Chapter

Leprosy: Prevention and Control

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Abstract

Hansen's disease is one of the most ancient diseases that is still prevalent in the world. The causative agent, Mycobacterium leprae (*M. leprae*) has a long incubation period, clinical features after infection are identified late and these acid fast bacilli cannot be cultured – making leprosy a difficult disease to eradicate. Therefore the prevention and control of disease becomes more important. The shift of treatment from dapsone monotherapy to multidrug therapy regimen has given a new hope. The multidrug therapy coupled with the newer vaccines promise better results to prevent further transmission. Globally and locally the efforts to decrease the burden of leprosy by using different strategies has resulted in elimination of leprosy. But there is still a long way to go to make world free of this dreaded disease.

Keywords: leprosy, prevention, vaccine, disability, multidrug therapy, rehabilitation

1. Introduction

Mycobacterium leprae (*M. leprae*) is an acid fast bacilli that is the causative agent of leprosy disease which mainly effects the skin and peripheral nerves. In olden times leprosy was common in temperate climates (e.g. Europe), today it is mainly confined to tropical and subtropical regions. Mode of transmission in leprosy is mainly through inhalation of droplets containing the bacteria. But skin contact is also claimed by many leprologists. The disabilities and deformities associated with leprosy due to neuropathy leads to long-term consequences, including. This in turn is associated with stigma.

The immunity of the host plays an important role in disease progress and control. Thus, fortunately 95% of patients exposed to *M. leprae* will not develop this disease. The variation in incubation period ranges from 2 to 20 years, or even longer.

Leprosy has been successfully eliminated as a public health problem in 2000 globally and at the national level in 113 countries out of 122 by 2005 [1]. Elimination of leprosy is defined by World Health Organization as a point prevalence below 1 per 10,000 population [2]. However, the number of new patients diagnosed with leprosy is still significant, at more than 200,000 in 2016 globally. The new case detection rate of the disease (NCDR) is only slowly declining (**Figure 1**) [3].

The long incubation period, silent symptoms, long duration MDT and unavailability of effective vaccine makes this disease difficult to identify, treat and eradicate. To add to the misery the stigma associated with the disease is another challenge. In such circumstances, prevention and control of disease gains utmost importance.

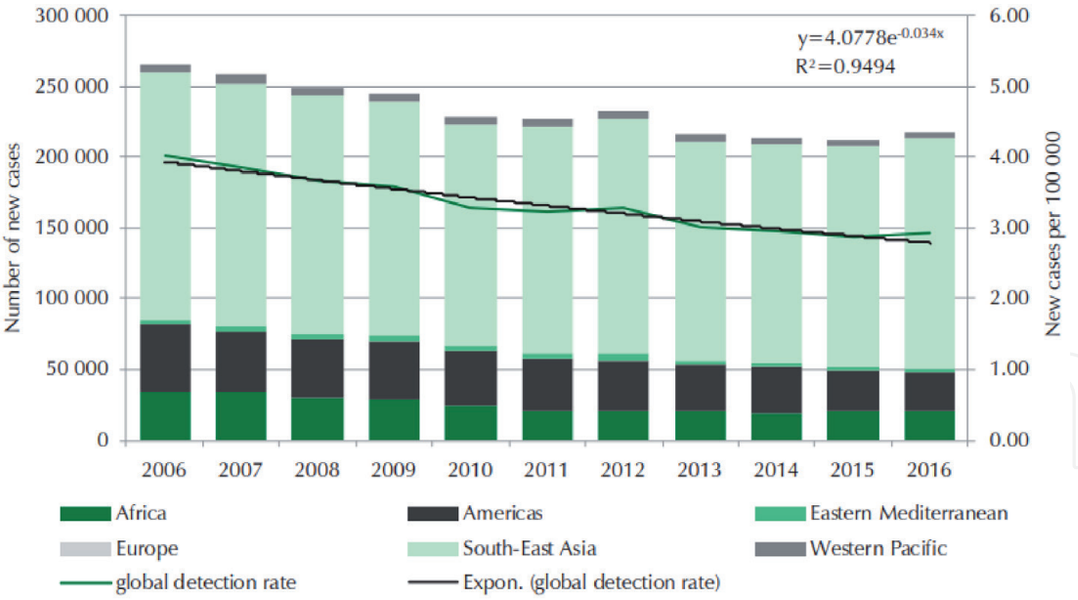

Figure 1.
Trend in case detection and case detection rate, by WHO region, 2006–2016 [3].

