

Circumcision and non-HIV sexually transmitted infections

Andrew E. MacNeily, MD, FRCSC,* Kourosh Afshar, MD, FRCSC†

Cite as: *Can Urol Assoc J* 2011;5(1):58-9; DOI:10.5489/cuaj.11009

As urologists, we are frequently asked questions about the foreskin by colleagues, patients and their families, as well as our own friends and family members. It seems not a month passes without a statement in the lay-press identifying a benefit to circumcision with respect to STI transmission in the developing world. We are then asked if this information applies to babies in Canada. Then the debate begins again about the pros and cons of circumcision. In 2007, *CUAJ* published a spirited point-counterpoint article on the pros and cons of newborn circumcision.^{1,2} This opinion piece is a follow-up to that article, with a focus on emerging data regarding the impact of circumcision on the transmission of non-HIV sexually transmitted infections (STIs).

Evidence supporting the effectiveness of adult circumcision for the reduction of HIV acquisition in men is strong and is based on several randomized controlled trials performed in the developing world.³⁻⁵ However, until recently, the same could not be said regarding other STIs. This was mainly due to the lack of randomized trials. The core of our knowledge surrounding the relationship between circumcision and non-HIV STIs stems from observational studies that are prone to bias and confounder effects. Common examples of the flaws in existing studies include the variety of methods of ascertaining the exposure or the outcomes, inclusion of diverse patient populations (geographically, culturally, baseline risk), and differing ages of circumcision (i.e., before or after sexual debut). Consequently, there are conflicting results among studies which reflect the heterogeneity seen in all systematic reviews on this topic. That said, a summary of our observations may prove useful for the purposes of patient and physician education.

Human papillomavirus

Human papillomavirus (HPV) is the most common STI worldwide, with more than 100 different identified genotypes.⁶ High-risk types 16 and 18 are responsible for up to 70% of cervical cancers and type 16 is implicated in about 50% of penile cancers. Low-risk HPV genotypes are causal in the development of genital warts. The virus gains access to the

basal epithelial layers of the anogenital mucosa via microabrasions and overall 90% of HPV infections are cleared within 2 years as a result of cell-mediated immune responses.⁷ The focus of HPV research has been mainly on women because the risk of HPV-related cervical cancer is high. However, the body of data supporting circumcision to reduce HPV infection and cervical carcinoma is somewhat confusing. It has long been observed that the prevalence of cervical carcinoma is low where circumcision is widely practiced; this has usually been attributed to a decreased prevalence of HPV on the circumcised penis. However, a recent meta-analysis on HPV and circumcision concluded that the published literature does not support the claim that the procedure reduces the risk of genital HPV infection.⁸ In conjunction with the advent of an effective female vaccination against HPV prior to the onset of sexual activity, this study suggested that the argument in favour of circumcision as a preventative measure was weak.⁹ In contrast to this conclusion, a rigorous randomized controlled trial conducted in Uganda was published online in *The Lancet* this January 2011.¹⁰ In more than 1200 heterosexual couples, adult male circumcision reduced the prevalence of high-risk HPV in their female partners by 28%. It is thought that circumcision reduces penile HPV carriage at the urethra, coronal sulcus and shaft leading to a decreased incidence and increased clearance in female partners probably by lowering re-infection.¹¹ Although this study did not directly assess for cervical neoplasia, persistent high-risk HPV infection is a prerequisite for its development.¹² It is reasonable to assume that the reduction in the HPV infection rate will result in reduced cervical cancer in the future, but proof of this assumption will require years of follow-up. Overall, the literature suggests that circumcision may partially prevent cervical carcinoma, particularly in countries that do not have well-established programs for cervical screening and HPV vaccination. It may evolve that in developing countries HPV vaccination and circumcision will be seen as complementary tools to prevent cervical carcinoma.

Other non-ulcerative STIs

In a prospective multi-centre American study involving more than 2000 men attending STI clinics, there was evidence

for an increased incidence of gonorrheal infection in non-circumcised men (odds ratio 1.5), but no difference with respect to Chlamydial infection.¹³ In contrast, a randomized controlled study in Kenya examining circumcision status and acquisition of *Chlamydia*, *Gonorrhea* and *Trichomonas vaginalis* found no reduction of infection in circumcised men.¹⁴ A meta-analysis of 30 observational studies did not show any association between circumcision status and gonococcal or chlamydial urethritis. Interestingly, when high-risk populations were examined, circumcision was associated with a significant risk reduction for the same STIs.¹⁵ In addition, in a 2008 prospective study of almost 6000 women from Zimbabwe, Uganda and Thailand, there was no difference in female acquisition of *Chlamydia*, *Gonorrhea* or *T. vaginalis* according to the circumcision status of their partners.¹⁶ In summary, at this time it would appear that aside from HPV, circumcision does not confer a risk-reduction for non-ulcerative STIs.

