Mother-to-child-transmission of HIV/AIDS in Africa: Ethical problems and perspectives

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Anton A van Niekerk

Director: Centre for Applied Ethics
University of Stellenbosch
Private Bag X1
Matieland. 7602
South Africa

1. Introduction

It is commonplace to identify and bewail a plethora of problems in the developing world generally, and in Africa in particular. Poverty, illiteracy, famine, political instability, natural disasters, and many more misfortunes dominate the history of this part of the world over the past 50 years. It was therefore adding uncalled (undeserved?) insult to already overwhelming injury when HIV/AIDS visibly[1] struck the (also developing) world since the mid-1980's. In spite of all the other calamities that Africa has to deal with, it nevertheless is no exaggeration to claim that HIV/AIDS nowadays constitutes the most serious health and social crisis and challenge that has ever befallen that continent.

There are a range of ethical problems raised by the phenomenon of HIV/AIDS on the continent of Africa, and a large literature exists about many of these problems. In the course of this chapter, I shall occasionally refer to this literature. I myself have dealt with problems evoked by poverty as the social context for HIV/AIDS in Africa, the lack of political will to address the issue, the challenges surrounding the need for changes in people's sexual behaviour, issues of women's vulnerability to the epidemic, the disenchantment of intimacy as a result of the discourse on AIDS, and issues of public versus private health elsewhere (cf. Van Niekerk 2002a and 2002b). In his article, I shall focus on the ethical problematic raised by the issue of mother-to-child-transmission (MTCT) of HIV in Africa.

Before I address two ethical problems in connection with this matter, I shall first deal with the relevant facts about MTCT. This will be followed by a discussion of two ethical problems, viz. the issue of the morality of placebo-controlled trials for drugs to prevent MTCT in Africa, and the issue of the lack of political leadership and responsibility to implement proven programs that will combat MTCT. In conclusion, I shall discuss a number of insights that these disputes yield for our understanding of our powers over disease in the contemporary world, the implications of these issues for our understanding of scientific methodology in medicine, the dangers of politicizing a health problem such as HIV/AIDS, the need for renewed reflection on the global disparities in the provision of health care, and the need for imaginative and responsible political leadership and co-operation between the developed countries, Africa and the pharmaceutical corporations to address and combat a catastrophe of unprecedented global proportions.

1. Mother-to-child-transmission (MTCT) of HIV in Africa

MTCT of HIV/AIDS in Africa represents one of the most contentious issues in the current debate about ethical problems related to HIV infection and management. HIV/AIDS, as is well known, is as yet an incurable viral infection. There also is, as yet, no available vaccine; at the time of writing this article, reports are in the

[1] Whether the disease was prevalent in earlier times, and not as such known or visible, is still a matter of considerable contention and speculation. The anthropologist Virginia van der Vliet argues that AIDS is probably a fairly recent phenomenon, and might have lingered unobtrusively in small African villages over a period of time, only emerging in its visible manifestation and spreading rapidly since because of modernising influences such as urbanisation and its accompanying altered sexual mores. Cf. Van der Vliet, 1996: 10-51.

press about the results of the clinical trials of the world's first systematic attempt at a vaccine, the so-called AidsVax. Researchers ascertained that this vaccine, based on the B and E strains of the virus (which are not prevalent in Africa), is safe, but that it protected only 3.8% of people injected with it (Altenroxel, 2003: 1). Many other trials, some of them also based on the C strain of the virus that is the one affecting Africa, are currently researched and planned and will probably get underway soon, but the trials are set to last for many years. Normally a vaccine would have to be proved at least 70% effective to be considered for registration; however, given the severity of the problem in Africa, a 30% success rate might well be considered efficacious, given the fact that, in a country such as South Africa where 1500 people are infected daily, such a vaccine could then theoretically prevent 450 infections per day (Ibid.)!

HIV is transmitted through the exchange of bodily fluids during homo- and hetero-sexual intercourse as well as by the sharing of needles by (ab-)users of drugs administered intravenously; this is known as "horizontal" transmission, i.e. transmission from one person to another. The most significant other mechanism for infection is the so-called "vertical" transmission from a pregnant woman to her unborn child. In the absence of both a cure and/or a vaccine, MCTC of HIV, however, does represent the one area where a significant reduction in the infection rate, and the concomitant saving of lives and relief of suffering, can be achieved. It is a well-established fact that the use of antiretroviral treatment during pregnancy can prevent the transmission of the virus from mother to child; the success rate with certain drugs is in the order of 50% (with highly active antiretroviral therapy in the USA the transmission rate is 1% - a 30-fold reduction). It is therefore doubly ironic and tragic that this very possibility – one of the few potential areas of "success" in combating this deadly epidemic - has become the arena of so much controversy, both as regards the legitimacy of the research methodology on which the trials to establish the efficacy of these drugs were concerned, as well as concerning the utilization of the opportunity to implement programs for MTCT prevention by authorities, particularly in South Africa. In what follows, I shall use the South African situation as a case study of how tragically a pertinent opportunity was and still is being forfeited in this regard.

