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The effectiveness of barrier methods of contraception in preventing the spread of HIV

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Introduction

Barrier methods of contraception fall into two, sometimes overlapping, categories: (1) physical barriers (male and female condoms), which prevent the passage of sperm and other constituents of semen to the partner's genital tract; and (2) chemical barriers, which form a more varied class of products and delivery systems. These latter products contain a spermicide that inactivates sperm (and other cells), delivered in a cream, gel, foam, film or other diffusion agent for the active ingredient. The overlap includes combination methods in which a physical barrier is used with the spermicide (such as the vaginal sponge, diaphragm and cervical cap). The spermicidal agent in most products sold in the United States is nonoxynol-9, a non-ionic surfactant detergent. European products contain benzalkonium chloride, and a popular Japanese foaming tablet contains menfegol, also a detergent.

Public interest in barrier methods has been renewed because this is the only class of contraceptives that can reduce the risk of contracting sexually transmitted diseases [1,2]. Because cultural and motivational factors influence the consistency with which these methods are applied, and their correct use, their effectiveness varies widely between groups [3,4]. Moreover, the prevalence of barrier contraceptive use is low in most countries, especially in sub-Saharan Africa where the prevalence is generally 1% or less.

Two kinds of data have been collected on the relationship between barrier methods and sexually transmitted diseases. The first comes from *in vitro* studies which do not mimic the vicissitudes of actual barrier use but can indicate the theoretical effectiveness of barriers. The second, and more important, type of data comes from *in vivo* epidemiologic studies conducted in human populations. These allow calculation of: (1) the perfect use effectiveness, which prevails among persons who use the product correctly at every coital act; and (2) the typical use effectiveness, which is the average success rate among diverse groups of users who may use the product incorrectly and/or inconsistently [5].

Male condom studies

In vitro data

The impermeability and integrity of various types of condoms have been well tested in the laboratory. Variable results have been obtained from laboratory studies on the passage of sexually transmitted organisms according to the size of the organisms tested, the condom membrane material and the quality of the condom. Despite the methodologic limitations in many of these studies, notably small numbers tested, the results generally show that high-quality latex condoms are impermeable to the passage of HIV and other organisms.

In vivo data

Although there are no definitive data on the protection conferred by condoms against sexually transmitteed disease, most studies suggest substantial reductions in the risk of disease [6,7]. These replicated and biologically plausible findings lent credibility to recommendations for condom use even before convincing evidence of their effectiveness against HIV appeared.

After a series of early cross-sectional studies, prospective investigations demonstrated a temporal link between condom use and lack of HIV infection which strongly supported the protective effect of condoms (Fig. 1) [8–16]. For instance, four studies among African sex workers which compared condom users with non-

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users reported relative risk estimates of 0.3 for ever versus never use [9], 0.5 for always/sometimes versus rarely/never use [10], 0.1 for ever versus never use [12] and 0.3 for >75% use versus <50% use [15].

The most convincing data come from prospective studies of serodiscordant couples, because of the known regular exposure to an infected partner. Several studies of heterosexual discordant couples have compared HIV seroconversion rates in couples using condoms with non-users (Fig. 1), including two compelling studies from Europe in the past year.

In a multicenter Italian study, 343 seronegative female sexual partners of HIV-infected men were followed for a median of 24 months [14]. Among the 305 women who continued to have vaginal intercourse with an infected man, 3.9 infections occurred per 100 woman-years. The HIV incidence rate was greatly reduced in women whose partners always used condoms compared with those who used them inconsistently or never (rate ratio from proportional hazards regression 0.1; 95% confidence interval 0.0–0.5). Inconsistent condom users did not benefit (see below).

In a multinational European collaborative study, 378 seronegative regular partners of infected men or women were enroled; two-thirds of the partners continued to have vaginal or anal intercourse and were included in the analysis [16]. The overall HIV seroconversion rate was 2.3 per 100 person-years. About half of the couples used condoms at every coital act, and no seroconversions occurred among these (95% confidence interval 0–1.5 per 100 person-years). For the 121 couples who used condoms inconsistently, the HIV incidence rate was 4.8 per 100 person-years (95% confidence interval 2.5–8.4), even though 50% of the inconsistent users reported using condoms at least half the time. These two studies show that consistent condom use confers substantial protection against HIV transmission, but that inconsistent use carries considerable risks of HIV infection.

