

MICROBICIDES

A New Defense Against
Sexually Transmitted Diseases

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PREFACE

For more than 30 years, The Alan Guttmacher Institute (AGI) has focused its attention on research and programs to improve the reproductive health of individuals and couples, both in the United States and around the world. While the prevention of unintended pregnancy has been, and continues to be, a major goal of the Institute's work, AGI is increasingly looking at other important aspects of reproductive health. One of these is the prevention of sexually transmitted diseases (STDs).

Even though STD prevention has been a serious epidemiological issue for years, most laypeople have not been very comfortable discussing or even thinking about the topic. In the 1980s, as awareness of HIV and AIDS grew, the stakes were raised, and people were forced to start talking more openly about both HIV and other STDs. Despite increased public attention, however, STD prevention remains a difficult objective, since no aspect of it is simple.

STDs can result from numerous pathogens and can be transmitted in many ways. For example, they can be spread through vaginal, anal and oral sex. HIV and some other STDs also may be transmitted if an infected individual shares needles for injection-drug use or if blood used for a transfusion is tainted. In addition, STDs do not affect only adults. Infants and children whose mothers are infected can acquire some of these diseases in the womb, during delivery or through breastfeeding. These considerations make the prevention of STDs extremely complex—for physicians, health counselors, research scientists, policymakers, and the average man and woman.

Worldwide, prevention is being pursued mainly through efforts to reduce risky sexual practices. These efforts involve encouraging sexually active individuals to limit intercourse to one uninfected partner or to use condoms every time they have sex—particularly if they do not know their partner's risk status or if they know that their partner is infected. In addition, prevention is being approached on other fronts: needle exchange programs for injection-drug users; the screening of donor blood supplies; and the use of drug therapies and, sometimes, cesarean section to avoid transmission from infected women to their infants. Moreover, work continues on the development of vaccines, including one that would provide immunity from the most deadly STD—HIV.

Still, efforts to promote primary STD prevention through safer sexual behavior have been hampered by the limited options available. The surest courses of action are abstinence from intercourse, except in a completely monogamous relationship with an uninfected partner, total avoidance of sex with an infected person, and correct and consistent condom use. At best, these practices require considerable self-discipline. For women, they are not always feasible. Many women are unable to insist that their partner use a condom every time they have sex and do not know about or do not like other methods that might offer some protection. And some women who believe that they are in a mutually monogamous relationship with an uninfected partner do not know that he actually has other partners or is infected with an STD.

Nobody expects that vaginal microbicides, whatever form they take, will be a magic bullet in the fight against STD infection.

Another strategy being pursued is research to develop new female-controlled methods of STD prevention. These methods are known as vaginal microbicides—literally, products that kill or deactivate dangerous microbes. Some of the more promising ones are being tested in large-scale trials, and a few manufacturers are coming close to seeking the Food and Drug Administration’s approval of their products.

Yet a number of questions about microbicides remain unanswered. Will they prevent only HIV or other STDs as well? Will they provide effective protection against both STDs and pregnancy? How long after application will a microbicidal product be effective? What mode of dispensing them will be most effective and most acceptable to women? The answers to some of these questions will be determined by the limitations of the scientific formulations available. The answers to others will reflect perceptions of what women want and think they would use. Ideally, women will one day be able to choose from among a wide range of microbicides, as they now choose from among a range of contraceptives.

Nobody expects that vaginal microbicides, whatever form they take, will be a magic bullet in the fight against STD infection. And many health experts believe that the condom will remain the primary and most effective weapon for couples to use in preventing STDs. Nevertheless, this seems an appropriate moment to evaluate some of the societal and economic considerations that are driving the search for vaginal microbicides. To that end, this report provides

- estimates of the extent of STD infection in the United States today, and some evidence of the monetary cost of treating these diseases;
- information on particular groups of Americans whose patterns of heterosexual behavior probably place them at greatest risk of contracting STDs;
- discussion of limitations in the methods now available to prevent STDs from spreading;
- information about current research on microbicides; and
- results of an AGI survey of women’s perceptions about their risk of contracting STDs and their interest in using microbicides when these products become available.

The report concludes with a discussion of prospects and policy recommendations for the future.

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SEXUALLY TRANSMITTED DISEASES: RISK FACTORS, LEVELS AND CONSEQUENCES

The emergence of HIV as a disease spread through sexual intercourse, combined with growing public awareness about the problems associated with other sexually transmitted diseases (STDs),¹ has transformed the context of many people's sexual lives. Now, in addition to the familiar need to avoid unwanted pregnancy, couples must worry about avoiding STDs. But preventing pregnancy and preventing STDs often require different approaches, because the most widely used contraceptive methods in the United States (the pill and sterilization) do not offer any protection against sexually transmitted infections.

Even though HIV is the infection most feared by sexually active people, all STDs can have highly unpleasant, and often painful, effects; many lead to serious long-term health problems. Moreover, infection with some STDs makes individuals more susceptible to contracting HIV.² And infection with any STD can be psychologically devastating, a source of acute personal embarrassment and sometimes destructive of personal relationships.

The risk of contracting STDs comes from being exposed to an infected person, and the more sexual partners a person has, the higher the risk.³ Other important factors determining the likelihood of STD infection are the potency of the microbe in question, the susceptibility of the uninfected partner, the type of sexual behaviors people engage in, whether couples use a protective method and the timeliness and effectiveness of medical treatment the infected partner obtains.⁴ In addition, women have a greater risk than men of

contracting an STD from an infected partner, because these diseases are more readily passed to women;⁵ young women, who have relatively few antibodies and a biologically immature cervix, are especially susceptible to infection.⁶

Some people who have acquired an STD—especially women—do not show symptoms of infection. But even when infected individuals have symptoms, they often do not know where to go for treatment, may not be able to afford a doctor or clinic visit, or may attempt to treat themselves with over-the-counter remedies. And others simply keep their STD infection a secret and hope it will go away.

Furthermore, while detection and treatment of STDs are crucial to infected people's well-being, not all of these diseases are curable. Infections caused by bacteria (or sometimes protozoa or fungi)—chlamydia, gonorrhea and syphilis, for example—can be cured with appropriate antibiotics. Those caused by viruses—including two of the most common STDs, genital herpes and human papillomavirus (HPV), the infection that can cause genital warts or cervical cancer—are incurable, although their worst symptoms can be treated or alleviated. The most threatening of all sexually transmissible viral infections, HIV, can be treated only through the use of very expensive drugs to delay the development of AIDS.

Whether curable or not, many STDs can cause long-term health problems for infected individuals. Some of these diseases can result in infertility or cancer. Women who have an infection while pregnant

are at risk of experiencing a spontaneous abortion, stillbirth, infant death or premature delivery; their infants may have a low birth weight, as well as such long-term health problems as chronic respiratory problems, blindness and mental retardation.⁷ Furthermore, because infections in women often have no symptoms or are difficult to diagnose, women are less likely than men to seek treatment; as a result, they tend to have more severe long-term health complications from STDs than men.⁸

STDs Touch the Lives of Millions of American Men and Women

Each year, an estimated 15 million new STD infections occur among Americans aged 15 and older (Figure 1, page 8). The most common are HPV (an estimated 5.5 million new infections), trichomoniasis (five million), chlamydia (three million), genital herpes (one million) and gonorrhea (650,000). Far less common, but still occurring in substantial numbers, are syphilis (70,000) and sexually transmitted hepatitis B (77,000) and HIV (20,000).⁹

Because some of the most common STDs are incurable, viral infections, the total number of Americans with a continuing infection (prevalence) is much higher than the number newly infected each year (incidence). An estimated 45 million Americans older than 14 (one in five in that age-group) suffer from genital herpes, and 20 million (almost one in 10) from HPV (Figure 2, page 9). More than one-half million each have sexually transmitted hepatitis B and HIV.¹⁰

Increasingly, HIV infection in the United States is being spread through heterosexual activity, rather than through same-sex contacts or injection-drug use. Between 1992 and 1997, the proportion of people with AIDS who were women rose from 14% to 19%.¹¹ Moreover, in 1998, 23% of new AIDS diagnoses and 32% of new HIV infections were reported among women.¹²

Treatment of STDs Costs the Health Care System Billions of Dollars Each Year

The U.S. health care system spends an estimated \$8.4 billion each year to treat the short- and long-term consequences of STDs (Figure 3, page 10).¹³ This total is a highly conservative estimate, because it covers only direct medical costs; it does not include lost wages and productivity as a result of STD-related illness in the population, or human costs in terms of the pain and grief that can result from infertility, ectopic pregnancies, death or disability.

