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**Physican, do no harm**

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Recent publicity about unethical trials raises a number of questions about research in developing countries. It also reminds us of the limitations of accepted safeguards: some of the trials under attack passed ethical review boards in the funding countries and have the approval of the local governments.

Some months ago, the New England Journal of Medicine carried a comment on 15 ongoing clinical trials testing cheaper drug regimens to prevent maternal-foetal transmission of HIV in Africa and Asia. Some 16,000 pregnant, HIV-positive women were enrolled in the placebo-controlled trials. The problem: these trials began after AZT had been found to prevent such transmission by 50% or more, and is recommended to all HIV-positive pregnant women in western countries. In other words, thousands of women in the trials were getting sugar pills to test the efficacy of the new regimens. If they had been enrolled in trials in the West, they would have received a standard course of AZT.

Nine of the trials are funded by the US Centers for Disease Control or the US National Institutes for Health.

The following points were made, in professional journals and the lay press: Placebo controls in any trial are unacceptable once an effective treatment is found. The research question cannot be: is the drug better than nothing, but is it as good as the other (more expensive) drug. The NEJM argued that earlier trials contained enough data on the shorter regimens being experimented with now, to show that they were better than a placebo.

The argument that placebo-controlled trials are more rapid, and need fewer numbers, is unacceptable: researchers cannot put their trial participants at risk for such reasons.

The existent standards of care are the consequence not of medical choices but economic policies which make effective drugs exorbitant. An ethicist working in reproductive health asks, "Why couldn't the government have taken AZT over as the people's property, as the French government did with RU486?"

A response from the CDC and the NIH acknowledged the inherent tension between participants' risk and the public's benefits, but argued that the logistic problems of administering AZT in Africa, the drug's toxicity in malnourished women, and the cost, made them look for simpler, cheaper alternatives. And "The most compelling reason to use a placebo-controlled study is that it provides definitive answers to questions about the safety and value of an intervention in the setting in which the study is performed, and these answers are the point of the research." However, logistic problems and cost cannot be reasons for withholding AZT from the control group. Further, the interventions were of known (though lesser) efficacy, according to the NEJM.

A supplement in the Monash Bioethics Review suggests that much research today is poorly formulated, repetitive, and not publicly accounted for. It also attacks the "placebo orthodoxy" in clinical trials, noting the limitations of such trials, and suggesting alternative means. Coincidentally, perhaps, soon after the controversy erupted it was found no longer necessary to use placebo controls.

Much has also been made of the fact that the trials passed ethics boards in funding countries, that they received the women's informed consent, had the support of the local governments. This is only evidence that such ethics boards are fallible, at best. And governments may, and do, violate their responsibility to people. Even responsible governments may be unable to refuse offers of such trials. Are they really in a position to oppose international funders when the proposal before them offers them a chance to treat a few people, and maybe get a cheap treatment in the long run?

Likewise, individual women who give their "informed consent" in such trials would naturally choose the chance of getting an effective drug, even if they turn out to be the unlucky ones to get a placebo instead; they would never get treatment otherwise. The fact is: ethical issues may sometimes need to be seen in economic terms. The research question was defined not by science but by an essential drug's cost. Why should any essential drug be beyond the reach of the vast majority of people who need it? Interestingly, governments and international organisations may be willing to bargain for cheap drugs when it comes to contraceptives.

There are some parallels to be drawn between the HIV trials and the ICMR trials on cervical cancer in which 1,158 women with cervical dysplasia were "monitored" to observe the rates of progression to cancer. Investigators say that they did not obtain written consent because most of the women were illiterate. Seventy-one women developed cancer; at least nine developed invasive cancer without treatment. Sixty-two women developed cervical carcinoma in situ before they were treated.

Investigators do not seem to have informed the women that their lesions were known to progress to cancer. Worse, any treatment seems to have been stopped once the study was over. In other words, the women who took part in the study trusting that they would receive better health care than otherwise, were allowed to fend for themselves, even die.

HIV and, to some extent, cervical cancer, is a product of poverty and powerlessness. It could also be argued that in both situations, the health care system is looking for cheaper interventions without challenging the forces that make current interventions so expensive, or inaccessible. Third, did the study examine a new question? Finally, in both cases the women could not have given informed, voluntary consent; they trusted the investigators because they had no other health care.

A 1995 article- in the journal Science notes that establishing institutional review boards and obtaining meaninful consent are acknowledged to be two major problems in ensuring ethical human research. This issue will become even more important in the future, as developing countries, particularly those with large burdens of "interesting" diseases, are seen as ideal research settings. For example, HIV infection is so prevalent in a country like Nairobi that a study that would take 15 years in the US can be done in 18 months, and for a lot less.

Especally if you don't have to use AZT.

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**Readers are invited to send reports and comments for our April issue on the ethics of clinical trials in India.**

**" I will feel reassured only after I get my job back"**

A recent Bombay high court judgement affirmed the HIV-positive individual's right to employment. Separately it also held that HIV-positive people can approach the court without disclosing their identities. The court directed that the public sector corporation which had employed the petitioner, MX, give him work as long as he was able, and also pay him Rs 40,000 for the four years that he was unemployed

MX is among the millions of unsung heroes of our times, courageous and resilient in the face of crippling adversity. It is no passing irony that his employer who kept him dangling first as a contract worker, then as a casual worker and finally fired him just before he was to be made permanent, is a public sector corporation. We reprint his story, with his consent.

I ran away from home when I was 12. There was always a shortage of food. I used to work as an agricultural labourer and earn some money but there was only grinding poverty to be faced each day. I ran away from poverty... "A lorry driver took me to a refinery where I was put to work painting drums I slept wherever I found some shelter. Later I joined the company as a contract worker. That was in 1982. I used to load 205-litre drums on to a truck...

"I went back home for the very first time after 12 years, after getting a telegram saying my parents had died. They of course had only used it as a way of getting me there to get married. Thereafter I went home each year that I was working with the company...

"In 1993 I was given a letter saying I was to be made permanent. The company doctor sent me to a private clinic for what I later understood was the HIV test. The doctor at the private clinic told me I had tested positive but I should reconfirm the findings at JJ hospital. I took both reports to the company where the doctor told me that though I had tested HIV positive I was fit enough to work and that I would be made permanent. However, I still worked as a casual employee for the next three months after which I was given a letter telling me that I was suspended from work as I was HIV positive...

"I approached whoever would hear me and pleaded my case specially as I had a wife and two children to support. Many officers told me they could not help and directed me to another official. The doctor at JJ hospital gave me a lot of courage and sent a letter to the management to absorb me but that did not work either. Another senior doctor even wrote to the company director... Finally, this doctor referred me to the advocate who fought my case...

"The first time I went to court I felt I would get justice there but then again I wasn't so sure. Though I was told that I could have as many as 15 years before the virus actually took its toll I never felt ill or tired. I have accepted that I have the virus. It does not frighten me except that I want to provide for my family...

"When I lost my job, my wife sold her jewellery and I eventually began driving an autorickshaw. I haven't gone home since I was removed from the company. I can't afford it. When my only sister got married I did not attend the marriage as I could not afford to take anything home for the family or for her..

"I will feel reassured only after I actually start working at the company and use the back wages to repay some of my debts. Providing for my children's education is my major task.... Life has been a harsh struggle. I cannot bear to see the suffering of poor people on the street. My friends laugh at me when I weep in films that show the disparity between the rich and the poor. I don't see movies anymore."

Excerpts.from 'MX tells his story'. H. Rustomfram. From The Lawyers Collective 12(5), 1997.