Department of Health

The South African National TUBERCULOSIS Control Programme Practical Guidelines 2004

Preface & Acknowledgements

PREFACE

At no time in recent history has tuberculosis been as great a concern as it is today. Despite highly effective drugs, morbidity and mortality due to Mycobacterium tuberculosis is increasing, a phenomenon that is being largely fuelled by the HIV epidemic. Since the inception of the National TB Control Programme in 1996, there has been an increase in case detection but with generally poor case holding marked by high interruption of treatment and loss of patients to follow up.

HIV not only increases the number of TB cases but also alters the clinical course of TB disease. Co-infected patients also suffer increased mortality mainly due to late diagnosis and other opportunistic infections. Early diagnosis and effective treatment of TB among HIV-infected patients are critical for curing TB, minimizing the negative effects of TB on the course of HIV and interrupting the transmission of M. tuberculosis to other persons in the community. Proper case management of TB can significantly prolong the lives of people living with HIV and AIDS.

The strategy of TB treatment is based on standardized short-course chemotherapy regimens and proper case management to ensure successful completion of treatment and cure.

The most cost-effective public health measure to control TB is the identification and cure of the infectious cases, i.e. patients with smear-positive pulmonary TB. However the objective of the TB programme is to cure all patients including those diagnosed with smear positive PTB, smear negative PTB and extra-pulmonary TB, in both adults and children.

Decreasing the number of previously treated cases through high cure rates and low interruption rates among new patients will prevent the escalation of drug resistance. The causes of drug resistance include inadequate treatment regimens prescribed by health staff, poor case holding of patients, erratic drug supply, poor drug quality or use of expired drugs, as well as patient error and non-adherence in following prescribed regimens and misuse of tuberculosis drugs.

Directly observed treatment (DOT) has been shown to be a key factor in achieving high cure rates and preventing drug resistance. Evidence from both developed and developing countries has shown that the likelihood of drug resistance can be reduced by ensuring patient adherence through direct supervision of treatment.
This document aims to assist health care workers in the successful management of tuberculosis thus ensuring a high successful treatment completion rate and a low interruption rate for all new smear positive cases.

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List of abbreviations

AFB	Acid-Alcohol Fast Bacilli
AIDS	Acquired Immune Deficiency Syndrome
ART	Antiretroviral Therapy
BCG	Bacille Calmette - Guerin
CBO	Community Based Organisation
CHW	Community Health Worker
CDC	Communicable Disease Coordinator
DOH	Department of Health
DOT	Directly-Observed Treatment
DOTS	Directly-Observed Treatment, Short course
E	Ethambutol
ETR	Electronic TB Register
GDF	Global Drug Facility
GFATM	Global Fund to fight AIDS, Tuberculosis and Malaria
H	Isoniazid
HIV	Human Immunodeficiency Virus
HIS	Health Information System
HR	Isoniazid/ Rifampicin
HSA	Health Services Area
IEC	Information, Education and Communication
IUATLD	International Union Against Tuberculosis and Lung Disease
KNCV	Royal Netherlands Tuberculosis Foundation
KZN	KwaZulu-Natal
MDRTB	Multidrug-Resistant Tuberculosis
NGO	Non-Governmental Organisation
NTCP	National Tuberculosis Control Programme
PHC	Primary Health Care
PN	Professional Nurse
PMTCT	Prevention of Mother-To-Child HIV Transmission
PPM	Private-Public Mix
QA	Quality Assurance
R	Rifampicin
RSA	Republic of South Africa
S	Streptomycin
SHR	Streptomycin/ Isoniazid/ Rifampicin
SHRZE	Streptomycin/ Isoniazid/ Rifampicin/ Pyrazinamide/ Ethambutol
STI	Sexually Transmitted Infections
SWOT	Strengths, Weaknesses, Opportunities, Threats
TB	Tuberculosis
TBCO	TB Coordinator
TBCTA	Tuberculosis Coalition for Technical Assistance
VCT	Voluntary Counselling and Testing
VHW	Village Health Worker
WHO	World Health Organisation
Z	Pyrazinamide

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1 Introduction

1.1 Global epidemiology and burden of disease

Nearly one-third of the global population is infected with Mycobacterium tuberculosis and at risk of developing the disease. More than 8 million people develop active tuberculosis every year, and about two million die on an annual basis worldwide.

Over 90% of global TB cases and deaths occur in the developing world, where 75% of cases are in the most economically productive age group (15-54 years). Co-infection with HIV significantly increases the risk of developing TB. Countries with a high prevalence of HIV, particularly those in sub-Saharan Africa, are witnessing an increase in TB. At the same time, multi-drug resistance caused by poorly managed TB treatment, is a growing problem in many countries around the world.

1.2 Reasons for the global TB burden

According to the WHO, the main reasons for the increasing global TB burden are:

- poverty and the widening gap between rich and poor in various populations;
- poor programme management in terms of inadequate case detection, diagnosis and cure;
- the impact of the HIV-pandemic; and
- the collapse of health infrastructure in countries experiencing deep economic crisis or civil unrest.

1.3 TB in South Africa

According to the latest world report of the WHO, South Africa ranks 9th on the list of 22 countries hardest hit by TB. South Africa reports more than 100 000 TB cases yearly. This is an incidence rate of more than 500/100 000 population. The latest successful treatment completion rates, recorded in 2002, are 68% with interruption rates of 13%.

South Africa's main challenges in TB control are:

- late presentation of patients to health facilities,
- late detection of TB, and
- high interruption rates.

1.4 Objectives of the National Tuberculosis Control Programme

The overall objectives of the NTCP are to:

- reduce mortality and morbidity attributable to TB;
- prevent the development of drug resistance; and
- ensure accurate measurement and evaluation of programme performance.

The targets for TB control in South Africa are to:

- cure 85% of newly detected cases of sputum smear-positive TB;
- detect 70% of TB cases; and
- reduce interruption rates to less than 5%.

The NTCP, together with other major stakeholders, developed a Medium Term Development Plan (MTDP) in 2001. This plan addresses the main TB strategy and activities that must be implemented in order to meet the set targets. The National Department of Health has committed itself to reach these targets by 2005; this is in accordance with the Amsterdam Declaration signed in 2000.

1.5 The structure of the NTCP

The NTCP consists of four levels within the general health services, namely:

- The Central unit, or national level, functions through the National Department of Health to co-ordinate, facilitate and evaluate tuberculosis services countrywide.
- The Provincial level is responsible for implementation and budgeting.
- The District level is the key element for the management of primary health care and is the most peripheral unit of the health services administration.
- The Health unit level functions within a district to provide primary health care. This level incorporates all the rural hospitals, health centres, dispensaries and clinics within a specific area.

This structure may vary to some extent, for example in some provinces a regional level has been established between the provincial and district levels.

1.5.1 Core activities at national level

The main function of the national unit is to provide support and technical guidance to the provinces on the following key activities:

- Countrywide implementation of the DOTS strategy.
- Training of provincial TB co-ordinators on all elements of the DOTS strategy.
- Supervisory visits.
- Laboratory visits to ensure proper diagnosis and follow-up of TB patients.
- Ensuring an efficient recording and reporting system for monitoring patients and programme performance.
- Strengthening collaboration between TB and HIV/AIDS programmes to ensure better management of co-infected patients.
- Raising public awareness about the seriousness of TB.
- Co-ordination of research activities.

1.5.2 Core activities at provincial level

The key functions at provincial level are:

- Collaboration with district management teams in planning TB activities so that the provincial work plan is the sum of the district work plans.
- Organising training and conducting supervisory/support visits, including laboratory and pharmacy personnel who perform activities related to TB control.
- Ensuring that a district's needs for TB drugs, forms and laboratory materials are supplied asrequired.
- Supervising record keeping of the TB case registers and laboratory registers.
- Collaborating with staff working in the HIV/AIDS programme to ensure better management of patients.
- Collaborating with other agencies and NGOs, as well as private doctors, who provide care for TB patients.

1.5.3 Core activities at district level

TB control and primary health care (PHC) are interdependent. Rapid progress in TB control will not occur unless TB control is integrated into the PHC-system. Similarly, a PHC-programme cannot be truly effective unless it includes TB control. But when TB control and PHC are integrated, TB case detection and case holding can be improved and extended to entire populations.

The key reasons why TB control should be integrated into PHC are:

- TB is highly prevalent in South Africa with its most frequent clinical manifestation, coughing, also being one of the most common presenting symptoms among patients attending PHC services.
- Effective TB control depends not only on access to diagnostic and treatment services, but also on active community participation.
- TB control contributes substantially to socio-economic development by reducing the burden of disease and death in the most productive age groups.

The key functions at district level are to:

- Co-ordinate training activities at district level.
- Develop an efficient patient referral system to ensure continuity of care.
- Co-ordinate and establish community-based DOTS programmes.
- Conduct support visits to health facilities including NGOs, laboratories and pharmacies.
- Submit quarterly reports on case finding and treatment outcomes.
- Ensure that diagnostics and drugs are available at all times.
- Plan and budget for TB activities.
- Participate in advocacy and social mobilisation activities.

The district TB-co-ordinator, who may be responsible for other programmes in addition to TB, should be part of the district management team.

2 The TB Control Policy Package

In order to achieve the targets for TB control, the TB programme needs to be strengthened significantly in the following areas:

- General public health services need to enhance their capacity to sustain and expand DOTS implementation without compromising the quality of case detection and treatment.
- Community involvement in TB care and a patient-centered approach need emphasis and promotion to improve both access to and utilisation of health services.
- Collaboration and synergy among the public, private and voluntary sectors are essential to ensure accessible and quality-assured TB diagnosis and treatment, under the guidance of provincial health authorities.
- The increasing impact of HIV on TB incidence and mortality calls for new partnerships and approaches.
- A surge in drug-resistant TB requires effective implementation of the DOTS strategy as well as measures to cure existing MDR-TB cases.

2.1 The DOTS Strategy

The DOTS strategy reinforces five essential elements:

1. Sustained political commitment to increase human and financial resources and make TB control a nation-wide priority integral to the national health system.
2. Access to quality-assured TB sputum microscopy for case detection among persons presenting with, or found through screening to have, symptoms of TB (the most important symptom being a prolonged cough of more than 2 weeks). Special attention is necessary for case detection amongst HIV infected people and other high-risk groups, such as household contacts of infectious cases and people in institutions.
3. Standardised short-course chemotherapy to all cases of TB under proper case-management conditions, including direct observation of treatment. Proper case management conditions imply technically sound and socially supportive treatment services.
4. Uninterrupted supply of quality-assured drugs with reliable drug procurement and distribution systems.
5. Recording and reporting system enabling outcome assessment of each and every patient and assessment of the overall programme performance. This forms the basis for systematic programme monitoring and correction of identified problems.

2.2 Key operations for DOTS implementation

The key operations for implementation of the DOTS strategy are to:

- establish a NTCP with a strong central unit;
- prepare a programme development plan (Medium Term Development Plan);
- develop a training plan;
- ensure that a good microscopy service is functioning and meeting the programme's aim of ensuring a 48-hour turn-around time of smear results;
- organise treatment services within the PHC system, giving priority to directly observed short-course chemotherapy;
- secure a regular supply of drugs and diagnostic material; and
- design and implement a supervisory planfor the key operations at the intermediate and district level.

Other important key operations essential to strengthen and sustain DOTS implementation include information, education, communication and social mobilisation, involving private and voluntary health care providers, economic analysis and financial planning, and operational research.

3 Transmission and Pathogenesis of TB

3.1 Transmission of tuberculosis

Tuberculosis is spread from person-to-person through the air by droplet nuclei, which are small particles 1 to 5 µm in diameter containing M. tuberculosis bacilli. Droplet nuclei are produced when persons with pulmonary or laryngeal tuberculosis cough, sneeze or sing. They may also be produced by aerosol-producing investigations such as sputum induction, bronchoscopy and through manipulation of lesions or processing of tissue or secretions in the laboratory.

Droplet nuclei, containing two to three M. tuberculosis organisms, are so small that air currents normally present in any indoor space can keep them airborne for long periods of time. Droplet nuclei are small enough to reach the alveoli within the lungs, where the organisms replicate.

Although patients with tuberculosis also generate larger particles containing numerous bacilli, these particles do not serve as effective vehicles for TB-transmissionas they do not remain airborne, and if inhaled, do not reach the alveoli. Organisms deposited on intact mucosa or skin do not invade tissue. When large particles are inhaled, they impact on the wall of the upper airways, where they are trapped in the mucous blanket, carried to the oro-pharynx, swallowed or expectorated.

Four factors determine the likelihood of transmission of M. tuberculosis:

1. the number of organisms being expelled into the air;
2. the concentration of organisms in the air determined by the volume of the space and its ventilation;
3. the length of time an exposed person breathes the contaminated air; and
4. presumably the immune status of the exposed individual.

HIV-infected persons and others with impaired cell-mediated immunity are more likely to become infected with M tuberculosis after exposure - and subsequently develop TB - than persons with normal immunity. However, they are no more likely to transmit M tuberculosis than those with normal immunity.

There are five closely related mycobacteria grouped in the M tuberculosis complex: M. tuberculosis, M. bovis, M. africanum, M. microti and M. canetti. Mycobacterium tuberculosis is transmitted through the airborne route and there are no known animal reservoirs. Mycobacterium bovis may penetrate the gastrointestinal mucosa or invade the lymphatic tissue of the oropharynx when ingested in milk containing large numbers of organisms. Human infection with M bovis has decreased significantly in developed countries as a result of the pasteurisation of milk and effective tuberculosis control programs for cattle.

Pulmonary tuberculosis is the infectious and the most common form of the disease, occurring in over 80% of cases. Extra-pulmonary tuberculosis is a result of the spread of infection (mycrobacteria) to other organs, most commonly pleura, lymph nodes, spine, joints, genito-urinary tract, nervous system or abdomen. Tuberculosis may affect any part of the body.

The most infectious cases are those with a positive smear by microscopy (smear positive cases).
Those in whom micro-organisms cannot be seen directly under the microscope (smear negative cases) are much less infectious. Extra-pulmonary cases are almost never infectious, unless they have pulmonary tuberculosis as well. One cough can produce 3 000 droplet nuclei.

Transmission generally occurs indoors, where droplet nuclei can stay in the air for a long time. Direct sunlight quickly kills tubercle bacilli, but they can survive in the dark for several hours.
The two main factors that determine an individual's risk of exposure are:

- the concentration of droplet nuclei in contaminated air, and
- the length of time the person breathes that air.

3.2 Pathogenesis of tuberculosis

After inhalation, the droplet nucleus is carried down the bronchial tree and implants in a respiratory bronchiole or alveolus. Whether or not an inhaled tubercle bacillus establishes an infection in the lung, depends on both the bacterial virulence and the inherent microbicidal ability of the alveolar macrophage that ingests it. If the bacillus is able to survive initial defenses, it can multiply within the alveolar macrophage.

The tubercle bacillus grows slowly, dividing approximately every 25 to 32 hours within the macrophage. As mycobacterium tuberculosis has no known endotoxins or exotoxins, there is no immediate host response to infection. The organisms grow for two to twelve weeks, until they reach 10Δ to 10^4 in number, which is sufficient to elicit a cellular immune response that can be detected by a reaction to the tuberculin skin test.

Before the development of cellular immunity, tubercle bacilli spread via the lymphatics to the hilar lymph nodes and from there through the bloodstream to more distant sites. Certain organs and tissues are notably resistant to subsequent multiplication of these bacilli. The bone marrow, liver and spleen are almost always seeded with mycobacteria, but uncontrolled multiplication of the bacteria in these sites is exceptional. Organisms deposited in the upper lung zones, kidneys, bones and brain may find environments that favour their growth. Numerous bacterial divisions may occur before specific cellular immunity develops, limiting multiplication.

Individuals with latent tuberculosis infection, but not active disease, are not infectious and thus cannot transmit the organism. It is estimated that approximately 10% of individuals who acquire tuberculosis infection will develop active tuberculosis. BCG immunisation gives up to 80% protection against the progression of TB from infection to disease. However, the main benefit of BCG is the protection against the development of the serious forms of TB (TB meningitis, miliary TB) in children.

The risk is highest in the first two years after infection, when half the cases will occur. The ability of the host to respond to the organism may be reduced by certain diseases such as silicosis, diabetes mellitus, and diseases associated with immuno-suppression, e.g., HIV Infection, as well as by corticosteroids and other immunosuppressive drugs. In these circumstances, the likelihood of developing tuberculosis disease is greater.

HIV-infected persons, especially those with low CD4 cell counts, develop tuberculosis disease rapidly after becoming infected with M tuberculosis.

3.3 Primary infection

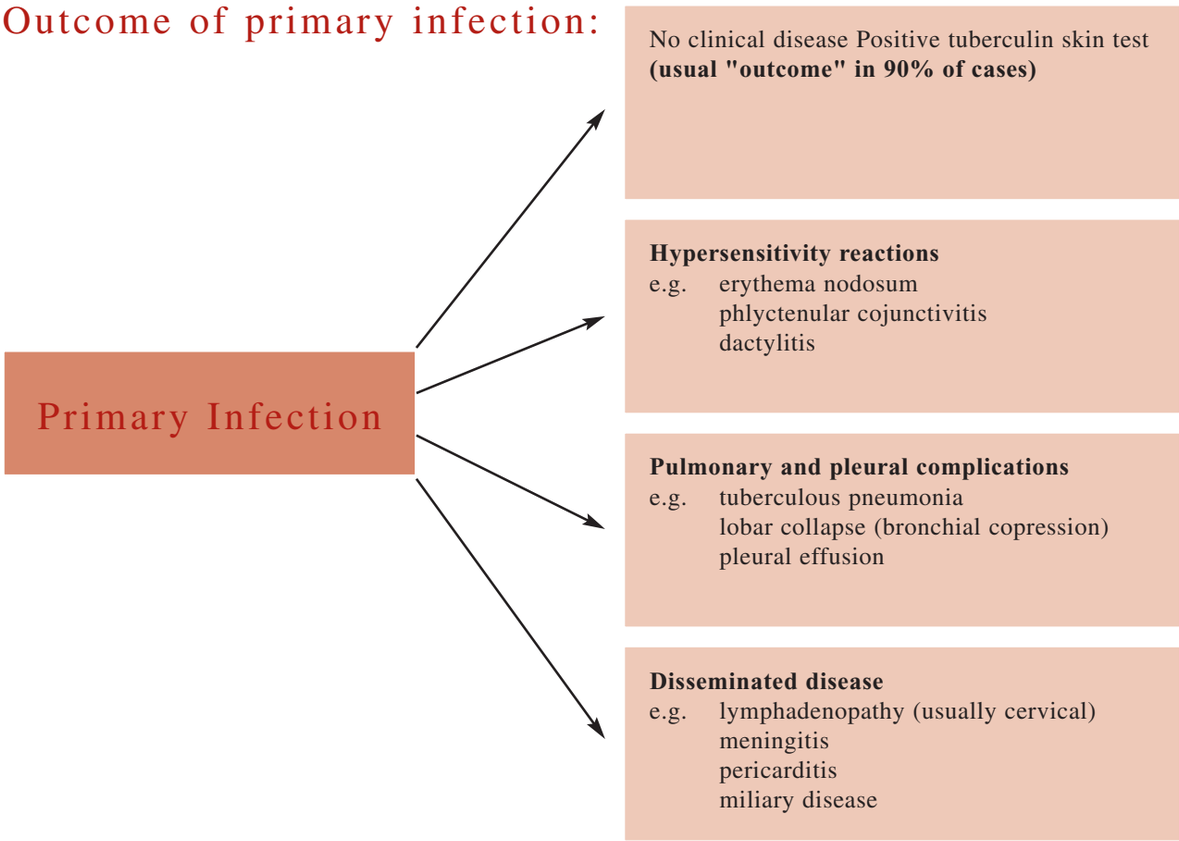
Primary infection occurs on first exposure to tubercle bacilli. Inhaled droplet nuclei are so small that they avoid the muco-ciliary defences of the bronchi and lodge in the terminal alveoli of the lungs. Infection begins with multiplication of tubercle bacilli in the lungs. This is the Ghon focus. Lymphatics drain the bacilli to the hilar lymph nodes. The Ghon focus and related hilar lymphadenophathy form the primary complex. Bacilli may spread in the blood from the primary complex throughout the body.

The immune response (delayed hypersensitivity and cellular immunity) develops about 4-6 weeks after the primary infection. The size of the infecting dose of bacilli and the strength of the immune response determine what happens next. In most cases, the immune response stops the multiplication of bacilli. However, a few dormant bacilli may persist. A positive tuberculin skin test would be the only evidence of infection. The immune response in a few cases is not strong enough to prevent multiplication of bacilli, and disease occurs within a few months.

3.4 Post-primary TB

Post-primary TB occurs after a latent period of months or years after primary infection. It may occur either by

Outcome of primary infection:



Following primary infection, rapid progression to intra-thoracic disease is more common in children than in adults. Chest X-rays may show intra-thoracic lymphadenopathy and lung infiltrates.

reactivation or by re-infection. Reactivation means that dormant bacilli, persisting in tissues for months or years after primary infection, start to multiply. This may be in response to a trigger, such as weakening of the immune system by HIV infection. Re-infection means a repeat infection in a person who previously had had a primary infection.

Post-primary TB usually affects the lungs but can involve any part of the body. The characteristic features of post-primary PTB are the following: extensive lung destruction with cavitation; positive sputum smear; upper lobe involvement; usually no intrathoracic lymphadenopathy.

4 Diagnosis Of TB

4.1 Symptoms and signs of TB

The most common symptoms of pulmonary tuberculosis are:

- persistent cough for more than 2 weeks; every patient who is presented to a health facility with this symptom should be regarded as a "tuberculosis suspect",
- sputum production which may be blood-stained,
- shortness of breath and chest pain,
- loss of appetite and loss of weight,
- a general feeling of illness (malaise),
- tiredness and loss of motivation, and
- night sweats and fever.

A patient showing these symptoms who is, or was, in contact with a person with infectious tuberculosis is more likely to be suffering from tuberculosis. Symptoms of extra-pulmonary tuberculosis depend on the organ involved. Chest pain from tuberculosis pleurisy, enlarged lymph nodes and sharp angular deformity of the spine are the most frequent signs of extra-pulmonary tuberculosis.

4.2 How is Diagnosis of Tuberculosis Confirmed?

In all instances, individuals identified as tuberculosis patients must have an examination of their sputum performed to determine whether or not they are infectious cases of tuberculosis, prior to the commencement of their treatment. The examination consists of microscopic examination of the sputum specimen (smear microscopy).
Smears may be prepared directly from clinical specimens or from concentrated preparations. The acid fast staining procedure depends on the ability of mycobacteria to retain dye when treated with mineral acid or an acid alcohol solution. Two procedures are commonly used for acid fast staining: the carbofuschin methods, which include the Ziel-Neelsen and Kinyoun methods, and a fluorochrome procedure using auramine-O or auramine-rhodamine dyes. If micro-organisms (commonly referred to as acid-fast bacilli, or AFB) are detected by this method then the patient is said to have smear positive tuberculosis. It is important to carry out smear microscopy because it correctly and efficiently identifies the cases that are infectious and therefore have the highest priority for care.

4.2.1 Sputum collection, labeling, storage and transport

At least two sputum specimens should be taken from a TB suspect:

- **First specimen:** At the first interview with the patient a "spot specimen" is collected. This specimen is obtained immediately after the patient undergoes a bout of coughing and the back of the throat is cleared. This should always be undertaken with the supervision of a health worker.
- **Second specimen:** The patient is then given a sputum container for the collection of an early morning specimen, usually the following day.

4.2.2 Sputum labeling

Correct labeling is essential as it will save time and prevent errors. Label the container first, very clearly with:

- Name of clinic/hospital.
- Name of patient and clinic/hospital number.
- Indicate whether the specimen is pre-treatment (suspect), follow-up (2-3 months) or end-of-treatment specimen (5-7 months).
- Write clear instructions regarding what investigations are required.
- Write the appearance of the sputum (e.g. mucoid, lumpy, green, offensive, etc).
- Date the specimen clearly and time of collection of the specimen.

4.2.3 Sputum collection

Note: The container should always be labelled as the lids may get mixed up.

This is an extremely important procedure:

1. The person must rinse out their mouth with water.
2. Explain the steps in a slow and concise manner.
3. Ask the patient to be very careful and direct the sputum into the container so as not to contaminate the outside.
4. Demonstrate a deep cough from the bottom of the chest, beginning with deep breathing.
5. Supervise the collection, but do not stand in front of the patient.
6. This procedure should occur in a well ventilated area or outside, but in private and without others watching.
7. Give the patient the container, without the lid.
8. Be ready to replace the lid on the container immediately.
9. Once specimen is in the container, make sure the lid is securely closed by pressing down on the centre of the lid down until a click is heard.
10. Wash your hands after handling the sputum specimen.
11. Remember! The person must be encouraged to produce a specimen even if this resembles saliva.