Spermicide studies

In vitro data

In the laboratory, nonoxynol-9 spermicides inactivate many pathogens, including gonococci, chlamydiae, herpes virus, treponemes, trichomonads and organisms causing bacterial vaginosis [17,18]. The detergent effect of nonoxynol-9 is non-specific, and it is toxic to both the normal vaginal flora as well as exogenous pathogens [19].

Laboratory studies on HIV have demonstrated that the organism is quite sensitive to several spermicidal compounds, including nonoxynol-9 [20], benzalkonium chloride [21,22], and menfegol [23], and also to the germicidal compounds betadine and chlorhexidine [24]. Free HIV is inactivated at nonoxynol-9 concentrations as low as 0.05%, whereas commercially available products in the United States generally contain nonoxynol-9 at concentrations of 2–12%. Even after dilution by vaginal fluids and semen, a lethal vaginal concentration should be attained during routine use of the spermicidal products.

Most HIV in semen is not free virus, but is contained in potentially infectious lymphocyte cells [25]. Thus spermicides must disrupt human lymphocytes to prevent sexual transmission of HIV. Approximately 10 times the

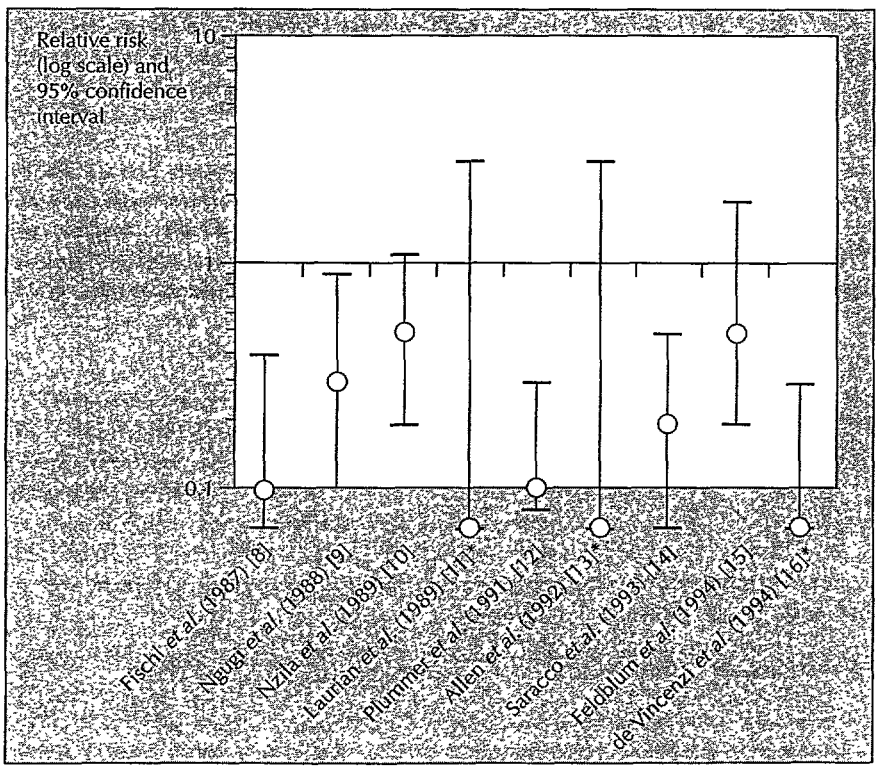

Fig. 1. Studies of condom use and HIV infection in heterosexuals. *In these studies, no infections occurred among the condom users, so that the relative risk estimate and its lower confidence limit are zero.

nonoxynol-9 concentration that is lethal to free virus will disrupt lymphocyte membranes [26]. However, this level is well within the capabilities of commercial spermicidal products; nonoxynol-9 is designed to disrupt spermatozoal cell membranes and the products contain sufficient concentrations to do so.

In vivo data

Numerous epidemiologic studies in a variety of settings using different study designs have consistently demonstrated that spermicide use reduces the incidence of both gonorrhea and chlamydial infection [27–29]. Several observational studies comparing the relative protection against a bacterial sexually transmitted disease have indicated that the typical effectiveness of condoms and spermicides is similar (see below).

