

Commentaries

The Serostatus Approach to Fighting the HIV Epidemic: Prevention Strategies for Infected Individuals

ABSTRACT

In the United States, HIV prevention programs have historically tailored activities for specific groups primarily on the basis of behavioral risk factors and demographic characteristics. Through the Serostatus Approach to Fighting the Epidemic (SAFE), the Centers for Disease Control and Prevention is now expanding prevention programs, especially for individuals with HIV, to reduce the risk of transmission as a supplement to current programs that primarily focus on reducing the risk of acquisition of the virus.

For individuals with HIV, SAFE comprises action steps that focus on diagnosing all HIV-infected persons, linking them to appropriate high-quality care and prevention services, helping them adhere to treatment regimens, and supporting them in adopting and sustaining HIV risk reduction behavior. SAFE couples a traditional infectious disease control focus on the infected person with behavioral interventions that have been standard for HIV prevention programs. (*Am J Public Health*. 2001;91:1019–1024)

Robert S. Janssen, MD, David R. Holtgrave, PhD, Ronald O. Valdiserri, MD, MPH, Melissa Shepherd, ABJ, Helene D. Gayle, MD, MPH, and Kevin M. De Cock, MD, FRCP, DTM&H

The AIDS epidemic, although first recognized only 20 years ago, has had a profound impact in communities throughout the United States. By mid-2000, more than 750 000 Americans with AIDS had been reported and more than 430 000 Americans had died.¹ After peaking in the mid-1980s, HIV incidence in the United States stabilized in the late 1980s and early 1990s.² The Centers for Disease Control and Prevention (CDC) estimates that the number of new infections has remained stable at approximately 40 000 per year since 1992.³ An estimated 800 000 to 900 000 Americans were infected with HIV at the end of 1998; of these, as many as 300 000 were unaware of their infection status.³

Additional approaches are required to break the grip of HIV in the United States. With as many as 5 million people at behavioral risk for HIV through unsafe sex and drug use,⁴ HIV prevention programs have historically been based on behavioral risk factors and demographic characteristics such as race/ethnicity, sex, and age. Activities have been tailored to meet the needs of specific groups without regard to serostatus. Although secondary prevention efforts to reduce associated morbidity and mortality are naturally focused on individuals with HIV, specific primary prevention efforts to reduce transmission from HIV-infected individuals to the uninfected have been limited. The CDC is currently expanding prevention programs to include new and enhanced activities based on HIV serostatus, particularly targeting individuals with HIV, as a way to break the current steady state of HIV transmission.

Prevention Strategies for Individuals With HIV

The CDC has launched a new strategy for HIV prevention called the Serostatus Ap-

proach to Fighting the Epidemic (SAFE) (Figure 1). SAFE is aimed at those who are infected with HIV—including those currently unaware of their serostatus—as well as those who have been tested and found to be uninfected but are at continued high behavioral risk (Table 1). This commentary presents the CDC's strategies for individuals with HIV, which consist of 5 action steps that focus on diagnosing HIV infection in all infected individuals, linking them to appropriate high-quality care and prevention services, and supporting them in adhering to treatment regimens and in adopting and sustaining HIV risk reduction behavior. To make the best use of limited resources, such efforts must use accurate surveillance data, including HIV incidence and prevalence; HIV, AIDS, and sexually transmitted disease (STD) case data; and behavioral data to focus care and prevention efforts on the communities and localities where HIV transmission is most intense.

