Perspectives

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Perinatal Issues • Cervical Cancer Screening • Other Issues

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About This Issue

This issue features 3 Perspectives articles. A review article summarizes issues of HIV infection in women as presented by Carmen D. Zorrilla, MD, at the 9th Annual Ryan White CARE Act Clinical Update in Washington, DC, in August 2006. Dr Zorrilla focused her talk on perinatal issues and on surveillance for cervical cancer. A second article from the same conference summarizes a presentation by Robert S. Janssen, MD, on the recently revised Centers for Disease Control and Prevention (CDC) recommendations for HIV screening. The CDC has recently recommended universal opt-out HIV testing. Finally, there is an ongoing resurgence of syphilis in HIV-infected patients. This and other sexually transmitted diseases in HIV infection are discussed in a review article based on a presentation given by Jeanne Marrazzo, MD, MPH, at an International AIDS Society-USA–sponsored Continuing Medical Education course in New York in October 2006.
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Perspective

HIV Infection in Women: Perinatal Issues and Cervical Cancer Surveillance

Issues of HIV infection in women include perinatal care to prevent mother-child transmission and screening for cervical dysplasia. Antiretroviral therapy has been very successful in reducing perinatal transmission rates. Ongoing issues in this setting include absence of relevant pharmacokinetics data for new drugs and formulations, implementation of new resistance testing guidelines, and recent apparently conflicting findings on the potential role of protease inhibitor treatment in preterm delivery. Recent findings also include a similar low transmission rate with vaginal delivery and emergency cesarean delivery versus elective cesarean delivery in women on antiretroviral therapy with HIV viral load of less than 1000 copies/mL, and a low rate of postpartum morbidity in women undergoing elective cesarean delivery. Recent changes in recommendations for cervical cancer screening in the general population should not be applied to HIV-infected women. However, the recent finding that HIV-infected women with CD4+ cell counts greater than 500μL do not have a greater rate of squamous intraepithelial lesions than women without HIV infection suggests that the former can be followed less frequently if they have normal Pap tests. This article summarizes a presentation on HIV infection in women made by Carmen D. Zorrilla, MD, at the 9th Annual Ryan White CARE Act Clinical Update in Washington, DC, in August 2006. The original presentation is available as a Webcast at www.iasusa.org.

Perinatal Issues

Preconception Care

Among the issues involved in pregnancy and childbirth for HIV-infected women are preconception care and counseling. Preconception care “aims to promote the health of women of reproductive age before conception and thereby improve pregnancy-related outcomes. Improving preconception health can result in improved reproductive health outcomes, with potential for reducing social costs as well” (MMWR Mortal Morbid Wkly Rep, 2006). It is important for all women and crucial for women living with HIV who have postponed but now want to achieve pregnancy, particularly HIV-infected women who are receiving antiretroviral therapy. Since about half of pregnancies in the general population are unplanned, preconception counseling and care should also be extended to women of reproductive age even if they are not actively seeking a pregnancy (Henshaw, Fam Plann Perspect, 1998).

Health care visits for women of reproductive age are opportunities to provide preconception care. A question such as: Are you planning a pregnancy? or, Could you become pregnant? might be a springboard to a discussion and may facilitate planning of the diverse reproductive options available (contraception, pregnancy preparation, infertility evaluation and so forth). Antiretroviral treatment options may differ if future pregnancy is a possibility. For new patients in HIV care, suspicion for and detection of early pregnancy is essential to appropriate management, including avoidance of potentially teratogenic drug treatments and the initiation of preventive strategies such as folic acid supplementation.

Perinatal Care

Transmission of HIV can occur in utero, during birth, and during breastfeeding. Although rates of transplacental transmission appear to be low, HIV has been found in fetal brain and liver tissues after spontaneous abortion, indicating that the virus can infect internal organs during development. Most transmission occurs during labor and delivery. Because most transmissions occur during birth, the reduction of perinatal HIV transmission has been very successful.

HIV-seropositive women can be identified during prenatal care and antiretrovirals can be given to reduce the risk of transmission. Breastfeeding increases the risk of transmission by 16%, with risk increasing with duration of breastfeeding. Interventions such as scheduled cesarean deliveries and infant formula are important in the reduction of perinatal HIV transmission.

Drug Therapy

The use of antiretroviral therapy during pregnancy followed by postexposure treatment for the newborn has been highly successful in preventing perinatal transmission of HIV in the United States. The number of cases of perinatally acquired infection in 2004 decreased by approximately 95% from the peak reported incidence in 1992, largely because of antiretroviral drug therapy during pregnancy. Data on pharmacokinetics during pregnancy are needed for new drugs and new formulations. New resistance testing recommendations need to be implemented. Also, whether use of protease inhibitors (PIs) in pregnancy is associated with increased risk of preterm delivery needs to be determined.

Obtaining information on antiretroviral pharmacokinetics in pregnancy is of particular importance in the case of PIs, since blood levels of most PIs are reduced in pregnancy. Currently there are no data in pregnancy for the newer agents fosamprenavir, tipranavir, atazanavir, and darunavir. Lopinavir/ritonavir capsules (135/50 mg) have been replaced with the higher-dose tablet...
formulation (200/100 mg), for which there are also no data in pregnancy.

Exposure to lopinavir/ritonavir during late pregnancy was lower than in the postpartum period and than in non-pregnant historic controls at the Pediatric AIDS Clinical Trials Group (PACTG) 1026 study (Stek et al, AIDS, 2006). The following statements are available at the US Department of Health and Human Services website (aidsinfo.nih.gov): “Increasing the dose of lopinavir/ritonavir in the third trimester to 4 capsules twice a day achieved adequate exposure during the third trimester but resulted in higher levels by 2 weeks postpartum (Stek et al, CROI, 2006). Another study of 16 HIV-infected primarily antiretroviral naive pregnant women who were receiving standard dosage of lopinavir/ritonavir throughout pregnancy found that 94% had trough levels above 1000 ng/mL (the minimum trough level required to inhibit wild-type HIV), and most (88%) had virologic suppression.” (Lyons et al, CROI, 2006).

The saquinavir hard-gel capsule (1200 mg) has replaced the soft-gel capsule (800 mg) in regimens with lower-dose (100 mg) ritonavir. Although the drug in the soft-gel capsule formulation had good pharmacokinetics in pregnancy, there are few data thus far on the drug in the hard-gel formulation.

“In a pharmacokinetic study of 4 pregnant women receiving saquinavir hard-gel capsule 1000 mg/ritonavir 100 mg-based regimen twice daily, trough concentrations ranged from 656 ng/mL to 2169 ng/mL and peak concentrations from 845 ng/mL to 4002 ng/mL. The minimum trough concentration for wild-type virus is 100 ng/mL.” (Hanlon et al, CROI, 2006). In a separate population pharmacokinetic study of 15 pregnant women receiving saquinavir hard-gel capsule 1000 mg/ritonavir 100 mg-based regimen twice daily, the projected median trough level was 1041 ng/mL (range, 96 ng/mL-2238 ng/mL). One woman had a trough level of less than 100 ng/mL but achieved adequate levels at an increased dose of 1200 mg saquinavir hard-gel capsule/100 mg ritonavir (Khan et al, IAC, 2004). Finally, in a study of 2 women who received saquinavir hard-gel capsule 1200 mg/ritonavir 100 mg given once daily, trough levels were 285 ng/mL and 684 ng/mL and the area-under-the concentration curve (AUC0-24) were 28,010 ng-hour/mL and 16,790 ng-hour/mL, above the target AUC of 10,000 ng-hour/mL (Lopez-Cortes et al, HIV Clin Trials, 2003). Thus, the available data suggest that 1000 mg saquinavir hard-gel capsule/100 mg ritonavir given twice daily should achieve adequate trough levels in HIV-infected pregnant women, but data are too limited to recommend once-daily dosing. Saquinavir hard-gel capsule should always be given with low-dose ritonavir boosting (Hanlon et al, CROI, 2006).