4.2.4 Sputum storage

- Place the sputum bottle in a plastic bag to prevent contamination.
- Store sputum specimen in a fridge if transport is not immediately available. Do not store in a freezer.
- Send the specimen as soon as possible.
- Record the date on which the specimen has been sent to the laboratory in the suspect register.

4.2.5 Transportation of sputum specimens

- Specimens should be transported to the laboratory in a cooler bag. High temperatures during transit will kill bacilli.
- During transportation, specimens should be kept out of direct sunlight.
- Explain to the driver the reasons for transporting the specimens, thereby ensuring that specimens go directly to the laboratory.

Sputum result turn around time (TAT) refers to the duration of time from the taking of a specimen from the patient to the receiving of the results at the health facility.

Note: Each workday, a responsible person should check the sputum register to see which results are outstanding and then contact the laboratory to find out where the results are. Close co-operation with the laboratory will produce quick results, resulting in sputum positivepatients being started on the correct treatment as soon as possible. The target of the NTCP

4.2.6 Sputum Results

The results of the laboratory reports are subject at times to human and material error. Some of the errors include: clerical errors, reagents problems, bad quality of specimens, process errors and lack of quality control. A laboratory result that does not tie up with other clinical information must be interpreted with care. The number of bacilli (AFB) seen in a smear reflects the patient's infectivity.

4.3 When to do Sputum Examination

The laboratory must record the number of bacilli seen on each smear as follows:

Number of bacilli seen on a smear		Results reported
No AFB	Per 100 oil immersion field	0
1-9 AFB	Per 100 oil immersion field	1-9 (indicate number seen), scanty
10- 99 AFB	Per 100 oil immersion field	1+
1-10 AFB	Per 1 oil immersion field	2++

Two specimens are taken on three separate occasions during the course of treatment of patients with PTB.

4.3.1 Pretreatment

When PTB is first suspected; send 2 specimens on consecutive days for TB microscopy for both new and retreatment cases. For retreatment cases, a sputum sample for culture and sensitivity should also be taken.

4.3.2 During treatment

Two specimens should be sent for microscopy just before the end of intensive phase of treatment (at 2 months of treatment for new patients and at 3 months for re-treatment patients).
During TB treatment, all pulmonary TB patients should be monitored by sputum smear microscopy. Sputum for culture and susceptibility testing is only required if patient still remains smear positive at the end of intensive phase.

4.3.3 At the end of treatment

Two specimens should be sent after 5 months of treatment for new patients and 7 months for re-treatment cases.

4.4 Role of other investigations in TB control

4.4.1 Chest X-rays

While chest X-rays are quick and convenient, reliance on them as the primary source for confirmation of diagnosis results in unnecessary treatment. X-rays are necessary in suspects who cannot produce sputum and they must therefore be interpreted in the light of their history and clinical findings.

Many diseases mimic TB on chest X-rays and this may lead to incorrect diagnosis. X-rays may show lung fibrosis or destruction due to old TB and this may also lead to over diagnosing of pulmonary TB.

Indications when chest X-rays are needed

1. When the sputum results are positive:
- Suspected complications, e.g. a breathless patient needing specific treatment (pneumothorax or pleural effusion).
- Frequent or severe haemoptysis.
- To help in diagnosing other lung diseases.
- Only one of the two pretreatment smears is positive.

2. When the sputum results are negative:
If you clinically still suspect TB despite negative smears, the patient should have a chest X-ray to help you make a decision regarding diagnosis and treatment.

3. During and at the end of treatment:
These will only be necessary if there are specific clinical reasons and the progress is not satisfactory.

4.4.2 Culture and drug susceptibility testing

Culture is more sensitive than smear microscopy, detecting a higher proportion of cases among patients with symptoms. The specificity is also higher as each live bacillus forms colonies on culture. However it is an expensive and slow diagnostic technique, not accessible to most patients and takes at least 4 weeks to provide a definitive result. Culture should be used only for paucibacillary tuberculosis patients who are not easily diagnosed by microscopy, such as smear negative pulmonary and extra-pulmonary tuberculosis.

Indications for the need to use culture

- History of previous unsuccessful TB treatment (interruption, failure, relapse).
- In cases where drug susceptibility testing is necessary.
- Patients who remain positive at the end of the intensive phase of treatment and or at the end of the treatment period.
- Patients who have two negative smears, not responded to a course of antibiotics and clinically TB is suspected.

4.4.2.1 Culture methods

Solid medium most commonly used for culture:

1. Lowenstein Jensen Medium (LJ) - this is the conventional egg based medium
2. Middle Brook 7H10/ 7H11- agar based medium

The liquid medium commonly used for culture:

1. Semi-automated Radiometric System BACTEC 460, which uses radiation technology.
2. Automated Non-Radiometric Systems, which use fluorometric technology - Mycobacterial Growth Indicator Tube (MGIT) and the colorimetric technology - BacT/ALERT Instrument

These are used in conjunction with solid medium as back up. The detection of bacilli occurs within seven to fourteen days with liquid medium as compared to three to four weeks with solid medium.

4.4.2.2 Drug susceptibility testing

Susceptibility tests are used to determine the susceptibility or resistance of a patient's bacillary strain to the different anti-tuberculosis drugs.

There are two types of susceptibility testing

- **Indirect:** performed after obtaining colonies in culture before testing and results are available only two to three months after sampling
- **Direct:** performed directly on the sample if it is rich in bacilli. In which case the results are available in 4-6 weeks

4.5 Tuberculin Skin Test

The tuberculin test has limited value in clinical work, especially where TB is common. The tuberculin test measures the body's immune system response to an injection of tuberculin purified protein derivative (PPD). Following infection with M. tuberculosis, a person develops hypersensitivity to tuberculin. Tuberculin injected into the skin of an infected person produces a delayed local reaction after 24-48 hours. We quantify this reaction by measuring the diameter of skin duration at the site of the reaction. Various conditions may suppress this reaction. The reaction indicates hypersensitivity. In other words, the reaction only shows that the person has at some time been infected with M. tuberculosis.

Note: A tuberculin test does not measure immunity. By itself, it does not indicate the presence or extent of tuberculosis disease; it only indicates infection.

The Mantoux test injects a known amount of PPD between layers of skin (intradermally) - ensure that the injection goes into and not under the skin. Measure the reaction to the test at the site of the injection 48-72 hours later. Measure the diameter of the reaction at widest point of the raised, thickened area, then record the results in millimetres. To help measure accurately, mark the edges of the duration at the widest point with a pen and measure the exact distance between the two points.

4.5.2 What does a positive tuberculin skin test mean?

4.5.1 Interpreting positive skin test results

Tuberculin Test		Previous BCG	No previous
BCG	HIV+		

- A positive test indicates infection with TB, but not necessarily TB disease.
- In a child under 5 years a strongly positive skin test indicates recent (6 weeks or more) infection that is a risk factor for progression to disease. In the presence of other features, i.e. history of TB contact, signs and symptoms of TB and X-ray changes, a positive tuberculin skin test is suggestive of TB disease in children.

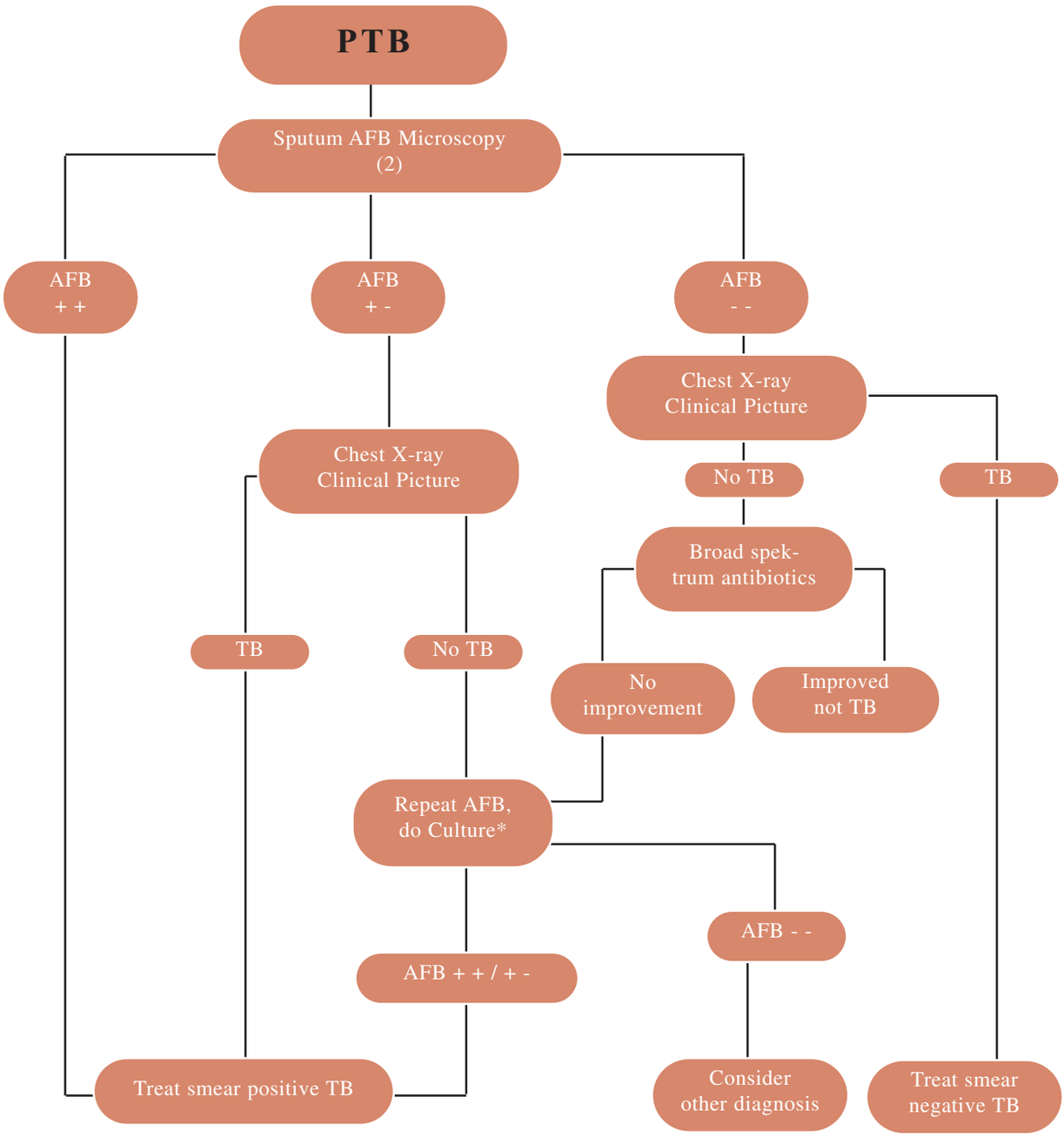
A positive reaction occurs after previous BCG immunisation and should remain positive for several years thereafter. This reaction is usually weaker than the reaction to natural infection of *M. tuberculosis.*

4.5.3 What does a negative tuberculin skin test mean?

A negative tuberculin skin test does not exclude TB. Various conditions may cause a negative reaction even if a child has TB. Conditions that may suppress the tuberculin skin test and give a false negative result include: HIV infection, malnutrition, severe viral infections (e.g. measles, chicken pox), cancer, immuno-suppressive drugs (e.g. steroids), severe disseminated TB.

- A positive reaction is only one piece of evidence in favour of the diagnosis in children.
- Because of increased risk, children under the age of 5 years who have a positive skin test and no symptoms and signs of TB should be put into chemoprophylaxis (Isoniazid 5mg/kg) for six months.

4.6 Management plan for pulmonary tuberculosis (PTB)



*Culture results should not delay the intiation of theraphy; the decision to treat pulmonary TB can be based on the history, clinical findings and chest x-ray findings, where the smear is negative or one negative and the other positive.

5 TB case definitions

The diagnosis of TB refers to the recognition of an active case, i.e. a patient with symptomatic disease due to M. tuberculosis. Beyond making the diagnosis of TB, it is also necessary to define the type of TB case for appropriate treatment and the outcome of treatment for evaluation.

5.1 Why case definitions?

- For proper patient registration and case notification.
- To evaluate the trend in the proportions of new smear-positive cases and smear-positive relapse and other treatment cases.
- To allocate cases to standardised treatment categories.
- For cohort analysis.

5.2 Why match treatment to standardised category?

- To allow priority to be given to infectious cases.
- To avoid under-treatment of sputum smear-positive cases and therefore to prevent acquired resistance.
- To increase cost-effective use of resources and to minimise side-effects for patients by avoiding unnecessary over-treatment.

5.3 What determines case definitions?

- Site of TB disease.
- Severity of TB disease.
- Bacteriology (sputum smear result).
- History of previous treatment of TB.

5.3.1 Site of TB disease: pulmonary or extra-pulmonary

- Pulmonary TB refers to disease involving the lung parenchyma. Therefore tuberculous intrathoracic lymphadenopathy (mediastinal and/or hilar) or tuberculous pleural effusion, without radiographic abnormalities in the lungs, constitute a case of extra-pulmonary TB.
- A patient with both pulmonary and extra-pulmonary TB constitutes a case of pulmonary TB.
- The case definition of an extra-pulmonary case with several sites affected depends on the site representing the most severe form of disease.
- Extra-pulmonary TB refers to TB of the organs other than the lungs: e.g. pleura, lymph nodes, abdomen, genito-urinary tract, skin, joints and bones, meninges.

5.3.2 Severity of disease

Severe extra pulmonary disease	Less severe extra pulmonary disease
Meningitis	Lymph node
Military	Bone (excluding spine)
Pericarditis	Peripheral joint
Peritonitis	Adrenal gland
Bilateral or extensive pleural effusions	Pleural effusion (unilateral)
Spinal	
Intestinal	

5.3.3 Bacteriology or sputum smear result

Smear-positive PTB case:

- There are at least 2 sputum smears positive for AFBs or
- 1 sputum smear positive for AFBs and chest X-ray abnormalities consistent with active TB or culture positive TB, or 1 sputum smear and clinically ill.

It is advisable that even if the first specimen is positive pre-treatment, another specimen should be taken. This will reduce the chances of a false-positive result as administrative errors may occur.

Smear-negative PTB case:

- At least 2 sputum smears are negative for AFBs.
- Chest X-ray abnormalities are consistent with active TB.

5.3.4 History of previous treatment

It is important to define a case according to whether or not the patient has previously received TB treatment in order to identify those patients at increased risk of acquired drug resistance and prescribe appropriate treatment.

New case:

A patient who has never had treatment for TB or who has taken anti-tuberculosis drugs for less than four weeks.

Re-treatment case:

A patient who has taken treatment for TB before and either relapsed, defaulted or had treatment failure.

- **Relapse:** A sputum smear positive pulmonary TB patient who received treatment and was declared cured (sputum smear negative) at the end of the treatment period and now developed sputum smear positive pulmonary TB again.
- **Treatment after failure:** A pulmonary TB patient who is still sputum smear positive at the end of the treatment period.
- **Treatment after default:** A patient who completed at least one month of treatment and returns after having interrupted treatment for two months or more, and still smear-positive (sometimes smear-negative but still with active TB as judged on clinical and radiological assessment).

Other:

- **Transfer out:** A patient already registered for treatment in one district who has been transferred to another to continue treatment.
- **Chronic case:** Patient who remains sputum smear positive after completing a supervised re-treatment regimen.

5.4 Recording treatment outcome in smear-positive TB

Note: Although smear-negative pulmonary cases and extra-pulmonary cases may also be treatment failures, relapses or chronic cases, this should be supported by pathological or

patients

- **Cure:** Patient who is smear-negative at, or one month prior, to the completion of treatment and also on at least one previous occasion.
- **Treatment completed:** Patient who has completed treatment but without proof of cure, smear results are not available on at least two occasions prior to the completion of treatment.
- **Treatment failure:** Patient who remains or is again smear-positive at five months after starting treatment.
- **Died:** Patient who dies for any reason during the course of TB treatment.
- **Treatment interrupted:** Patient whose treatment was interrupted for more than two consecutive months before the end of the treatment period.
- **Transfer out:** Patient who has been transferred to another reporting unit (e.g. district) and for whom the treatment outcome is not known.
- **Moved:** Patient who is moved to another facility within the same district.

6 Extra-pulmonary tuberculosis

Extra-pulmonary tuberculosis covers all forms of tuberculosis in which the disease process occurs outside the lungs. Many forms of extra-pulmonary tuberculosis originate from lymphatic or haematogenic spread of mycobacteria from a primary focus in the lung. Diagnosis of extra-pulmonary TB is often difficult, so diagnosis may be presumptive after excluding other conditions and may require invasive procedures to obtain diagnostic specimens.

The most common types of extra-pulmonary tuberculosis are:

- TB meningitis
- TB lymphadenitis
- Miliary tuberculosis
- TB Pleural effusion
- Tuberculous empyema
- Tuberculous pericardial effusion
- Ascites
- TB of the bones

The basic principles of treatment for pulmonary tuberculosis also apply to extra-pulmonary forms of the disease. Regimens of 6 months are supposed to be as effective in extra-pulmonary as in pulmonary disease. In some instances of severe disease longer therapy may be necessary. Such a decision should be taken by a specialist. Bacteriologic evaluation of extra-pulmonary tuberculosis may be limited by the relative inaccessibility of the sites of disease. Thus response to treatment often must be judged on the basis of clinical and radiographic findings.

The use of adjunctive therapies such as surgery and corticosteroids is more commonly required in extra-pulmonary tuberculosis than in pulmonary disease. Corticosteroid treatment is often used in treating some forms of extra-pulmonary tuberculosis, specifically meningitis and pericarditis. Treatment recommendations are also complicated by the paucity of data from controlled clinical trials of extra-pulmonary forms of TB.

Many specialists strongly believe that treatment for severe forms of extra-pulmonary TB (meningitis, military, pericarditis, spine) should be given for 9 months instead of the WHO recommended 6 months regimen. The continuation phase is extended from 4 months to 7 months. The decision to extend treatment should only be made by a specialist after individual assessment of the patient. Certain severe forms of EPTB require treatment with steroids. A specialist managing the patient should also make such a decision.

6.1 TB Meningitis

Before the advent of effective anti-tuberculosis chemotherapy, tuberculous meningitis was uniformly fatal. Tuberculous meningitis remains a potentially devastating disease that is associated with a high morbidity and mortality. HIV-infected patients appear to be at increased risk for developing tuberculous meningitis but the clinical features and outcome of the disease are similar to those in patients without HIV infection. Several studies have been done to support this evidence. Patients presenting with more severe neurological impairment such as drowsiness, obtundation, or coma have a greater risk of neurological sequelae and a higher mortality. TB meningitis is life threatening with serious complications if not treated promptly:

- Patients present with gradual onset of headache and decreased consciousness.
- Examination reveals neck stiffness and positive Kernig's sign (flex one of the patient's legs at hip and knee with the patient lying on back, and then straighten the knee - resistance to straightening the knee and pain in the low back and posterior thigh suggest meningeal inflammation).

- Diagnosis rests on clinical grounds and lumbar puncture to examine cerebrospinal fluid and the following features indicate a positive test:
  - Clear CSF
  - Elevated pressure
  - High levels of protein (>1g/ l)
  - High lymphocyte count (30-300/mmΔ)
  - Low glucose
- Patients with suspected TB meningitis should be referred to hospital without delay.

6.1.1 Differential diagnosis for TB meningitis

Disease	White Cell count	Protein	Glucose	Microscopy
Tuberculous meningitis	Elevated L > PMN PMN (raised initially)	Increased	Decreased	Presence of AFB (rare)
Inadequately treated bacterial meningitis	Elevated bothPMN and L	Increased	Decreased	Presence of bacteria after Gram staining (rare)
Viral meningitis	Elevated L > PMN	Increased	Normal	Negative
Cryptococcal meningitis	Elevated L > PMN	Increased	Decreased	Presence of parasites after India ink staining.
Acute syphilis	Elevated L > PMN	Increased	Normal	
Late stage Trypanosomiasis	Elevated L > PMN	Increased	Decreased	Motile trypanosomes
Tumour (carcinoma/ Lymphoma)	Elevated L > PMN	Increased	Decreased	Cytology shows malignant cells
Leptospirosis	Elevated L > PMN	Increased	Decreased	Leptospires
Amoebic meningitis	Elevated L > PMN	Increased	Decreased	Amoebae

6.2 Tuberculous Lymphadenopathy

- Persistent generalized lymphadenopathy (PGL) develops in up to 80% of HIV- infected individuals and requires no treatment - in PGL, lymph nodes are non- tender, <2 cm in size and symmetrical.
- Lymph node disease, including tuberculous lymphadenopathy, should be suspected if lymph nodes are tender, painful, nonsymmetrical, matted, fluctuant, rapidly growing or associated with fever, night sweats or weight loss.
- If clinical features suggest a cause of lymphadenopathy other than PGL, refer to a doctor who will do a needle (18G or 19G) aspirate of the lymph node (TB is diagnosed if the aspirated material is caseated and a smear of the aspirate reveals acid-fast bacilli).
- If no diagnosis is made after a needle aspirate, a lymph node biopsy should be done.
- Tuberculosis may also cause mediastinal or intra-abdominal lymphadenopathy which may be detected by X-ray, ultrasound or computerised axial tomography (CT scan) - this may be treated empirically, unless the nodes are accessible to aspiration at a tertiary health facility, aspiration may be guided by CT scan, fluoroscopy or ultrasound.

6.3 Miliary TB

Miliary TB results from widespread blood borne dissemination of TB bacilli. This is either the consequence of a recent primary infection or the erosion of a tuberculous lesion into a blood vessel.

6.3.1 Clinical features:

The patient presents with constitutional features (fever, night sweats and weight loss). He may have hepatosplenomegaly and choroidal tubercles (fundoscopy). Miliary TB is an under-diagnosed cause of end stage wasting in HIV-positive individuals.

6.3.2 Diagnosis:

Chest X-ray shows diffuse, uniformly distributed, small miliary nodules ("miliary" means "like small millet seeds"). Full blood count may show pancytopenia (this may also be seen as a result of HIV). Liver function tests may be abnormal. Bacteriological confirmation is sometimes possible from sputum, C.S.F., or bone marrow.

6.4 Tuberculous Serous Effusions

Inflammatory tuberculous effusions may occur in any of the serous cavities of the body, i.e. pleural, pericardial or peritoneal cavities. They are a common form of TB in HIV- positive patients.

- Patients usually have systemic and local features.
- Microscopic examination of the aspirates from tuberculous serous effusions rarely show AFB because the fluid forms as an inflammatory reaction to TB lesions in the serous membrane.
- TB culture is of no immediate help because a culture result takes up to six weeks or more.
- The aspirate is an exudate (the protein content is more than 30g/L). A biochemical test is not required to diagnose an exudate: let the aspirated fluid stand for a while - if it clots, it is an exudate.
- In populations with a high prevalence of HIV, TB is the commonest cause of an exudative serous effusion.

6.5 Tuberculous Pleural Effusion

Typical clinical features are chest pains, breathlessness, tracheal and mediastinal shift away from the side of the effusion and decreased chest movement and stony dullness on percussion on the side of the effusion.

6.5.1 Diagnosis

- Chest X-ray shows unilateral, uniform white opacity, often with a concave upper border.
- Pleural aspiration: the fluid is straw coloured, an exudate, protein content > 30g/l and is usually straw coloured, and the white cell count is high [1 000 - 2 500 per mmΔ] with predominantly lymphocytes, the Adenosine Deaminase (ADA) which is a measure of the lymphocyte count is raised > 30 IU
- Since the number of bacilli present is relatively small, AFB are not usually seen on microscopy of centrifuged specimens of pleural fluid, however, culture may be positive. If facilities are available, a closed pleural biopsy can be done with an Abrams needle for histological diagnosis. Since the distribution of TB lesions in the pleura is patchy, the diagnostic yield of closed pleural biopsy is about 75% and multiple biopsies increase the yield.

Differential diagnosis of an exudative pleural effusion includes malignancy, post-pneumonic effusion and pulmonary embolism.

6.6 Tuberculous Empyema

This usually arises when a tuberculous cavity in the lung ruptures into the pleural space. The physical signs are the same as those of a pleural effusion, but aspiration reveals thick pus. Send the pus to the laboratory for examination for TB, Gram stain and bacterial culture. If facilities are available a closed pleural biopsy is useful for diagnosis.

The main differential diagnosis is bacterial empyema. A succussion splash is a splashing sound heard with the stethoscope while shaking the patient's chest - if heard, it indicates a pyopneumothorax (pus and air in the pleural space) - after chest X-ray confirmation, insert a chest drain with underwater seal.