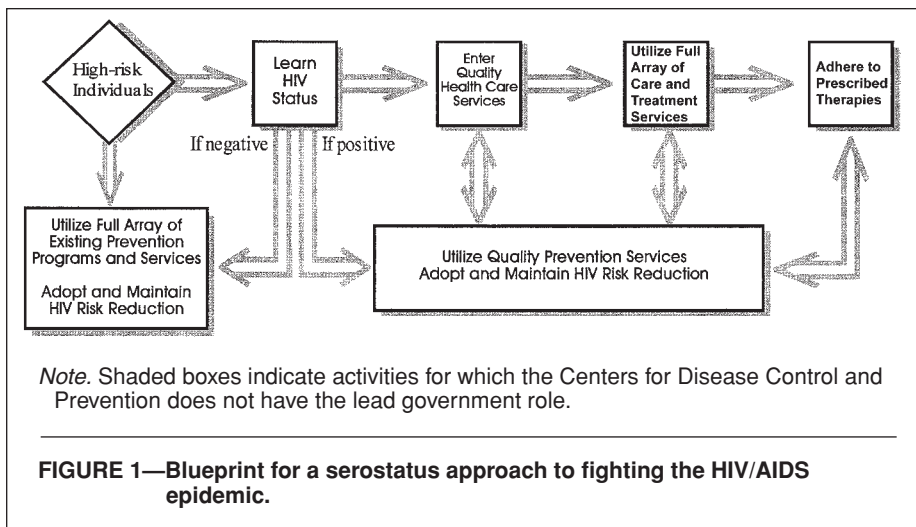
Essential Components of SAFE

The 5 SAFE steps are as follows: (1) Increase the number of HIV-infected persons who know their serostatus. (2) Increase the use of health care and preventive services. (3) Increase high-quality care and treatment. (4) Increase adherence to therapy by individuals with HIV. (5) Increase the number of

The authors are with the National Center for HIV, STD, and TB Prevention, Centers for Disease Control and Prevention, Atlanta, Ga.

Requests for reprints should be sent to Robert S. Janssen, MD, Division of HIV/AIDS Prevention, Centers for Disease Control and Prevention, 1600 Clifton Rd (Mail Stop D-21), Atlanta, GA 30333 (e-mail: rxj1@cdc.gov).

This commentary was accepted February 2, 2001.



individuals with HIV who adopt and sustain HIV–STD risk reduction behavior.

1. Increase the number of HIV-infected persons who know their serostatus

There are both medical and public health benefits to increasing knowledge of HIV status as early after infection as possible.

Medical benefits of HIV diagnosis. Individuals who have early knowledge of their HIV infection can benefit from prophylaxis for opportunistic infections; treatment of STDs, substance abuse, and mental health conditions; access to social services; and, when appropriate, use of combination antiretroviral therapy (ART).⁵ Prophylaxis of opportunistic infections has been important in reducing HIV-

related morbidity⁶; treatment of STDs can reduce the risk of HIV transmission; treatment of substance abuse and mental health problems can reduce HIV risk behavior.⁷ It is ART, though, that has had the most dramatic effect on morbidity and mortality. HIV-infected individuals in care are now living longer than before the advent of highly active antiretroviral agents,⁸ and one study suggests that some HIV-infected individuals receiving ART may have a normal life expectancy.⁹ AIDS is no longer 1 of the 15 leading causes of death in the United States.¹⁰ Quality of life for individuals with HIV has improved substantially, although the drugs' side effects can be troublesome and even life threatening. Recent information about side effects has resulted in a recommendation to delay the initiation of ART.⁵

Public health benefits of HIV diagnosis. Although 70% of individuals with HIV remain sexually active after they learn they are infected,^{11,12} it is clear that when people know they are HIV infected, they are significantly more likely to take steps to protect their partners than when they were unaware of their infection.^{12–15} It is probable, then, that a high proportion of HIV infections are being transmitted by people unaware of their HIV status. The only data that address this issue directly are from the Options Project in San Francisco, where 15 of 39 newly infected people were infected by individuals who did not know their serostatus (F. Hecht, written communication, February 1, 2001).

Another important public health reason for considering people with HIV as a priority population for HIV prevention programs is that ART may reduce infectiousness. If low viral load is associated with a lower risk of transmission and if antiretroviral drugs reduce viral load, then antiretroviral drugs may reduce transmission. High plasma viral load is an important risk factor for all modes of HIV transmission.^{16–22} In 2 studies in Africa, the risk of heterosexual transmission increased approximately 2.5-fold for every 10-fold increase in plasma viral load.^{23,24} Several studies have demonstrated a correlation between plasma HIV RNA and concentration of HIV RNA in semen and cervicovaginal secretions.^{25–28} ART reduces both plasma and genital fluid viral load; persons with the greatest decline in plasma HIV RNA concentration are most likely to show undetectable genital fluid HIV RNA.^{26–28} Although cell-associated virus is frequently present when seminal HIV RNA is

TABLE 1—Serostatus-Specific HIV Prevention Interventions

Population	HIV Prevention Interventions
Unaware of serostatus; behavioral risk of infection	Provide current, essential HIV-related information Encourage voluntary HIV counseling and testing among those at increased risk, including anonymous testing Reduce stigma of HIV disease and services
Recently tested HIV negative; no apparent behavioral risk of infection	Educate to provide HIV prevention messages to family, friends, partners
Recently tested HIV negative; behavioral risk of infection	Offer intensive individual or small-group counseling Develop community-level interventions Establish linkages to STD, substance abuse, mental health, hepatitis, and social services as needed Provide prevention case management for those at highest risk Develop structural interventions (e.g., sterile syringe access)
Tested HIV positive	Provide intensive prevention services Offer partner counseling and referral services Establish linkages to STD, substance abuse, mental health, hepatitis, and social services as needed Provide prevention case management Develop structural interventions (e.g., decrease discrimination)

