors, it also increases serum levels of a number of other, non-HIV medications.

Protease inhibitors have been associated with a number of metabolic complications: insulin resistance and symptomatic diabetes mellitus; hyperlipidemia (high levels of fat, including cholesterol, in the blood); and body fat accumulation syndromes, including increased fat in the neck and intra-abdominal

Editorial: The First Combination Treatment

Robert Marks, Editor

I don't hear much about HIV vaccines these days, but I do hear a lot about Bill and Melinda Gates. If there is a successful AIDS vaccine, or more importantly, if an effective preventive vaccine is successfully distributed after being developed, the Gates Foundation's will likely have played a major role in this triumph. A vaccine without distribution will be a failure.

In the world of HIV treatment—the real world of HIV care compared to the, alas, hypothetical world of the vaccine—the first combination treatment was not the famous drug "cocktail" that included a nucleoside reverse transcriptase inhibitor and a couple of protease inhibitors. It was the combination of any HIV treatment and the AIDS Drug Assistance Program.

ADAP was not a distribution plan and network, in and of itself, but it gave U.S. states the mechanism they needed to get drugs to people who needed them and who would not have otherwise afforded them. Since ADAP was designed to cover the full range of HIV-related medications, it did not need to wait until the advent of triple combination treatment to achieve huge extensions in the lives of people with HIV. (Of course, in many countries, universal health care provided this benefit without the necessity of special legislation that is funded at the discretion of Congress.)

In this issue of *FOCUS,* Stephen Follansbee and Michael Montgomery review the current state of both essential aspects of this true combination: medications and access to medications. They highlight the continuing successes and challenges and suggest the obstacles that both science and policy must overcome—in the United States and abroad—before HIV becomes a chronic, managable disease.

For reasons ranging from political grandstanding to authentic attempts to balance resources with need, some people have questioned the position of AIDS as exceptional among diseases. HIV care is now better funded than care for many other diseases. The problem with AIDS exceptionalism, however, is not that HIV has received "special treatment," but that policy makers have not followed the examples of scientists and clinicians.

While researchers working with other illnesses have taken advantage of HIV-related discoveries about virology, immunology, and antiviral treatment, policy makers have not adapted the ADAP model to extend the lives and improve the well-being of individuals with other diseases and our society. Instead of singling AIDS out, we should be applying its potent combination of care as broadly as possible.

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areas. The potential for fat accumulation is of great concern for many patients and affects both medication choice and adherence.

There are several new classes of anti-HIV medications. Enfuvirtide (Fuzeon) is a twice-daily injectable fusion inhibitor. It prevents the fusion of the virus particle to an uninfected cell's membrane, a step that is necessary for the HIV genes to enter the cell and start the process of viral replication. Enfuvirtide is potent, but viral resistance to it develops quickly if it is not combined with other potent antiviral medications. In addition, enfuvirtide injections are cumbersome and injection site reactions, mostly prolonged pain, swelling, and redness, are common. There is no second-generation fusion inhibitor for individuals who fail this medication.

There is a lot of interest in the integrase inhibitors, oral medications that target the integration of the newly synthesized viral DNA (made by the reverse transcriptase enzyme of the virus) into the host cell DNA. These medications appear to be potent and a few candidates are in various stages of development. None are FDA-approved, but some patients with advanced HIV infection are receiving one medication in this class through the pharmaceutical manufacturer's Early Access Program (EAP).

Lastly, there is research into drugs that interfere with HIV's process of attaching to the membrane of an uninfected cell, which precedes viral fusion. One intravenous compound that blocks the attachment of virus to the CD4+ molecule is undergoing evaluation. Oral compounds are under development that interfere with the second attachment step. Several of these CCR5 attachment inhibitors have been associated with liver toxicity. One is further in development and appears promising. Unfortunately, a person with advanced HIV disease is less likely to have a virus that utilizes the CCR5 attachment step. It has been more difficult to develop a medication that interferes with the alternative route of attachment (CXCR4) which is more commonly seen in very advanced patients.

One last treatment deserves comment. There are a number of individuals whose antiviral treatment regimens have led to excellent control of the virus, but who experience poor or even declining CD4+ cell count levels. Interleukin-2 (Proleukin), which is licensed in the United States for treating various malignancies, is known to

increase levels of circulating CD4+ cells. What is not known is whether interleukin-2-induced rises in CD4+ cell counts result in improved health or life-expectancy among people with HIV. Two large, ongoing studies are investigating the role of interleukin-2 in improving HIV-related outcomes.