The US Department of Health and Human Services released recommendations for antiretroviral resistance testing in pregnant women in mid-2006. Drug resistance testing is recommended for: (1) all pregnant women not currently receiving antiretrovirals before starting treatment or prophylaxis and (2) all pregnant women receiving antenatal antiretroviral therapy who have virologic failure with persistently detectable HIV RNA or who have suboptimal viral suppression after initiation of antiretroviral therapy.

Lack of availability of resistance testing might present issues in settings with limited resources. Particular attention to the quick turnaround of results is necessary due to the short time interval for antiretroviral treatment during pregnancy. Health care providers for pregnant women living with HIV need to ensure that testing results are available in a short turnaround time in order to start optimal therapy or implement treatment change if necessary.

The experience with PI-containing regimens during pregnancy has been diverse and sometimes conflicting. Some data indicate that PI-containing regimens are associated with preterm delivery, resulting in a trend among European practitioners to avoid PIs during pregnancy. In a recent report, outcome of pregnancy was evaluated in a cohort of 999 women followed up at the University of Miami from 1990 to 2002 according to whether they had received antiretroviral monotherapy (n = 492), a combination without a PI (n = 373), a combination with a PI (n = 154), or no therapy (n = 358; Cotter et al, J Infect Dis, 2006). Treatment with a PI-containing combination was associated with an increased risk of preterm delivery (odds ratio [OR], 1.8; 95% confidence interval [CI], 1.1-3.0) compared with any other combination. No differences were observed in risk for low birth weight or stillbirth. A confounding factor in this analysis was that PI treatment during pregnancy was given to those women who had already been receiving PI treatment, who had low CD4+ cell count or high viral load, or who had exhibited poor clinical response to prior treatment.

These findings appear to be consistent with increased risk of preterm delivery in women receiving PI treatment in a European cohort reported in 2000. In this report, preterm delivery occurred in 16% of women using no antiretroviral therapy (n = 2819), 17% using monotherapy (n = 555), 22% using a non-PI combination (n = 188), and 29% using a combination including a PI (n = 101; European Collaborative Study and Swiss Mother and Child HIV Cohort Study, AIDS, 2000). On the contrary, a PACTG analysis indicated that preterm delivery occurred in 27% of women receiving no antiretroviral therapy (n = 66), compared with 18% for those receiving monotherapy (n = 256), 11% for those receiving a non-PI combination (n = 533), and 15% using a combination including a PI (n = 617).

In Dr Zorrilla’s setting the women at highest risk for preterm delivery are the women not receiving therapy because these women often are not receiving prenatal care and might exhibit other risk behaviors that place them at risk for preterm delivery. An examination of outcomes of PI use in 233 pregnancies showed an HIV transmission rate of 0.9%, prematurity rate (>37 weeks) of 22% (20% excluding multiple [twin and triplet] pregnancies), and an extreme prematurity rate (>32 weeks) of 2.5%. As expected, premature delivery was more common in multiple gestations (9.2-fold increased risk) and with injection drug use as the HIV risk fac-
Transmission Rate
1.8% 1.8% 4.3% 7.4% 0.8% 2.3%

Table 1. Rates of HIV Transmission in 3081 Deliveries in Pediatric AIDS Clinic Trials Group 367 Chart Abstraction Study

<table>
<thead>
<tr>
<th>HIV-1 RNA Level</th>
<th>Elective cesarean delivery</th>
<th>Vaginal delivery or emergency cesarean delivery</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1000 Copies/mL</td>
<td>Single drug 1.8%</td>
<td>7.4%</td>
</tr>
<tr>
<td></td>
<td>Antiretroviral therapy 2.3%</td>
<td>1.8%</td>
</tr>
<tr>
<td>&lt;1000 Copies/mL</td>
<td>Single drug 1.8%</td>
<td>4.3%</td>
</tr>
<tr>
<td></td>
<td>Antiretroviral therapy 0.8%</td>
<td>0.5%</td>
</tr>
</tbody>
</table>

Adapted from Shapiro et al, CROI, 2004.

There are currently no published data regarding these issues.

Active genital tract herpes simplex virus (HSV-1 or -2) infection is an indication for cesarean delivery among women in the general population. Recurrent genital manifestations of herpes infection are an indication for antiretroviral treatment during pregnancy. The strong association between self-report or clinical manifestation of genital HSV infection and HIV transmission was recently pointed out again by a retrospective analysis of 402 pregnancies in New York City between 1994 and 1999. In the context of an overall HIV transmission rate of 11.4%, the transmission rate for women with HSV infection was 28.6% (OR, 4.8; 95% CI, 1.3-17.0; \( P = .02 \); Chen et al, Obstet Gynecol, 2005). A limitation of this analysis was the lack of HSV cultures or HSV DNA testing to confirm the clinical or self-report diagnoses. Although cesarean delivery may expose women to morbidity not associated with vaginal delivery, a recent study indicates that the risk is not so great as has been previously thought.

In the National Institute of Child Health and Development International Site Development Initiative Perinatal Study in Latin American and Caribbean countries, overall risk for postpartum morbidity was low in both vaginal and cesarean deliveries, with elective cesarean delivery being associated with a statistically nonsignificant 16% increase in risk compared with vaginal delivery (Duarte et al, Am J Obstet Gynecol, 2006). In this prospective cohort study, unadjusted ORs (95% CIs) for morbidity were 1.16 (0.5-2.7) for elective cesarean delivery before labor or rupture of membrane (n=260) and 2.96 (1.3-6.7) for cesarean delivery with labor or rupture of membrane (n=139) compared with vaginal delivery (n=299).

Cervical Cancer Screening

In addition to annual examinations, the American College of Obstetricians and Gynecologists still recommends annual screening with conventional Pap or thin prep tests for cervical cancer for women under 30 years of age. For those 30 years or older, screening options consist of annual cytology, less frequent screening (every 2-3 years) in those with 3 consecutive normal test results, and combined human papillomavirus (HPV) DNA testing and cervical cytology. These guidelines, however, are for women in the general population. Until more data are available, they cannot be extended to women with HIV infection, since it is known that HIV-infected women are prone to cervical squamous intraepithelial lesions (SIL).

In examining the cumulative incidence of SIL according to baseline HPV DNA, HIV serostatus, and CD4+ cell count, the Women’s Interagency HIV Study showed that the incidence of SIL in HIV-infected women with CD4+ cell counts below 500/µL was greater than...
that in women without HIV infection on multivariate analysis, with the rate in HIV-infected women with higher CD4+ cell counts being comparable to that in HIV-seronegative women.

