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Editorial

HAART in India: Heartening prospects & disheartening problems

The war against HIV/AIDS is fought on many fronts. India's reasonably successful tactics of interventions owe much to the vision and pioneering leadership of the Indian Council of Medical Research (ICMR). In 1985 American scientists developed reagents to detect antibodies to HIV (then called HTLV-III). The same year, the 'ICMR Centre of Excellence in Virology' at Christian Medical College, Vellore, established a laboratory for HIV[1-3]. We searched for evidence of entry or spread of HIV in southern India, using initially reagents gifted by J.L. Sever and D. Madden[1]. Surveys among recipients of multiple blood transfusions[1] and tribals with high prevalence of sexually transmitted diseases (STDs) gave negative results (unpublished). In the third survey during February and March 1986, of sex workers in government's custodial care in Tamil Nadu, conducted with permission from the Health Minister H.V. Hande, we found that infection had already reached Chennai, Madurai and Vellore [2,3].

HIV positive men with STDs detected in Vellore completed the picture of the chain of heterosexual transmission[2,4], a finding contrary to the then prevalent view of exclusive rectal transmission between homosexual men. The need and norms of screening blood donors and for counseling before and after testing were established[5,6]. The ICMR Centre described infection in monogamous women, themselves without risk-behaviour, and its inevitable consequence of vertical transmission[7]. Retrospective evidence showed transmission even in 1984[5]. All these pioneering studies, supported by the ICMR, provided the basis for designing interventions.

With vision and wisdom, the ICMR under the leadership of (Late) V. Ramalingaswami established HIV testing centres in every State capital by mid-1986. India is the first country to track the spread of infection and estimate prevalence rates by sero-epidemiology. Others had used surveillance data on clinical AIDS to estimate infection-prevalence by extrapolation. We knew that multiple infectious diseases plus immune deficiency of under-nutrition would confound and mask the clinical diagnosis of AIDS in India and disease surveillance was non-existent. Until the National AIDS Control Organisation (NACO) set up under the Ministry of Health and Family Welfare took over in 1992, ICMR functioned as the public health agency to spread messages of awareness and prevention, train physicians, ensure safe blood transfusions and prevent nosocomial transmission. NACO carried the work forward, increased testing centres, improved sampling procedures and strengthened blood-safety and hospital infection control. Among the entire vertical, single-disease public health initiatives in India, HIV control appears to be the most efficient. However, much remains to be done from the viewpoint of infected persons, to provide care, treat with drugs and dignity and eliminate discrimination and breach of human rights.

NACO had promoted the guidelines for treatment of opportunistic infections and provided support to States /Union territories to implement it in public sector hospitals. That improved the quality of life of many an HIV positive person, who would eventually succumb to AIDS. Appropriate anti-retrovirus therapy is life-saving for the individual. Like in tuberculosis (TB), three drugs have to be given simultaneously to prevent the pathogen developing drug resistance. This combination therapy is called highly active anti-retrovirus treatment (HAART). But unlike in tuberculosis, HAART is life-long. The world in general and India in particular were slow to recognize that HAART is not only the tool for the individual's restoration to health, but also an ingredient in public health intervention for retarding the spread of HIV[8,9]. When treatment is part of public health intervention for reducing the incidence of infection, like in our national health programmes against tuberculosis, leprosy and malaria, the Government underwrites the cost of diagnosis and treatment. Should not the same principle apply for HIV/AIDS also? NACO has fortunately accepted this principle. On the last World AIDS day (1 December 2003), then Union Health Minister Sushma Swaraj

announced that the government has indeed accepted this policy to provide HAART to those who suffer from AIDS. This is in accordance with the World Health Organisation's intention to treat 3 million with HAART by 2005, according to the '3 by 5' plan. On April 1, 2004, NACO launched the supply of the fixed drug combination or cocktail of zidovudine, lamivudine (nucleoside reverse-transcriptase inhibitors, NRTI) and nevirapine (non-nucleoside reverse trabscriptase inhibitor, NNRTI) to eight government hospitals in Bangalore, Chennai, Hyderabad, Imphal, Kohima, New Delhi and Mumbai. NACO has also initiated training of physicians in the correct use of HAART. Antiviral treatment will not only improve quality of life of the afflicted, but also give hope and courage where neither existed, and encourage their willing disclosure of infection in order to receive treatment[8]. The risk-perception of the uninfected will thus become more immediate, children will be protected from infection and discrimination, and through all these, HAART will become part of the prevention of spread of HIV infection. Indian pharmaceutical companies have helped this process by manufacturing generic drugs and reducing the global market prices of these highly valued medicines. According to Gulick[10], India-made fixed drug combination of zidovudine, lamivudine and efavirenz (NNRTI) recommended for poor countries by the WHO is right for rich countries as well.