Note. STD=sexually transmitted disease.

undetectable,²⁹ animal model data suggest that transmission by cell-associated virus may be less efficient than transmission by cell-free virus.^{30,31} The reduction of HIV transmission through the use of antiretroviral treatment is most clearly seen in the reduction of mother-to-child transmission.³²⁻³⁵ All of these data suggest that ART probably reduces the infectiousness of HIV during sexual and drug-using exposures, although the evidence is still indirect. The spread of a sexually transmitted agent in a population is related to the rate of partner change, the agent's transmissibility, and the duration of infectiousness.³⁶ By lowering viral load, ART can potentially reduce the duration as well as the degree of infectiousness and therefore reduce HIV transmission at the population level, provided that partner change, condom use, and sexual practices remain unchanged.

Because of these individual and public health benefits of HIV diagnoses, the CDC is giving additional emphasis to encouraging those at high risk for infection to seek testing and is expanding access to voluntary testing as a part of SAFE (Table 2). The CDC is piloting a media campaign called "Know Now" to encourage testing through raising individual awareness of the benefits of knowing HIV status among risk populations in high-prevalence, geographically circumscribed areas. This campaign is using marketing strategies and multiple forms of media to address motivation for and psychologic barriers to testing.³⁷ Such media campaigns are also targeting stigma associated with testing and a diagnosis of HIV infection.

An important method for making HIV testing more accessible is use of simple, rapid tests. These can be performed without labora-

tory support and offer the possibility of providing preliminary results within minutes after blood or oral secretions are collected. No such tests are currently available in the United States, although they are available in most other parts of the world. Studies have shown that when used in combination, rapid tests can provide results equal in predictive value to Western blot-based testing strategies.³⁸ When available in the United States, they will provide opportunities to dramatically increase the availability of HIV testing in a variety of settings and thus increase the number of people who know their HIV status.³⁹ Simple, rapid tests can be used for outreach by community-based organizations at social events such as community health fairs or gay pride festivals, or at bars, clubs, or street corners where large numbers of people at risk for HIV infection may congregate. In addition, rapid tests can be used for routine voluntary testing in emergency rooms or other medical settings where HIV prevalence may be elevated. Routinely offering HIV tests to all patients aged 15 to 54 years in high-HIV-prevalence acute care hospital settings,⁴⁰ and in other high-prevalence settings such as drug detoxification units and STD clinics, should increase the number of people who are aware of their serostatus. Through revised guidelines for HIV counseling and testing, the CDC is encouraging the routine offering of voluntary HIV testing in medical settings where large numbers of HIV-infected people may seek care for non-HIV-related illnesses.⁴¹ Expansion of voluntary HIV testing is also needed in nonmedical facilities such as correctional institutions where HIV-infected injection drug users are likely to be found.

2. Increase the use of health care and preventive services

Although three quarters of individuals with HIV seek medical care within 6 months of learning of their HIV infection,⁴² some individuals, for a variety of personal, social, economic, or other reasons, delay seeking services for up to 5 years.^{13,43} Data are limited on the use of prevention services by individuals with HIV. Better information is also needed on the performance of current referral systems. While the CDC will work with its partners to improve its programs that link people from publicly funded HIV testing settings to care and prevention services,⁴⁴ providers in other settings in which testing occurs will need to develop feasible links to care and prevention service providers. State and local health departments and community-based organizations can create better links between prevention and care programs, increasing access to both. Case management related to clinical care and social services or

TABLE 2—Examples of Essential Components of Centers for Disease Control and Prevention Programs Focusing on Individuals With HIV

