EPIDEMIOLOGY

Demographics Leprosy is almost exclusively a disease of the developing world, affecting areas of Asia, Africa, Latin America, and the Pacific. While Africa has the highest disease prevalence, Asia has the most cases. More than 80% of the world's cases occur in a few countries: India, China, Myanmar, Indonesia, Brazil, Nigeria, Madagascar, and Nepal. Within endemic locales, the distribution of leprosy is quite uneven, with areas of high prevalence bordering on areas with little or no disease. In Brazil the majority of cases occur in the Amazon basin and two western states, while in Mexico leprosy is mostly confined to the Pacific coast. Except as imported cases, leprosy is largely absent from the United States, Canada, and northwestern Europe. In the United States, ~4000 persons have leprosy and 100–200 new cases are reported annually, most of them in California, Texas, New York, and Hawaii among immigrants from Mexico, Southeast Asia, the Philippines, and the Caribbean.

The comparative genomics of single-nucleotide polymorphisms support the likelihood that four distinct strains exist, having originated in East Africa or Central Asia. A mutation spread to Europe and subsequently underwent two separate mutations that were then followed by spread to West Africa and the Americas.

The global prevalence of leprosy is difficult to assess, given that many of the locales with high prevalence lack a significant medical or public health infrastructure. Estimates range from 0.6 to 8 million affected individuals. The lower estimate includes only persons who have not completed chemotherapy, excluding those who may be physically or psychologically damaged from leprosy and who may yet relapse or develop immune-mediated reactions. The higher figure includes patients whose infections probably are already cured and many who have no leprosy-related deformity or disability. Although the figures on the worldwide prevalence of leprosy are debatable, incidence is not falling; there are still an estimated 500,000 new cases annually.

Leprosy is associated with poverty and rural residence. It appears not to be associated with AIDS, perhaps because of leprosy's long incubation period. Most individuals appear to be naturally immune to leprosy and do not develop disease manifestations after exposure. The time of peak onset is in the second and third decades of life.

The most severe lepromatous form of leprosy is twice as common among men as among women and is rarely encountered in children. The frequency of the polar forms of leprosy in different countries varies widely and may in part be genetically determined; certain human leukocyte antigen (HLA) associations are known for both polar forms of leprosy (see below). Furthermore, variations in immunoregulatory genes are associated with an increased susceptibility to leprosy, particularly the multibacillary form. In India and Africa, 90% of cases are tuberculoid; in Southeast Asia, 50% are tuberculoid and 50% lepromatous; and in Mexico, 90% are lepromatous. (For definitions of disease types, see Table 203-1 and "Clinical, Histologic, and Immunologic Spectrum," below.)

Transmission The route of transmission of leprosy remains uncertain, and transmission routes may in fact be multiple. Nasal droplet infection, contact with infected soil, and even insect vectors have been considered the prime candidates. Aerosolized *M. leprae* can cause infection in immunosuppressed mice, and a sneeze from an untreated lepromatous patient may contain $>10^{10}$ AFB. Furthermore, both IgA antibody to *M. leprae* and genes of *M. leprae*—demonstrable by polymerase chain reaction (PCR)—have been found in the nose of individuals from endemic areas who have no signs of leprosy and in 19% of occupational contacts of lepromatous patients. Several lines of evidence implicate soil transmission. (1) In endemic countries such as India, leprosy is primarily a rural and not an urban disease. (2) *M. leprae* products reside in soil in endemic locales. (3) Direct dermal inoculation (e.g., during tattooing) may transmit *M. leprae*, and common sites of leprosy in children are the buttocks and thighs, suggesting that microinoculation of infected soil may transmit the disease. Evidence for insect vectors of leprosy includes the demonstration that bedbugs and mosquitoes in the vicinity of leprosaria regularly harbor *M. leprae* and that experimentally infected mosquitoes can transmit the infection to mice. Skin-to-skin contact generally is not considered an important route of transmission.

In endemic countries, ~50% of leprosy patients have a history of intimate contact with an infected person (often a household member), while, for unknown reasons, leprosy patients in nonendemic locales can identify such contact only 10% of the time. Moreover, household contact with an infected lepromatous case carries an eventual risk of disease acquisition of ~10% in endemic areas as opposed to only 1% in nonendemic locales. Contact with a tuberculoid case carries a very low risk. Physicians and nurses caring for leprosy patients and the coworkers of these patients are not at risk for leprosy.

Although multilocus variable-number short-nucleotide tandem-repeat (VNTR) analyses have generally demonstrated considerable variability among isolates, highly similar and even identical VNTR results have been obtained with isolates from a limited number

TABLE 203-1 CLINICAL, BACTERIOLOGIC, PATHOLOGIC, AND IMMUNOLOGIC SPECTRUM OF LEPROSY

Feature	Tuberculoid (TT, BT) Leprosy	Borderline (BB, BL) Leprosy	Lepromatous (LL) Leprosy
Skin lesions	One or a few sharply defined annular asymmetric macules or plaques with a tendency toward central clearing, elevated borders	Intermediate between BT- and LL-type lesions; ill-defined plaques with an occasional sharp margin; few or many in number	Symmetric, poorly marginated, multiple infiltrated nodules and plaques or diffuse infiltration; xanthoma-like or dermatofibroma papules; leonine facies and eyebrow alopecia
Nerve lesions	Skin lesions anesthetic early; nerve near lesions sometimes enlarged; nerve abscesses most common in BT	Hypesthetic or anesthetic skin lesions; nerve trunk palsies, at times symmetric	Hypesthesia a late sign; nerve palsies variable; acral, distal, symmetric anesthesia common
Acid-fast bacilli (BI[a])	0–1+	3–5+	4–6+
Lymphocytes	2+	1+	0–1+
Macrophage differentiation	Epithelioid	Epithelioid in BB; usually undifferentiated but may have foamy changes in BL	Foamy change the rule; may be undifferentiated in early lesions
Langerhans giant cells	1–3+	—	—
Lepromin skin test	+++	—	—
Lymphocyte transformation test	Generally positive	1–10%	1–2%
CD4+/CD8+ T cell ratio in lesions	1.2	BB: NT; BL: 0.48	0.50
M. leprae PGL-1 antibodies	60%	85%	95%

[a]See text.

Abbreviations: BB, mid-borderline; BL, borderline lepromatous; BT, borderline tuberculoid; TT, polar tuberculoid; LL, polar lepromatous; BI, bacteriologic index; NT, not tested; PGL-1, phenolic glycolipid 1.