HIV seroprevalence in pregnant women in South Africa, where statistics[2] are based on the attendance of country-wide antenatal clinics (and where anonymous testing is done regularly and systematically), averages 23%, rising up to 33% in the worst-hit provinces (MacIntyre & Gray, 2000: 30-31). The UNAIDS figures of December 2002 show a decrease – about 15% - in the infection rate for women under the age of 20. However, for women in the age range of 20-29, the infection rate is still around 30% (UNAIDS Epidemic Update December 2002). When breast feeding (which exacerbates the possibility of transmission) occurs, these figures can reach 35%, as some studies have shown. "With a conservative estimate of 800 000 births per year in South Africa, this suggests that 70 000 infants are affected annually" (MacIntyre & Gray, 2000: 30). Many more children

[2] For an analysis of the problems related to reliable statistics about HIV in Africa, cf. chapter 2 of this volume.

are born uninfected, but become infected with HIV as a result of being breastfed by HIV-positive mothers.

The possibility of a significant reduction of MTCT was first proven in 1994 when the Paediatric AIDS Clinical Trial Group (PACTG) did a comprehensive clinical trial in the USA with the anti-retroviral drug Zidovudine (AZT)[3]. It was conclusively shown that a regime – the so-called (and now famous) 076 regime - of this drug reduced vertical transmission of HIV from 25% to 8%, i.e. by two thirds (De Zulueta, 2001: 290-291). These findings have repeatedly been confirmed, and have even been improved upon. A study in France, for example, showed that HIV positive women who received the 076 regimen had a transmission rate of only 0.8% (Mandelbrot, Chenadec et al., 1998).

Is this regimen then not the answer to the serious MTCT problem in developing countries that we are seeing? In theory possibly, but not in practice. For this there are mainly two reasons. The first is a simple matter of cost; the 076 regimen is prohibitively expensive. Up till quite recently, a single treatment program costed more than US$800 - a sum that is several hundred times the annual per capita health care allocation in many developing countries (Resnik, 1998: 289), particularly in Africa. Schüklenk points out that the producer of zidovudine, Glaxo-Wellcome, offered the drug to women in developing countries at a price of between US$50-150 – something that might be affordable in a country such as Taiwan, but which is still way beyond the financial capacity of most African countries (Schüklenk, 1998: 317). In 2003, three milligram Zidovudine in South Africa costed R1989.00 (US$331 at February 2005 exchange rate) plus dispensing fees per prescription. The second reason is that the 076 protocol is a very complex regimen that requires a great deal of labour, takes a long time to be administered effectively, requires careful surveillance in order to address possible side-effects, etc (Resnik, 1998: 289). Given the short supply of qualified health care workers, particularly in the rural parts of most African countries, these represent almost insuperable barriers.

There was, consequently, an urgent need to investigate the efficacy of antiretroviral therapies that could be administered by means of short courses to HIV positive women late in their pregnancies. Several trials were conducted in Thailand, Côte d'Ivoire, Burkina Faso and South Africa in which significantly shortened regimens of AZT were tested. The drug was administered in oral form from the 36th week of pregnancy for four weeks, followed by a single loading dose at the onset of labour, and twice daily for seven days after delivery. Significant reductions of MTCT – up to 38% in many cases – were noted in comparison with control groups, even in cases where breastfeeding continued (MacIntyre & Grant, 2000). On the score of both problems identified above with the conventional 076 protocol, these regimens seemed preferable to the needs of developing countries. The cost of a single treatment program was significantly cut; the alternative treatment regimen uses US$80 worth of AZT as compared to the US$800 worth of the drug in the 076 protocol (Resnik, 2001: 289-290). Because the patients are

[3] Zudovudine is marketed under the brand name of Retrovir (formerly called azidothymidine [AZT]). It is made available in tablet, capsules and a syrup. Each film-coated tablet contains 300 mg of Zudovudine and the inactive ingredients hypromellose, magnesium stearate, microcrystalline cellulose, polyethylene glycol, sodium starch glycolate, and titanium dioxide

treated for much shorter periods of time, the complexity of administering the drug was also significantly reduced.

The drug regimen that has been the cause of the most controversy and debate in South Africa, however, is Nevirapine[4]. It is a "fast-acting and potent antiretroviral with a long half-life" (MacIntyre & Grant, 2000). It was originally tested in a trial called the "HIVNET 012 trial" in Uganda. The trial investigated the use of a single 200mg dose administered orally to women at the onset of labour, followed by a single dose of 2mg/kg administered to infants within 72 hours of birth. This regimen was then compared to one in which "intrapartum ZDV [i.e. AZT] and one week of infant ZDV treatement" (Ibid.) were administered. Almost all babies were breast-fed. It was found that, in the Nevirapine group, the transmission rate, at the time when the newborns were 14-16 weeks of age, was 13.1%, contrary to 25.1% in the group with which they were compared (i.e. the group that received AZT as indicated above). The efficacy of Nevirapine was thus found to be 47%. The side effects of the two regimens were similar, and both were well tolerated (Ibid.). The wholesale cost of this regime is quoted as being US$4 per mother/child – almost incomparably cheaper than the original AZT regimens used in the developed worlds (De Zulueta, 2001: 298).