6.7 Tuberculous Pericardial Effusion

Diagnosis usually rests on suggestive systemic features and ultrasound:

- Cardiovascular symptoms include: chest pain, shortness of breath, cough, dizziness andweakness due to low cardiac output, leg swelling, right hypochondrial pain (liver congestion), abdominal swelling (ascites).
- Cardiovascular signs include: tachycardia, low blood pressure/pulsus paradoxus, raised jugular venous pressure, impalpable apex beat, distant heart sounds, pericardial friction rub, signs of right-sided heart failure (eg, hepatosplenomegaly, ascites, and oedema).
- Chest X-ray may show a large globular heart, clear lung fields, and pleural effusion.
- ECG may show tachycardia, flattening of ST and T waves, low voltage QRS complexes.
- Treatment is the same as for all types of TB (see "Treatment of TB") but corticosteroids can be added. Treatment without pericardiocentesis usually results in resolution of tuberculous pericardial effusion.
- In cases of cardiac tamponade the effusion should be aspirated by a specialist. If not properly treated pericarditis may evolve towards constriction over the following months.

Note: In high TB/HIV prevalent populations, TB is the most likely treatable cause of pericardial effusion. It may be safer for the patient to start presumptive anti-TB treatment than to undergo diagnostic pericardiocentesis.

6.8 Peritoneal tuberculosis

Clinical features include systemic features and ascites with no signs of portal hypertension; there may be palpable abdominal masses (mesenteric lymph nodes). Bowel obstruction may develop from adhesion of caseous nodules to bowel.

6.8.1 Diagnosis

- Always do a diagnostic ascitic tap - the aspirated fluid is usually straw coloured, but is occasionally turbid or blood stained - the fluid is an exudate, usually with more than 300 white cells per mm^3 - white cells are predominantly lymphocytes (polymorphs predominate in spontaneous bacterial peritonitis which is a common complication of cirrhosis).
- Investigate for pulmonary TB.
- Abdominal ultrasound may show retroperitoneal or mesenteric lymph node enlargement
- Diagnosis is usually presumptive - in doubtful cases, a macroscopic examination and bacteriological or histological examination of the samples may be considered in a hospital where exploratory surgery or laparoscopy can be performed.

6.9 Tuberculosis of the spine

This is a severe form of tuberculosis when there are neurological sequelae. It is seen both in children, usually within three years following primary infection, and in adults. In many cases more than one intervertebral disc space is involved. As the disease develops, the vertebral body adjacent to the disc space is affected; an abscess is formed and spreads either forward towards the mediastinum or the retroperitoneal space, to the vertebral body with compression of the spinal cord, or back along the vertebral column eventually appearing as a subcutaneous "cold" abscess. Collapse of adjacent vertebral bodies affected by tuberculosis may lead to angulated kyphosis. Thrombosis of the anterior spinal artery caused by the inflammation may lead to transverse myelitis and paralysis.

Involvement of cervical vertebrae may signal its presence by pain in the neck and shoulders. It may lead to rigidity of the neck, a cervical cold abscess behind the sternocleidomastiod muscle, and more rarely neurological signs leading to progressive tetraplegia.

Involvement of the dorsal vertebrae is indicated by localized back pain, deformity of the spine, and in extreme cases an angulated kyphosis (gibbus): the chief risk is spinal cord compression and paraplegia. In lower back lesions the abscess can appear behind the trunk.

Involvement of the lumbar vertebrae is indicated by lower back pain. The abscess can drain along the psoas muscle towards the inguinal area or towards the spine. A large draining abscess in the inguinal region "cold abscess" is indicative of tuberculosis of the spine.

Clinical features of vertebral tuberculosis are:

- Back pain, stiff back, reluctance to bend the back
- Referred pain radiating out from the site of origin (cervico-brachial, intercostals, crural, sciatic)
- Localised swelling, sometimes an obvious lump or abnormal curvature of the spine
- A child that refuses to walk, paralysis or weakness of the lower limbs due to pressure on the spinal cord.

Physical examination is non-specific until complications (gibbus, cold abscess, and neurological signs) appear. X-rays of the spine show disc space narrowing and erosion of the adjacent vertebral bodies, wedge shaped collapse and angulation. Biopsy of abscess if possible may be done for microscopy and culture to confirm the diagnosis.

A well-fitted orthopaedic brace is sometimes needed to immobilise the affected area. Surgical treatment is necessary if there is compression of the spinal cord and the patient has weakness or paraplegia of the lower limbs - these patients should be referred to a specialist urgently. Differential diagnosis includes degenerative disc disease, infectious spondylitis and cancerous vertebral metastases.

Note: The principles of treatment for patients with EPTB are the same as for PTB (Regimen 1 for new cases and Regimen 2 for re-treatment cases). The severe forms of extra-pulmonary TB may be treated for a period of nine months by extending the continuation phase (two months intensive and seven months continuation phase). The decision to extend treatment should only be made by a specialist after individual assessment of

7 Principles of treatment

The key to stop the spread of TB in a community is to start treating as soon as possible patients who are coughing up living TB bacilli. For treatment to be effective, it is crucial that correct drugs are given for the correct period of time.

The aims of the treatment of TB are to:

- cure the patient of TB;
- prevent death from TB or its complications;
- decrease transmission of TB to others; and
- prevent the development of acquired drug resistance

7.1 The essential TB drugs

There are three main properties of anti-TB drugs: bactericidal, bacteriostatic (sterilising) and the ability to prevent resistance. The anti-TB drugs possess these properties to different extents.

In a tuberculosis lesion there are various populations of bacilli:

- Metabolically active
- Intermediately active
- Semi dormant bacilli (persisters), which undergo occasional spurts of metabolism.
- Dormant bacilli which may become active

Different anti-TB drugs act against different populations of bacilli. Bacilli may occur extra-cellularly or intra-cellularly. The pH in the intercellular spaces is usually neutral or alkaline, whereas it is acid intra-cellularly. Some TB drugs act best in an acid environment; others better in a more alkaline pH.

Isoniazid (H) acts:

- On both alkaline and acid media (mainly alkaline)
- On intra-cellular and extra-cellular bacilli.
- Predominantly on rapid and intermediate growing bacilli and has limited action on slow growers.

Its action commences after 24 hours of administration. It is bactericidal with a high potency, killing more than 90% of the total population of TB bacilli during the first few days of treatment.

Rifampicin (R) acts:

- In both alkaline and acid media.
- On both intracellular and extracellular bacilli.
- On all bacterial populations including dormant bacilli.

Action commences within one hour of intake. It is bactericidal with a high potency therefore rifampicin is the most effective sterilising anti- TB drug and makes short course chemotherapy possible

Pyrazinamide (Z) acts:

- Only in an acid medium.
- On intracellular bacilli only (inside macrophages).
- Mainly on slow growing bacilli.

Achieves its sterilising action with 2-3 months. It is bactericidal with a low potency.

Essential TB drug (abbreviation)	Recommended dose (dose range in mg/kg)	
	Five times per week	Three times per week
Isoniazid (H)	5 (4 - 6)	10 (8 - 12)
Rifampicin (R)	10 (8 - 12)	10 (8 - 12)
Pyrazinamide (Z)	25 (20 - 30)	35 (30 - 40)

Ethambutol (E) acts:
- In both alkaline and acid media.
- On all bacterial populations.

It is bacteriostatic with a low potency therefore minimises the emergence of drug resistance.

Streptomycin (S) acts:
- Only in an alkaline medium.
- Mainly on extracellular bacilli.
- On rapidly growing bacilli.

Streptomycin is bactericidal with a low potency.

7.2 Fixed dose combination tablets (FDC)

The use of FDCs has several advantages over individual drugs. First, prescription errors are likely to be less frequent as dosage recommendations are more straightforward and adjustment of doses according to patient weight is easier. Secondly, the number of tablets to be ingested is fewer and thus may encourage patient adherence, thirdly, if treatment is not observed, patients cannot be selective in the choice of drugs to ingest.

7.3 Recommended standard treatment regimens for adults (8 years and older)

7.3.1 New case (a patient who has never been treated for TB in the past or who has taken anti-tuberculosis drugs for less than four weeks)

Treatment regimens have an initial (or intensive) phase lasting 2 months and a continuation phase usually lasting 4 months. During the intensive phase consisting of 4 drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol), there is rapid killing of tubercle bacilli. Infectious patients become rapidly non-infectious (within approximately 2 weeks). Symptoms abate. The vast majority of patients with sputum smear-positive TB become smear-negative within 2 months. In the continuation phase fewer drugs (isoniazid, rifampicin) and are necessary but for a longer time. The sterilizing effect of the drugs eliminates the remaining bacilli and prevents subsequent relapse.

7.3.2 Re-treatment cases

Previously treated patients include all TB patients who were treated as new cases for more than one month in the past and are now smear or culture positive (failure, relapse, return after default). They have a higher likelihood to have drug resistance, which may have been acquired through inadequate prior chemotherapy. The re-treatment regimen has an initial phase of 3 months - two months with 5 drugs (isoniazid, rifampicin, pyrazinamide, ethambutol and streptomycin), one month with 4 drugs ((isoniazid, rifampicin, pyrazinamide, ethambutol) and a continuation phase of 5 months with 3 drugs (isoniazid, rifampicin, ethambutol). Three drugs (rifampicin, Isoniazid, Ethambutol) are given throughout the treatment period. This regimen can cure patients excreting bacilli still fully sensitive to the drugs and those excreting bacilli resistant to isoniazid and or streptomycin. Under proper case management conditions, MDR-TB cases are those most at risk of failure in the re-treatment regimen.

7.4 Standard code for TB treatment regimen

Each antituberculosis drug has an abbreviation: R (Rifampicin), H (Isoniazid), Z (Pyrazinamide), E (Ethambutol) and S (Streptomycin). A TB treatment regimen consists of two phases: an initial phase and continuation phase. The number before a phase is the duration of that phase in months. Letters in parentheses indicates fixed dose combinations of those drugs. A subscript number (i.e. 3) after a letter or letters in parentheses indicates the number of doses of that drug per week. If there is no subscript number, treatment is daily (five

times a week).

7.4.1 Examples

2(HRZE)/ 4 (HR) 3

The initial phase is 2 (HRZE) The duration of the phase is two months. Drug treatment is daily, with isoniazid, rifampicin, pyrazinamide and ethambutol in fixed dose combinations. The continuation phase is 4 (HR) 3 The duration is four months, with isoniazid and rifampicin, in fixed dose combinations, three times per week.

2(HR) ZE/ 6 (HE)

The initial phase is 2 (HR) ZE. The duration of the phase is two months. Drug treatment is daily, with isoniazid, rifampicin in fixed dose combination plus pyrazinamide and ethambutol. The continuation phase is 6 (HE). The duration of the phase is six months. Drug treatment is daily, with isoniazid and ethambutol in fixed dose combination.

Effective anti-TB drug treatment means properly applied Short Course Chemotherapy:

Regimen 1: New cases, age above 8 years and adults

New smear-positive patients, new smear-negative patients and extra-pulmonary TB.
(R-Rifampicin, H-Isoniazid, Z-Pyrazinamide, E-Ethambutol)

Pre-treatment body weight	Two months initial phase given FIVE times a week	Four months continuation phase			
		When given THREE times a week		When given FIVE times a week	When given times a
	RHZE (150,75, 400,275)	RH (150,75)	RH (300,150)	RH (150,150)**	RH (300,150)
30-37 kg	2 tabs	2 tabs		2 tabs	
38-54 kg	3 tabs	3 tabs		3 tabs	
55-70 kg	4 tabs		2 tabs		3 tabs

Regimen 2: Re-treatment cases

Previously treated TB patients after cure, after completion, default and failure.
(R-Rifampicin, H-Isoniazid, Z-Pyrazinamide, E-Ethambutol)

Pre-treatment body weight	Two months initial phase given FIVE times a week		3rd month initial phase	Five months continuation phase When given FIVE times a week			
	RHZE (150,75, 400,275)	Streptomycin * (g)	RHZE (150,75,400 ,275)	RH (150,75)	E (400)	RH (300,150)	E (400)
30-37 kg	2 tabs	0.5	2 tabs	2 tabs	2 tabs		
38-54 kg	3 tabs	0.75	3 tabs	3 tabs	2 tabs		
55-70 kg	4 tabs	1.0	4 tabs			2 tabs	3 tabs
>71 kg	5 tabs	1.0	5 tabs			2 tabs	3 tabs

Note:	Fixed dose combination tablets available for adults	
	RHZE (150,75,400,275mg) RH(300,150mg)	RH(150,75mg) RH(150,150mg)

Regimen 2: Re-treatment cases

Previously treated TB patients after cure, after completion, default and failure.
(R-Rifampicin, H-Isoniazid, Z-Pyrazinamide, E-Ethambutol)

Pre-treatment body weight	Two months initial phase given FIVE times a week		3rd month initial phase	Five months continuation phase When given THREE times a week			
	RHZE (150,75, 400,275)	Streptomycin * (g)	RHZE (150,75,400 ,275)	RH (150, 150) **	E (400)	RH (300,150)	E (400)
30-37 kg	2 tabs	0.5	2 tabs	2 tabs	2 tabs		
38-54 kg	3 tabs	0.75	3 tabs	3 tabs	3 tabs		
55-70 kg	4 tabs	1.0	4 tabs			3 tabs	4 tabs
>71 kg	5 tabs	1.0	5 tabs			3 tabs	4 tabs

* *Streptomycin should NOT be given during pregnancy and to those over 65 years.*
** *RH (150,150) should only be used when treatment is given THREE times weekly in the continuation phase only.*

- Keep strictly to the correct dose and the duration of treatment.
- Cure of the new PTB patients depends on taking Regimen 1 for 6 months.
- Cure of re-treatment PTB patients depends on taking Regimen 2 for 8 months.

7.5 Side effects of the main anti- TB drugs and their management

Patient must take treatment 5 days a week, Monday to Friday. No treatment is necessary on Saturday and Sunday. In hospitals, treatment is given for seven days a week. Intermittent therapy (3 times a week), if used, may be given in the continuation phase only.

No trials of therapy should be given. A patient either has TB and should be treated, or

7.5.1 Isoniazid (H)

Adverse effects:

- Peripheral neuropathy (tingling and numbness of the hands and feet).

- Hepatitis, more often in patients older than 35 years (rare).
- Generalised skin rash (occurs rarely).
- Fever.
- Joint pains.

Management:
- **Mild itching:** continue drug treatment, reassure the patient, give calamine lotion and if necessary antihistmine.
- **Fever and generalised skin rash:** stop all drugs and give antihistamine.
- **Neuropathy:** give 10 mg -25 mg of pyridoxine, daily.
- **Drug induced hepatitis:** stop anti-TB treatment, do liver function tests. If there is a loss of appetite, jaundice and liver enlargement, do not give treatment for at least 1 week or until the liver functions have returned to normal. In most patients INH can usually be given later without the return of hepatitis.

Isoniazid inhibits the breakdown of epileptic drugs i.e. phenytoin and carbamazepine. Dosages of these drugs may need to be reduced during the treatment period.

7.5.2 Rifampicin (R)

Adverse effects:
- **Gastro-intestinal:** nausea, anorexia and mild abdominal pain, diarrhoea occurs less frequently.
- **Cutaneous reactions:** mild flushing and itchiness of the skin.
- **Hepatitis:** This is uncommon unless the patient has a history of liver disease or alcoholism.
- Serious side effects like influenza syndrome and shock may occur in patients who take the medicine intermittently instead of daily. Stop the treatment and refer the patient.
- The patient should be warned that rifampicin colours the urine, sweat and tears pink (urine looks orange-pink).

Drug interactions:
Rifampicin stimulates liver enzymes, which may the break down other drugs more rapidly than normal, e.g. oral

A severely ill patient may die without anti-TB drugs. In this case, treat the patient with 2 of the least hepatotoxic drugs, streptomycin and ethambutol. When the hepatitis resolves,

anticoagulants (warfarin), oral diabetic drugs, digoxin, phenobarbitone and other anti-epileptics.
Contraception:
The dose of contraceptives should be increased in patients on rifampicin. Depo provera 150mg should be given 8 weekly instead of 12 weekly. Nur-Isterate 200mg should be given 6 weekly instead of 8 weekly. Combined oral contraceptives with at least 0.05mg of ethinyloestradiol should be prescribed. The pill free interval should be shortened from 7 to 4 days. Intra Uterine Contraceptive Devices (IUCDs) may be recommended. WARN the patient that the effect of rifampicin may last up to 2 months after the treatment is stopped.

7.5.3 Streptomycin (S)

Adverse effects:
- Cutaneous hypersensitivity, rash and fever.
- Ototoxicity (damage to eighth cranial nerve). Damage to the vestibular (balancing) apparatus is shown by dizziness, sometimes with vomiting. Unsteadiness is more marked in the dark.
- Deafness.
- Anaphylaxis. Streptomycin injection may be followed by tingling around the mouth, nausea and occasioally by sudden collapse. Treat as for any anaphylactic reaction and do not give streptomycin again.

- Deafness in unborn children. Streptomycin should be avoided during pregnancy because it crosses the placenta.

Contra-indications:
Do not give to patients with existing renal disease, as it will impair renal function more. Older people (>65 years) have reduced renal function and should not be given streptomycin.

Management:
- Skin reactions: treat as for allergic skin reactions.
- Damage to vestibular apparatus: treatment must be stopped immediately.
- Ringing in the ears or loss of hearing: if the drug is stopped immediately, the symptoms will usually clear over weeks, if not, the damage will be permanent.
- Do not give streptomycin to patient above 65 years, to pregnant women or to young children.

7.5.4 Ethambutol (E)

Adverse effects:
- Progressive loss of vision caused by retrobulbar neuritis, usually manifests first as loss of colour vision and usually presents after the patient has been on treatment for at least two months. This is usually caused by excessive doses of ethambutol.
- Skin rash.
- Joint pains.
- Peripheral neuropathy.

Management:
If the patient complains about visual disturbance, stop treatment immediately. Skin rashes and joint pains usually respond to symptomatic treatment.

Contra-indication:
Ethambutol should not be given to children under the age of 8 years who are unable to tell you that they are losing their sight. The patient should be warned about the possible changes in vision and informed to report any changes in the eyesight.

7.5.5 Pyrazinamide (Z)

Adverse effects:
- **Liver damage:** Anorexia, mild fever, tender enlargement of the liver and spleen may be followed by jaundice.
- **Arthralgia:** This is common and mild. The pain affects both large and small joints, the level of uric acid is increased and gout may occur.
- Skin rash on sun exposed areas.

Management:
- **Hepatotoxicity:** Do not give the drug again if severe hepatitis occurs.
- **Arthralgia:** Treatment with aspirin is usually sufficient. Allopurinol may be required for the treatment of gout.

7.5.6 Pyridoxine (Vitamin B6)

It is unnecessary to give pyridoxine routinely. The use of alcohol during drug therapy should be discouraged or restricted. However, pyridoxine should be added for TB patients who are alcohol abusers, pregnant, diabetic or epileptic. The protective dose is 10-25 mg daily. This dose should never be exceeded in pregnancy.

7.6 Symptom-based approach to management of drug side

	Drug(s) responsible	Management
Minor: Continue anti-TB drugs		
Anorexia, nausea, abdominal pain	Rifampicin	Give tablets last thing at night
Joint pains	Pyrazinamide	Aspirin
Burning sensation in feet	Isoniazid	Pyridoxine 25mg daily
Orange / red urine	Rifampicin	Reassurance
Major: Stop drugs responsible		
Skin itching / rash (anaphylactic reaction)	Streptomycin	Stop streptomycin, treat as for hypersensitivity reaction
Deafness (no wax on auroscopy)	Streptomycin	Stop streptomycin
Dizziness (vertigo and nystamus)	Streptomycin	Stop streptomycin if severe
Jaundice (other causes excluded)	Most anti-TB drugs dice resolves, then re-	Stop anti-Tb drugs until jaun introduce one by one
Vomiting and confusion (suspected drug-induced pre-icteric hepatitis)	Most anti-TB drugs	Stop anti-TB drugs, urgent liver function tests
Visual impairment	Ethambutol	Stop ethambutol
Generalised reaction, including shock and purpura	Rifampicin	Stop rifampicin

8 Monitoring the treatment response

Patients with sputum smear positive pulmonary tuberculosis should be monitored by sputum smear examination. These are the patients for whom bacteriological monitoring is possible. For patients with sputum smear negative PTB and EPTB, clinical monitoring is the usual way of assessing the response to treatment. In patients who were culture positive, culture can be used to confirm cure or treatment failure and to determine susceptibility pattern in failure cases.

8.1 New cases

Response to treatment should be monitored by sputum smear examination. In general, two sputum specimens should be collected for smear examination at each follow up sputum check. Sputum smears should be performed at the end of the intensive phase of treatment (second month) and in the last month of treatment period (sixth month). Negative sputum smears indicate good treatment progress. At the end of the second month of treatment, most patients will have a negative sputum smear and will then start the continuation phase of treatment. *If a patient has a positive smear at this time, this may indicate one of the following:*

- Most frequently, that the initial phase of therapy was poorly supervised and that patient adherence was poor
- Sometimes, that there is a slow rate of progress with sputum smear conversion, i.e. if a patient had extensive cavitations and heavy initial bacillary load
- Rarely, that the patient may have drug resistant TB that does not respond to first line drugs

Whatever the reason, if the sputum smears are positive at the end of the second month, the initial phase with four drugs is prolonged for one month, after which the smears are repeated and the continuation phase of treatment with two drugs is started. Sputum smears are then performed. If the patient is still positive at the end of the third month, cultures for sensitivity testing should be done in the last month of treatment (6th month). If the sputum is still positive the patient is categorised as a case of treatment failure and started on the re-treatment regimen afresh. At the same time culture and susceptibility should be done, if sensitive continued on the re-treatment regimen and if resistant referred accordingly.

If a patient has a negative smear at two months but positive at the end of the treatment period (in the sixth month), the patient should be declared a treatment failure and re registered as such and started on regimen 2 from the beginning. Sputum smear negative patients should be monitored clinically, body weight is a useful progress indicator. *At the end of the second month of treatment sputum smears should be done for the following reasons:*

- Error at the time of diagnosis.
- Drug resistance.
- Non adherence to treatment.

When the patient has completed the initial intensive phase of treatment and the sputum is negative, then the continuation phase of treatment can be started. If the sputum smears are positive at the end of the two months, the patient is classified as a treatment failure and started on the regimen 2 from the beginning.

8.2 Re-treatment cases

Sputum smear examination is done at the end of the intensive phase of treatment (end of the third month) and at the end of the treatment period (eighth month). If the patient is smear positive at the end of the third month, the initial phase of treatment with four drugs is extended by another month and sputum smears are examined again at the end of the fourth month. If still positive at the end of the fourth month, culture and sensitivity testing is done and patient started on the continuation phase until results are available. If resistant to two of the three drugs used in the continuation phase referred accordingly.

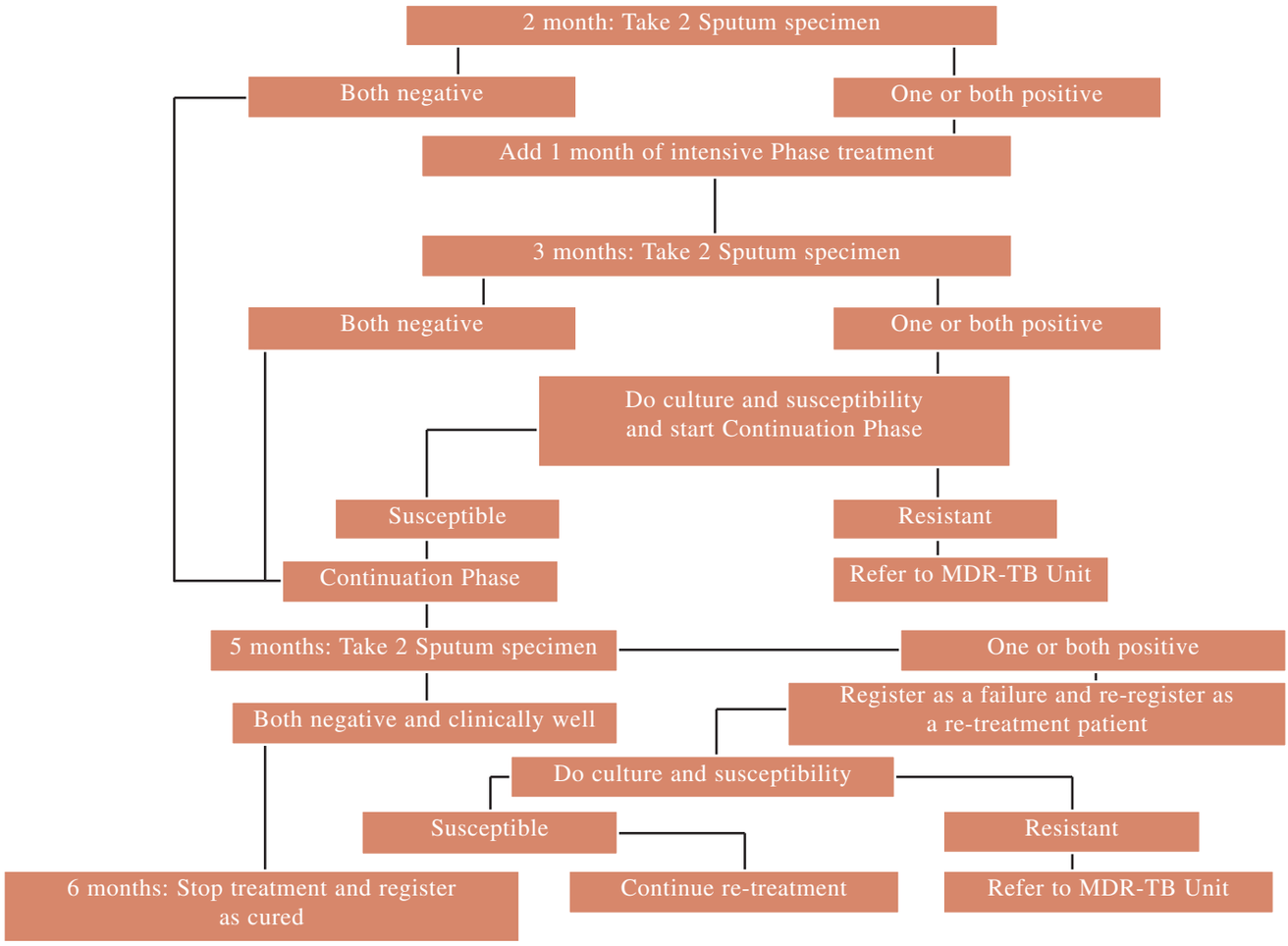
If the smears are negative at the end of the intensive phase the patient is started on the continuation phase of treat-

ment and smear examination repeated at the end of the treatment period if negative the patient is then documented as cured. If positive culture and sensitivity tests are conducted and patient documented as treatment failure and once results available referred accordingly.