Viral STDs account for by far the largest part of the overall cost (\$6.4 billion). The bulk of these expenditures (roughly \$4.5 billion) goes to treating sexually contracted HIV and AIDS; the next highest share (about \$1.6 billion) is taken up by the treatment of precancerous cervical lesions and cancer of the cervix caused by HPV.

Most of the \$2 billion associated with bacterial STDs is for treating pelvic inflammatory disease, which may result when chlamydia or gonorrhea infection is left untreated. Thus, timely medical treatment of those infections not only prevents their spread to sexual

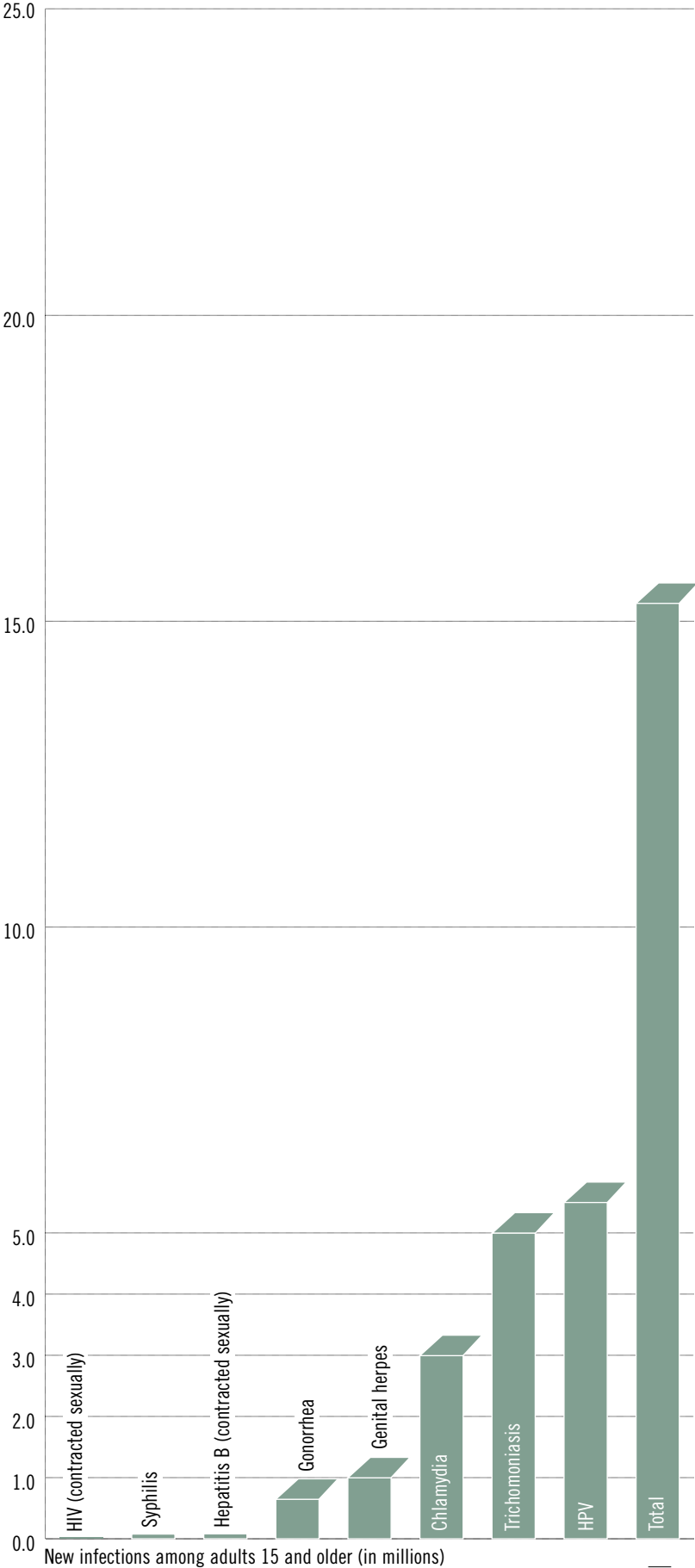


Figure 1 An estimated 15 million new STD infections occur each year among U.S. men and women.

Source: reference 9.

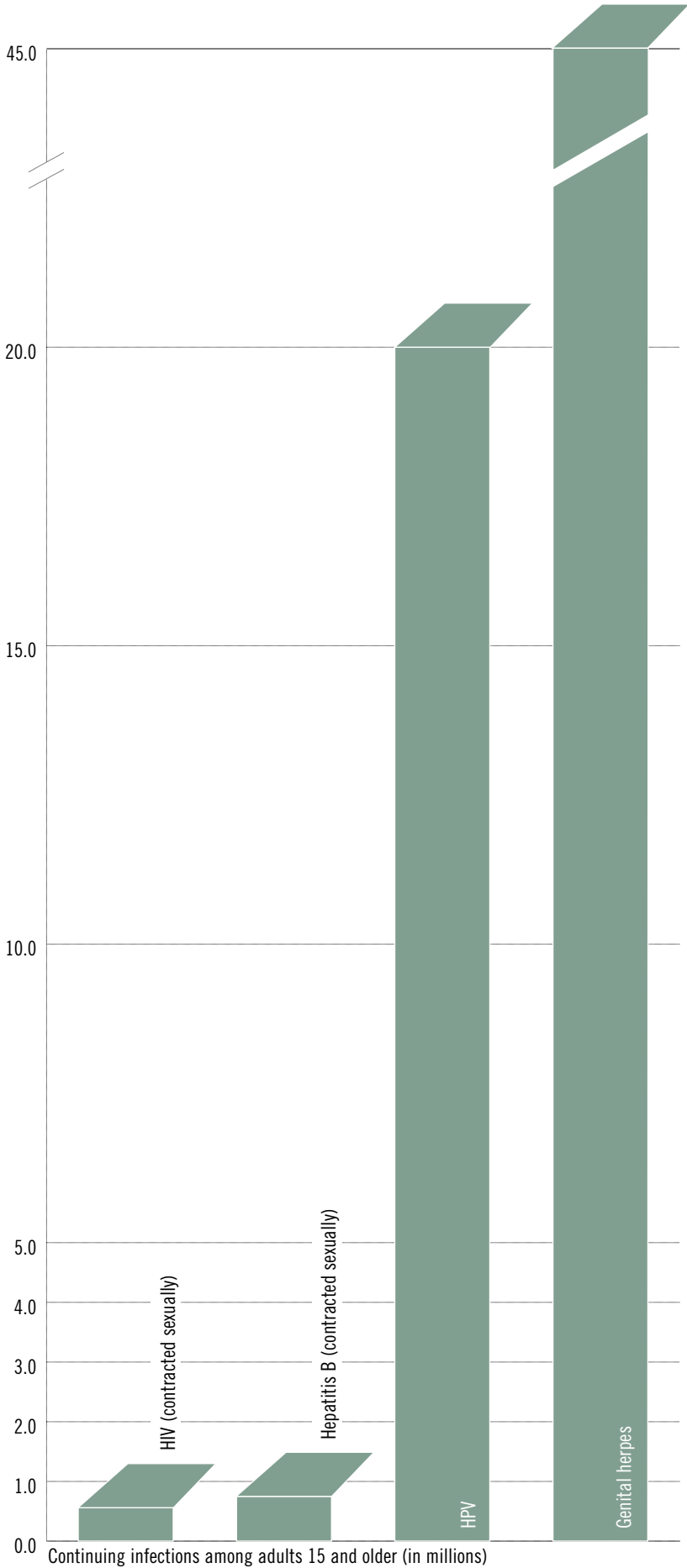


Figure 2 Millions of men and women are infected with viral STDs, for which there is no cure.

