

CDC HIV/AIDS Science Facts:

Male Circumcision and Risk for HIV Transmission and Other Health Conditions: Implications for the United States

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This fact sheet summarizes information in four areas of male circumcision: 1) male circumcision and risk for HIV transmission; 2) male circumcision and other health conditions; 3) risks associated with male circumcision; and 4) status of HIV infection and male circumcision in the United States.

What is Male Circumcision?

Male circumcision is the surgical removal of some or all of the foreskin (or prepuce) from the penis [1].

Male Circumcision and Risk for HIV Transmission

Several types of research have documented that male circumcision significantly reduces the risk of HIV acquisition by men during penile-vaginal sex.

Biologic Plausibility

Compared with the dry external skin surface, the inner mucosa of the foreskin has less keratinization (deposition of fibrous protein), a higher density of target cells for HIV infection (Langerhans cells), and is more susceptible to HIV infection than other penile tissue in laboratory studies [2]. The foreskin may also have greater susceptibility to traumatic epithelial disruptions (tears) during intercourse, providing a portal of entry for pathogens, including HIV [3]. In addition, the microenvironment in the preputial sac between the unretracted foreskin and

the glans penis may be conducive to viral survival [1]. Finally, the higher rates of sexually transmitted genital ulcerative disease, such as syphilis, observed in uncircumcised men may also increase susceptibility to HIV infection [4].

International Observational Studies

A systematic review and meta-analysis that focused on male circumcision and heterosexual transmission of HIV in Africa was published in 2000 [5]. It included 19 cross-sectional studies, 5 case-control studies, 3 cohort studies, and 1 partner study. A substantial protective effect of male circumcision on risk for HIV infection was noted, along with a reduced risk for genital ulcer disease. After adjustment for confounding factors in the population-based studies, the relative risk for HIV infection was 44% lower in circumcised men. The strongest association was seen in men at high risk, such as patients at sexually transmitted disease (STD) clinics, for whom the adjusted relative risk was 71% lower for circumcised men.

Another review that included stringent assessment of 10 potential confounding factors and was stratified by study type or study population was published in 2003 [6]. Most of the studies were from Africa. Of the 35 observational studies in the review, the 16 in the general population had inconsistent results. The one large prospective cohort study in this group showed a significant protective effect: the odds of infection were 42% lower for circumcised men [7]. The remaining 19 studies were conducted in populations at high



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risk. These studies found a consistent, substantial protective effect, which increased with adjustment for confounding. Four of these were cohort studies: all demonstrated a protective effect, with two being statistically significant.

Ecologic studies also indicate a strong association between lack of male circumcision and HIV infection at the population level. Although links between circumcision, culture, religion, and risk behavior may account for some of the differences in HIV infection prevalence, the countries in Africa and Asia with prevalence of male circumcision of less than 20% have HIV infection prevalences several times higher than those in countries in these regions where more than 80% of men are circumcised [8].

International Clinical Trials

Three randomized controlled clinical trials were conducted in Africa to determine whether circumcision of adult males will reduce their risk for HIV infection. The study conducted in South Africa [9] was stopped in 2005, and those in Kenya [10] and Uganda [11] were stopped in 2006 after interim analyses found a statistically significant reduction in male participants' risk for HIV infection from medical circumcision.

In these studies, men who had been randomly assigned to the circumcision group had a 60% (South Africa), 53% (Kenya), and 51% (Uganda) lower incidence of HIV infection compared with men assigned to the wait-list group to be circumcised at the end of the study. In all three studies, a few men who had been assigned to be circumcised did not undergo the procedure, and vice versa. When the data were reanalyzed to account for these occurrences, men who had been circumcised had a 76% (South Africa), 60% (Kenya), and 55% (Uganda) reduction in risk for HIV infection compared with those who were not circumcised. The Uganda study investigators are also examining the following in an ongoing study: 1) safety and acceptability of male circumcision in HIV-infected men and men of unknown HIV

infection status, 2) safety and acceptability of male circumcision in the men's female sex partners, and 3) effect of male circumcision on male-to-female transmission of HIV and other STDs.

Male Circumcision and Male-to-Female Transmission of HIV

In an earlier study of couples in Uganda in which the male partner was HIV infected and the female partner was initially HIV-seronegative, the infection rates of the female partners differed by the circumcision status and viral load of the male partners. If the male's HIV viral load was <50,000 copies/mL, there was no HIV transmission if the man was circumcised, compared with a transmission rate of 9.6 per 100 person-years if the man was uncircumcised [7]. When viral load was not controlled for, there was a nonsignificant trend toward a reduction in the male-to-female transmission rate from circumcised men compared with uncircumcised men. Such an effect may be due to decreased viral shedding from circumcised men or to a reduction in ulcerative STDs acquired by female partners of circumcised men [12]. A clinical trial in Uganda to assess the impact of circumcision on male-to-female transmission reported that its first interim safety analysis showed a nonsignificant trend toward a higher rate of HIV acquisition in women partners of HIV-seropositive men in couples who had resumed sex prior to certified postsurgical wound healing and did not detect a reduction in HIV acquisition by female partners engaging in sex after wound healing was complete [13].

