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## **Study Presents New Information on Male Circumcision to Prevent Spread of HIV in Africa**

*Preliminary data highlight importance of wound healing and effects on women*

Montreux, Switzerland (March 6, 2007) – Researchers at a World Health Organization and UNAIDS consultation on male circumcision today presented preliminary data from a trial examining circumcision's effects in HIV-infected men and the impact on HIV transmission from these men to their female partners. The preliminary results highlight the need for men to refrain from sex following surgery until their wounds are completely healed and for women to be fully informed about the need for sexual abstinence until there is complete wound healing in their male partners. The data were announced today by researchers from the Rakai Health Sciences Program and Makerere University in Uganda and the Johns Hopkins Bloomberg School of Public Health in Baltimore, Md. The preliminary data were made available to the WHO/UNAIDS meeting because they were deemed to be relevant to the development of guidance for countries regarding male circumcision and HIV prevention.

Previously released findings from three other trials showed that male circumcision provides HIV-uninfected men with 50-60 percent protection from acquiring HIV through sex with infected female partners. The study announced today investigated the impact of circumcising HIV-infected men on HIV transmission to their uninfected female partners, as well as safety of surgery and risks and benefits for these HIV-infected men.

The data reported today come from a randomized trial in Rakai, Uganda that follows 997 HIV-infected men. A proportion of these men had HIV-uninfected long-term female partners who were enrolled and followed. The trial was undertaken because prior observational studies suggested that circumcised HIV-infected men might be less likely to transmit HIV to their female partners than uncircumcised HIV-infected men. These new findings are derived from an interim analysis reviewed by the trial's Data and Safety Monitoring Board (DSMB) on March 1, 2007.

The new data indicate that rates of post-surgical complications are similar in HIV-infected and HIV-uninfected men. Preliminary data from the study also indicated that HIV-infected men who were circumcised had a 50 percent lower rate of genital ulceration.

Although the results were not statistically significant, the data also indicate a trend toward increased risk of transmission from circumcised men who resumed sex before their wounds were certified to be healed.

At the time of the DSMB review, there were 70 HIV-infected men with initially uninfected partners who had been concurrently enrolled in the circumcision arm of the trial and had at least one follow up visit over two years. Among these couples, 11 women became infected. In the control arm, there were 54 HIV-infected men, who remain uncircumcised, with concurrently enrolled, initially uninfected female partners with at least one follow up visit over two years. During follow up, four of these women became infected. These data did not reach statistical significance. Preliminary data suggests that the increase in transmission was likely attributable to men resuming sex before their wounds were certified to be healed. This information could change as further data are accrued.

The preponderance of the infections in both arms occurred during the first 0-6 month follow up interval. Therefore, further analyses focused on this early 0-6 month period. Preliminary data looking at 113 HIV-infected men whose HIV-uninfected female partners were followed for the first six months indicate a trend toward increased risk of transmission from circumcised men who resumed sex before their wounds were certified to be healed. These data also did not reach statistical significance.

In the first six-months following surgery, there were three transmissions to women from the 12 HIV-infected circumcised men who resumed sex before complete wound healing was certified. By contrast, from 55 HIV-infected circumcised men who waited to resume sex until after certified wound healing, there were six transmissions to initially uninfected women. The latter is similar to the proportion of transmissions from uncircumcised HIV-infected men in the control arm of the trial (four transmissions among 46 men to their initially uninfected female partners).

Post-surgical wounds normally took about four weeks to heal completely, and participants were strongly advised to abstain from sex until healing was certified through examination by a clinical officer. All study participants, both men and women, were provided with repeated HIV prevention education, offered free HIV counseling and testing, and provided with free condoms. HIV-infected study participants have access to free HIV care and antiretroviral treatment if indicated.

The trend toward a higher transmission rate from HIV-infected men who resumed sex before there was certified wound healing raises important questions about how to design circumcision programs in Africa, where many men do not know their HIV status. These issues will be considered by the WHO/UNAIDS consultation. This also highlights the need to reinforce other HIV prevention messages, such as abstinence, reducing the number of sex partners, and correct and consistent use of condoms.

“Because the total number of men who resumed sex before certified wound healing is so small, the finding of increased transmission after surgery may have occurred by chance alone. However, we need to err on the side of caution to protect women in the context of any future male circumcision program,” said Dr. Maria Wawer, the study’s principal investigator and a researcher at the Johns Hopkins Bloomberg School of Public Health. “Women make up a majority of people living with HIV in Africa, and these results demonstrate that women need to be educated about the risks and benefits of male circumcision. They need to be full participants in HIV prevention programs.”

Earlier observational data suggesting HIV-infected men who were circumcised transmit the virus less frequently to their female partners involved mostly men who had been circumcised before they were sexually active. The current trial found that adult male circumcision does not provide protection to female partners of HIV-infected men within the first six months after surgery. Nevertheless, currently available data cannot assess whether a protective effect might result in the longer term. The investigators noted that in trials of circumcision among HIV-uninfected men published last month in *The Lancet*, benefit was not observed until six to 12 months after surgery, suggesting that wound healing might also have been a relevant factor for the acquisition of HIV by HIV-uninfected men.

“Male circumcision has the potential to prevent millions of HIV infections, and we must think clearly and carefully about how best to safely expand access to the procedure in Africa,” said Dr. David Serwadda, the principal investigator from the Rakai Health Sciences Program in Uganda. “Male circumcision should always be performed in a professional surgical setting, with appropriate HIV-prevention education and follow-up care. Expanding healthcare capacity, training healthcare workers, and developing sound policies can help ensure that circumcision is safely provided to men.”

The trial will continue to follow participants and collect additional data on the longer term impacts of male circumcision performed in HIV-infected men. Enrollment into the study was closed when the trial’s DSMB found that enrolling additional participants would be unlikely to prove the investigators’

hypothesis that circumcision of HIV-infected men reduces HIV transmission to women over the short-term.

“While male circumcision has extraordinary potential to prevent HIV infection, these new findings remind us that we must proceed with thought and care in developing strategies to expand male circumcision in Africa,” said Dr. Kevin De Cock, the head of the World Health Organization’s HIV/AIDS department. “Circumcision of adult males is a surgical intervention that needs to be performed by trained medical personnel, and issues such as wound healing, condom use, other prevention approaches, and HIV testing must be considered very carefully. Even under the best of conditions, male circumcision must be implemented as part of a comprehensive program for HIV/AIDS prevention, treatment and care.”

The data announced today will be examined this week, along with data from other recent trials, at an international consultation convened by WHO and the UNAIDS Secretariat. The consultation will address the full range of policy, operational and ethical issues that will help guide countries about where and how male circumcision can be best implemented, promoted and safely performed.

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