For now, the existing recommendations regarding surveillance of lower genital tract neoplasia in HIV-infected women should generally be followed. These include inspection of the external anogenital area as part of an annual physical exam and taking of samples of all suspicious external lesions for biopsy. Two Pap tests taken 6 months apart should be obtained within the first year of HIV diagnosis. If the results of both are negative, tests can be repeated annually in those women with CD4 + cell counts greater than 500/μL.

In those with lower counts and in those with abnormal findings Pap tests should be done every 6 months and combined with HPV testing. Colposcopy should be performed in all cases in which Pap tests reveal atypical squamous cells of undetermined significance (ASCUS) or worse. Cervical intraepithelial neoplasia (CIN) should be treated, with excisional techniques (loop electrosurgical excision procedure) being favored over cryosurgery. Localized vulvar and anal intraepithelial neoplasia should be treated conservatively — for example, with carbon dioxide laser vaporization, fulguration, or trichloroacetic acid. It should be noted that trichloroacetic acid is nonteratogenic and can thus be safely used during pregnancy or in women who might become pregnant.

All extensive external anogenital and intra-anal lesions should be monitored biannually. Antiretroviral therapy significantly enhances regression of CIN. There is a high rate of recurrence of CIN after surgery in HIV-infected women.

**Suggested Reading**


May S, Lester P, Illardi M, Rotheram-Borus MJ. Childbearing among daughters of parents with HIV. Am J Health Behav. 2006;30:72-84.

Mirochnick M, Stek A, Capparelli E, et al. Adequate lopinavir exposure achieved with a higher dose during the third trimester of...
pregnancy. [Abstract 710.] 13th Conference on Retroviruses and Opportunistic Infections. February 5-8, 2006, Denver, CO.


Perspective

HIV Testing: Rationale for Changing Recommendations

HIV testing is an important and effective strategy for preventing HIV infection. Infected individuals who know their HIV serostatus are less likely to engage in high-risk sexual behavior, and it is estimated that knowledge of HIV serostatus in unaware persons could reduce new infections by more than 30%. The availability of rapid testing for HIV expands testing opportunities. Expanded routine, voluntary, and opt-out screening in health care settings is needed to reduce the number of persons who are unaware of their HIV-infected status, get newly diagnosed patients into care, and reduce transmission of HIV infection. This article summarizes a presentation on revisions to Centers for Disease Control and Prevention HIV screening recommendations made by Robert S. Janssen, MD, at the 9th Annual Ryan White CARE Act Clinical Update in Washington, DC, in August 2006. The original presentation is available as a Webcast at www.iasusa.org.

HIV testing is an important and effective HIV prevention strategy, and the availability of rapid testing expands testing opportunities. Expanded routine, voluntary, and opt-out screening in health care settings is needed to reduce the number of persons who are unaware of their HIV-infected status, get newly diagnosed patients into care, and reduce transmission of HIV infection. The Centers for Disease Control and Prevention (CDC) has issued revised recommendations for HIV testing of adults, adolescents, and pregnant women in health care settings.

Epidemiology and Risk

The number of persons living with HIV/AIDS has increased over the past decade with the continued occurrence of new infections and the reduction in AIDS mortality due to potent antiretroviral therapy and improved medical care. It is estimated that 1,039,000 to 1,185,000 persons in the United States are living with HIV infection, with some 252,000 to 312,000 (24%-27%) being unaware of their infection (Glynn et al, Nat HIV Prev Conf 2005). Data from 33 states with name-based reporting indicate that there were approximately 112,000 diagnoses in men and 45,000 in women from 2001 to 2004. Among men, transmission occurred via sex among men who have sex with men (MSM) in 61% of cases, heterosexual sex in 17%, injection drug use (IDU) in 16%, and IDU and MSM in 5%. In women, transmission occurred via heterosexual sex in 76% of cases and via IDU in 21%. As shown in Figure 1, the highest rates of HIV/AIDS diagnosis for 2004 in these 33 states were among black men, black women, and Hispanic men. Prevention of perinatal HIV infection in the United States has been very successful, with the number of cases in 2004 representing a reduction of approximately 95% since the peak number of cases in 1992 (CDC, Surveillance Report, 2005).

![Figure 1. Estimated annual rate of HIV/AIDS diagnoses in 33 states in 2004. AVPI indicates Asian/Pacific Islander; AI/AN, American Indian/Alaska Native; W, women; M, men. Adapted from the Centers for Disease Control and Prevention: HIV/AIDS Surveillance Report, 2005.](image-url)
greater than 30%.

Unawareness of HIV serostatus is common in high-risk and high-prevalence populations. Data from 1767 MSM in Baltimore, Los Angeles, Miami, New York, and San Francisco in the National HIV Behavioral Surveillance System showed HIV prevalence of 25%, with 48% of infected individuals being unaware of their infection. Unawareness rates were 79% in those aged 18 to 24 years and 70% in those aged 25 to 29 years. The highest prevalence was among black MSM (46%), who also had the highest rate of being unaware of infection (67%) (CDC, MMWR Morb Mortal Wkly Rep, 2005).

The need for increased testing is also emphasized by the high proportion of infected individuals who are diagnosed later in their disease course. Data from 2000 to 2003 in 16 sites indicate that among 4127 persons with AIDS, 45% were diagnosed with HIV infection within 12 months of their AIDS diagnosis (“late testers”). Compared with those tested early (more than 5 years before AIDS diagnosis), late testers were more likely to be younger (18-29 years old), heterosexual, less educated, and black or Hispanic. The need for HIV testing outside of routine medical settings is emphasized by the fact that only approximately 5% of late testers and 10% of early testers had infection diagnosed by testing during a routine medical checkup. The most common reason for testing among late testers was illness (~65%) and that among early testers was “self/partner at risk” (~50%: CDC MMWR Morb Mortal Wkly Rep, 2003).

Rapid HIV Tests

The availability of rapid HIV tests promises to make a major contribution to testing as a preventive measure. One important use of these tests will be as a remedy to the high rates of non-return for results of conventional HIV testing. For example, data from 2000 indicate that 31% of individuals with positive conventional test results at publicly funded sites did not return to the sites to receive test results. In addition, rapid testing technology can answer the need for immediate information or referral for treatment choices in perinatal settings and postexposure treatment settings. Further, it is highly suitable for screening in high-volume, high-prevalence settings.

US Food and Drug Administration (FDA)-approved rapid tests include the 4 clinically available tests—2 of which have Clinical Laboratory Improvements (CLIA) waivers, meaning that clinical laboratories can apply for certification—as well as 2 more recently approved tests. Sensitivity and specificity of the first FDA-approved rapid test in 2004 and 2005 involving 14 project areas and 347 testing sites (Wesolowski et al, AIDS, 2006) are shown in Table 1. Specificity of the test was high for both whole blood and oral fluid, with the positive predictive value using oral fluid being lower than that with whole blood. Use of the rapid test was associated with a higher proportion of patients being notified of both negative and positive results. Among patients receiving the rapid test, the project area-specific median (range) percentages were 99.5% (93.7%-100%) for receipt of negative results, 100% (89.8%-100%) for receipt of preliminary positive results, and 89.7% (49.4%-100%) for receipt of confirmed positive results. By comparison, among patients having conventional EIA testing, 77.3% (30.4%-98.5%) received negative results and 81% (33.3%-100%) received confirmed positive results.

