Between 8 and 12 percent of couples around the world have difficulty conceiving a child at some point in their lives, and in some areas that figure reaches one-third or more of couples. In some developing countries, for example Nigeria, infertility is the leading reason for gynecological consultations. Where infertility is widespread, couples seeking help can place a heavy burden on limited health care resources.

Defining Infertility

Couples are considered infertile if they do not conceive over a 12-month period of unprotected intercourse, but experience shows that many of these supposedly “infertile” couples will eventually conceive, even without treatment. For example, 38 percent of couples attending an infertility clinic in India conceived before any treatment began, and another 27 percent conceived before their treatment was completed. Similarly, a Chilean study found that only 4 percent of women were infertile after their first eight years of marriage, although 26 percent had experienced a delay in conception that lasted longer than 12 months.

Infertility affects both men and women. Yet women, particularly developing country women, may bear the sole blame for barren marriages; in many areas, infertility is a socially acceptable basis for divorce by the husband. The most comprehensive study of infertility—a WHO study of 5,800 infertile couples seeking help at 33 medical centers in 22 developed and developing countries—found that men were either the sole cause or a contributing factor to infertility in more than half of couples. Overall, the studies found that female causes accounted for between 25 to 37 percent of infertility worldwide (with larger proportions in sub-Saharan Africa and Southeast Asia), male causes accounted for between 8 to 22 percent, and both male and female causes accounted for between 21 to 38 percent (see Figure 1).
This multinational study also found that most infertile couples around the world suffer from primary infertility, which means that the woman has never conceived. Sub-Saharan Africa is a striking exception to this pattern: in this region most couples (52 percent) suffered from secondary infertility—that is, a woman cannot conceive even though she previously has conceived. Latin America also has a relatively high rate of secondary infertility: 40 percent. In contrast, only 23 percent of infertile couples in Asia and 16 percent in North Africa suffered from secondary infertility.

Levels and Causes of Infertility

While differences in data sources and analyses make it difficult to accurately measure or compare infertility rates, it is clear that the level and causes of infertility vary widely, both among and within countries. For example, the Demographic Health Survey (DHS) and World Fertility Survey (WFS) have demonstrated that the prevalence of infertility in sub-Saharan Africa ranges from 11 to 20 percent in the 27 countries surveyed. A closer examination of the data shows that these national rates conceal wide ethnic and geographic variations. For example, Namibia’s national infertility rate of 19 percent is an average of rates ranging from 14 to 32 percent among the country’s major ethnic groups.

What accounts for the variation in infertility levels? Everywhere there is a core of about five percent of couples who suffer from anatomical, genetic, endocrinological, and immunological problems that cause infertility. The remainder are infertile largely because of preventable conditions, including:

- sexually transmitted, infectious, and parasitic diseases,
- health care practices and policies, and
- exposure to potentially toxic substances in the diet or the environment.

The factors that contribute to these conditions vary from region to region. Reproductive tract infections, particularly sexually transmitted diseases (STDs), are the leading preventable cause of infertility. The WHO multinational study found that 64 percent of infertile women in sub-Saharan Africa had diagnoses that could be attributed to infection, about double the rate of other regions (see Figure 2). Tubal problems and other infection-related diagnoses also are associated with postpartum and postabortion complications.

Other infectious and parasitic diseases—and the medications used to treat them—contribute to infertility. For example, in India, where 40 percent of the population is exposed to tuberculosis (TB), genital TB contributes to female infertility. In Africa, schistosomiasis, malaria, and sickle-cell disease all contribute to infertility. It has been proposed that the success of malaria-control programs may help explain a reduction in infertility rates in Tanzania over the past 20 years.

Health care practices and policies also contribute to infertility, most notably unhygienic obstetric practices, which lead to postpartum infections. Septic abortions and their complications are another important factor. The results of the WHO study suggest that repeated pregnancies play a greater role in the etiology of infertility in Africa and Latin America, while repeated abortions are more important in Asia and developed countries. Inappropriate gynecological practices also may lead to infertility. In Egypt, for example, physicians routinely misdiagnose cervical erosion and then treat it inappropriately with cervical electrocautery, potentially causing infertility in the process. In Nigeria, where hernia repairs are routinely left to inexperienced surgeons, there is a pattern of male infertility due to vascular injuries sustained during these procedures.

