Management of Tuberculosis

A Guide to the Essentials of Good Practice

Sixth Edition
2010

International Union Against Tuberculosis and Lung Disease

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Preface

While a great deal of progress has been made in the fight against tuberculosis, the disease still poses a serious and even increasing problem in many low-income countries, affecting the health and social welfare of millions of people. Fighting tuberculosis is a challenge to all who are concerned about health and development. Providing treatment with antituberculosis drugs has made it possible to cure most patients suffering from this potentially fatal disease. Successful treatment, however, presupposes adequate drugs, close supervision of staff, direct observation of drug swallowing and monitoring of treatment results by bacteriological examination. In spite of the progress made, there continues to be a need for explicit and straightforward guidance on how to carry out the routine tasks required for the successful fight against tuberculosis.

This sixth edition of the Guide (first published in 1986) contains a description of tuberculosis, its diagnosis, treatment, the organisation and management of tuberculosis services and the structure within which such services can be delivered, even in the very poorest countries. Evaluation of the tuberculosis situation and of the interventions designed to bring it under control are discussed. This edition also addresses the challenges posed by HIV infection and drug-resistant tuberculosis, and provides a clear rationale for the cascade of treatment regimens if there is failure, relapse or return after default from the first course of treatment.

The Union hopes this Guide will help those struggling to provide high-quality care for tuberculosis patients, even in remote locations and even when resources are severely limited. It will also be of interest to health services planners and managers as well as those in charge of training health care workers.

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Glossary

AFB	acid-fast bacilli
AIDS	acquired immunodeficiency syndrome
ART	antiretroviral treatment
BCG	bacille Calmette-Guérin
BMU	basic management unit
CPT	cotrimoxazole preventive therapy
CTM	cotrimoxazole
DOTS	originally an acronym for directly observed treatment, short course, DOTS became the term used to describe the tuberculosis control strategy recommended by the WHO
HIV	human immunodeficiency virus
IGRA	interferon-gamma release assay
IRIS	immune reconstitution inflammatory syndrome
MDR-TB	multidrug-resistant tuberculosis
NTP	National Tuberculosis Programme
TB	tuberculosis
WHO	World Health Organization
XDR-TB	extensively drug-resistant tuberculosis

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Introduction

Tuberculosis is a great problem in most low-income countries. It is the single most frequent cause of death from a single agent in individuals aged 15 to 49 years. In some countries, especially in sub-Saharan Africa, the human immunodeficiency virus (HIV) is the driving force in the overlapping epidemic with tuberculosis. Activities directed against tuberculosis and HIV as public health problems are the direct responsibility of government health authorities.

The International Union Against Tuberculosis and Lung Disease (The Union) is the oldest international non-governmental organisation dealing with health. It started its activities as a series of conferences following the first international conference of specialists of internal medicine in 1867. It was first officially registered in 1902 as the Central International Bureau for the Prevention of Consumption, and started its monthly publication *Tuberculosis* in German, French and English. It has gained immense experience in collaborating with partners in providing care for millions of tuberculosis patients in some of the poorest countries in the world, through the vehicle of National Tuberculosis Programmes (NTPs). This Guide summarises that experience.

In recognition of the association between tuberculosis and HIV in settings where both are frequent, this revision of the Guide contains more information about their interface than previous editions. In recognition of the development of drug-resistant tuberculosis, which may hinder the progress in tuberculosis control, the Guide considers the implications of drug resistance that may result from treatment with inadequate antituberculosis treatment regimens and expands the discussion on drug-resistant tuberculosis.

The target audience for this Guide is the person responsible for the tasks at the basic management unit (BMU)* of the NTP, often a nurse or paramedical professional. While the Guide itself may not necessarily find its way into the hands of all these individuals, the authors wish to provide

*A BMU is defined in terms of management, supervision and monitoring responsibilities. More details on the organisation of the BMU can be found in section 5.2.2.

NTPs, and all those who work alongside them, with the basic information concerning the management of tuberculosis services, in the hope that this knowledge can be transferred, adapted to the local situation and provided in the local language to empower those whose responsibility it is to carry out this crucial task of organising these services at the most basic management level. Knowledgeable, skilled, dedicated and empowered basic unit managers are the key to relieving the suffering of millions of patients, reducing the impact of tuberculosis on the community and, in this way, contributing to reducing poverty among those affected.

In setting out to combat a problem such as tuberculosis, it is essential to have a clear concept of aims and priorities. The *aims* of the fight against tuberculosis are:

- *for a community*: to reduce the spread of tuberculosis micro-organisms and, by this means, to hasten the disappearance of this disease from society;
- *for individual patients*: to cure their disease, to quickly restore their capacity for activities of daily living and to preserve their position in their family and community.

Among the *priorities* of tuberculosis activities, the first is the appropriate *treatment and cure* of tuberculosis patients, especially those patients who are the most potent source of transmission of tuberculosis micro-organisms. Because tuberculosis is so frequent, may affect any part of the body and is such a serious disease, it must be a high priority for any practitioner who provides health care in low-income countries, and tuberculosis services must be incorporated into all health services. Tuberculosis can be controlled successfully only in the context of an NTP. Such a programme must operate within the routine health services of each country. Paramedical personnel usually perform the everyday tuberculosis activities (case finding and treatment) as part of the many activities of the general health services. It is essential that such personnel be properly trained, motivated and supervised.

In countries where HIV fuels tuberculosis, it is important to recognise that diagnosis and care of co-infected individuals is directed and overseen by the NTP and the National AIDS Programme. It is essential that the two programmes work together to plan, implement and evaluate joint tuberculosis and HIV services and programme activities.

The general population must be mobilised to participate, including patients and community organisations, as well as groups of health profes-

sionals. It is important to make clear to the population that tuberculosis is curable, that HIV infection can be prevented and treated and that there is no justification for discrimination or stigma. Community participation is essential to encourage individuals with symptoms suggestive of tuberculosis to present themselves to the health services for diagnostic examination for both tuberculosis and HIV and to ensure that tuberculosis patients continue to take their treatment until they are cured. Community participation can also play a crucial role in ensuring that tuberculosis cases who have been found to be HIV-infected continue their HIV care and receive necessary support after completion of tuberculosis treatment.

While the majority of tuberculosis patients come from the general community, the disease is especially a problem for "high-risk" groups in the population. These groups (the poor, persons incarcerated in detention centres, those with insecure housing, undocumented migrants and other marginalised groups) are often hard to reach with the usual public health services. They also contribute disproportionately to a cycle of poverty that frequently prevents economic development. The general principles of tuberculosis programmes apply also to these groups, but services for them may need to be adapted to address the broader context of their lives and circumstances. The above may also apply to HIV and AIDS: HIV diagnosis and care may not be accessible to certain marginalised communities, such as injection drug users or commercial sex workers, in addition to those identified above.

In many countries, non-governmental agencies provide tuberculosis services. They often work under difficult conditions in remote areas where they provide the only medical services available. Their activities should nevertheless always be undertaken in coordination with government offices and must follow the guidelines of the NTP. This especially applies to patients with multidrug-resistant tuberculosis, for whom services should be provided under the direction of the NTP, and not as separate projects by non-governmental organisations or private specialists.

Tuberculosis can only be conquered when all those affected by the disease are cared for by principles that follow the essentials of good practice. As the disease can affect virtually any organ of the body, patients may present at any location where health services are provided. While the ability to improve quality of tuberculosis services depends crucially on the good practice of the managers at the level of the basic management unit, any person providing health services must understand and be able to deliver high quality services for any tuberculosis patient that is encountered.

2
Tuberculosis

2.1. What do we know about this disease?

Patients with tuberculosis can present themselves at any location where health services are provided. Therefore, all those who provide health services need to understand some basic information about this disease.

2.1.1. What is tuberculosis?

Tuberculosis is an infectious disease caused in most cases by a micro-organism called *Mycobacterium tuberculosis*. The micro-organisms usually enter the body by inhalation through the lungs. They spread from the initial location in the lungs to other parts of the body via the blood stream, the lymphatic system, the airways or by direct extension to other organs.

- *Pulmonary tuberculosis* is the most frequent form of the disease, usually comprising over 80% of cases. It is the form of tuberculosis that can be contagious.
- *Extra-pulmonary tuberculosis* is tuberculosis affecting organs other than the lungs, most frequently pleura, lymph nodes, spine and other bones and joints, genitourinary tract, nervous system, abdomen or virtually any organ. Tuberculosis may affect any part of the body, and may even become widely disseminated throughout the whole body.

2.1.2. How does tuberculosis develop?

Tuberculosis develops in the human body in two stages. The first stage occurs when an individual who is exposed to micro-organisms from an infectious case of tuberculosis becomes infected (*tuberculous infection*), and the second is when the infected individual develops the disease (*tuberculosis*).

How are tuberculosis micro-organisms spread?

The likelihood that a patient with tuberculosis may infect another person is determined by the number of micro-organisms within the lungs and their ability to spread into the surrounding air. Patients with pulmonary tuberculosis in whom the micro-organisms are so numerous as to be detectable using a microscope to examine sputum specimens (*smear-positive cases*) are the most infectious cases. Those in whom micro-organisms cannot be detected directly under the microscope (*smear-negative cases*) are very much less infectious, and the severity of their disease is usually less than that of the smear-positive cases. *Extra-pulmonary cases* are almost never infectious, unless they have pulmonary tuberculosis as well.

The infectious tuberculosis patient expels micro-organisms into the air in tiny droplets when talking, coughing, laughing or sneezing. These small droplets dry rapidly, become "droplet nuclei" carrying the micro-organisms and may remain suspended in the air of a room for several hours. Any person entering the room may inhale these micro-organisms. If the micro-organisms establish themselves in the lungs of the person who inhaled them and begin to multiply, *tuberculous infection* has occurred. Exposure to the micro-organisms is greatest among those in close and prolonged contact with an infectious case (i.e., those living in the same household with a smear-positive patient).

The micro-organisms are rapidly destroyed by exposure to sunlight and their concentration in the air is reduced by good ventilation. Except in the event of close and prolonged contact with an infectious case of tuberculosis, the chance of getting infected from a single contact with a tuberculosis patient is very small. Most individuals who become infected have no symptoms or evidence of illness in association with this infection.

What happens after infection?

Among those who do become infected, most (estimated at 90%) will never become ill with tuberculosis unless their immunity is compromised. The micro-organisms may remain dormant within the body for a long time. Some individuals who have become infected subsequently develop disease (*tuberculosis*). They are most likely to develop disease in the months immediately following infection, but continue to experience a risk of developing tuberculosis throughout the remainder of their lives. Tuberculous infection does not prevent re-infection. Re-infection may occur and tuberculosis may develop even among tuberculosis patients who have been cured.

2.1.3. How does HIV affect tuberculosis?

Infection with HIV progressively leads to extensive destruction of the immune defence mechanisms of the body. As a result, those infected with HIV become ill with severe and often deadly infections to which persons without HIV infection would not usually be susceptible. These conditions are called opportunistic infections. Tuberculosis is one such "infection" frequently affecting HIV-infected persons.

The development of tuberculosis following tuberculous infection is usually prevented by the actions of the immune system; this explains why, in most people, only a relatively small proportion of those individuals who have been infected with tuberculosis micro-organisms go on to become ill with the disease. When the protection provided by the immune system is reduced by HIV infection, the tuberculosis micro-organisms (either from new infection, or dormant within the body of an individual who has been previously infected) may begin to multiply, causing tuberculosis. This means that the development of tuberculosis can be a warning sign indicating co-infection with HIV.

By accelerating the development of tuberculosis, HIV co-infection results in a rapid increase in the number of tuberculosis patients in a given community, which secondarily increases the likelihood that other members, both with and without HIV infection, will be exposed and infected, thereby more and more rapidly increasing the number of tuberculosis patients. Moreover, tuberculosis patients who are infected with HIV may find that their HIV-related disease develops more rapidly and they may quickly become seriously ill and die.

Because HIV is so closely linked to tuberculosis, in settings where the two diseases are common tuberculosis patients should be routinely offered testing and counselling for HIV, and those with HIV infection should be routinely screened for tuberculosis.

2.1.4. What is drug-resistant tuberculosis and how does it develop?

Large populations of tuberculosis micro-organisms always contain some micro-organisms that have spontaneously mutated to become resistant to a drug. Consequently, treatment with a single drug in a patient with a large population of micro-organisms kills those micro-organisms that are susceptible to the drug but allows those that are spontaneously resistant to the drug to multiply. When the micro-organisms in a patient are resistant to all but one of the drugs that is given to the patient, the treatment has the same effect as if a single drug were being given alone. Resistance to drugs becomes

clinically important when the patient has disease caused by a whole population of micro-organisms that are resistant to the drugs essential for treatment. Resistance always begins as a man-made problem, as it is the result of inadequate treatment somewhere along the chain of transmission.

For practical purposes, drug resistance in tuberculosis micro-organisms is divided into resistance in patients who have *never previously been treated for tuberculosis for as much as one month (new patients)*, and resistance in patients who have *previously been treated for tuberculosis for as much as one month (previously treated patients)*.

- In *new patients*, resistance occurs when a patient develops tuberculosis after being infected by another patient who has resistant micro-organisms.
- In *previously treated patients*, resistance may have developed during the previous course of treatment because of incorrect treatment,* for example treatment with a single drug in patients with smear-positive pulmonary tuberculosis (sometimes referred to as monotherapy), or administration of powerful drugs to a patient harbouring tuberculosis micro-organisms resistant to all but one of the drugs given to the patient.

Micro-organisms with resistance to at least the two most important drugs, isoniazid and rifampicin, are termed *multidrug-resistant* (MDR). The majority of patients with this type of resistance cannot be treated effectively with regimens that use only first-line drugs. They need to be treated with the so-called second-line drugs.† Unfortunately, in the last few years there has also emerged the problem of extensively drug-resistant tuberculosis (XDR-TB), which is defined as MDR-TB plus resistance to any fluoroquinolone and any of the second-line injectable drugs such as amikacin, kanamycin or capreomycin. Further consideration about the diagnosis and management of XDR-TB is outside the scope of this Guide.

2.1.5. What is the significance of drug resistance for a tuberculosis programme?

The steady increase in multidrug-resistant tuberculosis in various parts of the world over recent years is of great concern.

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*However, in good programmes, resistance observed in previously treated patients is often resistance that was already present before they started the first treatment and that caused failure or relapse.

†Second-line drugs include prothionamide, clofazimine, kanamycin and fluoroquinolones.

Although most patients with multidrug-resistant tuberculosis could be successfully treated with a combination of second-line drugs, the cost of some of these drugs is very high and adverse drug events are frequent, treatment takes a very long time and all drugs must be taken under direct observation. In recent years an increasing number of countries have included treatment of multidrug-resistant tuberculosis in their National Tuberculosis Programmes (NTPs), since special external funding has been made available. To obtain this external funding, a proposal outlining how patients with multidrug-resistant tuberculosis will be managed must usually be approved by the Green Light Committee (GLC), a committee of experts in drug-resistant tuberculosis hosted by the World Health Organization (WHO) (refer to the most recent WHO Guidelines for the programmatic management of drug-resistant tuberculosis).[4]

In some countries where efficient tuberculosis services have been provided over many years, the level of multidrug-resistant tuberculosis has been kept at a very low level and has not shown any increase. In these countries, multidrug-resistant tuberculosis is mainly found among patients who are detected when they fail first-line treatment and retreatment regimens. The NTP should set up an effective system for identifying multidrug-resistant cases and providing these few patients with second-line drugs. This is both to ensure cure of all tuberculosis cases and to reduce further spread of resistant strains, as long as the increased cost and workload of services for multidrug-resistant cases do not adversely affect the management of those patients without multidrug-resistant disease and thus produce even more cases of resistance. Other factors to consider in deciding whether to introduce care for multidrug-resistant tuberculosis into the NTP include the risk of allowing mismanagement and further amplification of resistance to second-line drugs due to poor quality of care if such patients continue to be cared for by health care providers outside the NTP, as well as the devastating cost of this condition for patients and their families.

In some countries, a high proportion of new cases and more than one third of previously treated cases have multidrug-resistant strains. In these settings, it is urgent to provide adequate treatment with second-line drugs. However, unless effective measures are taken to prevent further development of multidrug resistance through effective treatment of patients with susceptible strains, the impact of treating multidrug-resistant tuberculosis will be very limited.

The first priority should therefore always be to ensure an effective basic tuberculosis programme so that resistance is prevented. If an effective

NTP is in place, treatment of multidrug-resistant patients will have an additional impact in controlling tuberculosis.

2.2. How is tuberculosis diagnosed?

Diagnosis is defined as "the process of determining health status and the factors responsible for producing it".[1] In this instance, it means the process by which a health care worker decides that the patient has tuberculosis.

2.2.1. When should tuberculosis be suspected?

The most frequent symptoms of pulmonary tuberculosis are:

- persistent cough for 2 weeks or more: every patient presenting with this symptom should be designated a *tuberculosis suspect*;
- sputum production, which may be blood-stained (haemoptysis), shortness of breath and chest pain;
- loss of appetite and loss of weight, a general feeling of illness (malaise) and tiredness (fatigue), night sweats and fever.

Any patient presenting with any of these symptoms should be suspected of having tuberculosis. If the patient is, or was, in contact with a patient with infectious tuberculosis, such a person is even more likely to be suffering from tuberculosis.

Symptoms of extra-pulmonary tuberculosis depend on the organ involved. Chest pain from tuberculous pleurisy, enlarged lymph nodes and sharp angular deformity of the spine are some of the presenting symptoms or signs of extra-pulmonary tuberculosis.

2.2.2. Among whom is tuberculosis most likely to be found?

Tuberculosis cases are most frequently found among the following:

- patients who present themselves on their own initiative at a health facility with symptoms suggesting tuberculosis;
- those (especially children and young adults) living in the same household with smear-positive patients;
- those infected with HIV;
- those found to have an abnormality that has the appearance of tuberculosis when a chest radiograph has been taken for clinical investigation of a sick patient.

Tuberculosis will be detected most efficiently where health care providers and community members are highly aware of the symptoms suggestive of tuberculosis.

2.2.3. How is a diagnosis of tuberculosis confirmed?

A diagnosis is proposed by the health care worker after considering the history given by the patient (the symptoms) and the evidence resulting from physical examination of the patient (the signs). The process of diagnosis involves identifying the most likely condition to explain the symptoms and signs and listing other conditions that might explain the symptoms (the differential diagnosis). A variety of tests are conducted to confirm the diagnosis.

What is the value of bacteriology?

Each individual suspected of having tuberculosis, regardless of HIV status, must have an examination of sputum to determine whether or not that individual has infectious tuberculosis. Sputum examination must be carried out before starting treatment. The examination consists of microscopic examination of a specimen of sputum that has been spread on a slide and stained by the Ziehl-Neelsen or fluorescence method (smear microscopy). If micro-organisms (frequently referred to as acid-fast bacilli, or AFB) are detected by this method, the patient is said to have smear-positive tuberculosis. Smear microscopy is currently the only means by which the diagnosis of tuberculosis can be confirmed in the majority of patients in most low-income settings. It is also important to carry it out because it efficiently identifies those cases that are most infectious.

