

## Challenges Facing the Control of Leprosy in the Indian Context<sup>†</sup>

Vanaja Prabhaker Shetty,<sup>1</sup>PhD

Leprosy is a chronic infectious disease caused by *Mycobacterium leprae* and mainly affects the skin, peripheral nerves, the eyes and the mucosa of the upper respiratory tract. There has been a decline in the global annual new case detection rate (NCDR) for leprosy since 2001. The global burden of leprosy in the beginning of 2008 was 212,802 cases, with only 6 countries having a prevalence rate (PR) of >1/10,000. Though India has been declared as having achieved leprosy elimination in 2005, a large proportion of international figures still come from India.<sup>1</sup>

Some key milestones in the development of leprosy control strategies are as follows:

In 1948, the World Health Organization (WHO) acknowledged the magnitude of leprosy and enlisted leprosy control work as the sixth priority. In 1952, a WHO expert committee advocated the abolition of the compulsory isolation of leprosy patients, and recommended a strategy based on early detection and regular treatment for all leprosy patients on ambulatory basis.<sup>2</sup>

As early as 1955, the Government of India (the GOI) had launched its National Leprosy Control Program (NLCP), which was based on a survey, education and treatment (SET) strategy at the national level.<sup>3</sup> Diaminodiphenyl sulphone (DDS) was the only weapon in the hands of doctors and paramedical workers who were engaged in leprosy control.

In 1981, responding to the widespread problem of secondary and primary resistance to DDS, the WHO recommended the use of multi-drug therapy (MDT) as a standard treatment for leprosy in leprosy control programmes.<sup>4</sup> The WHO also provided technical support and ensured uninterrupted supply of MDT drugs free through its global partners to the GOI. In 1983, the GOI renamed the NLCP as the National Leprosy Eradication Program (NLEP) and continued with the SET strategy.<sup>5</sup> Registration of all new cases and prompt treatment with MDT and compliance reached record levels.

In the year 1991, the WHO resolved to “eliminate leprosy as a public health problem by the year 2000”.<sup>6</sup> For this purpose, a “public health problem” was defined as fewer than 1 leprosy case per 10,000 population. The assumption was that below this prevalence level, based on historical

experience in Scandinavia and Western Europe, the reduced transmission of *Mycobacterium leprae* would result in a lower incidence of infection and natural extinction. Leprosy became eliminable with the use of MDT. The WHO also set targets to achieve this goal. The GOI in turn adopted several operational strategies to intensify MDT coverage to endemic regions. The GOI introduced fixed duration MDT i.e. 6 months for PB and 12 months for MB cases, in 1996, and undertook a “cleaning of register” exercise during 1996 to 1997.

At the end of 2000, the WHO declared that leprosy had been eliminated as a global public health problem. The failure to realise the target date for “elimination” in India and several other countries, made the WHO propose a plan called “The Final push: 2000 to 2005”.<sup>7</sup> The target date was shifted to 2005. The final push strategy included (1) the integration of leprosy services into general health services to improve access to treatment; (2) capacity building to enable general healthcare staff to diagnose and treat leprosy; (3) improved logistics to ensure the provision of adequate stocks of MDT at health centres.

During 2004 to 2005, the GOI drew a strategic plan of action with a focus on endemic districts through Focused Leprosy Elimination Plan (FLEP), and awareness campaigns at district and block levels.<sup>5</sup> A major thrust had been on reducing the prevalence of leprosy. In the beginning of 2005 the supplementary policy directives issued by the GOI, based on the “Katmandu recommendation”<sup>8</sup> has changed the course of leprosy control work at all levels. The latter document suggested the following steps (1) stop all new case detection, (2) all new cases detected to be registered and given MDT only after validation by authorities in each area, (3) delete names of the patients from the registers as they receive the last pulse, and (4) do not register single lesion leprosy cases for now. These recommendations were strictly implemented and thus India achieved the goal of elimination of leprosy by the end 2005 at the country level.<sup>9</sup>

The WHO elimination goal indeed created a broad and strong commitment to the fight against leprosy. However, the number of new cases detected globally has changed very little. This is mainly explained by the disappointing additional impact of MDT on transmission. The strong

<sup>1</sup> The Foundation for Medical Research, Mumbai, India

Address for Correspondence: Dr Vanaja Prabhaker Shetty, Senior Scientist and Deputy Director, The Foundation for Medical Research, 84-A, RG Thadani Marg, Worli, Mumbai 400018, India.

