Adolescent females and women continue to be one of the fastest growing groups with HIV disease in the United States and globally, and most are between the ages of 15 and 44, the peak reproductive years. In 1985, the Centers for Disease Control and Prevention (CDC) recommended that HIV-infected women delay pregnancy until more was known. A decade later, while much remains unclear, research has yielded important findings that have changed the landscape for HIV-infected women in their childbearing years.

A variety of studies in the United States place the risk of vertical transmission (from mother to fetus) at between 13 percent and 30 percent. Recent results from the National Institutes of Health (NIH) AIDS Clinical Trials Group (ACTG) 076 study found that zidovudine (ZDV; AZT) had a significant inhibitory affect on HIV transmission from mother to fetus. Additionally, the CDC, the American College of Obstetricians and Gynecologists Pediatric AIDS Foundation, and others now recommend that all women, especially those who are pregnant, be given the opportunity to learn of their HIV infection status through voluntary HIV testing and counseling. This article will briefly review these issues and other factors that HIV-infected women may consider when making reproductive decisions and HIV-related treatment choices once pregnancy is underway.

The Science

In order to make an informed decision, women need to be given the facts that are available about HIV infection and pregnancy. Transmission from mother to baby can occur as early as the first trimester, although it now appears that the majority of transmission—perhaps 60 percent—occurs late in pregnancy or during labor and delivery itself. Perinatal transmission rates vary, ranging from 15 percent to 30 percent in the United States and resulting in 1,000 to 2,000 HIV-infected infants born in 1993.* HIV can be passed from breast milk (adding an additional 15 percent risk) which is why seropositive women who have access to safe, affordable infant nutrition alternatives should be encouraged to consider refraining from breastfeeding. Studies have shown lower perinatal transmission rates in Europe—13 percent to 17 percent—and higher rates in Africa and other developing nations—around 30 percent.

ACTG 076 has demonstrated that these rates—the result of multiple factors—can be influenced by treatment to help impede transmission. The study found that in HIV-infected women with T-helper cell counts of greater than 200, ZDV therapy after the fourteenth week of pregnancy, during labor and delivery, and after delivery to infants resulted in a two-thirds reduction of HIV transmission from mother to fetus.1 HIV was transmitted to 8 percent of the infants in the treatment group versus 25 percent of the infants in the placebo group. In response to these results, the U.S. Food and Drug Administration approved the use of ZDV for pregnant women and the U.S. Public Health Service issued guidelines on such use.2

The 076 data—encouraging in many regards—should be interpreted with some caveats. While the study found few side effects in the ZDV-treated group, long-term follow-up is necessary to define all possible effects. As this information becomes available, pregnant women will also have to balance the possible benefits of ZDV against risks to their fetuses. Other unanswered questions include whether the ACTG 076

*All children born to HIV-infected women carry maternal antibodies for up to 15 months, and thus, using standard antibody assays, will test seropositive at birth. About three-quarters of these children are not actually HIV-infected, and will “serorevert,” that is, lose maternally-acquired antibody over time. Tests which detect evidence of HIV itself, such as polymerase chain reaction (PCR), viral culture, and p24 antigen, are usually used to determine whether or not an infant is truly HIV-infected.
Editorial: Considering Pregnancy
Robert Marks, Editor

In the world of HIV, there are few topics more sensitive or complex than discussions of transmission from mother to fetus and few acts more irrevocable than the decision to continue or terminate a pregnancy. In light of this situation, counselors are understandably prone to compromise a basic tenet of therapy: avoid directing the client.

But it is precisely when the stakes are so high that it is most critical for the final outcome to be unmistakably the client’s decision. In such situations, the provider is obliged to present the information necessary to ensure that the client can make an informed decision; but the client is not obliged to bear in mind this information.

