

MASTER CLASS

HIV and Nonpregnant Women



E. ALBERT
REECE, M.D.,
PH.D., M.B.A.

Since the beginning of the HIV/AIDS epidemic in the 1980s, women have been affected with this dreaded disease. Many have been at risk of acquiring the virus, many have become infected, and some consequently have been at risk of transmitting the virus to their offspring.

Ob.gyns. have played a major role in the dramatic decrease in mother-to-child transmission since its peak in 1992; prenatal screening followed by the use of anti-retroviral therapy in women found to be HIV infected has reduced the risk of HIV transmission from a woman to her child to less than 2%.

Among nonpregnant women, our frequency of HIV testing has been variable, depending, for many of us, on the prevalence of HIV/AIDS in our communities and on our knowledge and/or perception of each patient's risk level.

In recent years, this selective approach to testing has been deemed faulty. It is an approach that has been subject to our own biases of risk and to misperceptions of many of the women we care for. Moreover, a risk-based approach has increasingly conflicted with the changing

face of AIDS/HIV infection – most notably, the rise in heterosexual transmission and the fact that 1 in 5 infected individuals (including our patient's sexual partners) are estimated to be unaware of their infection.

Studies have shown that many women who are found to be HIV positive did not consider themselves to be at risk. Had we seen these women, we might not have considered them to be at risk either. According to the most recent HIV Surveillance Report from the Centers for Disease Control and Prevention, 30% of HIV-positive women were tested for HIV late in their illness (that is, diagnosed with AIDS within 1 year of testing positive). Had they been diagnosed earlier, these women could have had years added to their lives with the early and ongoing use of highly active antiretroviral therapy.

For these and other reasons, there are significant public health advantages to the recommendation issued by the CDC 5 years ago that health care providers routinely test (with patient notification and an opportunity to decline) all patients aged 13-64 years.

As providers for women of all ages, it is important that we are aware of changing trends and issues in the HIV epidemic and that we are attentive to the CDC's recommendations. It is for this reason that I have invited Dr. Arlene D. Bardeguet to address the role that the

ob.gyn. plays in HIV prevention and testing in non-pregnant women.

Dr. Bardeguet serves as professor in the department of obstetrics, gynecology and women's health and director of HIV services at the New Jersey Medical School, Newark, N.J. Her special interest and expertise in HIV-infected women is evident in her clinical work and patient care, her research and writing, her teaching, and her work in the policy arena.

Here, she explains why HIV prevention strategies, including HIV pre- or postexposure prophylaxis, should become part of our routine clinical care. She also details how we can care for perinatally infected adolescents and how we must address the risks faced by our older patients. As providers of women's health through the age spectrum, she explains, we have an important role to play in the prevention of HIV acquisition and transmission. ■

DR. REECE, who specializes in maternal-fetal medicine, is vice president for medical affairs at the University of Maryland, Baltimore, as well as the John Z. and Akiko K. Bowers Distinguished Professor and dean of the school of medicine. He said he had no relevant financial disclosures. He is the medical editor of this column. Contact him at obnews@elsevier.com.

HIV Prevention, Testing of Nonpregnant Women

It is fairly well appreciated that more than 1.7 million individuals living in the United States are now infected with HIV. What may be less appreciated by patients and physicians is that the impact of the epidemic on women has grown significantly over time.

In 2008, using a new national surveillance system, the Centers for Disease Control and Prevention reported that women comprised more than one-fourth (27%) of the 56,300 people estimated to have been newly infected with HIV in 2006. That is, an estimated 15,000 women were newly infected with HIV in 2006 alone (JAMA 2008;300:520-9).

As ob.gyns., we care for women of all ages, from adolescents through women in their senior years. Therefore, we are in the unique position to be able to identify HIV-infected individuals who could benefit significantly from early monitoring and treatment and to decrease the risk of transmission on a broader level. We can protect our patients, and they in turn can protect their partners and future children. This is a tremendous opportunity that we should not miss.

In 2006, the CDC moved away from HIV testing recommendations that were risk based and advised routine screening for HIV infection for all patients aged 13-64 years. It recommended that physicians notify their patients that testing will be performed unless they decline.

The American College of Obstetricians and Gynecologists weighed in the next

year, saying that universal testing with patient notification is more effective in identifying infected patients than is targeted risk-based testing, largely because many women found to be infected with HIV did not consider themselves to have been at risk. Opt-out testing is less cumbersome, ACOG pointed out, because it removes the requirement for lengthy pretest counseling and for detailed, testing-related informed consent.

