28. Screening for Human Immunodeficiency Virus Infection

RECOMMENDATION

Clinicians should assess risk factors for human immunodeficiency virus (HIV) infection by obtaining a careful sexual history and inquiring about injection drug use in all patients. Periodic screening for infection with HIV is recommended for all persons at increased risk of infection (see ***Clinical Intervention***). Screening is recommended for all pregnant women at risk for HIV infection, including all women who live in states, counties, or cities with an increased prevalence of HIV infection. There is insufficient evidence to recommend for or against universal screening among low-risk pregnant women in low-prevalence areas, but recommendations to counsel and offer screening to all pregnant women may be made on other grounds (see ***Clinical Intervention***). Screening infants born to high-risk mothers is recommended if the mother's antibody status is not known. All patients should be counseled about effective means to avoid HIV infection (see Chapter 62).

Burden of Suffering

It is estimated that 0.8–1.2 million persons in the U.S. are infected with the human immunodeficiency virus (HIV-1) and that 40,000–80,000 new infections occur each year.[1,2] Most people infected with HIV eventually develop the acquired immunodeficiency syndrome (AIDS), defined by opportunistic infections or severe immune dysfunction.[3] Within 10 years of infection with HIV, about 50% of persons develop clinical AIDS, and another 40% or more develop other illnesses associated with HIV infection.[4] A small proportion (5–10%) of persons remain well 10–15 years after HIV infection,[5] but there is currently no available curative treatment for AIDS. Of the 476,899 cases of AIDS reported to the Centers for Disease Control and Prevention (CDC) through June 1995, 62% had died, including over 90% of those diagnosed before 1988.[6] HIV infection is now the leading cause of death among men ages 25–44, and the fifth leading cause of years of potential life lost before age 65.[7,8] By the end of 1995, it is projected that there will be 130,000–205,000 persons living with AIDS in the U.S., at an annual cost of treatment in excess of $15 billion.[9]

High-Risk Groups. Men who have sex with men and injection drug users (IDUs) together accounted for over 80% of AIDS cases reported in 1994.[6] HIV infection is widely prevalent in these groups.[10] In seroprevalence surveys conducted in 1991–1992 at STD clinics and drug treatment facilities, the median prevalence of HIV infection among men having sex with men was 26% (range 4–47%)[a] and ranged from 2–7% among IDUs in Western cities to 12–40% among IDUs on the East Coast.[10] HIV infection is also prevalent among heterosexual persons with other STDs (median 0.6%), prisoners (range 1–15%), and residents of homeless shelters (range 1–21%).[10] Very high rates of HIV infection (up to 30%) have been detected among inner-city young adults who smoke crack, especially among women who exchange sex for drugs.[11] More than 10,000 cases of AIDS have been attributed to transfusion of infected blood or blood components (i.e., clotting factor) between 1977 and 1985, but the current risk of becoming infected from blood or tissue products is extremely low.[12]

Pregnant Women. By July 1995, over 5,900 cases of AIDS had been attributed to perinatal infection.[6] An estimated 0.17% of all childbearing women in the U.S. were infected with HIV in 1991–1992, but prevalence varied from 0–0.05% in 16 states to 0.6% in New York State. Of 144 urban family planning clinics conducting blinded surveillance, 13 reported a prevalence of HIV infection over 1%.[10] Of the estimated 7,000 infants born to infected mothers each year, 80% are born in 20 states where prevalence of antibody-positive newborns was 0.1% or greater.[13] The probability of vertical transmission from mother to infant is between 13% and 35%,[14–16] increasing with severity of disease in the mother.[17]

General Population. The distribution of new AIDS cases may not reflect the changing pattern of the HIV epidemic due to the long delay between infection and clinical AIDS. Heterosexual transmission is the most rapidly growing source of new AIDS cases, accounting for 10% of new AIDS cases in 1994 (up from 2% in 1985).[6] It is the leading cause of new HIV infections in American women.[6,18] Young black and Hispanic women in large East Coast cities are at greatest risk (due to the higher prevalence of HIV in their male partners and the more efficient transmission of virus from men to women during intercourse),[19] but women of all races experienced comparable increases in heterosexually acquired AIDS cases between 1992 and 1994.[18] Large surveys in 1991–1992 of Job Corps applicants ages 16–21 (seroprevalence 0.27%), military recruits (seroprevalence 0.06%), and pa-