This can be frustrating to well-intentioned clinicians who respect a woman’s choice but who feel compelled by the data. I confronted this frustration myself as I edited Ann Kurth’s article in this issue of FOCUS. I had added the word “should” in a paragraph, meaning to emphasize the counselor’s obligation to present the client with the full range of information about ZDV treatment: the ways in which HIV may be transmitted from mother to fetus or infant; the likely rates of transmission without antiviral intervention; the likely rates of transmission with antiviral intervention; the effects of antiviral medication on the mother’s health, the fetus’ health, and the pregnancy. But I found instead that my words defined an obligation for the client: to consider these factors.

Kurth and the authors of the second article in this issue—Mindy Benson and Maureen Shannon—describe the full range of information related to pregnancy decision-making and some idea of what issues clients may want to consider. But their “shoulds” are for the most part reserved for clinicians, and these embody the obligation to present an accurate and complete picture of the medical factors involved and to avoid the ethical pitfalls inherent in acting jointly as clinician, investigator, and counselor.

Psychotherapists may be somewhat removed from the medical realities of ZDV and nevirapine prophylaxis, but they are not removed from the crises many women face when negotiating decisions about pregnancy. Their most important role in facilitating this decision may not be to ensure informed consent but to insulate a pregnant client and her decision-making process from outside pressures, particularly moral ones, to consider one factor or another—to construct an incubator in which she has the freedom and comfort to reach a decision with which she can live and thrive.

References
An ethical counseling framework will recognize that most women are motivated by what they perceive to be the best interests of their children as well as of themselves.


particularly in T-helper cell subsets. But, several prospective studies have largely concluded that pregnancy has only a minor effect on the clinical course of HIV disease, although the normal trend towards T-helper cell decreases in pregnancy is about 10 percent to 20 percent greater in HIV-infected versus uninfected women. Recent evidence also shows that HIV infection itself apparently does not lead to poor obstetrical or fetal outcome. The poor outcomes seen in mothers and babies in some studies may have been related more to active substance use than to HIV itself.

Because T-helper cell counts are important markers for HIV-related diagnosis and treatment, HIV-infected pregnant women should monitor their T-helper cell levels at least every trimester, especially if their counts are below 300. Ideally, HIV-infected women who choose to continue with a pregnancy should receive care from a team of providers including clinicians specializing in HIV-related care, pediatric care, addiction services where appropriate, as well as prenatal care and psychosocial support. Throughout pregnancy, providers and pregnant women will want to consider the value of aggressive prophylaxis and treatment of opportunistic infections—particularly Pneumocystis carinii pneumonia—which can threaten both mother and baby.

**Decision-Making about Pregnancy**

HIV-infected women who become pregnant face several dilemmas in defining the impact of HIV disease on themselves or a given pregnancy, two of which are particularly notable. First, despite the research advances outlined above, it is difficult to predict for a given individual the actual risk of HIV transmission from mother to fetus, nor is there any intervention that guarantees prevention of such transmission. Second, reproductive decisions—like those around sexual behaviors—are not always related to facts alone.

Rather, decisions are influenced by a variety of factors such as grief and hope in the face of loss, faith in religious or medical systems, pressures from partners or society, concerns about ill effect on health for self or infant, and moral beliefs about the value of life or the acceptability of abortion and societal and personal meanings of reproduction. Many of these factors—which are often cited as influencing both the decision to continue and to terminate pregnancy—resemble those confronted by seronegative women.

Childbearing has profound meaning across culture and class, and it is inevitable that these meanings will be heightened for women who face a chronic, stigmatized, life-threatening illness.

Rebecca Denison, editor of WORLD, a newsletter for women living with HIV disease, offers the following questions to facilitate the decision-making process:

- Are you able and willing to love and care for a baby, whether or not he or she is infected?
- How will pregnancy affect your health?
- Do you have the support of a partner, family members or friends who can help you care for a child?
- Who will care for your child—teach your child about his or her culture, remember you, and raise your child according to your values—if you become sick or die?
- In what ways (good or bad) will having a baby change your life?
- What are the reasons that you want (or do not want) to have a child?
- Do you feel pressured by others to have (or not have) a child?
- Do you have enough information to make an informed decision?

