From data to evidence

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Male circumcision as HIV prevention between controversies and scientific investigation

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Abstract

The randomized controlled trial (RCT) is considered the scientific foundation of medical practice in evidence based medicine. Therefore, the evidence it brings should put an end to controversies. But this was not the case if we look at the demonstration of the protective role of male circumcision (MC) against HIV/AIDS infection. Although based on a series of epidemiological investigations, culminating in RCTs, the benefits of MC are a controversial subject in the medical and scientific community. The RCTs are considered too reductionist; they allow for control during the investigation but are divorced from real-life conditions. In fact, evidence appears as a social construction, relying on more than objective factors, sometimes prejudices and misconceptions. Articles published on MC in scientific journals over nearly two decades and the reactions they elicited, both inside and outside the medical community are analysed. Data produced within RCTs have been criticized, notably for the gap between efficacy and effectiveness, experimentation and experience. Even though it is reduced, uncertainty is not dispelled by RCTs. In any case, this does not influence the scaling up of MC, which depends on both scientific evidence and the personal beliefs of the actors —researchers, decision-makers and the public.

Key words : HIV/AIDS, Male circumcision, Evidence-based medicine, sociology, controversy, Africa.

Introduction

Medicine is as much empirical knowledge as experimental science. It must describe the experience of illness as well as the individual variations that characterize it. Reality, which gives rise to experience, is considered deceptive. Personal experience, even a long series of converging experiences, has no value for establishing evidence. The statistical methods of epidemiology aim at neutralizing the variability of data. Only randomised controlled trials (RCT) and their methodological arsenal, freed from the contingencies of real life, can make a decisive contribution. Quasi-experimental methods are substituted for observation, by comparing groups according to controlled variables. But it remains impossible to control all the possible variables and questions are raised about those variables escaping control.

From descriptive to prospective epidemiology, then to RCTs, the goal of medical research is to exercise increasing control over empirical phenomena, the individual experiences of illness, in order to untangle a jumble of unstable facts (Fleck, 1981). Ultimately, it is the consensus among the researchers with regard to the framework of analysis, the methodological tools and the results that confers reliability and legitimacy on the evidence. Therefore, “integrating evidence is invariably a subjective process, dependant on the skills and values of the individuals who are trying to synthesize multiples pieces of diverse medical evidence” (Mulrow & Lohr, 2001, 257).

In evidence-based medicine (EBM), a higher level in the scientific process is reached. "Evidence was to be the practical form in which science entered into clinical consideration" (Daly, 2005, 12). There is no longer direct contact between a clinician and her patient, but rather an anonymous framework that allows the elimination of subjective factors and intrusive interactions in order to attain that ideal: an "impersonal standard of scientific integrity" (Marks, 1997, 3). Challenging consensus-based judgments, the RCT is supposed to provide an indisputable explanation. It aims at “a move from eminence-based decisions to evidence-based decisions” (Eisenberg, 2001, 371). It is the culmination of a rigorous methodology based on the careful and critical examination of articles published in peer-reviewed journals and on reviews of the research literature. However, proponents of EBM are themselves aware of its limits. “The greater conceptual hurdle is to generate a science appropriate for

the whole of clinical practice, in all its complexity, including the social and political context of patients and the health care system" (Daly, 2005, 2). As are its opponents :" the quantitative, essentially epidemiological definition of evidence in EBM was most often identified as problematically restrictive" (Lambert, 2006, 2640).

Framed by its hypotheses, its variables and its methods, the RCT leaves aside a whole series of phenomena. "Even the simplest RCT is the product of a negotiated order, replete with decisions — some contested, some not— and unexamined assumptions" (Marks, 1997, 134). Clinical research is a social enterprise, even a power struggle, "an activity conducted in a manner similar to politics, by groups of individuals with differing beliefs and interests, who must somehow persuade one another to enter into a temporary and partial alliance, and who then either succeed or fail to persuade others to act in concert with them" (ibid., 243). In contrast to a functional view of scientific demonstration, there are critics who emphasize the temporal and relative nature of evidence, a social construction as much as a scientific one (Berkvits, 1998; Dobrow et al., 2004).

Science advances through a collective effort based on the "style of thought" of a scientific community (Fleck, 1981). In the process of demonstrating the protective role of male circumcision (MC) against HIV infection, we can trace the increasing complexity of approaches that follows the hierarchy of evidence used in EBM (Mulrow & Lohr, 2001). Then, as data accumulate, there is a decrease in differences between various methods and explanatory frameworks following the elimination of artifacts and intrusive hypotheses.