[a]Data from patients at STD clinics, by selecting for high-risk sexual practices, will overstate the rate of infection in the general population of homosexual and bisexual men.

tients at urban hospitals (range 0.1–5.8%) indicate that the prevalence of HIV infection varies markedly among different demographic groups and geographic areas.[10] The rate of AIDS and the prevalence of HIV are substantially higher in Atlantic Coast states than in Midwest and Mountain states, in large metropolitan areas (population 500,000 or greater) than in smaller cities or rural areas, and in black and Hispanic young persons than in whites, Native Americans, or Asians/Pacific Islanders.[6,10,20] Blinded screening of over 20,000 primary care patients in smaller cities and rural areas detected HIV in 0.15% of all patients without known disease, however.[10] The regional variations in HIV prevalence generally mirror the local prevalence of infection among drug users. IDUs account for a large proportion of new HIV infections[21] and are a leading source of heterosexual and perinatal transmission of HIV.[6]

Accuracy of Screening Tests

The initial screening test to detect antibodies to HIV is the enzyme immunoassay (EIA). Commercially available EIAs use antigens from whole disrupted virus (first generation), recombinant viral proteins (second generation), or chemically synthesized peptides (third generation).[22] EIA results are considered "reactive" only when a positive result has been confirmed in a second test of the original sample. In subjects with clinical AIDS, the sensitivity of EIA is close to 100%, but newly infected individuals may not develop detectable antibodies for periods of weeks to months after infection.[23] The median interval between infection and seropositivity has been estimated at 3 months with earlier EIAs, with 95% seroconverting within 6 months.[24] Estimates based on more sensitive third-generation EIAs, which may be positive within 1 week of peak antigen levels, suggest that the "window" period with current tests is substantially shorter (3–4 weeks).[25,25a] Specificity of EIA is above 99.5% with most tests. Third-generation EIAs had specificities of 99.7–99.9% when tested against uninfected controls.[25–27] False-positive results can be caused by nonspecific reactions in persons with immunologic disturbances (e.g., systemic lupus erythematosus or rheumatoid arthritis), multiple transfusions, or recent influenza or rabies vaccination.[28,29] Food and Drug Administration (FDA) approval has been granted to rapid tests (<15 minutes) using colorimetric assays,[30] and to an EIA-based test using oral fluid samples collected with a cotton pad.[31,32] Although these tests are sensitive and specific (>99%), neither method is recommended for the definitive diagnosis of HIV infection.[33]

To prevent the serious consequences of a false-positive diagnosis of HIV infection, confirmation of positive EIA results is necessary, using an independent test with high specificity. The Western blot (WB) is the most

commonly used confirmatory test in the U.S. Indirect immunofluorescence assay (IFA), which is less expensive and less time-consuming, is also approved for confirmatory testing.[34] The specificity of WB is close to 100% under controlled settings,[35] but it is dependent on the skill and experience of the laboratory and on criteria used to determine positive WB results.[33,35] The sensitivity of WB was 98.5% and specificity 92.5% in a 1989 CDC quality control survey of 140 laboratories;[26] most errors involved misclassification of positive or negative samples as "indeterminate." Criteria for interpreting WB have been developed to improve accuracy in clinical testing.[35] Many laboratories doing a large volume of HIV testing achieved sensitivities and specificities of 100%.[36]

The precise false-positive rate of current HIV testing is not known. A false-positive rate of less than 1 in 100,000 was reported in experienced, centralized laboratories using careful quality control procedures.[37,38] In practice, false-positive diagnoses can result from contaminated or mislabeled specimens,[39] cross-reacting antibodies,[33] failure to perform confirmatory tests,[40] misinterpretation of WB patterns, or misunderstanding of reported results by clinicians or patients.[41] In one study, 8 of 900 women referred for treatment of HIV were not infected on repeat testing.[40] To prevent errors due to mistakes in specimen handling or WB interpretation, a consensus laboratory panel recommended confirming all new diagnoses of HIV with tests on a freshly obtained specimen.[42]