2. Burden of disease

In 2017, 192,713 patients were on treatment globally which makes the prevalence rate of 0.25 per 10,000 population [4]. Total of 210,671 new cases were reported in same year from 150 countries making NCDR of 2.77 per 100,000 population. **Figure 2** below shows the trends over the past decade (2008–2017) in new case detection of leprosy cases globally in the reporting countries of World Health Organization (WHO) [4].

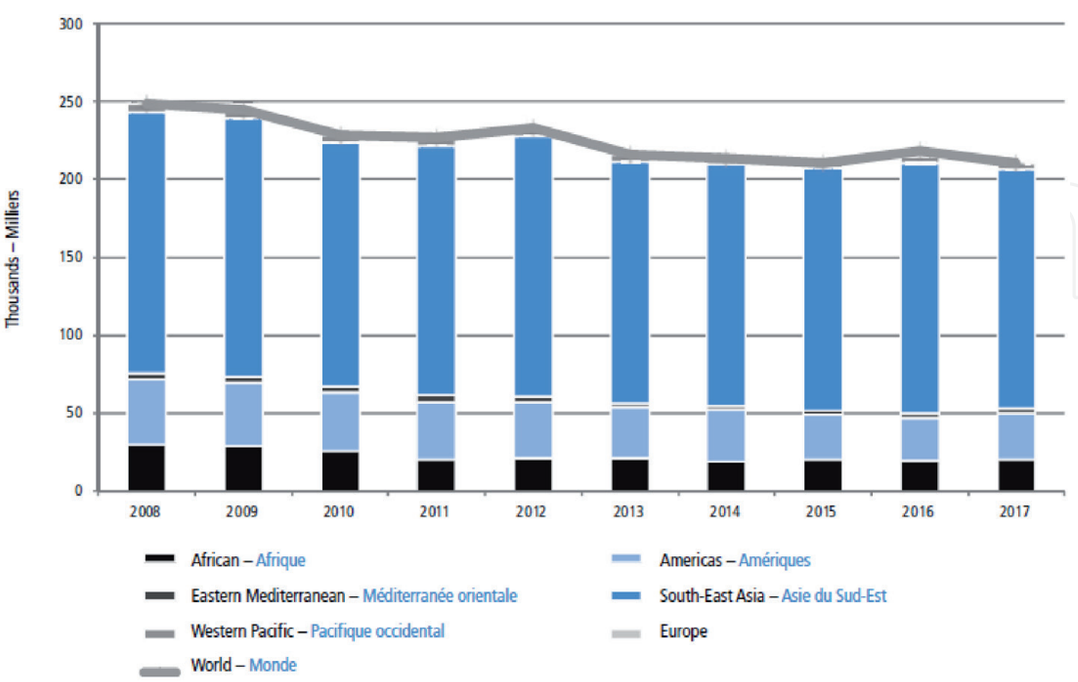

Figure 2.
Country-wise trends of detection of new leprosy cases from 2008 to 2017 [4].

3. Control of leprosy

The three main goals of control of leprosy are

a. To detect the pathology early and treat the patient completely.

b. To prevent the transmission to the others.

c. To prevent the disabilities and other complications.

Thus the following modalities are adopted to control leprosy:

1. Medical measures

2. Social support

3. Program management

4. Evaluation

4. Medical measures

4.1 Estimation of the burden of leprosy

The control of leprosy starts with the estimation of size and magnitude of the problem. Most common epidemiological survey method of collection of data is "Quick random sample survey." Information about the prevalence of leprosy, age and sex-wise distribution, various forms of leprosy and the health facilities available should be gathered. Roughly the total prevalence of leprosy in an area would be about 4 times that of the cases found among school children [5, 6]. These estimates are essential to plan, implement and to evaluate the results of the control program.

