

Quinacrine Sterilisation Trials: A Scientific Scandal?

Mohan Rao

The quinacrine trials raise a host of questions regarding the safety of this method of sterilization and the methodology used to assess this. Even more importantly they point the conditions created by the dominant discourse on these matters, in which a scientific scandal can be perpetrated with such impunity.

THERE is no doubt that understanding how the rubric of macro- economic changes under the structural adjustment program impinges on the determinants of the population issue is of singular importance. How, for instance, do food security issues reflect on morbidity levels and on infant and child survival? How does the casualisation of the labor force, it's increasing feminization and indeed the feminization of poverty, tell on the demand for family planning? How do cut- backs in social sector spending affect the supply of health and family planning services?

These are extremely critical issues. Unfortunately, not enough attention has been paid to them in either academic or policy making circle. But these are not the issues I wish to discuss here. Instead I shall relate the scandalous story of the quinacrine sterilization of women in India. Imbricate in this text are a plethora of sub- texts, discussion of which may throw light on the less obvious, but equally invidious, nature of changes under the package of liberalization and globalization, which while celebrating the concept of reproductive rights, pursues the neo- eugenic agenda of sterilization of poor women in the country.

I

Quinacrine, a synthetic anti- malarial belonging to the acridine group of drugs, was used in the treatment of malaria during the 1930s and 1940s, till it was replaced by better drugs such as chloroquine. It has also been used successfully in the treatment of giardiasis and systemic lupus erythematosus. Current interest in the drugs stem from the novel use discovered for it about two decades back as a method for chemical sterilization of women and the issues of safety, efficacy and ethics that have trailed its 'trails' around the globe. These trials have taken place in 19 third world countries: currently all countries of South Asia are seats of this scandal.

The method was developed in Chile by a Jaime Zipper in the 1970s. Zipper has earlier experimented with chemicals like formaldehyde and sulphuric acid to cauterize the fallopian tubes of laboratory animals. Soon, assisted by two American doctors who were to become the lions of the world- wide quinacrine sterilization movement, Elton Kessel and Stephen Mumford. Zipper tried out quinacrine sterilization in three public hospitals involving more than a thousand women over the next decade and a half (Saheli, Quinacrine: The Sordid Story of Chemical Sterilization of Women, New Delhi,1997).

The procedure involves the Trans- cervical introduction of pellets of quinacrine into the fundus of the uterus in the early proliferative phase of the menstrual cycle using a modified copper - T inserter. While various schedules have been tried, that most common currently involves the insertion of seven pellets of 36 milligrammes of quinacrine performed either once or twice. Following insertion, the pellets dissolve in the uterus in about half an hour and then, it has been suggested, sets up a local inflammatory reaction specifically in the fallopian tubes. The fibrosis and scar tissue that ensues leads to tubal occlusion and thus sterilization. Since tubal occlusion takes up to 12 weeks to be complete, an additional contraceptive is usually provided for this period along with the first insertion of quinacrine. Typically, a long- acting injectable contraceptive such as the controversial Depo Provera is used.

The quinacrine sterilizations do not require anaesthesia or trained personnel and can be performed in areas with no access to health facilities. While these are thought to be some of the method's operational advantages, given the nature of family planning programmes and the poor development of public health facilities in many developing countries, it is precisely these factors which endow the method with a high potential for abuse. That these are not merely Cassandra's fears is brought home in a documentary on these trials in New Delhi. Entitled 'The Yellow Haze', this documentary , made by the students at the Mass Communication Department of Jamia Milia Islamia University, features an interview with a woman who, having approached a clinic for the insertion of copper- T is sent back sterilised with quinacrine. The sponsors of these trials around the world, Elton Kessel runs an NGO named International Federation for family Health (IFFH) while Stephen Mumford runs one evocatively named Centre for Research on Population and Security (CRPS) both based in North Carolina, US. Earlier Kessel was the founder of the organisation named Family Health International(FHI) which both assisted Zipper in his trials and was involved with equally questionable trials with Norplant in Bangladesh (Mohan Rao, 'Surreptitious Sterilisations 'Health for the Millions, Vol 23, No 4, July - August 1997).