1. Increase number of HIV-infected persons who know their serostatus.
 - Create campaigns to emphasize benefits of early diagnosis of HIV.
 - Educate to reduce fear of knowledge of serostatus.
 - Create campaigns to diminish discrimination against HIV-infected persons.
 - Create campaigns to reduce stigma associated with HIV infection.
 - Train providers of high-risk persons on benefits and strategies of early HIV diagnosis.
 - Create campaigns to encourage voluntary HIV testing.
 - Continue to support anonymous testing.
 - Make testing venues more responsive to client needs.
 - Facilitate use of rapid tests.
 - Increase voluntary testing in health care facilities.
 - Increase voluntary testing of pregnant women.
 - Increase voluntary testing in prisons and jails.
 - Increase voluntary testing among sex and needle-sharing partners of HIV-infected persons.
 - Increase availability of home collection kits and testing through outreach programs.
2. Increase use of services.
 - Increase links between prevention and care programs.
 - Improve access to HIV/AIDS care through community-based organizations.
 - Upon discharge, link prisoners to care and prevention services.
 - Increase proportion of pregnant women receiving antenatal care.
3. Increase quality care and treatment.
 - Increase proportion of HIV-infected pregnant women receiving ART.
 - Educate health care workers and HIV-infected persons about HIV/AIDS treatment.
 - Monitor and evaluate quality of HIV/AIDS care.
 - Institute surveillance for effectiveness and side effects of ART.
4. Increase adherence to therapy by individuals with HIV.
 - Evaluate and implement strategies for increasing adherence, including directly observed therapy.
 - Monitor adherence to therapy.
 - Monitor antiretroviral drug resistance.
5. Increase number of individuals with HIV who adopt and sustain HIV-STD risk reduction behavior.
 - Increase availability of prevention services for individuals with HIV (e.g., counseling, prevention case management, peer opinion leader, small-group interventions).
 - Develop, implement, and evaluate specific risk reduction strategies for individuals with HIV.
 - Monitor behaviors and outcomes in individuals with HIV.
 - Teach health care providers to perform HIV and STD risk assessment for their HIV-positive patients.
 - Increase STD screening, diagnosis, and treatment for individuals with HIV.
 - Increase delivery of prevention messages to HIV-positive patients by health care workers.
 - Provide adequate and appropriate substance abuse treatment.

Note. ART=antiretroviral therapy; STD=sexually transmitted disease.

prevention case management (case management with risk reduction counseling)⁴⁵ can also increase use of both care and prevention services.

3. Increase high-quality care and treatment

In 1996, one third to two thirds of individuals with HIV were not receiving appropriate HIV/AIDS care, either because they were unaware that they were infected with HIV or because care services had not been accessed or delivered.⁴⁶ While the Health Resources Services Administration (HRSA) and the Health Care Financing Administration (HCFA) are the leading federal agencies in providing support for HIV care, the CDC will continue to be a part of Public Health Service efforts to continually update guidelines for optimal ART⁵ and for prophylaxis of opportunistic infection.⁶ In addition to HIV and AIDS surveillance, the CDC is developing population-based studies to monitor the quality, use, and impact of care.

4. Increase adherence to therapy by individuals with HIV

Toxicity, poor adherence to HIV treatment regimens, and pharmacologic problems such as poor drug absorption can cause failure to achieve viral suppression and development of drug resistance. Patients' failure to adhere to the complicated dosage requirements of ART may be the most important reason for these negative outcomes of treatment.^{47,48} In addition, drug-resistant viruses can be transmitted to uninfected individuals.^{49,50} Improving therapeutic adherence can reduce the frequency of drug resistance, but it will not eliminate it.

The CDC, in collaboration with other federal agencies, is conducting research on more effective interventions to increase adherence, including evaluating the feasibility of directly observed therapy. Directly observed therapy for tuberculosis has been feasible with simpler regimens of fixed duration,⁵¹ but because adherence to ART regimens is so important, trials of directly observed therapy for HIV are needed even if treatment regimens remain complex and of long-term—possibly lifetime—duration.⁵

5. Increase the number of individuals with HIV who adopt and sustain HIV-STD risk reduction behavior

Many individuals with HIV feel healthier when undergoing ART than they did before such treatments became available. In addition, the impression that HIV is a treatable chronic disease, and that ART reduces infectiousness, may be leading to increases in risk behavior among HIV-infected individuals and those at

highest risk for HIV infection.⁵² In a number of cities in the United States, increasing rates of gonorrhea among men who have sex with men suggest that unsafe sexual behavior may be reemerging in this community.⁵³ While most individuals who learn that they are infected reduce their risk behavior, a considerable fraction continue to have unprotected sex.⁵⁴ In a recent outbreak of primary and secondary syphilis in King County, Washington, among men who have sex with men, nearly three quarters of whom were HIV infected.⁵⁵

