

Tuberculosis

care and control in refugee and displaced populations

An interagency field manual
Second edition

Tuberculosis care and control in refugee and displaced populations

An interagency field manual – 2nd edition



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TUBERCULOSIS CARE AND CONTROL IN REFUGEE AND DISPLACED POPULATIONS

An interagency field manual

SECOND EDITION

Edited by M.A. Connolly, M. Gayer and S. Ottmani

STOP TB DEPARTMENT AND DISEASE CONTROL
IN HUMANITARIAN EMERGENCIES PROGRAMME
WORLD HEALTH ORGANIZATION

OFFICE OF THE UNITED NATIONS HIGH COMMISSIONER FOR REFUGEES



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CONTENTS

| | |
|---|-----------|
| Acknowledgements | vi |
| Abbreviations | vii |
| Foreword to the second edition | viii |
| Executive summary | x |
| Glossary | xii |
| 1. Introduction..... | 1 |
| 1.1 Global burden of TB | 1 |
| 1.2 Natural history of TB | 1 |
| 1.3 TB in refugee and displaced populations | 2 |
| 1.4 HIV/TB | 4 |
| 1.5 Multidrug-resistant TB | 6 |
| 2. Implementation of TB programmes | 10 |
| 2.1 Criteria for implementation | 10 |
| 2.2 Steps in implementation | 10 |
| 2.3 Training | 12 |
| 2.4 Supply of drugs, reagents and equipment | 14 |
| 2.5 Financial management | 14 |
| 3. Management of TB in adults | 16 |
| 3.1 Diagnosis of TB in adults | 16 |
| 3.2 Treatment aims and definitions | 22 |
| 3.3 Treatment regimens | 23 |
| 3.4 Treatment adherence | 29 |
| 3.5 Patient management | 30 |
| 3.6 TB and reproductive issues | 32 |
| 4. Management of TB in children | 33 |
| 4.1 Epidemiology | 33 |
| 4.2 Clinical presentation and diagnosis | 34 |
| 4.3 HIV and TB in children | 35 |
| 4.4 Management of childhood TB | 35 |
| 4.5 Management of childhood contacts of infectious adults | 37 |

| | |
|---|-----------|
| 5. Prevention of TB | 39 |
| 5.1 Key principles | 39 |
| 5.2 Health education | 40 |
| 6. Monitoring of TB programmes | 41 |
| 6.1 Recording and reporting | 41 |
| 6.2 Evaluation of the patient | 41 |
| 6.3 Outcome definitions | 42 |
| 6.4 Evaluation of laboratory activities | 42 |
| 6.5 Evaluation of TB programme performance | 43 |
| 7. Operational issues for TB programmes | 49 |
| 7.1 Contingency planning for TB programme interruptions | 49 |
| 7.2 Linking with the NTP and ensuring sustainability | 51 |
| 7.3 Expansion of TB programmes in refugee and displaced populations | 53 |
| 7.4 Transfers into a TB programme | 53 |
| 7.5 Repatriation and transfers out of the TB programme | 56 |
| 7.6 Private sector | 58 |
| 7.7 Special groups | 59 |
| 7.8 Building partnerships | 61 |
| 7.9 Phasing down/handover of TB programmes to the NTP | 63 |

| | | |
|--------------------|---|-----|
| Appendix 1 | The Stop TB Strategy | 64 |
| Appendix 2 | Roles of key agencies | 66 |
| Appendix 3 | Sample memorandum of understanding | 68 |
| Appendix 4 | Job descriptions and responsibilities of TB programme staff | 69 |
| Appendix 5 | Estimating drug requirements..... | 72 |
| Appendix 6 | Adverse effects of TB drugs..... | 80 |
| Appendix 7 | Laboratory requirements for sputum smear examinations | 81 |
| Appendix 8 | Estimating the quantity of forms, registers and health education materials | 89 |
| Appendix 9 | Supervisor's checklist | 90 |
| Appendix 10 | Health education messages | 93 |
| Appendix 11 | TB care and control after natural disasters | 95 |
| | Bibliography and resources | 98 |
| | Web sites | 100 |
| | Additional references | 101 |

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ABBREVIATIONS

| | |
|---------------|---|
| ART | antiretroviral therapy |
| BCG | bacille Calmette-Guérin (vaccine) |
| DOTS | The internationally recommended strategy for TB control until 2005, and the foundation of the new Stop TB Strategy introduced in 2006 |
| DST | drug susceptibility testing |
| FDC | fixed-dose combination drug |
| GLC | Green Light Committee |
| HIV | human immunodeficiency virus |
| IDP | internally displaced person |
| IPT | isoniazid preventive therapy |
| IUATLD | International Union Against Tuberculosis and Lung Disease |
| MDR-TB | multidrug-resistant TB |
| MOH | ministry of health |
| NGO | nongovernmental organization |
| NTP | national TB control programme |
| PPD | purified protein derivative |
| PTB | pulmonary tuberculosis |
| TB | tuberculosis |
| TST | tuberculin skin test |
| TU | tuberculin unit |
| UNHCR | Office of the United Nations High Commissioner for Refugees |
| VCT | voluntary counselling and testing (for HIV infection) |
| WFP | World Food Programme |
| WHO | World Health Organization |
| XDR-TB | extensively drug-resistant TB |

FOREWORD TO THE SECOND EDITION

Tuberculosis (TB) is a major global public health problem that causes more than 1.5 million deaths annually. The incidence of TB worldwide has increased by 1% over the past years. Coinfection with the human immunodeficiency virus (HIV) is an important contributing factor in many countries, mainly those of sub-Saharan Africa. Today, caring for TB patients and controlling the spread of TB are complicated by the emergence of multidrug-resistant TB (MDR-TB) and, to some extent, extensively drug-resistant TB in many countries, particularly those of the former Soviet Union. However, substantial progress has been made in the implementation of effective TB programmes in a growing number of countries worldwide.

Refugees and internally displaced persons (IDPs) are at increased risk of developing TB and of poor access to TB care and control services. Conflict is the most common cause of large population displacement, which often results in relocation to temporary settlements (e.g. camps). Factors including malnutrition and overcrowding in camp settings further increase the vulnerability of these populations. Health care is provided mainly by humanitarian agencies, including nongovernmental organizations (NGOs), often under United Nations coordination where a ministry of health (MOH) may not be in place. As a result, NGOs are crucial implementing partners for TB care and control in these populations. In countries where a national TB control programme (NTP) run by the MOH is in place, it is important that NGOs link up with the NTP to implement the same policies. In this manual, the term TB programme is used to describe TB care and control activities provided by NGOs to refugee and displaced populations, whereas the term NTP refers to MOH-led activities.

Natural disasters can also lead to large population displacement, although the displacement is often of much shorter duration and the implementation of health care programmes by NGOs is consequently based on a shorter time frame. In this setting, the role of NGOs would be to support the NTP in the affected country.

In order to provide guidance to humanitarian agencies (e.g. NGOs) on the implementation of effective TB programmes for refugee and displaced populations, the World Health Organization (WHO) and the Office of the High Commissioner for Refugees (UNHCR) have collaborated to produce this manual. The implementation of a TB programme is an important component of health care services for refugees and IDPs once basic primary health care services are in place. The aim of this manual is to increase implementation of TB programmes in refugee and displaced populations wherever possible, while ensuring that these programmes meet accepted standards of quality and outcome. Despite the challenges of these settings, experience over the past 10 years in the implementation of TB programmes for refugee and displaced populations has shown that TB can be effectively diagnosed and treated among these vulnerable populations. For instance, in 2005, the WHO global target to control TB (70% case detection and 85% treatment success) was reached in Somalia, where civil war has been ongoing for more than 15 years.

The principles of TB care and control set out in this document are based on the Stop TB Strategy, formerly known as the DOTS strategy. The application of these principles to refugee and IDP settings comprises much of the purpose and the content of this document. Operational issues specific to such settings, such as criteria for implementing and for discontinuing TB care and control activities, cross-border coordination, contingency planning for interruptions to programme implementation, repatriation, transfers in/out and phasing down of a TB programme, are addressed.

There have been a number of developments since the first edition in 1997, including the introduction of the new Stop TB Strategy in 2006. The sections on HIV and MDR-TB have been expanded and updated to reflect developments in this area. There is a new chapter on operational issues for TB programmes that outlines scenarios encountered specifically in refugee/IDP settings. The sections on drugs and therapeutic regimens have been updated to reflect the move to using fixed-dose combination drugs. The appendices include tools, including cross-border transfer forms, which have been used in a wide variety of refugee/IDP settings. There is also a new appendix on TB care and control following natural disasters.

It is hoped that this manual will encourage humanitarian agencies to increasingly take up the challenge of implementing TB programmes in refugee/IDP settings and provide crucial care for this treatable disease.

EXECUTIVE SUMMARY

This manual is intended to inform humanitarian agencies, including nongovernmental organizations, United Nations organizations and donors, of the issues relating to the care of patients with tuberculosis (TB) and controlling the spread of the disease in refugee and displaced populations. The manual will serve as a tool for health coordinators at the field level for the implementation, monitoring and evaluation of TB programmes in these settings. The main targets are those agencies providing health care to refugee and displaced populations, ministries of health or United Nations organizations coordinating these services and donor agencies providing financial support.

Recent field experience has demonstrated that a TB programme can be implemented effectively and produce good treatment outcomes, in appropriately chosen refugee and displaced population settings. TB care and control are not a priority in the acute phase of an emergency when mortality rates are high due to acute respiratory infections, diarrhoeal diseases, measles, malaria in endemic areas, and malnutrition. The priorities during this phase are the provision of adequate food, water, shelter, sanitation and basic drugs and the control of common acute communicable diseases. A TB programme should not be initiated until death rates have been reduced to less than 1 per 10 000 population per day, basic needs are provided, and essential clinical services and supplies are available.

A TB programme should be implemented only if the security situation is sufficiently stable to enable implementation of activities and if no major movements of the camp or the population served are anticipated in the near future. At a minimum, programme funding should be sufficient to enrol patients for 12 months and complete the treatment of all members of this cohort—a minimum of 18 months.

Whenever possible, the national TB control programme (NTP) of the host country should be involved in the development of the TB programme. The policies of the NTP in the country of origin should also be taken into consideration if refugees are likely to be repatriated. Coordination with UNHCR in the planning stage is critical in order to minimize the risk of patients interrupting treatment when camps or populations are moved.

The priorities of a TB programme are first to identify and treat infectious TB patients with smear-positive pulmonary TB and those with severe forms of the disease. Cure of infectious patients is the most effective means of reducing TB transmission in the family and community. However, the impact of TB treatment on a population may be demonstrable only after a number of years of programme operation—longer than the likely span of many emergency programmes. TB treatment can be justified in these settings on the basis of the humanitarian benefit to individual patients. Once the programme is established, it is appropriate to treat as many other forms of TB as possible if resources permit.

The recommended strategy to control TB is the Stop TB Strategy (Appendix 1). This new strategy has six components, one of which ("pursuing high-quality DOTS expansion and enhancement") includes five basic key elements – the most relevant being for refugee and displaced populations:

- political commitment and sustained financing;
- case detection through quality-assured bacteriology;
- standardized short-course chemotherapy with supervision and patient support;
- an effective drug supply and management system;
- monitoring and evaluation system, and impact measurement.

Quality-controlled smear microscopy for TB diagnosis and treatment should be provided free of charge and integrated into the primary health care services for refugee and displaced populations.

Many refugees and displaced persons may come from, or seek refuge in, countries with a high prevalence of infection with human immunodeficiency virus (HIV). Hence TB/HIV coinfection may be prevalent in these populations. A high rate of HIV should be considered a factor increasing the priority of TB treatment and control. TB patients coinfecting with HIV respond well to standard TB treatment. TB and HIV programmes should therefore be closely coordinated.

Provision of food may be important in TB programmes in malnourished populations and can serve a useful function as an incentive, but food supplementation is not routinely necessary for successful TB treatment.

GLOSSARY

The definitions given below apply to the terms as used in this manual. They may have different meanings in other contexts.

Acid-fast bacilli (AFB)

Bacteria that do not lose their stain when exposed to acid or acid–alcohol mixture during the staining process, i.e. bacteria of the *Mycobacterium tuberculosis* complex and all non-tuberculous mycobacteria.

Annual risk of TB infection

The risk of an uninfected person becoming infected with the TB organism in a one-year period.

Bacille Calmette–Guérin (BCG)

A live vaccine against TB derived from an attenuated strain of *Mycobacterium bovis*, a species of the *M. tuberculosis* complex.

Case-fatality rate

The proportion of patients with a disease who die from the disease within a given period.

Chronic cases (re-treatment failures)

A patient with TB who is sputum smear- or culture-positive at the end of the fifth month or at the end of a standard re-treatment regimen with essential TB drugs and fully supervised. These patients are likely to harbour, and potentially to excrete, drug-resistant organisms.

Close contact

A person who has shared the same space in an enclosed environment (e.g. household or sleeping quarters) for a prolonged period with a person with active TB disease and who is therefore considered to be at risk of infection with *M. tuberculosis*.

Cohort analysis

An assessment of the treatment outcomes of all members of a group of patients who were diagnosed, registered and planned to have the same treatment. Analysis is usually carried out at a specified time (usually three months) after the last patient entered in the cohort was expected to have completed treatment.

Contact investigation

The process of identifying close contacts of index cases, for which public health measures (such as tuberculin skin testing or chest radiography) may be required.

Continuation phase of treatment

The second period of TB treatment, after the initial phase, when treatment is maintained with a reduced number of TB drugs.

Diagnosis of TB

The clinical activity of using any available method (clinical examination, personal history, bacteriology, radiology, histology, tuberculin test, analysis of cerebrospinal fluid in meningitis) to establish the diagnosis of pulmonary or extrapulmonary tuberculosis.

Directly-observed therapy

The administration of each dose of medication, such as swallowing TB tablets, observed by health staff or another designated, trained and monitored individual in the community.

Epidemic

The occurrence in a community of a number of cases of an illness that are clearly in excess of the expected number.

Extensively drug-resistant tuberculosis (XDR-TB)

Multidrug-resistant tuberculosis plus resistance to (i) any fluoroquinolone and (ii) at least one of three injectable second-line drugs (capreomycin, kanamycin and amikacin).

Haemoptysis

Cough productive of blood, or sputum containing blood.

Incidence

The number of new cases of a disease in a defined population during a specified period of time, e.g. TB incidence is usually reported as cases/100 000 population per year.

Initial (intensive) phase of treatment

The first period of TB treatment during which a combination of drugs is given to kill as many of the TB organisms as possible, as quickly as possible, for a period of 2–3 months.

Internally displaced person (IDP)

Persons sharing the characteristics of refugees (see below), but displaced within the boundaries of their own country.

Mycobacterium tuberculosis

The tubercle bacillus that is the most common causative infectious agent of TB disease in humans.

Refugee

A person who "owing to a well-founded fear of being persecuted for reasons of race, religion, nationality, membership of a particular social group, or political opinion, is outside the country of his nationality, and is unable to or, owing to such fear, is unwilling to avail himself of the protection of that country...". *UNHCR Convention relating to the Status of Refugees* (adopted on 28 July 1951 by the United Nations Conference of Plenipotentiaries on the Status of Refugees and Stateless Persons convened under General Assembly resolution 429 (V) of 14 December 1950; entry into force on 22 April 1954, in accordance with article 43).

Short-course chemotherapy

Treatment with TB drugs for 6 or 8 months' duration based on the combination of at least three major TB drugs: isoniazid, rifampicin and pyrazinamide.

Smear conversion rate

The proportion of treated patients who convert from sputum smear-positive to sputum smear-negative within a specified period of time, usually after 2 or 3 months of the initial phase of TB treatment.

Sputum smear examination

A laboratory technique in which sputum is smeared on glass slides and stained with an acid-fast stain, normally using the Ziehl–Neelsen method, and subsequently examined by microscopy for the presence of AFB.

Sputum smear-positive pulmonary TB*

either: a patient with at least two sputum specimens positive for AFB by microscopy;

or: a patient with at least one sputum specimen positive for AFB by microscopy and radiographic abnormalities consistent with pulmonary TB;

or: a patient with at least one sputum specimen positive for AFB by microscopy, plus sputum culture positive for *M. tuberculosis*.

Sputum smear-negative pulmonary TB*

either: a patient who fulfils all the following criteria:

- at least three sputum specimens negative for AFB on microscopy;
- radiographic abnormalities consistent with active pulmonary TB;
- no response to a course of a broad-spectrum antibiotics;
- a decision by a physician to treat with a full curative course of TB chemotherapy.

or: a patient who is severely ill and meets all of the following criteria:

- at least two sputum specimens negative for AFB by microscopy;
- radiographic abnormalities consistent with extensive pulmonary TB (interstitial or miliary);
- a decision by a physician to treat with a full curative course of TB chemotherapy.

or: a patient whose sputum smears were negative but in whom a positive sputum culture result is received subsequently.

TB case detection

The public health activity of identifying infectious cases of pulmonary TB, namely pulmonary TB cases excreting tubercule bacilli that can be detected by microscopy. The most important group for case detection includes adults attending health facilities for any reason and presenting with cough for more than two weeks.

* See Box 3 (page 20) for other possible definitions in HIV-prevalent and resource-constrained settings.

TB suspect

Any person who presents with symptoms (in particular a cough for more than two weeks) or signs (including radiological abnormalities) suggestive of tuberculosis. TB suspects may directly attend a health facility because of symptoms, or be identified during public health procedures such as screening of high-risk groups.

Tuberculin skin test (TST) or Mantoux test

A skin test to assess infection with the TB organism, whereby purified protein derivative (PPD) is injected intradermally to identify people who have been sensitized to mycobacterial antigens by infection with *M. tuberculosis*, non-tuberculous mycobacteria or vaccination with BCG.

Tuberculosis (TB)

The disease caused by infection with *M. tuberculosis*, the tubercle bacillus. TB can infect almost any tissue or organ but most commonly affects the lungs.

- **active TB:** tuberculosis disease associated with symptoms or signs, including findings on physical examination.
- **extrapulmonary TB:** tuberculosis of organs other than the lungs, including TB of the pleura, lymph nodes, abdomen, genitourinary tract, pericardium, skin, joints and bones, and meninges.
- **infectious TB:** active tuberculosis that is transmissible to others, i.e. contagious, usually determined by a positive sputum smear in case of pulmonary or laryngeal disease.
- **latent TB infection:** infection with *M. tuberculosis*, diagnosed by a positive TST or serum antigen-stimulated IFN- γ release assay without clinical evidence of disease.
- **multidrug-resistant TB (MDR-TB):** tuberculosis caused by strains of *M. tuberculosis* that are resistant to at least both isoniazid and rifampicin, two of the essential TB drugs.
- **pulmonary TB:** tuberculosis affecting the lung parenchyma.

Ziehl–Neelsen staining method

The standard laboratory method of staining TB smears. It involves staining a heat-fixed smear with an aqueous solution of a dye (usually basic fuchsin) containing chemicals (usually phenol) to help the dye penetrate into the cell, washing the smear with acid, alcohol or acid/alcohol and then counterstaining (usually with methylene blue).

1. INTRODUCTION

1.1 GLOBAL BURDEN OF TB

The World Health Organization (WHO) estimates that there were 8.8 million new cases of tuberculosis (TB) with 1.6 million deaths worldwide in 2005. These deaths comprise 25% of all avoidable adult deaths in developing countries. Some 95% of TB patients and 98% of TB deaths are in developing countries, where 75% of TB patients are in the most economically productive age group (15–50 years). After increasing at a rate of 1% per year over previous years, the TB incidence was stable or in decline in all six WHO regions in 2005. However, the total number of new TB cases is still rising slowly.

1.2 NATURAL HISTORY OF TB

WHO estimates that up to one third of the world's population is infected with *Mycobacterium tuberculosis*, the bacterium that causes TB. Once infected, a person stays infected for many years, probably for life.

People with active pulmonary TB are the source of TB infection. These people shed TB bacilli in the community. The route of transmission of TB bacilli is airborne through droplets produced by TB patients when they cough or sneeze. These droplets typically contain tubercle bacilli and usually evaporate, diminish in size, become droplet nuclei and remain suspended in the air for several hours. If inhaled, a droplet nucleus is small enough in size to reach an alveolus in the lung. A person who breathes in air including droplet nuclei containing tubercle bacilli may become infected with TB bacilli (Figure 1). Ventilation and ultraviolet light reduce the risk of transmission.

The vast majority (90%) of people who are infected with the TB organism do not develop active TB disease. In these healthy, asymptomatic individuals, the only evidence of infection is usually a positive tuberculin skin test (TST).

Infected people can develop active TB disease at any time. The risk of developing TB disease is high in the first few years following infection, then decreases for a prolonged period of time. Various physical or emotional stresses may trigger the progression of infection to disease, the most important being weakening of immune resistance, especially by HIV infection. TB can affect most tissues and organs, but it most commonly involves the lungs.

TB treatment can cure more than 90% of patients with drug-susceptible TB. Without treatment, approximately 50% of active pulmonary TB patients who are HIV-negative will be dead after 5 years (the death rate is commonly higher in HIV-positive patients), 25% will be healthy (self-cured by a strong immune defence) and 25% will remain ill with chronic, potentially infectious, TB.

1.3 TB IN REFUGEE AND DISPLACED POPULATIONS

The Office of the United Nations High Commissioner for Refugees (UNHCR) estimated the number of refugees, internally displaced persons (IDPs) and other people of concern to UNHCR to be more than 32 million in 2006. More than 85% of refugees originate from, and remain within, countries with high burdens of TB.