Treatment Timing and Combination

In general, decisions regarding the first HIV antiviral medication regimen should consider potency, durability, convenience of administration, minimization of side effects, compatibility with other medications, and options for change should there be an adverse reaction. It is generally believed that the first treatment regimen has the best chance of being the one that will succeed. There has been little change recently in standards of care regarding the optimal time to initiate treatment. In the United States, 40 percent of individuals with HIV present with advanced disease, that is, CDC-defined AIDS manifesting as an opportunistic infection or malignancy. There is no controversy over the decision to initiate HIV antiviral treatment in these individuals.

HIV care is a more gratifying experience for clinicians who remember the early days of the epidemic: in the United States alone, treatment has saved 2.8 million years of life since 1989.

For asymptomatic individuals with higher CD4+ cell counts, guidelines, which have been recently updated, offer a broad range of medication choices depending on patient and provider circumstances and preferences.[3,4] Decision-making criteria include the individual's willingness to start treatment, his or her anticipated adherence to a treatment regimen, the individual's viral load, and the individual's CD4+ cell count and the rate of decline of that CD4+ cell count.

The guidelines also include advice about medication combinations. There are combinations, for example, zidovudine and stavudine, that should not be used because of antagonistic interaction. There are three-drug combinations—for example, Trizivir, which is a fixed combination of abacavir, lamivudine, and zidovudine—that should not be used because of lack of potency.

Among treatment-related issues, the most controversial are planned treatment interruptions. There have been a number of studies that have investigated the potential for treatment interruption to lower the risk for long term side-effects; reduce the cost of treatment; and auto-immunize the individual to HIV by allowing, at first, a rebound in viral growth and viremia that might stimulate the body's immune system to help fight the virus.[5]

The largest study to date, the SMART study, investigated two strategies. The "GO" strategy sought to maintain viral suppression, adjusting HIV antiviral drugs as necessary if the individual developed intolerable side effects or viral resistance. The "STOP" strategy sought to use the CD4+ cell count to dictate the use or interruption of HIV medications. In the STOP group, researchers discontinued medications when CD4+ cell count exceeded 350, which is generally felt to be a "safe" level. When CD4+ cell count fell below 250, researchers resumed medication until CD4+ cell counts again rose above 350. At an average of 13 months of follow-up, the study found an increasing difference in risk for serious events, including death, favoring the GO group who stayed on treatment. While ongoing analyses are investigating explanations for this difference, this and other studies suggest that scheduled or CD4+ count-driven treatment interruptions are generally not advisable.

Other Medical Issues

Among HIV-positive individuals who are doing well virologically (viral loads below the level of detection) and immunologic ally(increased and stabilized CD4+ cell counts above 200), it is difficult to determine whether medical complications are related to HIV disease, the medications used to treat HIV, or conditions that would have been seen in a non-HIV-infected population. Chief among these concerns are cognitive impairment, bone and skeleton problems, heart disease, and drug-drug interactions that can lead to a variety of serious conditions.

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A few patients who have apparently achieved good control of the virus, as manifested by a viral load below the level of detection, develop progressive cognitive impairment.[6] This may be related simply to the fact that the central nervous system acts as a viral "reservoir" that is not easily penetrated by antiviral medications. It is not clear, however, whether medications that do penetrate into the cerebral spinal fluid prevent cognitive impairment.[7] There are a number of studies looking into this phenomenon and investigating its possible mechanisms and treatment options.

There is an increased incidence of bone mineral abnormalities and other skeletal problems among people with HIV. A decrease in bone density (osteopenia and osteoporosis) is commonly described but not well understood.[8] It is associated with progression of untreated HIV disease and can be arrested with antiviral treatment. Hypophosphatemia (decreased blood levels of phosphate, one of the components of bone) is associated with tenofovir treatment and may increase the risk for osteomalacia (softening of the bones). Although it is unclear why, osteonecrosis of the head of the femur is increasingly common among people with HIV.[9] This leads to hip pain and may require surgical treatment, including total hip replacement.

Incidence of cardiovascular disease, including heart attacks, is higher in patients with HIV disease. While the exact mechanism of this problem is not clear, HIV providers are increasingly focusing on reducing all risk factors for heart disease. For example, they are encouraging people with HIV to cease smoking, tightly control high blood pressure, and better manage blood sugar, cholesterol, and triglyceride levels.