4.2 Early Case Detection

The objective is to detect all the cases as early as possible and to register them. Active case finding is important as the disease is symptomless in the early stages. Cases can be detected by the Contact surveys, Group surveys and Mass surveys. Contact surveys consists of examination of all household contacts with a lepromatous case, particularly children, in areas with prevalence less than 1 per 1000. Contact surveillance of households is recommended for a minimum period of 10 years after case is declared bacteriologically negative, and for 5 years in households with a non-lepromatous case from the time of diagnosis of the index case. Group surveys are done in areas where prevalence of leprosy is more than 1 in 1000 population. This consists of screening certain groups such as school children, slum dwellers, military recruits, industrial workers, etc. through "Skin camps." Lastly, mass surveys consists of examination of each and every individual by house-to-house visits in hyperendemic areas (prevalence – 10 or more per 1000 population). These are generally carried out by repeated annual examinations of school children which yield better results at relatively low cost [5, 6]. The data of each case is entered in the standardized proforma developed by WHO.

4.3 Chemotherapy

Since an effective vaccine is unavailable for leprosy the secondary prevention (early treatment) becomes more important. Until 1981, Dapsone (Diamino Diphenyl Sulphone—DDS) was used to treat leprosy which resulted in the development of resistance and relapse, making leprosy control difficult.

Multidrug Therapy: In 1982, WHO recommended Multidrug Therapy (MDT) for all leprosy patients. Introduction of MDT has opened a new avenue in the control of leprosy in the world. Aim of MDT is to convert the infectious case into noninfectious as soon as possible, so as to reduce the reservoir of infection in the community.

The main objectives of MDT are:

- To ensure early detection of the cases.
- To interrupt the transmission of infection.
- To prevent drug resistance, relapse and reaction.

The advantages of MDT over dapsone monotherapy are:

1. Shorter duration of treatment,
2. Better patient compliance,
3. High cure rate,
4. Cost-effectiveness and
5. Ease in health delivery system.

There are two types of MDT regimens used depending on the symptoms and signs shown by the patients - Paucibacillary (PB) and Multibacillary (MB). Recommended Regimens are discussed below [3, 5–7]:

i. Multibacillary leprosy:

MDT is recommended for following groups of patients:

- All smear positive cases.
- Skin lesions more than five in number.
- More than one nerve trunk thickening.
- All cases of relapse/reactivation and all cases who have been treated with Dapsone monotherapy earlier.

The drugs used in Multibacillary MDT and dosages are:

Rifampicin: 600 mg once monthly, supervised.
Dapsone: 100 mg daily, self administered.
Clofazimine: 300 mg once monthly, supervised and 50 mg daily, self administered.

Duration of treatment for Multibacillary leprosy is 12 months, can be extended to 18 months and continued where possible up to smear negativity. Sometimes LL/BL patients with high bacilli may need 2–3 years or more of MDT for achieving bacteriological negativity.

ii. Paucibacillary leprosy:

The drugs and dose schedule is:
Rifampicin 600 mg once a month for 6 months supervised.
Dapsone 100 mg daily for 6 months self administered.
Paucibacillary leprosy is treated for 6 months.

MDT is not contraindicated in patients with HIV infection.
Each MDT blister pack contains tablets for 4 weeks treatment. For easy identification color coding of the blister pack is done, that is, with different colors for multibacillary and paucibacillary cases both in adults and children.

The treatment in both PB and MB cases varies depending on the age of the patient. The patients between 10 to 14 years are treated as paediatric cases, while >14 years are considered adult. The standard treatment regimen for MB leprosy in adults is given for 12 months. The drugs in each blister pack are (**Figure 3**):

Two capsules of Rifampicin of 300 mg (600 mg once a month) to be taken as single dose under supervision.
Clofazimine 3 capsules of 100 mg each to be consumed once a month as single dose under supervision and 50 mg daily for next 28 days.
Dapsone 100 mg as single dose and then daily once for 1 month.