Little epidemiologic research has been conducted specifically on spermicide use and HIV infection, and only two studies have been published. In the first, a group of Nairobi prostitutes were studied, half of whom were randomly allocated to use a contraceptive sponge with nonoxynol-9; each placebo user inserted one glycerine suppository or, later in the study, a water-based cream before her first partner of the day [30]. The two groups were similar in most respects, but the sponge group had a higher prevalence of genital ulcers at enrolment than the comparison group (16 versus 3%). The cumulative 24-month HIV seroconversion rates were 56 and 41% in the sponge and comparison groups, respectively ($P=0.08$ by log-rank test). In a univariate survival analysis, the HIV rate ratio for sponge use was 1.7 (95% confidence interval 0.9–3.0); adding genital ulcers at admission to the model slightly reduced the rate ratio.

Despite its randomized design, this study had several important limitations. The study could not be blinded. The lubricating suppository used by comparison group women may have rendered intercourse less traumatic and perhaps reduced the incidence of lesions [31]. It is unclear how condom use was controlled in the analysis [32]. Despite random allocation to groups, the much higher prevalence of genital ulcers (and other sexually transmitted disease differences) in the sponge group at enrolment suggests the presence of unmeasured behavioral differences as well.

As the authors state, the effects of the contraceptive sponge may differ substantially from those of other spermicidal products. The sponge contains a high dose of nonoxynol-9 (1 g) and remains in place for at least 6 h with each insertion. Thus any vaginal irritation associated with nonoxynol-9, and any disruption of the normal vaginal flora, will tend to be greater. Finally, the sponge tends to dry the vagina and so it may increase trauma and ulceration secondary to intercourse.

In the second published study [33], women in Cameroun with multiple sexual partners underwent up to 12 monthly clinic visits for interviews, examinations and sexually transmitted disease tests, and for renewed supplies. The 273 HIV-seronegative participants were given latex condoms and 100-mg nonoxynol-9 suppositories, and were encouraged to use both at every coital act. During a mean follow-up of 8.1 months, 19 HIV infections occurred, an incidence of 10.4 infections/100 woman-years. In a second analysis, which better separated the effects of condom use and nonoxynol-9 use [15], the HIV incidence decreased as consistency in the use of nonoxynol-9 increased. In the proportional hazards regression analysis, the HIV rate ratio for women who used nonoxynol-9 for more than 75% of coital acts not protected by condoms was 0.4 compared with women who used nonoxynol-9 less than half the time (95% confidence interval 0.1–1.3). But since the participants were not randomly assigned to nonoxynol-9 use, this finding may have been affected by selection bias (although no measurable evidence of bias was evident).

In summary, these two recent investigations of the relationship between nonoxynol-9 use and HIV provide conflicting findings: in one, spermicide use was associated with HIV acquisition, while in the other, spermicide use was protective.

Irritation with spermicide use

Family planning researchers know that spermicides cause discomfort to some users (an allergic reaction to the spermicidal lubricant tectol has also been described [34], although the offending constituent of the lubricant was not identified). Speculation arose in 1988 that the irritating effect of spermicides might increase the risk of HIV infection [35]. The term irritation has not been standardized, but has at least two components, the symptoms reported by the users and the physical changes that are produced by the spermicide and observed by clinicians. Symptoms are important in that they may affect acceptability, compliance and continued use. Observed signs of tissue damage may be important in that they may increase the risk of infection. Unfortunately, the association between symptoms and signs of irritation does not appear to be consistent enough either to guide patient counseling or to allow the use of one as a surrogate for the other. Only a detailed visual examination can determine whether signs of irritation are present.

Family planning studies

Data on spermicidal discomfort that have been obtained during contraceptive effectiveness studies provide some insight into the level of symptomatic irritation that most women would experience. These studies generally include couples among whom the frequency of spermicide use is low to moderate. Typical couples have intercourse two or three times a week, and most women insert only one dose of spermicide per coital act.

From 1 to 8% of participants in Family Health International studies conducted among women attending family planning clinics have reported discomfort after use of a spermicide, regardless of the spermicidal ingredient

or the delivery system (Table 1). These are maximum estimates, because the percentages were derived from the first follow-up visit before the drop-out rate became substantial. Discontinuation from the study because of discomfort is an indicator of the severity of the irritation problem. Twelve-month life-table discontinuation rates have generally been in the range of 5–10 per 100 women [40].

Table 1. Percentage of women complaining of discomfort after 1 month in spermicide contraceptive clinical trials.

