

Male Circumcision for Prevention of HIV and Other Sexually Transmitted Diseases

Patricia Flynn, MD^a, Peter Havens, MS, MD^b, Michael Brady, MD^c, Patricia Emmanuel, MD^d, Jennifer Read, MD, MS, MPH, DTMandH^e,
Laura Hoyt, MD^f, Lisa Henry-Reid, MD^g, Russell Van Dyke, MD^h, Lynne Mofenson, MD^a

^aDepartment of Infectious Diseases, St Jude Children's Research Hospital, Memphis, Tennessee; ^bDivision of Infectious Diseases, Department of Pediatrics, Medical College of Wisconsin, Milwaukee, Wisconsin; ^cDepartment of Pediatrics, Columbus Children's Hospital, Columbus, Ohio; ^dDepartment of Pediatrics, University of South Florida, Tampa, Florida; ^ePediatric, Adolescent, and Maternal AIDS Branch, National Institute of Child Health and Human Development, Rockville, Maryland; ^fDepartment of Pediatric Infectious Diseases, Children's Hospitals and Clinics of Minnesota, St Paul, Minnesota; ^gDepartment of Adolescent and Young Adult Medicine, Stroger Hospital of Cook County, Chicago, Illinois; ^hDivision of Infectious Diseases, Department of Pediatrics, Tulane University School of Medicine, New Orleans, Louisiana

The authors have indicated they have no financial relationships relevant to this article to disclose.

A RECENT commentary in *Pediatrics* reviewed the documented medical benefits of newborn male circumcision, including protection against balanoposthitis, phimosis, infections of the urinary tract in male infants, and protection against human papillomavirus-associated genital cancers and HIV and *Chlamydia* infection in adolescents and adults.¹ Low rates of minor surgical complications (0.2%–0.6%) and safety and efficacy of local anesthesia were noted. The ability of newborn circumcision to protect against sexually transmitted diseases (STDs) was also shown in a recently published cohort study from New Zealand.² Recent large randomized clinical trials in South Africa, Kenya, and Uganda demonstrated reduction of HIV-acquisition risk by male circumcision performed outside the newborn period, showing the role of adult male circumcision in prevention of STDs in adolescents and adults.^{3,4}

An association between lack of male circumcision and acquisition of HIV infection was first noted in 1986.⁵ Over the next 10 years, more than 35 studies including ecologic, cross-sectional, case-control, and cohort studies in general and high-risk populations throughout the world evaluated the possible protective effect of male circumcision against HIV acquisition.^{6–8} A systematic review summarized the studies from sub-Saharan Africa and showed an estimate of the adjusted relative risk of HIV acquisition of 0.42 (95% confidence interval [CI]: 0.34–0.54; protection of 58%) in circumcised compared with uncircumcised male subjects.⁷ The impact of male circumcision on prevention of HIV acquisition was greater in high-risk groups than in the general population.⁶ A cohort study has also suggested that transmission of HIV to female partners of men with HIV may be lower when the male partner is circumcised.^{9–11}

To define more accurately the potential role of male circumcision in prevention of HIV acquisition, investigators have undertaken 3 large randomized clinical trials in southern and eastern Africa. The results of the first of these trials were published in 2005.³ In that study, 3274 uncircumcised men in South Africa were randomly assigned to either be circumcised immediately after randomization (intervention group) or at the end of the study (control group). The trial was stopped early, after a mean follow-up of 18 months, when the results of an interim intention-to-treat analysis revealed a significant protective effect of circumcision of 60% (95% CI: 32%–76%). When the data were analyzed to take into account men who were actually circumcised in the control group or not circumcised in the intervention group, the protective benefit of circumcision was 76% (95% CI: 56%–86%). Similar protection was demonstrated by the other 2 large trials, which were stopped early when results of an interim analysis showed that circumcision of adult men has protective efficacy of 53% (in the Kenya study) or 48% (in the Uganda study).⁴

Male circumcision may act directly to reduce the risk

Abbreviations: STD, sexually transmitted disease; CI, confidence interval

Opinions expressed in these commentaries are those of the authors and not necessarily those of the American Academy of Pediatrics or its Committees.

This article was coauthored by Drs Read and Mofenson in their private capacity. No official support or endorsement by the Department of Health and Human Services or the National Institutes of Health is intended or should be inferred.

www.pediatrics.org/cgi/doi/10.1542/peds.2006-3694

doi:10.1542/peds.2006-3694

Accepted for publication Jan 16, 2007

Address correspondence to Peter Havens, MS, MD, Medical College of Wisconsin, Pediatric Infectious Diseases, Suite C450, PO Box 1997, Milwaukee, WI 53201-1997. E-mail: phavens@mcw.edu
PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275); published in the public domain by the American Academy of Pediatrics

of HIV acquisition by reducing the ability of the virus to attach to and enter cells. The inner mucosal surface of the foreskin contains a higher density of Langerhans cells (a target cell for HIV infection) than stratified squamous epithelium (which is on the surface of the penis) and is more susceptible to HIV infection in vitro.¹² The foreskin is also more susceptible to trauma, which may increase susceptibility to HIV infection during sexual activity.¹³⁻¹⁵ Alternatively, the effect of circumcision on prevention of HIV acquisition may be indirect. Infections with ulcerative STDs including syphilis, chancroid, and herpes are reduced in men who have had a circumcision.^{13,16,17} Because these ulcerative STDs are associated with increased HIV-acquisition risk, reduction in other STDs may partially explain the reduced HIV-acquisition risk associated with male circumcision.