The first approved rapid test was also used in the Mother Infant Rapid Intervention at Delivery (MIRIAD) study, for testing of women in labor for whom HIV serostatus was unknown (Bulterys et al, JAMA, 2004). Among 7680 women screened in 12 hospitals in 5 cities, 54 (0.7%) new HIV infections were identified. Rapid testing yielded 6 false-positive results and no false-negatives; EIA yielded 15 false-positive results. Specificity was 99.92% with rapid testing and 99.80% with EIA; positive predictive values were 90% and 76%, respectively.

<table>
<thead>
<tr>
<th>Number of tests</th>
<th>Project-specific Median (Range) Percentages</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HIV seropositive</strong></td>
<td><strong>Estimated specificity</strong></td>
</tr>
<tr>
<td><strong>Rapid Test</strong></td>
<td></td>
</tr>
<tr>
<td>Whole blood</td>
<td>135,724</td>
</tr>
<tr>
<td>Oral fluid</td>
<td>26,066</td>
</tr>
<tr>
<td><strong>Conventional Test</strong></td>
<td>31,811</td>
</tr>
</tbody>
</table>

Data are using the first rapid HIV test approved by the US Food and Drug Administration. Adapted from Wesolowski et al, AIDS, 2006. PPV indicates positive predictive value.
Improving Scope and Yield of Testing

Data from 2000 to 2003 indicate that some 38% to 44% of adults aged 18 to 64 years have been tested for HIV in the United States, and that 16 to 22 million persons aged 18 to 64 years are tested annually. Most testing is done through private doctors or health maintenance organizations (Table 2). However, testing in hospitals, emergency departments (EDs), outpatient clinics, and in public community clinics accounts for greater proportions of positive test results. For example, testing in public clinics accounts for 9% of tests but 21% of positive test results.

The former CDC recommendations for HIV testing in adults and adolescents included routine screening in settings with high HIV prevalence (≥1%), targeted testing based on risk assessment, and annual testing for sexually active MSM. However, these recommendations do not appear to have increased testing in many settings, including the acute care setting. For example, in 108 million ED visits in 2000, including 68.3 million by patients aged 18 to 64 years, HIV serology was performed in 215,000; in 2002, there were 110 million ED visits, including 69.6 million by patients aged 18 to 64 years, and HIV serology was performed in 163,000.

HIV screening is feasible in acute care settings and can be facilitated by use of rapid tests and opt-out testing, in which testing is routine but can be refused by the client. A program of rapid test ED screening showed that an estimated 3.2% of tests were positive at Johns Hopkins ED in Baltimore, 2.7% at Grady ED in Atlanta, 2.3% at Cook County ED in Chicago, 1.3% at King-Drew Medical Center in Los Angeles, and 1.2% at Alameda County Medical Center in Oakland, compared with 1.1% of tests at CDC-funded counseling and testing sites. In an examination of the feasibility of voluntary, opt-out testing in sexually transmitted disease (STD) clinics in Texas in 1996 and 1997, the strategy increased the proportion of eligible clients receiving testing to 97% (23,020 of 23,686) compared with 78% (14,927 of 19,184) with voluntary, opt-in testing. The number of positive tests increased from 168 to 268. Since that time, opt-out testing has been routine, with proportions of eligible clients receiving HIV testing being 90% or more since the second half of 1998, and 95% or more since 2003.

An early examination of opt-out screening in pregnant women showed that whereas only 35% accepted testing with opt-in consent, with some feeling that agreeing to testing implied high-risk behavior, 88% accepted testing offered as routine opt-out testing, with clients exhibiting markedly less anxiety regarding testing. Previous CDC recommendations for pregnant women included: routine, voluntary testing as early as possible as a part of prenatal care; simplified pre-test counseling; flexible consent process; HIV rapid testing and treatment during labor and delivery for women without prenatal testing; and re-screening in the third trimester for select, high-risk women.

Revisions of Recommendations for Screening

Recent revisions of CDC recommendations for HIV testing include universal screening in health care settings (CDC, MMWR Morb Mortal Wkly Rep, 2006). The rationale for revising the previous recommendations included the facts that many HIV-infected persons access health care but are not tested for HIV until they are symptomatic and that awareness of HIV infection leads to substantial reductions in high-risk sexual behavior. The adoption of a universal screening strategy is facilitated by the reduced need for pre-test counseling associated with the high levels of knowledge about HIV in the general population. Further, there is inconclusive evidence about prevention benefits from typical counseling for persons who test negative. Screening in the antiretroviral therapy era is cost-effective as well.

A recent report concluded that even in relatively low-prevalence areas, cost effectiveness of routine HIV screening is similar to that of commonly accepted interventions (Sanders et al, N Engl J Med, 2005), estimates were $15,078 and less than $50,000 per quality-adjusted life year for HIV prevalence rates of 1% and greater than 0.5%, respectively. Another analysis concluded that routine, voluntary screening for HIV once every 3 to 5 years is justified on both clinical and cost-effectiveness grounds in all but the lowest-risk populations, and that one-time screening in the general population may also be cost-effective (Paltiel et al, N Engl J Med, 2005).

Revised recommendations for HIV screening are shown in Table 3. The new recommendations include routine, voluntary screening for all persons aged 13 to 64 years in health care settings, with screening not to be based on prevalence or risk. Opt-out screening is recommended, with the patient having

Table 2. Sources of HIV Tests and Positive Tests

<table>
<thead>
<tr>
<th>Source</th>
<th>HIV tests (%)</th>
<th>Positive tests (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Private doctor or health maintenance organization</td>
<td>44</td>
<td>17</td>
</tr>
<tr>
<td>Hospital, emergency department, outpatient clinic</td>
<td>22</td>
<td>27</td>
</tr>
<tr>
<td>Public community clinic</td>
<td>9</td>
<td>21</td>
</tr>
<tr>
<td>HIV counseling/testing facility</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Correctional facility clinic</td>
<td>0.6</td>
<td>5</td>
</tr>
<tr>
<td>Sexually transmitted disease clinic</td>
<td>0.1</td>
<td>6</td>
</tr>
<tr>
<td>Drug treatment clinic</td>
<td>0.7</td>
<td>2</td>
</tr>
</tbody>
</table>

1Adapted from Centers for Disease Control and Prevention, MMWR Morb Mortal Wkly Rep, 2004.
2Adapted from the supplement to HIV/AIDS Surveillance 2000-2003 (Centers for Disease Control and Prevention, unpublished data)
Table 3. Revised HIV Screening Recommendations

Non-pregnant Adults and Adolescents
Intended for all health care settings, including inpatient services, emergency departments, and urgent care, sexually transmitted disease, tuberculosis, public health, community, substance abuse, and correctional facility clinics.
- Routine, voluntary HIV screening for all persons aged 13 to 64 years in health care settings, not based on prevalence or risk
- Repeat HIV screening of persons with known risk at least annually
- Opt-out HIV screening with the opportunity to ask questions and the option to decline; include HIV consent with general consent for care
- Prevention counseling in conjunction with HIV screening in health care settings not required
- Provision of clinical HIV care or establishment of reliable referral to qualified providers
- Review and revision of state and local regulations as needed
- Consideration of “sunset” provision in low-prevalence settings:
  - Initiate screening
  - If HIV prevalence shown to be less than 1 per 1000, continued screening no longer warranted

