Editors' Summary. For men and women both, the most common preventable cause of infertility is infection. In some areas infection-related infertility is so widespread that it constitutes not only a personal problem but also a public health challenge. Pelvic inflammatory disease in women, due to sexually transmitted disease (STD) and other infections, probably accounts for more than half of all female infertility in many regions. Although the woman is usually blamed when a couple cannot have children, male factors explain about one-third of all infertility. Low sperm count, often the result of infection, is the most important male factor.

Infertility can mean either primary infertility — that is, inability to have any children at all — or secondary infertility — inability to have additional children — after several years of trying. Treatment of either primary or secondary infertility is difficult and costly, and the results uncertain. Therefore, public health programs should focus on prevention, which is much more practical and cost-effective. Programs to prevent infertility can stress:

- improved diagnosis, treatment, and control of sexually transmitted diseases,
- public education about STDs for men and women,
- expanded family planning services for men as well as women, stressing barrier methods and the pill,
- improved delivery and maternal health care.

Infertility may be most common in tropical Africa, where researchers have identified communities in which more than 30 percent of couples are childless. Infertility also occurs more often than usual in some Asian countries and in the Caribbean region. In Sudan, Indonesia, and Jamaica, for example, nationwide surveys suggest that more than 6 percent of married women reach age 40-49 without having any children. In most developing countries, 2 to 3 percent are childless. In the US the percentage of couples remaining childless is almost 8, but an unknown part of that is voluntary.

Female Infertility

The major causes of female infertility — which accounts for 50 to 70 percent of all infertility — are:

- infections and resulting damage or blockage of the fallopian tubes,
- hormonal or ovulation disorders, and
- endometriosis (growth of endometrial tissue outside the uterus).

In developed countries, hormonal disorders and endometriosis account for a large part of infertility, but they can be treated with increasing effectiveness. Drugs such as clomiphene citrate can be used to induce ovulation; drugs or surgery can be used in the early stages of endometriosis to prevent endometrial growths from damaging reproductive organs.

More common in developing countries — and most difficult to treat under any circumstances — is infertility caused by the aftereffects of various genital infections, including STDs. Infections can lead to permanent scarring and blockage of the fallopian tube, making fertilization impossible. They also can cause inflammation that disrupts sperm and egg transport. Some STDs, such as syphilis, can infect a fetus in the uterus, causing intrauterine death. Some, such as herpes, can infect the child at birth, reducing the chances for survival.

The most frequent type of infection in the fallopian tubes is pelvic inflammatory disease (PID). The term PID is now widely used to describe infections that have ascended into the upper reproductive tract. The most frequent cause of PID is gonorrhea. Gonorrhea can spread rapidly through populations and produces few immediate symptoms in the female. Therefore it is likely to go untreated, spread to
the tubes, and cause infertility. Other infections that can lead to tubal infertility are Chlamydia and possibly mycoplasmas — both sexually transmitted.

Childbirth and abortion can be major sources of infections that cause infertility. Infection is especially likely when these events take place under unhygienic conditions involving untrained personnel and when women with complications cannot reach hospitals. Women who have vaginal or cervical infections at the time are also at high risk.

**Male Infertility**

Much less is known about male infertility, partly because men are less likely to seek full examination or treatment. Male infertility results primarily from low concentrations of sperm in semen (low sperm count) or abnormal sperm. In developing countries male infertility, like tubal infertility in women, is often caused by untreated genital infections, many of them sexually transmitted. These infections may persist for years, spread through the reproductive organs, and cause inflammation and scarring that can block sperm transport. The same STDs that cause female infertility — especially gonorrhea, chlamydial infection, and possibly mycoplasmas — also affect males.

**Prevention**

Clearly, the most effective approach in the long run is to prevent the spread of infections that lead to infertility. Public health programs that would contribute to this goal include:

- **STD control programs.** These require individual and institutional efforts to identify and treat all STD cases as rapidly and effectively as possible, thus checking the spread of disease and its later complications.
- **STD education programs.** An important part of any control program, these involve public education of men and women at greatest risk to be sure that they know about the causes, symptoms, and dangers of STDs, and how and where to obtain treatment. Emphasis can be placed on the fact that limiting the number of sexual contacts will reduce the chances of acquiring an STD and possibly becoming infertile.
- **Training programs for traditional midwives.** These can teach those who attend childbirth and provide female health care how to reduce the risk of infection during uncomplicated births and when to refer women to health centers for further attention.
- **Basic family planning services.** Family planning programs can promote use of condoms, spermicides, diaphragms, and oral contraceptives — all of which protect against infections that can lead to infertility. Family planning can reduce the incidence of induced abortion by making contraceptives readily available and educating people about proper use.
- **Expanded family planning, STD, and/or basic infertility services.** In addition to promoting appropriate contraceptives, these programs can help identify and treat STDs and can help infertile couples obtain an initial evaluation of their condition at minimal cost.

Much of infertility is preventable, especially where rates of infertility are high because of disease. But controlling sexually transmitted disease and promoting the use of appropriate contraceptives require a sustained public health effort with national political support. This effort must emphasize the shared responsibility of men and women, since infertility is a shared problem. It will not be solved without appropriate and responsible behavior by both sexes and concerted, long-term efforts by health care providers.

**End of Editors' Summary.**

**EXTENT OF THE PROBLEM**

The extent of infertility varies considerably among countries and within countries. Couples everywhere, however, are distressed if they are unable to produce the offspring they want, and particularly if they are childless. Some may find their lives significantly disrupted by infertility. In many cultures the ability to have children is an important sign of an individual's worth. Couples want sons, who can inherit their land and name. They want children to care for them in old age and, in some religions, to pray for them after their death. For women, failure to have children can lead to social disgrace and divorce (499). While the social and psychological consequences of infertility differ, in virtually every culture most people feel that it is important to have children (343, 398).

**National Data**

Demographic studies usually measure infertility in one of two ways:

1. Childlessness at the end of reproductive life or
2. The absence of recent live births or pregnancies.
On the extent of childlessness, the most comprehensive national data come from the World Fertility Survey (WFS) (625) (see Population Reports, The World Fertility Survey: Current Status and Findings, M-3, July 1979). Overall, in the mid to late 1970s levels of childlessness among married women age 40 to 49 ranged from 1.3 percent in South Korea to 6.7 percent in Indonesia. The average for all 27 surveyed countries was 3.4 percent. The percentage was above this average in two of four African countries surveyed — Lesotho, at 5.5 percent, and Sudan, at 6.3 percent. Among 10 Asian and Pacific countries, childlessness was above the average in only two, Fiji, at 4.3 percent, and Indonesia, at 6.7 percent. In 4 of 11 Latin American and Caribbean countries, childlessness was high — between 4.5 and 6.5 percent. These countries were the Dominican Republic, Guyana, Jamaica, and Trinidad and Tobago, all in the Caribbean region. In both Middle Eastern countries surveyed, Jordan and Syria, levels of childlessness were below 3 percent (see Table 1).

WFS data have definite limitations for studying infertility, however. First, they reflect the experience of currently married women only. If some women are divorced because they are childless, the actual extent of childlessness is underestimated. Also, national data may obscure substantial regional differences within some countries. A further shortcoming of data on childlessness is that they do not cover couples who become infertile after having one or more children. Where childlessness is common, however, secondary infertility usually is also common (170).

Census data also have identified countries where childlessness is relatively common. African censuses in the 1950s and 1960s found that childlessness among women age 50 and older reached 32 percent in Gabon, 18 percent in Zaire, 14 percent in the Central African Republic, and 10 percent in Sudan (56). More recently, in the US 7.7 percent of ever-married women age 45 to 49 were childless in 1980 (620). It is not known how much of US childlessness is voluntary, however.

### Table 1. Percentage of Women Age 40-49, Continuously Married for at Least Five Years, Who Are Childless, World Fertility Survey Reports, 1974-1979

<table>
<thead>
<tr>
<th>Place</th>
<th>Date</th>
<th>Number of Women Surveyed</th>
<th>% Childless</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AFRICA</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kenya</td>
<td>1977-78</td>
<td>1,079</td>
<td>2.7</td>
</tr>
<tr>
<td>Lesotho</td>
<td>1977</td>
<td>567</td>
<td>5.5</td>
</tr>
<tr>
<td>Senegal</td>
<td>1978</td>
<td>622</td>
<td>3.1</td>
</tr>
<tr>
<td>Sudan</td>
<td>1978</td>
<td>478</td>
<td>6.3</td>
</tr>
<tr>
<td><strong>ASIA &amp; PACIFIC</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bangladesh</td>
<td>1975-76</td>
<td>826</td>
<td>2.2</td>
</tr>
<tr>
<td>Fiji</td>
<td>1977</td>
<td>955</td>
<td>4.3</td>
</tr>
<tr>
<td>Indonesia</td>
<td>1976</td>
<td>1,285</td>
<td>6.7</td>
</tr>
<tr>
<td>Korea, Rep. of</td>
<td>1974</td>
<td>1,461</td>
<td>1.3</td>
</tr>
<tr>
<td>Malaysia</td>
<td>1974</td>
<td>968</td>
<td>3.1</td>
</tr>
<tr>
<td>Nepal</td>
<td>1976</td>
<td>990</td>
<td>2.8</td>
</tr>
<tr>
<td>Pakistan</td>
<td>1975</td>
<td>2,290</td>
<td>2.1</td>
</tr>
<tr>
<td>Philippines</td>
<td>1978</td>
<td>1,661</td>
<td>2.8</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>1975</td>
<td>906</td>
<td>2.3</td>
</tr>
<tr>
<td>Thailand</td>
<td>1975</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LATIN AMERICA &amp; CARIBBEAN</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colombia</td>
<td>1976</td>
<td>620</td>
<td>2.9</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>1976</td>
<td>648</td>
<td>2.2</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>1975</td>
<td>334</td>
<td>4.5</td>
</tr>
<tr>
<td>Guyana</td>
<td>1975</td>
<td>663</td>
<td>5.3</td>
</tr>
<tr>
<td>Haiti</td>
<td>1977</td>
<td>412</td>
<td>3.2</td>
</tr>
<tr>
<td>Jamaica</td>
<td>1975-76</td>
<td>511</td>
<td>6.5</td>
</tr>
<tr>
<td>Mexico</td>
<td>1976-77</td>
<td>1,188</td>
<td>3.5</td>
</tr>
<tr>
<td>Panama</td>
<td>1976</td>
<td>601</td>
<td>2.7</td>
</tr>
<tr>
<td>Paraguay</td>
<td>1979</td>
<td>627</td>
<td>3.2</td>
</tr>
<tr>
<td>Peru</td>
<td>1977-78</td>
<td>1,294</td>
<td>2.0</td>
</tr>
<tr>
<td>Trinidad &amp; Tobago</td>
<td>1977</td>
<td>648</td>
<td>4.9</td>
</tr>
<tr>
<td><strong>MIDDLE EAST</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jordan</td>
<td>1976</td>
<td>722</td>
<td>2.2</td>
</tr>
<tr>
<td>Syria</td>
<td>1978</td>
<td>970</td>
<td>2.9</td>
</tr>
</tbody>
</table>

Source: Vaessen, M. [World Fertility Survey] (625)

Educational materials publicize three important ways to guard against infertility: (1) prevent and treat pelvic inflammatory disease (PID), a major source of infertility in women; (2) prevent and treat sexually transmitted diseases (STDs), which lead to PID and pregnancy loss in women and cause infertility in men as well; (3) use contraceptives such as condoms or spermicides, which protect against STDs, or the pill, which protects against PID. Programs in family planning, primary health, and STD control all have roles to play in preventing infertility.
What Is Infertility?

Infertility is defined in various ways. Medical, demographic, and popular usages often differ. A useful definition in assessing the need for public health programs, in planning medical treatment services, and in talking with couples is the inability to conceive, impregnate, or carry a pregnancy to term.

Definitions of infertility are often based on a couple's experience trying to achieve pregnancy over a period of time. From a medical point of view, a couple is considered possibly infertile if pregnancy has not occurred within one or two years of unprotected intercourse (671). Demographic studies often define a couple as infertile if the woman reports no pregnancies or live births within a certain number of years of unprotected intercourse — usually the past one, two, or five years. US and UK studies substantiate these definitions. A US study found that over 90 percent of couples desiring pregnancy achieved pregnancy within one year; 96 percent, within two years (606). A UK study of women stopping contraception to become pregnant found that over 90 percent had a child within two years; 96 percent, within three years (629).

A number of terms are commonly used in discussions of infertility. Infecundity is the inability to conceive or to impregnate. In medical literature the term infecundity often is synonymous with infertility. For instance, the World Health Organization (WHO) defines infertility as the inability to achieve conception within two years (671). Pregnancy wastage is the failure to carry a pregnancy to term, including both spontaneous abortion at any stage of pregnancy and stillbirth (671). Primary infertility means a couple has never achieved conception. Secondary infertility means at least one conception has occurred, but the couple is currently not able to achieve pregnancy (671). In popular use, the terms primary and secondary infertility also include the inability to carry a pregnancy to term. Sterility implies complete and permanent inability to conceive or impregnate, even after treatment (55).

Childlessness — a common measure of infertility — means that a couple has not produced any children, whether due to infecundity, pregnancy wastage, contraception, or induced abortion (55). While demographers distinguish between fertility, as childbearing performance, and fecundity, as childbearing ability, this report follows medical and popular usage, which equates the two.

A second measure of infertility is the percentage of married women who have not had a child or a pregnancy for a certain number of years, even though they were not using any contraception. By this measure, WFS data show especially high levels of infertility in Africa and in certain Asian countries (see Figure 1). This measure, however, may exaggerate the extent of infertility where women practice prolonged breastfeeding and/or postpartum abstinence. Also, this type of measure covers not just pathological infertility but also the normal decline in female fertility that accompanies age (see box, p. L-124).

In some countries levels of infertility are high enough to have a noticeable effect on total fertility, or average size of a completed family. According to a recent estimate, in 17 African countries taken together, infertility reduces total fertility by an average of one birth per woman, from 7.3 to 6.3. Where infertility is very common, as in Gabon, total fertility may be reduced by as much as 3.2 births per woman, from 7.3 to 4.1 (170). It has been suggested that infertility has been an important reason for decreases in population size in certain areas of Africa (495, 501). Among the Fulani of North Cameroon, infertility is thought to be responsible for a birth rate that is lower than the death rate (143). Many areas of declining population where infertility is a problem also are affected by out-migration, endemic disease, and high rates of child mortality (209, 392, 492, 626). Thus it is difficult to determine the effect of infertility without birth rates and other data.

Regional Variation

Within many countries levels of childlessness vary widely among regions (327, 495). In Africa research on the causes of infertility has been conducted for over 30 years, resulting in a large body of demographic, sociologic, and anthropologic literature (495). This research has uncovered areas with very high levels of infertility. In some regions of the Central African Republic the late 1950s, for instance, as many as 40 percent of women age 45 and older had never given birth to a live infant (496, 498, 499). Among Upper Volta villages studied by Anne Retel-Laurentin, the average number of live births reported by women age 45 and older varied from 2.1 to 4.6, and childlessness varied from 11 to 25 percent (30, 494). STDs and other diseases are thought to account for most of the infertility: where STDs were more common, rates of infertility were high (492, 494, 500, 501).