Source: reference 10.

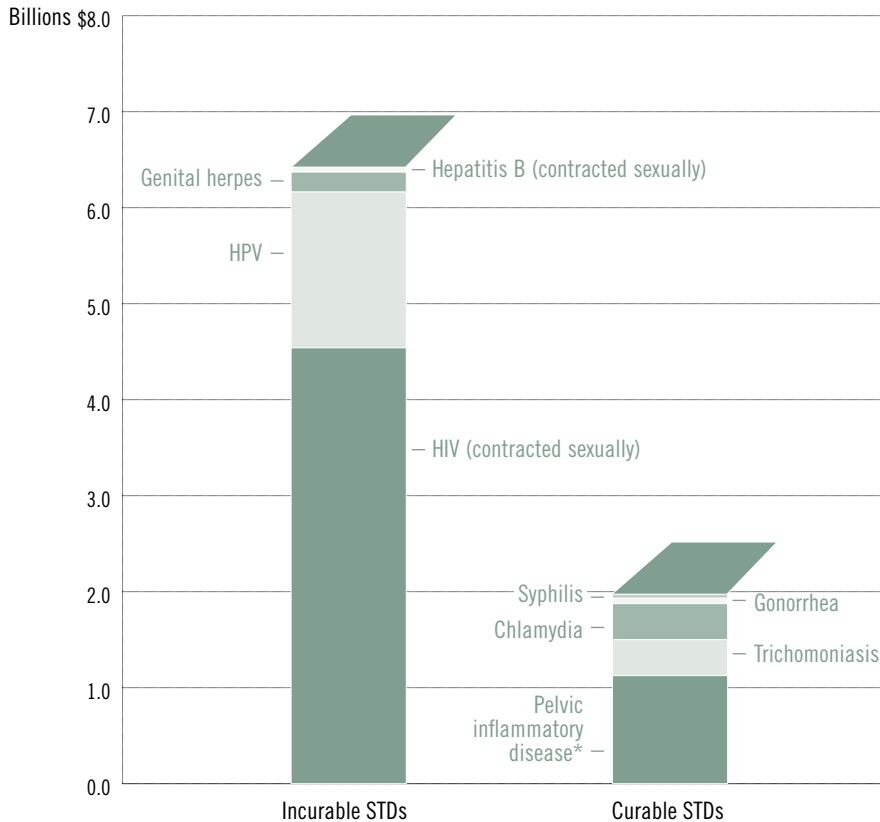


Figure 3 The U.S. health system spends more than \$8 billion each year on the treatment of STDs.

*Pelvic inflammatory disease is not an STD, but it may be a consequence of untreated chlamydia or gonorrhea.

Source: reference 13.

partners, but also reduces the much more costly burden of long-term consequences of untreated STDs.

Younger Americans Are at Greatest Risk of STDs

STDs largely affect young people (see box, page 13), because they are the most likely to be single and to be involved in sexual relationships with more than one person over a short period of time. For example, among U.S. women aged 15–44 who have had intercourse during the past year, 34% (17 million) are at increased risk of STD infection because they or their partner had more than one sexual partner in the past year.* Among teenagers and unmarried women, however, the proportions are almost doubled (Figure 4).¹⁴

The greatly elevated risk among younger people is particularly salient because both women and men are marrying later today than they did in the past. The average U.S. woman spends nearly one-quarter of her potential reproductive life (that is, the years from menstruation to menopause) being sexually active but unmarried. For the typical woman, seven years pass between the time she first has sexual intercourse and the time she marries; the typical man spends even more years sexually active and single—about 10.¹⁵

*While these estimates provide a useful indicator of general risk levels, they probably understate the true number of individuals with a direct risk of contracting an STD, primarily because in most surveys, Americans underreport their sexual activity. The estimates are further limited because they include only reports of heterosexual relationships.

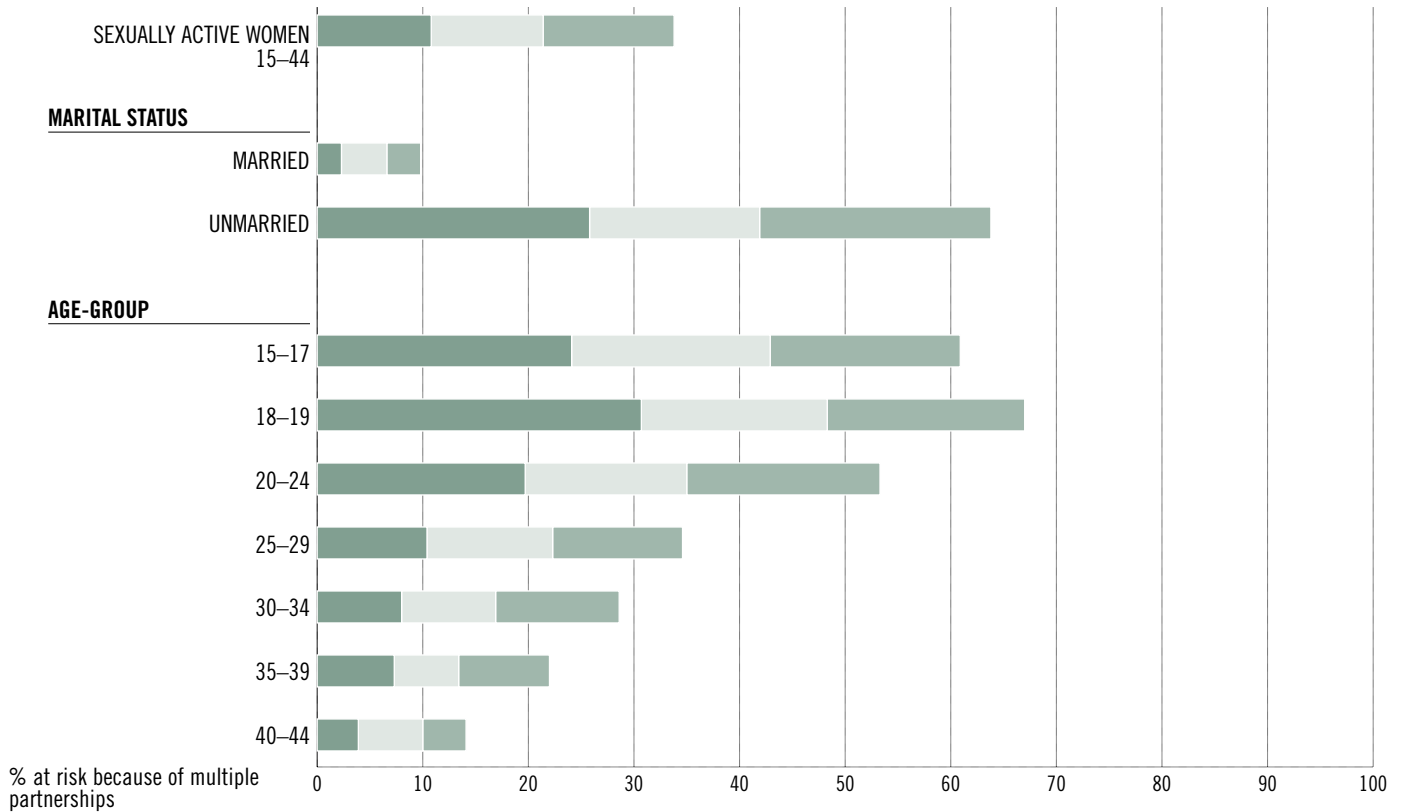


Figure 4 One-third of sexually active women are at risk of infection because they or their partner have had multiple partners during the last year.