Pregnant Women
- Universal opt-out HIV screening
  - Include HIV in panel of prenatal screening tests
  - Consent for prenatal care includes HIV testing
  - Notification and option to decline
- Second test in third trimester for pregnant women:
  - Known to be at risk for HIV
  - In key jurisdictions
  - In high-prevalence health care facilities
- Opt-out rapid testing for women with undocumented HIV serostatus in labor or delivery
  - Initiate antiretroviral prophylaxis on basis of rapid test result
- Newborn testing if mother’s serostatus unknown

Adapted from Centers for Disease Control and Prevention, MMWR Morb Mortal Wkly Rep, 2006.

the opportunity to ask questions and the option to decline testing.
These recommendations are intended to apply to all health care settings, including inpatient services, EDs, and urgent care, STD, tuberculosis (TB), public health, community, substance abuse, and corrections facility clinics. For low-prevalence settings, “sunset” provisions may be considered, in which screening can be discontinued if HIV prevalence is found to be below 1 per 1000 population.

Revisions for pregnant women (Table 3) include universal opt-out screening, a second test in at-risk women during the third trimester of pregnancy, opt-out rapid testing for women without documented HIV serostatus during labor or delivery, and testing of newborns of mothers with unknown infection status.

Expanded HIV screening raises a number of issues, including the question of who will pay for the testing. It is hoped that the recommendation for universal screening will stimulate payors to reimburse for testing as they do for other types of screening. There will still be a need for publicly funded testing. Expanded testing will also require renewed attention to ensuring that access to care is available for newly diagnosed patients. Although routine testing helps to remove the stigma of testing, there is still work to be done in reducing the stigma of diagnosis.

An increased number of diagnoses also entails increased demands in terms of partner notification. In this regard, important steps for clinicians and case managers include: communicating with health department partner services staff to become familiar with the services and how to access them; asking at the patient’s initial visit about sex and drug injection partners and whether they have been informed of risk; screening patients for behavioral risks and STDs that may indicate a need for further discussion about partners; and referring patients to the health department for assistance with partner notification.


Dr Janssen has no relevant financial affiliations to disclose.

Suggested Readings


Marks G, Crepaz N, Janssen RS. Estimating sexual transmission of HIV from persons aware and unaware that they are infected with the virus in the USA. AIDS. 2006;20:1447-1450.


Perspective

Syphilis and Other Sexually Transmitted Diseases in HIV Infection

An ongoing resurgence of syphilis and continued transmission of other common sexually transmitted diseases (STDs) in HIV-infected patients is fueled by a number of factors, including “prevention burnout” resulting from fatigue with long-term, safer-sex behavior, use of recreational drugs (notably methamphetamine), and false sense of security associated with HIV serosorting and elevated CD4+ cell count. Annual screening for common STDs is recommended for HIV-infected patients. Issues in syphilis and herpes simplex virus-2 (HSV-2) diagnosis and treatment are discussed. New problems are briefly reviewed, which include the increased reporting of lymphogranuloma venereum and the increased frequency of fluoroquinolone-resistant gonorrhea. The recently revised Centers for Disease Control and Prevention guidelines for treatment of syphilis, HSV-2 infection, chlamydial infection, and gonorrhea are summarized. This article summarizes a presentation on syphilis and other STDs made by Jeanne Marrazzo, MD, MPH, at an International AIDS Society–USA Continuing Medical Education course in New York, in October 2006. The original presentation is available as a Webcast at www.iasusa.org.

Syphilis and other sexually transmitted diseases (STDs) are resurgent in HIV-infected patients. Factors involved in ongoing STD transmission include: improvements in HIV therapy leading to increased well-being and survival attended by resumption of risky sex behaviors; “prevention fatigue” (ie, burnout over safer-sex practices); increased use of recreational drugs (eg, methamphetamines, poppers, and erectile dysfunction drugs); use of the Internet as a venue to meet sex partners, especially anonymous partners; and what appears to be false assurance afforded by HIV serosorting or elevated CD4+ cell counts. With regard to the latter, for example, a study of 338 men who have sex with men (MSM) in primary HIV care found that those who reported participating in insertive anal sex were 5 times less likely to use condoms when their partners were HIV seropositive than when they were HIV seronegative. Similarly, those with higher CD4+ cell counts were 20% more likely to have unprotected receptive anal sex than those with lower CD4+ cell counts (Bachmann et al, Sex Transm Dis, 2005). For these reasons, annual screening for common STDs is recommended in HIV-infected patients, with more frequent screening being warranted if risk behaviors are reported.

Syphilis

After a 2005 STD update presentation made by Dr Marrazzo in Washington state, a course attendee opined “She spent too much time on syphilis. I’ll never see a case.” Such a mind-set probably ensures that this will be the case, since the diagnosis can easily be missed if one is not looking to make it. Reported syphilis cases have increased markedly in MSM in King County, Washington since 1997 (Figure 1; Public Health-Seattle and King County [PHSKC] data, 2004). A similar resurgence is being observed in many metropolitan locales and more rural settings throughout the country. If one is not finding cases of syphilis among HIV-infected patients in metropolitan centers, one may not be looking hard enough. In Dr Marrazzo’s venue, more than half of syphilis cases in MSM are in HIV-infected men, with 4% of cases in heterosexual patients occurring in those with HIV infection. The median

Figure 1. Early syphilis incidence among men who have sex with men (MSM) by HIV serostatus in King County, Washington from 1997 to 2004. (Public Health-Seattle and King County data, 2004).

Dr Marrazzo is an Associate Professor of Infectious Diseases at the University of Washington in Seattle.
age of syphilis cases in MSM in Dr Marrazzo’s venue is 34 years.

Methamphetamine deserves special mention as a risk factor for STD transmission. Its use is common on the West Coast and in rural areas and it is becoming more common on the East Coast. There are clear epidemiologic links between methamphetamine and the current syphilis outbreak in MSM. The drug, which is very easy to obtain or make (recipes can be found online), reduces social inhibitions, increases libido and prolongs sexual arousal, allows for sustained energy level and lack of sleep, and results in reduced use of barrier protection (Krawczyk et al, MMWR Recomm Rep, 2006). It may also exert an independent biologic effect in increasing HIV viral load and may directly suppress CD4+ cell function.

Syphilis is caused by Treponema pallidum. Primary syphilis often presents with a chancre, or ulcer, and is usually followed in 3 weeks to 3 months by secondary syphilis, evidenced by a “trepnmonic event” consisting of rash, fever, and neurologic symptoms. Nephrotic syndrome and even glomerulonephritis may occur in this stage. This is followed by a long latent period (eg, 5-50 years) before onset of tertiary syphilis consisting of neurologic disease, gummas (a necrotic lesion that can occur in bone or brain), and cardiac disease.