So far, so good. However, this battlefront is not easy terrain. In this issue of IJMR there is a review paper on obstacles to successful antiviral treatment[11]. SJ Potter and colleagues in Sydney, Australia alert us on the problem of the development of drug resistance during HAART, due to viral and host factors that facilitate the emergence of HIV variants. All those who are concerned with introducing HAART in India must read this article. The authors elaborate on the contributory factors for drug resistance, namely the existence of virus reservoirs within the host, high rates of HIV turnover and of spontaneous mutation, selective pressure from drugs, pharmacokinetics of drugs and problems of patient tolerance/adherence to strict regimens. In addition to these genuine causes, in India we have another problem, namely erratic and unscientific drug prescription, the 'therapeutic anarchy'. India's experience with treatment for TB confirms that therapeutic anarchy prevails in the country. While there are several reasons for this state of affairs, one glaring problem was that the academic institutions (medical colleges and postgraduate training centers, both in government and private sectors) were not given due partnership role in designing, training or implementing the diagnosis and treatment guidelines of the Revised National TB Control Programme (RNTCP). Thus generations of doctors have been passing out learning TB diagnosis and treatment from teachers who follow by and large textbooks written by specialists in the West or even in India, who themselves were not part of the RNTCP designers or partners. Re-training all of them with RNTCP guidelines is nearly impossible. Doctors prescribe anti-tuberculosis drugs without full knowledge of the pluses and minuses of drug combinations and giving wrong doses and durations of treatment. Only lately has the RNTCP taken corrective steps of establishing centres for directly observed treatment (DOT) for which academic and private institutions are selected for participation. Although this modification is in the right direction, it remains 'too little too late'. Any registered practitioner of modern medicine can treat TB using any drug, since all of them are available through pharmacies. Inappropriate drug use has contributed to the emergence of multidrug resistant tuberculosis which is emerging at a worrying rate. We do not want history repeated with HAART with medical profession causing the emergence of drug resistant HIV.

NACO must establish precise criteria to commence HAART, the drug and dose combinations, and the exact principles and modalities of monitoring those on treatment and validate them through research. The ICMR must function as the research wing of the government's health care and public health programmes. For this, the Departments of Health and Family Welfare must articulate their questions and address them to the ICMR. In the case of RNTCP, such partnership works well, but not in the case of HIV control. In some rich countries the principle of 'hit early hit hard' was the original approach to therapy. That is not necessary in India. As long as a person has good quality of life in spite of HIV infection, HAART can be withheld; this makes medical as well as economic sense. Criteria must be set as to what clinical conditions are diagnostic of AIDS that signals the need for HAART. When opportunistic diseases including tuberculosis are diagnosed, the first step is to apply specific therapy against them, but not to start HAART. A point of time will arrive when HAART

is the smart intervention. Instead of leaving the decision tree to the individual physician's own criteria, there must be a mechanism to ensure strict adhesion to strict criteria, developed and validated through research. Perhaps the decision to go on HAART must be made by a panel of three physicians. CD4 cell counts may not be available everywhere, but other simple tests such as haemoglobin, haematocrit, total lymphocyte count *etc*., must be available for monitoring progress. In case a person relapses in spite of HAART, there must be access to more sophisticated tests and expertise to alter the regimen. In this century it is not too much to ask to put every person on HAART on a computer register with programmed alert for timely follow up. In fact, computerization will lighten the task, which would be cumbersome if done manually. As HAART is being introduced, the exact guidelines of criteria to commence treatment and methods of monitoring progress must be made available to all physicians irrespective of institutional affiliation or independent work style. Every medical college and postgraduate training centre should be given the detailed protocols and also appropriate curriculum material so that uniform teaching could take place. NACO should prepare such curricular material and work closely with the Medical Council of India to introduce them without any more loss of time. This year all medical interns and final year students must be targeted for a short course on HAART. Next year onwards it should be included in teaching Pharmacology, Medicine and Paediatrics. Thus at least tomorrow's doctors will know what HIV treatment is all about.

In the past we have done some bad things with good intentions. Thus we have chest diseases clinics more or less exclusively to detect and treat pulmonary TB and fever clinics to detect and treat malaria. The erstwhile leprosy clinics have been disbanded, but leprosy diagnosis and treatment have not yet been fully integrated with primary health care system. Primary care physicians are inadequately trained in leprosy. Against this backdrop we have little choice but to begin with HIV treatment centres, parallel to the TB clinics. Could not every chest clinic for TB be converted to TB and HIV centre? Care should be taken not to infect HIV positive persons with TB and vice versa in such centres. Could not HIV therapy also be given with direct observation/supervision, for DOHAART (directly observed HAART), as has been successfully experimented in Haiti? Will NACO and RNTCP agree to work together? Will HIV counseling, voluntary testing and treatment in the same premises inhibit TB patients coming to chest clinics? This question deserves an answer through a multi-centre study.

Alternatively, NACO may dialogue with each state health ministry and develop a list of reputed medical care institutions in every district and town/city. State AIDS control societies may be the channel of such dialogue. Among such carefully chosen institutions, suitable ones may be selected as HAART centres, if they agree to comply with all requirements. This process may take several months. Care must be taken so that people have easy access to such treatment centres. NACO must also develop clear guidelines as to who is eligible for free-of-charge HAART and who is not.

Obviously all HAART centres must be prepared to function as voluntary counseling and testing centres as well. All these must be initiated in parallel processes, so that HAART can be started in many more centres than those presently established in seven major cities during 2004 itself. Perhaps some 50-100 centres in well-established institutions will give us the practical experience and a list of practical problems to be addressed when expanding the network to all major hospitals in the country. They can also act as training centres for physicians in other centres yet to be opened. Ultimately there should be sufficient centres of HAART so that people have access within a reasonable distance. In order to avoid the haphazard use of antiretroviral drugs by registered medical practitioners, drug marketing may be restricted to these centres and taken off of the shelves of pharmacies. But then, how will persons who are willing to pay for the drugs themselves get them? These and many similar issues will have to be addressed and resolved without delay in order to make the policy of HAART a reality in India.

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