3. Two ethical problems raised by randomized placebo controlled trials for shortened drug-regimens to prevent MTCT of HIV.

The results of the trials for shortened, affordable and manageable drug regimens to prevent MTCT in developing nations were seemingly quite positive and provided laudable opportunities to set in place arrangements that could significantly reduce MTCT in (South) Africa. Yet, the whole enterprise was, from the beginning, steeped in a serious controversy, and has, up till now, hardly been translated into a comprehensive program of MTCT prevention in South Africa. For this apparent anomaly, there are two reasons of moral import, the first associated with the research process leading to the development of these drugs, and the second with the political impediments to the implementation of the knowledge yielded by these developments. I will deal with each in turn.

3.1 The ethics of the trials

The first ethical issue that dominated discussion of the moral management of MTCT in the previous decade, was whether double-blinded, randomized placebo controlled trials (RPCT) for the shortened regimens of antiretroviral drugs in the developing world were at all ethical. The use of RPCT in the assessment of drugs is accepted world-wide. RPCT, as is well known, amounts to a procedure where the research subjects are divided into two groups. Over a fixed period of time, the one group receives the new drug, and the other a "placebo", i.e. the equivalent of no relevant drug at all (or the so-called "sugar pill"). Neither the research subjects

[4] The name "Nevirapine" is currently commonly in use in South Africa. The drug is in fact marketed by Boehringer Ingelheim under the brand name Viramune. It is structurally a member of the dipyridodiazepinone chemical class of compounds. It is available in tablets for oral administration. Each tablet contains 200 mg of nevirapine and the inactive ingredients microcrystalline cellulose, lactose monohydrate, povidone, sodium starch glycolate, colloidal silicon dioxide and magnesium stearate.

nor the health care professionals administering the drugs are aware of which patients belong to which group; that information is only available to the managers of the trial, who are not in contact with the patients. Full, written informed consent has to be given by all participants. The rationale for the procedure is to assess whether the drug in question makes any notifiable difference to the condition for which it is administered; the only sure way to assess that is to compare its outcome in patients who actually use it with those of patients not using it at all.

The controversy over the use of RPCT in the case of the shortened regimens of antiretrovirals in Africa was sparked by an article by Lurie and Wolfe (Lurie & Wolfe, 1997) in which it was claimed that these trials were unethical since they violated an important moral rule that has been accepted for RCPT all over the developed world: if a new drug is tested for a condition for which there is a known, established and effective treatment, the patients in the control group have to, at least, receive this treatment, and not a mere placebo. Put differently: the use of placebo in drug trials is morally only justifiable when the researchers are in a state of *equipoise* at the outset of a trial. That simply means that a placebo may only be used when there exists no evidence that a treatment is more effective than placebo (Resnik, 1998: 290). If an effective drug for the condition is available and a new drug has to be tested, the drug trial ought, accordingly, not to be a randomized double blind placebo controlled trial, but rather a so-called "equivalency" trial. Paquita de Zulueta explains this as follows: "The use of a placebo is not a necessary or specific feature of the RCT [i.e. the randomized controlled trial], but it is required for answering the research question 'Is this treatment better than nothing?' An alternative question might be 'Is this treatment as good as, or nearly as good as, the accepted effective treatment?' The latter question would call for an equivalency trial (preferably a double blind trial to eliminate bias) as recommended by Lurie and Wolfe" (De Zulueta, 2001: 293).

Marcia Angell, executive editor of the *New England Journal of Medicine* (NEJM - arguably the most prestigious journal for medical science in the world), wrote, in addition, an editorial (Angell, 1997) in which she compared the RPCT in Africa with the infamous Tuskegee syphilis study that ran in the USA from the 1930's to the 1970's, and in which poor, uneducated men were continued to be used as a "control group" in a syphilis drug study long after it was clear that penicillin is an effective drug for their disease. The Africa trials were, in turn, defended by Harold Varmus, Director of the National Institutes of Health (NIH) and David Satcher, Director of the Center for Disease Control and Prevention in the United States (CDC). They argued that the critics of these trials were unfair and did not fully grasp the scientific, social and economic complexities of the research.[5] As a result of this controversy David Ho (*Time* Magazine's Man of the Year in 1996 because of his landmark research on antiretroviral "cocktails") and Catherine Wilfert resigned from the board of the NEJM in protest of the editorial by Angell. (Marc Lallemant has, in the mean time, successfully conducted a ZDV equivalence study in Thailand.)[6]

[5] See discussion by Resnik, 2001: 287.
[6] Personal communication by Mark Cotton.