Email: fmr@fmrindia.org

<sup>†</sup> World Leprosy Week (21-27 January)

reduction in registered prevalence is not based on a decreasing incidence, and can be explained by the shortening of treatment duration and cleaning of the registers.<sup>10</sup>

As per the “Global strategy for further reducing the leprosy burden and sustaining leprosy control activities 2006-2010”, national leprosy programmes are urged to encourage people to come forward for treatment, and recommend limiting leprosy services to health facilities.<sup>11</sup> Voluntary reporting systems for leprosy patients have some inherent problems related to a low level of community awareness, high social stigma, atypical skin lesions, and the insidious presentation of neurological symptoms. On the contrary, active case searching from community facilitates early case detection, reducing the risk of permanent disabilities, and may interrupt the transmission.

One of the cornerstones of the NLEP is information, education and communication (IEC) in the community. A study done by the Foundation for Medical Research (FMR) during June to November 2007 in one rural and one urban setting in Maharashtra, India, showed a high prevalence of leprosy (PR = 6.7 and 2.6 per 10,000, as against the state average of 0.7/10,000), with a high proportion of multibacillary (MB) and child cases among them.<sup>12</sup> This study underscored a need to inquire into factors affecting access to leprosy care, and also to understand people’s perceptions and reactions to leprosy in the context of IEC activities implemented in this area.

With reference to these objectives, a study on situational analysis was undertaken in the rural area. Several patients detected in the survey were unaware about their disease, which questions the role of IEC activities for leprosy. It was noted that self-perceived stigma is more prevalent in the study area; however, patients acknowledged family level support. Barriers such as the distant location of PHC’s, highly irregular supply of drugs, no transport facilities, long waiting time, and no confidentiality in the public health sector were reported (unpublished). Further, a Special Selective Drive (SSD) under NLEP in the state of Maharashtra, India, carried out by FMR at Karjat Taluka of Raigad district and Gadchiroli district between February and April 2009 also showed a large backlog of undetected cases.

The NCDR was 14 and 13/10,000 respectively in the 2 districts as against the state average of 1.1/10,000. A casual inquiry into access to healthcare showed a combination of 3 factors, i.e. irregular supply of drugs, poor diagnostic skills of the health staff and commuting problem resulting in denial of timely treatment in over 50% of the cases (unpublished). A high proportion of child cases (24%) with multiple case families and grade 2 disability (~18%) reflects continued transmission and delay in diagnosis. Collectively, these findings point impaired access to health services for the population or its delayed utilisation.

A study from North West Bangladesh depicted a prevalence of previously undiagnosed leprosy of about 13/10,000 population compared to the registered leprosy cases 2.3/10,000.<sup>13</sup> Another study in Brazil showed that 28.4% of leprosy cases in the community were not identified by the health system between 2001 and 2005.<sup>14</sup>

Our findings allow recommending measures for improving the NLEP programme. We recommend 1) encouraging active case detection and arranging for special case detection activities, 2) strengthening IEC activities and making it more patient centric, 3) capacity building of healthcare functionaries on various aspects of early detection, nerve function assessments and self-care methods.

The assumption underlying the elimination strategy is that MDT will reduce transmission by reducing the number of contagious individuals in the community but evidence to support this assumption is lacking. How much of transmission the control strategy can prevent depends on 2 unresolved issues. Is the incubation period contagious and are close contacts of patients infected rapidly.<sup>15</sup>

The international task force for disease eradication considers leprosy as not now eradicable, obstacles being lack of a specific and sensitive diagnostic tool, social stigma and the potential reservoir in armadilloes<sup>16</sup> and also in primates cannot be ruled out.

