Indian J Med Res 124, December 2006, pp 608-610

Commentary

Participation in HIV vaccine trials: Listening to participant & community concerns

The terrible truth about the HIV/AIDS pandemic is that it affects men, women and children indiscriminately. In India, almost half of all infections are among women, a population with few risk factors beyond those that men place them at[1]. Additionally, as the number of orphaned children from AIDS increases, we need to realize that disease risks arise from one's social positioning, making vulnerable groups unable to negotiate adequate education, security from exploitation, and safe sex practices[2,3]. The search for a scientific intervention capable of slowing the pandemic resembles a quest for a holy grail, a search almost unattainable, but with the potential to stop suffering of a Himalayan proportion. Effective prevention interventions exist, focused on peer-based condom use and behaviour change for vulnerable groups. These strategies need to be complemented by additional prevention tools. Scientists are placing their efforts with prevention strategies such as circumcision, pre-exposure prophylaxis and microbicides; but the most elusive is an HIV vaccine[4].

In this issue, Suhadev *et al* present their important findings from a socio-behavioural study in Tamil Nadu, India, addressing barriers to participating in an HIV vaccine trial[5]. The authors report that concerns amongst Indian populations are similar to those from other countries *viz.*, the potential for adverse events related to the vaccine, for stigma from participating in a sexually relevant clinical trial, and for practical issues about how participation in a clinical trial may disrupt their daily schedules[6]. Suhadev *et al* strongly recommend that educational activities aimed at potential trial populations may help to quell concerns and improve enrolment. The authors quite rightly demonstrate the difficulties of enrolling adequate community representation of high-risk groups, different ethnicities and an appropriate representation of women[7].

As with any clinical trial, enrolling the appropriate population is challenging. In an HIV vaccine trial, the outcomes of most interest will be the number of HIV infections per group (vaccine or placebo arms). In order to achieve appropriate power to detect efficacy in these clinical trials, we need to recruit participants at high enough risk that multiple infections will be documented by the end of the trial. To enroll these populations, we would look to individuals with expected risk-factors, such as men that visit sex workers, sex workers themselves, men that have sex with men, intravenous drug users; amongst others that have less obvious risk factors. As one reads this brief list, you can infer that participation in a clinical trial assessing HIV vaccines likely suggests that the participants have a risk factor. This study demonstrates that the very recruitment issue is a barrier for otherwise benevolent participants, participants that recognize the importance of clinical trials, but do not want to be subject to stigma from family members, physicians, insurance suppliers and immigration.

The barriers highlighted in this study[5] may well be incorrect from a scientific perspective (*e.g.*, becoming seropositive from the vaccine), but demonstrate that these public perceptions are widespread in India and internationally[6]. If we are to

effectively reduce clinical trial participation barriers, we need to aim our educational messages at both potential participants and the community at large. India is making important steps at combating HIV prevalence, however, a greater emphasis must now be placed at combating HIV related stigma[8].

Enrolling in a clinical trial does indeed have risks associated with it, and the argument that a HIV vaccine is desperately needed cannot overshadow the protection of participants[9]. The immediate and long-term safety of vaccines is poorly understood and the medical community stands deeply divided over the safety of even conventional vaccines, such as influenza[10]. As the scientific community races towards as many as 32 HIV vaccine trials around the world[11], we need to be cautiously optimistic that any new intervention has the realistic potential to provide protection from infection. AIDS vaccine initiatives have focused on a variety of different vaccine strategies, including mucosal immunity, cell-mediated immunity, and humoral immunity; without achieving consensus from the vaccine community that any one or several approaches holds the greatest promise[12]. The VAXGEN trial illustrates that inappropriate use of trial funding and use of the limited resource of participants was permitted, despite the widespread expectation that the vaccine would be ineffective[13]. The argument used to permit the clearly ineffective intervention to continue in a trial setting was that the trial demonstrated that the infrastructure to conduct efficacy trials existed[14]. For the AIDS activist community around the world, the failure of this trial diminished much good will and public support for vaccine trials. By unrealistically hyping the potential benefits of clinical trials, without properly addressing the potential difficulties and harms associated with participation, we are misleading participants and they may quickly grow tired of assisting in participation. This current study illustrates that participants have a high expectation of potential success of a vaccine, clearly more so than most vaccine scientists.

Participants in trials may have difficulty in understanding scientific concepts such as randomization, placebo and power. However, as clinical trialists, it is not only our duty to ensure that we educate them about these concepts and dispel myths regarding adverse events, but it is our duty to ensure that participation in the trial does not place them at an increased risk of social stigmatization, potential violence and economic discrimination. Educational activities need to focus on the wider community, addressing both the stigma related to trial participation as well as promoting the charitable contributions that participants are making.

Indeed, scale up of effective prevention services for vulnerable groups is a key element of a vaccine strategy for several reasons. First, such strategies help identify the highest risk population that are suitable for trials[7]. Second, such strategies can be key elements of social inclusion of otherwise marginalized populations[15]. Third, scale up of vulnerable group interventions would enable a delivery infrastructure for vaccines, when finally introduced[16].