Data from other countries also show marked regional differences in infertility. According to African censuses from the 1950s and 1960s, among women age 50 and older childlessness varied by region from 3 to 40 percent in Zaire, 2 to 21 percent in Sudan, 18 to 46 percent in Gabon, and 10 to 19 percent in the Central African Republic (56). In Tanzania a 1973 survey found that childlessness among women age 40 to 44 ranged from 4 percent in one region to 21 percent in another (226). In Cameroon a recent study of women age 15 to 50 found that primary infertility — never having conceived — varied between 3 and 17 percent among regions. Secondary infertility varied between 14 and 39 percent (313). In Indonesia in the mid-1970s, 6.7 percent of married women age 40 to 49 were childless (625), but in some regions 15 percent of married women age 30 and over were childless (245).

Ethnic and racial differences in infertility have been observed in places as disparate as Zaire and the US. In Equateur Province, Zaire, for example, childlessness among women age 45 to 49 varies from about 6 percent among the Ngbaka and Batwa-Batsha peoples to 65 percent among the Mbelo (530). In the US a 1976 survey showed that about twice as many noncontracepting black couples as white couples had not achieved pregnancy in the previous year — 18.4 percent compared with 9.1 percent (404). Levels of infertility may differ because of differences in the prevalence of STDs or because of differences in access to adequate care for STDs and during childbirth.
Figure 1. Percentage of Noncontracepting, Nonpregnant Women, Continuously Married for Last Five Years, Reporting No Live Births in Last Five Years, by Age Group, World Fertility Survey Reports, 1974-1979

Source: Vaessen, M. (World Fertility Survey) (625)
Childlessness is more common in cities than rural areas wherever the pattern has been studied — among women of various age groups in Indonesia (245), Kenya (407), Niger (141), Tanzania (73), and Zaire (516, 596). This may be because STDs are more common in cities (36). In cities the presence of recently arrived, unmarried migrants and the disruption of traditional family units contribute to the spread of STDs (27, 60, 628).

Effect of Marriage Patterns

Infertility often is relatively common in areas where marriages tend to be unstable and where many people have multiple sexual partners (495). Marital instability, premarital intercourse, and brief consensual unions — all of which may increase the number of sexual partners — can lead to infertility by facilitating the spread of STDs (143, 498, 515). At the same time, marital instability may be the result of infertility (437). In some societies women are divorced because of childlessness, or women leave infertile marriages hoping to conceive with a new partner (143, 436, 499).

Polygyny (more than one wife) may increase the likelihood of infertility (233, 437, 495, 517), probably because STDs can be transmitted quickly among all wives in a polygynous marriage. At the same time, where polygyny exists, lack of offspring with one wife may encourage a man to take other wives (437). A 1977 Kenyan survey found that, among women age 44 to 49, 6 percent of co-wives were childless, while only 2 percent of sole wives were childless (226). Women in polygynous marriages may have coitus less often, which also could help to explain such a difference.

Trends

Is infertility becoming more or less common? Data are few, so it is not possible to assess worldwide trends. Zaire and

Throughout tropical Africa — especially in the central region — areas where infertility is common have been identified through numerous medical, demographic, and anthropologic studies. (Adapted from Retel-Laurentin, A. Infecondité en Afrique noire: maladies et conséquences sociales. Paris, Masson, 1974.)

In the US, by contrast, survey data suggest that infertility among young married women increased slightly between 1965 and 1976 (405). Infertility, defined as no pregnancy after one or more years of intercourse without contraception, increased from 4.5 to 7.4 percent among those age 15 to 29, a statistically significant change (405). Rates of STDs and pelvic inflammatory disease (PID) increased markedly during this period (see box, p. L-131). By contrast, among older women, infertility declined from 15.5 to 12.6 percent. Methodologic problems make it difficult to be sure of the accuracy of these percentages (387), but the results agree with clinicians’ observations of increasing infertility problems among young US women (154, 401). These data suggest an impact of increasing STDs on infertility even where treatment is available.

When is infertility a public health problem? There is apparently no “baseline” level of infertility or childlessness which, if exceeded, indicates that infertility is a public health problem rather than only a couple’s private concern (55). Among the Hutterites, a healthy, high-fertility North American religious sect not at high risk of sexually transmitted diseases and not using contraception, only 2 to 3 percent of married women were childless at age 45 (689, 691). It is not clear, however, whether rates would be similar in other populations without STDs and contraception. Regardless of the level of childlessness or infertility, wherever preventable infections such as STDs are a major cause of infertility, public health programs can play an important role in helping couples to achieve their desired family size (56) (see pp. L-134-143).

FEMALE INFERTILITY, PID, AND DISEASE

Female factors probably account for about 50 to 70 percent of all infertility (22, 49, 401). In clinical studies female factors may be overestimated as a cause of infertility, however, because men are less likely to be examined and because unexplained infertility is often arbitrarily attributed to the female.

The immediate causes of female infertility are fairly well understood. They can involve structural or physiologic abnormalities in any part of the female reproductive tract (see Figures 2 and 3). For example:

- Ovaries may fail to produce a viable egg, preventing the possibility of conception.
- Fallopian tubes may be blocked, distorted, or infected, preventing normal movement of the egg or sperm in the tubes.
The uterus may be distorted or the uterine lining (endometrium) inadequate or infected, preventing implantation or survival of the embryo.

- The cervix may be malformed, infected, or secrete abnormal mucus, preventing sperm from reaching the upper reproductive tract.

- Systemic infection or hormonal imbalance may result in fetal death.

In many developing areas, or wherever general health care is poor, a large proportion of female infertility is caused by tubal infection and blockage. As shown below, surveys of infertility patients indicate that tubal factors are the chief cause of female infertility in various developing countries.

<table>
<thead>
<tr>
<th>Clinic Location and Ref. No.</th>
<th>Number of Women</th>
<th>% With Tubal Abnormalities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nairobi, Kenya (368)</td>
<td>104</td>
<td>73</td>
</tr>
<tr>
<td>Libreville, Gabon (409)</td>
<td>228</td>
<td>44</td>
</tr>
<tr>
<td>Kef, Tunisia (182)</td>
<td>114</td>
<td>56</td>
</tr>
<tr>
<td>Highlands</td>
<td>220</td>
<td>86</td>
</tr>
<tr>
<td>Papua New Guinea (102)</td>
<td>634</td>
<td>62</td>
</tr>
<tr>
<td>North Sulawesi, Indonesia (49)</td>
<td>634</td>
<td>62</td>
</tr>
</tbody>
</table>

Although data are few, chronic pregnancy wastage also may be more common in areas where health conditions are poor. In 1971 in regions of Upper Volta where childlessness was common, the spontaneous abortion and stillbirth rate was 31 percent — 15 to 20 percent higher than expected (494).

In developed countries, or where general health care is adequate, the major causes of female infertility, in addition to tubal damage, are ovulation disorders and complications of endometriosis (see Table 2). (Endometriosis is a condition in which endometrial tissue, like that in the uterine, grows on the ovaries, fallopian tubes, and other organs, often causing adhesions — bands of fibrous tissue that cause organs to adhere to one another abnormally.) Clinical series of infertile couples in Denmark, Israel, the US, and Singapore suggest that ovulation disorders account for about 20 to 30 percent of female infertility; tubal problems, for about 15 to 25 percent; and endometriosis, for 10 to 15 percent. (The distinction between endometriosis and tubal problems is not always clear since endometriosis may cause tubal obstruction.) In 10 to 20 percent of couples, neither a male nor a female cause for infertility can be found (see Table 2). Clinical series such as those shown in Table 2 often reflect the specialties of clinics, differing diagnostic techniques, the motivation of couples to attend the clinic, their ability to pay, and other factors (55, 274, 693). Thus these reports may not be precise indications of the causes of infertility.
Pelvic Inflammatory Disease

The major cause of tubal blockage leading to infertility is pelvic inflammatory disease (PID) — an infection often originating in the cervix that ascends to the upper reproductive tract. Women with PID are infertile during the infection. Also, PID can lead to fluid-filled swellings, adhesions, scarring, and other permanent damage to the fallopian tubes (367). In general, a woman with PID is more likely to become permanently infertile if the disease is severe, if treatment is delayed, or if she has suffered multiple episodes of PID. In developed countries an estimated 15 to 20 percent of women who develop PID become permanently infertile (648, 649, 651). In developing countries the proportion probably is higher, since women with PID are less likely to be treated. Before antibiotics were available, an estimated 60 percent of PID cases may have led to infertility (649).

Lars Westrom in Lund, Sweden, has documented the links between PID and infertility. Some 900 women treated for acute PID between 1960 and 1974 were followed to their first pregnancy or, if not pregnant, until 1979. Overall, 15 percent of the former PID patients who were at risk of pregnancy never became pregnant. Of the women who had had severe PID (as diagnosed by laparoscopy), 30 percent were infertile, compared with 13 percent with moderate PID and 6 percent with mild PID. Also, the more episodes of PID, the greater the risk of infertility (648) (see Figure 4).

Westrom also has shown a link between PID and ectopic pregnancy. In an earlier study one of 24 pregnancies among 415 PID patients was ectopic compared with one of 147 among 100 controls (647). Ectopic pregnancy often leads to rupture of a fallopian tube — a life-threatening emergency that usually requires surgical removal of the tube.

The major sources of PID are:
- sexually transmitted diseases,
- postpartum infection,
- postabortion infection (410).

### Table 2. Causes of Infertility in Clinical Series of Couples Seeking Treatment, Selected Studies, 1962-1980

<table>
<thead>
<tr>
<th>Author, Date, Country &amp; Ref. No.</th>
<th>No. of Couples</th>
<th>Male Factors</th>
<th>Female Factors</th>
<th>Both Male &amp; Female</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DEVELOPING COUNTRIES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Barten 1978, Indonesia (49)</td>
<td>863</td>
<td>30</td>
<td>64</td>
<td>NA</td>
<td>6</td>
</tr>
<tr>
<td>Chukudebelu et al. 1979, Nigeria (126)</td>
<td>114</td>
<td>48</td>
<td>50</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Garcia Martinez et al. 1977, Mexico (181)</td>
<td>500</td>
<td>12</td>
<td>87</td>
<td>NA</td>
<td>2</td>
</tr>
<tr>
<td>Ledward 1980, Saudi Arabia (324)</td>
<td>56</td>
<td>20</td>
<td>61</td>
<td>5</td>
<td>14</td>
</tr>
<tr>
<td>Nakamura et al. 1971, Brazil (415)</td>
<td>919</td>
<td>28</td>
<td>67</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Ratnam et al. 1976, Singapore (485)</td>
<td>709</td>
<td>23</td>
<td>55</td>
<td>NA</td>
<td>22</td>
</tr>
<tr>
<td><strong>DEVELOPED COUNTRIES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dor et al. 1977, Israel (150)</td>
<td>665</td>
<td>23</td>
<td>52</td>
<td>8</td>
<td>18</td>
</tr>
<tr>
<td>Jones &amp; Pourmand 1962, US (261)</td>
<td>555</td>
<td>15</td>
<td>66</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>Katayama et al. 1979, US (275)</td>
<td>459</td>
<td>18</td>
<td>68</td>
<td>NA</td>
<td>15</td>
</tr>
<tr>
<td>Sorensen 1980, Denmark (573)</td>
<td>196</td>
<td>10</td>
<td>72</td>
<td>NA</td>
<td>15</td>
</tr>
<tr>
<td>Thomas &amp; Forrest 1980, Australia (664)</td>
<td>291</td>
<td>6</td>
<td>61</td>
<td>10</td>
<td>23</td>
</tr>
</tbody>
</table>

- Percentages are expressed as percentages of all diagnosed causes of infertility, not as percentages of individuals or of couples.
- May include some cases of male infertility.
- Excludes 177 couples with multiple causes of infertility not specified by sex.
- Includes couples also listed under "Both Male & Female."
Among the STDs, gonorrhea and chlamydial infections are the most common causes of PID-related infertility (see Table 3). Other factors that increase the risk of PID are dilation of the cervix, which occurs during childbirth or induced abortion, and use of an IUD, especially among women exposed to STDs (211) (see p. L-124).

**Sexually Transmitted Diseases**

**Gonorrhea.** Worldwide, gonorrhea is almost certainly the most common preventable cause of PID and tubal infertility (see box, p. L-131). Caused by the bacteria Neisseria gonorrhoeae, gonorrhea is highly contagious through sexual contact. The chances of a man's acquiring gonorrhea from a single exposure are between 20 and 35 percent (672); for a woman the chances are probably double those for a man (91). Because individuals never develop protective immunity, the disease can spread rapidly through a population. In women cervical gonorrhea is often asymptomatic. Thus women are much less likely to seek treatment than men, who usually notice a burning sensation at urination and urethral discharge within a week after infection (37). An estimated 8 to 20 percent of women with untreated cervical gonorrhea develop gonococcal PID (161, 293, 652). The risk depends largely on how quickly the disease is treated.

Gonococcal PID — defined as PID in women who also have cervical gonorrhea (136) — can produce severe clinical symptoms, but it usually responds quickly to antibiotics. The symptoms include abdominal pain, tenderness of the fallopian tubes, fever, and vaginal discharge of pus (136, 284, 591, 593). Where adequate medical facilities are available, most women with these symptoms probably seek treatment quickly and thus decrease the risk of permanent tubal damage.

When gonococcal PID is not treated, the disease can be very damaging. The bacteria multiply rapidly in tubal tissue (106) but after a week or two appear to die out. Then a variety of secondary invaders — usually bacteria that ascend from the vagina — may infect the damaged tissue (134, 359, 400). These often cause more damage than the initial gonococcal infection (190, 359, 593), since many are difficult to treat.

In some developed and developing countries, gonorrhea causes more than 40 percent of PID cases. In the US between 40 and 50 percent of women with PID have positive endocervical gonorrhea cultures (131, 134, 161, 594). Similar figures are reported in Africa. In Uganda a study of 86 PID patients found that at least 38 percent had cervical gonorrhea (204). In a Kenyan study 43 percent of 53 PID patients had gonorrhea (108), and in Zambia a study found that 46 of 100 PID patients had gonorrhea (484). Gonorrhea is not always a major cause of PID, however. In India, where gonorrhea does not appear to be widespread, only 9 percent of 800 PID patients had gonorrhea (549).

A comparison of two regions in Uganda suggests a close association between high levels of gonorrhea and PID, on one hand, and infertility, on the other. In one region, Teso, 18 percent of women had positive cultures for gonorrhea, 17 percent of women had evidence of PID, and the birth rate was relatively low — 37 births per 1,000 population annually. In the other region, Ankole, 2 percent of women had positive cultures for gonorrhea, none had PID symp-

**Chlamydial infections.** Another common sexually transmitted disease that can cause tubal infertility is chlamydial infection. It is caused by a bacteria-like organism, Chlamydia trachomatis, that lives within the cells of its host (533, 536). In women, infection results in cervicitis. A recent study in Sweden found that 8 percent of women with cervical chlamydial infections had PID (652).

