

## Leprosy: A Time for Elimination by 2020

Mohamud A Verjee\*

Medical Student Affairs, Division of Medical Education, Weill Cornell Medicine, Qatar

### Abstract

Leprosy is a vestigial disease, found endemically in pockets of countries globally. With a long history, it began to decrease in the 1980's when its prevalence fell from over five million to less than 180,000. Modern treatment is effective and provides a cure with triple therapy available at no cost to those affected. With a lengthy incubation period, but fortunately a low infectivity and contagion index, it can be eliminated if detected early in the onset period. Commonly, the primary presenting clinical features are peripheral neuropathy, skin lesions, and in a late stage, limbic destruction, although multiple organ systems can be affected. WHO champions the reduction of leprosy globally, producing weekly reports and an operating manual for leprosy management. The mission ahead is to eliminate the disease, with a priority to rid pediatric leprosy entirely by 2020. The morbidity and suffering of the disease are preventable with diligence and rigor. This review summarizes the disease, efficacy of treatment, and elucidates current policies of the WHO in the task to eliminate leprosy.

**Keywords:** Leprosy; Hansen's disease; WHO; Lepromatous; Tuberculoid; Endemic; Multidrug therapy

### Introduction

White and Franco-Paredes's paper (2015), [1] detailed a comprehensive account of leprosy, also known as Hansen's disease (HD). It is a chronic infectious disease manifested by progressive skin lesions and peripheral nerve damage over an incubation period of approximately 5 to 20 years. [2] However, immune-compromised individuals and those with comorbidities such as HIV can develop characteristic *lepromatous* skin lesions within only a year. The disease goes back to biblical times with its appearance of facial disfigurement causing fear and avoidance of those affected regarded as outcasts. Limbs are particularly susceptible to the loss of digits on hands and feet, nasal degradation, and respiratory compromise. Untreated, the loss of mobility coupled with muscle weakness and the inability for self-care are significant long-term outcomes. Some who are severely affected never seek treatment because of socio-economic reasons, primarily poverty, stigma, ignorance, or the simple failure to recognize subtle skin changes, while tolerating other insidious clinical signs and symptoms.

From 1995, WHO elected to provide multi-drug therapy (MDT) to all globally identified patients with leprosy, sponsored by the Nippon Foundation until 2000. Subsequently, philanthropy continued from the Novartis Foundation, with a pledge to keep medication free as a humanitarian action until the year 2020. An excess of 16,000,000 patients with leprosy received MDT in a twenty-year period [2].

### Role of WHO

In the 1980's, the number of people with leprosy totalled 5,200,000 [3,4]. By 2016, in WHO's six recognized global regions, 216,108 new leprosy cases occurred in 145 countries. By the end of 2016, analysis of the disease in 173,358 patients confirmed a prevalence rate of 0.29/10,000 [2]. Nine out of every one hundred infections are in children. Dr. Erwin Cooreman, the Team Leader of WHO's Global Leprosy program, reflects "The world has the tools, the right medicines and the political will – yet we are falling short of detecting the disease in time, particularly among children" [5].

### Leprosy Dissemination

Disseminated by droplet spray, leprosy is challenging to spread by human-to-human contact unless there is consistently close-living

proximity with an infected individual [6]. It is not highly contagious. Handling infected nine-banded armadillos [7], in South America, does increase transmission risk. A slow-growing bacterium, *Mycobacterium leprae* (*M. leprae*), is the responsible pathogen. Leprosy is endemic in India, Brazil, Nepal, Micronesia, Sri Lanka, Pakistan, Tanzania, Mozambique, Madagascar, and Cambodia. Migrant travel from these countries gives rise to sporadic cases appearing in nonendemic nations including Europe, Canada, and the United States. In 2013, India had the highest proportion of new cases reaching 59%, followed by Brazil 14%, and Indonesia 8% [8]. Many, when newly diagnosed, already have significant impairments, for example, in Pakistan where the figure is currently 15%.

While confirmation of leprosy in newcomers is not an apparent public health issue in specific places, it still needs active treatment. Modern India and Brazil have the highest reported number of new cases annually [9]. The Rawalpindi Leprosy Hospital, now renamed the Aid to Leprosy Patients Hospital, was set up by the British Leprosy Mission in 1904. Before the partition of India and Pakistan, patients from all over British India sought treatment there as well as using the institution as a shelter. Close living families can be treated empirically for prophylactic purposes as justified. The primary objectives are to diagnose and treat patients with the disease promptly and reduce any further deterioration in their nerve damage and standard functions.