Indeterminate Western Blot Results. Indeterminate WB results, due to antibody patterns that do not meet full criteria for positive test, occur in 3–8% of EIA-positive specimens.[33,43] In a survey of over 1 million newborn specimens for maternal HIV antibody, <1 in 4,000 screened samples produced an indeterminate WB result.[43a] An indeterminate WB result may indicate evolving antibody response in recently infected subjects, but in low-risk persons it usually represents the presence of nonspecific antibodies. Follow-up of nearly 700 EIA positive/WB indeterminate blood donors documented seroconversion in only eight subjects, all but one of whom reported a high-risk behavior.[43–45] An indeterminate WB is more significant in high-risk subjects, but the risk of seroconversion is variable (13–28%).[44,46] Antibodies to p24 antigen were present in 29 of 30 subjects who subsequently converted.[43,44] A new indeterminate WB in subjects who were previously seronegative is more likely to represent recent infection.[47] Seroconversion usually occurs within 2–3 months (range 2–16 weeks in one study).[44] A stable indeterminate WB after 6 months can be assumed to be due to nonspecific antibody reaction rather than HIV infection.[33,48]

Viral Culture and Polymerase Chain Reaction Assays. Viral culture is the most specific test for HIV infection, but it is time-consuming, expensive, technically difficult, and insufficiently sensitive for use as a screening test.[22] Poly-

merase chain reaction (PCR) can detect viral genetic material in subjects who have not yet developed antibodies, but trace levels of contamination can produce false-positive results.[22] In proficiency testing of five experienced laboratories, sensitivity of PCR was 98–100% and specificity was 96–100%.[49] With newer, more sensitive EIAs, the additional value of screening with PCR is small in adults. In over 250 high-risk persons with nonreactive EIAs, PCR detected only two confirmed cases of HIV.[50–53] Since PCR is not 100% specific, a large proportion of positive PCR results in seronegative patients may be false positives. Despite their limitations as screening tests, viral culture, PCR, and viral antigen assays are useful for evaluating patients with symptoms of acute HIV infection.

Diagnosis of HIV in Infants. Diagnosing infection in infants born to HIV-infected mothers is difficult, since maternal antibodies to HIV are present in both infected and uninfected infants. Uninfected infants serorevert an average of 10 months after birth, but maternal antibody may persist up to 18 months.[54] Viral culture and PCR are highly specific for infection in infants, although PCR is occasionally positive in infants who eventually serorevert and are presumed not to be infected.[55] Reported sensitivity for culture is 60–90%[22,56] and 84–98% for PCR, increasing after 3 months.[57,58] Using culture and/or PCR, an estimated 50% of infected infants can be identified at birth, and up to 90% by 3 months.[59] Other tests for perinatal infection include assays for viral antigen (sensitivity 30–60%)[56,59] and IgA (sensitivity 50–80%).[59,60]

Screening by Risk Factor Assessment. Patient history is an important but imperfect way to assess risk for HIV infection. Patients may conceal high-risk behaviors, and others (especially women in high-risk areas) may be unknowingly at risk from an infected sex partner. In high-prevalence family planning clinics, testing women who reported drug use or an IDU partner detected only 41–57% of all cases.[61,62] Offering testing routinely to all women resulted in greater acceptance (up to 96%),[61] and detected 87% of all HIV infections.[62] Even in low-prevalence areas such as Sweden, 37% of infected pregnant women did not report clear risk factors for HIV.[63] There are few data comparing the sensitivity of targeted versus routine screening in male patients. In a seroprevalence study in primary care practices, physicians were not aware of HIV risk factors in roughly one third of infected patients.[10]

Consent, Confidential Versus Anonymous Testing, and Partner Notification. There is general consensus that informed consent should be obtained prior to HIV testing.[14,64] The diagnosis of HIV has serious consequences, and compulsory testing may discourage persons from seeking care. Alternate forms of consent—right of refusal (i.e., passive consent) versus explicit consent, active recommendation versus nondirective counseling—have

been considered to facilitate screening during pregnancy.[13,65] Universal newborn screening without consent of the mother was considered but rejected by the New York State legislature.[66]

Half of all states require confidential reporting of HIV-infected persons by name to state or local health departments, and all require reporting of AIDS patients.[6,67] Partner notification (contact tracing) can alert exposed persons to the need to be tested. Between 50% and 90% of sex partners can be identified through organized partner notification programs,[68] and costs per case identified compare favorably to screening high-risk groups.[69]

In one trial, offering the option of anonymous testing resulted in higher rates of testing.[70] Two thirds of all patients at a public clinic (and a majority of seropositive patients) chose anonymous testing over confidential testing.[71] Test kits that would allow individuals to submit specimens (blood or saliva) collected at home for anonymous testing, using coded identifiers, are being considered by the FDA.[71a]

Frequency of Testing. The appropriate frequency of HIV screening is not known, but it depends in part on the incidence of new infections. Rates are highest among IDUs in Northeastern cities (3–6 infections/100 patient-years [py]),[21] compared to less than 1/100 py in homosexual men in most cities,[72] and 0.04/100 py among military personnel aged 25–29.[73] Due to the low incidence of new infection and increased sensitivity of new tests, repeat testing simply to confirm an initial negative EIA is rarely indicated.