In general, the symptoms of chlamydial PID are less severe than those of gonococcal PID. Many women may be asymptomatic (210, 591, 650). Yet the tubal damage caused by chlamydial PID appears to equal or exceed that caused by gonococcal PID (397). In Weström's study of 415 PID patients, women with nongonococcal PID, including chlamydial PID, were almost four times more likely to be infertile than women with gonococcal PID. Other factors also may have contributed to this difference, however (647).

It is difficult to gauge the incidence of chlamydial PID, mainly because the disease-causing organism is difficult to culture (673) and also because other STDs often mask its effects (650). In Swedish, Finnish, and US clinics where tests for the organism are routine, 20 to 30 percent of PID patients have chlamydial infections (161, 362, 452). Very little information on chlamydial infections is available from developing countries.

Infertile women often have evidence of current or past chlamydial infection. In the US 35 percent of 172 infertile women had high chlamydial antibody titers; 75 percent of the women with high titers were infertile because of tubal
Table 3. Summary of Relationships Between Female Infertility and Diseases in Developing Countries

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cause/Effect Relationship</th>
<th>Epidemiologic Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sexually Transmitted Diseases</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>Yes—well-established</td>
<td>Major</td>
</tr>
<tr>
<td>Chlamydial Infections</td>
<td>Yes—few data</td>
<td>Unknown</td>
</tr>
<tr>
<td>Syphilis</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td><strong>Mycoplasmas</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M. hominis</td>
<td>Possible</td>
<td>Unknown</td>
</tr>
<tr>
<td>U. urealyticum</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td><strong>Other Conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postpartum infection</td>
<td>Yes—well-established</td>
<td>Possibly major</td>
</tr>
<tr>
<td>Postabortion infection</td>
<td>Yes—well-established</td>
<td>Probabl y major</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Malaria</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>Possible—few data</td>
<td>Probably great where disease is common</td>
</tr>
</tbody>
</table>


Problems (268). In Finland 57 percent of 128 infertile women had such antibodies, compared with 29 percent of 68 pregnant women. The highest antibody levels were found in 9 infertile women with proven tubal blockages (475).

**Mycoplasmas.** These sexually transmitted organisms are commonly found in the human reproductive tract (598). Some studies have found that women with PID are more likely than controls to harbor one type of mycoplasma — Mycoplasma hominis (161, 364). Mycoplasma infections often coincide with gonococcal or other infections (161, 364). Thus it is not clear whether they damage tubal tissue or merely coexist with other infections known to be damaging.

**Other Diseases**

**Genital tuberculosis.** Genital tuberculosis (TB) usually develops after an infection in the lungs (165, 537, 665) and causes scarring and adhesions that can block the tubes (284). Little is known about the prevalence of genital TB or about the proportion of women with pulmonary TB who develop genital TB. Genital TB generally is asymptomatic. Signs and symptoms of tubal disease, such as bleeding and pain, may occur many years after the initial infection, if they occur at all (165, 286, 434, 537). Thus, women often are unaware that they have genital TB until they try to have children. Even endometrial biopsies may fail to detect the disease in about half of the cases (665).

In India, where pulmonary TB is common (668), genital TB may cause about 10 percent of female infertility. Among women undergoing curettage or endometrial biopsy for infertility, genital TB has been found in 4 to 6 percent (157, 454, 549). Laparoscopic examinations, which identify more cases, found that 11 percent of over 500 infertile Indian women had genital TB (296, 297).

**Schistosomiasis.** A number of researchers have suggested that schistosomiasis caused by the schistosome S. haematobium (also called bilharziasis or snail-fever), a water-borne parasitic disease common in many African countries, may be another cause of tubal infertility (96, 354, 408, 681). It has also been suggested that schistosomiasis causes pregnancy wastage. Retel-Laurentin observed that, in regions of the Central African Republic and Upper Volta where infertility is common, the rate of spontaneous abortion or stillbirth was 30 to 40 percent for women with urogenital schistosomiasis but no STDs, compared with 5 to 20 percent in women with neither schistosomiasis nor STDs (492, 493, 497). How schistosomiasis would cause infertility is not clear, however (95, 184, 423, 639). A variety of mechanisms have been proposed — all related to the presence of schistosome eggs in the genital tract (352, 353, 354, 681). Only a small portion of women with schistosomiasis, however, have schistosome eggs in the genital tract, and damage is usually minimal (74, 119, 158, 186). Controlled studies to date have failed to link infertility or ectopic pregnancy to schistosomiasis (74, 177, 186).

**PREGNANCY WASTAGE AND DISEASE**

Pregnancy wastage is common. As many as 45 percent of all pregnancies may be lost before women even recognize that they are pregnant (159, 172, 228). About 15 percent of recognized pregnancies end in spontaneous abortion (316, 511). Most of these pregnancy losses result from unpreventable, random genetic or developmental abnormalities of the fetus that are incompatible with life. Other unpreventable causes include malformed uterus or cervix and inadequate production of the hormone progesterone, which is necessary to maintain pregnancy (287, 511). (See Figure 2.) Among the most important preventable causes of pregnancy wastage are:

- STDs
- certain systemic diseases and infections.
Syphilis and Other STDs

Syphilis is an important preventable cause of pregnancy wastage in some countries. Caused by the spirochete Treponema pallidum, syphilis can progress from a primary stage, characterized by a painless genital chancre, to a secondary stage, characterized by a general body rash, to a latent stage that may last for years before the serious systemic effects of tertiary syphilis, such as insanity and heart disease, occur. Pregnancies in women with primary and secondary syphilis often end in spontaneous abortion, stillbirth, perinatal death, or the birth of a child with congenital syphilis (293). For instance, a US study in the late 1940s and early 1950s found that, among 220 pregnancies in women with untreated primary or secondary syphilis, 38 percent ended in spontaneous abortion, stillbirth, or neonatal death; 41 percent resulted in a syphilitic infant. By contrast, of 82 women with late syphilis, when the disease is much less infectious, 74 percent delivered healthy, full-term infants (252).

Syphilis was a serious problem throughout much of the world before penicillin became widely available in the mid-1950s (662). Scattered reports of a high incidence of congenital syphilis suggest that it remains a serious problem in a number of African countries including Cameroon, the Central African Republic, Senegal, Uganda, Upper Volta, Zaire, and Zambia (293, 497), and in some parts of Asia (see box, p. L-131).

How much impact does syphilis have on the fertility of a population? In some regions of the Central African Republic in the late 1950s and early 1960s the syphilis rate among married women was about 50 percent. Some 40 percent of women age 45 and older in these regions were childless, and women in this noncontracepting population had an average of only two children (496, 498).

In a major study in Upper Volta, Retel-Laurentin documented in 1971 that fertility was lowest where syphilis rates were highest, and vice versa (30, 494).

<table>
<thead>
<tr>
<th>Region</th>
<th>High-Fertility (%)</th>
<th>Medium-Fertility (%)</th>
<th>Low-Fertility (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Syphilis rate</td>
<td>11%</td>
<td>26%</td>
<td>36%</td>
</tr>
<tr>
<td>Birthrate</td>
<td>236</td>
<td>166</td>
<td>134</td>
</tr>
<tr>
<td>Childlessness</td>
<td>11%</td>
<td>22%</td>
<td>25%</td>
</tr>
<tr>
<td>Abortion and stillbirth rate</td>
<td>22%</td>
<td>24%</td>
<td>31%</td>
</tr>
</tbody>
</table>

In these regions all identified syphilis cases and their contacts were treated in 1971 and again in 1976. Between 1971 and 1976 syphilis rates dropped by about 5 percent in each of the regions. Fertility rates increased in all three regions — to 266 in the high-fertility region, 226 in the medium-fertility region, and 201 in the low-fertility region (30). The pregnancy wastage rate for the period 1972 to 1976 dropped slightly to an overall 24 percent for the three regions (30). A variety of other diseases also were common in the regions (497). WHO researchers have suggested that the fertility differences in these regions may have been due more to gonorrhea than to syphilis or other diseases (56). Syphilis and gonorrhea often occur in the same populations (250).

Mycoplasma infections. Infections of the endometrium with the mycoplasma Ureaplasma urealyticum are thought to cause pregnancy wastage (173), but the evidence is not clear. Abnormally high rates of spontaneous abortion have been observed among women with these infections (2, 173, 477). Also, the infections appear to be more common among infertile couples (175, 194, 305, 588). Moreover, there have been reports that treating infertile women for mycoplasma infections improved their chances of pregnancy (174, 477, 588). A well-controlled double-blind trial did not confirm this, however (218). Also, mycoplasmas are present in nearly half of all sexually active adults (599), the majority of whom have no fertility problems.

Genital herpes. The main risk of a genital herpes infection to a pregnant woman is that her infant may contract herpes during birth. An infant has a 50 percent chance of acquiring the infection if born while herpes in the mother is in one of its periodic active stages. Of infants that become infected, 60 percent die (293). Herpes infections also can be transmitted to a developing fetus (557, 663), but only when the virus is circulating through a woman's bloodstream. This happens only during the first episode of herpes, not during later episodes (577).

Other Diseases

Malaria. Experience with malaria control programs suggests that malaria is an important cause of spontaneous abortion. For example, in Sri Lanka before malaria control, the birth rate dropped markedly in the months after the peak of the malaria season. After malaria control the distribution of births was more uniform (424). How would malaria cause abortion? Low birth weights indicate that malarial infection of the placenta can impair fetal nutrition (29, 94, 103, 344, 378). Impaired fetal nutrition is assumed to increase the risk of abortion as well as the risk of low birth weight (201). High fever in early pregnancy also could cause abortion (201, 373). Even if malaria only slightly increases the risk of abortion, it could cause much pregnancy wastage in some areas because it is so common.

Toxoplasmosis. Toxoplasmosis may be an important cause of abortion in women who have an acute episode during
pregnancy. Transmitted mainly through cat feces and raw meat, toxoplasmosis may produce mild, transient fever, fatigue, enlarged lymph nodes, and, in severe cases, extensive damage to the brain, eyes, muscles, heart, liver, or lungs. In some cases the fetus is infected through the placental blood supply.

In many countries toxoplasmosis is a common cause of fetal death. In Zaire a 1970 study suggested that toxoplasmosis may have caused about 10 percent of stillbirths (644). It is estimated to cause more than 10 percent of pregnancy wastage in southern India (449). Surviving infants may suffer defects such as blindness and mental retardation. Since immunity generally develops after infection (56, 340, 509, 667), toxoplasmosis does not cause habitual abortion (191, 283, 310, 574).

Many other common infectious diseases, when contracted early in pregnancy, can cause high fever or fetal infection, resulting in abortion. These diseases include influenza, pneumonia, scarlet fever, and rickettsiae (56, 318, 474, 520, 547). While the risk to an exposed pregnancy can be great, there is no danger to subsequent pregnancies after the disease episode (474, 520).

**Effects of Childbirth and Illegal Abortion**

Postpartum and postabortion infections are common in many parts of the world. If untreated, these infections can spread to the tubes, sometimes causing tubal infertility. In many countries toxoplasmosis is a common cause of fetal death. In Zaire a 1970 study suggested that toxoplasmosis may have caused about 10 percent of stillbirths (644). It is estimated to cause more than 10 percent of pregnancy wastage in southern India (449). Surviving infants may suffer defects such as blindness and mental retardation. Since immunity generally develops after infection (56, 340, 509, 667), toxoplasmosis does not cause habitual abortion (191, 283, 310, 574).

**AGE AND FEMALE INFERTILITY**

Biologically, a woman's reproductive life begins at menarche and ends at menopause. Demographically, fertility rates are measured in terms of women age 15 to 44 or sometimes 49. In fact, a woman's natural fecundity varies considerably over the years between menarche and menopause. It is low immediately after menarche and before menopause, when hormonal patterns may be quite irregular. It probably peaks between ages 18 and 30.

At what age does the risk of infertility significantly increase? Interest in this question has developed mainly because many women, especially educated women with professional careers, are delaying childbearing — sometimes even until their 30s.

Clearly, sexually active women's risk of infertility increases with age partly because they have more time to develop PID, to have an induced abortion leading to complications, or to develop other reproductive health problems (220, 617). It is generally believed as well that women's fertility declines considerably even before menopause because the ova produced are more often defective, and therefore pregnancy wastage is more common. Also, ovulation becomes less frequent. A marked drop in fertility has been thought to occur at about age 35 (462).

A recent French study strongly suggested that women's fertility drops sharply at around age 30 rather than at age 35 (167). Over 2,000 nulliparous women whose husbands were azoospermic were surveyed after undergoing artificial insemination by donor, mostly with frozen sperm. Failure to conceive after one year of monthly inseminations was much more common in women over age 30 than in younger women (167):

<table>
<thead>
<tr>
<th>Age</th>
<th>% Failing to Conceive</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30</td>
<td>26</td>
</tr>
<tr>
<td>31-35</td>
<td>39</td>
</tr>
<tr>
<td>36+</td>
<td>46</td>
</tr>
</tbody>
</table>

Some physicians have concluded from these data that women thinking about delaying childbearing until their late 20s or early 30s should be warned of an increasing risk of infertility (144).

In general, World Fertility Survey data also suggest that the risk of infertility increases more sharply at ages 35-39 than at any younger age (see Figure 1, p. L-117). In most of the 27 countries surveyed, the increase in the percentage of continuously married women with no live births in five years was substantially greater between the age groups of 30-34 and 35-39 than between 25-29 and 30-34. In about one-fourth of the countries, however, the risk of infertility increased steadily beginning at age 30 (625). US data for 1976 also show a gradual increase in infertility with age rather than a sharp increase at any specific age (405).

The controversy over the exact relationship between female infertility and age has not yet been settled (78, 224). It is clear that the risk of infertility increases with age. Yet, as Bongaarts states, for many women who want to postpone childbearing "the risks ... may well be quite small compared to the benefits" (76).
Uganda, for example, postabortion and postpartum infection are thought to be second only to gonorrhea as a cause of female infertility (204). Infections occur after childbirth or abortion because microorganisms ascend more easily through a cervix that is dilated. Also, tissue remaining in the uterus may promote bacterial growth. The organisms causing infection may be present in the anus or vagina normally. Also, they spread from a cervical infection or are introduced by dirty hands or instruments.

The prevalence of specific infections varies geographically. For instance, in Ethiopia 19 of 45 women with postpartum infection (42 percent) had positive gonorrhea cultures (461). In India, however, 86 percent of postpartum infections studied were caused by staphylococcal or fecal bacteria; no gonococci were found (627). Chlamydial infections also can be an important cause of postpartum and postabortion infection. In a U.S. study women with chlamydial infections during pregnancy were 2.5 times more likely to develop postpartum infections than women without chlamydial infections (631). In a Swedish study women with endocervical chlamydial infections were over five times more likely to develop PID within four weeks after first-trimester induced abortion than uninfected women (478). The mycoplasma M. hominis also may cause postpartum and postabortion infections (219, 598), but its importance is unclear (372).