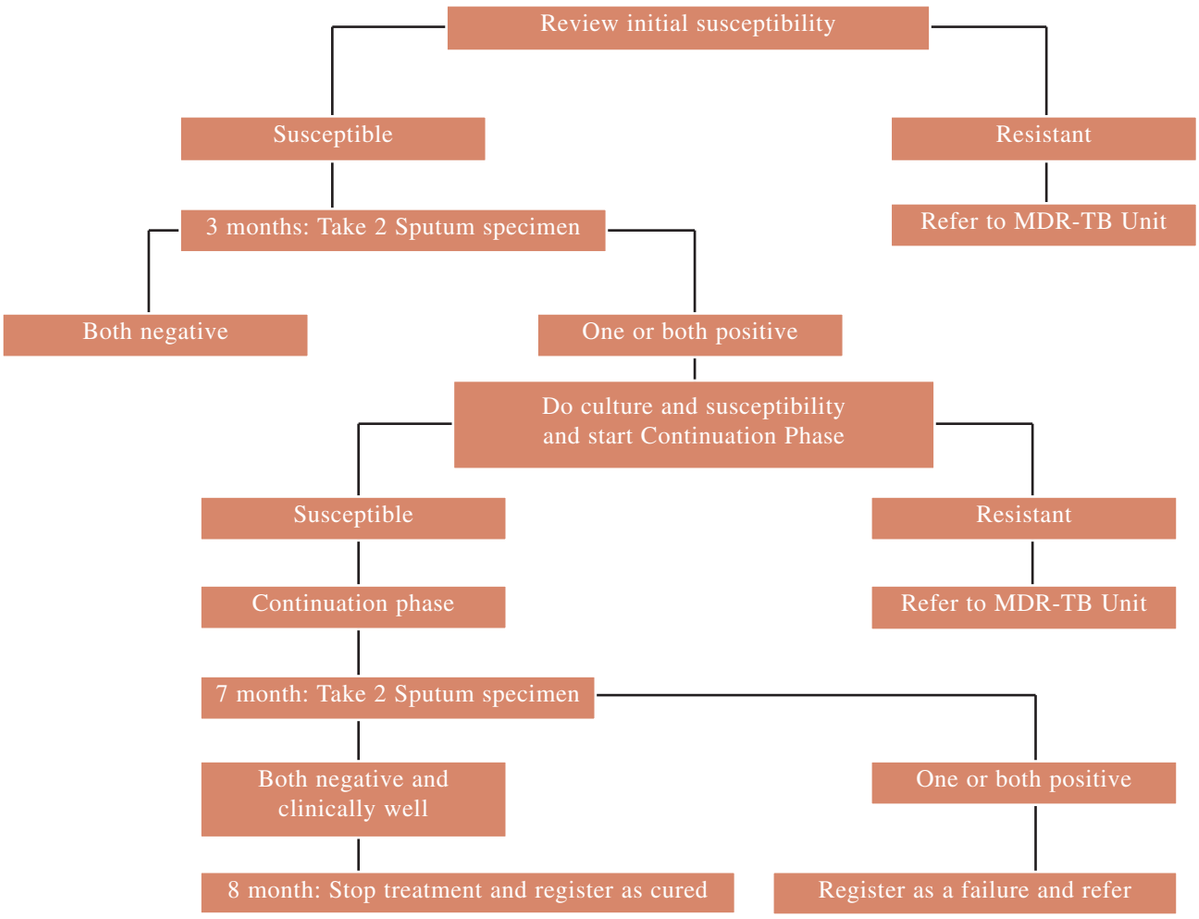
8.3 Extra-Pulmonary Tuberculosis

Response to treatment can be monitored only through clinical observation and as in smear negative disease the weight of the patient is a useful indicator.

Monitoring of new PTB adult patients.



Monitoring of retreatment adult patients



9 Adherence to treatment

The public health priority of the NTCP is to cure smear-positive cases, while preventing the emergence of drug resistance. Ensuring adherence to treatment is necessary to achieve this priority. TB is curable if patients are given a complete and uninterrupted course of drug therapy and if they take these medications as prescribed. However poor adherence to TB medication is a common problem resulting in inadequate treatment. *The consequences of inadequate and incomplete treatment are serious:*

- Prolonged illness and disability for the patient.
- Infectiousness of the patient causing continued transmission of TB in the community.
- Development of drug resistant TB.
- The possibility of death.

TB is a complex disease that carries biological, social, economic and cultural ramifications for the patient. Health care providers should be mindful of the strong impact this disease can have on all aspects of the patient's life and the need for a comprehensive approach to the management of the patient.

Although the necessary tools are available, the successful treatment of TB cannot be achieved by clinical medicine alone. Treatment success is influenced by the health care system and by the behaviours of both patients and health care providers. *Other factors that may influence treatment outcomes are:*

- Personal and social characteristics of patients and health care workers
- Culturally determined knowledge and beliefs of patients and providers
- Health care infrastructure that supports TB treatment.
- Quantity and quality of information about TB that is available to patients and the public.
- Extent of patient's knowledge about TB.
- Quality of training that the health care workers have received

Patients and health care workers share responsibility for treatment outcomes, therefore the provider must do every thing possible to educate, support, influence and persuade the patient to take their medication as prescribed and to complete treatment.

9.1 Adherence

Adherence to treatment means following the recommended course of treatment by taking all the prescribed medications for the entire length of time necessary. Patients' adherence is a key factor in treatment success. In many parts of the country, a significant proportion of patients stop treatment before the end, for various reasons. The premature interruption of treatment presents a problem for patients, their family members, those who care for them, and for health workers.

Promoting adherence through a patient-centered approach, which includes facilitating access to treatment, choosing with the patient the most convenient time and place for direct observation of treatment and, when possible, providing other social and medical services, is much more effective than spending resources on defaulter tracing. Facilitating access includes providing drugs and laboratory service for diagnosis free of charge, reducing the time and cost to the patient to obtain treatment, and providing good and rapid attention.

Convenience to the patient must be balanced with the assurance of regular drug intake and monitoring, important to give the patient the best chances of cure. When patients receive self-administered treatment, they often take drugs irregularly, and tracing is difficult and often unproductive. In addition, there is a much longer period between interruption of treatment and initiation of treatment after tracing the patient.

It is vital for health staff and community workers to offer polite and efficient attention, and to consider the patient's needs at every contact with the patient.

9.2 What is directly observed treatment (DOT)?

Directly observed treatment is an important element in the WHO recommended policy package for TB control. Directly observed treatment means that an observer watches the patient swallowing the tablets, in a way that is

sensitive and supportive to the patient needs. This ensures that a TB patient takes the right drugs, in the right doses, at the right intervals. In practice, it means providing a treatment supporter acceptable to the patients, to enable them to complete treatment.

The supporter may be a health worker or a trained and supervised community member. The district coordinator is responsible for coordinating training and monitoring the performance of the community treatment supporters. There must be a clearly defined line of accountability from the district coordinator to the clinics and treatment supporter. It is important to ensure confidentiality and that directly observed treatment is acceptable to the patient. The TB drugs should remain with the treatment supporter and only given to the patient at the time of intake.

9.3 Why directly observed treatment?

Directly observed treatment is required to ensure treatment adherence. It helps reinforce patient's motivation to continue treatment and counter the tendency of some to interrupt treatment, as it is impossible to predict who will or will not comply. Directly observed treatment also ensures the accountability of health care workers to ensure that patients take their TB treatment and helps prevent emergence of drug resistance.

DOT is recommended in:

- The initial phase of treatment, at least for all smear-positive cases.
- The continuation phase of rifampicin-containing (three/ five times weekly regimens.

It is therefore important to note that DOT is recommended for the entire period of treatment. If a TB patient misses one attendance for directly observed treatment, it is necessary to trace the patient back immediately.

9.4 How to apply directly observed treatment to fit patients' needs

A TB patient who has to travel far for treatment is less likely to adhere to treatment. One of the aims of the TB programme is to organize TB services such that the patient has TB treatment as close to home (or the workplace) as possible.

For those patients that live close to a health facility, it should be encouraged that they take treatment from the health facility. This should be the chosen alternative if it fits the patient's convenience. Some TB patients live far away from a health facility. For those patients that live far away from the health facilities the treatment supporter will be a community health worker or a trained local community member.

In general members of the patient's family should not be encouraged to be the treatment supporters but should provide the necessary support and encouragement to the patient to finish treatment. Collaboration with other programmes allows the identification of staff from these programmes (e.g. home-based care) who, with suitable training and monitoring, may support TB patients. For patients who are working DOT can be offered in their workplace provided there is a trained health care worker or colleague who can support the patient through out the treatment period and ensure that the patient reports to the clinic on the dates scheduled for follow up.

9.5 Community treatment supporters

The following points need to be considered when setting up community DOT:

- Existing community groups and organisations should first be approached to determine how they might be able to make a contribution to community TB care, rather than setting up new systems, groups and organisations.
- Selection of community volunteers should be a cooperative activity including health care workers involved in TB, patients, community representatives and community group leaders.
- Community volunteers need regular support, motivation, instruction and supervision by relevant staff to ensure that quality outcomes are maintained.
- Training requirements may vary depending on the setting, ranging from "on the job instruction" by NTP staff

to more formal short courses of instruction supported by regular updates
- Regular audit and reporting of results is important to define and clarify the community contribution to TB care in each program.

Implementation of directly observed treatment depends on the setting, facilities, resources and environment. There must therefore be flexibility in applying directly observed treatment, with adaptation in different ditricts and provinces. Major factors that influence treatment interruption are access to treatment (distance, transport costs, time and wages lost, quality and speed of drug delivery), knowledge level about TB and the need to complete treatment, and flexibility for transfer to another facility.

For any chosen method of supervision and administration of treatment, the programme must show high sputum smear conversion and cure rates, under routine conditions in both rural and urban areas. Within a province, a district that demonstrates a successful method of implementing directly observed treatment can be a model for other districts.

9.6 Interruption of treatment

Directly observed treatment adapted to patients' needs and to the working conditions of health care workers is certainly the best method of avoiding treatment interruption. However, even with directly observed treatment, there may be treatment interruptions.

9.6.1 Preventive measures to decrease treatment interruption

At the time of registration of a tuberculosis patient starting treatment, it is important to set aside enough time to meet with the patient (and preferably also with the patient's family members). This is an important opportunity to advise and counsel the patient. During this meeting it is vital to record the patient's physical address and other physical addresses (e.g. partner/ spouse, parents, work place, place of study) in order to maximize the probability of locating patients who interrupt treatment.

Where resources permit, it is helpful for a health staff member to accompany the patient to his/her residence following the initial meeting. Also, it is important to identify potential problems, which the patient may face during the initial phase of treatment. A visit to the patient's home before or during the initial phase of treatment allows verification of the patient's exact address and at the same time provides an opportunity to arrange for screening of all household contacts, especially children under the age of 5 years.

Health staff must inform the patient about the duration of treatment and the need to consult ahead of time in case of permanent or temporary change of address to facilitate continuation of treatment.

In the meeting with the patient at the end of the initial phase of treatment the patient can inform the health worker about plans (work, family, moving house) for the following months of the continuation phase of treatment. In addition, all visits of the patient to the health worker should reinforce the need for regular and complete intake of treatment and elicit any problem that may cause interruption.

9.6.2 Corrective measures to decrease the duration of treatment interruption

When a patient doesn't keep an arranged appointment to receive treatment, it is necessary to inquire after the patient, using the contact addresses previously obtained and appropriate means of tracing the patient. It is important to find out the cause of the patient's absence in order to take appropriate action and continue treatment.

9.6.3 What to do when a patient returns after interrupting treatment

The management of patients who have interrupted treatment is complex and takes into consideration multiple variables (immune status, degree of remission of the disease with the previous treatment, drug susceptibility),

Table 1: Actions in interruption of TB treatment

Interruption for less than one month			
· Trace patient · Solve the cause of interruption · Continue treatment and prolong it to compensate for missed doses.			
Interruption for one to two months			
Action 1	Action 2		
· Trace patient · Solve the cause of interruption	If smears negative or EPTB	Continue treatment and prolong it to compensate for missed doses	
· Do 2 sputum smears · While waiting, continue treatment	If one or more smears positive-Send sputum for culture and susceptibility	Treatment received: < 5 months	Continue treatment and prolong it to compensate for missed doses
		> 5 months	Regimen 1: start Regimen 2 Regimen 2: Treat un until culture & sensi tivity & refer
accordingly			
Interruption for two months or more (defaulter)			
Action 1	Action 2		
· Do 2 sputum smears + · Solve the cause of culture and susceptibility interruption	Negative smears or EPTB	Re start TB treatment on the same regimen that the patient was on, if the patient was still on the intensive phase, re start the intensive phase again and if the patient was on the continuation phase, start the continuation phase again	
	One or more smears positive	Regimen 1	Start Regimen 2
		Regimen 2	Restart treatment until culture & sensitivity, refer if resistant

which may be difficult to measure. A simple decision tree is suggested in table 1.

9.7 Strategies for improving Adherence

9.7.1 In adults

1) Quality interaction with the patient:

- Create a partnership.
- Ask patient whether they do take the TB drugs and do not assume that they do.
- Give each patient adequate time at each visit.
- Be positive do not intimidate or frighten the patient.

- Treat the person and not the disease.
- Understand and address different cultural beliefs and values.
- Adapt treatment to lifestyle.
- Make referrals to social welfare, where necessary.

2) Patient education:

- Give the vital information first in the patient interview
- Be conscious and clear with instructions as the patient might be anxious after hearing the diagnosis.
- Be clear about the length of the treatment regimen.
- Do not overload the patient with too much information at one time.
- Use educational materials that are culturally and linguistically appropriate for the patient.
- Assess the patient's beliefs about TB and if possible integrate the beliefs into the treatment plan.
- Review instructions, question patient to ensure understanding.
- Clarify patient's questions and respond clearly.
- Give written instructions.
- Describe specific adherence behaviours required.

3) Treatment:

- Tailor the treatment plan to patient's suitability, and offer options
- Give clear instructions about medication side effects
- Ensure proper record keeping for each patient on treatment
- Follow up quickly on missed appointments
- Fast track patients coming for treatment and follow up
- Ensure that staff is supportive to patients
- Ensure that the physical environment is comfortable to patients
- Ensure confidentiality
- Offer a holistic approach in addressing the patient's needs

9.7.2 In children and adolescents

Children with TB present specific problems for adherence. However there is very little information about the rates of adherence among children or methods for improving it. Many children with TB have few or no symptoms of the disease and many do not experience dramatic improvement in symptoms when given appropriate treatment. Because of the characteristic of the disease in children, there might be difficulty convincing the parents that their children are ill and need treatment and that the treatment needs to given as prescribed.

To improve adherence among children work with the parents or caregivers who will administer medications to the children. You cannot assume that parents will give the medication as prescribed, as some parents are non-adherent.

1) Provide anticipatory guidance:

Talk with parents about the potential problems they might experience once treatment is initiated. *Children may:*

- Resist taking medication
- Experience adverse reactions to the medication
- When parents are aware of potential problems they may be better equipped in dealing with them and assist with the treatment.

2) Ensure DOT

Direct observation of treatment must be ensured by either a facility healthcare worker, community health worker, parent or caregiver with proper documentation of each and every dose taken. Supplementing DOT with incentives or enablers to encourage co-operation from the child might be beneficial.

Adolescents are at high risk for poor adherence because of concerns about stigma and the fact that they might not

Treatment regimens in special curcumstances

10

10.1 Treatment for pregnant women

Untreated tuberculosis represents a far greater hazard to a pregnant woman and the foetus than does treatment of the disease. It is important to ask a woman before starting TB treatment if she is pregnant. Most TB drugs are safe for use in pregnant women, the exception is streptomycin which is ototoxic to the foetus and should not be used in pregnancy.

Co-administration of Rifampicin with any of the protease inhibitors (Ritonavir, Indinavir, and Nelfinavir) or non-nucleoside reverse transcriptase inhibitor (Nevirapine) is contraindicated. These drugs may inhibit or induce cytochrome P-450 isoenzymes and thus altering the serum concentration of rifampicin.

Rifampicin induces the Cytochrome P-450 and may substantially decrease blood levels of the antiretroviral drugs resulting in the potential development of resistance. If protease inhibitor or non-nucleoside reverse transcriptase inhibitor is to be started after giving Rifampicin, then at least two weeks should elapse after the last dose of Rifampicin. This time gap is necessary for reduction of the enzyme inducing activity of Rifampicin prior to commencement of antiretroviral drugs.

10.2 Treatment for breastfeeding women

A woman who is breastfeeding and has TB should receive a full course of TB treatment. Timely and properly applied chemotherapy is the best way to prevent transmission of tubercle bacilli to her baby. All the TB drugs are compatible with breastfeeding and a woman taking them can safely continue to breastfeed her baby.

If the mother is sputum smear positive the child should be given prophylactic isoniazid (5mg/ kg/ daily) for six months and continue breastfeeding. BCG vaccination should be postponed until the end of isoniazid prophylaxis. If the mother is sputum smear negative, the child is vaccinated and no chemoprophylaxis is necessary.

10.3 Treatment for women taking the oral contraceptive pill

Rifampicin interacts with the contraceptive pill with a risk of decreased protective efficacy against pregnancy. A woman who is receiving contraception may choose between the following two options while receiving treatment with rifampicin. Following consultation with a physician, she could take an oral contraceptive pill containing a higher dose of oestrogen (50 mcg), alternatively she could use another form of contraception.

10.4 Treatment for patients with liver disorders

Isoniazid, rifampicin and pyrazinamide are all associated with hepatitis. Of the three, Rifampicin is least likely to cause hepatocellular damage, although the drug is associated with cholestatic jaundice, Pyrazinamide is the most hepatotoxic.

The patients with the following conditions can receive the usual short-course chemotherapy regimen provided that there is no clinical evidence of chronic liver disease: hepatitis virus carriage, a past history of acute hepatitis, excessive alcohol consumption. However, hepatotoxic reactions to TB drugs may be more common in these patients and should be anticipated.

10.5 Established chronic liver disease

Patients with liver disease should not receive Pyrazinamide. Isoniazid plus Rifampicin plus one or two non-hepatoxic drugs such as streptomycin and Ethambutol can be used for total treatment duration of eight months. Alternative regimens are 9 RE or SHE in the initial phase followed by 3HE in the continuation phase, with a total treatment duration of 12 months. Therefore recommended regimens are 2 SHRE / 6 HR, 9 RE or 2 SHE / 1O HE.

10.6 Acute hepatitis (e.g. acute viral hepatitis)

Uncommonly a patient has TB and concurrent acute hepatitis unrelated to TB or TB treatment. Clinical judgment is necessary. In some cases it is possible to defer TB treatment until the acute hepatitis has resolved. In other cases when it is necessary to treat TB during acute hepatitis, the combination of SE for 3 months (3 SE) is the safest option, if the hepatitis has resolved the patient can then receive a continuation phase of six months isoniazid and rifampicin (6 HR). If not, SE should be continued for a total of 12 months.

10.7 Treatment of patients with renal failure

Isoniazid, rifampicin and pyrazinamide are either eliminated almost entirely by biliary excretion or metabolized into non-toxic compounds. These drugs can, therefore, be given in normal dosage to patients with renal failure. In severe renal failure, patients should receive pyridoxine with isoniazid in order to prevent peripheral neuropathy. Streptomycin and ethambutol are excreted by the kidney. Where facilities are available to monitor renal function closely it may be possible to give streptomycin and ethambutol in reduced doses. The safest regimen to be administered in patients with renal failure is 2 HRZ/ 4 HR.

11 TB in children

The number of children who are infected with tuberculosis and who progress to disease depends on the intensity of the epidemic, the age structure of the population, the prevalence of HIV and the quality of the TB program. In South Africa many children develop disease and die from tuberculosis. For this reason the management of children exposed to infectious cases and the diagnosis and treatment of tuberculosis is important.

11.1 Transmission of TB in children

The source of TB infection in a child is usually an adult (often a family member) with pulmonary TB. When the source case is sputum smear positive the likelihood of infecting children (and others) is much greater than if the source case is sputum smear negative but culture positive. Smear negative culture positive cases however are also infectious and are responsible for approximately 20-33% of infections.

When children are discovered to be infected or to have TB disease, the family members and other people in close contact with the child should be investigated in an attempt to find the source case, which is often unknown. The younger the child with TB is, (especially children younger than two years of age), the more likely it is that the source case will be present in the household.

11.2 Risk for infection

The following factors increase the risk of infection:

- Long duration of the exposure.
- High intensity of exposure. Smear positive patients are the most infectious, smear negative culture positive are less infectious and extra pulmonary TB cases are the least infectious.
- Children under two years of age with a mother or caregiver suffering from TB.
- Malnutrition.
- HIV positive children.

11.3 Outcome of children infected with tuberculosis

1. The most common outcome is that most infected children do not develop clinical disease. They are able to contain the infection. They are labeled as being TB infected and are characterized as having no symptoms or signs. Their tuberculin skin test is positive.
2. Some children develop of hypersensitivity responses to the tuberculoprotein which present with erythema nodusum, phentycular conjunctivitis and dactylitis. These presentations are seldom seen and normally self-limiting.
3. Progression to pulmonary and extra pulmonary disease. The most common form of childhood disease is intrathoracic lymph node enlargement
4. The progression to disseminated disease with the development of extra pulmonary disease. Including miliary TB and TB meningitis.
5. Infected adolescents, when they progress to disease develop adult type lung disease with lung apical involvement and the characteristic cavity formation.

TB disease is classified as pulmonary and extra pulmonary disease. Disease is classified as pulmonary disease when the lung tissue is involved. Extra pulmonary TB is the most common form in children and includes TB lymph node enlargement, TB meningitis, TB effusions (pleural, pericardial and peritoneal), miliary TB and skeletal TB.

11.4 Risk factors for the progression from infection to disease

1. **Age of the child:** young children especially those under two years of age have the highest risk of developing disease as well as of progressing to disseminated disease. Another high risk group is adolescents who are

infected for the first time during adolescence. Children going to primary school have the lowest risk of progressing from infection to disease as well as for developing serious disease.

2. Children with immune suppression especially HIV infected children. Other children at high risk are severely malnourished children, especially children suffering from kwashiorkor, and following a bout of measles
3. **Recent infection:** Most children, who will progress to disease, do so within 12 months of infection.

11.5 Clinical presentation

Children can present with TB at any age but the commonest age is between zero and four years of age and in adolescence. TB can present as an acute pneumonia or more commonly as a chronic disease. Being a chronic disease most of the symptoms are very non-specific and often overlap with other chronic diseases especially HIV.

The most common clues to the diagnosis are:

- Contact with a smear positive pulmonary TB source case. The likelihood of infection and disease is increased if there is close contact (family member, person living in the same household or caretaker) with an infectious source case. Other information about the source case, which is important, is the response to treatment, as failure to respond might indicate exposure to a drug resistant source case.
- Failure to gain weight, and loss of appetite without obvious cause should raise the suspicion of TB. Children with weight loss, especially when documented on the "Road to Health" chart should be investigated for TB. A child in a feeding rehabilitation programme who fails to gain weight is also at high risk and should be investigated for TB.
- Chronic cough for more than 14 days especially if the child fails to respond to a course of antibiotics (amoxycillin)
- An audible wheeze or a brass like cough that does not respond to a bronchodilator is suggestive of airway compression from enlarged intrathoracic glands.
- Painless enlarged lymph glands, which occur most commonly in the neck and do not respond to a course of antibiotics.
- Two or more episodes of fever and especially if the fever is present for more than seven days without an obvious cause (such as malaria) for the fever.

