

International Rectal Microbicide Working Group (IRMWG)
Teleconference – January 19, 2007
Notes by Linda Hughes – (thanks Linda!)

Today's call will focus on the subject of Male Circumcision and its preventative effect on the transmission of HIV. Slides accompanying today's presentations provided by Dr. Tim Farley and Dean Peacock can be accessed www.lifelube.org

Jim Pickett takes a moment to thank Roy Wadia and Jerry Galea for putting this call together and reminds us all to Recruit, Recruit, Recruit to the IRMWG. There are currently more than 350 IRMWG participants from 35 countries. Invite anyone who may be interested in simply learning more about our work or becoming more involved. Tell them to send Jim Pickett an email to sign up (jpickett@aidschicago.org)

Here is the roll call. Please send corrections/additions to jpickett@aidschicago.org.

1. Gus Cairns, London
2. Marina Seval, France
3. Andrew Brannigan, Israel
4. Philip Bates, Vancouver
5. Shalonie Evans, CA
6. Robert Reinhardt, CA
7. Charlie Price, UCLA
8. Janet Madsen, Vancouver
9. Steve Wakefield, WA, HIV Vaccine Trials Network
10. Dr. Ian McGowan, UCLA (IRMWG Steering Committee)
11. Ross Cranston, UCLA
12. Linda Hughes, WA, Polydex
13. Jodi Jacobsen, Washington, D.C. Center for Health and Gender Equity
14. Jim Pickett, Chicago (IRMWG Steering Committee)
15. Ellen Marshall, CO
16. Trina Nelson, Chicago
17. Dr. Rowena Johnston, NY amfAR (IRMWG Steering Committee)
18. Deidre Grant, NY, AVAC
19. Mitchell Warren, NY, AVAC
20. Julie Davids, RI CHAMP (IRMWG Steering Committee)
21. Lei Chou, NY CHAMP
22. Sean Barry, NY CHAMP
23. Naomi Goodman, MA
24. Sheely Thompson, D.C.
25. Oren Siffon, D.C.
26. Michelle Ball, AIDS Committee of Ottawa, Ottawa
27. Michelle from AVAC, NY
28. Jerry Galea, Lima, Peru (IRMWG Steering Committee)
29. Ximena Salazar, Lima *Universidad Peruana Cayetano Heredia*, School of Public Health, Lima, Peru.
30. Ana Maria Rosasco, Lima *Universidad Peruana Cayetano Heredia*, School of Public Health, Lima, Peru.
31. Eddy Segura, Lima *Universidad Peruana Cayetano Heredia*, School of Public Health, Lima, Peru.
32. Jose Pajuelo, Lima *Universidad Peruana Cayetano Heredia*, School of Public Health, Lima, Peru.
33. Manju Chatani, Accra, Ghana, AMAG, (IRMWG Steering Committee)
34. Kevin Fisher, AVAC

35. Dawn Smith, CDC, Atlanta
36. Adam Graham, Ottawa
37. Marc-Andre LeBlanc, Global Campaign for Microbicides, Ottawa (IRMWG Steering Committee)
38. James Sykes, D.C., AIDS Institute
39. Cindra Feuer, NY
40. Dr. Tim Farley, Geneva, Switzerland
41. Dean Peacock, Cape Town, SA

Dr. Tim Farley began with his presentation.

Very impressed by the global diversity of the callers on today's teleconference, hello to all my friends around the world and thank you for being here today.

Dr. Farley is the Coordinator, Control of Sexually Transmitted Infections, World Health Organization

The first slide is the Outline of topics I will be covering today. As you can see, I will be discussing the evidence of protective effect of Male Circumcision (MC) against female to male HIV transmission and look at some ecological, randomized and observational trials.

Dr. Farley read the balance of his Outline slide but there was significant background interruption. Everyone was asked to put his or her phone set on MUTE to continue.

The 3rd slide is a map of the world where circumcision prevalence rates are noted in various colors. Note that circumcision is highly prevalent in West Africa where it is common practice to perform neonatal circumcision on infants, the rate is not so high in mid Africa, where the practice is performed mostly in adolescent boys more as a right of passing ceremony and sometimes entails just a small incision or slit and does not necessarily remove a significant portion of the foreskin, and in Europe where MC is relatively rare, usually performed for medical reasons rather than cultural.

MC is highly prevalent in Africa, but many are performed by Traditional circumcisers for cultural and religious reasons. It can be a simple procedure, but there are risks associated with the procedure and this particular point is heavily weighed at WHO – the benefits against the potential harm.

The benefits of MC are many as outlined in the next slide. This first report on the effects of circumcision was a well-conducted study. The data showed that while urinary tract infections in infants are not necessarily rare, uncircumcised boys had a 12-fold higher risk of contraction.

The following benefits are some of the first ecological data we have and are mostly observational – they were not conducted as separate studies. The reductions in Chancroid and penile cancer incidence is notable, a 63% decrease in human papilloma virus transmission with circumcised men is considerable. Cervical cancer rates in women partners of circumcised men also decreased by 2 to 6%.

