

## Male circumcision and HIV

### Recent developments – December 2006

On 13 December 2006, the US National Institutes of Health, after a recommendation of the Data and Safety Monitoring Board (DSMB), announced that it had decided to stop two trials in Kenya and Uganda because the interim results showed an approximate halving of risk of HIV infection in men who were circumcised.

The trial carried out in Kisumu, Kenya by researchers from the University of Nairobi, University of Illinois at Chicago, the University of Manitoba, and RTI International completed enrolment in September 2005 of 2784 men aged 18 to 24 years old and showed that adult male circumcision reduced by 53% the risk of becoming infected with HIV. It did not address whether male circumcision has any effect on the risk of transmitting HIV.

The trial, carried out in Rakai, Uganda by researchers from Makerere University, the Uganda Virus Research Institute, Johns Hopkins University, and Columbia University New York, completed enrolment in July 2005 of 4996 men aged 15 to 49 years old and showed that adult male circumcision reduced by 48% the risk of becoming infected with HIV. It did not address whether male circumcision reduces the risk of transmitting HIV.

A trial in South Africa, supported by the French Agence nationale de recherches sur le sida (ANRS) and known as the Orange Farm Intervention Trial, was stopped in 2005, when an interim analysis showed at least a 60% reduction in HIV infection among circumcised men.

A further trial, led by researchers at Johns Hopkins University, assessing the impact of male circumcision on the risk of HIV transmission to female partners is currently under way in Uganda, with results expected in 2008. The effect of male circumcision on reducing the risk of HIV transmission among men who have sex with men has not been studied in a randomized controlled trial.

### Background

Male circumcision is the surgical removal of the tissue covering the head of the penis. Data from observational studies, conducted since the mid 1980s, show that circumcised men have a lower prevalence of HIV infection than uncircumcised men. A UNAIDS study in four urban populations in sub-Saharan Africa investigated behavioural and other factors that could account for the large disparities seen in HIV prevalence across different African regions. Low prevalence of male circumcision and high prevalence of genital ulcers, which are more common in uncircumcised men, emerged as two of the principal determinants for the differences in HIV levels found in sub-Saharan Africa. A systematic review of eight prospective observational studies has shown that circumcised men have a lower risk of HIV infection, even after adjustment for differences in sexual behaviour. An observational study in Uganda observed a lower incidence of male-to-female transmission of HIV if the man was circumcised.

Several biological explanations for a protective effect of male circumcision against HIV infection have been proposed. One is that HIV can more easily reach HIV-1 target cells, including CD4+ T cells, macrophages, dendritic and Langerhans cells expressing CCR5 and

CXCR4 HIV-1 co-receptors which are present at high density in the inner foreskin epithelium and sub-mucosa. Whereas the outer surface of the foreskin and the glans penis have thick protective layers of keratin, the inner foreskin has almost none. Another possible explanation is that small tears in the delicate skin of the inner surface of the foreskin during sexual intercourse could allow a portal of entry for HIV. A further explanation is that whereas the circumcised penis dries rapidly following intercourse, the protected mucosal surface of the inner foreskin permits HIV and other pathogens to survive longer. Yet another is that male circumcision helps prevent some sexually transmitted infections, principally those characterized by genital ulcers that are associated with an increased risk of HIV infection.

### **Policy implications**

It is anticipated that news of these results will heighten interest in male circumcision from governments, non-governmental institutions, and the general public in a number of countries, in addition to increasing demand for male circumcision services.

Governments considering whether and how to enhance the availability of safe male circumcision services will need to consider how to contextualize male circumcision within comprehensive HIV prevention programming and what prominence to afford male circumcision services in relation to other health services given current financial and human resource constraints. At the same time, the risk of unsafe circumcision is high if safety is not accorded high priority. Meeting increasing demand while minimizing post-operative complications will require appropriately trained practitioners, adequate equipment, and close follow-up and care.

After considering ethical, human rights, financial, human resource, safety and other issues, countries that decide to expand male circumcision services will need to ensure that it is promoted in a culturally appropriate way and that it is implemented safely. Populations must understand that male circumcision does not afford complete protection against HIV infection, and that circumcised men can still become infected, even if the likelihood may be reduced compared to uncircumcised males exposed to similar risk. Education about the procedure itself and about its implications for HIV prevention will be essential. Men and women must understand that circumcised men can still become infected with the virus and if HIV-positive, can infect their sexual partners. Male circumcision should never replace other known effective prevention methods and should always be considered as part of a comprehensive prevention package, which includes correct and consistent use of male or female condoms, reduction in the number of sexual partners, delaying the onset of sexual relations, and HIV testing and counselling.

At the level of individuals, just as combination treatment for people with HIV-related disease is more effective than single drug therapy, combination prevention for sexually active people is more effective than reliance on a single HIV prevention method. Men who are at risk of HIV exposure, regardless of their circumcision status, should be counselled to use condoms and reduce concurrent partnerships. Correct and consistent condom use provides protection against unintended pregnancies, HIV infection or re-infection, and other sexually transmitted infections. Male circumcision affords lower protective efficacy against HIV infection than correct and consistent condom use, has a lower or uncertain protective efficacy against some sexually transmitted infections and provides no protection against pregnancy.

### **Current UN Work Plan activities**

WHO is coordinating the preparation and implementation of the Second UN Work Plan on Male Circumcision and HIV which focuses on addressing the technical support needs of countries which opt to include male circumcision within comprehensive HIV prevention

programming as a result of the growing evidence of the partially protective effect of male circumcision on HIV.

UNAIDS has been coordinating implementation of the first UN Work Plan on Male Circumcision and HIV, which focused on increasing the safety of current practices and assisting countries to assess technical, financial, human rights, legal, ethical and practical aspects relevant to deciding on the role of male circumcision within comprehensive HIV prevention programming.

WHO, UNAIDS and their partners will continue to work together to provide coordinated, consistent, and up-to-date guidance and support to governments and other development partners regarding male circumcision and HIV, including in both service delivery and monitoring. These groups will also work cooperatively to identify the best means of increasing the delivery of safe circumcision services in countries that choose to do so.

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