Effectiveness of Early Detection

Detection of asymptomatic HIV infection permits early treatment to slow disease progression, interventions to reduce perinatal transmission, and counseling to prevent transmission of virus to uninfected sex partners or persons sharing injection needles.

Effectiveness of Early Therapy in Asymptomatic Adults. Antiretroviral medications (e.g., zidovudine [ZDV or AZT], didanosine, zalcitabine) reduce mortality in AIDS patients and delay progression to AIDS in symptomatic HIV infection.[74,75] Due to eventual resistance developed by the HIV virus,[76] however, there is no clear benefit of initiating antiretroviral therapy (with current drugs as monotherapies) before patients become symptomatic.[74,77,78] In an overview of six randomized, controlled trials (RCTs) of ZDV for asymptomatic HIV infection, there was no long-term benefit of early treatment versus deferred treatment (begun at onset of symptoms) on survival or progression to AIDS.[79] For asymptomatic patients with more advanced immunodeficiency (CD4 200–500/μL), early ZDV delayed progression to AIDS or AIDS-related complex over the short-term but did not

improve outcomes beyond the first 1–2 years.[74,79,80] In Concorde, the largest and longest trial—over 1,700 men and women with asymptomatic HIV infection followed over 3 years—there was no significant difference between patients receiving early versus deferred treatment in the combined incidence of AIDS or death (18% in each group), or in total mortality (8% and 6%, respectively).[81] The early benefits from delaying disease progression are offset by the adverse effects of ZDV (e.g., nausea, headache, and fatigue).[82] Early combination antiretroviral therapy, by reducing drug resistance, may be more effective than monotherapy in reducing viral burden and delaying immunodeficiency, but long-term clinical trials of these approaches have not yet been completed.[83,84]

Chemoprophylaxis can reduce the risk of *Pneumocystis carinii* pneumonia (PCP) in patients with more advanced immunodeficiency. The annual incidence of PCP rises to 18–25% in persons with CD4 < 200/μL,[85,86] and half of all HIV-infected persons are still asymptomatic at this stage of disease.[85,87,88] In retrospective analyses, prophylaxis with trimethoprim-sulfamethoxazole (TMP-SMX) or inhaled pentamidine reduced the incidence of primary PCP by 67–83%,[86,89–91] delayed onset of AIDS by 6–12 months, and prolonged survival in those with low CD4 count by almost 1 year.[92–94] In a recent 3-year trial, TMP-SMX, dapsone, and inhaled pentamidine were equally effective as initial therapy for primary prophylaxis against PCP.[95] TMP-SMX was more effective in shorter studies[89,90,96] and for patients with CD4 < 100,[95] and it is recommended as the preferred prophylactic agent;[97] long-term therapy is limited by the high incidence of side effects (e.g., leukopenia, fever, rash, or gastrointestinal side effects). TMP-SMX and dapsone also provide protection against toxoplasmosis,[98,99] an uncommon complication of asymptomatic HIV infection in the U.S.[95] Long-term benefits of chemoprophylaxis are limited by the continuing decline in immune function.[92]

HIV-infected persons infected with *Mycobacterium tuberculosis* are at increased risk of developing active tuberculosis, primarily at CD4 counts below 500/μL. In a randomized trial among asymptomatic HIV-infected persons in Haiti, an endemic tuberculosis area, chemoprophylaxis with isoniazid reduced the incidence of tuberculosis nearly 75% and delayed progression to AIDS.[100] In a U.S. cohort study, isoniazid prophylaxis reduced tuberculosis among HIV-positive, PPD-positive drug users.[101,102] Decision analyses suggest that the benefits of prophylaxis may outweigh risks in both PPD-positive and anergic patients with HIV when exposure to tuberculosis is prevalent (e.g., in IDUs, homeless persons, and immigrants from endemic areas; see Chapter 25).[103] Chemoprophylaxis with rifabutin is also effective against *Mycobacterium avium* complex (MAC), but few asymptomatic patients have sufficiently advanced disease (CD4 < 75/μL) to warrant MAC prophylaxis.[97]