- Woman and her partner had multiple partners
- Woman had multiple partners
- Woman's partner had multiple partners

Source: reference 14.

What Can People Do to Protect Themselves Against STDs?

Given the risk-laden world they live in, people have a number of choices about how to conduct their sexual lives. They can abstain from sex until they marry. However, marriage is not a complete guarantee of monogamy. (At a minimum, even among married women, 10% are at risk because they or their husbands have had more than one sexual partner in the past year—see Figure 4.) And in some monogamous relationships, one partner may be infected with an incurable STD acquired during a previous relationship. Unmarried people can choose to have intercourse with only one (uninfected) person or to engage in sex only if a condom is used.

When used correctly and consistently at every act of intercourse, the condom is the chief proven method of avoiding the transmission of most STDs.¹⁶ Notably, it is becoming increasingly popular in the United States. In 1988, 13% of sexually active women 15–44 said they and their partner were using the condom, alone or in combination with another contraceptive method; by 1995, that proportion had risen to 19%, and it was considerably higher than average (32–34%) among teenagers and women who had never been married (Figure 5, page 12).¹⁷

Almost half of women (47%) who have had more than one sexual partner in the past year used a condom during that time.¹⁸ But this still leaves large numbers of American women and men possibly exposed

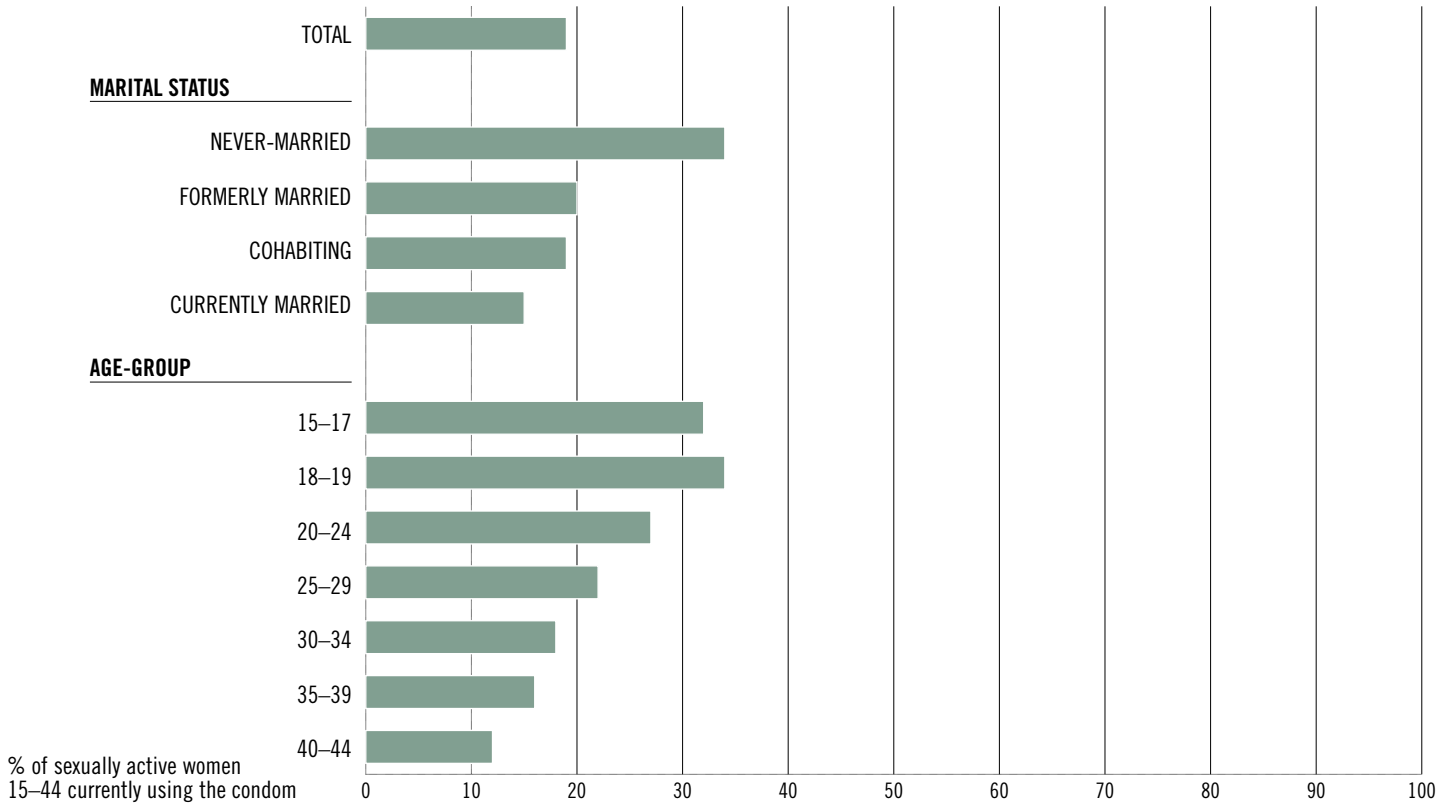


Figure 5 Never-married women and teenagers are the most likely to report condom use.

Source: reference 17.

to STDs and without any protection. The reasons are not hard to understand. Many men find that the condom reduces their sexual pleasure, and some couples dislike having to interrupt sex to use it.

But many women lack protection not only because of personal attitudes and tastes. Some lack the authority in a sexual relationship to insist on either consistent condom use or mutual fidelity. Some do not have sufficient self-confidence or financial independence to walk away from a relationship in which their partner's refusal to use a condom places them at risk. Some women are uncomfortable talking about sex or negotiating condom use. Others are fearful that a request for condom use may be interpreted as suspicion of their partner's infidelity, or acknowledgment of their own. Some women do not want their partner to use a condom because they want to have a child.

Women whose partners do not use condoms could decide to use the female condom, although clinical trials indicate that it is not as effective in preventing pregnancy (or, probably, STDs) as the male condom.¹⁹ This method is more expensive than the male condom, and its use requires agreement between partners. By and large, then, the decision to use or not use a condom—whether male or female—often rests with the male partner.

Women also have another option available to them, although many do not know about it. Nonoxynol-9, the active ingredient in a number of over-the-counter birth control methods available in the United States, provides some level of protection against STDs.

STDs Particularly Affect Younger Americans

- *Some 25% of new STD infections each year in the United States occur among men and women aged 15–19.*¹
- *Another 42% of these infections occur among 20–24-year-olds.*²
- *Among women with newly diagnosed HIV infection, 25% are aged 13–24.*³
- *Some 39% of men and 44% of women with AIDS were 20–34 when the disease was diagnosed.*⁴ *Given that it takes, on average, 10 years for an HIV-infected person to develop AIDS, these proportions suggest that many American adults with AIDS were in their teens or early 20s when they contracted the virus.*

References

1. Eng TR and Butler WT, eds., *The Hidden Epidemic: Confronting Sexually Transmitted Diseases*, Washington, DC: National Academy Press, 1997.
 2. *Ibid.*
 3. Centers for Disease Control and Prevention, U.S. HIV and AIDS cases reported through December 1998, *HIV/AIDS Surveillance Report*, 1998, Vol. 10, No. 2, Tables 7 and 8, pp. 16–17.
 4. *Ibid.*, Table 7, p. 16.
-

Nonoxynol-9 Offers Protection Against Bacterial STDs, but Important Questions Remain

Nonoxynol-9 offers users a roughly 15–25% level of protection against gonorrhea, chlamydia and trichomoniasis. Thus, among 100 women who might typically become infected with these bacterial infections, 15–25 would be protected if they used any of the methods containing nonoxynol-9—jelly for use with the diaphragm, vaginal suppositories, vaginal cream and foam, contraceptive film and the contraceptive sponge.²⁰ This level of protection is undoubtedly less complete than that provided by consistent and correct use of the condom. However, these methods are within the control of the woman, which is a distinct advantage if her partner refuses to use a condom or does not use it every time sex occurs.