It has been long observed that the prevalence of HIV/AIDS infection in African countries is inversely proportional to the frequency of MC. But it took more than two decades for that relationship to be scientifically proven. An RCT showed that it protects men from getting HIV (Auvert et al., 2005) and this result was confirmed by two other RCTs (Bailey et al., 2007; Gray et al. 2007). These data have been questioned. While MC is one of the oldest surgical operations in the world, it remains highly controversial. Where some people identify an effective and definitive means for avoiding sexually transmitted diseases, other see useless surgery, unacceptable mutilation, both barbarous and reactionary, a religious or cultural heritage and an endeavour of puritans opposed to sexual

satisfaction. The hypothesis that MC protects against HIV infection came to light in 1986. And it was only some twenty years later in 2005 that the first RCT was published showing that it protected men from the risk of HIV infection. Twenty years to unravel the tangle of hypotheses, counter-hypotheses, confirmations, refutations; twenty years of impassioned debate. Here, I will retrace the steps taken during two decades of research, emphasizing the complex intermingling of scientific investigation and social factors. An examination of the nature of evidence in a scientific project —the process of demonstration of the preventive role of MC—constitutes the central theme of this article.

Methodology

I undertook a search of medical and scientific peer-reviewed journals for articles about MC as potential HIV prevention in Africa and for letters that comment on them. The Pubmed, Medscape, Embase, Aidsline databases, as well as the databases of identified journals, were searched. All articles used statistical methods. Comments on published articles have a different status; they do not rely on scientific investigation, have not been peer reviewed and can express opinions. The correspondence sections offer space for debate. The retrieved articles and letters were categorized manually to capture the range of comments, arguments and critics. My review seeks to follow the research process that had led to carrying out RCTs —a process based on arguments and counter-arguments relative to MC— and then to examine the reactions to these RCTs. It does not encompass their scientific reliability nor the appropriateness of methods used[1]. Using a sociological approach, it concerns their discourse, their objectives and conclusions, as they are stated by the authors.

The randomized controlled trials

A RCT carried out between 2002 and 2005 in South Africa found evidence of the protective effect of MC (Auvert et al., 2005). It was terminated early during an intermediary analysis by an independent committee because the results were judged so positive that it would not have been ethical to continue depriving half of the 3274 participants of the benefits of MC, if they wished to undergo it. HIV-negative participants, aged 18 to 24 years, were randomly divided into two groups, half being

[1] Analyses of the internal validity of the research projects are found in the literature and integrated into our approach.

circumcised at the start of the research. All volunteers received information on HIV prevention and other sexually transmitted diseases, as well as free condoms[2]. They were followed up at regular intervals in order to verify that sexual behaviours were comparable in the two groups. When the research was interrupted, 20 circumcised participants were HIV infected against 49 uncircumcised ones, giving a 60% rate of protection.

In view of these results, WHO and UNAIDS remained cautious and awaited confirmation by two similar research projects carried out in Kenya (Bailey et al., 2007) and in Uganda (Gray et al., 2007) before deciding on a prevention policy. These two trials were also terminated early and confirmed the prophylactic function of MC. The trial carried out at Kisumi in Kenya followed a similar procedure and obtained results very close to those of Auvert et al. (2005). The trial carried out at Rakai in Uganda (Gray et al., 2007) on 4996 men is similar to the preceding ones, except for the wider age range studied (15-49 years). Depending on the way data are analyzed, the preventive efficacy of MC varied from 51% to 60%. The results of these RCTs are remarkably similar. Their authors thus recommend the practice of MC in populations where that practice is rare and where high transmission rates of HIV are mainly attributable to heterosexual contacts. They also emphasize that protection is only partial and that information is needed in order to avoid a slackening of preventive behaviours.

These RCTs produced their results after nearly two decades of intense discussions on the protective role of MC against HIV, which I will now examine.

The antecedents

Biological foundations

In 1986, Fink and Alcena assumed a link between HIV infection and absence of MC. “Because the majority of men from Central Africa are not circumcised,…there is frequent mini-ulceration of the foreskin of the penis. This represents an easy portal of entry for the virus…” (Alcena, 1986, 446)[3]. The biological basis for MC protection was described later by Szabo and Short (2000): the foreskin

[2] As in the following two RCTs, the ethical aspects of the investigation were carefully taken into consideration (Cleaton-Jones, 2005).
[3] Citation pages will not be mentioned when the articles were published or reproduced on Internet sites without mention of a page number.

contains more Langerhans target cells for HIV. By reducing the surface of the foreskin, MC reduces these target cells. Atashili (2006) disputes the evidence and states that the foreskin has an immunological function as MC does not get rid of all the target cells.

Converging evidence: Observations on the protective function of MC

Although indigenous African healers recommend MC for protection against sexually transmitted infections (Green et al., 1993), the first epidemiological studies on the distribution of HIV infection in Africa found contrasting situations (Moses et al., 1990). The main question was to find out if these were attributable to MC. This was the purpose of more than forty observational studies. In an approximate study of 409 African ethnic groups, Bongaarts et al. (1989) concluded that MC provided an explanation for the disparity of HIV prevalence in Africa. Cameron et al. (1989) used a prospective methodology and confirmed the link between the absence of MC, genital ulcers — two interrelated factors — and HIV infection, studying prostitutes with a 85% HIV-prevalence and their clients.