Effectiveness of Early Therapy in Asymptomatic Children. There are few randomized trials of interventions in asymptomatic HIV-infected children, but TMP-SMX is safe and effective for PCP prophylaxis in other immunocompromised children.[104] PCP may be the first indication that infants are infected with HIV: 44% of the children who developed PCP in one study had never been evaluated for HIV.[105] Between 7% and 20% of children with HIV develop PCP within the first year of life (peak incidence between 3 and 9 months),[105,106] and mortality is high (up to 30%).[107] Adverse reactions (rash, cytopenia) from TMP-SMX occur in up to 15% of HIV-infected children. New CDC guidelines for PCP prophylaxis in infants recommend prophylaxis for all HIV- infected or possibly infected infants during the first year of life.[107] Studies are currently under way to evaluate the benefit of different antiretroviral therapies in asymptomatic children.

A variety of precautions are routinely recommended for HIV-infected children and adults, due to the increased susceptibility to viral and bacterial infections:[108–110] vaccination against influenza, pneumococcus, hepatitis B, and *Haemophilus influenzae;*[111] avoidance of oral (live virus) polio vaccine in children;[112] attention to nutrition;[113] avoiding uncooked foods and high-risk sexual practices; and more frequent Papanicolaou (Pap) screening for women (due to an increased risk of invasive cervical cancer).[67,114] The benefit of these interventions in persons with asymptomatic HIV infection has not been determined.

Effectiveness of Early Intervention in Asymptomatic Pregnant Women. A randomized placebo-controlled trial (ACTG 076) demonstrated that a regimen of ZDV begun between weeks 14 and 34 of pregnancy and continued through delivery and for 6 weeks in newborn infants significantly reduced perinatal HIV infection (8.3% vs. 25.5%) among infants born to seropositive mothers with mildly symptomatic HIV infection (CD4 > 200/μL).[16] ZDV is associated with a low incidence of severe side effects in mothers or infants, but the long-term effects on the health of infants, and on the course of HIV disease in mothers, are not known. Cesarean delivery is also associated with lower rates of vertical transmission; a trial of operative versus vaginal delivery in HIV-infected pregnancies is under way in Italy.[115]

Identifying seropositive women during pregnancy may have other important benefits: some women may be candidates for PCP prophylaxis; male partners can be advised to be tested and to use condoms; infants can be monitored for evidence of HIV infection and started on appropriate therapy; and early involvement of social services may facilitate care for infected mothers and infants. Infected mothers are advised to avoid breastfeeding: a meta-analysis of cohort studies estimated that breastfeeding increases vertical transmission by 14%.[116] The extent to which early detection actually leads to these benefits is difficult to estimate. There is no clear

effect of testing and counseling on fertility decisions: in two U.S. studies, pregnancy rates were similar for HIV-positive and HIV-negative women.[117] Infected women were more likely to choose abortion than uninfected women in one study,[118] but the large majority of women with HIV chose to continue the pregnancy.[63]

Effectiveness of Testing and Counseling to Prevent Transmission of HIV. Determining whether HIV testing and counseling reduces HIV transmission is complicated by many factors:[119] a paucity of well-controlled trials; variable quality of counseling interventions; reliance on intermediate endpoints, such as self-reported changes in behavior; differences between screened and unscreened patients in observational studies; population-wide changes in high-risk behavior; and the uncertain importance of testing versus counseling. The effect of testing and counseling varies with the specific behavior and population being targeted.[117] Programs that targeted couples in which one member was infected provide the strongest evidence of the benefits of testing and counseling: compared with historical controls, counseled couples increased regular condom use and significantly reduced the rate of seroconversion in partners.[120–123]

Among homosexual men, high-risk sexual practices and new HIV infections have declined substantially since the development of HIV tests. Community-wide changes may have been more important than identification of seropositive persons, however, and there are worrisome signs of persisting unsafe practices among younger gay men.[124] Condom use is generally higher among seropositive men than seronegative or untested men, but longitudinal studies suggest increasing use of condoms across all groups.[125–127] Unprotected anal intercourse and number of sex partners have declined over time in both tested and untested men. The absolute change in risk may be greater in seropositive men, who engage in higher-risk behavior at baseline.[128] A substantial proportion of seropositive men continue to have sex with multiple partners and engage in oral intercourse; 5–15% continue unprotected anal intercourse.[128]

