NET EN:
ANOTHER CHAPTER IN THE SAGA OF INJECTABLE CONTRACEPTIVES

The issue of injectable contraceptives is once more in the spotlight. In August 2000, the Supreme Court gave an extremely significant order on what has come to be known as the 'Net En Case'. The Government of India affidavit in this case states that 'the Ministry of Health and Family Welfare is proposing to introduce Net En injectable as a new contraceptive in National Family Welfare Programme in such places only where adequate facilities for follow-up and counselling are available.' In our opinion, the order is a clear admission by the Government that mass use of Net En in the Family Planning [FP] programme is not advisable in view of the potential risks associated with such a use and a serious need for close monitoring and follow up.

In 1986, Stree Shakti Sanghatana (Hyderabad), Saheli (Delhi), Chingari (Ahmedabad) and several individuals filed a writ petition in the Supreme Court of India asking for a stay on the Phase IV clinical trials of the injectable contraceptive Net En (Norethisterone Enanthate). The step became necessary following exposure of attempts by a Primary Health Centre in Patancheru in Andhra Pradesh to use Net-En as a contraceptive injection in a family planning camp without paying any heed to the notions of informed consent.

History of the Net-En Case

The case was filed against the Union of India through the Secretary, Ministry of Health and Family Welfare (MOHFW), Indian Council of Medical Research (ICMR), State of Andhra Pradesh and the Drugs Controller General of India (DCI) and had focussed on the following issues:

- The **hazards of Net En** – Both short term and long term hazards are reported. Hazards include menstrual chaos, adverse impact on the hypothalamus-pituitary axis in the brain which could lead to undesirable effects on other systems of the body, long term risks such as the possibility of cancer, risk to progeny due to in utero exposure, and severe uncertainty about return of fertility after discontinuation.
- Violation of medical ethics, since there was **no informed consent** – women recruited for Net En trials were not given adequate information regarding the hazards of the drug, nor were they informed that they were part of a trial with an unapproved drug.
- **Inadequate health facilities** for administering long-acting hormonal injectable contraceptives. The health delivery system does not have sufficient facilities for ruling out contra-indications (such as pregnancy, liver disease, breast malignancy, uterine/cervical hyperplasia, clotting problems, heart disease), monitoring and extended follow-up of the woman and her progeny after discontinuation of the contraceptive.
- The **potential for abuse** of a long-acting injectable contraceptive in a target oriented government population control programme. There is also the possibility of the contraceptive being administered without the knowledge of the woman. The prevalence of an 'injection culture' makes it all the more amenable for misuse. Further, given that women do have a genuine need for effective contraception, they may 'accept'/ 'choose' the injectable if only the convenience is highlighted, and the potential hazards downplayed by propaganda of the government and pharmaceutical company. For instance, women in Patancheru PHC were only told: "Injection le lo, bachcha nahin hoga." ("Take this injection, you won't get pregnant.")

The Writ petition strongly voiced our objections to introducing Net En into the rural health network and the mass Family Planning Programme. Most of these objections still stand, since the abysmal state of the government health-delivery system is too well known to need repetition.

The Net En Case was partly an outcome of the concerns women's groups and health activists had begun voicing in early 1980s. Following public hearings in the UK and US to assess the safety of injectable contraceptives the controversy over these long-acting hormonal contraceptives became widely known all over the world. The hazards of injectables became a reality in India when news about clinical trials on Net En became public. Following the first ICMR press release in 1983 declaring its intention to introduce Net En into the Family Planning Programme, women's groups and health groups like the Drug Action Network and Medico Friends Circle were trying to gain

information about the clinical trials which was systematically denied. In 1983 and 1984, ICMR initiated a Phase IV (Programme Introduction) Study in urban and rural centres to assess the acceptability of Net En in order to introduce injectable contraceptives in the National Family Welfare Programme (FWP). Patancheru was one of the centres of this trials, and the starting point for a nation-wide campaign.