Drug-drug interactions are of increasing concern. The complexity of HIV antiviral treatment is magnified by the fact that many antiviral medications share two characteristics: they induce or inhibit cytochrome P450 enzymes at the same time as they rely on the enzymes of the cytochrome P450 system for their own metabolism and elimination. This interaction extends to a variety of natural health products.[10] For example, failure of indinavir (Crixivan) has been attributed in some individuals to the concurrent use of St. John's wort, which, as a potent inducer of the cytochrome CYP 3A4 enzyme system, led to lowered indinavir levels.

Several cases of rhabdomyolysis (the breakdown of skeletal muscle cells leading to the release of myoglobin) and renal failure (since myoglobin is toxic to the kidneys) have been reported in individuals using ritonavir-based HIV antiviral regimens, which led to a roughly 50-fold rise in some of the cholesterol lowering medications called "statins." Likewise, ritonavir-based regimens have been implicated in several cases of Cushing's syndrome, due to corticosteroid excess among patients also using a fluticasone-containing nasal spray for allergies or oral spray for asthma.

Conclusion

HIV treatment has become a more gratifying experience for clinicians who remember the early days of the epidemic. The challenge of treatment today is to balance the possibility of increased quality and duration of life with the risk of long-term side-effects, some of which are yet to be described. In addition, it has become more important than ever to understand all the medications a patient is taking, including a list of natural health products and over-the-counter preparations, to minimize the risk of increased toxicity or decreased effectiveness of HIV antiviral treatments.

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Clearinghouse: HIV Medical Care

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Loue S. Preventing HIV, eliminating disparities among Hispanics in the United

The Promise of ADAP

Michael Montgomery, MEd

While waiting for a flight in the Frankfurt airport in 1998, I became engaged in conversation with a reporter for a German newspaper. To his question regarding what I did in "the States," I described, with not a little pride, California's AIDS Drug Assistance Program (ADAP)—for which, at the time, I had responsibility. After a lengthy discussion of ADAP, the reporter shrugged and said, "Of course, in Germany we do not have that problem."

Despite the U.S. Congress's indifference to it, ADAP has been a monumental success in ensuring that low-income people with HIV have access to HIV-related prescription drugs.

In the United States, of course, we do have that problem. If the Ryan White CARE Act is a band-aid applied to compensate for the absence of universally available health care, ADAP is "the safety net beneath the safety net," providing coverage for a host of medications for people with HIV who could not otherwise afford them. In 2005, there were over 134,000 enrollees in ADAPs nationally.[1]

Funding the HIV Treatment Revolution

The advent of zidovudine (AZT; ZDV) nevertheless ended a period of profound treatment hopelessness, during which HIV's reputation as a "death sentence" was repeatedly, mercilessly reinforced. Soon after the U.S. Food and Drug Administration approved AZT, HIV-positive people who were sufficiently poor and disabled to qualify for Medicaid had access to the drug for free. For people not eligible for Medicaid, the drug was prohibitively expensive.

In response to the prodding of AIDS activists, legislatures in several states provided funding to assure access to AZT, even for those who would not meet traditional criteria for public disability programs. In 1987, Congress appropriated funds to support states in their efforts to pay for AZT, creating what would later become ADAP. By 1990, ADAP was incorporated by Congress as one of five mandated activities under Title II of the Ryan White CARE Act. While states had flexibility in determining ADAP eligibility and the treatments ADAP would cover, the federal support of the program assured nationally at least rudimentary access to AIDS treatment.

For several years, individual state ADAPs, which remained dependent upon the willingness of their local legislatures to supplement federal funding, grew at different rates. Most, but not all, states were able to add new HIV antiviral treatments as they were approved by the FDA. For the most part, ADAPs developed quietly and expanded slowly.

With the 1995 FDA approval of the first protease inhibitor, followed in 1996 by two more and the demonstrated efficacy of combination therapies, the demand on ADAP exploded. Making these medications available without further restricting financial eligibility required significant budget increases. In fiscal year 1996, Congress created dedicated funding for state ADAPs. In 1997, the combined budgets for all ADAPs nationally totaled $385 million, more than double the 1996 budget and triple the 1995 budget.[2] In 1995, California's

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See also references cited in articles in this issue.

ADAP had a $17 million budget. By 2006, it had grown to more than $300 million.

