Prevention of transmission of leprosy: The current scenario

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Abstract

With the worldwide implementation of WHO multidrug therapy in the 1980s, the global burden of leprosy has decreased. However, the annual new case detection rate around the world has remained nearly static over the past decade with India, Brazil, and Indonesia contributing the majority of these new cases. This has been attributed to the ongoing transmission of Mycobacterium leprae from existing untreated cases and partly to the intensive new case detection programs operative in endemic areas. The WHO has called for a “global interruption of transmission of leprosy by 2020”. Targeted chemoprophylaxis of contacts may help bring down the number of new cases. The single-dose rifampicin currently in use for post-exposure prophylaxis (PEP) has limitations and so newer antileprosy drugs and regimens have been trialed for chemoprophylaxis. BCG re-vaccination in combination with chemoprophylaxis for the prevention of leprosy transmission has not been very encouraging. The use of the anti-phenolic glycolipid-1 (PGL-1) antibody test to detect subclinical cases and administer targeted chemoprophylaxis was unsuccessful owing to its low sensitivity and technical difficulties in a field setup. There is a pressing need for newer multidrug chemoprophylactic regimens using second-line antileprosy drugs. The Netherlands Leprosy Relief has proposed an enhanced PEP++ regimen. A simple but highly sensitive and specific serological test to detect subclinical cases at the field level needs to be developed. Although there are a number of challenges in the large-scale implementation of strategies to halt leprosy transmission, it is important to overcome these in order to move towards a “leprosy-free world.”

Key words: Chemoprophylaxis, immunoprophylaxis, leprosy, PEP++regimen

Introduction

Leprosy is a chronic infectious disease caused by Mycobacterium leprae (M. leprae). It is thought to be transmitted by droplets from untreated patients with a high bacillary load to susceptible individuals. Owing to the high risk of transmission, all contacts of an “active case” are potential “future cases” which may further give rise to new cases exponentially. The management of contacts of leprosy cases is therefore a priority.

The implementation of multidrug therapy (MDT) has resulted in the reduction of leprosy prevalence globally. However, despite the free availability and effective utilization of MDT worldwide, the decline in newly detected cases over the past 10 years has been slow; from 249,007 cases in 2008 to 210,671 cases in 2017. The current global annual new case detection rate (ANCDR) is 2.7/100,000 population, marginally lower than in previous years. India, Brazil, and

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Indonesia contributed to 80.2% of the global new case load in 2017. The gradual decrease in ANCDR is not an unexpected phenomenon for a chronic infectious disease such as leprosy with long and unpredictable incubation period. The implementation of “leprosy case detection campaigns” as national programs in some countries facilitating detection of new cases may also be partly responsible for the relatively stagnant statistical data in recent years.

In 2012, the World Health Organization (WHO) set “roadmap targets” to reduce the global impact of 17 neglected tropical diseases including leprosy. A target for the “global interruption of transmission of leprosy by 2020” was set with the aim of bringing down the number of incident new cases from existing cases and, in the long run, eradication of leprosy. “Breaking the chain of transmission” as a leprosy control strategy has now gained momentum around the world. This not only includes early diagnosis and treatment but also treatment of the contacts of new cases who could harbor subclinical infection with the potential to later develop manifest disease. However, many challenges need to be overcome to reach this goal including optimal contact-tracing, confirmation of subclinical infections by appropriate diagnostic tests, establishment of an effective chemoprophylactic regimen, and large scale implementation of these regimens in leprosy-endemic countries.

**Contacts of a “case of leprosy”**

**Susceptibility to develop leprosy**

An individual who is in prolonged association (≥20 h/week) with an index case of leprosy is considered to be a “contact.” Following exposure to an untreated case, only 5%–20% of the contacts may develop clinical features of leprosy.

Several factors determine susceptibility to leprosy [Table 1].