Whenever tuberculosis is suspected, at least two specimens must be collected for examination by microscopy. Whenever possible, they should be obtained within 24 hours, as follows:

First specimen. During the patient's first visit, a specimen is collected on the spot; this specimen is obtained, after coughing and clearing the back of the throat, under the supervision of a health care worker, in a well-ventilated area, preferably in the open air. Obtaining a spot specimen implies that, before the patient leaves the health facility at the end of the consultation, a specimen has been obtained for submission to the laboratory.

Second specimen. The patient is then given a sputum container for collection of an early morning specimen before the second visit, which should be on the next working day.

One positive smear result is sufficient to register the patient as a sputum smear-positive patient and to start treatment. If the first spot specimen is positive and if the patient does not return for the second visit, a search must start immediately to find and enrol the patient on treatment, thus preventing further transmission of micro-organisms in the community and deterioration of the patient's condition.

It is reasonable to routinely examine only two specimens, rather than three. This, however, should be determined as policy by the authorities of the NTP and not decided individually.

Those patients whose sputum smears are negative but who are thought to have tuberculosis should be reviewed by a Medical Officer prior to commencing treatment. The Medical Officer may wish to proceed in the following manner in order to determine whether or not the patient actually has tuberculosis, prior to commencing treatment. If chest radiography is available, it may be performed. If the chest radiograph demonstrates shadows in the lung fields consistent with a pulmonary infectious disease, a course of broad spectrum antibiotics may be given. If the patient continues to show symptoms after completion of the antibiotics, a second series of two sputum smear examinations may be performed and, if still negative, the Medical Officer may choose to treat the patient for tuberculosis and record the patient as a case of smear-negative pulmonary tuberculosis. The "trial of treatment", whereby the response of a patient to a short period of antituberculosis treatment is used to decide whether or not the patient has tuberculosis, is poor practice and should not be done.

Is X-ray useful?

Diagnosis by means of radiographic examination in patients suspected of tuberculosis presents a challenge. Abnormalities identified on a chest radiograph may be due to tuberculosis or to a variety of other conditions and the pattern on the radiograph is not specific for tuberculosis. Some individuals who have previously had tuberculosis that is now healed (and therefore does not require treatment) may have a chest radiograph that resembles tuberculosis requiring treatment. Chest radiographs may be helpful in those patients who are not sputum smear-positive, but they can only be read reliably by an experienced Medical Officer.

What about the tuberculin test?

A tuberculin skin test is sometimes used by health care workers to help in the diagnosis of tuberculosis. The response to the intradermal injection of tuberculin is read 48–72 hours later, requiring the patient to revisit the clinic after the injection was administered. The interpretation of a test result is often very difficult, as a positive test may be caused by conditions other than tuberculosis and a negative test does not always rule out tuberculosis. Furthermore, tuberculin is not routinely available in many peripheral health institutions. It is expensive, has a very short shelf life, must be kept protected from light and heat, and requires some technical skill in administration and reading. Thus, in most instances, health care workers are forced to work without this test. A significant reaction to the test indicates the presence of infection but cannot indicate whether or not the patient has the disease. Many patients with advanced immunosuppression related to HIV will fail to react to the test even when they have the disease. Interferon-gamma release assays (IGRAs) have recently been proposed as a possible solution to some of the problems encountered with the tuberculin skin test. They are more specific than the tuberculin skin test, particularly in people who have received BCG, and they require only one visit by the patient. However, like the tuberculin skin test, they cannot distinguish between infection and disease. The tests are costly, they require specific laboratory equipment and there is a need for a venous blood sample to be drawn. Currently, there is no evidence to support the use of IGRAs in routine practice.

How is tuberculosis diagnosed in children?

Diagnosis of tuberculosis in children is difficult. It is even more difficult in HIV-positive children or in infants (whose own HIV status cannot easily be confirmed even when their mothers are HIV-positive). Great care should be taken to rapidly identify serious forms of tuberculosis such as disseminated tuberculosis, tuberculous meningitis, spinal tuberculosis and tuberculosis in immunosuppressed children. These can be life-threatening conditions and they require prompt diagnosis and treatment if death or disability is to be avoided. This is especially true in very small children (under 2 years of age), and particularly in children who have been in contact with smear-positive pulmonary tuberculosis patients.

In the majority of instances, however, childhood tuberculosis is a mild disease. Nevertheless, children with tuberculosis should be treated to

prevent complications and to ensure that they do not subsequently develop tuberculosis from reactivation of their infection. Only a very small proportion of children have tuberculosis that is smear-positive, and many children cannot produce sputum for examination. The points of most importance in determining a diagnosis in children, in order of priority, are:

- a history of contact with a case of infectious (sputum smear-positive) tuberculosis, particularly in the same household;
- an abnormal chest radiograph showing unilateral and sometimes bilateral lymphadenopathy and/or shadows in the lung field indicating infiltration.

In the absence of the above, it is less likely that the child has tuberculosis.

Any child under 5 years of age in contact with a smear-positive case who is not perfectly healthy must be carefully evaluated by a competent Medical Officer to decide if tuberculosis is present. If the child has signs or symptoms suggesting tuberculosis, it should be assumed that the child has tuberculosis, and the child should be given a full course of treatment. Those children under 5 years of age in contact with a smear-positive case of pulmonary tuberculosis who are perfectly healthy should be considered for preventive chemotherapy.*

2.2.4. Who should be considered to be a case of tuberculosis?

Any person diagnosed with tuberculosis should be recorded as a case. Those who have tuberculosis micro-organisms visible on microscopic examinations of sputum should be recorded as *smear-positive*. All other cases should be recorded in such a way as to distinguish them from smear-positive cases (as *sputum smear-negative* or as *sputum smear-negative extra-pulmonary* cases). All those with a positive smear recorded in the laboratory register and for whom no record has been made in any tuberculosis register should be entered into the register and evaluated with all other patients even when they are given no antituberculosis treatment at all. This includes all tuberculosis patients who never return after the sputum specimen has been examined, those who die before the start of treatment

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*For further details, see *Management of the Child with Cough or Difficult Breathing. A Guide for Low-Income Countries*.[2] For up-to-date dosage guidelines visit the WHO website at http://www.who.int/selection_medicines/committees/subcommittee/2/TB.pdf[3]

and all patients who start treatment for tuberculosis in hospital but cannot be traced after leaving the hospital.

2.2.5. How does HIV infection influence the diagnosis?

Tuberculosis is one of the most frequent opportunistic diseases in HIV-infected individuals in countries where both diseases are prevalent. Consequently, in all countries where tuberculosis and HIV are frequent, all those identified as having HIV infection should be systematically investigated for tuberculosis. Tuberculosis can occur at any stage during the course of HIV infection. In early HIV infection, when the immune defence mechanisms of the body are almost normal, tuberculosis presents with symptoms and signs that are similar to the symptoms and signs in an HIV-negative tuberculosis case, and a high proportion of cases in adults are smear-positive. However, when HIV infection progresses and the immune defence mechanisms of the body weaken, the presentation of the case may be unusual, and extra-pulmonary forms are more frequent. In these cases, the clinical presentation may be quite different from what is expected and sputum smear examination may be more frequently negative. It should be noted that individuals with advanced destruction of immune defence mechanisms may be symptom-free for some time, even though tuberculosis micro-organisms can be seen in their sputum. Some of these patients do not have chronic cough; some may present with non-specific symptoms, such as loss of weight and chronic fever; chest radiographs may have abnormal shadows in lung fields or intra-thoracic lymphadenopathy or they may be normal.

Although the appearance of tuberculosis varies according to the degree of destruction of the immune defence mechanisms in the body, positive smears still occur among those infected with HIV. Thus, sputum smear examination plays a vital role in the diagnosis of tuberculosis even in those countries where HIV infection is frequent. If the sputum examination is performed correctly, the majority of patients with pulmonary tuberculosis and HIV infection will be found to be smear-positive. Thus, the most contagious cases can be diagnosed rapidly.

Patients who are not sputum smear-positive must be offered treatment. However, other tests beyond the scope of this Guide would be required to confirm their diagnosis. If these tests are not currently available, the diagnosis must be confirmed by a Medical Officer before treatment is initiated.

2.2.6. How do we know if a patient has drug-resistant tuberculosis?

The confirmation of the diagnosis of tuberculosis in most countries is based on sputum smear microscopy. To detect resistance and to exclude disease caused by other mycobacteria, other methods for species identification and drug susceptibility testing are needed. These methods are complex, slow and expensive, and are not widely available in most countries or are used only for specific patient groups (for example, those with a high risk of multidrug resistance). In virtually all patients, even where drug susceptibility testing is available, treatment must be started without knowledge of the susceptibility of the micro-organisms to the drugs.

If drug resistance is already present, there is a possibility that the treatment might create more resistance. The recommendations put forward in this Guide are developed specifically to prevent this from occurring. Changes to the recommendations may compromise their ability to reduce the possibility of promoting further resistance. However, when the recommendations are strictly followed, tuberculosis can be successfully treated in the vast majority of cases, without knowledge of the susceptibility patterns of individual patients and without promoting drug resistance.

The measurement of drug resistance is an important topic, but the details of how this is carried out are beyond the scope of this Guide.

3
The human immunodeficiency virus

Where both tuberculosis and HIV are significantly present in a community, a patient with tuberculosis has a much greater chance of also having HIV infection, while someone who is HIV-infected has a much greater chance of developing tuberculosis. Consequently, as noted above, every tuberculosis patient should be offered testing for HIV. Every person with (or suspected of having) HIV infection should, at every contact with the health services, be interviewed carefully to determine whether or not tuberculosis is likely to be present. It is particularly important to look for tuberculosis as early as possible in the process of testing for HIV because an environment where persons with HIV gather (such as a general medical clinic or a centre for testing for HIV) is a location where tuberculosis is likely to occur, leading to spread from one person to another. Moreover, strict policies have been recommended for preventing spread of micro-organisms in all health care settings and must be rigorously enforced (see the most recent WHO policy on tuberculosis infection control in health-care facilities, congregate settings and households[5]).

All those who provide care for tuberculosis and HIV patients (including all general medical services) must have a thorough knowledge of both conditions. The philosophy of care must be "two diseases, one patient, one system".

3.1. What is HIV?

HIV is the organism that causes HIV infection in humans and, over time, as the person's immune system deteriorates, the acquired immunodeficiency syndrome (AIDS). It belongs to the group of retroviruses that have an unusual ability to integrate themselves into the genetic material of the organism they infect. HIV grows mainly in certain cells called CD4+ T lymphocytes, or simply CD4 cells. These cells are an important part of the immune defence mechanisms that are responsible for protecting the person against various infections and cancers.

When a person becomes infected with HIV, the virus enters a CD4 cell and joins the cell's own genetic material. Numerous new copies of the

virus are produced. Eventually, they break out of the CD4 cell, which dies as a result. New viruses look for other CD4 cells, enter into them and the process is repeated. In this way, the number of CD4 cells in the body progressively decreases over the years and the number of HIV viruses increases. This leads to progressive destruction of the immune defence mechanisms. The infections occurring as a consequence of reduced immunity caused by HIV infection are called opportunistic infections/diseases; tuberculosis is one of the most frequent and important of these.

The destruction of the immune defence mechanisms means that disease-causing organisms can invade the body unchallenged, multiply and cause serious disease.

Two to six weeks after becoming infected with HIV, a person may develop a condition called an acute HIV syndrome, characterised by flu-like symptoms that subside on their own. Thereafter, the person has no symptoms of illness, although remaining infectious, and can spread HIV to another person, most frequently through sexual intercourse when a condom is not used. This phase without symptoms may last from a few years up to 10–15 years.

As HIV infection progresses and the immune defence mechanisms weaken, the person starts to become ill, and may develop skin rashes, herpes zoster (shingles), chronic diarrhoea, fever, weight loss and symptoms of other HIV-related illnesses. The final stage of HIV infection is called AIDS and it frequently lasts 1 to 2 years before death, unless antiretroviral treatment is given. Tuberculosis, bacterial pneumonias, fungal infections of the skin and mouth, HIV wasting syndrome, central nervous system conditions and Kaposi's sarcoma are common diseases in individuals with AIDS. Approximately 30% of HIV-infected adults develop some symptoms and signs of HIV infection in the 3 years after becoming infected, and approximately 50% develop AIDS within 7 to 8 years.

The WHO has developed a clinical staging system for HIV infection, with Stage 4 indicating AIDS-defining conditions. The diagnosis of pulmonary and extra-pulmonary tuberculosis in an adult person with HIV infection indicates the presence of clinical Stage 3 and 4, respectively. In a child, the presence of tuberculous lymphadenopathy indicates Stage 3.

3.1.1. How is HIV spread?

HIV spreads most frequently from person to person through exchange of body fluids, especially during sexual intercourse. HIV may also spread

through transfusion of infected blood or blood products and the sharing of HIV-contaminated needles and syringes. HIV can also spread from an infected pregnant woman to her unborn baby during pregnancy or to her newborn baby during labour and through breast-feeding.

In health care settings, HIV (and other blood-borne organisms) can spread if syringes and needles are re-used (only disposable syringes and needles should ever be used and, after use, carefully discarded) or if a health care worker suffers a needle stick injury with a used needle.

There is no evidence that HIV transmission occurs through everyday contact, hugging or kissing, food or drink, or mosquito or other insect bites.

3.1.2. How can we prevent the spread of HIV?

The most common route of HIV transmission is through sexual intercourse. For this reason, everyone must make every effort to prevent sexually transmitted HIV infection by all possible means and at all times. Sexually active individuals need to act in a responsible and healthy manner. This includes knowing whether they are HIV-infected or not. Whenever one partner has had sexual intercourse with more than one other person and when couples have sexual intercourse where one person is infected with HIV and the other is not (discordant couples), there is a risk of sexual transmission of HIV. In these circumstances, correct and consistent use of a condom during sexual intercourse can significantly reduce the risk of HIV transmission.

The most effective approach for reducing sexual transmission of HIV is for all individuals to delay the age at which they start to have sexual intercourse, to reduce the number of lifetime sexual partners (most effective when a person has only a single lifelong partner) and to reduce the number of concurrent sexual partners (i.e., the number of partners with whom a person is having sexual intercourse at the same time). When individuals are unable or unwilling to meet these conditions and when individuals are not certain that they or their partner is not infected with HIV, a condom should always be used during sexual intercourse.

Other ways to prevent the spread of HIV include programmes for the prevention of mother-to-child HIV transmission, provision of safe blood and blood products, needle exchange facilities for injecting drug users, careful use of syringes and needles by health care workers, and information and education programmes. Strong evidence has also emerged that

male circumcision can reduce the risk of HIV infection in men who have been circumcised.

3.2. How is HIV infection diagnosed?

HIV infection is usually diagnosed through detection of antibodies to the virus in the blood. Production of these antibodies begins 2 to 8 weeks after infection. The period following infection, before antibodies become detectable, is known as the "window period". Other methods of diagnosis of HIV infection can also be used, but they are not usually readily available for the majority of people in low-income settings.

Simple and rapid HIV tests are recommended so that special laboratory equipment or highly trained staff are not needed. They can be carried out on blood specimens obtained by a finger prick, or on saliva. For the result of the HIV test to be recorded as positive, it must be positive on two tests using different test principles. Rapid HIV test results can be confirmed using other tests, such as enzyme immunoassay. Because all rapid tests do not perform equally well, each country's National AIDS Programme will determine the best combination of tests to use.

Results of rapid tests are available within 15 to 30 minutes. Thus, individuals who have received pre-test counselling and who consented to testing can be informed of the result and receive their post-test counselling all on the same day. The test results must remain confidential, as should all medical information about patients.

Offering an HIV test should be a routine part of the investigation of every tuberculosis patient. This is now called "provider-initiated HIV testing and counselling". This approach differs from the traditional "voluntary counselling and HIV testing", where the decision for HIV testing is left entirely with the patient and the emphasis is on extensive pre-test counselling and the social and preventive implications of being HIV-infected. With provider-initiated HIV testing and counselling, the HIV testing is requested by the health care worker; there is a greater emphasis on "opting out" (patients undergo an HIV test as part of the routine service unless they specifically decline); and there is a higher priority on post-test rather than pre-test counselling. The important thing is that the patient must always feel free to refuse the test.

The counselling and psychological support around HIV testing should include:

- determining the patient's knowledge about HIV and the association between HIV and tuberculosis;
- providing detailed information about HIV and the association between HIV and tuberculosis;
- determining whether the individual has any characteristics that are associated with a greater chance of getting HIV infection (HIV risk factors—such as multiple sexual partners or having recently had a blood transfusion);
- describing what is involved in performing the test;
- discussing the possible impact of a positive or negative result; and
- explaining how someone who is HIV-infected can access care.

For an individual found to be HIV-negative, the post-test counselling session should explore how to remain uninfected. For those found to be positive, post-test counselling offers an opportunity for support and provision of key facts about HIV and tuberculosis, other HIV-related conditions, available treatment and promotion of sexual behaviour that reduces the chance of infecting others and/or contracting other sexually transmitted infections or being superinfected with other HIV strains.

3.2.1. What is the role of diagnosing HIV infection among tuberculosis patients?

The link between HIV and tuberculosis is well known in many communities. Patients with tuberculosis may therefore be well aware of the possibility of HIV co-infection (and vice versa) and have in mind that they may be infected. It is important that, at the time of tuberculosis investigations, diagnosis and commencement of tuberculosis treatment, the health care worker finds out whether a patient with tuberculosis knows his/her HIV status. If it is not known, or a negative result was obtained more than 3 months ago, then HIV counselling should be given and testing offered. It is important to consider the advantages and disadvantages of providing patients with this service together with their tuberculosis services, or having it provided elsewhere within the health care services. Counselling should ideally be considered as a continuous process that ensures good communication with the patient found to be HIV-infected and his/her support person or family member. This contact can be nurtured during the period of tuberculosis treatment, as the treatment necessitates multiple visits. These visits also offer an opportunity to counsel and test the patient's sexual partner(s) and children for both tuberculosis and HIV.

There are important benefits of patients knowing their HIV status. If a patient is HIV-infected, the diagnosis may provide an explanation for symptoms the patient has already been experiencing. It also opens the door to the use of preventive drugs and it can help the patient to access antiretroviral drugs, where they are indicated. The information and counselling that patients receive when finding out their HIV status can help them prevent the spread of HIV to others (sexual partners or children, in the case of a mother). Indeed, it is dangerous for people not to know their HIV status, as accessing HIV care is essential for protecting their own health, and avoiding transmission is essential for protecting the health of others. Knowing one's HIV status should be the norm rather than the exception.

If a tuberculosis patient refuses HIV testing, multiple consultations during tuberculosis treatment allow the health care worker to reinforce the value of knowing one's HIV status and to enquire about the reasons for refusal.