In 1997, a National Institutes of Health consensus conference on HIV prevention interventions called for increased research to identify interventions to support infected individuals in adopting and sustaining risk reduction behavior,⁵⁶ and several studies have been subsequently initiated by the National Institute of Mental Health and by the CDC. The CDC will strongly encourage health departments, HIV prevention community planning groups, and community-based organizations to include people with HIV among priority populations for prevention programs. In addition, simple risk assessment tools are needed for physicians to assess the risk behavior of their HIV-infected patients and to provide referral for those needing prevention interventions. Preliminary information suggests that even when they are enrolled in primary care, sexually active individuals with HIV are not receiving adequate HIV prevention counseling or adequate diagnosis and treatment of other STDs.⁵⁷ The CDC is collaborating with the Infectious Diseases Society of America and federal agencies to develop recommendations for prevention activities in care settings. With the vast majority of prescriptions for ART being written by a few thousand physicians across the country, it is feasible to offer training to these caregivers to recognize ongoing risk behavior and refer people appropriately for prevention services. Because many individuals with HIV are already in publicly financed systems of care,⁴⁶ the CDC will work closely with HCFA and HRSA to increase prevention services in those settings. However, new resources are needed to increase the availability to all individuals with HIV infection of current prevention services, such as risk reduction counseling, peer group support, peer-based prevention case management, STD treatment, substance abuse treatment, and mental health services.

Some mathematical models suggest that much HIV transmission occurs from individuals who are recently infected and whose plasma viral loads are therefore high.⁵⁸ If preventing transmission from such individuals is essential for controlling the epidemic, partner counseling and referral services are crucial, because, in combina-

tion with serologic methods that detect recently acquired HIV infection, they enable the identification of persons with early HIV infection.⁵⁹ Using such methods for rapid assessment of sexual or injection-drug-use networks can lead to the interruption of chains of active transmission by helping network members adopt and sustain risk reduction behavior.

Potential Impact and Resource Needs

The CDC has established the goal of reducing new HIV infections in the United States by 50% in 4 years.⁴⁴ We estimate that to reach that goal, it is critical to increase by 30 000 each year the number of infected people who become aware of their serostatus and are linked to appropriate care and prevention services. In addition, full and appropriate prevention services must be provided for all individuals with HIV infection. These activities will require an additional public investment of \$300 million per year. These additional resources would be directed at (a) a highly targeted HIV counseling and testing effort to identify undiagnosed HIV-seropositive persons, provide expanded voluntary testing, and develop and implement effective referrals to prevention and care services; (b) comprehensive HIV prevention services for each seropositive person whose ongoing behavior could lead to HIV transmission; and (c) HIV prevention services such as counseling for high-risk HIV-seronegative clients identified through the counseling and testing effort, particularly current partners of HIV-infected individuals. Increasing the number of individuals with HIV who know their status will increase the number in care and will require increases in public financing for care through Medicaid and the Ryan White CARE Act.

Such an investment will save not only lives but money. Given that in 1997 each averted HIV infection saved society approximately \$154 000 in discounted lifetime treatment costs of HIV disease,⁶⁰ an additional \$300 million would have to avert only about 2000 HIV infections to produce these cost savings. Preliminary modeling analyses, based on literature on the effectiveness of behavioral intervention, suggest that SAFE programs might actually avert approximately 20% of HIV infections (8000 cases) per year (CDC, unpublished data, 2000). Thus, maintaining current prevention programs for high-risk uninfected persons and fully implementing the CDC's SAFE initiative could reduce HIV incidence by nearly 60% (approximately 23 000 cases) and reduce the number of HIV-infected people with unknown serostatus by 80% in 4 years.

Partnerships

An important aspect of SAFE activities for those with HIV is developing new partnerships with organizations that historically have not been involved in HIV prevention and expanding traditional public health partners. The CDC has mobilized a public-private partnership, "X-AIDS ACT NOW! National Partnership Council," to fight the epidemic. More than 50 organizations, including medical care organizations, the pharmaceutical industry, private industry, and the media, as well as national and community-based HIV prevention organizations, make up the core of the partnership. These organizations are creating alliances that will motivate, coordinate, and direct private sector resources to address the specific needs of SAFE.

Conclusion

Historically, HIV prevention programs have focused primarily on developing risk reduction interventions for those at high risk for becoming infected with HIV. In 1999, a review of 55 state and city applications to the CDC for funds for HIV prevention programs demonstrated that only 18 (32.7%) listed HIV-infected individuals as a priority population for HIV prevention programs. Although there are millions of people in the United States at "behavioral risk" for HIV infection, transmission can occur only from people who are infected with the virus. As the number of individuals with HIV continues to increase because of ART, so does the urgency for lifelong prevention strategies customized for them. The 1996 International AIDS conference in Vancouver, British Columbia, marked the beginning of a new treatment era in the AIDS epidemic, making knowledge of serostatus and linkage to prevention and treatment services more important than ever before.

