Editorial

ACCOMPANIED MDT (AMDT)—MORE QUESTIONS THAN ANSWERS

Accompanied MDT (AMDT),\textsuperscript{1,2} an essential element of the ‘flexible and patient-friendly MDT delivery systems’ recommended by WHO, is a policy in which the patient is provided the entire supply of MDT drugs at the time of diagnosis\textsuperscript{3,4}—6 months of medication for a paucibacillary (PB) patient and 12 months for a multibacillary (MB) patient, while asking ‘someone close to or important to the patient assumes the responsibility of helping him or her complete a full course of treatment’.\textsuperscript{5} Recently, the Global Alliance for Leprosy Elimination (GAEL) and the WHO Technical Advisory Group on Elimination of Leprosy (TAG) have recommended that ‘AMDT should be widely implemented in order to increase accessibility of all patients (to MDT).’\textsuperscript{5,6} because of the prestige of these institutions, the AMDT policy has been widely implemented in the field.

AMDT is one of the more controversial technical policies that have been introduced into leprosy control, because it deviates fundamentally from the principle of supervised administration of the monthly component of standard MDT regimens,\textsuperscript{4} and may therefore damage seriously the quality of treatment by MDT. The purpose of this paper is to call attention to the flaws of AMDT. Because poor adherence is also a common phenomenon among tuberculosis (TB) patients, as the result of which directly observed treatment (DOT) has been widely applied as the ‘standard of cure’ for treatment of TB, the relevant experience from TB programmes is reviewed.

Poor adherence to self-administration of treatment: a common phenomenon among leprosy and TB patients

Adherence or compliance of patients is crucial to the success of treatment. The terms ‘adherence’ and ‘compliance’ have been used alternatively in many publications. However, ‘adherence’ is a better term than ‘compliance’, because the former reflects the active role of the patient in self-management of treatment and the importance of cooperation between patient and provider, whereas the latter term connotes that the patient is docile and subservient to the provider, an undesirable characteristic.\textsuperscript{5} Consequently, ‘adherence’ is used throughout this paper.

Poor adherence to self-administration of treatment is a common behavioural problem\textsuperscript{5} among patients suffering from chronic diseases,\textsuperscript{6,7} including TB\textsuperscript{8–10} and leprosy.\textsuperscript{11–13} Almost 45 years ago, Fox underscored the problem of achieving high rates of adherence to treatment among ambulatory TB patients.\textsuperscript{5} Despite all efforts, ‘irregularity (had) been a problem
Throughout the course of treatment,' Fox concluded that, whereas the issue of which oral medications to use was important, it was 'less fundamental' than the regularity of self-administered treatment. Subsequently, numerous papers14,15 have confirmed Fox's observation. Sbarbaro estimated that at least 35% of patients, regardless of socio-economic background, culture, or educational achievement were poor adherents to treatment,16 and stated that the treatment behaviour of most patients is unpredictable.17

Among leprosy patients, the magnitude of poor adherence to dapsone self-administration became apparent only when the urinary dapsone:creatinine ratio method18,19 for monitoring the ingestion of dapsone was established and tested in many leprosy control centres. A review of the results of urine testing concluded that only about half of the prescribed dapsone was actually ingested.11 Furthermore, studies also revealed that mere attendance at the clinic or collecting drugs by leprosy or TB patients was not a reliable indicator of regular drug self-administration.8,20 Because rifampicin, the key component of MDT regimens, was expected to be administered under supervision,4 only limited studies have been carried out since the introduction of MDT to determine the adherence of leprosy patients to self-administration of the daily component of MDT regimens. Although Becx-Bleumink reported better adherence to self-administered dapsone among PB patients treated with MDT than among those treated with dapsone monotherapy,21 only 70%20 to 80%21 of patients were found to adhere to self-administration of the daily component of MDT regimens when the monthly component was administered under supervision, suggesting that, even with MDT, adherence to the self-administered component of MDT regimens remains poor. Since the large-scale implementation of AMDT policy, no information is available concerning adherence to self-administration of MDT drugs among patients received the entire supply of MDT drugs at the time of diagnosis.1–3

Unsupervised outpatient TB treatment has often been associated with a poor cure rate, despite the existence of proven drug regimens.22 Poor adherence has been identified as a serious obstacle to the completion of treatment among individual patients, as a major barrier to the control and elimination of TB at the public health level, and as one of the important causes of the emergence and rapid increase of drug resistant, particularly multidrug resistant, strains of Mycobacterium tuberculosis.5,23 The failure of many leprosy patients to achieve clinical and bacteriological quiescence despite prolonged periods of dapsone monotherapy has been attributed to poor adherence.11–13 In addition, irregular treatment with dapsone was thought to be a major factor leading to the development of dapsone resistance.11 Until now, no study has been carried out to assess the therapeutic implications of poor adherence among patients treated with MDT; however, one may not exclude the possibility of some MB relapse as a consequence of poor adherence to the monthly administration of MDT, rifampicin, and the emergence of rifampicin resistant strains of M. leprae among MB patients who fail to adhere to the self-administered, daily component of MDT regimen.