Where HIV infection is relatively frequent, tuberculosis services can provide an entry point to HIV diagnosis and care by providing joint services and/or referral to relevant care elsewhere within the general health services to HIV-infected tuberculosis patients and their family members. In planning for joint services, the core functions of a tuberculosis programme, i.e., case finding and treatment, must not be compromised. Great care should be taken to ensure that infection control measures are followed, particularly in areas where cases of pulmonary tuberculosis may be in contact with immunocompromised patients.

3.2.2. How is HIV diagnosed in children?

Due to passively transferred maternal anti-HIV antibodies, antibody-based HIV tests cannot be used for diagnosis of HIV infection in infants and children up to the age of 18 months. A positive HIV test can therefore mean a true HIV infection or just the passage of maternally transferred HIV antibodies in a child who does not have HIV infection. However, a negative HIV test does exclude HIV infection. Only tests that detect the virus itself can be used to diagnose HIV infection in such cases. These tests are not routinely available. Some infants and children develop symptoms and signs suggestive of HIV infection at an early age. In these situations the diagnosis of HIV can be made on clinical grounds.*

*For up-to-date guidance visit the Child Lung Health Division website of The Union at http://www.theunion.org/lch/education-and-publications.html

3.3. How are HIV infection and AIDS treated?

Antiretroviral drugs are becoming increasingly available and affordable in many countries. These medicines dramatically improve the quality of life of HIV-positive individuals and prolong their lives. However, they do not cure HIV infection. HIV-infected persons may continue to spread the virus if care is not taken to prevent the transmission of HIV during sexual intercourse.

In addition to antiretroviral treatment, HIV-positive individuals can benefit from the management and prevention of opportunistic infections.

3.3.1. What constitutes care and prevention of opportunistic infections? What is cotrimoxazole preventive therapy?

Every new infection challenges the immune defence mechanisms of the body. In the case of an HIV-positive individual, such episodes may put additional strain on weakening or already frail defence mechanisms. To minimise this strain, it is essential that various infectious conditions and opportunistic infections be diagnosed promptly and treated efficiently. This constitutes care of opportunistic infections.

Cotrimoxazole is a fixed-dose combination of sulfamethoxazole and trimethoprim. It effectively protects against several disease-causing organisms, such as *Pneumocystis jirovecii* (formerly *P. carinii*), toxoplasma, isospora, many common pathogens causing pneumonia, diarrhoea and malaria. Its regular use leads to reduced illness and death from these conditions in HIV-infected persons. When cotrimoxazole is given daily, it is referred to as cotrimoxazole preventive therapy (CPT).* If there is no contraindication to cotrimoxazole preventive therapy, it is advisable to introduce it as soon as possible after the diagnosis of HIV infection alongside the tuberculosis treatment.

Given the difficulty in diagnosing HIV infection in infants and young children, it is recommended that cotrimoxazole preventive therapy be given to all babies born to HIV-positive women from 6 weeks to 18 months, the age at which HIV infection can be excluded or confirmed.

3.3.2. What is antiretroviral treatment?

As with antituberculosis treatment, using antiretroviral drugs in combination improves their effects and reduces the risk of development of drug resistance. Antiretroviral treatment, sometimes also called highly active

*The usual dosage for an adult is one tablet containing {trimethoprim 160 mg and sulfamethoxazole 800 mg} per day.

antiretroviral treatment, is a combination of at least three drugs. The goal of antiretroviral treatment is to restore and maintain the immune defence mechanisms by increasing the CD4 cell count and slowing down the replication of HIV in the body. This reduces the occurrence of opportunistic infections and cancers. Antiretroviral treatment can prevent the selection of drug-resistant HIV strains by preventing the virus from multiplying. Finally, by reducing the HIV load in plasma and other body fluids, antiretroviral treatment can reduce (but not eliminate) the risk of HIV transmission to a sexual partner and from the mother to her baby during pregnancy, delivery and breast-feeding.

Taking antiretroviral treatment consistently is as important as taking tuberculosis treatment consistently. As in tuberculosis treatment, it is advisable to use fixed-dose combinations where possible, to simplify dosing of drugs and to ensure better adherence to all the drugs in both the initial and continuation phases. It is necessary to monitor adverse reactions to antiretroviral treatment because these reactions may cause the patient to stop or interrupt treatment. Treatment has to be lifelong, and resistance may develop after some time. It is therefore important that treatment response be monitored at regular intervals.

Antiretroviral treatment does not cure HIV infection. A person taking it remains infectious. Persons taking antiretroviral treatment must therefore use condoms correctly and consistently whenever they have sexual intercourse. Despite the various advantages such treatment can bring to the lives of HIV-infected individuals, they may face a time when no further effective treatment can be offered or found, and only palliative care should then be provided.

3.3.3. When should antiretroviral treatment be started?

The decision to start antiretroviral treatment is seldom an emergency, except when a patient is severely ill with disseminated tuberculosis. A stepwise approach is proposed:

- make a firm diagnosis of HIV infection;
- assess the clinical stage of the HIV infection in the HIV-positive patient;
- treat existing active opportunistic diseases, including tuberculosis, and start cotrimoxazole preventive therapy; and
- counsel the patient and a supporting family member about adverse drug effects, how to take the drugs, and the importance of taking the drugs regularly for the rest of the patient's life.

HIV-infected patients with extra-pulmonary tuberculosis should be prepared for antiretroviral treatment and started on treatment in due course, regardless of their CD4 cell counts. Ideally, HIV-infected patients with pulmonary tuberculosis should first have their CD4 cell count measured. The indication to start antiretroviral treatment is often based on the CD4 cell count. If CD4 count capability is not available, then HIV-infected patients with pulmonary tuberculosis can be started on antiretroviral treatment.

It is essential, in all cases, to refer to the National AIDS Programme antiretroviral treatment guidelines for specific instructions on how to care for the patients.

3.3.4. How does antiretroviral treatment affect tuberculosis?

HIV-infected individuals who are taking antiretroviral treatment may develop the immune reconstitution inflammatory syndrome. This is thought to be due to "awakening immunity" as the immune defence mechanisms start to recover in response to the antiretroviral drugs. HIV-infected patients whose immune status is very low (i.e., they have a very low CD4 count) are at higher risk of developing this syndrome than those whose immune status is not so compromised. The recovery or reconstitution of immune defence mechanisms may be complicated by episodes in which previously sub-clinical/latent opportunistic infections or partly treated opportunistic infections are unmasked and present with symptoms and signs. In settings where tuberculosis is common, tuberculosis is frequently the opportunistic disease that becomes unmasked in patients on antiretroviral treatment. Other reasons why a patient may be getting worse must be excluded, including not taking treatment regularly, drug resistance, development of a new opportunistic infection or adverse drug reactions from the antiretroviral treatment. Antituberculosis and antiretroviral treatment should be continued in all cases. However, certain seriously ill patients may need a course of oral corticosteroids. The immune reconstitution inflammatory syndrome is thought to be one of the most important complications in tuberculosis patients co-infected with HIV.

HIV-infected individuals who are taking antiretroviral treatment have a lower risk of developing tuberculosis than HIV-infected individuals who are not taking it. However, the risk remains higher than in individuals free from HIV.

4
Treating tuberculosis

4.1. How is tuberculosis treated?

If the diagnosis of tuberculosis is made at an early stage of the disease and the patient is not seriously ill (either from tuberculosis or other diseases), it is possible to cure virtually any patient of tuberculosis. This is achieved if they are treated properly and the micro-organisms causing their disease are not resistant to the drugs frequently used for treatment of tuberculosis. Patients with multidrug-resistant tuberculosis (caused by micro-organisms that are resistant to at least isoniazid and rifampicin) are much more difficult to cure. In HIV-infected individuals with tuberculosis, the top priority is to efficiently treat tuberculosis.

4.1.1. What are the principles of tuberculosis treatment?

What is the basis of treatment?

Antituberculosis drugs are the most important component of all treatment of tuberculosis. This treatment is one of the most efficient means of preventing the spread of tuberculosis micro-organisms. The requirements for adequate treatment are:

- an appropriate *combination* of at least four antituberculosis drugs initially to prevent the development of resistance to those drugs;
- prescribed in the correct *dosage*;
- taken *regularly* by the patient;
- for a *sufficient period* to prevent relapse of the disease after completion of treatment.

Treatment must be given to every patient with a diagnosis of tuberculosis and should be given *free of charge* to the patients.

When should treatment be started?

Treatment should not be started until a firm diagnosis has been made. Treatment should always be started as soon as possible after finding a

positive smear in a patient suspected of having tuberculosis. Rarely (when the clinical condition appears inconsistent with the diagnosis of tuberculosis, or when doubt exists about the quality of the laboratory services), treatment might be deferred until a second positive result has been obtained or the patient has been referred to an experienced Medical Officer. As previously noted, the "trial of treatment" has no place in the diagnosis of tuberculosis.

What are the phases of treatment?

Treatment of tuberculosis cases should always include an *initial intensive phase*. An initial course of the combination of drugs recommended in this Guide is effective in eliminating most of the micro-organisms and in minimising the influence of small numbers of micro-organisms that are resistant to drugs. The intensive phase in all new patients (never previously treated for as much as one month) should be given for 2 months. The role of the intensive phase is to prevent failure to respond to the treatment.

The *continuation phase* is important to ensure that the patient is permanently cured and does not relapse after completion of treatment. The continuation phase does not require as many drugs, but does require a sufficient length of time to be sure the patient is permanently cured.

4.1.2. What if the patient has been treated previously?

Before treatment is started, it is essential to question all patients closely, carefully and repeatedly to determine whether or not they have previously taken treatment for tuberculosis. Any patient who has previously been treated for as much as one month must be suspected of having micro-organisms resistant to one or more drugs and/or not having taken all the drugs correctly. Such patients require very careful follow-up and a different form of treatment from those who have never been treated before. Occasionally patients are reluctant to reveal that they have been treated previously. For this reason, it is a wise policy to question patients several times using a reassuring manner. Some patients will still carry the Tuberculosis Patient Identification Card from their previously treated episode of tuberculosis, and this should contain information about previous tuberculosis registration number, type of tuberculosis and date of starting antituberculosis treatment.

4.1.3. What is directly observed treatment and how is it used?

The regimens proposed in this Guide will cure most newly diagnosed cases of tuberculosis, without promoting drug resistance. To achieve this, it is vital that the patient regularly takes the total quantity of drugs in the manner they were prescribed. To ensure that this occurs, frequent and careful supervision is necessary. During the intensive phase of treatment, a trained and supervised person (a health care worker whenever possible) must *directly observe* that the patient swallows every dose of the combination of drugs given. This is recommended in order to avoid the promotion of drug resistance. It is important to agree with the patient on the most convenient way to provide the treatment. In general, family members are not recommended as treatment observers. Treatment is, unless otherwise indicated, given to patients as outpatients. Either the patient comes to a health facility, which should be as close as possible to the patient's home, or the treatment observer goes to the patient's house. Occasionally the patient will need to have accommodation arranged at the treatment centre, in a hostel or in some other location. When the patient is very ill, it may be necessary for the patient to be admitted to hospital.

When the patient has completed the prescribed duration of treatment, the drugs should be stopped. Additional treatment is unnecessary if all the drugs prescribed have been taken. Although it is distinctly unusual for tuberculosis to relapse after adequate treatment, patients should be told to report for re-examination if symptoms suggesting tuberculosis recur.

4.1.4. What do we use for treating tuberculosis?

There is only a limited number of drugs currently available for the treatment of tuberculosis. For this reason, they must be used with great care in order not to promote resistance to these drugs. The presence of resistance, and particularly of multidrug resistance, makes the treatment much less likely to be successful.

Which drugs are most effective?

The most important drugs for the treatment of tuberculosis are isoniazid (H), rifampicin (R), pyrazinamide (Z), ethambutol (E) and streptomycin (S). Some drugs are available in fixed-dose combined preparations that may contain two, three or four antituberculosis drugs. There are fixed-dose combinations that contain:

- rifampicin with isoniazid {RH};
- ethambutol with isoniazid {EH};
- rifampicin with isoniazid and pyrazinamide {RHZ};
- rifampicin with isoniazid and ethambutol {RHE};
- rifampicin with isoniazid, pyrazinamide and ethambutol {RHZE}.

These fixed-dose combinations reduce the number of pills that a patient must swallow each day. It is very important to check the recorded expiry date for the drugs provided and to manage the drugs accordingly, using the first-in, first-out process.

The use of rifampicin and streptomycin for diseases other than mycobacterial diseases should be restricted to very carefully considered indications. Drugs used for the treatment of tuberculosis should be strictly controlled. They should only be available to patients through the National Tuberculosis Programme. They should not be available from the private market.

What do the antituberculosis drugs contain?

There is international agreement on the recommended dosage of each antituberculosis drug, which is calculated per kilogram of body weight.

This Guide proposes that a limited variety of preparations be available for each drug. This simplifies the management of the supply of drugs. It will enhance safety in prescription and will allow the correct dosage to be given. The preparation with the lowest content is usually recommended for treatment of adults: {RH} 150 mg/75 mg; Z 400 mg; E 400 mg; {EH} 400 mg/150 mg; S 1 g. These preparations (and the particular combinations of these preparations, known as regimens) have been used in this Guide as an example to illustrate the principles of the NTP, to illustrate how the drugs are used in practice. Other combinations (and regimens) are available and may be recommended by NTPs. These other choices may be equally effective, but the standard of good practice in each country is determined by the NTP and must be followed by all practitioners.

How are antituberculosis drugs used?

For both the patient and the community, it is essential to prevent the development of drug-resistant tuberculosis. A patient who fails on a first course of treatment is more likely to have resistant micro-organisms. Resistance to one drug may lead to the development of resistance to any

Table 4.1 Optimal dosages for essential antituberculosis drugs in adults

Drug	*Daily dose in mg/kg (range)*
Isoniazid	5 (4–6)
Rifampicin	10 (8–12)
Pyrazinamide	25 (20–30)
Ethambutol	20 (15–25)
Streptomycin	15 (12–18)

other drug when that drug is given as a sole companion to one to which the micro-organism is already resistant.

The principles of choosing a treatment strategy

The tuberculosis treatment recommended by an NTP has to be based on a strategy that cures most of the patients and reduces the risk of creating incurable (drug-resistant) patients who persistently transmit their tuberculosis micro-organisms to the community.

How to choose the appropriate treatment regimen

The choice of the appropriate treatment regimen depends on the patient's history of prior treatment. The treatment follows a sequence or cascade of regimens, in which at every stage the chosen regimen gives the greatest chance of cure in a patient who has had an unsuccessful outcome on the previous regimen. The drug composition is also chosen in such a way that the simplest, easiest and most tolerated regimen is used first, followed by a more complicated regimen if this is unsuccessful.

In the previous guides of The Union, the regimens were based on the availability of only six essential drugs that were recommended in a way that reduced to a minimum the risk of multidrug-resistant tuberculosis, because medications to treat and cure multidrug-resistant tuberculosis were not available for all patients who needed them in a national programme. The first-line regimen was thus a regimen of 8 months' duration that used rifampicin in the intensive phase only. Patients whose tuberculosis was due to a fully susceptible strain of bacilli had an excellent chance of cure, although at the same time the chance of cure was reduced in patients whose tuberculosis was due to isoniazid-resistant bacilli. When patients failed (or returned after default or relapsed), they were more likely to have

tuberculosis caused by isoniazid-resistant (but rifampicin-susceptible) bacilli, as the risk of acquiring rifampicin resistance was very low. Consequently, they could still be cured with a retreatment regimen, also of 8 months' duration, that contained rifampicin throughout the entire course of treatment.

The 8-month first-line treatment regimen is now discouraged by the WHO and is used in very few countries. In a clinical trial conducted by The Union, the 6-month regimen with rifampicin throughout has been shown to have higher efficacy (fewer failures and relapses) than the previously recommended 8-month regimen. However, this poses a problem under field conditions, because programmes are now confronted with patients who are true failures, i.e., who have multidrug-resistant tuberculosis that cannot be cured with the former retreatment regimen. Evidence is emerging that a proportion of rifampicin resistance is acquired, particularly with intermittent regimens, and ethambutol and/or pyrazinamide may not prevent the acquisition of resistance after the end of the initial intensive phase. The Union consultants agree that, for the continuation phase, daily rather than intermittent treatment should be prescribed for this phase of treatment. Ethambutol and/or pyrazinamide resistance will rarely emerge, and these drugs can continue to be used throughout the sequence of three treatment steps proposed in this Guide.

Step 1: Choice of the first-line treatment regimen

The first-line regimen is used for patients who have never been previously treated for as much as one month. Rifampicin plus isoniazid are given daily for a total of 6 months. During the first 2 months, the intensive phase, the regimen is strengthened by pyrazinamide plus ethambutol (2 RHZE/4 RH). This regimen has been proven in clinical trials to be the most efficacious as long as it is taken daily in the correct dosages and the bacteria are susceptible to the drugs. The chance of selecting drug-resistant mutants is highest when the bacterial load is greatest, i.e., when the patient is sputum smear-positive. Directly observed treatment during the intensive phase has proved effective in diminishing this risk, and should always be applied, preferably by a health care professional. Where possible, the safest approach is to directly observe the whole course of treatment, i.e., both the intensive and continuation phases. However, at minimum, arrangements must be made to ensure that every dose of drug in the intensive phase of treatment is swallowed under direct observation.

Table 4.2 For new cases of tuberculosis (never previously treated), number of tablets to be taken daily for adults on treatment according to weight and the content of the tablets

Month of treatment	*Drug*	*Weight in kg*		
		30–39	*40–55*	*>55*
1–2 Intensive phase	{RHZE} (R 150 mg, H 75 mg, Z 400 mg, E 275 mg) combined tablets	2	3	4
3–6 Continuation phase	{RH} (R 150 mg, H 75 mg) combined tablets	2	3	4

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

The directions for administration of drugs according to the weight of the patient are given in Table 4.2.

Step 2: Choice of the first-line retreatment regimen

Smear-positive patients who have taken drugs for treatment of tuberculosis for as much as one month in the past must be given a retreatment regimen. Previously treated patients include:

Relapses. These are patients who become smear-positive again after having been treated for tuberculosis and declared "Cured" or "Treatment completed" after their previous treatment.

Treatment after failure. These are patients who, while on treatment, are smear-positive at 5 months or later during the course of treatment.

Treatment after default. These are patients who return to treatment and are smear-positive after having interrupted treatment for more than 2 months. Those who have a negative smear on returning to treatment after defaulting should not be newly recorded, but should continue their original treatment until completion of the total quantity of drugs prescribed. A record of their treatment can be kept on the original treatment card, on which it is recorded that the patient returned for completion of treatment.

The first-line retreatment regimen recommended is of 8 months' duration, with rifampicin and isoniazid throughout, and is supplemented by

the three drugs pyrazinamide, ethambutol and streptomycin during the first 2 months (2 RHZES/6 RH). All drugs are given daily, with the same recommendation for directly observed treatment as the initial regimen.