### Clinical Signs and Symptoms

While the clinical emphasis is on irreversible neurological damage with skin lesions and anesthesia, mucous membranes, soft tissue, facial features, the reproductive system, connective tissues including bone and the circulatory system can be involved.

\*Corresponding author: Mohamud A Verjee, Medical Student Affairs, Division of Medical Education, Weill Cornell Medicine, Qatar, Tel: +974 4492 8504; Fax: +974 4492 8555; E-mail: [mov2002@qatar-med.cornell.edu](mailto:mov2002@qatar-med.cornell.edu)

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Multiple organ systems are involved, as seen in (Table 1), with details of their complications.

The types of reaction to leprosy infection are detailed in (Table 2), summarizing the clinical responses and differences between tuberculoid and lepromatous expressions, the two primary forms of the disease.

### Introduction and Use of Medications

Dapsone proved to be the breakthrough medication in the 1940's but by the 1960's, resistance to its beneficial effect developed. Curative monotherapy existed for over thirty-five years. Antibiotics with multidrug therapy (MDT) started from 1982 after the recognition of bacillary resistance with dapsone monotherapy. Today's treatment regime consists of six to twelve months of dual therapy with rifampicin, and dapsone for all, adequate for clearing *tuberculoid* leprosy. Clofazimine is added as a third drug for *lepromatous* leprosy to eliminate the *M. leprae* pathogen and provide a full cure with twelve months therapy (WHO, Global 2013) [9]. Patients are non-infectious after only a month of treatment when compliant. Other complimenting medications used are non-steroidal anti-inflammatory preparations (NSAIDs) for pain and inflammation, with appropriate doses of prednisone. Thalidomide returned to strictly monitored use for leprosy treatment after its devastating teratogenic reputation. Prescribed as a sedative, then for nausea and hyperemesis to expectant mothers, its exposure to a developing fetus in pregnancy caused severe congenital disabilities, predominantly phocomelia. *Phoco* means "seal" and "*melia* means a "limb," when describing a shortened limb as if resembling a "seal's flipper."

Affected systems	Complications
Ophthalmic	Visual deficit affecting mucous membranes, blindness from iritis and scleritis and open-angled glaucoma
Upper respiratory tract	Respiratory mucosa disruption
Facial soft tissue	Nasal deformities, congestion and epistaxis
Reproductive	Infertility (male and female), erectile dysfunction (male)
Renal	Chronic renal failure
Locomotor	Muscle weakness and atrophy, soft tissue inflammation and foot drop
Skin	Anesthesia, permanent subcutaneous swellings, ulcers, rashes, superficial nodules, the predilection for damage to macrophages, histiocytes and keratinocytes and erythema nodosum leprosum (ENL)
Nervous	Peripheral neuropathy especially limbic, the predilection for Schwann cells to dedifferentiate, demyelination and sensory loss
Bone	Lepromatous tumor deposits in metastasis
Circulatory	Endothelial damage, vasculopathy and vessel necrosis

Table 1: Systems involved.

Type 1 – Tuberculoid	Type 2 – Lepromatous
Intense cell-mediated response seen	Multidrug therapy can stimulate Type 2
Few <i>M. leprae</i> bacilli present – 0-5 lesions	More <i>M. leprae</i> bacilli present >5 lesions
Lower levels of antibodies to <i>M. leprae</i>	Erythema nodosum leprosum (ENL)
Inflammation and tenderness common	Can be recurrent or chronic
More often seen if neuritic pain present	Antibody-antigen complexes in tissues
Starts in 1st six months of MDT treatment	Prolonged cellular dysfunction notable

Table 2: Types of reaction to leprosy.

The Leprosy Post-Exposure Prophylaxis (LPEP) program, set up in collaboration with the Novartis Foundation, exists to study whether single dose rifampicin is useful for prophylaxis to persons in contact with known leprosy patients [10].

### Detection of *M. leprae*

Detection is confirmed by a skin biopsy and confirmation of acid-fast bacilli by Ziehl-Neelsen's stain. An alternate method today tests DNA confirmation of *M. leprae* by a polymerase chain reaction (PCR).

### WHO Response

In 2014, WHO produced a weekly epidemiological record with its *Global leprosy update, 2014: need for early case detection* [11].