The Campaign Against Injectable Contraceptives

As part of the campaign against hazardous contraceptives, the struggle against injectable contraceptives has been vigorous and visible. Protesting against unethical trials and misuse of contraceptives has been a significant part of the women's movement in India. Initiated by city-based autonomous women's groups and health action groups, the campaign widened to include a wide spectrum of progressive organisations including women's wings of left parties and democratic rights groups.

Women's groups in India were aware of the controversy surrounding Net-En and Depo-Provera [a brand name of another progestin-only injectable contraceptive - Depot Medroxy Progesterone Acetate (DMPA)] in the US and UK, where women's organisations and health activists had been raising questions about the health risks associated with long acting injectable contraceptives, and the potential for abuse. Though there was extreme secrecy surrounding the clinical trials in India, women's groups struggled to gather data and highlight instances of abuse of hazardous contraceptives.

The methods of protest have been forceful as well as innovative. From lobbying, dharnas, sit-ins and demonstrations targeted at the Ministry of Health and Family Welfare, ICMR and other official bodies, to gheraoing the Drugs Controller in his own office to gate-crashing into meetings, the voices of resistance have been loud and clear. And the reactions have been as strong - the local press termed as 'unladylike' the action of jumping over the wall to storm the meeting organised by Max Pharma in 1994 in Delhi to launch Depo Provera in India!

The legal avenue, in the form of public interest litigations have also formed part of our strategy to prevent the introduction of injectables in India. The earliest legal action in Bombay to stall the import of Depo Provera was followed by cases in the Supreme Court against Net En and Depo Provera.

Reaching out to the public has been an important part of the campaign. Producing easy to understand material - booklets, posters, hand-outs and pamphlets and leafleting in crowded localities, we have tried to take the debate out on to the streets. Songs about the hazards of injectables were composed and sung, skits were performed, and slogans coined.

Repeated Attempts to Introduce Injectable Contraceptives

Over the years a variety of reasons have been given under the garb of 'choice' and 'cafeteria approach' for the introduction of newer and newer contraceptives in the FWP. Most of these have been long-acting hormonal contraceptives which are administered by health-care providers and are not in the control of women themselves. Instead of women controlling their own fertility and making choices about their bodies, the provider agencies i.e. the governmental machinery is bent on making 'choices' for the women, especially the rural and poor women. Pharmaceutical industries are more keen to introduce injectable contraceptives for their own monitory benefit. Thus, it is obvious that the government in collusion with the pharmaceutical industry is interested in the introduction of provider controlled injectable contraceptives for the mass use.

Following the public attention on the unethical trials in Patancheru in 1986 and the controversy over the advisability of introducing Net En into the FWP, it appeared that Net En was placed on the back burner, while clinical trials on Norplant [a long acting hormonal implant], hormonal vaginal rings and nasal sprays were set in motion. Lower dose injectables, and once-a-month injectables, combined estrogens-progestin preparations which had fewer side-effects, anti-fertility vaccines were also being researched.

Yet, simultaneously, there were ongoing efforts to register and introduce the injectables in the market. Moreover, the proposal to introduce injectables into the government FWP was not given up completely. The DCI had given approval for the import and marketing of Net En by private

practitioners in 1986. This fact was kept a closely guarded secret, and became known only in 1994, when Net En was officially launched in India for 'social marketing'. Depo Provera was officially launched for 'social marketing' in 1994. Women's groups responded with strong protests since the case against Net En was still pending in court, and the issues raised in the petition had not been satisfactorily answered by the government. In 1994 Jagori and others also filed another court case asking for a ban on Depo Provera. The approval for marketing had resulted in a situation where indiscriminate over-the-counter sale of these hazardous drugs was rampant.

