HIV and AIDS offer tremendous opportunities for research given the need for discovering new strategies and agents for preventing and treating disease. The urge for developing new drugs and vaccines and the financial stakes involved pose ethical challenges to research workers in the field. Nowhere is this more relevant than in developing countries and more so in disadvantaged groups such as women and children. The ones who are most in the need of protection and those who need to be given access to the benefits of new developments are also the ones who are most likely to be exploited.

In several countries, HIV infection and AIDS are more commonly encountered amongst vulnerable populations; individuals who are poor, uneducated and hence powerless. They have a limited understanding of the disease, and a much more limited insight into their problems. Although newly infected individuals are not at risk of death in the near future, they are often pressured into entering clinical trials. They are approached at a time when they are in emotional shock and hence very vulnerable. It is questionable if informed consent is properly implemented and if the prospective subjects understand the concept, its process of administration and its implications. Sastry et al[1] evaluated the overall understanding of key issues regarding informed consent about HIV/AIDS amongst pregnant women in the state of Maharashtra, in India. They estimated that, after group education and counseling (GEC), only 58% of women had understood six out of eight key issues. It has been suggested that ethics boards should be more innovative and explore the suitability, feasibility and effectiveness of new methods of conveying information (perhaps through videotapes or obligatory information sessions with independent counselors) to enhance understanding amongst prospective research subjects for HIV-related research studies.[1] This concept is appealing and should perhaps be utilized for all major trials and especially those that are industry sponsored and more so in developing countries. Sastry et al[2] have determined that 72% of women understood key issues when visual aids were used during group counseling sessions. Moreover, when these same visuals were used during individual counseling sessions, 96% of women comprehended key issues pertaining to informed consent.

There has been much debate and discussion in the scientific community about ensuring justice for trial participants. It is necessary that potential volunteers are adequately informed of both the long-and short-term consequences of initiating prolonged regimes of multiple anti-retroviral drugs. Ethically it is necessary to ensure that these participants have sustainability of care and access to drugs, even after the trial ends. Different groups have come up with innovative approaches to ensure that research participants continue to be provided with care through co-payments, pharmaceutical donations and drug funds.[1] However, the very concept of providing sustained care has, paradoxically, led to another ethical dilemma: Would the decision to participate in the trial or not be influenced by the prospect of receiving care and effective drugs? Wouldn’t this act as an undue inducement? The likelihood of these considerations influencing the prospective volunteer is much more in resource–poor settings, since these projects often offer better quality care than that available through the public health sector.[3]

Various corporate or political groups may attempt to influence and control the study design; this is another matter for concern.[3] Researchers might subordinate subjects’ welfare to the objectives of the study especially when the research question is extremely important and in their perception could provide an answer that would substantially improve the care in future.[4] This is especially true of trials pertaining to HIV and anti-retrovirals. Even well-meaning researchers may treat human subjects as a means to an end with their welfare being considered secondary to the ultimate research goal.

Placebo-controlled trials produce much faster results and are favored by the scientific community but in a situation such as HIV/AIDS, where accepted modes of intervention are available, it is unethical to conduct placebo-controlled trials. The AIDS clinical trials group (ACTG) Study 076 was the first randomized, controlled trial in which administration of the anti-retroviral drug zidovudine to HIV-positive pregnant women was proved to reduce the incidence of maternal-infant transmission of HIV infection.[5] Undoubtedly, there are many other anti-retrovirals as well as other methods for reduction of perinatal HIV transmission. These would necessarily have to be evaluated in randomized, double blind controlled studies. However, it is necessary that the control group receives an accepted mode of intervention such as zidovudine or nevirapine and not a placebo. In fact, these modalities should be made available to all the patients.
It is unethical to have volunteers receiving placebo when a drug regimen, which has been proven to reduce transmission significantly is available. However, even after the ACTG study was completed, Lurie and Wolfe\textsuperscript{46} identified 18 randomized, controlled trials of interventions to prevent perinatal HIV transmission with ethical guidelines being violated in 15 trials. The studies were designed to evaluate a variety of interventions, such as the use of anti-retrovirals, Vitamin A and vaginal washing in a total of over 17,000 women.

In the two studies being performed in the United States, the patients in all the study groups had unrestricted access to zidovudine or other antiretroviral drugs. In 15 of the 16 trials in developing countries, however, some (and at times none) of the patients were provided with antiretroviral drugs. Nine of these 15 studies being conducted outside the United States were funded by the US government through the CDC or the National Institutes of Health (NIH), 5 were funded by other governments and 1 was funded by the United Nations AIDS Program. The studies were being conducted in Côte d’Ivoire, Uganda, Tanzania, South Africa, Malawi, Thailand, Ethiopia, Burkina Faso, Zimbabwe, Kenya and the Dominican Republic. These 15 studies clearly violated ethical standards, which should have been as exacting as in the case of research carried out in the sponsoring country.

Trials that emanate from developed countries and that are conducted either partially or completely in developing countries are more susceptible to ethical violations. As Lurie and Wolfe correctly point out, acceptance of a standard of care that does not conform to the standard in the sponsoring country results in a double standard in research. These double standards, which permit research designs and practices that would be unacceptable in the sponsoring country, create an incentive to use under-privileged populations with least access to healthcare in resource-poor countries as research subjects. Government bodies responsible for matters of public health and research have a huge responsibility. They must ensure that prospective subjects are offered appropriate and adequate information to base their decision on and are provided with optimum care during and after the trial in an ethically conducted research study.

The organizations indulging in research should be prompt in giving wider publicity to the research findings. For example, the National AIDS Control Organization (NACO), which is the nodal body for work on HIV/AIDS in India, has been successful in demonstrating the feasibility of short-term zidovudine prophylaxis for prevention of vertical transmission of HIV infection from the infected mother to her baby in a study conducted in India from April 2000 to July 2001 and the results are available at the NACO website.\textsuperscript{[7]}

The HIVNET012 trial demonstrated the use of nevirapine prophylaxis in HIV positive pregnant women.\textsuperscript{[8]} Subsequently, NACO incorporated the distribution of Nevirapine to HIV positive women in labor as a part of the Prevention of Parent to child transmission (PPTCT) Program in India. From January 2003 to June 2004, 4771 mother-baby pairs have received Nevirapine prophylaxis.\textsuperscript{[9]} NACO should publish the results of the study so that the benefits and limitations of the interventions can be gauged by the scientific community and other resource poor communities can learn from these results.

The prophylactic use of anti-retrovirals in pregnancy for protecting the neonate has raised a number of ethical issues. Continuing research has led to the availability of new, more potent antiretroviral regimens to prevent vertical transmission of HIV infection to the fetus and baby. Further, new evidence is available regarding the safety of use of highly active antiretroviral therapy (HAART) in pregnant women. It is also known that administration of a single-dose of nevirapine could result in the development of resistant HIV strains. This could limit treatment options available to these women in future. A 7-day tail of AZT plus 3TC (Lamivudine) is used to reduce the risk of NVP resistance and the same has been incorporated in the WHO guidelines.\textsuperscript{[10,11]} However, WHO continues to include single dose nevirapine without the AZT plus 3TC tail as one of the alternative regimens for preventing parent to child transmission of HIV.\textsuperscript{[10,11]} In view of the potential for resistance is it appropriate for WHO to continue with this regimen in its guidelines?

With increasing globalization, the number of trials pertaining to HIV, in developing countries will only increase. A large proportion of these trials will be funded either by developed nations or the industry. The issue of protection of disadvantaged groups will be a major concern and it is necessary to ensure that the rights of research subjects are not trampled upon and that the research is conducted in conformity with the highest ethical standards.

**References**