A 2007 survey of almost 400 medical staff at San Francisco General Hospital,



Arlene D. Bardeguet, M.D., M.P.H.

which serves a population with a high HIV prevalence, showed that clinicians in obstetrics/gynecology and HIV infectious disease specialists were significantly more likely to routinely test their patients than were physicians in other

specialties (J. Acquir. Immune Defic. Syndr. 2009;50:114-6).

As the authors say, however, this isn't surprising given the fact that ACOG, the CDC, and other national organizations have long called for universal prenatal HIV testing.

Other studies have suggested that compliance with the CDC recommendations is low – that many ob.gyns. as well as other primary care physicians – do not routinely offer HIV testing outside of the prenatal context. Even in high prevalence areas such as New Jersey, we have documented that many providers miss the opportunity to offer the test to all their patients, deeming them unlikely to be infected. This approach hinders early

access to care for potentially infected patients and fails to address an unknowing risk of transmission to partners.

We need to think differently.

We do not ask patients: Do you want a chlamydia test? A Pap smear? A cholesterol test? We tell them, instead, that we're going to check their cholesterol levels, or that it's time for their Pap smear, or that we'd recommend a chlamydia test. We need to present HIV testing in the same way – as part of the routine battery of tests that will be performed unless the patient declines. Studies have shown, interestingly, that more patients accept recommended HIV testing when they know it's routinely offered to everyone, without an assessment of risk.

Furthermore, we need to do so in spite of race and in patients of all ages, with all the generations of women whom we see.

As ob.gyns., we must be cognizant of the changing face of HIV infection in women in the last 30 years and realize the unique challenge that we now face as the infection encompasses patients from a broader age spectrum than just those in their reproductive years. We have witnessed both an increased number of HIV infections in the older population and increased survival among individuals on highly active antiretroviral therapy (HAART), including those who were perinatally infected.

We also must appreciate that women who are engaged in a relationship with a known HIV-infected partner, regardless of their age, can prevent acquisition with barrier methods such as condom use or postexposure prophylaxis as delineated by the CDC for serodiscordant couples.

Women Older Than 50

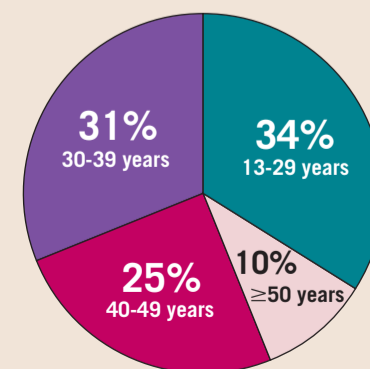
Studies have consistently demonstrated that many women are sexually active into their 60s. Even when we appreciate this, we tend to dismiss the possibility that any of our older patients might have HIV infection. We tend to assume that our patients are in stable relationships and presume there is no value to HIV testing.

It's important to appreciate, however, that the number of people aged 50 years and older who are living with HIV/AIDS has been increasing in recent years. It is estimated that almost one-fourth of all people with HIV/AIDS in the United States are age 50 years and older. While this is partly because HAART has extended the lives of many HIV-infected people, it is also attributed to newly diagnosed infections in people over 50 years.

The 2008 CDC analysis that showed that women comprised more than one-fourth of the individuals newly infected with HIV in 2006 also found that 25% of the new in-

Continued on following page

Estimated New HIV Infections By Age, 2006



Source: Centers for Disease Control and Prevention

Continued from previous page

fections were in individuals (men and women) aged 40-49 years (13,900 out of 56,300). Another 10% were in individuals aged 50 years and over (5,800 of 56,300). Approximately 30% of the infections were a result of heterosexual contact. Earlier data from the 1990s similarly showed over 10% of new AIDS cases occurring in people older than age 50 years.

Women of all ages can wrongly believe they are not at risk of contracting HIV. In one recent survey examining patient attitudes about HIV testing and knowledge about their own risk status, only 2% of approximately 850 women of various ages considered themselves at high risk for HIV infection despite the fact that almost half of them reported having had unprotected sex at some point with more than one partner. The women were patients of ob.gyn. members of ACOG's Collaborative Ambulatory Research Network (Matern. Child Health J. 2009;13:355-63).

Older women are generally even less knowledgeable about HIV transmission and how to protect themselves than are younger women, and they are not concerned about undesired pregnancy. For these reasons, many older women may not be practicing safer sex, increasing their risk for HIV and other sexually transmitted infections.