There is an unsolved problem of bacterial persistence and relapse due to persisters. Contrary to expectations, use of MDT has not altered the problem of persistence of *M. leprae* bacilli, that by definition are drug sensitive organisms that remain dormant.<sup>17</sup> Understanding the biology of dormant organism is important and needs to be addressed at a different level. Findings from a recent prospective cohort study by FMR indicate a poor sterilising effect of a 12-month regime of MDT in MB cases. Over 15% of 65 borderline lepromatous (BL) cases assessed at 6 months post-release from 12 months MDT regime showed presence of viable *M. leprae* as evidenced by the growth in foot pads of non-immunosuppressed mice.<sup>18</sup>

There is lack of an efficient surveillance system for relapse, drug resistance and treatment dropouts. With the introduction of a new untested short-term treatment regime, it is imperative to record the number of relapse cases. Also, there is no recording and tracking system to assess the number of patients who discontinued their treatment. This is a matter of concern in view of the public health risk posed by the likelihood of infection due to active relapse cases and treatment dropouts.

Relapses following MDT in both paucibacillary (PB) and MB cases are being reported worldwide, and so is the stray incidence of resistance of *M. leprae*, proven either in the mouse foot pad or using molecular tools.<sup>19,20</sup> We record on an average 10 to 12 referral relapse cases per year. One

concern is that, of the 21 referral relapse cases following 12 months MDT that were recorded during the past 3 years, 5 (20%) had relapsed for the second time. Acknowledging the seriousness of the matter, the WHO now has taken an initiative for drug resistance surveillance using molecular tool.<sup>21</sup> There is also a need for backing this study with a broader understanding of drug resistance pattern, role of efflux transporters<sup>22</sup> and state of persistence of *M. leprae* and correlation with clinical outcomes.

Though it is common knowledge that many leprosy patients, particularly in urban areas, are treated by the private sector; from which no documented figures are available. It is important to be vigilant, as this affects leprosy control efforts overall.

Lastly, appropriate and timely treatment of nerve function impairment (NFI) is of paramount importance in leprosy, and MDT is not effective in the control of nerve damage. Nerve function assessment (NFA) is important for the diagnosis of leprosy per se, but has even more crucial role in the prevention and early treatment of NFI. Nerve conduction studies (NCS) provide valuable information for detecting NFI and evaluating appropriate therapeutic regimes. In a cohort of 400 newly detected MB cases by NCS, >95% of patients showed impairment of one or more nerves at registration, regardless of reaction, indicating that nerve damage is more widespread than clinically ascertained, and that reaction episodes increase nerve damage.<sup>23</sup>

Recent research findings have drawn attention to opportunities to improve and extend the use of corticosteroids for the treatment and control of reactions and NFI.<sup>24</sup> The mode of action of corticosteroids in the amelioration of nerve function is not clear and needs further study.

#### Acknowledgements

*I want to acknowledge the help of Ms. Fatema Khambati in organising the references. FMR work quoted is part of team work carried out at FMR.*

