HIV infection and circumcision: cutting through the hyperbole

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Abstract

The objective of this study was to determine whether the justifications given for promoting mass circumcision as a preventive measure for HIV infection are reasonable and whether mass circumcision is a feasible preventive measure for HIV infection in developing countries.

The medical literature concerning the practice of circumcision in the absence of medical indication was reviewed regarding its impact on HIV infection and related issues. The literature was analysed with careful attention to historical perspective.

Our results show that the medical literature supporting mass circumcision for the prevention of HIV infection is inconsistent and based on observation studies. Even if the two ongoing randomised controlled trials in Africa show a protective benefit of circumcision, factors such as the unknown complication rate of the procedure, the permanent injury to the penis, human rights violations and the potential for veiled colonialism need to be taken into account. Based on the best estimates, mass circumcision would not be as cost-effective as other interventions that have been demonstrated to be effective.

Even if effective, mass circumcision as a preventive measure for HIV in developed countries is difficult to justify.

INTRODUCTION

The explosion of publicity accorded to the HIV/AIDS pandemic can in part be attributed to the lack of clear understanding of the disease mechanism and the apparently inescapable mortality attributed to the acquisition of HIV. The public's awareness and fear of HIV have resulted in changes in sexual behaviours such as increased condom use, which has been less comprehensive and long-lasting than originally expected.[1] Regrettably, some have capitalised on the fear generated by the HIV/AIDS pandemic to promote personal or political agendas.[2-5] In the medical establishment, this has been manifested in the scientifically dubious promotion of male circumcision as a preventive measure for HIV infection.[2]

HISTORY OF CIRCUMCISION PROMOTION

This is not the first time that circumcision has been promoted as a panacea for an incurable disease. As a medical procedure, circumcision was first introduced in the nineteenth century in English-speaking countries as a means of preventing and 'curing' masturbation, which was then believed to cause everything from epilepsy, insanity, tuberculosis, spinal paralysis, to hip dysplasia.[6] As the germ theory of disease developed and the understanding of disease processes improved, the true aetiologies of the illnesses for which circumcision was believed to hold the cure were elucidated. During the Cold War, mass involuntary circumcision of the newborn was implemented in the USA, giving the practice a cultural foothold.[6] New medical-sounding justifications, however, were sought to justify its continued use as a routine neonatal surgery since the traditional justifications for preventing masturbation and 'nervous diseases' were no longer as persuasive to the public or the medical profession. The prevention of cancer, sexually transmitted diseases (STDs) and urinary tract infections were each in turn invoked to justify infant male circumcision, although the medical evidence supporting such claims ranged from paltry to imaginary.

A clear pattern has emerged: any incurable disease that happens to be the focus of national attention at any given time will be used by US circumcision advocates as an excuse for the continued imposition of mass circumcision. In the 1870s, epilepsy was the focus of national attention, so circumcision advocates claimed that circumcision could cure and prevent epilepsy.[6] In the 1940s, STDs were the focus of national attention, so circumcision advocates claimed that circumcision could cure and prevent

the spread of STDs.[6] Likewise in the 1950s, cancer was the focus of national attention, and again circumcision advocates claimed that circumcision could cure and prevent a variety of cancers including penile cancer, cancer of the tongue, prostate cancer, rectal cancer and cervical cancer.[6] Since the late 1980s, HIV and AIDS have become the focus of national attention, and circumcision advocates have, predictably, claimed that circumcision can prevent HIV infection.[6]