This regimen is recommended based only on expert opinion, due to the scarcity of data available from clinical trials for retreatment regimens. The rationale for the recommendation is as follows. During treatment, sputum smears may remain positive for a prolonged time, even if the bacilli are no longer alive. The problem is even greater with regimens that contain rifampicin in the continuation phase compared with regimens that limit rifampicin to the intensive phase. Thus, failures (smear-positive specimens at 5 months or later) may be due to dead bacilli being expectorated, especially if the patient had extensive disease at the start of treatment.

If failures are mistakenly attributed to multidrug-resistant bacilli, this may result in the provision of treatment that is more expensive and less well tolerated, and which uses less efficacious drugs that must all be given under direct observation for a much longer period. This has strong negative implications for both patient and tuberculosis programme alike. This Guide thus proposes using an initial retreatment regimen that is still based on first-line drugs.

Patients may harbour an isoniazid-resistant strain. For such patients the addition of streptomycin during the intensive phase will most probably contribute to protecting rifampicin. If the bacilli are multidrug-resistant (i.e., resistant to both drugs), streptomycin might be lost as a treatment option during the intensive phase of treatment for multidrug resistance. This is considered a minor loss, however, as treatment of multidrug-resistant tuberculosis will always be based on another injectable drug (amikacin, kanamycin, capreomycin), with rare cross-resistance.

Ethambutol is not added to the continuation phase in this regimen because there is no evidence that it reduces the risk of failure due to acquired rifampicin resistance. Furthermore, it may prove useful to retain susceptibility to this drug for use in subsequent regimens in case the strain is already resistant to both isoniazid and rifampicin.

Duration of treatment is extended to 8 instead of only 6 months, to compensate for the possible loss of isoniazid (or other drugs, as long as this does not include both isoniazid and rifampicin), and therefore to ensure a better chance that all bacilli are killed with the longer treatment duration. The regimen is continued unless laboratory tests are available to prove that there is multidrug resistance or treatment fails according to the

Table 4.3 For patients given retreatment for tuberculosis, number of tablets to be taken for adults according to weight and the content of the tablets

Month of treatment	*Drug*	*Weight in kg*		
		30–39	*40–55*	*>55*
1–2 (daily)	{RHZE} (R 150 mg, H 75 mg, Z 400 mg, E 275 mg) combined tablets	2	3	4
	S	0.5 g	0.75 g	1.0 g*
3–8 (daily)	{RH} (R 150 mg; H 75 mg) combined tablets	2	3	4

*Patients aged 45 years and over should receive 0.75 g; streptomycin should ***not*** be given to pregnant women.
H = isoniazid; R = rifampicin; Z = pyrazinamide; E = ethambutol; S = streptomycin.

usual criteria, whichever comes first. The directions for administration of drugs according to the weight of the patient are given in Table 4.3.

Patients who are proven to have multidrug-resistant tuberculosis or who fail on this first-line retreatment regimen will require treatment for multidrug-resistant tuberculosis. This is based on the use of second-line drugs.

Step 3: Choice of the second-line retreatment regimen

The selection of the second-line drug retreatment regimen is also hampered by a lack of strong data from clinical trials. The standards for the treatment of multidrug-resistant tuberculosis are published by the Green Light Committee, hosted by the WHO.[4] These standards should be the reference on which the NTP bases its recommendations. The majority of the experts in The Union share the concern that the regimens proposed in these standards are too long and focus too much on drug efficacy rather than on overall regimen effectiveness. The recommended regimens do not take sufficient account of the influence of adverse drug events on patient adherence, and they are also expensive.

Therefore, an alternative regimen that has been tested extensively under programme conditions in the Damien Foundation Projects in Bangladesh might be considered when formulating a national policy.

The treatment of multidrug-resistant tuberculosis in this project was developed sequentially starting with a standard regimen proposed by the

WHO. This first regimen was highly efficacious in preventing failure and relapse, but it also resulted in large losses of patients who refused to complete treatment due to adverse drug reactions, mostly due to prothionamide. Progressively, and after careful analysis of the results in each step, a regimen was finally identified that resulted in a relapse-free effectiveness of close to 90%, with outcomes very similar to those obtained among new cases treated in the same project.

This regimen contains gatifloxacin, pyrazinamide, ethambutol and clofazimine throughout treatment. During the intensive phase, this drug combination is supplemented by kanamycin, isoniazid and prothionamide. The intensive phase is given for a minimum of 4 months, but is prolonged if the sputum smear examination at the end of 4 months of treatment remains positive, until the monthly sputum smear examinations are negative. The continuation phase is fixed at 5 months, whatever the final duration of the intensive phase. The results may be especially relevant for settings where the prevalence of resistance to fluoroquinolones and second-line injectables among multidrug-resistant strains is low, which is likely the case in most low-income countries. The detailed results of this study are available in the international biomedical literature.[6] Like any other regimen for multidrug-resistant tuberculosis, there is international agreement that each dose of drugs must be directly observed throughout treatment. The directions for administration of the drugs according to the weight of the patient are given in Table 4.4.

What adverse effects can the drugs have?

Adequate treatment of each case for the full duration of the prescribed regimen is very important if success in treatment is to be achieved. Any change to the treatment regimen due to what appear to be adverse effects must be made only after careful consideration.

Treatment of tuberculosis is prolonged over a number of months. During such a period of time in anyone's life, some events might occur which, if they occur in someone taking drugs, may be thought to have been caused by these drugs. Particularly frequent events of this type include skin rashes and abdominal complaints. In studies of the use of isoniazid, in which the comparison group was given no active drug (placebo), it was noted that of all the episodes that doctors considered to be caused by reactions to drugs, approximately half were in fact caused by something else.

Table 4.4 For patients given a second-line retreatment regimen for tuberculosis, number of tablets to be taken for adults according to weight and the content of the tablets

		Weight in kg		
Month of treatment	*Drug*	*25–32*	*33–50*	*>50*
1–4 (daily) (may be prolonged)	Gatifloxacin* (400 mg)	1	1.5	2
	Z (400 mg)	2.5	4	5
	E (400 mg)	1.5	2	3
	H (300 mg)†‡	1	1.5	2
	Prothionamide (250 mg)†	1	2	3
	Clofazimine (50 mg)	1	2	2
	Kanamycin§	15 mg/kg	15 mg/kg	15 mg/kg
5–9 (to 12) (daily) (5 months fixed)	Gatifloxacin (400 mg)	1	1.5	2
	Z (400 mg)	2.5	4	5
	E (400 mg)	1.5	2	3
	Clofazimine (50 mg)	1	2	2

*While adverse drug events related to dysglycaemia have been reported in some populations, e.g., the elderly, this has not been a major problem in the Bangladesh project. Nonetheless, product availability may become limited and necessitate consideration of an alternative fourth-generation fluoroquinolone, such as moxifloxacin.
†For isoniazid and prothionamide, the highest dosages are given from 55 kg onwards only.
‡For the treatment of MDR-TB, isoniazid is used in a higher dosage than for first-line treatment, thus 300 mg tables are utilised.
§Patients aged 45 years and over should receive max. 0.75 g; kanamycin should be given intermittently in case of extension of the intensive phase; kanamycin should ***not*** be given to pregnant women.
Z = pyrazinamide; E = ethambutol; H = isoniazid.

When do drugs need to be stopped without further consideration?

Very infrequently, reactions occur that require the drugs to be stopped and the patient to be hospitalised for management. They include the following:

Generalised reactions including shock, purpura and fever. This is very rare but may be caused by rifampicin, pyrazinamide or streptomycin if it is used. The drug thought to be responsible for the reaction should *never be given again.*

Impairment of vision in a patient on ethambutol (rarely, isoniazid can also be responsible). Patients developing impaired

vision (including reduced colour discrimination, blurring or spots) should report immediately for examination. If ethambutol is thought to be responsible, it should *never be given again*.

Patients who are pregnant must never be given injectable antituberculosis drugs due to the risk of damage to the foetus.

What symptoms indicate that drugs need to be stopped while the cause is investigated?

Jaundice or severe abdominal discomfort may be caused by hepatitis. It is most frequently due to rifampicin, but may also be caused by pyrazinamide or isoniazid. Furthermore, the hepatic toxicity of isoniazid and rifampicin is at least additive. Any patient with these symptoms should be referred to the Medical Officer for further consideration.

Skin rash is most frequently due to isoniazid, streptomycin or pyrazinamide. If the patient is clinically well (does not suffer from advanced tuberculosis or serious forms such as meningitis or disseminated disease), it is best to stop all drugs and recommence them when the reaction has subsided. If the symptoms recur, the patient should be referred to the Medical Officer.

Dizziness may be caused by injectable drugs. This is most frequent in older individuals. Correct dosage and duration of treatment are important to prevent occurrence of these adverse drug events.

What reactions do not require interruption of treatment?

Numbness or tingling may be caused by isoniazid. When it occurs, it can be treated by supplementing the isoniazid with vitamin B_6 (also known as pyridoxine) at a dose of at least 50 mg daily.

Joint symptoms may be caused by pyrazinamide. Check the dosage by weight, as these symptoms are usually caused by overdosage. They may be easily alleviated with acetylsalicylic acid.

All patients on **rifampicin** should be advised to expect a **red/orange colour to body fluids** (tears, saliva, sputum, sweat and urine), which is not dangerous.

It is important to **determine if the patient is taking oral contraceptives**, anti-epileptic drugs, corticosteroids, oral treatment for diabetes, oral anticoagulants or certain types of antiretroviral drugs. These instances may require adjustment of dosage or the use of alternative family planning methods.

4.2. What factors might affect treatment?

4.2.1. How does HIV affect tuberculosis treatment?

The principles of tuberculosis treatment are the same for patients with and those without HIV infection. The tuberculosis treatment regimens, in principle, are the same. It must be stressed that even in co-infected patients, the top priority is to treat tuberculosis first.

Patients infected with HIV usually have a response to treatment similar to those who are not infected with HIV, with a few exceptions:

- they are more likely to die during the course of treatment, usually from causes other than tuberculosis;
- they may be more likely to experience toxic reactions to drugs than those who are not HIV-infected and their treatment must be adjusted for this reason.

4.2.2. How does antiretroviral treatment affect tuberculosis treatment?

Some questions remain unanswered in this regard. For example, what is the best time to start antiretroviral treatment in individuals who have been diagnosed with both tuberculosis and HIV? One has to consider the high pill burden, drug-drug interactions, overlapping drug toxicities and occurrence of immune reconstitution inflammatory syndrome. Even in the absence of firm evidence, it would appear reasonable in most instances to start antiretroviral treatment at the end of the intensive phase, because some time is required to perform the HIV test, complete the biological assessment before antiretroviral treatment, carry out post-test counselling and, importantly, prepare the patient and the treatment supporter to ensure that the treatment is taken regularly and consistently. If the patient has advanced HIV infection and is very ill and appears likely to die, starting antiretroviral treatment earlier after the start of tuberculosis treatment should be considered.

Another question to be addressed is the choice of where the antiretroviral treatment is administered both during and after tuberculosis treatment. Should it be available in the tuberculosis clinic or in the antiretroviral treatment clinic, in both, or in a combined clinic? Again, there is not yet sufficient experience for the best approach, although countries are piloting collaborative tuberculosis and HIV services and gathering relevant information. In every situation, it is important to balance the

benefits and risks. If patients are made to attend two different facilities, it is possible that they may not understand the importance of taking their treatments regularly and that they may fail to attend their essential regular appointments. However, if tuberculosis clinics are given the responsibility of providing antiretroviral treatment, there is a danger that the tuberculosis clinics will become overburdened and that infection control will be hindered. Equally, if antiretroviral treatment clinics are given the responsibility of providing antituberculosis treatment, there is a danger that the majority of co-infected patients will be managed in antiretroviral treatment clinics, and without strict infection control measures there is a danger of transmission of tuberculosis micro-organisms to HIV-infected patients.

It is recommended to follow the national antiretroviral treatment policy and guidelines for all decisions about when to start ART in co-infected tuberculosis patients and what type of treatment regimen to use.

HIV infection can be spread through the exchange of blood or blood products. Tuberculosis micro-organisms are spread through airborne transmission. Because of the association between tuberculosis and HIV infection, great care must be taken in tuberculosis and HIV care programmes, and in health services in general, to prevent the spread of both of these infections. The highest standards of hygiene must be observed, particularly when there is a risk of exposure to blood or blood products, when caring for tuberculosis patients. The use of injections should be limited as much as possible. Where they cannot be avoided, every health care worker should strictly adhere to the principle: *a sterilised needle and syringe for each injection in each individual patient*, followed by destruction of the syringe and needle that were used. Given the risk of co-infection by HIV and tuberculosis in places where HIV is frequent, as well as the danger of other blood-borne infections, particular attention should be paid to the safe disposal of injection material that has been used for streptomycin injections.

A health care worker who is HIV-positive should avoid exposure to tuberculosis patients because of the greatly increased risk of developing tuberculosis if infected.

Moreover, wherever HIV-positive patients come together (in clinics, hospital wards, hospices and community support groups), careful attention should be paid to any possibility of the occurrence of tuberculosis in these patients, and every effort should be made to diagnose and treat tuberculosis very rapidly, if it does occur.

4.2.3. How does drug resistance affect treatment?

Large populations of tuberculosis micro-organisms, such as those in patients who are sputum smear-positive, always contain some mutants spontaneously resistant to drugs. If a correct combination of drugs is prescribed and is taken fully and regularly by the patient, this resistance is overcome and does not pose a problem. This is one of the main reasons why a greater number of drugs is used during the intensive phase of treatment until the population of micro-organisms has been rapidly reduced and why treatment must be observed to have been taken in its entirety. This important principle must be respected to prevent the development or extension of clinically important resistance to additional drugs.

Once developed, resistance to antituberculosis drugs can have an impact on tuberculosis, by causing the emergence of further resistance (where an insufficient combination of drugs is used) or by rendering the patients difficult to cure (if resistance to isoniazid and rifampicin coincide in an individual patient). The recommendations put forward in this Guide propose the steps that are most likely to be successful in preventing multidrug-resistant tuberculosis.

Recommendations for the management of multidrug-resistant tuberculosis have been published by the WHO.[4] Management of such cases is the responsibility of the National Tuberculosis Programme.

4.2.4. What if the patient is pregnant or breast-feeding?

Pregnant women with tuberculosis should start or continue their treatment for tuberculosis in the same way as other patients. When the patient has a nursing infant, it is of particular importance to continue breast-feeding, as its discontinuation poses a serious risk to the health of the infant.

4.3. What about those exposed to tuberculosis?

Those who live in the same household as any patient who is smear-positive have a higher risk of having tuberculosis themselves. If they have any symptoms, they should be requested to come for a medical examination. Any child in the household under 5 years of age who has symptoms that suggest tuberculosis should be given treatment and registered as a case of tuberculosis. All other children under 5 years of age who are healthy should be given preventive chemotherapy, even if they have previously been vaccinated with BCG.

4.3.1. What is preventive therapy and its role?

Preventive therapy is the treatment of those infected with *Mycobacterium tuberculosis* (tuberculous infection) who do not have the disease (tuberculosis). The infection can be identified in healthy individuals using a tuberculin skin test. The risk of developing tuberculosis in those who are tuberculin skin test positive is low unless the infection has been acquired relatively recently or the person is also HIV-positive. Preventive therapy in such persons can substantially reduce the chance of developing tuberculosis.

This Guide recommends daily preventive treatment with isoniazid for a period of 6 months, at a dose of 5 mg/kg body weight for adults and 10 mg/kg for children. While a 9-month course of isoniazid preventive therapy is more efficacious, a major limitation is that completion rates are typically low, and every effort should be made to ensure that treatment is taken for least 6 months.

Tuberculin is commonly not available. The group with the greatest need for preventive therapy is children under the age of 5 years who are living in the same household as a newly diagnosed smear-positive tuberculosis patient. The chance that the child has been infected is high, as is the chance that the child will develop tuberculosis. New smear-positive patients must be questioned carefully to determine if there are children in their household. These children must then be examined and treated as outlined above.

How does HIV affect preventive treatment?

Isoniazid preventive therapy is a useful personal health measure for HIV-infected individuals who are also infected by *Mycobacterium tuberculosis*. Before giving preventive treatment, it is important to ensure that the person does not have tuberculosis, as monotherapy with isoniazid would result in resistance to that drug.

4.3.2. Can a patient on treatment for tuberculosis infect others?

Treatment is effective in rapidly diminishing the infectiousness of any patient with susceptible micro-organisms. This is because the drugs rapidly reduce the number of micro-organisms and the patient's cough rapidly subsides, resulting in fewer micro-organisms expelled into the air. In most settings, no special precautions for preventing the spread of micro-organisms need be taken once the patient is on treatment; the best prevention is to

ensure that patients are diagnosed and started on treatment rapidly, and that the drugs are being taken regularly.

This is not true, however, if the micro-organisms are multidrug-resistant, in which case great care must be taken to avoid transmission to those around the patient. Where multidrug-resistant tuberculosis is frequent, great care must be taken to avoid contact, as much as possible, between those who have (or are likely to have) tuberculosis and any person likely to have HIV infection.

Good ventilation must be provided wherever tuberculosis patients (or those likely to have tuberculosis) gather. Hospitalising tuberculosis patients should be avoided whenever possible; if they are admitted to hospital, the best ventilation possible should be provided for the area. The latter is also true for patients living in communal settings (residential schools, prisons). Moreover, tuberculosis patients with multidrug-resistant micro-organisms (and those likely to have tuberculosis) who cannot avoid communal living should be given accommodation in an area away from other patients, particularly HIV patients. Outpatient waiting areas should preferably be laid out as wide open verandahs. Moreover, areas where those who may have, or are confirmed to have, tuberculosis are requested to produce sputum for smear examination should be well ventilated and away from areas attended by other people. Every effort should be made to collect the specimen out of doors in the open air.

Prevention of transmission within health care facilities should be part of a careful plan with a series of priorities, beginning with administrative controls (high degree of clinical suspicion of infectious tuberculosis patients, their rapid identification and separation from other patients and prompt initiation of tuberculosis treatment), followed by environmental controls (maximisation of natural ventilation and control of air flow) and personal respiratory protective devices. Such devices for health care personnel require regular change of filtering elements, a condition necessary to ensure their effectiveness that is difficult to achieve where resources are limited. Surgical masks are effective in reducing the chance that patients disseminate droplets to the environment, but are ineffective in preventing health staff from being infected.

5
Caring for the patients

The quality of the care given to patients and the thoroughness with which it is followed are important determinants of successful treatment and of reduction in the risk of becoming infected. Poor treatment increases the number of infectious cases in a community.

5.1. How should the patients be followed?

Because the treatment is prolonged, great care must be taken to ensure that patients continue to take their treatment correctly for the total duration prescribed.