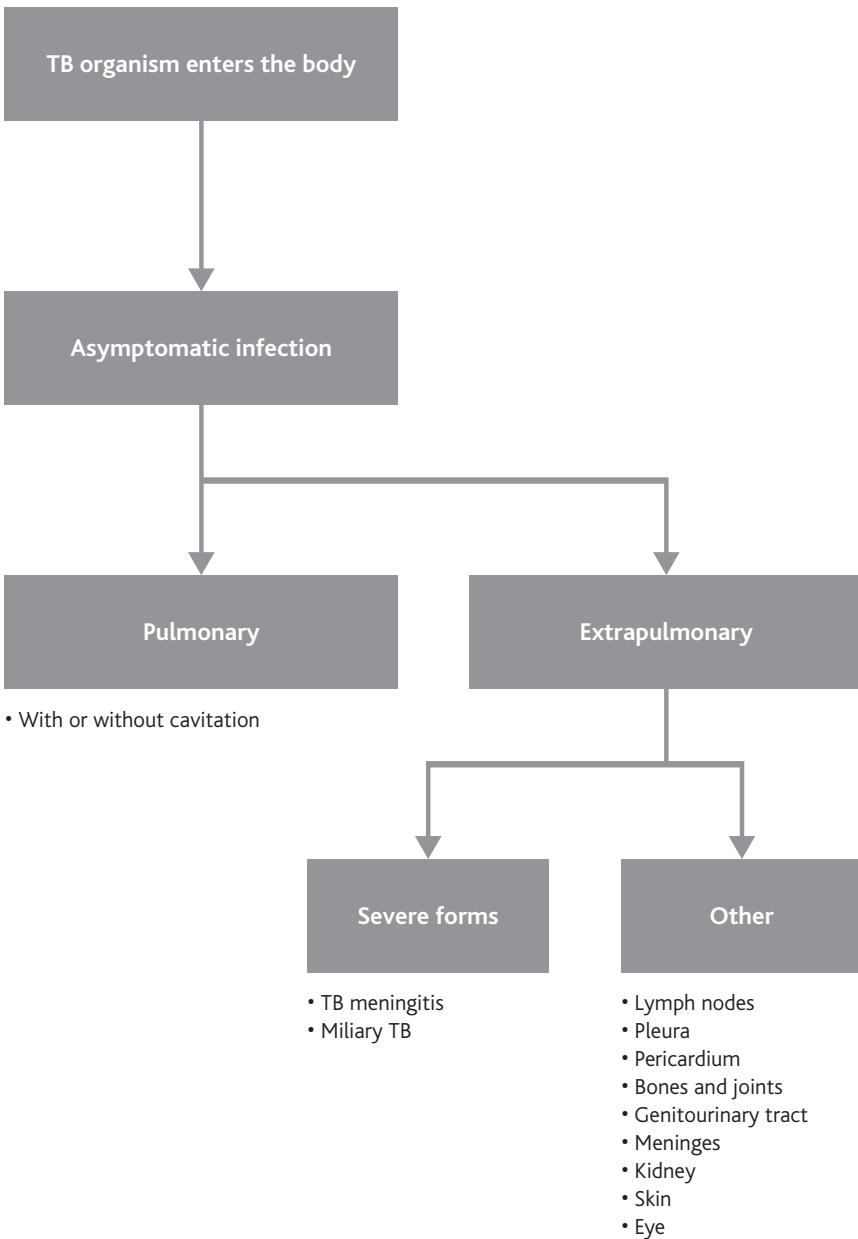
Refugees and displaced populations are at particularly high risk of developing TB. The crowded living conditions of these populations can facilitate the transmission of TB infection. Coexistent illness, particularly HIV and poor nutritional status, can also weaken their immune system and make them more vulnerable to developing active TB. TB is an increasingly important cause of morbidity and mortality among refugee and displaced populations.

SUDAN, KENYA, REPUBLIC OF INGUSHETIA

In 1985, 26% of deaths among adult refugees in Somalia and between 38–50% of all deaths among refugees in camps in eastern Sudan were attributed to TB.

In north-east Kenya in 1994, the incidence of new infectious TB patients in camps was four times the rate in the local population.

In Ingushetia in 2000, the TB notification rate for displaced Chechens was almost twice as high as the resident Ingush population.

Figure 1 Classification of TB

1.4 HIV/TB

Infection with HIV promotes the progression of recent and latent *M. tuberculosis* infection to active TB, and also increases the rate of recurrent TB. HIV infection is also the most potent factor known in promoting progression from infection to active TB disease. Approximately 10% of HIV-negative people with latent TB infection will progress to active TB disease over their **lifetime**; in comparison, up to 10% of HIV-positive people with latent TB infection will develop active TB disease **each year**.

TB is a leading cause of HIV-related morbidity and mortality particularly in resource-constrained settings. The rising incidence of TB in Africa, mainly attributed to HIV, is sufficient to offset the stable or falling TB incidence in most of the rest of the world. TB is among the leading cause of death among people infected with HIV worldwide. In some countries (particularly sub-Saharan Africa), up to 70% of TB patients are HIV coinfecting.

While the symptoms and signs of TB in patients coinfecting with HIV are generally similar to those in non-infected individuals, atypical clinical and radiological presentations are more common in immunosuppressed patients. The likelihood of sputum smear-negative pulmonary TB is higher among HIV-positive patients, which makes the diagnosis difficult. Studies show that the proportion of smear-negative pulmonary TB among people living with HIV/AIDS ranges between 30–60%. Similarly, extrapulmonary TB, particularly involving the lymph nodes and pleura, but also the pericardium and meninges, is more common among the HIV-infected. Although the diagnosis may be difficult among HIV-infected individuals, the treatment of TB is the same, and the cure rate of TB treatment is similar in HIV-coinfecting and HIV-negative patients. The likelihood of recurrence (including reinfection with a new organism) is somewhat higher in the HIV-infected. The case-fatality rate is substantially higher among the HIV coinfecting, the excess deaths resulting mainly from non-TB complications of HIV. Thioacetazone should be avoided in HIV-positive patients in whom severe, even life-threatening, adverse drug reactions occur much more frequently.

WHO has a recommended policy guidance on collaborative TB/HIV activities that targets the dual epidemics of TB and HIV. The policy recommends that HIV/AIDS and TB programmes (including those for refugees/IDPs) should create a mechanism to collaborate in order to promote patient-centred services among these populations (summarized in Box 1). Establishing a joint coordinating body, which works at all levels of the system dealing with refugees/IDPs at national, regional, district or local levels; equal or reasonable representation of the two programmes is important. A joint plan that defines the roles and responsibilities of each programme and resource allocation including deployment of sufficient human resources and increased capacity in health care delivery to implement collaborative TB/HIV activities among refugees should be developed. Intensified TB case-finding should be established in all settings offering voluntary HIV counselling and testing (VCT), AIDS care and treatment for refugees and IDPs. A referral system should be established between VCT, AIDS care and treatment, and TB diagnostic and treatment centres.

Box 1 Collaborative TB/HIV activities

1. Establish the mechanisms for collaboration

- Set up coordinating bodies for TB/HIV activities at all levels
- Conduct surveillance of HIV prevalence among TB patients
- Carry out joint TB/HIV planning
- Monitor and evaluate

2. Decrease the burden of TB in people living with HIV/AIDS

- Establish intensified TB case-finding
- Introduce isoniazid preventive therapy after excluding active TB
- Ensure control of TB infection in health care and congregate settings
- Ensure refugees and IDPs are included in national TB programmes, particularly when national drug requirements are being calculated, including isoniazid for preventive therapy

3. Decrease the burden of HIV in TB patients

- Provide HIV testing and counselling
- Introduce HIV prevention methods
- Introduce co-trimoxazole preventive therapy
- Ensure HIV/AIDS care and support
- Introduce antiretroviral therapy

All TB patients should be offered VCT and, if found positive, should receive appropriate HIV prevention, treatment and care services, including antiretroviral therapy (ART). Co-trimoxazole preventive therapy should be offered to eligible patients living with HIV/AIDS who have active TB. TB services (including in refugee centres) should incorporate comprehensive HIV prevention strategies for patients, targeting sexual, parenteral or vertical transmission, or should establish a referral linkage with HIV/AIDS services to do so. When active TB is safely excluded, people living with HIV/AIDS should receive isoniazid preventive therapy (IPT) as part of the package of care. Information about IPT should be made available to all people living with HIV/AIDS. Isoniazid should be given in a dose of 300 mg per day for 6 to 9 months.

A core set of indicators and data collection tools based on the WHO guidelines for monitoring and evaluation should be developed and data collected for monitoring and evaluation of collaborative TB/HIV activities.

Recently, there has been some progress in expanding access to ART among HIV-infected individuals in resource-poor countries. While refugees and displaced people are likely to be among the last groups to benefit from this therapy, there may be situations where refugees are already receiving ART or where an ART programme is implemented. Concurrent therapy with TB and antiretroviral drugs can be very complex, with potentially serious drug interactions between TB drugs (primarily rifampicin) and antiretroviral drugs. Some patients experience an initial clinical deterioration (immune reconstitution syndrome) with the initiation of ART. If concurrent treatment of the two diseases is considered, it is essential to seek expert advice regarding choice of ART regimens and other aspects of case management.

1.5 MULTIDRUG-RESISTANT TB

Drug resistance is a growing threat to TB care and control worldwide. Multidrug-resistant TB (MDR-TB) – defined as resistance to at least both rifampicin and isoniazid – poses a major challenge to TB control. MDR-TB is manmade, caused by inappropriate choice of drugs or inadequate support for adherence to treatment. Preventing the development of drug resistance through the maintenance of well-functioning TB programmes is the most critical element in the response to MDR-TB.

More than 400 000 MDR-TB cases emerge every year as a result of the misuse of TB drugs and of the transmission of drug-resistant strains. MDR cases are difficult to treat and costly to manage – drugs alone can cost US\$ 20 000 per treatment course. Mortality is usually very high in the presence of HIV coinfection. Poor management of MDR-TB is resulting in extensively drug-resistant TB (XDR-TB). XDR-TB is MDR-TB with resistance to any fluoroquinolone and at least one of the three injectable second-line drugs. It is almost impossible to cure in resource-poor settings. This variant of MDR-TB is now reported in several countries and has been associated with rapid death in those coinfecting with HIV in South Africa.

Accurate and timely diagnosis are the core components of MDR-TB case management. MDR-TB must be diagnosed correctly before it can be treated effectively. Quality-assured culture and drug susceptibility testing (DST) are indispensable. Internal quality control and external quality assurance should be in place, including a link for proficiency testing with a recognized reference laboratory. In many country settings with well-functioning TB programmes, DST is carried out only in patients with an increased risk for MDR-TB, such as patients in whom Category I or Category II regimens have failed.

The management of second-line TB drugs is complex, especially when individualized treatment regimens are used. The treatment strategy consists of a rational method for designing the optimal treatment regimen, a method to deliver this regimen under direct observation, and a plan for monitoring and managing adverse drug reactions. Treatment of MDR-TB takes up to 24 months, and success rates can be lower than in drug-susceptible TB.

Most of the second-line TB drugs are much more costly than first-line drugs. They are frequently changed because of side-effects, delayed DST results and poor response to treatment. Moreover, the management of MDR-TB cases requires a recording system with differently defined categories for patient registration, culture and DST results, and monitoring treatment delivery and treatment response for 24 months. Cohort analysis includes interim indicators and treatment outcomes after two or more years, and treatment outcomes by treatment regimen and DST results.

WHO and its partners created the Green Light Committee (GLC) in 2000 in response to the threat of MDR-TB. The GLC is a multi-institutional partnership that works to provide access to second-line TB drugs to patients in need while preventing the creation of resistance to these drugs, which are currently the *last* line of defence against TB. No other global mechanism apart from the GLC currently ensures the efficacy of available second-line TB drugs.

Evidence from pilot projects in Estonia, Latvia, Peru, the Philippines, and the Russian Federation, which are benefiting from the GLC mechanism, shows that the management of MDR-TB under programmatic conditions is feasible and cost-effective when implemented in the context of a well-functioning TB control programme and based on WHO MDR-TB management policy guidelines.

Given the complexity and cost of treating MDR-TB, the priority for nongovernmental organizations (NGOs) working with refugee and displaced populations is to ensure that the Stop TB Strategy using first-line TB drugs is effectively implemented. This will reduce the risk of MDR-TB and the need to use second-line TB drugs in these difficult situations.

AZERBAIJAN – TREATMENT OF MDR-TB IN NAGORNO KARABAKH

In Nagorno Karabakh, lack of regular drug supplies, unaffordable diagnosis and treatment, and inadequate case management followed the fall of the Soviet Union and the war between Armenia and Azerbaijan. In October 1997, a TB programme based on WHO–IUATLD protocols was implemented by an NGO. After 17 months, the rate of successful treatment outcome was 78% for new smear-positive cases, but among re-treatment cases there was a 25% combined failure/mortality rate. In March 2001, a decision was made to adapt treatment to individual DST.

Diagnosis

Sputum samples were collected in duplicate on CPC medium for all smear-positive patients, stored at 4 °C, and sent to the IMT Antwerp for first- and second-line DST by proportion method on Lowenstein–Jensen.

Treatment

All patients were started on standard Category I or II regimens according to treatment history. From March 2001, the treatment was adapted to the susceptibility pattern after receipt of the DST results.

MDR patients received individualized therapy with at least four drugs with proven sensitivity from among the following: kanamycin, capreomycin, ethionamide, ofloxacin, cycloserine and *p*-aminosalicylic acid granules, at maximal doses when possible; ethambutol was added if the DST results showed susceptibility.

- The intensive phase included an injectable agent for at least 6 months, or 6 months beyond the date of the initial negative culture if still culture-positive at month 3.
- The continuation phase included three known sensitive drugs, plus pyrazinamide, planned for a total of 24 months of therapy or at least 18 months of culture-negative status.
- Sputum smear, culture and liver or renal function tests were done monthly during the intensive phase and then every 3 months.
- Social aid (food, firewood, transportation costs) was provided and housing arranged for those in need during the continuation phase, as was patient education on TB-related topics.
- Other drug-resistant TB patients received adapted treatment schemes.

Results

From March 2001 to September 2002:

- in addition to 162 new TB cases and 17 re-treatment TB cases who were treated with standardized short-course chemotherapy, 15 MDR-TB cases and 36 other resistant cases were treated. Among these, the cure rate was 60% and 97% respectively.

RESOURCES

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2. IMPLEMENTATION OF TB PROGRAMMES

The objectives of a TB programme are to detect at least 70% of TB cases existing in the population and to cure at least 85% of them. Identifying and curing smear-positive pulmonary TB patients should be a priority.

2.1 CRITERIA FOR IMPLEMENTATION

The following **criteria** are essential before a decision is made to implement a TB programme for refugee and displaced populations:

- data from the refugee or displaced population indicate that TB is an important health problem;
- the emergency phase is over (death rates are <1 per 10 000 population per day);
- basic needs of water, adequate food, shelter and sanitation are met;
- essential clinical services and basic drugs for common illnesses are available;
- basic health services are accessible to a large part of the population so that TB suspects can be identified and appropriate investigation or referral arranged.

The **basis** of an effective TB programme is the Stop TB Strategy (see Appendix 1). In refugee and displaced populations, at least the following five key elements, included in the first and major component of this strategy, must be considered a priority:

- political commitment to TB control with sustained financing;
- case detection through quality-assured bacteriology;
- standardized treatment with supervision and patient support;
- an effective drug supply and management system;
- monitoring and evaluation system, and impact measurement.

2.2 STEPS IN IMPLEMENTATION

A number of steps are involved in the assessment, planning, initiation, implementation and monitoring of a TB programme in a refugee/IDP setting (see Figure 2).

The first step is to **assess the burden** of TB among the population. Data on incidence of TB in the country of origin of the affected population should be obtained. This may be supplemented by data from health care facilities providing basic health care to the affected population. Subsequently, the situation should be assessed to determine whether the initiation **criteria** for a TB programme have been met (see 2.1 above).

Establishment of **political commitment** at various levels of relevant leadership is critical. In addition, **awareness** should be **raised and support mobilized among both host and refugee/IDP populations**. Aside from broad support for the TB programme, specific objectives include support for treatment adherence and defaulter tracing and for measures to limit the availability of TB drugs outside the programme.

Programme planners should be familiar with the characteristics of the **NTP** – regimens used, programme results, and its potential contribution to and involvement in the development and implementation of the planned programme. Similarly, knowledge about the characteristics, such as regimens used, of the NTP of the country of origin of a refugee population would be important if the population had to be repatriated. Where possible, it is highly desirable to harmonize treatment regimens with those of the NTP to which patients might be transferred.

Secure **funding** must be identified. The usual minimum would be funding sufficient to admit patients for a 12-month period and to follow that cohort through to treatment completion—a total commitment of at least 18 months. Stopping a successful programme solely for lack of funds would be medically and ethically undesirable, so there should be an expectation of ongoing funding if the need for the programme persists and the programme is successful. A **budget and workplan** should be written.

It may be useful to explore other **links with the health system** in the host country if a refugee population is being served. In some cases, the host country may have X-ray facilities and other specialized resources and could function as a referral centre for the TB programme. In other circumstances, a host country population in the area of a refugee camp might not have access to TB treatment, a potential source of discord if TB care is available to the refugees. In that case, it may be appropriate to include the local population in the programme and provide support for local facilities.

One **lead agency** must be identified as taking responsibility for oversight of the TB programme. In addition, it is recommended that a TB coordinator be identified for per 50 000 population served.

A **memorandum of understanding** must be developed (see Appendix 2) by the TB programme coordinator (e.g. from an NGO) with the lead health agency (e.g. ministry of health (MOH), WHO or UNHCR). Where UNHCR is the coordinating agency, close collaboration is critical to ensure completion of therapy in the event of repatriation or population movement.

Staffing requirements must be estimated, job descriptions developed, staff recruited, training needs assessed and the costs and logistics of training estimated.

Any need for **patient accommodation** must be determined and plans made to house a small number of very ill patients. In some settings, a larger group of patients may need to be housed in order to receive treatment because of distance to the treatment centre or other reasons.

Existing **laboratory** resources – human and material – should be assessed to determine equipment needs and staff and training requirements, and be costed. A source for quality control must also be determined.

A **recording system** must be established based on the Stop TB Strategy template, and the appropriate forms and registers obtained.

Monitoring and evaluation of the programme must be ensured and regular supervisory visits should be planned, if possible with NTP counterparts.

A **simple, locally-adapted protocol** for implementation of the TB programme should be developed through consultation with the agency or agencies involved in TB care. The protocol should include steps in management of a patient with suspected TB, diagnostic algorithms, TB treatment categories and drug regimens, in line with the Stop TB Strategy. Consideration should be given to the regimen of the host NTP and the country of origin if the population concerned is refugees. The recording and reporting system as well as that for monitoring and evaluation must also be incorporated.

The protocol should also include the management of drug stocks in order to prevent TB drugs being taken and circulated freely in the community, and contingency plans for episodes of insecurity, unexpected movement of the camp or population, and repatriation or transfers to another programme. These must address the care of patients in such circumstances; arrangements should be made in advance with the anticipated programme of destination, whether in the same or another country, and with UNHCR, to ensure treatment completion. Copies of this local protocol should be available in all treatment facilities.

KENYA

In 1992, in the north-eastern part of Kenya, an influx of refugees from Somalia attending the local TB treatment centres led to the near collapse of these services. As a result, the National Leprosy and TB Programme developed guidelines for the diagnosis and treatment of refugees with TB inside the camps based on its existing practices. Voluntary workers from the refugee community supported by NGO and MOH staff supervised patients taking their drugs daily during the 7 months of treatment. UNHCR ensured that funds and drugs were continuously available.

2.3 TRAINING

Training is one of the key elements of a successful TB programme. All staff involved in the programme require basic knowledge of TB, its diagnosis, appropriate treatment and monitoring. Training must be conducted by people who are themselves well-trained in TB care and control through the Stop TB Strategy. The NTP, WHO and NGOs dealing with TB care and control may be sources of such trainers.

Health staff who have worked in TB care and control in their countries of origin may be found among the refugee or displaced population. These persons may be able to provide useful background information on community knowledge and cultural beliefs, as well as on treatment regimens and practices used previously. They can also be potential members of the programme staff.

All health care workers providing services to refugees or displaced populations should be familiar with the function of the TB programme and the need to identify and refer TB suspects for sputum smear examination. A critical element of training is to educate and raise the awareness of *primary health care workers* who will be the first contact of most TB patients, and on whom therefore, diagnosis and case-finding depend. They must be knowledgeable about the symptoms and signs suggestive of TB, particularly cough of long duration (more than 2 weeks), the need for sputum examination and the process for arranging sputum examination and subsequent follow up.

Laboratory staff will require training – even if already skilled in acid-fast bacilli (AFB) smear microscopy – in programme operation, the quality control process and record management.

Staff training should occur locally where possible, using existing materials, e.g. from the host country or country of origin, adapted to local settings. WHO has published detailed training modules. Appendix 4 provides job descriptions. The topics covered should include the following:

- transmission of TB,
- clinical signs and symptoms of TB,
- diagnosis of TB, including collection of sputum samples and the role of the laboratory,
- treatment of TB, including regimen categories, dosages and drug side-effects,
- patient education and follow up,
- contact investigation,
- management of a TB clinic,
- record keeping and management of medical supplies (especially drugs and laboratory reagents),
- community education,
- monitoring and evaluation.

The training of health workers should result in provision of services for TB care in line with the *International standards for tuberculosis care*.

2.4 SUPPLY OF DRUGS, REAGENTS AND EQUIPMENT

Required steps:

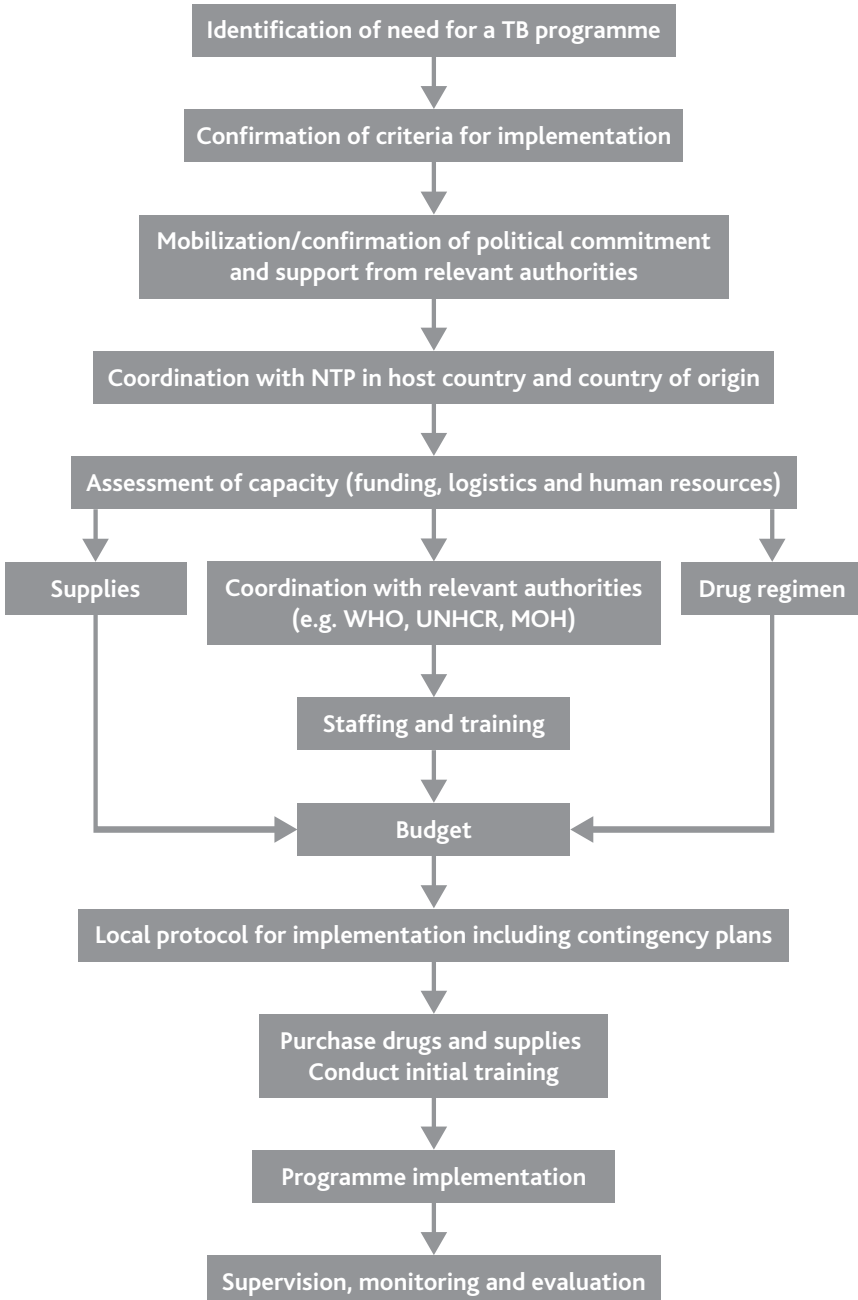
- Identify the responsible officer for procurement of drugs and materials.
- Estimate the numbers of patients requiring TB treatment in the first year (plus 6 months' reserve stock) (see Appendix 5).
- Identify potential suppliers and the costs.
- Estimate the cost of freight, insurance, customs duties or taxes.
- Estimate the time from placing the order to the arrival of drugs at the central store.
- Prepare a budget for the cost of drugs, laboratory supplies and other requirements including shipping and related costs.
- Find suitable, secure, storage facilities.
- Purchase the drugs and supplies.
- Monitor usage and recording through periodic store inspections.