Newborn circumcision may be preferable to circumcision at an older age because of its enhanced safety.¹⁸ Questions remain about the possibility that circumcised men may practice riskier sex because of presumed protection. The protective effect of circumcision on reducing HIV transmission found in Africa, where HIV is predominantly heterosexually transmitted and HIV prevalence is high, may not be directly applicable in the United States, where HIV in men is predominantly transmitted by male-to-male sex and HIV prevalence is lower. However, newborn circumcision has been shown to prevent later acquisition of STDs in young adult men in New Zealand, which suggests that the protective effect is not confined to developing countries.²

Since 1999, 16 states have eliminated Medicaid payments for circumcisions that were deemed "not medically necessary,"¹⁹ justifying that decision in part on the basis of the American Academy of Pediatrics statement that "potential medical benefits...are not sufficient to recommend routine neonatal circumcision."²⁰ Data now demonstrate the benefit of male circumcision as an intervention for the prevention of STDs including HIV and genital cancers. Therefore, if parents choose circumcision for their newborn male child, or if an adolescent decides that circumcision might be appropriate to reduce risk of STD acquisition, it is a medically rational choice that should be included in government health or private insurance benefits. Circumcision, like vaccination, may be an effective intervention for disease prevention in the United States as well as in other countries. Advisory groups in the United States need to carefully consider how recent data on the preventive efficacy of adult male circumcision might change current recommendations for care of newborns and adolescents in the United States.

Editor's note: The American Academy of Pediatrics is presently reviewing its 1999 Circumcision Policy Statement, reaffirmed May 2005.

REFERENCES

- Schoen EJ. Ignoring evidence of circumcision benefits. *Pediatrics*. 2006;118:385-387
- Fergusson DM, Boden JM, Horwood LJ. Circumcision status and risk of sexually transmitted infection in young adult males: an analysis of a longitudinal birth cohort. *Pediatrics*. 2006;118:1971-1977
- Auvert B, Taljaard D, Lagarde E, Sobngwi-Tambekou J, Sitta R, Puren A. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial [published correction appears in *PLoS Med*. 2006;3:e298]. *PLoS Med*. 2005;2:e298
- US National Institutes of Health. Adult male circumcision significantly reduces risk of acquiring HIV [press release]. 2006. Available at: www3.niaid.nih.gov/news/newsreleases/2006/AMC12_06.htm. Accessed December 13, 2006
- Fink AJ. A possible explanation for heterosexual male infection with AIDS. *N Engl J Med*. 1986;315:1167
- Siegfried N, Muller M, Deeks J, et al. HIV and male circumcision: a systematic review with assessment of the quality of studies. *Lancet Infect Dis*. 2005;5:165-173
- Weiss HA, Quigley MA, Hayes RJ. Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis. *AIDS*. 2000;14:2361-2370
- Moses S, Plummer FA, Bradley JE, Ndinya-Achola JO, Nagelkerke NJ, Ronald AR. The association between lack of male circumcision and risk for HIV infection: a review of the epidemiological data. *Sex Transm Dis*. 1994;21:201-210
- Gray RH, Kiwanuka N, Quinn TC, et al. Male circumcision and HIV acquisition and transmission: cohort studies in Rakai, Uganda. Rakai Project Team. *AIDS*. 2000;14:2371-2381
- Quinn TC, Wawer MJ, Sewankambo N, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. *N Engl J Med*. 2000;342:921-929
- Gray R, Wawer M, Thoma M, et al. Male circumcision and the risks of female HIV and sexually transmitted infections acquisition in Rakai, Uganda. Presented at: 13th Conference on Retroviruses and Opportunistic Infections; February 5-8, 2006; Denver, CO
- Patterson BK, Landay A, Siegel JN, et al. Susceptibility to human immunodeficiency virus-1 infection of human foreskin and cervical tissue grown in explant culture. *Am J Pathol*. 2002;161:867-873
- Weiss HA, Thomas SL, Munabi SK, Hayes RJ. Male circumcision and risk of syphilis, chancroid, and genital herpes: a systematic review and meta-analysis. *Sex Transm Infect*. 2006;82:101-109; discussion 110
- Halperin DT, Bailey RC. Male circumcision and HIV infection: 10 years and counting. *Lancet*. 1999;354:1813-1815
- Szabo R, Short RV. How does male circumcision protect against HIV infection? *BMJ*. 2000;320:1592-1594
- Quigley MA, Weiss HA, Hayes RJ. Male circumcision as a measure to control HIV infection and other sexually transmitted diseases. *Curr Opin Infect Dis*. 2001;14:71-75
- Hira SK, Kamanga J, Macuacua R, Mwansa N, Cruess DF, Perine PL. Genital ulcers and male circumcision as risk factors for acquiring HIV-1 in Zambia. *J Infect Dis*. 1990;161:584-585
- Centers for Disease Control and Prevention. Male circumcision and risk for HIV transmission: implications for the United States. 2006. Available at: www.cdc.gov/hiv/resources/factsheets/PDF/circumcision.pdf. Accessed January 31, 2007
- National Conference of State Legislatures. Circumcision and infection. State health notes 9-18-2006. Available at: www.ncsl.org/programs/health/shn/2006/hl475.htm#circumcision. Accessed November 6, 2006
- American Academy of Pediatrics, Task force on Circumcision. Circumcision policy statement. *Pediatrics*. 1999;103:686-693