Reference	Method	Women (%)
[36]	Menfegol tablet	4.7
[37]	Belgrade: nonoxynol-9 sponge	4.4
	Belgrade: menfegol tablet	1.7
	Taiwan: nonoxynol-9 sponge	1.8
	Taiwan: menfegol tablet	1.9
	Bangladesh: nonoxynol-9 sponge	2.0
	Bangladesh: menfegol tablet	0.7
[38]	Menfegol tablet	0.6
	Nonoxynol-9 foam	1.6
[39]	Nonoxynol-9 tablet	2.2
	Menfegol tablet	8.5

Spermicide irritation studies

Two studies were designed to measure the incidence of irritation following the use of nonoxynol-9. In a Bangkok phase I study, 15 sexually inactive women inserted 150-mg nonoxynol-9 vaginal suppositories four times a day for 2 weeks [41]. Each woman underwent a pelvic examination with colposcopy at admission, after 1 week and after 2 weeks. Six out of 14 women (43%) had cervical or vaginal lesions following this intense nonoxynol-9 regimen. In four of these six women the lesions appeared to be a result of sloughing of a thin layer of cervical tissue adjacent to the vaginal fornices.

In a subsequent phase II study in the Dominican Republic, a larger number of sexually inactive women inserted varying numbers of 150-mg nonoxynol-9 suppositories daily for 2 weeks [42]. A comparison group used a placebo lubricating suppository four times a day. The frequency of nonoxynol-9 use ranged from one insertion every other day to four insertions per day. Each woman had colposcopies at admission, after 1 week and after 2 weeks.

Symptoms of irritation included dysuria, genital itching and genital burning. During the follow-up, no consistent rise in self-reported irritation symptoms occurred with an increasing frequency of nonoxynol-9 use. Only in the group who used nonoxynol-9 four times a day did symptoms increase over the rate reported by placebo users [42].

Signs of irritation included erythema and epithelial disruption. In contrast to the symptoms, clinical signs of irritation did increase with frequency of nonoxynol-9 use. Erythema and tissue disruption were equally frequent among the women who inserted nonoxynol-9 every other day as among the placebo users. The incidence of signs of irritation was about twofold higher among women who used nonoxynol-9 once or twice a day, and fivefold higher among the women who inserted four nonoxynol-9 suppositories daily, than among those who inserted placebo suppositories [42]. The presence of symptoms was only weakly predictive of signs of irritation.

The World Health Organization (WHO) sponsored a study of frequent menfegol insertion that was similar in design to the nonoxynol-9 study. Preliminary reports indicate that the results are similar to those for nonoxynol-9, in that frequent menfegol tablet insertion was associated with elevated rates of genital irritation. One recent study indicated that spermicide use was not associated with vaginal inflammation/discharge, but this cross-sectional study grouped various spermicidal methods, failed to describe diagnostic criteria and failed to ascertain the frequency of spermicide use [43].

Nonoxynol-9 prophylaxis studies

To gain statistical power, epidemiologic studies of the use of nonoxynol-9 and the risk of sexually transmitted disease have enrolled women with multiple sex partners and with a high incidence of sexually transmitted disease. The participants use nonoxynol-9 with moderate to high frequency, usually inserting more than one dose of spermicide per day.

In Nairobi, sponge users were advised to replace the sponges after every two or three partners, and to wear the sponge for 6 h after last intercourse [30]. Women in both the sponge and placebo groups reported a mean of 34 sexual partners per week during the study, and an estimated 14 sponges were used per week. Self-reported discomfort was far higher in the nonoxynol-9 group. Genital ulcers (epithelial breaks) at all sites were also higher in the sponge group (Table 2), although most of the ulcers were vulvar and differences in vaginal and cervical ulcers were slight.

In the Bangkok prophylaxis study, the effect of vaginal film containing about 70 mg nonoxynol-9 was examined [29]. The massage parlor workers in both groups reported a mean of 11 partners per week, and most washed their vaginas after intercourse. Discomfort was more common in the nonoxynol-9 than placebo group, but was less frequent than in the Kenya study. The excess in discomfort with the use of nonoxynol-9 occurred only with more than eight insertions per week. The ulcers were mostly vulvar and were clinically diagnosed as herpes. There was no difference in the percentage of women with ulceration according to nonoxynol-9 use, the rate in both groups being two per 100 woman-weeks (Table 2). Also, no excess of ulcers occurred in the higher frequency nonoxynol-9 insertion stratum.

