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Editorial

Global leprosy scenario: Eradication, elimination or control?

With new discoveries, emerge new promises. In the early 1940s, Faget *et al*[1], a health officer at the Carville National Leprosarium, Louisiana, USA, recognized that a sulphonamide drug (promin), effective against tuberculosis in animals, might work against leprosy. Following his documentation of encouraging results of promin in the first 22 lepromatous patient volunteers at Carville[1], a wave of enthusiasm swept through the world; people thought leprosy would now be conquered. Similar was the response with the advent of dapsone and subsequently with the strategy of Survey, Education and Treatment that shaped leprosy control programmes in various nations[2]. With multidrug therapy (MDT) for leprosy, the euphoria and hope for conquering the war against leprosy reached a greater height. Unfortunately, in the midst of such exciting developments, two promising prophylactic vaccines, one based on leprosy-derived mycobacteria, Indian Cancer Research Centre-bacilli and Bacillus Calmette–Guerin plus killed *Mycobacterium leprae*[3,4], lost due attention.

Public health concerns around leprosy

A disease is considered a public health problem on account of its magnitude as well as the morbidity and mortality it could wreck. The year 1966 onwards, global estimates of leprosy prevalent cases ranged from 10 to 12 million[5]. From early days, leprosy was recognized as a disease of public health concern on account of the deformities, disabilities and disfigurement it inflicted and community reactions it evoked. The disease created terror and communities were afraid of its transmissibility. Public health response in the medieval period was of isolation and ostracism for leprosy patients! Effective control of a problem of such magnitude thus merits engagement with the involvement of the affected community, public health managers as well as of the community at large, ensuring the availability of effective interventions and above all a political will.

Public health response

Modern day's public health response began after dapsone became available in the 1950s[6]. Leprosy chemotherapy was considered to be the silver bullet to cure leprosy and thus prevent deformities. Social aspects; social aetiology, social effects and social therapy got side-lined to secondary status. Problems associated with dapsone mono-therapy were identified within a decade after its introduction; dapsone resistance, requirement of long-term treatment and persistence of small number of viable dapsone-sensitive bacilli ('persisters') isolated from lepromatous leprosy patients on dapsone for 10-12 year[7], being the major ones. Continued use of dapsone mono-therapy was a prescription for widespread occurrence of dapsone resistance and thus got the MDT introduced. The WHO Study Group in 1982 considered the shift from dapsone to MDT essentially to prevent transmission, curing patients and to prevent drug resistance[8].

Historically, our efforts to manage leprosy, as a public health problem, have centred on finding shorter and user-friendly drug regimens suitable for programmatic implementation without compromising cure of patients. This has been the case with the advent of dapsone, fixed duration MDT, single-dose rifampicin, ofloxacin and minocycline (ROM) for single-patch leprosy or uniform-MDT[9]. Two core considerations characterized these efforts, (*i*) shorter but efficacious treatment and (*ii*) prevention of disabilities. These interventions were responsible to bring down the prevalence substantially.

India enthusiastically followed suit by launching National Leprosy Eradication Programme in 1983. The World Health Assembly (WHA) resolution of leprosy elimination in 1991 was a landmark decision[10]. It was the expectation that once the level of leprosy prevalence came down to a low level of <1/10,000 population, leprosy would be limited to

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Box. Definitions

Eradication: Zero cases and zero risk of cases (beyond the concept of 'interruption of transmission', leading to extinction of pathogen)

Elimination: Zero cases but with continuing risk

Elimination of disease as a public health problem: Reduction of cases below what is considered to be a public health risk

Control: Reduction in cases by some defined amount[11]

smaller areas and would die down over a period of time (Box).

Impact of chemotherapy

The Indian Association of Leprologists conducted a workshop on the impact of MDT on trend of leprosy[9]. Reports from several districts in different parts of India with experience of MDT over seven years were made available for consideration and analysis. Analysis of this data showed that after the introduction of dapsone in leprosy control programme, leprosy prevalence came down due to patients, not having active signs of leprosy getting removed from active registers, migration or death of some patients and some patients getting cured by dapsone[12]. A similar effect was seen after introduction of MDT. However, new case detection did not show a declining trend. Introduction of MDT over 7-8 years did not show the expected reduction in new case detection. Before the recommendation of MDT-based therapeutic intervention by the World Health Organization (WHO) in 1984, screening of patients and treatment of leprosy with dapsone reduced the disease burden by 45-70 per cent in highly endemic states in India. In 1988, the sixth WHO expert group defined a case of leprosy as one with clinical manifestations of leprosy and who needs treatment for leprosy[13]. Removal of names of patients without active leprosy needing treatment brought down the prevalence dramatically. Several voluntary groups diversified their activities by adding other health issues in their programmes or shifting their attention to countries, which were struggling to achieve similar feats. Lowering of prevalence was expected to have big impact on generation of funds for leprosy work of non-governmental organizations. Experts continued to remind national governments and the WHO that this achieved level of elimination was not expected to lead to the eradication of leprosy. Britton and Lockwood[14] commented that the widespread implementation of MDT was associated with a fall in the prevalence of leprosy but no reduction in the case-detection rate globally. They observed that the situation demanded continuation of leprosy control activities for decades. In Malawi, leprosy decline started even before MDT and MDT did not hasten its fall[15]. The International Leprosy Association Technical Forum report concluded in 2003 that the WHO elimination goal (achieving below 1 case per 10,000 population) resulted in a broad and strong commitment to the fight against leprosy[16]. However, the number of new cases detected globally remained more or less unchanged without any impact on transmission. In line with the global trend and when leprosy got eliminated as a public health problem, a merger of leprosy-specific services with general health services happened as the natural evolution.