Although the bacillary load of the index case is the foremost factor determining the risk of disease transmission, contacts of paucibacillary (PB) index cases are also at risk. In a series of children with leprosy, Jain et al. recorded 38% PB contacts in the household and neighborhood. Contacts harbouring *M. leprae* may remain asymptomatic for long periods before they develop active disease. The risk of acquiring leprosy for different categories of contacts are presented in Table 2.

**Table 1: Risk factors for acquiring leprosy**

| Factors                      | Higher risk | Lower risk | Comments                                                                 |
|------------------------------|-------------|------------|--------------------------------------------------------------------------|
| **Patient-related**          |             |            |                                                                          |
| Type of leprosy in the index patient | MB and PB with 2-5 lesions | Single-lesion PB | MB and PB with 2-5 lesions have similar risk |
| Smear positivity in the index patient | Positive | Negative |                                                                          |
| Treatment status of the patient | Untreated/incompletely treated/defaulter | On regular treatment/completed treatment | Bimodal pattern in a study |
| **Contact-related**          |             |            |                                                                          |
| Age                          | Older age   | People between 20-29 years may be at lower risk | Risk increases from 5 to 15 years with peak between 15-20 years Age >30 years |
| Gender                       | Male        | Female | This observation is variable in different studies |
| Physical distance with index case | Core household relatives | Other contacts living under the same roof and next door neighbors | Neighbors of neighbors have further lower risk |
| Genetically related individuals | Children, parents, siblings | | Genetically related persons are at higher risk, irrespective of physical distance |
| BCG scar                     | Absent      | Present | Risk of developing leprosy *per se* and the type of leprosy are genetically determined. The susceptibility gene loci may be variable in different countries |

**Table 2: Types of contacts in leprosy**

| Types of contacts | Definition | Remarks | Remarks |
|-------------------|------------|---------|---------|
| Household contact | Resides under the same roof and shares the kitchen with the index case | Risk of acquiring leprosy: Four times more than general population | MB index cases: 5-10 times risk |
| Neighbor contact  | Resides in the same locality, next door to an index case | Risk of acquiring leprosy: MB index cases: 3-5 times risk | MB index cases: 3-5 times risk |
| Social contact    | Coming to close vicinity of an index case (≥20 h/week), e.g., peers at educational institutions, colleagues at work, and religious associates | Risk of exposure is higher in enclosed rooms and overnight stay with a case than a day-time meeting in a room Short regular contacts are as vulnerable as single one of long duration |
Contact tracing and management

Household contacts are often more amenable to antileprosy interventions such as clinical examination and prophylactic therapy. The “new-case detection campaigns” and “contact tracing programs” that are operative in some endemic countries aim to detect and treat yet unidentified cases to reduce the source of infection. Contacts of these new cases can be targeted with chemoprophylaxis to break the “chain of transmission”. Chemoprophylaxis can be administered either to individual high-risk contacts, or as a blanket intervention of the entire population around a newly detected case.

Chemoprophylaxis

Chemoprophylaxis is the “administration of drugs, including antibiotics, to prevent the development or progression of an infection to active manifest disease.” Preventing the entry of *M. leprae* into a new host is impractical, but chemoprophylaxis may abort the progression of disease in contacts who have acquired the organism. Hence, chemoprophylaxis in leprosy is aptly termed as post-exposure prophylaxis (PEP).

Trials on chemoprophylaxis of leprosy

Pre-MDT era

Dapsone and acedapsone

The prophylactic value of dapsone in treating contacts of leprosy cases was first reported by Dharmendra (1965) from India. Several randomized controlled trials (RCT) describing dapsone as an effective chemoprophylactic agent soon followed with efficacy rates varying from 34% to 99%. Lower efficacy rates of 28%–46% were reported from other endemic countries such as Korea, Uganda, and Philippines. Dayal and Bharadwaj reported an 86% efficacy rate of dapsone chemoprophylaxis in high-risk childhood contacts. Acedapsone was also studied in childhood contacts of lepromatous and smear-positive leprosy patients with efficacy rates of 44%–54%.