2.5 FINANCIAL MANAGEMENT

The following items must be included in the budget estimates:

- health staff salaries,
- drugs and other medical supplies,
- laboratory equipment and reagents,
- stationery and other clinic needs,
- training costs,
- transport of staff and supplies,
- physical infrastructure including housing for patients,
- generator and fuel (if not already in place).

Figure 2 Key steps in implementation of a TB programme in refugee and displaced populations



3. MANAGEMENT OF TB IN ADULTS

3.1 DIAGNOSIS OF TB IN ADULTS

The management of TB should conform to the *International standards for tuberculosis care*.

The most important symptom in the identification of TB suspects in adults (over 15 years of age) is:

- cough of long duration (more than 2 weeks).

Patients with TB may also have other symptoms or signs such as:

- significant weight loss
- fever or night sweats
- haemoptysis
- chest pain
- breathlessness
- tiredness
- loss of appetite.

In refugee and displaced populations, the priority of the TB programme is to detect smear-positive pulmonary TB cases using sputum microscopy, and to cure them. Smear-positive patients are the main source of TB infection in communities. The diagnosis of TB is more accurate in this group than in smear-negative TB cases.

Each TB suspect should have three sputum samples examined by light microscopy. An early morning sputum sample is more likely to contain TB organisms than a sample produced later in the day.

In practice, each TB patient should provide three sputum samples during a two-day period ("spot–morning–spot"):

• **Day 1**

Sample 1 – The patient provides an "on-the-spot" sample in a container under supervision on presentation to the health facility. He or she is then given a labelled sputum container to take home for an early morning sample the following morning.

• **Day 2**

Sample 2 – The patient brings to the health facility an early morning sputum sample collected upon awakening.

Sample 3 – The patient provides another "on-the-spot" sample at the health facility when he/she brings sample 2.

Smears should be stained using the Ziehl–Neelsen method. Any patient suspected of TB with two positive smears is a TB patient who must then be registered as smear-positive pulmonary TB case and commenced on TB treatment.

If the initial three smears are negative, but pulmonary TB is still suspected because of persistent symptoms, the suspect should be given broad-spectrum antibiotics (e.g. amoxicillin or co-trimoxazole, **but not rifampicin or a quinolone antibiotic**), to treat bacterial respiratory infection, for at least one week. If symptoms persist after antibiotic treatment, the patient should be re-examined by sputum smear microscopy of three new samples as described above. Patients should also be assessed for other causes of cough – e.g. asthma or chronic lung diseases such as bronchiectasis – and for the response to any therapy directed at those problems. Box 2 shows the criteria for diagnosis of sputum smear-positive and sputum smear-negative pulmonary TB.

Pulmonary TB refers to disease involving the lung parenchyma. Tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion without lung involvement is a case of extrapulmonary TB. A patient with both pulmonary and extrapulmonary TB should be classified as a case of pulmonary TB.

PULMONARY TB, SMEAR-POSITIVE

Smear-positive pulmonary TB cases represent at least 65% of the total number of pulmonary TB cases in adults, and 50% or more of all TB cases when microscopy laboratory services are available and appropriately carried out, and diagnostic criteria are properly applied. Note that these proportions may be lower in populations with high HIV incidence.

Additional cases of TB may be found among close contacts of known active pulmonary TB cases – family members or people sleeping in the same quarters. New patients should be routinely questioned about the presence of symptomatic individuals in their homes or families. Symptomatic contacts should be screened for TB as described above – a relatively efficient means of case-finding.

PULMONARY TB, SMEAR-NEGATIVE AND EXTRAPULMONARY TB

In the absence of TB culture, even with access to X-ray facilities, the diagnosis of **smear-negative pulmonary TB** is unavoidably imprecise. Without the use of chest radiography, a diagnosis of smear-negative pulmonary TB is likely to be even less specific. In refugee situations, it is common not to have ready access to X-ray facilities, but it may be possible to refer patients for X-rays or other hospital services. While a chest X-ray cannot diagnose TB, typical radiological findings can suggest a diagnosis of TB. A normal X-ray, typical findings of another disease or the absence of findings compatible with TB, make a diagnosis of TB unlikely. Characteristic X-ray findings as read by an experienced physician, in the presence of symptoms consistent with TB and in the absence of a likely alternative diagnosis, may suffice to establish a diagnosis of smear-negative pulmonary TB. In the complete absence of radiography, a clinical judgement must be made by a medical officer. Figure 3 provides a standardized management plan for suspected TB patients.

Once a TB programme has been established, cases of **extrapulmonary TB** should also be treated. Extrapulmonary TB refers to TB of organs other than the lungs, e.g. pleura, lymph nodes, abdomen, genitourinary tract, skin, etc. Diagnosis should be based on, whenever possible, one culture-positive specimen or histological evidence or on strong evidence consistent with active extrapulmonary TB followed by a decision made by a clinician to treat with a full course of TB chemotherapy.

Some cases of extrapulmonary TB may be easy to identify:

- chronic enlargement of lymph nodes, usually cervical, particularly when there is spontaneous progression to sinus formation.

Other cases are usually suspected, and should be referred to a hospital if possible:

- for urgent assessment, definitive diagnosis and care, e.g. suspected severe, life-threatening forms, such as miliary TB or TB meningitis;
- for further investigation such as X-ray, ultrasound or biopsy in case of suspected TB pericarditis, osteoarticular TB (including suspected vertebral TB), TB peritonitis, or renal TB.

Severity of TB disease. Bacillary load, extent of disease and anatomical site are considerations in determining the severity of TB disease and therefore in selecting the appropriate treatment. Involvement of an anatomical site results in classification as severe disease if there is a significant acute threat to life (e.g. pericardial TB), a risk of subsequent severe handicap (e.g. spinal TB) or both (e.g. meningeal TB). Miliary, disseminated TB is considered to be severe. The following forms of extrapulmonary TB are classified as severe: meningeal, pericardial, peritoneal, bilateral or extensive pleural effusion, spinal, intestinal, genitourinary. Lymph node, pleural effusion (unilateral), bone (excluding spine), peripheral joint and skin TB are classified as less severe.

Box 2 Criteria for diagnosis of sputum smear-positive and sputum smear-negative pulmonary TB in adults**Pulmonary TB, sputum smear-positive**

either: a patient with at least two sputum specimens positive for AFB by microscopy;

or: a patient with at least one sputum specimen positive for AFB by microscopy and radiographic abnormalities consistent with active pulmonary TB as determined by a clinician;

or: a patient with at least one sputum specimen positive for AFB by microscopy, which is culture positive for *M. tuberculosis*.

Pulmonary TB, sputum smear-negative

either: a patient who fulfils all the following criteria:

- at least three sputum specimens negative for AFB on microscopy
- radiographic abnormalities consistent with active pulmonary TB*
- no clinical response to a course of broad-spectrum antibiotics
- decision by a medical officer to treat with full course of TB chemotherapy.

or: a patient who fulfils **all** the following criteria:

- severely ill
- at least two sputum specimens negative for AFB by microscopy
- radiographic abnormalities consistent with extensive pulmonary TB (interstitial or miliary),* and
- decision by a medical officer to treat with full course of TB chemotherapy.

or: a patient whose sputum smears were negative but whose sputum culture result is positive.

This group includes cases without smear result, which should be exceptional in adults but is relatively more frequent in children.

* In the complete absence of radiography, a clinical judgement must be made by a medical officer

Box 3 Revised WHO recommendations for diagnosis of TB in HIV-prevalent and resource-constrained settings

Pulmonary TB, smear-positive

One sputum smear examination positive for acid-fast bacilli (AFB) **and**
Laboratory confirmation of HIV infection or
Strong clinical evidence of HIV infection.*

If there is no laboratory confirmation of HIV infection or if the patient has no strong clinical evidence of HIV infection, the criteria to establish diagnosis of smear-positive pulmonary TB presented in Box 2 should be used.

Pulmonary TB, smear-negative

At least two sputum specimens negative for AFB **and**;
Radiographical abnormalities consistent with active TB **and**
Laboratory confirmation of HIV infection **or**
Strong clinical evidence of HIV infection* **and**

Decision by a clinician to treat with a full course of anti-TB chemotherapy

If there is no laboratory confirmation of HIV infection or if the patient has no strong clinical evidence of HIV infection, the criteria to established diagnosis of smear-negative pulmonary TB presented in Box 2 should be used.

Extrapulmonary TB

The criteria for diagnosis of extrapulmonary TB are:

One specimen from an extrapulmonary site culture-positive for *Mycobacterium tuberculosis* or smear-positive for AFB

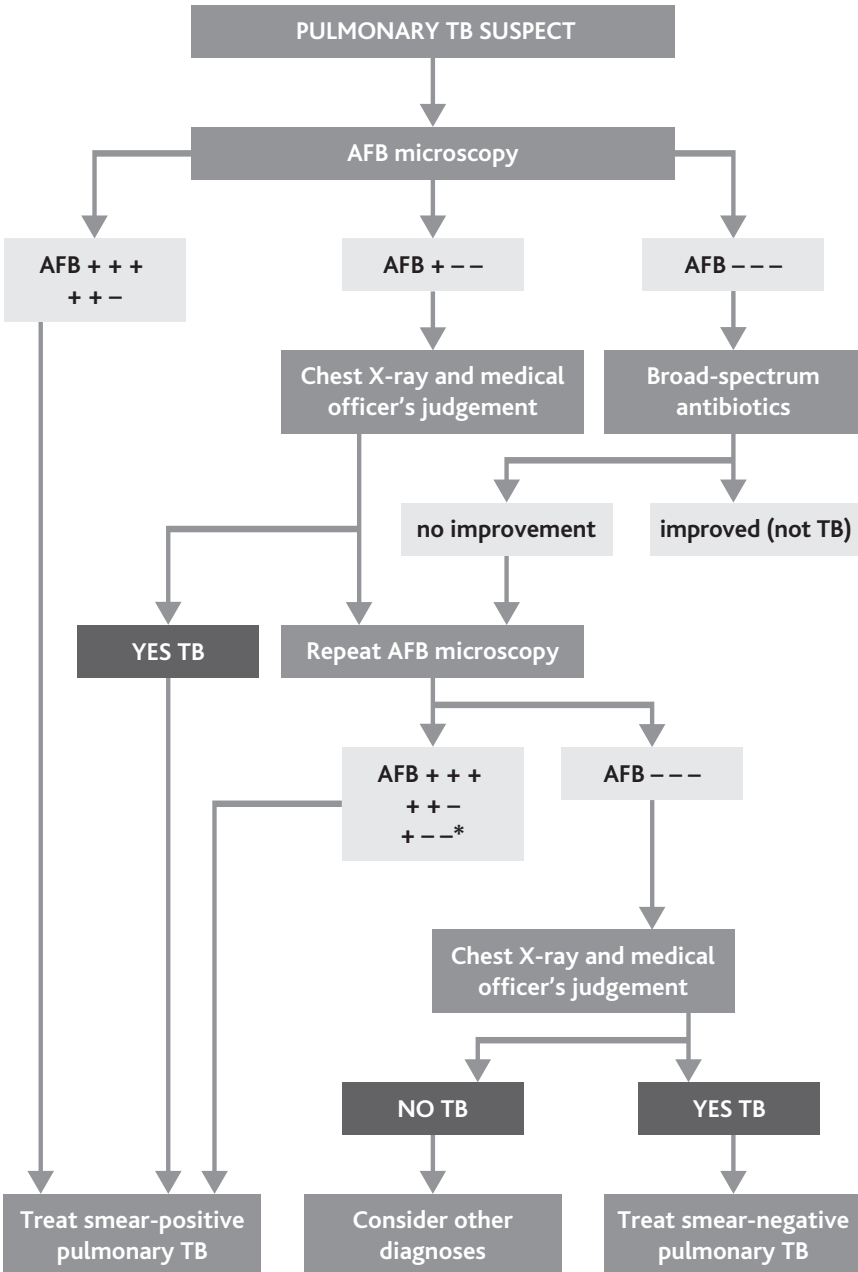
or

Histological or strong clinical evidence consistent with active extrapulmonary TB and

A decision by a clinician to treat with a full course of anti-TB chemotherapy.

These criteria are used whether or not the patient has laboratory confirmation of HIV as well as whether or not the patient presents strong clinical evidence of HIV.*

*Depending on clinical assessment and national and/or local policy, a person of unknown HIV status may be classified as HIV-positive for the purposes of diagnosis and management.

Figure 3 Standardized management plan for suspected TB cases^a

^a Adapted from *Treatment of tuberculosis. Guidelines for national programmes*, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).

* If AFB negative and then one + on repeat microscopy, reassessment by medical officer and/or chest X-ray should be done.

DEMOCRATIC REPUBLIC OF THE CONGO (FORMER ZAIRE) – GOMA

In 1994, 750 000 Rwandan refugees arrived in Goma, and four camps were established in the Kivu Region. In coordination with the Zairian NTP, TB programmes were implemented in the refugee camps in 1995. Smear-positive cases represented 91% of pulmonary TB cases and 72% of all TB cases.

Of the 357 new smear-positive TB patients registered, the cure + treatment completion rate was 71%, 13% died, 8% defaulted and 6% transferred out. The high death rate was related to the high prevalence of HIV, the estimated HIV prevalence among the TB patients was 60%.

3.2 TREATMENT AIMS AND DEFINITIONS

The aims of TB treatment are:

- to cure the patient of TB;
- to prevent death from TB or its late effects;
- to prevent relapse of TB;
- to decrease transmission of TB to others;
- to prevent the development of acquired drug resistance.

It is vital to achieve these aims while preventing the selection of resistant bacilli in infectious patients.

In order to prescribe appropriate treatment, a case should be defined according to whether or not the patient has previously received treatment for TB. Once the diagnosis is made, and before beginning treatment, **every patient must be questioned carefully about whether or not they have ever taken TB drugs before**. This distinction is also essential for epidemiological monitoring of the TB epidemic at regional and country levels.

The patient should be classified according to the following criteria:

- site of disease (pulmonary or extrapulmonary),
- bacteriological status (sputum smear-positive or not), and
- history of TB treatment (new or previously treated).

The following definitions are used:

- **New.** A patient who has never had treatment for TB or who has taken TB drugs for less than one month.
- **Relapse.** A patient previously treated for TB who has been declared cured or treatment completed, and is diagnosed with bacteriologically positive (smear or culture) TB.
- **Treatment after failure.** A patient who is started on a re-treatment regimen after having failed previous treatment.

- **Treatment after default.** A patient who returns to treatment, positive bacteriologically, following interruption of treatment for two consecutive months or more.
- **Transfer in.** A patient who has been transferred from another TB register to continue treatment.
- **Other.** All cases that do not fit the above definitions. This group includes chronic case, a patient who is sputum-positive at the end of a re-treatment regimen.

Note. Smear-negative pulmonary and extrapulmonary cases may also be relapses, failures, returns after default or chronic cases. This should, however, be a rare event, supported by pathological or bacteriological evidence (culture).

3.3 TREATMENT REGIMENS

The chemotherapeutic regimens are based on standardized combinations of five essential TB drugs:

- rifampicin
- isoniazid
- pyrazinamide
- ethambutol
- streptomycin.

Each of the standardized chemotherapeutic regimens¹ consists of two phases:

- An initial (intensive) phase. This phase lasts 2–3 months during which 3–5 drugs are given daily under direct observation to reduce the number of TB organisms to very low levels.
- A continuation phase. This phase lasts 4–6 months during which 2–3 drugs are given 3 times a week under direct observation or, in some cases (e.g. during repatriation of refugees), 2 drugs are given daily for 6 months unsupervised, in a fixed-dose combination form.

Actual swallowing of every dose of rifampicin-containing treatment must be directly observed by a health worker, or a trained and supervised community member.

¹ Regimens are written in short form with the number of months the medication is to be given in front of the letter and the doses per week written after the letter. If there is no number after the letter, a daily dosage is given (or 6 times per week, excluding, for instance, Sundays). The symbol "/" separates the different phases of the therapy, e.g. 2 RHZE / 4 H3R3 means that for the first 2 months of treatment rifampicin, isoniazid, pyrazinamide and ethambutol are given daily. This is followed by 4 months of rifampicin and isoniazid given regularly but each drug is given only 3 times per week.

FIXED-DOSE COMBINATION DRUGS

The use of fixed-dose combination drugs (FDCs) is strongly recommended as it eliminates the possibility of taking a single TB drug, and subsequently avoids TB monotherapy. This markedly reduces the risk of promoting resistance, particularly to rifampicin, the drug most critical to the success of short-course TB therapy. FDCs have other advantages over individual drugs. First, prescription errors are likely to be less frequent because dosage recommendations are more straightforward and adjustment of dosage according to patient weight is easier. Second, the number of tablets to ingest is smaller and may thus encourage patient adherence. Third, if treatment is not to be observed, patients cannot be selective in the choice of drugs to ingest.

However, FDCs also have disadvantages. First, if prescription errors do occur, excess dosage (risk to toxicity) or sub-inhibitory concentrations of all drugs (favouring development of drug resistance) may result. Second, health care workers may not apply directly observed therapy believing that adherence is automatically guaranteed with FDC administration. Third, poor rifampicin bioavailability has been found for some FDCs, particularly in 3- and 4-drug combinations. Quality assurance is therefore essential. Finally, using FDCs does not obviate the need for separate drugs for a minority of patients who develop drug toxicity.

WHO strongly recommends the use of FDCs for the treatment of TB; only products of proven bioavailability should be used. The recommended formulations currently available are shown in Table 1.

Table 1 Fixed-dose combination drugs from the WHO Model List of Essential Medicines (revised April 2002)^a

| Drug (abbreviation) | Dose form | Strength for daily use | Strength for intermittent use 3 times weekly |
|---|---|-------------------------------------|--|
| rifampicin + isoniazid (RH) | Tablet | 150 mg + 75 mg 300 mg + 150 mg | 150 mg + 150 mg |
| | Tablet or pack of granules ^b | 60 mg + 30 mg | 60 mg + 60 mg |
| ethambutol + isoniazid (EH) | Tablet | 400 mg + 150 mg | |
| rifampicin + isoniazid + pyrazinamide (RHZ) | Tablet | 150 mg + 75 mg + 400 mg | 150 mg + 150 mg + 500 mg |
| | Tablet or pack of granules | 60 mg + 30 mg + 150 mg | |
| rifampicin + isoniazid + pyrazinamide + ethambutol (RHZE) | Tablet | 150 mg + 75 mg + 400 mg + 275 mg | |

^a The fixed-dose combination R 150 mg + H 75 mg + E 275 mg is currently available from the Global Drug Facility. The process of including this drug combination in the WHO model list of essential medicines has been recently initiated.

^b For paediatric use.

TREATMENT CATEGORIES

Treatment categories are essential for prioritization of TB treatment according to public health risk – Category I is the highest priority. These categories are summarized in Table 2.

Table 2 Recommended TB treatment regimens for each treatment category^a

| TB treatment category | TB cases | Initial (intensive) phase | Continuation phase |
|-----------------------|---|---|---|
| I | New smear-positive pulmonary TB New smear-negative pulmonary TB with extensive parenchymal involvement New cases of severe forms of extrapulmonary TB | 2HRZE ^b or 2H ₃ R ₃ Z ₃ E ₃ ^b | 4H ₃ R ₃ (6 HE) ^c |
| II | Sputum smear-positive Relapse Treatment failure Treatment after interruption | 2SHRZE/ 1HRZE | 5H ₃ R ₃ E ₃ |
| III | New smear-negative pulmonary TB (other than in Category I) Less severe forms of extrapulmonary TB. | 2HRZE ^d or 2H ₃ R ₃ Z ₃ E ₃ ^d | 4H ₃ R ₃ (6 HE) ^c |

E, ethambutol; H, isoniazid; R, rifampicin; S, streptomycin; Z, pyrazinamide.

^a Adapted from *Treatment of tuberculosis. Guidelines for national programmes*, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).

^b Streptomycin may be used instead of ethambutol. In meningeal TB, ethambutol should be replaced by streptomycin.

^c This regimen may be associated with a higher rate of treatment failure and relapse compared with the 6-month regimen with rifampicin in the continuation phase.

^d Ethambutol may be omitted during the initial phase of treatment for patients with non-cavitary, smear-negative pulmonary TB who are known to be HIV-negative and for young children with primary TB.

CATEGORY I

The Category I regimen is prescribed to:

- smear-positive cases who have never previously been treated or have only received treatment for less than one month
- severely ill patients with other forms of TB (new smear-negative pulmonary TB with extensive parenchymal involvement, and new cases of severe forms of extrapulmonary TB)
- severe concomitant HIV disease.