Postpartum Infection

Postpartum infection causes many maternal deaths in developing countries and probably leads to secondary infertility in many who survive (56, 132, 201, 373, 616, 671). In several African hospitals, for example, postpartum infection accounts for 14 to 30 percent of maternal mortality (31, 88, 100, 351, 355). In an Ethiopian hospital 10 percent of all gynecologic patients had postpartum infection (461). In a 1973 Ugandan study about 10 percent of hospital admissions for acute pelvic inflammation were due to postpartum infections (204). In a recent Indian study 10 percent of hospital admissions for chronic pelvic inflammation were due to postpartum infection (549).

Obstetric difficulties, such as prolonged or obstructed labor, generally result in more bleeding and trauma than normal labor (222) and thus more danger of infection (139, 320, 323, 469, 474, 585). Cephalopelvic disproportion (the fetal skull too large for the pelvic opening) contributes to obstructed labor and so to risk of infection. It may be more common where nutritional deficiencies early in pregnancy are among the causes of an intrauterine growth retardation (474, 487). Improperly performed abortions also can cause physical injury leading to infertility. Uterine trauma or lacerations of the vagina or cervix can cause cervical incompetence, intrauterine adhesions, and other complications that interfere with fertility (474). Obstructed labor, generally results in more bleeding and trauma than normal labor (222). For instance, among the Yoruba of Nigeria herbs are sometimes placed in the vagina to enhance uterine contractions and hasten delivery.

Postpartum infections are a major cause of secondary infertility when childbirth occurs under conditions that are unsanitary. (Y. Pouliquen/WHO)

In cases of obstructed labor, stronger uterine contractions may increase the risk of uterine rupture (258, 320, 321).

Postabortion Infection

Infection following induced abortion is an important cause of infertility in some countries (56, 124, 201, 229, 299, 416, 547, 671). Because abortions performed by untrained practitioners are often unsanitary or incomplete (332, 416), infection is common. A Macedonian study found signs of infection in 22 percent of abortion-related hospital admissions (561). Spontaneous abortion also may result in infection. This generally occurs only when the abortion is incomplete, and the infection usually is limited to the endometrium (374, 487). In a Bangladesh hospital study of 1,003 women admitted for incomplete abortion, 10 percent of those who had had induced abortions developed pelvic infections compared with only one percent of women who had spontaneous abortions (52).

Improperly performed abortions also can cause physical injury leading to infertility. Uterine trauma or lacerations of the vagina or cervix can cause cervical incompetence, intrauterine adhesions, and other complications that interfere with fertility (474). Subjects inserted through the cervix may perforate the uterus, leading to extensive pelvic infection (24, 332). Chemicals may destroy tissue, thus facilitating infection (323, 474, 487) and causing intrauterine adhesions (539).

A variety of other factors that may occasionally cause female infertility are relevant to public health programs because they are predictable and preventable. These include:

- alcohol, tobacco, certain drugs, and certain environmental pollutants,
- severe malnutrition,
- effects of female circumcision.

Other causes, which are not preventable, include genetic and hormonal disorders.
Alcohol, Tobacco, Drugs, 
and Environmental Pollutants

Alcohol. Evidence is mounting that alcohol can cause a range of fertility problems in women. Women with severe drinking problems—alcoholics—have reported difficulty conceiving. They often have a variety of health problems, however, so the direct effects of alcohol cannot be assessed (50). Moderate and heavy drinkers who become pregnant have greater risk of pregnancy loss (289), and, if they do not abort, their children may have various physical and mental problems (140, 215, 266). A recent prospective study found that pregnant women who drank more than 100 g of alcohol a week (about 10 drinks) were more likely to have babies whose weight was below the tenth percentile. The risk for these women was more than double that for women who drank about 50 g per week (676). Even in small amounts alcohol may be unsafe for pregnant women (333, 572, 624).

Tobacco. Smoking also can have an adverse effect on reproduction. Pregnant women who smoke have a greater chance of developing complications that can result in perinatal death, particularly placenta previa (a placenta that covers part or all of the cervical opening). The risks of smoking are especially marked among poorly nourished women who lack prenatal care (128). Smoking clearly increases the chances that an infant will be of low birth weight (450). Also, smoking probably increases the risk of spontaneous abortion (128, 223, 376). The more cigarettes smoked per day, the greater the risks (288). (See Population Reports, Tobacco—Hazards to Health and Human Reproduction, L-1, March 1979.)

Drugs. Certain over-the-counter, prescription, and illicit drugs may lower a woman's fecundity (430). Habitual use of barbiturates or narcotics is thought to inhibit regular ovulation (376). Some powerful drugs used to treat serious illnesses such as cancer and chronic kidney disease can stop ovulation completely (46, 280, 376). Tetracycline, often used in treatment of STDs, affects the developing bones and teeth of a fetus and so should not be taken during pregnancy. Some prescription drugs, including certain antidepressants, narcotic analgesics, and tranquilizers have been suspected of promoting congenital malformations and pregnancy wastage (84). Controlled studies to date, however, generally have not shown a clear association between these prescription drugs and effects on the fetus (271).

Environmental pollutants. Various substances used in industry and agriculture may affect a woman's fecundity (345, 374, 430). Lead poisoning both reduces the ability to conceive and increases pregnancy wastage (6, 514). Radiation and many pesticide residues also can increase pregnancy wastage (46). There is a need for more controlled studies to determine whether associations exist between specific pollutants and infertility (270).

Under starvation conditions, ovulation and menstruation may stop. During the Dutch famine of 1944-45, the Bangladesh famine of 1974-75, and the Kampuchean famine of 1978-79 birth rates dropped by about 50 percent. They increased nine months after food became available (234, 281, 406, 582).

Female Circumcision

Female circumcision clearly endangers the health of girls and women, but the relationship to infertility is uncertain. Practiced chiefly in certain African and Middle Eastern countries, the operation varies from excision of the tip of the clitoris to removal of the clitoris, labia minora, and labia majora—termed Pharaonic circumcision (40, 43, 373). It is generally performed on girls between the ages of 4 and 10 (43, 466). All female circumcisions involve a short-term risk of infection, hemorrhage, shock, and urinary retention. Pharaonic circumcisions are especially dangerous and may cause long-term complications (43, 373, 412).

Clinicians in Sudan suspect that Pharaonic circumcision predisposes women to ascending infections and infertility. This is because scarring and closure of the external genitalia prevent proper drainage of urine and menstrual blood and because tearing, which facilitates infection, is likely to occur at childbirth (412, 525). Controlled studies of circumcision, infection, obstetric difficulties, and infertility have not been carried out, however. A Sudanese survey of the medical histories of 7,505 women, 95 percent of whom had undergone Pharaonic circumcision, found that short-term complications of the operation were common. Yet infertility was reported by only about 2 percent. It occurred in most cases because the circumcision had made full penile penetration impossible (42).

Unpreventable Infertility

Certain causes of female infertility can neither be predicted nor prevented. Some, such as ovulation disorders and endometriosis, often can be treated and corrected. Other, less common problems, such as genetic disorders that result in defective ova or repeated abortions, are not treatable (227, 552).

Ovulation disorders. In most developed countries and in some countries of Asia and the Middle East, infrequent ovulation or the absence of ovulation (anovulation) are the most common cause of female infertility (see Table 2). Often accompanied by amenorrhea, ovulation disorders result from disruption of the hypothalamic-pituitary-ovarian axis, the complex feedback system of hormonal signals necessary for normal menstrual cycles and the maintenance of pregnancy. Among the causes of ovulation disorders are the following:

- Hyperprolactinemia, a high serum concentration of the pituitary hormone prolactin, can inhibit ovulation, possibly by blocking various ovarian hormone receptors and thus causing a hormonal imbalance (58). Up to 40 percent of hyperprolactinemia cases may be caused by pituitary tumors (178).
- Polycystic ovarian disease—often called Stein-Leventhal syndrome— inhibits ovarian function. It is characterized by enlarged ovaries with many follicular cysts, amenorrhea, abnormal hair growth, and obesity (44, 80). Almost all women with this disease are infertile.
Thyroid gland disorders disrupt the hypothalamic-pituitary-ovarian axis. Too much thyroid hormone results in too little circulating estrogen; too little thyroid hormone results in too much estrogen (44). In either case the normal effects of estrogen on the hypothalamus are absent, and ovulation is prevented.

Stress may disrupt ovulation by affecting the autonomic nervous system, which in turn affects the endocrine system (147, 544). The exact mechanisms are not known, but temporary amenorrhea often coincides with a particularly stressful event (90, 176).

For additional information on hormonal disorders, see the publications in the box on p. L-136.

Endometriosis. An important cause of female infertility in developed countries (see Table 2), endometriosis is characterized by the growth of endometrial tissue on the fallopian tubes, ovaries, and other pelvic organs. Women with endometriosis are much more likely to be infertile than women without endometriosis (642). In one case-control study infertility was 20 times as common among women with endometriosis as among those without endometriosis (586).

The causes of endometriosis are not fully understood (87, 164, 411). The most widely accepted explanation is that during menstruation some endometrial tissue passes through the fallopian tubes and implants on other organs (10, 87, 642). Under the influence of hormones during each subsequent menstrual cycle, this tissue grows and may shed, resulting in more implants. The implants eventually cause scarring and adhesions, both of which may distort the tubes and ovaries, interrupting ovum transport and causing infertility (285).

Cervical and uterine factors. Some congenital uterine or cervical abnormalities cause infertility. Cervical stenosis (a small cervical canal) and septate uterus (a uterus divided into two chambers) are two examples (262). Other cervical and uterine abnormalities are sometimes a consequence of induced abortion or childbirth (see p. L-125). For instance, uterine adhesions occasionally follow uterine surgery or curettage of the endometrium (238, 280).

Cervical mucus disorders can prevent passage of sperm or immobilize it. Hormonal imbalances such as low estrogen levels may cause inadequate cervical mucus or mucus so thick that it blocks sperm (142, 212). A small proportion of infertile women may produce antibodies that immobilize sperm in the cervix or cause sperm to stick together — often called "hostile cervical mucus" (18, 72, 269, 386, 541). How these antibodies act is not fully understood (556).

For additional information on endometriosis, see the publications in the box on p. L-136.

Male infertility, STD, and disease

Male factors are thought to be the major cause of infertility in about 30 percent of all infertile couples and to contribute to infertility in another 20 percent (22, 202). For instance, a study of 275 Bangladeshi men attending an infertility clinic with their wives concluded that 29 percent of the men were probably infertile (122). In Singapore a study of 709 infertile couples found evidence of male infertility...
in 23 percent (485) (see Table 2, p. L-120). A US survey of 1,000 infertile couples found that about 30 percent of the men were infertile and another 15 percent were probably subfertile (600).

The contribution of male factors to infertility may often be underestimated, however, since infertility investigations traditionally have concentrated on women rather than men (154, 221, 394). The woman is almost always the first member of an infertile couple to be examined and usually is studied more intensively than the man. In many cases men are examined only when all possible female factors have been ruled out. Gynecologists are generally not knowledgeable about male infertility and often refer men to urologists, who themselves may have only limited knowledge of male infertility (394). Many men may refuse examination because they mistakenly believe that sexual potency is proof of fertility (303). For all these reasons, knowledge about male infertility and its treatment lags behind knowledge of female infertility (154, 394, 614).

Male infertility is most often caused by one of two conditions, either blockage of sperm ducts or disorders in sperm production. Both result in poor semen quality — semen that contains too few sperm and/or abnormal sperm. A less common condition is sexual malfunction that prevents ejaculation of semen.

Most men who seek medical help are classified as either azoospermic (having no sperm in semen) or, more likely, oligospermic (having a low concentration of sperm in semen) (214, 325). Subfertility is generally defined as a sperm count below 20 million sperm per milliliter of semen (23, 57). Many men with low sperm counts also have a high proportion of abnormally shaped sperm or of sperm that do not move normally. The reasons for poor semen quality can be determined in only about 10 to 15 percent of cases (107, 214). The remaining cases are usually classified as "idiopathic oligospermia" — oligospermia without apparent cause (614).

### Table 4. Summary of Relationships Between Male Infertility and Diseases in Developing Countries

<table>
<thead>
<tr>
<th>Disease</th>
<th>Cause/Effect Relationship</th>
<th>Epidemiologic Importance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sexually Transmitted Diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gonorrhea</td>
<td>Yes—well-established</td>
<td>Major</td>
</tr>
<tr>
<td>Chlamydial infections</td>
<td>Yes—few data</td>
<td>Unknown</td>
</tr>
<tr>
<td>Mycoplasmas</td>
<td>Possible</td>
<td>Probably minor</td>
</tr>
<tr>
<td>U. urealyticum</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other Diseases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>Yes—well-established</td>
<td>Unknown</td>
</tr>
<tr>
<td>Bancroftian filariasis</td>
<td>Possible—few data</td>
<td>Probably minor</td>
</tr>
<tr>
<td>Leprosy</td>
<td>Yes—well-established</td>
<td>Minor</td>
</tr>
<tr>
<td>Mumps</td>
<td>Yes—well-established</td>
<td>Minor</td>
</tr>
<tr>
<td>Schistosomiasis</td>
<td>Yes—well-established</td>
<td>Unknown</td>
</tr>
</tbody>
</table>


In some developing countries one of the most commonly identified causes of poor semen quality is genital infection, usually with STDs (672) (see Table 4). When untreated, these infections can lead to complete blockage of sperm ducts, causing azoospermia (97, 325). In developed countries untreated genital infections and thus azoospermia are less common. Varicocele, a defective testicular vein or veins that cause abnormal blood flow to the testes, is often blamed for oligospermia in developed countries (153, 369), but its role in infertility is not clearly established. Other factors that contribute to abnormal semen include genetic abnormalities, hormonal imbalances, exposure to environmental pollutants, certain diseases, such as mumps, and possibly development of sperm antibodies (see Figure 5).

### Sexually Transmitted Diseases

In men, as in women, untreated genital infection causes infertility by creating inflammation or blockage in the upper reproductive tract. Often due to STDs, these infections begin in the urethra (termed urethritis). If not adequately treated, they may spread to the vas deferens. It is estimated that in 25 to 30 percent of cases, infection reaches the epididymides (termed epididymitis) (62, 83) (see Figure 6). Epididymitis is a more serious condition than urethritis. Most men with epididymitis are temporarily subfertile simply from the infection itself (61, 429, 610). In addition, infections may cause scarring that partially or completely blocks sperm transport. An estimated 20 percent will have permanently impaired fertility (61). When epididymitis is not treated, the percentage becoming infertile may be as high as 50 to 80 (83). In India a study of 70 men with signs of current or past epididymitis found that 27 percent were azoospermic and another 34 percent had sperm counts of fewer than 40 million per ml of semen (396).

Untreated urethritis leading to epididymitis is relatively rare in developed countries, since most men who have symptoms are treated promptly with antibiotics. In some developing countries, however, untreated urethritis is a substantial problem (640, 673). Many men are not treated for urethritis for months or even years. For instance, clinic studies in Nigeria and Uganda found that, on average, men had symptoms for about 2½ years before they sought the help of medical personnel (282, 574). Moreover, where antibiotics are available without prescription, as in most developing countries, men usually attempt to treat themselves — often inadequately or inappropriately — before they seek professional help (444).