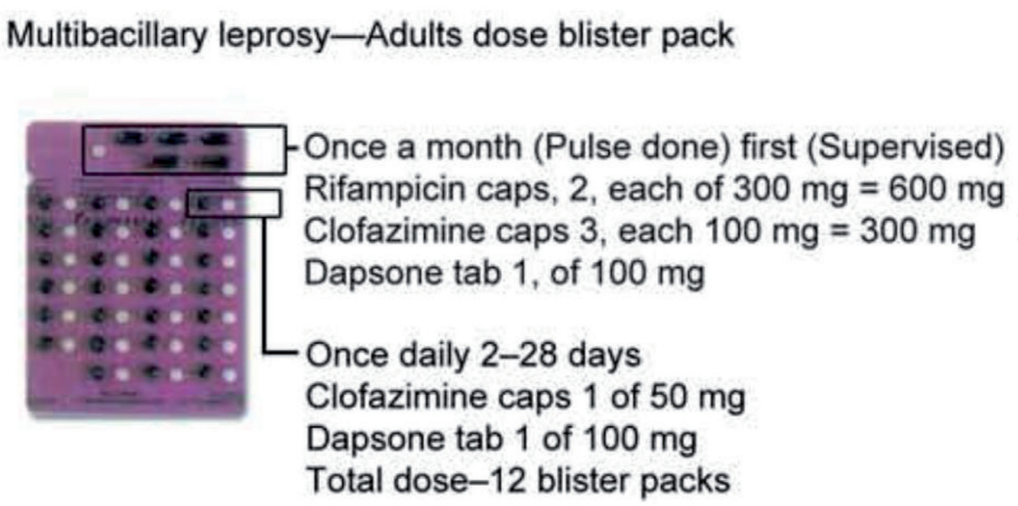

Figure 3.
MDT for adult MB type of leprosy [2, 7].

The standard adult treatment regimen for PB leprosy is (**Figure 4**):

Rifampicin: 600 mg once a month.
Dapsone: 100 mg daily.
Duration: 6 months (6 blister packs of 28 days each).

Treatment regimen for MB leprosy in children (ages 10–14 years) is (**Figure 5**):

Rifampicin: 450 mg once a month.
Clofazimine: 150 mg once a month, and 50 mg every other day.

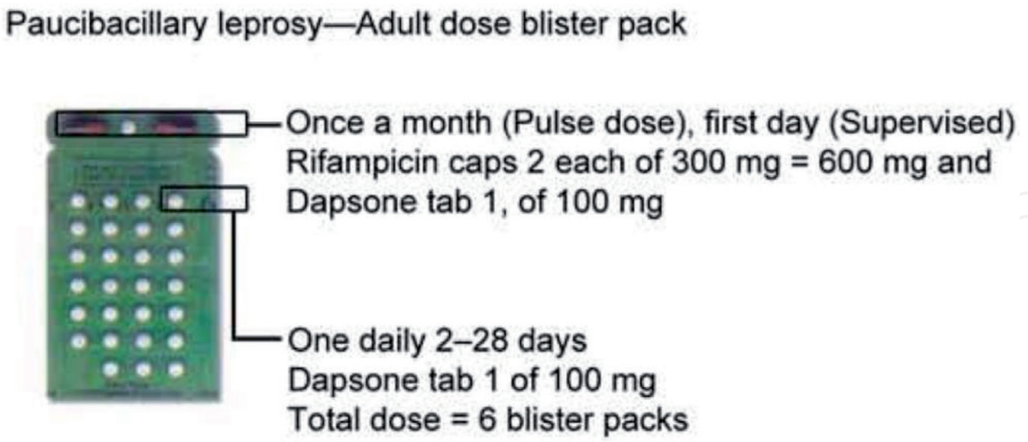

Figure 4.
MDT for adult PB type of leprosy [2, 7].