In the Cameroon cohort study [33], non-users of nonoxynol-9 were not followed, and the mean number of nonoxynol-9 insertions was 3.4 per week. Discomfort

Table 2. Signs of irritation reported by sex workers in nonoxynol-9 studies.

Vehicle, reference, unit of measurement, site of use	Ulcers with nonoxynol-9	Ulcers without nonoxynol-9
Sponge (1000 mg) [30], events per physical examination (×100)		
All genital sites	15	8
Vaginal/cervical	5	3
Film (70 mg) [29], events per 100 woman-weeks		
	2	2
Suppository (100 mg) [44], events per 100 woman-months		
Cervical, low frequency	9	–
Cervical, medium frequency	2	–
Cervical, high frequency	3	–
Vaginal, low frequency	3	–
Vaginal, medium frequency	1	–
Vaginal, high frequency	1	–

Frequency of use: low, ≤10 insertions per month; medium, 11–15 insertions per month; high, >15 insertions per month.

attributed to nonoxynol-9 was common (49%), as was discomfort attributed to condoms (37%). Ulcers were quite common during this follow-up, as they had been at admission (about one-third of women), perhaps reflecting diagnostic custom. Limiting the analysis to women who were ulcer-free at admission, the incidence of cervical and vaginal ulcers did not increase with the frequency of nonoxynol-9 use, and was, in fact, highest among the lowest frequency nonoxynol-9 users (Table 2) [44].

These studies indicate that discomfort in sex workers is more common than in family planning cohorts. As in the irritation studies when women were challenged with high doses of nonoxynol-9, the rate of ulceration depends on the dose. More frequent insertions and higher dose products (both of which prevailed in the Nairobi study) [30] lead to elevated rates of epithelial disruption. When the nonoxynol-9 doses are lower, the increased risk is modest or absent.

Condom irritation

Other barrier methods have not been subjected to the same detailed examination of irritation effects as has been done for spermicide use, even though the male latex condom, for example, has the potential to produce genital irritation. No study has examined the effect on the epithelium of using one or more latex condoms daily.

Latex allergies may cause problems for condom users at risk of HIV infection [45]. In a small Finnish study of health-care workers with latex-glove contact dermatitis, allergic reactions were reported by 24% of the patients after condom use [46]. As latex exposure becomes more widespread, reports of latex allergy seem to be increasing, but so far there have been no studies on the relationship with the transmission or acquisition of sexually transmitted infections.

Consistency of use and barrier effectiveness

The consistency of use of a barrier is probably more important in determining its ultimate effectiveness than is its efficacy under conditions of perfect use. In two studies of nonoxynol-9 use and the incidence of cervical gonorrhea and chlamydial infection, the incidence rates (and rate ratios) of sexually transmitted disease generally decreased with better spermicide compliance [28,29].

This implies that more consistent use of a less efficacious barrier method may be more effective in preventing sexually transmitted disease than less consistent use of a more efficacious one [47–49]. Thus, while the male condom is more efficacious if used consistently, a less efficacious female-controlled method may have a greater individual and public health impact if used more often. At least one computer model shows that even if the use of a spermicide is less efficacious than condoms in preventing HIV and results in a moderate reduction in the use of condoms, the number of new HIV infections in a high-risk group may be reduced if the overall proportion of coital acts protected by at least one of the two methods is increased [50].

In some observational studies condoms and spermicides were associated with a similar protective effect against such sexually transmitted diseases as cervicitis, gonorrhea, trichomoniasis, and hospitalized pelvic inflammatory disease [29,51–54]; two of these studies also took the frequency of unprotected intercourse into account. These results not only indicate that studies should be designed to examine the effectiveness of existing female-controlled methods (including the diaphragm and cervical cap) in the prevention of HIV [55]; they also lead to a counseling and policy dilemma in that a method of limited efficacy can yield a major public health benefit, but individuals might not wish to rely on such a measure. Product labeling and counseling of people at risk have to make a clear distinction between absolute protection ('prevents infection') and partial protection ('reduces the risk of infection'). Another important counseling point is that single-episode efficacy and the cumulative efficacy diverge widely as the number of exposures to an infected person increases. A method that is more than 99% effective for a single coital act can give an 18% cumulative failure rate with 100 exposures over time ($1-0.998^{100}=0.18$).

How consistently must condoms be used?