The largest trial so far was carried out in Vietnam where more than 31,000 women went quinacrine sterilisation between 1989 and 1993. The publication of a paper on these trials in the Lancet in 1993 provided them with a great deal of Scientific legitimacy (D T Hieu et al, '31,781 Cases of Non - Surgical Sterilisation with Quinacrine Pellets in Vietnam.' Lancet,342, July 24,1993). However, this publication raised a huge controversy (about which more later) and, following the WHO's recommendations, the Ministry of health called off the trial .A retrospective study of tie trial was carried out in 1994 but the report still awaits publication (Marge Berer, 'The quinacrine controversy continues', Reproductive Health Matters, 6 November 1995). In June 1994, the WHO Consultation on Female Sterilisation Methods called for the conduct of four per - clinical toxicology studies on quinacrine before approval of the drug for clinical testing. It categorically stated that human trials should be stopped forthwith pending the outcome of these toxicological studies(WHO, progress in Human reproduction, No 36,1995). FHI undertook these studies with financial assistance from USAID. The rationale adduced was that in view of the scientific and ethical questions raised by the method, having answers to these questions would be to the public good; and further, that a safe and non- surgical method of sterilization would be cheaper than surgical sterilization.

The September 1995 issue of the FHI newsletter Network reporter that three out of four studies on quinacrine were positive, that is, they showed quinacrine to be mutagenic. Mutagenicity, the capacity to induce somatic changes in cells, is indicative of possible carcinogenicity or cancer causation. While not all mutagenic substances are carcinogenic, nevertheless further laboratory tests on animals are essential as per internationally accepted scientific norms in order to exclude carcinogenicity. Problems however arouse with the next step involving trial on female rodents: problems with the route of insertion, the dosage, the number of insertions, and above all, the heavy mortality load among the animals which had to be subject to repeated anaesthesia during the course of the trials. FHI estimated that to conduct further studies would cost up to eight million dollars and would take at least eight years. In view of all these factors, USAID decided to stop the funding of these studies.

In Chile, meanwhile, there was an uproar following the receipt of a September 1994 memo from Mumford's Centre, the CRPS which stated that the Chilean government was considering replacing surgical sterilization with Quinacrine sterilization in the country's two most populous regions. It jubilantly states that the Chilean government's plans vindicated the efforts of the pioneers of the quinacrine method of sterilization in the face of WHO's 'ridiculous' position. The memo turned out to be false; it nonetheless provided an impetus to activists to probe the entire conduct of these trials.

A broad-based coalition named Open Forum for reproductive health and rights voiced four main concerns as they agitated for a halt to these trials. These were; (1) Unresolved issue of safety, for in, addition to possible toxicity(including carcinogenicity), side effect and failure, quinacrine should also be assessed for embryotoxicity in the event of failure of the method; (2) The WHO recommendation that human clinical trials not be conducted till toxicology studies were satisfactorily conducted; (3) The need for informed consent procedures that had been completed lacking these trials; and(4) The need for scrutiny of the trial documents by an ethics committee to assess both safety and ethical standards that had been followed (Lezak Shallot, 'Business as Usual for Quinacrine Sterilisation in Chile'. Reproductive Health Matters 6, November 1995).

The Chilean ministry of health withdrew its support in November 1994 while the public hospitals were asked to review their internal ethics procedure. However, Zipper and his team are reportedly continuing its trials in private clinics with financial support of CRPS.

In India, quinacrine sterilisation is been carried out with " hundreds of doctors involved " according to an early convert to the cause, Biral Mullick. Mullick, who runs an NGO named Humanity Association in Calcutta, admits in a quinacrine promotional video made for the IFFH, to have sterilised 10,000 women over the past two decades. He has also claimed to have trained over 200 village health workers from all over the country in quinacrine sterilisation even as he frankly admits that financial constraints prevent follow - up his cases. Mullick obtains his supplies from the CRPS and has published his finding along with Kessel and Mumford in international scientific journals. In Bangalore, between July 1994 and July 1996, Pravin Kini, Sita Bhateja and B. Rajagopal completed trials on 600 women. They have initiated a two - year project through a trust named Contraceptive and Health Innovations Project (CHIP) to sterilize 25,000 women. With supplies provided by IFFH, CHIP has mobilised about 300 doctors from all over Karnataka to carry out his project.