There are other non-specific signs including night sweats, breathlessness (due to pleural effusion), peripheral edema (due to pericardial effusion) or painful limbs and joints (due to erythema nodosum or dactylitis).

Although TB in children is a chronic disease, there are danger signs which require an immediate response as they could indicate serious and often life threatening forms of TB, like TB meningitis.

These danger signs include:

- headache (especially if accompanied by vomiting), irritability, drowsiness, neck stiffness and convulsions (signs of TB meningitis);
- big liver and spleen (signs of disseminated TB);
- breathlessness and peripheral edema (signs of pericardial effusion); and
- severe wheezing (signs of severe bronchial compression).

11.6 Tuberculin Skin Test (TST)

The tuberculin skin test measures the hypersensitivity to tuberculin purified protein derivative (PPD). A positive tuberculin test, measured after 48-72 hours does not indicate the presence or extent of tuberculosis disease; it only indicates TB infection. There are various types of tuberculin skin tests available including Mantoux, Tine, Monospot skin tests. The recommended is the Mantoux skin test. In a child who has not had BCG, a Mantoux skin test is defined as "positive" when the diameter of skin induration is 10mm or greater. In a child who has had BCG, an induration of 10-14mm may be due to vaccination or TB infection while a 15 mm or greater induration is regarded as indicative of infection and therefore "positive". A negative tuberculin skin test does not exclude TB infection and some induration e.g. 5-14 mm is supportive if the clinical features and contact history are suggestive.

The tuberculin test is less likely to be positive in a child with TB if the child also has:

- Severe malnutrition
- HIV infection
- Disseminated TB such as miliary disease or TB meningitis
- Immunosuppressive drugs e.g. high dose steroids

In HIV infected children the TST is less likely to be positive and for this reason a Mantoux skin test result of 5 mm and greater is regarded as indicating infection.

11.7 Chest radiography

Chest radiography is often very useful in making the diagnosis of TB in children. The chest radiographs must however be of good quality and the results depend on the expertise of the person reading them.

The most common radiological signs of childhood TB are:

- An enlarged hilar region of the lung and a broad mediastinum due to enlarged hilar or mediastinal glands. Often compression of the airways due to the enlarged lymph glands can be observed. The enlarged lymph glands can occlude the airway leading to collapse of a lobe.
- The parenchymal lesion can enlarge causing widespread opacification in a segment or lobe of the lung.
- Acute dissemination causes widespread fine millet-sized (1-2 mm) lesions (Miliary TB).
- Pleural effusions that usually occur in children older than six years.

The changes on chest radiography are often non-specific so the TB should not be diagnosed from the radiograph alone. The usefulness of the chest radiograph in HIV infected children is reduced due to the overlap with other HIV related lung diseases e.g. Lymphoid Interstitial Pneumonia (LIP).

11.8 M. tuberculosis identification and culture

Pulmonary TB in children is usually smear negative because the disease is paucibacillary (few organisms) and it is difficult to obtain sputum samples from children. For these reasons samples are often not collected or tests are not performed.

In complicated cases or cases where the diagnosis is unsure it is often of value to collect gastric aspirates, hypertonic saline induced sputum, nasopharyngeal aspirates or fine needles aspirates from peripheral lymph nodes for staining and culture.

In adolescents the clinical and radiological pictures are similar to those in adult patients and sputum for smear microscopy must be collected.

11.9 The impact of HIV on the diagnosis of TB in children

HIV makes the diagnosis of TB in children even more difficult for the following reasons:

- Several of the symptoms are common to both HIV related lung disease and TB e.g. chronic cough, weight loss and persistent fever.
- The interpretation of the tuberculin skin test is even less reliable as there is a higher false negative rate.
- The chest radiographic pictures overlap with HIV related lung diseases like LIP (Lymphoid Interstitial Pneumonia) being very similar to miliary TB.
- The radiological features of TB in HIV infected children can be similar to those of HIV non-infected children, but the picture can also be atypical.
- Differential diagnosis of pulmonary TB in HIV-infected children is much broader and includes: bacterial pneumonia, viral pneumonia, fungal lung disease, pneumocystis carinii pneumonia (PCP), pulmonary lymphoma and Kaposi sarcomata.
- If there is uncertainty of the diagnosis, the child should be treated with antibiotics for five-seven days and the chest X-ray repeated after two weeks depending on the clinical picture of the child.

11.10 Approach to the diagnosis of TB in children and adolescents

The approach to the diagnosis of TB in children depends on the resources that are available. In some areas the availability of TST and chest radiographs is limited. In these areas the scoring system (see below) would be a valuable tool to make the diagnosis of TB. In other areas where the tests are available the accuracy of the diagnosis can be improved and the over-diagnosis of childhood TB prevented. In these areas the scoring system would be a valuable screening tool to identify the children that might have TB and need further investigation.

11.11 A score system for the diagnosis of TB in children

A score system is one way of trying to improve the diagnosis of childhood TB by the careful and systematic collection of diagnostic information. A score system is there to help in the clinical judgment. The scoring system was developed as a screening instrument and leads to the over-diagnosis of TB in HIV infected children.

Table 2: Score chart for diagnosis of TB in children

Feature	0	1	2	3	4	Score
GENERAL						
Weeks of illness	< 2	2 - 4		> 4		
Nutritional status [% weight for age]	> 80%	60-80%		< 60%		
Family history of TB	None	reported by family		proved sputum positive		
Tuberculin test				positive		
Malnutrition				not improving after 4weeks		
Unexplained fever			No response to treatment			
LOCAL						
				Lymph nodes		
				Joint or bone swelling		
				Abdominal mass or ascites		
				CNS signs, Abnormal CSF		
X-rays				Broad mediastinum due to enlarged hilar glands	Angle deformityof spine	
TOTAL						

Table 2 shows a score chart for the diagnosis of childhood TB or screening for TB:
[> : more than; < : less than.]
A score of 7 or more indicates a high likelihood of TB.

Name of Child: ----------

---------- ----------

Date: Completed by:

11.11.1 How to apply/read score system

The score system can also be used to make the diagnosis of TB or to screen for TB if tuberculin and a chest radiograph are not available.

Example:
Score the following patient for TB: A young child has weight loss (weight < 60% for age) with no family member with TB, skin test is not available, has bouts of unexplained fever with no response to antibiotic and positive lymph nodes in the neck.

FEATURE	SCORE
Weight less than 60%	3
Family history of TB	0
Tuberculin Test	0
Unexplained fever, no response to treatment	2
Lymph nodes	3
TOTAL	8

Any score of 7 or more is suggestive of TB.

11.12 Approach to the diagnosis of intra-thoracic TB when TST and chest radiography are available

When the TST and chest radiograph are available the score system is used as the screening instrument and the patient has the necessary tests performed. TB is then diagnosed using the modified WHO criteria. The specificity is further enhanced by the ability to do cultures.
The child TB is diagnosed as follows:

11.12.1 Possible TB

When the patient has a normal chest radiograph and has one of the following:
1. Smear positive household contact
2. Symptoms of chronic disease e.g. weight loss, chronic cough etc.
3. Positive tuberculin skin test Children with possible TB are either followed up or receive chemoprophylaxis or treatment of latent infection (see Chemoprophylaxis and treatment of latent infection)

11.12.2 Probable TB

When the patient has a chest radiograph suggestive of intrathoracic TB and one of the following:
1. Smear positive household contact
2. Symptoms of chronic disease e.g. weight loss, chronic cough etc.
3. Positive tuberculin skin test Children with probable TB and children with culture positive TB are registered and treated for TB

11.13 Management of childhood TB

11.13.1 DOT (Direct Observation of Treatment)

DOT is applicable to all patients with tuberculosis, including children. High success rates are achievable in children with uncomplicated intrathoracic TB and less severe forms of EPTB such as TB lymphadenopathy and pleural effusion. All children with severe forms of tuberculosis (meningitis, spine, peritonitis, miliary, skeletal) should be referred to hospital for opinion on the management as drug therapy might be given for a longer time but should still receive direct observed therapy.

11.13.2 Non-drug therapy

The parents should receive advice on an adequate diet for the child and malnourished children should be referred for rehabilitation. When a young child is diagnosed with any form of TB, the parents should be carefully evaluated to make sure whether one of them was perhaps the source case.

11.14 TB treatment for children up to 8 years of age

11.14.1 Regimen 3

Recommended regimens for treatment of uncomplicated intrathoracic tuberculosis and EPTB such as lymph gland and pleural effusion in children. Fixed drug combinations are preferable as they prevent the development of MDR TB. The patient should be continued on the pre-treatment body weight throughout the treatment period, there is no need to adjust the dosages based on weight gain.

11.14.2 Fixed dose combination tablets available for children

Pre-treatment body weight phase treatment times a week	4 months continuation phase treatment given	2 months initial given five five
times per week		
	RHZ 60,30,150	RH 60,30
3-4 kg	fi tab	fi tab
5-7 kg	1 tab	1 tab
8-9 kg	1fi tabs	1fi tabs
10-14 kg	2 tabs	2 tabs
15-19 kg	3 tabs	3 tabs
20-24 kg	4 tabs	4 tabs
25-29 kg	5 tabs	5 tabs

In those circumstances that children cannot take treatment for five times a week in the continuation phase and there is guarantee of strict supervision, treatment can be taken three times weekly in the continuation phase only. The following table shows the suggested drugs and doses for continuation phase treatment.

Pre-treatment body weight phase treatment times a week	4 months continuation phase treatment given	2 months initial given five three
times per week		
	RHZ 60,30,150	RH 60,60
3-4 kg	fi tab	fi tab
5-7 kg	1 tab	1 tab
8-9 kg	1fi tabs	1fi tabs
10-14 kg	2 tabs	2 tabs
15-19 kg	3 tabs	3 tabs
20-24 kg	4 tabs	4 tabs

RHZ (60,30,150mg), RH (60,30mg) and RH (60,60mg) only used for the three times weekly regimen. All fixed dose combination tablets for children are dissolvable

11.15 Management of adolescents with pulmonary TB

	Recommended dose ranges in mg/ kg	
	5 times a week	3 times a week
Isoniazid	4-6 (5)	8-12 (10)
Rifampicin	8-12 (10)	8-12 (10)
Pyrazinamide	20-30 (25)	30-40 (35)
Streptomycin	12-18 (15)	12-18 (15)
Ethambutol	15-20 (15)	25-35 (30)

Adolescents should be treated like adult patients, those with first time TB using regimen 1 and re-treatment cases using Regimen 2.

11.14 Response to therapy

Children should be monitored on a monthly basis for the first two months. Children responding to therapy will have resolution of symptoms and will gain weight. The chest radiograph is a poor indicator of response as the hilar and mediastinal lymph glands can enlarge as a result of the improvement in the immunity of the child. After six months only approximately 66% of children who had abnormal chest radiographs at the beginning of treatment, will have normal chest radiographs. In an asymptomatic child a routine chest radiograph is not indicated during or at the end of therapy.

Adolescent patients with sputum smear positive TB should be followed up by the same regimen as adult patients and should have repeat sputum examinations done after two and at five months treatment.

11.15 Management of child contacts of infectious cases

Active contact tracing of children who are household contacts of smear-positive PTB cases is recommended. Screening should include a thorough history, clinical examination, tuberculin test and chest radiography. Those that are found to have TB should be treated with a full course of TB treatment. Those who are well and less than

five years of age with no signs of infection or disease should receive chemoprophylaxis as they have a high risk for developing disease and disseminated TB.

The recommended regimen is isoniazid 5mg/ kg/ day, five times a week for six months. It should not be forgotten that all age groups are at risk for developing TB especially those less than five years of age. A group often forgotten is those less than one year whom have the highest risk of serious and disseminated disease. Children older than five years who are well do not require prophylaxis but only clinical follow-up as they have the lowest risk of serious and disseminated disease.

11.16 Management of children with latent infection

Any HIV positive child with a positive TST and who is asymptomatic, even if not in contact with a sputum smear positive source case of TB, has a high risk of developing disease. For this reason any child under the age five years with a positive TST should be treated for latent infection with INH 5mg/ kg/ day, five times a week for six months. An alternate regimen is to treat the children with latent infection with INH and Rifampicin (60/ 30) for three months but this requires strict DOT.

Note: Children may also be infected by a smear-negative PTB source case, but because the risk for these children is lower than after exposure to a smear positive source case, these children often receive less attention. However, if resources allow it, these children should be managed as

11.17 Diagnosis of TB Meningitis in Children

TB meningitis is a very serious form of TB in children. Complications include obstruction of cerebrospinal fluid (CSF) flow, hydrocephalus, inappropriate anti-diuretic hormone secretion, hemi- or quadriplegia, convulsions, deafness, blindness and mental retardation.

Symptoms:
- Headache
- Irritability
- Drowsiness
- Convulsions
- Weight loss

History:
- Contact with a TB patient

Physical signs:
- Signs of meningeal irritation (neck pain and resistance to neck flexion)
- Cranial nerve palsies
- Altered level of consciousness

Investigations:
- Lumbar puncture (CSF findings: raised protein, low glucose, low chloride, lymphocytes
- predominate, gram stain negative - acid fast bacilli are seldom found)
- Mantoux test is often, but not always, positive
- Chest radiograph may be normal or abnormal

11.18 Treatment of TB Meningitis in Children

11.19 Indications for the use of steroids in children with

TB

Tuberculous Meningitis		
	Management	**Comments**
Non-drug treatment	Monitor neurological status on a regular basis. Attend to nutritional status. Nasogastric feeding is usually needed initially.	All patients need physio therapy and occupational therapy.
Drug treatment 3-month initial phase	Rifampicin + isoniazid + Pyrazinamide +ethionamide *Rifampicin,oral,20mg/kg/24hrs as a singledose. *Isoniazid,oral,20mg/kg/24hrs as a single dose. *Pyrazinamide, oral, 40mg/24hrs as a single dose; maximum 2g per 24 hrs. *Ethionamide,oral,20mg/Kg/24 hrs as a singledose; maximum 1g per 24 hrs.	
6-month continuation phase	Discontinue pyrazinamide. Continue with rifampicin, isoniazid and ethionamide using the doses above. Treatment is then given once daily for 5 days per week.	
Steroids	Prednisone, oral, 2-4mg/kg/24 hrs in 3 divided doses for 4-6 weeks. Then taper to stop over 14 - 21 days.	
Hydrocephalus	Acetazolamide oral, 100 mg/kg/24 hrs in 3 divided doses; maximum 1g/day. AND Furosemide,oral, 1-2 mg/kg/24 hrs as a single daily dose for at least 4-6 weeks.	Refer non-communicating hydrocephalus for ventriculo-peritoneal shunt
Convulsions	Diazepam, slow IV, 0.2-0.3 mg/kg, to control acute seizures. *Maintenance: Phenobarbital, oral, 5-10mg/kg/24hrs in 2 divided doses, until the patient is free of convulsions for at least 14 days. Taper to stop over 1 week	

Note: TB meningitis is a very serious form of TB and should not be treated at primary health care facility but should be urgently referred to a tertiary level.

The following are indications for oral steroids in children with TB:

- TB meningitis
- TB pericarditis
- Mediastinal lymph glands obstructing the airways.
- Severely ill children with disseminated TB (miliary).

Dosage:

- Prednisone 2-4 mg/kg/24 hours orally in 3 divided doses for 4-6 weeks can be added to the anti-TB drugs - taper to stop over 2 weeks.

12 TB, HIV AND AIDS

12.1 Introduction

HIV infection leads to progressive immunodeficiency and increased susceptibility to infections, including TB. As HIV infection progresses, CD4 lymphocytes decline in number and function. The immune system is less able to prevent the growth and local spread of M Tuberculosis.

Early diagnosis and effective treatment of TB among HIV-infected patients are critical for curing TB, minimizing the negative effects of TB on the course of HIV and interrupting the transmission of M Tuberculosis to other persons in the community. Proper case management of TB can significantly prolong the lives of people living with HIV and AIDS. Tuberculosis can occur at any point in the course of progression of HIV infection.

HIV fuels the TB epidemic in several ways:

- Promotes progression to active TB disease in people with recently acquired and with latent M Tuberculosis infection.
- HIV is a risk factor for reactivation of latent tuberculosis infection to active disease.
- People living with HIV and AIDS are more prone to tuberculosis infection when exposed to M.Tuberculosis.
- HIV increases the rate of recurrent TB, which may be due to either endogenous reactivation (relapse) or exogenous re-infection.
- In the absence of HIV infection, only about 10% of people infected with M Tuberculosis get sick with TB during their lifetime. In people who are co-infected with HIV and TB, about 50% will develop active TB disease at some stage which translates to a ten fold increase in risk for HIV positive individuals.
- The increasing TB disease in persons living with HIV and AIDS poses an increased risk of TB transmission to the general community.

HIV not only increases the number of TB cases but also alters the clinical course of TB disease. As HIV related immuno suppression increases, the clinical pattern of TB disease changes, with increasing numbers of smear negative pulmonary TB and extra pulmonary TB cases. TB is more likely to be disseminated and more difficult to diagnose as immuno suppression progresses. Co-infected patients also suffer increased mortality mainly due to late diagnosis and other opportunistic infections. Currently about 55% of TB patients are co-infected with HIV in the country

12.2 Diagnosis of HIV in TB Patients

12.2.1 When to suspect HIV co-infection in TB patients

Symptoms suggestive of HIV infection are:

- weight loss
- diarrhoea (>1 month)
- pain on swallowing (suggests oesophageal candida)
- burning sensation of feet (suggests peripheral sensory neuropathy)

Histories suggestive of HIV infection include:

- Herpes Zoster (shingles)
- Recurrent pneumonia
- Bacteraemia
- Sexual partner with HIV infection
- Sexually-transmitted infection

Physical signs suggestive of HIV infection include:

- Oral thrush
- Oral hairy leukoplakia

- Extensive herpes of Zoster (shingles)
- Scar of herpes Zoster
- Kaposi's sarcoma
- Pruritic papular rash
- Symmetrical generalised lymphadenopathy
- Persistent painful genital ulceration

HIV infection should be suspected if, during the course of other investigations the following results are found:
- Unexplained anaemia
- Leucopenia or thrombocytopenia
- Bacteraemia

12.2.2 HIV Testing

The definitive diagnosis of HIV infection rests on a positive HIV test. Therefore all TB patients should receive HIV information and education and offered counseling and HIV testing.

12.3 Diagnosis of TB in HIV positive patients

Pulmonary tuberculosis is the most common manifestation of tuberculosis in adults infected with HIV. Tuberculosis can occur at any point in the course of progression of HIV infection. The clinical pattern of tuberculosis correlates with the patient's immune status. If TB occurs in the early stages of HIV infection when immunity is only partially compromised, the features are more typical of tuberculosis, commonly with upper lobe cavitations, and the disease resembles that seen in pre-HIV era.

As immune deficiency worsens, HIV-infected patients present with atypical pulmonary disease resembling primary tuberculosis or extra-pulmonary and disseminated disease, commonly with hilar lymphadenopathy and lower lobe infection, or miliary type of infiltrations. It is important to note that HIV-infected patients with pulmonary TB may have a normal chest X-ray.

Mycobacterium TB infection develops when the CD4 count falls below 400/mI as compared to other infections which develop when the CD4 counts falls much below 250/mI. This means that one of the earlier infections to occur in an HIV positive case is Mycobacterium tuberculosis, it may therefore happen that TB is diagnosed much earlier than the HIV infection in co-infected patients.

12.3.1 Diagnosis of Pulmonary Tuberculosis

Clinical features:
Generally there is no difference between HIV positive and HIV negative patients. However, among HIV-infected patients, cough is reported less frequently, probably because there is less cavitations, inflammation and endobronchial irritation as a result of decrease in cell-mediated immunity. Similarly, haemoptysis, which results from caseous necrosis of the bronchial arteries, is less common in HIV-infected patients.

Mantoux test:
Though useful for measuring the prevalence of tuberculous infection in a community, it has limited value for individual adult diagnosis. Furthermore, with progression of immune deficiency and decrease in CD4 counts, cutaneous anergy to mantoux test increases.

Sputum Microscopy:
Sputum microscopy is the cornerstone to diagnosis of TB even in high HIV-prevalence areas. Patients suspected of having TB should have two sputum specimens examined for Acid Fast Bacilli (AFB). HIV infected, smear pos-

itive patients tend to excrete significantly fewer organisms per ml of sputum than HIV- negative patients, which can lead to AFB being missed if the appropriate number of sputum samples as well as high power fields are not examined by microscopy.

The following table shows how the clinical picture, sputum smear result and chest X-ray appearance often differ in early and late HIV infection:

Features of PTB	Stage of HIV infection	
	Early	Late
Clinical picture	Often resembles post-primary TB	Often resembles primary TB
Sputum smear results	Often positive	Often negative
Chest X-ray appearance abnormalities	Often cavities	Often infiltrates, no cavities, no

12.3.2 Extra-pulmonary Tuberculosis

Extra-pulmonary disease has been reported in up to 70% of HIV-related TB cases when the CD4 lymphocyte count is less than 100. The main types of extra-pulmonary TB seen in HIV-infected patients are lymphadenopathy, pleural effusion, pericardial effusion, and miliary TB. The definitive diagnosis of extra-pulmonary TB is often difficult because of the scarcity of diagnostic facilities. Presentation of extra-pulmonary TB is generally no different in HIV-infected compared with HIV negative patients.

However, HIV-related TB lymphadenopathy can occasionally be acute and resemble an acute pyogenic bacterial infection. Diagnosis can be made using simple techniques such as needle aspiration, inspection of biopsied lymph nodes for macroscopic caseation, and examination of direct smears from the cut surface. In TB meningitis, the CSF may be completely normal in HIV-infected persons. Disseminated TB may be difficult to diagnose. Pericardial TB is not rare and may be diagnosed presumptively based on the characteristic balloon-shaped appearance of cardiac shadow on chest X-ray.

12.3.3 Childhood Tuberculosis

Similar to adults, pulmonary TB is the most common manifestation of TB in HIV-positive children. The diagnosis of pulmonary TB in children less than 4 years old has always been difficult and HIV-infection further compounds the problem. Mantoux test is often negative and most cases are diagnosed according to non-specific clinical and radiographic criteria.

12.4 Implications of diagnostic difficulties

The advent of HIV has made the diagnosis of TB more difficult, and false diagnosis of TB probably occur frequently among patients affected by other HIV-related illnesses. these false-positive diagnoses in most cases account for a small proportion of all forms of TB notified, and thus do not negate the huge increases observed in TB notifications in HIV-endemic areas.

12.5 Treatment of TB in HIV-infected patients

In general, anti-TB treatment is the same for HIV-infected and HIV-negative TB patients.

Note: Thiacetazone is not recommended drug in the management of tuberculosis in South

Thiacetazone causes severe cutaneous reactions. Exfoliative Dermatitis or Steven Johnson syndrome may occur and can be fatal. Steven Johnson's Syndrome is a special type of hypersensitivity reaction. It is characterised by generalised bullous eruption, sometimes haemorrhagic involving skin and mucous membranes. In HIV positive patients, cutaneous reaction with Thiacetazone occurs more frequently and is more severe. Adequate sterilization and safe disposal of syringes and needles should be ensured whenever streptomycin is administered.

12.6 Response to treatment

Patients who complete treatment show the same clinical, radiographic and microbiological response to short-course treatment irrespective of whether they are HI V positive or negative. The only exception might be on weight gain, which is usually slower in HIV-positive than in HIV-negative patients.

12.7 Case fatality

HIV-infected patients have a much higher mortality during and after anti-TB treatment compared with HIV-negative patients. Approximately 30% of HIV-infected, smear positive TB patients die within 12 months of starting treatment, and about 25% of those who complete treatment will die during the next 12 months. This is partly due to TB itself, but largely due to other HIV-related problems like septicemia, diarrhea, pneumonia, anaemia, Kaposi's sarcoma, cryptococcal meningitis.
Direct observation of treatment (DOT) is even more important for HIV-infected TB patients. Self-administration

Note: HIV infected smear negative pulmonary TB patients may have a worse prognosis than HIV positive patients with smear positive pulmonary TB. Delays in the diagnosis of TB have been associated with worse outcomes, so initiation of treatment as soon as TB is

of treatment is associated with higher case fatality rates. This not only improves their quality of life, but also has been shown to prolong their life span by an average of two years. DOT can prevent emergence of MDR -TB and also will reverse the trend of MDR-TB.

12.8 Drug resistance

Outbreaks of multi-drug resistant TB have been reported in patients with HIV infection in other countries. HIV itself does not cause multi-drug resistant TB, but it fuels the spread of this dangerous condition by increasing susceptibility to infection and accelerating the progression from infection to disease.

12.9 Recurrence

When TB recurs after previous cure, there are 2 possibilities:

- **True relapse:** reactivation of persisters not killed by anti-TB drugs.
- **Re-infection:** due to re-exposure to another source of infection.

The proportions of recurrences due to these 2 possibilities are not known.