In a nine-question survey of 514 urban women aged 50 years and older (mean age of 62), the majority of women scored poorly, answering four or fewer of the questions correctly. Eighty-four percent correctly identified unprotected heterosexual sex as a moderate- to high-risk activity, but only 13% identified condoms as being very effective in preventing HIV, and 18% said condoms are not at all effective (J. Amer. Geriatr. Soc. 2004;52:1549-53).

In another study aimed at assessing differences in the characteristics of individuals (both men and women) who refuse testing and those who accept it, investigators found that HIV test refusal was associated with female gender, white race, older age, and higher educational level (AIDS Patient Care STDS 2006;20:84-92).

Older women must be educated about their risk of heterosexual transmission and the fact that the risk for HIV acquisition has been increasing since 1994 in the United States. They need to understand that normal physiologic changes in the menopausal period such as thinning of the vaginal mucosa, increased susceptibility to vaginal abrasions during intercourse, and changes in their immune response can make them more vulnerable to disease acquisition or progression.

It also is important to educate them about the effectiveness of condoms and the importance of knowing the HIV status of their partners, because it is estimated that approximately 21% of infected individuals in the United States do not know their HIV status.

Most of all, our patients should understand that 30 years into the epidemic, we have demonstrated excellent survival in individuals on treatment, particularly among those who were diagnosed early and who are receiving HAART. A recent report from the CDC shows that average life expectancy after HIV diagnosis in the

general population increased from 10.5 to 22.5 years from 1996 to 2005 (J. Acquir. Immune Defic. Syndr. 2010;53:124-130).

Interestingly, as the report points out, studies have shown that although HIV-infected women had a greater life expectancy to begin with, they showed a lesser magnitude of improvement than did men, particularly white men. (Women's life expectancy changed from 12.6 to 23.6 years.) This observation highlights the importance of earlier diagnosis and link to care.

Knowing about the successes of HAART is important because women are less likely to opt out of HIV testing when they perceive the benefits. We can explain to patients – especially those who are apprehensive about the test – that the test is integrated into the annual health care panel (along with cholesterol and triglyceride testing, and genital cytology), and that, contrary to decades ago, we can treat and control HIV disease once it is diagnosed, which is more than we can do for certain types of cancer.

Our patients need to understand that it can be a manageable chronic disease as long as it is detected and effectively addressed early in the course of their infection. Today, we have access to a wide array of pamphlets and videos that we can offer in the waiting area to help patients understand this and appreciate the value of HIV testing.

Serodiscordant Couples

Thus far, there is limited standardization or consensus on how and when to provide counseling, testing, and prevention strategies for women who are involved in HIV serodiscordant relationships. However, most experts recommend that patients whose partners are HIV positive should be tested for HIV infection annually and encouraged to use effective prevention strategies such as the male or female condom.

Screening and treatment for sexually transmitted diseases should be done annually as coinfection can increase the risk of HIV transmission. In one of the studies demonstrating an impact of STD treatment – a randomized trial conducted more than 15 years ago in rural Tanzania – improved STD education and treatment reduced HIV incidence by about 40% (Lancet 1995;346:530-6).

In cases in which an unplanned sexual encounter with an HIV-positive partner occurs without protection, postexposure prophylaxis should be considered and given as soon as the event is identified, preferably within 48 hours. The CDC's recommendations for the use of antiretroviral postexposure prophylaxis, issued in 2005, call for a 28-day course of HAART (MMWR 2005;54[RR02]:1-20)

Decisions about the optimal post-exposure therapy involve various factors, including the partner's antiretroviral history, adherence to the regimen, and most recent viral load. We may need to counsel patients, however, that having undetectable virus in the blood does not necessarily mean there will not be any virus in the genital tract. Discrepancies between serum and genital viral load have been reported among HIV-infected men and women on HAART.

If a woman engages in unprotected sex with a male of unknown serostatus, she can request postexposure prophylaxis. In this case, she should be counseled about the risks and benefits of postexposure HAART, as she may expose herself to

program should include suppressive antiretroviral therapy for the infected partner (who may yet be eligible for such therapy under current recommendations for CD4 cell count), screening and pretreatment for other sexually transmitted infections, and unprotected sexual intercourse that is limited to times of peak fertility (AIDS 2010;24:1975-82).