Other doctors and NGOs are also part of the Kessel- Mumford network. Among them are Ajay Ghosh in Calcutta, Ashi Sarin in Patiala, Rohit Bhatt in Baroda and Maya Sood in New Delhi. Maya Sood's involvement is amazing since she is the head of the department of obstetrics and gynecology at the Lady Harding Medical college, one of the largest teaching hospitals in New Delhi. Although the 'trial' conducted here was on a small number of women as part of a student's post - graduate research it raises vital issue as to how the ethics committee of the hospital could have granted permission for the study without seeking the approval of the mandating authority in the country, the Drug controller of India. This represents, as it were, the thin edge of the wedge with the involvement of

doctors in the government sector hitherto immune from this malady. Again, supplies were provide by Kessel. Indeed Sood candidly states that she would carry out a much larger study should Kessel provide her with the necessary resources.

Co- ordinating the supply of drugs and equipment in the country is J K Jain, former BJP member of the Rajya Sabha and the owner of Jain Studios and the Jain medical centre in New Delhi. Jain Studios has made a promotional video of quinacrine sterilisation which is being distributed all over the world by Kessel and Mumford. Jain Medical Centre, besides a Nursing home, is also the New Delhi address of the IFFH of which Jain has been the president over the last six years.

Kessel and Mumford obtain financial support from a host of private American foundation and individuals including the Leland Fikes Foundation and the Ted Turner foundation among others, although the latter has now ceased to be a donor. They are linked to racist - right- wing groups such as the federation for American Immigration Reform and the American for Immigration Control. In a documentary telecast on BBC entitled the Human Laboratory, they are on record that as patriotic Americans, they believed that the US cannot have a free Immigration policy lest it be swamped by immigrants who would turn the country into one more third nations. They also obtain funding from a section of the ecology movement, the eco- fascists, who believed that the growth of the third world population constitutes the gravest threat to the global environment . Mumford, Kessel and Mullick also state in a paper that ' not to be ignored is the most important role that sterilisation must play in maintaining peace and security given the world's overpopulation' ; indeed the former two claim that they received support from the highest echelons of the US security establishment in their endeavors.

There have, of course been protests with several lead editorials in national newspaper calling a halt to these trials. In Calcutta activist of the Ganatantrik Mahila Samiti led by Malini Bhattacharya, former member of parliament, forced the closure of Mullick's clinic. The government of West Bengal has since initiated an enquiry into Mullick practice. In Banglore demonstrations have been held by a broad coalition of women's groups and health activist outside the clinic of Sit Bhateja and Pravin Kini. In New Delhi a demonstration 's by women's groups was held outside the Jain clinic.

The government of India denies granting approval to any of these trials in parliament in reply to a question tabled by Ashok Mitra, the minister of state in the department of legal affairs stated that the government of India was aware that the WHO had specifically recommended that pending further studies, trial

with quinacrine on human population be stopped forthwith . he stated that the government had only permitted the Indian council of medical research to carry out a study in 1992 but that the high failure rate early in the study compelled its termination Subsequently " approval for clinical trials of quinacrine pellets had not been granted to any investigator by the Drug Controller General of India". Further, the minister also stated that " no drug manufacture has been granted license to manufacture quinacrine and the drug is not imported". However, in the same statement, the minister stated that the government was not aware that quinacrine sterilisation were being performed in the country.

Petitions from women's group have also been presented to the minister of health calling for a ban on quinacrine sterilisations and punishment of the doctors who have been performing them in contravention of the laws of the land. Despite all these efforts, doctors in the private sector and some NGOs are continuing with these trials which defy all international norms for the conduct that the faculty of the Centre of Social Medicine and Community Health, JNU, along with the All India Democratic Women's Association have approached the Supreme Court with a public interest litigation.

II

The quinacrine trials raise a host of questions regarding the safety of this method of sterilisations and the methodology used to assess this. Above all, they raise issues regarding the conditions under which such a scientific scandal can be perpetrated with such apparent immunity.