How consistently must a barrier be used to confer protection against HIV? Empirical data on this question are best for the male condom. The two recent European studies provide some clues. In both studies, consistent condom use provided substantial protection against HIV infection. In the Italian study, however, the infection rate

was actually higher in the inconsistent condom users than among those who never used condoms (9.7 versus 5.7 per 100 woman-years, difference not significant) [14]. In the multinational European study, the seroconversion rate among inconsistent users was 4.8 per 100 person-years [16]. Couples who used condoms for at least half of their coital acts, but not every act, had about the same cumulative incidence of seroconversion as those who did not use condoms at all (10.3 versus 15.0%; $P > 0.60$). Taken together, these studies suggest that only consistent use confers measurable protection against HIV transmission.

Yet studies among sex worker cohorts indicate that inconsistent condom use can have a measurable public health impact where people have multiple sexual partners [56]. For example, sex workers in Cameroon using condoms for more than 75 and 50–75% of coital acts had HIV rate ratios of 0.3 (95% confidence interval 0.1–1.2) and 0.4 (95% confidence interval 0.1–1.2), respectively, compared with a referent group using condoms less than 50% of the time [15]. Among sex workers in Kenya, a 90% reduction in HIV infection occurred among women who reported any condom use at all (odds ratio 0.1; 95% confidence interval 0.1–0.3) [12].

How can these discrepant findings from different contexts be reconciled? Among persons with multiple sexual partners, a minority of whom are seropositive, 50% condom use will reduce the probability of contact with an infected partner by half (assuming condom use is independent of the HIV status of the partner). In contrast, among HIV-discordant couples, inconsistent condom use does not reduce the probability of contact with an infected partner; numerous unprotected coital acts take place, leading to little or no measurable benefit from the condom use.

Although neither study addressed condom breakage, this may not be as important as is commonly feared. Male condoms break in 3–5% of coital acts [57–59], but much of this breakage is attributable to incorrect condom use and is concentrated in a small minority of condom users. In models of the contraceptive effectiveness of condoms, small changes in consistency of use far outweigh large changes in breakage rates [60]. Thus the public health issue is usage, not breakage.

Methodologic issues

Measurement of sexual behavior

To measure the prophylactic effectiveness of barrier methods, variables such as coital frequency, numbers of sexual partners and use of barrier methods must be accurately measured. Partner selection may also be important. However, there is no standard by which sexual behavior can be validated. At the community level, the reported use of condoms can be compared with the incidence of sexually transmitted diseases. However, the relationship between the occurrence of these diseases and either the frequency of unsafe sexual behavior or the consistency of condom use is temporal rather than etiological [61]. At the individual level, some researchers have used test–retest reliability as an indicator of validity, with low reliability suggesting poor validity [62]. Others have measured agreement among heterosexual [63,64] and homosexual [65,66] partners in the reporting of selected sexual behaviors. Finally, self-reported sexual information obtained by interview has also been 'validated' against data gathered prospectively using a daily coital log [67].

Three approaches generally optimize accurate measurement: (1) prospective recording of sexual activity using a pictorial coital log as a calendar, on which coital episodes and each combination of use of barrier methods can be ascertained; (2) closely spaced recall periods; and (3) separate interviews with sexual partners [68]. These measures also allow researchers to consider the impact of various combinations of barrier contraceptive use, such as condoms and spermicides used together versus condom use only. Importantly, a more specific definition of contraceptive use allows more precise estimates of any dose–response relationship between the use of a barrier contraceptive and prevention of HIV or other sexually transmitted diseases.

Recent cross-sectional studies have used sexual activity records as outlined above but have shown no association between condom use and HIV infection [69,70]. Retrospective reports of condom use, however, may be inaccurate. Futhermore, cross-sectional data cannot fix the time of condom use in relation to the infection [71], allowing misclassification of condom use at the actual time of infection.

The conceptualization of condom use is also relevant. Condom use at last intercourse may be accurately recalled, but the variable reveals little about longer-term exposure [72]. Condom use may be collinear with a history of sexually transmitted disease, leading to spurious results in multiple regression [72]. Moreover, a dichotomized condom variable may allow considerable residual confounding during regression analysis, compared with a continuous measure of condom use [73]. These potential problems can all be tested during data analysis.

