Research on anti-fertility vaccines: serious concerns for women's health

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Scientific research to control women's fertility by causing immune reactions has been continuing for almost three decades all over the world. This search for 'suitable targets within the body' has been extremely controversial, with women's groups and health activists globally opposing the 'vaccine-approach' to contraception that treats pregnancy as a disease. In 1998, Saheli published a monograph titled, "Target Practice: Anti-Fertility Vaccine Research and Women's Health", that traced the development of the various Anti-Fertility Vaccines (AFVs), highlighted the unethical and unsound scientific basis of this research, the health hazards it poses for women and the social implications of their use. The following article draws entirely upon this monograph, copies of which, along with complete references, are available from Saheli.

AFVs or immuno-contraceptives aim to induce an immune response in thebody in order to interrupt the process of reproduction. Theoretically, the intervention can be made at most stages of reproduction. In the case of AFVs, researchers must not only "choose" a target antigen that plays a critical role in reproduction, they must also make the body component appear "foreign" to induce the immune system to attack it.

AFVs traditional vaccines

There are several frameworks within which the difference between vaccines for infectious disease control (traditional vaccines) and AFVs can be discussed, such as the biological basis, immunological targets, recipient population, etc. Other grounds, which have a bearing on risk-benefit analysis, include differing perspectives of developers, providers and users and the right of the State to impose programmes of control. Almost all of these differences are grounded in the social, economic and gendered aspects of societies.

While traditional vaccines aim to provide protection against debilitating or life-threatening diseases, AFVs aim to prevent conception, a normal physiological process which is not a disease. The action of traditional vaccines is directed against foreign or 'non-self' antigens in the body, while AFVs direct their action against 'self' antigens. Such vaccines that aim to trigger an auto-immune response in the body necessarily interfere with its self-tolerance. Consequently, they carry the potential for inducing auto-immune disease. Furthermore, traditional vaccines use the specific "memory" of the immune system to continue to protect the body against re-infection and confer long-term/lifelong protective immunity. In contrast, AFVs are expected to offer contraceptive cover for a short, defined time period, and be reversible to allow conception. But the 'switching off' action of immuno-contraceptives has not yet been established, and the long-term effects of changing the immune status of the body still need scientific evaluation. In the case of disease control, traditional vaccines may often be the only means of prevention available. But while evaluating AFVs, it is important to remember that numerous safe and effective alternate methods of contraception are already available to women.

Research on AFVs is being carried out by the World Health Organisation (WHO), the National Institute of Immunology (NII), New Delhi, the Indian Institute of Science (IISc), Bangalore, the Population Council, New York, USAID and other institutions all over the world. While most AFVs are still at the animal trial stage or Phase I human trials, the Anti-hCG vaccine developed by NII has reached Phase II trials. But many trials have flouted ethical norms of biomedical research, and shown little regard for women's health. In exposing some major violations, we have considered the Helsinki Declaration, the CIOMS Guidelines and ICMR Guidelines for Biomedical Research on Human Subjects.

Basis for human trials

Research on human subjects should be based on adequate laboratory and animal experimentation, and knowledge sufficient to predict potential hazards.

Violations: Much remains to be learnt about the immune system itself. Since AFVs induce immune reactions to cause contraception, this has many implications. One of the most important concerns is of cross-reactions that have been widely reported in published studies. And uncertainty remains about whether these are beneficial or problematic. Other potential hazards include hyper-sensitivities, auto-immune diseases and permanent infertility. No conclusive evidence is available to either rule these out, or predict them accurately, so the human trials that have been conducted have been based on insufficient information, and are therefore premature and unethical. In India in 1974, Anti-hCG Vaccine trials were also conducted on 6 women prior to completion of animal studies.

Risk-benefit assessment

Predictable risks must be carefully compared with foreseeable benefits before human trials are initiated, and the interests of the subject must prevail over the interests of science and society.

Violations: Despite almost three decades of research on AFVs, failure rates are unacceptably high, immunological safety has not been established, long-term toxicity and teratological effects not ruled out and the effect on the foetus not conclusive.

Other concerns include the hazards of repeated immunisation and the unpredictability of immune response among trial subjects. The interaction between AFVs and HIV infection has

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also not been adequately studied. Yet, human trials of AFVs have continued. Since AFVs expose healthy people of reproductive age, mostly women in the prime of their lives to an range of health hazards, the risks these women may have to face are totally unacceptable. The cost effectiveness of "treating" large numbers with "immunisation against pregnancy" cannot gain precedence over concerns for women's health.