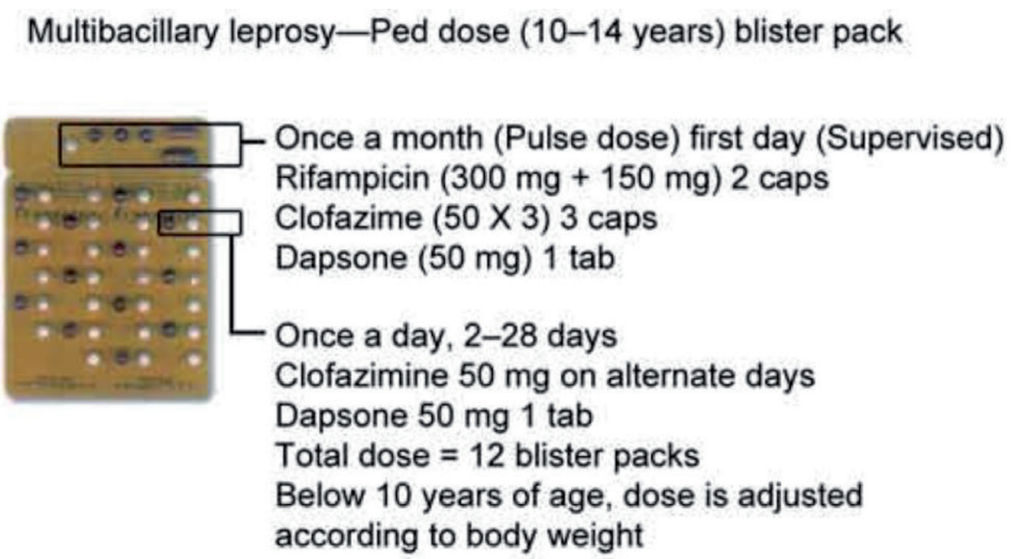

Figure 5.
MDT for pediatric MB type of leprosy [2, 7].

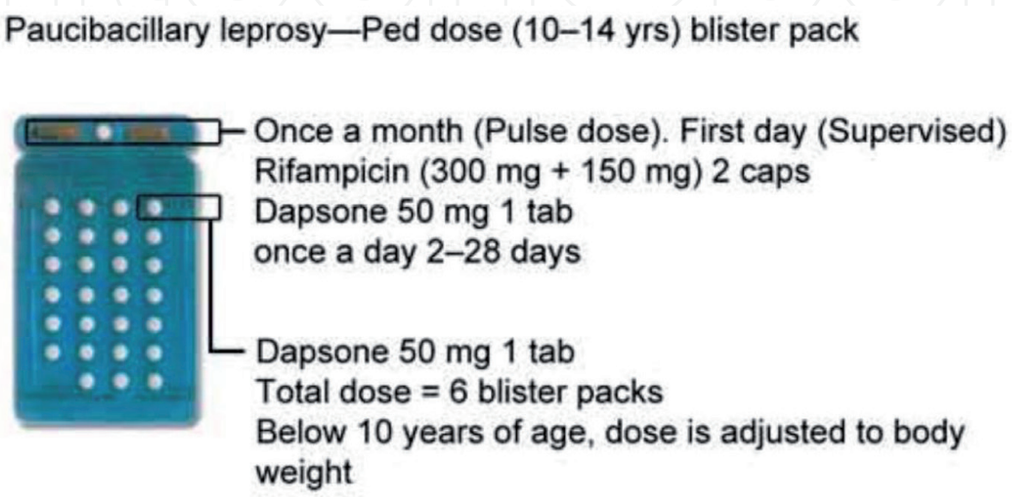

Figure 6.
MDT for pediatric PB type of leprosy [2, 7].

Dapsone: 50 mg daily.
Duration: 12 months (12 blister packs of 28 days each).
Treatment regimen for PB leprosy in children (ages 10–14 years) is (**Figure 6**):

Rifampicin: 450 mg once a month.
Dapsone: 50 mg daily.
Duration: 6 months (6 blister packs of 28 days each).

MDT is provided free-of-charge globally through an agreement between a pharmaceutical company and WHO. WHO manages distribution of MDT to countries in coordination with national leprosy programs.