Leprosy is not regarded as a public health problem today as its prevalence of <1 case per 10,000 people meets the agreed criteria when it occurs. It remains a severely debilitating disease. Concerns about its mobility abound with new cases crossing continents and arising in non-endemic countries as well as endemic ones. WHO developed a Global Leprosy Strategy, 2016 – 2020: *Accelerating towards a leprosy-free world* [12] and adopted a three-pillar core approach.

1. Strengthen government ownership, coordination, and partnership.
2. Stop leprosy and its complications.
3. Stop discrimination and promote inclusion.

Targets for the Strategy included

1. Zero disabilities for new pediatric patients.
2. A grade-2 disability rate of <1 case per 1,000,000.
3. Zero countries with legislation allowing discrimination on the basis of leprosy.

Also, WHO produced an *Operational Manual 2016 – Global Leprosy Strategy 2016 – 2020* [13], with stakeholders including non-governmental organizations, to "reduce the burden of leprosy while providing more comprehensive and timely care following the principles of equity and social justice".

### Classification

The classification of Leprosy is involved with four different methods used to date [14,15].

1. WHO system: *Multibacillary* and *Paucibacillary*
2. Ridley-Jopling classification in the US with five entities
3. ICD-10, developed by WHO, uses Ridley-Jopling, adding an "indeterminate" "I" type
4. MeSH uses three groupings – lepromatous, tuberculoid, and borderline.

### Leprosy – Types

Two predominant types of leprosy are recognized. The first, *lepromatous (Multibacillary leprosy)* is the more severe variety with multiple skin lesions signified by an atypical rash. The second, *tuberculoid (Paucibacillary leprosy)* is a milder form with few skin lesions (less than five to none). It is both less infectious and contagious, with a notable scarcity or absence of the leprosy mycobacterium. Diagnosticians agree on a hybrid or "borderline" variety with

pathologically mixed lepromatous and tuberculoid features, with further subdivisions suggested. Also, leprosy may only involve neural tissue, with absent skin lesions, making the disease even harder to confirm without a detailed neurological investigation. [16,17] A careful travelogue history may infer a better sense of likelihood if the patient originates from one of the earlier named countries.

## Genetics

Cell-mediated immunity defects in specific genes, LPRS 1 to 6, may render patients more susceptible to developing leprosy. There appears to be a biochemical link with Parkinson's disease. The differentiation of clinical lepromatous leprosy emerging, as opposed to the tuberculoid form, requires further study [18].

## Monitoring Global Spread

WHO keeps close vigilance on the disease, especially with occurrences confirmed in non-endemic nations. It is often difficult to trace the origin of the source, particularly with mass migratory movements precipitated by famine, war, strife, and a wish to find a new and more prosperous life elsewhere without any rigorous health regulations or checks being in place in the country of their origin.

While medical treatment is effective in halting the progression of leprosy, nerve damage is effectively permanent, and extensive rehabilitation with some surgical intervention may be required. The objectives are to cure and to maintain independent living for those without afflictive body or organ damage. Dependent care often ensues for those with focal tissue damage and functional loss of limb movement.

For specialist care in the United States, the National Hansen's Disease Program (NHDP), [19] is a treatment and care facility in Baton Rouge, Louisiana, US, based at the Ochsner Medical Center. It also oversees ambulatory leprosy care at eleven US clinics, provides leprosy management training, medical education for healthcare workers, and supports biomedical research. Further information is available at <https://www.hrsa.gov/hansensdisease>.

## Conclusion

The existence of modern day leprosy is an anachronism. Reducing morbidity and mortality are within reach with the complete eradication of the infection. Safe medications are effective and curative, with Leprosy Post-Exposure Prophylaxis (LPEP) now added to treatment regimes to minimize close contact transmission. The reduction of leprosy globally since the 1980's is apparent. While there is no medication cost to the sufferer, patients can sustain severe disability with all the outcomes of permanent neural damage and limb deformities if left undiagnosed and consequently, untreated. Providing healthcare facilities in endemic and non-endemic areas, educating populations and providing timely intervention after detection of the disease is paramount. However, as the condition becomes less frequent, facilities for treatment may close for lack of need. Physicians and healthcare workers may then lack the experience of managing leprosy. This deficit could lead to a paradoxical resurgence of the disease in endemic nations, existing beyond the planned pediatric infection elimination date of 2020.

## Declaration of Conflict of interest

None.

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