To this list can be added several other questions. What is the extent of a woman’s caretaking responsibilities for other children if any? What kind of emotional and practical support can she count on receiving from family, partners, friends, and coworkers? To what extent has she come to terms with her own infection and her sense of the future? Some women who discover their HIV infection status may wish to terminate pregnancy quickly, feeling that they are doomed. Some of these women may later become pregnant again and choose to continue subsequent pregnancies, once they have had time to adjust to an HIV diagnosis and the realization that they “aren’t going to die tomorrow.” (Women who wish to terminate pregnancy will need referrals to facilities that do not discriminate based on HIV infection status.)
Framework for Reproductive Counseling

In April 1995, the CDC finalized public comment on new guidelines for HIV counseling and voluntary testing for pregnant women. The new guidelines recommend that health care workers counsel all pregnant women regarding the risks and benefits of HIV antibody testing, coupling this with voluntary testing and referral and information about treatment options for those found to be HIV-infected. The CDC concluded that voluntary testing, unlike mandatory testing, would not discourage pregnant women from seeking prenatal care but would help them establish trusting relationships with their providers.

Non-directive counseling—by which a woman is given all available information but not told or advised what decision to make—is critical to ensure that women are able to make these fundamental decisions for themselves. HIV-infected women should be given all available information about their options during pregnancy, including information about ACTG 076, self-care and health promotion, and other interventions that may help reduce the risk of perinatal transmission. These discussions must be specific to each woman and to each pregnancy or possible pregnancy and take into account life goals, clinical condition, and support framework. It is useful to explore with each woman what a pregnancy means to her; for example, pregnancy may function as a way of expressing hope, focusing on something other than her own illness, leaving behind a legacy, or fulfilling a socially and psychologically significant role.

Providers should be clear that there are no guarantees of a seronegative birth, even if ZDV is used. While a woman should not be made to feel that having an HIV-infected child is a failure, it may be useful for her to examine what she might feel were this to occur and use these feelings to help guide her decision to continue a pregnancy. An ethical counseling framework to help women negotiate the balance between transmission reduction and the effects of ZDV treatment on maternal health will recognize that most women are motivated by what they perceive to be the best interests of their children as well as of themselves. It is important for counselors to discuss not only whether women will take ZDV but also her related concerns about the loss of physical and social functioning, death and dying, and long-term child care.

Finally, while reproductive counseling should incorporate new scientific information, it is important to acknowledge that there is still much that is not known about perinatal transmission. In these circumstances, “I don’t know” is an acceptable and important response. Reproductive decision-making involves difficult choices, and while providers can assist in this process, they cannot offer answers.

Conclusion

The most effective way to prevent pediatric HIV disease is to prevent infection in women. Renewed emphasis on this goal would require more prevention and testing outreach to male partners; more accessible and female-friendly addiction treatment; and greater stress on women’s roles beyond reproduction. Short of preventing infection in women, scientific advances such as those seen in ACTG 076 may give women and their providers more with which to reduce perinatal transmission risks. Providers can assist with this complex, painful, and sometimes affirming process by offering women access to information and supporting them in their decisions.

References


Nevirapine: Ethical Dilemmas and Care for HIV-Infected Mothers
Mindy Benson, PNP, MSN and Maureen Shannon, CNM, FNP, MS

The groundbreaking results of the AIDS Clinical Trial Group (ACTG) 076 protocol have proved that antiviral medications can reduce HIV transmission from mother to fetus, at least for a select population of relatively healthy women. These results—zidovudine (ZDV) therapy reduced perinatal transmission rates from as much as 25.5 percent to only 8.3 percent—were more than anyone dared hope possible. But for many women in the United States, ZDV therapy is not a viable option. These women may be at a later stage in disease progression or may have entered care late in the course of pregnancy, may have had ZDV therapy prior to pregnancy, may be unable or unwilling to follow the study regimen, or may be unable to tolerate ZDV. In the developing world, ZDV remains too expensive and difficult to administer following the ACTG 076 protocol.