A major criticism pertains to issues of safety. The proponents of the method claim that risk - benefit assessment, the cornerstone of clinical trials, favoured the use of quinacrine sterilisations in populations where maternal mortality is high contraceptive prevalence, low. Further, that toxicologists maintain that the dose and duration of exposure are the clinical factors when humans are exposed to mutagenic or carcinogenic substances. Thus quinacrine, as an anti - malaria, had been used orally in higher doses, over a longer period of time, on a larger population with little deleterious effects.

What these arguments miss out are rather salient. First, they assume that maternal mortality is caused primarily by unwanted pregnancies which contraceptive would avert. It needs hardly be stated that a large proportion of maternal deaths occur among women with wanted pregnancies. Second, that causes due to reproduction account for merely 2 per cent of deaths among women in India. Even in the reproductive age group they account for 12 per cent of deaths. Indeed these causes do not thus account for the high maternal mortality rate in developing countries: the vast majority of these deaths are

primarily due to diseases of poverty: under- nutrition, anaemia and infectious disease and the lack of access to health care facilities in the event of complications of pregnancy. Contraceptive or sterilisation alone thus has extremely limited role to play in declines of maternal mortality. If this were indeed the case, countries such as Brazil and Indonesia- the latter marked by a particularly aggressive family planning programme- which have witnessed remarkable declines in the birth rate, should also have experienced commensurate declines in the maternal mortality rate which has not occurred.

The argument that quinacrine was used extensively as an anti - malarial and that therefore quinacrine as a sterilisation agent is without danger, is equally specious. Quinacrine was used as an anti - malarial only till such time as better alternatives like chloroquine became available. Further , the extremely high mortality rate malaria at that point in time far outweighed the risks due to quinacrine. Unlike the case with malaria in the past, there are alternative forms of terminal contraceptive today such as vasectomy for men and tubectomy for women.

The literature on quinacrine frequently argues that there were no deaths in the 40 - day period following quinacrine sterilisations in 100,000 women. There are however a number of problems with this facile presentations of data. Included in this huge number are presumably the 31,781 women sterilised in Vietnam which formed the basis of the Lancet publication . The New York based Association for Voluntary Surgical Sterilisation found serious scientific flaws in this study(C S Carignan et al, The Quinacrine Method of Nonsurgical Sterilisation: Report of an Experts Meeting, AVSC Working Paper No 6, July 1994). The data on side effects and failure rates, for instance, were not derived from the full sample of women but on varying subsets among them. The findings from these subsets were then extrapolated to the entire sample.

Again, it is unclear as to how the ectopic pregnancy rate was calculated; in one province, two out of nine pregnancies were ectopic - a hugely unusual occurrence. And yet, according to AVSC, " this troubling finding is not mentioned in the analysis of ectopic pregnancies". AVSC thus maintains that " it is not possible to include that quinacrine pellets are safe and effective non - surgical method of sterilisation".

In addition, given the fact that a variety of protocols of dosage, number of insertions and adjuvants have been followed - a quaint methodology characteristic of all the trials in India also - it is not methodologically legitimate that mortality rates are calculated from data obtained by diverse, and often unspecified, methods. Indeed to further undermine the credibility of the data, it

has been revealed that there known deaths due to quinacrine sterilisations have not been reported in the findings.

Questions can also be raised about the standard cut- off date of 40 days for determining mortality risks after surgery being used in the case of quinacrine sterilisation. Potentially fatal ectopic pregnancies can occur as long as a woman sterilised with quinacrine is in the reproductive age group. The use of this cut-off date thus does not constitute a long enough period to assess the mortality risks associated with this method. Indeed, given the fact that what apparently characterizes these trials is the complete lack of follow- up, it is questionable as to whether legitimacy can be granted to any of these findings at all.

