Circumcision—the surgical removal of the foreskin of the penis—is usually performed for medical, religious, or cultural reasons. In many parts of Africa, circumcision is traditionally practiced among adolescents and young adults as a rite of passage into adulthood. Since 1986, after the publication of a leading report on HIV among African heterosexuals by urologist Aaron Fink, there has also been growing evidence that circumcision might offer some protection against HIV transmission. Several observational studies followed Fink’s report, and many of these studies have shown that in African societies where circumcision is common, HIV infection prevalence is lower.

A landmark 2000 study of mixed-HIV status heterosexual Ugandan couples further generated excitement about circumcision as an HIV prevention tool. Women participants in the study were HIV-positive; their male partners were HIV-negative. Forty of the 137 uncircumcised men in the study became infected over a period of 30 months, but none of the 50 circumcised participants became infected during this time. Most, but not all, observational studies have confirmed the result that circumcision protects men engaged in vaginal sex against HIV infection. This article reviews the biology of how circumcision might confer this protection, offers recent data demonstrating the HIV prevention effects of circumcision, and discusses some of the potential applications of these data for HIV prevention in Africa.

How Circumcision May Protect

The uncircumcised penis includes two primary features that the circumcised penis lacks: an inner and outer surface of the foreskin, which covers the head of the penis, and the frenulum, which connects the foreskin to the rest of the penis. The tougher, outer part of the foreskin provides some protection against HIV entry through the surface of the penis. The inside surface of the foreskin is more vulnerable and contains many cells (called Langerhans cells) that are believed to be especially receptive to infection by HIV. Circumcision reduces not only the surface area of vulnerable, non-keratinized skin but also the number of a specific type of cell—Langerhans cells—that could come into contact with HIV during sex. While some authors have argued that a chemical compound (Langerin) produced by Langerhans cells prevents HIV entry through the penis, there is little evidence as yet to support this assertion.

Another reason that circumcision is thought to reduce HIV acquisition is that the frenulum, also removed during circumcision, is particularly susceptible to trauma during sexual intercourse. Such trauma (in the form of small tears) provides a portal for infection. Genital ulcerations caused by chancroid and syphilis also create such portals for infection. By protecting against the acquisition of these and other sexually transmitted diseases, circumcision decreases the risk of HIV infection. Finally, improved hygiene sometimes follows circumcision, because without the foreskin to trap secretions, the penis remains cleaner. Thus, inflammation is less likely, which also reduces the chance of acquiring HIV infection.

Experimental Evidence

Despite the fact that the majority of observational studies had demonstrated that circumcision could be beneficial, some researchers and policymakers were not fully persuaded by this evidence. With
**Editorial: The Kindest Cut?**

Michelle Cataldo, LCSW, Clinical Editor

Late last year I read the reports on circumcision and HIV with interest, optimism, and some uncertainty. I was optimistic that a promising new intervention had been discovered in the fight against AIDS in Africa. I felt uncertain because I wasn’t sure about how the findings might be applied outside the confines of a research study. While I am familiar with the circumcision of infants, I wondered if large numbers of adult men would choose to be circumcised. Would circumcised men feel less need to use condoms? Was there any protective effect for the circumcised man’s partner—male or female? What were the implications outside the groups of African heterosexual men that populated the research studies?

Having continued to follow the study evidence, and with the help of the articles by the authors in this issue, I am less uncertain and still optimistic. That optimism, however, is measured.

Adamson Muula, the author of the lead article, describes the evidence for circumcision as an HIV prevention intervention in Africa. He explains why this evidence, which has been building for years, is finally strong enough to establish circumcision as a proven, replicable intervention there. His review of the literature suggests that, at least hypothetically, many African men would find circumcision acceptable. However, he also notes that many questions remain unanswered. While we now know that circumcision protects men from acquiring HIV from women during vaginal sex, it is still unclear whether an HIV-positive man’s circumcision status makes him more or less likely to transmit HIV to female or male partners, whether circumcision protects during anal as well as vaginal sex.