Each state ADAP determines its own financial eligibility criteria, resulting in an income range that extends from no more than 125 percent to no more than 700 percent of the federal poverty level. Furthermore, each state determines the drugs that it will reimburse under ADAP, varying from HIV antiviral medications only to open formularies that cover all prescribed medications.

The Waning of Federal Support

As federal commitment to full funding of ADAP waned in the early 2000s, states struggled to meet a steadily growing demand. To ensure the stability of their programs for enrolled clients, many states resorted to waiting lists and other cost-saving mechanisms. Even in states that managed to enroll new clients without restriction, client concerns about the threat of cuts revealed the essence of ADAP: not only does it ensure access to life-sustaining medications, it also offers peace of mind. ADAP, a person with HIV trusts, will be there even if he or she loses a job and health insurance. Conversely, ADAP clients are increasingly willing to re-enter the work force, even without full prescription coverage at their new jobs. ADAP further provides an ethical underpinning and counteracts historical antecedents by ensuring treatment access to people in populations that have been distrustful of public health systems.

In the absence of adequate increases in federal funding, program administrators and advocates worked with state legislative bodies to find funds in already over-committed budgets. Through the ADAP Crisis Task Force initiative, undertaken by the National Alliance of State and Territorial AIDS Directors (NASTAD), the states collectively began to negotiate for manufacture rebates, discounts, and price freezes on drugs they purchased. It is estimated that this public/private partnership has saved ADAPs more than $300 million over the last three years. States that have been unable to adequately supplement federal ADAP funds have taken drastic steps to maintain some HIV medical access. In addition to reducing financial eligibility and limiting drugs on the formulary, several states require financial contributions from participants, a further disincentive to participation.

ADAP has been a monumental success in ensuring that low-income people with HIV have access to HIV-related prescription drugs.[2] This has been accomplished in spite of Congress's indifference to health care access, as exhibited by the inadequate federal ADAP funding. In response, state AIDS program administrators, state legislatures, and even pharmaceutical manufacturers have had to struggle to maintain as close to universal access to HIV medications as is possible.

Access to HIV care should not be an accident of geographic residence. A physician treating a person with HIV in the rural South should have in her or his arsenal the same battery of treatments as a physician in San Diego. As suggested in a report by the National Academy of Science's Institute of Medicine, assuring universal access requires the creation of a national ADAP—an entitlement program like Medicaid that would ensure the availability of a minimum formulary of medications to all uninsured, HIV-positive people. Such entitlement programs, whose yearly funding is assured and based solely on need, are less attractive to legislators, no matter how meritorious, because they eliminate budgetary discretion.

Conclusion

Recently, the Centers for Disease Control and Prevention (CDC) issued guidance on HIV testing that calls for routine HIV testing in medical and other settings. This initiative poses an ethical dilemma: once infections are identified, is there a commitment to provide treatment? How can we encourage people to be tested if we do not ensure access to care?

For all their shortcomings, state-administered ADAPs have been profoundly successful in providing access, even if unequal, to life-extending medications. Care for other conditions—Alzheimer's disease, for example—has not similarly benefited from the organized support of activists and, as a result, people with these illnesses do not have access to comparable programs. This is a shame, since ADAP has not only directly delivered medications to tens of thousands of HIV-positive people, it has also provided hope to thousands more who know that should life make an unexpected turn, they will have access to the medications upon which their lives depend.

Comments and Submissions

We invite readers to send letters responding to articles published in *FOCUS* or dealing with current AIDS research and counseling issues. We also encourage readers to submit article proposals. Send correspondence to rob.marks@ucsf.edu or to Editor, *FOCUS*, UCSF AIDS Health Project, Box 0884, San Francisco, CA 94143-0884.

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Michael Montgomery, MEd, recently retired as the Chief of the California Office of AIDS. Before that, he was Chief of OA's ADAP Section in 1996-1997, during which California's ADAP was restructured, and Chief of OA's HIV Care Branch in 1998-1999. In 2005-2006, he served as Chair of the National Alliance of State and Territorial AIDS Directors and remains involved with the group.

Recent Reports

Rationing AIDS Drug Resources

Linas BP, Zheng H, Losina E, et al. Optimizing resource allocation in United States drug assistance programs. *Clinical Infectious Diseases*. 2006; 43(10): 1357–1364. (Massachusetts General Hospital; and Harvard University.)