5.1.1. Are all the patients on treatment?

Many studies have shown that tuberculosis patients often present of their own accord to the general health services, but may not be properly diagnosed and initiated on tuberculosis treatment. For this reason, periodic visits should be made to the adult medical outpatient department of the facility where patients are being diagnosed to determine the number of persons seeking care in the facility and ensure that those who should be referred for examination for tuberculosis are actually given this examination. A general rule that is helpful in evaluating the comprehensiveness of tuberculosis services is the "30-10-10" rule, which indicates that approximately 30% of adults consulting general care facilities will present because of respiratory symptoms, 10% of whom will have prolonged respiratory symptoms and will thus be eligible for sputum smear examination. Of these, possibly 10% may be sputum smear-positive (although this percentage has a wide range, depending on accessibility of services and proper selection of suspects, and has commonly been shown to be as high as 20% or more in many sub-Saharan African countries and frequently as low as 5% in Latin America). The actual percentage is easily obtained from the tuberculosis microscopy laboratory register, and comparisons can be made between different basic management units in the same area. If the number

of examinations is substantially different from the expected average obtained from regular supervisory visits to the laboratories (be it higher or lower), the reasons for the differences need to be explored.

A periodic review, usually once a week, should be undertaken to compare the names of the patients identified as smear-positive in the laboratory with the list of patients commenced on treatment or referred to another health facility for treatment, to ensure that no patients identified in the laboratory go without treatment.* Moreover, the laboratory results of all those patients who have been commenced on treatment who are not smear-positive should be confirmed in the laboratory to ensure that their examinations have actually been performed and are negative.

5.1.2. How can we encourage full participation of the patient?

The successful treatment of the patient requires that the patient understands what is happening. A patient who understands the nature of the disease and its treatment is more likely to follow the treatment required to achieve cure. The relationship developed between the patient and the health care worker is key to achieving success in treatment and requires investment of time and energy. Health care workers should adopt a positive attitude with their patients and pay attention to the importance of privacy. They should listen carefully to the patient to ensure that the patient clearly understands the messages being communicated, and fully engage the patient in preparing plans for treatment and follow-up.

The patient and, if possible, at least one member of the patient's close social network in whom the patient has confidence, should clearly understand the answers to the following questions:

- What is tuberculosis?
- How does a person get it?
- What measures can be taken to limit it?
- How is tuberculosis treated?
- Can the disease be cured?
- Is treatment free of charge?
- What drugs are used and for how long?
- How is the treatment followed?
- What are the possible adverse effects of the drugs?
- What should be done if a certain adverse effect occurs?

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*The result of this cross-checking should be written in the corresponding column of the *Tuberculosis Laboratory Register* (Appendix, Form 2).

In addition, in settings where HIV is prevalent:

- How is it associated with HIV?
- Does the patient know his/her HIV status?
- What are the benefits of knowing one's HIV status?
- What care can be offered if the patient is found to have HIV infection in addition to tuberculosis?

If the patient understands the disease and its treatment, this information can be passed on to the community and, as a result, other individuals with tuberculosis may be encouraged to come forward to seek diagnosis and treatment.

Besides helping the patient to understand key aspects of the disease and its treatment, it is important that the health care worker has a clear understanding of the problems the patient may face in taking the treatment and attending the clinic regularly. These may be psychosocial and linked to how the patient and the community understand and interpret the disease. They may also be linked to difficulties in accessing the clinic regularly, for example, due to the cost of transport, the distance to be walked or inconvenient clinic opening hours. All problems that the patient may encounter should be systematically examined before treatment is initiated, and solutions to overcome them should be found together with the patient and the designated treatment supporter that the patient has selected.

A useful addition to understanding how well the services are functioning and what problems patients face in the management of tuberculosis is to occasionally visit selected patients in their homes to interview them and their family about their knowledge of tuberculosis and the difficulties they face in following the treatment. This has the potential to identify shortcomings in the health services that can be easily addressed.

5.1.3. How do we monitor progress during treatment?

The results of sputum smear examination should be recorded (see section 5.4.1) for all patients before starting treatment. Bacteriological follow-up examinations in smear-positive patients are the most important means of assessing progress. After 2 months of intensive phase treatment, a single sputum specimen in these patients must be examined by microscopy. Regardless of the result, patients should start the 4-month continuation phase.

In all smear-positive patients, a single microscopic examination is done at 5 months. If the result is negative, treatment should be continued until completion. If any acid-fast bacilli are identified (regardless of the grade of the positive result), the result should be confirmed by a second positive result before declaring the patient a treatment failure who must be given the retreatment regimen.

One single sputum microscopy examination is repeated on the final visit at 6 months. If negative, the patient is declared cured. Patients with positive smears on this examination (confirmed by a second examination) are declared treatment failures and must be given the retreatment regimen.

Patients who occasionally miss an appointment during the continuation phase should have the total amount of time of treatment that was missed added to the originally planned duration. If the patient is still on treatment at the time of the evaluation 9 months after the close of the quarter in which the patient was registered, the outcome of treatment of the patient is recorded as "defaulted". For monitoring of treatment for multidrug-resistant tuberculosis, the reader is referred to WHO guidelines.[4]

5.2. What is the most efficient way to deliver tuberculosis services?

Because tuberculosis is a widespread disease, and preventing it requires a high quality of medical care for individual patients, the organisation and system through which this care is given is an important element in achieving success in tuberculosis services.

5.2.1. How should the tuberculosis services be structured?

The responsibility for tuberculosis services rests with the government. These activities must be organised in the form of a National Tuberculosis Programme (NTP). The aims of an NTP are as follows:

- to rapidly diagnose and cure as many of the infectious cases of tuberculosis as possible, and in this way to reduce the rate of spread of tuberculosis micro-organisms;
- to maintain vigilance in the detection of all new infectious cases that will continue to arise during the entire lifetime of that group in the population that has already been infected prior to the application of control measures;
- to limit the excess transmission of tuberculosis micro-organisms resulting from the presence of HIV infection in the community.

To achieve these aims, an NTP must:

- *be country-wide*, with a focus on areas where the greatest proportion of the population lives. It requires a strong urban component (urbanisation is increasing rapidly and tuberculosis is a particularly serious problem in overcrowded urban areas). Achieving country-wide scale-up of tuberculosis services should nevertheless be carefully planned, without endangering the quality already achieved;
- *be permanent*, ensuring that the cases continuously arising from those already infected with tuberculosis micro-organisms will be rapidly identified and rendered non-infectious (a process that must continue throughout the lifespan of the last heavily infected group in the population);
- *be adapted* to the realities of each community within which it operates, taking note of the *characteristics* of the population;
- *take into account* access to health facilities and the convenience of services for the patients;
- *pay attention* to the attitude of health care personnel;
- *be integrated* within the general health services of the community, as tuberculosis is one of the most important causes of ill health in low-income countries and patients present with their symptoms at every level of the health service;
- *collaborate with the National AIDS Programme*, particularly in settings where HIV fuels tuberculosis, to plan, implement and monitor joint services for co-infected tuberculosis patients.

The modern NTP is based on the Stop TB Strategy, promoted by the World Health Organization and launched on World TB Day in 2006.[7] This strategy has grown from the experience of The Union and its partners, which is described in this Guide. "High-quality DOTS expansion and enhancement" is the first of six components in the Stop TB Strategy, and is described as the cornerstone that provides the foundation for the remaining five components. Thus, NTPs must aim to further strengthen the five basic elements outlined in his Guide, namely:

- *sustained political commitment* to increase human and financial resources;
- uninterrupted supply of *quality-assured drugs*;
- access to *quality-assured tuberculosis sputum microscopy*;

- *standardised short-course chemotherapy* for all cases of tuberculosis under proper case-management conditions, including direct observation of treatment at least during the intensive phase of treatment;
- *recording and reporting system* enabling outcome assessment.

With its five remaining components, the Stop TB strategy aims to expand the scope of the DOTS strategy to address constraints and challenges in tuberculosis control:

- address TB-HIV, MDR-TB and other special challenges;
- contribute to health systems strengthening;
- engage all care providers;
- empower people with tuberculosis and communities;
- enable and promote research.

5.2.2. How should the service be organised?

The structure of the tuberculosis service should follow a three-level organisation, with a peripheral level (where the services are provided), an intermediate level (which provides support) and a central level (which coordinates the progress of tuberculosis services).

The basic management unit

The peripheral level should be based upon the principle of a **basic management unit** (BMU). The BMU is the cornerstone of the tuberculosis service; it is defined as a functional area serving, on average, a population of 50,000 to 150,000 (up to 300,000 in large cities). It is part of the general health services and comprises:

- One health facility offering diagnostic and treatment services, with at least a direct smear microscopy laboratory (usually a hospital or a large health centre). At more peripheral levels of the health service, serving a smaller unit of population, the quality of diagnostic services, and particularly sputum smear microscopy, is very difficult to ensure. Experience from many countries shows that one such facility per BMU offers an adequate balance between access to, and quality of, diagnostic services. Treatment will often be started at a facility where the diagnosis is established but continuing treatment can be organised at the health facility nearest to the patient.
- One or several health facilities offering only screening examination to identify those suspected of having tuberculosis, referral and treat-

ment services (these are often satellite health centres or posts in the area). They will refer patients presenting with respiratory symptoms for diagnostic examination, or send sputum or smears for microscopy to the BMU, and will provide continuing treatment for those found to have the disease and started on treatment elsewhere.

- Some community-based or non-governmental organisations refer suspects and deliver treatment within the community. However, any such services must be under the direct supervision of the governmental services at the BMU. Therefore, even when such services are provided outside the public sector, the government must be held responsible for their results.

Each BMU should have a Tuberculosis Coordinator. This person, usually a paramedical professional, is responsible for ensuring that tuberculosis activities (case finding and treatment) are correctly implemented throughout the BMU. Ideally, this coordinator should have demonstrated capacity in organising tuberculosis case finding and treatment at facility level. The BMU Tuberculosis Coordinator is usually part of the area health management team and has a supervisory role. This post may be a full-time or a part-time position, depending on the workload.

The BMU Tuberculosis Coordinator is responsible for the regular supervision of all the health units within the BMU that are involved in the tuberculosis service. Supervision involves the following tasks:

- ensuring uninterrupted availability of treatment supplies and adequate stock management within the unit;
- ensuring that all patients commenced on treatment have had a sputum smear examination performed;
- ensuring that the correct treatment regimen is applied to all patients (in particular, ensuring that those patients eligible for the retreatment regimen are correctly identified and treated);
- organising the treatment of patients, ensuring that the entire intensive phase of treatment is given under direct observation by a trained person, often a health care worker;
- ensuring that the organisation of tuberculosis care in all facilities in the BMU is designed to facilitate enrolment on, and adherence to, treatment;
- ensuring that living arrangements for patients who must remain away from home to receive treatment do not put the successful completion of treatment at risk;

- regularly comparing the *Tuberculosis Register* and the *Tuberculosis Laboratory Register* to make sure that all patients diagnosed with positive smear microscopy are enrolled on treatment or, if they cannot be retrieved, are entered in the *Tuberculosis Register* as defaulters;
- ensuring actions aimed at promoting adherence to treatment and preventing defaulting (such as patient education and communication), and retrieving all patients who do not appear at regular appointment times;
- completing the *Tuberculosis Treatment Card* regularly and keeping the BMU *Tuberculosis Register* in order and up to date;
- compiling the reports of the facilities in the BMU, and reporting the results of tuberculosis activities in the BMU, in particular the cohort analysis of case finding and treatment outcome;
- in settings where HIV is frequent, ensuring that all patients with tuberculosis are offered HIV diagnostic and care services or referral to an appropriate unit for these services;
- coordinating with staff at the BMU level responsible for other programmes such as HIV/AIDS, Leprosy and Laboratory Services.

The intermediate level

In order to maintain a high quality of service, a system of training and supervision must be in place to support the BMU Tuberculosis Coordinator. For this reason, each group of 5–10 BMUs should have an individual (an intermediate or higher-level coordinator) responsible for ensuring that this occurs. In most instances, this individual is a physician or paramedical officer who acts as a "reference" in the area to determine what is to be done when problems arise. This individual carries out the tuberculosis activities in addition to other responsibilities (often providing specialist services for chest diseases or other communicable diseases). The person can also be an epidemiologist or public health person who is part of the provincial health team. The Provincial/Regional Tuberculosis Coordinator is responsible for:

- advising in the nomination of health care workers who are responsible for managing the care of tuberculosis patients;
- supporting and supervising the activities of the BMU Tuberculosis Coordinators, who must be visited at least quarterly (or more frequently in the case of poor performance);
- providing training for all new personnel and refresher training for those who require special attention in the light of their performance;

- ensuring uninterrupted availability of diagnostic and treatment supplies, stationery such as *Tuberculosis Treatment Cards*, *Patient Identity Cards* and *Tuberculosis Registers*, and adequate stock management at the BMU and intermediate levels;
- maintaining a system of quality control of sputum smear microscopy;
- reviewing and ensuring the quality of the regular reports of activities submitted from the BMU level and reviewing progress made with the BMU Tuberculosis Coordinators each quarter; such a review is better when it can be made in a participatory way with the BMU Tuberculosis Coordinators, for instance during a quarterly meeting at the intermediate level;
- co-ordinating with health authorities at intermediate levels to ensure adequate resources are mobilised to permit accessibility of diagnostic and treatment services throughout the district. In particular, adequate access should be provided for specific populations such as prisoners and displaced communities. This includes, for example, advocating the creation of new BMUs, treatment facilities, mobile clinics or community-based schemes within existing BMUs, and contributing to the preparation of plans for obtaining sufficient resources to sustain the tuberculosis service;
- coordinating with the central level to ensure regular supervision, training, supply and reporting, and with colleagues responsible for other programmes such as HIV/AIDS, Leprosy and Laboratory Services.

The central level

Within the Ministry of Health, there must be a Central Tuberculosis Unit with a full-time director and support staff to ensure that the NTP functions appropriately. In settings where HIV infection is frequent, the programme director and staff must appreciate the threat that HIV poses to tuberculosis services and the fact that tuberculosis services can only be successful if they collaborate with the prevention, care and management of HIV. The Central Tuberculosis Unit should maintain links with the central government departments responsible for primary health care, hospital care, laboratory services, pharmaceuticals, planning, human resource development and training and finances.

The Director must take responsibility for all tuberculosis-related activities in the country. The functions of the Central Tuberculosis Unit include the following:

- planning, monitoring and evaluating the development of the NTP, including work plans, budgets, reports and administration. These activities are usually implemented in close co-operation with the central government department responsible for the control of communicable diseases and the department of planning;
- co-ordinating, monitoring and evaluating the implementation of the national tuberculosis control strategies by the different partners in the sector according to the national tuberculosis control plan;
- ensuring, through training and supervision, that the technical recommendations of the NTP are correctly applied in the participating health facilities and encouraging operational research to help find solutions to local challenges;
- co-ordinating with the central government department responsible for laboratories to ensure that the network of laboratories is properly defined and supervised, that quality control activities are carried out correctly and that training is appropriate;
- communicating with the National Tuberculosis Reference Laboratory on quality assurance of smear microscopy and surveillance and diagnosis of multidrug resistance;
- ensuring, in collaboration with the logistics and supply system in the central government department responsible for health, the timely and adequate procurement, proper storage and regular delivery of diagnostic and treatment supplies throughout the country, assuring adequate quantities, including a buffer stock based on reports of case-finding results;
- reviewing and ensuring the quality of the reports of tuberculosis activities submitted from the intermediate level;
- regularly supervising and supporting the Provincial/Regional Coordinators;
- ensuring that all the institutions that deal with patients but that are not related directly to the central government department responsible for health (teaching hospitals, city hospitals, government departments responsible for other health institutions, private care providers) are included in the NTP as soon as they agree to follow NTP guidelines, and that they receive training, supervision and supplies, and provide reports;
- collaborating with the National AIDS Programme to ensure that:

i) patients who are affected by both tuberculosis and HIV are properly cared for and that exposure of HIV-infected individuals to tuberculosis micro-organisms is avoided;
ii) HIV-infected patients are evaluated for signs of tuberculosis at every contact during care of opportunistic infections and/or antiretroviral treatment and if a person is suspected of having tuberculosis, she/he is referred to the nearest BMU or receives care at the most appropriate facility for diagnosis and treatment of tuberculosis;

- ensuring diagnosis and treatment of patients with multidrug-resistant tuberculosis, which is usually centralised to one specialised national unit that manages all such treatment;
- informing all central government authorities of the activities, importance and resource needs of the NTP.

5.2.3. Is there a need for external evaluation?

Periodic external evaluation by recognised experts in tuberculosis control should be undertaken in all countries for review of technical aspects of the programme and their implementation. Such reviews provide an independent assessment of the programme and give support to programme personnel in their attempts to gain a hearing from decision makers in order to make necessary changes.

5.3. How is the laboratory service organised?

A well-functioning laboratory is the first requirement for successful management of tuberculosis. If the diagnosis is not made reliably and if follow-up of treatment is not trustworthy, all other activities will be affected.

5.3.1. What is the basis of the laboratory examination?

Sputum smear examination is essential for every person with prolonged respiratory symptoms and for the follow-up of tuberculosis patients. Because of this, it is necessary to have laboratory services that reach the entire population. Such laboratory services should be provided within the context of the already existing health service structure, and the duties of sputum smear examination should be included among the other duties

of the laboratory personnel already present within the health service. There is no need for specialised personnel to perform sputum smear microscopy within the general health service. Because tuberculosis contributes to such an extent to the health problems of most countries, every general laboratory technician within the health service should have the skills to perform this diagnostic procedure.

The recommended method for routine confirmation of a diagnosis of tuberculosis is the microscopic examination of smears of sputum specimens stained using the Ziehl-Neelsen or fluorescence microscopy method. For this purpose, a good-quality binocular microscope with an electrical light source (or a mirror where electricity is unavailable) is essential. The microscope must be equipped with the appropriate objectives (a 100× oil immersion objective for the Ziehl-Neelsen technique, or a 20× plus a 40–50× dry no-coverslip objective for the fluorescence technique), and it should have a movable stage.*

5.3.2. What are the tasks of the laboratory service?

The tasks of the laboratory service with respect to tuberculosis are:

- to confirm tuberculosis diagnosis (including the correct classification of cases);
- to monitor the treatment of sputum smear-positive cases;
- to carry out surveillance of resistance to antituberculosis drugs;
- to ensure the diagnosis of cases with multidrug-resistant tuberculosis through a case-finding strategy that is tailored to the situation in the country;
- to provide rapid HIV testing according to National AIDS Programme guidelines in areas of high HIV prevalence.

The network of microscopy centres

The diagnosis of tuberculosis must be made as close as possible to the home of each patient, while maintaining the high quality of the testing procedures. To accomplish the first two of the above tasks, a network of laboratory centres carrying out sputum smear microscopy at an adequate technical level must be maintained.

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*The technical aspects of sputum smear examination are provided in the Union's *Technical Guide for Sputum Examination for Tuberculosis by Direct Microscopy*[8] and *Priorities for Tuberculosis Bacteriology Services in Low-Income Countries*.[9]

The laboratory technicians in the general health services must be competent to carry out sputum smear microscopy; this requires that they be trained, motivated and properly supervised.

It is important to plan services in such a way that they are accessible to the population and yet maintain an adequate level of quality. To accomplish this, it is generally recommended that one microscopy centre should be developed for at least each unit of the population containing between 50,000 and 150,000 inhabitants (i.e., corresponding to a BMU), according to the incidence of tuberculosis and the geographic distribution of the population. Plans to extend the network far into the peripheral level must take into account the requirements in human resources in order to assure the technical quality of the examinations.