Informed consent

In the absence of conclusive data from laboratory and animal tests to rule out possible short- and long-term side-effects, it is unethical for researchers to make claims of safety and reversibility of the method under trial. It is only when participants are fully aware of the possible risks and of the areas where full knowledge of hazards is not yet known (e.g. effect on offspring), that their participation can be called genuinely 'informed'.

Violations: In the Anti-hCG Vaccine trials in India, the entire procedure of informed consent was unethical. Information about possible side-effects or hazards was absent in the Informed Consent Form and Information Brochure prepared by NII. Conducting trials from Family Planning Centres in government hospitals, where approved contraceptives are offered, further exposes a strategy to capitalise on women's ignorance and vulnerability.

Trials on lactating women

Pregnant or nursing women should not be subjects of any trials except those designed to protect or advance the health of pregnant or nursing women, foetuses or nursing infants.

Violation: In another instance of blatant violation, Dr.G.P.Talwar conducted clinical trials of the Anti-hCG vaccine on 20 postpartum women through 2 Indian centres. Despite having published papers quoting the study, Talwar publicly denied having done so when challenged by women activists at the VII International Congress of Reproductive Immunology in Delhi, October 1998.

Right to compensation

Research subjects who suffer physical injury as a result of participation must receive financial and other assistance to compensate temporary or permanent impairment or disability.

Violation: Besides a WHO-HRP trial where the Swedish government covered potential damages from clinical trials, there are few instances of compensation/health insurance cover for AFV trial subjects. Participants in India have had no such cover or assurance of treatment/ medical attention.

Follow-up

In contraceptive trials, especially with methods like AFVs that impact both the immune system and the reproductive system, it is essential that women be followed up for a length of time to assess side-effects or problems. In the light of prior experiences like the diethyl-stilbestrol (DES) tragedy, where some adverse effects became apparent only after the children born to trial subjects attained puberty or reached the reproductive age, it is safer to err on the side of caution. Yet, it is shocking that no established guideline on human trials has laid down norms for such follow-up. Even the WHO has only made a "recommendation" to follow up progeny until puberty. Not surprisingly, both research and funding institutions, relieved of the 'burden' of having to conduct long term follow up, are content to make unsubstantiated claims.

Violation: According to published reports of Talwar's Anti-hCG Vaccine trial, only 94 out of 162 women interviewed 'volunteered' for long term follow-up.

When the NII was questioned by women's groups about why follow-up was not built into the study design, they had no explanation to offer. WHO conducted long-term follow-up of the subjects of its Anti-hCG Vaccine trials in Australia, only when urged to do so by its Gender Advisory Panel in February 1996. Not surprisingly, a decade after the trials, only 1 out of 45 subjects could be traced.

The same apathy is apparent in the follow-up of children born during or after the trials. In more than 20 years since the first human trials of the Anti-hCG vaccine, offspring born to women who became pregnant during the trials either accidentally or intentionally, have not been systematically followed up and no data exist to rule out adverse effects.

Funding agencies involved in the trials of AFVs have also been equally irresponsible. Canada-based International Development and Research Centre (IDRC) which funded the Phase II trials of the Anti-hCG vaccine in India, professed a commitment to long-term follow-up of the women till 2003. But in 1998, it retracted its stand and concluded that "women and their children have received conscientious follow-up care which has produced no evidence of complications due to their participation in the vaccine study". Such premature conclusions are extremely unscientific and totally unacceptable.

The unethical research of AFVs is only a case in point. Many long-acting, invasive, provider-controlled contraceptives have been developed, researched and marketed with the same disregard for ethical norms and the participants in the trials. In a country like India, with a state-run health programme and an overriding population control ideology, this has serious implications for the health and well-being of millions of women and men.

Selected references:

1. Indian Council of Medical Research: *Policy Statement on Ethical Considerations Involved in Research on Human Subjects*, ICMR, New Delhi, 1980.

2. Indian Council of Medical Research: *Draft Ethical Guidelines on Biomedical Research Involving Human Subjects*, ICMR, New Delhi, 1997.

3. Schrater, AF: *Contraceptive Vaccines: Promises and Problems*, in: Holmes HB *(ed) Issues in Reproductive Technology, An Anthology*, 1992.

4. WHO/HRP:*Report of the Second Meeting of the HRP Gender Advisory Panel*, Geneva, January 1997, WHO, Geneva, 1996.

5. Proceedings of a *Symposium on Assessing the Safety and Efficacy of Vaccines to Regulate Fertility*, convened by the WHO/ HRP, Geneva, June 1989.

6. Saheli: "*Target Practice", Anti-Fertility Vaccine Research and Women's Health.* 1998. Available from Saheli for Rs.25 + Rs.10 mailing cost.

A complete list of referances is available from the authors.