An increasingly important question is whether nonoxynol-9 can prevent the transmission of viral STDs, particularly HIV. Its protective effect as evidenced in laboratory studies is difficult to interpret, because of differences in the ways the various products deliver nonoxynol-9 and in the amount of it that they contain. And at higher doses, some women—especially those who use the product frequently—experience irritation of the vaginal lining, which can make HIV transmission easier. The Centers for Disease Control and Prevention has concluded, therefore, that women should not be encouraged to use this product for HIV prevention.²¹

Some health officials and women’s health advocates, by contrast, feel that women should be informed about all methods that can, *or*

might, help prevent HIV transmission. They argue that when condom use is not possible, the use of products containing moderate or low doses of nonoxynol-9, in combination with a diaphragm, if possible, is one way for women to reduce their risk of viral STDs.²²

Research is under way to answer many questions about the benefits and risks associated with the use of nonoxynol-9 to protect against STDs. For the moment, however, messages about its desirability as a method of preventing viral STDs are still guarded.

MICROBICIDES: NEW OPTIONS FOR WOMEN

In response to the global AIDS epidemic and heightened concern about other STD infections, scientists are intensifying the search for technologies to prevent these diseases—especially methods that women can use. The new products for women—vaginal microbicides—are not yet available, but some are being tested in a number of countries.²³

Microbicides can use one or more of the following mechanisms of action to combat infection: They can *block* infection by creating a barrier between the pathogen and the vagina. They can *kill* or otherwise immobilize pathogens. Or they can *prevent a virus from replicating* once it has infected the cells that line the vaginal wall. Vaginal microbicides will probably be produced in many forms—gels, creams, suppositories, film, sponges and vaginal rings.²⁴

Because STDs are caused by different types of pathogens, a microbicide that works against one will not necessarily protect against another. So scientists are trying to develop products that will be effective against a wide range of pathogens, including HIV. The challenge is to develop products that are highly effective against infectious organisms but low in toxicity and nonirritating during repeated vaginal use.²⁵

Some microbicides being investigated will prevent pregnancy as well as protect against STDs, while others will not. The development of a noncontraceptive microbicide will be important for women who have an HIV-positive partner but who want to have children.

Many Novel Approaches Are Being Explored in the Development of Microbicides

At least 60 vaginal microbicial products are in various stages of development. Some are based on existing products used in new ways or new combinations; others are based on completely new compounds.²⁶

- *Antibodies*, one of the body's main defense systems, are the basis for vaccine technology. Scientists have found ways to isolate the antibodies that counteract HIV and other infections and to mass-produce them. These technologies raise the possibility of delivering antibodies directly to the vagina, allowing them to combat pathogens before infection occurs.
- *Detergents and surfactants* disrupt the outer membranes of cells and the outer shell of viruses. Nonoxynol-9 is a detergent; another detergent that is used as a spermicide (octoxynol-9) is also being explored as a potential microbicide, as are compounds that are used in shampoo, toothpaste and contact lens solution.
- *Gels* that coat the vagina may prevent HIV from entering the cells of the vaginal lining. One promising gel is an inexpensive substance derived from seaweed.
- *Peptides* are small protein molecules that line every surface of the body—eyes, skin, lungs, tongue and intestinal tract—and kill bacteria within minutes of contact. If applied in concentrated quantities at the site of potential infection, peptides may kill off pathogens before they cause infection.

The ideal would be a situation in which different formulations of microbicides were available for use in different phases and contexts of women's and men's sexual lives.

- *pH regulators* maintain the natural acidity (pH level) of the vagina, making it inhospitable to HIV. (The virus cannot live in the normal acidity of the healthy vagina; however, semen is alkaline, and the vagina becomes more alkaline during intercourse, allowing HIV to survive.) One formulation under investigation also creates a physical barrier that helps block the passage of pathogens into the cells of the vagina and cervix.

- *Antiretroviral products* interrupt the replication of a virus once it enters a cell. Many antiretroviral drugs initially explored as potential AIDS therapies were abandoned because they were not easily absorbed into the bloodstream. But these compounds might work well in vaginal microbicides, because they could be applied to the skin and would not have to be absorbed systemically.

Testing the Efficacy and Safety of Microbicides Will Take Many Years

All new drug formulations are subjected to lengthy (and therefore costly) laboratory, animal and human trials before the Food and Drug Administration (FDA) approves them for use in the United States. Testing involves a number of carefully phased stages (see box).

Once the FDA has granted approval of a drug, its manufacture and labeling, the new product becomes available for physicians to prescribe or for sale over the counter, without a prescription. But the manufacturers must continue to submit periodic reports to the FDA, including any reports of adverse reactions.

Only one in every 1,000 compounds that start off in laboratory testing make it to clinical trials, and only one in five of those are eventually approved for marketing.²⁷ The rigorousness of the process largely explains why it typically takes so long and costs so much to bring a new pharmaceutical product onto the market.

Many scientific questions about microbicides are still to be resolved. These include the potential of a microbicide developed for vaginal use to be adapted for rectal use (which would make the product useful both for women and for men who have sex with men), how long particular products will be effective once applied and their safety over long periods of repeated use.²⁸

Although not all the leads being pursued will end up as microbicial products, experts agree that many have the potential to become useful, effective and safe methods of reducing STD infection. The ideal would be a situation in which different formulations of microbicides were available for use in different phases and contexts of women's and men's sexual lives, as is now the case with contraceptive methods.

The U.S. Drug Approval Process

- Preclinical laboratory tests. *Laboratory (in vitro) and animal studies are conducted to demonstrate the compound's general safety and potential effectiveness. Because vaginal microbicides may be used in conjunction with other methods—the male or female condom, for example—their ingredients must also be evaluated to ensure their compatibility with materials used for these methods.*
- Phase I clinical trials. *These studies, typically involving about 20–80 healthy volunteers, determine a drug's safety in humans. Among the questions examined are the product's safe dosage range; how it is absorbed, distributed, metabolized and excreted; and the length of time it remains active in the body. For topical vaginal products, evidence indicating vaginal irritation or ulceration is also examined.*
- Phase II clinical trials. *Usually conducted among approximately 100–300 volunteers, these trials further assess the product's safety and effectiveness. For microbicides, they also evaluate preliminary evidence of the product's biological plausibility as a preventive against the disease-causing organism in question.*
- Phase III clinical trials. *Health professionals monitor 1,000–4,000 participants, usually recruited in clinic or hospital settings, to confirm the product's efficacy and identify any adverse reactions.*
- New drug application. *Following completion of all phases of preclinical and clinical trials, the developer must file a new drug application with the Food and Drug Administration. The application must include an analysis of all the data collected; a typical application runs about 100,000 pages. For new drugs approved in 1997, the average time from submission of the new drug application to government approval was about 16 months.*

Source: Spilker, BA, The drug development and approval process, <<http://www.phrma.org/charts/approval.html>>, accessed Aug. 9, 1999.