5. Surveillance

Clinical surveillance of the patients after completion of treatment is an important part of MDT to ensure complete cure. For paucibacillary cases follow up for at least once a year for 2 years after completion of treatment and for multibacillary cases at least once a year for 5 years [3–5].

6. Immunoprophylaxis

Early diagnosis of cases, aggressive treatment and proactive measures to avoid complications and disabilities is the backbone for the success of any comprehensive program. In addition to accurate reporting and control measures, effective preventions will be needed to achieve elimination. Search for an effective vaccine either to be used alone or in combination with a drug has been going for a long time.

Presently BCG (Bacillus Calmette-Guerin) is the only vaccine that has shown some protection against *M. leprae* bacillus. A single dose of BCG gives 50 percent or higher protection against the disease. It is the most widely used vaccine in the world, yet the degree of protection it confers is not yet confirmed. The meta-analysis of many experimental studies concludes that the vaccine gives approximately 26% protection against leprosy. But the protection level decreases with time. To overcome this problem more than one dose of vaccine is advised.

Other variants of vaccination are also suggested.

a. **Adding killed *M. leprae* to BCG:** Various modifications have been suggested, such as the addition of killed *M. leprae* to BCG. This method almost doubles the vaccine efficacy in some populations as concluded by few studies. But the same cannot be said for patients below 15 years.

b. **Vaccination with *M. indicus pranii* (*Mycobacterium W*)**: This strain discovered in India. Testing of the MIP vaccine took place in 2005 and showed that it was effective for seven to 8 years, after which a booster dose would be needed to maintain the immunity. Recently the vaccine was approved by the Drug Controller General of India to be rolled out in a project involving five districts in the states of Bihar and Gujarat, where there are high rates of leprosy. Leprosy patients and their close contacts will benefit from this project, making India the first country in the world to have a large-scale leprosy vaccination initiative [8].

Another milestone in prevention of leprosy is the discovery of the vaccine candidate, called LepVax. Scientists at Infectious Disease Research Institute (IDRI), along with national and international collaborators including the

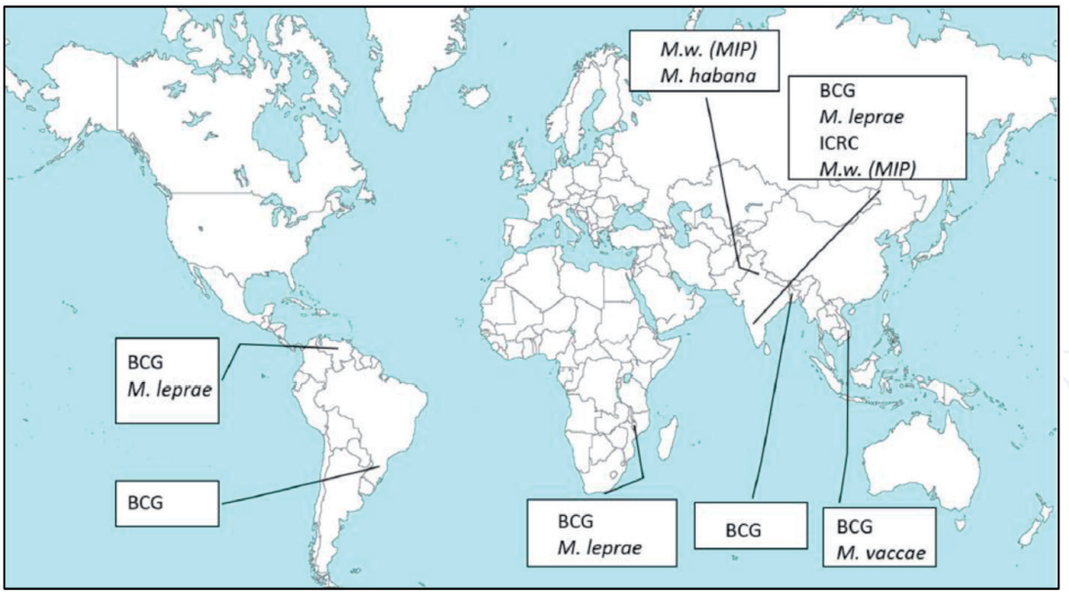

Figure 7.
Locations of leprosy vaccine testing.

