CORRESPONDENCE

Treating patients with HIV

Your issue on faced when treating people with HIV discusses a very important subject.

I started my medical career around the time that HIV was first detected. My first personal encounter with the disease was some years ago, when a fellow physician and personal friend was diagnosed as HIV positive. The problems in treating a HIV positive patient were becoming clear at the time. Unfortunately, they remain the same today.

Even well-off people with HIV find it difficult to continue treatment in the long term. For the others, it is just impossible. This is true even after the costs of drugs came down. Only one of the 300 or so patients I have treated could afford HAART therapy (three drugs including a protease inhibitor). Therapy must often be administered to an entire family. Monitoring tests are also expensive. Add to this the loss of pay for patient and attendants. Stigmatisation of the family. In the hospital, immunodeficient people are at risk of infection from nearby patients and passing resistant infections to others. Health professionals are given inadequate protection against infections of all sorts.

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Reference:

1. Health professionals and HIV. *Issues in Medical Ethics* 2002; 10: 79-95.

What about the mother?

This refers to your article on concerns regarding the MTCT trials. (1) NACO's programme to prevent mother to child transmission of HIV, although 'ambitious', was awaited by obstetricians all over the country, particularly in the high prevalence states, for almost five-six years. Many institutes have evidence that seropositivity of HIV amongst women who come in for prenatal care is above 1%, sometimes as high as 4-7%.

It is recommended internationally that all pregnant women should be counselled about the risk of HIV transmission, perinatal transmission and the effect on the foetus, clinical manifestations of HIV infection, preventive measures, the availability of screening tests, the non availability of curative drugs and vaccines, and the existence of antiretroviral drugs. After this, they should be offered testing. This can be described as the most reasonable and effective approach to prevent transmission of HIV from mother to foetus. (2)

One of the primary aims of counseling pregnant women regarding HIV is to inform them about the disease, its mode of transmission and means of prevention and thus lead to primary prevention of the disease. This is accomplished in antenatal clinics where more than 90% of patients receive universal counseling.

Another aim of the PMTCT Programme is to improve antenatal care. This is also taking shape, social workers, nursing staff and counsellors are now counseling women on nutrition, immunisation, contraception, breast feeding, besides HIV-AIDS. This is a welcome change. Antenatal waiting rooms are also getting a face-lift, thanks to PMTCT. However, though the programme is well conceived, the choice of intervention, particularly the ante-retroviral therapy, cannot be justified.

After knowing the HIV status, sometimes as early as the first trimester, a seropositive pregnant woman is not supported with any intervention till the onset of labour. The drug Nevirapine is offered when a patient has received no antenatal care and has come to the hospital at the onset of labour. In the PMTCT programme, except for emergency admissions, most women are supposed to be aware of their sero-status during the antenatal period and will be asking for some action on part of the obstetrician to reduce the transmission to her child.

Why should women not be given the advantage of better antiretroviral therapy, a safer mode of delivery and good infant feeding options? The short course ante-retroviral therapy with Zidovudine has been successfully tried in Thailand as well as by NACO in their initial feasibility trials. It is surprising that NACO recommends nevirapine as a final intervention programme saying that this the most it can give pregnant women who are HIV positive. The amount spent on training, workshops and meetings could be better utilised by giving the target beneficiary the best treatment rather than the poor compromise chosen by NACO.

Dr Sucheta Mundle, lecturer in obstetrics and gynaecology, GMC, Nagpur.

Reference:

1. Rajalakshami TK. Programme to prevent mother to child transmission of HIV: Some concerns. *Issues in Medical Ethics* 2002; 10: 92-93.

Everybody does it

The case study 'Cross subsidy in public hospitals' (1) refers to an everyday practice. We have regularly called for more than one lumbar puncture needle, or more than a few disposable needles, and more than one endotracheal tube, so that we can use these on 'poor' patients. I never thought about the implications of such practices as the writer has expressed them. I am trying to hold together a system which is falling apart, while serving my patients. I should challenge the system. Instead, what I am doing is bailing it out.

Ashish Goel, MGIMS, Wardha

Reference:

1. Sreejit EM. Cross-subsidy in public hospitals. *Issues in Medical Ethics* 2002; 10: 100-101.

Questionable ethics and confused regulation

Citalopram, an anti-depressant, was administered by Sun Pharma, on daily labourers as part of bioequivalence studies demanded by an importer. Some patients developed complications; one of them developed gangrene as well as renal complications.

Bioequivalence studies are done establish the therapeutic equivalence of a branded product and its generic (non-branded) version. In India there are no guidelines for bioequivalence studies. Guidelines of the WHO, USFDA and

National Institutes of Health say that such studies should involve, in principle, adult, healthy volunteers. To what extent underfed volunteers can be called healthy is a moot question. Worse, it is not clear if they were adequately informed about what they were getting into.

