

Caution on circumcision cuts South Africa's AIDS researchers

When scientists announced in July that circumcising adult males can drastically cut the rate of HIV infection, international agencies urged caution, saying it would be best to wait for results from further studies. But in South Africa, where HIV prevalence is the highest in the world, some experts say there's little time to waste.

Since 1986, there have been more than 40 observational and biological studies indicating that circumcision can protect men from HIV infection (*Lancet* 5,165–172; 2005, *AIDS* 14, 2361–2370; 2000). But the latest study, led by the Agence Nationale de Recherches sur le SIDA in Paris, is the first randomized control trial.

The researchers followed 3,274 sexually active men between the ages of 18 and 24 in the poor, high-risk community of Orange Farm near Johannesburg. Circumcising the men cut their risk of infection with HIV by about 60%, they found. Two other large randomized trials funded by the US National Institutes of Health are under way in Uganda and Kenya (*PLoS Med.* 2, e293).

In some studies, as many as 70% of participants said they would be willing to be circumcised if it could protect them from HIV infection, notes

Bertran Auvert, lead investigator of the French study. The next step, he says, is to implement circumcision along with other interventions such as condoms and STD clinics.

But others are more cautious. "I think if the studies consistently show an effect, then we're looking at a potentially valuable intervention for controlling HIV transmission," says Jimmy Volmink, director of the South African Medical Research Council's Cochrane Centre. Although the study shows some protection, it's not clear whether that protection will remain effective in the long term, he says. "I feel one controlled trial done in a particular context is not sufficiently strong evidence to start implementing wide-scale policy change."

Before applying the results, scientists will have to consider cultural issues, Volmink adds. For example, some South African tribes such as the Xhosa and the Pedi follow certain rituals in circumcising young men. In July, local newspapers reported that more than 20 young men had died in South Africa as the result of botched circumcisions. In some cases, practitioners use the same blade to circumcise several boys,

potentially increasing the risk of HIV infection. Spreading the message that circumcision prevents HIV infection could increase the number of unskilled—and unsafe—practitioners, he says.

There are biological reasons that might explain how circumcision cuts HIV risk. Langerhans immune cells found under the foreskin are prime targets for HIV. The virus can also survive longer in the moist environment between the glans and foreskin. Because lesions from sexually transmitted diseases that increase the risk of HIV infection often occur under the foreskin, removing it could reduce the risk. Circumcision may also reduce the risk of invasive penile cancer in men and cervical cancer in their female partners.

The ongoing studies are likely to confirm circumcision's protective effect in HIV infection, so policymakers should start planning to implement it now, says Francois Venter, clinical director of South Africa's Reproductive Health Research Unit. "If we had an AIDS vaccine this good, we would roll it out tomorrow," he says. "There wouldn't be a debate. We would vaccinate the whole country."

Lauren Beukes, Cape Town

Price of mice to plummet under NIH's new scheme

For many scientists, mice are the animal models of choice because they are supposed to be cheap and easy to manipulate. But in recent years, neither has been particularly true, forcing scientists to shell out precious grant money for mice lacking certain genes.

The US National Institutes of Health (NIH) is embarking on an ambitious initiative to make the animals affordable. The agency hopes to build an inventory with about 25,000 mouse lines—although a few practical hurdles remain.

With an initial \$10 million, the NIH has already purchased 251 knockout mouse lines from Deltagen and Lexicon Genetics, the two primary suppliers. In exchange, the companies will curtail intellectual property rights and provide data on the physical characteristics of each mouse line. Depending on the response from the research community, the NIH may buy up to 2,500 more lines from the companies, says Chris Austin, director of the NIH Chemical Genomics Center.

Researchers rely on knockout mice, which lack specific genes, to study disease and screen drugs. Of the nearly 25,000 genes in the mouse genome, about 10,000 have thus far been knocked out. Of those, about one-



Mighty mouse: Making a single line of knockout mice can take up to a year and cost \$100,000.

third of the mouse lines are owned by private companies or scattered among various academic and nonprofit labs. Three mouse banks partially funded by the NIH store most of the remaining lines.

Making a new knockout line is not easy: it can take up to a year and cost up to \$100,000, notes Muriel Davisson, director of genetic resources at The Jackson Laboratory in Bar Harbor, Maine, one of the three NIH mouse banks.

Buying a mouse line from a company is no cheaper. For instance, California-based

Deltagen charges \$26,200 for two pairs of live knockout mice. Additional embryos, sperm and embryonic stem cells can run up another \$15,000. Even then, the mice often come attached with intellectual property strings. Company employees sometimes co-author papers and some companies demand royalties on any discoveries or products.

The NIH mouse banks charge about \$115 per mouse and hold no licensing restrictions for academic researchers. The agency plans to move the purchased lines to mouse banks at the Jackson Laboratory, the University of California in Davis and the University of North Carolina. It will also build a catalog of mice made in academic labs and collaborate with other international programs, including one in the European Union, to avoid duplication, Austin says.

The mouse banks will store the majority of the mice as frozen embryos and thaw them as needed. But researchers often prefer live mice, says Austin, and cages take up a lot of space, leading to concerns about the banks' storage ability. "It's a very real problem," says Austin. "The repositories will have to add capacity in order to take on this large amount of mice."

Emily Waltz, New York