Data on MC were synthesized in review articles. Analyzing a series of observational studies, Caldwell and Caldwell (1994) emphasized the polemical aspect of this question. "The role of male non-circumcision has been presented in epidemiological studies which claimed a level of statistical association usually accepted as approaching proof in other investigations. These studies have been largely ignored for reasons that may not be entirely scientific." (23). Moses et al. (1994) reviewed 30 observational studies: out of 26 cross-sectional studies[4], 18 showed an association between MC and lower risk. They stressed the reliability of the data. "Most of the Bradford-Hill criteria of causation are met: strength of association, consistency, temporality, biologic gradient and theoretical plausibility, coherence, analogy" (207). They dismissed an objection often cited by opponents of MC: the spread of the infection in Africa because of contaminated blood.

In a study of 837 married men in Rwanda (Seed et al., 1995), the men living in rural areas, mostly uncircumcised and supposedly less exposed to HIV risk had a higher rate of HIV infection than the men living in urban areas, mostly circumcised. New confirmation of data in favor of MC was reported

[4] Cross-sectional studies provide a "snapshot" of the frequency of a disease in a population at a particular point in time.

in a prospective research on trucking company employees (Lavreys et al., 1999) where the circumcision status was verified by physical examination[5]. The uncircumcised men had a 4-fold increased risk of HIV infection.

Halperin and Bailey (1999) reviewed ten years of studies on the association between MC and HIV infection. They concluded that "it is time for the international health community to add MC services to the current limited armamentarium of AIDS prevention measures in countries with a high prevalence of heterosexually transmitted HIV and STDs… [Otherwise] medical professionals and public health authorities may inadvertently be harming the very individuals whom they are trying to help" (1814). Two articles compared the prevalence of HIV infection in four African cities that had contrasting rates of HIV infection: moderate in Cameroon and Benin or very high in Kenya and Zambia (Auvert et al. 2001). Data analyses controlled for confounding factors such as religious, cultural practices, sexual behaviours, and confirmed the population level association between HIV and lack of MC.

Agot et al. (2004) used a rigorous methodology to confirm that MC is associated with reduced risk of acquiring HIV among men. A serology test for HIV was carried out on two groups of Luo men from Kenya for whom HIV infection was analyzed in relation to the presence or absence of MC, verified by medical examination. But according to Franco (2004), that research did not enable the debate to progress, even though its authors had made great efforts at "disentangling the possible biological effects of circumcision from its inextricable links to religious beliefs, cultural factors and sexual practices" (134). While data in favour of MC were accumulating, the question of its acceptability was was investigated among various sub-Saharan African populations where the practice was not widespread. In a review of this question, Westercamp and Bailey (2007) concluded: "it is doubtful … that we learn a great deal more by additional acceptability studies that pose hypothetical questions to participants" (353).

Doubts and caution

Discordant opinions were voiced. In a review article, Vincenzi and Mertens (1994) expressed several criticisms that were picked up and amplified in numerous subsequent publications. They contested the

[5] Commonly used in the preceding studies, self report is less reliable.

biological plausibility of MC: "it is unclear what the portal of entry is for HIV" (156). Data were judged heterogeneous and contradictory, lacking a coherent explanatory model. They cited numerous biases: hygiene practices, sexual behaviour, misclassification of exposure, reliability of self-reports, and also a supposed "publication bias" in favour of articles positive to MC. Finally, they wondered if the interpretation of the data relied on "faith[6] or evidence". Rather, the effects of MC should be subject to an objective scientific analysis and not be debated in an impassioned and emotional fashion, they conclude, after throwing oil on the fire of subjectivity.

Reservations were voiced in several epidemiological studies and reviews that confirmed the beneficial effects of MC (O'Farrell & Egger, 2000; Weiss et al., 2000). Resistance to HIV infection could be due to religious proscriptions and strict rules of hygiene that affected risk. A cohort study was carried out on 5507 seronegative men and 410 serodifferent couples (Gray et al., 2000). The data were confusing because a part of the participants was Muslim. The results of a national study in South Africa (Connolly et al., 2008) confirmed that MC does not protect against AIDS when it is practiced too late, on sexually active adults and outside a medical setting.

