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Editorial

Leprosy stigma & the relevance of emergent therapeutic options

In the history of modern medicine, in terms of physical stigma, leprosy is a predominant disease and the probable reason is that the disease, even in the lepromatous spectrum, does not account for mortality but only for the visible deformity which proves to be a major cause of life-long stigamtization[1]. Stigma has been defined by Goffman[2] as 'an attribute that is deeply discrediting, and the stigmatized individual is one who is not accepted and not accorded the respect and regard of his peers; one who is disqualified from full social acceptances'. Stigma was sub-divided into three main groups, with the physical deformity of face being the predominant. This definition is appropriately relevant to leprosy where the oft depicted facial morphology of the neglected lepromatous patient is the universal depictive connotation of leprosy. The other deformities including facial plaque of the non-lepromatous patient (especially if in reaction), facial palsy, claw hand deformity, foot-drop or the hypopigmented macules which are conspicuous on dark skin. The perception ingrained in the general conscience is such that leprosy in all its varied forms is infectious and its carriers worthy of being discriminated.

The earliest reliable evidence of leprosy in India can be found in the *Sushruta Samhita*, written in a period about 600 BC, which mentioned chaulmoogra oil as a treatment for leprosy[3]. The litany of perilous misconceptions about leprosy abounds in endemic countries including India[4]. The following are particularly prevalent and disturbing: (*i*) In India, there is an ingrained concept of heredity which is said to explain all the ills that plague human life. (*ii*) Another view considers deformity as divine punishment, which is in turn equated with leprosy. This misconception is encouraged by the fact that patients who recover, and appear perfectly normal, keep their disease a secret. (*iii*) Deformed beggars reinforce the association between leprosy and poverty. (*iv*) As majority of the misconceptions harboured by the lay public are not removed yet, the bulwark of measure should revolve around disease awareness, its early diagnosis and successful treatment.

The stigma in leprosy is at three levels - the patients (self-perceived stigma), the relatives and the community. A study from Nepal noted that varied myths still surround the disease, with only 62.6 per cent being aware of it being caused by a bacteria and a significant proportion (36%) associating it with various other irrelevant causes, including bad blood, curse, heredity and bad deeds. Only 43.8 per cent knew that leprosy is transmitted by prolonged close contact with leprosy patients, and surprisingly, 25.7 per cent reported religious rituals as its treatment[5]. Knowledge of the disease reduces stigma, and thus, extensive information, education and communication (IEC) campaigns might be an important way to remove this issue. It is important to understand that stigma and lack of knowledge among lay public lead to late care-seeking behaviour which further increases the chances of deformities, leading to stigma[6].

From the patients' perspective, the disease affects various aspects of life including marriage, employment and social interaction, especially with the presence of visible deformities (specific or non-specific)[7]. A study from Ghana reported that persons cured of leprosy preferred to stay in the leper colony. This was due to self-stigma, isolation and neglect, and would make effective treatment inconsequential in leprosy[8].

While the Global Partnership for Zero Leprosy[9] has delineated three goals of zero transmission, zero disability and zero discrimination, the first goal is difficult to achieve and the last goal is based on the prevention of the second

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goal. While effective education and more emphasis on leprosy training in the medical curriculum is the need of the hour, probably one of the most effective methods to reduce stigmatization is early diagnosis and appropriate treatment. A recent study found that patient delay (of more than three months) and healthcare provider delay (of more than one month) were two significant risk factors for disability among adult leprosy cases[10]. It is thus useful to intervene early and effectively with appropriately tailored therapy with the twin goals of effectively reducing transmission and preventing disability. There are varied and important treatment scenarios (Table) which are useful to refresh and implement beyond merely dispensing the multidrug therapy (MDT) kits. Even though the emergent focus is on disabilities, simple concerns are rarely addressed such as clofazimine pigmentation which add to the stigma of leprosy[26]. Although clofazimine forms the bulwark of therapy, largely as resistance to it is unproved to date, there is a need to possibly look at novel biomimetic preparations which have equal efficacy and cause no skin pigmentation[27]. Furthermore, the fixed duration treatment is at variance with ground reality where patients with bacteriological index (BI) >4 at diagnosis usually get extended therapy. It is important to remember that relapses take about seven years to appear[28] and there is a dearth of studies that examine this aspect consequent to uniform MDT regimen.