Current status

After introduction of MDT, the registered number of leprosy patients decreased substantially, from more than five million in the 1980s to 133,802 cases in 2021 with a prevalence of 16.9 per million population[17]. However, new cases kept on appearing without much change in the rate demonstrating continued transmission of *M. leprae*. The years 2020 and 2021 witnessed difficulties in case detection due to the COVID-19 pandemic. From 2011 to 2019, there was a slow decline in new case detection from 34.8 to 26.3 per million population, a drop of about two per cent per year[14]. During the same period, child case detection also followed a declining trend from 12.3 to 7.6 per million child population[17].

Adoption of the WHA resolution on leprosy elimination in 1991 was strongly supported with specific actions such as Leprosy Elimination Campaigns and Special Action Plans for Elimination of Leprosy. These initiatives aimed at case detection through various ways and providing MDT services, with focus on 'Cases of Consequence'. Due to self-healing nature of early leprosy and to avoid overdiagnosis and inflation, case detection efforts got shifted to cases of consequence. Global case detection rates essentially showed spurts on account of these processes, rather than the actual trends. Outreach of the national programmes expanded to unearth several undetected cases.

Presently reported new cases have about 40-50 per cent of pauci-bacillary (PB) and 50-60 per cent multi-bacillary (MB) cases. Most of the case detection activities performed in regular periodical way show a very high proportion, close to 70 per cent of single patches, about 20 per cent PB leprosy with 2-5 patches and the remaining 5-10 per cent of MB cases. If this

is what we expect, then our new case detection in programme situations should be verified. Are we missing a sizeable proportion of PB cases? This kind of change might not be on account of a secular course of shifting leprosy pattern from PB to MB in a short span of a decade or two. A declining case detection rate in child population and low levels of grade 2 disabilities in new cases also call for careful objective assessment. When ROM single dose was adopted for treating single-patch cases in the year 1998, these cases remained in leprosy registers for a single day. Leprosy prevalence came down dramatically almost overnight. After four years, this category of single-patch leprosy was removed and these cases apparently were almost 'forgotten' from leprosy new case detection counts.

Further challenges

As we know today, leprosy is not restricted to human beings alone. Armadillos do have leprosy in natural course and transmission from armadillos to man has been documented[18]. Increasing leprosy in armadillos as well as zoonotic infections have also been reported in the south-central and south-eastern United States[18]. Perhaps, this is unlikely to have any real epidemiological impact on human leprosy situation. Importantly, leprosy bacilli can survive in moist soil for days together[19]. We have no tools to eradicate *M. leprae* from the nature.

Leprosy elimination & interruption of transmission

The WHO published guidelines for diagnosis, treatment and prevention of leprosy in 2018[20]. Single-dose rifampicin was recommended as post-exposure prophylaxis (PEP) for contacts of leprosy patients. WHO identified different levels in the achievement of eventual elimination of leprosy[17]. In the first stage, interruption of transmission is envisaged. At this stage incidence of leprosy on account of indigenous or autochthonous transmission comes to zero level in children. In the final stage, local transmission in all the age groups is expected to be achieved for at least three consecutive years. It is further stipulated that the whole population would be covered for early case detection, effective surveillance and data management would be established and disability care for the patients is ensured[17]. Worth noting in this regard is that the global child case detection rate in 2021 was 4.5; the target is to reduce the rate to 0.8 per million children by 2030[21].

To conclude, compared to *M. tuberculosis*, *M. leprae* is a half dead bacillus[22]. However, it perhaps would take a few thousand years to lose all its pathogenicity. With a mindset of a finite game plan, we are therefore dealing with a disease having a much wider time span. In the process, we set targets for our programmes without realizing the hurdles we create and even lose the trust of several stakeholders. We consider these targets as absolute goals, without realizing that these are essentially milestones to be achieved, which are based on our current understanding and public health tools and technologies available at the time of setting these targets. Moreover, when these are not achieved, we call them aspirational goals! The time has come to revisit this paradigm and bring change in programmatic parlance and approach. While case finding, cure and rehabilitation should still remain as key elements in the comprehensive package of intervention to manage leprosy in today's world, more innovations need to be added to this package and the focus has to be different from only 'drugs for cure'. We need to remember, while a substantial progress has been made towards controlling leprosy, there still is a long way ahead to reach our vision.

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