Also in this issue of *FOCUS*, David Templeton and Andrew Grulich explore the implications of the new research evidence on circumcision for resource-rich countries. In these settings, condoms are more often used, sex between men is a more common transmission route than heterosexual sex, and more men are already circumcised. For these and other reasons, Templeton and Grulich are skeptical about the prospect that circumcision can significantly reduce new HIV infections in higher-income countries. Further, because condom use is so much more effective in preventing HIV than circumcision is, they note that any abandonment of condoms in favor of reliance on circumcision could increase HIV risk.

New circumcisions will have the greatest impact in the settings with high rates of HIV and few other effective prevention options. In some parts of the world, that impact could be enormous. The prospect of an HIV prevention intervention with a 60 percent efficacy rate in sub-Saharan Africa, where nearly two-thirds of the people with HIV in the world live, is thrilling.

More research is needed to address still-unanswered questions about this intervention. I’m hopeful that in the meantime, safe, sanitary circumcision by skilled practitioners will be offered to men in developing countries who want it to protect their own health and that of their partners.

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**References**

the experiment and deny those in the control arm the benefits of circumcision.

Over the course of the median follow-up period of 18 months, Auvert and colleagues found that circumcision was 61 percent protective. In other words, the circumcised group had only 39 percent of the number of new HIV cases as the uncircumcised group.

Other studies, including one by Robert Bailey and colleagues in Kisumu, Kenya, and another by Ronald Gray and colleagues in Rakai, Uganda, were in progress at the time Auvert and colleagues published their findings. Gray’s randomized trial enrolled 4,996 uncircumcised, HIV-negative men between 15 and 49 years of age.

About half of the men (2,474) were randomly assigned to receive immediate circumcision, and the other half (2,522) were assigned to receive circumcision delayed for 24 months. HIV testing was repeated at 6-month, 12-month, and 24-month follow-up visits.

In Bailey’s study, 2,784 HIV-negative men between the ages of 18 and 24 were randomly assigned either to be circumcised (1,391 participants) or to have circumcision delayed (1,393 participants). The results in both trials showed that circumcised men were 60 percent less likely to have acquired HIV despite the fact that sexual behaviors were similar between subjects in the circumcised and uncircumcised groups.

Circumcision: A New “Vaccine”? Because of its success in preventing HIV transmission from women to men during vaginal sex, circumcision has been described as similar to a vaccine with a 60 percent efficacy. Like a vaccine (although no effective vaccine for HIV currently exists), circumcision does not completely remove the risk of contracting the virus. For some populations, however, it could be part of a “comprehensive prevention package.”

In both recent African trials, circumcised men were 60 percent less likely than uncircumcised men to have contracted HIV, despite similar levels of risk behavior.

A serious concern is that circumcisions performed in unhygienic situations or by unskilled practitioners could lead to infections or blood-borne illnesses, including HIV. Further, even if circumcisions are performed safely, there are questions about their long-term HIV-protection effectiveness: all three randomized controlled trials were stopped after just under two years, so it is not known whether the protective effect of circumcision endures or wanes over time. In addition, a limitation of the African randomized controlled trials was the presumption that all the study subjects, or at least most of them, were exclusively heterosexual, and that they engaged only in vaginal intercourse. The protective effect of circumcision for the insertive partner in anal sex with either female or male receptive partners is unknown.

Each of the randomized controlled trials excluded some participants because of factors such as preexisting medical conditions that would have made circumcision dangerous. This was necessary to ensure that adverse events such as bleeding and infections were minimized among the study participants. Unfortunately, this also means that the “healthy” young men of the study group may not be representative of all the


Acceptability of Circumcision in Africa

Even if circumcision is highly effective, how acceptable is it to adult men in Africa? While many studies have reported that circumcision is very acceptable to African men, these studies often have small samples, making it difficult to generalize their findings. Further, many studies test acceptability with hypothetical questions such as “We do not know as yet whether circumcision protects men from catching HIV infection. But in case it [circumcision] did, would you accept being circumcised if it turns out that circumcision could protect you from catching HIV?”

Questions like the one above may assume that knowledge of the HIV-protective effectiveness of an intervention alone influences the decision to accept or not accept circumcision. In real life, there are many considerations, including cultural issues, concerns about safety, and the cost of the procedure, that influence such a decision. Despite these limitations, circumcision appears to be highly acceptable to men in most studies.