The effects of screening in injection drug users are less consistent. Among drug users in treatment, drug use and needle sharing decline after HIV counseling and testing but also declined among unscreened patients.[117,129] In a community survey, IDUs who had received testing and counseling were half as likely to share needles as untested subjects.[130] Testing has inconsistent effects on high-risk sexual behavior among drug users. Seropositive IDUs are more likely to report condom use in some cross-sectional studies, but 30–70% use condoms only occasionally or not at all.[117,131]

Counseling and testing patients at STD clinics has had variable results. Rate of recurrent STDs was unchanged 1 year after testing in one study,[132]

was lower among HIV-positive than HIV-negative subjects in another (15% vs. 23%),[133] and declined among seropositive patients while rising among seronegative patients in a third.[134] In one randomized trial, testing and counseling reduced unprotected intercourse more than counseling alone.[135] Other longitudinal studies suggest little change in sexual behavior in seronegative subjects after testing and counseling. Routine testing and counseling among students at a college health clinic did not improve low rates of condom use.[136] Among women tested in community health clinics, seronegative women did not reduce sexual risk factors after testing and counseling, compared with untested controls.[137]

Efforts to modify high-risk behaviors in infected and high-risk persons are often hindered by substance abuse, poverty, limited education, denial, or economic necessity (i.e., prostitutes). A minority of seropositive persons abstain completely from sex or drug use after diagnosis. Those who do not may have trouble obtaining condoms or clean needles but may not inform sex partners that they are infected.[138] Female partners of infected men may minimize risk or be unable to get their male partner to consistently use a condom.[139]

Adverse Effects of Testing and Counseling. The diagnosis of HIV infection can have significant adverse effects, among them intense anxiety, depression, somatization, or anger.[140,141] Among 1,718 newly diagnosed patients with HIV, 21% met criteria for depression at first visit, but psychological distress was related more to symptoms than diagnosis and diminished with time.[142] Testing reduces anxiety in high-risk persons who are seronegative. Despite recent efforts to improve public perceptions and attitudes, the stigma associated with the diagnosis of HIV/AIDS is still significant.[143] Disclosure of test results can result in disrupted personal relationships, domestic violence, social ostracism, and discriminatory action, such as loss of employment, housing, health insurance, and educational opportunities.[144] Recent legislation and the expanded case definitions for AIDS may help prevent some forms of discrimination and help ensure medical care for those with more advanced infection. Information on the frequency or consequences of false-positive diagnoses are largely anecdotal. Although retesting and follow-up can resolve most errors, misdiagnosis may cause irreparable harm (divorce, abortion, etc.). Finally, negative test results may provide false reassurance unless patients are counseled about their continuing risk of infection from drug use and high-risk sexual activity.

Recommendations of Other Groups

Counseling and HIV testing of high-risk individuals are recommended by the CDC[14] and numerous medical organizations: the Canadian Task Force on the Periodic Health Examination (CTF),[145] the American Academy of Family Physicians,[146] the American Medical Association (AMA),[147] the

American College of Obstetricians and Gynecologists (ACOG),[114] the American College of Physicians, and the Infectious Disease Society of America.[148] High-risk individuals include men who have sex with men; persons seeking treatment for STDs; injection drug users and their sex partners; recipients of transfusion between 1978 and 1985; and persons who have had multiple sex partners or exchanged sex for money or drugs. Bright Futures[149] and the AMA Guidelines for Adolescent Preventive Services (GAPS)[150] recommend offering HIV testing to all at-risk adolescents, including those with more than one sex partner in the last 6 months.

The CDC recommends that health care facilities where the prevalence of infection exceeds 1%, or the AIDS diagnosis rate is greater than 1 / 1,000 hospital discharges, consider routine, voluntary screening among patients aged 15–54 years.[151] The AMA approves of routine HIV testing in the clinical setting, based on local considerations such as planned medical procedures and local seroprevalence.[147] GAPS[150] and AAFP[146] recommend offering screening to sexually active adolescents and adults from high-prevalence communities.