**Supervised administration: a solution to the problem of poor adherence to treatment in leprosy and TB**

Although a number of alternative means exist to improve adherence,5 supervised (or directly observed) administration is the only proven way to ensure that a patient receives treatment with the correct drugs, in the correct dosage, at the correct intervals.26,27 Based on the experience with the supervised administration of TB treatment, one of the principles of the
MDT regimens recommended by the WHO Study Group on Chemotherapy of Leprosy for Control Programmes was that the monthly component of the regimens—rifampicin alone for PB leprosy and rifampicin plus a supplementary larger dose of clofazimine for MB leprosy—should be administered under the supervision of a health worker. However, it was felt that it was not feasible to supervise administration of the daily component, which was therefore intended to be self-administered. A decade later, when the ‘direct observed therapy, short-course’ (DOTS) strategy was introduced, its designers emphasized the need for supervision of therapy in TB programmes. An essential element of the DOTS strategy is directly observed treatment (DOT)—watching patients taking their medications—at least during the intensive phase (the first 2 months) of treatment. This policy has been endorsed by the great majority of health authorities as the ‘standard of cure’ for TB treatment.

Implementation of supervised therapy is certainly not easy in the field, especially in areas in which the health infrastructure is weak. Because supervised therapy requires that a trained individual personally supervise and verify that the patient swallows the prescribed medication, and places responsibility for the patient’s outcome on the health service, it requires dedicated staff, effective leadership and sufficient resources, and is therefore far more demanding than leaving the patient to self-administer his treatment. Because MDT strategy requires that leprosy patients swallow only the monthly component of MDT regimens under supervision, supervised therapy in leprosy programmes is significantly less demanding operationally for both patients and health services than the DOT approach in TB programmes.

Since their introduction, both MDT and DOTS strategy have been intensively implemented in the field. By the time of the seventh meeting of the WHO Expert Committee on Leprosy in 1997, more than 8.4 million leprosy patients had completed treatment with MDT with monthly rifampicin administered under supervision. By the year 2000, 148 countries, both rich and poor, had adopted the DOTS strategy for TB control. Published data demonstrated that DOT approach has improved TB treatment outcomes in a wide range of settings. Today, WHO’s TB programme continues to promote the implementation of DOT in the field.

**Discontinue supervision of therapy and implement AMDT in leprosy programmes?**

Recently, to accelerate the leprosy elimination process, WHO’s leprosy programme and its TAG have changed dramatically their position on supervised therapy. They have concluded that, after the first dose of MDT, supervision of the subsequent monthly component of MDT regimens is no longer essential; further, based on this conclusion, they have recommended large-scale implementation of AMDT. Some members of TAG even believe that monthly supervision ‘hampers integration and is not user-friendly’, and that ‘providing patients with a full course of treatment on their first visit is both patient- and staff-friendly and will improve compliance’.

In fact, the WHO Study Group emphasized more than 20 years ago that the MDT delivery system should be flexible and convenient for patients. The concepts of convenience and flexibility were intended only to ensure administration of the monthly component of MDT regimens, and hence the regularity of treatment, neither ignored the ubiquitous problem of poor adherence of patients nor denied the need for supervision of monthly drug administration. As long as regularity of treatment is ensured, the patient is treated with kindness and
respect, and the supervision is acceptable, accessible and convenient to the patient and accountable to the health service, there is no reason to believe that such supervision is not patient-friendly. On the other hand, no drug-delivery system that cannot ensure the administration of the monthly component of MDT regimens can be considered patient- and staff-friendly.

The recommendation to discontinue supervision of monthly drug administration appears to be a simple solution to the difficult problem of implementing supervised therapy, but the solution is obviously wrong. Not only have WHO and TAG confused the operational difficulties of implementing supervised therapy with the technical justifications for discontinuing its application, and ignored completely the fact of poor adherence of patients to self-administered medication; more importantly, the recommendation lacks evidence-based justification. Furthermore, the recommendation also neglects the importance of regular contacts between health workers and leprosy patients, which facilitate early detection and management of various complications, crucial for prevention of impairments.

**AMDT, an ill-defined policy**

Experience with AMDT has yet to be documented, and virtually no information is available with respect to the adherence to MDT among patients under AMDT. Moreover, it is unclear whether this approach has ever been tested in the field.