The identification and treatment of “early” syphilis (ie, primary, secondary, or latent syphilis) within 1 year of acquisition is crucial since there is low likelihood of transmission thereafter. The chancre of primary syphilis is typically (but not invariably) painless and has a heaped-up border and a nonpurulent base (Figure 2). In some cases, it can be mistaken for a herpes simplex virus (HSV) lesion. It can occur as a vaginal, vulvar, or cervical lesion in women; internal lesions (vaginal, vulvar) are nearly always asymptomatic. Chancre associations with positive nontreponemal serology (ie, rapid plasma reagin [RPR] or Venereal Disease Research Laboratory [VDRL]) in only approximately 70% of cases. The rash in secondary syphilis (Figure 2) is typically maculopapular and classically involves the hands or soles of the feet. However, the rash can assume almost any form (eg, pustular, vesicular). Other characteristic findings include condyloma lata that may occur at any moist body site and are particularly common in the perianal area. Oral mucous patches are common and often are misidentified as aphthous ulcers or other types of lesions.

Standard serologic tests for syphilis are the RPR and VDRL, which provide quantitative measurement of antigen (cardiolipin–lecithin–cholesterol antigen) that is not specific to T pallidum. These tests are also used to assess treatment response, with a 4-fold decline in antigen titer over 6 months being considered evidence of adequate response. The test used in initial diagnosis should also be used for assessing response, since there can be a 2-fold difference in measured antigen titer between the different tests. The treponemal tests, T pallidum particle agglutination
those not on antiretroviral therapy. Those with low CD4+ cell counts and with poorer response being observed in is problematic in HIV-infected patients, and 24 months (compared with 6, 12, nontrepo-
mal testing done at 3, 6, 9, 12, 18, without HIV infection, with nontrepo-
more frequent intervals than in patients

Patients consists of standard stage-ap-
nication (TP-PA) and fluorescent trepone-
mal antibody absorption (FTA-ABS), are qualitative tests used to confirm initially positive VDRL or RPR results. A treponemal enzyme immunoassay is another test often used for screening. However, false-positive results can occur with this test, particularly in low-prevalence settings. Positive findings should be con-
firmed with a standard nontreponemal test titer to guide management. Some prac-
titioners recommend LP for all HIV-in-
fected patients with syphilis, regardless of disease stage. A more conservative approach is to perform LP in any pa-
ient with neurologic or ophthalmic signs or symptoms, and to base the decision in other patients on CD4 + cell count and syphilis titer (Figure 3; Marra et al, J Infect Dis, 2004).

Neurologic or ophthalmic signs or symptoms

No
RPR ≥ 1:32
No

CD4+ count ≤ 350 cells/µL

Yes

HIV seropositive

No

Consider LP

No LP

Figure 3. One approach to decision whether to perform lumbar puncture in patients without neurologic or ophthalmic signs or symptoms of syphilis. Adapted from Marra et al, J Infect Dis, 2004.

LP indicates lumbar puncture; RPR, rapid plasma reagin.

Treatment for syphilis in HIV-infected patients consists of standard stage-appropriate treatment (see below). Serologic follow up should be performed at more frequent intervals than in patients without HIV infection, with nontreponemal testing done at 3, 6, 9, 12, 18, and 24 months (compared with 6, 12, and 24 months in patients without HIV infection). Clearance of neurosyphilis is problematic in HIV-infected patients, with poorer response being observed in those with low CD4+ cell counts and those not on antiretroviral therapy.

Risk of neurosyphilis is increased 3- to 4-fold when the CD4+ cell count is below 350/µL and by 19-fold if there is also a finding of serum VDRL titer above 1:32. Currently, there is no consensus on the use of lumbar puncture (LP) to guide management. Some practitioners recommend LP for all HIV-infected patients with syphilis, regardless of disease stage. A more conservative approach is to perform LP in any patient with neurologic or ophthalmic signs or symptoms, and to base the decision in other patients on CD4+ cell count and syphilis titer (Figure 3; Marra et al, J Infect Dis, 2004).

Neurologic findings may include hearing loss or any other cranial neuropathy; ophthalmic findings can include uveitis or retinitis. Abnormality of any cerebrospinal fluid (CSF) parameter should be considered evidence of central nervous system (CNS) involvement in the setting of positive serology, consistent exam findings, or known exposure. Such abnormalities include elevated white blood cell (WBC) count (usually lymphocytes; a 5-fold or higher elevation is typical, although some authors have used an increase of 20-
fold or higher to account for HIV-related pleocytosis), elevated protein level, positive CSF VDRL (CSF VDRL has a false-negative rate of 50%-70%), and positive FTA-ABS or TP-PA (the latter 2 tests are very sensitive, but not specific when applied to CSF; this means they are helpful if they are negative).

All individuals who have had sexual exposure to a patient with syphilis within the past 90 days should have treatment. The Centers for Disease Control and Prevention (CDC) have recently issued revised recommendations for STD treatment. Those for syphilis are shown in Table 1. Benzathine penicillin (L.A. or long-acting) which contains 2.4 million units (MU) of benzathine penicillin G, is recommended for primary, secondary, or early latent syphilis. No other penicillin formulation should be used, including penicillin G benzathine, a mixture of 1.2 MU benzathine penicillin G and 1.2 million MU procaine penicillin G (which has been mistakenly used).

There has been some use of more than one injection of benzathine penicillin in HIV-infected patients in this setting, but there is no evidence to support any better outcomes using this approach. Further, benzathine penicillin is in short supply, and it is probably better to preserve additional doses for use in treating late latent infection. Use of azithromycin results in development of rapid resistance to the drug. For those who cannot tolerate penicillin or have a history of anaphylaxis, oral doxycycline can be used, although it is probably an inferior regimen.

A newer option for early syphilis is ceftriaxone 1g given intravenously or intramuscularly daily for 8 to 10 days. Parenteral penicillin G is used for neurosyphilis, with ceftriaxone 2g per day being an option in those who cannot tolerate penicillin. Desensitization can be considered in patients who are allergic to both penicillin and cephalosporins.

Herpes Simplex Virus-2

Genital infection with herpes simplex virus-2 (HSV-2) is a largely hidden epidemic. Approximately 20% of the adult US population is seropositive for
HIV RNA level. HSV-2 may increase susceptibility to HIV via disruption of normal barriers (eg, skin ulceration) and recruitment of target CD4+ cells to the site of viral activity, and directly promote replication of HIV. HSV-2 may increase infectiousness of HIV by increasing HIV shedding at the mucosal surface, irrespective of whether lesions are present, and via the increased recurrences and severity of recurrences of HSV-2 that occur with coinfection.

HSV-2 testing requires use of type-specific HSV-2 gG-based serology that accurately distinguishes HSV-2 from HSV-1 infection. Several type-specific kits are commercially available, with some variation in reported sensitivity, specificity, and cost. The Western blot assay is considered the gold standard but is not commercially available, is relatively expensive and is less specific and sensitive than some kit assays. Although the recently published CDC guidelines do not recommend universal screening for HSV-2, they recommend testing in all HIV-infected individuals, MSM, and individuals with multiple sex partners, as well as in individuals with recurrent symptoms and negative culture, those with clinical diagnosis without laboratory confirmation, those with sex partners who have genital herpes and who want to know their own infection status, and those who request testing.