Increasingly, men and women in developing countries face exposure to environmental and workplace pollution, which can play a role in infertility.
Researchers have documented high levels of arsenic in the semen of infertile men who live in areas of Mexico where drinking water is contaminated. Similarly, the semen of some infertile Nigerian men contains high levels of aflatoxins, the metabolites of fungi that infest staple foods in many tropical countries. Infertility in Egypt and Singapore has been linked with workplace exposure to heat, pesticides, and other chemicals.

Lastly, cultural and social factors can play an important role in causing infertility. Marital and sexual customs such as age at marriage, the number of sexual partners, and female genital mutilation, can influence the risk of genital infection. The use of tobacco, alcohol, and caffeine, all have been implicated in infertility: Egyptian men who smoke tobacco in traditional waterpipes face more than twice the risk of infertility as other men. Cultural traditions may even have genetic ramifications. Generations of close-cousin marriage in Arab cultures have been linked with two causes of infertility: a congenital testicular defect (Sertoli-cell syndrome) and the immunological problem of anti-sperm antibodies.

The Role of Infection

For a great many women in developing countries, infertility results from untreated pelvic inflammatory disease (PID), a sequela of an STD or other reproductive tract infection. PID can scar the fallopian tubes, either blocking them completely or damaging the mucosa and cilia needed for them to function. The risk of tubal-factor infertility doubles with each successive episode of PID (see Figure 3) and is five times greater after a severe infection than a mild infection. Prompt treatment, within three days of developing symptoms (lower abdominal pain, vaginal discharge, abdominal tenderness, fever), reduces the risk of infertility by a factor of three.

Many episodes of PID are caused by the ascent of gonococcal and chlamydial cervical infections to the upper reproductive tract: Some 93 percent of women with bilateral tubal occlusion studied in Thailand, Hungary, and Slovenia had antibodies to Chlamydia trachomatis and/or Neisseria gonorrhoeae. Chlamydial infection poses a special problem, because it frequently is asymptomatic and therefore goes untreated, even as it causes severe tubal damage. Postpartum and postabortion infections also may lead to PID; these are special problems where deliveries take place in unhygienic conditions and where unsafe abortion is common.

While research results are conflicting, STD infections seem to have less of an impact on male fertility. However, STDs and other diseases, such as schistosomiasis, do cause inflammations of the male genital tract, and these may impair sperm production or block sperm release.

Managing Infertility in Developing Countries

Evaluating and treating infertile couples can be a costly process. At the extreme, offering couples the latest in assisted reproduction technology, such as in vitro fertilization, may cost upwards of US$50,000 per live birth. Given limited health care budgets and a wide range of serious health problems, it is important to ask what kinds of infertility programs are appropriate in low resource settings. Where infection is the leading cause of infertility, prevention will help far more couples, at less expense, than treatment.

Preventing Infection. Reducing the prevalence of STD and associated cases of PID calls for complementary prevention and management interventions, preferably integrated with existing reproductive health services. STD control as part of primary health care was summarized in the previous issue of Outlook (Volume 15, Number 2). In many settings, informing men and women that STDs may cause infertility at the same time as encouraging them to take preventative measures and seek treatment when symptomatic has proved useful.

Reducing the incidence of postpartum infections can be achieved through ensuring safer birth practices, including training traditional birth attendants how to ensure hygiene during deliveries, and by developing mechanisms to help women with potentially complicated deliveries to deliver in clinics. The most effective ways to reduce postabortion infections are (1) to promote family planning, because effective contraception eliminates the need for abortion; (2) to provide treatment for postabortion complications at a variety of health facilities; and, (3) where the law allows, to increase access to safe pregnancy termination services.