The whole concept of the AMDT policy is extremely vague. First, whether AMDT is to be applied as a routine or only in special situations is not clear, although the WHO Study Group stated clearly that only in special situations may the involvement of community members in MDT delivery become necessary. In other words, as a routine, the administration of monthly component of MDT regimens should be supervised by a health worker. Although the effectiveness of MDT supervised by health workers with that of MDT supervised by community or family members has not been compared, such a comparison has been made in TB programmes. Because the cure rate was significantly higher among TB patients supervised by health workers, who were more likely to practice ‘actual DOT’, the preferred choice of DOT supervisor was the health worker. In arguing the case for AMDT, Daumerie cited the results of a highly controversial trial in Pakistan, because cure rates did not differ significantly among patients supervised by a health worker, supervised by a family member or unsupervised, it was concluded that DOT did not provide additional benefit in terms of cure rate. However, Daumerie cited only the results of the trial from a newsletter, and neglected the strong criticisms of this trial published subsequently in the journal *The Lancet* by the national TB programme in Pakistan and by WHO. Cure rates among the patients of all three groups were low—only slightly greater than 60%, largely the result of minimal primary-health-care integration, weak managerial capacity and poor adherence. Moreover, the three groups of patients were not comparable because of inadequate randomization. Therefore, the conclusion that DOT did not improve the cure rate has been questioned.

Because of inadequate development of the health infrastructure in many endemic countries, the health worker is not always accessible or acceptable to the patient, and it is clearly not feasible to assign only health workers as supervisors, using a member of the community as supervisor is an obligatory alternative in special situations. However, under AMDT, it is unclear who may be chosen to supervise the patient’s treatment. The only
description provided is ‘someone close to or important to the patient’,\textsuperscript{2} who could be a community or family member; it is unclear whether there is an order of preference. Published experience indicates that community health workers\textsuperscript{36} or community volunteers, such as community leaders, village elders, tribal chieftains, religious leaders, teachers, shopkeepers, neighbours, and even cured patients can successfully supervise TB treatment.\textsuperscript{28,31,32,36} Nevertheless, opinions differ regarding supervision by family members, which is common in some DOT programmes;\textsuperscript{31,32} most workers believe that supervision by family members is less reliable and even ineffective,\textsuperscript{28,31,37} and some national TB programmes, such as that of India, have clearly defined the DOT supervisor as someone outside the family.\textsuperscript{37} WHO’s TB programme believes that only in some cases may a family member supervise treatment, and the family member must be regularly supervised by a community health worker.\textsuperscript{38}

Third, how an AMDT ‘helps’\textsuperscript{2} a patient to complete a full course of treatment is not described; is he expected to observe the patient swallow each monthly dose of treatment? In some TB programmes, situations in which a DOT supervisor who simply accompanied the patient but did not observe him to swallow the drugs were considered ‘actual non-DOT’.\textsuperscript{32}

Finally, training and supervising the community members by health workers have been shown to be critically important for the success of DOT for TB treatment,\textsuperscript{36,30} but how best to train and supervise the AMDT is unclear.

Although a number of essential questions about AMDT remain to be answered, AMDT has been rapidly and intensively implemented in the field. In an increasing number of national programmes, the total quantity of MDT blister packs is provided at the time of diagnosis to all patients, including those patients living rather close to treatment centres, but the AMDT supervisor either does not exist or lacks training and supervision. Consequently, one cannot be certain that the MDT drugs are indeed self-administered by the patients. Can so reckless a policy be termed ‘patient- and staff-friendly’?

Conclusion

Because of poor adherence of patients to self-administration of treatment, supervised therapy is the only way to ensure regularity of treatment. That other approaches to ensure regularity of treatment will suffice is only wishful thinking. Although implementation of supervised therapy in the field is not easy, it has been routinely applied for the treatment of leprosy and TB patients, and is still being applied as routine policy for TB programmes; therefore, there is no reason to discontinue supervised therapy in leprosy programmes. Leprosy patients residing close to a health facility, who probably represent the majority of patients in most endemic countries, should be encouraged to visit the health facility once monthly, and to swallow the monthly drug in front of a health worker. For patients residing far away from a health facility, the supervisor could be a health outreach worker or a trained local community member, preferably someone outside the patient’s family. To standardize the procedures of supervised therapy, national leprosy programmes should update its manual or technical guidelines, and strengthening the training and supervision activities, ensure that all general health workers dealing with leprosy patients possess the skills essential for diagnosis and treatment. All community volunteers who have been assigned as AMDT supervisors must receive adequate training and regular supervision by health workers.

With large-scale implementation of AMDT, the quality of treatment is a matter of real concern. Without a guarantee of quality, quantitative achievement or a declaration of leprosy
elimination is meaningless. To avoid building the leprosy elimination monument on sand, we must not consider only the short term. Every effort should be made to maintain and improve the basic quality of diagnostics and treatment in the field; these tasks are as important as increasing the accessibility of MDT to the patients. It is time to replace wishful thinking with evidence-based practice, and discontinue the implementation of AMDT as a routine in the field. In addition, research should be encouraged to develop a fully supervisable, monthly-administered MDT regimen, all components of which are administered once monthly; such a regimen would greatly ease the task of supervision, and also reduce significantly the risk of emergence of rifampicin resistant leprosy resulting from non-adherence of patients to the self-administered, daily component of MDT.

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References