Reviews looked at confounding factors (Bailey, Plummers & Moses, 2001; Hayes, 2001; Quigley, Weiss & Hayes, 2001) and concluded that data in favor of MC were not sufficiently convincing. A series of questions were raised, notably, the types of MC, its protection against other sexually transmitted infections, the reasons for practicing MC, the impact of the age at which it is carried out, and its scientific foundations. In a letter reacting to an article favourable to MC by Halperin et al. (2002), Gray et al. (2002) recommend caution and the setting up of RCTs. To which the former reply by evoking mounting biological evidence. A Cochrane review[7] was carried out (Siegfried et al., 2003) emphasized the methodological heterogeneity of the studies, as well as their inconsistent quality, and concluded that "there is no strong evidence of the effects of male circumcision to try to reduce the spread of HIV/AIDS". "…Observational studies are inherently limited by confounding which is

[6] The use of this word doubtless relates to the religious dimension of MC, not mentioned directly here.
[7] The Cochrane collaboration aims to be a global resource for systematic review and a critical appraisal of research articles. Set up by experts according to a highly codified procedure, Cochrane reviews are a basic reference.

unlikely to be fully adjusted for." It was necessary to await results of RCTs before promoting MC in Africa.

Publications on MC are characterized by repetition: researchers redo similar investigations and analysis and come to similar conclusions. Redundancy is the rule, even if it is not easily discernible because publications appear in diverse formats — journals specializing or not in HIV infection — and do not reach the same audience.

The offensive against MC: the denunciation of a conspiracy

The issue of MC was caught between studies that attempted to untangle cause from effect on one hand and stubborn resistance, on the other. Opponents of MC expressed their viewpoint mainly in letters in reaction to published scientific articles and in websites. Van Howe (1999) considered MC as scientifically unfounded and dangerous. He denied that studies carried out in Africa shown that circumcised men were less exposed to HIV risk: they supposedly have more partners and condoms did not stay on their penises. Darby (2004) repeated the usual methodological arguments: selection bias, religion as a confounding variable, inadequate statistical analysis. Boyle (2004) evoked the fact that the approach used by researchers, themselves supposedly circumcised, —if this was the case he prudently added— was biased. Thus, researchers were accused of abusive proselytizing.

Szabo and Short's (2000) biological arguments were attributed to a retrograde and puritanical Victorian period, to backward tribal customs, to hundred years of pressure by circumcisers playing on fears. The foreskin could not have been an "error of nature", i.e. of God (Cruz, 2000). According to Van Howe et al. (2000), "HIV transmission is heavily dependent on certain sexual behaviours, not anatomy" (1467). The criticized authors condemned their opponents' dogmatic position. "It would be unfortunate if the zealous opponents of neonatal male circumcision in developed countries… distracted attention from the glaring fact that in Central and Southern Africa, where 24.5 million people are infected with HIV, circumcision could offer some immediate protection against spread of the disease" (Szabo & Short, 2000, 1594).

Boyle (2003) described numerous negative effects of MC. It provokes an "emotional defence against (one's) own painful feelings of grief for a lost body part and reduced sexual function" (427). The catalogue of these undesirable effects was eclectic: unhappiness, anger, sadness, feeling incomplete, cheated, hurt, concerned, frustrated, abnormal, and violated. The circumcised men would be prone to alcohol dependence and the use of drugs, as well as solitude, marital problems, anti-social behaviours, domestic violence, rape, sexual abuse of children, theft and suicide. In front of this bleak picture, the practice of MC is described as "wishful fantasy" provoking "a calamitous worsening of the HIV/AIDS epidemic" (328). For Hill and Denniston (2003), 90% of the sub-Saharan African epidemic was not due to heterosexual transmission as only 30% of infections were attributable to sexual activity. The other infections would be due to iatrogenic transmission through blood that could only be increased by MC practiced under poor hygienic conditions. Besides, MC could change sexual behaviours by increasing risky practices. The authors raised the threat of what "Africans" or "African males" may think or do, "abused and exploited by scientists who recommend the circumcision policy, sensitive of previous colonial exploitation and suspicious of the biological warfare origin of the virus" (496)[8]. They warned against the political consequences of the probable failure of MC: "African males would have sacrificed their erogenous tissue for a false hope of preventing HIV infection"(ibid.).

As more evidence accumulated in favour of MC, the criticisms became more caustic. For Hellsten (2004) [9], MC, a "genital mutilation", absurd and irrational, would open the door to allowing all sorts of mutilations: "We would have no justification for stopping (parents) cutting off their children's ears, fingers or noses if their religion or cultural beliefs demand it". MC would bring about "a sexual disinhibition, and for women, unsafe, maybe also forced, sex". The reasons to practice MC were a "mere smokescreen[10] to cover up the actual social, political or economic reasons that are behind the preservation of genital mutilation in any given cultural context". A conspiracy was denounced. "Medical data with counter results [are] ignored or misinterpreted in order to maintain the practice". But the worst was yet to come. "In a modern, American, market oriented society male circumcision

[8] Here, Hill and Denniston repeat word for word a sentence from an article by Ntozi (1999, 99) that puts forward a measured position on MC and recommends proceeding to RCTs.
[9] Consulted on the Internet site: http://www.cirp.org/library/ethics/hellsten1/ (Accessed March 17, 2010)
[10] The italics are the author's, to emphasize the terms used for denouncing a well-hidden conspiracy.

became a form of commercial exploitation of children when physicians, in cooperation with transnational biotechnology corporations, looked for the sales of marketable and economically profitable products made from harvested human foreskins that could further be used in the pharmaceutical industry". Medicine is in league with the powerful and dangerous pharmaceutical industry in an illegal trade. And this in the name of a science without ethical bounds that "can be a double edge sword that readily lends itself as an alibi for strongly held preferences and cultural biases".