The next slide graphs the HIV prevalence with MC prevalence. It's nearly 20 years old now, from 1989 but clearly shows the declining HIV prevalence where MC is widely practiced.

Bob Bailey and Don Halperin did a Lancet paper on MC around 2000 or 2001 I believe. From it, these next slides further illustrate where MC is low, below 20%, HIV is higher and where MC is above 20%, like in the West African countries, prevalence is much lower. We then illustrate this with another chart showing prevalence rates by country. Again, prevalence rates are highest where MC rates are lowest, as in some African countries where HIV prevalence is more than 25% and MC is performed the least. Prevalence rates drops to nearly 2% where the MC is 80%.

Lower rates are shown in Asian countries, but similarly the rates of HIV are higher in areas where MC is lowest. China doesn't have a high prevalence of MC but still has relatively low HIV prevalence.

In the next slides the adjusted odds ratio is demonstrated, where the lines represent different studies and each point represents the protective effects of MC. This is quite interesting as the data is adjusted to include behavior issues and the effects of MC. For instance the Rakai study reported 0 infections among the 50 circumcised participants - this is really very impressive but is still only observational – not really sure how much weight we can put on this data, but here and on the next slide where the rates of transmission of HIV from circumcised and uncircumcised men to women partners is demonstrated, uncircumcised men with low viral loads had low transmission to women rates and the higher viral load men (over 50,000) has a negligible rate of protection to women whether circumcised or not. In any event, the authors think there is a protective rate of circumcision.

Three MC trials were launched in 2000 – 2001 – 2002. Orange Farm was the first to publish, not the first to complete, but the first to publish. MC is fairly common practice here and it is provided as a medical service, and was offered for free. A narrow age range of participants was selected for this trial, completed in April of 05. The slide says that analysis was expected in November 04, this is an error and should say November 05.

In Rakai, the age range was significantly wider and a greater number of men participated (5000). In Kisumu, a smaller number of men were enrolled.

In the Orange Farm trial, of the 1,538 men enrolled in the intervention arm, 18 infections resulted. In the 1,590 men from the control group, 51 infections resulted. There is not a major difference in the time periods noting the numbers of HIV conversion early in the trial, the next few and the last few months of the trial, but consistently across the time periods there is a measurable protective effect to intervention by MC. In this group, some men had circumcision performed at the beginning of the trials and experienced an increased protective effect.

The Rakai and Kisumu trial results are on the next slide, Rakai experiencing a 48% reduction in risk of HIV transmission and Kisumu experiencing a 53% reduction.

This data is uncannily close to the observational data.

- Side note mentioned here about future discussions on policy shift to account for preliminary data but realistically won't happen until after results of ongoing studies is received.

Full trial analysis is ongoing and is expected some time in mid 2007. These results are not likely to be presented at CROI.

Next we move on to Biological Mechanisms. In a healthy penis the preputial sac is an immunologically active environment. The foreskin tissue is rich in HIV target cells. Some MC procedures remove the entire inner aspect of the foreskin, and some MC's leave quite a substantial amount of skin behind. A full circumcision exposes the glans and can result in keratinization of the glans and shaft, thereby making the penis less vulnerable to infection. The intact foreskin is also associated with problems related more to infants and young boys than to grown men.

Another trial is still enrolling, looking to determine protective rates on women partners of circumcised men. Evidence is intriguing so far, but scanty. Follow up with the women partners of the circumcised Rakai study participants will be available in 2008.

On the next slide, ratios of HIV transmission among MSM was studied but it is difficult to determine whether these studies accounted for insertive/receptive differences which could potentially have a high

impact on the data. WHO and UNAIDS are working to concentrate efforts to adapt studies to monitor this.

Next we look at various implications of the data. Where there is a low MC prevalence, the impact on HIV transmission appears to be high. We need to be concerned about messaging to avoid undermining existing safer sex messages and strategies, and in high risk groups, even if MC delays infection, it may not for long. More studies are needed to determine the impact realized by insertive AI and where there may not be much data from receptive AI, especially from those partners who are exclusively receptive, then MC is unlikely to have any impact.

Look to some time in March for more data on this.

Next we move on to the current priorities of the UN partners. Of course our primary target is the adolescent, young men, where we will realize the biggest return – impact on HIV.

One of the enormous challenges is with improperly trained service providers. In some places like Swaziland and Lesotho there are no MC service providers. Neonatal MC is another challenge – it may be somewhat difficult to impose MC on a baby or small boy that is unlikely to face HIV for another fifteen to twenty years. Other key challenges we face are itemized on the next slide, one being that we must consider circumcision campaigns carefully so as to avoid inadvertently promoting high risk behavior.

Questions for Dr. Farley will be reserved to the end of both presentations. Now we invite Dean Peacock to walk us through his.