Because infections often are not properly treated, they may be a major cause of sperm duct blockage and resulting azoospermia in developing countries (672). For instance, a South Korean survey of infertile men found that about 40 percent were azoospermic and 20 percent had evidence of epididymitis (325). A Colombian survey of infertile men found that 30 percent were azoospermic and 37 percent had evidence of genital infection (97).

**Gonorrhea.** In men, untreated gonorrhea can lead to urethral abscess, urethral stricture, and inflammation of the prostate gland as well as epididymitis (37, 68, 282, 550, 640, 664). Many of the complications of gonorrhea can lower sperm counts, although untreated epididymitis is the most serious cause. In one Ugandan clinic, for in-
Figure 5. Relationships of Selected Direct and Indirect Causes of Male Infertility

STOs - gonorrhea
- chlamydial infections
- mycoplasmas (?)
Certain nonsexually transmitted organisms

- Epididymitis or other complications
- Blocked sperm ducts

- Certain systemic diseases such as tuberculosis
- Congenital disorders
- Varicocele (?)
- Hormonal imbalance
- Environmental factors
- Alcohol, certain drugs, tobacco

- Sperm production disorders
- Poor semen quality

- Sperm antibodies (?)
- Lack of testicular function

- Psychological factors (?)
- Sexual dysfunction
- Certain systemic diseases

Genetic factors
- Certain hormonal disorders
- Complications of mumps

stance, among 1,000 male STD patients, 91 had urethral stricture caused by chronic or recurring gonorrhea (282).

A Ugandan study compared the health of men and women in the Teso region, where gonorrhea was common and fertility relatively low, and in the Ankole region, where gonorrhea was uncommon and fertility high. Evidence of past epididymitis, as indicated by thickened epididymes, was much more common in Teso men. Although active gonorrhea infections were relatively uncommon, 28 percent of Teso men had thickened epididymes, compared with only 4 percent of Ankole men. Some 44 percent of childless men in Teso had thickened epididymes (38). The difference in fertility between the two regions is not necessarily due entirely to male infertility, however, since a similar difference in STD prevalence was found among women (see p. L-121).

Chlamydial infections. Studies in developed countries show that Chlamydia is the chief cause of nongonococcal urethritis. In the US from 40 to 50 percent of nongonococcal urethritis is chlamydial (82, 216). Symptoms of chlamydial urethritis usually are less severe than those of gonococcal urethritis. Perhaps because chlamydial urethritis may therefore go untreated, in developed countries more cases of epididymitis may be due to chlamydial infections than to gonorrhea. Gonorrhea still seems to be a more common cause of urethritis in developing countries (342, 383), although the proportion of chlamydial cases usually is unknown due to the difficulty of culturing the organism.

Mycoplasmas. The mycoplasma U. urealyticum causes perhaps as many as 20 to 25 percent of nongonococcal urethritis cases in the US (82, 216), but it is not known how often epididymitis and infertility result (175, 306, 598). A recent US study, however, suggests that asymptomatic infections may be important to male infertility — or perhaps to female infertility. The study followed 161 infertile couples for three years. Both husband and wife were treated for mycoplasma infection. In 129 couples the husband's infection was cured, and 60 percent of women had a pregnancy ending in a live birth. In 32 couples the husband's infection recurred after treatment. Only 5 percent had a successful pregnancy (608). Because other infertility-related infections may have been cured along with the mycoplasma infection and because many of the wives' infections were also presumably cured by treatment, further studies are necessary.

Other Diseases

Tuberculosis. Urogenital TB causes infertility in men by scarring and blocking the epididymis or, less commonly, through infection of the prostate, seminal vesicles, or vas deferens (20, 86, 379). Urogenital TB develops following infection of the lungs, but, as in women, symptoms of urogenital TB in men may not develop until many years after pulmonary infection (123). The proportion of men with pulmonary TB who later develop urogenital TB is unknown (199), although records from Scotland in the 1960s showed that the number of reported cases of male urogenital TB was 4 to 9 percent of the number of reported pulmonary TB cases (93).

Filariasis. Some investigators think that an important cause of male infertility is Bancroftian filariasis (373, 392, 421), a widespread disease in hot, humid areas that is caused by a mosquito-borne filarial worm (670). The parasites concentrate in the genital lymphatic system, blocking lymph drainage. Inflammation and swelling may occur in the testes, scrotum, epididymis, or vas deferens.
Epidemiologic studies on filariasis and infertility have produced contradictory findings. In Gabon men with microfilaria — filarial larvae in the blood — were significantly more likely than other men to have fewer than three children (311, 618). By contrast, a Philippine study found no relationship between microfilaria and fertility or between lymphatic obstructions and fertility (208). Medical evidence of a link between filariasis and infertility is largely anecdotal (392, 421, 448).

**Leprosy.** The lepromatous form of leprosy also has been implicated as a cause of infertility. In the Philippines a 33-year study found that wives of men with lepromatous leprosy had 40 percent fewer births after the onset of symptoms than did wives of healthy men (564). Frequency of intercourse was not recorded, however. A 1952 US study of 179 men with leprosy found that 28 percent had atrophied testicles (200). Recent studies in India and Malaysia indicate that men with lepromatous leprosy also may develop high levels of sperm antibodies (526, 633, 634) (see p. L-132).

**Mumps.** In postpubertal males mumps can lead to orchitis (inflammation of the testes) and in severe cases to later atrophy of the testes (20). Among every 100 men who develop mumps, about 20 also develop mumps orchitis, and one or two of these will be affected in both testicles (308). Most men recover from mumps orchitis without fertility impairment (20). In a 1951 Swedish study, however, 98 men with a history of bilateral mumps orchitis reported an average of 1.1 impregnations each, compared with 2.1 each among age-matched controls who had not had mumps orchitis (56, 308).

**Schistosomiasis.** In infested men eggs of the schistosome *S. haematobium* — the strain common in African countries — frequently are found in seminal vesicles and occasionally in other parts of the male reproductive tract (118).

In addition to certain infectious diseases, a variety of factors may impair sperm production and so cause male infertility. These include hormonal and genetic abnormalities and exposure to external influences that impair sperm production. Varicocele is often diagnosed as a cause of infertility, but it is not clear whether this condition adversely affects sperm production.

**Varicocele**

Varicocele is caused by improperly functioning valves in one or more testicular veins. It allows excess venous blood to flow around the testis. Some researchers think that this excess blood flow interferes with sperm production by raising the temperature or increasing serum levels of toxic metabolites in the testes (33).

The relationship between varicocele and male infertility is not clear, however. In the US varicocele is found in 20 to 40 percent of men attending infertility clinics (206). In about half, sperm counts are low, sperm motility is poor, and a high proportion of sperm cells are immature and abnormal (53, 155, 348). In the other half, however, sperm production is not affected. In fact, varicocele is a relatively common condition. It occurs in 10 to 15 percent of all US men, including men who are not infertile (206, 347).

Some studies report that surgical repair of varicocele (varicocelectomy) improves semen quality in 60 to 70 percent of cases and that pregnancies follow in 40 to 50 percent of cases (155, 206, 347). Other studies have found no significant differences in semen quality or pregnancy rates between men with corrected varicocele and men with uncorrected varicocele (428, 513).

**Hormonal, Genetic, and Immunologic Factors**

Hormonal imbalances that cause infertility are much less common in males than in females (22, 600). Parity because of this, even less is known about the problem in men than in women. Best understood are the effects of severe hormonal abnormalities caused by genetic disorders. For instance, men with Klinefelter's syndrome — a genetic disorder found in 0.2 percent of men — have low testosterone levels and are azoospermic. Some may also experience breast development and atrophied testes (28). In Kallman's syndrome, another genetic disorder, the hypothalamus fails to secrete gonadotropin-releasing hormone and thus the pituitary does not produce follicle-stimulating hormone (FSH) or luteinizing hormone (LH).
Incidence of Infertility-Related STDs

Gonorrhea, syphilis, and chlamydial infections — the three STDs that most clearly cause infertility — are epidemic in many areas. The most reliable data on their incidence come from developed countries, where both gonorrhea and syphilis usually must be reported. Underreporting is a problem, however, especially among private physicians. Data on chlamydial infections come from scattered reports only, since these infections are difficult to diagnose and usually need not be reported. In most developing areas, although STDs are clearly a public health problem (56, 648, 672, 673, 674), information is limited. National data, where available, greatly underreport cases, especially among women (27, 455, 643).

Gonorrhea

Gonorrhea is one of the most common diseases in developed and developing countries (668). In many countries gonorrhea appears to have become more common during the 1960s and 1970s, as shown below:

<table>
<thead>
<tr>
<th>Country</th>
<th>Reference Number</th>
<th>Reported Cases of Gonorrhea per 100,000 Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canada</td>
<td>565</td>
<td>129 (1969) — 205 (1973)</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>257</td>
<td>120 (1965) — 492 (1977)</td>
</tr>
<tr>
<td>Cuba</td>
<td>643</td>
<td>8 (1972) — 104 (1978)</td>
</tr>
<tr>
<td>Denmark</td>
<td>655</td>
<td>264 (1969) — 331 (1973)</td>
</tr>
</tbody>
</table>

According to clinical reports, gonorrhea may be very common in many African countries. In Nairobi, Kenya, 18 percent of 200 women attending a family planning clinic had gonorrhea (240). In Cameroon 12 to 15 percent of 1,326 women at maternity or child health centers had gonorrhea (422). It is estimated that in Kampala, Uganda, 10,000 people per 100,000 population have gonorrhea; in rural Uganda, 3,000; and in Nairobi, Kenya, 7,000 (36).

Intensive gonorrhea control efforts have stopped the rise in gonorrhea rates or even reduced rates in a few countries. In Sweden an intensive gonorrhea control program led to a drop in the gonorrhea rate between 1970 and 1975 — from about 500 per 100,000 to about 300. The rate may have begun increasing again after 1975, however (636). In the US, stepped-up control efforts started in 1972. The gonorrhea rate peaked in 1975 at 473 and has been stable through 1980 (692).

Gonorrhea is becoming increasingly resistant to penicillin, the antibiotic most often used as treatment. Totally resistant strains, called penicillinase-producing N. gonorrhoeae (PPNG) (also called β-lactamase producing), were first identified in the Philippines and West Africa in 1975. They have since been found in over 50 countries and probably occur in many others (112, 669, 686). In some African, Asian, and European areas PPNG strains now make up a major portion of all identified strains — 20 to 30 percent in some clinics in Kenya and Ghana and 50 percent in some clinics in Bangkok, Thailand, for example (669).

Pelvic inflammatory disease (PID) — often caused by gonorrhea or chlamydial infection — also has become more common. In the US, where about half of PID episodes are associated with gonorrhea (131, 134, 161, 594), the increase in PID paralleled the increase in gonorrhea through the early 1970s (654). After the gonorrhea control program was stepped up in 1972, hospital admissions for PID slowed and the number of visits to private physicians for PID decreased (527, 529).

Similarly, in some developing countries, PID cases may be up to 30 percent of all PID cases among women (305). Still, at present nearly one million US women a year suffer from PID and its aftereffects — pain, infertility, and ectopic pregnancy (135).

Syphilis

Vigorous public health campaigns have checked the spread of syphilis in some countries, but in others rates have been increasing. The incidence rate in the US remained stable from 1961 through 1979 at about 9 to 12 cases per 100,000 (623). In Canada, Denmark, Sweden, West Germany, and the UK, rates were stable from 1969 at least through 1973 at fewer than 10 cases per 100,000 (565). In Cuba a program begun in 1972 that emphasized screening and prophylactic treatment of syphils kept the rate stable from 1974 through 1978 (643).

Increasing rates are reported in many areas, however. In Costa Rica the rate increased fourfold between 1965 and 1976, from 45 to 185 (257). In Papua New Guinea the rate tripled between 1973 and 1978, from 39 to 117. In the same period the other South Pacific islands, taken together, experienced a 13-fold increase, from 5 to 65 (660, 661).

Although the incapacitating effects of tertiary syphilis are less common worldwide than they were 40 years ago (674), congenital syphilis and its effects remain serious health problems in a number of developing areas where syphilis rates may be high (674). In Lusaka, Zambia, for instance, about 7 percent of newborns have congenital syphilis (231, 232). In India about 5 percent of stillbirths or neonatal deaths have been attributed to congenital syphilis (380, 413).

Chlamydial Infections

Although information is scant, chlamydial infections seem to be widespread and increasing in many areas (536). In the UK nonspecific or nongonococcal urethritis is about 1.8 times as common as gonococcal urethritis (565). Since Chlamydia accounts for 30 to 60 percent of nongonococcal urethritis in many clinic populations (82, 216, 673), the rate of chlamydial infection in the UK may be close to the gonorrhea rate. Based on similar data (113, 371), the US rate is estimated to be about 200 per 100,000.

Chlamydial infections probably are common in developing countries also (673), although perhaps less so than in some developed countries. A recent Gambian study found that 14 percent of 65 men with gonorrhea had simultaneous chlamydial infections and 21 percent of 20 men with nongonococcal urethritis had chlamydial infections (342). Although a study in Nairobi found that only 4 to 9 percent of patients attending family planning clinics, antenatal clinics, and STD clinics had acute chlamydial infections, blood tests showed evidence of past infection in 91 percent of women and 80 percent of men (433). While blood test results may sometimes reflect a past infection with another chlamydial strain (673), these data suggest that infections with C. trachomatis may be common in Nairobi.
Because FSH and LH are necessary to stimulate the testes to develop and release testosterone, puberty never takes place (637). Failure of the hypothalamus or pituitary—sometimes caused by a pituitary tumor—also can affect FSH and LH secretions. The result is impotence, atrophied testes, and/or loss of secondary sex characteristics (552). Recently, individual studies have linked low sperm counts to high FSH levels (426) or low LH levels (465), but these reports have not yet been confirmed.

Occasionally, a man produces antibodies that, when present in the semen, reduce the motility of sperm. These sperm antibodies may be more likely to develop when sperm come in contact with tissues outside the sperm ducts. For instance, in vasectomized men, sperm may enter the tissues that surround the blocked vas deferens. Some men who have had vasectomies surgically reversed remain involuntarily infertile. A substantial proportion of these men have antibodies to sperm (26, 51, 458, 555). Other aftereffects of vasectomy—such as permanent damage to the epididymes or testicular cells—may have more effect on semen than antibody production, however (241, 558).

**Environmental Pollutants, Alcohol, Drugs, and Tobacco**

**Environmental pollutants**. Exposure to toxic substances, radiation, or extreme heat may affect male fertility (376, 430). Radiation impairs sperm production, but the effect seems to be temporary in most cases (521). Exposure to high levels of pesticides reduces sperm counts (104, 653). Occupational exposure to lead can reduce sex drive and sperm counts (85, 309). Extreme heat may reduce male fertility, since the optimum temperature for sperm production is about 2°C below normal body temperature (463). A Mexican survey of 200 men in infertile marriages—65 percent of whom had sperm counts below 30 million per ml of semen—found that 30 percent were exposed to extreme heat and 78 percent wore tight supporting trusses which raised the scrotal temperature during work (459).