Another disturbing development was the involvement of non-governmental organisations (NGOs) in distributing these contraceptives through their health programmes. Yet, the real danger - of mass use of injectables in the FWP was still kept at bay. However, it was apparent that the government was still making moves to include injectables in the FWP. In 1992, in the light of National Family Health Survey (NFHS) data which showed that only 5.5% couples use reversible modern methods of contraception, MOHFW in its Action Plan for Revamping the FWP in India, decided to place more emphasis on reversible methods, especially 'for younger couples with high fertility potential' in the form of injectable contraceptives to 'be introduced under the programme, initially under controlled conditions and gradually on a wider scale.' In this move, the Government of India [GOI] was backed by the World Bank, under whose recommendation the it was launching the revamped Reproductive and Child Health Programme. Further, in a workshop held in Mumbai in December 1998 on 'Improving Contraceptive Choices in the National Family Welfare Programme' by the Institute for Research in Reproduction, an ICMR Institute, it became apparent that the GOI was once again eager to introduce Net En into the FWP. Minutes of the workshop clearly note that Forum for Women's Health, CEHAT and other women's groups and health groups in Mumbai strongly protested against this proposal, raising issues about potential hazards, as well as the potential for abuse.

The recommendations of this meeting state: 'Taking into consideration the available infrastructure at Primary Health Centres; the need for counselling; screening and appropriate back-up for medical interventions; injectable contraceptives should preferably be introduced selectively in suitably equipped centres and hospitals. It is stressed that the introduction should be gradual with emphasis on good clinical practice and rigorous post-introduction surveillance of the side effects and patient care.'

Privatisation and the Role of NGOs: Cause for Concern

The increasing privatisation of health care, and the entry of NGOs into the field of health and family planning in particular, has thrown up a gamut of issues from lack of accountability to monitoring of their activities. Several NGOs have even been conducting medical research and trials of contraceptives - such as Quinacrine, RU-486 the 'abortion pill', and Depo Provera. International funding agencies financing these NGOs have clear intentions of population control. The World Bank's population activities have been focussed on 'increasing government commitment to developing a policy framework for fertility decline as a national development objective, and providing loans and credits for implementing population programs.' In other words, the World Bank has made population control a conditionality for loans and grants-in-aid to Third World governments. The Reproductive and Child Health Programme launched following the sectoral review undertaken by GOI and the World Bank envisages a significant role for both the private health sector as well as NGOs.

NGOs, with their flexible structure and closer outreach to people, appear to have more credibility and sincerity in implementing programmes. The government has sought to utilise this factor to the fullest extent. Many NGOs are little more than implementing agencies for the government with funding from foreign donor agencies. Depending on funding for their very existence leaves little scope to critique the donor driven agenda - be it family planning or the new catch all concept of 'reproductive health'.

Thus, although neither Net En nor Depo Provera have been officially cleared for 'mass use', NGOs such as DKT International, Mumbai, the Family Planning Association of India (FPAI) and Marie Stopes Clinics / Parivar Sewa Sansthan, with branches all over the country, have included Depo Provera in their 'reproductive health package' in an attempt to 'increase choices in spacing methods'.

Post Marketing Surveillance: Lip Service Instead of Follow up

Experience with hormonal preparations like the infamous Diethyl Stilbestrol (DES), oral contraceptives and hormonal IUDs has shown that some long-term side-effects and effects on progeny are not discovered immediately. The animal and clinical trials required in most countries before contraceptives are introduced, ensure that contraceptives are safe and effective in the short run. Only continued Post Marketing Surveillance (PMS) of larger numbers of women, however, can detect side-effects that are rare or appear only after a long period.

Rigorous PMS is also necessary because there are wide differences in the way in which different populations react to injectables. In India, no study has followed up Net En users for more than two years. On the recommendation of the ICMR, DCI approved the marketing of Net En in 1986, and Depo Provera in 1993 for the private market. In both instances, this approval was granted with the 'advice' to the drug company that PMS be conducted. Till date, no PMS on Net En has been made public.

The PMS recently completed [released in September 2000] by Pharmacia-Upjohn, manufacturers of Depo Provera, is a clear case of how PMS is used as lip service instead of genuine attempt for follow up of drug

recipients on a large scale and over a prolonged period. In the first place, though the study claims to be an 'extensive five year long study' it is based on data collected from 1079 subjects recruited between June 1994 and December 1997 and followed only over five 3-monthly injections i.e. for a period of 15 months. There is no logic for this, since the intended duration of Depo-Provera is as a spacing method for at least 2 to 3 years. Fifteen months is inadequate to assess long-term effects, declaring Depo-Provera 'safe' on the basis of this survey speaks for the shoddy standards accepted by the Indian government.