In response, the Pediatric AIDS Clinical Trial Group has continued to develop other trials that might offer evidence of reduction of perinatal transmission. The ACTG 250 protocol, a phase I clinical trial evaluating the safety and pharmacokinetics of nevirapine, is a good example of an alternative to ZDV therapy that might be available to a wider population. A discussion of the nevirapine trial offers insights into not only the leading edge of antiviral therapy, but also the counseling dilemmas clinician-investigators face when helping pregnant women with HIV disease decide about experimental treatments.

Nevirapine and Clinical Trials

Nevirapine is a non-nucleoside HIV reverse transcriptase inhibitor. It differs in structure from currently approved nucleoside analogs—ZDV, ddI, and ddC—although both classes of drug act by binding to the reverse transcriptase enzyme. In studies of both adults and children older than three months of age, nevirapine has demonstrated an ability to dramatically reduce HIV viral burden. Repeated administration of nevirapine alone continues to produce this effect on viral burden for approximately four weeks, after which time HIV develops resistance to it.

Despite nevirapine’s dramatic effect on viral burden, the short time until resistance makes it an unlikely candidate for long-term therapy. However, since 50 percent to 70 percent of perinatal transmission is believed to occur during labor and delivery, nevirapine may be effective in reducing perinatal transmission. In order to confirm nevirapine’s safety and determine the optimal dose for pregnant women and infants, the ACTG established nine ACTG 250 sites in the United States and Puerto Rico.

The staff at many of these perinatal ACTG sites are both clinicians and investigators, offering clients both care and opportunities to participate in clinical trials. While trials provide clients access to potentially beneficial treatments that would be otherwise unavailable to them, many of the perinatal sites do not require trial participation in order to receive clinical services. Nonetheless, for staff at these sites, provid-

See also references cited in articles in this issue.


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See also references cited in articles in this issue.
ing care and gathering data can result in a blurring of the lines between clinician and investigator and posing conflicts of interest.

Ethical Dilemmas

Several ethical issues arise in such situations. First, even in the best designed and carefully planned trials, there is a concern—however remote—that an intervention may lead to adverse effects for mother, infant, or both. In the case of nevirapine, rare but severe reactions, including rash (which may involve life-threatening shedding of skin and mucous membranes) and hepatitis, have been associated with daily therapy in a small number of patients. The ACTG 250 protocol attempts to respond to these concerns by administering less than half the daily dose associated with these reactions for a shorter period of time: a single dose for mothers and no more than a single dose daily for seven days for infants.

Second is the possibility that clients will feel obliged to enroll in a clinical trial to please the clinician-investigator. A client may assume that her clinician is offering the trial because the clinician thinks the woman should participate. Here it is crucial for the clinician-investigator to maintain clear boundaries between his or her roles. Although the investigator may believe that trials such as ACTG 250 will probably reduce perinatal transmission and may be an ideal option for a particular woman, the clinician is ethically bound to present the information in a nonjudgmental manner.

The optimal counseling approach is to present scientific data and protocol requirements, then respond to the client’s questions and concerns. Maintaining appropriate boundaries during this process can be particularly difficult as the bond between clinician and patient intensifies during pregnancy. Obviously, the treatment decision must remain the woman’s, not the clinician’s.

Thorough, non-directive, and culturally appropriate presentations of information about complex research studies require an investment of time from both clinicians and clients. These discussions should cover: data about perinatal transmission rates—with and without ZDV use; the possible benefits of the trial; unknown long-term adverse outcomes for the woman and her infant; information about study protocol including the existence of placebo arms when applicable; and notice of the right of the woman to withdraw from the study without compromising her or her infant’s health care at the clinic. In the case of ACTG 250, clinician-investigators must inform women that while there are no placebo arms in the trial, some strata of the trial involve different administration protocols: although all the mothers receive nevirapine during labor, some of their infants receive no drug, others receive a one-time dose, and a third group receive a single daily dose for up to a week.