No one really expects an effective HIV vaccine to provide 100 per cent protection from infection. Indeed, even a vaccine that can provide 50 per cent protection would have a tremendous impact on slowing the HIV/AIDS epidemic in India, but it will be no panacea[16]. Disinhibition, or increased risky behaviour, is the major concern from any partially effective vaccine, as the public and scientists may have difficulty in distinguishing partial from full protection[6]. This current study lends some credence that at-risk populations recognize the importance of condoms, even if a vaccine existed. Although all of this formative research is conducted regarding a hypothetically effective vaccine, it demonstrates that the public and high risk groups in particular, are aware of the effectiveness of established prevention strategies such as condoms, and that further efforts to promote and make accessible male and female condoms are the most likely successful strategy to continue addressing this disease[3].

As the world races toward an effective HIV prevention strategy, scientists and policy makers must be guided by evidence, not by desperation[4]. We are still far off from having an effective prevention strategy and despite the promises made by political leaders at the recent International AIDS Conference in Canada about imminent effective strategies such as circumcision, pre-exposure prophylaxis and microbicides; we have no more effective strategies than we did at the beginning of this epidemic: condoms, clean needles, and peer-based education[3]. As Suhadev *et al* demonstrate, the public deserves appropriate awareness about clinical trials and HIV/AIDS in general, and we need to listen to them to understand their concerns instead of assuming that scientists know best.

Edward J. Mills* & Prabhat Jha
B.C. Centre for Excellence in
HIV/AIDS, St. Paul's Hospital
Vancouver BC &
Centre for Global Health Research
St. Michael's Hospital
University of Toronto
Toronto, Ontario, Canada
******Corresponding author*:
e-mail: millsej@mcmaster.ca

References

1. UNAIDS. Report on the global AIDS epidemic. http://*www.unaids.org/en/HIV_data/2006GlobalReport/default.asp* (Accessed Oct 31, 2006). 2006.
2. Menon-Johansson AS. Good governance and good health: The role of societal structures in the human immunodeficiency virus pandemic. *BMC Int Health Hum Rights* 2005; *5* : 4.
3. Jha P, Nagelkerke JD, Ngugi EN, Prasada Rao JV, Willbond B, Moses S, *et al*. Public health. Reducing HIV transmission in developing countries. *Science* 2001; *292* : 224-5.
4. Mills E, Siegfried N. Cautious optimism for new HIV/AIDS prevention strategies. *Lancet* 2006; *368* : 1236.
5. Suhadev M, Nyamathi AM, Swaminathan S, Venkatesan P, Sakthivel R, Shenbagavalli, *et al*. A pilot study on willingness to participate in future preventive HIV vaccine trials. *Indian J Med Res* 2006; *124* : 631-40.
6. Mills E, Cooper C, Guyatt G, Gilchrist A, Rachlis B, Sulway C, *et al*. Barriers to participating in an HIV vaccine trial: a systematic review. *AIDS* 2004; *18* : 2235-42.
7. Mills E, Nixon S, Singh S, Dolma S, Nayyar A, Kapoor S. Enrolling women into HIV preventive vaccine trials: an ethical imperative but a logistical challenge. *PLoS Med* 2006; *3* : e94.
8. Kumar R, Jha P, Arora P, Mony P, Bhatia P, Millson P, *et al*. Trends in HIV-1 in young adults in south India from 2000 to 2004: a prevalence study. *Lancet* 2006; *367* : 1164-72.
9. World Medical Association. Declaration of Helsinki, Article 5. *http://www.wma.net/e/policy/b3.htm*. 2000.
10. Jefferson T. Influenza vaccination: policy versus evidence. *BMJ* 2006; *333* : 912-5.
11. IAVI. Ongoing trials of preventive AIDS vaccines. *http://www.iavireport.org/specials/OngoingTrialsofPreventiveHIVVaccines.pdf*. Accessed November 2, 2006.
12. Burton DR, Desrosiers RC, Doms RW, Feinberg MB, Gallo RC, Hahn B, *et al*. Public health. A sound rationale needed for phase III HIV-1 vaccine trials. *Science* 2004; *303* : 316.
13. Watanabe ME. Skeptical scientists skewer VaxGen statistics. *Nat Med* 2003; *9* : 376.
14. VaxGen vaccine trial fails the test but may offer insights. *AIDS Alert* 2003; *18* : 41, 43-5.
15. Basu I, Jana S, Rotheram-Borus MJ, Swendeman D, Lee SJ, Newman P, *et al*. HIV prevention among sex workers in India. *J Acquir Immune Defic Syndr* 2004; *36* : 845-52.
16. Rao Seshadri S, Subramaniyam P, Jha P. The Potential Demand for and Strategic Use of an HIV-1 Vaccine in Southern India. World Bank Policy Research Working Paper No. 3066. Available at SSRN: *http://ssrn.com/abstract=636428. World Bank Policy Research Working Paper No. 3066*; 2003.