Male Circumcision and Other Health Conditions

Lack of male circumcision has also been associated with sexually transmitted genital ulcer disease and chlamydia, infant urinary tract infections, penile cancer, and cervical cancer in female partners of uncircumcised men [1]. The latter two conditions are related to human papillomavirus (HPV) infection. Transmission of this virus is also associated with lack of male

circumcision. A recent meta-analysis included 26 studies that assessed the association between male circumcision and risk for genital ulcer disease. The analysis concluded that there was a significantly lower risk for syphilis and chancroid among circumcised men, whereas the reduced risk of herpes simplex virus type 2 infection had a borderline statistical significance [4].

Risks Associated with Male Circumcision

Reported complication rates depend on the type of study (e.g., chart review vs. prospective study), setting (medical vs. nonmedical facility), person operating (traditional vs. medical practitioner), patient age (infant vs. adult), and surgical technique or instrument used. In large studies of infant circumcision in the United States, reported inpatient complication rates range from 0.2% to 2.0% [1, 14, 15]. The most common complications in the United States are minor bleeding and local infection. In the recently completed African trials of adult circumcision, the rates of adverse events possibly, probably, or definitely attributable to circumcision ranged from 2% to 8%. The most commonly reported complications were pain or mild bleeding. There were no reported deaths or long-term sequelae documented [9, 10, 11, 16]. A recent case-control study of two outbreaks of methicillin-resistant *Staphylococcus aureus* (MRSA) in otherwise healthy male infants at one hospital identified circumcision as a potential risk factor. However, in no case did MRSA infections involve the circumcision site, anesthesia injection site, or the penis, and MRSA was not found on any of the circumcision equipment or anesthesia vials tested [17].

Effects of Male Circumcision on Penile Sensation and Sexual Function

Well-designed studies of sexual sensation and function in relation to male circumcision are

few, and the results present a mixed picture. Taken as a whole, the studies suggest that some decrease in sensitivity of the glans to fine touch can occur following circumcision [18]. However, several studies conducted among men after adult circumcision suggest that few men report their sexual functioning is worse after circumcision; most report either improvement or no change [19–22]. The three African trials found high levels of satisfaction among the men after circumcision [9, 10, 11, 16]; however, cultural differences limit extrapolation of their findings to U.S. men.

HIV Infection and Male Circumcision in the United States

In 2005, men who have sex with men (MSM) (48%), MSM who also inject drugs (4%), and men (11%) and women (21%) exposed through high-risk heterosexual contact accounted for an estimated 84% of all HIV/AIDS cases diagnosed in U.S. areas with confidential name-based HIV infection reporting. Blacks accounted for 49% of cases and Hispanics for 18%. Infection rates for both groups were several-fold higher than the rate for whites. An overall prevalence of 0.5% was estimated for the general population [23]. Although data on HIV infection rates since the beginning of the epidemic are available, data on circumcision and risk for HIV infection in the United States are limited. In one cross-sectional survey of MSM, lack of circumcision was associated with a 2-fold increase in the odds of prevalent HIV infection [24]. In another, prospective study of MSM, lack of circumcision was also associated with a 2-fold increase in risk for HIV seroconversion [25]. In both studies, the results were statistically significant, and the data had been controlled statistically for other possible risk factors. However, in another prospective cohort study of MSM, there was no association between circumcision status and incident HIV infection, even among men who reported no unprotected anal receptive intercourse [26]. And in

a recent cross-sectional study of African American and Latino MSM, male circumcision was not associated with previously known or newly diagnosed HIV infection [27]. In one prospective study of heterosexual men attending an urban STD clinic, when other risk factors were controlled, uncircumcised men had a 3.5-fold higher risk for HIV infection than men who were circumcised. However, this association was not statistically significant [28]. And in an analysis of clinic records for African American men attending an STD clinic, circumcision was not associated with HIV status overall, but among men with known HIV exposure, circumcision was associated with a statistically significant 58% reduction in risk for HIV infection [29].

Status of Male Circumcision in the United States

In national probability samples of adults surveyed during 1999–2004, the National Health and Nutrition Examination Surveys (NHANES) found that 79% of men reported being circumcised, including 88% of non-Hispanic white men, 73% of non-Hispanic black men, 42% of Mexican American men, and 50% of men of other races/ethnicities [30]. It is important to note that reported circumcision status may be subject to misclassification. In a study of adolescents, only 69% of circumcised and 65% of uncircumcised young men correctly identified their circumcision status as verified by physical exam [31].