MOST COMMONLY USED REGIMEN 2HRZE (OR 2H₃R₃Z₃E₃) 4H₃R₃

The duration of this regimen is 6 months. For the first 2 months of treatment (intensive phase), isoniazid, rifampicin, pyrazinamide and ethambutol are given daily or three times a week under direct supervision (see Table 3 for dosage). At the end of the second month, a sputum smear examination should be carried out. Most patients will have a negative result on sputum microscopy – they can then progress to the continuation phase. This phase lasts for 4 months, with isoniazid and rifampicin given 3 times per week, under direct supervision. If the sputum smear examination is positive at the end of the second month, the initial phase is prolonged for a third month. Then, the patient starts the continuation phase regardless of the sputum smear result at end of the third month.

If the sputum smears are still, or become, positive at the end of the fifth month, this patient is classified a **treatment failure**. Assuming that supervision was consistent, such patients have a relatively high probability of drug resistance. The patient is re-registered, and commences a full course of the re-treatment regimen as a Category II patient.

The other commonly used regimen is 2HRZE (fully supervised) 6HE (in an FDC tablet, daily and self-supervised administration, usually with at most monthly visits); therefore, this treatment regimen, 2HRZE/6HE, takes a total of 8 months.

A third regimen, which has been used in nomadic and unstably displaced populations, is the "Manyatta regimen" – current version: 4HRZE fully supervised 3HE in FDC, self-supervised.

Table 3 Recommended dosages of essential TB drugs^a

| Drug | Daily administration mg/kg (maximum dose) (dose range) | Three times weekly mg/kg (maximum dose) (dose range) |
|--------------|--|--|
| isoniazid | 5 (300) (4–6) | 10 (600) (8–12) |
| rifampicin | 10 (600) (8–12) | 10 (600) (8–12) |
| pyrazinamide | 25 (2 g) (20–30) | 35 (3 g) (30–40) |
| streptomycin | 15 (1 g) (12–18) | 15 (1 g) (12–18) |
| ethambutol | 15 (2 g) (15–20) | 30 (25–35) |

^a Drug doses need to be adjusted for weight gain at the end of the initial phase (2nd or 3rd month).

CATEGORY II

The Category II regimen is indicated in patients who were previously treated and are **now sputum smear- or culture-positive**; these patients include:

- treatment interruption cases
- treatment failure cases
- relapse cases.

This re-treatment regimen is **fully supervised throughout both the intensive and the continuation phases of treatment** and is as follows: in the intensive phase, rifampicin, isoniazid, pyrazinamide and ethambutol are given daily for 3 months supplemented by streptomycin daily for the first 2 months; in the continuation phase, rifampicin, isoniazid and ethambutol are given 3 times per week for 5 months.

Sputum smear examination is performed: (i) at the end of the third month of treatment (i.e. at the end of the intensive phase), (ii) at the end of the fifth month of treatment (i.e. during the continuation phase), and (iii) at the end of the eighth month of treatment (i.e. at the end of treatment). If the patient is sputum smear-negative at the end of the third month of treatment, the continuation phase should be initiated with HRE three times a week. If the patient is sputum smear-positive at the end of the third month, the intensive phase of treatment is extended, with HRZE, for one more month before proceeding to the continuation phase. All the patients who are positive at the end of the third month should progress to the continuation phase, regardless of the sputum smear result at the fourth month of the intensive phase. Patients who remain or become smear positive at the end of the fifth month or at the end of the treatment course are “chronic cases” and have a high risk of being MDR-TB cases. Particular attention should be paid to minimize indoor exposure of other people to these patients. The treatment for MDR-TB with second-line drugs is indicated if all the requirements to manage MDR-TB cases are fulfilled (see section 1.5).

CATEGORY III

The Category III regimen is indicated for those who are:

- new smear-negative pulmonary TB cases
- cases of non-severe forms of new extrapulmonary TB (including symptomatic primary disease in children).

These patients receive the same treatment regimen as Category I patients. However, ethambutol may be omitted during the initial phase of treatment in patients with limited parenchymal involvement, non-cavitary smear-negative pulmonary TB who are known to be HIV-negative and in children with patent primary TB. The 8-month regimen (2HRZ/6HE) has not been thoroughly evaluated in extrapulmonary TB, but would probably be satisfactory for the treatment of non-severe forms of disease.

Sputum smear-negative pulmonary TB patients should be monitored clinically; body weight is a useful progress indicator. Sputum smears should be checked at the end of the intensive phase of treatment (second month of treatment). If the results are positive (i.e. a smear-negative pulmonary TB case became smear-positive), there are three possibilities: (i) the results of the diagnostic examination were wrong; (ii) the results of the follow-up examination are wrong; or (iii) the patient has indeed become sputum smear-positive. The appropriate action in this situation is to repeat the sputum smear examination to exclude laboratory error. If the results are still positive, the following actions should be taken: (i) the Category III regimen should be stopped; (ii) the treatment outcome should be exceptionally registered as “treatment failure”; and (iii) the patient should be re-registered as “other” and put on a Category II regimen.

Table 4 provides the recommended dosage schedules for adults with fixed-dose combination drugs.

Table 4 Dosage schedules for treatment of new adult TB cases using fixed-dose combination drugs

| Patient body weight (kg) | Intensive phase | | | Continuation phase | |
|-----------------------------------|--|------------------------------------|-------------------------------------|-------------------------|-----------------------------|
| | 2 months | | | 4 months | or 6 months ^a |
| | Cat I | Cat III | Cat III | | |
| | Daily or 3 times daily | Daily | 3 times weekly | 3 times weekly | Daily |
| | RHZE 150 mg +75 mg +400 mg +275 mg | RHZ 150 mg +75 mg +400 mg | RHZ 150 mg +150 mg +500 mg | RH 150 mg +150 mg | EH 400 mg +75 mg |
| 30–39 | 2 | 2 | 2 | 2 | 1.5 |
| 40–54 | 3 | 3 | 3 | 3 | 2 |
| ≥55 | 4 | 4 | 4 | 4 | 3 |

H, isoniazid; R, rifampicin; Z, pyrazinamide; E, ethambutol.

Fixed dose combination tablet including 150 mg rifampicin + 75 mg isoniazid + 275 mg ethambutol can be procured from the Global Drug Facility of the Stop TB Partnership.

^a 4RH may be replaced by 6EH daily when supervision of treatment is not possible. However, data from a recent clinical trial have shown that 6EH results in higher rates of treatment failure and relapse in comparison to 4RH in the continuation phase of treatment.

3.4 TREATMENT ADHERENCE

Ensuring patient adherence to treatment is essential to ensuring the cure of the patient, the prevention of resistance and the success of the programme. Conditions for enhancing treatment adherence include:

- direct observation of treatment either by a health worker or a trained and supervised community member;
- vigorous efforts to educate the patient about adherence at treatment initiation and throughout the treatment course;
- home visits to trace non-compliers and patients as soon as they interrupt their treatment;
- good relationship between staff and patient;
- continuing education for staff, community leaders and the refugee/IDP populations;
- clinic setting acceptable to patients and staff;
- education of the family and recruitment of their support in maintaining patient adherence;
- individual assessment of defaulting risk and development of individualized solutions.

THAI – CAMBODIAN BORDER

A TB programme tailored for the Khmer refugees in the camps achieved an excellent adherence rate. After their sputum was found to be positive for TB, each patient was required to attend a four-day course for one hour per day. This course covered most aspects of TB, its spread and its treatment.

A housemate was chosen to help take responsibility for the TB patient during the course of treatment. Patients were required to teach their housemate what had been taught at the course. A home visit was made by members of the TB staff, including the health worker, who would follow the patients throughout their treatment course. The visit was to evaluate household contacts for symptoms of TB and to assess how much the housemate had learnt from the patient. Factors which were felt important to ensure treatment completion were that patients had a stable residence, were not looking for missing family members and thus likely to leave, and had a regular source of food. When the patient was recruited into the TB programme, a contract was signed by all the parties before treatment. The refugee signed a commitment to attend the clinic regularly for the entire duration of the treatment.

SOMALIA

A successful TB programme was established despite the security problems in the country. Excellent adherence rates were achieved and new patients were attracted from other areas as word spread of the programme's success.

All patients received treatment in accordance with the Stop TB strategy. In addition to medications, patients were provided with three meals per day, lodging for themselves and their family if they were not from the local area, and education for their children. A mosque was provided in the premises for use by patients and their families. A contract was signed by the patient, their supporter and the TB staff before the commencement of therapy.

Initially, TB was a stigmatizing disease in the area and many patients avoided medical assistance for fear of being labelled. This is changing as more patients are being cured.

Refugee populations often have high rates of malnutrition. Food supplements contributed to the nutritional rehabilitation of malnourished TB patients as well as other refugees. Extra food, however, is not a prerequisite for an individual response to TB treatment nor is provision of food supplementation a routine prerequisite for initiating a TB programme. In some settings, the programme needed to provide a basic ration to enable patients to stay at the health centres to receive supervised treatment. Food can also have considerable value as an incentive to support adherence and treatment completion. Other incentives should be introduced with caution – articles such as bednets, with a health benefit, are preferred.

3.5 PATIENT MANAGEMENT

The majority of TB patients can be treated as outpatients, unless they are severely ill. Outpatient treatment is given daily or three times a week by the designated health worker responsible for TB or by basic health care workers in peripheral-level units. In some programmes, non-health care workers such as teachers, storekeepers or even family members have been used to directly supervise treatment. If supervision by non-health care community members is found to be necessary, for example, because of distance between the patient's residence and the health centre, it is important to seek local advice regarding culturally appropriate supervisors. It is also critical to implement a robust system for their training and supervision and to ensure that drug administration is consistently documented.

Both the diagnosis and the treatment of TB should be fully integrated into the general health services for that population, while maintaining a disease-specific management and information system.

Indications for hospitalization are:

- severe disease (e.g. meningitis, extreme wasting, haemoptysis) requiring nursing care and close observation;
- serious complications of treatment (e.g. severe skin reactions or jaundice);
- other serious concomitant diseases (e.g. malaria, diabetes, hepatic insufficiency, renal insufficiency);
- logistic difficulties (e.g. providing treatment for a TB patient from a remote village who cannot walk to receive treatment). In some refugee and emergency settings, it may be necessary to provide some form of simple accommodation as distinct from hospital care, to allow patients to receive supervised therapy.

In hospital, TB patients recently started on treatment should be separated from other patients (especially children and those infected with HIV) in a well-ventilated area. The patients and their families should receive regular education on preventive measures, especially on covering the mouth when coughing. Each patient should have a covered container for sputum and the contents must be disposed of safely.

TB patients receiving treatment in the community do not routinely require isolation. They soon become less infectious after effective treatment has been instituted. The risk to household members will usually have been greatest before the index patient's diagnosis and treatment initiation and is best addressed by contact investigation as described above.

It is important to ensure that TB treatment does not lead to the creation of new transmission risks in the community. This could occur, for example, if a patient just starting treatment was to move into a household with small children in order to be close to the clinic. The problem would be even more serious if it transpired that the patient had drug-resistant disease. Judgement should also be exercised in the case of smear-positive patients treated in the community, who have particularly high risk of transmission to vulnerable groups through their work (e.g. primary-school teachers).

3.6 TB AND REPRODUCTIVE ISSUES

Pregnant women are treated with the same regimens as others but **streptomycin must not be given** because of its ototoxicity for the fetus. All women should be asked if they are pregnant before commencing treatment. Pregnant women should be advised that successful treatment of TB is important for successful outcome of pregnancy. All women should be asked to notify the TB clinic if they become pregnant during the course of TB treatment.

A breastfeeding woman who has TB should receive a full course of TB treatment. Appropriate treatment of the mother is the best way to prevent transmission of TB to her baby. All TB drugs are compatible with breastfeeding. The infant of a smear-positive mother must be given isoniazid as a contact.

Women should also be advised that oral contraceptives are likely to be ineffective while the patient is taking rifampicin and that alternative methods of contraception should be used.

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4. MANAGEMENT OF TB IN CHILDREN

4.1 EPIDEMIOLOGY

Children are usually infected with TB by an adult or an older child with sputum smear-positive pulmonary TB, often a family member. Less commonly, they may be infected by contact with sputum smear-negative (e.g. culture-positive) cases. The best way to prevent childhood TB is therefore by proper identification and treatment of infectious patients. Case notifications of childhood TB usually vary from 3% to more than 25% of all TB cases registered with the NTP. Children can present with TB at any age. The frequency of childhood TB depends on the intensity of transmission in the community, the age structure of the population, the available diagnostic tools and whether contact investigation is routinely and efficiently undertaken. The ratio of pulmonary TB to extrapulmonary TB in children is usually around 1 in 3 but varies, depending on factors such as age, ability to examine contacts and possible genetic factors.

Children may also be infected with *M. bovis* by drinking untreated milk from infected cows. They often present with cervical TB adenitis or intestinal TB but can also develop pulmonary TB or disseminated disease.

The risk of infection in children depends on the extent of exposure to infectious droplet nuclei. For example, if a mother has sputum smear-positive pulmonary TB, her infant is more likely to become infected because of the very close contact and the higher risk of inhaling a large number of infectious droplets. The greater the exposure to cases with infectious TB disease, the greater the likelihood of infection.

The majority of infected children do not develop TB disease in childhood. The only evidence of infection is likely to be a positive TST. The likelihood of developing disease is greatest shortly after infection and declines steadily with time. Infants and young children aged under 5 years are at particular risk of developing disease. If infected children do develop disease, the majority will present with symptoms within one year of infection. For infants particularly, the time-span between infection and disease may be as little as 6–8 weeks. Various immunosuppressive conditions may facilitate progression of infection to disease, including HIV infection, measles, whooping cough and protein-calorie malnutrition. These conditions are also most common in infancy and early childhood.

4.2 CLINICAL PRESENTATION AND DIAGNOSIS

The commonest type of TB in children is extrapulmonary TB, mainly intrathoracic. Other common forms include TB lymphadenopathy, TB meningitis, TB effusions (pleural, pericardial and peritoneal) and spinal TB. The diagnosis of respiratory TB in children is difficult because there is some confusion between primary infection (often without obvious lesions in the lungs) and pulmonary TB. Pulmonary TB is usually smear-negative. This is because many children present with primary rather than reactivation (cavitary) pulmonary TB and because the majority of children with pulmonary TB are too young to produce sputum for smear microscopy. Smear-positive pulmonary TB is more likely to be diagnosed in post-pubertal children. The incidence of pulmonary TB is normally lowest between the ages of 5 and 12 years and then increases slightly again in adolescence, when it presents more like adult pulmonary TB.

APPROACH TO DIAGNOSIS

The diagnosis of pulmonary TB is difficult in children, particularly in resource-poor settings. Important features include:

- contact with a smear-positive pulmonary TB case;
- respiratory symptoms for more than 2 weeks, not responding to broad-spectrum antibiotics;
- weight loss or failure to thrive especially when not responsive to therapeutic feeding programme;
- positive test to the standard dose of tuberculin (2 tuberculin units (TU) or RT23 or 5 TU of PPD-S): 10 mm or more in unvaccinated children, 15 mm or more in BCG-vaccinated children; however, with severe TB and /or advanced immunosuppression, the TST may be negative.

There are no specific clinical findings for diagnosis of pulmonary TB in children. There may be clues to other diagnoses such as asthma, bronchiectasis, whooping cough, inhaled foreign body or cardiac disease. Chest X-ray findings are often not specific and certainly not diagnostic. Upper and mid-lobe infiltrates are more common, while cavitary lesion is uncommon. The usefulness of TST and chest X-ray is further reduced in malnourished or HIV-infected children. However, radiographic and clinical findings suggestive of TB become more valuable when it has been established that the child has been in close contact with a diagnosed case of pulmonary TB, especially smear-positive PTB. The bacteriological confirmation is usually not possible in normal conditions, let alone in refugee and displaced populations; the diagnosis of pulmonary TB in children is most often presumptive.

The diagnosis of extrapulmonary TB in children may be more straightforward because of characteristic clinical features (e.g. spinal deformity, scrofula – lymph node suppuration via sinus to skin).

TUBERCULIN SKIN TEST (TST)

A positive TST does not indicate the presence or extent of TB disease; it only indicates infection. In a child who has not had Bacille Calmette–Guérin (BCG) vaccination, a TST is defined as "positive" when the diameter of skin induration is 10 mm or more. In a child who has had BCG, an induration of 10–14 mm may be due to vaccination or TB infection. A negative TST does not exclude TB infection and some induration, e.g. 5–14 mm, is supportive if the clinical features and contact history are suggestive. The TST is less likely to be positive in a child with TB if the child also has severe malnutrition, HIV infection or disseminated TB such as miliary disease or TB meningitis.

4.3 HIV AND TB IN CHILDREN

HIV makes diagnosis and management of TB in children more difficult (as with adults) for the following reasons:

- Other HIV-related disease, such as lymphocytic interstitial pneumonitis, may present in a similar way to pulmonary TB or miliary TB.
- Interpretation of TST and chest X-ray is less reliable.
- When TB/HIV coinfection is common in adults, a positive contact history is less specific if the contact is the child's parent. The child is at risk of becoming infected with both diseases.
- Children with TB and advanced HIV disease may not respond to TB treatment.

4.4 MANAGEMENT OF CHILDHOOD TB

High treatment success rates are achievable in children with active TB. There has been understandable caution with the use of ethambutol in children too young to report early visual deterioration, but ethambutol has been safely used in infants and young children at the recommended dosages. The recommended daily dose of ethambutol is higher in children (20 mg per kg/day) than in adults (15 mg per kg/day) because of the differences in pharmacokinetics.

The recommended treatment regimens and dosages for the treatment of childhood TB are in general the same for children and adults (see Tables 5 and 6). This is because uniformity is likely to reduce confusion and therefore improve overall compliance. However, there are some important differences between children and adults that may affect drug choice and dosage. Recommended dosages are based on research in adults, and yet metabolism of drugs varies with age. The effectiveness of the recommendation of ethambutol plus isoniazid for the maintenance or continuation phase has never been studied in children, whereas rifampicin plus isoniazid has proven efficacy. Mortality is high and long-term sequelae are common with TB meningitis; to prevent them, diagnosis and treatment of TB meningitis must be rapid. In children with TB meningitis, streptomycin (or ethionamide at the daily dose of 20 mg/kg) should be used instead of ethambutol because ethambutol does not cross the blood–brain barrier. Corticosteroids (usually prednisone) are recommended in TB meningitis in a dosage of 2 mg per kg/day for 4 weeks; this dose should then be slowly reduced over 1–2 weeks before stopping. Corticosteroids are also useful in lobar or segmental opacity caused by a lymphadenopathy. All children with suspected meningitis or miliary TB should be hospitalized initially until their clinical status has stabilized. Children with TB meningitis are at high risk of long-term disability and therefore benefit from specialist care, where this is available.

Table 5 Recommended TB treatment regimens for children

| Clinical presentation | Intensive phase | Continuation phase |
|--|--|---|
| New smear-positive pulmonary TB | 2HRZE | 4H ₃ R ₃ |
| New smear-negative pulmonary TB with extensive parenchymal involvement (acute miliary, segmental or lobar opacity) | or 2H ₃ R ₃ Z ₃ E ₃ | 6HE ^a |
| New cases of severe forms of extrapulmonary TB (disseminated acute TB, abdominal, spinal and pericardic TB) | | |
| TB meningitis | 2SHRZ ^b | 4RH ^c |
| New smear-negative pulmonary TB (other than in Category I) | 2HRZ | 4H ₃ R ₃ |
| Less severe forms of extrapulmonary TB (TB adenitis, mediastinal lymphadenopathy) | or 2H ₃ R ₃ Z ₃ | |
| Previously treated smear-positive pulmonary TB: | 2HRZES/1HRZE | 5H ₃ R ₃ E ₃ |
| • Relapse | | |
| • Treatment failure | | |
| • Treatment after interruption | | |

E, ethambutol; H, isoniazid; R, rifampicin; S, streptomycin; Z, pyrazinamide.

^a A regimen including a continuation phase with 6HE may be associated with higher rates of treatment failure and relapse compared with a regimen including a 4RH continuation phase.

^b For the treatment of TB meningitis, some experts recommend ethionamide in the intensive phase instead of streptomycin because ethionamide crosses both healthy and inflamed meninges, whereas streptomycin crosses meninges mainly when they are inflamed.

^c Other authorities recommend longer duration of continuation phase in the treatment of TB meningitis (7 to 10 months RH).

Table 6 Dosage schedules for treatment of non-severe smear-negative TB in children using fixed-dose combination drugs

| Patient body weight (kg) | Intensive phase (2 months) | | Continuation phase (4 months) | |
|--------------------------|----------------------------------|-----|-------------------------------|---------------------|
| | Daily | | Daily | or 3 times weekly |
| | RHZ 60 mg + 30 mg + 150 mg | | RH 60 mg + 30 mg | RH 60 mg + 60 mg |
| <7 | 1 | 1 | 1 | 1 |
| 8–9 | 1.5 | 1.5 | 1.5 | 1.5 |
| 10–14 | 2 | 2 | 2 | 2 |
| 15–19 | 3 | 3 | 3 | 3 |
| 20–24 | 4 | 4 | 4 | 4 |
| 25–29 | 5 | 5 | 5 | 5 |

H, isoniazid; R, rifampicin; Z, pyrazinamide.

4.5 MANAGEMENT OF CHILDHOOD CONTACTS OF INFECTIOUS ADULTS

Children less than 5 years of age have a greatly increased risk of progression to serious forms of active TB following infection. Moreover, TB infection in this group is much more likely to have occurred recently than would be the case in older individuals. Therefore, household or “sleeping shelter” contacts, aged under 5 years, of smear-positive TB cases should be a priority for contact investigation and chemoprophylaxis (see below).

Active tracing of children who are household contacts of smear-positive PTB cases is highly recommended. Ideally, screening should include at least a thorough history, clinical examination, TST and chest X-ray. Those with a diagnosis of active TB are then treated. Those who are well and aged under 5 years should receive prophylaxis (isoniazid 5 mg/kg daily). This will significantly reduce the likelihood of their developing TB disease. Breastfeeding children of sputum smear-positive mothers are the most important group for preventive therapy. Prophylaxis should be for at least 6 months and requires regular (e.g. every 2 months) follow up. Children aged over 5 years who are well do not require prophylaxis, only clinical follow up.

Children may also be infected by smear-negative PTB cases, and, even though transmission is less common, routine contact investigation needs to be organized whenever possible.

In high HIV prevalence settings, TB contact investigations can be an opportunity for both TB and HIV case-finding.

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5. PREVENTION OF TB

5.1 KEY PRINCIPLES

The detection and cure of infectious cases of TB are the most effective methods of preventing TB transmission and controlling the disease in the community.