LINKING CIRCUMCISION AND HIV/AIDS

Against this historical backdrop, the HIV/AIDS pandemic is merely the latest incarnation of a 130-year-old pattern of circumcision promotion by a small, but very influential, portion of the medical community in circumcising first world countries.[7-12] The idea that circumcision can prevent AIDS was developed by Fink, a long-time advocate of mass circumcision. Fink introduced the hypothesis in a letter to the *New England Journal of Medicine*,[13] which he later admitted was based purely on speculation rather than hard data.[14] Seeking to capitalise on public anxiety over the spread of HIV, other advocates of mass circumcision sought to develop Fink's hypothesis by producing geographical analyses of Africa, which studied maps rather than men, which they argued could be used to legitimise mass circumcision in the US. Using decades-old anthropological data and extrapolating HIV incidence rates, an association between the foreskin and HIV was suggested.[15] Next came a number of observational studies suggesting an association between the foreskin and an increased risk of HIV infection in men, mostly in Kenya, who exhibited high-risk behaviours.[16, 17] These studies compared disparate populations that were distinguishable on other relevant independent variables, such as religion, social class, tribal affiliation, sexual practices and presence of genital ulcer disease. Subsequently, the degree of association of the initial studies and the infectivity attributed to the foreskin could not be replicated in the same population by the same team of investigators.[18]

Partner studies in which associations were suggested between the HIV status of a woman and the circumcision status of her sexual partner have overall failed to support an association.[19, 20] Likewise, general population surveys have, as a whole, failed to demonstrate a strong association.[19, 20] It is only when limiting the analysis to African studies and using values obtained following multivariate analysis that an association can be extracted from these studies.[21] One of the challenges in interpreting these various observational studies is determining whether circumcision status may be a risk factor or a marker for other risk factors. The fundamental flaw in multivariate analysis is that to be accurate it is assumed that the variables controlled for are independent of one another. Many of these variables, including sexual, religious and hygienic practices, as well as economic status, appear to be linked to tribal affiliation, which in turn is strongly correlated with circumcision status.[22] These multiple, highly-correlated, confounding factors influencing sexual behaviours and HIV susceptibility create a co-linearity problem that can make these regression models unstable and yield unreliable results. Consequently, without more reliable data it is irresponsible to place blame for HIV's spread on normal penile anatomy.

Many of the studies suggesting an association between circumcision status and HIV infection tested a wide assortment of factors, fishing for significant risk factors without making the proper adjustments for multiple comparisons. As a result, many of the positive associations asserted could be due merely to oversampling.

Meta-analysis has demonstrated significant between-study variability independent of the vagaries of geography, study design and circumcision's prevalence within a community,[19] and has suggested the possibility of publication bias, whereby studies failing to find a correlation between circumcision status and HIV infection are either never submitted for publication or are passed over by editors.[20] Observational studies, when compared to randomised controlled trials, have been shown to consistently overestimate odds ratios by 30%.[23] In light of this unexplained heterogeneity and possible publication bias, any conclusion based on these observational studies should be viewed with scepticism.[24]

On the basis of weak scientific evidence, many circumcision proponents have called for universal circumcision in Africa.[2-4] Although the next logical step in this scientific inquiry might be a randomised controlled trial, problems exist with such a project. A trial involving permanent amputation of a body part, the benefit of which is largely unproven, is fraught with ethical pitfalls and would not be likely to be approved in a developed nation. The subject would certainly need to be fully informed, and the potential for manipulation of the information provided would need to be prevented. Studies have already demonstrated that pro-circumcision propaganda can effectively influence attitudes regarding circumcision.[25-30] Despite the clear ethical contraindications, two randomised controlled trials to determine if a relationship exists between HIV status and circumcision to be undertaken in Africa have received funding from the US National Institutes of Health. Both studies are markedly overpowered so as to find a statistically significant difference where a significant clinical difference may not exist.[31-33] A report in the lay literature suggests that compliance following randomisation may pose a serious threat to the study's completion.[34] Therefore, the subsequent analysis must employ an intent-to-treat approach, as otherwise serious bias would be introduced into the results.

FACTORS TO CONSIDER BEFORE RECOMMENDING A CIRCUMCISION PROGRAMME

In the unlikely event that a randomised controlled trial demonstrates a benefit, the decision to recommend universal circumcision in Africa would need to take several additional factors into consideration.

1) How does universal circumcision compare in efficacy, cost and complications to other interventions aimed at reducing HIV infection?