Ulcerative STIs

The first systematic review and meta-analysis of the literature examining this issue in 2006 concluded that there was a strong protective effect of adult circumcision against chancroid and syphilis, with a weak protective effect against herpes simplex virus type 2.¹⁷ A year later, a similar meta-analysis combined an examination of both ulcerative and non-ulcerative STIs. The authors found that there was a trend towards a reduction in ulcerative diseases in circumcised males, but firm conclusions were not possible due to inadequate data, publication bias and significant between-study heterogeneity.¹⁵ Although this meta-analysis employed sound statistical methods, it was performed by only one author without the requisite multiple blinded reviewers of all articles incorporated into the data. On balance, there does seem to be support in the literature at this time for the efficacy of circumcision in reducing the acquisition of ulcerative STIs.

Conclusion

The data regarding the benefits of adult circumcision for the prevention of HPV are compelling. For other non-ulcerative STIs the benefits of circumcision appear minimal. In addition, it would appear that the current literature supports adult circumcision in the developing world for the prevention of ulcerative sexually transmitted diseases. The implications for HIV acquisition are important since ulcerative STIs are a known risk factor for this. The data regarding the benefits of adult circumcision for the prevention of HPV are also compelling. For other non-ulcerative STDs, the benefits of circumcision appear minimal. Overall, the effectiveness of circumcision in the prevention of any STI should be assessed

by taking all factors into account, including baseline prevalence of the disease in question, sexual behavior, use rates of condoms and sociodemographic group. Translating findings from adult studies, mainly performed in the developing world, into policies regarding neonatal circumcision in the developed world would be premature and inappropriate at this time.

*Department of Urologic Sciences, University of British Columbia, Vancouver BC; †Department of Urologic Sciences and Clinical Epidemiology, University of British Columbia, Vancouver BC

Competing interests: None declared.

This paper has been peer-reviewed.

References

- MacNeilly AE. Routine circumcision: the opposing view. *Can Urol Assoc J* 2007;1:395-7.
- Houle AM. Circumcision for all: the pro side. *Can Urol Assoc J* 2007;1:398-400.
- Gray RH, Kigozi G, Serwadda D, et al. Male circumcision for HIV prevention in men in Rakai, Uganda: a randomized trial. *Lancet* 2007;369:657-66.
- Bailey RC, Moses S, Parker CB, et al. Male circumcision for HIV prevention in young men in Kisumu, Kenya: a randomized controlled trial. *Lancet* 2007;369:643-56.
- Auvert B, Taljaard D, Lagarde E, et al. Randomized, controlled intervention trial of male circumcision for reduction of HIV infection risk: the ANRS 1265 Trial. *PLoS Med* 2005;2:e298.
- Aral SO, Holmes KK. The epidemiology of STIs and their social and behavioral determinants: industrialized and developing countries. In: Holmes KK, Sparling PF, Stamm WE et al. eds. *Sexually transmitted diseases*. 4th edition New York: McGraw-Hill; 2008:72-3.
- Veldhuijzen NJ, Snijders PJF, Reiss P, et al. Factors affecting transmission of mucosal human papillomavirus. *Lancet Infect Dis* 2010;10:862-74.
- Van Howe RS Human papillomavirus and circumcision: a meta-analysis. *J Infect* 2007;54:490-6.
- Rambout L, Hopkins L, Hutton B, et al. Prophylactic vaccination against human papillomavirus infection and disease in women: a systematic review of randomized controlled trials. *CMAJ* 2007;177:469-79.
- Mawer MJ, Tobian AAR, Kigozi G, et al. Effect of circumcision of HIV-negative men on transmission of human papillomavirus to HIV-negative women: a randomized trial in Rakai, Uganda. *Lancet* published online January 7, 2011. DOI:10.1016/S0140-6736(10)61967-8.
- Nielson CM, Schiaffino MK, Dunne EF, et al. Associations between male anogenital human papillomavirus infection and circumcision by anatomic site sampled and lifetime number of female sex partners. *J Infect Dis* 2009;199:7-13.
- Schiffman M, Castle PE, Jeronimo J, et al. Human papillomavirus and cervical cancer. *Lancet* 2007;370:890-907.
- Disaker RA, Peterman TA, Kamb ML, et al. Circumcision and STD in the United States: cross sectional and cohort analyses. *Sex Transm Infect* 2000;76:474-9.
- Mehita SD, Moses S, Agot K, et al. Adult male circumcision does not reduce the risk of incident *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, or *Trichomonas vaginalis* infection: results from a randomized controlled trial in Kenya. *J Infect Dis* 2009;200:370-8.
- Van Howe RS. Genital ulcerative disease and sexually transmitted urethritis and circumcision: a meta-analysis. *Int J STD AIDS* 2007;18:799-809.
- Turner AN, Morrison CS, Padian NS, et al. Male circumcision and women's risk of incident chlamydial, gonococcal, and trichomonal infections. *Sex Transm Dis* 2008;35:689-95.
- Weiss HA, Thomas SL, Munabi SK, et al. Male circumcision and risk of syphilis, chancroid and genital herpes: a systematic review and meta-analysis. *Sex Transm Infect* 2006;82:101-10.

Correspondence: Dr. Andrew E MacNeilly, Faculty of Medicine, The University of British Columbia Gordon & Leslie Diamond Health Care Centre Level 6, 2775 Laurel St., Vancouver, BC V5Z 1M9; amacneilly@cw.bc.ca