Methods of preventing TB transmission include ensuring good ventilation and reducing crowding in health clinics, and ensuring hospitalized smear-positive patients are kept in a separate ward. Particular care must be taken to separate infectious TB patients from HIV-positive individuals and young children.

People living in close contact (household or sleeping quarters) with smear-positive pulmonary TB patients should first be assessed for features suggestive of active TB; if active TB is diagnosed, they should be treated. Household contacts aged less than 5 years who do not have TB should be given 5 mg per kg/day isoniazid chemoprophylaxis for at least 6 months, depending on local recommendations. This course of preventive therapy can significantly reduce the risk of TB occurrence in a child already infected with tubercle bacilli. One week after completion of the course of chemoprophylaxis, any child not previously vaccinated should be given BCG.

For infants of newly diagnosed sputum smear-positive mothers, breastfeeding should continue and the infant should not be separated from the mother. Transmission is likely to have occurred already, and the infant is at greater risk of dying from other causes if breastfeeding is stopped. If the infant is well, he or she should be given isoniazid prophylaxis for at least 6 months. However, if at the end of the third month of chemoprophylaxis: (i) the child remains well, (ii) his or her TST is negative, and (iii) the mother has converted to sputum smear-negative, IPT can be stopped. If these conditions are not met, the course of chemoprophylaxis should be continued for at least the remaining 3 months. BCG should be given one week after completing IPT. If the infant becomes unwell, TB should be suspected.

Since HIV prevalence is the most powerful determinant of TB occurrence in high HIV prevalence countries, HIV prevention is a critically important element of TB prevention in the longer term (see section 1.4).

BCG has been shown to be effective in preventing severe forms of TB such as meningitis and miliary TB in children, but has no consistent impact on transmission in a population. BCG is strongly recommended for all newborn children in refugee and displaced population settings and any children up to the age of 5 years who have not already received it. Re-vaccination with BCG is not recommended.

5.2 HEALTH EDUCATION

The goals of community education are:

- to reduce stigmatization of TB;
- to encourage and promote early presentation of TB suspects, specifically those with persistent cough (>2 weeks);
- to raise awareness of the importance of (i) TB treatment and (ii) treatment adherence for both the individual patient and the community.

The most important messages to teach (see also Appendix 11) are:

- TB is curable.
- Anyone can contract TB.
- Refugees and displaced persons are at greater risk of developing TB.
- The most important symptom of TB is a cough of long duration (>2 weeks), sometimes with other symptoms such as weight loss, chest pain, shortness of breath and fevers or sweats.
- Early diagnosis and treatment cure the patient most quickly **and** are the best ways to stop TB from spreading.
- Appropriate treatment makes patients non-infectious rapidly, but cure takes 6 or 8 months.
- All patients must complete the full course of treatment, even though they may feel well much earlier.
- Poor adherence leads not only to failure of treatment but also to development of drug resistance – a risk to both patient and community.
- Controlling TB is a community responsibility.
- All patients should be treated sympathetically and with respect, not only by health staff but also by community members.
- Children are especially at risk if not treated and may develop severe, even fatal, disease.
- Coughing spreads TB bacilli.

Teaching materials need to be translated into the local language and be appropriate to the level of education and literacy of the population, making maximal use of pictures and diagrams to illustrate the material. Cured patients are often helpful teachers and supporters of new patients.

6. MONITORING OF TB PROGRAMMES

6.1 RECORDING AND REPORTING

Systematic record keeping is an essential requirement for a successful TB programme. Good records are necessary in order to follow and manage individual patients effectively, to determine whether the programme is performing according to accepted standards and to identify problems that may require corrective measures.

Key requirements are:

- accurate record keeping;
- regular reporting;
- regular analysis;
- regular feedback to all staff involved and to those who need to be informed.

Records which must be kept are:

- register of TB suspects (patients who are suspected of TB and referred for laboratory investigation);*
- TB laboratory register (patients who are screened for TB and smear diagnosis);
- individual patient's record;
- TB register (patients started on TB treatment).

It is essential for an orderly referral process to be in place. A link should be established between the TB suspect register and the TB laboratory register as well as between the TB laboratory register and the TB register. The TB coordinator must check that all patients with positive sputum results are entered into treatment and into the TB register in a timely manner. Follow up to ensure the patient has actually commenced the treatment is essential.

6.2 EVALUATION OF THE PATIENT

The health worker supervising each patient's treatment is responsible for identifying any symptoms or signs that might indicate serious adverse drug effects or concurrent illness, and referring appropriate patients to the clinician. Where possible, patients should be assessed by a doctor weekly for the first month, then every 2 weeks during the second month, and monthly for the duration of their treatment.

* The outpatient register may be used as a TB suspect register in some settings.

The following elements are essential to evaluate individual patient progress:

- sputum-smear result after 2 months of treatment; if positive at 2 months, sputum microscopy to be repeated at 3 months after an additional month of intensive phase therapy;
- sputum-smear result at the end of month 5 of treatment;
- sputum-smear result at the completion of therapy (month 6 or 8).

6.3 OUTCOME DEFINITIONS

At the end of the treatment course for each TB patient, the TB coordinator should record the outcome in the TB register using the definitions of standard treatment outcomes shown in Box 4.

6.4 EVALUATION OF LABORATORY ACTIVITIES

The following information should be routinely reported:

- number of TB suspects registered in the TB laboratory register (A);
- number of sputum samples examined (B);
- number of sputum samples with positive microscopy (C);
- number of smear-positive patients (D);
- proportion of positive sputum samples among sputum samples examined (C divided by B);
- proportion of smear-positive patients among number of TB suspects registered in TB laboratory (D divided by A);
- re-checking system of slides for quality assurance, according to the international recommendations: yes/no;
- if yes, the percentage of false-positive and false-negative slides.

Box 4 Definitions of standard treatment outcomes

| | |
|-----------------------------|---|
| Cured | A patient who is sputum smear-negative in the last month of treatment and on at least one previous occasion. |
| Completed treatment* | A patient who has completed treatment but who does not meet the criteria to be classified as cured or treatment failure. |
| Defaulted | A patient whose treatment was interrupted for 2 consecutive months or more. |
| Died | A patient who dies for any reason during the course of treatment. |
| Treatment failure** | A patient who is sputum smear-positive at 5 months or later during treatment. |
| Transferred out | A patient who has been transferred to another recording and reporting unit and for whom the treatment outcome is not known. |

* Treatment success is defined as the sum of patients cured and those who have completed treatment.

** Includes a patient who was initially smear-negative before starting treatment and became smear-positive after completing the initial phase of treatment.

6.5 EVALUATION OF TB PROGRAMME PERFORMANCE

In most refugee and displaced population situations, the coordinating health agency (e.g. UNHCR) implements a surveillance system with weekly or monthly reporting of priority diseases by NGOs. Monthly TB reports on case-finding and treatment outcomes should feed into this surveillance system. The TB data reported should include the number of new TB patients diagnosed (smear-positive, smear-negative, and extrapulmonary) by age (under 5, and 5 years and over) and the number of TB patients whose treatment is completed and are cured. **These figures are not sufficient to evaluate a TB programme.**

The evaluation of a TB programme should also assess the following:

- case-finding;
- early treatment result through smear conversion at month 2 and 3 of treatment;
- cohort analysis (see below) for treatment outcome 12 months after registration of TB patients.

CASE-FINDING

From the TB register, and on a quarterly basis, the following elements should be computed:

- number of new sputum-positive PTB cases; this number should be also stratified by age group and sex;
- number of new smear-negative PTB cases;
- number of new PTB with smear examination not done or not available;
- number of new extrapulmonary TB cases;
- number of re-treatment TB cases; this number should be also stratified by subcategory of re-treatment (relapse, treatment failure, treatment interruption and other re-treatment subcategory).

Every three months, these numbers must be reported on a standardized form by every health facility with a TB register to the TB programme coordination unit.

Ideally, other information needs to be analysed by the TB programme coordinator:

- if the register of TB suspects is implemented in the basic health facilities, the number of TB suspects identified in this register should be compared with the number of TB suspects registered in the TB laboratory; this comparison highlights the proportion of the TB suspects screened for TB among the TB suspects identified in the basic health facilities;
- also, the proportion of contacts screened for TB among the number of TB contacts identified should be assessed;
- from the TB laboratory register, the number of sputum examinations performed per TB suspect needs to be regularly evaluated.

EARLY TREATMENT RESULT (SMEAR CONVERSION AT MONTH 2 OR 3)

In order to assess the progress of the treatment impact, it is essential to monitor the sputum smear conversion at the end of month 2 or 3 of treatment. This information should be collected on a quarterly basis from the TB register. The conversion rate at month 2 or 3 should be calculated for new smear-positive pulmonary TB cases only.

The expected smear conversion rate, even in refugee situations, should be higher than 80%. If a programme is achieving conversion rates of 80% or less, it should be reviewed immediately. It suggests a serious problem with one or more elements of the programme. Possibilities include:

- direct observation of treatment is not being performed properly or patients may be lost to follow up;
- misclassification of patients (re-treatment patients classified as new patients);
- laboratory error (false-positive results);
- poor quality or bioavailability of drugs;
- drug resistance;
- note that a minority of patients with very advanced disease and particularly with large cavities and a high bacillary load, may be somewhat slower than average to clear their smear positivity.

If the smear conversion rate at 60 days is less than 80%, the TB control services should be assessed carefully, the problem identified and corrective measures devised and applied.

COHORT ANALYSIS

Cohort analysis involves calculation of the rate of each outcome shown in Box 4 for the cohort of patients. A cohort is a group of patients who were diagnosed and registered for treatment during a specific time period (usually 3 months). Evaluation of treatment outcome in new smear-positive pulmonary TB cases is used as a major indicator of programme quality. Outcome in other patients may be separately analysed for new smear-negative pulmonary cases, new extrapulmonary TB cases and each subcategory of re-treatment patients.

Cohort analysis is the key management tool for evaluating the performance of the TB programme. It allows the identification of problems, so that the TB programme coordinator can take appropriate actions to overcome them and improve programme performance.

The TB programme coordinator should use the information included in the TB register and perform cohort analysis of treatment outcome every 3 months and at the end of every year. This analysis should be carried out 3 months after all patients included in the cohort have completed their course of treatment.

QUARTERLY REPORTS

At the end of every quarter, the TB programme coordinator should establish three reports in order to monitor the activities and performance of TB control. The information for these reports should be collected on standardized forms from the TB register:

- The report on **case-finding** should be established within the month following the quarter that has finished.
- The report on **smear conversion** at month 2 or 3 of treatment should be done for the quarter before the quarter for which the report on case-finding has been established.
- The report on **cohort analysis** should be carried out the same quarter for which the report on case-finding has been recently done, but of the previous year.

For instance, if we are currently at the end of April 2006, the TB programme coordinator should establish: (i) the report on case-finding for the quarter 1 January–31 March 2006; ii) the report on smear conversion for the quarter 1 October–31 December 2005; and (iii) the report on cohort analysis for the quarter 1 January–31 March 2005.

These reports should be submitted to the NTP, if present. Also, feedback information should be provided to the staff involved in TB control activities.

Table 7 details the causes of and possible solutions to poor treatment outcomes.

The recording and reporting system has been recently revised in order to meet the indicator needs of the new Stop TB Strategy.

Table 7 Poor treatment outcomes – causes and possible solutions

| Treatment outcome | Causes | Possible solutions |
|--|---|--|
| Died | High prevalence of HIV | Interventions to minimize HIV transmission; consider co-trimoxazole prophylaxis; antiretroviral therapy, if available |
| | Late diagnosis | Ensure primary health workers consistently recognize TB suspects and send sputa for examination Promote community awareness of TB symptoms, especially chronic cough |
| | Concurrent illness | Identify obstacles to access to health facilities, and correct them Strengthen knowledge and skills of staff in recognizing and managing prevalent diseases |
| Failed treatment Low conversion rate at month 2 or 3 of treatment (early indicator) or final outcome | Defaulting and poor adherence to treatment | Investigate causes Reinforce direct observation of TB drug intake Enhance defaulter prevention and tracing |
| | False-positive follow-up smears | Independent review of the positive slides in question. Reinforce routine and timely quality control |
| | Misclassification or choice of wrong regimen: e.g. re-treatment patients given a regimen for new patients | Improve supervision of the health facility and, specifically, of classification at entry and following treatment guidelines |
| | Drug quality/bioavailability Trading in drugs | Assess drug source re: quality and bioavailability of drugs Investigate. Reinforce direct observation of TB drug intake |
| | Suspected primary resistance to both rifampicin and isoniazid | Confirm by culture and sensitivity Devise local protocol – depending on local resources and capacity |
| Defaulted | Inadequate/ineffective health education | Ensure that appropriate, understandable health education is provided to patients at entry and during treatment Reinforce education to families, community and authorities to understand the importance of completion of treatment for TB Added attention to staff morale |
| | Unfriendly behaviour of health staff | |
| | Inconvenient hours, prolonged wait for supervised doses | Explore obstacles to expeditious care with health staff and identify solutions |
| | Non-adherent patients and defaulters not followed up No default tracing system established | Explore reasons for defaulting (e.g. distance from clinic, alcohol use) and possible solutions. Ensure adequate human and transport resources for defaulter tracing; community involvement |
| | Transfer not done correctly | Increase supervision; review arrangements between transferring and receiving programmes Involve UNHCR when population or camp transfer occurs |
| | Patient leaves camp or moves due to instability in the area | Contingency plan for insecurity, previously established Arrangements for transfer of patients to NTP at destination |

RESOURCES

Managing TB at national level – A training course. Geneva, World Health Organization, 1996 (WHO/TB/96.203).

Managing TB at district level – A training course. Geneva, World Health Organization, 1996 (WHO/TB/96.211).

Management of tuberculosis – Training for health facility staff. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.314a–l).

Revised TB recording and reporting forms and registers - Version 2006 (WHO/HTM/TB/2006.373; available at: http://www.who.int/tb/dots/r_and_r_forms/en/index.html).

Technical guide for sputum examination for tuberculosis by direct microscopy. *Bulletin of the International Union Against TB.* 1978. Suppl. No. 2.

Treatment of tuberculosis. Guidelines for national programmes, 3rd ed. Geneva, World Health Organization, 2003 (WHO/CDS/TB/2003.313).

Management of tuberculosis: a guide for low-income countries, 5th ed. Paris, International Union Against Tuberculosis and Lung Disease 2000.

Tuberculosis handbook. Geneva, World Health Organization, 2003 (WHO/TB/98.253).

7. OPERATIONAL ISSUES FOR TB PROGRAMMES

7.1 CONTINGENCY PLANNING FOR TB PROGRAMME INTERRUPTIONS

TB programme implementation may be interrupted as a result of unplanned population movements or breakdowns in security. The unique problems of continuity faced by programmes delivered under insecure circumstances must be taken into account, firstly in the decision to institute a TB programme and secondly in contingency plans adapted to the specific situation. These include considerations of **quantity and security of drug stocks** to be held on site in order to minimize the risk that TB drugs will “leak” into the community should the programme have to withdraw at short notice.

More importantly they include an assessment, in discussion with local staff and other key players such as the MOH and NGOs, of the most likely types of disruptions to TB programme continuity, their anticipated duration (from a few hours to permanent) and the most appropriate contingency plans based on this information. Potential disruptions could include unstable situations in the area or within the camp or population, or sudden unanticipated relocation of refugees/IDPs. If such a situation appears imminent, it may be appropriate to distribute a supply of drugs to each patient, balancing the risks of interrupting treatment with those of allowing TB drugs in the community at large. These reserve supplies should be prepared when each patient enters the programme. Box 5 shows the actions to take if TB treatment is interrupted.

Box 5 Actions to take if TB treatment is interrupted

Interruption for less than 1 month

- Trace patient
- Assess if cause of interruption can be rectified
- Continue treatment and prolong it to compensate for missed doses

Interruption for 1–2 months

Action 1

- Trace patient
- Assess if cause of interruption can be rectified
- Do 3 sputum smears
- Continue treatment while waiting for results

Action 2

If smears negative or extrapulmonary TB:

- Continue treatment and prolong it to compensate for missed doses.

If one or more smears positive:

Treatment received <5 months:

- Continue treatment and prolong it to compensate for missed doses.

Treatment received >5 months:

- Category I: start Category II
- Category II: refer (may evolve to chronic)

Interruption for 2 months or more (defaulter)

- Do 3 sputum smears
- Solve the cause of interruption, if possible
- No treatment while waiting for results

If negative smears or extrapulmonary TB:

- Clinical decision on individual basis whether to restart or continue treatment, or no further treatment

If one or more smears positive:

- Category I: start Category II
- Category II: refer (may evolve to chronic)

SUDAN

During a prolonged period of low intensity war and recurrent insecurity in south Sudan, arrangements were made to prepare for each patient at programme entry a "runaway bag" containing one month's supply of isoniazid plus ethambutol in a fixed-dose combination. The runaway bags could be rapidly distributed in the event of insecurity, which was expected to last more than a few days. Contingency plans were made to contact local staff on the ground and arrange regrouping to resume treatment, within a month.

THAILAND – MAELA REFUGEE CAMP

In 1987–1988, conflict in Burma led to the influx of refugees into Thailand. Since then, some 100 000 Karen Burmese refugees have remained in Thailand. Maela camp is a closed Karen refugee camp in Tak Province, with a population of about 40 000 with the transfer of refugees in 1997 from Shoklo camp.

A TB programme started in 1987 in Shoklo and was transferred to Maela in 1997 as well as other health facilities. In order to ensure treatment compliance, TB patients were admitted to a “TB village” next to the camp where they stayed with their family for the whole duration of treatment. They were housed in bamboo huts similar to the ones in the camp. Food was provided by the programme during the entire duration of treatment. As for all health services, TB diagnosis and treatment were free of charge. Regular health education messages were provided. Treatment was given daily under strict supervision by medical personnel.

From October 2001 to October 2002, the results for all new cases were: cure + treatment completed = 172/257 (67%); death = 19/257 (7%); failure = 9/257 (3%); default = 57/257 (22%).

Further investigations to explain this unusually high default rate in a closed camp situation showed that most of the defaulters were patients from outside the camp (Thai Karens, illegal migrants, unregistered refugees). These patients attended the health structures in the camp in order to have access to free treatment. They often gave false addresses in the camp and were consequently impossible to trace when interrupting the treatment. Moreover, these patients faced greater economic constraints than the refugees and were more likely to interrupt their treatment.

Despite all efforts of the health personnel, the economic or administrative constraints faced by a population in a complex emergency can result in high defaulter rates. Prevention of default must be a priority but must not lead to the denial of treatment to some patients.

7.2 LINKING WITH THE NTP AND ENSURING SUSTAINABILITY

Management of TB demands a longer time frame and a developed infrastructure to ensure the TB programmes implemented are effective and sustainable. In comparison, addressing the more immediate health and nutritional needs in acute humanitarian emergencies by delivering basic primary health care services does not require the same level of structure or coordination with national disease control programmes.

Linkage with the NTP of the host country is key to ensuring the sustainability of TB programmes in refugee populations. Apart from ensuring that drug regimens accord with national protocols and that standard reporting forms and registers are used, the NTP manager should be involved in the development of the local TB implementation protocol, quality control, supervisory visits, trainings, meetings of TB coordinators and in the monitoring and evaluation process of TB control. For internally displaced populations, coordination with the NTP in the country is equally crucial. In situations where repatriation programmes for refugees are being implemented, the NTP in the country of origin should be involved from the beginning of the transfer process to ensure those on treatment complete the course.

UNITED REPUBLIC OF TANZANIA

In refugee camps in the United Republic of Tanzania, NGOs provide TB diagnosis and treatment services, monitor and supervise patients and conduct health education activities. The TB programme is incorporated into the Tanzanian National Tuberculosis Control Programme and assessments of drug supply and data collection are conducted by the NTP.

AFGHANISTAN

In early 2002, when WHO reopened its office in Kabul, Afghanistan, after years of emergency operation-oriented activities in Pakistan, the NTP was barely existent. It dealt mainly with treatment of TB cases in Kabul and surrounding districts. Its authority was completely unrecognized outside Kabul, and NGOs filled gaps without clear policies and technical guidance. Key steps in ensuring sustainability included:

- Appointment of regional TB coordinators (accountable to the NTP, supported by WHO) as an essential measure in strengthening control activities in remote areas.
- National workshop on communicable disease control conducted, to endorse the DOTS strategy as the national strategy for TB control and highlight the leading role of the NTP.
- Preparation of a multi-year (2002–2005) strategic plan for DOTS expansion.
- Establishment of an Interagency Coordinating Committee, an advisory body for the MOH on issues related to TB control and a forum for all stakeholders to debate implementation of the Stop TB strategy.
- Supervisory visits by NTP manager to regions, in order to affirm the coordinating role of the MOH regarding TB control activities countrywide.
- Expansion of partnerships between the NTP and various actors in TB control by means of memoranda of understanding, entailing TB drug and food distribution and abidance to national guidelines.
- Celebration of World TB Day in both Kabul and the provinces to help raise awareness about the programme and attract more partners under the NTP umbrella.

7.3. EXPANSION OF TB PROGRAMMES IN REFUGEE AND DISPLACED POPULATIONS

Once a TB programme has started and is achieving conversion rates of at least 85% at month 2 of treatment in new sputum smear-positive cases, and treatment success rates of 85% and over in at least one clinic, this implies that the TB programme can be implemented effectively. At this stage, expansion of the programme from that clinic can occur. The clinic should be designated a "demonstration and training centre". Ideally, a programme should aim for cure rates of 85%. However, in refugee and displaced populations, other outcome measures such as case-fatality rate may be high because of concomitant disease, malnutrition and HIV; and treatment interruption, transfer-out rates or defaulter rates can be high because of instability.

Expansion should be gradual. Many staff will need to be trained effectively. Higher level supervisors or outside sources will need to assist in training, as the ongoing operations of the demonstration and training centre must not be neglected. However, if expansion is too slow, the programme at the initial site may be compromised by an influx of patients from more remote areas, resulting in poor treatment adherence and an increase in defaulter rates.

Training should include the primary health staff at peripheral-level health facilities who have responsibilities for case-finding and supervising treatment of TB patients. Laboratory staff must also be trained before expansion can proceed.

7.4 TRANSFERS INTO A TB PROGRAMME

Although most TB patients are expected to complete treatment at the centre where they were first registered, a plan should be devised to deal with patients who transfer into or out of the programme. The plan will depend on what is known about the TB programme of origin/destination, the regimens used and the quality of the programme.

Direct transfers, accompanied by treatment records, who originate from well-functioning TB programmes that use similar treatment regimens should continue their current regimen to completion with routine follow up including sputum examinations.