Treating and managing the side effects of drugs in MDT are largely ignored aspects of treatment, more so with the newer drugs. Resistance testing is sparse, and hence, such cases can transmit resistant strains to the community. Reports of reactions occurring in infections with resistant strains are an ominous, though largely ignored, aspect as such cases, with the added effects of concomitant steroids and oral immunosuppressants, can predispose to dissemination of the resistant strains[29,30]. Nerve damage is the most important problem in leprosy, which is not surprising considering the marked tropism of *Mycobacterium leprae* for Schwann cells (SC). *Trypanosoma cruzi* and *M. leprae* are two unique organisms with a predilection for the SC[31]. *M. leprae* has undergone a reduction in its genome, which enabled it to attain the lowest guanine-cytosine content (approximately 58%) among mycobacteria, and this process, referred to as genomic 'reductive evolution',

Table. Therapeutic interventions and their role in control of leprosy and consequent prevention of stigmatization

Special therapeutic scenarios	
Therapeutic intervention	Alternative suggestion
Clofazimine pigmentation (an important stigmatizing factor)	Substitute by ofloxacin 400 mg/day or minocycline 100 mg/day[11-13]
Rifampicin resistance/ intolerance	Alternative regimen with clofazimine, ofloxacin and minocycline for 6 months followed by clofazimine and ofloxacin for 18 months[11-13]
Pregnancy and lactation	Continue/start MDT as indicated Clofazimine is excreted in breast milk but largely safe to use[11-14]
Concomitant tuberculosis	Rifampicin in antitubercular doses; in addition to MDT[11-13]
Newer therapeutic recommendations/advances in leprosy and their constraints	
Intervention	Constraint
Single-dose rifampicin[15]	Protection for low bacillary load and paucibacillary disease only; no significant protection beyond two years; more protection for further contacts than household contacts
Immunoprophylaxis (BCG/ *Mw* vaccine)	Repeat BCG vaccination recommended in some countries[16] but minimal or no evidence of any additional benefit over routine vaccination at birth[17] *Mw* has been studied in India before with encouraging effects[18]; further trials on going in five districts of high endemicity in India[19]
U-MDT	Concerns of higher relapses and disability progression in MB leprosy; longer follow ups required to clarify these aspects[20]
Immunotherapeutic use of *Mw*/MIP vaccine	Trials conducted in India[21-23] have shown efficacy (as adjunct to MDT) in achieving faster bacillary clearance in patients with high bacillary index A higher incidence of reversal reactions reported in a few studies, while the incidence of type 2 reactions has been shown to be similar to control groups or lower[24,25]

U-MDT, uniform MDT; MB, multibacillary; MDT, multidrug therapy; BCG, Bacillus Calmette-Guérin; MIP, *Mycobacterium indicus pranii*