Where other diseases are a common cause of infertility, aggressive campaigns to control their spread may have an impact. For example, reducing the incidence of tuberculosis or treating affected women before TB spreads to the genital tract would

![Percent of Women with Tubal Factor Infertility following PID, by Number of Episodes](image)
prevent many cases of female infertility in India. Likewise, testicular biopsies of Nigerian and Ghanaian men, which found a high incidence of inflammatory lesions, suggest that efforts to control and treat schistosomiasis would reduce levels of male infertility in addition to female infertility in these countries.

Evaluating Infertile Couples. While preventing reproductive tract infections may be the most effective way to reduce infertility problems in developing countries, this long-term strategy does not address the strong demand for infertility treatment in many regions. Frequently, overburdened clinics in developing countries take a haphazard approach to evaluating the infertile couples who come to them for help. Health providers may offer advice or treatments without conducting a complete evaluation—sometimes without even seeing both partners.

While providers may differ on the number of visits and tests recommended for an infertility work-up, the first step is always to take a complete history (covering various medical issues, including prior reproductive tract infections, sexual behavior, contraceptive use, and prior fertility) from both partners. This itself may mark a change from accepted practice in countries such as Kenya where infertility is assumed to be a female disorder and husbands rarely accompany wives to infertility clinics. Health workers also should collect information on any factors known to be important locally in causing infertility, for example, female genital mutilation or exposure to pesticides. Ideally, the initial visit also includes physical examinations of both partners, management of STDs and other reproductive tract infections, evaluation of hormone levels, and a semen analysis.

A key component of an infertility evaluation is for the woman to chart her menstrual cycles at home for several months. This may be as simple as recording the dates when her periods begin and end or, where more intensive instruction is possible, recording basal body temperatures and mucus changes to verify ovulation. Also valuable—but requiring more equipment and trained personnel—are a postcoital test of the woman's cervical mucus to identify sperm transport problems, an endometrial biopsy to identify luteal phase defects, and a laparoscopy and/or hysterosalpingogram to look for blockages or abnormalities of the fallopian tubes and uterus.

Treatments. After a thorough evaluation, most infertile couples do receive a firm diagnosis. Before deciding on a treatment, however, health workers must consider both its cost and the probable results. When ovulatory problems are diagnosed, drugs such as clomiphene citrate and bromocriptine may be used to induce ovulation, while antibiotics can be prescribed in STD-related cases. Artificial insemination, either with the husband's or a donor's sperm, is a relatively simple and inexpensive approach to overcoming many male fertility problems, as well as problems with the woman's cervical mucus. It does, however, require laboratory facilities for the preparation of the sperm and to screen for HIV infection of donor semen.

In many cases, the diagnosis is an abnormality or blockage in the reproductive organs which calls for surgery. Success rates vary, depending both on the procedure and the extent of the damage. In men, varicocelectomy (repair of a varicose vein in the testicle) has proven successful, while surgical repairs of vas obstructions are less so. In women, surgery to repair tubal scarring has had limited success. While microsurgery has shown better results than macro-surgery in these cases, conception rates for all techniques are less than 40 percent and a high proportion of the pregnancies are ectopic. The less damage the patient has sustained, the better the prognosis.

The introduction of in vitro fertilization (IVF) in 1978 created a new treatment option for women suffering from damaged and blocked tubes. IVF employs advanced technologies to recover mature ova, fertilize them in the laboratory, and then implant them in the uterus, thus bypassing the fallopian tubes. Centers for IVF and other assisted reproduction techniques in Latin America, Asia, and Africa have achieved results comparable to those in developed countries, but success rates everywhere are limited: about 15 to 20 percent of women have a clinical pregnancy, three-quarters of these have viable births. In addition to the high costs, centers in developing countries may have difficulty ensuring access to appropriate facilities and supplies.

In 5 to 15 percent of infertile couples, even a thorough evaluation will not find a cause for their problem (see Figure 1). To help these couples conceive, health workers can explain the menstrual cycle and advise them when and how often to have intercourse. Timing is important because conception can only take place if intercourse occurs during about a four-day period, the three days preceding ovulation and one day following. Techniques developed for natural family planning can help infertile couples predict ovulation and maximize the chances of conception. These techniques include tracking the number of days in the woman's menstrual cycle, charting her temperature each day, and monitoring the appearance and texture of her cervical mucus. Several excellent resources are available regarding these techniques (for example, see Network, Volume 12, Number 1, Fall 1996). Family planning clinics are a natural venue for offering these services (see box).