It is crucial that clinicians not only present information but also help women articulate their own responses to this information and express the conflicts they may have about participating in trials. It is also essential to offer clients written information about trials as well as referrals to social support resources.

Third, facing the complexity of such information, clinician-investigators may feel pressure to streamline the presentation and discussion of a protocol as a means of reducing the time required to complete this process. Ultimately, this can result in improper or inadequate informed consent, or conversely, declined enrollment in response to confusion about the study and its implications.

Finally, funding issues exacerbate clinically based ethical dilemmas. The research establishment rewards, with continued funding, sites that successfully accomplish projected trial recruitment. The result is that clinicians must negotiate a precarious balance between providing appropriate clinical care and enrolling the number of participants that will secure not only the current trial but future ones.

Conclusion

The exciting results of ACTG 076 have reminded providers that state-of-the-art HIV perinatal services should include access to clinical trials. To facilitate access, clinician-investigators must attempt to remain objective interpreters of scientific information as well as supportive advocates for women facing reproductive and treatment decisions.

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References


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Predicting Perinatal HIV Transmission

A New York study of pregnant women found that T-helper cell counts, T-suppressor cell levels, and possible mode of delivery were all linked to higher HIV transmission rates from mother to fetus. Women at risk for HIV infection due to drug use, exposure, or seropositive status were enrolled in the study between 1986 and 1992 at six different medical centers. The sample consisted of 246 HIV-infected women—193 of whom were enrolled prenatally and 53 of whom were enrolled at time of delivery—and 347 uninfected women who comprised a control group.

Participants were interviewed to determine risk for HIV infection, demographic characteristics, and medical history. They underwent laboratory tests and physical examinations every two months and at delivery.

During the period of analysis, 221 HIV-infected women delivered live infants. Of these births, 172 of the infants had determined infection status, and 28 percent were seropositive; 49 of the infants had undetermined status because they were lost to follow-up or died before HIV infection status could be determined.

Several characteristics were significantly related to HIV transmission, including T-helper cell counts below 280 (resulting in a 48 percent transmission rate); T-suppressor cell percentages above 51 percent (resulting in a 41 percent transmission rate); and vaginal delivery rather than cesarean (32 percent versus 18 percent transmission rate). The highest transmission rate of 62 percent was observed in women with both low T-helper cell counts and T-suppressor percentages above 51 percent.

Analysis of the data revealed that T-helper cell counts and T-helper cell percentages related to similar trends in transmission rates. Analyzing T-suppressor cell counts, however, did not show a significant difference in transmission rates. It was only when current T-suppressor cell counts were expressed as a percentage of baseline counts that researchers detected higher transmission rates.

Despite these strong associations, some transmitting women had normal counts, so no factor or combination of factors in the analysis can be said to be a specific predictor of maternal transmission. The data indicate that the relationship between mode of delivery and HIV transmission is worthy of further research, and that women with low T-helper cell counts and elevated T-suppressor cell levels should be advised of their increased risk of transmission.

Attitudes toward Childbearing
Lai KK. Attitudes toward childbearing and changes in sexual and contraceptive practices among HIV-infected women. Cleveland Clinic Journal of Medicine. 1994; 61(2): 132-136. (University of Massachusetts Medical Center.)

A small survey of HIV-infected women of childbearing age found that subjects did not receive sufficient counseling about reproduction and contraception. The study, primarily of White women, contradicts earlier surveys comprised of women of color.

Researchers recruited 46 women through the HIV Clinic at the University of Massachusetts Medical Center between 1990 and 1991. Thirty-three of the participants were White, 12 were Hispanic, and one was African American. Questionnaires and structured interviews determined the women’s demographic data, attitudes toward childbearing, and changes in sexual behavior.