For Van Howe et al. (2005), epidemiological research on MC wrongfully depicted itself as scientific. "Several opinion pieces published in the medical literature have been portrayed as 'studies'…Scientific efforts to understand, contain and prevent HIV infection are more likely to be successful when the scientists involved in this endeavour can gather and analyze data objectively and rationally rather than use AIDS as yet another excuse to promote an old blood rite" (264). Researchers, again supposedly circumcised themselves and considering "their incomplete penis…[as] superior to the intact penis" (ibid.), were accused of proselytising in favour of a "barbaric" practice. "Should healthy body parts be amputated to conform to cultural and religious practices of scientists from outside cultures?" (ibid., emphasis added) In their determination to combat MC, its opponents advanced arguments without proof, derived from conspiracy theory, or even based on xenophobia and racism.

After the RCTs: back to "real life"

As the "gold standard" of medical research[11], the RCTs was expected to put an end to debate, at least concerning its scientific aspects, since issues of implementation and acceptability may widen the gap between efficacy and efficiency. They constitute a working model where researchers can exercise maximum control. In the real world, things could be very different. The publication of the RCTs gave rise to numerous letters where critics repeated the same arguments and continued to question the

[11] "Because the randomized trial and especially the systematic review of several randomized trials is so much more likely to inform us and so much less likely to mislead us, it has become the 'gold standard' for judging whether a treatment does more harm than good" (Sackett et al., 1996, 72).

methodology. The detractors of MC would not cease their struggle. Their goal was henceforth to slow down or even prevent the scaling up that was to be undertaken.

Circular arguments against MC

The criticism was focused on the quality of evidence. The RCTs took place over a short period. What is the impact of MC over the long term? They were accompanied by very intense follow-up and counseling. What would happen when these conditions were no longer present? Garenne (2006) questioned whether the effects of MC could be maintained over the long term, using the analogy of insufficiently safe contraceptive methods. According to him, the 60% protection shown by Auvert et al. (2005) only represents a decrease in the annual risk. MC will have less impact on HIV infection after several years.

Arguments against MC repeated criticisms from before RCTs (Potterat et al., 2006) as though evidence was not valid. “Male circumcision is not the vaccine we are looking for” stated Green et al. (2008) who also made an appeal to the “real world” and the “long-term” in their indictment of MC. “Thousands of African men now line up to get circumcised in the mistaken belief that it will save them from HIV […] The public is misled; false hope is promoted from uncertain conclusions” (193, emphasis added). The world health community should scrutinize the data and examine “several other factors that might have influenced and skewed the results” (ibid.), especially the supposed high proportion of non-sexual transmission. MC is dangerous because of contaminated medical instruments, exposure to blood, a false sense of security, and risk compensation behaviours. African males[12] would be too happy to do without condoms and trust an erroneous message about protection. MC would decrease the number of Langerhans cells, which, it is supposed, protect against transmission by attacking HIV. Myers and Myers (2008) again condemned a pro-circumcision lobby impatient to achieve their ends by the promotion of a license for unprotected sex

A rejoinder emanated from numerous experts —academicians, members of international organizations and major foundations, "surprised at the degree of resistance to something which seems to them both

[12] This all-encompassing term is repeated several times in the article. It evokes the stereotypes with regard to their difficulty in controlling their sexuality.

self-evidently good and worthwhile, and also entirely consistent with the 'scientific' biomedical paradigm within which they operate" (Dopson et al., 2003, 317). Wamai et al., 2008, restated the fact that scientific evidence was "overwhelming", that the HIV epidemic was devastating and the many other prevention strategies disappointing; early termination of the RCTs was because of the high level of efficacy of MC; the data were consistent and that the observed effects were "virtually identical to that seen in many previous observational studies"(400). South African, Kenyan and Ugandan cohorts are being followed up. "There is no reason why the protective effect of foreskin removal would decline over time" (ibid.), and there is no increase in reported risky behaviour. Addressing the statement that many infections were not due to heterosexual contacts, the authors replied that "this theory has been repudiated by the WHO and virtually all reputable scientists" (ibid.). They repeated that no serious or permanent complications of MC were reported in the RCTs, designed to control for confounding factors. They indeed adhered to ethical rules and "it is unethical to deny safe MC services in high prevalence settings" (401). In conclusion, "as more and more people in sub-Saharan Africa become needlessly infected with HIV, the time has come for urgent and decisive leadership, not circular and unscientific arguments about an intervention whose efficacy has been proven beyond a reasonable doubt." (403).