Relapse: The relapse rate of TB is low in HIV-infected TB patients who complete a rifampicin containing short-course treatment regimen. The use of non-rifampicin containing regimens and treatment interruptions due to drug reactions are associated with an increased risk of relapse of TB. Similarly relapse is more in self-administered treatment as compared to directly observed treatment.

12.10 Response of HIV-infected TB patients to TB treat-

ment

Clinical course during treatment: Common HIV-related infections (pneumonia, and diarrhoea and their complications, fungal infections) cause considerable morbidity during treatment of HIV-infected TB patients and contribute to the increased case fatality rate. Patients should be monitored during treatment to identify and treat these infections early.

12.11 Cotrimoxazole prophylaxis

Prophylaxis against inter-current infections may decrease morbidity and mortality in HIV-infected TB patients. Cotrimoxazole is highly effective in preventing pneumocystis carinii pneumonia and toxoplasmosis. It also has activity against pneumococcus, Salmonella and Nocardia. Cotrimoxazole has been shown to decrease hospitalisations and mortality in HIV infected TB patients. UNAIDS and WHO have recommended that cotrimoxazole should be used for prophylaxis for adults and children living with HIV/AIDS in Africa as part of a minimum package of care.

The national HIV/AIDS Policy Guideline for the 'Prevention and treatment of opportunistic and HIV related diseases in adults recommends trimethoprim/ sulphamethoxazole (cotrimoxazole) 160/ 800mg (960mg) daily for all HIV positive patients (whether they have TB or not) who:

- have symptomatic HIV disease (WHO Clinical stage 2,3 or 4), or
- have a CD4 count less than 200 cells/mm^3, or
- have already had pneumocystis carinii pneumonia.

HIV positive people with TB are all in WHO clinical stage 3 or 4. It is therefore recommended that all HIV positive TB patients be offered cotrimoxazole prophylaxis as follows:

- Wait until the patient has completed one month of TB treatment - this is to be able to differentiate between side effects from anti-TB drugs and side effects from cotrimoxazole.
- Counsel patients on the effectiveness and side effects of cotrimoxazole (i.e., explain to patients that cotrimoxazole can help prevent pneumonia and other infections, that it is only effective while the patient takes it so that it should be taken for the rest of their lives and that it can cause a rash and other side effects).
- If a patient chooses to accept it, provide cotrimoxazole 960mg (2 single strength or 1 double strength tablet) daily. The recommended dosage for children is trimethoprim 5mg/kg, sulphamethoxazole 25mg/kg. Cotrimoxazole syrup contains trimethoprim/ sulphamethoxazole 40/200mg and the recommended dosage is therefore 0.625 ml/kg (see table 2).

Table 2: Cotrimoxazole prophylaxis dosing schedule for children (approxi-

Weight	Cotrimoxazole (ml)
<5 kg	2.5 ml
5-9.9. kg	5 ml
10-14.9 kg	7.5 ml
15-21.9 kg	10 ml or 1 single (480mg) strength tablet
>22 kg	15 ml or 1.5-2 single (480mg) strength tablets

12.12 TB Preventive therapy

TB can be prevented in people living with HIV/AIDS by offering isoniazid prophylaxis (TB preventive therapy). In these individuals, TB preventive therapy has been shown to decrease the risk of TB disease and should be part of a package of care for people living with HIV and AIDS. It does not aim to control TB on a public health scale and it is not an alternative to the DOTS strategy for controlling TB. It is a very effective intervention for HIV

infected individuals prior to starting ARV.

Exclusion of active Tuberculosis: It is essential to exclude active tuberculosis in every patient prior to starting preventive therapy. This is critical in order to avoid giving one drug to patients with TB disease who require the full treatment.

Patients interested in TB preventive therapy should be specifically asked about signs and symptoms of tuberculosis:
- Cough > 2 weeks
- Fever > 2 weeks
- Night sweats
- Weight loss of > 1.5 kg in the past 4 weeks: weight should be measured at each clinic visit to allow documented evidence of weight loss. A weight loss of > 1.5 kg should be considered a positive screen indicator.
- Pleuritic chest pains, haemoptysis should also prompt investigations for TB.

All patients with 1 or more of the symptoms and signs must be investigated further for TB and are not immediately eligible for TB preventive therapy: 3 sputum specimens must be collected for the following investigations:
- 2 sputum specimen for microscopy
- 1 sputum specimen for culture

Trials have shown that a chest X-ray does not improve case detection and is an additional barrier for people to access the intervention. Emphasis is on sputum samples and, where appropriate, on identification of extra-pulmonary TB. Chest X-ray is not recommended in the screening for TB preventive therapy.

12.12.1 Eligibility for TB Preventive Therapy

Clinical trials have shown that the benefit of TB preventive therapy is greater in HIV positive people with positive tuberculin skin test.

Particular attention should be given to the following populations: miners, prisoners, TB contacts and health care workers. Patients with symptoms and signs suggestive of TB must be investigated for TB (see figure1). If they are not confirmed with TB (smear and culture are both negative) and their condition improves, should be re-assessed after 3 months for TB preventive therapy. Asymptomatic HIV positive people, with a negative tuberculin skin test should not be offered TB preventive therapy. Tuberculin skin test (Mantoux technique) should be offered to all HIV infected individuals.

All HIV positive people with no symptoms and signs suggestive of active TB, with a positive tuberculin skin test are eligible for TB preventive therapy.z

12.12.2 Who is Not Eligible for TB Preventive Therapy?

1. Patients with active liver disease or active alcohol abuse should not be offered TB preventive therapy because of potential hepatotoxicity of the drug used for preventive therapy.
2. Patients with history of TB treatment:
   - Patients who had active tuberculosis in the past 2 years should not be considered.
   - Patients who were treated for tuberculosis more than 2 years earlier may be considered because they may have already been re-infected with TB.
3. Patients on anti-retroviral therapy should not be offered TB preventive therapy, as there is currently no evidence of added benefit. Patients who receive TB preventive therapy and who require to start antiretroviral

therapy can complete their TB preventive therapy even if the ARV treatment is started as there is no interaction between isoniazid and the current ART regimen used.

12.12.3 Recommended regimen

- The standard regimen for TB prevention therapy is: Isoniazid (INH) 5mg/kg daily (maximum 300mg per day)
- The recommended duration is: 6 months
- Additional vitamin B6 (Pyridoxine) is part of the vitamin complex that HIV infected individuals receive in sufficient dosage to prevent the eventual occurrence of peripheral neuropathy.
- At this stage the TB preventive therapy should be given once only and the protective effect is expected to last for 18 months. Thereafter the patient should be monitored regularly for development of TB symptoms.

12.12.4 When and how to start

Information about tuberculosis, including preventive therapy, should be made available to all people living with HIV/AIDS. TB preventive therapy must be discussed and adequately planned to ensure full understanding and adherence by the patients. During the post-test counselling, the patient is informed about the possibility of TB preventive therapy and is told to come if s/he is interested. It is not recommended to offer TB preventive therapy immediately after breaking the HIV result to the patients or clients.

For people who know their HIV status for one month or longer, a two-visit schedule is recommended as follows:

- **First visit:** The known HIV infected patient is offered TB screening (symptomatic). This screening is essential to exclude any active tuberculosis that would require full treatment. The health worker must systematically enquire on the existence of the signs and symptoms discussed above and investigate as appropriate. It is only when the patient is free of the above symptoms that s/he is offered to have the tuberculin skin test.
- **Second visit:** Three days (48-72 hrs) later, the patient is seen for reading the result. If the skin test is positive, the patient is offered TB preventive therapy with adequate provision of information

During ongoing counselling sessions, the patients will be informed about HIV, side effects of Isoniazid (particularly hepatitis), the importance of adherence, the symptoms of active TB and the importance of seeking care if they develop symptoms. The counselling should explain that TB preventive therapy decreases the risk of getting TB but the TB may still occur despite it. Patients starting TB preventive therapy should be given one-month supply at a time. They are expected to cover the 6 months therapy within a period of 9 months.

12.12.5 Monitoring

Patients are monitored monthly for adherence, development of side effects (peripheral neuropathy; major: jaundice, vomiting and confusion due to hepatitis) and early detection of active TB.

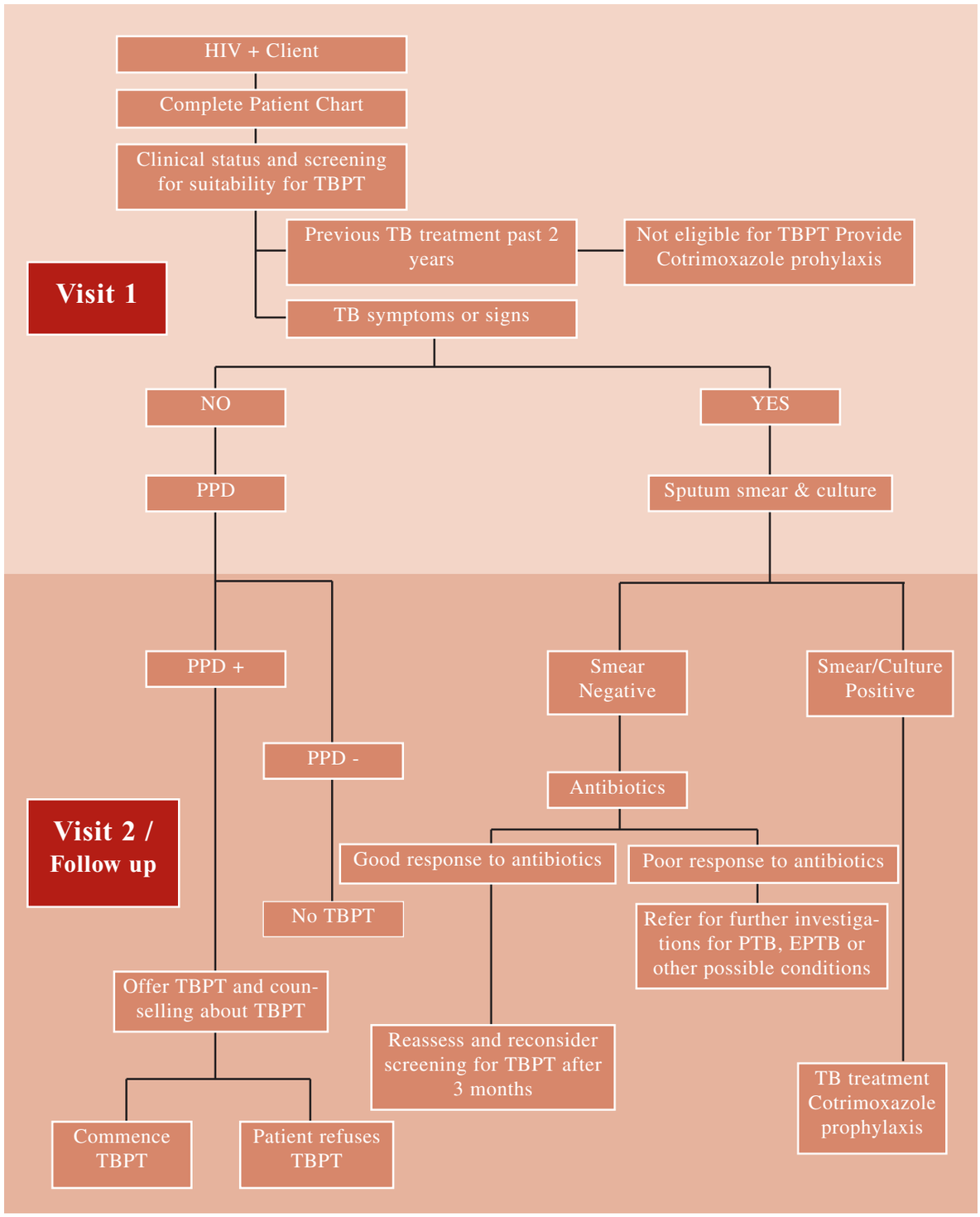
- If the patient develops active TB, stop the preventive therapy and start the full TB treatment regimen.
- In case of peripheral neuropathy, prescribe 100 mg pyridoxine (vitamin B6) daily until symptoms disappear.
- If the patient develops signs and symptoms suggestive of hepatitis, stop INH preventive therapy immediately and refer for further investigations and assessment.
- If the patient interrupts therapy, enquire about the possible reasons for interrupting and counsel on the importance of adherence appropriately. Restart the therapy after ensuring that obstacles to adherence have been addressed. Ensure that the 6 months therapy is taken within a 9 months period. If the patient interrupts for the second time, consider stopping the therapy.

12.13 Side effects of anti-TB drugs in TB/HIV patients

Adverse drug reactions are more common in HIV-positive than in HIV-negative TB patients. Risk of drug reaction increases with increased immuno-suppression. Most reactions occur in the first 2 months of treatment.

Skin rash is the commonest reaction; fever often precedes and accompanies the rash. Mucous membrane involve-

Figure 1: Screening Algorithm for TB Preventive Therapy (TBPT)



ment is common. The usual drugs responsible are streptomycin and rifampicin. Severe skin reactions, which may be fatal, include exfoliative dermatitis, Stevens-Johnson syndrome and toxic epidermal necrolysis.
Other reactions:
The commonest reactions necessitating change in treatment include GI disturbances and hepatitis. There may be an increased risk of rifampicin associated shock and thrombocytopenia.

12.14 Anti-tuberculosis therapy and antiretroviral therapy

Note: Steven Johnsons syndrome is common in countries that use Thiocetazone as part of TB treatment. In South Africa, Thiocetazone is NOT recommended.

To date no cure is available for HIV/AIDS. It is only the opportunistic infections in HIV/ AIDS, which can be treated. The antiretroviral drugs, which are used in HIV positive patients, are effective in slowing down the replication of the virus. These drugs are the protease inhibitors, nucleoside reverse transcriptase inhibitors and non-nucleoside reverse transcriptase inhibitors. Nucleoside reverse transcriptase inhibitors like Zidovudine, Didanosine, Zalcitabine, Stavudine, Lamivudine and Abacavir can be safely co-administered with anti-tuberculosis drugs.
Rifampicin stimulates the activity of the cytochrome P450 liver enzyme which metabolizes PIs and NNRTIs. This can lead to a reduction in the blood levels of PIs and NNRTIs. PIs and NNRTIs can also enhance or inhibit this same enzyme system, and lead to altered blood levels of rifampicin. The potential drug interactions may result in ineffectiveness of antiretroviral drugs, ineffective treatment of TB, an increased risk of drug toxicity as well as potential development of resistance.

Note: Co-administration of Rifampicin with any of the protease inhibitors (Ritonavir, Indinavir and Nelfinavir) or non-nucleoside reverse transcriptase inhibitor (Nevirapine,

Rifamycins induce Cytochrome P-450 and may substantially decrease blood levels of the antiretroviral drugs resulting in the potential development of resistance. Isoniazid, ethambutol, pyrazinamide and streptomycin can be concurrently used with protease inhibitors or non-nucleoside reverse transcriptase inhibitors.

If protease inhibitor or non-nucleoside reverse transcriptase inhibitor is to be started after giving rifampicin, then at least two weeks should elapse after the last dose of rifampicin. This time gap is necessary for reduction of the enzyme inducing activity of rifampicin prior to commencing of antiretroviral drugs.

12.15 Concomitant Tuberculosis

12.15.1. Patient develops tuberculosis while on antiretroviral therapy

Antiretroviral therapy should be continued throughout TB treatment, with changes to the regimen and monitoring as follows:

- **Regimen 1:** A change to efavirenz is recommended for patients on nevirapine wherever possible. If this is not possible (e.g. intolerant of efavirenz or significant risk of falling pregnant), nevirapine may be continued in selected cases, with monthly ALT monitoring. Discuss these cases with an antiretroviral expert.
- **Regimen 2:** Lopinavir / ritonavir 400/100mg every 12 hours should change to lopinavir / ritonavir 400/400 mg every 12 hours (increasing the dosage of ritonavir by adding three extra capsules of ritonavir). This should be continued until 2 weeks after completion of TB treatment, when the extra ritonavir can be stopped.

12.15.2 Patient presents with TB before commencing ARVs

- If the patient has no history of WHO Stage 4 illness, and has a CD4 count of more than 200 cells/mmΔ, antiretroviral therapy is not yet needed. Treat the patient's TB; the need for antiretroviral treatment should be reassessed on completion of TB treatment.
- If the patient has a history of WHO Stage 4 illness and/or a CD4 count of less than 200 cells/mmΔ, start TB treatment; add ARV after two months.
- If the patient has a CD4 count of less than 50 cells/mmΔ or other serious HIV-related illness, make sure that the patient is tolerating TB treatment before initiating ARVs (complete at least two weeks of TB treatment before initiating ARVs). Patients in this group should be started on first-line therapy consisting of stavudine, lamivudine and efavirenz (nevirapine should generally be avoided because drug levels might decrease and there is a danger shared hepatotoxicity might increase).

Patients should be pre-emptively counselled about the following:

- Treatment for TB together with ARV therapy involves taking a large number of tablets and they may struggle with adherence.
- When antiretroviral treatment is commenced, the patient's TB symptoms may transiently worsen as part of immune reconstitution.

12.16 BCG and HIV

WHO and UNICEF recommend that asymptomatic HIV infected children should receive BCG vaccination as per the immunisation policies. However, these should be withheld in a child with symptomatic HIV infection. BCG when given to a symptomatic HIV positive will lead to disseminated BCG disease.

Figure2: How to Treat Adult Patients with Concomitant

TB develops while on	TB infection is present before start-
Continue ARV therapy throughout TB treatment Patients on first-line therapy containing nevirapine should generally be swapped to efavirenz as follows: First-line therapy: 1. Stavudine 40mg (or 30mg if <60kgs) every 12 hours + 2. Lamivudine 150mg every 12 hours + 3. Efavirenz 600mg at night Second-line regimen needs to be changed to a regimen compatible with standard TB therapy as follows: Second-line therapy: 1. Zidovudine (AZT) 300mg every 12 hours + 2. Didanosine (ddI) 400mg once a day (250mg daily if <60kg) on an empty stomach + 3. Lopinavir/ritonavir 400/400mg every 12 hours	CD4+ count > 200/mmΔ (and no other HIV-related symptoms): Start TB treatment. Assess the need for ART after completing TB therapy, using CD4 and clinical criteria CD4+ count < 200/mmΔ: Delay ARVs until after two-months intensive phase of TB therapy. Then start first line therapy as below, CD4+ count of < 50/ mmΔ or other serious HIV illness: introduce ART as soon as the patient is stabilized on TB therapy (no less than two weeks between starting TB therapy and starting ART). First-line therapy: 1. Stavudine 40 mg (or 30mg if <60kg) every 12 hours + 2. Lamivudine 150mg every 12 hours + 3. Efavirenz 600mg at night

Remember:
Patients on TB medication and ARVs are taking a large number of tablets - do pre-emptive counselling to

12.17 Counseling of co-infected patients

Table 3: Shared side effects of TB and antiretroviral therapy

Side effects	Antiretroviral treatment	Tuberculosis treatment
Nausea and vomiting	didanosine, zidovudine, ritonavir, saquinavir	Pyrazinamide
Hepatitis	nevirapine, efavirenz	rifampicin, isoniazid, pyrazinamide
Peripheral neuropathy	stavudine, didanosine	Isoniazid
Rash	nevirapine, efavirenz	rifampicin, isoniazid, pyrazinamide

12.17.1 HIV counseling and testing of individual TB patients

It is important to offer voluntary counselling and testing (VCT) to TB patients for the following reasons:

- The opportunity for patients to know their HIV status and prognosis.
- Early diagnosis and management of other HI V-related illnesses.
- Avoidance of drugs associated with a high risk of side-effects.
- Increased condom use and decreased HIV transmission.
- Opportunities for prevention of other infections (e.g. using cotrimoxazole).

A policy of compulsory HIV testing (even if this were legal) of TB patients would be counter productive. This type of policy would result in patients deterred from seeking care, decreased case-finding in at-risk groups and reduced credibility of health services.

Counselling with assurance of confidentiality is essential before and after HIV antibody testing. The patient gives explicit informed consent to have the test, i.e. the patient understands what the test involves and the implications of testing. Counselling is a dialogue between the patient and the counsellor, who provides information and support.

12.17.2 Counseling an HIV-positive patient diagnosed with TB

An HIV positive TB patient needs to be counseled on the various aspects of both TB and HIV.

- What is TB?
- Modes of spread of TB.
- Treatment of TB: how long it will be, the necessity of completing treatment and how the patient will be monitored.
- Necessity of doing sputum smear examination
- Necessity of taking treatment
- Contact screening
- Sputum disposal by patient
- lf side effects develop, contact a health worker immediately

13 Multi-drug Resistant Tuberculosis

At no time in recent history has tuberculosis been as widespread a concern as it is today. Despite highly effective drugs, disease and deaths due to Mycobacterium tuberculosis are increasing worldwide and are being fuelled by the widespread HIV epidemic. A most serious aspect of the problem has been the emergence of multidrug-resistant (MDR) tuberculosis, which poses a threat to individual patients as well as to communities.

MDR tuberculosis is defined as tuberculosis disease caused by strains of M. tuberculosis that are resistant in vitro to both rifampicin and isoniazid, with or without resistance to other drugs. As with other forms of drug resistance, MDR tuberculosis is a man-made problem, being largely the consequence of human error in any or all of the following:

- management of drug supply;
- patient management;
- prescription of chemotherapy; and/or
- patient adherence.

Most common medical errors leading to the selection of resistant bacilli:

- Prescription of inadequate chemotherapy (eg. three drugs during the initial phase of treatment in a new patient smear-positive with bacilli resistant to isoniazid).
- Adding one extra drug in the case of treatment failure, and often adding a further drug when the patient relapses after what amounts to monotherapy.

Most common errors observed in the management of drug supply:

- Frequent or prolonged shortages of antituberculosis drugs due to poor management.
- Use of two or three drugs when four or five first-line drugs should be given.
- Use of tuberculosis drugs (or drug combinations) of unproven bioavailability.
- Poor management practices multiplying the risk of successive monotherapies and selection of resistant bacilli.
- Health care workers not ensuring that a good relationship is built with the patient from the start, eg. not taking time to show an understanding of the patient's situation nor taking a problem-solving approach.
- Patient's lack of knowledge due to poor information, or not repeatedly checking on patient understanding and practice.
- Poor case-management, eg. careless attitudes, lack of friendly support, treatment not directly observed.
- Frequent staff changes, with no focal point for ensuring correct clinical practice.
- Poor staff morale, compounded by lack of regular support and supervision.
- Poor record keeping and follow-up of patients, compounded by poor referral systems.

Patient-related factors:

- Patient cooperation or adherence is most often a problem when the patient
- is homeless,
- has an alcohol or drug problem,
- is unemployed and/or looking for a job,
- when a family member has been unsuccessfully treated previously, or
- when access to health care is difficult.

An in-depth discussion with the patient at the initiation of treatment can help to decrease these constraints. The disuccsion can clarify the expectations of both the patient and the health care staff, help the patient try to solve barriers to adherence and assist in building a supportive relationship.

Since the mid-eighties, patients with MDR tuberculosis have been diagnosed in each of the nine provinces in South Africa, and a recent national survey by the Medical Research Council indicated a rate of 1.6% MDR in new tuberculosis cases and 6.6% in previously treated cases. This translates into at least 6 000 new cases of MDR tuberculosis in South Africa each year.

MDR tuberculosis is difficult and expensive to treat. The social and economic burden of this problem is already evident in South Africa where the cost of treating a case of MDR tuberculosis is up to 25 times the cost of treating an uncomplicated drug-susceptible case.

There is also ample reason to believe that the full brunt of MDR tuberculosis is still to be faced in the country. Several epidemiologic and genetic studies have confirmed ongoing transmission of drug-resistant tuberculosis. Nosocomial outbreaks of MDR tuberculosis associated with HIV infection have been documented, while HIV-infected patients being treated in hospitals for drug susceptible tuberculosis have been re-infected with MDR strains.

Experience in other countries has shown that patients with active, untreated MDR tuberculosis can infect large numbers of HIV-positive individuals, leading rapidly to significant outbreaks of MDR tuberculosis with high case-fatality rates. It is therefore of the utmost importance that MDR tuberculosis be prevented by rigorous adherence to the principles of the Tuberculosis Control Programme (the DOTS* strategy) and by patiently and consistently building partnerships with patients, their families and communities to cure tuberculosis at the first attempt.

To achieve tuberculosis control world-wide, the World Health Organization (WHO) considers the implementation of sound tuberculosis control based on the DOTS strategy a top priority. However, WHO recognises that MDR tuberculosis poses a considerable risk to the effectiveness of DOTS programmes. Therefor, WHO strongly encourages pilot projects to assess the feasibility and cost effectiveness of DOTS-Plus interventions in tuberculosis control programme settings, provided that DOTS is in place.

The National Tuberculosis Control Programme (NTCP) of the Department of Health developed a strategy in 2000 to treat patients with MDR tuberculosis in South Africa. This policy recommended that MDR tuberculosis treatment be provided as part of the NTCP in areas where the DOTS strategy has been implemented successfully. Each of the nine provinces currently provides MDR tuberculosis treatment through NTCP structures.