A 2006 qualitative study assessed community acceptance of circumcision by using focus groups of 159 men and women across tribal and regional areas in Malawi. In general, respondents said they approved of circumcision if it were effective in preventing HIV infection. They also cited other benefits, including enhanced sexual pleasure among men and women, better penile hygiene, and improved social standing among peers. Respondents reported that the appropriate time to circumcise boys would be at roughly 12 years of age, because younger boys might not be able to take care of circumcision wounds themselves. A limitation of this kind of study methodology is that while researchers could obtain the general consensus of the group, it was not clear that the study subjects were in any way representative of the larger population.

A 2007 study on the acceptability of circumcision in Zambia found that in communities in which circumcision was not practiced often, the main facilitators for acceptance were the promise of improved genital hygiene, HIV and sexually transmitted infection prevention, and a low cost for the procedure. The main barriers were cultural tradition, high cost, pain, and concerns for safety. Most participants reported that they would seek circumcision for themselves or their partners or sons if the procedure were free or at a minimal cost and were proven to reduce the risk of HIV and other sexually transmitted diseases.

A 2007 review of 13 studies from nine countries found that the proportion of uncircumcised men willing to be circumcised ranged from 29 percent to 87 percent, with a median of 65 percent. The proportion of women favoring circumcision for their partners ranged from 47 percent to 79 percent, with a median of 69 percent. Finally, the proportion of women who said they would be willing to have their sons circumcised ranged from 50 percent to 90 percent, with a median of 71 percent; among men, the proportion ranged from 70 percent to 90 percent, with a median of 81 percent. It is important to remember that these responses were to a hypothetical situation and might have been very different if circumcision were actually being offered.

Conclusion

The methodological strength and persuasive outcomes of recent research suggest that circumcision may be adopted as a national health policy in southern African countries. Future research may determine whether circumcision has any effect on transmission from HIV-positive men to their sexual partners, both male and female, through both vaginal and anal sex. Nonetheless, for a continent stricken by extremely high rates of HIV, circumcision may offer an effective, enduring, acceptable, and relatively inexpensive approach with great power to protect many people.
Circumcision and HIV: Implications for Developed Countries

David James Templeton, MBChB and Andrew Edwin Grulich MBBS, PhD

The evidence that circumcision may reduce the risk of HIV acquisition by men during vaginal sex has been building for 20 years. Researchers first noted an association between circumcision and decreased HIV risk in Africa in 1986, and subsequently, a range of observational studies conducted in diverse African populations has suggested a protective effect in men. Among female partners of HIV-positive men with low to moderate viral loads, observational data suggest that circumcision may reduce transmission of HIV. Results of an ongoing trial in Uganda assessing the efficacy of circumcision for prevention of male-to-female HIV transmission are eagerly awaited. Until recently, however, concern about the effects of cultural and religious factors raised questions about the efficacy of circumcision as a prevention approach.

In 2005, the first randomized trial of circumcision for HIV prevention reported a 60 percent reduction in HIV incidence among heterosexual men in South Africa. Recently, two randomized trials in Uganda and Kenya reported a similar protective effect. Based on these data, researchers have now concluded that circumcision is an effective tool for HIV prevention in Africa. A recent World Health Organization/UNAIDS policy review recommended the introduction of circumcision programs in key geographic settings for Africa in areas where HIV prevalence is high throughout the population, and where current circumcision rates in young men are low.

The debate has now begun about whether these results can be generalized to other settings. This raises questions about both the efficacy of circumcision as a prevention tool for homosexuals in more developed settings and about its utility as a prevention measure among men who have sex with men.

How Generalizable Are the Data?

Almost all the evidence on the association between HIV and circumcision comes from African studies. The most comprehensive meta-analysis included only two cohort studies from outside Africa, both in men attending sexually transmitted disease clinics. One of these was in the United States, and one was in India. In each of these, researchers found that circumcision was protective, although, in the U.S. study, this finding was not statistically significant.

