reactions. Clofazimine (200–300 mg/d) is of questionable benefit but in any event is far less efficacious than glucocorticoids.

Type 2 Treatment of ENL must be individualized. If ENL is mild (i.e., if it occurs without fever or other organ involvement and with occasional crops of only a few skin papules), it may be treated with antipyretics alone. However, in cases with many skin lesions, fever, malaise, and other tissue involvement, brief courses (1–2 weeks) of glucocorticoid treatment (initially 40–60 mg/d) are often effective. With or without therapy, individual inflamed papules last for <1 week. Successful therapy is defined by the cessation of skin lesion development and the disappearance of other systemic signs and symptoms. If, despite two courses of glucocorticoid therapy, ENL appears to be recurring and persisting, treatment with thalidomide (100–300 mg nightly) should be initiated, with the dose depending on the initial severity of the reaction. Because even a single dose of thalidomide administered early in pregnancy may result in severe birth defects, including phocomelia, the use of this drug in the United States for the treatment of fertile female patients is tightly regulated and requires informed consent, prior pregnancy testing, and maintenance of birth control measures. Although the mechanism of thalidomide's dramatic action against ENL is not entirely clear, the drug's efficacy is probably attributable to its reduction of TNF levels and IgM synthesis and its slowing of polymorphonuclear leukocyte migration. After the reaction is controlled, lower doses of thalidomide (50–200 mg nightly) are effective in preventing relapses of ENL. Clofazimine in high doses (300 mg nightly) has some efficacy against ENL, but its use permits only a modest reduction of the glucocorticoid dose necessary for ENL control.

Lucio's Phenomenon Neither glucocorticoids nor thalidomide is effective against this syndrome. Optimal wound care and therapy for bacteremia are indicated. Ulcers tend to be chronic and heal poorly. In severe cases, exchange transfusion may prove useful.

PREVENTION AND CONTROL

Vaccination at birth with bacille Calmette-Guérin (BCG) has proved variably effective in preventing leprosy: the results have ranged from total inefficacy to 80% efficacy. The addition of heat-killed *M. leprae* to BCG does not increase the effectiveness of the vaccine. Because whole mycobacteria contain large amounts of lipids and carbohydrates that have proved in vitro to be immunosuppressive for lymphocytes and macrophages, *M. leprae* proteins may prove to be superior vaccines. Data from a mouse model support this possibility.

Chemoprophylaxis with dapsone may reduce the number of tuberculoid leprosy cases but not the number of lepromatous cases and hence is not recommended, even for household contacts. In addition, single-dose rifampin prophylaxis is of doubtful efficacy. Because leprosy transmission appears to require close prolonged household contact, hospitalized patients need not be isolated.

In 1992, the WHO—on the basis of that organization's treatment recommendations—launched a landmark campaign to eliminate leprosy as a public health problem by the year 2000 (goal, <1 case per 10,000 population). The campaign mobilized and energized nongovernmental organizations and national health services to treat leprosy with multiple drugs and to clean up outdated registries. In these respects, the effort has proved hugely successful, with >6 million patients completing therapy. However, the target of leprosy elimination has not yet been reached. In fact, the success of the WHO campaign in reducing the number of cases worldwide has been largely attributable to the redefinition of what constitutes a case of leprosy. Formerly calculated by disease prevalence, the count is now limited to cases not yet treated with multiple drugs. Worldwide, the annual incidence of leprosy has not fallen. Furthermore, after the completion of therapy, when a patient is no longer considered to represent a "case," half of all patients continue to manifest disease activity for years; relapse rates (at least for multibacillary patients) are unacceptably high; disabilities and deformities go unchecked; and the social stigma of the disease persists.

During most of the twentieth century, nongovernmental organizations, particularly Christian missionaries, provided a medical infrastructure devoted to the care and treatment of leprosy patients—the envy of those with other medical priorities in the developing world. With the public perception that leprosy is near eradication, resources for patient care are rapidly being diverted, and the burden of patient care is being transferred to nonexistent or overloaded national health services and to health workers who lack the tools and skills needed for the disease's diagnosis and classification and for the selection of nuanced therapy (particularly in cases of reactional neuritis). Thus the prerequisites for a salutary outcome increasingly go unmet.

204 Nontuberculous Mycobacterial Infections

Steven M. Holland

Several terms—nontuberculous mycobacteria (NTM), atypical mycobacteria, mycobacteria other than tuberculosis, and environmental mycobacteria—all refer to mycobacteria other than *Mycobacterium tuberculosis*, its close relatives (*M. bovis, M. caprae, M. africanum, M. pinnipedii, M. canetti*), and *M. leprae*. The number of identified species of NTM is growing and will continue to do so because of the use of DNA sequence typing for speciation. The number of known species currently exceeds 150. NTM are highly adaptable and can inhabit hostile environments, including industrial solvents.

EPIDEMIOLOGY

NTM are ubiquitous in soil and water. Specific organisms have recurring niches, such as *M. simiae* in certain aquifers, *M. fortuitum* in pedicure baths, and *M. immunogenum* in metalworking fluids. Most NTM cause disease in humans only rarely unless some aspect of host defense is impaired, as in bronchiectasis, or breached, as by inoculation (e.g., liposuction, trauma). There are few instances of human-to-human transmission of NTM, which occurs almost exclusively in cystic fibrosis. Because infections due to NTM are rarely reported to health agencies and because their identification is sometimes problematic, reliable data on incidence and prevalence are lacking. Disseminated disease denotes significant immune dysfunction (e.g., advanced HIV infection), whereas pulmonary disease, which is much more common, is highly associated with pulmonary epithelial defects but not with systemic immunodeficiency.

In the United States, the incidence and prevalence of pulmonary infection with NTM, mostly in association with bronchiectasis (Chap. 312), have for many years been several-fold higher than the corresponding figures for tuberculosis, and rates of the former are increasing among the elderly. Among patients with cystic fibrosis, who often have bronchiectasis, rates of clinical infection with NTM range from 3% to 15%, with even higher rates among older patients. Although NTM may be recovered from the sputa of many individuals, it is critical to differentiate active disease from commensal harboring of the organisms. A scheme to help with the proper diagnosis of pulmonary infection caused by NTM has been developed by the American Thoracic Society and is widely used. The bulk of nontuberculous mycobacterial disease in North America is due to *M. kansasii*, organisms of the *M. avium* complex (MAC), and *M. abscessus*.

In Europe, Asia, and Australia, the distribution of NTM in clinical specimens is roughly similar to that in North America, with MAC species and rapidly growing organisms such as *M. abscessus* encountered frequently. *M. xenopi* and *M. malmoense* are especially prominent in northern Europe. *M. ulcerans* causes the distinct clinical entity Buruli ulcer, which occurs throughout tropical zones, especially in western Africa. *M. marinum* is a common cause of cutaneous and tendon infections in coastal regions and among individuals exposed to fish tanks or swimming pools.