A monograph on Citalopram says, "The possibility of a suicide attempt is inherent in depression and may persist until remission occurs. Therefore, high-risk patients should be closely supervised throughout therapy with Citalopram hydrobromide and consideration should be given to the possible need for hospitalisation. In order to minimise the opportunity for overdose, prescription for Citalopram should be written for the smallest quantity of drug consistent with good patient management." Clearly giving Citalopram to 'healthy' people seems to present a risk. Giving it to underfed, poor people, seems to be an even worse choice.

The Sun Pharma company says the trial was part of Phase IV post-marketing surveillance (PMS). However, PMS is done on patients who have been prescribed the drug for the said condition.

The same monograph on Citalopram says that, "to date, no information is available on the pharmacokinetic or pharmacodynamic effects of citalopram in patients with severely reduced renal function." Did the patients have a history of renal dysfunction? Did the company check?

A WHO guideline on bioequivalence studies reads, "Health monitoring, before, during and after the study must be carried out under the supervision of a qualified medical practitioner licensed in the jurisdiction in which the study is conducted." The Sun Pharma medical director is quoted in the papers as saying 'How can we be held responsible?'

The researchers claim to have taken informed consent. This is meaningless when the research subject is non-literate, poor and otherwise weak in bargaining power.

Sun Pharma claims to be subjecting every batch or export consignment to bioequivalence studies, albeit at the insistence of the importer. The guidelines do not mention such a practice which is both absurd and fraught with dangers.

Soon after this controversy, Sun Pharma advertised in the newspapers asking for volunteers for trials. Is the public entitled to know what these trials are for and which ethical guidelines are followed? If they are for bioequivalence will the Drug Controller explain why we need bioequivalence studies for every export consignment? If Parliament could pass a law fro the Right to Information in public affairs for the country, what about the right of the public at large to know what kind of trials are going on and on whom and for what purpose?

The recent post-liberalisation hype is to project India as a favored destination for clinical trials. But our very advantages – a large population, genetic diversity and low costs — are compounded by: poor or no regulatory laws, and ignorance on research ethics and law among the public and even health professionals.
The application fee for phase I clinical trials will be Rs 50,000 and the fee for both phase II and phase III trials, is just Rs 25,000 each. Many companies will of course get "informed consent" of illiterate poor people, and probably women, and will be targeted with drugs known and unknown. Citalopram is just an indicator.

Chinu Srinivasan, Rohit Prajapati, Kiritbhai Bhatt, Trupti Shah, Masoor Saleri, People's Union for Civil Liberties, Baroda..

Ethical use of animals in scientific research

A number of articles have appeared in the press recently regarding a visit to the National Institute of Immunology (NII), New Delhi, by an inspection team of the Committee for the Prevention of Cruelty in Scientific Experiments on Animals (CPCSEA). The articles were extremely critical of the condition of the monkeys kept in the NII and its use of animals in scientific research. One article stated that the CPCSEA had recommended closure of the primate house at the NII, in effect terminating all research at the Institute involving these animals.

Delhi Science Forum (DSF), a non-profit public interest organisation of scientists, technologists and social scientists working in areas of science and technology policy, is extremely concerned at these developments at NII which are but the latest of a series of similar actions by CPCSEA in different institutions. These actions reveal disturbing trends in the structure and functioning of CPCSEA and also have serious implications for the future of scientific research in India.

DSF designated a three-member team to visit NII and examine the issue covering not only the conditions and use of animals at NII but also the functioning of the CPCSEA. DSF spoke with CPCSEA team members and sought their views but was unable to obtain a copy of the team's report from either the team or CPCSEA.

Contrary to the allegation that animals are kept in overcrowded enclosures, DSF found that the 207 primates at NII are kept in 13 large outdoor enclosures (5 more are under construction) and additional indoor enclosures for observations and rotation, with small chambers in some outdoor enclosures with provision for heating or cooling depending on season. Enclosures are cleaned four times a day, about an hour after each feeding period. NII also has operating theatres and three full-time veterinarians. Therefore, the animal facilities at NII provide ample space, are in good condition, and are well-maintained.

Against the allegation that over 90% of the monkeys are infected with TB, NII records and DSF's observations show that only 2 adult monkeys out of 207 have TB, and these, along with one female's infant, are in quarantine, under observation and treatment. NII records show that all incoming monkeys are quarantined and tested for TB, such testing also being conducted regularly for all the monkeys, with infected monkeys being treated and painlessly put to sleep as per approved procedure if not cured.

Among the more sensational allegations was that the monkeys at NII were undernourished. DSF examined the monkeys' dietary and nutritional status besides feeding practices at NII. Monkeys at NII are fed four times a day, with special pelletised feeds, channa, bread with vitamin and other nutritional supplements (both additional for pregnant and lactating animals), fruits and vegetables. Monkeys at NII thus obtain more than the internationally recommended standard of 70-

100 kCal/kg of bodyweight per day.