Recommended treatment of first episodes and recurrences and recommended suppressive therapy in HIV-infected persons are shown in Table 2. One change in recommendations in the recent guidelines is the omission of the 5-times daily acyclovir regimen from the options for treating recurrence, simply because of its lack of convenience. The new guidelines add the possibility of using valacyclovir therapy (500 mg orally once daily) to prevent transmission of HSV-2 to uninfected partners. Indications may include serodiscordant couples (evidence of benefit is available only for serodiscordant heterosexual couples thus far), persons with numerous sex partners, MSM, and HIV-infected individuals. Annual assessment of the discordant partner for seroconversion is recommended if this strategy is used.

Proctocolitis: Lymphogranuloma Venereum

In a recent case, a 34-year-old man with HIV infection and CD4+ cell count of 200/µL presented with rectal discharge, bleeding, and pain that had begun 2 months before presentation. Colonoscopy showed rectal ulcers with inflammation, friable mucosa, and no abscess. He had been treated for chlamydial infection, gonorrhea, and syphilis. The symptoms had recurred recently, with severe pelvic pain radiating to his back. Diagnostic tests for Chlamydia trachomatis from the rectal mucosa were obtained and the patient was started on oral doxycycline. The patient was found to have lymphogranuloma venereum (LGV), which is caused by LGV strains of C trachomatis. LGV is endemic in Southeast Asia, South America, the Caribbean, and Africa.

The classic presentation involves inguinal lymphadenopathy and genital ulcers. Cases of LGV-related proctitis

### Table 1. Centers for Disease Control and Prevention Guidelines for Treatment of Syphilis

<table>
<thead>
<tr>
<th>Stage</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| Primary, Secondary, and Early Latent | - Benzathine penicillin (L-A) single dose IM 2.4 MU
- Do not use other penicillin formulations
- Do not use azithromycin
- Doxycycline 100 mg po bid × 14 d (inferior)
- Ceftriaxone 1 g IV or IM daily × 8-10 d (alternative) |
| Late Latent | - Benzathine penicillin IM 2.4 MU weekly × 3 doses (7.2 MU total)
- Doxycycline 100 mg po bid × 28 d (inferior) |
| Neurosyphilis | - Aqueous penicillin G 18-24 MU/d × 10-14 d
- Procaine penicillin G 2.4 MU/d PLUS probenecid 500 mg po qid × 10-14 d
- Ceftriaxone 2 g IV daily × 10-14 d (alternative) |

Adapted from Centers for Disease Control and Prevention, MMWR Morb Mortal Wkly Rep, 2006.

IM indicates intramuscularly; IV, intravenously.

Table 2. Centers for Disease Control and Prevention Guidelines for Treating Genital Herpes Simplex Virus-2 Infection in HIV-infected Patients

<table>
<thead>
<tr>
<th>Type</th>
<th>Treatment</th>
</tr>
</thead>
</table>
| First Episode (Same as in HIV-seronegative Patients) | Acyclovir 400 mg tid × 7-10 d
Acyclovir 200 mg 5x/d × 7-10 d
Famciclovir 250 mg tid × 7-10 d
Valacyclovir 1 g bid × 7-10 d |
| Episodic Treatment of Recurrences | Acyclovir 400 mg tid × 5-10 d
Famciclovir 500 mg bid × 5-10 d
Valacyclovir 1 g bid × 5-10 d |
| Suppressive Treatment | Acyclovir 400-800 mg bid or tid
Famciclovir 500 mg bid
Valacyclovir 500 mg bid |

Adapted from Centers for Disease Control and Prevention, MMWR Morb Mortal Wkly Rep, 2006.
Table 3. Centers for Disease Control and Prevention Guidelines for Treatment of Chlamydial Infection

<table>
<thead>
<tr>
<th>General</th>
<th>Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Azithromycin 1 g po, single dose, directly observed</td>
</tr>
<tr>
<td></td>
<td>Doxycycline 100 mg po bid × 7 d</td>
</tr>
<tr>
<td>Alternative</td>
<td>Ofl oxacin 300 mg po bid or levofloxacin 500 mg qd × 7 d</td>
</tr>
<tr>
<td></td>
<td>Erythromycin 500 mg po qid × 7 d</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>In Pregnancy</th>
<th>Recommended</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Azithromycin 1 g po × 1</td>
</tr>
<tr>
<td></td>
<td>Amoxicillin 500 mg po tid × 7 d</td>
</tr>
<tr>
<td>Alternative</td>
<td>Erythromycin base 500 mg po qid × 7 d</td>
</tr>
<tr>
<td></td>
<td>Erythromycin base 250 mg po qid × 14 d</td>
</tr>
<tr>
<td></td>
<td>Erythromycin ethylsuccinate 800 mg po qid × 7 d</td>
</tr>
<tr>
<td></td>
<td>Erythromycin ethylsuccinate 400 mg po qid × 14 d</td>
</tr>
</tbody>
</table>

Adapted from Centers for Disease Control and Prevention, MMWR Morb Mortal Wkly Rep, 2006.

have been seen in the United States, usually involving HIV-infected individuals or MSM and usually involving the L2 LGV serovar. The cases typically have involved delayed diagnosis.

Proctocolitis can be caused by chlamydial infection, HSV infection (typically HSV-2), gonorrhea, syphilis, and occasionally enteric pathogens (more common when upper colon symptoms are present). Nucleic acid amplification tests have not been cleared by the US Food and Drug Administration (FDA) for use with rectal specimens, but they can be used in diagnosis if they are validated by a local laboratory. Cell culture also can be used if available.

Specific diagnosis of LGV is difficult. Identification of LGV serovars requires serotyping of isolates obtained by direct culture of the rectal mucosa, or nucleic acid amplification test genotyping, and neither is widely available. Serologic tests are recommended but can be done only by specialized reference laboratories (there are approximately 20 such laboratories in the United States). The tests are technically demanding and titers for LGV proctocolitis are not well defined. If LGV is suspected, presumptive treatment should be considered and the local health department contacted. Treatment consists of doxycycline 100 mg twice daily for 21 days, longer than the recommended treatment duration for other chlamydial infections (Table 3).

Gonorrhea

In another recent case, a 28-year-old HIV-infected man presented with purulent urethral discharge. Gram stain revealed Gram-negative intracellular diplococci. He had no known allergies to medications. He reported unprotected receptive oral sex with other men. Management of this case may include presumptive treatment with a single oral dose of cefixime, if available (see Table 4 for other options) and should include empiric treatment for all sex partners within the previous 60 days. Since the finding of chlamydial infection is common when gonorrhea is present (the converse is not true), the patient should also be given a regimen aimed at both gonorrhea and chlamydial infection (eg, addition of azithromycin or doxycycline).

Management in this case should not include presumptive treatment with a single dose of a recommended fluoroquinolone if oral cefixime is not available. Rates of fluoroquinolone resistance in Neisseria gonorrhoeae are increasing and are very high among MSM throughout the United States, in general in West Coast states, and in individuals who have acquired a resistant strain of the organism prevalent in Southeast Asia and Hawaii. In the United States, overall rates of resistance are approximately 8% in heterosexual persons and 23% in MSM. Current CDC guidelines thus recommend against using fluoroquinolones for gonorrhea in MSM. For these reasons, a sexual history and travel history should be taken before prescribing a fluoroquinolone for gonorrhea. Current general recommendations for gonorrhea treatment are shown in Table 4. It should be noted that a CDC recommendation against using quinolones for any gonorrhea is expected.

