The Anti-Fertility Vaccine That Never Was

❍ **Sonya Ghosh**

The research on the controversial anti-hCG anti fertility vaccine that scientists in major institutes in India have been struggling to develop for the last three decades raises many ethical questions that need to be debated. Questions have been raised by women's groups since the 1970s about compromising rights of women in the name of 'population control'. Instead of giving individual women more options to prevent pregnancy and protect against AIDs and sexually transmitted diseases, the anti fertility vaccine is designed to be easily administered to large numbers of women using the least resources. If administered to illiterate populations the issues of user control and informed consent are further cause for concern. Most of the research is directed towards women even though these vaccines can be used by both men and women. However, the government has now realised that inappropriate animal models were used and have halted the project.

What is the Anti hCG vaccine?

A rise in the level of hormone hCG indicates that a woman is pregnant as it is secreted by the early embryo and triggers release of other hormones to enable the fertilised egg to remain implanted in the uterus. If hCG is blocked, the level of progesterone declines and the blastocyst (fertilised egg 5 days after fertilisation) is expelled, terminating pregnancy. The anti-hCG vaccine consists of a part of the hormone which induces an antibody reaction and blocks hCG**.**

Two prototypes of the anti hCG vaccine are being developed globally, one by the World Health Organisation (WHO) HRP in Geneva and the other by National Institute of Immunology (NII) by Dr. G.P. Talwar and his colleagues.

Inconclusive Trials

The WHO Task Force guidelines on Immunological Methods for Fertility Regulation attempts to limit cross-reactivity. Cross-reactivity between hormones is a key concern because hCG resembles a family of hormones produced in the pituitary gland. A vaccine that immunises against hCG could affect these other hormones causing other disorders. To avoid cross-reaction, World Health Organisation HRP(**??)** decided to develop a vaccine based on a peptide that has no similarity to the pituitary hormones. However, NII under Dr. Talwar decided that cross reactivity is not important. A prototype vaccine based hCG was carried out by Population Council in the 1970s, All India Institute of Medical Sciences tested another similarly based injectable prototype vaccine in 23 healthy, young women. Eight pregnancies occurred in this group creating a controversy on the ethics of using fertile women in such studies since the effect of this vaccine on their babies is not known. (Shahani SM, Kulkarni PP, Patel KL et al, 1982, "Clinical and Immunological Response to Pr-B-hCG TT Vaccine". *Contraception*. 25:421-34).

The Anti Fertility Project

The Indian Council for Medical Research (ICMR) launched a multi crore project called "Immunological Approaches to Fertility Control" (IAFC) to develop safe and reversible contraceptive agents, a project destined to become a classic example of futile research, inexplicable delays and unjustified expense and needless animal experimentation. Initially funded by the Ministry of Health and Family Welfare with an outlay of Rs.14.63 crores (1983-92) it was transferred to Department of Biotechnology (DBT) in 1987. The government sanctioned Rs.5.77 crores to National Institute of Immunology and to five other governmental institutes on the controversial vaccine.

Going Against Own Findings

NII researchers spent five years experimenting on rodents, bonnet monkeys and baboons, before starting Phase1 clinical trials. These trials showed that though all the women generated antibodies against hCG above the determined efficacy level. The antibody response was variable among the participants, an outcome that the extensive animal trials were unable to predict. The researchers, however, declared satisfaction with the vaccine, and its fully reversible nature. But extended Phase1 trials (completed in September 1990) refuted these findings,

raising the question as to how the previous trial had shown 'encouraging' results.

Flexible Definitions

After Phase1 trials, key scientists decided to cross-expand the parameters of defining what constitutes a 'normal' menstrual cycle of women and defined it as 22-35 days. On this basis they concluded that 90 per cent of the women undergoing the trials had normal menstrual cycles. According to this mode of analysis, a woman who had a regular 24-day cycle before vaccination which changed to 32 days post-vaccination, would fall within the range of normal. This enabled the scientists to disregard irregular cycles. Instead, insertion of IUD, irregular use of contraception or lactation were cited as reasons for fluctuation in menstrual cycle length.

Ignoring Negative Reactions

Phase II trials initiated in May 1990 indicated similar results with 85 per cent women seen to have "normal" cycles.

Variation in immune response and resulting pregnancy risk was a problem that emerged clearly in Phase II clinical trials held at the AIIMS, Safdarjung Hospital and the PGIMER: even though 80 percent of women generated antibodies that were clearly above the safe level (revised to 50ng/ml from 20ng/ml in Phase 1 trials). One pregnancy occurred in a woman even with this antibody level. 26 pregnancies occurred in women with low antibodies. Of these, four opted to deliver their babies which were reportedly normal and follow-up was only done till the age of three-and-a-half years, instead of 10 years, as recommended by IDRC, and WHO guidelines.

The unacceptability of this vaccine became clear on three counts after the Phase II trials:

- the antibodies produced were too variable for an acceptable product.
- a high failure rate

Phase III trials, intended to conclude by 1992, have not been held till date. Dr. Talwar retired from NII to continue developing the vaccine at his independent Talwar Research Foundation, which work he claims DBT will fund. Dr. Vinayak of DBT confirmed that after two decades the vaccine was still in its developmental phase, that Phase III trials have not yet begun and that funding to this project had been downgraded. It remains to be seen how DBT will phase out the anti fertility vaccine funding so as not to attract public attention to its investment of crores together with other blunders (already noted in detail in the CAG report, 1994, at *http://www.cagindia.org/reports/scientific/1994_book1/index.htm)* and whether it will indeed fund the vaccine being developed by Dr. Talwar, and on what grounds and to what extent.

