

Leprosy in 21st century

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The progress in the management of leprosy, one of the oldest known diseases, has been rather slow. Apart from peculiarities of *Mycobacterium leprae* (inability to grow in artificial media) and disease (long and variable incubation period, variable clinical presentations), lack of interest on the part of developed nations and pharmaceutical companies (as leprosy is mainly a disease of people from low socioeconomic status) have been responsible for this slow progress. Research in last 2-3 decades has led to a better understanding of disease, its pathogenesis and management. One of the major breakthroughs in leprosy management was introduction of multi-drug therapy (MDT) by World Health Organization (WHO) in 1982. WHO MDT has helped us not only treat millions of leprosy patients but also prevent transmission of leprosy to community to some extent.¹ As a result, leprosy has achieved goal of global elimination.² However, still some endemic areas of leprosy persist and new cases are being detected every day.^{3,4} This calls for reinforcement of ongoing efforts against leprosy and formulation of new strategies.

There has been significant progress in understanding leprosy because of recent work. But, there is still need for further research in leprosy as there are many lacunae in our understanding. Some of the areas of concern

include understanding pathogenesis; genetic and immunological basis of disease manifestation; pathogenesis and management of leprotic neuropathy; new and effective antileprotic drugs; and vaccines against leprosy.

Leprosy has a new causative agent!

In 2008, a new agent *Mycobacterium lepromatosis* has been identified as the second cause of leprosy. Leprosy was considered to be caused by *M. leprae* and not much efforts were made to study the genetics of causative agent. Gene analysis of causative agent of diffuse lepromatous leprosy (DLL) patients showed overall 7.4% difference from *M. leprae*, suggesting new species. Interestingly, DLL has been known in Mexico and Costa Rica for more than a century. Later, *M. lepromatosis* has been documented as a cause of leprosy in Brazil, Singapore, Myanmar and Canada, suggesting wide existence of this newly discovered species. In a study on 120 patients from Mexico, *M. lepromatosis* was identified in 55 cases, *M. leprae* was identified in 18 cases, and both species caused disease in 14 cases. They found that all DLL cases were caused by *M. lepromatosis*. Also, new species was associated with severe leprosy disease, as well as, severe lepra reactions.^{5,6} Considering the clinical and therapeutic implications, efforts should be made to perform genetic analysis of agents in leprosy patients in south Asia.

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Progress in serodiagnosis of leprosy

Diagnosing leprosy early is of paramount importance as timely initiation of treatment can make a big difference in final outcome. Leprosy has long and variable incubation period. Also, early cases of leprosy mimic so many conditions commonly encountered in clinical practice. Less bacterial load makes it very difficult to diagnose early cases of leprosy by demonstrating acid-fast bacilli. Discovery of phenolic glycolipid (PGL-I) paved the way for serodiagnosis of leprosy. PGL-1 is cell surface bound molecule and its level correlates with bacilli burden (bacterial index). Untreated LL and BL cases have shown PGL-1 detection rate between 88% and 96%. TT and BT cases with BI of 0 do not have detectable PGL-1 in their sera. Another usefulness of PGL-1 lies in the fact that active synthesis and release of PGL-I has been shown to be a marker of *M. leprae* viability. Hence, monitoring the serum levels of PGL-I after initiating multidrug therapy (MDT) can help us ascertain the efficacy of drug treatment. Considering the limitations of PGL-1 in patients with low BI (<3) and paucibacillary cases, attempts were made to find another method of serodiagnosis. Soon, ELISA technique was developed to detect antibodies to PGL-1 in serum of suspected cases. Now lateral flow device to detect human IgM antibodies to PGL-I is available to be used in field conditions.⁷ Another *M. leprae*-derived major membrane protein-II (MMP-II) has been utilized for serodiagnosis of leprosy and has shown to be better index marker than PGL-I. However, MMP-II too shows low detection rate in PB cases. Recently identified molecules like ML2028 (Ag85B) and ML2038 (bacterioferritin) are capable of detecting antibody responses in the majority of PB patients.⁸ Genetically engineered fusion protein called Leprosy IDRIDiagnostic (LID)-1 appears very promising as immune response to LID-1

appears to be strikingly more elevated and to occur much earlier than the anti-PGL-1 IgM response.⁹