Various drawbacks of dapsone chemoprophylaxis has limited its use for this purpose. With support from the Damien Foundation, Belgium, nine double-blind RCTs (SDR vs. placebo) were conducted in household contacts of leprosy cases in India. With short-term administration does not clear dormant *M. leprae*. Low bactericidal effect requires long term prophylaxis; issue of compliance by otherwise asymptomatic contacts. Emergence of dapsone resistance.

Post-MDT era

Rifampicin Chemoprophylaxis

Rifampicin is bactericidal and a single dose kills up to 92.1% of *M. leprae* rendering the patient nearly noninfectious. In the first trial of rifampicin chemoprophylaxis among contacts of leprosy patients in southern Marquesas, a single dose of rifampicin (25 mg/kg) was observed to have a protective effect of 40%–50% at the 4th and 10th years. An Indonesian trial with two doses of rifampicin at 3.5 months intervals showed a protective effect of 75% at 3 years which was higher among distant contacts, as compared to household and neighbourhood contacts; this effect waned by 6 years to become nearly similar to the controls.

In the landmark COLEP study conducted in two districts of north-west Bangladesh a single-dose of rifampicin (SDR) or placebo was administered to close contacts of newly diagnosed leprosy patients and followed up biannually for 4 years. The overall decrease in the incidence of leprosy at 2 years was 57%, but there was no significant difference between the groups at 4 years. As with the Indonesian trial, a greater protective effect on distant contacts (as compared to household contacts in whom the protective effect was <30%) was noted. *M. leprae*–specific anti-phenoic glycolipid-1 (anti-PGL-1) antibody negative contacts achieved higher protection as compared to seropositive cases.

Box 1: Drawbacks of dapsone chemoprophylaxis

- Favourable pharmacokinetics as a chemoprophylactic agent against leprosy; but short term administration does not clear dormant *M. leprae*.
- Low bactericidal effect requires long term prophylaxis; issue of compliance by otherwise asymptomatic contacts.
- Emergence of dapsone resistance.
Trials on multidrug chemoprophylactic regimen

Various drug combinations have been used to formulate a highly bactericidal chemoprophylactic regimen with a longer-lasting protective effect. Placebo-controlled trials with ROM therapy (single dose rifampicin 600 mg, ofloxacin 400 mg, and minocycline 100 mg) have not demonstrated superiority over SDR. The disadvantages of ROM chemoprophylaxis are presented in Box 3.

Newer antileprosy drugs as chemoprophylactic agents

An ideal antibiotic for chemoprophylaxis must have certain properties [Box 4].

Several second-generation antileprosy drugs are highly bactericidal against M. leprae in animal and human studies including the ansamycins (rifapentine, rifabutin), fluoroquinolones (moxifloxacin, ofloxacin, pefloxacin), macrolides (clarithromycin), and tetracyclines (minocycline). New antileprosy regimens using these drugs have been studied extensively and experience gathered from their use in the treatment of leprosy can be applied to make use of these as chemoprophylactic agents. [Table 3] However, implementation of these regimens on a large scale is limited by high cost, increased risk of adverse drug reactions and other technical factors. Some studies have also shown that regimens using second-line antileprosy drugs are either not beneficial or only marginally superior to the existing WHO-MDT even in rifampicin-resistant cases.

Prospects of new drugs as chemoprophylactic agents

The relative merits of these second-generation antileprosy drugs as chemoprophylactic agents over rifampicin are presented in Table 4.

Although rifampicin resistance has been documented, it is thought that the possibility of rifampicin resistance arising in patients with subclinical leprosy is very low as they are estimated to harbor fewer than 10⁶ M. leprae in total or <10⁵ viable M. leprae. Based on this assumption as well as the confidence arising from its long use both as a chemotherapeutic and chemoprophylactic agent, rifampicin still remains the drug of choice for leprosy chemoprophylaxis.