The social sciences: an added dimension?

In 2007, a review meeting[13] was organized at Montreux by the WHO and UNAIDS to compare different points of view, notably those of sociologists and anthropologists. Many participants were opposed to MC, and did their part in fuelling controversy. If the research evidence was clear, consensus was far from achieved (Berer, 2007).

Niang and Boiro (2007) emphasized the complexity of the social and symbolic meanings of MC in West Africa: Senegal and Guinea-Bissau. It has a sacred dimension of spiritual purity as well as a sacrificial function. The foreskin is considered a source of disease and malediction. The initiation during which MC is carried out is a kind of death followed by resurrection, and a spiritual preparation. Men circumcised at the same time are strongly bound together. It is a period of sexual education

[13] www.who.int/hiv/pub/malecircumcision/meetingreport_nov07/en/index.html/ (Accessed March 17, 2010)

aiming to instil temperance. Is it possible to reconcile these meanings with an alien public health perspective?

Reacting to the fact that MC is "just a snip", as it was described by a participant in a former WHO/UNAIDS meeting, Aggleton (2007) maintains that "few if any investigations contain robust controls for confounding factors such as social background, sexual behaviour or penile hygiene." (19) The strengthening advocacy in favour of MC is based on collusion between public health and social control. Since prevention programs have been failures, he argues, there is a backlash to biomedical acts and moral constraints. The results of the RCTs should be criticized for faulty science. "Evidence from recent trials, which at the very least requires continued scientific scrutiny, is now trumpeted as 'truth'. Opponents… have been silenced and marginalized under the onslaught. Curious alliances have arisen between clinicians, advocates, religious leaders and moral entrepreneurs" (20). Such statements are very much in line with a frequent position taken by opponents of MC, based on the revelation of a conspiracy.

Dowsett and Couch (2007) again took up the arguments of the staunch opponents of MC. They evoked the "euphoria" of participants at the international conference in Toronto in 2006, while "many were less sanguine" (34) and pushed aside, notably the sociologists and anthropologists who were "sceptical about the narrow form of "science" being touted as the only form of evidence needed […] The clamour for circumcision silenced many questions, overrode any misgivings and swept sceptics to the sidelines" (ibid.). MC is a discriminatory procedure promoted as an "African solution". It would surely lose its benefits in real world settings. The methodology of the RCTs is also disputed: findings were taken out of context, the double-blind was impossible, the counselling intensive. The adverse effects of MC will develop over time. It is necessary to remain "wary of the indecent haste with which the discussion about MC has been swept up in a tide of enthusiasm based on only one, albeit significant, part of the evidence base needed for recommending such a radical public health initiative" (42).

Other participants at this meeting envisaged the practical details and the difficulties of MC scaling up. Gruskin (2007) noted that WHO and UNAIDS had not explained what an appropriate MC was, since

that operation is characterized by numerous variations. He worried that circumcised men would not follow preventive recommendations. Buvé et al. (2007) warned against precipitation and advised to "hurry up slowly" (Festina Lente), considering that "the biggest challenge is how to deliver a complex prevention package that combines a surgical procedure with a behaviour change intervention"(58). How could MC be practiced under proper conditions in insufficient health services? "The biggest bottleneck when going to scale with MC will be the lack of human resources" (59).

Preparing the scaling up

WHO and UNAIDS, and other organizations — notably, the US President Emergency Plan for AIDS relief (PEPFAR), the Bill and Melinda Gates Foundation — became strongly involved when the three RCTs produced converging data. It became essential to set up policies of preventive MC in African countries where the epidemic was very active, with necessary safety precautions while respecting human rights. Hallett et al. (2008) recommend combining MC, motivation to change behaviours and antiretroviral treatments (ART), because of the synergy of their effects. According to Podder et al., (2007), "the combined use of male circumcision and ART is more effective in reducing disease burden than the combined use of male circumcision and condoms for a moderate condom compliance rate" (2447). The protective effects of MC were so marked that men will have to take a lot of risks in order to cancel them out (Waver et al., 2005). The prevention of millions of infections among men was expected, and also among women in the long term, through the mechanism of herd immunity (Nagelkerke et al., 2007; White et al., 2008). The protection from STIs afforded by MC will also have to be taken into account, since it lowers the risk of HIV infection. Moreover, because of the early termination of the RCTs, evaluation at the population level may be inaccurate and underestimate the incremental level of impact, which may be larger at the population level and over a longer time scale when coverage increases (Boily et al., 2008).

Between July and November 2006, consultation meetings and task forces were organized by WHO and UNAIDS with local authorities and key actors in many countries of Central and Southern Africa[14].