A Piercing Observation

A 20-year-old woman presented to the emergency department anxious because her partner’s “Prince Albert” penile piercing was noted to be missing soon after vaginal intercourse (Das et al, Obstet Gynecol, 2005). Exams were
unremarkable. However, pelvic film revealed a small discoid shape, consistent with the metal bearing used to fasten the penile ring, in the lower abdomen-upper pelvic region, suggesting the object had migrated through the cervix and uterus into the fallopian tubes. The patient had been prepared for diagnostic laparoscopy when an astute physician obtained a complete sexual history, finding that the patient had performed oral sex on her partner prior to vaginal intercourse. Laparoscopy was postponed, and the follow-up pelvic film 1 week later was normal.

A thorough sexual history is invaluable to accurate diagnosis and management.


Financial disclosure: Dr Marrazzo has served as a paid lecturer for Merck and 3M, as a consultant for Quidel and Mission Pharmacal, and is on the Speaker’s Bureau for Merck and 3M.

Suggested Readings


Letter

To the Editor: Thank you for the superb review on structured treatment interruptions (STIs) summarized by Dr Benson. The article generously cites our work regarding treatment interruptions. Most of the summary is perfectly accurate. There are, however, 2 points to which I would like to draw your attention.

First, regarding the Swiss-Spanish Intermittent Therapy Trial, the summary states: “improved host cellular responses could not be achieved in most patients with chronic HIV infection, although a small number of patients appeared to have a short-term response.” Figure 1 demonstrates robust stimulation of HIV-specific immune response as measured by enzyme-linked immunospot analysis (ELISPOT). Results shown are in all 71 patients for whom results from weeks 0 and 52 were available. All patients stayed off therapy between weeks 40 and 52. Responders have a statistically significant lower number of spot-forming cells (SFCs) than nonresponders (P = .01; Mann-Whitney test). The response is about an order of magnitude greater than the immune response to most experimental vaccines.

The essential point of the paper is summarized in the right side of this figure. Although there was a robust immune (ELISPOT) response, it did not correlate with better control of viremia after cessation of antiretroviral therapy. To the contrary, patients with more ELISPOT values tended to have a higher HIV-1 RNA rebound. The real issue is not that STIs failed to stimulate the immune response, but that this stimulation is irrelevant to control of HIV viremia while the patient is off the drugs.

Secondly, regarding the Staccato trial, the summary states: “No differences in low-density lipoprotein cholesterol or triglyceride levels were observed...” There were differences in favor of the STI group, many of which were statistically significant as can be seen in Table 1.

Bernard Hirschel, MD
Geneva University Hospital
Geneva, Switzerland

Dr Hirschel has no relevant financial affiliations to disclose.

Table 1. Lipid Values in Scheduled Treatment Interruption (STI) and Continued Therapy (CT) Groups

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>24 Weeks</th>
<th>48 Weeks</th>
<th>ERT</th>
<th>End of Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>STI</td>
<td>CT</td>
<td>STI</td>
<td>CT</td>
<td>STI</td>
</tr>
<tr>
<td>Total Cholesterol</td>
<td>5.1</td>
<td>5.3</td>
<td>4.8</td>
<td>5.2*</td>
<td>4.7</td>
</tr>
<tr>
<td>(μmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LDL-Cholesterol</td>
<td>3.2</td>
<td>3.3</td>
<td>3.1</td>
<td>3.4*</td>
<td>3.1</td>
</tr>
<tr>
<td>(μmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Triglycerides</td>
<td>2.0</td>
<td>2.1</td>
<td>1.6</td>
<td>2.1†</td>
<td>1.6</td>
</tr>
<tr>
<td>(μmol/L)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>59.4</td>
<td>59.9</td>
<td>60.0</td>
<td>59.8</td>
<td>59.7</td>
</tr>
</tbody>
</table>

All patients received 12 to 24 weeks of antiretroviral therapy between the end of the randomized treatment (ERT) and the final visit. Adapted from Ananworanich et al, Lancet, 2006. *P<.01; †P<.05

References


In reply: Thank you for your clarifications. My intention related to the review of the Swiss-Spanish Intermittent Therapy Trial was to make the same point that you did, that is, that stimulation of a broad immune response with structured treatment interruption was not correlated with an improved ability to control viremia off therapy. Secondly, with regard to the Staccato trial results, the study had not been published yet at the time I reviewed the data for this article, so I had access only to the information that was presented briefly at the 13th Conference on Retroviruses and Opportunistic Infections. Your further explanation of the lipid results is appreciated.

Constance A. Benson, MD
University of California San Diego
San Diego, CA

Dr Benson has served as a scientific advisor to Achillion, Boehringer Ingelheim, GlaxoSmithKline, Johnson & Johnson, and Merck, and receives research support from Gilead.

Figure 1. Left: numbers of HIV-specific, interferon-γ-producing, CD8+ spot forming cells per million peripheral blood lymphocytes (HIV-IFN-CD8+ SFC/10⁶ PBL). Right: number (and median) of SFC/10⁶ PBL in responders and nonresponders. Adapted from Fagard et al, Arch Intern Med, 2003.
Educational Programs of the International AIDS Society–USA

Established in 1992, the International AIDS Society–USA is a not-for-profit, HIV clinical specialist-education organization. The mission of the International AIDS Society–USA is to improve the treatment, care, and quality of life of persons with HIV and AIDS through balanced, relevant, innovative, and state-of-the-art education and information for practitioners who are actively involved in HIV and AIDS care. The organization’s educational activities are particularly intended to bridge clinical research and patient care.

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Chinazo Cunningham, MD, and Hillary V. Kunins, MD
CME Credit Available: 1.5 hours

Diagnosis and Management of Immune Reconstitution Syndrome in HIV-infected Patients
Jaime C. Roberston, MD, and Carl J. Fichtenbaum, MD
CME Credit Available: 1 hour

The Importance of Viral Fitness and Drug Resistance in Chronic and Recent HIV Infection
Mark A. Wainberg, PhD, and Dan Turner, MD
CME Credit Available: 1 hour

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Chairs: Ronald T. Mitsuyasu, MD and Constance A. Benson, MD

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April 27, 2007
Westin Peachtree Plaza
Chairs: Michael S. Saag, MD, and Jeffrey L. Lennox, MD

Chicago, IL
May 7, 2007
Marriott Downtown Chicago
Chairs: John P. Phair, MD, and Harold A. Kessler, MD

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May 23, 2007
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Chairs: Henry Masur, MD, and Michael S. Saag, MD

San Francisco, CA
May 31, 2007
Grand Hyatt San Francisco
Chairs: Robert T. Schooley, MD, and Stephan E. Follansbee, MD

10th Annual Ryan White CARE Act Clinical Update
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For clinicians in RWCA-funded clinics only
June 14-16, 2007
Hyatt Regency Phoenix
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October 19, 2007
New York Marriott Marquis
Chairs: Douglas T. Dieterich, MD and Roy M. Gulick, MD, MPH

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