An analysis of this debate shows a clear conflict between a deontological and a consequentialist approach to the problem. In a deontological approach, the moral argument takes one or more moral "principles" or "rules" as point of departure, and apply them to the situation at hand. The position defended by Lurie, Wolfe and Angell is a deontological approach wherein the rule governing RPCT and equivalency trials is clearly formulated and stuck to at all costs and at all times. The idea of "double standards" for research on human subjects in the first and third world respectively, is rejected out of hand. Such double standards, it is argued, will result in nothing but the exploitation of the third by the first world. Respect for human subjects and beneficence require us to, at all costs, maintain the ethical standards for research on humans that are prevalent in the West and that are formulated in Codes of Research Ethics such as the Helsinki Declaration and the Code of the Nuffield Council on Bioethics. In fact, in a spirited defence of this position, where she addresses the issue of cost and applicability of Western standards in Africa, De Zulueta even makes the following statement: "The revised version of the Helsinki Declaration [which the author endorses] reinforces the deontological or 'clinical care' ethic, as opposed to the utilitarian ethic. Some might argue that the revised guidelines will create serious obstacles to carrying out research that could benefit poorer nations. Others would argue that this is the price that has to be paid if the moral responsibilities of researchers to individual participants are maintained" (De Zulueta, 2001: 307-308). What would the implication of this statement be? Is the author seriously arguing that, if the standards that govern the research on drug trials in the first world cannot be maintained *at all times* when doing research in the developing world, the latter research should simply *not ever be attempted*, even if arrangements are made by local people who conduct the research that are adapted to local circumstances and possibilities? This is a position that could hardly be taken seriously by people who are the actual victims of such a deadly pandemic such as HIV/AIDS, and for whom participation in a drug trial often constitutes the only opportunity of accessing drugs that might relieve their suffering.

The argument in favour of placebo-controlled trials are normally developed along broad consequentialist lines. Consequentialism as approach to moral reasoning requires that only the consequences of an act be considered when deciding on the moral status of the act. Utilitarianism, as the best known variety of consequentialism, requires that the greatest good for the most people involved be sought when assessing the moral status of an act. The consequentialist argument in this regard contains the following three aspects[7]:

1. The recognized regimens of antiretrovirals that do quite successfully prevent MTCT in the developed nations, such as the AZT 076 regime, is prohibitively expensive and entirely unaffordable for women living with AIDS in Africa. In a country such as South Africa, the bulk of the HIV positive women (estimated at about two and a half million) are dependent on public sector medicine and have no form of health insurance. That means that they are entirely dependent on the state for health care. A simple calculation shows that, if we take the number of pregnant women that would require treatment in a single year to be 1.5 million, and the 076 regimen is assumed to cost

[7] I broadly draw on the discussion of Resnik, 2001: 293-304 for these arguments.

US$800 per person (1998 figures), it would cost the South African Government US$1.2 billion (i.e. ZAR7.2 billion). The entire budget for AIDS support in the most recent[8] (February 2003) of the South African Parliament, however, is ZAR3.3 billion, a third of the amount required. Note also that South Africa is one of Sub-Saharan Africa's richest countries. There is, therefore, no realistic chance that something approaching the 076 AZT regimen can be utilized in most other Sub-Saharan states. The only hope for HIV positive mothers wishing to prevent MTCT to their newborns, is significantly shortened (and hopefully more affordable) drug regimens. The development of such regimens is therefore absolutely essential if we want to assure that, at least in the one area where infection can be contained, such containment occurs.

It can therefore generally be argued that placebo trials promote concerns such as social utility and justice for the most people possible under the dire constraints of the African context in which the effort is being made to improve the lives of HIV/AIDS victims, particularly children. The clear aim of the trials is to develop safe, cheap and effective treatments for, if not all, then at least for considerably more Africans than would have been the case without the knowledge yielded by these trials. The aim of social utility, understood as meeting urgent social and medical needs, is thus served. Resnik also points out the "the trials promote justice by providing a fair distribution of the benefits and burdens of research…The studies provide physicians and public health administrators in developing nations with practical answers about preventing perinatal transmission of HIV. Another way of putting this point is that the research satisfies the Declaration of Helsinki's requirement of reasonable availability" (Resnik, 2001: 300).

2. Placebo controls are required for the sake of scientific rigour. They are the best way to ensure the safety and efficacy of the new drugs. Equivalency trials are not called for when testing the shortened regimens of antiretrovirals in Africa. Specifically, it cannot be simplistically assumed that the 076 AZT protocol has been sufficiently established to require that all research subjects be treated with AZT as the minimum required standard of care. The research questions underlying the two regimens are different. What was now being investigated in Africa was not a safe way of preventing MTCT in the developed world, but a safe way of preventing MTCT in Africa. Resnik points out that the research question has changed in two respects. First, what was pertinent was whether the shorter and cheaper regimens were as effective as no treatment at all. The standard level of care for HIV positive women in Africa is, unfortunately, mostly no treatment at all. Second, the disputed studies operate in a population of research subjects that differ considerably from the ones targeted when the 076 regimen was tested. For example, children were used in the Nevirapine study, and children, in medicine, represent a completely different set of variables to deal with. The general condition and health risks of pregnant women in developing countries differ markedly from those in developed countries (cf. the high incidence of malaria and tuberculosis in the former). All of these factors require, according to

[8] At time of original writing

authors such as Varmus, Satcher and Resnik, a placebo control group in order to establish the safety and efficacy of the new drugs that were tested for the shortened regimens (Resnik 2001: 295-296).