A consideration of the biology of circumcision’s protective effects may aid in determining whether the African results can be generalized. Some biological mechanisms are likely to be universal, including the high density of CD4+ receptor-containing cells (Langerhans cells) on the inner surface of the foreskin and a susceptibility of the foreskin to abrasions. However, in Africa, lack of access to running water probably results in less frequent washing of the genitals, and it is possible that this increases the transmission of HIV and other sexually transmitted infections. A high rate of ulcerative sexually transmitted infections also increases the likelihood of disease transmission. To the degree that these factors are less present in more developed countries, the protective effect of circumcision may be lessened. Further, in the United States, for example, most adult men are already circumcised, and the risk of HIV acquisition is low compared with the risk in Africa. These factors alter the risk-benefit analysis of the utility of circumcision between the two types of settings.

Condons are so effective in preventing HIV that in populations with high levels of condom use, there is little potential for circumcision to reduce HIV incidence.


In many countries, sex between men is a more common route of HIV transmission than heterosexual sex, yet there is little data on circumcision as an HIV prevention tool in this population.

In many countries, sex between men is a more common route of HIV transmission than sex between men and women. Still, there are few data on circumcision as a potential HIV prevention tool in this population. The only prospective data from the U.S. HIVNET vaccine preparedness study, which reported that HIV incidence was 1.5 percent among circumcised men and 2.8 percent in uncircumcised men. This protective effect remained, even after statistical multivariate analysis.

At face value this result appears curious, since the majority of new HIV infections among men who have sex with men are acquired via receptive anal sex, because the transmission probability is so much higher than during insertive anal sex. Only two cross-sectional studies have been published: one reported an association between circumcision and lower HIV prevalence; and one reported no association between circumcision and HIV prevalence. Further data are urgently required to clarify these seemingly conflicting results. Gay men in many developed country settings report high levels of condom use; in Australia, consistent condom use for anal sex with casual partners is reported by 70 percent or more of gay men. If circumcision leads to a perception of invulnerability to HIV, with consequent reduction in condom usage, there

FOCUS Now Quarterly

This issue of FOCUS marks our transition to a quarterly, digital-only publication. We have also made changes (both major and subtle) in our format. In response to your suggestions, we have created a new section, “Related Resources,” that replaces our former “Recent Reports” and “Clearinghouse” sections. In the coming months, you may notice further changes as we strive to make FOCUS even more readable and useful to you. We welcome your comments and suggestions in this process. Please contact Michelle Cataldo, Clinical Editor, at michelle.cataldo@ucsf.edu with your thoughts.
may be an even greater risk than in heterosexuals that circumcision would be associated with an increased HIV risk.

There are particular populations in developed countries in which circumcision may offer potential benefit. In the United States, for instance, African American and Hispanic men are less likely to be circumcised than White men, and these groups also bear the brunt of sexually transmitted HIV. The acceptability of adult circumcision to these groups and its potential to reduce HIV incidence among communities that have not traditionally embraced circumcision warrant further study. Even within these groups, it is crucial that circumcision be promoted only as part of a “combination prevention” intervention including intensive promotion of condom use.

At an individual level, it is likely that the increased public discussion of circumcision will result in patient requests for adult circumcision, which is less safe and more expensive than circumcision performed on infants. At the same time as news of circumcision’s potential as an HIV prevention tool has been touted in developing countries, rates of circumcision continue to fall in resource-rich countries such as Australia and the United States, which previously had very high circumcision rates. When confronted with a request for adult circumcision, physicians should respond cautiously and counsel patients that circumcision is not an equally effective alternative to condom use.

Conclusion

In Africa, circumcision joins the proven armamentarium of HIV prevention tools. These include condom use, identification and treatment of sexually transmitted infections, and HIV antiviral drugs for prevention of mother-to-child transmission of HIV. Because the nature of the HIV epidemic is different in developing than in developed ones, current data are insufficient to recommend circumcision as a means of HIV prevention in developed countries.

Authors

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Related Resources

Journal Articles

Abdool Karim Q. Prevention of HIV by male circumcision. *BMJ*. 2007; 335(7609): 4–5. Reviews the challenges of integrating the provision of circumcision as an HIV-prevention method with existing sexual health services, including the underfunding of sexual health services in general, the need to identify appropriate personnel to perform circumcisions, and the fact that circumcision wounds may not be healed before sexual activity resumes.