The aggressive diagnosis and treatment of STDs and various treatment modalities in the African context have been shown to be clinically effective and reasonably cost-effective.[35-37] Our preliminary calculations indicate that to be competitive with these proven interventions, even granting for the sake of argument the proponents' claims for the effectiveness of circumcision, a circumcision would need to cost less than $1.52 (unpublished data). Estimates of the costs of a sterile circumcision in Africa, excluding the cost of treating any complications from the surgery are $15.[38] Surgery

thus does not seem an economically or a medically logical intervention for this infection. Since the spread of HIV infection is primarily caused by behaviour, many AIDS researchers believe that behavioural interventions hold the most hope in the long term.[39]

2) The surgical complications of the procedure, which are believed to be higher in developing nations, need to be considered. Although no study has been completed to address this issue comprehensively, circumcision in developing nations entails additional risks of tuberculosis,[40] tetanus,[41, 42] and severe complications.[43, 44] Immediate complications following neonatal circumcision in North America occur in 2% to 6% of infants,[45, 46] while delayed complications, such as meatal stenosis requiring meatotomy, occur in 5% to 10% of circumcised boys.[47]

The US pro-circumcision information campaigns targeted at Africa are beginning to increase the number of requests for the procedure from African men who have been understandably misled into believing that it will make them immune to HIV infection.[25-31] If this pattern continues, the demand for circumcision may outstrip the capacity to provide the procedure in a controlled setting. Non-sterile procedures performed by untrained individuals, who would undercut the price of sterile procedures, would result in a higher rate of complications and perhaps a higher rate of HIV infection. Ironically, a higher number of boys in Africa could then die at the hands of their circumciser than the total that ostensibly might have been protected from HIV infection. Without better information regarding complications, a recommendation for universal circumcision is unfounded.

3) The permanent untoward effects of the amputation have been largely ignored. Circumcision removes the vast majority of fine-touch neuroreceptors found on the penis. Studies of the foreskin have revealed it to contain highly complex, specialised tissue.[48] By contrast, the glans has primarily free nerve endings, which can only sense deep pressure and pain.[49] The anatomical changes caused by circumcision may be responsible for the differing sexual practices seen in circumcised men,[22] as well as for coital techniques that make the experience less satisfactory for their female partners.[50] Those touting the benefits of the amputation of the foreskin appear universally unaware or unwilling to acknowledge its immunological, protective and erogenous functions. This is to be explained by the fact that circumcision advocates are almost always circumcised men from circumcising cultures.[51]

4) Careful scrutiny must be given to legal, ethical and human rights considerations surrounding the removal of healthy tissue from non-consenting minors to allegedly protect them from a behaviour-based disease that may not exist or for which they may not be at risk when they reach sexual maturity.[52]

5) The potential for bias in the information transmitted during the informed consent process in older males has been established.[26] Using a selective bibliography, a convincing argument can be made in favour of circumcision.[53] Such an approach may be attractive to a healthcare provider or investigator wishing to promote the practice. Clearly, such coercion - with amputation taking the place of education - is not in the best interests of the patient. The public may be left, whether intended or not, with the impression that circumcision provides complete protection from HIV infection. An increase in high-risk behaviours might ensue. Following circumcision, a male still needs to engage in safe sexual practices to avoid acquisition of HIV. This needs to be emphasised, and statements that circumcision provides a 'natural condom'[54] are counter-productive.

6) It is likely that a recommendation for universal circumcision in Africa would be interpreted as thinly-veiled colonialism. In addition to raising human rights issues, such a call for circumcision would come into conflict with the role of circumcision status as a sign of tribal affiliation. Assimilation is probably the greatest threat to tribal/cultural identity. Imposition of circumcision on cultures where it has not been previously practised thus poses a serious threat to tribal/cultural identity. Should healthy body parts be amputated to conform to the cultural and religious practices of scientists from outside cultures whose only rationale is they believe that it may confer some benefit? Attempts to change cultural practices are often unwelcome and strenuously resisted. Every attempt should be made to counter the AIDS epidemic within the cultural context of those targeted. Therefore, cultures that currently do not circumcise should not be induced to adopt the practice.[55]

7) The removal of the majority of the male genital mucosa would diminish the effectiveness of the mucosal vaccines being developed.