New strategies for leprosy control

It is now evident that WHO MDT alone cannot control leprosy. Newer strategies like active case detection through contact surveillance have shown promising results. Earlier, emphasis was on screening family members of index leprosy case. Now some studies have shown that contact surveillance including neighbor contacts (in a radius of 200 meters) results in higher case detection rate. In fact, the rates of case detection were similar between household contacts and neighbors.¹⁰ Hacker *et al.*¹¹ in their study, concluded that "cases diagnosed through contact surveillance are detected earlier in the disease progression, have lower initial and final bacterial indices, have lower initial and final disability grades, and have a lower prevalence of disease reactions."¹¹

Another important tool in leprosy control could be chemoprophylaxis and immunoprophylaxis of contacts. A single dose of rifampicin (SDR) has shown to offer protective effect of approximately 60%, effective in the first 2 years after the intervention. Bacillus Calmette-Guérin (BCG) vaccination has shown some protective effect against leprosy. A meta analysis showed BCG having overall protective effect of 26% in experimental studies, and of 61% in observational studies. The protective effect of SDR and BCG vaccination appears to be additive, approximating 80%.^{12,13} Considering these findings, it is imperative that future leprosy control strategy should include chemoprophylaxis and immunoprophylaxis of contacts. Both rifampicin and BCG vaccine are cheaper cost-wise; hence, implementation of such a strategy on mass level would not

posesignificant stress on resource-poor developing countries.

References

1. Rao P N, Jain S. Newer management options in leprosy. *Indian J Dermatol*. 2013;**58**:6-11.
2. World Health Organization. Global leprosy situation, weekly epidemiological record. 2015;**36**:461-76
3. Ghayas AS, Saaiq M, Mahmood-ur-Rahman. Clinical observations in leprosy cases treated at Diamer district of Gilgit-Baltistan, Pakistan. *J Pak Med Assoc*. 2013;**63**:1415-7.
4. Singal A, Sonthalia S. Leprosy in post-elimination era in India: Difficult journey ahead. *Indian J Dermatol*. 2013;**58**:443-6.
5. Han XY, Silva FJ. On the age of leprosy. *PLoS Negl Trop Dis*. 2014;**8**(2):e2544.
6. White C, Franco-Paredes C. Leprosy in the 21st century. *Clin Microbiol Rev*. 2015;**28**:80-94.
7. Spencer JS, Brennan PJ. The role of *Mycobacterium leprae* phenolic glycolipid I (PGL-I) in serodiagnosis and in the pathogenesis of leprosy. *Lepr Rev*. 2011;**82**:344-57.
8. Geluk A, Duthie MS, Spencer JS. Postgenomic *Mycobacterium leprae* antigens for cellular and serological diagnosis of *M. leprae* exposure, infection and leprosy disease. *Lepr Rev*. 2011;**82**:402-21.
9. Duthie MS1, Balagon MF, Maghanoy A, Orcullo FM, Cang M, Dias RF *et al*. Rapid quantitative serological test for detection of infection with *Mycobacterium leprae*, the causative agent of leprosy. *J Clin Microbiol*. 2014;**52**:613-9.
10. Campos DC, Dutra AP, Soares VL, Carvalho PA, Camargo LM. New strategies for active finding of leprosy cases in the Amazonian region. *Rev Soc Bras Med Trop*. 2015;**48**:488-90.
11. Hacker MA, Duppre NC, Nery JA, Sales AM, Sarno EN. Characteristics of leprosy diagnosed through the surveillance of contacts: a comparison with index cases in Rio de Janeiro, 1987-2010. *Mem Inst Oswaldo Cruz*. 2012; **107**:49-54.
12. Richardus JH, Oskam L. Protecting people against leprosy: chemoprophylaxis and immunoprophylaxis. *Clin Dermatol*. 2015;**33**:19-25.
13. Chaptini C, Marshman G. Leprosy: a review on elimination, reducing the disease burden, and future research. *Lepr Rev*. 2015;**86**:307-15.