Various limitations of chemoprophylaxis and the stigma associated with implementation have been discussed in Box 5.

Combined Chemoprophylaxis and Immunoprophylaxis

The protective effect of BCG vaccine against leprosy is based on antigen sharing between M. tuberculosis and M. leprae. There is ample evidence of the protective effect of BCG vaccine in leprosy prevention. A meta-analysis of evidence drawn from seven experimental studies showed a protective effect of 26%, whereas an overestimated value of 61% was obtained from 19 observational studies. In another meta-analysis (excluding observational studies), 78.3% of the 29 studies showed significant protective effect. In trials, cohort studies, and case–control studies statistically significant protective effects of 43%, 62%, and 59% were seen respectively.

Role of neonatal BCG vaccination in prevention of transmission of leprosy

In most parts of the world, mandatory BCG vaccination at birth is part of “Expanded Programme of Immunization (EPI, WHO)”.

Protective effects of BCG vaccination in leprosy are discussed in Box 6.

Chemoprophylaxis among contacts having neonatal BCG vaccination

Individually, SDR and neonatal BCG vaccination each may provide around 60% protection against transmission of M. leprae to household contacts, but when an already BCG-vaccinated contact receives SDR, the protective effect increases to about 80%. However, as with SDR prophylaxis, greater benefits accrue to contacts of PB cases and for distant contacts. Both SDR chemoprophylaxis and
Table 4: Prospects of new drugs as chemoprophylactic agents with advantages and disadvantages over rifampicin\textsuperscript{34,40,53-58}

| Drugs       | Advantages                                                                 | Disadvantages                                                                 | Relevant studies                                                                 |
|-------------|----------------------------------------------------------------------------|------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Rifapentine | Long-acting ansamycin\textsuperscript{50}                                  | Costlier                                                                     | M. leprae viability study on infected mice:                                      |
|             | Longer half life; 14-18 h versus 3 h in rifampicin                        |                                                                               | -Five doses of rifapentine are equivalent to 20 doses of rifampicin\textsuperscript{65} |
|             | Killing power following single dose is 99.6\% vs 92.1\% in rifampicin     |                                                                               | -Single dose of both drugs ineffective to kill M. leprae\textsuperscript{65}     |
|             | Marginally effective against rifampicin-resistant M. leprae\textsuperscript{53} |                                                                               |                                                                                 |
| Moxifloxacin| Very high bactericidal effect against M. leprae\textsuperscript{49}       | Fluoroquinolones are “category C” drugs in pregnancy and lactation          | Moxifloxacin (10 mg/kg/day) has been used in children aged 7-15 years with        |
|             | Longer half life than rifampicin and superior safety profile when compared with other fluoroquinolones\textsuperscript{50} |                                                                               | multidrug-resistant tuberculosis, showing good tolerance.\textsuperscript{77}   |
| Clarithromycin| Rapid tissue penetration ability with high plasma and tissue level      | Relatively short-acting, with less effect on slow-growing M. leprae\textsuperscript{30} | Hence, it must always be administered in combination with another drug          |

\textit{M. leprae}: Mycobacterium leprae

Box 4: Characteristics of an ideal antibiotic for chemoprophylaxis\textsuperscript{34}

- Rapid gastro-intestinal absorption without local side effects
- Rapid tissue penetration and even distribution in infected cells
- Slow elimination, so long plasma half life achieved resulting in enhanced efficacy (helpful in formulating ‘single dose regimen’)
- Relatively milder adverse effect profile
- Safe in children, elderly and pregnant women

Box 5: Factors limiting implementation of a chemoprophylactic regimen\textsuperscript{55,60}