3. It has been argued that the use of placebos are desirable in situations where the prescribed doses of AZT or other drugs required for equivalence trials were unaffordable. The argument in this regard is that, if the trials are performed by Africans and adapted to local conditions and to the capacity of the researchers performing them, and if sufficient informed consent is attained from the research subjects, it is paternalistic, if not downright imperialistic and maleficent to oppose such trials. This sentiment is expressed by Dr. David Ho, referred to above, in an article in *Time* from which I quote the following passage: "These clinical trials…were created for Africans by Africans with the good of their people in mind and with their informed consent. The studies were designed to be responsive to local needs and to the constraints of each study site. African scientists have argued that it is not in their best interest to include a complicated and costly AZT regimen for the sake of comparison when such a regimen is not only unaffordable but logistically infeasible. They have, instead, opted for a study design that is achievable in practice and is likely to provide lifesaving answers expeditiously, even though it includes a group of women receiving a placebo. While the inclusion of this placebo group would not be acceptable in the US, the sad truth is that giving nothing is the current standard of care in Africa" (Ho, 1997: 59).

   I agree with Resnik (2001: 300) that this consequentialist argument suffers from the crassness often attached to arguments where the end justifies just about any means. It is dubious to argue that economic considerations should dictate experimental designs. Placebo controls should, preferably, only be used when required in terms of scientific rigour, otherwise people (i.e. those receiving placebos) are clearly and exclusively used to benefit others without any identifiable benefit to themselves. If placebos are not used for the sake of scientific rigour, and only for the sake of getting the trials funded, they are used for the wrong reasons. Over and against this, the consequentialists argue that, without funding, procured in this (possibly morally dubious) way, the trials would never take place and no one would benefit. It is clear that the large pharmaceutical companies can, in this respect, come to the aid and provide funding in such a manner that the use of placebos are limited to situations where the canons of scientific method, and nothing else, require them.

An area of major concern in the literature is the legitimacy of the informed consent acquired form participants in these trials in Africa. Udo Schüklenk, for example, remarks that "the voluntariness of the HIV women's consent is…questionable. Is it not a coercive offer to force terminally ill pregnant women to choose between joining a placebo-controlled trial which gives them a shot at an established HIV intervention, and no treatment at all?" (Schüklenk, 1998: 315). The counter-question, of course, is: what is the alternative? If this trial really is her only chance of "getting a shot" at, at least, attempting to assure the survival of her unborn child, and every attempt is made (which of course does not always happen) to help her to make an informed, competent and voluntary choice, are we

to forfeit her the opportunity purely because we have doubts about the voluntariness of her act?

De Zulueta, in turn, has misgivings about Western criteria for informed consent, but then continues to argue that "if you cannot obtain consent that fulfils 'Western' criteria, there is a *stronger* case for absolute stringency in fulfilling article 1.10 of the Helsinki Declaration (1996 version) which states: 'The researcher should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress'" (De Zulueta, 2001: 303). Marcia Angell also doubts whether informed consent does give sufficient protection from exploitation "because of the asymmetry of knowledge and authority between researchers and their subjects" (Angell, 1997: 847).

I have already raised the issue of what alternatives are available to trying to acquire as much informed consent as possible from people who are, admittedly, often illiterate, frightened, quite ill and dependent on the researcher. Another factor is the question whether all these concerns about informed consent are not indicative of an unjustified paternalism as regards the practice of informed consent in Africa. Why does it have to be assumed that people in developing countries are necessarily so gullible and without understanding that their oral or written consent cannot be taken seriously? Resnik rightfully argues in this regard that we will be well advised not to over-emphasize Western models and procedures of informed consent when dealing with people in Africa. He writes: "One method that researchers have used to improve informed consent in HIV research in the third world is to employ trusted community leaders to convey information to people in local populations." (Resnik, 2001: 301). This idea has, in turn and by implication, been sharply criticized by Ijsselmuiden & Faden (1992: 830-833) and Ekunwe (1984: 23) who are very doubtful of the assumed bona fides of such community leaders in countries with poor human rights records.

This is a difficult problem, although I am convinced that it is also problematic to simply apply Western standards of informed consent to indigenous Africans. The African's idea of personhood is much less related to Western ideas of individual autonomy, and is much more closely related to family ties and community-based. Decisions are therefore seldom made by people as entirely independent individuals, as is assumed in most Western models of informed consent. A broader understanding of this phenomenon is required whenever reflecting on informed consent in Africa.[9] For example, in a recent Masters dissertation for the M.Phil (Bioethics) degree at the University of Cape Town, Paul Roux argues persuasively for the thesis "that the process of informed consent, although appropriate in Africa as an exercise in the recognition of autonomy, when applied in the case of African women may have the unexpected and deleterious effect of isolating her from a traditional support base and enhance the likelihood of non-disclosure of HIV status, and should therefore be adapted to meet the needs of this special situation" (Roux, 2001). This "adaptation", according to the author, mainly entails involving the family much more in the process of obtaining consent. Roux argues that his research has shown that this approach greatly contributes to a

[9] Cf. for this argument Moodley, 2002: 209-213

lesser risk of stigmatisation when these women reveal their HIV status in their communities.