The frequency cited argument that approval for quinacrine for the treatment of other disease precludes the need for a license to use it as an agent for female sterilisation is completely baseless. Under the Drugs and Cosmetics Act of India, a new drug is defined to include" a drug already approved .. which is now proposed.. with a new claims. Viz, indications, dosage form and route of administration". The Drug Controller of India has only granted approval for the use of quinacrine in tablet form, orally, for the treatment of malaria, giardiasis and amoebiasis. The drug is thus not approved for female sterilisation. Indeed it has not received this approval from any authority globally including the US. The US Food and Drug Administration recently issued a warning on the internet where quinacrine was being promoted as a method of self - sterilisations. The warning states that the kit being advertised " uses pellets of quinacrine hydrochloride , an unapproved drug which can cause ectopic pregnancies, abnormal pregnancies and permanent damage to a woman's reproductive organs".

While it is of course necessary to critique the methodology of these trials, it is equally important to understand in what context such experiments can be blithely carried out, recalling the eugenic experiments with chemical sterilisation carried out in the Nazi concentration camps. The victims in that grand design were Jews, gypsies, communists, gays and all those deemed unfit by the science of eugenics. The women now being subjected to this method of sterilisation are the poor in the third world deemed to be the cause of every possible social problem by the science of demography. Among the concatenation of factors which have coalesced to make the quinacrine scandal possible is the assumption about the reproductive profligacy of the poor. There is such an overwhelming consensus about this among the elites in India, that the only discussion is how to do something about it. Most often the solution is found in contraceptive technology directed at women.

This becomes extremely easy given the euphoria created by the non-liberal discourse on rights including 'reproductive rights' and 'reproductive choice', in international circles. What is elided in this discourse is that to talk of reproductive rights in the face of the lack of right to food, employment, water, access of education, health and indeed even the survival of children - in other words all the accoutrements of survival with dignity - is to make a travesty of women's rights. The reification of such a concept of reproductive rights in the west thus makes it absolutely compatible with the violation of the rights of poor women in countries like India with quinacrine sterilisation. There is after all, nothing remarkably new about this women in third world countries have often enough in the past paid the cost, in health and well-being, for the benefits by way of improved contraceptives, which have primarily accrued to women in the west: the low dose contraceptive pill, for instance was refined after trials with extremely risky high dose combinations in Puerto Rica. In India itself we have had trials with Norplant and with the anti-fertility vaccine.

There is however something unique about the quinacrine trials. This is for the first time that contraceptive trials on human populations are being undertaken country by private agencies and NGOs. None of the investigating individuals and organizations have sought received permissions from the mandating authority in the country, the Drug Controller of India. Hitherto all institutions undertaking such research - and it is important to underline that they were institutions and not individuals- were accountable to the parliament and followed guidelines laid down by the Indian Council of Medical Research which broadly followed international guidelines in this regard. The quinacrine trials, on the other hand, completely bypass all such agencies of monitoring and accounting. In other words, we have a completely unregulated and free market of human research at the command of dubious private institutions of the west with poor women of the country forming the sample.

What has made this extraordinary situation possible, I would suggest, is the changes under the structural adjustment programme. The efforts at the 'rolling back' of the state, which forms the heart of the programme of globalisation and liberalisation, have led to the undermining of the public institutions of research and of monitoring and regulation of public health. In this case ICMR has been reduced to issuing a few newspaper notices deprecating the trials. At the same time under the rallying cry of privatisation, what appears to have occurred is a privatisation of public health with NGOs and private individuals been encouraged by private institutions in the west to carry out research in the country: we have also had the example of banned uveal tissue research being carried out in a corporate sector hospital in Hyderabad beside a host of entirely shoddy research being carried out on reproductive morbidity in various places around the country. While the Indian state has withdrawn from its commitment

to primary health care, the World Bank itself has changed its perception of intervention in the population sector from a broad-based 'developmentalist' one to a more technology based one of a " minimum essential clinical package " with the removal of constraints on method availability including excessively restrictive screening requirements and necessary or duplicative approval procedures"(World Bank, World Development Report 1993: Investing in Health,OUP, New York, 1993). The commitments made at the Cairo conference to enhance women's health and reproductive rights notwithstanding, the impunity with which US based NGOs are providing the lead in violation of human rights in southern countries, informs us of the need to monitor health systems rendered vulnerable by the incorporation of the Indian economy in the global market.