In his article, Michael Montgomery discusses the formidable financial challenges that ADAPs across the nation face, challenges that have caused some states to implement waiting lists. In the study below, researchers investigated which of two approaches would best meet the needs of HIV-positive clients in Massachusetts: a first-come, first-served model or a model that prioritized those with the most compromised immune systems. The excerpt below is adapted from the cited article and its abstract:

A mathematical model showed that with limited resources, AIDS Drug Assistance Programs would serve more diverse populations and patients with significantly more advanced HIV disease if they used CD4+ cell count-based enrollment criteria rather than a first-come, first-served approach. Using a cohort of Massachusetts ADAP clients from fiscal year 2003, the model showed that while the first-come, first-served approach would serve more clients, the CD4+ cell count approach would serve clients who were at greatest risk of dying from HIV-related causes.

ADAPs would serve more diverse populations and patients with significantly more advanced HIV disease if they used CD4+ cell count-based enrollment criteria rather than a first-come, first-served approach.

In fiscal year 2003, the Massachusetts ADAP served 3,560 clients at a direct cost of $10.3 million. With the hypothetical use of CD4+ cell count-based eligibility (a current or lowest CD4+ cell count less than or equal to 350), Massachusetts ADAPs would have served 2,253 clients (37 percent fewer than were actually served in fiscal year 2003) and appreciated savings of $2.7 million. Given the same hypothetical budget constraints and using first-come, first-served eligibility, Massachusetts ADAPs would have served 2,406 clients (32 percent fewer than were actually served in fiscal year 2003).

Further analysis divided the patients who would have been treated by the first-come, first-served approach. The median CD4+ cell count of those who would have come first and been served was 659. This number was much higher than the median CD4+ cell count of 257 for those who would have come later and not been served. This suggests that the first-come, first-served approach treats healthier patients at the expense of less healthy ones. In addition, a CD4+ cell count-based scheme would have served a greater proportion of non-White individuals (65 percent versus 55 percent for the first-come, first-served approach), non-English speakers (24 percent versus 19 percent for the first-come, first-served approach), and unemployed people (69 percent versus 61 percent for the first-come, first-served approach).

Disparities in HIV Care

Hirschorn LR, McInnes K, Landon BE, et al. Gender differences in quality of HIV care in Ryan White CARE Act-funded clinics. *Women's Health Issues*. 2006; 16(3): 104–112. (Harvard University; Tufts University; and the U.S. Health Resources and Services Administration.)

Heslin KC, Andersen RM, Ettner SL, et al. Racial and ethnic disparities in access to physicians with HIV-related expertise. *Journal of General Internal Medicine*. 2005; 20(3): 283–289. (Charles R. Drew University; and the University of California, Los Angeles.)

Despite incredible progress outlined in both articles of this issue, there remain disparities in the delivery of HIV antiviral treatment and other aspects of HIV-related care. The two studies described below, one from Harvard Medical School and the other from Charles R. Drew University and UCLA, examine how aspects of HIV service delivery vary by the gender and race or ethnicity of the clients being served.

In the Harvard study, a national sample of Ryan White CARE Act-funded clinics found that women were less likely than men to receive services and treatment central to HIV-related care despite the fact that they were seen more regularly than men.

Researchers reviewed the records of 9,015 patients (2,860 women and 6,155 men) who received care at 69 primary care clinics. Outcome measures included: HIV antiviral therapy use, HIV viral suppression, *Pneumocystis jiroveci* pneumonia (formerly known as *Pneumocystis carinii* pneumonia [PCP]) prophylaxis, and other disease prevention efforts. Women were significantly less likely than men to receive HIV antiviral therapy, receive PCP prophylaxis, or be

screened for hepatitis C virus, although women were seen more regularly than men.

Sites were divided into three categories: those that served high (40 percent or greater) percentages of women, those that served medium (25 percent to 39 percent) percentages of women, and those serving low (0 percent to 24 percent) percentages of women. Sites serving high percentages of women delivered similar or better care for both men and women than other sites. However, although sites serving a higher percent of women had more support services—such as case management and on-site obstetrician-gynecologists—and provided Pap smears at higher rates, women at such sites remained less likely than men to receive important HIV care, including HIV antiviral therapy and PCP prophylaxis, suggesting that the type of site does not explain disparities in care.

According to the Charles R. Drew University study, two key indicators of physician competence to treat HIV suggest potential disparities in HIV care across race and ethnicity. Professional medical associations recommend that physicians who treat HIV patients have a measurable form of disease-specific expertise, such as infectious disease certification or treatment of a high volume of HIV-positive patients.