The following conclusions can be drawn form this discussion:

- There is, particularly in view of the prohibitive costs associated with conventional regimens for antiretroviral treatment, a serious need for cheaper and simplified (preferable shorter) regimens of these drugs to prevent MTCT in Africa.
- Randomized placebo controlled trials for shortened drug regimens to manage MTCT in Africa are justified *if the research question is of such a nature that scientific rigour requires it*.
- If scientific needs justify equivalency trials rather than placebo trials and the latter is prohibited because of expense, special appeals ought to be made to foreign governments and pharmaceutical companies to provide the standard level of care required by equivalency trials.
- It is a mistake – and overly paternalistic - to judge the quality of informed consent in Africa merely by the standards applied in the West. Models of informed consent appropriate for Africans ought to be researched much more intensively. Steps ought at all times to be taken to ensure that the beneficial results of drug trials in the third world be made available to the people in whose communities this research was done.

3.2 Denial of the problem and lack of political will to prevent MTCT in South Africa

The debates referred to in the previous section are intriguing, and although the ethical issues have not been settled, they did not prevent the actual research for shortened drug regimens to prevent MTCT – placebo based or not – to actually take place. As I have indicated, a number of new drugs (of which Nevirapine is the best-known) or shortened regimens of existing drugs (e.g. Zidovudine) have been developed and have been proved to be highly efficient in preventing MTCT.

That then leaves the question as to why the development of a comprehensive program of providing these drugs to pregnant women and newborns has been so slow in coming (it has only been, theoretically, introduced in 2004; some would argue at least 10 years too late!), and, once the program has been introduced, why it is so slowly and seemingly reluctantly implemented. Benatar writes in this regard about the situation in South Africa: “While government’s recent commitment to providing antiretroviral treatment is welcome relief from long-standing vaccilation, the rollout programme, like implementation of the strategic plan, is far too slow (only about 65 000 of the 500 000 who require antiretroviral treatment are currently receiving this). Many lives have been sacrificed through denial and delay. There is urgent need to correct these shortcomings” (Benatar, 2005: 9). This reluctance to get on with what is so obviously required constitutes one of the most serious moral issues associated with the pandemic in South Africa, and will, in all probability, be acknowledged by future generations as, morally speaking, one of the really tragic (if not outrageous) eventualities that accompanied the epidemic in current times. A golden opportunity has thus been lost to relieve the suffering of thousands in a situation where millions are, in any case, suffering and dying, as the figures often in this book clearly indicate.

Why is the South African government so hesitant to address the problem and provide the antiretrovirals to prevent MTCT? The current Minister of Health has, firstly, consistently expressed fears that Nevirapine – the drug with clearly the best potential, particularly because of its low cost (US$4 per regimen) and the relative simplicity of its administration – is dangerous because of its possible toxicity. In addition, the argument has often been made by the Minister in the press that Nevirapine has not been approved by the American Medicine's Control Board and is thus not being used in the USA. Why should it then be "dumped", with all its alleged "dangers", on the South African populace?

These concerns are not at all justified. Firstly, there are no indications that Nevirapine is unacceptably toxic. McIntyre and Gray, two eminent scientists in the field whose work I have already referred to extensively, state explicitly: "These trials of antiretroviral interventions [they refer, in particular, to Nevirapine] have included several thousand African mother-infant pairs. To date, none of these trials has demonstrated significant toxicity or serious side-effects in mothers or infants" (2000: 31). This finding about toxicity was also confirmed by all the relevant scientific literature, and has also been confirmed by research done by South Africa's Medicines Control Board in 2003, which officially, following a request for such research by the Minister, found the drug to be "safe and efficient" (as has also been found by the National Institutes of Health in the United States) (Brümmer, 2003: 2).

Secondly, even if the drug had a level of toxicity, would that necessarily rule out its use, given the gravity of the ailment that it might prevent in newborns? If we only were to use entirely non-toxic drugs in medicine, most of the currently world-wide utilized regimens of chemotherapy for diseases such as leukemia and lymphoma – regimens that, particularly in the case of children, have dramatically improved the prognoses for these life threatening diseases – must have been ruled out, since they all are, to a greater or lesser extent, toxic and require careful surveillance when administered. Surely the seriousness of the MTCT of HIV would justify a level of toxicity in a drug if the drug can prevent such transmission? While it is unrealistic to expect the "perfect" drug, the point about Nevirapine, to refer to the last quotation again, is, in fact, that it does not seem to be toxic at all.