At a time of increasing risk behavior in some communities with high HIV prevalence and among an increasing number of individuals with HIV infection, SAFE strategies for HIV-infected persons represent a logical evolution of prevention in an era of improved treatment. Such an approach couples a traditional infectious disease control focus on the infected person with behavioral interventions that have become standard elements in HIV prevention programs. In this new era, for individual as well as public health reasons, every person infected with HIV should be voluntarily diagnosed, evaluated medically, treated according to state-of-the-art guidelines, and provided with appropriate prevention services.

In combination with current programs focusing on HIV-negative individuals, SAFE

offers an unprecedented opportunity for significantly reducing HIV transmission and HIV-associated morbidity and mortality. □

Contributors

R. S. Janssen, D. R. Hotgrave, and K. M. De Cock led the writing of this commentary. R. O. Valdiserri, M. Shepherd, and H. D. Gayle contributed ideas and helped with writing and reviewing the manuscript.

References

- Centers for Disease Control and Prevention. *HIV/AIDS Surveillance Report*. 2000;12(No.1):1-42.
- Rosenberg PS, Biggar RJ. Trends in HIV incidence among young adults in the United States. *JAMA*. 1998;279:1894-1899.
- Centers for Disease Control and Prevention. Guidelines for national human immunodeficiency virus case surveillance, including monitoring for human immunodeficiency virus infection and acquired immunodeficiency syndrome. *MMWR Morb Mortal Wkly Rep*. 1999;48(RR-13):1-29.
- Anderson JE, Wilson RW, Barker P, Doll L, Jones TS, Holtgrave D. Prevalence of sexual and drug-related HIV risk behaviors in the US adult population: results of the 1996 National Household Survey on Drug Abuse. *J Acquir Immune Defic Syndr*. 1999;21:148-156.
- Department of Health and Human Services. Guidelines for the use of antiretroviral agents in HIV-infected adults and adolescents. The living document: January 28, 2000. Available at: <http://www.hivatis.org/trgdlns.html>. Accessed March 28, 2001.
- 1999 USPHS/IDSA guidelines for the prevention of opportunistic infections in persons infected with human immunodeficiency virus: US Public Health Service (USPHS) and Infectious Diseases Society of America (IDSA). *MMWR Morb Mortal Wkly Rep*. 1999;48(RR-10):1-59.
- Metzger DS, Navaline H, Woody GE. Drug abuse treatment as AIDS prevention. *Public Health Rep*. 1998;113(suppl 1):97-106.
- The CASCADE Collaboration. Survival after introduction of HAART in people with known duration of HIV-1 infection. *Lancet*. 2000;355:1158-1159.
- Justice AC, Chang CH, Fusco J, West N. Extrapolating long-term HIV/AIDS survival in the post-HAART era. In: *Abstracts of the 39th Interscience Conference on Antimicrobial Agents and Chemotherapy*; San Francisco, CA; September 26-29, 1999. Washington, DC: American Society for Microbiology; 1999. Abstract 1158:489.
- Martin JA, Smith BL, Mathews TJ, Ventura SJ. Births and deaths: preliminary data for 1998. *Natl Vital Stat Rep*. 1999;47(25):6-7.
- Wiktor SZ, Biggar RJ, Melbye M, et al. Effect of knowledge of human immunodeficiency virus infection status on sexual activity among homosexual men. *J Acquir Immune Defic Syndr*. 1990;3:62-68.
- Wenger NS, Kusseling FS, Beck K, Shapiro MF. Sexual behavior of individuals infected with the human immunodeficiency virus: the need for intervention. *Arch Intern Med*. 1994;154:1849-1854.
- Kilmarx PH, Hamers FF, Peterman TA. Living with HIV: experiences and perspectives of HIV-infected sexually transmitted disease clinic patients after posttest counseling. *Sex Transm Dis*. 1998;25:28-37.
- Higgins DL, Galavotti C, O'Reilly KR, et al. Evidence for the effects of HIV antibody counseling and testing on risk behaviors. *JAMA*. 1991;266:2419-2429.
- Hays RB, Paul J, Ekstrand M, Kegeles SM, Stall R, Coates TJ. Actual versus perceived HIV status, sexual behaviors and predictors of unprotected sex among young gay and bisexual men who identify as HIV-negative, HIV-positive and untested. *AIDS*. 1997;11:1495-1502.
- Schaffer N, Roongpisuthipong A, Siriwasin W, et al. Maternal viral load and perinatal HIV-1 subtype E transmission. Bangkok, Thailand. *J Infect Dis*. 1999;179:590-599.
- Mofenson LM, Lambert JS, Stiehm ER, et al. Risk factors for perinatal transmission of human immunodeficiency virus type 1 in women treated with zidovudine. *N Engl J Med*. 1999;341:385-393.
- Garcia PM, Kalish LA, Pitt J, et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. *N Engl J Med*. 1999;341:394-402.
- Busch MP, Operskalski EA, Mosley JW, et al. Factors influencing human immunodeficiency virus type 1 transmission by blood transfusion. *J Infect Dis*. 1996;174:26-33.
- Operskalski EA, Stram DO, Busch MP, et al. Role of viral load in heterosexual transmission of human immunodeficiency virus type 1 by blood transfusion recipients. *Am J Epidemiol*. 1997;146:655-661.
- Lee T-H, Sakahara N, Fiebig E, Busch MP, O'Brien TR, Herman SA. Correlation of HIV-1 RNA levels in plasma and heterosexual transmission of HIV-1 from infected transfusion recipients. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1996;12:427-428.
- Ragni MV, Faruki H, Kingsley LA. Heterosexual HIV-1 transmission and viral load in hemophilic patients. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1998;17:42-45.
- Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *N Engl J Med*. 2000;342:921-929.
- Fideli U, Allen S, Musonda R, et al. Virologic determinants of heterosexual transmission in Africa. In: *Program and Abstracts of the 7th Conference on Retroviruses and Opportunistic Infections*; San Francisco, CA; January 30-February 2, 2000. Alexandria, Va: Foundation for Retrovirology and Human Health; 2000. Abstract 194:111.
- Ghys PD, Fransen K, Diallo MO, et al. The associations between cervicovaginal HIV shedding, sexually transmitted diseases and immunosuppression in female sex workers in Abidjan, Côte d'Ivoire. *AIDS*. 1997;11:F85-F93.
- Gupta P, Mellors J, Kingsley L, et al. High viral load in semen of human immunodeficiency virus type 1-infected men at all stages of disease and its reduction by therapy with protease and nonnucleoside reverse transcriptase inhibitors. *J Virol*. 1997;71:6271-6275.