[14] The minutes of these meetings are available on the site: http://www.who.int/hiv/pub/malecircumcision/en/ (Accessed March 17, 2010)

In December 2006, a general meeting was held in Geneva[15]. The aim was to identify countries where MC was little practiced and where the prevalence of HIV was high, and to get them involved in prevention policies using MC. A brochure[16], "Male circumcision, Africa's unprecedented opportunity", repeats an estimation by Williams et al. (2006): MC has the potential to avert about 5.7 million new HIV infections and 3 million deaths over 20 years in sub-Saharan Africa. Strategy manuals described the various aspects of scaling up[17]. Guidelines explained circumcision techniques. Surgical kits were developed. It was also necessary to determine needs for research and information in order to ensure a successful scaling up, to determine what local human resources were available and to train medical personnel. How to get the support of traditional healers was an issue that needed to be tackled as well.

"What else do we need to know?" asked Muula (2007) in a cautionary note, since "taking the language of epidemiology and applying it to individuals is extremely problematic" (363). There were numerous calls for levelheadedness. "The excitement the results of these trials will surely generate should not cause us to forgo true diligence in investigating whether or how the clinical evidence can be translated into routine practices" (Newell & Bärnighausen, 2007, 618). The same advice came from Sawires et al. (2007): "enthusiasm generated from the three trials might not lead to accelerated scale-up… Strong science alone does not result in rapid, widespread roll-out" (708). It would however be unethical not to take the preventive opportunities offered by MC seriously (Rennie et al., 2007). It was apparently as effective as the vaccine everyone has been looking forward to (Klausner et al. 2008).

Warnings increased about risk compensation and disinhibition. "Avoiding the sexual dissatisfactions of condom use and the desire to have more sex partners are likely to be significant motivations for men to seek circumcision" (Kalichman et al., 2007). It is recommended to wait for complete healing before resuming sexual activity. An assessment was done in Kenya at Bungoma (Bailey et al., 2008) where MC is widely practiced, either in medical facilities or by traditional healers. Unsurprisingly, there were more complications when the operation was performed by the latter. Therefore, there was a

[15] See: www.who.int/hiv/pub/malecircumcision/meetingreport_dec06/en/index.html/ (Accessed March 17, 2010)
[16] www.who.int/hiv/pub/malecircumcision/Africa_opportunity/en/index.html/accessed
[17] www.who.int/hiv/pub/malecircumcision/op_guidance/en/index.html/ (Accessed March 17, 2010)

need for infrastructure, personnel, training, follow-up and an effort at information to avoid the harmful effects of MC. Kagumire (2008) was not optimistic concerning the situation in Uganda because of the president's opposition to MC.

According to the cost estimate by Auvert et al. (2008), substantial expenditures will be needed for the first five years of the roll-out of MC in sub-Saharan Africa. But they are offset by the expected health benefits. The participation of numerous actors — political leaders, activists, teachers, street leaders, churches and health workers— is essential for scaling-up. Political support should be strong and continuous.

A review (Byakika-Tusiime, 2008) concluded there is unequivocal evidence of the positive effects of MC. A second Cochrane review (Siegfried et al., 2009) stated that it was no longer necessary to continue RCTs on MC, as those already done were reliable. It nevertheless concluded that there was greater sexual risk-taking among circumcised men, which contradicts the assertions of the authors of the RCTs. In their own secondary analysis, Mattson et al. (2008) show a decrease in risk-taking. Moreover, a comparable rate of incidental STIs was observed in the two groups, circumcised or not.

Epilogue

Following publication of the RCTs and when the question of scaling up was addressed, caution was the appropriate attitude and optimism was measured. However, in the field, things are sometimes going faster than wished for by the experts, especially in some of the sub-Saharan African countries severely affected by AIDS. However this preventive option requires strong political backing (Katz & Wright, 2008). In Swaziland, which has the highest prevalence in the world (26%), the prime minister became personally involved in implementing MC and men hurry to be circumcised. With a prevalence of 24% among 15-49 year olds, Botswana launched a large program of MC. But other countries, especially South Africa (18% prevalence), are more reticent to develop MC.

Countries suffering the most from the HIV epidemic are at a crossroad. MC is a new prevention tool with proven efficacy. It is the only preventive technique that has proved itself since the promotion of condoms. But all the difficulties of implementing safe MC, combined with other means of prevention

because of its partial efficacy, are now going to be discovered in the field. There are many obstacles, from opposition or political inertia to a lack of financial and manpower resources, to disagreement among scientists. And acceptance by the public, so often brought up in the literature, does not seem the most critical problem.