NII has Standard Operating Procedures for care of animals and their use in experiments which are monitored and overseen by NII's Ethics Committee. DSF found not only that conditions and treatment of animals at NII were satisfactory but also that records were basically sound, properly maintained and procedures broadly conforming to international standards were being followed. Of course, there is always room for improvement and NII scientists and managers appeared open and willing to discuss any measures that may be recommended in this regard.

Not all the CPCSEA team members agree with the opinions as reflected in sections of the press and reiterated by some members to DSF. This makes the non-availability of the team report all the more serious and, if action is being taken or contemplated based on such unsubstantiated individual opinions, this raises grave concerns about pre-determined, motivated and biased functioning of CPCSEA.

DSF explicitly recognises the necessity for regulation of use of animals in scientific research to ensure ethical and proper treatment of animals and pursuit of research in accordance with clearly prescribed rules. The fact that the CPCSEA is a statutory body, with rules governed by law, is a positive aspect not only ensuring compliance but also benefiting scientific research and practice. The rules under the relevant Act are also broadly as endorsed by the scientific community in India and abroad.

While the CPCSEA as constituted gives representation to scientific departments and the research community, apart from animal rights activists, in practice and in the manner it functions, the latter have virtually taken over the CPCSEA and its various bodies, and have subverted the statutory body. CPCSEA today appears to act not to regulate the use of animals in scientific research but to completely stop it now and prevent it in future.

Some fundamental defects in the constitution of the CPCSEA under the relevant Act urgently require to be addressed. The NII episode, as well as previous ones at JNU, Indian Institute of Science, AIIMS, National Institute of Nutrition and other research institutions in both the public and private sectors, brings out sharply that the CPCSEA now appears to be functioning as police, prosecutor, judge and hangman, resulting in arbitrariness and lack of transparency and accountability.

The CPCSEA should be overhauled, and its advisory, inspection and other bodies completely reconstituted, with due representation of the scientific community apart from those with concerns for animal welfare. Inspection reports should be shared with the concerned institution for greater transparency, to enable peer review and full participation of research institutions in the regulatory process
CPCSEA should be brought under the ministry of science and technology with proper structures and mechanisms for transparency and accountability

In the case of NII, no action should be taken on the basis of this inspection team's report since the entire process has been deeply flawed and vitiated.

Finally, DSF calls upon the scientific community to vigorously debate these issues, evolve a consensus and work towards a thorough overhaul and reform of this important regulatory body.

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Abortion pill or murder marketed?

I draw your attention to the distribution and marketing of Mifepristone and Misoprostol by Sun, Cipla and Zydus Alidac Pharmaceuticals. These drugs for abortion are supplied to practising gynaecologists to be given to patients after obtaining their consent. The money is to be collected from the patient by the physician, who in turn turns it over to the drug representative. This is highly irregular, unethical and illegal and cannot be equated with drug dispensing by primary physicians at their dispensary.

Second, the drug is meant for the medical termination of pregnancy (MTP). This must be done according to the MTP Act, 1971, only by an *approved physician, in an approved centre and for approved conditions* (Threat to mother's life, congenital anomalies, rape induced pregnancy and pregnancy due to contraceptive failure, the last only in the case of married women).

According to the promotional literature, the pill is to be distributed for abortion at home. This is contrary to the provisions of the MTP Act. It makes no difference that in the consent form circulated by drug companies and to be signed by the patient, the patient agrees to take the pill in the physician's clinic. According to the MTP Act, a gynaecologist's consulting chamber is not recognised for the purpose of MTP. In any case, the abortion takes place at home and is not in conformity with the MTP Act. The possibility of failure and profuse bleeding is substantial and would expose the patient to grave risks, especially in rural settings. The risk is greater for unwed women for whom pregnancy is looked down upon, and who may therefore not contact proper services and may abort and bleed at home. Besides, the pill is being distributed through qualified and unqualified medical practitioners in the country, though under the MTP Act only a practitioner registered with the appropriate Medical Council can terminate a pregnancy. This is virtually marketing murder for paltry monetary gains with the open connivance of medical professionals.

Also, the distribution of full-text articles reproduced from the *New England Journal of Medicine*, *British Journal of Obstetrics and Gynaecology* and the *Journal of American Medical Women's Association* as promotional material, with or without the permission of the journals and the authors, is unethical. It amounts to lending the name by authors for promotion of brand/drug and amounts to 'association' under the MCI Act.
This marketing strategy to promote the abortion pill as an 'in-house' abortion method is dangerous and will claim hundreds of lives in the prevalent health care scenario in India. Unsafe abortion under the garb of MTP is already claiming many lives in the country.

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