Measurement of irritation

The definition of irritation needs to be standardized and studied in relation to the risk of infection. Colposcopy has become the basis for assessing the irritation produced by vaginal products, and WHO has developed a manual to standardize the procedure. However, more research is required to evaluate the impact of this standard. In earlier studies [41,42], for example, colposcopes found signs that were visible to the unaided eye. Thus a wider array of methods for measuring irritation should be compared: unaided vision; hand-held magnification; colposcopy (to assess epithelial disruption and/or vascu-

lar changes); biopsy (to assess cellular changes); and even molecular techniques. Despite the complex technology that can be brought to bear to define the condition, the clinical significance of vaginal/cervical irritation remains unclear.

Another unresolved issue in irritation studies is the confounding of symptoms and signs by the presence of vaginal infections. Some vaginitis causes itching and discomfort; in severe cases lesions occur independently of any spermicide effect. At the same time, spermicide use may affect the risk of vaginal infection [27,53]. Thus the presence of vaginitis needs to be considered in future studies.

Research needs

Current spermicides

In *AIDS 1994: A Year in Review*, Stone and Hitchcock [74] laid out a research agenda for prophylactic barrier methods, some of which is taking place now. Consensus-building meetings sponsored by WHO in late 1993, and by the United States Public Health Service in 1994, have helped to clarify regulatory and clinical issues in the development of new barrier products. Both gatherings emphasized the crucial need to determine whether currently available nonoxynol-9 spermicides reduce the incidence of HIV infection. Consensus emerged on the following ethical, scientifically sound study design to measure that association:

(1) A randomly allocated controlled trial in which all participants are given male condoms.

(2) Half the women are allocated to the use of an active spermicide product with the other half using a placebo product.

(3) Women are counseled to use both a condom and the vaginal product at every coital act.

(4) The study is large enough study to measure HIV rate ratios within frequency strata.

(5) The study is to include colposcopic examinations and regular appraisals of participant safety by a data and safety monitoring board.

Two studies meeting these design criteria are under way, with funding from the United States National Institute of Allergy and Infectious Diseases (NIAID), and others may be conducted by WHO.

Spermicides may benefit HIV prevention in ways other than those discussed above. For example, they may render already infected women less infectious by inactivating free and cell-associated virus in genital secretions. Spermicide use may also protect men from HIV infection.

New ingredients

Discomfort from current spermicides is a problem for some users and leads to inconsistent use and/or cessation of use. Thus, the development of less irritating yet effective compounds is important. The Contraceptive Research and Development Program (CONRAD), the Population Council, WHO, Family Health International, NIAID and others are working towards that end. Moreover, provision should be made for studying prophylactic effectiveness and the potential for irritation both preclinically and in phase I and II studies, rather than just in the postmarketing phase.

Irrespective of their microbicidal effect, new compounds may or may not be spermicidal. Women's advocates and researchers have called for the development of non-spermicidal microbicides that will protect women from sexually transmitted diseases while allowing conception to occur [75]. This type of product would be especially helpful in areas where fertility is highly valued yet sexually transmitted diseases are prevalent.

Physical barriers

If female condoms can be used consistently, they should reduce the risk of HIV infection [76]. The product's cost may restrict its accessibility, but its association with HIV infection should be studied. Devices such as the diaphragm and cervical cap may also reduce the risk of HIV.

Behavioral questions

Behavioral research is needed at both the individual and community level. In individuals, the determinants of consistent and prolonged use of barrier methods should be studied. Little is known of the reasons why women adopt and continue to use female barriers. The impact of new products should be evaluated. For example, will female condom use have an impact on male condom use? Will new plastic male condoms lead to a higher prevalence of male condom use?

When more is known about the use of spermicide in relation to the risk of HIV, intervention at the community level should be considered. The impact of social marketing of a spermicide product can be evaluated by descriptive and analytic epidemiologic methods. Studies are needed in order to compare the effect of condom promotion versus condom plus spermicide promotion in similar populations.

Summary

Because barrier methods provide protection against bacterial sexually transmitted diseases, these methods are valuable public health adjuncts irrespective of their effect on HIV. Male latex condoms offer substantial protection against HIV infection. Women at risk of sexual acquisition of HIV infection need one or more prophylactic methods that they can control. While the available spermicide products may serve this purpose, current data do not allow firm causal inferences. Large and well designed epidemiologic studies are required to examine the association between female use of barrier methods and

HIV infection. These are difficult and costly to perform, however, and to date have yielded conflicting results. Finally, prospective studies in high-incidence cohorts are necessary, and the relationships between spermicide use, local irritation, the vaginal flora and HIV incidence rates must be clarified.

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