13.1 When to suspect MDR TB

- Retreatment patients who remain sputum smear positive after three months' of intensive Therapy.
- Treatment failure and defaulter cases.
- Close contacts of MDR tuberculosis cases.
- Chronic cases.

13.2 Diagnosing MDR TB

MDR TB is a laboratory diagnosis; it is only diagnosed by TB culture and susceptibility testing.

13.3 Management of MDR TB

- Refer MDR TB patients to an MDR TB unit where experienced clinicians can treat the patient according to the "Guidelines for the Management of Drug-resistant Tuberculosis Patients in South Africa". If you are unsure of which facility is designated as an MDR TB unit in your province.
- Management of MDR TB should be characterised by:
  - rational drug susceptibility testing of specimens from MDR tuberculosis patients;
  - provision of a social worker for counseling and support;
  - provision of key nursing staff to provide continuity during the treatment period;
  - direct observation of treatment throughout the course of treatment;
  - keeping updated registers;
  - monitoring compliance;
  - developing measures for rapid recall if patients interrupt their treatment;
  - increasing education and motivation of patients; and
  - tracing and evaluating contacts rapidly.

13.4 MDR TB contact management

Contact management for MDR TB should be the same as in contacts of pulmonary TB. There is no evidence to support giving such contacts MDR TB drugs as chemoprophylaxis. Early diagnosis before there is lung damage and correct treatment is the best way to improve outcomes of those infected with MDR TB.

13.5 HIV counselling and testing

All MDR tuberculosis patients should receive voluntary counseling and testing (pre- and post test) for HIV.

14 Non Tuberculosis Mycobacteria

14.1 Epidemiology and pathogenesis

Most non tuberculous mycobacteria (NTM) organisms have been isolated from water and soil. The best studied of these has been M. avium complex.

14.1.1 Prevalence in Humans

Although first observed soon after Koch's discovery of the tubercle bacillus, NTM were not widely recognized as human pathogens until the 1950s. The prevalence now appears to be increasing as a result of HIV and AIDS with M.Gvium complex being the most commonly reported infection in patients with AIDS.

14.2 Non tuberculous mycobacteria (NTM)

Synonyms: Mycobacteria other than tuberculosis (MOTTS), Atypical mycobacteria.

The term Mycobacterial species , may be misleading, as it includes Mycobacterium tuberculosis (MTB) as well as the non tuberculous mycobacteria(NTM), and is the term used on preliminary reports by some laboratories prior to completion of identification tests.

The non tuberculous mycobacteria (NTM) are environmental bacteria, found in soil, plants, animals, fish, and water. They are not spread from person to person. There are over a 100 different NTM, and new ones continue to be identified. They are generally less virulent than MTB, but may cause a variety of diseases ranging from localized pulmonary disease, to lymphadenopathy, skin lesions, wound infections, and disseminated disease particularly in patients with advanced HIV disease. Pulmonary disease from NTM resembles TB, and is seen in miners, patients with underlying chronic lung disease and occasionally presents as bronchiectasis predominantly in middle aged females.

NTM are acid fast bacilli, and cannot be differentiated from TB bacilli on direct microscopic examination of a sputum or lymph node aspirate. However, pulmonary disease in Africa is overwhelmingly due to infection with Mycobacterium tuberculosis, and acid fast bacilli seen on sputum should be regarded as TB bacilli. NTM are cultured in the same way as TB bacilli, and differentiated from TB bacilli using biochemical test and growth characteristics, or rapid molecular tests such as probes and PCR. Some of the biochemical tests take several weeks to complete. The importance of differentiating NTM from TB bacilli is that they require a different approach to management.

In many cases, the NTM isolated is a contaminant in the specimen, and the patient does not need treatment. In some patients, the NTM is merely colonizing an old TB cavity or area of damaged lung, and is not causing any disease. The decision about whether the NTM in the specimen is pathogenic, a contaminant or a colonizer is difficult and needs to be made by an expert. The clinical and radiological details, type of specimen, the number of isolates, and the specific NTM identified are all taken into consideration. Mycobacterium avium complex isolated from blood in an HIV/AIDS patient is always significant and requires urgent treatment.

Most NTM are resistant to standard TB drugs treatment. There are standard treatment regimens for each specific NTM, and sensitivity testing is not routinely performed. **NTM infections are sometimes misdiagnosed as MDRTB, but should never be treated as MDRTB.**

Note: Once a patient has been diagnosed with MOTTS, he/she should be referred to a specialized centre for further management

Admission and discharge criteria for TB patients

15

15.1 Introduction

Hospital care for TB patients is indicated in certain circumstances, and it is vital that there should be admission and discharge criteria in order to ensure optimal care for all TB patients. TB patients are only admitted to hospital care when either their clinical condition warrants it and/or access to community-based care is not available.

It is equally important that TB patients should be discharged to outpatient care at clinics as soon as they can be managed effectively in the community with DOT support. TB patients are not routinely admitted to a hospital. TB hospitals admit only patients with active TB who are referred from hospitals or clinics.

The aims of admission and discharge criteria and processes for TB hospitals are:

- To ensure that patients referred to TB hospitals by referral hospitals and clinics are appropriate referrals in accordance with admission criteria
- To ensure the successful completion of the intensive phase of TB treatment in sputum positive TB patient, where access to a clinic or community based support is not possible.
- To provide appropriate and effective care for TB patients that require hospitalization until they are well enough to be treated at a clinic or in the community.
- To reduce treatment interruption by ensuring continuity of care when patients no longer need to be treated in hospital. According to the discharge plan.
- In areas where there are no TB hospitals this would apply to the TB wards

15.2 Admission criteria for TB patients to TB hospitals

15.2.1 Referral from PHC clinics to TB hospitals

Admission is indicated if one or more of the following criteria are met. In all cases, a completed TB referral form should accompany referrals for admission from hospitals and clinics. This form must include relevant basic personal, clinical and diagnostic information e.g. confirmed sputum smear results for AFB or other reasons for making the diagnosis of TB (clinical findings, X-ray report or other).

- Medical reasons for admission are when patients diagnosed with TB are too ill or too weak to go home, including severely emaciated TB patients without other complications.
- Re- treatment TB cases that need streptomycin injections that cannot be managed at a PHC clinic.
- Social or socio-medical reasons for admission are when clinic or community supported care cannot be achieved, particularly in the case of high-risk groups like alcohol / drug dependents, mentally disturbed patients or previously non-compliant patients.

15.2.2 Referral from Public hospitals to TB hospitals

Admission is indicated if one or more of the following criterion is met. In all cases, a completed TB referral form should accompany referrals for admissions from public hospitals. This form must include relevant basic personal, clinical and diagnostic information e.g. confirmed sputum smear results for AFB or reasons for making the diagnosis of TB (Clinical findings, X- ray report or other).

- Patients diagnosed with TB who are too ill or too weak to go home, including severely emaciated TB patients without other complications.
- Re-treatment TB cases that need streptomycin injections that cannot be managed at a PHC clinic.
- If clinic or community supported care cannot be achieved, particularly in the case of high-risk groups like alcohol / drug dependents, mentally disturbed patients or previously non-compliant patients.

Please note:

- A patient with two negative sputum smears for AFB may not have TB at all but sputum should be sent for TB culture to exclude PTB. Reassess the patient according to the differential diagnosis of PTB e.g. Congestive Cardiac failure, Asthma, Chronic obstructive lung disease, Bronchiestasis, or Bronchial carcinoma. These patients should not initially be admitted to a TB hospital.
- Treating MDR-TB patients requires experience and special expertise. MDR-TB patients must be referred for evaluation, prescribing of treatment and follow-up at a specialised unit.
- PTB patients with medical conditions e.g. Diabetes mellitus, epilepsy and severe hypertension should be stabilized before referral.
- Severely ill extra-pulmonary TB patients (TB meningitis, TB spine, TB pericardi-

15.3 Essential elements of inpatient care in the TB hospitals

15.3.1 Clinical Management

- Ensure proper diagnosis for pulmonary TB sputum e.g. sputum smears for AFB and / or chest X-rays.
- Extra-pulmonary cases diagnosed by histology or chemical pathology.
- Ensure criteria for admission are met.
- Ensure proper classification of the cases e.g. new or re-treatment cases.
- Ensure correct anti-TB regimens prescribed.
- Emsure proper registration and motivation of the patient

15.3.2 Health Education for TB patients

Health education plan for each patient to be developed and implemented within 2 weeks of admission.

15.3.3 Offering VCT services to all TB patients

Trained counsellors to offer and provide counselling and HIV tesing to every TB patient during the course of their stay.

15.3.4 Social development

An Integrated plan to be established between the TB hospitals and the Social Welfare department in preparation for discharge. Social evaluation to be undertaken on TB patients to assess eligibility for support grants.

15.3.5 DOT support

Within one week of hospitalization, an individual patient plan for DOT management should be developed, e.g. confirm correctness of address, and arrange to meet with a potential DOT supporter as well as family member(s).

15.3.6 Management of other HIV related diseases

All dually infected patients should be on prophylactic co-trimoxazole treatment. Once they are clinically ready

for discharge, TB patients with HIV infection can be referred to home-based care services or "step-down" facilities.

15.4 Criteria for referral of TB patients from TB hospitals to district/regional hospitals

Patients should be referred to a secondary or tertiary care hospital whenever their clinical condition warrants more specialised care than the TB hospital can provides.

This includes:

- All severe complications due to TB disease that need intensive care management e.g. massive haemoptysis, severe dyspnoea and empyema.
- Severe drug reactions e.g. acute liver failure, Steven Johnson syndrome.
- HIV related diseases that need specialised medical care e.g. Cyptococcal meningitis.

15.5 Discharge criteria from the TB hospitals to PHC clinics

TB patients should be discharged from TB in patient care units as soon as the following two criteria are met:

- Medically stable (no dyspnoea, no haemoptysis, not severely emaciated and afebrile) and able to care for him/herself (or as soon as family or community-based care is arranged).
- Able to access treatment at a clinic and be monitored either by going to a clinic or by a DOT supporter.

15.6 Discharge process

Within 2 weeks of admission a discharge plan must be completed which ensures:

- Continuation of care (recruitment of DOT supporters, contact with the most accessible clinic).
- Patient education on TB management (e.g. infection control measures to be taken, duration of treatment and importance of compliance with the treatment).
- Patient and DOT supporter to meet before discharge from the hospital.
- Nutritional support should be arranged for patients with an inadequate access to food at home. A social worker needs to be involved to arrange support for such needy patients.

Referral to a local clinic or another hospital should always be done by:

- Completing the pink referral form in detail with all the relevant information. One copy is for the patient to take with to the clinic, one copy to be sent to the referral clinic and one is kept at the hospital.
- The green patient card should be updated before the patient leaves the TB hospital and the clinic or DOT supporter should keep it updated until the treatment is completed.
- If possible the patient should physically be delivered to the clinic, or be accompanied by a DOT supporter or Social worker on discharge, or the clinic should collect the patient. Where this is not possible, follow up with the clinic, should be made to confirm that patient arrived.

16 Infection Control

Anecdotal evidence suggests that concurrent increases in the incidence of TB are being observed among health care workers in the country. Recent studies of the risk of nosocomial transmission of M. tuberculosis performed in developing countries have shown that health care workers caring for infectious TB patients are at risk of M. tuberculosis infection and disease. Non-existent or ineffective TB infection control (IC) measures facilitate transmission in health care facilities.

The majority of patients are seen at primary health care level, therefore it is important to ensure that the measures for prevention of spread of infection do not only focus on hospitals but should address all levels of health care:

- Clinic level
- Hospital level
- TB hospitals and MDR-TB units

There are three levels of infection control (IC) measures - administrative (managerial), environmental, personal respiratory protection. Administrative controls are the most important since environmental controls and personal respiratory protection will not work in the absence of solid administrative control measures.

16.1 Administrative control measures

These reduce the risk of exposure for health care workers and patients, if this risk can be eliminated altogether then there is no need for the other control measures.

These measures include early diagnosis, prompt isolation and initiation of treatment of potentially infectious patients.

Risk assessment needs to be conducted for all facilities and an infection control plan developed to address the risks that have been identified with proper monitoring of the implementation of this plan. High risk areas are mainly outpatient departments, TB wards, TB hospitals, bronchoscopy suites, laboratories, and sputum induction / collection rooms

16.2 Environmental control measures

In cases where infectious particles cannot be eliminated various environmental control methods can be used in high-risk areas to further reduce the concentration of infectious particles in the air. These measures include improving ventilation, controlling the direction of flow of air. The implementation of these measures should be guided by the assessment of risk as well as availability of resources. There should be enough windows to allow for more ventilation and these should open to the outside and not to other wards and where possible the windows should be on opposite sides of the room to allow for cross ventilation. Doors can be kept open to maximise ventilation provided these do not open to other wards or rooms. In areas where maximum natural ventilation is not possible overhead fans can be installed to enhance ventilation in settings where windows can remain open, by facilitating circulation and mixing of air.

Mechanical ventilation can be used in areas where there may be high concentrations of infectious droplets. These are systems that facilitate air entry into the room and extraction from the room to the outside. The most cost effective are exhaust fans, these are placed in windows but it is important to ensure that airflow is adequate and that air flows across the room.

Exhaust ventilation systems that allow for exchange of air in the room as well as extraction of air to the outside. Negative pressure ventilation where the room is kept at negative pressure to the outside thus ensuring that air is drawn into the room and exhausted directly to the outside.

Ultraviolet germicidal irradiation (UVGI) may be used as an adjunctive measure. Ultraviolet rays kill the bacilli

but for this to be effective the contaminated air has to come into contact with the rays, therefore circulation of air is important and it is ineffective in humid and dusty environments. These are expensive, have to be installed properly for maximum effect and a regular programme of maintenance is essential.

16.3 Personal respiratory protection

Personal protection refers to the use of respirators that contain a special filter material that protects the wearer from inhaling the bacilli. They are used as the last resort where all the other measures have not completely eliminated the risk. They are most appropriately used for short term protection against high risk exposures i.e. during sputum inducing procedures, bronchoscopies, autopsies.

The recommended respirators are a type that covers the mouth and nose and fitted with a special particulate filter to filter out very small particles, i.e. N95 respirators wich are simple and the most reasonable device for use in the health care setting. Surgical masks are meant to prevent the spread of infectious particles from the person wearing the mask to others therefore do not protect the person wearing it from inhaling the particles as they have a limited filtration capacity. These are recommended on infectious patients under certain circumstances on a short term basis as this could perpetuate stigma.

17 Monitoring and evaluation in the National TB Control Programme

A key element of the DOTS Strategy is the establishment and maintenance of a system to monitor case detection and treatment outcomes. It is essential for efficient programme management since it provides a basis for evaluating the progress made in achieving programme targets, supervision of staff and for monitoring and surveillance.

Monitoring is the observation of programme performance to ascertain whether activities are accomplished as planned. It aims to identify problems quickly so that they can be solved without delay. Monitoring is carried out at both the services delivery unit through direct contact with health workers and at the management office by examining periodic reports.

Evaluation refers to the periodic assessment of progress towards operational targets and epidemiological objectives. Although a managerial activity, evaluation is usually carried out less frequently than monitoring and includes more than checking activities. For instance, it also includes measurement of indicators, such as percentage of patients cured, to assess progress in achieving targets and objectives

Accurate keeping of records on all individual patients and periodic reporting with statistics on patients and activities together with explanatory remarks is essential for planning, forecasting, procuring and distribution of drugs as well as laboratory material as well as evaluating control measures implemented in the TB programme.

The standardised forms utilised by the NTCP include (forms in annexe):

- **Suspect Register (GW):** which is kept in facilities, to record symptomatic patients reporting to that facility.
- **Laboratory request form for Sputum Examination:** this is kept in all facilities.
- Tuberculosis Laboratory Register, kept at laboratories performing sputum examination.
- **Patient treatment card (GW 20/15):** a patient-held for all patients on TB treatment.
- **Clinic/Hospital card (GW 20/12):** which is kept in all facilities and used to collect all the information about the patient (demographic, disease classification, treatment regimen, monitoring and outcomes).
- **Tuberculosis Register (GW 20/11):** Kept in all facilities and is used to record key information (demographic, disease classification, treatment regimen, monitoring and outcomes) on each registered patient.
- **Transfer form (GW20/14):** kept in all facilities and used to report on the key patient information from the register required when the patient is transferred from one district to another.

Reports:

- **Quarterly report on case finding:** filled at (sub) district level.
- **Quarterly report on smear conversion:** Completed at (sub)/ district level, reports on the previous quarter's cohort.
- **Quarterly report on treatment outcomes for smear positive cases of pulmonary TB**: completed at (sub)/ district for the cohort registered 12-15 months earlier.
- **Quarterly report on programme management:** compiled at (sub)/ district level, and is mainly a narrative report.

17.1 Information flow

The information collected at facility level in the clinic or hospital card is entered into the register and all these have to be updated regularly. Analysis and validation of the data should be done at facility level with facility reports completed quarterly From the facilities this is passed on to the sub district where it is collated and analysed.

17.2 Electronic TB Register

This is a programme management tool used at sub / district level. The information submitted to the sub / district is entered into the electronic register and data validation as well as analysis is done using this tool. *The following reports can be generated by the system:*

a. Report on Case finding
b. Report on Sputum Conversion
c. Report on Treatment Outcome
d. Facility Profile Reports

Aggregated data are exported to the DHIS (district health information system) at sub / district level. Data is then transmitted electronically from the sub / district level to provincial level where it is aggregated and analysed before it is passed on to national level.

17.3 Evaluation

The most important part of evaluating case finding is to compare the expected and the observed rates (per 100 000 population) of smear positive pulmonary TB cases. The observed rates can be determined from the quarterly report on case finding. The expected rates can be estimated from TB prevalence studies.

In general it is expected that at least 2% of adult outpatients will be chest symptomatic, and that 5-15% of chest symptomatics examined will be sputum positive. Diagnostic practises can be evaluated by determining the proportion of smear positive cases among all pulmonary cases diagnosed. If the proportion who are smear positive is much less than half, either smear examinations are being done poorly, or there is over diagnosis of smear negative TB or both. Cohort analysis is the important part of evaluation of the programme. The most important indicator of programme success is the cure rate of new smear positive cases, which should be greater than 85%.

17.4 Programme Monitoring Indicators

The dates for analysis of data at district level for treatment outcomes of patients, who started treatment for example in year 2004, should be as follows:

Start of treatment	Date of analysis
01 January 2004 to 31 March 2004	First week of April 2005
01 April 2004 to 30 June 2004	First week July 2005
01 July 2004 to 30 September 2004	First week October 2005
01 October 2004 to 31 December 2004	First week January 2006

17.4.1 Case finding

Indicator	Description	Source	Collection	Level	Range/notes
1. Proportion of smear positive pulmonary cases among TB suspects	No. of smear positive pulmonary cases detected divided by the total number of suspects	Laboratory register	Supervision	All	5-20%
2. Case detection rate new smear positive pulmonary cases	No. new smear positive pulmonary cases as percentage expected number of	R&R	Quarterly report	National	70% WHO objective(1)

Indicator	Description	Source	Collection	Level	Range/notes
3. Proportion pulmonary smear positive cases out of all pulmonary cases	No. All smear positive pulmonary cases divided by total number of pulmonary cases	R&R	Quarterly report	All	50-70%
4. Retreatment ratio	No. of smear positive retreatment cases (relapses and other retreatments) divided by the sum of new smear positive pulmonary patients and retreatment cases.	R&R	Quarterly report	All	6-8% Only ss+ RRx cases counted, not other RRx cases
5. Accessibility of laboratory services	No. laboratories with sputum smear services divided by no. all laboratories. (in NHLS)	Progress reports	Half-yearly evaluation meetings	Province National	Area specific
6. Smear result turn around time	Number of days elapsed between receiving sputum specimens from the patient and receiving results Definition is important. Delay in sending s hould be part of undesirable delay.	Sputum referral form Laboratory register	Supervision	All	0-48 hours
7. Proportion of HIV + TB cases out of all TB cases	Number of HIV + TB cases divided by the total number of	TB register	Quarterly report	All	

17.4.2 Case holding

Indicator	Description	Source	Collection	Level	Range/notes
1. Ratio smear positive pulmonary patients put on treatment	No. smear positive pulmonary patients in TB register divided by no. in Laboratory register or Suspect register	TB register Laboratory register or suspect register	Supervision	All	95-100%
2. Conversion rate at 2 (3) months	No. smear positive cases that convert from smear positive to smear negative at 2 (new smear positive patients) and 3 (retreatment patients) months	R&R	Quarterly report	All	> 85%
3. Treatment outcome	Cure, completion, success, failure, death, default and transfer rates for different patient categories	R&R report	Quarterly	All	> 85%
4. Access and acceptance of VCT	Proportion of TB patients receiving VCT out of all registered	Progress reports	Yearly evaluation meeting	Province National	

(1) WHO target of 70% is utilised for national purposes. However, calculation of the case detection rate is problematic because it is difficult to establish the denominator of real incidence, due to HIV/TB and absence of reliable data on the Annual Risk of Infection.

(2) At any given time drugs stocks should not be below the given target, to ensure efficient drug distribution and uninterrupted drug supply. It means that reserve stocks in each province should be 12 m/s at the moment that a new supply is delivered.

(3) Initial resistance: Convention is that this should ideally be 0%, not more than 1%. Acquired resistance should be low as well, but will be somewhat higher than IR.

17.4.3 Program management

Indicator	Description	Source	Collection	Level	Range/notes
1. DOT(S) coverage	No. districts implementing DOTS strategy as percentage of all districts in province/country No. of clinics offering DOT services, as percentage of all PHC clinics No. of patients receiving community-based DOT as percentage of all patients	Progress report	Half-yearly evaluation meeting	Province National	100% Area specific indicator given that all patients get DOT
2. Supervision	Proportion of supervisory visits conducted as proportion of visits programmed	Progress Reports	Quarterly report	Province National	75%
3. Reporting	Proportion of correct quarterly reports timely at provincial level	R&R	Quarterly report	Province National	100%
4. Drug accounting	Proportion and type of drugs and supplies used in a quarter compared to the estimates for that quarter	R&R	Quarterly report	Province National	90-110%
5. Drug stocks	Various stocks of TB drugs at district, provincial, expressed in Month/Supplies	Quarterly drug stock reports	Quarterly	Unit, District, Province	· 3 m/s · 3 m/s · 6 m/s
6. Sputum smear Quality control	Proportion of slides false positive or negative in QA samplProportion of agreement in sputum smear quality control	QA report	Supervision	Province National	**(2)** FP: 0-2% FN: 0-5%95% or higher
7. Training	Proportion of training sessions conducted as proportion of sessions programmed	Progress Reports	Quarterly report	All	>80%
8. Drug Resistance	Prevalence and trends of drug resistance, MDR-TB	Project report	Survey	Province National	IR: 0-1% AR: 2-4%

Annexure1: Essential tuberculosis A1

1. Isoniazid

Group: antimycobacterial agent
Tablet: 100mg 300mg
Injection: 25 mg/rn/in 2-ml ampoule

General information

Isoniazid, the hydrazide of isonicotinic acid is highly bactericidal against replicating tubercle bacilli. It is rapidly absorbed and diffuses readily into all fluids and tissues. The plasma half-life, which is genetically determined, varies from less than one hour in fast acetylators to more than three hours in slow acetylators. It is largely excreted in the urine within 24 hours, mostly as inactive metabolites.

Clinical information

Uses

- A component of all TB chemotherapeutic regimens currently recommended by WHO.
- Isoniazid alone is occasionally used to prevent:
  - Transmission to close contacts at high risk of disease.
  - Progression of infection to primary complex in recently infected, asymptomatic individuals.
  - Development of active TB in immunodeficient individuals.

Dosage and administration

Isoniazid is normally taken orally but it may be administered intramuscularly to critically ill patients.

Treatment (combination therapy)

Adults and children:

- mg/kg (4-6 mg/kg) daily, maximum 300 mg
- 10 mg/kg three times weekly

Preventive therapy:

- **Adults:** 300 mg/kg daily for six months at least
- **Children:** 5 mg/kg daily (maximum 300 mg) for six months at least

Contraindications:

- Known hypersensitivity
- Active hepatic disease

Precautions

Monitoring of serum concentrations of hepatic transaminases, where possible, is useful in patients with pre-existing chronic liver disease. Patients at risk of peripheral neuropathy as a result of malnutrition, chronic alcohol dependence or diabetes should additionally receive pyridoxine, 10 mg daily. Where the standard of health in the community is low, this should be offered routinely. Isoniazid interacts with anti-convulsants used for epilepsy. It may be necessary to reduce the dosage of these drugs during treatment with isoniazid.

Use in pregnancy

Whenever possible, the six-month regimen based upon isoniazid, rifampicin and pyrazinamide should be used.

Adverse effects

1. Isoniazid is generally well tolerated at recommended doses. Systemic or cutaneous hypersensitivity reactions occasionally occur during the first weeks of treatment.