- Constant source of funds required
- Training and supervision of health personnel
- Preparedness for adverse drug reactions with newer drugs, as it may create negative impact among the beneficiaries
- Chemoprophylaxis is not a substitute, but complimentary to ‘new case detection’ so contact tracing strategies must be continued
- Health workers must maintain patient confidentiality to avoid operational difficulty at field set up

Box 6: Protective effects of Bacillus Calmette-Guérin vaccination in leprosy\textsuperscript{64,65}

- BCG has a protective effect (20-90\%) against leprosy\textsuperscript{44,34}
- Neonatal BCG vaccination can provide long term protection against leprosy
- Patients without neonatal BCG vaccination are at higher risk of progression to MB disease\textsuperscript{61}
- Contacts of a newly diagnosed leprosy case who have had neonatal BCG vaccination have half the risk of acquiring the disease\textsuperscript{61}

PB: paucibacillary; MB: multibacillary

BCG vaccination individually do not optimally protect the close contacts of MB and smear-positive index cases.\textsuperscript{65}

Role of BCG revaccination in prevention of transmission of leprosy

The COLEP study showed that BCG immunoprophylaxis potentiated the protective effect of chemoprophylaxis.\textsuperscript{66} A cluster RCT to compare the effect of BCG immunoprophylaxis alone with a combination of BCG immunoprophylaxis and SDR chemoprophylaxis among contacts of newly diagnosed leprosy patients (MALTALEP study, Bangladesh) is ongoing.\textsuperscript{66}

In a study from Brazil\textsuperscript{65,66} 56\% protective effect of BCG vaccination has been demonstrated in contacts of patients with leprosy irrespective of their neonatal vaccination status. Based on this, BCG revaccination to leprosy contacts has been adopted as a government policy in that country.\textsuperscript{66,68,69} Another study from Malawi found that a second dose BCG vaccine conferred 50\% protection against leprosy.\textsuperscript{7} However, the role of BCG revaccination later in life is debatable.\textsuperscript{65,66,68}

The immunoprophylactic effects of four vaccines, BCG, BCG + killed M. leprae, Mycobacterium \textit{w} (\textit{Mw}), and ICRC, were evaluated in double-blind RCT conducted in South India.\textsuperscript{70} \textit{Mw} showed the lowest protective effect of 25.7\% while that of BCG, ICRC and BCG + killed M. \textit{leprae} were 34.1\%, 65.5\% and 64\% respectively.\textsuperscript{70,71} The authors concluded that the ICRC and BCG + killed \textit{M. leprae} vaccines had potential for prevention of leprosy.\textsuperscript{70} There was no evidence of beneficial effect of additional dose of BCG vaccination during first year, but statistically significant higher value was recorded during follow up.\textsuperscript{70,71}

In a cluster-randomized community trial (BCG-REVAC), a large cohort of normal Brazilian school children were administered an additional dose of BCG vaccine to assess its impact in prevention of transmission of both tuberculosis and leprosy.\textsuperscript{65} At 6 years 8 months, there was no difference in the occurrence of new leprosy cases among the revaccinated and non-revaccinated groups.\textsuperscript{64}

Thus, revaccination of household contacts with BCG does not appear to be a viable strategy in prevention of leprosy. However, neonatal BCG vaccination as part of EPI must be made compulsory in leprosy-endemic countries. BCG vaccination at birth may be encouraged through special
campaigns, especially in the states with high endemicity for leprosy and in the families with sufferers of leprosy.\textsuperscript{63} During active or passive surveillance for new leprosy cases, screening for a BCG scar must be made mandatory and if a new case or a household contact lacks a BCG scar, vaccination should be carried out immediately. It must be emphasized that concomitant administration of vaccine at a later date and chemoprophylaxis is contraindicated; if chemoprophylaxis is given first, then BCG administration should be deferred by at least 24 hours, while if BCG is administered first then chemoprophylaxis should be delayed by 1 month.\textsuperscript{42} This involves two visits by health workers thereby increases costs.