WOMEN'S PERCEPTIONS OF THEIR STD RISK AND INTEREST IN MICROBICIDES

In a 1998 telephone survey, The Alan Guttmacher Institute (AGI) asked a large, nationally representative sample of sexually active American women aged 18–44 whether they were worried about HIV and other STDs; whether they would use microbicides if these methods became available; and their preferences regarding the possible characteristics of microbicial products.²⁹

One in Four Sexually Active Women Are Worried About STDs and Would Use Microbicides

Overall, nearly three in 10 sexually active women are worried about contracting HIV or another STD, including 23% who would be at least somewhat interested in using a vaginal microbicide and 6% who would not. In addition, 17% would be interested in such a product but are not worried about contracting an STD (Figure 6).

Nine in 10 women who express an interest in using a vaginal microbicide say that one reason for their interest is that they want to be in control of protecting themselves against STDs. One-third say that such a method appeals to them because they or their partners do not like using a condom, and one in seven would use it because they sometimes have more than one partner in a given time period.

Women who are neither worried about STDs nor interested in using microbicides offer various reasons to explain their position: They trust their sexual partners; they are satisfied with the condom and see no need for a different kind of preventive method; they believe they are not at risk of getting an STD; their partners would

object to their using a microbicide; or they would not be comfortable using such a product.

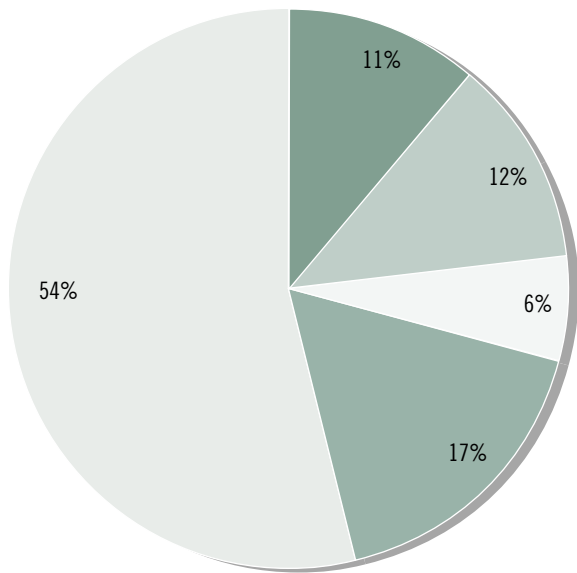
Microbicides Are an Attractive Option to a Wide Variety of Women

Even though the idea of using a vaginal microbicide is only a theoretical possibility, it seems to have a very broad-based appeal for American women. The vast majority of those surveyed—94%—would be at least a little interested in using such a product if they ever found themselves at possible risk of contracting an STD. Women in all age, race, marital and income groups share this interest.

Furthermore, while only one in four women overall are worried about their STD risk and are interested in microbicides, the proportion is much higher among certain groups. It is almost six in 10 among women who are neither married nor living with a partner; close to half among those who are low-income, black or Hispanic; and about four in 10 among women younger than 25 (Figure 7, page 20). Among women who have had more than two partners in the past year, those whose partner is not monogamous and those who use condoms to prevent STDs, roughly two-thirds are worried about STDs and would be interested in microbicide use (not shown).

What Would Women Consider an Ideal Vaginal Microbicide?

Women who said that they would consider using microbicides now or in the future if they were in a situation of risk, or that they would



% of sexually active women 18–44

Figure 6 Almost three in 10 sexually active women are worried about getting an STD, and the majority of these would be interested in using vaginal microbicides.

- Worried/very interested
- Worried/somewhat or a little interested
- Worried/not interested
- Not worried/interested
- Not worried/not interested

Source: reference 29.

have been interested in such products at some point in the past—virtually all of those surveyed—were asked a series of questions about the features they would like to see in a vaginal microbicide.

The majority of women surveyed said that the ideal microbical product could be applied several hours before sexual intercourse (67%) and would be available without prescription in a drugstore (71%). There is, however, little agreement about the form the product should take. Four in 10 women would prefer a cream or jelly formula, three in 10 a suppository and the rest a sponge or film (Figure 8, page 21).

When asked how likely they would be to use a method that had to be reapplied before each act of sexual intercourse, only 13% of women said they probably would not use such a product.

Interestingly, being able to use a microbicide without their partner’s knowledge is not as important a consideration for women as might be expected. Women were evenly divided among those who would be more likely to use a product if their partner knew about it, those who would be more likely to use it if he did not know and those who would be equally likely to use it in either case. These findings reinforce those of an earlier study, which indicated that although many women think it is important to be able to use spermicidal products without their partners’ knowledge, not all rank secrecy as a necessary characteristic.³⁰

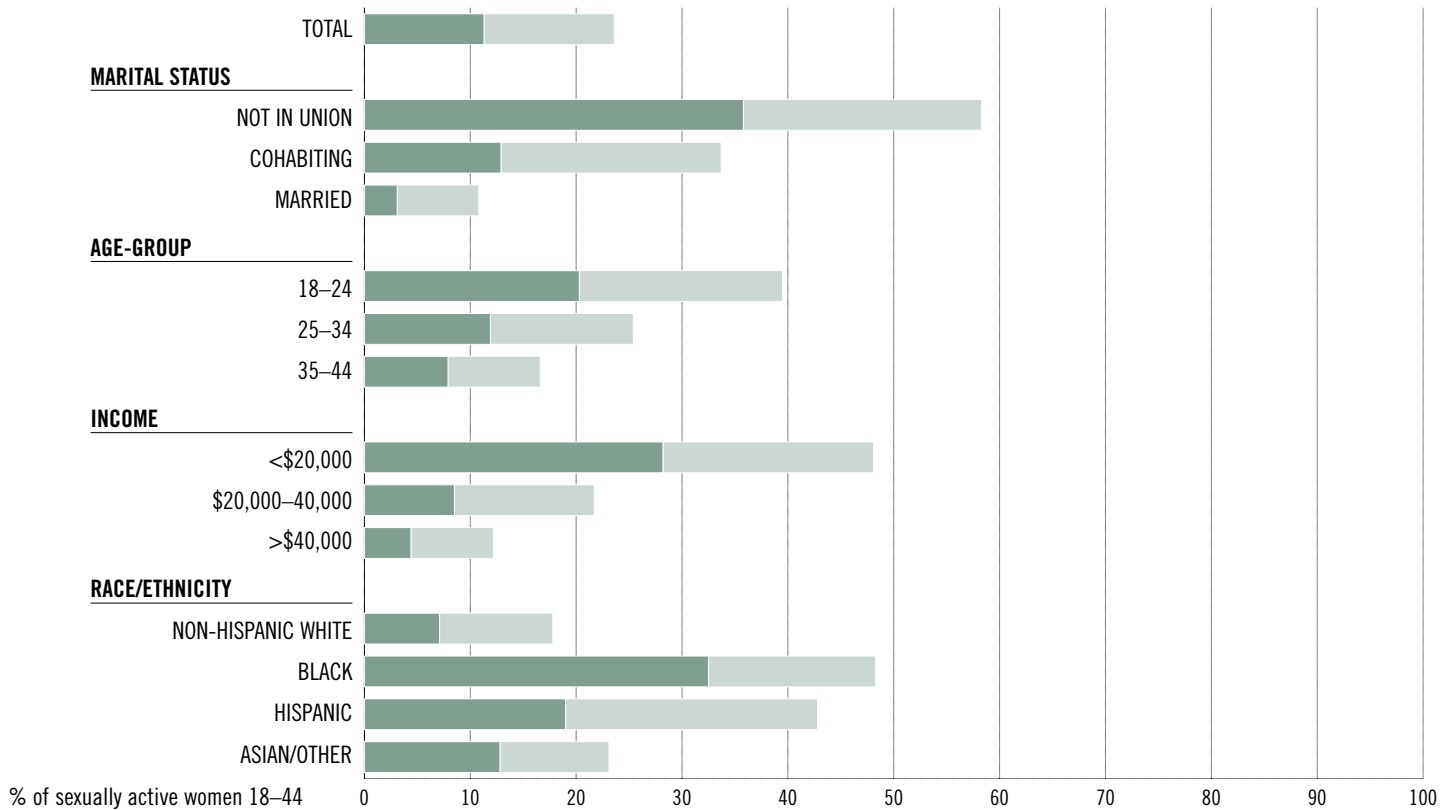


Figure 7 Women who are unmarried, younger than 25, poor and black or Hispanic would be the most likely to use microbicides.