Assuring the quality of smear microscopy

Quality assurance of laboratory examinations is essential if the tests are to be meaningful and useful in the care of the patient. In the case of sputum smear microscopy for AFB, good quality assurance often has a large impact on its sensitivity, sometimes even doubling the number of cases detected. Substantially improving specificity is more difficult, as false positives are relatively infrequent. Quality assurance must consist of internal and/or external checks, followed by corrective actions as required. If internal quality control were done perfectly, quality would be assured sufficiently. However, as this is still the exception rather than the rule, external quality assessments are needed. Correct and efficient quality assessment of smear microscopy is a demanding task. It requires very good organisation, the ability to follow precise guidelines, and also a considerable investment in human resources, depending on the method chosen.

Detailed information on establishing and carrying out these activities is included in the Union publication *Priorities for Tuberculosis Bacteriology Services in Low-Income Countries*.[9]

Culture and susceptibility testing

Sputum smear microscopy must have the highest priority in the care of tuberculosis patients. More sophisticated tests (such as culture, susceptibility testing, molecular technology) should not be undertaken outside the National Tuberculosis Reference Laboratory until an adequate network of laboratories for smear microscopy has been developed that serves the whole community and which has a good system of quality assurance. In many countries it is not possible to provide the entire population with

a diagnostic service that is based upon culture and susceptibility testing. The role of culture and susceptibility testing is primarily to conduct surveillance of drug resistance and to confirm multidrug resistance in individual cases for treatment purposes.

The determination and surveillance of antituberculosis drug resistance is useful as a means of monitoring the adequacy of a tuberculosis programme. The development and/or promotion of clinically important resistance of micro-organisms to drugs can always be traced to a source that is a man-made problem, and is frequently a reflection of individual or programmatic malpractice (the prescription or provision of inappropriate or inadequate treatment regimens and/or treatment without direct observation, resulting in potential monotherapy). When increasing levels of drug resistance are detected using a system of surveillance, prompt action must be taken to try and prevent further occurrence. The development of resistance to drugs (and particularly to isoniazid and rifampicin) severely compromises the ability and substantially increases the cost for the health services to cure the individual patient and to bring the tuberculosis problem under control.

Detailed information on establishing and carrying out these activities is included in the Union publication *Priorities for Tuberculosis Bacteriology Services in Low-Income Countries*.[9]

5.4. How do we monitor care?

The adequate care of tuberculosis cases requires that records be kept on each individual patient, with periodic reporting of the results of case finding and of treatment. This is essential in order to ensure that the patient is correctly treated and that adequate supplies of essential materials are provided. In addition, the information that is routinely collected and reviewed allows the identification of problems that may arise with the management of the patients and of the system. The documents used to record and report the care of the patients should be simple, clear and kept to the absolute minimum that is required for adequate care. The following description provides a guide for the recording of patients as they appear to the health facility and comprises the minimum number of records and reports necessary to ensure the proper care of the patients.

5.4.1. What records are necessary?

Records of diagnostic examinations

All individuals who present themselves to the general health service and are suspected of having tuberculosis are required to have a sputum smear

examination. The initial sputum sample is requested during the first consultation with the health care worker, at which time the *Request and Reporting Form for Sputum Smear Examination* (Appendix, Form 1) is completed. When the sputum sample is received in the laboratory, the information on the individual patient is entered in the *Tuberculosis Laboratory Register* (Appendix, Form 2). As indicated in this sample form, each patient examined for diagnosis will have at least two sputum examinations, the results of which are entered on a single line in the laboratory register.

In the *Request and Reporting Form for Sputum Examination*, the result of each sputum smear examination is entered in the appropriate box for the first or second specimen in the column entitled "Result". Sputum smear results should be recorded as follows: "neg" for negative, "1 to 9" AFB (the exact number of AFB per 100 fields for *scanty* positive), "1+" for 10–99 AFB per 100 fields, "2+" for 1–10 AFB per field on at least 50 fields, or "3+" for ⩾10 AFB per field on at least 20 fields.

These results should be recorded in the *Tuberculosis Laboratory Register* in the same way, in the column entitled "Results of specimen". All positive results should be entered into the register in red ink for ease of identification. The reason for the examination should also be filled in by entering a tick in the "Diagnosis" column or filling in the month of treatment under "Month of follow-up".

In settings where HIV is frequent, BMUs may perform rapid HIV tests. The appropriate forms designed by the National AIDS Programme and supplied to the BMUs through agreed mechanisms should be used.

Records of cases of tuberculosis

If the patient is designated a tuberculosis case, a *Patient Identity Card* will be issued, completed by a health care worker and kept by the patient (Appendix, Form 4). This card contains the name, address, sex and age of the patient. It identifies the tuberculosis register number and the name of the BMU. The type of tuberculosis (disease site) as well as the date and results of bacteriological examination at the time of diagnosis, the date the treatment was commenced and the regimen prescribed are recorded. Spaces are provided for the dates of follow-up appointments and the results of follow-up sputum examinations. The *Patient Identity Card* is a confidential document, as it contains medical information. Patients, and particularly illiterate patients, should be informed of this and instructed to present the card only to other health care workers, as they may need to know the patient's condition before other treatments are prescribed.

At the same time, a *Tuberculosis Treatment Card* (Appendix, Form 3) is completed. This card is kept at the health service where the patient receives treatment. When a sputum examination result is received by the laboratory, the result should be recorded immediately on the *Tuberculosis Treatment Card*. The card should also include information about tobacco use by the tuberculosis patient to facilitate tobacco cessation intervention.*

In high HIV prevalence areas, information on HIV testing, results of HIV testing, cotrimoxazole preventive therapy and antiretroviral treatment should be included in the *Tuberculosis Treatment Card* and the *Tuberculosis Register.*

At the end of each working day, the responsible health care worker must collect all the tuberculosis treatment cards of the patients that have been seen during the day and transcribe the relevant information into the BMU *Tuberculosis Register* (Appendix, Form 5) in the unit where the patient is managed—particularly the results of follow-up smear examinations.

Once each week, the personnel responsible for the treatment of patients must meet with those responsible for carrying out sputum smear microscopy in the laboratory, to ensure that all patients recorded in the *Tuberculosis Laboratory Register* as sputum smear-positive have been enrolled on treatment (or referred to another BMU for initiation of treatment). Those found positive in the laboratory and for whom no record has been made in any other register should be entered into the register, traced, started on treatment and evaluated with all other patients.

Often the BMU will include several health units where tuberculosis patients receive tuberculosis treatment. If these units have a considerable number of cases, it may be practical to have a Unit Tuberculosis Register to facilitate supervision. The Tuberculosis Coordinator will copy the information from the Unit Tuberculosis Register into the BMU *Tuberculosis Register.*

In completing the *Tuberculosis Register*, great care should be taken to ensure that the information is correctly recorded and regularly updated. When a patient is newly detected, precise information should be entered. Patients should be recorded in numerical order by the date when they become known to the health care worker responsible for tuberculosis activities in the BMU and responsible for the *Tuberculosis Register.* Numbering

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*For information on tobacco cessation intervention, please refer to the Union Guide *Tobacco Cessation Interventions for Tuberculosis Patients*.[10]

Big cities and large referral institutions

In some big cities, large hospitals diagnose a substantial number of tuberculosis patients, but do not treat them or do not follow them to ensure they complete treatment (that is, they are not functioning as a BMU). After discussion and agreement with the health care workers of those institutions, these patients should all be referred to more convenient BMUs where they will be registered and continue their treatment. Such hospitals, if they do not function as a BMU, will not send quarterly reports to the NTP, and the patients will be reported from the BMU where they were initially registered. Care must be taken to ensure that all such patients are truly registered in the referral BMU, even those who have died at the hospital before being referred to the BMU. In these hospitals, a focal tuberculosis person should be identified to centralise information and management of tuberculosis drugs; a referral register may be used to facilitate the documentation and follow-up of all patients who are referred to other facilities.*

A similar problem is often encountered in centres that were historically dedicated to the care of tuberculosis patients and that attract substantial numbers of patients who come from long distances and who are not able to receive their treatment in the centre where the diagnosis was made. After discussions, these patients should be referred to a more convenient BMU where they will be registered and reported; the name of the BMU to which the patient is referred should be written in the column "TB number or referral BMU" of the *Tuberculosis Laboratory Register* (Appendix, Form 2) in the centre where the diagnosis has been made.

The decision about where to decentralise treatment to should be based on the following practical considerations. The first is to decide on the distance that the patient would have to travel to receive care. A second consideration is to determine the maximum number of patients who should routinely be provided with care in a given location (for example, depending on the situation, not more than 100 or 200 patients per year). Very often, services are overloaded with up to ten times this number of patients and cannot maintain a high quality of care. Those entrusted with organising health services need to take workload into consideration when it comes to thinking about providing basic services at the highest possible quality. These guidelines must be drawn up taking the local situation into account and in discussion with patients, communities and health service planners.

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*This reference register could include the following columns: Date / Name / Sex / Age / New patient or already registered / Type of tuberculosis / Hospital admission / Patient contact / Date of discharge from hospital / Name of the BMU referred to / Date of arrival in this BMU / Remarks, including death if during hospitalisation.

commences with number 1 (one) at the beginning of each calendar year, regardless of when the patient was diagnosed or commenced treatment. Drawing a line after the last patient registered in a given quarter or starting registration for a new quarter on a new page of the register facilitates the counting of patients at reporting time.

All tuberculosis patients detected and/or enrolled on treatment at the BMU should be registered in the *Tuberculosis Register.* This includes those patients who may have died or defaulted prior to starting treatment or who had been hospitalised prior to being referred to the BMU. Patients enrolled on treatment and registered at another BMU, then transferred to this BMU to continue treatment should be recorded in the *Tuberculosis Register* as *transfer in*.

It is important to ensure that each patient is correctly recorded and treated. This includes identification of the correct "disease site":

- *pulmonary* cases are those with tuberculosis of the lungs, including those who are sputum smear-positive and those who are sputum smear-negative, in the latter case provided a minimum of two sputum examinations have been performed;
- *extra-pulmonary* cases are all other patients, including those with pleural and miliary tuberculosis (the specific site should be recorded).

The correct "type of case" (defined as "category" in WHO tuberculosis treatment guidelines) necessary to determine the proper treatment is one of the following:

- a *new* case is one who has never been treated previously for as much as one month;
- a *relapse* case is one who, having previously been treated, was declared cured or treatment completed prior to becoming sputum smear-positive;
- *treatment after failure* is a patient who, while on treatment, is smear-positive at 5 months or later during the course of treatment, and who starts retreatment;
- a patient is recorded as *treatment after default* who had been on treatment for one month or longer and who returned to the health service sputum smear-positive after having interrupted treatment for 2 or more months and who starts retreatment;
- a patient is recorded as *transfer in* when the patient was originally registered as a case in another Tuberculosis Register but transferred

to the current facility to continue care; this patient retains his/her previous registration number from the previous BMU, and is not given a new registration number from the new BMU;
- all other patients are entered under the column *other*. This section includes chronic patients, smear-negative or extra-pulmonary cases who have been treated previously. Chronic cases are those patients who could not be cured by the most powerful regimen used in a given programme (retreatment or treatment for multidrug-resistant tuberculosis).

For all patients with smear-positive pulmonary tuberculosis, it is extremely important to determine correctly whether or not they have previously been treated for as much as one month. The incorrect designation of such patients will result in incorrect treatment of the patient. The correct assignment of previously treated patients to one of the three groups *relapse, treatment after failure* and *treatment after default* allows precision in evaluation. Patients who are registered as relapses, failures and treatment after default are given a new registration number.

The most strongly positive result should be recorded in the appropriate box in the column entitled "Results of smear examination" in the *Tuberculosis Register*. The result should be recorded exactly as recommended for the tuberculosis laboratory. All positive sputum results should be entered into the register in red ink for ease of identification. The laboratory serial number and the date the examination was performed should be entered into the column next to the result of the examination.

Treatment outcome

The result of treatment of each individual patient should be recorded as soon as it becomes available, as follows:

- *cured* indicates a sputum smear-positive patient who was smear-negative at the last month of treatment and on at least one previous occasion;
- *treatment completed* indicates a patient who completed treatment but for whom smear examination results are not complete enough to classify the patient as cured. (This outcome includes patients for whom the final smear examination was not done);
- *failure* designates any new patient who is smear-positive (and confirmed by a second specimen) at 5 months or later during treatment;
- *died* is recorded for a patient who died for any reason after diagnosis and before the end of their treatment;

- *defaulted* is recorded for any patient who has failed to collect drugs for more than 2 consecutive months after the date of the last attendance during the course of treatment. Those who are still on treatment at the time of the evaluation of treatment results (12 months after the close of the quarter in which the patient was entered into the tuberculosis register) should also be recorded as defaulted;
- *transfer out* indicates any patient who was transferred to another BMU to continue treatment and for whom treatment results are unknown.

The first of these events to occur is recorded as the outcome of the treatment.

In settings where HIV is frequent, it is recommended to systematically collect information on HIV, as indicated in the *Tuberculosis Register* (Form 5).

5.4.2. How are the results reported?

Reporting the results of case finding and of treatment outcome every 3 months (quarterly) permits tuberculosis activities to be evaluated and allows the early identification of problems in the health services providing care to the patients. While more frequent reports may be required for certain other conditions, reports on activities related to tuberculosis are not necessary at intervals of less than every 3 months; the reports are used primarily for assessing the performance of tuberculosis control services and calculating supply requirements (and secondarily for planning future activities). All quarterly reports are prepared from the *Tuberculosis Register* and the *Tuberculosis Laboratory Register*: they are only as accurate as the information recorded in these registers. The quarterly reports should be prepared the second week following the end of each quarter (the second week of April, July, October and January) for the quarter being evaluated. These reports should be submitted to the authorities (in this case, the Provincial/Regional Tuberculosis Coordinator) no later than the end of the month in which they were completed (end of April, July, October and January). Once they have been verified for accuracy and coherence, and validated by the appropriate supervisory level, they should be forwarded to the central level, where they are compiled and tabulated, no later than the end of the quarter in which they are prepared.

Quarterly Report on Tuberculosis Case Finding (Appendix, Form 6)

This report is completed systematically by counting the number of cases recorded in the *Tuberculosis Register* during the quarter that has just ended. Any case classified as "Transfer in" is not reported, but any case classified as "Other" should be reported. A patient is classified as having sputum smear-positive tuberculosis if any microscopic examination of sputum shows AFB. Any patient may be treated for tuberculosis (depending on the assessment of a Medical Officer), but only those who have negative sputum smear examinations are classified as sputum smear-negative cases.

The order in which the cases are counted is noted in Table 5.1.

The HIV block is then filled out, distinguishing two groups of patients: new sputum smear-positive and all tuberculosis patients (including the new sputum smear-positive cases). The number of patients for whom an HIV test result is available (either after or before the diagnosis of tuberculosis) is entered, as well as the number of positive tests. This information is collected in a cohort manner for the quarter that has just ended. Patients registered in previous quarters and tested in the quarter are not included.

The next step in preparing the *Quarterly Report on Tuberculosis Case Finding* is to determine the number of new cases of smear-positive pulmonary

Table 5.1 Preparing the *Quarterly Report on Tuberculosis Case Finding*: counting the cases in each quarter

Disease site	*Pre-treatment sputum smear result*	*Category of case*
1. Pulmonary	Positive	New
2. Pulmonary	Positive	Relapse
3. Pulmonary	Positive	Treatment after failure
4. Pulmonary	Positive	Treatment after default
5. Pulmonary	Neg/ND	New <5 years of age
6. Pulmonary	Neg/ND	New 5–14 years of age
7. Pulmonary	Neg/ND	New ⩾15 years of age
8. Extra-pulmonary	Neg/ND	New
9. Pulmonary	Neg/ND	Other (pulmonary cases entering in none of the above categories)

ND = not done.

Table 5.2 Determining the distribution of new smear-positive cases by age group and sex

Males	*Age group*	*Females*
2	0–4	3
1	5–14	1
3	15–24	2
7	25–34	7
5	35–44	4
3	45–54	2
3	55–64	1
4	65+	1
28	Total	21

tuberculosis by age category and sex. This can be done using the method illustrated in Table 5.2. Using this method, identify cases whose pre-treatment smear result is recorded as positive and then look across to be sure that the patient is recorded as "new" under the heading "Category of case". If the patient is smear-positive and "new", determine the age and sex. Then record the case record on a separate sheet of paper using the method outlined in Table 5.2. For example, for a woman aged 33 years, you would add a "|" to the right side of the age group 25–34; a man aged 51, add a "|" to the left of the age group 45–54. The sum of the cases should tally with the number of new smear-positive cases found after adding the counts of the lines in Table 5.1.

A copy of the *Quarterly Report on Tuberculosis Case Finding* should be carefully kept on file at the centre, because it will be used 12 months later for reporting on the results of treatment.

Quarterly Report on the Results of Tuberculosis Treatment (Appendix, Form 7)

At the same time as the report on case finding is completed (the second week of January, April, July and October), a *Quarterly Report on the Results of Tuberculosis Treatment* (Appendix, Form 7) should also be completed. The quarter for which the report should be prepared is the same quarter as the report on case finding, but 12 months earlier. The treatment result for every case should have been recorded by this point in time. For example, in the second week of the third quarter, the form should be completed for the results of treatment for patients registered in the second quarter of the previous year. It is completed separately for three types of cases: new sputum smear-positive cases, retreatment sputum smear-positive cases, and all the other forms together that were notified in the *Quarterly Report on Tuberculosis Case Finding* (Form 6) (smear-negative or smear not done pulmonary cases, extra-pulmonary, other). Those cases recorded as *transfer in* must *not* be included in the report, as the treatment results of such cases should be sent to the unit from which the patient was transferred and reported in that unit.

When preparing the *Quarterly Report on the Results of Tuberculosis Treatment*, the BMU should consult its own filed copy of the *Quarterly Report on Tuberculosis Case Finding* for the same quarter. From this case-finding report, take the number of cases to be reported and enter it in the first column of the *Quarterly Report on the Results of Tuberculosis Treatment* (indicated by the asterisk). The total number of cases evaluated within each category (according to the type of case) should tally with the number entered in this section. The number of cases evaluated and reported for outcome should again tally with the numbers reported in the *Quarterly Report on Tuberculosis Case Finding* for the same quarter (previously completed). Where the number is different, an explanation must be provided.

To complete the report on treatment results, information needs to be obtained from the *Tuberculosis Register* under the section entitled "Results of treatment". Where more than one result occurs in a single patient, the result that will be recorded is the event that occurs first, i.e., if an individual remained smear-positive at 5 months but subsequently died (or defaulted or was transferred out), that patient must be evaluated as smear-positive (failure). If no treatment result is recorded in the register at the time the report is prepared, the patient must be evaluated as having defaulted. When a patient has been transferred to another unit to continue treatment, the outcome of the treatment at the unit to which the patient was transferred should be obtained and entered into the register. Those patients evaluated as *transfer out* should be those for whom the outcome of treatment remains unknown.