Based on a couple's history, the health worker also may advise behavioral changes that could increase the likelihood of conception. Such advice...
What Can a Family Planning Clinic Do?

By addressing the problem of infertility, family planning clinics demonstrate their commitment to helping people achieve their personal reproductive goals, whether that goal is to postpone a birth, to end childbearing, or to conceive as soon as possible. Every family planning facility, no matter how limited their staff and equipment, can at least educate women and men about infertility issues.

One aspect of this education is to reassure clients that the family planning methods they use do not cause infertility—a common misunderstanding. Specifically, providers should know that:

- barrier methods protect against STDs, therefore can protect against tubal infertility.
- oral contraceptives (OCs), injectable contraceptives, and contraceptive implants have not been linked to infertility, though sometimes return to fertility can be delayed by a few months after discontinuation of OCs and injectables.
- IUDs inserted in women with an STD infection may accelerate ascending infections and therefore increase the risk of tubal infertility. Ensuring that a potential IUD user is not at risk of STD can almost completely eliminate the risk.
- Education about infertility and fertility awareness gives couples the knowledge they need to conceive more quickly or to prevent another birth. It can help dispel local beliefs that infertility is always the “woman’s fault” and teach the importance of preventing and seeking early treatment for STDs.

In addition, education may encourage infertile couples to seek help early before their problems become untreatable. Some family planning clinics also may choose to offer basic infertility evaluations and treatment. Because family planning workers already are familiar with reproductive health issues and possess both clinical and counseling skills, they can readily be trained to take histories, perform physical exams, collect blood and semen samples, and teach women how to chart their menstrual periods.

might include increasing the frequency of coitus; discontinuing the use of lubricants during intercourse and of douching afterwards; elevating the woman’s hips during and after intercourse; gaining or losing weight to produce regular ovulatory cycles; and reducing the intake of coffee, alcohol, or tobacco.

Counseling. No matter how wide or how limited a clinic’s treatment options may be, counseling is always essential. When there is no obvious physical reason for a couple’s problem, counselors can reassure them that nothing is seriously wrong and advise them how to increase the chances of conception. When there is a firm diagnosis, counselors can explain the problem to the couple and give them a realistic idea of the treatment options and their likely success. When there is little or no hope, counselors can help clients cope with the bad news, including their personal disappointment and the strains on their marriage, and suggest adoption as an alternative.

For example, while the infertility clinic at Bawku Hospital in Ghana has seen only 15 percent of its clients become pregnant, the education and counseling offered by the clinic has helped infertile women and couples understand and cope with their personal disappointment and social pressures. By heightening the awareness of reproductive problems, the clinic also has encouraged increasing numbers of women to seek help for STDs, gynecological complaints, and family planning needs.

Program Implications

Infertility in developing countries is widespread and, in many instances, preventable. Given limited resources, programs should focus on reducing STDs, postpartum and postabortion complications, and the endemic diseases that cause infertility rather than on offering high-technology treatments to infertile couples. Yet, couples suffering the personal disappointment and social stigma of infertility cannot be ignored. By training health care workers to carry out systematic, but limited, evaluation and treatment protocols, it is possible to make diagnoses, offer counseling, and conduct basic treatments without adding substantially to existing health care costs.


TABLE 1

<table>
<thead>
<tr>
<th>Location</th>
<th>Vertical transmission rates(^{†}) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>22-43</td>
</tr>
<tr>
<td>Asia</td>
<td>48</td>
</tr>
<tr>
<td>Caribbean</td>
<td>24</td>
</tr>
<tr>
<td>United States</td>
<td>17-30</td>
</tr>
<tr>
<td>Europe</td>
<td>14-27</td>
</tr>
</tbody>
</table>

\(^{†}\) Data from selected countries. Source: Adapted from John and Kreiss, 1996 and Working Group on Mother-To-Child Transmission of HIV, 1994.

