

Management of patients after MDR-TB treatment failure

13.1 Chapter objectives

The objectives of this chapter are:

- To describe the clinical approach in suspected MDR-TB treatment failure.
- To discuss indications for suspending treatment for patients in whom a Category IV regimen has failed.
- To outline the supportive care options for patients in whom all the possibilities of MDR-TB treatment have failed.

13.2 Assessment of patients at risk for failure

Patients who do not show signs of improvement after four months of treatment are at risk for treatment failure. In all patients who show clinical, radiographical or bacteriological evidence of progressive active disease, or reappearance of disease after month 4 of treatment, should be considered as being at high risk for treatment failure.

The following steps are recommended in such patients:

- The treatment card should be reviewed to confirm that the patient has adhered to treatment.
- The treatment regimen should be reviewed in relation to medical history, contacts and all DST reports. If the regimen is deemed inadequate, a new regimen should be designed.
- The bacteriological data should be reviewed. Often, the smear and culture data are the strongest evidence that a patient is not responding to therapy. One single positive culture in the presence of an otherwise good clinical response can be caused by a laboratory contaminant or error. In this case, subsequent cultures that are negative or in which the number of colonies is decreasing may help prove that the apparently positive result did not reflect treatment failure. Positive smears with negative cultures may be caused by the presence of dead bacilli and therefore may not indicate treatment failure. Repeated culture- and smear-negative results in a patient with clinical and radiographical deterioration may indicate that the patient has a disease other than MDR-TB.

- The health-care worker should confirm that the patient has taken all the prescribed medicines. A non-confrontational interview should be undertaken without the DOT worker present.
- A non-confrontational interview of the DOT worker alone should also be carried out. Questions should be asked to rule out the possible manipulation of the DOT worker by the patient. If manipulation is suspected, the DOT worker should be switched to another patient, and the patient with suspected treatment failure should be assigned to a new DOT worker.
- Other illnesses that may decrease absorption of medicines (e.g. chronic diarrhoea) or may result in immune suppression (e.g. HIV infection) should be excluded.
- If surgical resection is feasible, it should be considered.

MDR-TB treatment often consists of a treatment cycle; if no response is seen, reassessment of the regimen and treatment plan and formulation of a new plan of action are necessary. Patients who have persistent positive smears or cultures at month 4 but who are doing well clinically and radiographically may not require a regimen change. Whenever a regimen change is indicated because of treatment failure, a new regimen is started (with at least four effective drugs) and options for adjunctive treatment – most commonly surgery – can be considered. Adding one or two drugs to a failing regimen should be avoided. Changes in treatment can be made as early as 4–6 months if conversion is not seen and if there is clinical deterioration.

13.3 Indications for suspending treatment

It takes 3–4 months to evaluate whether a change in treatment plan has been effective. If the patient continues to deteriorate despite the measures described in the previous section, treatment failure should be considered. There is no single indicator to determine whether a treatment regimen is failing. Although there is no simple definition for treatment failure, there often comes a point during the treatment when it becomes clear that the patient is not going to improve. Signs indicating treatment failure include:

- persistent positive smears or cultures past month 8–10 of treatment;
- progressive extensive and bilateral lung disease on chest X-ray with no option for surgery;
- high-grade resistance with no option to add two additional agents;
- overall deteriorating clinical condition that usually includes weight loss and respiratory insufficiency.

It is not necessary for all of these signs to be present to identify failure of the treatment regimen. However, a cure is highly unlikely when they are all present.

The epidemiological definition of treatment failure for recording outcomes (see Chapter 4) is often different from that used in the process of suspending therapy in a patient when the therapy is failing. The epidemiological definition is an outcome to account for the patient in a treatment cohort analysis, while the clinical decision to suspend therapy is made after the clinical search for all other options has been exhausted and cure of the patient is considered to be highly unlikely.

13.4 Suspending therapy

Treatment can be considered to have failed and suspension of therapy is recommended in cases where the medical personnel involved are confident that all the drugs have been ingested and there is no possibility of adding other drugs or carrying out surgery.

There are two important considerations in suspending therapy or changing it to a supportive care regimen. The first is the patient's quality of life: the drugs used in MDR-TB treatment have significant adverse effects, and continuing them while the treatment is failing may cause additional suffering. The second is the public health concern: continuing a treatment that is failing can amplify resistance in the patient's strain, resulting in resistance to all known antituberculosis drugs; the "super-resistant" strain may cause subsequent infection of others.

13.5 Approach to suspending therapy

The approach to suspending therapy should start with discussions among the clinical team, including all physicians, nurses and DOT workers involved in the patient's care. Once the clinical team decides that treatment should be suspended, a clear plan should be prepared for approaching the patient and the family. This process usually requires a number of visits and takes place over several weeks. Home visits during the process offer an excellent opportunity to talk with family members and the patient in a familiar environment. It is not recommended to suspend therapy before the patient understands and accepts the reasons to do so, and agrees with the supportive care offered.

13.6 Supportive care for patients in whom all the possibilities of MDR-TB treatment have failed

A number of supportive measures can be used once the therapy has been suspended. It is very important that medical visits continue and that the patient is not abandoned. The supportive measures are described in detail in the Integrated Management of Adolescent and Adult Illness guidelines produced by WHO in a booklet titled *Palliative care: symptom management and end-of-life care (1)*. The supportive measures are summarized in Box 13.1.

BOX 13.1**End-of-life supportive measures**

- **Pain control and symptom relief.** Paracetamol, or codeine with paracetamol, gives relief from moderate pain. Codeine also helps control cough. Other cough suppressants can be added. If possible, stronger analgesics, including morphine, should be used when appropriate to keep the patient adequately comfortable.
- **Relief of respiratory insufficiency.** Oxygen can be used to alleviate shortness of breath. Morphine also provides significant relief from respiratory insufficiency and should be offered if available.
- **Nutritional support.** Small and frequent meals are often best for a person at the end of life. It should be accepted that the intake will reduce as the patient's condition deteriorates and during end-of-life care. Nausea and vomiting or any other conditions that interfere with nutritional support should be treated.
- **Regular medical visits.** When therapy stops, regular visits by the treating physician and support team should not be discontinued.
- **Continuation of ancillary medicines.** All necessary ancillary medications should be continued as needed. Depression and anxiety, if present, should be addressed.
- **Hospitalization, hospice care or nursing home care.** Having a patient die at home can be difficult for the family. Hospice-like care should be offered to families who want to keep the patient at home. Inpatient end-of-life care should be available to those for whom home care is not available.
- **Preventive measures.** Oral care, prevention of bedsores, bathing and prevention of muscle contractures are indicated in all patients. Regular scheduled movement of the bedridden patient is very important.
- **Infection control measures.** The patient who is taken off antituberculosis treatment because of failure often remains infectious for long periods of time. Infection control measures should be continued (see Chapter 15).

13.7 Conclusion

Suspension of therapy should be considered only after all other options for treatment have been explored. Suspending therapy in a patient who has failed MDR-TB treatment is a delicate situation and difficult for family members and caregivers; but it is especially difficult for the patient as treatment is often viewed as his or her only hope. Strong support, care and sympathy must be given to the patient and family.

Reference

Palliative care: symptom management and end-of-life care. Geneva, World Health Organization, 2004 (WHO/CDS/IMAI/2004.4).