8) The demand for male circumcision may translate into an increased demand for female circumcision, since the justifications for both practices are strikingly similar.[56]

LACK OF BIOLOGICAL PLAUSABILITY

In order for the scientific community and the public to accept circumcision as a preventive measure for HIV, a biological basis for the intervention is needed. Circumcision proponents have responded by propagating speculations as if they were fact in the apparent hope that, if repeated often enough, they will be regarded as fact. Such assertions include:

a) The claim that the preputial mucosa is more prone to abrasion than the externalised mucosa of the glans of the circumcised penis.[57] In fact, a study by a prominent circumcision proponent found a trend in the opposite direction.[58] In a similar vein, women reported more problems with adequate coital lubrication with their circumcised partners than with their genitally intact partners.[50] Regrettably, the impact of 'dry sex' on the risk of HIV in the male partner has been largely unexplored.[59]

b) The suggestion that the subpreputial space is more likely to harbour sexually transmitted viruses and to promote their propagation.[57] Recent studies have shown that genital warts are more common in the circumcised male.[60] When the studies exploring the association between circumcision status and human papilloma virus infections are combined in a meta-analysis, the summary effect indicates no association (random effects model OR=1.24, 95%=0.91-1.69) (unpublished data). Likewise, a large American study found circumcised men to be at higher risk for genital herpes,[22] while meta-analysis fails to support an association (random effects model OR=1.15, 95%=0.92-1.45) (unpublished data).

c) The assertion that the preputial mucosa is rich in Langerhans cells, which are believed to be the port of entry for HIV. This assertion is based primarily on

an opinion piece published by vocal advocates of mass circumcision.[4] What is needed to decide this to date undocumented assertion, is data on the density of Langerhans cells in the prepuce of sexually active men with and without STDs. Such information, which would facilitate a determination of the importance of this factor, has not been published.[61] Moreover, inflammatory T-cells may be needed for HIV to enter a Langerhans cell, suggesting that a predisposing infection may be a necessary condition for HIV infection.[62] Clearly, further study is needed.

IMPACT ON NORTH AMERICA

Circumcision advocates appear unduly hasty in their desire to implement universal circumcision in Africa, despite weak support for their endorsement and the significant number of unanswered issues. We contend that the rush to intervene has little to do with preventing HIV infection in Africa and may have more to do with a conscious and/or unconscious impulse to help perpetuate and promote the practice in North America. There is ample indirect evidence to support this contention.

1) The call for universal circumcision in Africa did not emanate from Africa, but rather from North American physicians and researchers, most of whom had a long history of vocal advocacy of mass circumcision in the US.[2, 3, 57]

2) A large amount of coverage in the North American lay press has been devoted to the studies suggesting an association between the foreskin and HIV infection among males in Africa, despite clear concessions that the African experience differs in a number of significant ways from the American experience.[63] The American experience, as far as can be determined, in certain respects has been the opposite of that in Africa, with homosexual men, rather than heterosexual women, as the focus of the early pandemic. None of the published studies in the US has been able to demonstrate a clear association among heterosexuals between HIV and presence of the foreskin.[22, 64, 65] One study found a marginally significant association in homosexual men.[66] These results are suspect in that the investigators relied on history, which is known to be unreliable, to determine circumcision status. Geographic analysis of developed nations demonstrates that circumcision is associated with higher rates of HIV infection.[19] This result is driven by the US where the incidence of heterosexually-acquired HIV infection is double to triple that documented in western Europe.[67] Other differences between North America and Africa include the predominant HIV strain and the principal sexual mixing patterns.