Thus, the number of women of reproductive age infected with human immunodeficiency virus (HIV) increases, more and more infants are placed at risk of the disease. Studies have found that women infected with HIV transmit the virus to between 14 and 48 percent of their children (see Table).\(^{1,2}\) Transmission rates are typically lower in developed countries (below 25 percent) than in developing countries (above 25 percent). Results of recent studies on mother-to-infant HIV transmission are helping programs develop effective interventions to reduce the prevalence of HIV among children.

HIV can be transmitted from mother to child at three different times—in utero, at delivery, and during breastfeeding.\(^3\) The presence of the virus in fetal tissues demonstrates that HIV can cross the placenta. Studies of twins support the idea that transmission may occur during delivery: second-born twins, who have a quicker passage through the birth canal (and thus have less exposure to cervico-vaginal secretions and, possibly, blood) than their first-born siblings, have lower rates of infection. Half or less of all infected newborns test positive for HIV shortly after birth; they are assumed to have been infected in utero. Other infected infants only develop detectable levels of virus in the bloodstream after the first week of life; they are assumed to have been infected immediately before or during delivery.

Infants also may be exposed to maternal HIV after birth, through breast milk. According to a meta-analysis of six prospective studies, 14 percent of children of HIV-infected mothers contracted HIV through breastfeeding.\(^4\) The data suggest that breastfeeding may account for more than one-third of all infants infected in areas such as sub-Saharan Africa where breastfeeding is universal and HIV is highly prevalent. Breastfeeding infants of women who become infected with HIV postnatally are at especially high risk of infection: the virus is transmitted to 29 percent of these infants.

### Maternal and Obstetric Risk Factors

Prospective studies of children born to mothers infected with HIV have examined potential risk factors for transmitting the disease. One consistent finding is that disease progression in the mother—as measured by markers such as a low CD4+ lymphocyte count—is significantly related to the risk of transmitting HIV to the child. Infants born to women with more severe cases of HIV are from 2 to 3.5 times more likely to be infected than children born to women with milder illness.\(^3,4,5,6,7\) Concurrent infections with sexually-transmitted diseases (STDs) or other vaginal infections also may increase the risk of HIV transmission.\(^3,4\)

Early rupture of the fetal membranes also appears to be a significant risk factor for HIV transmission, possibly because it increases infants’ exposure to infected cervico-vaginal secretions during delivery. For example, in a multi-center U.S. study, the transmission rate was 25 percent when the membranes ruptured more than four hours before delivery, compared with a rate of 14 percent when less time elapsed before delivery.\(^6\)

Certain obstetrical procedures may increase the risk of HIV transmission. In two French cohorts, transmission rates were twice as high (34 percent versus 19 percent) when women had undergone...
procedures during pregnancy that might disturb the placenta or cause subclinical bleeding, particularly amniocentesis and amnioscopy. There are conflicting data on whether procedures used during labor and delivery, such as episiotomy, internal fetal-scalp electrodes, and the use of instruments, influence the risk of HIV transmission.

A meta-analysis of six prospective studies has found significantly lower maternal HIV transmission rates for Caesarean deliveries (14 percent) compared with vaginal deliveries (20 percent). In theory, Caesarean sections could reduce HIV transmission during delivery by limiting infants' exposure to infected cervico-vaginal secretions. The meta-analysis did not control for other key variables, such as the mother's viral load, however, and other studies have produced contradictory findings.

While the data on obstetric risk factors are far from definitive, they do suggest some changes in the care of pregnant women infected with HIV. For example, health care providers should actively diagnose and treat STDs and vaginal infections in HIV-infected pregnant women; they should avoid invasive procedures during pregnancy; they should not intentionally rupture the fetal membranes to induce or accelerate labor; and they should try to hasten delivery after the membranes rupture. As for Caesarean sections, even if they are proven to reduce the rate of HIV transmission, the potential benefit must be weighed against the cost of the procedure and its known risks—risks that may be greater for HIV-infected women than others.