Perinatally Infected Women

An increasing number of perinatally infected adolescents has been identified and engaged in care throughout the United States. This population is unique in that many were initially exposed to monotherapy or

dual antiretroviral regimens and thus have developed resistance to several antiretroviral regimens. In addition, their adherence to HAART is lower than required to avert failure on current regimens.

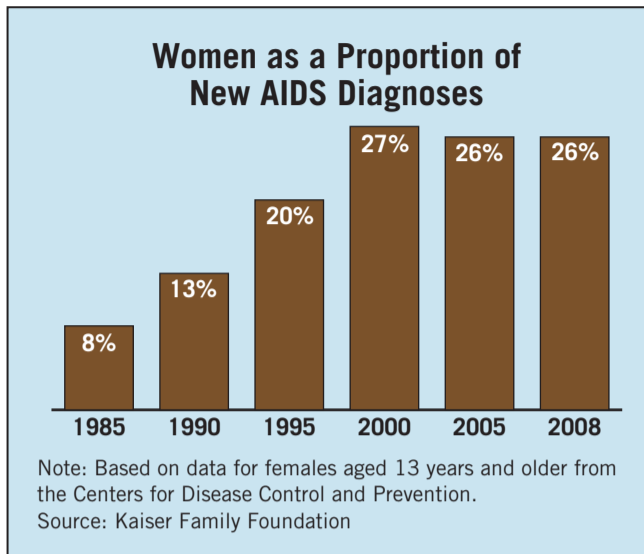
They are a population that presents a challenge to ob.gyns. because many have high-risk sexual behaviors, and when they become pregnant, they are at high risk for operative delivery due to inadequate viral suppression.

We recently reported on the pregnancy outcomes of 10 perinatally infected adolescents referred to the high-risk obstetric clinic at our institution and delivered between 1997 and 2007. Neonatal outcomes were generally favorable, but these young women had a high rate of operative delivery (62%, compared with our institutional rate of 33%) due to the failure to achieve undetectable viral load (Am. J. Obstet. Gynecol. 2009;200:149.e1-5).

Our goals for these women should therefore include supporting and counseling on treatment adherence and on the selection of well-tolerated HAART regimens that can rapidly suppress viral load. We should also minimize the use of operative deliveries when feasible to avert compromise of their future reproductive health, and provide adequate contraceptive counseling to prevent unplanned pregnancies. We also must engage the partners of these young women in HIV prevention strategies and HIV testing (in our cohort, most of the sexual partners were seronegative males) and work with them in preventing the acquisition of other sexually transmitted infections. Abnormal cervical cytology and STIs affected 80% of the patients in our cohort, and high rates of STIs have been reported in other cohorts of HIV-infected adolescents.

Engaging the patients in care and viral suppression prior to conception and educating their partners to avert HIV acquisition will be among the highest priorities in years to come, especially since this group is more disenfranchised from the health care system and less likely to engage in pregnancy prevention and planning.

Dr. Bardequez said she had no relevant financial disclosures. ■



unnecessary toxicities.

When faced with these situations we can obtain guidance from, or work in partnership with, the infectious disease provider who is managing the HIV-infected partner, or we can contact state or national phone lines for linkage to immediate care. Some health departments have established nonoccupational post-exposure prophylaxis programs in their jurisdictions. Overall, it is important that we be aware of the availability of post-exposure HAART and its possible risks and benefits.

In the near future, a woman whose partner is HIV positive should be able to benefit from antiretroviral microbicides used before or after intercourse. In the double-blind, randomized, and well-publicized CAPRISA (Centre for the AIDS Programme of Research in South Africa) 004 trial, a 1% vaginal gel formulation of tenofovir reduced HIV acquisition by approximately 39% overall and by 54% in women with high adherence to the protocol for gel application (Science 2010;329:1168-74). Another phase III trial of tenofovir is ongoing.

The field of safe reproduction for HIV serodiscordant couples also is advancing, such that women and their partners have various options for conceiving with minimal risk of transmitting the infection.

A large body of evidence suggests that reproductive technology – that is, sperm washing and artificial insemination – can help HIV-affected couples safely conceive, and the results of further CDC-sponsored research aimed at evaluating outcomes in couples who have used these techniques to conceive are expected soon. For many couples, however, such technologies are economically inaccessible.

Experts are looking at periconception preexposure prophylaxis as a potential strategy for preventing HIV transmission in couples trying to conceive. Under this approach, the seronegative partner would take antiretroviral drugs during periods of attempted conception, with the goal of preventing initial viral replication. Clinical trials evaluating its safety and efficacy are ongoing.

Other components of a risk-reduction