Another part of the *Quarterly Report on the Results of Tuberculosis Treatment* concerns tuberculosis patients with HIV infection. The number of HIV-positive tuberculosis patients during this quarter is reported (this number is not always the same as in the *Quarterly Report on Tuberculosis Case Finding* because some patients have tested positive after the form has been completed). These HIV-positive tuberculosis patients will be classified according to their count (CD4 cells/μl) as: "<200" or "200–350" or ">350" or "Unknown". The "Number of tuberculosis patients given cotrimoxazole" in this cohort of patients should be reported, as well as the "Number of tuberculosis patients given antiretroviral treatment", irrespective of when they began the cotrimoxazole prophylaxis or the antiretroviral treatment.

When completed, the report must be forwarded to the next level of the health service (and eventually to the central level), as noted above, and a copy should again be carefully kept on file for future reference.

For multidrug-resistant tuberculosis, special treatment cards, registers and quarterly reports of case finding and treatment results are described in the WHO guidelines (2008).[4] A patient who is diagnosed with multidrug-resistant tuberculosis while on first-line treatment or retreatment and who is started on a treatment regimen with second-line drugs should have the treatment outcome category *failure*, with the comment "changed to MDR-TB treatment".

5.5. What supplies are needed and how are they managed?

In order to have the best success in the management of tuberculosis patients, it is necessary to ensure that supplies are continuously available. This is even more important for tuberculosis patients than might be the case with some other types of illnesses. The NTP is responsible at all times for the regular supply and sufficient stocks of drugs and other supplies for all its participating facilities. The types of supplies that are necessary to adequately manage cases of tuberculosis are:

- laboratory supplies, including sputum containers, slides and reagents for making the sputum smears;
- antituberculosis drugs; and
- programme forms and stationery required for patient management and preparation of records and reports.

5.5.1. How are supplies managed?

Because successful treatment depends on patients taking their prescribed drugs regularly and without interruption for a long period of time, an uninterrupted supply of drugs is essential. Moreover, the uninterrupted availability of single-use injection material helps prevent the transmission of HIV and hepatitis viruses. Only a strict system of supply management, following clear procedures for ordering appropriate amounts and keeping accurate stock records, can prevent disruptions in the supply chain and ensure that all necessary supplies are always in stock in the required quantities. A supply management system also permits proper accounting of supplies and materials, as consumption can be compared with requirements, which are estimated by reports of case finding.

How are drugs ordered?

The ordering described here is for the BMU serving a population of 50,000–150,000. At this level it is most convenient to order supplies once every

quarter and to allow for an additional "reserve" stock in case of irregularity of supply.

Ordering and maintenance of treatment supplies is determined from the results of case finding, which are recorded in the *Quarterly Report on Tuberculosis Case Finding*. Ordering of these supplies is done at the same time as case finding is reported (in the second week after the end of the quarter, i.e., the second week of April, July, October and January). Treatment supplies are ordered using the *Quarterly Order Form for Treatment Supplies* (Appendix, Form 8). The quantity of materials required for the treatment of patients each quarter is determined as follows:

- The number of patients to be treated is determined from the *Quarterly Report on Tuberculosis Case Finding* that has just been completed for the preceding quarter.
- The number of patients is entered under the column headed "Cases". The sum of the new cases (smear-positive, smear-negative and extra-pulmonary cases) is in the first column (2{RHZE}/4{RH}), and the sum of the first-line retreatment cases (relapse, treatment after failure, treatment after default – 2S{RHZE}/6{RH}) in the second column.
- The quantity of each type of drug that is required in a quarter is determined by multiplying the number of cases by a "factor"—this factor is the average number of tablets to be taken by a patient during the entire course of treatment—and taking the sum of all the numbers in the two columns (A + B).
- The reserve stock, i.e., drugs required as a buffer in case of an increase in the number of suspects or patients or due to a delay in receiving a delivery of drugs, is equal to the amount required for the specified interval, usually a quarter; this figure (C) is entered into the second section of the form, under D and under E.
- The quantity of drugs in the store (pharmacy) at the end of the quarter must be counted and entered under (F). Drugs that are beyond their expiry date should not be counted.
- The total quantity to be ordered is calculated by adding the quantity of drugs required for the patients registered during the quarter (D) and the quantity of the reserve stock needed (E), then subtracting the quantity of drugs in the store (F), i.e., D + E − F.

In case of severe adverse drug reactions, it is important to ensure that single antituberculosis drugs are also available. They should be reserved

for some main hospitals and can be ordered on the same order form under "Other".

How is an uninterrupted supply maintained?

In many countries, the transfer of information (post and telecommunications) is difficult and transportation of goods is unreliable, so delays can occur. As a result, supplies may not always reach health facilities in time if they are located a long distance from the store where the supplies are kept. It is very important to make allowances for the problems of communication and transportation. This is accomplished by placing orders at regular intervals in time (usually every quarter), and by calculating, with every order, a "reserve" stock of supplies at all levels where stocks are kept. In this way, every patient can be assured of receiving all the drugs necessary to be cured of tuberculosis.

Reserve stocks are necessary at the levels where a coordinator is placed. The quantity of reserve stock to be ordered at intermediate and peripheral levels should be equivalent to the requirements of the period between deliveries, usually one quarter, to avoid stock-outs and overstock. It is determined on the same *Quarterly Order Form for Treatment Supplies* (E).

Maintaining a reserve stock in this manner ensures that all patients receive regular treatment. As is apparent, the numbers of cases requiring different forms of treatment that have been determined from the *Quarterly Report on Tuberculosis Case Finding* are not exact figures. The numbers of patients transferred into and out of the BMU while on treatment and the number of patients who die or default also influence the requirements. However, the reserve stock ensures that sufficient drugs will be available for the coming period, and the correction for the differences noted will automatically occur when the next order for drugs is completed in the following quarter.

The quantity of drugs dispensed should be compared with the number of patients reported, to determine if they tally. The process to achieve this is the opposite of the one used to calculate drug requirements on the *Quarterly Order Form for Treatment Supplies*. The quantity of each drug used in the quarter should be divided by the corresponding "factor" on the form. For each drug, the corresponding number of patients that could have been treated is thus calculated and these numbers are compared to ensure first that dispensing is coherent between drugs; second, these numbers are compared with the number of patients who have actually received drugs according to the register. Major differences may indicate loss of drugs. This is an effective way to increase awareness and prevent losses of drugs, especially rifampicin.

How are stocks of treatment supplies maintained?

Misuse of tuberculosis drugs is prevented by using fixed-dose drug combinations. It is also controlled by having correct storage conditions at all levels in the system. Stocks of tuberculosis drugs should be kept in secure, dry, adequately ventilated places. Drug management requires strict controls. Stocks specifically provided for the treatment of tuberculosis should be clearly identified as such, whenever the same drugs are used by several different programmes (e.g., streptomycin, which is used to treat tuberculosis and plague).

Expired drugs may be less effective and their use may contribute to the development of drug resistance by tuberculosis micro-organisms. Managing drug stocks properly at all levels in the system will ensure that expired drugs are not delivered to patients.

At all levels in the system, stocks of tuberculosis drugs should be kept according to the date of expiry of each batch of each individual drug. Drugs that expire first should always come out of the stock first.

For each individual drug and for each batch expiring at a certain date, a stock card should be maintained. All drugs received (in) and delivered (out) should be recorded, and the balance on the card should always tally with the physical stock.

Expired drugs should not be disposed of at peripheral level but should instead be returned to the Central Store, where they should be physically destroyed, for example by incineration. Return of expired drugs to the Central Store should be recorded on stock cards.

Sufficient stocks of single-use injection materials (syringes, needles and water for injection) should always be maintained so that streptomycin and other injectables can be delivered to patients safely.

5.5.2. How are laboratory supplies managed?

The quantities of materials required for the laboratory are small. For this reason, materials can be supplied every half year (every other quarter) rather than every quarter. The reserve requirement is always best estimated as being the equivalent of one quarter of the supplies.

The most accurate method to calculate the needs for sputum smear microscopy supplies is based on a reported number of smears examined plus the amount of supplies left in stock. The calculations are made by the supplying authority, counting for each smear: 3 to 5 ml of the various staining solutions, 1 slide and 1 sputum container, 0.1 ml immersion oil

(for Ziehl-Neelsen microscopy, not for fluorescence) and 1 ml burning spirit, etc. After adding the reserve allowed and subtracting the balance in stock, the calculated requirements are rounded to the nearest packing unit. This calculation is easy, provided the *Quarterly Report for Peripheral Sputum Smear Laboratory Performance and Stock Situation* (Appendix, Form 9) is used properly. It should be customised by each programme, mentioning on the form the exact names of the staining and destaining solutions, and adding other items as needed.

The form is completed as follows:

1) Patients

- the number of patients with a positive smear result whose "reason for examination" in the laboratory register is "diagnosis" is entered as well as the total number of patients who are examined for "diagnosis" (suspects)
- the number of patients with a positive smear result whose "reason for examination" in the laboratory register is "follow-up" is entered as well as the total number of patients who undergo a follow-up examination

2) Smears

- the number of AFB smears is entered by type (diagnosis or follow-up) and result; the type of staining—Ziehl-Neelsen or fluorescence—should also be indicated.

3) Stocks on hand

- the amount of materials currently in stock (estimated, does not have to be exact measurements); note that the requested amounts do not have to be filled in, as the calculation remains the responsibility of the supplying level, using a computer spreadsheet if available. However, a regular physical estimate and reporting of the balance in stock is essential and is the responsibility of each laboratory.

In the absence of a report on smears examined, the basis for calculating the needs is the number of reported sputum smear-positive patients detected at the BMU's laboratory, as a proxy for the number of smears performed. Because many tuberculosis suspects must be examined to find one patient with sputum smear-positive tuberculosis, the proportion of positive smears among the diagnostic smears examined must then be taken into account. This proportion can vary greatly, from less than 5% to over

30%. Thus, if 10% are smear-positive cases, then 10 suspects need to be examined for each smear-positive case. As each suspect should also have two (or three, depending on the collection strategy used) sputum examinations, and each case should have three additional examinations during follow-up, the number of slides that need to be examined for each smear-positive case is $(1 \times 10 \times 2) + 3 = 23$, where the proportion of smear-positive cases among suspects is 10%. Where it is 20%, i.e., where only five suspects need to be examined to detect one case but three sputum samples are required for screening, the calculation is $(1 \times 5 \times 3) + 3 = 18$.

5.5.3. What other supplies are needed?

To maintain the quality of care of patients, other materials are also required. In particular, a regular supply of forms, registers and other recording materials is needed to ensure that patients are correctly managed. Determination of the volume of materials required is based on the regular reports on the results of case finding. A list of items required should be prepared and a stock kept at the unit.

6
Protecting the community

6.1. What is the rationale for a tuberculosis programme?

Tuberculosis is one of the frequent fatal infectious diseases for which effective interventions exist. The burden of tuberculosis is heavy for tuberculosis patients and their families. At the community level, tuberculosis often affects the poor, contributes to their increased vulnerability and slows down or even prevents their socio-economic progress.

Poor treatment of tuberculosis patients can make the tuberculosis situation even worse. This is due to the fact that, while it is relatively easy to prevent death due to tuberculosis, it is more difficult to cure a patient permanently and thus to prevent the patient from spreading micro-organisms to uninfected members of the community.

Public health services aim to reduce the number of new cases of tuberculosis appearing each year to the point where the disease will no longer be a serious public health problem in a country. The aims of public health differ from those of clinical medicine in that efforts are focused on communities instead of individuals. Public health also implies the obligation to obtain and document results: patients must be cured. Public health is an organised and combined effort undertaken by teams of health care workers to detect all sources of infection, to put these patients on effective treatment and to follow them until they are cured. In this effort, various aspects of public health are equally important; these aspects include:

- diagnosis and care of patients;
- provision of necessary laboratory services;
- supply management;
- recording and reporting; and
- coordination of disease control activities and tasks.

Control of communicable diseases is an essential dimension of primary health care. The public health aims of tuberculosis services cannot be achieved by any single person alone. It requires a team effort and a partnership with patients.

6.1.1. Why is it possible to control tuberculosis?

Tuberculosis *can* be controlled worldwide. The reasons why this is possible are:

- the most powerful *source* of the infection is a person who is sick with the disease and who can thus be relatively easily identified;
- the rate of *spread of micro-organisms* can be quickly reduced if the infectious cases are identified and effectively treated as quickly as possible;
- the *transmission of micro-organisms* is relatively inefficient, so that any reduction in the number of sources of infection and the period of time each is infectious will inevitably improve the epidemiological situation;
- the basic *tools* required to carry out the tasks (sputum smear microscopy and drug treatment) exist, are simple and can be applied efficiently even in difficult socio-economic conditions.

How does HIV affect the situation?

The introduction of HIV infection into the community has upset the balance between tuberculosis micro-organisms and the human host by compromising the immune defence mechanisms which, under normal circumstances, almost always hinder the transition from tuberculous infection to tuberculosis in the individual. As a result, HIV-infected individuals, once they acquire *Mycobacterium tuberculosis*, are much more likely to develop tuberculosis within weeks or months of infection and to become infectious themselves. The number of infectious cases in the community increases considerably, thereby increasing the risk of exposure to as yet uninfected members of the community. Where individuals infected with HIV gather together (often in health care facilities), exposure to infectious tuberculosis cases is more likely.

However, the introduction of HIV into the community does not alter the following points:

- *identification of infectious cases* is unchanged, as sputum smear microscopy remains the most efficient means of determining the infectious potential of individuals;
- *cure of infectious cases* is possible in the presence of HIV infection, as the treatment regimens remain as powerful, regardless of the presence of HIV;
- the *basis of tuberculosis services* (case finding and treatment) is therefore unchanged.

Nevertheless, the *urgency* of widespread delivery of tuberculosis services cannot be overemphasised, as without these measures the transmission of tuberculosis micro-organisms will increase rapidly.

Indeed, the introduction of HIV into the community is a definite challenge to the public health aims of tuberculosis services in settings where both diseases are frequent. Tuberculosis cannot be conquered if HIV transmission is not prevented. HIV may pose a threat to the efficiency and quality of a tuberculosis programme through co-infected patients who are not treated with antiretroviral drugs and through undiagnosed tuberculosis among HIV-infected individuals. The tuberculosis programme may become overwhelmed with tuberculosis cases (new, retreatment and multidrug-resistant), as a result of HIV co-infection, even in the presence of a well-functioning antiretroviral treatment programme with satisfactory coverage. It is imperative that this fact be recognised and that NTPs and National AIDS Programmes collaborate closely with other relevant departments in the ministries of health, such as human resources planning, training and financial planning and management.

How does drug resistance affect the situation?

An important objective of the management of tuberculosis is to avoid making things worse than they already are. Inadequate management of tuberculosis patients is the most frequent cause of drug resistance. Inadequate management is, if possible, even more hazardous in settings where HIV is frequent, as it leads to drug-resistant tuberculosis cases in persons with diminished immune defence mechanisms, which is a recipe for disaster for individuals, their families, communities and the NTP. If tuberculosis patients are managed as recommended in this Guide, the chance of development of drug-resistant tuberculosis will be much lower and the spread of existing drug resistance will be reduced. If there is already widespread multidrug resistance, the outcome of treatment of patients will be affected in direct relation to the extent of the problem.

A poorly organised or managed NTP is a frequent cause of drug resistance and often reflects misdirected priorities for the programme. Where the emphasis and resources are directed primarily to specialised services for chronic resistant cases, a frequent occurrence where these cases are numerous, the problem is compounded. This is because new drug-resistant cases are created faster than they can be cured. Simply treating the unfortunate cases of multidrug-resistant tuberculosis, without addressing the reason why they occurred in the first place (correcting poor case management),

will never succeed in overcoming the problem. The first priority for allocation of resources must *always* be the proper case management of those cases known to be curable, thus diminishing the creation of new resistant cases. In settings where the level of multidrug resistance is already high, however, prevention must be combined with adequate treatment of such cases. Such cases pose a risk to others: those who become infected by them are at risk of developing tuberculosis which will be multidrug-resistant, thus escalating the problem. This is even more important where those infected with resistant bacilli are also infected with HIV.

6.1.2. Can tuberculosis be prevented by vaccination?

It is generally accepted that BCG provides a considerable degree of protection (particularly in young children) against serious forms of tuberculosis such as disseminated tuberculosis and tuberculous meningitis. Vaccination in childhood has little impact in controlling the spread of tuberculosis micro-organisms in the community because the type of tuberculosis prevented by BCG is usually not the infectious form (smear-positive pulmonary tuberculosis), as this form is infrequent in childhood.

In most countries, BCG vaccination is included in the Expanded Programme on Immunization (EPI). The EPI recommends that the vaccine should be given at birth or as early in life as possible, and that it should not be given to children who are known to be HIV-positive. The vaccine is injected intradermally into the upper portion of the left arm, at a dose of 0.05 ml for those up to 1 year of age (and at a dose of 0.1 ml for those more than 1 year of age). There is no scientific justification for revaccination with BCG.

Evidently, the development of a more effective vaccine must have high priority in the global strategy to control tuberculosis.

6.2. What should be done in locations where the National Tuberculosis Programme does not function?

In some locations, particularly when the political situation is unstable, the NTP does not function. Very often, voluntary and other non-governmental organisations take on the challenge of dealing with tuberculosis patients as part of the general health services they provide. On humanitarian grounds, health care personnel may be required to treat patients even when conditions are far from ideal. Nevertheless, some important considerations need to be taken into account.

6.2.1. Why is a National Tuberculosis Programme necessary?

Poor treatment of tuberculosis patients has been clearly shown to have a harmful impact on the tuberculosis situation. This is due to the fact that, while it is relatively easy to prevent death due to tuberculosis, it is more difficult to cure a patient permanently. When patients do not die but are not cured of their disease, they remain in the community with a risk of spreading infection to uninfected members of the community, thus increasing the burden of disease in the community.

Poor treatment keeps alive contagious patients who might otherwise have died. Poor treatment may therefore increase the number of sources of infection in a community. Poor treatment has another, very serious consequence. Patients who are treated for tuberculosis but fail to be cured are at a high risk of developing *chronic and resistant* tuberculosis. Thus, in addition to increasing the risk of transmission of tuberculosis micro-organisms, the strain of micro-organisms being spread is resistant, and when it is multi-resistant, it is also very difficult to cure with the treatment regimens currently available in most countries. *If you cannot ensure that a patient will be treated properly, you must urgently create the conditions in which diagnosis and treatment of tuberculosis can be safely provided. It is of utmost importance to identify such patients, counsel them to reduce their chances of infecting others and to ensure the highest standards of infection control in all institutions where such patients may be encountered.*

6.2.2. How can care be given safely?

If the NTP does not function, certain guidelines should be followed:

- In order not to hinder national efforts to construct a proper, functioning NTP, all tuberculosis services should be provided in accordance with the existing national tuberculosis policies, lines of communication should be established with whatever national tuberculosis structures exist, and regular reports should be submitted to them.
- Treatment of tuberculosis patients should be initiated as soon as a microscopy service has been established.
- Only standardised regimens following international recommendations should be used.
- The intensive phase of rifampicin-containing regimens must be directly observed. *Failure to follow this principle will increase the risk of*

development of resistance to drugs, will endanger the life of the patient and will create a danger to the community. The greatest risk of using rifampicin in an uncontrolled manner, especially during the intensive phase, is the creation of resistance to both isoniazid and rifampicin, which means that the patient requires expensive second-line drugs taken for a prolonged period to be cured.