**Alcohol**. Alcoholic men often produce less testosterone. The testes may eventually atrophy, and the breasts may become enlarged (1, 21, 637). Moderate drinking does not seem to reduce fertility in otherwise normal men, but in men with borderline sperm counts moderate drinking may reduce fertility (1).

**Drugs**. Powerful therapeutic drugs such as those used in cancer therapy or for the control of mental disorders often cause temporary or permanent infertility, probably by directly affecting testicular cells (46, 151, 187). Less is known about the effects of illegal drugs, such as marijuana, cocaine, opium, or heroin, due to the difficulty of collecting data. Preliminary reports suggest that heavy marijuana smokers have lower sperm counts, lower sperm motility, and more abnormal sperm than other men (1).

**Tobacco**. Cigarette smokers also probably affect male fecundity. Reports from the UK and Egypt concluded that, on average, cigarette smokers have fewer motile sperm and more abnormal sperm than nonsmokers (163, 548). By contrast, a recent US study of men in infertile marriages found no difference in semen quality between smokers and nonsmokers (512). In some infertile men, however, semen quality improved markedly when they stopped smoking (21).

**INFERTILITY THERAPY**

Infertility therapy is often unsuccessful. Only about one-quarter to one-half of all couples treated achieve a live birth (150, 261, 275, 485, 573, 604). The chances of success depend mostly on the cause of infertility.

In general, when infertility is caused by prior infection—either tubal damage in females or epididymal or vas blockage in males—the prognosis is poor. Surgical repair of either condition, even when performed by experienced surgeons on carefully selected patients, leads to pregnancy in no more than 20 to 30 percent of cases (152, 510). When pregnancies occur after surgery for blocked fallopian tubes, 6 to 15 percent are ectopic (196, 256, 510). Thus live birth rates are even lower. Studies in Senegal and Kenya reported live birth rates of only 6 percent after tubal surgery (239, 632). By contrast, ovulation disorders often respond to treatment. In clinics in both developed and developing countries, pregnancy rates as high as 50 to 60 percent have been reported (19, 67, 300, 476).

For some conditions, treatment may make little difference. For instance, with mild endometriosis in women, varicocele in men, and unexplained infertility, pregnancy rates often are about the same for treated and untreated couples (13, 129, 428, 543).

Where it is available, infertility therapy is often long and costly (291, 522). Several different diagnostic procedures may be necessary. Even then, the cause may remain unexplained in as many as 20 percent of couples (see Table 2). Costly drugs taken for a long period or expert surgery may be tried before pregnancy occurs or patients and/or doctors decide against further treatment. In one Latin American clinic seven visits per couple were the average. In 20 percent of couples, between 11 and 40 visits were necessary (55). It was estimated that in 1980 in Paris, an average birth following infertility therapy cost the equivalent of about $8,000 (US), including delivery. Without infertility therapy, a birth cost an average of about $1,750 (55).

Many government health services lack adequate personnel, drugs, and equipment to diagnose and treat infertility. Only couples who can afford to travel to health centers, or who can turn their own businesses over to a partner, can access comprehensive services. Even there, a full array of diagnostic procedures and drugs may not be available except in developed countries. In an informal survey of 21 developing-country physicians attending an infertility therapy training course in the US, all but two reported that lack of facilities and equipment, and shortage of drugs, were major barriers to providing infertility services (470).

Although a variety of diagnostic and treatment procedures are used by infertility specialists, only simple procedures that can be used by general health care providers are discussed here. For detailed information on more sophisticated procedures, see the box on p. L-136.

**Simple Diagnostic Procedures**

There are at least six relatively simple diagnostic procedures that can be used to try to discover the causes of infertility.
The first step in an infertility evaluation is a comprehensive medical and reproductive history of both members of the infertile couple. Any report of genital infection in the man or woman or of menstrual disorders in the woman is especially important. Both partners should have physical examinations. The genitals should be carefully examined for any abnormalities that might indicate a hormonal or genetic disorder or an infection (287, 553).

For the man, the major test for evaluating fertility is semen analysis (567). Semen usually is collected through masturbation and within a few hours examined for (1) total volume, (2) millions of sperm per milliliter of ejaculate (sperm count), (3) motility of sperm, (4) shape and size of sperm, and (5) presence of bacteria or white blood cells, indicating infection. Ideally, more than one sample should be taken, since semen quality varies over time (568).

For the woman, simple ovulation detection tests are often used to diagnose infertility. The indicators of ovulation usually monitored are basal body temperature shift and cervical mucus changes (221). Body temperature rises about 0.2 to 0.9°C about one or two days after ovulation, responding to a rising level of progesterone. Daily monitoring of body temperature may reveal whether ovulation has occurred. Cervical mucus changes in consistency and quantity over the menstrual cycle. Just after menstruation it is absent or present in small amounts. Shortly before ovulation it is sticky, cloudy, and more copious. Around the time of ovulation it is plentiful and becomes slippery and clear. (For more explanation of these two methods of ovulation detection, see Population Reports, Periodic Abstinence: How Well Do New Approaches Work?, 1-3, September 1981.) Endometrial biopsies also can be used to assess whether ovulation occurs and whether the endometrium develops normally (431, 503).

Although more difficult than other tests, tubal patency tests — carbon dioxide insufflation (Rubin’s test) and hysterosalpingography — are important because they indicate whether a woman’s tubes are blocked. In an insufflation test, carbon dioxide is injected through the cervix. The passage of the gas through the uterus and tubes is then monitored with a pressure gauge. Hysterosalpingography is more accurate and provides information about both the uterus and tubes (505). It involves injection of radiopaque dye through the cervix followed by X-ray examination (553) (see photos, this page). Tubal patency tests must be performed by physicians and must never be undertaken when there is evidence of a cervical infection or PID, since the tests can spread the infection.

Where equipment and trained personnel are available, laparoscopy also may be used to diagnose female infertility, particularly when the results of other tests are inconclusive. The direct view of the abdominal cavity through the laparoscope permits clearer diagnosis of adhesions, PID, endometriosis, and ovarian growths (179, 304, 600).

Information about both men and women can be obtained from another simple diagnostic test, the postcoital test. Also called the Sims-Huhner test, this test involves taking a sample of cervical mucus two to three hours after coitus near the time of ovulation. The mucus is examined under a microscope at high power (400 times magnification). Although standards vary (189, 611), about 10 to 20 motile sperm per high-power field is considered normal (274, 553, 600, 611). If too few sperm are found or if sperm are abnormally shaped or nonmotile, semen problems or “hostile cervical mucus” are suspected.

Simple Treatment Procedures

Although most infertility treatments involve surgery and/or long-term medication, some problems are easily treated. Couples with no identifiable cause of infertility may be only subfertile and often achieve pregnancy with the help of simple strategies such as timing coitus to coincide with ovulation. Couples who are infertile due to current asymptomatic infections — usually gonorrhea or chlamydial or mycoplasma infections — can be given antibiotics to cure the infection (see Figure 7).

If sperm count is moderately low and cannot be treated or if a husband has problems with ejaculation, one approach that can be tried is artificial insemination with husband’s semen (AIH). The aim of AIH is to assure that the maximum number of sperm reach the fallopian tubes. AIH involves collecting semen — often just the first portion of the ejaculate, which contains the highest concentration of sperm — and placing it at the entrance to the cervix, inside the endocervical canal, or in the uterus at about the time of ovulation (600). Reported pregnancy rates after AIH generally are low — from 4 to 30 percent (107, 149, 576, 581). A recent US study of 61 couples in whom infertility was due to the man reported a higher rate — 53 percent — when couples were taught how to do a basic AIH procedure at home (148).
In Vitro Fertilization

Since P.C. Steptoe and R.G. Edwards announced the birth of the first “test-tube baby” in 1978 (584), infertility treatment through in vitro fertilization and embryo transfer has attracted much attention. While the procedure appears promising, it is still considered experimental and is used only as a last resort for carefully selected patients (263, 635).

Medical groups in at least 10 developed countries have started services for in vitro fertilization and embryo transfer (263). As of early 1983 about 400 pregnancies and 150 live births, including three sets of twins and one of triplets, had occurred as a result of the procedure (7, 169, 263).

Currently, to be eligible for in vitro fertilization and embryo transfer, couples must have tried other infertility treatment without success (263, 635). In many cases the woman has irreparable tubal damage, severe endometriosis, or hostile cervical mucus. Some couples have unexplained infertility or mild oligospermia (263).

Most medical groups that perform in vitro fertilization use hormonal therapy first to stimulate ovarian activity and then to induce ripening of the ovarian follicles that release the ova. One or more ripe ova are recovered by laparoscopy and then incubated for about six hours before a carefully washed sperm sample is added. If fertilization occurs, the eggs are further incubated until the 2- to 8-cell stage is reached. Then they are transferred into the uterus. To maximize chances of implantation, the patient must remain stationary for four hours or more, followed by about 36 hours of bed rest. Progesterone is administered daily for 10 days to decrease the chances of abortion (133, 264, 265, 326, 336, 337, 366, 603, 615).

Only one published series reports the number of pregnancies achieved per laparoscopies performed. In the second half of 1981 an Australian team performed 128 laparoscopies, recovering ova in 115 cases (90 percent). Fertilization occurred in 89 (70 percent), leading to embryo transfer in 83 (65 percent). Pregnancy was established in 10 women (8 percent of laparoscopies or 12 percent of embryo transfers) (337). Most recent series report a somewhat higher rate of pregnancies per embryo transfer — about 20 percent (169, 263, 264, 326, 635). Currently, there are no published reports on the proportion of live births resulting from the procedure.

In vitro fertilization is expensive. In the US, for example, medical, hospital, and laboratory costs vary from about $2,500 to $7,500 per cycle (169, 263). Actual costs for the patients include travel to and living expenses at a treatment center — about $1,500 per cycle. Since many couples repeat the procedure for several cycles (337), the total cost may exceed $10,000. While the knowledge being gained may eventually benefit many infertile couples, at present this sophisticated new treatment is available only to a small number of infertile couples.

In women with ovulation disorders, a few relatively simple drug therapies can be used. Clomiphene citrate (Clomid), the most common, induces ovulation by counteracting the ovulation-suppressive effects of estrogen during the first portion of the menstrual cycle. Clomiphene citrate is taken orally, usually for five days beginning on about the fifth day of the menstrual cycle. If a dose of 50 mg per day does not bring on ovulation, doses of up to 250 mg per day may be given in subsequent cycles. About 70 to 80 percent of selected women ovulate as a result of this therapy. Pregnancy rates usually range from about 30 to 50 percent (19, 67, 300, 476). Spontaneous abortion rates often are relatively high, however — between 20 and 25 percent (180, 256).

Clomiphene citrate has few serious side-effects but in many countries it is relatively expensive. At lower doses patients may occasionally have some ovarian enlargement and abdominal discomfort. At higher doses some patients also experience visual disturbances or hot flashes (180). The risk of multiple births appears to be small. For instance, in one series of 50 term pregnancies after clomiphene therapy, 3 resulted in twins (67). Physicians from Egypt, Fiji, Thailand, and Yemen report that clomiphene costs between $15 and $20 (US) per cycle (470). The price in the US is similar. In some countries — Bangladesh, for one — it is not available (122).

Bromocriptine is sometimes used to induce ovulation in women with high prolactin levels. A regimen of 7.5 mg per day lowers prolactin levels, and ovulation usually resumes after 30 to 90 days of treatment (44, 605). Reported pregnancy rates after return of ovulation range from 50 to about 90 percent (64, 171). Spontaneous abortion rates are relatively low — about 12 percent (256). Bromocriptine costs about $40 per month in the US. In developing countries it is even more expensive. For instance, in Egypt bromocriptine can cost about $100 (US) per month (470).

The range of simple treatments that can be used by general health care providers is relatively limited. Most infertility treatments are more sophisticated and expensive. One relatively new procedure, in vitro fertilization, is an example of how complex treatments can become (see box at left). Clearly, this therapy, along with many others, is out of the reach of most infertile couples.

Prevention

Prevention is always better than treatment. In the case of infertility, prevention is doubly important because treatment is expensive and its success, uncertain (56, 204, 418). Although some causes of infertility cannot be prevented, public health programs can prevent much infertility that is due to infection by paying more attention to the major reasons for infection:

- sexually transmitted diseases,
- poor obstetric care,
- illegal abortion.

Public health programs aimed at these causes of infertility are not easy to implement. First, they require a level of political support that is often difficult to achieve (36, 658). Second, such programs compete for funding with programs to prevent or treat serious endemic diseases that
### Figure 7. Simple Treatment Regimens for STDs and PID

<table>
<thead>
<tr>
<th>Uncomplicated Urogenital Gonorrhea</th>
<th>PID</th>
<th>Uncomplicated Chlamydial and Mycoplasma Infections</th>
<th>Syphilis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Against penicillin-sensitive strains:</strong></td>
<td>For outpatients with gonococcal or nongonococcal PID:</td>
<td>Tetracycline HCl 500 mg orally 4 times daily for 7 days or Doxycycline 100 mg orally twice daily for 7 days Unsafe in pregnancy. Multiple doses required.</td>
<td>For primary or secondary syphilis:</td>
</tr>
<tr>
<td>Either</td>
<td>Single-dose therapy for uncomplicated gonorrhea plus either</td>
<td></td>
<td>Benzathine penicillin G 2.4 million units intramuscularly</td>
</tr>
<tr>
<td>Aqueous procaine penicillin G 4.8 million units intramuscularly or Amoxycillin 3.0 grams orally or Ampicillin 3.5 grams orally plus</td>
<td>Tetracycline HCl 500 mg orally 4 times daily for 10 days or Doxycycline 100 mg orally twice daily for 10 days plus</td>
<td>For patients with penicillin allergies:</td>
<td>For patients with penicillin allergies:</td>
</tr>
<tr>
<td></td>
<td>Metronidazole 1.0 g twice daily for 10 days</td>
<td>Tetracycline HCl 500 mg orally 4 times daily for 15 days Unsafe in pregnancy. Multiple doses required.</td>
<td></td>
</tr>
<tr>
<td><strong>For patients with penicillin allergies:</strong></td>
<td></td>
<td>Erythromycin 500 mg orally 4 times daily for at least 7 days Multiple doses required.</td>
<td>or Erythromycin (not the estolate) 500 mg orally 4 times daily for 15 days Multiple doses required.</td>
</tr>
<tr>
<td>Tetracycline 500 mg orally 4 times daily for 7 days or Doxycycline 100 mg orally twice daily for 7 days</td>
<td>Doxycycline 100 mg orally twice daily for 10 days plus</td>
<td>For congenital syphilis:</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Metronidazole 1.0 g twice daily for 10 days</td>
<td>In symptomatic infants or asymptomatic infants with abnormal cerebrospinal fluid:</td>
<td>Aqueous crystalline penicillin G, 50,000 units per kg of body weight, intramuscularly or intravenously twice daily for at least 10 days or Aqueous procaine penicillin G, 50,000 units per kg of body weight, intramuscularly daily for at least 10 days.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>In asymptomatic infants with normal cerebrospinal fluid:</td>
</tr>
<tr>
<td><strong>Against penicillin-resistant strains:</strong></td>
<td>Hospitalized patients: Combined regimens of several antibiotics active against a broad spectrum of pathogens. Drugs include doxycycline plus cefoxitin or doxycycline plus metronidazole. All administered intravenously in hospital, followed by oral regimen after discharge.</td>
<td></td>
<td>Benzathine penicillin G, 50,000 units per kg of body weight, single intramuscular dose.</td>
</tr>
<tr>
<td>Spectinomycin 2.0 g intramuscularly or Ceftriaxone 250 mg intramuscularly or Cefotaxime 1.0 g intramuscularly or Cefoxitin 2.0 g intramuscularly plus 1.0 g probenecid orally</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less effective in some places but less expensive and sometimes more available are:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kanamycin 2.0 g intramuscularly or Thalidomethenic 2.5 g orally</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ineffective against concurrent chlamydial infection.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Recommended by US Centers for Disease Control (3, 110, 115) and World Health Organization (669, 672, 673, 674) and the African Union Against the Venereal Diseases and the Treponematoses (683). Listed regimens generally are the simplest possible for each category of disease.