Worried about STDs/very interested in microbicides
 Worried about STDs/somewhat or a little interested in microbicides

Source: reference 29.

Some microbical products being developed are specifically intended to combat bacterial STDs. Others are targeted at HIV as well, or exclusively. Women were asked how interested they would be if a product were protective only against HIV or only against other STDs. Their responses make it clear that AIDS protection is by far women’s most urgent concern. One-half would be very interested if a vaginal microbicide offered protection only against HIV, but only one-quarter would be very interested if it were protective only against other STDs. Still, at least 80% of women would have some interest in using a product that protected them either against HIV or against other STDs, but not against both.

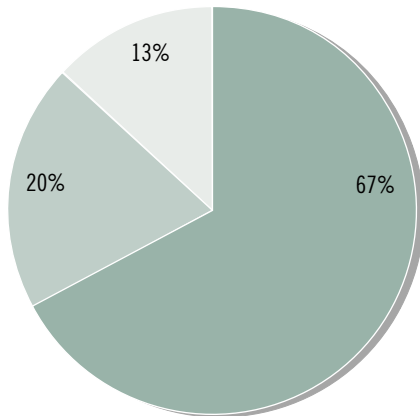
Three out of four women would be very interested in using a microbical product selling at roughly the cost of a condom (between 50 cents and one dollar) for each application, but only six out of 10 report a similar interest in a product priced at two dollars per application. Only 3% would have no interest in using a vaginal microbicide at either price.

Millions of U.S. Women Would Probably Be Interested in a Vaginal Microbicide

Among the nearly 60 million U.S. women between the ages of 15 and 44,³¹ an estimated 51 million are sexually active, and the findings from the telephone survey suggest that 15–16 million of them are worried about contracting an STD. Of these, 12.6 million would be interested in using a vaginal microbicide if such a product were

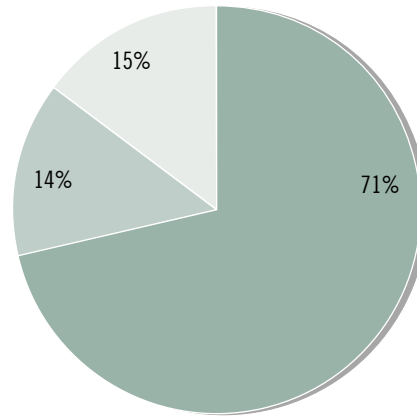
WHEN WOULD IT BE APPLIED?

- Could be applied several hours before sex
- Must be applied just before sex
- Either



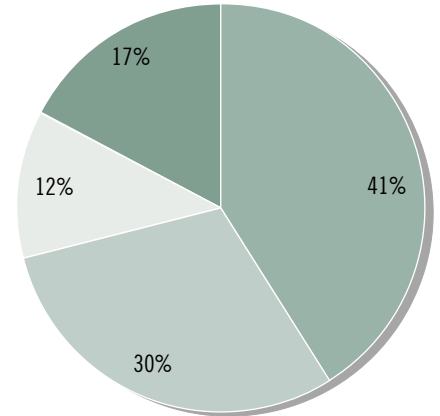
HOW WOULD WOMEN OBTAIN IT?

- Over the counter
- By prescription
- Either



WHAT FORM WOULD IT TAKE?

- Cream or jelly
- Suppository
- Sponge
- Film



% of sexually active women 18–44

Figure 8 Women say the ideal microbicide could be applied well before sex, would be sold over the counter and would come in a cream, jelly or suppository form.

Source: reference 29.

available—six million would be very interested, and 6.6 million somewhat or a little interested (Figure 9, page 22).*

These estimates are affected by considerations of both the efficacy and the cost of a microbidental product. Even if a product reduced the risk of STDs by only 70–80%, more than 11 million women would be interested in using it, including almost four million who would be very interested. With this level of effectiveness and a cost comparable to that of the condom (\$0.50–1.00 per application), the method would still have some appeal to more than nine million women (not shown). Doubling the cost would reduce the number of potentially interested women to 7.7 million, but more than three million women would still be very interested in using it.

*To estimate the numbers of women most likely to be worried about STDs and interested in using microbicides, we applied the responses obtained from 18–44-year-olds to the total estimated population of sexually active women aged 15–44.

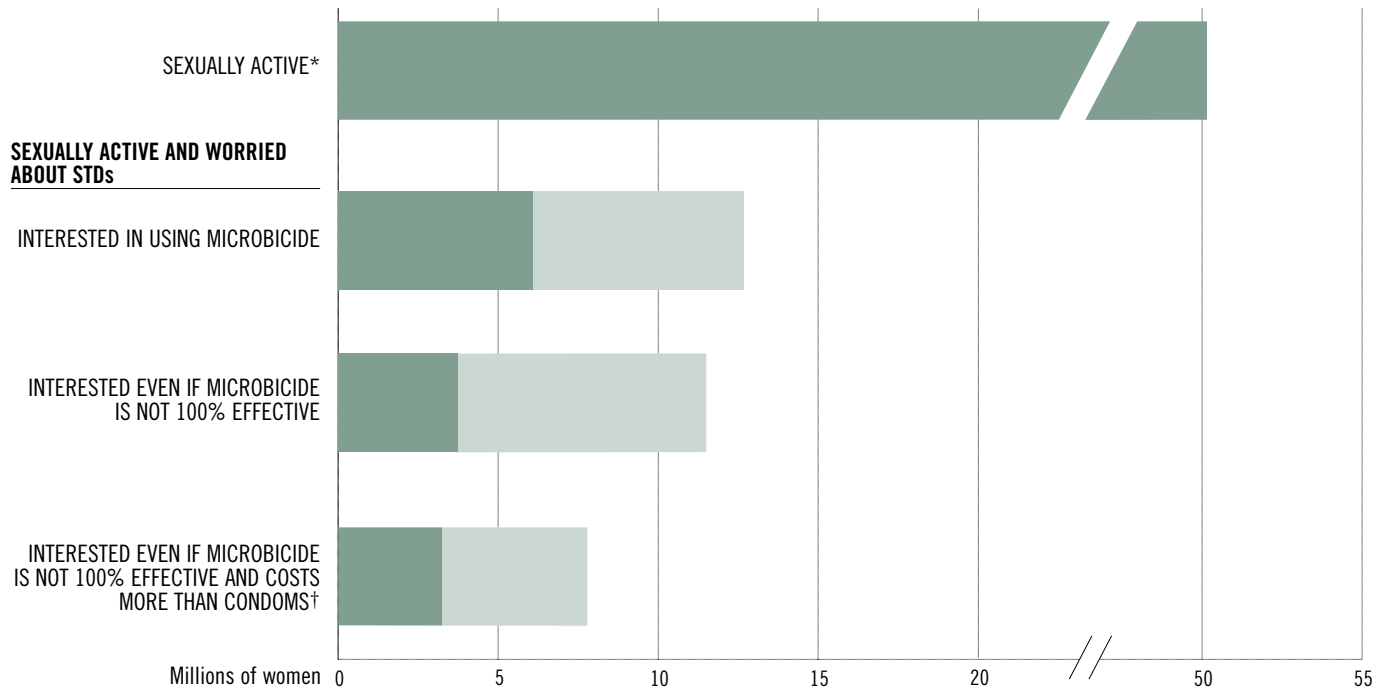


Figure 9 Millions of women would be interested in using a microbicide, even if the product were not totally effective and cost more than condoms.