Accurate knowledge of the risk of vertical transmission of HIV was very low: about half of the women surveyed believed that chances were about 50 percent, while the other half believed that the chances were 100 percent. Of the women who had received counseling following testing, only 59 percent reported that the topic of pregnancy had been discussed.

Positive HIV serostatus dramatically affected the group’s attitudes toward childbearing and contraception. Although 59 percent of the surveyed women said they wanted to have children prior to testing, only 17 percent still wanted to have children at the time of the survey. Seventy percent practiced birth control after their
test, in contrast to the 39 percent who had used birth control before being tested. Most of the survey respondents reported increased use of condoms, with 28 percent using condoms some of the time and 54 percent using them all of the time. Most women cited protection of self and partner—rather than avoiding pregnancy or protecting unborn children—as motivation for changing sexual behavior.

The results of the survey contradict a 1989 study that showed that the rates of elective abortion and repeated pregnancies were identical for both seropositive and seronegative women. A significant difference between this and previous studies is the ethnic origin of the respondents; unlike the primarily White sample of this survey, most other samples include a non-white majority of black or Hispanic respondents.

**Donor Insemination and HIV Transmission**


The American Fertility Society’s 1988 ban on “fresh” semen for artificial insemination is unwarranted, according to an essay on the risks and benefits of fresh and frozen semen. Frozen sperm, less viable than fresh sperm, requires special treatment, thus reducing the likelihood of insemination and increasing its cost.

The 1988 decision to use only frozen semen was based on concerns that the “window period”—after HIV exposure but before the development of measurable levels of antibodies—would make screening results too uncertain. Since that time, however, testing methods have become advanced enough to reduce the window from 42 months to as little as 45 days.

The negative publicity surrounding infected blood doubtlessly made the American Fertility Society particularly careful to avoid unwitting infection of insemination recipients. The risks involved in blood transfusion, however, differ from those of donor insemination in several important ways: the infectivity of HIV from sperm is considerably less than that of HIV from blood; HIV is more common in blood than in semen; and sperm donors, who are screened for other sexually transmitted diseases, are less likely to be HIV infected than blood donors, who are not screened according to their history of sexually transmitted disease. Nonetheless, since the donor population for sperm is comprised exclusively of men, who are at higher risk for HIV infection than women, the population of sperm donors is likely to have a higher seroprevalence than the population of blood donors.

The risk of HIV infection involved with fresh sperm insemination is remote. When compared to the other risks faced in pregnancy and infertility treatment, the benefits of fresh semen outweigh its risks. Screening and testing of donors should continue to confirm the evidence that fresh sperm is safe and should be considered for insemination.

**Perinatal HIV and Ethical Conflict**


Faced with limited resources and competing priorities of individual rights and public welfare, the perinatal and pediatric HIV pandemic is escalating in a global environment of ethical conflict, according to an essay that surveys the range of these conflicts. Pitting the health care entitlements of children against those of their mothers, reproductive rights and child protection laws must take into account a range of ethical dilemmas, including whether to continue pregnancy, antibody screening for children, maintaining patient confidentiality, and the mother’s role as surrogate decision-maker for her child.

**Next Month**

A major component of HIV-related counseling is about acknowledging and accepting death—even as clients focus on embracing life. This is most true when a client’s health has deteriorated to the point that he or she is living in a hospice. In the July issue of *FOCUS,* Barbara E. Hines, MA, MPH and Stephan M. Peura, respectively, the Coordinator of Client Services and the Administrator of the Corpus Christi Residence in Pittsburgh, Pennsylvania, provide an overview of the psychosocial issues clients face as they approach death and how these issues are expressed in the hospice setting. They also offer insights into how hospice responds to these issues.

Also in the July Issue, John Fryer, MD, a psychiatrist at Temple University in Philadelphia, describes the ways in which psychiatric care is applied in the hospice setting.
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