The U.S. Public Health Service (PHS) released new guidelines in 1995, recommending that all pregnant women be routinely counseled and encouraged to have HIV testing.[152] Similar policies have been approved by American Academy of Pediatrics (AAP)[65] and ACOG.[153] Pregnant women should be screened as soon as the woman is known to be pregnant; repeat testing may be indicated near delivery for women at high risk of infection. The CTF (prior to ACTG 076) concluded there was insufficient evidence to recommend for or against routine screening in pregnancy, due to the low rate of infection in Canada.[145] In cases where the HIV serostatus of the mother is not known, PHS and AAP guidelines suggest that health care providers educate the mother about benefits to her infant and encourage her to allow testing for the newborn.[65,152] A 1991 Institute of Medicine task force (before ACTG 076) recommended voluntary screening of all pregnant women in high-prevalence areas and of high-risk women in other areas, but it found insufficient evidence to recommend routine newborn screening.[64]

Both the AMA and the AAP have endorsed alternate procedures for pretest counseling and consent, including right of refusal, to facilitate routine testing in specific situations. Mandatory testing for HIV is currently required on entrance to the military, and for donors of blood, organs, and tissue; federal prisoners; and persons seeking to immigrate to the U.S. Individual state laws vary regarding mandatory testing, confidentiality of results, informed consent, and reporting of seropositive persons to public health officials.[67] The CDC recommends that seropositive persons be instructed how to notify their partners, but suggests that physicians or health department personnel should use confidential procedures to ensure that partners are notified.[14]

Discussion

Early detection of asymptomatic HIV infection can reduce morbidity and mortality in infected persons, but the long-term benefits are currently limited by the relentless course of disease in most patients. The most compelling argument for early detection is the potential to prevent transmission of HIV, which may occur over many years before infected persons develop symptoms of HIV infection. Although there is only indirect evidence that screening reduces the incidence of new HIV infections, even small changes in transmission will have important public health benefits.

Screening is most important in the high-risk groups that currently account for the large majority of AIDS cases and new HIV infections.[154] The ability of ZDV to reduce perinatal transmission of HIV provides strong evidence of the benefit of screening during pregnancy. In high-risk communities, offering HIV testing to all pregnant women is more acceptable to patients, easier to implement, and more sensitive than screening on the basis of self-reported risk factors. In areas where HIV infection is uncommon, however, the choice between targeted screening and universal screening is a policy decision. Universal screening may detect occasional cases of HIV infection among women without reported risk factors, but it will subject many women at negligible risk to the potential harms from a false-positive or indeterminate test result. If specificity of testing is 99.98%, routine screening in low-risk populations (e.g., pregnant women in low-prevalence states) will generate one false-positive and many additional indeterminate results for every true-positive. Although indeterminate and false-positive results can generally be resolved with follow-up testing, some women may decide to terminate the pregnancy before infection status can be definitively determined. Counseling and testing many thousands of low-risk women to detect a single case of HIV may also divert resources from more important issues. If routine testing can be provided with the combination of accuracy and low costs achieved by large, centralized screening programs,[37,63,155] the justification for universal screening would be stronger.

A growing number of HIV infections occur in persons who are infected through heterosexual contact. The risk of heterosexual transmission varies widely among different communities, with the highest risk among poor minority women in large cities and the rural South. In high-risk communities or clinics, routine screening of sexually active young women and men may be appropriate. In populations where prevalence of infection is low, more selective screening is likely to be more efficient: 5% of women and 12% of men report multiple sex partners within the last 12 months without consistent condom use.[156] Deciding what constitutes a “high-risk” community is a policy decision,[64] depending in part on available data and resources

for testing. A prevalence of 1/1,000 among newborns,[157] or an AIDS diagnosis rate of more than 1/1,000 hospital discharges,[151] has been used to justify routine screening in other settings. Community prevalence provides only a crude measure of individual risk, however, and should not replace careful assessment of high-risk behaviors in each patient.

Screening for HIV in high-risk groups is cost-effective under a wide range of assumptions. In an analysis of federally funded programs (where HIV prevalence was 2.6%) testing and counseling activities saved money even if only one new infection is avoided for every 100 seropositive subjects identified.[158] In Sweden, where prevalence of infection is only 0.01% in pregnant women, routine prenatal HIV testing costs approximately $10 per patient and $100,000 per case identified.[63] Screening is less cost-effective in asymptomatic adults if only the benefits from early treatment are considered.[154] Revised cost-effectiveness analyses of alternate screening strategies for asymptomatic persons are needed, incorporating new data on antiretroviral therapy in pregnant and nonpregnant adults, regional variations in prevalence, targeted versus universal screening, and the costs of testing and counseling in the primary care setting.