Transfers from a TB programme of unknown quality or with poor results (default rate >10%, cure rate <85%, 60-day sputum conversion rate <80%) should be treated as shown in Box 6.

Box 6 Procedure for transfer of patients into a TB programme

- Determine duration of previous treatment for all TB patients; perform two sputum smears on all patients.
- If **patients were initially smear-positive and are still smear-positive** on repeat sputum smear screening, and
 - a) have been treated for 1 month or more, commence on Category II regimen
 - b) if previous treatment was less than 1 month, start Category I treatment at day 0.
- If initially **smear-positive patients are now smear-negative** and
 - a) have received at least the full 2 months of appropriate intensive-phase treatment, complete a full continuation phase
 - b) have not completed 2 months of intensive-phase treatment, reinstitute Category I treatment from day 0.
- If **patients were initially smear-negative and are now smear-positive**, and
 - a) have received intensive treatment for 1 month or more, commence on Category II regimen
 - b) have received less than 1 month of intensive-phase treatment, start Category I from day 0.
- If **patients were initially smear-negative are still smear-negative**, and
 - a) have received appropriate intensive-phase treatment for 1 month or more, continue with the prescribed treatment
 - b) have received less than 1 month of intensive-phase treatment, start Category III from day 0 if TB is not severe.

CROSS-BORDER ISSUES

People may move regularly across country borders not only because of insecurity but also because of lack of access to health care in one country or for employment purposes. TB diagnosis and treatment can be compromised if close monitoring does not take place. Different TB regimens in different countries make this even more difficult, and communication where possible with authorities across the border is necessary to follow-up patients.

THAILAND

A TB programme run by an NGO in Mae Sot, Thailand, provides TB care for undocumented migrants, using the Stop TB strategy. Motorcycle-riders deliver the drugs to the homes of the migrants each day. Undocumented migrants are at risk of deportation, so a unique feature of this programme is the photo identity card given to patients. If arrested, they show their card and, on agreement with the government authorities of the province, will not be deported.

The TB programme operates in close cooperation with the local provincial health office.

Another activity along the border are small huts for TB patients behind the Kwai River Christian Hospital in Kanchanaburi Province. TB patients stay at these huts for six months or however long it takes to finish treatment. This makes it possible for undocumented migrants to safely receive the full treatment.

SOMALIA – SAMPLE CROSS-BORDER TRANSFER FORM

National Tuberculosis Control ProgrammeFrom (referring health facility): To (receiving health facility): Address and name of I/C TB: Name: TB ID number: Age: yr. Sex (tick): Female Male Nationality: Reason for transfer: Date of starting TB treatment: (day) (month) (year G.C)Type of TB: PTB/SS+ PTB/SS- EPTB If extrapulmonary, specify the site involved: Classification: New Re-treatment **Current treatment:**

Intensive phase

Continuation phase

| Drugs | Dosage | Total daily doses given | Drugs | Dosage | Total monthly doses given |
|----------------------|----------------------|-------------------------|----------------------|----------------------|---------------------------|
| <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> |
| <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> |
| <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> | <input type="text"/> |

Sputum results:

| Month | Date | Result |
|-------|----------------------|----------------------|
| 0 | <input type="text"/> | <input type="text"/> |
| 2/3 | <input type="text"/> | <input type="text"/> |
| 4/5 | <input type="text"/> | <input type="text"/> |
| 6/8 | <input type="text"/> | <input type="text"/> |

This treatment has been interrupted because of transfer since: / / (date (day/month/year))Drugs given to the patient for the travel time: (number of days)Date: / / Name: Signature:

Receiving unit: cut and send this portion back to your cross-border TB coordinator

From: (receiving health unit): **To: cross-border TB coordinator**The following patient has attended for further treatment on / / (date)Name: TB ID number: Date: / / Name: Signature:

7.5 REPATRIATION AND TRANSFERS OUT OF THE TB PROGRAMME

Repatriation or transfer may occur during the course of treatment if:

- there is a functioning TB programme in the area to which the patient is being transferred;
- a liaison exists between the two TB programmes and the refugee agency organizing the movement of the population, to coordinate transfer and minimize interruption of treatment.

When a mass repatriation is being planned, new patients (who are likely to repatriate within the next three months) should ideally repatriate or transfer out only when they have completed their intensive phase of treatment. If this is not possible, they should be considered for priority transfer or repatriation.

Key messages if repatriation or transfer is planned:

- preparation (stop recruitment of new patients into the programme);
- coordination between the two programmes and the NTPs of the two countries;
- set up administrative systems for the transfer – hand-held patient card plus transfer notes;
- harmonization of treatment protocols (see transfers-in);
- supply of drugs for the transfer process;
- pick-up at border and close follow up in the country of return.

It is very important that continuity of treatment occurs during transfer. Contact with the new treatment centre should be made by the clinic staff if possible prior to transfer. Forward planning and liaison between staff is particularly important if a large population is being transferred. If there is a difference in regimens used by the transferring and receiving programmes, a plan must be developed to resolve this. A reliable mechanism for transfer of records should be established. Ideally, at completion of treatment, the transferring programme should be notified as to the treatment outcome of transferred patients.

Each patient should have:

- their personal record card up to date and with the treatment plan for the rest of the course detailed; a copy of the card should be sent ahead of the patient to the new treatment centre if possible;
- sufficient quantities of ethambutol and isoniazid to allow travel and contact with the new clinic, e.g. one month's supply;
- If the transferring programme has a supply of drugs to complete therapy of a group of transferred patients, and the receiving programme lacks an adequate supply or time in which to order sufficient drugs, arrangements to have the drugs accompany the patient should be considered.

ERITREAN REFUGEES REPATRIATING FROM SUDAN

In 2003, Eritrean refugees repatriating from Sudan in treatment for TB who had already completed the intensive phase of treatment were provided with 4 weeks of medications and followed up by the implementing partner in Sudan, to be linked into the NTP once they reached their final destination.

In the original TB register, patients should be recorded as transferred out. However, every effort should be made to determine the final outcome and the register updated so that the outcome may be included in the statistics for the admitting cohort.

If the health services in the area into which the patient is being transferred are not functioning or able to cope with extra patients, or if satisfactory liaison cannot be made to avoid the interruption of treatment, it is preferable for the patients to remain in the camp or present treatment centre until treatment can be completed. The patients and their families should be advised that any disadvantages of delayed repatriation must be balanced against the specific risks of incomplete treatment. If the patient's departure from the treatment centre prior to treatment completion is unavoidable, consideration should be given to changing the regimen after the intensive phase to complete therapy with the continuation phase of the 2HRZE/6HE regimen, which permits self administration. When possible, repatriation or transfer should be delayed until at least the intensive phase has been completed. However, it is recommended that families are kept together, and patients should not be held back and separated from their families to complete this phase.

A list of patients receiving TB treatment should accompany every convoy and be handed over to the implementing partner once across the border. Careful records should be kept and active follow up implemented in the community, particularly as the returnee's final destination may be likely to be different from that recorded initially. The proportion of those who are lost to follow up should be reported to UNHCR or other concerned agency monthly. TB is often stigmatized, particularly where associated with HIV. Care must be taken to ensure confidentiality of diagnosis, which should not appear on any public document such as the manifest of vulnerable people.

ANGOLA – DEMOBILIZED SOLDIERS

It is important that demobilized soldiers and dependents are also considered among the would be "returnees". In Angola, where a long quartering phase preceded the demobilization, this became particularly relevant. Soldiers on TB treatment had to be left behind until completion of treatment. It is essential that the agency involved in transport of these people be involved in a referral system assessing the attending capacity at the end-point.

7.6 PRIVATE SECTOR

Private practitioners tend to flourish in refugee/IDP settings. Breakdown and looting of national health care facilities and lack of trained staff often lead to refugees/IDPs seeking care in the private sector and purchasing drugs in private pharmacies if such services are available.

However, private pharmacies are weakly regulated in terms of drug quality, qualifications of the health care providers and particularly their knowledge of TB case management standards, NTP regimens and reporting requirements. Given that private practitioners will almost certainly be prescribing TB drugs, it is essential that awareness is raised and that appropriate training and support are provided to them to ensure proper TB diagnosis and case management under NTP supervision.

AFGHANISTAN

Reports from health workers and research conducted in 2003 on TB and gender show that the vast majority of patients seeking care in DOTS centres have previously seen a private practitioner for their symptoms. Most patients start treatment as prescribed by the private practitioner. In almost all cases, diagnosis is made on clinical grounds, without sputum examination; treatment is often not appropriate, does not include the DOT component; there is no regular follow up; and no reporting to health authorities by the private practitioner. Personal enquiries in private pharmacies have disclosed that TB treatment is largely available over the counter. Costs of a full course of treatment (six months) is in the range US\$ 50–60 and the most frequently prescribed medications include 3- or 4-drug FDCs of uncertain quality.

Ethical considerations prevent the ban of import or sale of TB drugs through the private sector because of the current lack of affordable access to DOTS by a large part of the Afghan population. WHO is supporting operational research on TB treatment in the private sector in Kabul, where most doctors operate. As in many other countries, physicians concentrate in major cities. As a consequence of arrangements during the previous political regimes, doctors are not allowed to work exclusively in the private sector but they can run their clinics after working hours in government employment, which is usually very poorly paid. Given that they can be reached through the public sector, this, in theory, makes it easier to address training and advocacy messages to private practitioners.

7.7 SPECIAL GROUPS

REFUGEE CAMPS

Refugee populations may be differentially affected by TB (and HIV coinfection) than host populations, often exacerbated by overcrowding and malnutrition but also treatment interruptions and poor access to health care. They may come from high TB burden populations or, conversely, be hosted in high TB burden countries.

ERITREA

TB case detection and treatment was strengthened as part of the response to very high levels of malnutrition among Somali refugees in Eritrea in 2002. UNHCR data from 2003 show an annual incidence six times that of the host population (1852/100 000 in the Somali refugees in 2003 versus 277/100 000 in the local Eritreans in 2001).

Health care services can be better in refugee camps compared to local services owing to good health care facilities and trained staff. TB control is not a priority in the emergency phase. However, once effective primary and community health care is established, including a network of trained and supervised community health workers, TB programmes should be introduced. Linkages with national programmes should be made early.

Refugees may be excluded from national programmes and global initiatives such as the Global Drug Facility and the Global Fund to Fight AIDS, Tuberculosis and Malaria. However, opportunities must not be missed for incorporation into the NTP to ensure appropriate use of protocols for diagnosis and treatment, standardized reporting, quality control for sputum microscopy, quality-assured drug supply, and monitoring and evaluation.

ISLAMIC REPUBLIC OF IRAN

Approximately 2.3 million Afghan refugees live in the Islamic Republic of Iran, most of them within communities in urban and sub-urban settings; less than 5% are in refugee camps, mainly in Sistan–Balochistan Province on the border with Afghanistan. In 2001, 20% of TB cases notified in the Islamic Republic of Iran were refugees; they accounted for approximately 44% of sputum smear-positive pulmonary TB cases identified in Tehran. The incidence of TB was generally higher among refugees than non-refugees; for instance, in Zabol District, in Sistan, the incidence of sputum smear-positive pulmonary TB was 60% higher in Afghan refugees than in Iranians. The NTP of Iran, whose activities are fully integrated in PHC settings, provides services free of charge to refugees with TB in public health facilities either in communities or in camps.

INTERNALLY DISPLACED POPULATIONS AND NON-CAMP REFUGEES

A major problem with IDP and non-camp refugees is that they may not be able to access national or NGO health services; mechanisms put into place for the stable population may not apply. IDPs, unlike refugees, may not have the same level of protection from the international community and national authorities may not address their needs. It is therefore vital that efforts are made to reach this vulnerable population and include them in health care services. Increased collaboration between the NTP and NGOs can increase population coverage and improve the efficiency with which TB care and control activities are implemented in displaced populations. Proactive measures should be taken, including the use of community health workers and mobile clinics.

UGANDA

Almost 30% of Uganda's population is internally displaced. Refugees from other countries make up 15% of the displaced population in Uganda. Uganda is a high TB burden country, with the incidence of all TB cases of 363 per 100 000 population. Although Uganda is one of the countries reported to be implementing the DOTS strategy, sub-national data from 2002 show that only 28 out of 56 districts were at various stages of implementing DOTS, with 16 districts not implementing DOTS at all. Most of the 1 418 432 registered IDPs are hosted in eight districts where DOTS was not being fully implemented.

The average national treatment success rate (60%), and that in districts with IDPs and refugees (58%), was similar. However, IDPs accounted for only 1.7% of TB cases notified to the NTP. UNHCR-run treatment centres consistently achieved higher average treatment success rates (67%). Despite challenges experienced in the course of providing services to refugee populations, it is noted that where UNHCR has a presence, TB programme activities are better implemented.

Specific efforts must be made to reach IDPs if Stop TB Strategy targets are to be reached.

ASYLUM SEEKERS

A patient suspected of TB must be managed according to the *International standards for tuberculosis care*.

If the patient is already a TB patient, treatment must be resumed as if the patient were transferring into a programme (see algorithm in Box 6).

It is important that appropriate reception standards are followed:

- Access to adequate care must be free and non-discriminatory.
- Detention should be opposed (no grounds for detention to reduce risk of TB transmission).
- There should be no compulsory screening for HIV in TB patients.
- Clear guidelines must be provided to staff processing applications to allay fears of work-based transmission.

7.8 BUILDING PARTNERSHIPS

Building partnerships with NGOs and civil society, in settings where vulnerable civilian populations with varied health needs have become detached from or have never experienced a health service capable of controlling a growing burden of TB, can make a big difference in terms of quality and scope of care.

It is important to note that similar problems arise in stable populations when profound economic and social difficulties lead to the breakdown of a once efficient service. In the Russian Federation, for example, as well as in many of the newly independent countries of the former Soviet Union, a rapid rise in TB incidence, fuelled by the emergence of HIV and MDR-TB, has overwhelmed a health service never designed to withstand the fiscal and social problems that it is facing. The problems of poverty-stricken populations in these circumstances mirror those experienced by refugee and displaced populations, and this section could apply equally to them.

In most settings with refugee and displaced populations, there are a number of different care providers outside the government. While the size, type and role of these actors vary greatly across contexts, it is potentially to everyone's advantage to involve different actors in TB care and control activities. The first step in creating a partnership is to map all relevant public and private actors in a given setting. Each of the actors will need to have clear, and complementary, roles, through an establishment of terms of reference for each of the partners. Selection of delegated roles and responsibilities needs to be consistent with mission and capacity of each of the partners. It is essential for the agency initiating partnership building (the local NTP if possible) to have a strong stewardship capacity in order to guide and oversee collaboration between different partners. The recommended modality or "tool" of a partnership is a memorandum of understanding, which acknowledges the identity and autonomy of the partners.

Partnership building is key in terms of harnessing the contribution of different care providers, whereby there should be flexibility to involve NGOs – even if they are currently not involved – in TB- or health-related work. In contexts where there are existing partnerships with communities, their involvement in health activities should be acknowledged and supported.

SOMALIA

A partnership was formed between WHO and the World Food Programme (WFP) in Somalia for TB care and control activities to ensure the achievement of mutual objectives: WFP provided food aid to TB centres over 2003–2005 towards the WFP objective "to improve the nutritional status of vulnerable people". This in turn contributed to WHO's overall goal in Somalia with regard to TB, which is to increase TB cure rates. In a letter of understanding, terms of collaboration were set out: WFP would consult WHO when making decisions on identifying TB centres to be supported with WFP food aid; agreeing on numbers of beneficiaries to support with food aid per centre; agreeing which TB centres to suspend or terminate WFP food aid support; agreeing on renewing WFP food aid support to TB centres. Furthermore, WFP food aid was to be provided to TB patients throughout their medical treatment, whether they were registered as in- or out-patients at the TB centre.

7.9 PHASING DOWN/HANDOVER OF TB PROGRAMMES TO THE NTP

The TB programme should be phased down if:

- population displacement or closure of the camp is expected;
- funding is no longer available (a situation that should be considered preventable – generally indicative of flawed planning and/or inadequate political commitment);
- security problems are seriously interfering with programme efficiency, e.g. making regular supply of drugs impossible;
- it proves impossible, for whatever reason and despite vigorous efforts, to address the factors associated with poor outcomes – to achieve defaulter rates of <10% and 60-day sputum conversion rates of >70% – among smear-positive patients.

If closure of the camp or population movements can be anticipated, plans specific to the local situation should be made regarding (i) completion of therapy for those already in treatment (see "Transfers out") and (ii) when and how to discontinue admissions to the programme.

In general, any circumstance that does not permit completion of therapy for the individual or group should be considered unacceptable. Interrupting fully supervised treatment with an appropriate drug regimen confers an increased risk of relapse, depending on the stage at which the treatment interruption occurs.

Stopping new admissions to the TB programme before the complete closure of the programme is a separate but related decision. It will create personal and ethical difficulties for both health staff and patients since it involves refusing treatment to new patients even while providing it to established patients.

Following closure of a TB programme in an area, the TB register should be sent to the NTP so that enrolled patients may be followed up to completion of treatment. Ensuring links with the NTP will be critical in ensuring continuation of TB care and control activities as much as possible.

APPENDIX 1 – THE STOP TB STRATEGY

- Vision:** A world free of TB
- Goal:** To dramatically reduce the global burden of TB by 2015 in line with the Millennium Development Goals (MDGs) and the Stop TB Partnership targets
- Objectives:** Achieve universal access to high-quality diagnosis and patient-centred treatment
- Reduce the human suffering and socioeconomic burden associated with TB
- Protect poor and vulnerable populations from TB, TB/HIV and multidrug-resistant TB (MDR-TB)
- Support development of new tools and enable their timely and effective use
- Targets:** MDG 6, Target 8: Halt and begin to reverse the incidence of TB by 2015
- Targets linked to the MDGs and endorsed by Stop TB Partnership:
- By 2005: detect at least 70% of new sputum smear-positive TB cases and cure at least 85% of these cases
 - By 2015: reduce prevalence of and deaths due to TB by 50% relative to 1990
 - By 2050: eliminate TB as a public health problem (<1 case per million population)

COMPONENTS OF THE STOP TB STRATEGY

1. Pursue high-quality DOTS expansion and enhancement

- a. Political commitment with increased and sustained financing
- b. Case detection through quality-assured bacteriology
- c. Standardized treatment with supervision and patient support
- d. An effective drug supply and management system
- e. Monitoring and evaluation system, and impact measurement

2. Address TB/HIV, MDR-TB and other challenges

- Implement collaborative TB/HIV activities
- Prevent and control MDR-TB
- Address prisoners, refugees and other high-risk groups and special situations

3. Contribute to health system strengthening

- Actively participate in efforts to improve system-wide policy, human resources, financing, management, service delivery, and information systems
- Share innovations that strengthen systems, including the Practical Approach to Lung Health
- Adapt innovations from other fields

4. Engage all care providers

- Public–public, and public–private mix approaches
- International Standards for TB Care

5. Empower people with TB, and communities

- Advocacy, communication and social mobilization
- Community participation in TB care
- Patients' Charter for Tuberculosis Care

6. Enable and promote research

- Programme-based operational research
- Research to develop new diagnostics, drugs and vaccines

APPENDIX 2 – ROLES OF KEY AGENCIES

In order to implement an effective TB programme, it should be planned and operationalized at several levels:

NATIONAL LEVEL

- Where there is an effective NTP, the NTP will lead TB care and control activities, assisted by WHO, UNHCR and NGOs operating in the country, or
- where the NTP is not functional, the WHO Representative will lead in the development of a TB programme in close collaboration with appropriate national agencies, assisted by UNHCR and NGOs operating in the country. In this situation, efforts are to be made to develop an effective NTP.

INTERCOUNTRY LEVEL - especially during the repatriation phase and at other periods of mass population movement.

NTP managers of the host country, the recipient country and any third country (e.g. during transit), assisted by appropriate NGOs should organize TB control activities - this process will be assisted by various mechanisms:

- WHO regional participation,
- UNHCR participation, and
- intercountry (border) committees.

Where the NTP uses WHO/IUATLD endorsed regimens, then the regimen used for TB care and control should be that used by the NTP. If the NTP is using some other protocol, then advice should be sought from the WHO Representative in consultation with the NTP manager. When there is inconsistency between the host country and the country of origin, the decision on drug regimen should be referred to an intercountry (border) committee.

NATIONAL TB PROGRAMME

- Responsibility for all TB control activities in the country
- Delegation of TB control activities to recognized organizations, as appropriate
- Planning, implementing and evaluating the TB care and control activities in refugee and displaced populations
- Coordinating government, international and non-government organizations funding
- Drug procurement and distribution
- Training
- Supervision of TB care and control activities for refugees and displaced populations, and

- establishment of intercountry (border) committees to coordinate TB care and control activities in border areas.

KEY AGENCIES:

1. WORLD HEALTH ORGANIZATION

- Provide technical support such as development of guidelines and human resource development
- Advise on when to commence, and when not to commence, a TB programme
- Assist in the arrangements for procurement of quality-controlled drugs
- Assist in advocacy and fund-raising, and
- Take the lead role, in the absence of an effective NTP.

2. OFFICE OF THE UNITED NATIONS HIGH COMMISSIONER FOR REFUGEES

UNHCR has the responsibility to ensure that refugees and other populations of concern to UNHCR have access to essential preventive and curative health care, with the goal of minimizing avoidable morbidity and mortality. Services are delivered through partners. Role in TB care and control includes:

- Advocate for the inclusion of refugees and other persons of concern to UNHCR in national TB and HIV programmes, including provision of drugs
- Support linkages with NTP/WHO
- Assist in procurement of TB drugs
- Support planning, especially in anticipation of, and during, repatriation and mass population movement
- Coordination of health partners in some settings
- Funding of some partners.

3. NONGOVERNMENTAL ORGANIZATIONS

- Provide health care services to refugee and displaced populations
- Services may include primary health care, reproductive health, hospital care, therapeutic feeding programmes
- Monitor health, nutrition and human rights within refugee and displaced populations
- Implement TB control programmes in collaboration with WHO and NTP where one exists
- Specialized NGOs may conduct operational research.

APPENDIX 3 – SAMPLE MEMORANDUM OF UNDERSTANDING

Memorandum of understanding (MOU) between WHO and NGOs or agencies involved in the TB control programme of country X (January – December YYYY)



WHO Country X Office

Tel:

Fax:

E-mail:

Preamble

In order to ensure the provision of high quality TB care and control services, it is proposed that all Nongovernmental organizations (NGOs) or agencies involved in the approved TB control programme in Country X requesting WHO support will sign this memorandum of understanding (MOU).

