Clinics in Dermatology (2016) **34**, 24–31

ELSEVIER

Clinics in Dermatology

Epidemiologic trends of leprosy for the 21st century

Pieter A.M. Schreuder, MD, MSc[a,*], Salvatore Noto, MD, MSc[b], Jan Hendrik Richardus, MD, PhD[c]

[a]*Maastricht, The Netherlands*
[b]*Bergamo, Italy*
[c]*Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, The Netherlands*

Abstract Major gaps still exist in the knowledge about leprosy, particularly with regard to how it spreads. Leprosy epidemiology remains complicated due to the specific characteristics of *Mycobacterium leprae*. To describe epidemiologic trends for the 21st century, the first part of this paper gives an overview of the epidemiology of leprosy, followed by past trends and the present situation of new-case detection as a proxy of the incidence. The third part, regarding predicted epidemiologic trends for the 21st century, elaborates on the main topic of this paper. With limited diagnostic tools to detect infection with *M leprae*, other methods are necessary to estimate trends in incidence and transmission. A computer program has been developed for modeling the transmission and control of leprosy (SIMLEP). The effect of failure to sustain early case detection beyond 2005 on leprosy incidence and case detection is shown. Important unanswered questions are whether the incubation period is contagious and how rapid close contacts of leprosy patients are infected. As long as such key questions remain unanswered, it will be difficult to estimate the impact of control strategies on the transmission of *M leprae* on resulting disease incidence. In the meantime we can expect that the global new-case detection trends will stay more or less stable or only decrease slightly for many years to come. There is a need of new preventive interventions to change this situation and reduce the incidence of leprosy in the 21st century.

Introduction

Leprosy is one of the oldest diseases known to mankind, but major gaps remain in the knowledge about this disease, particularly with regard to how it spreads.[1] *Mycobacterium leprae* is the causative agent of leprosy and was described by Armauer Hansen in 1873. It was the first infectious agent to be linked to a specific disease. The fact that *M leprae* cannot be cultured in laboratory media (although there are some animal models, such as armadillo and nude mouse) has greatly hampered research into leprosy. Leprosy epidemiology remains complicated due to the specific characteristics of *M leprae*.

Epidemiology of leprosy

Leprosy has been prevalent in almost every part of the world at some stage in history. The irregular geographic

* Corresponding author.
E-mail address: impieter@hotmail.com (P.A.M. Schreuder).

http://dx.doi.org/10.1016/j.clindermatol.2015.11.001
0738-081X/

distribution of leprosy was always considered an enigma, and its occurrence in countries with cold climates is well documented. Epidemiologic surveillance in Norway, the United States, and Japan, covering periods from 1851 to 1981, found a consistent decline in incidence rates of leprosy.[2,3] In fact, leprosy incidence declined in most parts of the world before effective treatment became available.

Currently, the top five countries that are home to more than 80% of the new leprosy cases that are detected annually are situated in (sub) tropical regions: India, Brazil, Indonesia, Bangladesh, and Ethiopia.[4] Even within endemic countries, some regions, districts, and villages are more affected than others. Leprosy is nonrandom in its distribution.[1] For example, a study among highly endemic island populations in Indonesia found that leprosy patients are extensively clustered and not equally distributed among islands; furthermore, within highly affected islands there was an unequal distribution among the houses.[5]

Human beings are considered the main source of infection. Contact with a known leprosy case is a major risk factor; how the organism is transmitted from one individual to another remains uncertain[6] but is most likely by droplet infection. The entry of bacteria into the human host most likely takes place through the nasal mucosa, although the skin as port of entry has been suggested as well. Multibacillary (MB) leprosy patients, particularly lepromatous patients, shed large numbers of *M leprae* from their nose. It has been suggested that subclinical (no signs of the disease yet) MB patients may be already infectious. Contacts of MB patients have a 5- to 8-times higher risk of developing the disease compared with the general population.[7] It is not known whether paucibacillary patients are infectious at any stage of their disease.

Notwithstanding, in some areas with a high prevalence where there are relatively few MB patients there must be other important sources of infection.[1] A finding that favors the existence of other sources of infection is the widespread distribution of *M leprae* nasal carriage among the population who dwell in leprosy-endemic areas.[8] These silent carriers of *M leprae* may represent an important source of infection. Positivity rates among contacts and noncontacts in seroepidemiologic and polymerase chain reaction studies indicate that general populations in areas in which leprosy is endemic face high risks of exposure to *M leprae*.[8] One study found that in a highly endemic area for leprosy, not only household contacts of seropositive patients but also persons living in the vicinity of a seropositive patient were more likely to have antibodies against *M leprae* than the general population.[9] Both physical distance to a patient and high bacillary load of a patient have been identified as risk factors associated with the occurrence of leprosy among contacts.[10] Although it is assumed that *M leprae* spreads most easily within households of infected persons, in endemic areas social contacts within the neighborhood, village, or urban ward are also considered important for transmission.[11] In areas with declining leprosy incidences, proportionally more new patients may be expected from (extended) contacts than from the general population.

A case–control study from Brazil gives weight to the assumption that person-to-person is not the only form of *M leprae* transmission and that indirect transmission may occur and other reservoirs may exist outside the human body.[12] *M leprae* can survive for months outside the human body under favorable circumstances and could be a possible source of leprosy infection.[13,14] It is even possible that some human infections are the result of zoonotic transmission (armadillos, primates), although the risk is considered small.[1] The only evidence for a nonhuman reservoir is that pertaining to nine-banded armadillos in the southern United States.[15] A recent systematic review has described the current knowledge on the transmission of *M leprae*.[16]

Leprosy may present in many different clinical pictures, and its diversity is determined by the host immunity toward the causative agent. Although not completely understood, genetic differences between individuals as well as other factors influencing the immune status, like age, nutritional status, health status, and previous exposure and way of exposure to mycobacteria (via nose or skin, environmental, bacille Calmette-Guérin [BCG] vaccination) appear to influence the host reaction to *M leprae*.[10] In 2011, one researcher stated that it remains unclear whether genetic predisposition has a role in the development of leprosy.[17] Several studies have reported a protective effect of BCG vaccination against the development of clinical leprosy. BCG vaccination gives variable protection against leprosy in different study sites, ranging from 20% to 90%.[18] Also environmental mycobacteria may confer some degree of protection against leprosy.[19]

M leprae is slow growing and the incubation period is long, 2 to 12 years, ranging from 1 to 20 and more years, with an estimated average of 5 years.[17,20] Studies in regions with declining incidence rates have found increasing fractions of new patients with long incubation periods, resulting in increasing age of onset.[2,21] Clinical leprosy in infants in such regions is rare. Incidence rates rise to a peak between the ages of 10 to 20 years,[1] which is also indicated by data from Ethiopia.[22] Norwegian data show a peak in the 15 to 29 year age group.[3] The cohort analyses of Norway registry data by Irgens show that this peak incidence persisted over generally declining risk in consecutive birth cohorts.[1,3]

There appear to be regional differences in sex ratios of leprosy patients being diagnosed and treated. Reported male excess may be due in part to ascertainment bias.[1] Irrespective of the male/female ratio, proportionally more men than women are registered with MB leprosy,[23] with increasing ratios from borderline tuberculoid toward lepromatous leprosy. More men than women develop serious disabilities.

It is often stated that, in endemic countries, not more than 5% of those exposed to *M leprae* will develop clinical leprosy during their lifetime. But in Nauru (Micronesia, South Pacific), a single leprosy case was introduced in 1912