helped it to adapt to the host SC[32]. *M. leprae* promotes nuclear reprogramming and dedifferentiation of host SC into progenitor/stem-like cells that are vulnerable to *M. leprae* infection[32]. Thus, early detection of nerve impairment is an emergent need both for diagnosis and prevention of disabilities[33]. Nylon monofilaments (Semmes-Weinstein monofilaments) and voluntary muscle testing are current state-of-the-art tools that have been shown to correlate well with sophisticated tests[33,34]. The primary focus of reactions is to prevent nerve damage and to address the issue of neuropathic pain[34]. While steroids have been used, the regimens vary and the impact of steroids and other measures on preventing progression of nerve damage needs to be assessed[35]. The lumping of both downgrading and upgrading reactions into type 1 reaction (reversal reaction) is unfortunate as downgrading reactions are evidently seen in clinical practice and these do not require long duration of steroids and are easier to control. Downgrading reaction is a distinct reaction that occurs without treatment. The importance is that the steroid dose and duration are either less or steroid may not be required in type 1 downgrading reaction. This is because suppressing a heightened immune response (type 1 upgrading) is more difficult than suppressing a downgrading reaction[36]. Upgrading reactions are better documented than downgrading ones; the reason could be that patients under treatment are more likely to have their progress observed[36]. Another therapeutic relevance is that lumping downgrading reaction with upgrading reactions as reversal reactions entails such cases to treatment with long duration of steroids, and in tuberculosis (TB)-endemic countries, like India, there is a real risk of reactivation of TB with prolonged steroids[37]. A review of reported cases of leprosy and TB co-infections noted that 7 of 10 (70%) cases were on steroids before the diagnosis of TB, suggesting that steroids may be a risk factor for reactivation of TB in leprosy patients[38]. This highlights the need to include interferon gamma release assay (IGRA) in the workup before treatment of leprosy reactions in TB-endemic countries.

A very relevant issue for stigma remains disability management and this is woefully inadequate. The risk factors for disabilities include male sex, multibacillary leprosy and leprosy reactions with steroids, and possibly early and adequate treatment would be useful to prevent disabilty[39].

For a large number of medical professionals, dermatologists are the only trained task force to address leprosy and it is imperative to re-emphasize the various treatment options and the role of early diagnosis and intervention that can effectively manage and prevent disabilities and reactions (Table). Various methods of mitigating stigma have been suggested, mainly focusing on documenting the level of stigma in the communities and healthcare services and also assessing objectively its impact on patients[40]. It is therefore recommended to address the negative attitude against patients at the community level through outreach efforts. However, in countries where health budgets are already constrained by other diseases of national importance and where widespread illiteracy is a real issue, such laudable ideas usually do not succeed consistently. Therefore, the present measures need to be honed and implemented fully before hurriedly enforcing new measures including single-does regimen or vaccines (Table)[11-25], as it is important to understand the financial and logistical restraints for any national programme. Further, to convince dermatologists to implement 'novel' interventions is another challenge, largely ignored by the national and international bodies recommending guidelines in leprosy.

Thus, while stigma management and identification are important, it is our view that robust management of leprosy reinforcing the existent principles would be more effective in preventing disabilities than the laudable but complex issues that address stigma in recommendations. Stigma is ingrained into the conscience of the community and is a consequence of delay or lack of adequate treatment, and possibly to a large extent, 'prevention by early diagnosis and adequate treatment'[35] could be a more practical approach to manage stigma in leprosy.