What has been found about Nevirapine is that there is a possibility that HIV positive women who use it in a second or further pregnancy, might develop resistance to the drug (it works quite well in first pregnancies). However, there is uncertainty about whether all the information on this issue is yet available. What is clear, is that there were some (though not major) violations of Good Clinical Practice Guidelines (GCPG) when the original trials on Nevirapine were done in Uganda (the so called HIVNET 012 trial). This has caused South Africa's Medicine Control Council to express reservations about Nevirapine. The issue in this regard, however, is resistance and not toxicity. There seems to be general consensus in the medical fraternity that Nevirapine is safe to use when not administered in isolation, but in combination with other antiretroviral drugs. As has been argued by Natrass in chapter 3 of this volume, the cost-issue of these

combined drugs is rapidly becoming less of a problem because of the significant lowering of drug prices in recent times.

The minister's second concern about antiretroviral treatment in South Africa's public health sector, is the issue of cost. Is antiretroviral treatment to prevent MTCT affordable? Current estimates are that these treatments will cost the current tax payers in the vicinity of R90 million (US$15 million) per annum – literally a drop in the ocean of the (even South African!) government's current health budget. In addition, large pharmaceutical companies have gone to great lengths to cheapen the drugs, or to make them available free of cost. (Note the figures provided in chapter 3 about the significantly reduced costs of antiretroviral drugs in South Africa.)

Even more significantly, the popular, government-endorsed theory that the provision of antiretroviral drugs, not only to pregnant women and newborns, but to all South Africans living with AIDS, is totally unaffordable, has, most recently, increasingly been challenged. The economists Natrass, Geffen and Raubenheimer have, in a recent study (2003; cf. also Natrass 2004), shown that highly active antiretroviral therapy (HAART) is indeed affordable for the government, and much more advantageous for society than non-treatment. They added their set of cost-estimates to those of Johnson and Dorrington, and came to the conclusion that to provide HAART to people in the fourth stage of AIDS will cost less than ZAR1 billion (approximately US$117.6 million) and will reach a peak of R18.2 billion by 2015, when 2.3 million people in South Africa will be needing these drugs. If services such as counselling, prevention of MTCT and the treatment of other sexually transmitted diseases be added to this, the entire cost of the intervention, including infrastructure, will be R20.3 billion (about US$2.3 Billion) in 2015. This represents the highest limit of the costs. If we assume that the South African economy will grow by 2% (inflation adapted) in the Gross National Product (GNP) between now and 2015, it means that a full-fledged prevention and treatment program for HIV/AIDS will cost the public sector about 1.7% of GNP at the height of the epidemic. According to the World Health Organisation's Commission on Macroeconomics and Health, it is attainable for countries with a low and middle income to increase budget allocations for health to 1% of GNP by 2007, and to 2% of GNP by 2015. The cost projections by Natrass and colleagues are within these limits (Cf. Natrass 2003). That means that not only is the prevention of MTCT affordable to the South African government, but also the wholesale provision of antiretroviral drugs to the entire population in need of it.

This does represent a lot of money. Ought a country such as South Africa to be "tough" and rather sacrifice the HIV/AIDS generation for the sake of social utility? Innuendo of concern about "what will happen to the AIDS orphans if we save their lives" is also, from time to time, heard form the ranks of government and the ruling ANC party spokesmen. Natrass rightly has a twofold response that I fully agree with. The first is that treatment programs (with antiretrovirals) turn out to be prevention programs and might therefore contribute greatly to lowering the general infection rate in the population. But, as Natrass remarks, there is an even bigger ethical problem: "What does it mean for us as a society to opt for the route of sacrificing a whole generation? Do we really want to sacrifice other people that

can be treated for less than 2% of the GNP at the peak of the epidemic, thus restoring life and hope for them?" (Natrass 2003; my translation).

A third reason for the government's hesitance to embark on a full-scale program of (even) MTCT prevention is, in all probability, of a deeper nature. It has to do with a deep-seated scepticism of the scientific facts about the nature of the epidemic, fuelled by the influence of dissident scientists like Rasnick, Geshekter and Duesberg who question whether HIV causes AIDS at all (Cf. Duesberg, 1996; Rasnick, 2000 and Geshkekter 2000). It has become clear that the South African President has been under the influence of the dissidents for a long time – he even appointed some of them to a "task group" to "do research" to establish the relationship between HIV and AIDS – and has been exerting a very strong influence on the official position taken on these matters by the Minister of Health and other prominent members of the government and the ANC. The reader is, in this regard, referred to citations from both an article that President Mbeki wrote on this matter, as well as a speech that he made at the University of Fort Hare in 2001, provided in footnote 2 of chapter two of this volume. From these statements, the extent of his denial of the seriousness of the AIDS pandemic seems indisputable.