- (a) WHO shall provide TB drugs (dependent on adequate stock and funding) according to the number of cases on treatment (agreed upon with WHO) on a quarterly basis to the NGO for the approved TB programme. A proper inventory record of the drugs received and dispensed must be maintained.
- (b) WHO shall also provide, on written request from the NGO/agency, necessary on-the-job training for the NGO technical personnel in the management of TB patients, and in the laboratory backup support for the programme.
- (c) WHO shall provide, on written request from the NGO/agency, basic laboratory materials for the programme.
- (d) WHO shall carry out, as security conditions allow, on-site visits to the tuberculosis management centres of NGOs/agencies being supported to ensure that the TB treatment guidelines are being adhered to, and to get more acquainted with the success and difficulties of NGOs/agencies.
- (e) The NGO/agency, on starting a TB programme, must be ready to continue with the programme for a **minimum period of 12 (twelve) calendar months**, calculated from the first COHORT of patients who are started on treatment.
- (f) The NGO/agency will maintain and use prescribed WHO recording registers and forms. It will also follow all the policies and guidelines laid down in the guidelines for TB control in Country X published by WHO.
- (g) The NGO/agency shall complete and forward the quarterly report forms (TB 09, 10 & 11) to WHO by 15th of the following month after the reporting quarter.
- (h) If the NGO/agency wishes to continue its TB care and control activities beyond the validity of this MOU, a written request should be submitted to WHO. If the performance has been satisfactory, this MOU will be extended to cover a further period of one year and similar action will be taken for future periods.

For NGO/agency:

Date & Stamp

For WHO:

Date & Stamp

APPENDIX 4 – JOB DESCRIPTIONS AND RESPONSIBILITIES OF TB PROGRAMME STAFF

The number of personnel required and their job descriptions will depend on the local situation. Information on factors such as the number of refugees/IDPs and local population, the site and how spread out the population is will help to determine staffing needs. In large areas, where the affected population is dispersed in different camps or villages, local area coordinators may be required in addition to the overall TB coordinator.

LEAD AGENCY

- Ensure adequate funding is available for the programme
- Appoint a suitable TB coordinator
- Assist with the training of personnel, especially laboratory technicians
- Liaise with national authorities, donors and international agencies involved in refugee care
- Mobilize political commitment and support
- Ultimate responsibility, with input from WHO, UNHCR and country etc., for decision to initiate and terminate a TB programme and for determination of specific programme characteristics

TB COORDINATOR (the only position solely dedicated to TB control)

- Liaise with NTP
- Determine staffing requirements
- Develop job descriptions
- Hire staff
- Provide leadership, encouragement and advice for problem solving to all staff members
- Produce TB protocol for the refugee/IDP setting and their distribution to each treatment post
- Train camp or local area coordinators
- Set up the TB programme in all the camps (and any sites for internally displaced persons)
- Coordinate training of programme staff including two laboratory technicians for each laboratory

- Supervise overall functioning of the TB programme
- Ensure quality control of all aspects of the TB programme including the laboratory
- Calculate requirements for drugs and other supplies and order in sufficient time to ensure that adequate stocks are available at all times
- Ensure continuing education programmes for staff and the community
- Visit the laboratory regularly and record all new patients in the TB register
- Maintain the TB register
- Ensure follow up of all TB patients, especially transfers and difficult patients
- Monitor TB contact investigation activities
- Coordinate management of all TB-related information, including reporting

TB FOCAL POINT IN HEALTH CENTRE

- Identify TB suspects
- Request sputum smear examination for TB suspects identified
- Liaise with TB laboratory to ensure that all sputum smear examinations requested for TB suspects are performed
- Liaise with laboratory to ensure all sputum positive patients are followed up
- Ensure all records are kept up-to-date and are accurate
- Ensure all follow-up sputum tests are performed as required and results recorded
- Provide feedback of clinic results to community health workers and other staff
- Ensure all patients are treated with respect and compassion by clinic staff
- Ensure clinic hours are suitable for the patients and long waits are not encountered
- Ensure incentives are distributed appropriately
- Implement continuing education programmes in the clinic
- Ensure all those who fail to attend for treatment are followed up
- Check supplies are adequate (including emergency stock) and orders placed in a timely manner
- Liaise with camp or emergency setting coordinator, and
- Provide continuing education programmes for other staff and the community
- Identify and correct situations entailing preventable risks of transmission
- Ensure contact investigation activities are carried out

COMMUNITY HEALTH WORKERS

- Refer anyone with symptoms suspicious of TB to the clinic
- Educate community, patients and relatives regarding TB and its management
- Ensure directly observed therapy administration to patients for whom they are responsible
- Record all treatments given in clinic records and on patient's record card
- Identify defaulters, "returnees" and "missing"
- Follow up non-compliers and defaulters
- Refer contacts for assessment

LABORATORY TECHNICIAN

- Examine all smears sent for AFB examination and accurately report the findings. Reports should include whether the sample was saliva or sputum, whether AFBs were seen and if so in what numbers (e.g. scale from + to +++)
- Supply regular written reports to the clinic supervisor of all smear results, both positive and negative
- Keep a list of all new smear positive patients, the date of diagnosis, when and who notified
- Maintain the laboratory register updated
- Provide summary reports of laboratory activity and results
- Participate in the quality control process

APPENDIX 5 – ESTIMATING DRUG REQUIREMENTS

To carry out an initial order of drugs for the first year, the following steps are required:

- Define the treatment regimens to be adopted, then identify the drugs to be used for each category of patient as well as the drug combination and their dosages in function of the weight groups (see Tables 5.1 and 5.2)
- Calculate the drug requirement per patient for each category (see section 5.2 below)
- Estimate the number of smear-positive cases based on epidemiological data
- Estimate the number of adult patients in each category to be treated
 - When a large population is displaced, the proportion of patients whose treatment has been interrupted is high during the first year. For example, with Rwandan refugees (October, 1994), the estimate for each 100 000 population was:
 - 50 Category I patients (new smear positive cases with 10% severe smear-negative)
 - 20 Category II patients (failures, relapses, and smear-positive cases after interruption of treatment), and
 - 30 Category III patients
- Calculate total estimated drug requirements for adults
- Add 10% to the quantity of each drug (or combination drug) to provide for children and some wastage, and then
- Add 50% for reserve stock to the first purchase
- For planning purposes, add an additional 50% to costs, to cover transportation and distribution.

Review drug usage after the first three months and, based on consumption during that period, recalculate requirements for the rest of the year. Place orders well in advance to ensure continuity in supply. Note that requirements may increase if treatment is seen to be successful, as more suspected cases will be encouraged to come forward.

5.1 EXAMPLES OF NUMBER OF TABLETS OF TB DRUGS FOR TREATMENT IN FUNCTION OF THE DRUG COMBINATION, DOSAGE AND WEIGHT GROUPS

Table 5.1 Sample regimens with fixed-dose combinations of TB drugs in adults^a

| WEIGHT IN KG | 30–39 | 40–54 | ≥55 |
|---|-------|-------|-----|
| Initial phase – daily or 3 times weekly | | | |
| HRZE (75 mg + 150 mg + 400 mg + 275mg) | 2 | 3 | 4 |
| or HRZ (75 mg + 150 mg + 400 mg) ^b | 2 | 3 | 4 |
| Category II: add S (vial 1g) for 2 months. | 0.5 | 0.75 | 1 |
| Continuation phase – daily | | | |
| HE (150 mg + 400 mg) | 1.5 | 2 | 3 |
| Continuation phase – 3 times weekly | | | |
| HR (150 mg + 150 mg) | 2 | 3 | 4 |
| Category II: add E 400 mg for 5 months | 2 | 4 | 6 |

E, ethambutol; H, isoniazid; R, rifampicin; S, streptomycin; Z, pyrazinamide.

^a Adapted from Blomberg B et al. *Informal consultation on 4-drug fixed-dose combinations compliant with the WHO model list of essential drugs*, Geneva, 15–17 August 2002. Geneva, World Health Organization (unpublished).

^b HRZ (150 mg + 150 mg + 500 mg) is for use 3 times weekly.

Table 5.2 Sample regimens with fixed-dose combinations of TB drugs in children (paediatric formulations)^a

| WEIGHT IN KG | up to 7 | 8–9 | 10–14 | 15–19 | 20–24 | 25–29 |
|--|---------|------|-------|-------|-------|-------|
| Initial phase – daily or 3 times weekly | | | | | | |
| HRZ (30 mg + 60 mg + 150 mg) | 1 | 1.5 | 2 | 3 | 4 | 5 |
| E 400 mg | – | – | – | – | 1 | 1 |
| S vial 1g | 0.25 | 0.25 | 0.25 | 0.33 | 0.50 | 0.50 |
| Continuation phase – daily | | | | | | |
| HR (30 mg + 60 mg) | 1 | 1.5 | 2 | 3 | 4 | 5 |
| Continuation phase – 3 times weekly | | | | | | |
| HR (60 mg + 60 mg) | 1 | 1.5 | 2 | 3 | 4 | 5 |

E, ethambutol; H, isoniazid; R, rifampicin; S, streptomycin; Z, pyrazinamide.

^a Adapted from Blomberg B et al. *Informal consultation on 4-drug fixed-dose combinations compliant with the WHO model list of essential drugs*, Geneva, 15–17 August 2002. Geneva, World Health Organization (unpublished).

Distributing and administering four separate drugs simultaneously – and ensuring that all are available and taken together every time – poses considerable logistic and supervisory problems. In some countries with large TB programmes, special “blister packs” are produced in which three or four tablets, corresponding to the daily requirement for the particular treatment regimen adopted, are packaged together.

However, given the particular challenge in refugee/IDP settings, WHO recommends only using fixed-dose combination (FDC) drugs in these situations.

FDC tablets simplify the logistics of drug management and can reduce the risk of drug resistance.

5.2 ESTIMATING THE QUANTITY OF FIXED-DOSE COMBINATION DRUGS

Estimating the quantity of **FDCs** needed will depend on the approved drug treatment regimens for each category of TB patient. The new 4-drug FDC is the most suitable formulation for the two-month intensive phase of treatment. For the continuation phase, the 2-FDC containing isoniazid and rifampicin is commonly used. Before estimating drug requirements, the length of time between placing an order and receiving the medicines at all levels must be known; this is commonly called *lead* time. If this is 6 months or less, the procurement plan should cover the drug needs for one year as well as the necessary buffer stock. However, if the lead time is likely to be more than 6 months, a procurement order of more than one year's supply should be prepared.

In countries with good information systems, estimates of drug requirements should be based on the *number of notified* cases treated with the recommended standard chemotherapy regimens. In settings with poor baseline health information, such as may be found in refugee and displaced settings, an estimate of the number of TB cases expected should be made, for example by using NTP data or data from countries of origin of refugees.

The following example describes how to estimate drug needs:

1. Determine the amount of tablets or grams of each drug the programme needs to treat *one patient* in each treatment regimen for categories I, II and III (see Table for categories).
2. Estimate the total amount of tablets or grams of each drug the programme needs to treat *all TB patients* during ONE YEAR.
3. Specify the quantity of reserve/buffer stock needed at each level of the system.

EXAMPLE: CATEGORY I REGIMEN

Category I regimen is prescribed to new smear-positive PTB patients; new smear-negative PTB patients with extensive parenchymal involvement; patients with severe concomitant HIV disease or severe forms of extrapulmonary TB.

In this example:

- The estimated number of new smear-positive PTB to be treated (body weight band 40–54 kg) is **7 725**.
- If one assumes that the number of new smear-negative PTB cases represents 30% of the number of new smear-positive PTB (this percentage varies with TB prevalence and diagnostic practices), then the number of smear-negative PTB is: **$7\,725 \times 0.30 = 2\,318$** .
- Also, if one assumes that new cases of severe forms of extrapulmonary TB represent 20% of new smear-positive PTB cases then their number is: **$7\,725 \times 0.20 = 1\,545$** .
- Therefore total Category I cases to treat is: **$7\,725 + 2\,318 + 1\,545 = 11\,588$** .

EXAMPLE: CATEGORY II REGIMEN

The category II treatment regimen is prescribed to previously treated patients who are classified as relapses, treatment failures and returning defaulters. In many instances, the number of re-treatment cases is equivalent to 10–40% of the new smear-positive cases. In this example, 25% of the estimated number of new smear-positive PTB cases is used = **$7\,725 \times 0.25 = 1\,932$** .

EXAMPLE: CATEGORY III REGIMEN

The category III regimen is prescribed in cases of new smear-negative PTB (other than in Category I) and new less severe forms of extrapulmonary TB. In this example, the estimate is based on 15% of new smear-positive PTB cases for adults and 8% for children.

$7\,725 \times 0.15 = 1\,159$ (adults)

$7\,725 \times 0.08 = 618$ (children)

Total Category III cases to treat: **$1\,159 + 618 = 1\,777$** .

Therefore, total number of patients to treat for all three categories for one year = **$11\,588 + 1\,932 + 1\,777 = 15\,297$** .

Based on numbers calculated as in the example above, the quantities of each drug needed can be worked out in two steps:

1. Determine the number of tablets of each drug needed to treat one patient for each TB category, then
2. Multiply the number of tablets of each drug to treat one patient by the number of cases in each TB category.

For example:

Note: All calculations below are based on 28 doses per month for a daily regimen and 12 doses per month for a 3 times per week regimen as follows:

For a daily regimen
(one month = 28 doses)

2 months = 56 doses

3 months = 84 doses

5 months = 140 doses

6 months = 168 doses

For a 3 times per week regimen
(one month = 12 doses)

4 months = 48 doses

5 months = 60 doses

Example: Quantities needed for Category I regimen (adult patients with body weight band 40–54 kg): 2RHZE/4(RH)3:

| INTENSIVE PHASE: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
|--|---|-----------------|--------------------|------------------------------|
| FDC tablet containing: R150 mg/H75 mg/ Z400 mg/E275 mg | 3 tablets daily for 56 doses | = 168 x | 11 588 | = 1 946 784 |
| CONTINUATION PHASE – 3 TIMES WEEKLY: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
| FDC tablet containing: R150 mg/H150 mg | 3 tablets at once, 3 times weekly for 48 doses | = 144 x | 11 588 | = 1 668 672 |

Example: Quantities needed for Category II regimen (adult patients with body weight band 40–54 kg): 2SRHZE/1HRZE/5(RH)3E3:

| INTENSIVE PHASE: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
|--|---|-----------------|--------------------|------------------------------|
| FDC tablet containing: R150 mg/H75 mg/ Z400 mg/E275 mg | 3 tablets daily for 84 doses | = 252 x | 1 932 | = 486 864 |
| Streptomycin vials: S750 mg | 1 vial daily for 56 doses | = 56 x | 1 932 | = 108 192 |
| Water for injection vials: use with streptomycin | 1 vial daily for 56 doses | = 56 x | 1 932 | = 108 192 |
| CONTINUATION PHASE – 3 TIMES WEEKLY: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
| FDC tablet containing: R150 mg/H150 mg | 3 tablets at once, 3 times weekly for 60 doses | = 180 x | 1 932 | = 347 760 |
| Ethambutol tablet containing: E400 mg | 3 tablets at once, 3 times weekly for 60 doses | = 180 x | 1 932 | = 347 760 |

Example: Quantities needed for Category III regimen (adult patients with body weight band 40–54 kg): 2RHZE/4(RH)3:

| INTENSIVE PHASE: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
|--|--|-----------------|--------------------|------------------------------|
| FDC tablet containing: R150 mg/H75 mg/ Z400 mg/E275 mg | 3 tablets daily for 56 doses | = 168 x | 1 159 | = 194 712 |
| CONTINUATION PHASE – 3 TIMES WEEKLY: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
| FDC tablet containing: R150 mg/H150 mg | 3 tablets at once, 3 times weekly for 48 doses | = 144 x | 1 159 | = 166 896 |

Example: Quantities needed for children (body weight band 15–19 kg): 2RHZ/4(RH)3:

| INTENSIVE PHASE: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
|---|---|-----------------|--------------------|------------------------------|
| FDC tablet containing: R60 mg/H30 mg/ Z150 mg | 3 tablets daily for 56 doses | = 168 x | 618 | = 103 824 |
| CONTINUATION PHASE – 3 TIMES WEEKLY: | DOSE | ONE CASE | ADULT CASES | TABLETS FOR ALL CASES |
| FDC tablet containing: R60 mg/H60 mg | 3 tablets at once, 3 times weekly for 48 doses | = 144 x | 618 | = 88 992 |

A buffer stock should be included in the quantification of drug requirements. To do this, double the yearly total quantity in the above example. This will cover unexpected increases in TB cases, procurement lead time, delays in shipment and distribution, and drug loss due to damage. If quantifying for a district or health centre, then enough reserve stock should be added equal to the time it takes to replace stock (e.g. 1–3 months).

The Global Drug Facility (GDF) has developed Stop TB Patient Kits which are available through its direct procurement service and under certain conditions as free grants. The Stop TB Patient Kits contain all the drugs for a full treatment for one patient in the middle weight band of 40-54 kg. Inside the kit is an instruction booklet which explains how the kits can easily be adjusted for patients in the higher or lower weight bands.

These kits are available for Category I and III regimens – 2(RHZE)/4RH and 2(RHZE)/6EH – and for Category II regimen – 2S(RHZE)/1(RHZE)/5(RHE) – plus syringes and needles.

The Stop TB Kits ensure that the full regimen is available for every patient started on treatment and greatly simplify quantification, ordering and logistics of TB drugs (one patient = one kit). For full details see: <http://www.stoptb.org/GDF/>.

Appropriate prices for quality-assured TB drugs are proposed, in function of the packaging, drugs' combination and dosage, by GDF, Management Sciences for Health (MSH), and others in the following web sites:

http://www.stoptb.org/GDF/drugsupply/drugs_available.asp

<http://erc.msh.org/mainpage.cfm?file=1.0.htm&id=1&temptitle=Introduction&module=DMP&language=English>

<http://www.medeor.org/index2.htm>

<http://www.ida.nl/>

<http://user.online.be/orbipharma/engels/menu.htm>.

APPENDIX 6 – ADVERSE EFFECTS OF TB DRUGS

Most TB patients complete their treatment without any significant adverse drug effects.

Adverse effects are classified as minor or major. In general, a patient who develops minor adverse effects should continue TB treatment, usually at the same dose but sometimes at a reduced dose. The patient also receives symptomatic treatment. If a patient develops a major side-effect, the treatment or the offending drug is stopped. Patients with major adverse reactions may need to be managed in a hospital.

| Adverse effects | Drug(s) probably responsible | Management |
|--|--|--|
| MINOR | | |
| Anorexia, nausea, abdominal pain | pyrazinamide, rifampicin | Check for jaundice Give drugs with small meals or last thing at night |
| Joint pains | pyrazinamide | Aspirin |
| Burning sensation in the feet | isoniazid | pyridoxine 100 mg daily |
| Orange/red urine | rifampicin | Reassurance; patients should be told when starting treatment that is common and normal |
| MAJOR | | |
| Decrease in hearing Deafness (no wax on auroscopy) | streptomycin | Stop streptomycin; use ethambutol |
| Dizziness (vertigo and nystagmus) | streptomycin | Stop streptomycin; use ethambutol |
| Jaundice (other causes excluded), symptoms or signs of hepatitis | pyrazinamide, isoniazid and rifampicin, probably in that order of likelihood | Stop TB drugs (see below ^a) |
| Confusion (suspect drug-induced acute liver failure if jaundice present) | most TB drugs | Stop TB drugs. Urgent liver function tests and prothrombin time if available |
| Visual impairment (other causes excluded) | ethambutol | Stop ethambutol; may be replaced with streptomycin |
| Shock, purpura, acute renal failure | rifampicin | Stop rifampicin; treatment duration must be extended to 12 months |

^a If drug-induced hepatitis, stop all TB drugs. Reintroduce one at a time (in the order: rifampicin, isoniazid) in incremental dosages over several days for each drug, starting two weeks after jaundice has resolved. Note, rifampicin commonly produces asymptomatic jaundice without hepatitis. If hepatitis has produced clinical jaundice, avoid pyrazinamide: suggested regimen is 2SHE/10HE). Severely ill TB patients may die without TB drugs, in which case, use streptomycin and ethambutol and restart usual treatment after hepatitis has resolved.

APPENDIX 7 – LABORATORY REQUIREMENTS FOR SPUTUM SMEAR EXAMINATIONS

A BASIC TB LABORATORY

INTRODUCTION

TB laboratory work in emergencies will generally be limited to the examination of sputum smears by light microscopy. The laboratory used for this work (whether existing or new) should have certain features:

- A suitable building or room(s) appropriately laid out and furnished and with appropriate ventilation and temperature control.
- Adequate numbers of trained staff.
- Defined standard operating procedures for the methods used. These should also include protocols for internal and external quality assessment and a safety policy including full risk and hazard assessments and safety procedures.
- The appropriate equipment, reagents, stains, media, glassware and disposables.
- Adequate supplies of clean water and a good drainage system.
- Technical, engineering and logistic support.
- Good access and external communications.

In emergencies, the ideal laboratory facility may be difficult to achieve and some compromises may have to be accepted. However, no compromise with items affecting staff safety can be tolerated.

STAFF

The laboratory staff should be able to undertake certain defined tasks:

Technical

- Prepare and stain sputum smears
- Undertake Ziehl–Neelsen microscopy and record the results
- Maintain internal quality control
- Ensure safe working environment
- Clean and maintain equipment

Administrative

- Receive specimens and dispatch results
- Maintain the laboratory register
- Manage supplies of stains, reagents, glassware, stationery and other essentials

At least one staff member should have experience of running a laboratory, preferably in field conditions, and be able to undertake additional duties such as laboratory management and ordering stock.

PREMISES FOR TB LABORATORIES

Any building or room used as a laboratory should be structurally appropriate. It must be possible to clean/disinfect internal surfaces easily. Floors should be non-slip and easy to clean. Windows should fit, be able to open, and be provided with security grilles and mosquito screens where appropriate. External doors should be lockable and should ideally not open directly into the laboratory. If the laboratory cannot be locked when it is empty, suitable security measures (e.g. lockable cupboards) must be taken to protect valuable equipment such as microscopes. Good ventilation and temperature control are essential for good and safe working. Airflows should be away from and not towards staff working at the bench. A staff room and toilets should be provided.

LABORATORY LAYOUT

The microscopy room will need at least three distinct sections:

1. An area for specimen reception and for undertaking laboratory paperwork; this area may also be used for storage.
2. A well-lit area for slide preparation and staining.
3. An area for microscopy; if the electricity supply is poor, this should be in front of a window so that the mirror can be used.