Another example is the attention paid to a randomised controlled trial that was rejected by *The Lancet*. The reports of the results of this study have appeared in *Science*[68] and *The Wall Street Journal*,[69] but has yet to be published in a peer-reviewed journal. At the Third International AIDS Society Conference on HIV Pathogenesis and Treatment in Rio de Janeiro in July 2005, a study indicating that female circumcision was associated with a lower risk of HIV infection was presented,[70] yet this finding has received little or no attention. If the true aim is to reduce the incidence of HIV infection, one would expect physicians advocating a surgical preventive for males would also expend the same energy advocating a surgical preventive for females.

3) Several opinion pieces published in the medical literature have been portrayed as 'studies' in both lay and medical publications.[2-4] The authors have made no noticeable attempts to correct this mischaracterisation. This suggests that these authors are playing to the general public, especially in North America, in the manner most advantageous to their agenda, and dispensing with their obligation to avoid misrepresenting the importance and validity of their opinions.

4) The neonatal circumcision juggernaut in the US is beginning to lose steam. Despite efforts to halt and reverse the decline,[71-77] neonatal circumcision rates continue to fall in the US. In 1996, the Canadian Paediatric Society issued a policy statement that recommended against neonatal circumcision.[78] More recently, the Royal Australasian College of Physicians, as well as provincial paediatric organisations in British Columbia and Saskatchewan, have issued policy statements strongly condemning neonatal circumcision.[79-82] In 1999, the American Academy of Pediatrics (AAP) Task Force on Circumcision concluded that the medical evidence favouring circumcision was 'not sufficient to recommend routine neonatal circumcision'.[83] In response to this policy statement published in a journal read primarily by North American paediatricians, three leading circumcision advocates were allowed to publish a long opinion piece recounting the many supposed medical benefits of neonatal circumcision.[5] Despite one author's previous admission that studies of HIV in Africa did not pertain to North America,[63] the authors provided a selective recounting of the studies from Africa to suggest an association between the foreskin and HIV infection in the US.[5] The authors' assertions were publicly dismissed by the chairman of the AAP Task Force, prompting an additional letter to the editor by this trio, who cited new publications to support their position.[84] Two of these publications were, in fact, opinion pieces.[2, 85] The two genuine studies referenced had serious methodological flaws and were written by a member of this trio,[86, 87] calling their objectivity into question. Several years later, the lead author had yet another letter published in the same journal pushing the same message, i.e., that mass circumcision was necessary in the US to fight AIDS.[88]

CONCLUSION

Why are circumcision proponents expending so much time and energy promoting mass circumcision to North Americans when their supposed aim is to prevent HIV in Africa? The circumcision rate is declining in the US, especially on the west coast;[89] the two North American national paediatric organisations have elected not to endorse the practice, and the practice's legality has been questioned in both the medical and legal literature.[50, 90-94] 'Playing the HIV card' misdirects the fear understandably generated in North Americans by the HIV/AIDS pandemic into a concrete action: the perpetuation of the outdated practice of neonatal circumcision.

Amputation of highly erogenous genital tissue is viewed as barbaric by cultures that do not subscribe to the practice.[95] From a psychological standpoint, it can be inferred that, in cultures where circumcision is common, circumcisers desire to be empowered by their actions. Similarly, circumcised males are conditioned to believe that their incomplete penis is superior to the intact penis. Medical justifications, even though repeatedly proposed and disproven,[6] are a means by which these psychological objectives can be accom-

plished.

In the quest to conquer AIDS, as with any disease, medicine and science ought to be purged of all vestiges of superstition, personal agendas and wishful thinking. Medicine must ally itself with scientifically proven practices within the dictates of medical ethics, human rights and the law. Beliefs and fears alone, no matter how understandable, deeply held or traditional, cannot justify the amputation of healthy tissue. Scientific efforts to understand, contain and prevent HIV infection are more likely to be successful when the scientists involved in this endeavor can gather and analyse data objectively and rationally rather than use AIDS as yet another excuse to promote an old blood rite.

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