### Treatment Options

A multi-center clinical trial conducted in the U.S. and France in the early 1990s found that treating pregnant HIV-infected women and their infants with the antiretroviral drug zidovudine reduced transmission by two-thirds: 7.6 percent of infants in the zidovudine group contracted the virus compared with 22.6 percent in the placebo group. The only short-term side effect of the drug was to lower infants' hemoglobin levels temporarily.

Some questions remain about zidovudine treatment. It is not known which of the original protocol's three elements were responsible—either individually or in combination—for the drop in transmission: zidovudine was administered orally to women during the last trimester of pregnancy, intravenously to women during labor and delivery, and orally to newborns during the first six weeks of life. The long-term safety of zidovudine for infants continues to be evaluated.

Based on the compelling results of the clinical trial, however, the U.S. Public Health Service has recommended screening pregnant women for HIV and offering zidovudine to those infected. Cost-effectiveness studies in the U.S. show that this is far less expensive than caring for HIV-infected children.

Applying those results to developing country settings will be difficult because the cost and complexity of the zidovudine protocol are serious obstacles to its use.

### Breastfeeding

The risk of transmitting HIV from mother to child in breast milk must be weighed against the well-established health benefits of breastfeeding and the potential risks of bottle feeding. Breastfeeding protects infants against diarrheal diseases and respiratory tract infections and also contributes to women's and children's well-being by lengthening birth intervals. For infants who have been infected with HIV in utero or during delivery, breast milk also may deliver maternal HIV-specific antibodies that will improve their health and survival. Bottle feeding, in contrast, may threaten infants' health in settings where mothers cannot afford to buy sufficient formula, do not have access to clean water, and may not be able to clean bottles adequately.

Thus the balance of risks and benefits of breastfeeding by HIV-infected mothers varies depending on the pattern of infant mortality, the prevalence of HIV, and the ability to bottle feed safely. In industrialized countries, HIV-infected mothers routinely are urged not to breastfeed, because bottle feeding poses less of a threat to their infants than the possibility of HIV infection. In contrast, where infant mortality due to infectious disease and malnutrition is high—even if HIV prevalence is also high—the health benefits of breastfeeding outweigh the dangers of HIV. A 1992 WHO/UNICEF consensus statement recommended that HIV-infected women in these settings continue to breastfeed. In settings where the dangers of bottle feeding and the prevalence of HIV are moderate, the decision whether to breast or bottle feed is less clear.

As more is learned about the transmission of HIV through breastfeeding, the best intervention in developing countries may be to modify breastfeeding patterns. For example, if the risk of transmission is constant throughout the duration of breastfeeding, weaning infants early (perhaps at age 3-7 months in sub-Saharan Africa) might maximize the health benefits of breastfeeding while minimizing the risk of transmission. If the risk of transmission peaks during the first week after birth, with colostrum being more infectious than breast milk, then withholding breast milk for the first day or two of life might reduce transmission rates without denying infants the benefits of breastfeeding.

### Policy Implications

Research findings suggest that mother-to-infant transmission of HIV might be reduced by changing the obstetrical management of HIV-infected women,
by treating pregnant women with zidovudine, or by modifying breastfeeding patterns. Yet each of these interventions requires that pregnant women who are infected with the virus first be identified. A universal screening program, accompanied by appropriate counseling, is costly and difficult to implement. In the U.S., for example, providers fail to screen most pregnant women despite strong recommendations to do so, and many of those women who are identified as HIV-positive decline treatment.8

Additionally, interventions that may be cost-effective in developed countries are not always feasible or appropriate in developing countries. For example, routinely administering zidovudine or offering Caesarean sections to HIV-infected women is not possible financially or logistically in low-resource settings. Likewise, recommendations to avoid amniocentesis or internal fetal-scalp monitors are irrelevant where such procedures are rarely used. Furthermore, the balance between the benefits and risks of breastfeeding differs among countries. Research is under way on practical interventions that are better suited to developing countries. These include studies of shortened zidovudine regimens, modifications of breastfeeding patterns, the topical application of antiseptics at delivery, administration of Vitamin A to pregnant women, and passive immunization with antibodies.1, 3, 12

Mother-to-Infant HIV Transmission. ................. 6