The study design for this PMS lacks on other counts too. It does not address the issue of loss of bone-density and risk of osteoporosis (weakening of bones, leading to fractures) - something of great relevance in India where bone-density among women is already low. It does not study the risk of cancer or the question of predictable return of fertility or exposure of foetus to high levels of the drug in case of failure of the method!

As is common in many of such surveys, problems such as amenorrhoea (absence of menstruation), irregular bleeding, generalised weakness, migraine headaches and severe abdominal cramps have been considered by the researchers to be 'non-serious'. From a woman user's perspective, these side-effects could hamper her daily activities and seriously affect her feelings of physical and social well-being. It is important to remember that contraceptives are administered to young, healthy women in the prime of their lives. Any side-effects which impair their daily activities, productivity and well-being should be considered 'serious'. The benefit-risk assessment should differ from the risk-benefit assessment of a treatment for a disease.

The study also flouts international guidelines for ethical medical research. The use of lactating women as study subjects is a violation of the Code of the Council for International Organisations of Medical Sciences.

What are the implications of the PMS on Depo Provera for use of injectables in the government FWP?

The PMS shows that even in highly controlled conditions, one woman's pregnancy was not detected before administering the first dose of DMPA. Since the adverse effect of DMPA on progeny has not been ruled out, this is a serious issue. The likelihood of such occurrences in field conditions is obviously much higher.

The timing of injection schedule was not adhered to even in this controlled study. Injectables have to be administered during the first 5 days of the menstrual cycle, and subsequently regularly at the same time. In

the PMS study, several women were given injections at irregular intervals. Timing of injection has a direct bearing on effectiveness, and it is doubtful how this requirement will be adhered to in the already over burdened FP programme.

It is the above concerns which prompted the Drugs technical Advisory Board (DTAB) to take a cautious view of the introduction of injectables into the National FWP. In 1995 itself, the DTAB had ruled, 'Depo Provera is not recommended for inclusion in the Family Planning Programme.' Unless the critical issues of the inadequacies in the health infrastructure are remedied, introduction of injectables will be akin to inviting mass ill-health. The trend to privatise health care delivery as well as medical research needs to be viewed with apprehension.

End Note

It must not be forgotten that India is one of the largest markets for contraceptives in the world. With almost 40 million potential users the Indian contraceptive market is larger than the entire population of Switzerland, Norway, Sweden, and Australia put together. Little wonder that multinational pharmaceutical companies have been consistently wooing this market with aggressive propaganda, and the active collusion of the government machinery.

The Net EN court case, its follow-up and review of the ground situation in India over the last 15 years clearly indicates that the primary health care facilities have not improved, but rather have deteriorated over this period. Privatisation of healthcare is on the increase. India provides one of the largest markets for contraceptives in the world, thus attracting multinational pharmaceutical companies. The role of NGOs in healthcare delivery is dubious in view of their donor-driven agenda and also because of the absence of uniform regulations to conduct the research. Monitoring NGOs and ensuring quality research is essential. The growing trend of 'privatising' research has disturbing implications.

Post Marketing Surveillance in lieu of Phase IV clinical trials conducted by impartial scientific bodies is another outcome of the liberalised economy. Clinical trials and PMS conducted by the pharmaceutical company which directly stands to profit from the results of the research, raises serious doubts regarding 'scientific objectivity' of the data collected and its analysis. Divorcing the profit motive from genuine people-oriented research is essential.

Attempts to introduce injectable contraceptives into the FWP are gaining momentum, with pressure from NGOs, pharmaceutical companies and the government. Population policies in the states and Centre are being formulated to encourage the introduction of long-acting contraceptives, particularly injectables. These moves to enforce coercive population control policies and legitimise the use of hazardous contraceptives must be firmly resisted.

Taken from the Saheli (a women's resource group) Website: https://sites.google.com/site/saheliorgsite/health/hazardous-hormonal-contraceptives/net-en