The basic smear laboratory will need at least four tables or benches:

1. For receipt of specimens, laboratory registers and slide storage.
2. For smear preparation.
3. For staining (preferably with a sink).
4. Microscope bench (if there is no electricity or the supply is intermittent, this should be in front of a window).
5. For receipt of specimens, laboratory registers and slide storage.

Ideally, the laboratory should have only one door, which should be kept closed. Access to the laboratory should be restricted to authorized personnel only. There should be a window in one wall, preferably off a corridor or lobby through which specimens are received at the specimen reception bench.

The main laboratory area should contain all the facilities necessary for smear preparation. This area must have work-benches, a wash basin and storage cabinets. Laboratory reports will be completed here and passed to the reception bench where the laboratory register will be filled in and the results dispatched.

The laboratory room should have:

- Good ventilation and temperature control
- Good water supplies and a distiller if reagents are to be prepared in the laboratory. If the laboratory receives ready prepared strains, a demineralizer is needed.
- A glassware wash up and drying area
- Adequate electricity supplies
- Adequate drainage that cannot contaminate local water supplies
- An incinerator; a pit outside away from water, food storage, people, especially children, animals, etc., can be used as an incinerator, provided it is deep enough.
- Good lighting
- A means of sterilizing and/or disinfecting contaminated items (e.g. an autoclave or boiling water sterilizer)
- Stable benches that are resistant to chemicals and are at a comfortable height to work (90 cm is commonly used)
- Comfortable seating of the right height.

SAFE WORKING PRACTICES

Safe working in the laboratory depends on the observance of basic safety precautions and on good training of staff both in safety and in good bench work. Detailed information on safe working practices can be found in the WHO publications *Laboratory biosafety manual* and *Safety in health-care laboratories* (see resources).

SMEAR MICROSCOPY

Effective sputum smear microscopy is dependent in the first instance on good specimen collection. Appropriate wide mouthed screw-capped containers should be provided, staff trained in the proper collection of sputum and educational material developed for patients so that they can provide proper specimens. A collection and transport system may need to be developed to ensure that specimens arrive promptly and safely. These procedures, the techniques of smear microscopy (and methods of dealing with specimens other than sputum) and the recording of results are described in detail in Part II of the WHO publication *Laboratory services in tuberculosis control* (see resources) and are not therefore given here.

The basic equipment required by a sputum smear laboratory is given below.

BASIC REAGENTS AND EQUIPMENT FOR A SPUTUM SMEAR LABORATORY

- Sputum containers for collection and storage of specimens
- Wire loop (3mm ID) to spread sputum on the slide
- Alcohol/sand flask to clean the loop
- Microscope(s)
- Microscope slides (clean, grease free and unscratched) or frosted slides
- Writing diamond to mark the slides
- Forceps
- Bunsen burner or spirit lamp to sterilize the loop, fix the smears and flame the smears during staining
- Containers for waste disposal (metal for burnable waste, plastic for items to be disinfected)
- Staining racks
- Slide racks
- Ziehl–Neelsen stain
- 3% HCL-Ethanol or 20–25% H₂SO₄ for decolourizing smears
- Water to rinse smears

MICROSCOPES

The laboratory will need one or more binocular microscopes, which should have:

- Parfocal Achromat or Plan Achromat objective lenses of the following magnifications and numerical apertures:
 - 10x objective – NA 0.25
 - 40x objective – NA 0.65
 - 100 x (oil) objective – NA 1.25
- Eyepieces of 10x magnification
- An integral light source and a mirror unit (at least the latter)
- An Abbe type sub-stage condenser with a diaphragm
- A mechanical stage fitted with a vernier scale.

Provide a cover to keep the instrument clean when not in use. In the tropics, store the microscope in a box with a low wattage light bulb that is on all the time and with holes to allow air circulation to prevent the growth of fungus on the lenses.

In order to maintain technical proficiency, a microscopist should examine at least 10–15 smears per week but not more than 20 slides per day (or visual fatigue will reduce output quality). If larger numbers of slides must be examined each day, then either additional microscopists should be employed or a fluorescence microscopy system set up. This allows slides to be scanned much more rapidly and hence the workload per microscopist can be increased, but is more complicated and demanding on the laboratory than basic light microscopy. Details are given in Part II of “Laboratory Services in Tuberculosis Control” (see references).

MICROSCOPY EXAMINATION REQUIREMENTS FOR 2000 SPECIMENS

Binocular microscopy for use in daylight and electric power, with oil immersion objective (x 100), eye-pieces (x8 or x10) and spare bulbs for microscope. In hot and humid climates, a warm cupboard heated by 1 or 2 light bulbs (40 Watts) is also needed.

| Equipment | Number |
|---|---------------|
| Sputum containers, plastic, disposable, 45–50 ml | 3000 |
| Slides for microscope, 25 x 75, 1.1–1.3 mm thick (could be frosted) | 3000 |
| Applicators, wooden or nickel-chrome wire, 1 mm diameter | 3000 |
| Loop holder | 2 |
| Slide holder, metal, 40 cm x 5 cm, for 12–25 slides | 2 |
| Bunsen burner for use with butane gas or spirit lamps | 2 |
| Glass marker, diamond point | 2 |
| Timer, 0–60 minutes, with alarm | 1 |
| Forceps, stainless steel, for slides, 15 cm | 2 |
| Scissors, stainless steel, 25 cm | 1 |
| Slide rack, plastic, for 12–25 slides | 2 |
| Slide boxes for 100 slides | 2 |
| Funnel glass, 45 mm or 60 mm diameter | 4 |
| Bottles, brown glass, 100 ml | 4 |
| Wash bottles, plastic, 250 ml | 3 |
| Drop plastic bottles, 10 ml for immersion oil | 2 |
| Bucket, plastic, 12 ml | 2 |

| Reagents | Number |
|---|---------------|
| Acid-ethanol for Ziehl–Neelsen staining | 3 litres |
| Carbol fuchsin for Ziehl–Neelsen staining | 6 litres |
| Aqueous methylene blue | 4 litres |
| Immersion oil | 200 ml |

| Laboratory records, reports, miscellaneous items | Number |
|---|---------------|
| Laboratory request forms | 3000 |
| Laboratory register for TB | 1 |
| Pens, ball point, black or blue ink | 2 |
| Pens, ball point, red ink | 2 |
| Adhesive labels for sputum containers | 3000 |
| Lens tissue | 2 rolls |
| Balls of white absorbent cotton | 500 g |
| Filter-paper, 15-cm diameter, no. 1 | 4 boxes |
| Toilet tissues | 2 rolls |
| Still (apparatus for distilled water) | 1 |
| Towel and clean cloths | as needed |
| Masks and laboratory coats | as needed |
| Sodium hypochlorite | 10 litres |
| Methylated spirits | 2 litres |

The GDF has developed diagnostic kits that contain everything to perform correct AFB microscopy. They are available through the GDF direct procurement service and under certain conditions as free grants.

There are three different GDF diagnostic kits:

- The consumables kit, which contains all the consumable items to prepare 1000 slides, with among other things 1000 slides, the already prepared and ready for use reagents, disinfectant, methylated spirit and filter-paper. This kit can be ordered together with 1000 sputum containers.
- The equipment starter kit, which contains all the small materials needed to perform smear microscopy, such as staining racks, drying racks, spirit lamps, funnels, slides boxes, gloves, literature.
- The microscope kit, which contains a high-quality microscope equipped with mirror unit, but also with a battery for use during power cuts, a charger for the battery, a lamp unit for use with the battery, a surge protector and spare lamps and fuses.

The GDF has prepared a calculation spreadsheet for easy calculation of the number of consumables kits to be ordered based on the expected number of smear-positive patients.

The GDF web site: <http://www.stoptb.org/GDF/> can provide further details.

RESOURCES

WHO publications

Laboratory services in tuberculosis control. Parts I, II and III. Geneva, World Health Organization, 1998 (WHO/TB/98.258).

Health laboratory facilities in emergency and disaster situations. Alexandria, WHO Regional Office for the Eastern Mediterranean, 1994.

Laboratory biosafety manual, 2nd ed. Geneva, World Health Organization, 1993.

Maintenance and repair of laboratory diagnostic, imaging and hospital equipment. Geneva, World Health Organization, 1994.

Safety in health-care laboratories. Geneva, World Health Organization, 1997.

Selection of basic laboratory equipment for laboratories with limited resources. Alexandria, WHO Regional Office for the Eastern Mediterranean, 2000.

Other relevant publications

Collins CH, Grange JM, Yates MD. *Tuberculosis bacteriology: organization and practice*, 2nd ed. Oxford, Butterworth–Heinemann, 1997.

Cheesbrough M. *Laboratory practice in tropical countries (Part 1)*. Cambridge, Cambridge University Press, 1998.

Cheesbrough M. *Laboratory practice in tropical countries (Part 2)*. Cambridge, Cambridge University Press, 2000.

Davis J, Lambert R. *Engineering in emergencies: a practical guide for relief workers*, 2nd ed. London, ITDG Publishing and RedR, 2002.

APPENDIX 8 – ESTIMATING THE QUANTITY OF FORMS, REGISTERS AND HEALTH EDUCATION MATERIALS

Estimate the quantity of TB forms, registers and education materials needed during the first year. They will need to be ordered and distributed on a yearly basis.

Determine the minimum quantity of forms, registers and health education materials needed for the year.

Refer to the table below, which lists the recommended quantity of forms and registers. Depending on country or settings, additional forms may be needed.

| Name of forms and registers | Quantity needed per TB reporting unit |
|---|--|
| Tuberculosis Treatment Card | 1 per patient |
| Tuberculosis Identity Card | 1 per patient |
| Tuberculosis Suspects Register | 1 per health facility |
| Tuberculosis Laboratory Register | 1 per year |
| Tuberculosis Register | 1 per year |
| TB Laboratory Form Request for Sputum Examination | 13 for every new pulmonary smear-positive case |
| Quarterly Report on New and Re-treatment Cases of Tuberculosis | 12 per year (3 copies x 4 quarters) |
| Quarterly Report on the Results of Treatment of Pulmonary Tuberculosis Patients Registered 12–15 Months Earlier | 12 per year (3 copies x 4 quarters) |
| Tuberculosis Referral/Transfer Form | Based on proportion of patients who transferred out of the district during the previous year |
| Tuberculosis Culture/Drug Sensitivity Test Request/Report Form* | Country specific |

* if conditions allow

Add an additional 20% to the quantity of forms, registers and education materials needed.

To account for the increase in the number of TB patients and lost forms, add 20% to the quantity of forms, registers and educational materials needed. (You do not have to make this calculation for the registers because one of each register book should be sufficient for one year.)

APPENDIX 9 – SUPERVISOR’S CHECKLIST

Sample TB checklist for supervisory visits to health facilities providing services for TB diagnosis and treatment

Sample TB checklist for supervisory visits to health facilities providing services for TB diagnosis and treatment

Health facility District TB Coordinator

Health worker responsible for TB Date / /

Review *TB Treatment Cards* for all current TB patients and for those who completed treatment since the last supervisory visit.

Register all newly-detected cases. Update the *District TB Register* for other patients.

Also check TB Treatment Cards:

| | YES | NO |
|--|--------------------------|--------------------------|
| 1. Is each patient on the correct regimen? | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Are sputum examination results recorded correctly? | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. Is treatment regular and correctly recorded? | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Are patients undergoing smear examination at 2 months (3 months if Category II)? | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Are patients undergoing smear examination at 5 months and at the end of treatment? | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Are patients who are smear-positive at 2 months (3 months if Category II) receiving one more month of initial-phase drugs? | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. For each patient who has completed treatment, is the information on the <i>TB Treatment Card</i> sufficient to determine treatment outcome? | <input type="checkbox"/> | <input type="checkbox"/> |

Review *Register of TB Suspects and/ or TB Laboratory Register* (if available):

| | YES | NO |
|---|--------------------------|--------------------------|
| 1. Does the facility have a <i>Register of TB Suspects</i> ? | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. If yes, are the results of sputum-smear microscopy written in the <i>Register of TB Suspects</i> ? | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. If the facility has both a <i>Register of TB Suspects</i> and a <i>TB Laboratory Register</i> in the facility, do the microscopy results recorded on them match? | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Do the results on the <i>TB Register</i> match the results recorded on the <i>TB Treatment Card</i> ? | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Have all the smear-positive patients started treatment? | <input type="checkbox"/> | <input type="checkbox"/> |

Have there been changes in staff responsible for TB?

If yes, specify:

Sample TB checklist for supervisory visits to health facilities providing services for TB diagnosis and treatment (*continued*)

Quarterly: Ask the health worker responsible for TB about recent monitoring results. Has the health worker calculated the following indicators for appropriate quarters? If so, what are they?

Write the figures below

- | | |
|---|----------------------|
| 1. The proportion of outpatients aged >15 years who were identified as TB suspects? | <input type="text"/> |
| 2. The proportion of TB suspects tested who were sputum smear-positive? | <input type="text"/> |
| 3. The proportion of new sputum smear-positive TB cases that converted at 2 or 3 months (sputum conversion rate)? | <input type="text"/> |
| 4. The proportion of new sputum smear-positive cases that | |
| – were cured? | <input type="text"/> |
| – completed treatment? | <input type="text"/> |
| – defaulted? | <input type="text"/> |
| – failed treatment? | <input type="text"/> |
| – died? | <input type="text"/> |
| – were transferred out? | <input type="text"/> |

Ask whether health workers have any questions or problems:

| |
|----------------------|
| <input type="text"/> |
| <input type="text"/> |
| <input type="text"/> |
| <input type="text"/> |
| <input type="text"/> |
| <input type="text"/> |

Examine and ask about supplies. Is there:

YES NO

- | | | |
|--|--------------------------|--------------------------|
| 1. An adequate supply of TB drugs? | <input type="checkbox"/> | <input type="checkbox"/> |
| Are these drugs well maintained, not expired? | <input type="checkbox"/> | <input type="checkbox"/> |
| Note quantities in stock: | <input type="text"/> | |
| 2. An adequate supply of needles, syringes and diluent for injections? | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. An adequate supply of sputum containers? | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. A sterilizer in good working condition (if required)? | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. An adequate supply of: | | |
| – TB Treatment Cards, | <input type="checkbox"/> | <input type="checkbox"/> |
| – Request for Sputum Examination forms, | <input type="checkbox"/> | <input type="checkbox"/> |
| – Referral/Transfer forms? | <input type="checkbox"/> | <input type="checkbox"/> |

Sample TB checklist for supervisory visits to health facilities providing services for TB diagnosis and treatment (*continued*)

| Observe health workers with patients if possible. Do they: | YES | NO |
|--|--------------------------|--------------------------|
| 1. Ask all adult outpatients about cough and correctly identify TB suspects? | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. Send TB suspects to laboratory or collect sputum samples for examination? | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. Administer the correct drugs for the treatment regimen? | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. Watch patients swallow the tablets? | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. Tick the <i>TB Treatment Card</i> <i>after</i> watching the patient swallow the tablets? | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Correctly give a streptomycin injection <i>after</i> the tablets have been swallowed? (if applicable) | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. Give each injection with a sterile syringe and needle? (if applicable) | <input type="checkbox"/> | <input type="checkbox"/> |
| 8. Inform TB suspects/patients about TB in a considerate and appropriate manner? | <input type="checkbox"/> | <input type="checkbox"/> |

| Talk to TB patients. Do patients know: | P 1 | P 2 | P 3 |
|--|--------------------------|--------------------------|--------------------------|
| 1. What disease they are suffering from? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 2. The number of tablets to take per day? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 3. When to return for the next appointment? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 4. The duration of treatment? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 5. What to do when they experience problems (side-effects)? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 6. Why sputum examinations are needed? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 7. How TB spreads? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| 8. Who else in the household should be examined or tested for TB? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Ask whether the patient has any problems that may prevent completing treatment. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

Describe problems identified during this visit:

Comments (possible causes of the problems):

Recommendations:

APPENDIX 10 – HEALTH EDUCATION MESSAGES

The aim of TB control for a community is to decrease the risk of TB infection by breaking the chain of transmission of tubercle bacilli.

Public awareness can provide essential information on the extent of the TB problem in the community and can help prevent transmission. It is important for members of at-risk populations to understand the nature of TB disease and how it is diagnosed, treated and prevented.

At the national and community levels, health services should collect and analyse epidemiological data to identify populations with high TB incidence, so that TB prevention activities and public awareness campaigns can be appropriately directed. Public awareness campaigns should be initiated by national and local organizations to alert communities at high risk of TB about the increased TB threat.

Community public awareness campaigns should be focused on health services and religious, social and economic organizations. The media should be effectively utilized to communicate information about TB prevention. Local community media should deliver the information to the general public, high-risk communities and TB risk groups.

Key elements of community education:

- avoiding stigmatization of TB patients;
- curability of TB disease;
- early (self) referral of TB suspects;
- importance of adherence to treatment;
- contact screening.

The most important messages:

- TB in an adult should be suspected when the person has a productive cough lasting more than 2 weeks, with or without other symptoms such as significant weight loss or blood in the sputum.
- Visiting a health care facility early is very important if a person experiences chest symptoms compatible with TB.
- Given the contagious nature of TB infection, it can be spread from person to person, causing disability or even death in those not treated properly.
- Anyone may contract TB.
- TB is completely curable with adequate treatment.
- TB is largely preventable.
- Early treatment is important for best results and to prevent spread, especially to family members.
- Appropriate treatment is the best prevention.
- Children are especially at risk if not treated and may develop severe, even fatal, disease.
- All patients must take the full course of treatment.
- Steadiness in TB drug intake, as prescribed by a health worker, is an important element in treatment success.
- Treatment makes patients non-infectious within 1 month, but cure takes 6–8 months.
- Treatment must be completed even though the patient may feel better sooner.
- Failure to complete treatment may result in a recurrence that may be impossible to treat and may spread serious disease to others, especially children.
- Controlling TB is a community responsibility.
- All patients should be treated sympathetically and with respect.

TB suspects and TB patients should be taught simple measures to decrease the risk of transmitting TB including:

- covering the mouth whenever coughing or sneezing to prevent the spread of lung diseases;
- using sputum pots with lids;
- turning the head to one side while being examined by a doctor.

APPENDIX 11 – TB CARE AND CONTROL AFTER NATURAL DISASTERS

Natural disasters (floods, hurricanes, tornados, tsunamis, earthquakes, etc.) have potential consequences on incidence of TB, patient management and development of drug resistance.

In the immediate aftermath of a natural disaster, the following issues pose particular problems for TB care and control:

- **Crowded living conditions of displaced populations.** The prevention of overcrowding in temporary settlements is a priority in the acute phase as well as the prevention of malnutrition both of which increase people's susceptibility to infection.
- **Loss to follow up.** This may include difficulty in tracking existing TB patients among the displaced population, and continuing their treatment. This may result in the development and spread of drug-resistant TB strains.
- **Access to drugs in disaster-affected areas.** Patients who were on TB treatment in the disaster-affected areas may not have access to any appropriate drug distribution system if the normal health infrastructure is damaged or destroyed
- **Access to drugs in non-affected areas.** The distribution system of TB drugs and supplies implemented by the NTP is likely to be disturbed in the non-affected areas where the existing health infrastructure may be overwhelmed by the additional and urgent workload.
- **Inappropriate drugs administered.** TB patients who were on treatment in NTP services before the disaster may receive inappropriate TB drug prescriptions from other health care providers not trained in Stop TB strategy.
- **TB service providers.** Increased challenges of coordination if multiple TB service-providers are involved – NTPs must have the support they need in order to assure this vital function continues.
- **Disruption of TB services in non-affected areas.** TB care and control activities may be disrupted in non-affected areas during the acute phase (displaced people, increase in work load, redeployment of health workers usually involved in TB control to disaster area)
- **NTP management.** Members of the central units of NTPs may be assigned to other managerial tasks related to the disaster situation. This is likely to disturb, or even stop, the managerial activities of the NTPs particularly in the regions unaffected by the disaster where, in general, the majority of TB cases are located.

PRIORITY ISSUES TO ADDRESS IN THE ACUTE PHASE FOLLOWING A NATURAL DISASTER

- TB should be included in all rapid health assessments
- Assessing the number of TB patients already on treatment in the disaster-affected areas from the existing recording and reporting system and ensure the continuation of treatment by these TB patients
- Wide distribution of health education messages, targeting TB patients on treatment, on the need to continue their treatment through information channels accessible to patients in communities.
- Establishment by NTPs of lists of health facilities able to appropriately ensure TB drug distribution to patients in the affected communities and in regions close to affected areas.
- Restarting TB care and control activities under the leadership and coordination of NTPs in the affected areas and ensuring that sufficient TB activities are maintained in non-affected areas during the acute phase
- Wide distribution of lists of health facilities able to appropriately ensure TB drug distribution in the communities and among health care providers of the region, including newly arrived NGOs/organizations.
- Development by NTPs of an acute phase strategy to manage patients from affected areas who present for TB treatment provision in health facilities: this must include regular drug provision, referral mechanism for complications, sputum follow-up with appropriate changes in regimens, reporting and monitoring mechanism and process of transfer back to normal geographical area of care once services set up in affected area.
- Ensuring appropriate storage of TB drugs
- Ensuring TB drug supply to health facilities reported in the lists.
- Distribution of the national TB control guidelines and of the acute phase strategy defined by the NTPs to organizations supporting health facilities involved in TB care and control in affected and non affected areas.
- Monitoring and supervision by NTPs of TB care and control activities in the affected areas.
- Control, by the national health authorities, of TB drugs that might be provided through any new distribution systems.

AFTER THE ACUTE PHASE

- Evaluation, by NTPs, of TB care and control activities carried out in the acute phase in affected and non affected areas
- Pursue TB care and control activities at all levels in line with the NTP directives
- Plan implementation of Stop TB activities in the framework of the rehabilitation process in affected areas
- Adjust strategic plans of NTPs on the basis of changes determined by the consequences of the disaster on health services
- Advocacy efforts in order to maintain TB as health priority at national level
- Development of proposals to financially support the implementation of the TB control strategic plans within the ongoing international movement to rebuild the infrastructures in areas affected by natural disasters.

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Global Fund to Fight AIDS, Tuberculosis and Malaria: www.theglobalfund.org

Green Light Committee: www.who.int/tb/dots/dotsplus/management

International Committee of the Red Cross. www.icrc.org

International Dispensary Association: www.ida.nl

International Federation of Red Cross and Red Crescent Societies: www.ifrc.org

International Organization for Migration: www.iom.int

Management Sciences for Health: www.msh.or

Médecins Sans Frontières International: www.msf.org

Office of the United Nations High Commissioner for Refugees: www.unhcr.org

World Health Organization: www.who.int

WHO Stop TB publications: www.who.int/tb/publications/en/

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