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References

1. Bryceson A, Pfaltzgraff RE, editors. *Leprosy: Medicine in the tropics*. London: Churchill Livingstone; 1982.

2. Goffman E. *Stigma*: *Notes on the management of spoiled identity*. Englewood Cliffs, London: Penguin Books, Prentice-Hall Inc.; 1963.
3. Lowe J. Comments on the history of leprosy. *Lepr Rev* 1947; *18* : 54-64.
4. Mutatkar RK. *Society and leprosy*. Wardha, India: Gandhi Memorial Leprosy Foundation; 1979.
5. Singh R, Singh B, Mahato S. Community knowledge, attitude, and perceived stigma of leprosy amongst community members living in Dhanusha and Parsa districts of Southern Central Nepal. *PLoS Negl Trop Dis* 2019; *13* : e0007075.
6. Correia JC, Golay A, Lachat S, Singh SB, Manandhar V, Jha N, *et al*. "If you will counsel properly with love, they will listen": A qualitative analysis of leprosy affected patients' educational needs and caregiver perceptions in Nepal. *PLoS One* 2019; *14* : e0210955.
7. Marahatta SB, Amatya R, Adhikari S, Giri D, Lama S, Kaehler N, *et al*. Perceived stigma of leprosy among community members and health care providers in Lalitpur district of Nepal: A qualitative study. *PLoS One* 2018; *13* : e0209676.
8. Sottie CA, Darkey J. Living with stigma: Voices from the Cured Lepers' village in Ghana. *Soc Work Health Care* 2019; *58* : 151-65.
9. Global Partnership for Zero Leprosy. Available from: *https://zeroleprosy.org/*, accessed on January 22, 2020.
10. Srinivas G, Muthuvel T, Lal V, Vaikundanathan K, Schwienhorst-Stich EM, Kasang C. Risk of disability among adult leprosy cases and determinants of delay in diagnosis in five states of India: A case-control study. *PLoS Negl Trop Dis* 2019; *13* : e0007495.
11. Sardana K, Bhushan P, Khurana A. Chemotherapy. In. Sardana K, Khurana A, editors. *Joplings handbook of leprosy*, 6th ed. New Delhi: CBS Publishers; 2020.
12. WHO Study Group on Chemotherapy of Leprosy & World Health Organization. Chemotherapy of leprosy: Report of a WHO study group. WHO, Technical Report Series 847; 1994.
13. WHO Expert Committee on leprosy & World Health Organization. WHO Expert Committee on leprosy: eighth report. WHO, Technical Report Series 968; 2012.
14. Jacobson RR. Treatment of Leprosy. In: Hastings RC, editor. *Leprosy*. New York: Churchill Livingstone; 1994. p. 342.
15. Richardus R, Alam K, Kundu K, Chandra Roy J, Zafar T, Chowdhury AS, *et al*. Effectiveness of single-dose rifampicin after BCG vaccination to prevent leprosy in close contacts of patients with newly diagnosed leprosy: A cluster randomized controlled trial. *Int J Infect Dis* 2019; *88* : 65-72.
16. Düppre NC, Camacho LA, da Cunha SS, Struchiner CJ, Sales AM, Nery JA, *et al*. Effectiveness of BCG vaccination among leprosy contacts: A cohort study. *Trans R Soc Trop Med Hyg* 2008; *102* : 631-8.
17. BCG vaccines: WHO position paper - February 2018. *Wkly Epidemiol Rec* 2018; *93* : 73-96.
18. Sharma P, Mukherjee R, Talwar GP, Sarathchandra KG, Walia R, Parida SK, *et al*. Immunoprophylactic effects of the anti-leprosy *Mw* vaccine in household contacts of leprosy patients: Clinical field trials with a follow up of 8-10 years. *Lepr Rev* 2005; *76* : 127-43.
19. Kumar S. India resurrects forgotten leprosy vaccine. *Science* 2017; *356* : 999.
20. Penna GO, Bührer-Sékula S, Kerr LRS, Stefani MMA, Rodrigues LC, de Araújo MG, *et al*. Uniform multidrug therapy for leprosy patients in Brazil (U-MDT/CT-BR): Results of an open label, randomized and controlled clinical trial, among multibacillary patients. *PLoS Negl Trop Dis* 2017; *11* : E0005725.
21. Kamal R, Natrajan M, Katoch K, Arora M. Clinical and histopathological evaluation of the effect of addition of immunotherapy with *Mw* vaccine to standard chemotherapy in borderline leprosy. *Indian J Lepr* 2012; *84* : 287-306.
22. Narang T, Kaur I, Kumar B, Radotra BD, Dogra S. Comparative evaluation of immunotherapeutic efficacy of BCG and mw vaccines in patients of borderline lepromatous and lepromatous leprosy. *Int J Lepr Other Mycobact Dis* 2005; *73* : 105-14.
23. Kaur I, Dogra S, Kumar B, Radotra BD. Combined 12-month WHO/MDT MB regimen and *Mycobacterium* w. vaccine in multibacillary leprosy: A follow-up of 136 patients. *Int J Lepr Other Mycobact Dis* 2002; *70* : 174-81.
24. Sharma P, Misra RS, Kar HK, Mukherjee A, Poricha D, Kaur H, *et al*. *Mycobacterium* w vaccine, a useful adjuvant to multidrug therapy in multibacillary leprosy: A report on hospital based immunotherapeutic clinical trials with a follow-up of 1-7 years after treatment. *Lepr Rev* 2000; *71* : 179-92.
25. De Sarkar A, Kaur I, Radotra BD, Kumar B. Impact of combined *Mycobacterium* w vaccine and 1 year of MDT on multibacillary leprosy patients. *Int J Lepr Other Mycobact Dis* 2001; *69* : 187-94.
26. Job CK, Yoder L, Jacobson RR, Hastings RC. Skin pigmentation from clofazimine therapy in leprosy patients: A reappraisal. *J Am Acad Dermatol* 1990; *23* : 236-41.
27. Murashov MD, Diaz-Espinosa J, LaLone V, Tan JWY, Laza R, Wang X, *et al*. Synthesis and characterization of a biomimetic formulation of clofazimine hydrochloride microcrystals for parenteral administration. *Pharmaceutics* 2018; *10*. pii: E238.
28. Jamet P, Ji B. Relapse after long-term follow up of multibacillary patients treated by WHO multidrug regimen. Marchoux Chemotherapy Study Group. *Int J Lepr Other Mycobact Dis* 1995; *63* : 195-201.
29. Sinha S, Sardana K, Agrawal D, Malhotra P, Lavania M, Ahuja M. Multidrug resistance as a cause of steroid-nonresponsive downgrading type I reaction in Hansen's disease. *Int J Mycobacteriol* 2019; *8* : 305-8.
30. Arora P, Sardana K, Agarwal A, Lavania M. Resistance as a cause of chronic steroid dependent ENL: A novel paradigm with potential implications in management. *Lepr Rev* 2019; *90* : 201-5.
31. Neal JW, Gasque P. The role of primary infection of Schwann cells in the aetiology of infective inflammatory neuropathies. *J Infect* 2016; *73* : 402-18.