Explain Wasted Funding

Scientists responsible for this inconclusive research, funded by government and supported by public taxes cannot continue to hide behind the myth of 'progress of mankind' to carry out what increasingly appears a self serving activity: accountability must be enforced for state funded researchers and they must explain the lack of results. ❑

The Ethics of it All

Is The Non Human Primate Model Appropriate For Anti Fertility Studies?

The Rhesus monkey is a popular choice for testing pregnancy termination through hCG because of easy availability of this animal. It is also justified by scientists on grounds of alleged "monkey menace" in both urban and rural areas, an argument used also to justify the use of stray dogs in experiments. However, certain ethical questions arise in the use of the rhesus monkey:

➔ The convoluted cervix of the female rhesus makes manipulation difficult and blastocysts have to be recovered through a difficult surgical process. Is it ethical to subject the rhesus to successive surgeries on grounds of economy and easy availability when a species like the bonnet monkey would enable non surgical recovery of blastocysts as it has a straight cervix?

➔ These monkeys are caught from the wild and most suffer from tuberculosis. Is it ethical to present anti-fertility data recovered from monkeys that have suffered from and been treated for tuberculosis in articles in research journals without citing this fact?

➔ Will data recovered from animals which have been seriously sick contribute to any serious research or will it simply serve to earn promotions for the researchers?

➔ Can scientists repeatedly operate every cycle on the same female monkey simply because there is a data base on that monkey in terms of estrus cycles, pregnancy records, reproduction records, etc. Monkeys languish for years in animal houses because researchers do not collect data on younger monkeys: one 27 year old monkey has been in the animal house of a reputed medical college of Delhi for 19 years because of 'proven fertility'.

➔ Furthermore, such operated monkeys are not even given aseptic post operative care, (often even analgesics are denied). They are

moved back to their individual cages with other individually housed monkeys in rooms that lack basic heating and cooling. These scientists justified it on the grounds that the monkeys live in the wild without heating and cooling. They conveniently forget the fact that the monkeys held captive in their labs have been confined in individual cages sometimes for over 20 years without access to exercise or socialisation. Ironically, the term used in the research papers to describe these poor animal room conditions is 'semi natural conditions'.

John P. Hearns in his article "Primate Models for Early Human Pregnancy" (*Animal Models in Human Reproduction* ed. M.Serio and L.Martini. Raven Press, New York, 1980) notes: "The morphology and endocrinology in macaques and baboons differ in important aspects from that in humans" and raises the question of whether an appropriate animal model can be found to mimic that of the human female in early stages of implantation. He points out that there are important differences, for example the time of blastocyst in uterus is between 5-6days in the human whereas in the baboon it is 7-8 days and in the rhesus it is 8-9 days. Furthermore, days of gestation differ drastically between humans and non human primates.The choice of the baboon as a model raises further problems as the implantation process varies even between the various baboon species, apart from differences in relation to the human female already pointed out.

Marmosets, too, are an inappropriate model because of the slow rate of early embryonic development and its small size from which only 4ml of blood can be taken out per week to prevent anemia in the animal. ❑

The Profile of an Illegal breeder

The family of Shashi Suri has illegally procured and sold animals for experimentation for three generations.

A CPCSEA team made a surprise visit to his top story flat in Model Town. Initially he denied keeping animals on the premises but when we prevailed upon him to unlock the terrace, this is what we found: trays of mice were found strewn, some mice had died of cold (it was the month of December), others had eaten each other as no food or water had been given. In a tray under the water tank, a breeding rat had cannibalised her newborn babies and only the remnants could be seen. In another corner of the terrace was a bucket of stale water filled with frogs, half of which were found to have died. In other cages, rats and mice had not only died, but were left to rot and were crawling with maggots.

Mr. Suri is a popular supplier and has sold animals to Delhi University colleges, Maulana Azad Medical College and All India Institute of Medical Sciences. For a consideration he can even supply cats, dogs and monkeys caught off the road. His frog suppliers bring frogs in gunny bags and earthen pots from Bulandshahr and Guwahati by train.

Reliable and reproducible results from animal experiments can only be obtained if laboratory bred animals with identifiable genealogies and proper health parameters are used. Yet reputed institutes do not attach any importance to this crucial scientific fact. This raises questions as to the relevance of the data collected from experiments on such animals. Delhi University colleges continue to buy from him in violation of all laws, national and international.

Early Training into Malpractices

19 Delhi University colleges conduct zoology courses and come under the purview of the Department of Zoology

- None of these colleges have an animal holding facility , animals for dissection are kept in makeshift devices like buckets, sinks, old packing cases.
- Zoology courses taught have not been changed for 27 years.
- Banned animals (like the shark species fish scholeodon, some species of molluscs ,frogs, etc.) and small mammals are routinely bought from unregistered breeders.
- Colleges save money on anesthesia, prefering to repeatedly bang frogs and rats on tables to stun them for experiments .
- After experiments , animals are left to return to consciousness and die in dustbins and garbage heaps instead of being humanely euthanised
- There is a course requirement which requires each student to kill and display at least a 100 butterflies for a five mark slot.
- The central Department of Zoology of the University does not have an experimental room for operative procedures or a post operative recovery room. Rats on which scrotal surgery had been performed were kept in dirty and unwashed cages in the same room as other rats;
- The Depatment of Zoology animal house is infested with black ants which crawl into cages and share the animal feed
- Acquatic research is carried out in the Department: while changing the water manually, fish escape and are found dead on the floor.
- Dead animals are buried in make shift graves at the back of the institute
- No registers are maintained to record routine matters as dead animal disposal, stock maintained, purchase ,experimental animal issue register; death , euthanasia and necropsy ; feed purchase ; medicine purchase ; animal health and treatment.

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