Investigators linked data from a prospective cohort study of 2,207 people with HIV receiving care in the United States with a cross-sectional survey of the 404 physicians caring for these patients. Multivariate analysis estimated the association of patient race and ethnicity with the experience and training of their physicians and controlled for health status, socioeconomic status, other demographic characteristics, and geographic variation in provider supply. White and Latino patients were equally likely to have seen an infectious disease specialist; Black patients were 40 percent less likely than Whites or Latinos to have seen a specialist; and Alaskan Native, American Indian, Asian, Pacific Islander, or mixed racial background patients were 56 percent less likely than Whites or Latinos to have seen a specialist. Latino patients had physicians whose HIV patient volume was, on average, 24 percent higher than the physicians of White patients.

Epidemiology of AIDS-Related Cancers

Bower M, Palmieri C, Dhillon T. AIDS-related malignancies: Changing epidemiology and the impact of highly active antiretroviral therapy. *Current Opinion in Infectious Diseases.* 2006; 19(1): 14–19. (Chelsea and Westminster Hospital, London.)

In his overview article, Stephen Follansbee provides an update on HIV-related treatments. As the authors of the study described below note, HIV antiviral treatments have been particularly successful in the area of AIDS-related cancers. The following excerpt was adapted from the cited article and its abstract:

Three cancers in people with HIV denote an AIDS diagnosis: Kaposi's sarcoma, high-grade B-cell non-Hodgkin's lymphoma, and invasive cervical cancer. The incidence of both Kaposi's sarcoma and non-Hodgkin's lymphoma has declined with the widespread use of improved HIV antiviral treatment, and the outcomes for both diseases have improved. Moreover, HIV antiviral therapy alone produces a response in a majority of HIV-antiviral-naive patients with Kaposi's sarcoma.

In contrast, HIV antiviral treatment has had little impact on the incidence of human papilloma virus-associated tumors (cervical and anal cancer) in people with HIV. Many other cancers occur more frequently in people with HIV, but these are not AIDS-defining illnesses. As people with HIV live longer, an increased incidence of some other non AIDS-defining cancers is becoming apparent.

Next Issue

In recent years, it has become much easier to identify HIV infection even in individuals who have not yet produced antibodies. This development, particularly the use of RNA testing, has bolstered the theory that the period prior to antibody development—often called "acute" or "primary" HIV infection—is a crucial time in the course of HIV disease. In the February issue of *FOCUS,* **Frederick Hecht, MD**, Associate Professor of Medicine, and **Christopher Pilcher, MD**, Assistant Professor of Medicine, both of the University of California San Francisco, provide an overview of the science of acute infection. They explain why the time just after infection is so critical in terms of both care and prevention.

Also in the February issue, **Philippe Chiliade, MD**, Technical Advisor with Family Health International and former Medical Director of Whitman-Walker Clinic, discusses the experience of working with newly diagnosed, acutely infected individuals around treatment planning and transmission prevention.

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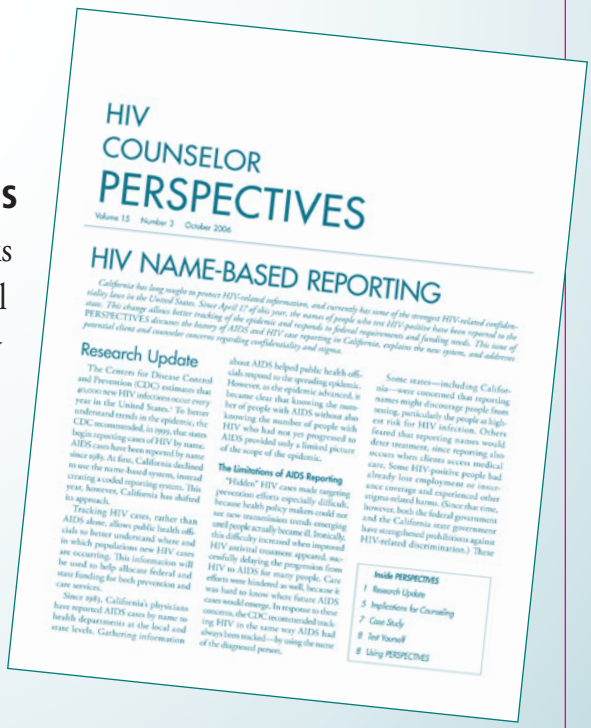
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