27. Vernazza PL, Gilliam BL, Dyer J, et al. Quantification of HIV in semen: correlation with antiviral treatment and immune status. *AIDS*. 1997; 11:987–993.
28. Vernazza PL, Gilliam BL, Flepp M, et al. Effect of antiviral treatment on the shedding of HIV-1 in semen. *AIDS*. 1997;11:1249–1254.
29. Zhang H, Dornadula G, Beumont M, et al. Human immunodeficiency virus type 1 in the semen of men receiving highly active antiretroviral therapy. *N Engl J Med*. 1998;339: 1803–1809.
30. Miller CJ. Mucosal transmission of simian immunodeficiency virus. *Curr Top Microbiol Immunol*. 1994;188:107–122.
31. Sodora DL, Gettie A, Miller CJ, Marx PA. Vaginal transmission of SIV: assessing infectivity and hormonal influences in macaques inoculated with cell-free and cell-associated viral stocks. *AIDS Res Hum Retroviruses*. 1998; 14(suppl 1):S119–S123.
32. Connor EM, Sperling RS, Gelber R, et al. Reduction of maternal-infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. *N Engl J Med*. 1994;331: 1173–1180.
33. Shaffer N, Chuachoowong R, Mock PA, et al. Short course zidovudine for perinatal HIV-1 transmission in Bangkok, Thailand: a randomised controlled trial. *Lancet*. 1999;353:773–780.
34. Morris A, Zorrilla C, Vajaranant M, et al. A review of protease inhibitor use in 89 pregnancies. In: *Program and Abstracts of the 6th Conference on Retroviruses and Opportunistic Infections; Chicago, IL; January 31–February 4, 1999*. Alexandria, Va: Foundation for Retrovirology and Human Health; 2000. Abstract 686:197.
35. Peters V, Marinovich A, Singh T, Lindgren ML, Bertolli J, Thomas P. Trends to reduce perinatal HIV transmission in New York City. In: *Program and Abstracts of the 7th Conference on Retroviruses and Opportunistic Infections; San Francisco, CA; January 30–February 2, 2000*. Alexandria, Va: Foundation for Retrovirology and Human Health; 2000. Abstract 707:207.
36. May MR, Anderson RM. Transmission dynamics of HIV infection. *Nature*. 1987;326:137–142.
37. Valdiserri RO, Holtgrave DR, West GR. Promoting early HIV diagnosis and entry into care. *AIDS*. 1999;13:2317–2330.
38. Stetler HC, Granade RC, Nunez CA, et al. Field evaluation of rapid HIV serologic tests for screening and confirming HIV-1 infection in Honduras. *AIDS*. 1997;11:369–375.
39. Kassler WJ, Dillon GA, Haley C, et al. On-site, rapid HIV testing with same-day results and counseling. *AIDS*. 1997;11:1045–1051.
40. Centers for Disease Control and Prevention. Recommendations for HIV testing services for inpatients and outpatients in acute-care hospital settings. *MMWR Morb Mortal Wkly Rep*. 1993;42(RR-2):1–6.
41. Centers for Disease Control and Prevention. HIV counseling, testing, and referral guidelines. *MMWR Morb Mortal Wkly Rep*. In press.
42. Osmond DH, Bindman AB, Vranizan K, et al. Name-based surveillance and public health interventions for persons with HIV infection. *Ann Intern Med*. 1999;131:775–779.
43. Samet JH, Freedberg KA, Stein MD, et al. Trillion virion delay: time from testing positive for HIV to presentation for primary care. *Arch Intern Med*. 1998;158:734–740.
44. *HIV Prevention Strategic Plan Through 2005*. Atlanta, Ga: Centers for Disease Control and Prevention; 2001.