CLINICAL INTERVENTION

Clinicians should assess risk factors for HIV infection in all patients by obtaining a careful sexual history and inquiring about drug use. Counseling and testing for HIV should be offered to all persons at increased risk for infection: those seeking treatment for sexually transmitted diseases; men who have had sex with men after 1975; past or present injection drug users; persons who exchange sex for money or drugs, and their sex partners; women and men whose past or present sex partners were HIV-infected, bisexual, or injection drug users; and persons with a history of transfusion between 1978 and 1985 (“A” recommendation).

Pregnant women in these categories, and those from communities (e.g., states, counties, or cities) where the prevalence of seropositive newborns is increased (e.g., ≥0.1%) should be counseled about the potential benefit to their infant of early intervention for HIV, and offered testing as soon as the woman is known to be pregnant (“A” recommendation). Repeat testing may be indicated in the third trimester of pregnancy for women at high risk of recent exposure to HIV. There is insufficient evidence to recommend for or against universal prenatal screening for HIV in low-prevalence communities (“C” recommendation). A policy of offering screening to all pregnant women may be recommended on other grounds, including patient preference, easier implementation, and increased sensitivity compared to screening based on community prevalence and reported risk factors. Careful quality control measures and patient counseling are essential to limit the potential adverse effects from inde-

terminate and false-positive test results during pregnancy. Testing infants born to high-risk mothers, with permission of mother, is recommended when antibody status of mother is unknown. ("B" recommendation).

There is insufficient evidence to recommend for or against routine HIV screening in persons without identified risk factors ("C" recommendation). Recommendations to screen sexually active young women and men in high-risk communities can be made on other grounds, based on the increasing burden of heterosexual transmission and the insensitivity of screening based on self-reported risk factors. Similarly, routine HIV screening may be reasonable in groups such as prisoners, runaway youth, or homeless persons, where the prevalence of high-risk behaviors and HIV is generally high. The definition of high-risk community is imprecise. Clinicians should consult local public health authorities for advice and information on the epidemiology of HIV infection in their communities. More selective screening may be appropriate in low-risk areas. Testing should not be performed in the absence of informed consent and pretest counseling, which should includes the purpose of the test, the meaning of reactive and nonreactive results, measures to protect confidentiality, and the need to notify persons at risk. Patients who wish to be tested anonymously should be advised of appropriate testing facilities.

A positive test requires at least two reactive EIAs and confirmation with WB or IFA, performed by experienced laboratories that receive regular external proficiency testing. A separate sample should be submitted for persons found to be seropositive for the first time, to rule out possible error in specimen handling. Patients with indeterminate WB results should be evaluated individually to determine whether findings are likely to represent recent seroconversion. Repeat testing should be performed 3–6 months after indeterminate test results, or sooner if recent seroconversion is suspected. A stable indeterminate WB pattern is not indicative of HIV infection.

Seropositive patients should receive information regarding the meaning of the results, the distinctions between casual nonsexual contact and proven modes of HIV transmission, measures to reduce risk to themselves and others, symptoms requiring medical attention, and available community resources for HIV-infected persons. Clinicians should explore potential barriers to changing high-risk behavior in seropositive and seronegative individuals. Guidelines for HIV counseling have been published by the PHS.[159] Seropositive persons should be evaluated for severity of immune dysfunction and screened for other infectious diseases such as tuberculosis (see Chapter 25). Guidelines for the management of early HIV infection and prevention of opportunistic infections have been published by the Agency for Health Care Policy and Research[67] and the CDC.[97,107,111] Arrangements for follow-up medical care are especially im-

portant for drug users, who may require assistance in gaining entrance to a drug treatment program (see Chapter 53). All seropositive individuals should be encouraged to notify sex partners, persons with whom injection needles have been shared, and others at risk of exposure. Seropositive cases should be reported confidentially or anonymously to public health officials in accordance with local regulations.

Persons with nonreactive test results should be informed that the risk of acquiring subsequent HIV infection can be prevented by maintaining monogamous sexual relationships with uninfected partners. Other measures to reduce the risk of infection (consistent use of condoms, etc.) should be specifically mentioned (see Chapter 62). The frequency of repeat testing of seronegative individuals is a matter of clinical discretion. Periodic testing is most important in patients who continue high-risk activities. In patients with recent high-risk exposure (e.g., sex with HIV-infected partner), repeat testing at 3 months may be useful to rule out initial false-negative tests.

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