Conclusion

From a scientific perspective, we have followed the slow process of establishing evidence and winning adherence to it. "The meaning and validity of scientific evidence is influenced as much by the sociocultural characteristics of readers and users as it is by meticulous use of research methods" (Berkvits, 1998, 1539). Scientific investigation does not take place in a self-contained world. It is tainted with emotions and prejudices: "the appeal to logic and science may fail if the rhetoric does not also engage with deeply held values and beliefs" (Dopson et al., 2003, 321). The turmoil in society does not stop at the doors to the laboratory. However, as research progresses, its methods get freed from parasitical hypotheses, and it concentrates on more limited objects. Nonetheless, even the RCTs are not the gold standards scientists are looking for: they raise objections concerning the artificial conditions making it possible and the narrowness of their scope (Cartwright, 2007; Lambert, 2006). "The design of RCTs […] makes their outcomes difficult to generalize over a diverse and heterogeneous patient population" (Mykhalovskyi & Weir, 2004, 1063). We end up at an insoluble paradox. How can proof be arrived at if it is not possible to simplify, to cut to the essential? But how can we simplify, or make models, without denaturing reality?

RCTs on MC were a challenge. They transferred a methodology based on drug testing, where the double blind was possible and decisive, to a surgical operation. This difficulty has not escaped the detractors of MC: it taints the orthodoxy of the investigation. Therefore, reproducibility and the accumulation of data became essential since they allowed compensating for biases and for idiosyncrasies of the researchers or participants.

RCTs are supposed to compete with clinical expertise, which has long been the rule in the medical arena; expertise that is learned through experience, in face-to-face contact with the patient — an approach that does neither use controlled comparison, nor rely on measurement and statistics. In

epidemiological studies on MC, do the accumulation and the convergence of data gathered outside an experimental context strengthen their reliability? As we have seen, measurement is not considered sufficient to substantiate evidence. Experimentation makes it possible to measure under controlled conditions, and therefore to limit variability. However, uncertainty remains. “Often, evidence is not so clear that there is no room for debate” (Rodwin, 2001, 442). Questions about measurement are unchanged: has one measured what it is pertinent to measure? Have the most operational variables been selected? Is the procedure adapted to its objective? The scientific controversies are focused on these aspects and remain unresolved. While combining measurement with experimentation improves the quality of evidence, it remains impossible to remove all uncertainty. Evidence conserves elements of uncertainty and subjectivity (Muhlrow and Lohr, 2001). It is founded on a shared frame of reference, that is similarities on interpretation, and on the “participants’ receptivity” (Dobrow et al., 2004, 214). It remains therefore a relative entity (Green, 2000 ; Goldenberg, 2006), open to “credibility struggles” (Epstein, 1996) and grounded in a legitimating process that defines which approaches and data will be considered relevant (Lambert, Gordon and Bogdan-Lovis, 2006).

Another important point is the emerging consensus about promotion of MC. In principle, evidence is expected to be universal. If recommendations concerning MC were to rely on evidence only, this preventive approach should be promoted everywhere, including in Western countries, especially those in which MC is rare. This is not the case. MC is presented as a solution for containing AIDS epidemics in Africa, and only there. This may be seen as a biomedical colonialism of a kind, or, at least, a patronizing attitude that may hurt recipients of this preventive message. The consensus about diffusion of MC in Africa may thus make the notion of "evidence" more relative, and even subvert it.

Beyond the scientific arena, the data of the RCTs did not change the most active opponents, those physicians who have long fought against the practice of MC. As clinicians, they have difficulty accepting epidemiological evidence, especially when they consider such evidence as contrary to their own experience. They participate in anti-MC organizations active in the United States and Great

Britain, countries where the practice of MC has long been widespread. Their denunciation of the barbarous nature of the operation is paired with a latent but noticeable ostracism apparent in recurrent innuendos aimed at the advocates of MC for religious motives.

International organizations became involved following the positive results of the RCTs. In their efforts to support a policy of scaling up MC, they had to take into consideration the idiosyncrasies of politicians for and against MC. This is one reason why wide differences are observed in reactions of sub-Saharan African countries. As for the public, it tries to "vote with its feet": in countries where the prevalence of AIDS is very high, demand is strong but facilities are not able to keep up. This brings us to the key question of politicization of evidence, that is the use of evidence to legitimate political decisions, as well as to its rhetorical uses. "Much of what is called evidence is, in fact, a contested domain, constituted in the debates and controversies of opposing viewpoints in search of event more compelling arguments" (Wood et al., 1998, 1735). Evidence is politicized during the complex transfer of population-level research onto an individual level. This translation process, several authors have pointed out, frequently distorts and subverts the original evidence (Eisenberg, 2001 ; Cartwright, 2007).

Evidence has not significantly changed the scope of actors' positions. Finally, it is "real life" that will resolve the question: implementation in the field, encouraged or impeded by political authorities convinced or not by research results promoted by international organizations, but also, and doubtless especially, by their personal convictions. From a scientific as well as a political point of view, passion and prejudice will still prevail.

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