According to the National Hospital Discharge Survey (NHDS), 65% of newborns were circumcised in 1999, and the overall proportion of newborns circumcised was stable from 1979 through 1999 [32]. Notably, the proportion of black newborns circumcised increased during this reporting period (58% to 64%); the proportion of white newborns circumcised remained stable (66%). In addition, the proportion of newborns who were circumcised in the Midwest increased during the 20-year period—from 74% in 1979 to 81% in 1999; the proportion of infants born in the West who were circumcised decreased from

64% in 1979 to 37% in 1999. In another survey, the National Inpatient Sample (NIS), circumcision rates increased from 48% during 1988–1991 to 61% during 1997–2000. Circumcision was more common among newborns who were born to families of higher socioeconomic status, born in the Northeast or Midwest, and who were black [33].

In 1999, the American Academy of Pediatrics (AAP) changed from a neutral stance on circumcision to a position that the data then available were insufficient to recommend routine neonatal male circumcision. The Academy also stated, “It is legitimate for the parents to take into account cultural, religious, and ethnic traditions, in addition to medical factors, when making this choice” [34]. This position was reaffirmed by the Academy in 2005. This change in policy may have influenced reimbursement for, and the practice of, neonatal circumcision. In a 1995 review, 61% of circumcisions were paid for by private insurance, 36% were paid for by Medicaid, and 3% were self-paid by the parents of the infant. Compared with infants of self-pay parents, those covered by private insurance were 2.5 times as likely to be circumcised [35]. Since 1999, 16 states have eliminated Medicaid payments for circumcisions that were not deemed medically necessary [36]. However, AAP has recently (2007) convened a panel to reconsider its circumcision policy in light of additional data now available.

Cost-Benefits and Ethical Issues for Neonatal Circumcision in the United States

A large retrospective study of circumcision in nearly 15,000 infants found neonatal circumcision to be highly cost-effective, considering the estimated number of averted cases of infant urinary tract infection and lifetime incidence of HIV infection, penile cancer, balanoposthitis, and phimosis. The cost of postneonatal circumcision was 10-fold the cost of neonatal circumcision [37]. Many parents now make decisions about infant circumcision based on cultural, religious, or parental desires rather than health concerns [38].

Some persons have raised ethical objections to asking parents to make decisions about elective surgery during infancy, particularly when it is done primarily to protect against risks of HIV and STDs that don't occur until young adulthood, but other ethicists have found it an appropriate parental proxy decision [39].

Considerations for the United States

A number of important differences from sub-Saharan African settings where the three male circumcision trials were conducted must be considered in determining the possible role for male circumcision in HIV prevention in the United States. Notably, the overall risk of HIV infection is considerably lower in the United States, changing risk-benefit and cost-effectiveness considerations. Also, studies to date have demonstrated efficacy only for penile-vaginal sex, the predominant mode of HIV transmission in Africa, whereas the predominant mode of sexual HIV transmission in the United States is by penile-anal sex among MSM. There are as yet no convincing data to help determine whether male circumcision will have any effect on HIV risk for men who engage in anal sex with either a female or male partner, as either the insertive or receptive partner. Receptive anal sex is associated with a substantially greater risk of HIV acquisition than is insertive anal sex. It is more biologically plausible that male circumcision would reduce HIV acquisition risk for the insertive partner rather than for the receptive partner, but few MSM engage solely in insertive anal sex [40].

In addition, although the prevalence of circumcision may be somewhat lower in U.S. racial and ethnic groups with higher rates of HIV infection, most American men are already circumcised, and it is not known whether men at higher risk for HIV infection would be willing to be circumcised or whether parents would be willing to have their infants circumcised to reduce possible future HIV infection risk. Lastly, whether the effect of male circumcision differs by HIV-1 subtype, predominately subtype B in the United States and subtypes A, C, and D in circulation

at the three clinical trial sites in Africa, is also unknown.

Summary

Male circumcision has been associated with a lower risk for HIV infection in international observational studies and in three randomized controlled clinical trials. It is possible, but not yet adequately assessed, that male circumcision could reduce male-to-female transmission of HIV, although probably to a lesser extent than female-to-male transmission. Male circumcision has also been associated with a number of other health benefits. Although there are risks to male circumcision, serious complications are rare. Accordingly, male circumcision, together with other prevention interventions, could play an important role in HIV prevention in settings similar to those of the clinical trials [41, 42].

Male circumcision may also have a role in the prevention of HIV transmission in the United States. CDC consulted with external experts in April 2007 to receive input on the potential value, risks, and feasibility of circumcision as an HIV prevention intervention in the United States and to discuss considerations for the possible development of guidelines.

As CDC proceeds with the development of public health recommendations for the United States, individual men may wish to consider circumcision as an additional HIV prevention measure, but they must recognize that circumcision 1) does carry risks and costs that must be considered in addition to potential benefits; 2) has only proven effective in reducing the risk of infection through insertive vaginal sex; and 3) confers only partial protection and should be considered only in conjunction with other proven prevention measures (abstinence, mutual monogamy, reduced number of sex partners, and correct and consistent condom use).

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