Dean Peacock introduced himself, from Cape Town, a member of the Sonke Gender Justice Network, an NGO focused on gender, HIV/AIDS, and human rights. And although not an expert in male circumcision, their group is looking into the support of MC campaigns in Swaziland and Lesotho. Sonke is working with USAID and others, currently seeking answers as to how to bring on and scale up efforts to provide MC services. A recent WHO meeting led us to the expectation that MC would be scaled up and Sonke embarked on several activities, including acts of civil disobedience to put pressure on the necessary issues.

We advocate for ARV's, first for pregnant women and then others in affected communities. We are looking into several of the issues facing a scale up of a male circumcision campaign, including the role of traditional circumcisers and health systems capacities. There are very few medical doctors available and therefore some MC is being performed by nurses, and this task-shifting issue is one that needs further advocacy. More resources will be necessary to properly train these nurses and paramedics in the performance and care of MC.

There is a consensus among UN agencies that scale up needs to occur within health service facilities but there has been very little action from governments, following the results of the Orange Farm MC trials. Our ART experience tells us that advocacy and activism will be essential to maintain pressure toward the inevitable scale up of MC programs in accredited health care facilities.

There are a number of traditional circumcisers – but we do not have very many details about the MC practices of these traditional service providers. Certainly there are known cases of amputation and onset of infections and that raises a lot of questions about the nature of the practice of traditional circumcisers.

(At this point in particular, there was a great deal of audio interference in Mr. Peacock's presentation from a participant on the call whose breathing into the phone obliterated some of what was being said. Please accept the writer's apologies for incomplete notes at this juncture)

In some countries traditional circumcisers are keen to play a role. HIV has overwhelmingly impacted many health care systems, and safe and effective prevention is desirable by medical professionals as well as the traditional providers. With long wait lists at some health care facilities, it is imperative that we maintain communication and planning with the traditional providers, not only to advocate for resources, but also to ensure that MC is one part of a broader prevention package.

Part of that broader prevention pack will have to include accompanying messages of gender equality and gender violence, a redefining of gender equitable models of manhood, a call for more money to be shifted into biomedical intervention and addressing concerns that MC will detract from efforts to address social and structural drivers, all the while maintaining a positive position on the use of condoms, AIDS education, treatment and stigma reduction.

Following the two presentations, questions from the teleconference participants were solicited. Dr. Farley began by picking up on some of Mr. Peacock's good points on the traditional MC providers. In East Africa, traditional circumcisers perform most circumcisions and we are unclear as to what to do about them.

We want to scale up medicalized services, but one of the problems is that only a small number of people are licensed to perform anesthesia. Some of the traditional methods of MC are simply unacceptable and it would be helpful if we could get the two factions to work in parallel, either by bringing the traditional circumcisers into the medical facilities or to implant medical resources into traditional practice, but this challenge is also country specific and would need to be tailored for appropriateness.

For instance, in Lesotho, the traditional circumcisers perform the ritual with a little nick of the dorsal slit, leaving a majority of the foreskin behind. In such cases we are seeing areas where there may be a high rate of circumcision but also a high rate of HIV prevalence.

We are however seeing rapidly evolving practice among the traditional circumcisers in Lesotho; it is excellent that cultural minds are so malleable and receptive to the findings of the research.

Q: How will this information affect the HIV prevention trials, specifically the rectal microbicide studies?

A: Farley - As circumcision becomes more acceptable, it would ideally be promoted as part of the prevention package, much the same way condoms or safer-sex counseling are being used today.

Q: What about the protection of women, or AI partners?

A: Farley - Obviously MC is not going to offer any further protection from HIV to receptive AI partners, but would have an impact on the protection of insertive AI partners.

Q: Farley - What is the acceptability of these studies, where are we trying to rollout MC, any data?

A: Quite a lot of research is being done on the acceptability issue, for instance in Botswana, Lesotho and KwaZulu Natal. People are devastated by HIV and so are coming to terms with the protective aspect of MC, saying 'OK - if it is going to have an effect of protection, then I don't mind'. Oddly, it seems easier to get them to adopt male circumcision than to stop female mutilation.

Grandmothers and mothers are bringing their baby boys into clinics in overwhelming numbers. With limited resources available these guardians were being turned away and told that MC could only be performed on babies whose health may be in jeopardy or some medical reason existed to do it. Word got out and soon these same grandmothers and mothers were revisiting the clinics claiming their sons

and grandsons suffered from a sore penis or some other malady they thought might convince the medical staff to circumcise their babies.

Women can play a large part in this cultural shift as well, simply by saying "I prefer sex with a circumcised man", in which case men would queue up for the procedure.

Q: Are there any studies on cost-effectiveness?

A: Farley - Yes, two or three have been published on cost-effectiveness of MC. It really is quite cost-effective. A review of the data available suggests that it might cost a few thousand dollars per HIV intervention, which is remarkably inexpensive, all things considered.

No more questions. Thank you all for participating. Notes will be forwarded by email in the coming days. Stay tuned for future IRMWG teleconferences and other notifications.