National Hansen's Disease Program and the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, with financial support from American Leprosy Missions, have developed this leprosy vaccine. Based on the preclinical studies, the LepVax, has progressed to Phase I clinical testing in the United States, the first stage of safety testing in human volunteers. The clinical trial is focused not only on safety but also evaluates the immune response of the individual to the vaccine.

c. **Indian cancer research center (ICRC) bacilli:** Another variant belonging to the *M. avium intracellulare* group, the ICRC bacilli are thought to induce lepromin conversion in lepromatous leprosy patients and in lepromin-negative leprosy-free individuals. Its efficacy was reported to be 65.5 percent [8].

d. ***M. vaccae:*** The studies with this soil-dwelling mycobacterial species combined with BCG showed to provide greater protection against leprosy, but a Vietnamese trial contradicted the results [8].

e. ***M. Habana:*** This bacilli has been reported to induce lepromin conversion when used as a live vaccine in monkeys, and protected mice against the development of leprosy [8].

Chemoprophylaxis alone provides two-year protective window while effective immunization will provide a much broader protective window. Thus many studies and research is going on to provide both chemoprophylaxis and immunization for immediate and short-term protection and longer-term protection respectively. This strategy could have better impact and distinct appeal in controlling and preventing leprosy. Such trials could also provide a gateway for the assessment and implementation of new emerging vaccines (**Figure 7**).

7. Chemoprophylaxis (post-exposure prophylaxis)

Chemoprohylaxis using effective antibiotics focuses on providing protection to people at risk such as close contacts – family members, neighbors, co-workers, health care providers for lepers etc. Due to the stigma of disease the leprosy cases

are found in clusters in all endemic regions, rather than being evenly dispersed over the whole area. Thus these high risk people can be identified and prophylaxis provided along with secondary prevention strategies. The process includes focused surveillance, contact tracing, early diagnosis and treatment. This helps in reducing the incidence and breaking the chain of transmission.

Chemoprophylaxis, as recommended by WHO Guideline Development Group (GDG), is done using single dose rifampicin (SDR) for contacts of leprosy patients both in adults and children of 2 years of age and above. Before starting the drug leprosy and TB disease are to be excluded. There should be no contraindications also for the use of rifampicin.

Other important considerations for the implementation of this chemoprophylaxis by programs are:

i. Adequate management of contacts.

ii. Consent of the index case to disclose his/her disease.

An RCT found that SDR reduces risk of leprosy over 5–6 years in leprosy contacts. For every 1000 contacts treated with SDR, there were four leprosy cases prevented after 1–2 years and three cases prevented after 5–6 years.

Recommended dosage schedules for SDR are given in **Table 1**.

The limitations of this approach are:

a. The protection is approximately for only 2 years.

b. High bacillary load cannot be eliminated using single dose.

c. Specific screening test needed to distinguish between contacts with high and low bacillary load.

Age/weight	Rifampicin single dose
Adults (≥15 years)	600 mg
10–14 years	450 mg
Children 6–9 years (weight ≥ 20 kg)	300 mg
Children <20 kg (≥2 years)	10–15 mg/kg

Table 1.
Rifampicin dose for chemoprophylaxis [3].

8. Deformity prevention and rehabilitation

Among communicable diseases, leprosy remains a leading cause of peripheral neuropathy and disability in the world, despite extensive efforts to reduce the disease burden. It is an important aspect of leprosy control. It means the medical, surgical, social, educational, and vocational restoration as far as possible of treated patients to normal activity so that they resume their place in the home, in society and industry [5–7]. Early treatment helps in disability limitation.

Rehabilitation: WHO has defined rehabilitation as "the combined and coordinated use of medical, social, educational and vocational measures for training and retraining the individual to the highest possible level of functional ability."