Very interested
 Somewhat or a little interested

*Women were considered sexually active if they had had sex in the past 12 months. †The AGI survey asked women how interested they would be in a microbicide that cost about two dollars per application, roughly twice the cost of a condom. **Source:** reference 29.

PROSPECTS FOR MICROBICIDE RESEARCH AND DEVELOPMENT

STDs impose a grievous human and economic burden on society, in part because female methods of protection are limited. And while a great deal remains to be learned about STD risk levels in the United States and about strategies to help women reduce their risk of these infections, well-documented medical, economic and societal considerations make a compelling case for supporting and accelerating the development of microbicidal products that women can control:

- STDs, including HIV and AIDS, have created a global health emergency that shows little sign of abating.
- These diseases threaten the health, and sometimes the lives, of millions of Americans.
- Every year, the treatment of STDs siphons off billions of dollars that might be used in other important health areas.
- STD infection rates in general are unacceptably high among U.S. women, and rates of some infections are rising among younger women.
- Women (and in some cases, their infants) are typically the hardest hit by STD infection.
- But women lack effective means of protecting themselves against possible STD infection.

The findings of the AGI survey suggest that if effective, reasonably priced vaginal microbicides were on the market, millions of American women who worry about STDs would probably purchase them. But what are the prospects of such products' finding their way into the drugstores of America anytime in the near future?

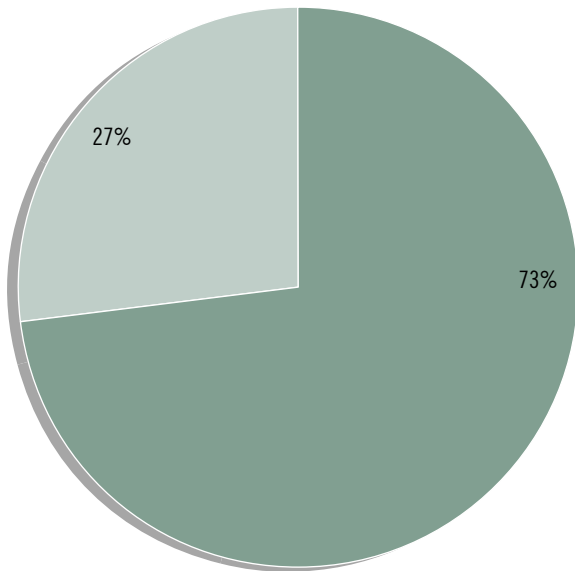
Microbicide Development Requires a Partnership Between Public and Private Funding Sources

The prospective costs of developing any of the promising microbicidal compounds are daunting—as much as \$20 million to meet rigorous FDA requirements for human safety testing, and no less than \$30 million to complete large-scale efficacy trials.³² Even though 35 small biopharmaceutical companies and about 25 not-for-profit agencies are active in microbicide development, their combined resources are extremely limited.

Consequently, research and development in the technology of STD prevention, despite some highly promising advances, has been painfully slow and inadequately financed. The slow pace of development is all the more frustrating in light of the number and promise of some new products that are stalled in the pipeline for lack of funds.

The private sector—concerned that microbicides would be a low-profit product and worried about possible product liability claims—has not been eager to invest in the process required to take these products from the laboratory to the pharmacy shelf. As a result, much of the onus for research and development rests on the public sector.

In 1996, Secretary of Health and Human Services Donna Shalala announced that the federal government would invest \$100 million in microbicide development over four years (\$25 million a year). The following year, federal funds in support of microbicide research



Federal spending, FY 1997 (\$24.7 million)

Figure 10 Only three out of four federal dollars supporting microbicide development are dedicated exclusively to that purpose.

- Microbicide-specific research
- Basic research with multiple purposes

Source: reference 33.

totalled \$24.7 million. Of this amount, \$18.1 million (73%) was earmarked specifically for microbicide product development and testing, and the rest for basic research with multiple purposes that may have some application to microbicides (Figure 10).³³

Early in 1999, the National Institutes of Health received a 15% increase in its appropriations from Congress, which adds more than \$2 billion to the budget available for federally funded medical research in the United States. This has encouraged an alliance of public interest groups to call for the Department of Health and Human Services to increase its investment in microbicide research to \$75 million a year.³⁴

The amount of government support requested is almost insignificant when compared with the \$8.4 billion being spent every year to treat STDs in the United States. The cost savings—not to mention the savings in human suffering and discomfort—that might result if growing numbers of women had the means to protect themselves against infection would be enormous.

Moreover, there is strong historical precedent for public support of urgently needed basic biomedical research. Many important medical breakthroughs—vaccines, for example—would not have happened if monetary profit had been the only motivation. Microbicides are one of a number of crucial “orphan” products—drugs and devices that will probably never reach the market without collaboration between public and private funding sources.

Until effective vaginal microbicides are available, women (and men) at risk of acquiring STDs need information about what they can do to protect themselves.

The Challenges Are Not Simply Financial

The development of all new drugs involves not only strong financial support but also complex technical and ethical issues.³⁵ For example, to produce reliable estimates of the safety and efficacy of a new method of preventing the transmission of HIV—a relatively rare disease in this country—trials must be conducted among very large numbers of sexually active people. But at some point, trials must also be conducted among selected populations likely to be exposed to a high risk of acquiring the infection. This is why clinical trials of microbicides are often carried out in developing countries that have high levels of HIV infection or among sex workers.

Other difficult issues arise in the selection of appropriate population study groups. Given the need to involve high-risk populations, some participants in microbicide trials will be exposed to partners with HIV or other STDs. Therefore, the protocols for ethically sound microbicide trials must include mandatory counseling of all participants about the importance of using condoms in addition to the product being tested. Under these conditions, trials can measure only whether a microbicide improves upon the protection afforded by condom use. However, some study women will inevitably find themselves in situations in which their partners refuse, or are unable, to use condoms consistently. Some trials, therefore, will focus on this group when evaluating the effectiveness of a microbicidal product.

Research scientists and community health advocates alike are well

aware of the complexities of microbicide testing. In 1998, scientists, advocates and policymakers from 19 countries met to discuss these concerns, and agreed unanimously that testing should be carried out in full consultation with the local community involved and with due consideration of proper ethical precautions.³⁶ However, it is not enough for these standards to be agreed upon in principle; community watchdogs and medical ethicists must be vigilant in ensuring that they are rigorously observed in practice.

Existing STD Prevention Strategies Must Not Be Overlooked

Until effective vaginal microbicides are available, women (and men) at risk of acquiring STDs need information about what they can do to protect themselves. After abstinence and mutual monogamy with an uninfected partner, condoms remain the most effective means for preventing these infections.³⁷ In addition, some health professionals and women's health advocates argue that although more research is needed on the efficacy and possible health ramifications of nonoxynol-9, this product should be routinely offered to women, since it is available in forms that women can use and offers some protection against gonorrhea and chlamydia.

In the meantime, family planning providers and gynecologists, as well as other health professionals, must make information about STD prevalence and the possible harmful consequences of infection—particularly infertility and cervical cancer—clear to all of their sexually active patients. Prevention messages and advice

It is impossible to overemphasize the urgency of the need for new forms of protection against STDs, particularly for women—here in the United States and around the world.

about how to engage in effective sexual negotiation and safer sex should become routine aspects of reproductive health counseling everywhere.

The Benefit of New Methods Will Reach Beyond U.S. Borders

It is impossible to overemphasize the urgency of the need for new forms of protection against STDs, particularly for women—here in the United States and around the world. The global AIDS situation has moved well beyond the status of a containable health emergency. The addition of a new and effective method of preventing STDs will represent a significant advance in its own right; it also will help the global fight against AIDS. Finally, it will be especially valuable if it enhances women's control over the circumstances and consequences of their sexual and reproductive lives.

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