*a For epididymo-orchitis, single-dose therapy for uncomplicated urogenital gonorrhea should be supplemented with tetracycline HCl 500 mg orally 4 times daily, doxycycline 100 mg orally twice daily, or erythromycin 500 mg orally 4 times daily, all for 10 days (669).

*b Where possible, hospitalization of PID patients is preferred.

*c Congential syphilis responds well to treatment, but treatment cannot reverse prenatal damage to bones, organs, or the central nervous system. Maternal screening and treatment during pregnancy can minimize prenatal damage.

*d Where cerebrospinal fluid testing is not available, regimens of crystalline or procaine penicillin can be used for all cases but require multiple doses. Some practitioners consider single-dose benzathine penicillin adequate for infants without central nervous system disease.
affect the entire population, such as malaria, schistosomiasis, and tuberculosis. Third, prevention programs require knowledge of which conditions or diseases are most prevalent — information that is not always available in regions where infertility is greatest (4, 56).

Nevertheless, preventive public health programs remain the most cost-effective approach to infection-related infertility. In the long run such programs not only reduce individual suffering but also reduce the increasingly heavy cost to the whole community of treating genital infections. In the US, for example, it is estimated that syphilis and gonorrhea control efforts in 1981, which cost the US government about $47 million, saved about $150 million in health care costs — $119 million by preventing complications of gonorrhea and syphilis, $24 million by preventing uncomplicated gonorrhea, and $6 million by preventing the spread of penicillin-resistant strains of gonorrhea (655).

Public health programs that would help prevent infertility include:

- STD control programs — organized efforts to limit the number of persons infected and to minimize the consequences of infection.
- STD education programs — public education to inform people of the causes, symptoms, and dangers of STDs, how to avoid infection, and how and where to obtain treatment.
- Programs to improve obstetric care — training for traditional practitioners and other nonphysicians who attend childbirth and provide women’s health care, teaching them how to reduce the risk of infection during uncomplicated births and when to refer women to health centers for further attention.
- Family planning programs — services to supply contraceptives, which give women an alternative to illegal abortion, and to promote especially the methods that protect against infection (see p. L-141).

STD Control Programs

Most organized efforts to combat STDs begin with medically oriented control programs. Public education, al-
though often added later, also is important. Comprehensive STD control programs involve (1) accurate reporting of STD cases, (2) early diagnosis and effective treatment of STDs and their complications, (3) finding and treating sexual contacts of infected persons, and (4) screening high-risk groups for STDs. A comprehensive program operates best where there are well-established health services with adequate resources, extensive cooperation, and good follow-up capabilities. In many developing areas, control efforts often must begin with specific, limited tasks — for instance, assessing the problem, treating the most common STDs, or screening for prenatal syphilis.

Syphilis was the target of early STD control programs, mainly because some of its effects (such as congenital syphilis, cardiovascular syphilis, and insanity) are obvious and serious. While syphilis was difficult to manage before penicillin became available, now relatively simple, inexpensive blood tests are available for screening and diagnosis, and a single dose of long-acting penicillin provides a cure (115, 674).

Gonorrhea is more difficult to control because it is more difficult to diagnose, requiring genital examination and smear or culture testing of urine, pus, or mucus (37, 662). Moreover, a large and increasing proportion of N. gonorrhoeae strains, especially in parts of Asia and Africa, are now resistant to penicillin and require alternative treatments (see p. L-131) (112, 460, 482). Efforts to develop a gonorrhea vaccine are underway (508). One US pharmaceutical company is currently analyzing results of a clinical trial involving about 3,500 volunteers given either an experimental gonorrhea vaccine or a placebo. If the vaccine proves effective, the company will seek approval for large-scale production (682).

Some STD control programs are beginning to include PID. In the US, for instance, the Centers for Disease Control are promoting better management of PID cases by (1) educating physicians and other health care personnel about PID; (2) preparing and disseminating treatment guidelines; (3) encouraging careful follow-up of cases; and (4) encouraging referral and treatment for sexual partners of women with PID (92). In addition, the epidemiology of PID is being described and publicized (267, 529).

The most successful national STD control program has been in the People's Republic of China. In fact, China is the only country that claims to have eradicated syphilis and perhaps gonorrhea, even though STD rates were high when the communist regime took power in 1949 (66, 183, 456). STDs were controlled through a massive effort, begun in the early 1950s, that included (1) eliminating prostitution, (2) providing STD treatment in all health facilities, (3) educating people about the symptoms of STDs and the need for treatment, and (4) putting political and social pressure on the public and health workers to find all cases and see that they were treated (66, 243, 456). STD incidence has remained low since this campaign mainly because political and social pressures in China discourage premarital and extramarital sexual relationships.

Other Asian programs emphasize controlling STDs in prostitutes. It is estimated that contact with prostitutes accounts for as much as 90 percent of reported STD cases in many Asian countries (480). Some countries have few STD clinics but make periodic attempts to diagnose and screen high-risk groups, such as prostitutes or servicemen, have been made in a number of countries but with limited and temporary impact (432, 607). Prenatal syphilis screening programs exist in a few countries, but often they reach only women attending specific clinics or hospitals (607). A few African countries are setting up larger programs. In Zambia a policy for STD control was adopted in 1981. A major objective is to reduce the high rate of perinatal

This poster aims to alert health professionals to the need for routine gonorrhea screening in order to help prevent PID. Swabs, usually from the cervix, are spread across culture medium in the pattern shown and later checked for growth of N. gonorrhoeae.

(Courtesy of Arizona Department of Health Services)
death due to congenital syphilis (41, 70, 231). The program is beginning with a pilot project to screen all women attending certain prenatal clinics in the city of Lusaka. Women with positive blood tests for syphilis will be treated, and their husbands contacted and treated if possible (41, 483). The Ministry of Health in Ethiopia, in conjunction with WHO and other agencies, is also undertaking a prenatal screening project because of the high rate of pregnancy wastage due to syphilis (685). The Central African Republic is expanding its STD control program. With WHO assistance, an STD clinic has been opened in the city of Bangui, and regional clinics are being established throughout the country (307). WHO is also working to increase communication among central African countries about the management and control of STDs (307).

How can countries with poor health conditions, limited health funding, and inadequate health facilities realistically approach STD control? The first step in most areas — after a brief assessment of the problem — is to improve diagnosis and treatment of STDs.

At present, STD management is inadequate in many areas. Where antibiotics are sold in retail outlets, people often buy whatever is available and treat themselves. For instance, in Nigeria a study of patients with nongonococcal urethritis found that half had taken at least three different antibiotics before visiting a clinic (17). Since people often buy the wrong antibiotics and stop taking the medication as soon as the symptoms disappear, self-treatment can lead to complications of the original infection and often promotes the development of antibiotic-resistant strains of STDs (17, 36, 607, 675).

Clinics also may treat STDs incorrectly. A Ugandan survey found that, in several health centers, gonorrhea was not inappropriately treated with several small doses of long-acting penicillin rather than the appropriate single dose — mainly because the practitioners did not understand how one injection could cure disease (33, 35). Also, since penicillin-resistant strains of gonorrhea are spreading rapidly in many areas (see box, p. L-131), clinics that continue to use only penicillin to treat gonorrhea risk treatment failures. The African Union Against the Venereal Diseases and Treponematoses recently suggested that, when penicillin fails in more than 10 percent of gonorrhea cases, programs need to "review and possibly change accepted regimens" to drugs effective against penicillin-resistant strains (683) (see Figure 7). Unfortunately, these drugs are usually more expensive than penicillin, and some cannot be given in single doses.

The most important step to improve STD care over the long run is training health care providers at all levels. Physicians may know little about STDs. In the US, for instance, medical students average less than a half hour of formal training on STDs in the four years of medical school (235). Formal and informal courses for all health workers, including pharmacists, are important, especially where STDs are a problem (641). Journal articles and professional meetings about STDs should be encouraged (27). Current issues in STD care, including updates on the prevalence of penicillin-resistant strains of gonorrhea, should be brought up in continuing education and in-service training programs. Pamphlets for pharmacists and pharmacy clerks may also be helpful.

**Simple Treatment Protocols**

Since 80 to 90 percent of people in developing countries live in rural or semirural areas, the burden of managing STDs will fall on the primary health care facilities that serve these areas (33). Most rural primary care facilities have little if any laboratory equipment to aid diagnosis, and the medical auxiliaries or pharmacists who staff them have limited medical training (33).

WHO has proposed that, in primary care centers without diagnostic facilities, STDs could be managed by simple treatment protocols based on the most common symptoms of STDs (381, 673, 693). When the symptom is urethral or vaginal discharge, these protocols involve treating for gonorrhea first (see Figures 8 and 9). For genital ulcers, patients in many African regions can be treated for both syphilis and chancroid first (693) (see Figure 10). Alternatively, treatment may depend on the appearance of ulcers: painless, well-rounded lesions are treated as syphilis; painful necrotic lesions, as chancroid; painful multiple vesicles, as herpes (381). If possible, patients are treated with a single-dose, inexpensive medication and told to return in seven days. If the symptoms are still present at follow-up, patients are treated for the most likely remaining cause — if urethral discharge, usually for nongonococcal urethritis; if vaginal discharge, often for trichomoniiasis or, where it is common, for chlamydial infection (381). (See Figures 8 and 9.) Specific protocols

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**Figure 8. A Simple Treatment Protocol for Urethral Discharge for Use Where Laboratory Diagnosis Is Not Possible**

- **Urethral discharge**
- **Gonorrhea treatment**
- **After 7 days**
  - **Discharge absent, cured**
  - **Discharge persists**
    - **Chlamydial/mycoplasma treatment**
    - **After 7 days**
    - **Discharge absent, cured**
    - **Discharge persists**
      - Refer

*For appropriate treatment regimens, see Figure 7.*

Figure 9. A Simple Treatment Protocol for Vaginal Discharge for Use Where Pelvic Examination and Laboratory Diagnosis Are Not Possible

<table>
<thead>
<tr>
<th>Vaginal discharge</th>
<th>Gonorrhea treatment</th>
<th>After 7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trace contacts</td>
<td>Discharge absent, cured</td>
<td></td>
</tr>
<tr>
<td>Discharge persists</td>
<td>Trichomoniasis treatment</td>
<td>After 7 days</td>
</tr>
<tr>
<td>Discharge persists</td>
<td>Candidiasis treatment</td>
<td>After 7 days</td>
</tr>
<tr>
<td>Discharge persists</td>
<td>Refer</td>
<td></td>
</tr>
</tbody>
</table>

- For appropriate treatment regimens, see Figure 7.
- In areas where chlamydial infections are common, Chlamydia/mycoplasma treatment may be the appropriate second step in this protocol.
- Effective regimens include: Clotrimazole 100 mg intravaginally daily for 7 days or nystatin 100,000-1,000,000 units (depending on geographical area) intravaginally daily for 14 days (669, 673).


would vary from place to place depending on the relative incidence of various STDs and on the patients — for instance, whether they describe symptoms accurately, whether they return for follow-up, and whether genital examinations can be conducted (381, 669, 693). Treatments used would vary according to the availability and cost of various drugs, the likelihood of compliance with multidose regimens, and the incidence of penicillin-resistant strains of STDs (381, 669). These protocols should not replace thorough diagnosis and treatment techniques where such techniques are available. Where they are not available, however, these protocols can at least provide a basis for simple management of STDs.

This type of simplified STD management was successful in a rural health center in Swaziland in 1978. All patients with urethral or vaginal discharge were treated for gonorrhea. Of 447 men with urethral discharge, 41 percent returned for follow-up after seven days. Five percent still had a discharge. All were then successfully treated for non-gonococcal urethritis with tetracycline. The men identified 192 female contacts, 94 of whom were traced and treated. The cost, including treatment and tracing, was $5.84 (US) per patient. Of 316 women with vaginal discharge, 38 percent required a follow-up treatment for trichomoniasis and 4 percent required a second follow-up treatment for candidiasis. One percent of the total had to be referred to a regional hospital (381, 693). In the Central African Republic a combined treatment regimen effective against the major causes of genital lesions — chancroid and syphilis — was used with all patients attending a Bangui clinic for genital lesions. No specific diagnoses were attempted. At follow-up 85 percent were cured (307).

Public STD Education Programs

Public education is crucial in any STD control program. It involves:
- informing the public about STDs — how they are transmitted and their long-term effects, especially PID and infertility;

Figure 10. A Simple Treatment Protocol for Genital Ulcers for Use Where Laboratory Diagnosis Is Not Possible

<table>
<thead>
<tr>
<th>Genital ulcer</th>
<th>Syphilis and chancroid treatment</th>
<th>After 7 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trace contacts</td>
<td>Improved, cured</td>
<td></td>
</tr>
<tr>
<td>No genital ulcer</td>
<td>Syphilis treatment</td>
<td></td>
</tr>
<tr>
<td>Genital ulcer</td>
<td>Continue chancroid treatment</td>
<td>After 7 days</td>
</tr>
<tr>
<td>Worse</td>
<td>Refer</td>
<td></td>
</tr>
</tbody>
</table>

- For appropriate treatment regimens, see Figure 7.
- Trimethoprim 80 mg/sulfamethoxazole 400 mg 2 tablets orally twice daily for 5 days or erythromycin 500 mg orally 3 times daily for 7 days (669). Limited data suggest that a single treatment of 8 tablets of trimethoprim 80 mg/sulfamethoxazole 400 mg also is effective (669, 683).

informing people that limiting the number of sexual partners minimizes the risk of acquiring an STD and, if they have an STD, that sexual contact should be completely avoided or condoms used during coitus;

- encouraging men and women at risk to use contraceptives that protect against STDs or PID (see p. L-141);

- assuring that people know where to go for appropriate STD treatment and that all patients, especially men, understand the importance of telling sexual partners about the need for treatment.

Obviously, the impact of public education depends greatly on the availability of appropriate contraceptives and, most importantly, treatment facilities.

