In developed countries, clinical experience with leprosy classification is limited; fortunately, however, the resources needed for skin biopsy are highly accessible, and those for pathologic interpretation are readily available. In developing countries, clinical expertise is greater but is now waning substantially as the care of leprosy patients is integrated into general health services. In addition, access to dermatopathology services is often limited. In such instances, skin smears may prove useful, but in many locales access to the resources needed for their preparation and interpretation also may be unavailable. Use of skin smears is no longer encouraged by the World Health Organization (WHO) and is often replaced by mere counting of lesions, which, together with a lack of capacity for histopathologic assessment, may negatively affect decisions about chemotherapy, increase the potential for reactions, and worsen the ultimate prognosis. A reasoned approach to the treatment of leprosy is confounded by these and several other issues:

1. Even without therapy, TT leprosy may heal spontaneously, and prolonged dapsone monotherapy (even for LL leprosy) is generally curative in 80% of cases.
2. In tuberculoid disease, it is common for no bacilli to be found in the skin prior to therapy, and thus there is no objective measure of therapeutic success. Furthermore, despite adequate treatment, TT and particularly BT lesions often resolve minimally or incompletely, while relapse and late type 1 lepra reactions can be difficult to distinguish.
3. LL leprosy patients commonly harbor viable persistent *M. leprae* organisms after prolonged intensive therapy; the propensity of these organisms to initiate clinical relapse is unclear. Because relapse in LL patients after discontinuation of rifampin-containing regimens usually begins only after 7–10 years, follow-up over the very long term is necessary to assess ultimate clinical outcomes.
4. Even though primary dapsone resistance is exceedingly rare and multidrug therapy is generally recommended (at least for lepromatous leprosy), there is a paucity of information from experimental animals and clinical trials on the optimal combination of antimicrobial agents, dosing schedule, and duration of therapy.

In 1982, the WHO made recommendations for leprosy chemotherapy administered in control programs. These recommendations came on the heels of the demonstration of the relative success of long-term dapsone monotherapy and in the context of concerns about dapsone resistance. Other complicating considerations included the limited resources available for leprosy care in the very areas where it is most prevalent and the frustration and discouragement of patients and program managers with the previous requirement for lifelong therapy for many leprosy patients. Thus, for the first time, the WHO advocated a finite duration of therapy for all forms of leprosy and—given the prohibitive cost of daily rifampin treatment in developing countries—encouraged the monthly administration of this agent as part of a multidrug regimen. Over the ensuing years, the WHO recommendations have been broadly implemented, and the duration of therapy required, particularly for lepromatous leprosy, has been progressively shortened. For treatment purposes, the WHO classifies patients as *paucibacillary* or *multibacillary*. Previously, patients without demonstrable AFB in the dermis were classified as paucibacillary and those with AFB as multibacillary. Currently, in light of the perceived unreliability of skin smears in the field, patients are classified as multibacillary if they have six or more skin lesions and as paucibacillary if they have fewer. (Unfortunately, this classification method has been found wanting, as some patients near the lepromatous pole have only one or a few skin lesions.) The WHO recommends that paucibacillary adults be treated with 100 mg of dapsone daily and 600 mg of rifampin monthly (supervised) for 6 months **(Table 203-2)**. For patients with single-lesion paucibacillary leprosy, the WHO recommends as an alternative a single dose of rifampin (600 mg), ofloxacin (400 mg), and minocycline (100 mg). Multibacillary adults should be treated with 100 mg of dapsone plus 50 mg of clofazimine daily (unsupervised) and with 600 mg of rifampin plus 300 mg of clofazimine monthly (supervised). Originally, the WHO recommended that lepromatous patients be treated for 2 years or until smears became negative (generally in ~5 years); subsequently, the acceptable course was reduced to 1 year—a change that remains especially controversial in the absence of supporting clinical trials.

TABLE 203-2 ANTIMICROBIAL REGIMENS RECOMMENDED FOR THE TREATMENT OF LEPROSY IN ADULTS

Form of Leprosy	More Intensive Regimen	WHO-Recommended Regimen (1982)
Tuberculoid (paucibacillary)	Dapsone (100 mg/d) for 5 years	Dapsone (100 mg/d, unsupervised) *plus* rifampin (600 mg/month, supervised) for 6 months
Lepromatous (multibacillary)	Rifampin (600 mg/d) for 3 years *plus* dapsone (100 mg/d) indefinitely	Dapsone (100 mg/d) *plus* clofazimine (50 mg/d), unsupervised; *and* rifampin (600 mg) *plus* clofazimine (300 mg) monthly (supervised) for 1–2 years

Note: See text for discussion and comparison of the WHO recommendations with the more intensive approach as well as the alternative WHO regimen for single-lesion paucibacillary leprosy.

Several factors have caused many authorities to question the WHO recommendations and to favor a more intensive approach. Among these factors are—for multibacillary patients—a high (double-digit) relapse rate in several locales (reaching 20–40% in one locale, with the rate directly related to the initial bacterial burden) and—for paucibacillary patients—demonstrable lesional activity for years in fully half of patients after the completion of therapy. The more intensive approach (Table 203-2) calls for tuberculoid leprosy to be treated with dapsone (100 mg/d) for 5 years and for lepromatous leprosy to be treated with rifampin (600 mg/d) for 3 years and with dapsone (100 mg/d) throughout life.

With effective antimicrobial therapy, new skin lesions and signs and symptoms of peripheral neuropathy cease appearing. Nodules and plaques of lepromatous leprosy noticeably flatten in 1–2 months and resolve in 1 year or a few years, while tuberculoid skin lesions may disappear, ameliorate, or remain relatively unchanged. Although the peripheral neuropathy of leprosy may improve somewhat in the first few months of therapy, rarely is it significantly alleviated by treatment.

Despite the drawbacks of the WHO's recommendations for multidrug therapy, these regimens have been used almost exclusively worldwide. Although two of the three recommended drugs (dapsone and clofazimine) are only bacteriostatic against *M. leprae* and bactericidal agents have been identified since the WHO formulated its recommendations, significant studies employing the available alternatives in newly designed regimens have not been initiated. Given the recent findings that moxifloxacin, like rifampin, is profoundly bactericidal in leprosy patients and that short-course chemotherapy for tuberculosis is possible only when two or more bactericidal agents are used, a moxifloxacin/rifamycin-based regimen including either minocycline or clarithromycin appears promising; such a regimen may prove to be more reliably curative than WHO-recommended multidrug therapy for lepromatous leprosy and may allow a considerably shorter course of treatment.

THERAPY FOR REACTIONS

Type 1 Type 1 lepra reactions are best treated with glucocorticoids (e.g., prednisone, initially at doses of 40–60 mg/d). As inflammation subsides, the glucocorticoid dose can be tapered, but steroid therapy must be continued for at least 3–6 months lest recurrence supervene. Because of the myriad toxicities of prolonged glucocorticoid therapy, the indications for its initiation are strictly limited to lesions whose intense inflammation poses a threat of ulceration; lesions at cosmetically important sites, such as the face; and cases in which neuritis is present. Mild to moderate lepra reactions that do not meet these criteria should be tolerated and glucocorticoid treatment withheld. Thalidomide is ineffective against type 1 lepra