**BCG vaccination may increase the risk of occurrence of leprosy**

Duppre \textit{et al.} from Brazil noted a higher incidence of tuberculoid leprosy in the contacts without neonatal BCG, during earlier months of the first year of vaccination at a later date.\textsuperscript{67,68} However, this risk reduced after the first year and this group of contacts subsequently achieved a protection of 80\%.\textsuperscript{64,69} This observation has not been substantiated further\textsuperscript{64,69} and one of the objectives of MALTALEP study is to reevaluate this finding.\textsuperscript{65}

**MIP vaccine used for immunoprophylaxis**

The immunoprophylactic effect of \textit{Mycobacterium indicus pranii} (MIP or \textit{Mw} vaccine) in contacts of leprosy patients is presented in Table 5.\textsuperscript{71-74} The results of these studies may be reevaluated for large scale applicability of this vaccine as an immunoprophylactic agent.

**Screening of Contacts to Detect Susceptibility to Leprosy**

There is no way of detecting susceptibility to leprosy in close contacts in order to use targeted chemoprophylaxis.\textsuperscript{2} Demonstration of anti-PGL-1 antibodies (IgM and IgG) among healthy contacts has shown a consistent association with future development of the disease\textsuperscript{75} with the risk being three times greater in seropositive individuals.\textsuperscript{75} However, the selection of cases for chemoprophylaxis on a large-scale based on this test does not appear practical (Box 7).

\textbf{Future Directions in Prevention of Transmission of Leprosy in High Endemic Countries}

SIMCOLEP is a micro-simulation model developed to study the transmission and impact of control measures of leprosy among the members of a household with an index case.\textsuperscript{78,79} The two components of the model are the “life history of individual family members” and the “natural course of infection with \textit{M. leprae}” and it takes into account the formation, dissolution, and change of the households, transmission of leprosy between existing and new households, and evaluation of the interventions aimed at these household members.\textsuperscript{7} The SIMCOLEP study design was based on the data generated from the COLEP study and the trial was conducted in the same geographical area with the aim to compare the efficacy and future outcome of various leprosy intervention programs.\textsuperscript{78,79}

At present, the global distribution of leprosy is uneven and cases are aggregated in three countries i.e. India, Brazil, and Indonesia.\textsuperscript{79} Although elimination has been achieved at the national level in both India and Indonesia, there are some high endemic states/areas contributing significantly to the disease burden in these countries as well as globally.\textsuperscript{79} This may be a hindrance in achieving the goal of “global interruption of transmission of leprosy by 2020 (WHO).”\textsuperscript{76} Blok \textit{et al.} have used the SIMCOLEP model to predict the trend of incidence of leprosy in the high endemic regions of these three countries until 2030.\textsuperscript{78,79} With the existing leprosy control strategies in these countries, a downward trend in the

| Author          | Intervention                                                                 | Result                                                                 |
|----------------|------------------------------------------------------------------------------|------------------------------------------------------------------------|
| \textit{Kar et al.} (1992)\textsuperscript{72} | Two doses of MIP vaccine administered to lepromin-negative contacts of MB leprosy patients | Conversion of 98.5\% lepromin-negative contacts to lepromin positive |
| \textit{Sharma et al.} (2005)\textsuperscript{73} | Administered 2 doses of MIP vaccine to household contacts and followed up them for 8-10 years | Protective efficacy 68% at 3-4 years and 60% at 7-8 years |
| \textit{Kamal et al.} (2017)\textsuperscript{74} | Double-blind placebo-controlled study: MIP vaccine added to standard MDT regimen in patients with borderline tuberculoid leprosy | Efficacy decreased to 39% after 10 years of vaccination |

The \textit{UCP-LFA} format detects both humoral and cellular markers of \textit{M. leprae} infection and is effective in detecting PB cases;\textsuperscript{76,77} it was found efficacious in trials conducted in Bangladesh and other countries in Asia, Africa, and South America.\textsuperscript{77}

\textbf{Table 5: Immunoprophylaxis trials with MIP vaccine\textsuperscript{72-74}}

MDT: multidrug therapy; MIP: \textit{Mycobacterium indicus pranii}

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Author          & Intervention                                                                 | Result                                                                 |
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ANCDR has been predicted by the year 2030; hence, it may be possible to achieve the goal of interruption of transmission at national level by 2020 as per the target set by the WHO. However, it would not be possible to achieve this goal in some thickly populated high endemic regions of these countries. To address this issue, enhanced control measures are required for these regions.

