

***Mycobacterium lepromatosis* Deserves Adequate Attention**

Identifying the etiology of any disease is a major step in moving towards understanding the mechanism(s) of pathogenesis, finding suitable tools for effective management, prevention and control. This step is of paramount importance in case of infectious diseases. However, there could be many hurdles in moving from etiology to management and control. Discovery of bacterial etiology by Norwegian physician Gerhard Armauer Hansen in 1873 was an important landmark not only for leprosy but for any infectious disease. This led to policy decisions by various governments of infection control – these measures like segregation measures, though not ethically correct and acceptable, yet these contributed to its containment and elimination / eradication from several countries. The path from its discovery to unravelling various important aspects of bacteriology was not easy. Despite many attempts, even 150 years later *Mycobacterium leprae* can at best be grown to a limited extent in *in-vitro* conditions and easy to handle model of mouse foot pad. While it can be grown in armadillos, the model itself is not easy to manage in laboratory conditions. Nevertheless, the efforts of so many clinicians, microbiologists/ molecular biologists, pathologists, immunologists, public health specialists, social scientists and others have generated knowledge which has helped in discoveries facilitating efficient management of leprosy. Disease is by and large contained to few countries and reduced to a smaller number of cases. On the negative side, disease is still an important problem in countries like India, Brazil,

Indonesia, Bangladesh. New cases and disabilities are still there, here the numbers do not count.

After achieving major successes with multi-drug treatment globally about 25 years ago, situation is stagnating. Though the numbers are progressively getting reduced yet persons suffering from extensive disseminating forms continue to be reported from several countries. Clinicians continue to encounter cases with severe reactions, Lucio/ Lucio like phenomenon, poor responders and disabilities. It is a reality that science of dissecting the disease and its known agent *Mycobacterium leprae* peaked between 1950-2000, after that few landmarks can be identified. Discovery of *Mycobacterium lepromatosis* in 2008 by Han et al as a second etiology of leprosy (Hansen's disease) is undoubtedly an important landmark. This species was found to be significantly different genetically from *Mycobacterium leprae*. Initially, clinically it was observed to be associated with diffuse lepromatous disease in Mexico and the Caribbean region.

It is a severe form of leprosy which manifests through nerve invasion and extensive skin ulcerations due to heavy burden of acid-fast bacilli in the body. *M. lepromatosis* has been detected in borderline leprosy cases (BL), lepromatous leprosy cases (LL) and leprosy reactional cases. This organism has also been reported from ENL cases (mostly necrotic ENL) in India. Interestingly, these strains appear to be heterogenous. In the recent years, there have been several reports of such cases of ENL published in Indian Journal of Leprosy and other

journals, some investigators have also reported Lucio like presentation in some cases. There is not enough data to comment whether such cases have increased or not. Overall, contribution of *M. lepromatosis* to reactional states is also not known. It would also be important to analyse the response of these cases to MDT and standard anti-reaction regimen(s). While the studies carried out so far are noteworthy, it is clear that such investigated cases represent a very small proportion, even in India.

Mycobacterium lepromatosis has been propagated in athymic nude mouse and has been reported to have a unique repetitive element RLPM, and a RLPM - PCR assay has been developed for rapid molecular diagnosis. It is thought that the RLPM and RLEP assays would be useful for the clinical diagnosis and surveillance of leprosy due to *M. leprae*, *M. lepromatosis* and also mixed infections. As techniques of genomic characterization are affordable and easily

available, it would be important to carry out larger studies in patient specimens from different regions across the spectrum of leprosy, including the reaction cases in India, other endemic and non-endemic countries. A consortium approach for focussing on specimens from severe forms of ENL can be a good approach. There is clear need to accelerate research on biology of *M. lepromatosis* including its growth, pathobiology in experimental animals and its relevance in understanding the molecular epidemiology of leprosy especially of reactional states. Multicentric and multi-country studies will be needed to progress faster in understanding the biology and applied aspects of disease caused by *M. lepromatosis*. Such knowledge may help in better management of disease and its complications. All such information would ultimately be useful in reducing its morbidity and ultimately achieving faster eradication of leprosy.

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