Given the almost cataclysmic nature of the AIDS epidemic in (South) Africa, this kind of denial can only be judged as morally dubious. Space will not allow me to explore fully the ethics of denial.[10] Denial is an acknowledged and even accepted psychological disposition in situations where people are struck by very bad news that they find difficult to accept. It represents one of the "phases" that Elisabeth Kübler-Ross (1975) identified in typical reactions of people who discover that they are terminally ill. As such it is well-known and can even evoke our sympathy. There is, however, no justification for the head of a state and/or government of a country with such a serious problem as our AIDS pandemic to become stuck in the first phase of people's typical response to bad news. AIDS is indeed bad news, and we would all have loved it if there were no AIDS. However, it is intolerable that the leadership of a country experiencing such a crisis creates the impression that it almost does not exist, or is not at all a priority. This behaviour must be morally condemned; it indeed creates the impression of irresponsibility. No wonder that, in recent times, more and more voices are raised with the prediction that the current South African leaders ought to be aware that their inaction and denial may be judged, sooner rather than later, as "crimes against humanity". Stephen Lewis, the current United Nations envoy for AIDS in Southern Africa is the latest international figure who has accused the South African government of "criminal negligence" (Hooper-Box & Battersby, 2003: 2) in its handling of the epidemic, particularly concerning its reluctance to roll out a program of MCTC prevention, in spite of having been ordered to do so by the highest court in the land.

4. Conclusions

The following short conclusions seem appropriate in view of the previous discussion.

[10] On the topic of denial, cf. Garvey, 2001: 3-20.

4.1 The phenomenon of HIV/AIDS has, probably more than anything else, proved our vulnerability to disaster, in spite of the unprecedented advances in medical science at the beginning of the 21st century. I have elaborated on this point at the end of chapter 4 of this volume, and will not repeat those remarks here, valid though they remain.

4.2 The dispute about the ethics of randomised placebo-controlled trials for the development of drugs to combat MTCT in Africa reiterates Stephen Toulmin's long-standing insight that "science is not an intellectual computing machine, but a slice of life" (Toulmin, 1961). Science is no value-free enterprise with methods, procedures and assumptions that are in no way influenced by the social contexts within which it operates and for which it becomes functional. As a "slice of life" science participates in the uncertainties and instabilities of our historical life as human beings. For a legitimate, accountable and adequate understanding of science we are compelled to reflect on the variety of relationships within which science can be practiced, ranging from its relation to labour and technology, to the relations to society and politics, as well as the relations to views of life and religious belief (Rossouw, 1980: 14-15).

This is well illustrated by the following observation by Ranaan Gillon: "…clinical research…always has two components: a component of pure research intended to produce generalisable medical knowledge, and a component of therapy, where the intention is to benefit the particular patient/subject's own health…The less a trial shares in that Hippocratic commitment, i.e. the less it is intended and likely to benefit the individual patient subject, the more it should be treated as non-therapeutic research aimed at benefiting others, and not the participant subjects, and therefore the more such a trial should incorporate the safeguards appropriate to non-therapeutic research, including the need for extensively informed consent" (Gillon, 2001: 263). This judgement makes clear that the nature of the science practiced cannot be divorced from the moral concern about the extent to which the investigated subjects will, eventually, benefit from the knowledge gained in the process. The issue of drug trials for the sake of reducing MTCT makes us aware of both the possibilities and the social responsibility of science, the tragedy of scarce and depleted resources, the need to act for people's benefit in spite of these impediments, and the possibility of hope that scientific innovation might incur in situations that otherwise seem hopeless.

4.3 The tragedy of the South African Government's neglect to act in accordance with people's real needs as far as MTCT in that country is concerned, unequivocally proves the dangers of an unjustified politicization of the discourse about HIV/AIDS and the concomitant problem of MTCT in Africa. Such politicisation holds the potential of exacerbating an already occurring catastrophe. HIV/AIDS is primarily a health problem and not a political problem, although we may recognize that socio-political factors, such as chronic poverty and illiteracy, can negatively impact on the pandemic. What is required in South Africa and other African countries is what e.g. happened in Uganda where the impact of the disease has been significantly curbed by a national, co-ordinated and comprehensive treatment and prevention campaign that had the prevention of MTCT as a core component.

4.4 Once the previous point has been made in its own right, it is also as important to acknowledge that the catastrophe compels us to reflect critically on the massive imbalances between the wealth of Africa and the West, and thereby to rethink the requirements for human well-being on a global scale. No other health phenomenon has in recent years more emphatically demonstrated the need for the development of a global bioethics. The reader is invited to read what has been argued in this respect in chapters five and six of this volume.

4.5 In conclusion: MTCT of HIV in Africa is a serious problem, but it can be managed in an affordable way, as has been argued. The most serious impediment to its humane and effective management is not a lack of knowledge, the unavailability of drugs, the infrastructure to make them available, or their unaffordability. It is the lack of political will and the denial of the seriousness of the problem on the part of the political leadership, particularly in South Africa. Once this leadership assumes its rightful responsibility, all the indications are that aid from the rest of the world, be it governments or pharmaceutical companies, will be forthcoming, and a very significant reduction in MTCT can be expected. Opportunities and good will in this regard abound. It is for the leadership in African countries to grab the day: co-operate with both countries and pharmaceutical companies who are willing to come to our aid, accept their offers, make the infrastructure available for the distribution of these drugs and do what is now possible to prevent an almost unspeakable tragedy.

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