REVIEW

Leprosy: a review on elimination, reducing the disease burden, and future research

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Summary  Leprosy, one of the oldest diseases known to man, is a stigmatising, potentially disabling disease. Throughout history, leprosy has been associated with fear, prejudice and immense social stigma. It remains one of the leading causes of deformity and physical disability from an infectious disease. Tremendous advances in leprosy control were made by the World Health Organization, and the ‘elimination of leprosy’, defined as a decrease of disease prevalence to less than 1 case per 10,000 population, was achieved by 2000. However, the reality is that true ‘elimination’ is yet to be achieved. Despite almost 30 years of effective multidrug treatment, the prevalence and incidence of leprosy have plateaued since 2005. Moreover, new cases with Grade 2 disability and new cases occurring in children remain unchanged since 2010, reflecting a failure in early leprosy detection, and indicating that transmission is clearly continuing. This review examines the challenges of elimination, and proposes further measures to reduce the disease burden, including future research possibilities.

Background

Leprosy, one of the oldest diseases known to man, is a stigmatising, potentially disabling disease. It is a chronic, infectious disease caused by Mycobacterium leprae. Clinical manifestations include skin, peripheral nerve, and eye lesions. Among communicable diseases, leprosy is a leading cause of permanent physical disability. However, early treatment is curative and averts disability. Leprosy is classified into paucibacillary (1-5 skin patches), and multibacillary (greater than 5 patches). There are multiple social determinants which impact upon leprosy control, as illustrated in Table 1.

To avoid drug resistance, multidrug treatment (MDT) consisting of dapsone, rifampicin and clofazimine, was recommended by the World Health Organization (WHO) in 1981, having a 98% cure rate.

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In the initial 3 years of MDT, the global leprosy prevalence reduced by a remarkable 45%5 sparking WHO’s governing body, the World Health Assembly, to pass a resolution in 1991 to ‘eliminate leprosy as a public health problem by the year 2000.’6 The elimination of leprosy, defined as a decrease of disease prevalence to less than 1 case per 10,000 population, was achieved by 2000. By 2006, all but six countries accomplished national elimination.5 In 2013, 96% of new cases globally were detected in only 14 countries (Figure 1).5

Despite almost 30 years of effective MDT, the prevalence and incidence of leprosy have plateaued since 2005 (Figure 2A).5

Moreover, new cases with Grade 2 disability (G2D) remain unchanged in 2013 compared to 2010, reflecting a failure in early leprosy detection (Figure 2B).5

Additionally, new cases occurring in children have not reduced, reported at 9.2% in 2013,5 indicating transmission is clearly continuing.7

DEFINING ELIMINATION AND CONTROL

The World Health Organization defines, disease elimination as the reduction of infection incidence to zero, and disease control as the reduction of disease incidence to a locally
Figure 1. Global leprosy prevalence rates. Data reported to WHO as of January 2012. Source: World Health Organisation.

Figure 2. Global burden of leprosy disease. (A) Incidence and prevalence of leprosy. (B) New cases with Grade 2 disability (G2D) and number of relapsed cases. *Grade 2 disability (G2D) is defined as visible deformity or damage present, or severe visual impairment. Graphs were created from data reported by WHO.
acceptable level. However, WHO defined *leprosy elimination* in terms of prevalence reduction, which is essentially a control target. Nonetheless, it was anticipated that a decrease in prevalence would ultimately lead to elimination. A fundamental assumption of the elimination strategy was that MDT reduced *M. leprae* transmission. However, unfortunately, there is no substantial evidence available supporting this. Evaluating the effect of MDT on transmission is difficult due to many factors. Firstly, leprosy has a long, variable incubation period, ranging from 2–20 years, and laboratory tools to detect leprosy in the early stages are lacking. Secondly, decreases in case detection have other causes, including the bacille Calmette-Guérin (BCG) vaccination. Finally, variable control measures used over time obscures interpretation of trend data.

**THE CHALLENGES OF ELIMINATION**

Although the goal was to eliminate leprosy as a public health problem, the terminology misled many people, including policy makers to believe that the goal was complete elimination. This may partly explain the reduction in leprosy programme funding, the decrease of academic work on leprosy, and why leprosy rarely features in medical school curriculum, even in endemic countries.