Preventive rehabilitation consists of prevention of development of disabilities in a leprosy patient by early diagnosis and prompt treatment. But once the patient becomes handicapped and suffers from the damage caused, should be trained and retrained to the maximum functional ability so that the patient becomes useful to self, to the family and to community at large by various measures such as medical (physical), surgical, psychological, vocational and social rehabilitation (Flow chart 20.10).

9. Health education

Health education is given to the patient, to the family and to the community at large about leprosy. The education should be directed to ensure general public and patients help them develop their own actions and efforts to change the perception about the disease and seeking professional help whenever required. Early recognition of symptoms, prompt diagnosis, health seeking behavior, personal care, treatment adherence and rehabilitation are important aspects of health education. The key messages included are about the cause of disease and the complete cure available to encourage people for early diagnosis and treatment. It also aims at helping people to change their attitude and behavior by removing the misunderstandings and misconceptions. Mass Health education also helps to eradicate social stigma, social ostracism and social prejudice associated with leprosy which is the biggest hindrance for the eradication of disease.

10. Social and financial support

The complications of the disease cause disfigurement and disabilities which in turn gives way to the stigma and strong discrimination of these patients. This results not only in physical and social isolation also financial dependency, ultimately forcing the leprosy patients to beg on streets for their survival. To address this issue WHO introduced the strategy of community-based rehabilitation (CBR). This intended to enhance the quality of life for lepers with disabilities through community initiatives. Community participation and using local resources to support the rehabilitation of people with disabilities within their own communities is the foundation of this concept [9, 10].

11. Programmatic measures

11.1 Prevention of leprosy globally

11.1.1 The enhanced global strategy for further reducing the disease burden due to leprosy 2011–2015

"Enhanced Global Strategy for Further Reducing the Disease Burden due to Leprosy for 2011–2015" was launched in 2009 by the World Health Organization. The target of the program was to reduce Grade 2 Disability rate (G2DR) in leprosy patients by at least 35% by the end of 2015 (G2DR is the number of new cases with grade 2 disability per 100,000 population). Since the elimination of leprosy in 2005, the prevalence is very less and thus G2DR has been proposed as an indicator. The advantage of G2DR as indicator is that, it is less susceptible to operational factors such as detection delay and is a more robust marker for mapping cases of leprosy in

any country. This will also help the program implementers to focus on interventions that reduce visible deformities by enhancing early detection and treatment of leprosy patients and ultimately reduce the number of new leprosy cases in the population. However by the end of 2015, only Thailand was able to achieve this target [11].

11.1.2 Global leprosy strategy 2016–2020: accelerating towards a leprosy-free world

In 2016, WHO launched the "Global Leprosy Strategy 2016–2020: Accelerating towards a leprosy-free world" [9].

The program aims to reinvigorate efforts to control leprosy and avert disabilities, especially among children still affected by the disease in endemic countries.

The strategy is built around three major pillars:

i. Strengthen government ownership and partnerships;

ii. Stop leprosy and its complications; and

iii. Stop discrimination and promote inclusion.

The strategy of this program is:

- To sustain expertise and increase the number of skilled leprosy staff;
- To improve the participation of affected persons in leprosy services;
- To reduce visible deformities and stigma associated with the disease;
- To call for renewed political commitment and enhanced coordination among partners;
- To highlight the importance of research and improved data collection and analysis.

The key interventions needed to achieve these targets include:

- Early case detection especially in children before visible disabilities occur thus reduce transmission;
- In highly endemic areas or communities detection of disease among higher risk groups through campaigns;
- Improving health care coverage and access for marginalized populations such as poor patients, patients in the difficult to reach areas and the areas of conflicts.

Customization of the strategic interventions in endemic countries is permitted to suit the national plans to meet the new targets. E.g. Screening all close contacts of persons affected by leprosy; initiating a shorter and uniform treatment regimen; and incorporating specific interventions against stigmatization and discrimination.

Its ultimate goal of this program is to further reduce the global and local leprosy burden, that is, (a) zero disabilities in children with leprosy-affected, (b) G2DR less than one per million population and (c) repeal of laws that discriminate leprosy patients of their rights.

Conflict of interest

Author declares no conflict of interest.

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