**Future directions of chemoprophylaxis: The PEP++ regimen**

The Netherlands Leprosy Relief proposed an enhanced chemoprophylaxis regimen (PEP++) with the aim of reducing leprosy transmission by 80%-90% from the existing 60%. A series of meetings were held with experts from all domains of leprosy control across the world. The criteria for choosing an optimal enhanced PEP regimen were set up: effective, safe, acceptable, affordable, feasible, and minimal chance of development of drug resistance. The expert committee concluded that the tentative PEP++ regimen should consist of 3 doses each of rifampicin (600 mg, weight-adjusted dose in children) and moxifloxacin (400 mg) at 4 weekly intervals (days 1, 29, and 57). In cases where moxifloxacin was contraindicated, clarithromycin (300 mg, weight-adjusted dose in children) could be used.

Two most bactericidal drugs (rifampicin and moxifloxacin) with longer half life and desirable pharmacodynamics were selected, the rationale being to enhance the protective effect with repeated doses and lowering the risk of inducing resistance. These two drugs are easily available, affordable, and with monthly dosage schedule, supervised administration is possible. The efficacy of the proposed PEP++ regimen is to be tested against SDR in cluster-randomized trials in close contacts of leprosy cases in high endemic regions of India, Brazil, and Indonesia.

However, through a recent circular (EMA/668915/2018, 5th October, 2018) the Pharmacovigilance Risk Assessment Committee (PRAC)” of the European Medicine Agency (EMA) has imposed restrictions on oral, parenteral, and inhalational use of quinolone antibiotics because of their rare but potentially long-lasting side effects on musculoskeletal and nervous systems. This has evoked a discussion regarding the use of moxifloxacin as the second drug in the PEP++ regimen on a large scale for healthy contacts of patients with leprosy. Taking account of this recommendation, the best PEP++ regimen for adults would be rifampicin (600 mg) in combination with clarithromycin (500 mg or 1000 mg).

Ongoing trials of a tetravalent subunit vaccine LepVax (89 kD chimeric fusion protein containing three prioritized antigens, ML2055, ML2380, ML2028, and additional ML2531, formulated in a toll-like receptor 4 ligand glucopyranosyl lipid adjuvant in stable emulsion (GLA se) in post-exposure experimental animals have shown an 85% reduction in *M. leprae* load at 12 months after vaccination. LepVax has a good safety profile besides having protective effects on cutaneous nerves and delays *M. leprae*-induced impairment of motor nerve function. In BCG-vaccinated animal models the antigen-specific responses to LepVax remain unaltered. All these characteristics favor its future use as an ideal immunoprophylactic agent.

**Conclusion**

Thirteen countries with ongoing leprosy transmission have signed the declaration “towards a world free of leprosy (Bangkok Declaration, 2013, WHO). Despite the use of dapsone chemoprophylaxis to prevent transmission of leprosy five decades ago, the search for an ideal chemoprophylaxis regimen continues.

Implementation of any leprosy control program in endemic countries is a challenge to policymakers in terms of funds, manpower, and the difficulty of reaching geographical areas with pockets of leprosy. This economic burden could be reduced if blanket intervention could be replaced with chemoprophylaxis specifically targeted to subclinical cases identified by simple, highly sensitive laboratory tests.

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**Conflicts of interest**

There are no conflicts of interest.

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