Although WHO abandoned the ‘elimination’ target in 2007, national leprosy rates are still emphasised, which may have unintended damaging consequences, as demonstrated in India for example. The pressure on outstanding countries to meet the elimination target by 2005 resulted in India meeting the target, however independent studies showed many undiagnosed patients, and it was found that measures were adopted to ensure fewer patients were registered, including not registering single lesion cases and not tracing contacts. Subsequently, India has reported approximately 130,000 new cases a year, keeping it in the ‘eliminated’ category. However, from 2004–2007 new case detection dropped by 75%, but the proportion of G2D cases increased by 38%. This indicates less active case finding, which may partly be due to a decreased incentive to find new cases, and has a devastating effect on leprosy morbidity.

Although it is important to set targets to provide direction for national programmes and secure political commitment, the targets used are imperative. Evidence has demonstrated that disability-based targets encourage early diagnosis and treatment, and prevent morbidity. Hence, there has been a shift from placing importance solely on ‘elimination’ and total new cases found, to emphasising disability rates, for instance, new cases of G2D.

Unfortunately, the celebration of the leprosy progress may have resulted in a loss of political commitment. Funding for leprosy programmes has been reducing by 5% per year globally, for the past 5 years. Currently, few countries have a surveillance-response system to provide epidemiological data, and implement required interventions. Moreover, many leprosy programmes have been left unsupported and the skills in diagnosis and management have dwindled. In some countries where marked success has occurred, unfortunately there has been an increase in multibacillary and disability cases.

In the face of other competing priorities (e.g. HIV, malaria, TB), a major challenge is for leaders across all sectors to reaffirm commitment and allocate increased resources at a global and national level. Where facilities are weak, sharing facility control programmes for other diseases should be considered. There is an urgent need to rebuild and sustain leprosy expertise, and to develop strategies globally and nationally, in collaboration with partners, to augment training programmes. Additionally, national efforts are needed to involve
dermatologists in the leprosy control programme to sustain high-quality leprosy services. To achieve this, it is vital that partnerships are solidified between governments, non-government organisations, the private sector, international agencies, professional associations and people affected by leprosy.

FUTURE MEASURES FOR REDUCING THE DISEASE BURDEN

Contact surveillance

The risk of acquiring leprosy for individuals living in households with multibacillary patients is 5–10 times higher, and with paucibacillary patients 2–3 times higher, than in people not living in such households. Unrecognised cases and subclinical infections in contacts contribute a significant proportion of all new leprosy cases. Hence, if case detection campaigns and mandatory contact tracing programmes were implemented nationally, this would undoubtedly reduce the disease burden.

Immunoprophylaxis

Ideally, disease control is best obtained by an effective vaccine. BCG vaccine, although imperfect, is used globally, with 85% of the world’s infants receiving it. The protection imparted by BCG against leprosy is highly variable for poorly understood reasons. A meta-analysis showed an overall protective effect of 26% [95% confidence interval (CI): 14–37%] in experimental studies, and of 61% [95% CI 51–70%] in observational studies. In recent studies it was demonstrated that an additional dose of BCG was more protective compared with a single dose, with protection lasting for decades. It has been proposed that an additional dose of BCG be given for all at risk groups in high endemic areas.

Chemoprophylaxis

There is much evidence for the use of chemoprophylaxis in asymptomatic contacts. A meta-analysis of seven randomised-controlled trials (RCTs) demonstrated that chemoprophylaxis provided 60% protection against leprosy. Rifampicin has an additive effect to BCG. An RCT showed that individually BCG and rifampicin provided 57% (95% CI: 24–75%) and 58% (95% CI: 30–74%) protection respectively, but the combined strategies had a protective effect of 80% (95% CI: 50–92%). It has been hypothesised that if national programmes gave one dose of rifampicin and BCG to asymptomatic contacts, it would prevent many potential cases and reduce ongoing transmission.

Preventing drug resistance

Several reports of rifampicin, dapsone and ofloxacin resistance have been published. If chemoprophylaxis were to be introduced, avoiding drug resistance is imperative, and stringent longitudinal observation is required so that timely measures to combat resistance can be developed.

Globally, more and more relapses are being reported. Relapse suggests treatment failure, caused by inadequate or irregular treatment. It is vital to continuously monitor relapse cases in relation to treatment completion and drug resistance in all national programmes.
Treatment adherence is a major factor in drug resistance. In developing countries, patients’ treatment is often interrupted due to drug shortage or poor access to health services. ‘Accompanied MDT’ has been advised by WHO to be considered in these settings, whereby a patient is given the entire treatment course on diagnosis, and nominates someone to accompany them to aid in understanding the treatment. Many patients also stop treatment due to lepra reactions, which are immunologically mediated episodes of inflammation. It is imperative that health care workers and the community remain educated via leprosy programmes, and know not to cease MDT during these reactions.