45. *HIV Prevention Case Management: Guidance*. Atlanta, Ga: Centers for Disease Control and Prevention; September 1997.
46. Bozzette SA, Berry SH, Duan N, et al. The care of HIV-infected adults in the United States. *N Engl J Med*. 1998;339:1897–1904.
47. Paterson D, Swindells S, Mohr J, et al. How much adherence is enough? A prospective study of adherence to protease inhibitor therapy using MEMS caps. In: *Program and Abstracts of the 6th Conference on Retroviruses and Opportunistic Infections; Chicago, IL; January 31–February 4, 1999*. Alexandria, Va: Foundation for Retrovirology and Human Health; 2000. Abstract 92:84.
48. Lucas GM, Chaisson RE, Moore RD. Highly active antiretroviral therapy in a large urban clinic: risk factors for virologic failure and adverse drug reactions. *Ann Intern Med*. 1999;131: 81–87.
49. Boden D, Hurlley A, Zhang L, et al. HIV-1 drug resistance in newly infected individuals. *JAMA*. 1999;282:1135–1141.
50. Little SJ, Daar ES, D'Aquila, et al. Reduced antiretroviral drug susceptibility among patients with primary HIV infection. *JAMA*. 1999;282: 1142–1149.
51. Centers for Disease Control and Prevention. Prevention and treatment of tuberculosis among patients infected with human immunodeficiency virus: principles of therapy and revised recommendations. *MMWR Morb Mortal Wkly Rep*. 1998;47(RR-20):1–51.
52. Lehman JS, Hecht FM, Wortley P, Lansky A, Stevens M, Fleming P. Are at-risk populations less concerned about HIV infection in the HAART era? In: *Program and Abstracts of the 7th Conference on Retroviruses and Opportunistic Infections; San Francisco, CA; January 30–February 2, 2000*. Alexandria, Va: Foundation for Retrovirology and Human Health; 2000. Abstract 198:112.
53. Centers for Disease Control and Prevention. Increases in unsafe sex and rectal gonorrhoea among men who have sex with men—San Francisco, California, 1994–1997. *MMWR Morb Mortal Wkly Rep*. 1999;48:45–48.
54. Marks G, Burris S, Peterman TA. Reducing sexual transmission of HIV from those who know they are infected: the need for personal and collective responsibility. *AIDS*. 1999;13: 297–306.
55. Centers for Disease Control and Prevention. Resurgent bacterial sexually transmitted disease among men who have sex with men—King County, Washington, 1997–1999. *MMWR Morb Mortal Wkly Rep*. 1999;48: 773–777.
56. *Consensus Development Conference Statement: Interventions to Prevent HIV Risk Behaviors*. Bethesda, Md: National Institutes of Health; February 11–13, 1997:1–41.
57. Erbeding EJ, Stanton D, Quinn TC, Rompalo A. Behavioral and biologic evidence of persistent high-risk behavior in an HIV primary care population. *AIDS*. 2000;14:297–301.
58. Jacquez JA, Koopman JS, Simon CP, Longini IM Jr. Role of the primary infection in epidemics of HIV infection in gay cohorts. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1994;7: 1169–1184.
59. Janssen RS, Satten GA, Stramer L, et al. New testing strategy to detect early HIV-1 infection for use in incidence estimates and for clinical and prevention purposes. *JAMA*. 1998;280: 42–48.
60. Holtgrave DR, Pinkerton SD. Updates of cost of illness and quality of life estimates for use in economic evaluations of HIV prevention programs. *J Acquir Immune Defic Syndr Hum Retrovirol*. 1997;16:54–62.