32. Chavarro-Portillo B, Soto CY, Guerrero MI. *Mycobacterium leprae's* evolution and environmental adaptation. *Acta Trop* 2019; *197* : 105041

33. Croft RP, Nicholls PG, Steyerberg EW, Richardus JH, Cairns W, Smith S. A clinical prediction rule for nerve-function impairment in leprosy patients. *Lancet* 2000; *355* : 1603-6.

34. van Brakel WH. Detecting peripheral nerve damage in the field: Our tools in 2000 and beyond. *Indian J Lepr* 2000; *72* : 47-64.

35. Lockwood DNJ, Nicholls P, Smith WCS, Das L, Barkataki P, van Brakel W, *et al*. Comparing the clinical and histological diagnosis of leprosy and leprosy reactions in the INFIR cohort of Indian patients with multibacillary leprosy. *PLoS Negl Trop Dis* 2012; *6* : e1702.

36. Sardana K, Sinha S, Bhushan P. Reactions in leprosy. Overview and type 1 reaction. In. Sardana K, Khurana A, editors. *Joplings handbook of leprosy*, 6th ed. New Delhi: CBS Publishers; 2020.

37. Rawson TM, Anjum V, Hodgson J, Rao AK, Murthy K, Rao PS, *et al*. Leprosy and tuberculosis concomitant infection: A poorly understood, age-old relationship. *Lepr Rev* 2014; *85* : 288-95.

38. Mangum L, Kilpatrick D, Stryjewska B, Sampath R. Tuberculosis and leprosy coinfection: A perspective on diagnosis and treatment. *Open Forum Infect Dis* 2018; *5* : ofy133.

39. de Paula HL, de Souza CDF, Silva SR, Martins-Filho PRS, Barreto JG, Gurgel RQ, *et al*. Risk factors for physical disability in patients with leprosy: A systematic review and meta-analysis. *JAMA Dermatol* 2019.

40. van Brakel WH. Global Partnership for Zero Leprosy Research Agenda Working Group Subgroup on Stigma. Available from: *https://zeroleprosy.org/wp-content/uploads/2019/06/GPZL-RWG-Stigma.pdf*, accessed on December 17, 2019.