Several individual studies of treatment of paucibacillary disease have reported results that concord with the WHO data (Pattyn *et al.,* 1987; Reddy and Mihinuddin, 1988; Orege, 1990; Pattyn *et al.,* 1990; Boerrigter *et al.,* 1991; Ekambaram and Rao, 1991; Becx-Bleumink, 1992; Pattyn, 1993). Other studies demonstrated satisfactory cure rates with 12 months of MDT, and closer analysis of their results showed that there was a good response by six months in the majority of cases (Chopra *et al.,* 1990; Grugni *et al.,* 1990; Kaur *et al.,* 1992; Ramu, 1992; Nadkarni *et al.,* 1993).

Initial results of treatment of multibacillary disease indicated that 2 years of therapy was likely to be satisfactory (WHO, 1994). Very short courses were tried with mixed results; however, follow-up of 10 years or more was ultimately deemed necessary to ascertain the true relapse rate, even when a good response was present (Becx-Bleumink, 1991; Pattyn *et al.,* 1992).

In 1996, it was reported that the combination of clofazimine and dapsone given daily for 12 weeks to nude mice infected with *M. leprae* was highly bactericidal, killing more than 99.99% of organisms. This suggested that it was not necessary to treat multibacillary disease for as long as 24 months, the WHO MDT regimen current at the time (Ji *et al.,* 1996a). This observation of the bactericidal nature of the combination was confirmed in a clinical trial in patients with multibacillary disease. Four of 10 patients treated with dapsone and clofazimine for 1 month had no viable organisms detectable on inoculation of lepromatous material in the mouse footpad (Ji *et al.,* 1996b).

In 1998, after the publication of the aforementioned studies suggesting that MDT could be shortened, the regimen for multibacillary disease was shortened to 12 months (WHO, 1998). The rationale was that the majority of effective bactericidal activity was from the use of rifampicin in a single dose that results in the killing of more than 99.999% of viable organisms, and that the now better understood bactericidal effect of the combination of clofazimine and dapsone would account for the remainder that were naturally rifampicin-resistant (Banerjee *et al.,* 1997).

Retrospective evaluation of cohorts of patients with multibacillary disease who did not complete 24 months of therapy confirmed the efficacy of 12 months of treatment; however, shorter durations appeared to result in higher relapse rates. All assessments were performed at relatively short post-treatment intervals of 5 years or less (WHO, 1998).

Field evaluations continue to demonstrate the fact that relapse rates for MDT of multibacillary disease remain low. In one report of 300 patients with multibacillary disease, treated with the WHO MDT regimen between 1986 and 2002, 163 were evaluable. In that group, there were three cases of relapse—one each at 2, 4, and 11 years after cessation of therapy. With a mean duration of follow-up of 7.1 years, the relapse rate was 0.26 per 100 person-years, indicating that relapse rates after MDT remain low. Many of the patients in this cohort received 18 months to 2 years of therapy (Poojabylaiah *et al.,* 2008).

In 1997, after a successful trial in India, an additional regimen of a single dose of rifampicin 600 mg, ofloxacin 400 mg, and minocycline 100 mg was approved as an experimental treatment for single-lesion paucibacillary leprosy. Long-term follow-up continues, and the incidence rate of suspected relapse is currently reported at 3 per 1000 person-years (WHO Technical Advisory Group on Leprosy Control, 2006; WHO, 2013).

WHO is also evaluating a single multidrug regimen for all forms of leprosy. This is termed the *Uniform Multidrug Therapy Regimen.* All patients are treated with 6 months of dapsone and clofazimine daily, and monthly rifampicin and clofazimine bolus. Early reports appeared encouraging (Kroger *et al.,* 2008), particularly in the multibacillary patients; however, the final report is still pending, and, as with many of the WHO short-course MDT regimens, long-term follow-up over 10 years is eagerly awaited.

Given that the drive for the use of shorter course therapy was based on the need to enhance compliance, rapidly reduce infectivity in multibacillary patients, and conserve scarce resources in the poorer countries where leprosy is most prevalent, many more conservative clinicians have opted for prolonged treatment, particularly in multibacillary cases. The USPHS National Hansen's Disease Program (HRSA, 2016) has continued with a more conservative approach and, after long-term evaluation (10–20 years) of short-course therapy in multibacillary patients, may opt to change if relapse rates remain low (Moschella, 2004).

The WHO MDT regimens remain the mainstay of treatment of all forms of leprosy with low relapse rates (WHO, 2012). These regimens have not changed since they were first introduced. Despite the WHO declaration of the elimination of leprosy as a public health problem in many countries, new cases continue to appear in those countries and asymptomatic carriers remain prevalent. Many contemporary challenges remain before this ancient disease can be considered to have been finally eradicated (Lockwood and Suneetha, 2005; Scollard *et al.,* 2006; Kar and Gupta, 2015).

7b. Other mycobacterial infections

Dapsone has modest *in vitro* activity against *M. ulcerans;* however, a trial of dapsone combined with rifampicin in a small number of patients showed disappointing results (Espey *et al.,* 2002). The DHFR inhibitor epiroprim when combined with dapsone appears to have strong bactericidal activity (Dhople, 2001), but as yet no trials of treatment have been reported.

Dapsone appears to have no clinically apparent prophylactic effect on *M. avium* complex infection in patients with advanced HIV disease (Stein *et al.,* 1998). In the multicenter AIDS cohort study of 1035 subjects, of whom 216 used dapsone at some time during the study period, there was a nonsignificant reduction of 30% in the incidence of MAC disease in those who had used dapsone. This confirmed the findings of a study that examined the incidence of MAC disease in a trial of dapsone prophylaxis for pneumocystis infection. In