Disability prevention and rehabilitation

Even after effective treatment, long-term morbidity and disability is problematic. Up to 60% of patients have peripheral nerve damage at diagnosis. Ongoing education of health care workers and the community is vital to prevent damage to hands, feet and eyes in those with peripheral neuropathy. Appropriate referral is important for acute complications and improved rehabilitation services are needed for those with disability to improve quality of life.

Reducing leprosy stigmatisation

The stigma of leprosy is still profound in many communities, and increased community awareness is necessary to motivate affected individuals to seek treatment. It is essential for programmes to foster partnerships with people affected by leprosy. Key actions to strengthen community involvement, and enable early disease presentation are outlined in Table 2. Increased community participation will aid in operationalising policy formulation and achieving successful policy implementation, to increase case finding, improve treatment adherence, and ultimately prevent disability.

Table 2. Strengthening community action and reducing stigmatisation

<table>
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<tr>
<th>Goal</th>
<th>Action</th>
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<tbody>
<tr>
<td>Increased involvement of persons affected by leprosy</td>
<td>• Advocate that people with leprosy provide information to the general public and media, to overcome educational, and cultural and social barriers</td>
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<td>• Encourage people with leprosy to be involved in public policy</td>
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<td></td>
<td>• Support empowerment workshops</td>
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<td></td>
<td>• Increase community education to address myths and misconceptions which generate discrimination and human rights abuses</td>
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<td></td>
<td>• Use a “people first” language i.e. “persons with leprosy,” rather than negative terms, such as “lepper”</td>
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<tr>
<td>Decreased community stigma of leprosy</td>
<td>• Encourage information, education and communication</td>
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<td></td>
<td>• Display of posters about leprosy in public places</td>
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<td></td>
<td>• Enlist the support of others to spread positive messages about leprosy, including community leaders, teachers, religious authorities and traditional practitioners</td>
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<td>Improved community education</td>
<td>• Place global pressure on countries to abolish laws containing discriminatory clauses against persons with leprosy</td>
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<td></td>
<td>• Support groups for women</td>
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<td></td>
<td>• Identify female leaders with leprosy to act as role models</td>
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<td></td>
<td>• Include all woman in empowerment workshops</td>
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<tr>
<td></td>
<td>• Incorporate women in delivery systems</td>
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</table>
FUTURE RESEARCH

Over a century after its’ discovery, *M. leprae* still cannot be cultured in vitro, and significant gaps persist in our understanding of its biology.\(^43\) The mode of transmission and period of infectivity remains unknown. It is undetermined if leprosy is transmitted during incubation or if there are healthy carriers. It was demonstrated that DNA from *M. leprae* exists in the nasal passages of asymptomatic individuals, however further research is needed.\(^44\) Also, effective screening tools are lacking, so early treatment depends on self-identification or a high-index of suspicion by clinicians.

The relevance of non-human and environmental reservoirs is yet to be studied.\(^45\)–\(^49\) Leprosy has been found in wild armadillos, and non-human primates, however the significance of this in human infection is unknown.\(^47\)–\(^49\) Several studies demonstrated an environmental reservoir in the soil of endemic regions.\(^45,46\)

These limitations massively hinder effective leprosy control, and further research is needed to develop new diagnostic and epidemiologic tools. Additionally, research into the logistics of prophylaxis implementation and cost–effectiveness of such policies would be beneficial, as would the development of new chemoprophylactic and immunoprophylactic regimens.

Conclusion

Elimination of a disease is truly difficult to achieve, especially one such as leprosy, which has such a long, variable incubation period and much remains unknown about its biology. Leprosy, an enigmatic disease, is one of the oldest diseases known to man, yet dramatic gaps remain in our basic understanding of this disease, including transmission and pathogenesis. Although substantial progress has been made in providing treatment to those with leprosy, further developments are needed. Future progress toward eradicating leprosy is dependent on a better understanding of the disease transmission and new tools to interrupt it. Hopefully, the progress made can be maintained and further advanced by the political will of governments, and ongoing research into this disease and its treatment. We urge all countries, governments, stakeholders, and individuals to reaffirm their commitment to reducing the burden of one of the world’s most devastating diseases, so that someday we can say leprosy is truly eliminated.

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