The need for STD education is great. Most people know little about how STDs are transmitted, what their symptoms are, or what long-term risks they pose (27, 99, 307, 414, 468, 607, 658). Few men realize that they should avoid sexual contacts during any genital infection or understand the health risks for women exposed to infection (34). In some rural areas of central Africa urethral discharge is thought to be a sign of puberty rather than a symptom of disease (36). In Ethiopia a common belief is that syphilis can be "weakened" and cured by having many sexual contacts (468). In Nairobi a survey of 200 relatively well-educated women attending a family planning clinic found almost total ignorance of the harmful effects of STDs and of ways to prevent STDs (240). In Madras, India, a survey of 200 men and women living in a slum found that less than one-quarter understood how STDs are transmitted or what the symptoms are. Women were particularly ill-informed (575).

The emphasis and approach of an STD education program must vary according to the population at greatest risk. Efforts should always be aimed at both men and women, however. If, as in some developing countries, the at-risk population is made up of low-income, nonliterate young adults, then radio or cinema messages emphasizing the importance of prevention and prompt treatment may be most appropriate. Where adolescents in school are particularly at risk, as in the US and many European countries (247, 298), in-school education may be appropriate. It may be controversial, however, and usually must be preceded by efforts to win support from parents and community groups (225, 488, 658). (See Population Reports, Population Education in the Schools, M-6, March-April 1982.)

Where funding is very limited, education should be directed at particularly high-risk groups such as prostitutes, men and women attending STD clinics, or others especially likely to have multiple sexual partners (27, 577). STD clinics can provide information to patients through posters, brochures, and, above all, through personal counseling by health personnel (27). Condom distribution and education about the protective effects of condoms, diaphragms, spermicides, and oral contraceptives should be emphasized in all STD treatment facilities. Where medication is available without prescriptions, pharmacists and pharmacy clerks should be given some training and simple illustrated materials for distribution.

Little is known about the impact of education programs on behavior, mainly because education is usually part of overall STD control programs and thus is not evaluated separately. Also, the desired behavioral changes—limiting the number of sexual partners, using condoms, and/or attending STD clinics—are affected by many other factors and are difficult to measure (298).

One Ugandan study did try to estimate the effects of STD education on behavior. Almost all male and female university students who attended a one-hour talk on STDs said immediately afterward that they would be more cautious about sexual contacts. Among men who attended the talk and who later sought STD treatment at the university clinic, however, the only clear change in behavior was that they reported for treatment earlier. The study could not determine whether the talk helped some people avoid STDs so that they did not need to come to the clinic (34).

In Sweden a nationwide public education program promoting condom use for protection against STDs may have helped lower the gonorrhea rate. The National Association for Sex Education began a condom promotion campaign in 1970 as part of an STD control effort involving the government, the schools, and private organizations. The campaign used posters, cartoon strips, point-of-purchase displays, and short films. At the same time, the schools began sex education programs. Within two years the number of condoms sold had increased by 50 percent. The incidence of gonorrhea had dropped by 20 percent. How much of this drop was due to increased condom use is not known. The increased number of treatment facilities also could have helped lower the gonorrhea rate (636).

**Improving Obstetric Care**

Improving obstetric care is difficult and calls for appropriate training of health care providers. These include traditional midwives, community health nurses, and formally trained midwives as well as physicians (464). Most in need of training are traditional midwives, often called traditional birth attendants (TBAs). In many developing countries TBAs deliver between 60 and 80 percent of babies (89, 357, 632, 666). This pattern continues partly because of a lack of trained personnel but also because some women prefer TBAs to trained medical personnel (see Population Reports, Traditional Midwives and Family Planning, J-22, May 1980). Thus, improving obstetrical care requires upgrading
the skills of those currently providing care as well as training new generations of health care providers.

Many developing countries, including Ecuador, Honduras, Sierra Leone, the Philippines, and Thailand, have set up TBA training programs (45, 356, 358, 590, 645). Others, such as Sudan, have developed formal programs to train young women to become village midwives and eventually replace the TBAs (213). Since the majority of TBAs are nonliterate women in their 40s and 50s, training programs for them use very simple teaching techniques with emphasis on practical skills. Courses describe when to refer patients with complications to a medical facility and emphasize basic hygienic practices such as washing hands. Most cover elementary prenatal and postnatal care. Training courses usually provide TBAs with simple delivery kits (357).

How successful TBA training programs are is unclear. In Honduras a 1977 evaluation suggested that trained TBAs referred more patients with complications than did untrained TBAs. Many TBAs continued to use unsafe practices, however (358). In Sierra Leone a study of TBA practices before and after training revealed that many TBAs reverted to traditional practices a few months after training (645). In Thailand a 1978 study tested knowledge of maternal and child health care and family planning on the part of trained and untrained TBAs. Trained TBAs were somewhat more likely than untrained TBAs to choose the correct answers (590). No large studies have yet compared the health or fertility of women attended by briefly trained TBAs or trained nurses with the health or fertility of those treated by untrained TBAs.

One barrier to improving obstetric care is mutual distrust between the medical profession and TBAs (559). In some areas, however, TBAs and physicians have begun to work together. In Taiwan TBAs often assist young obstetricians in setting up new practices as well as joining in partnerships with them at “birth stations” (273). In Guaiuba, a small town near Fortaleza, Brazil, TBAs were invited to attend deliveries at small birth stations where nurses and transportation to a hospital were always available (472, 684). The success of the Guaiuba project has prompted similar efforts elsewhere in Brazil (684).

THE ROLE OF FAMILY PLANNING PROGRAMS

Family planning programs can help to prevent infertility and, in some cases, can provide basic infertility services (221). By providing contraceptives such as condoms, diaphragms, spermicides, and oral contraceptives, family planning programs can help men and women protect themselves and their partners from sexually transmitted diseases and/or pelvic inflammatory diseases. By making all contraceptives readily available, family planning programs can reduce the incidence of illegal abortion, complications of which can lead to infertility. Many family planning clinics also can diagnose and treat STDs and thus help reduce the rate of PID and other complications of untreated STDs. Some may be able to offer basic infertility services so that infertile couples can obtain an initial evaluation at minimal cost.

Providing Contraceptives

Increasing the availability of contraceptives can help to prevent infertility in two ways: (1) by offering contraceptives that protect against infection as well as pregnancy and (2) by giving women who want to control their fertility a choice other than illegal abortion.

Condoms, when used throughout all sexual contact, effectively protect against gonorrhea and syphilis and probably other STDs as well (see Population Reports, Update on Condoms: Products, Protection, Promotion, H-6, September-October 1982). A study in a London STD clinic found that men who used condoms regularly and correctly were one-tenth as likely to contract gonorrhea or syphilis as men who did not use condoms. Even men who used condoms irregularly or incorrectly were 80 percent as likely to contract an STD (47). Family planning and STD programs need to place more emphasis on the value of regular condom use in preventing STDs and potential infertility (554).

Spermicides may provide both a mechanical and chemical barrier to infection since they are normally used with a spermicide. In the US an investigation of over 2,000 women attending a Louisiana family planning clinic found that women who used diaphragms or whose husbands used condoms had cervical gonorrhea about one-fifth as often as users of oral contraceptives (OCs) or IUDs (278). Spermicides require fitting by a physician or paraprofessional, however, and so may not be available to many women.

Spermicides, although not as effective in preventing pregnancy as diaphragms or condoms, are often readily available in retail stores and kill most organisms that cause STDs (109, 127, 138, 259, 471, 560). A recent US study found that spermicide users had a gonorrhea rate one-fourth that of users of oral contraception or voluntary sterilization (259). As with condoms and the diaphragm, spermicides provide best when used correctly and consistently (see Population Reports, Spermicides:—Simplicity and Safety are Major Assets, H-5, September 1979).

By protecting against STDs, condoms, diaphragms, and spermicides also protect against PID. A case-control study of 306 PID patients and over 1,175 controls found that condom users faced 70 percent the risk of PID as non-users; spermicide users, 60 percent; and diaphragm users, 40 percent (279). A recent study suggests that bacteria may attach to sperm and thus be carried to the uterus and fallopian tubes (609). This would help explain the protective effect of barrier methods against PID.

Oral contraceptives, as well as being highly effective for contraception, protect women against PID (442, 524, 546). Women who have used OCs for 12 months or longer face half as much risk of developing PID as non-users (see Population Reports, Update on Contraceptives:—Simplicity and Safety are Major Assets, H-5, September 1979). OC users who have used OCs should be told that, although conception may be delayed for a few months after discontinuing pills, it is not permanently prevented (331).

Long-acting progestins—injectables, implants, and others— may also help prevent PID. A recent WHO case-
Many clinics may be able to diagnose and treat common STDs. Studies suggest that IUD users are about 1.5 to 4 times more likely to develop PID than noncontraceptors (98, 211, 546, 648). Risk associated with IUD use is greater among women who have a number of sexual partners (162, 447), possibly because of greater potential for exposure to STDs. The reason for greater risk with IUD use is not certain. Bacteria may grow more rapidly in the fallopian tubes because of inflammation due to the IUD, the increased volume and duration of menstrual bleeding may promote bacterial growth; bacteria may ascend through the cervix more easily when an IUD is in place; and/or bacteria may be introduced into the uterus during IUD insertion (see Population Reports, IUDs: An Appropriate Contraceptive for Many Women, B-4, July 1982). A recent study shows that infections most often occur in the first few months after insertion, suggesting that the last explanation is most important (687).

Complications of poorly performed illegal abortions, including pelvic infection and infertility, are a common problem in developing countries where family planning services are limited. The ready availability of contraceptives may reduce the number of abortions in these areas. In Chile, as the figures below show, abortion complications declined as family planning use increased (253, 439):

<table>
<thead>
<tr>
<th></th>
<th>Early 1960s</th>
<th>1978</th>
</tr>
</thead>
<tbody>
<tr>
<td>% using contraception</td>
<td>5%</td>
<td>25%</td>
</tr>
<tr>
<td>Abortion deaths per 1,000 live births</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Abortion hospitalizations per 1,000 women age 15-44</td>
<td>25</td>
<td>15</td>
</tr>
</tbody>
</table>

Where nationwide family planning programs are not yet established, programs intended to reduce abortion complications may concentrate on providing contraceptives to women most likely to seek abortions. These women vary from region to region. In many Asian and South American countries older, married women with many children make up the bulk of those undergoing abortions. By contrast, in many African countries young, unmarried women undergo abortions more than other women (332). One African physician comments that in some areas of Africa simply assuring that school girls are aware of contraceptives and where to obtain supplies may be a step toward preventing abortion (435).

STD and Infertility Services

Providing STD diagnosis and treatment is a logical extension for many family planning programs. In some developed and developing countries, family planning programs may be the only source of medical care for many young, sexually active women. Also, family planning clinics often are the only available facilities that routinely perform genital and pelvic examinations (240). Thus, in areas where STDs are common, family planning clinics could diagnose and treat STDs and screen for asymptomatic STD infection. This would require appropriate facilities and training, however. Also, clinics would have to encourage men as well as women to attend — an approach important for family planning as well as for preventing infertility.

Some family planning clinics and regional health centers may be able to help couples with infertility problems (120, 221, 251, 287, 315). In many developing countries infertility services are available only at a few, hospital-based clinics. Thus, the majority of infertile couples have little opportunity even for a diagnosis. Those who can attend a clinic often have to wait a long time for basic tests. For instance, in Ibadan, Nigeria, women may wait six months to a year for hysterosalpingography (301).

In most family planning clinics, infertility services must be limited to procedures that do not require expensive equipment and can be performed by paraprofessionals rather than physicians. In the US, federally funded family planning clinics are required to offer infertility services. Officials note, however, that:

- Designing and implementing a comprehensive infertility program is a major undertaking for a family planning program that has worked primarily to prevent unwanted pregnancies. The responsibilities of contraceptive and infertility programs are so different that careful planning, assessment of needs, and ongoing evaluation of the program and resources available in the community are essential before even the most effective, experienced family planning service provider can launch a successful infertility program (621).

Some simple procedures that could be offered include:
- Counseling couples on fertility awareness — when and how often coitus should take place to maximize the chance of pregnancy,
- Obtaining medical histories from both husband and wife,
- Performing physical examinations of both husband and wife,
- Checking couples for asymptomatic STD infections that could cause subfertility,
- Determining whether ovulation takes place, using basal body temperature and/or cervical mucus records,
- Performing semen analyses,
- Counseling couples with potentially serious fertility problems about their options for further treatment and the anticipated long-term costs and chances for success.

Couples who are subfertile because of relatively simple problems such as asymptomatic cervicitis or improper timing of coitus could become pregnant with the help of such services. In the US, family planning clinics in rural Penn...
There are three ways that health workers can help permanently infertile couples. They can:

- Counsel couples in whom male factors cause infertility so that they do not continue to spend time and money fruitlessly seeking a cure,
- Counsel couples in whom female factors cause infertility about artificial insemination with a donor's sperm, and
- Advise couples interested in adopting a child of the opposite sex about sources of children to be adopted.

Infertile couples, especially childless couples, often find it difficult to accept their infertility and to begin thinking about adoption, artificial insemination, or remaining childless. These couples need accurate, realistic information about their infertility prognosis. Also, they often need help in dealing with the lack of understanding on the part of relatives and the community. Physicians and counselors can help by listening and responding sympathetically to couples' concerns.

When the man is sterile, some couples may choose to try having a child through artificial insemination by donor. The procedure is the same as for AIH (see p. L-133), except that donor sperm is used. The sperm donor is usually a man of ethnic and physical make-up similar to the infertile man's. Success rates in healthy women under age 35 usually are relatively high — between 50 and 80 percent within 3 to 12 cycles of insemination. The major problem is that artificial insemination by donor is not accepted in some cultures and religions. Roman Catholicism and Orthodox Judaism consider it to be adultery (389). In many African countries it may be unacceptable, although O.A. Ladipo reports that his patients in Ibadan, Nigeria, have accepted the procedure after counseling (302). In India infertile couples have readily accepted artificial insemination (479).

Adoption is the only way for most permanently infertile couples to have children. In developed countries children are usually adopted through public or private adoption agencies. Adoptions must be approved by the courts and by social welfare agencies. In most countries the supply of children to be adopted is not nearly enough to meet the demand.

In most developing countries adoption is less regulated than in developed countries. In many Polynesian societies, for example, adoption simply involves parents agreeing to give an infant to a neighbor or relative who is infertile or who has no small children. The biological parents retain many rights to their child, however (61, 507). In India the 1956 Hindu Adoptions and Maintenance Act allows any Hindu man to adopt a son if he does not already have a son or to adopt a daughter if he does not already have a daughter. A Hindu woman, however, may adopt a child only if her husband has abandoned her, is dead, or is of "unsound mind" (69). In Indonesia private hospitals may arrange for the adoption of unwanted babies (569). In Africa formal adoption is rare. Motherless children or children born out of wedlock are usually absorbed into extended families. Even when adoptable children are available, infertile couples may not accept adoption because they see adopting a child as a public admission of their infertility.

Infertility can be a source of suffering to women and men around the world. Therefore, wherever infertility is common, it is important to develop public health approaches to prevent infertility, to establish health facilities to diagnose and, when possible, to treat infertile couples, and to develop ways for permanently infertile couples to adopt children.


