Editorial

I take pleasure to present fourth issue of 2008 of Indian Journal of Leprosy to its readers. This issue focuses on treatment regimens for leprosy. As we know that control of leprosy as a public health problem has been one of the greatest success stories of modern times. Multidrug treatment (MDT) comprising of rifampicin, clofazimine and dapsone was introduced in the National Control Programmes in early 1980s. Since 1982, millions of leprosy cases have been treated and the global burden of the disease has tremendously been reduced. India reached its elimination levels (less than 1 per 10000 in 2006). Since then, the programme has been integrated with the general health services.

When MDT was introduced, it had 2 main goals. The first goal was to effectively block the transmission. While the highly bactericidal effect of rifampicin was observed in mouse foot-pad, similar trends were observed in human cases as well with intermittent administration of rifampicin. Second goal was to reduce the incidence of drug resistance to sulphones which was high at that time as well as to prevent emergence of resistance to other drugs like rifampicin. This goal again has been successfully been achieved. Another objective of the MDT was elimination of dormant persistor bacteria so that the relapses could be reduced. Even though rifampicin is the only drug shown to be partially effective against slowly replicating/non-replicating mycobacteria, this combination successfully reduces the persistor rates significantly thus bringing the relapsed rates to acceptable limits of less than 5% in most of the studies. It has been generally seen that except for highly bacillated cases, the problem of persistence and consequent relapses is very low in most of the paucibacillary as well as multi bacillary cases.

The persistence of dead skeleton and also viable organisms leads to another complication which manifests in the form of persisting clinical activity and repeated episodes of reactions. This was tackled by two alternate approaches. One approach includes addition of alternate drugs. Important alternate drugs are minocycline, ofloxacin and clarithromycin. There are large number of publications available which show that these drugs inhibit and/or kill *M. leprae*. The issue has been the designing of most effective combination of conventional drugs alongwith these alternatives. Initial approaches of using ofloxacin continuously in the intensive phase showed limited success. The paper being published in this issue reports long term follow-up of the results of monthly administration of ofloxicin and minocycline to standard MDT for a duration of one year. This study shows that this combination successfully eliminates the persistors which is also corroborated by low relapse rate including in the highly bacillated lepromatous cases. In other studies, these lepromatous cases have been observed to harbour viable persistors in a significant proportion and have high relapse rate even after 2 years of MDT.

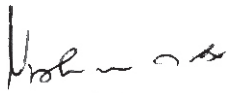
Another option tried to overcome the problem of persistence was addition of immunotherapy to chemotherapy This approach is also highly successful. Mycobacterial

preparations such as, heat killed *Mw*, live BCG, irradiated ICRC bacilli and *M. vaccae* have been observed to have good effect in terms of faster clearance of dead organisms, granuloma as well as low reaction and relapse rates in different studies. Interestingly, immunotherapy with BCG or *Mw* has been shown to decrease the persister rates also which can be co-related with a better clinical outcome. Results of these interventions in paucibacillary cases are awaited.

One major aim of multi drug treatment (MDT) was to have short term treatment regimen. While all different combinations of MDT (standard rifampicin + clofazimine + dapsone for MB cases) and dapsone + clofazimine have been found to be successful in limiting the treatment to six months or 1 year. No comparisons among different cut-off points of duration of therapy are published e.g. hardly any published data of comparison of 1 year vs 2 years fixed duration for MB cases specially in highly bacillated cases is available. Nevertheless, the regimen being published in this issue as well as any of the combined immunotherapy and chemotherapy regimens (both *Mw* and BCG are available) could be considered as a cafeteria choice for multibacillary cases specially with high bacterial burden.

Persistence of active lesions, episodes of late reaction and relapses were found to be a problem when the results of two drug MDT for paucibacillary cases started getting published. Extension of duration of treatment was shown to be useful and use of the same combination of dapsone, clofazimine and rifampicin was envisaged as a common regimen to treat all type of leprosy cases. This idea of a common regimen based on published results from JALMA in 1999 has been adopted by WHO as a uniform MDT for all leprosy cases. This regimen reduces the persisting lesional activity and reactions in PB cases which may be partly due to anti-reaction property of ofoclozamine. While the mechanisms would be speculative, the benefits are apparent. Initial results of global trial of uniform MDT have also been published and are very encouraging. This regimen, if proved successful after due follow-up would be very user friendly and easily applicable in the integrated set-up of public health service.

To conclude, there is still scope to improve the therapy of leprosy to make it more user friendly and also offer cafeteria choice to end users. Though this editorial does not discuss many other important developments, the idea is to keep the dynamism alive for the ultimate benefit of leprosy patients. Though the number of leprosy cases is getting reduced and we must continue to consolidate the success by implementing the presently available regimens and methods of management. Nevertheless, we must also continue to strive for excellence and improvement.



(V M Katoch)
Honorary Editor