Berer M. Male circumcision for HIV prevention: Perspectives on gender and sexuality. *Reproductive Health Matters*. 2007; 15(29): 45–48. Questions the ethics of prioritizing circumcision as a prevention intervention, since it is irreversible and more intrusive than condom use. Advocates health education for both sexes, notes that sexual negotiations between men and women are complex, and questions circumcision’s role in protecting women from HIV infection.

Buchbinder S. HIV epidemiology and prevention interventions. *Topics in HIV Medicine*. 2007; 15(2): 26–30. Summarizes presentations given at the 2007 Conference on Retroviruses and Opportunistic Infections, including reports on two Ugandan circumcision studies—one of which is the Rakai study that demonstrated circumcision’s significant protective effect for HIV-negative men. The second study examined the protective effect of circumcision of HIV-positive men against transmission to their female partners. This
study was stopped early because some men resumed sexual activity before their wounds had healed, increasing transmission risk to their female partners.

Dickerman JD. Circumcision in the time of HIV: When is there enough evidence to revise the American Academy of Pediatrics’ policy on circumcision? Pediatrics. 2007; 119(5): 1006–1007. Discusses circumcision’s protective effect against the human papillomavirus and penile cancer, as well as urinary tract infections in infants. Notes that circumcision rates have declined, and that decisions about circumcision infants are often emotionally and culturally based. Argues that a new policy statement by the American Academy of Pediatrics is needed to help parents make informed decisions about the procedure.

Dowsett GW, Couch M. Male circumcision and HIV prevention: Is there really enough of the right kind of evidence? Reproductive Health Matters. 2007; 15(29): 33–44. Questions the evidence supporting the joint WHO/UNAIDS March 2007 recommendation that circumcision be adopted as an HIV prevention intervention in areas of high HIV prevalence where transmission occurs predominantly among heterosexuals. Notes the exclusion of men who have sex with men from these studies, questions the safety of traditional African circumcision procedures, compares circumcision’s effectiveness unfavorably with that of condom use, and questions circumcision’s acceptability.

Edouard L, Okonofua F. Male circumcision for HIV prevention: Evidence and expectations. African Journal of Reproductive Health. 2006; 10(3): 7–9. Explains how circumcision may protect men who have vaginal sex with HIV-positive women against infection. Expresses concerns that there may be an insufficient number of skilled practitioners to accommodate increased demand, and raises issues regarding informed consent to the procedure.


Matovu JKB, Ssem pijja V, Makumbi FE, et al. Sexually transmitted infection management, safer sex promotion and voluntary HIV counseling and testing in the male circumcision trial, Rakai, Uganda. Reproductive Health Matters. 2007; 15(29): 68–74. Describes the 5,000-subject Rakai randomized clinical trial that demonstrated circumcision’s 51 percent to 60 percent efficacy for prevention of HIV acquisition by men from women.

Web Sites

Medline Plus: Circumcision. http://www.nlm.nih.gov/medlineplus/circumcision.html. This site offers numerous links to other Web sites with circumcision-related information, including the American Academy of Family Physicians, the American Urological Association, the American Academy of Pediatrics, the Mayo Clinic, and the National Institutes of Health Clinical Trials sites.

Next Issue

In the Fall 2007 issue of FOCUS, U.S. Centers for Disease Control and Prevention (CDC) researchers Charles B. Collins, Jr. PhD, Wayne D. Johnson, MSPH, and Cynthia M. Lyles, PhD, describe the process by which evidence-based behavioral interventions (EBIs) are developed, replicated, and disseminated. They also discuss the challenges and rewards of implementing and adapting evidence-based approaches in the field.

Also in the Fall issue, George Ayala, PsyD, Director of Health Promotion, Community Research, and Capacity Building at AIDS Project Los Angeles (APLA), offers a real-life illustration of this adaptation process. He and his team report on the collaboration among community members, public health providers, clinicians, and researchers that is necessary to adapt evidence-based interventions.