- Smear-positive patients who have been treated previously for as much as one month must be given a first-line retreatment regimen.
- Where regular supplies cannot be assured, a full treatment regimen should be set aside for each patient enrolled on treatment. This will ensure that every patient who commences treatment is able to complete it.

6.3. How can the situation be assessed and good results assured?

Assessment of the tuberculosis situation entails evaluation both of the epidemiological situation and of the interventions being applied in a given country. The interventions (the process by which the tuberculosis situation is modified) are evaluated using the quarterly reports on case finding and on treatment results, as described previously. Public health targets for interventions have been established at a global level and may be modified for the local situation during the implementation of a programme. Targets should focus as much as possible on items that something can be done about. A comparison of the results achieved with the targets that have been established forms the basis of evaluation of the control measures applied.

6.3.1. How are activities evaluated?

The most important evaluation is the regular review of results of tuberculosis treatment. Several results are of particular importance:

- The proportion of all cases that have *defaulted* from treatment reflects the organisation and performance of case management. The only way to achieve acceptable treatment results (the ultimate target of the treatment programme) is by reducing the proportion of patients who default. This indicates whether patients find the service accessible and appropriate, and often reveals the attitude of the health services personnel in providing care to patients. The most important target for a programme is to have a very low number of defaulters.

- The proportion of patients whose treatment result is *transfer* should be very low. Those who are transferred to facilities in the same general area should have their results obtained from that facility. Regular meetings of coordinators, during which these issues can be routinely discussed, will help solve problems related to the transfer of patients.

Other tuberculosis treatment outcomes to monitor over the course of time include the following:

- The proportion of cases who are *smear-positive* at 5 months or later after starting treatment (treatment failures) may be an indication of the efficacy of the regimen utilised and may also reflect the presence of dead bacilli, non-adherence to the prescribed treatment and the level of drug resistance in these patients.
- The proportion of patients who *died* may indicate the impact of the HIV epidemic in the community, multidrug-resistant tuberculosis, delay in diagnosis and the proportion of elderly tuberculosis patients.

The review of regular reports allows treatment activities to be evaluated. Progress in approaching the targets can be determined and various geographical areas of a country can be compared to identify problem areas. Comparing the performance of neighbouring areas that, in principle, share similar epidemiological, socio-economic and environmental constraints is helpful in determining which areas achieve better results, and may be used as a model from which to draw lessons. Trends over time can be defined (both positive and negative) in the results of treatment in a single location, and these will indicate the progress in quality of care in that location.

6.3.2. How is the size of the tuberculosis problem determined?

Evaluation of the tuberculosis situation (epidemiological surveillance) is important to assess the impact of interventions and to adjust the NTP's plan and budget in relation to the challenges identified. Several epidemiological indices can be used to measure the extent of the tuberculosis problem in a given community.

Rate of reported smear-positive cases

Obtaining the rate of reported smear-positive cases is inexpensive and feasible in most situations. The numerator is the number of new cases

of smear-positive tuberculosis diagnosed in a given area during a period of time. The denominator is the population of that area during the period.

This rate can only be used in countries where notification of smear-positive pulmonary tuberculosis is relatively complete and correctly compiled. Population estimates must be reliable to permit the calculation of rates and the determination of trends. This is the most practical means of surveillance in most countries, and its accuracy and completeness should have the highest priority among surveillance activities. When the denominator is not reliable, only trends in the numerator can be examined and not the rate.

Prevalence of smear-positive pulmonary tuberculosis

Information on the prevalence of smear-positive pulmonary tuberculosis can only be obtained from prevalence surveys. A well-conducted prevalence survey provides information on the number of infectious cases in a community at a given point in time, and sequential surveys can inform about changes in the epidemiological situation. They are, however, expensive and complicated to undertake reliably. Such surveys need to examine large numbers of people to find just a few tuberculosis patients. Because of this, they are not usually able to provide as much information as one would like.

Tuberculin surveys

The measurement of the frequency of significant reactions to the tuberculin skin test has been used to monitor the epidemiological situation of tuberculosis in a community. It is not easy to conduct an accurate tuberculin survey, as this must be based on a sample of the population that is representative of the general population. Moreover, certain technical aspects of the performance of the test and of the determinants of test reactions (e.g., vaccination coverage, the occurrence of infection with other mycobacterial species) may lead to difficulties in interpretation.

The determination of trends in tuberculin skin reactivity is more informative than a single determination of prevalence. Repeated surveys of representative samples of a population 5 to 10 years apart may give an estimation of the trend of transmission of tuberculosis micro-organisms to the population tested, but the technical limitations of such surveys often limit the amount of knowledge that can be gained from them.

6.3.3. How is the effect of HIV measured and monitored?

Because HIV infection may have a dramatic impact on the trend in tuberculosis, where the two infections coincide in a population it is important to determine the level and trend of HIV infection in tuberculosis cases. The determination of HIV seroprevalence and of its trend is accomplished relatively easily in a representative sample of all the new smear-positive cases of tuberculosis in a country. Tuberculosis is one of the most frequent opportunistic diseases to occur in HIV-infected individuals, and it has a "magnifying" effect in the determination of HIV prevalence. For this reason, tuberculosis patients are also a useful "sentinel" population to monitor the trend of the HIV epidemic in a country. HIV has already caused a dramatic rise in the numbers of tuberculosis patients in a number of countries, and this has resulted in a tremendous strain on the health services. Proper planning and budgeting can only be carried out when there is knowledge of how the two infections coincide in the community.

Synergies exist between tuberculosis and HIV/AIDS care. Certain lessons that NTPs have learned in the provision of diagnosis and treatment of the chronic condition of tuberculosis can be applied to the management of the chronic condition of HIV infection.

Additional indicators to monitor include:

- the proportion of tuberculosis patients *tested for HIV* who are given cotrimoxazole if found to be infected and antiretroviral treatment if indicated;
- the proportion of *partners* of HIV-infected tuberculosis patients *tested for HIV*;
- the proportion of *children* of HIV-infected tuberculosis patients *tested for HIV*;
- the proportion of HIV-infected tuberculosis patients *referred for HIV care*.

6.3.4. How is drug resistance assessed and monitored?

Resistance to antituberculosis drugs is a man-made problem whose original cause can always be traced to a poorly organised or managed NTP. Thus, the trend in resistance to antituberculosis drugs is a means of identifying deficiencies in the implementation of an NTP. To a certain extent, the pattern of resistance in a country predicts the effectiveness of the standardised treatment used in the programme.

The details of the methods used for drug susceptibility monitoring are beyond the scope of these guidelines, as different approaches will be adopted for different settings. Surveys of drug susceptibility in representative samples of new patients and in all patients from the three categories of previously treated patients (after cure, after failure, after default) are needed to measure drug resistance. However, these surveys of drug susceptibility in representative samples of new patients and retreatment cases represent a large burden, particularly for the reference laboratory, so that only very few countries have succeeded in monitoring drug resistance in this way. Continuously monitoring drug resistance among retreatment cases has proven more feasible and useful, as it yields early diagnosis of multidrug-resistant tuberculosis at the same time. This method also requires a representative sample, without selection of the clinically worst cases. In practice, as many as possible of the patients who have failed, relapsed and possibly also returned after default from treatment will be included. It may not always be possible to test susceptibility to all first-line drugs, depending on the preferred first-line technique. Molecular methods can be used for easy transport even from remote areas, but they cannot be used for all drugs, while transporting specimens for culture from which any test might be performed creates problems of contamination and viability of organisms. However, effective monitoring of drug resistance may very well concentrate on rifampicin resistance, which can be measured correctly by molecular methods.

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Appendices

Tuberculosis Programme

Request and Reporting Form for Sputum Smear Examination

Requesting facility: _____ Date: _____

Patient's name:

Age: _____ Sex: M ☐ F ☐

Complete address: _____

_____

_____

Telephone number (if available): _____

Reason for examination: Diagnosis ☐ Follow-up examination ☐

If follow-up, number of month of treatment: _____

Name and signature of person requesting examination:

_____

Results (to be completed in the laboratory)

Laboratory Serial No.: _____

Date	Specimen	Appearance*	Result *(tick one)*				
			Neg	Scanty (1–9)†	+	++	+++
	1						
	2						

* Visual appearance of sputum (blood-stained, muco-purulent, salivary)
† 1–9 bacilli per 100 fields; record the exact number of acid-fast bacilli seen

Date: _____ Examined by: _____

Signature _____

The completed form (with results) should be sent promptly to the referring facility

Tuberculosis Programme

Tuberculosis Laboratory Register

Year: _____

Lab Serial No.	Date specimen received	Name	Sex M/F	Age	Name of requesting facility	Address of patient attending for diagnosis	Reason for examination*		Results of specimen		Case tracking (only for SS+ for diagnosis) TB number or referral BMU†	Remarks
							Diagnosis *(tick)*	Month of follow-up	1	2		

* Tick the appropriate category from the *Request for Sputum Smear Examination*
† TB register number or name of the BMU to which the patient will be referred for treatment
SS+ = sputum smear-positive patient.

FORM 2

Tuberculosis Programme

Tuberculosis Treatment Card

TB No.: _____

Name: _____

Age: _____ Sex: M ☐ F ☐ Date of registration: _____

Address (and Tel):

_____

_____

Basic Management Unit (BMU): _____

Treatment Unit: _____

Disease site *(tick one):*

Pulmonary ☐ Extra-pulmonary ☐ Site (specify) _____

Category of patient *(tick one):*

New ☐ Treatment after failure ☐

Relapse ☐ Treatment after default ☐

Transfer in ☐ Other ☐ (specify) _____

I. INITIAL INTENSIVE PHASE

For patients on retreatment, former TB No.*: _____

Prescribed regimen and no. of tablets (or grams)

New
RZHE

Retreatment		
S		RZHE

Month	Date	Lab no.	Smear result	Weight (kg)	Date of next appointment
0					
2					
5					
End					

TB-HIV		
	Date	Result†
HIV test		
CD4		
CPT start		
ART start		

Cotrimoxazole 480 ☐ 960 ☐ Patient uses tobacco? No ☐ Yes ☐ If yes, willing to quit within the next 30 days? No ☐ Yes ☐

Day / Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

Enter X on day when drugs were swallowed under direct observation, and Ø on day when the patient doesn't come for treatment.

* Attach the previous card.

† HIV results: P = Positive; N = Negative; I = Indeterminate; ND = Not done; HIV-positive patients should be referred to the HIV clinic; CPT = cotrimoxazole preventive therapy; ART = antiretroviral treatment.

Please turn over

FORM 3

II. CONTINUATION PHASE

Regimen and number of tablets:

New cases (daily)	{RH}	Retreatment (daily)	{RH}
4 months		6 months	

CTM 480	
CTM 960	

Day / Month	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31

Enter X on day of observed administration or when drugs are collected. Draw a horizontal line ——• through the number of days supplied Ø = drugs not taken

Remarks: _____

_____

_____

_____

Treatment outcome Date of decision: _____

☐ Cure ☐ Treatment completed ☐ Treatment failure ☐ Died ☐ Default ☐ Transfer out; BMU name _____

Tuberculosis Programme

Patient Identity Card *(to be presented to any health worker consulted)*

Name _____

Address _____

Sex: M ☐ F ☐ Age: _____

Date treatment start: _____

BMU TB Register No.: _____

Name of the BMU: _____

Sputum smear microscopy				Weight (kg)
Month	Date	Lab No.	Result	
0				
2				
5				
End				

Disease site (tick one)

☐ Pulmonary ☐ Extra-pulmonary, specify: _____

Type of case (tick one)

☐ New ☐ Treatment after failure
☐ Relapse ☐ Treatment after default
☐ Transfer in ☐ Other, specify: _____

I. INITIAL INTENSIVE PHASE Start date: _____

Number of tablets

RHZE

Number of grams

S

II. CONTINUATION PHASE Start date: _____

RH

Appointment dates

Appointment date	Attended (Yes or No)

Notes: _____

FORM 4

Tuberculosis Programme

Tuberculosis Register (page 1/2)

Date registered	BMU TB No.	Name	Sex M/F	Age	Address	Treatment Unit	Treatment start date	Regimen*	Disease site P/EP	Type of case†					
										New	Relapse	Treatment after failure	Treatment after default	Transfer in	Other

* **New case:** RHZE
Retreatment: S

† **New:** never previously treated for as much as 1 month
Relapse: previously treated, declared cured, returns smear-positive
Transfer in: registered and started treatment in another unit

Treatment after failure: smear-positive ≥ 5 months after starting treatment, commenced on retreatment
Treatment after default: returned smear-positive after default, commenced on retreatment

FORM 5

Tuberculosis Programme

Tuberculosis Register (page 2/2)

Year:_____

Results of smear examination								Result of treatment *(tick)*‡							TB-HIV				
Before treatment		2 months		5 months		End treatment													
Result	Lab no./ date	Result	Lab no./ date	Result	Lab no./ date	Result	Lab no./ date	Date of result	Cured	Completed	Failure	Died	Defaulted	Transfer out	HIV result (P,N,I,D)§	CD4 count	CPT (Date)	ART (Date)	Remarks (Specify BMU if transferred, ART clinic, etc…)

‡ **Cured:** negative smear at end of treatment and on one previous occasion
Completed: completed treatment, but sputum examination not done for proof of cure
Failure: smear-positive at 5 months or later during treatment, confirmed by a second positive smear
Died: died from any cause while on treatment
Defaulted: failed to collect drugs for 2 months or more after date last seen
Transferred: sent to another BMU for continuation of treatment; treatment result unknown

§ HIV test: P = Positive; N = Negative; I = Indeterminate; ND = Not done.

Tuberculosis Programme

Quarterly Report on Tuberculosis Case Finding

Name of Basic Management Unit (BMU): _____	BMU Tuberculosis Coordinator:_____
Patients registered in quarter _____ of (year) _____	Signature: _____Date:_____

All cases registered in the quarter*

Pulmonary sputum smear-positive (SS+)				New pulmonary smear-negative or not done			New extra-pulmonary	Other†	**Total**
New cases	Relapses	Treatment after failure	Treatment after default	<5 years	5–14 years	≥15 years			

HIV test	No. patients tested	No. positive
New SS+		
Total TB		

* **Transferred in** patients are not included in this report.
† **Other:** there should be very few cases in this category; they include TB cases that do not fit in the other categories, in particular the rare retreatment smear-negative cases

New smear-positive cases only

Age group (years)														**TOTAL**		
0–14		15–24		25–34		35–44		45–54		55–64		65+				
M	F	M	F	M	F	M	F	M	F	M	F	M	F	Male	Female	Total

Quarters 1st quarter — 1 January to 31 March
2nd quarter — 1 April to 30 June
3rd quarter — 1 July to 30 September
4th quarter — 1 October to 31 December

FORM 6

Tuberculosis Programme

Quarterly Report on the Results of Tuberculosis Treatment

Cases registered in the quarter ending 12 months prior to reporting date

Name of Basic Management Unit (BMU): _____	BMU Tuberculosis Coordinator: _____
Patients registered in quarter _____ of year _____	Signature: _____ Date: _____

1 – Treatment results

Type of case	Cured	Treatment completed	Failure	Died	Defaulted	Transfer out	**Total**
New SS+ No. registered* _____							
Retreatment SS+ No. registered _____							
All other forms† No. registered _____							

* From *Quarterly Report on Tuberculosis Case Finding* for that quarter (patients transferred in are excluded from this report)
† Sputum smear-negative, extra-pulmonary, other (patients transferred in are excluded from this report)

2 – TB-HIV

Number of HIV-positive TB patients	Count (CD4/µl)				Number of TB-HIV patients on cotrimoxazole preventive therapy (CPT)	Number of TB-HIV patients on antiretroviral treatment (ART)
	Not done	<200	200–350	>350		

FORM 7

Tuberculosis Programme

Quarterly Order Form for Treatment Supplies at Basic Management Unit Level

Enter the number of cases enrolled in the previous three months (from the *Quarterly Report on Tuberculosis Case Finding*)

Item	2{RHZE}/4{RH}			2S{RHZE}/6{RH}			Total
	Cases	Factor	Total A	Cases	Factor	Total B	A+B= C
{RHZE}		x 210 =			x 210 =		
{RH} 150/75		x 420 =			x 630 =		
S 1 g		x 0 =	0		x 60 =		

Item	Running requirement	Reserve requirement	Currently in stock	Total order	Quantity given
	D (= C from above)	E (= D)	F	D + E – F	
{RHZE}					
{RH} 150/75					
S 1 g					
Water for injection (5 ml)*					
Syringes/needles*					
H 50 mg					
Other					

Name of BMU: _____

Date: _____

Name: _____

Signature: _____

* Same as number of vials for streptomycin

FORM 8

FORM 9

Tuberculosis Programme

Quarterly Report for Peripheral Sputum Smear Laboratory Performance and Stock Situation

Name of BMU:..... Name of Laboratory: …….. Patients registered in quarter _____ of (year) _____

1) Patients

Number of TB suspects for diagnosis with positive smear	Total number of TB suspects examined for diagnosis	Number of patients with positive smears on follow-up examination	Total number of patients examined for follow-up

2) Smears

ZN ☐ **FM** ☐	Positive	Scanty	Negative	**Total**
Number of smears examined for diagnosis				
Number of smears examined for follow up				
Total smears examined				

3) Stocks on hand at the end of the quarter ***(the quantities delivered will be filled in by the supplier)***

	Stock	Delivered		Stock	Delivered
Carbolfuchsin solution	……. l	……. l	Immersion oil	……. ml	……. ml
Auramine solution	……. l	……. l	Burning spirit	……. l	……. l
Counterstaining solution	……. l	……. l	Slides	……. pcs	……. pcs
Destaining solution	……. l	……. l	Sputum containers	……. pcs	……. pcs

Other requests: ……

Date: _____ Name and signature: _____

About The Union

Founded in 1920, the International Union Against Tuberculosis and Lung Disease (The Union) is dedicated to bringing innovation, expertise, solutions and support to address health challenges in low- and middle-income populations. With nearly 10,000 members and subscribers from over 150 countries, The Union has its headquarters in Paris and offices serving the Africa, Asia Pacific, Europe, Latin America, Middle East, North America and South-East Asia regions. Its scientific departments focus on tuberculosis, HIV, lung health and non-communicable diseases, tobacco control and research. Each department engages in research, provides technical assistance and offers training and other capacity-building activities leading to health solutions for the poor.

For more information, please visit www.theunion.org

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