#### REFERENCES

1. Global leprosy situation, beginning of 2008. *Wkly Epidemiol Rec* 2008;83:293-300.
2. Expert committee on leprosy; first report. *World Health Organ Tech Rep Ser* 1953;71:1-28.
3. Shetty S, Nandakishore, Shetty JN. National Leprosy Eradication Program. *Indian J Dermatol* 1997;42:55-64.
4. Chemotherapy of leprosy for control programmes: report of a WHO Study Group. *World Health Organ Tech Rep Ser* 1982;675:1-33.
5. Dhillon GPS, Barkakaty BN. National Leprosy Eradication Program in India: Achievements and Deficiencies. *Health Administrator*, Vol. XVIII:4-7.
6. Elimination of leprosy: resolution of the 44th World Health Assembly. Geneva: World Health Organization, 1991. Resolution No. WHA 44.9.
7. World Health Organization. The final push towards elimination of leprosy: strategic plan 2000-2005, Geneva 2000; WHO/CDS/CPE/CEE/2000.1.
8. National programme managers for leprosy elimination – Report of an Inter-country meeting, Katmandu, Nepal, 6-8th January 2005, WHO Regional Office for South-east Asia.
9. Announcement: India achieves national elimination of leprosy. *Indian J Lepr* 2006;78:101.
10. Shortening duration of treatment of multibacillary leprosy. *Wkly Epidemiol Rec* 1997;72:125-8.
11. World Health Organization. Global Strategy for Further Reducing the Leprosy Burden and Sustaining Leprosy Control Activities 2006-2010. Geneva: WHO, 2005. WHO/ CDS/ CPE/ CEE/ 2005.53.
12. Shetty VP, Thakar UH, D'souza E, Ghate SD, Arora S, Doshi RP, et al. Detection of previously undetected leprosy cases in a defined rural and urban area of Maharashtra, Western India. *Lepr Rev* 2009;80:22-33.
13. Moet FJ, Schuring RP, Pahan D, Oskam L, Richardus JH. The prevalence of previously undiagnosed leprosy in the general population of northwest Bangladesh. *PLoS Negl Trop Dis* 2008;2:e198
14. Grossi MAF, Moschioni C, Lambertucci JR, Antunes CMF. Estimation of hidden prevalence of leprosy during the period 2001-2005 in Minas Gerais, Brazil. *Proceedings of the 17th International Leprosy Congress, Hyderabad, February 2008.*
15. Britton WJ, Lockwood DNJ. What is necessary to eradicate leprosy? *Lancet* 2004;363:1209-19.
16. Centers for disease control and prevention. Recommendation of the International Task Force for Disease Eradication. *MMWR Recomm Rep* 1993;42:1-38.
17. Shetty VP, Mistry NF. Key issues related to bacterial persistors. In: Sood OP, Rattan A, editors. *Leprosy Elimination: Critical Issues*. New Delhi: Ranbaxy Science Foundation, 2002:177-86.
18. Shetty VP, Khambati FA, Ghate SD, et al. The effect of corticosteroids usage on bacterial killing, clearance and nerve damage in leprosy; Part 3 – Study of two comparable groups of 100 multibacillary (MB) patients each, treated with MDT + steroids versus MDT alone, assessed at 6 months post-release from 12 months MDT. *Lepr Rev* 2010;81 (in press).
19. Maeda S, Matsuoka M, Nakata N, Kai M, Maeda Y, Hashimoto K, et al. Multidrug resistant *Mycobacterium leprae* from patients with leprosy. *Antimicrob Agents Chemother* 2001;45:3635-9.
20. Shetty VP, Wakade AV, Ghate S, Pai VV, Ganapati R, Antia NH. Viability and drug susceptibility testing of *M. leprae* using mouse footpad in 37 relapse cases of leprosy. *Int J Lepr Other Mycobact Dis* 2003;71:210-7.
21. WHO. Guidelines for Global Surveillance of Drug Resistance in Leprosy. WHO 2009, SEA-GLP-2009.2.
22. De Rossi, Ainsa JA, Riccardi G. Role of mycobacterial efflux transporters in drug resistance: an unresolved question. *FEMS Microbiol Rev* 2006;30:36-52.
23. Capadia GD, Shetty VP, Khambati FA, Ghate SD. Effect of corticosteroid usage combined with multi-drug therapy on nerve damage assessed using nerve conduction studies: A prospective cohort study of 365 untreated multibacillary (MB) leprosy patients. *J Clin Neurophysiol* 2010;27(in press).
24. Rao PS, Sugumaran DS, Richard J, Smith WC. Multi-centre, double blind, randomized trial of three steroid regimens in the treatment of type 1 reactions in leprosy. *Lepr Rev* 2006;77:25-33.