2. The risk of peripheral neuropathy is excluded if vulnerable patients receive daily supplements of pyridoxine. Other less common forms of neurological disturbance, including optic neuritis, toxic psychosis arid generalized convulsions, can develop in susceptible individuals, particularly in the later stages of treatment and occasionally necessitate the withdrawal of isoniazid.
3. Hepatitis is an uncommon but potentially serious reaction that can usually be averted by prompt withdrawal of treatment. More often, however, a sharp rise in serum concentrations of hepatic transaminases at the outset of treatment is not of clinical significance, and usually resolves spontaneously during continuation of treatment.

Drug interactions

Isoniazid tends to raise plasma concentrations of phenytoin and carbamazepine by inhibiting their metabolism in the liver. The absorption of isoniazid is impaired by aluminium hydroxide.

Overdosage

Nausea, vomiting, dizziness, blurred vision and slurring of speech occur within 30 minutes to three hours of overdosage. Massive poisoning results in coma preceded by respiratory depression and stupor. Severe intractable seizures may occur. Emesis and gastric lavage, activated charcoal, anti-epileptics and IV sodium bicarbonate can be of value if instituted within a few hours of ingestion. Subsequently, haemodialysis may be of value. Administration of high doses of pyridoxine is necessary to prevent seizures.

Storage

Tablets should be kept in well-closed containers, protected from light. Solution of injection should be stored in ampoules protected from light

2. Rifampicin

Group: antimycobacterial agent
Capsule or tablet: 150 mg, 300 mg

General information

A semi synthetic derivative of rifamycin, a complex macrocyclic antibiotic, inhibits ribonucleic acid synthesis in a broad range of microbial pathogens. It has bactericidal action and a potent sterilizing effect against tubercle bacilli in both cellular and extra cellular locations. Rifampicin is lipid-soluble. Following oral administration, it is rapidly absorbed and distributed throughout the cellular tissues and body fluids; if the meninges are inflamed, significant amounts enter the cerebrospinal fluid.

A single dose of 600 mg produces a peak serum concentration of about 10 micrograms/ml in two to four hours, which subsequently decays with a half-life of two to three hours. It is extensively recycled in the enterohepatic circulation, and metabolites formed by deacetylation in the liver are eventually excreted in the faeces. Since resistance readily develops, rifampicin must always be administered in combination with other effective antimycobacterial agents.

Clinical information

Uses

A component of all six and eight month TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration

Rifampicin should preferably be given at least 30 minutes before meals, since absorption is reduced when it is taken with food. This however may not be clinically significant and food can reduce intolerance to drugs. **Adults and children:** 10 mg/kg (8-12 mg/kg) daily, maximum 600mg daily, two or three times weekly.

Contra-indications

- Known hypersensitivity to rifamycins
- Hepatic dysfunction

Precautions

Serious immunological reactions resulting in renal impairment, haemolysis or thrombocytopenia are on record in patients who resume taking rifampicin after a prolonged lapse of treatment. In this rare situation it should be immediately and definitely withdrawn. Careful monitoring of liver function is required in the elderly and in patients who are alcohol-dependent or have hepatic disease. Patients should be warned that treatment may produce reddish coloration of urine, tears, saliva and sputum, and that contact lenses may be irreversibly stained.

Use in pregnancy

Whenever possible, the six-month regimen based upon isoniazid, rifampicin and pyrazinamide should be used. Vitamin K should be administered at birth to the infant of a mother taking rifampicin because there is a risk of postnatal haemorrhage.

Adverse effects

1. Rifampicin is well tolerated by most patients at currently recommended doses, although gastrointestinal intolerance can be unacceptably severe. Other adverse effects (fever, influenza-like syndrome and tbrombocytopenia) are more likely to occur with intermittent administration, and skin rashes just as likely. Exfoliative dermatitis is more frequent in HIV-positive TB patients.
2. Temporary oliguria, dyspnoea and haemolytic anaemia have also been reported in patients taking the drug three times weekly. These reactions usually subside if the regimen is changed to one with daily dosage.
3. Moderate rises in serum concentrations of bilirubin and transaminases, which are common at the outset of treatment, are often transient and without clinical significance. However, dose-related hepatitis can occur which is potentially fatal. It is consequently important not to exceed the maximum recommended daily dose of 10 mg/kg (600 mg).

Drug interactions

Rifampicin induces hepatic enzymes, and may increase the dosage requirements of drugs metabolized in the liver. These include corticosteroids, steroid contraceptives, oral hypoglycaemic agents, oral anticoagulants, phenytoin, cimetidine, cyclosporin and digitalis glycosides. Since rifampicin reduces the effectiveness of the oral contraceptive pill, women should consequently be advised to choose between one of the following two options for contraception. Following consultation with a physician, she could take an oral contraceptive pill containing a higher dose of oestrogen (50mcg).

Alternatively she could use a non-hormonal method of contraception throughout rifampicin treatment and for at least one month subsequently. Current antiretroviral drugs (non-nucleoside reverse transcriptase inhibitors and protease inhibitors) interact with rifampicin. This may result in the ineffectiveness of antiretroviral drugs, ineffective treatment of TB or an increased risk of drug toxicity. Biliary excretion of radiocontrast media and sulfobromophthalein sodium may be reduced and microbiological assays for folic acid and vitamin B12 disturbed.

Overdosage

Gastric lavage may be of value if undertaken within a few hours of ingestion. Very large doses may depress central nervous function. There is no specific antidote and treatment is supportive.

Storage

Capsules and tablets should be kept in tightly closed containers, protected from light.

3. Isoniazid/Rifampicin

General information

Fixed combination of rifampicin and isoniazid intended to promote compliance. It is essential that all such products are shown to have adequate bio-availability.

Clinical information

Uses

Both drugs are components of all six and eight month TB chemotherapeutic regimens currently recommended by WHO.

Dosage administration

There are different dosage forms, for daily use and for intermittent use in adults and children.

For daily use

- **Tablets for adult use:**
- 150 mg isoniazid + 300mg rifampicin
- 75 mg isoniazid + 150 mg rifampicin
- **Tablet or pack of granules for paediatric use:**
- 30mg isoniazid + 60 mg rifampicin

For intermittent use (three times weekly)

- **Tablets for adult use:**
- 150mg isoniazid + 150mg rifampicin
- **Tablet or pack of granules for paediatric use:**
- 60 mg isoniazid + 60 mg rifampicin

4. Pyrazinamide

Group: antimycobacterial agent
Tablet: 400 mg

General information

A synthetic analogue of nicotinamide that is only weakly bactericidal against M tuberculosis, but has potent sterilizing activity, particularly in the relatively acidic intracellular environment of macrophages and in areas of acute inflammation. It is highly effective during the first two months of treatment while acute inflammatory changes persist and its use has enabled treatment regimens to be shortened and the risk of relapse to be reduced. It is readily absorbed from the gastrointestinal tract and is rapidly distributed throughout all tissues and fluids. Peak plasma concentrations are attained in two hours and the plasma half-life is about 10 hours. It is metabolized mainly in the liver and is excreted largely in the urine.

Clinical information

Uses

A component of all six and eight month TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration

Adults and children (for the first two or thee months):

- 25 mg/kg daily (20-30 mg/kg)
- 35 mg/kg (30-40 mg/kg) three times weekly

Contraindication

- Known hypersensitivity

· Severe hepatic impairment

Precautions
Patients with diabetes should be carefully monitored since blood glucose concentrations may become labile. Gout may be exacerbated.

Use in pregnancy
The six month regimen based upon isoniazid, rifampicin and pyrazinamide should be used whenever possible.

Adverse effects
Pyrazinamide may cause gastro intestinal intolerance. Hypersensitivity reactions are rare, but some patients complain of slight flushing of the skin. Moderate rises in serum transaminase concentrations are common during the early phases of treatment. Severe hepatotoxicity is rare. As a result of inhibition of renal tubular secretion, a degree of hyperuricaemia usually occurs, but this is often asymptomatic. Gout requiring treatment with allopurinol occasionally develops. Arthralgia, particularly of the shoulders, may occur and is responsive to simple analgesics (aspirin). Both hyperuricaemia and arthralgia may be reduced by prescribing regimens with intermittent administration of pyrazinamide.

Overdosage
Little has been recorded of pyrazinamide overdose. Acute liver damage and hyperuricaemia have been reported. Treatment is essentially symptomatic. Emetic and gastric lavage may be of value if undertaken within a few hours of ingestion. There is no specific antidote and treatment is supportive.

Storage
Tablets should be stored in tightly closed containers, protected from light.

5. Streptomycin
General information
An aminoglycoside antibiotic derived from Streptomyces griseus that is used in the treatment of TB and sensitive Gram-negative infections. Streptomycin is not absorbed from the gastrointestinal tract but, after intramuscular administration, it diffuses readily into the extracellular component of most body tissues and it attains bactericidal concentrations, particularly in tuberculous cavities. Little normally enters the cerebrospinal fluid, although penetration increases when the meninges are inflamed. The plasma half-life, which is normally two to three hours, is considerably extended in the new-born, in the elderly and in patients with severe renal impairment. It is excreted unchanged in the urine.

Clinical information
Uses
A component of several TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration
Streptomycin must be administered by deep intramuscular injection.

Adults and children
· 15 mg/kg (12-18 mg/kg) daily, or two or three times weekly.
· Patients over 60 years may not be able to tolerate more than 500-750 mg daily.

Contraindications
· Known hypersensitivity

- Auditory nerve impairment
- Myasthenia gravis

Precautions

Hypersensitivity reactions are rare; if they occur (usually during the first weeks of treatment) streptomycin should be withdrawn immediately. Once fever and skin rash have resolved, desensitization may be attempted.

Streptomycin should be avoided, when possible, in children because the injections are painful and irreversible auditory nerve damage may occur. Both the elderly and patients with renal impairment are also vulnerable to dose-related toxic effects resulting from accumulation. Where facilities are available to monitor and function closely it may be possible to give streptomycin in reduced doses to patients with renal impairment. Where possible, serum levels should be monitored periodically and dosage adjusted appropriately to ensure that plasma concentrations, as measured when the next dose is due, do not rise above 4 mg/mI.

Protective gloves should be worn when streptomycin injections are administered, to avoid sensitisation dermatitis.

Use in pregnancy

Streptomycin should not be used in pregnancy. It crosses the placenta and can cause auditory nerve impairment and nephrotoxicity in the fetus.

Adverse effects

Injections are painful and sterile abscesses can form at injection sites. Hypersensitivity reactions are common and can be severe. Impairment of vestibular function is uncommon with currently recommended doses. Dosage should be reduced if headache, vomiting, vertigo and tinnitus occur.

Streptomycin is less nephrotoxic than other aminoglycoside antibiotics. Dosage must be reduced by half immediately if urinary output falls, if albuminuria occurs or if tubular casts are detected in the urine. Haemolytic anaemia, aplastic anaemia, agranulocytosis, thrombocytopenia and lupoid reactions are rare adverse effects.

Drug interactions

Other ototoxic or nephrotoxic drugs should not be administered to patients receiving streptomycin. These include other aminoglycoside antibiotics, amphotericin B, cefalosporins, etacrynic acid, cyclosporin, cisplatin, furosemide and vancomycin. Streptomycin may potentiate the effect of neuromuscular blocking agents administered during anaesthesia.

Overdosage

Haemodialysis can be beneficial. There is no specific antidote and treatment is supportive.

Storage

Solutions retain their potency for 48 hours after reconstitution at room temperature and for up to 14 days when refrigerated. Powder for injection should be stored in tightly closed containers protected from light.

6. Ethambutol

Group: antimycobacterial agent
Tablet: 100 mg, 400 mg (hydrochloride)

General information

A synthetic congener of I ,2-ethanediamine that is active against M. tuberculosis, M. bovis and some non-specific mycobacteria. It is used in combination with other TB drugs to prevent or delay the emergence of resistant

strains. It is readily absorbed from the gastrointestinal tract. Plasma concentrations peak in 2-4 hours and decay with a half-life of 3-4 hours. Ethambutol is excreted in the urine both unchanged and as inactive hepatic metabolites, about 20% is excreted in the faeces as unchanged drug.

Clinical information

Uses

An optional component of several TB chemotherapeutic regimens currently recommended by WHO.

Dosage and administration

Adults:

- 15 mg/kg (15-20 mg/kg) daily
- 30 mg/kg (25-35 mg/kg) three times weekly
- **Children:** maximum 15 mg/kg daily
- Dosage must always be carefully calculated on a weight basis to avoid toxicity, and should be reduced in patients with impaired renal function.

Contraindications

- Known hypersensitivity.
- Pre-existing optic neuritis from any cause.
- Creatinine clearance of less than 50 mI/minute.

Precautions

Patients should be advised to discontinue treatment immediately and to report to a doctor should their sight or perception of colour deteriorate. Whenever possible, renal function should assessed before treatment.

Use in pregnancy

The six month regimen based upon isoniazid, rifampicin and pyrazinamide should be used. Ethambutol should be used if a fourth drug is needed during the initial phase.

Adverse effects

1. Dose-dependent optic neuritis can result in impairment of visual acuity and colour vision. Early changes are usually reversible, but blindness can occur if treatment is not discontinued promptly
2. Ocular toxicity is rare when used for 2-3 months at recommended doses.
3. Signs of peripheral neuritis occasionally develop in the legs

Overdosage

Emesis and gastric lavage may be of value if undertaken within a few hours of ingestion. There is no specific antidote and treatment is supportive.

Storage

Tablets should be stored in well-closed containers.

A2 Annexure 1: Clinically significant drug-drug interactions involving

Drug class	Drugs whose concentrations are substantially reduced by	Comments
Anti-infectives	Rifampicin	Saquinavir/ ritonavir can be used with Rifampicin, Lopinavir/ ritonavir can also be used with adjustment of ritonavir dosage
	Protease inhibitors (Saquinavir, Indinavir, Nelfinavir, Ritonavir, Lopinavir/ ritonavir)	Doses of Nevirapine and Efivarenz need to be increased
	NNRTI (Nevirapine, Efivarenz)	Azithromycin has no significant interaction
	Macrolide antibiotic (clarithromycin, erythromycin)	May require use of a drug other than doxycycline
	Doxycycline	Concentrations of these drugs may be sub therapeutic. Fluconazole may be used but dose might need to be increased
	Azole antifungal agents (Ketoconazole, Itraconazole, voriconazole)	Consider alternate form of malaria prophylaxis
	Mefloquine	Consider an alternate antibiotic
	Chloramphenicol	Consider alternate form of pneumocystis carinii treatment or prophylaxis
	Atovaquone	
Hormone therapy	Ethinyl estradiol, norethindrone	Women on oral contraception should be advised to add a barrier method of contraception
		May require alternate therapy
	Tamoxifen	May require increased dose of levothyroxine. Monitoring of serum TSH recommended
	Levo-thyroxine	
Narcotics		May require methadone dose increase
Anticoagulants	Methadone	May require 2-3 fold dose increase, monitoring prothrombin time recommended
	Warfarin	
Immuno-suppresive agents	Cyclosporine, tacrolimus	Monitoring of cyclosporin serum concentrations may assist with dosing
	Corticosteroids	Monitor clinically, may require 2-3 fold increase in corticosteroid dose
Anticonvulsants	Phenytoin, Lamotrigine	Therapeutic drug monitoring recommended may require anticonvulsant dose increase
Psychotropic drugs	Nortiptyline	Therapeutic drug monitoring recommended, may require dose increase or change to alternate psychotropic drug.
	Haloperidol, Quetiapine	Monitor clinically may require dose increase or use of alternate psychotropic drug

Drug class	Drugs whose concentrations are substantially reduced by Rifampicin	Comments
		Monitor clinically may require dose increase or use of alternate psychotropic drug
Hypolipidemics	Benzodiazepines (diazepam, triazolam, zolpidem, buspirone)	Monitor hypolipidemic effect, may require use of an alternate hypolipidemic drug
Sulfonurea hypoglycaemics	Simvastatin, Fluvastatin	Monitor blood glucose, may require dose increase or change to an alternate hypoglycaemic drug
Bronchodilators	Tolbutamide, chlorpropamide, glimepiride, repaglinide, glyburide	Therapeutic drug monitoring recommended, may require theophylline dose increase
Cardiovascular agents	Theophylline	Clinical monitoring recommended, may require change to alternate cardiovascular agent
	Verapamil, Nifedipine, Diltiazem	Clinical monitoring recommended, may require dose increase or change to alternate cardiovascular agent
	Propranolol, metoporol	Clinical monitoring recommended, may require dose increase or change to alternate cardiovascular agent
	Enalapril, Losartan	Therapeutic drug monitoring recommended, may require dose increase
	Digoxin (in patients with renal insufficiency), Digitoxin	Therapeutic drug monitoring recommended, may require quinidine dose increase
	Quinidine	Clinical monitoring recommended, may require change to alternate cardiovascular agent

A3 Annexure 3: Patient treatment card

NATIONAL TUBERCULOSIS CONTROL PROGRAMME GW 20/15

PATIENT TREATMENT CARD

Revised 2001

Health district _____ Treatment point _____

Clinic/Hospital _____ Telephone no _____

Surname _____

Full name(s) _____

y y

Register number cc cc cc

d d m m y y

Resgistration date cc cc cc Sex c Age (in years) cc

Transferred/Moved c N = Newly registered

M = Moved in from facility in the district

T = Transferred in from facility in another district

PATIENT CATEGORY

c(N)	New patient	c(RF)	Retreatment after failure
c(RC)	Retreatment after previous cure	c(RI)	Retreatment after interruption
c(RCA)	Retreatment after previous completion		

INTERNATIONAL CODE FOR DISEASE (ICD-10)

cA16.2	TB PULMONARY	cA16.7	TB primary	cA18.8	TB other organs
cA16.3	TB lymph nodes	cA17.0	TB meningitis	cA19.9	TB miliary
cA16.5	TB pleura/other resp org	cA18.0	TB bones/joints		

NOTIFICATION INFORMATION

Has patient been notified cYes cNo

d d m m y y

Date of notification cc cc cc

Completed by _____ Telephone number _____

REGIMEN AND DOSAGES

d d m m y y

Regimen 1 - New Adult c Regimen 2 - Retreatment Adult c Regimen 3 - Children c Treatment Start Date cc cc cc

a. INTENSIVE PHASE

				Other drugs (specify)				
Drug	RHZE	RHZ	S					Weight at Diagnosis
Number tabs								kg.

H = Isoniazid R = Rifampicin Z = Pyrazinamide E = Ethambulol S = Steptomycin

*The use of fixed - dose bombinations are a central part of national TB Programme guidelines.

	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			

b. CONTINUATION PHASE Other drugs (specify

Drug	HR	E					Weight at end of intensive phase
Number tabs							kg.

	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			

SPUTUM BACTERIOLOGY RESULTS (Enter date specimen collected)								
Pre - Treatment		End of intensive Phase (2/3 months)		Discharge		Culture **		
Smear Date(s)	Smear Result(s)	Smear Date(s)	Smear Result(s)	Smear Date(s)	Smear Result(s)	Specimen Date(s)	Culture Result	Suscept Results

**Non-converters and retreatment cases

TREATMENT SUPERVISOR

cRelative cEmployer cTeacher cCommunity health worker cClinic nurse

cOther

Name _____ Adress _____

_____ Telephone no _____ Code _____

TREATMENT OUTCOME

c**(C)** **Cured;** Patient who is smear-negative at, or one month prior to, completion of treatment and on at least one previous osccasion

c**(TC)** **Treatment completed** without bacteriologic proof of cure

c**(TF)** **Treatment failure**, patient remains, or becomes again smear-positive at 5 months or later during treatment

c**(D)** **Patient died** (any reason)

c**(TI)** **Treatment interrupted** for 2 or more months

c**(TRAN)** **Patient transferred** to another district; treatment outcome unknown

c**(MVD)** Check here if patient **MOVED** to another facility in the **SAME** district

NOTES _____

_____

_____

Discharged by (print name) _____

d d m m y y

Date of discharge c c c c c c

Annexure 4: Laboratory request form for sputum examination

A4

NATIONAL HEALTH LABORATORY SERVICE

PATIENT DETAILS

AALN8404

AALN8404

PLEASE PRINT CLEARLY

Surname

First Name

File Number

Identity Number

Date of Birth Age

Patient's Physical Address

Postal Code

Gender: Male c Female c

CLINIC DETAILS

Clinic Name

Sister's Name

Clinic (Responsibility) Code

Telephone Number

Fax Number

Health District

District Code

CLINIC DETAILS

Date Collected

Time Collected

Specimen Type

CLINICAL

Diagnosis

Curent Treatment

TB Sputum Specimen (a Tick)

Suspect | At 2-3mths

At 5-7mths | Other

TEST INVESTIGA-

TICK TEST REQUIRED a

TB Smear AFB

TB Culture for Mycobacterium TB bacilli

TB Sensitivity (HR + E)

TB Sensitivity other specify:

HIV Antibody

HB

RPR

Rh

Glucose

MCS (not TB)

Other tests:

AALN8404

AALN8404

AALN8404

AALN8404

Annexure 5: Laboratory result report.

NATIONAL HEALTH LABORATORY SERVICE

LABORATORIUM

Labno	:	MP 1006		
Patient	:	Patricia Nkomane Female		
Sender	:	Dr Gumege Mmamethlake Clinic	Age	: 25
Ref Dr	:	35/2003		
Hospital	:	12/11/2003	13/11/2003	
Hosp No	:	12/11/2003	16/11/2003	
Taken	:		Registered	:
Reported	:		First Report	:

LABORATORY REPORT

CLINICAL DATA : No clinical details supplied
SPECIMEN : Sputum : New case
TESTS ORDERED: TB Micro

TB MICROSCOPY

ZIEHL - NEELSEN STAIN
Result — Smear positive for Acid - fast bacilli
Positive ++ (10 per immersion field)

JM Khoza
Authorised by:

The results should be sent to the health facility within 48 hours.

Sender	:		Age	:
Ref Dr	:			
Hospital	:			
Hosp No	:			

Annexure 6: Patient clinic/hospital A6

SOUTH AFRICA

NATIONAL TUBERCULOSIS CONTROL PROGRAMME

PATIENT CLINIC/HOSPITAL CARD

Registration number cccc/cccc (y y y y)

Transferred/ Moved? c
N = Newly registered.
M = Moved in from facillity in this district
T = Transferred in from facillity in another district

Registration date cc/cc/cccc (d d m m y y y y)

Health District _____ Clinic/Hospital _____ Treatment point _____

Surename _____ Full name (s) _____

Home address _____

(First) _____

_____

Work address _____

_____

Telephone (H) _____ Telephone (W) _____

Home address _____

(New) _____

_____

Work address _____

_____

Telephone (H) _____ Telephone (W) _____

Race c
1 = African/Black
2 = Coloured
3 = Indian/Asian
4 = White
5 = Unspecified/Other

Gender c M/F

Age cc Years

Date of birth cc/cc/cccc (d d m m y y y y)

PATIENT CATEGORY

c (N)	New Patient		
c (RC)	Retreatment after previous cure	c (RF)	Retreatment after failure
c (RAC)	Retreatment after previous completion	c (RI)	Retreatment after interruption

INTERNATIONAL CODE FOR DISEASE

cA16.2	TB PULMONARY	cA16.7	TB primary	cA18.8	TB other organs
cA16.3	TB lymph nodes	cA17.0	TB meningitis	cA19.9	TB miliary
cA16.5	TB pleura/other resp org	cA18.0	TB bones/joints		

NOTIFICATION INFORMATION

Has patient been notified? cYes cNo

Date of birth cc/cc/cccc (d d m m y y y y)

Completed by _____ Telephone number _____

SPUTUM RESULTS

Pre - Treatment		End of intensive Phase (2/3 months)		Discharge		Culture **		
Smear Date(s)	Smear Result(s)	Smear Date(s)	Smear Result(s)	Smear Date(s)	Smear Result(s)	Specimen Date(s)	Culture Result	Suscept Results

** Non-converters and retreatment cases

REGIMEN AND DOSAGES

Treatment start date

Regimen 1 - New adult c Regimen 2 - Retreatment adult c Regimen 3 - Children c cc/cc/cccc

a. INITIAL INTENSIVE PHASE Other drugs (specify)

Drug	RHZE	RHZ	S					Weight at Diagnosis
Number tabs								kg.

H = Isoniazid R = Rifampicin Z = Pyrazinamide E = Ethambutol S = Sreptomycin

* The use of fixed-dose combinations is a central part of national TB Programme guidelines.

Use one of the following sybols in the upper space of the appropriate box and initial in the lower space after the drugs have been administered:

a= Medication takken under supervision at clinic.
X = Patient did not collect medication.
O = Patient did not have to collect medication (e.g. weekend).
- = Medication collected for self-administration or supervision elsewhere; draw horizontal line (-) to indicate number of days supply were given.

	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			

b. CONTINUATION PHASE

Drug	RH	E					Weight at Diagnosis
Number tabs							kg.

	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			

TREATMENT SUPERVISOR

c **Relative** c **Employer** c **Teacher** c **Community health worker** c **Clinic nurse** c **Other** _____

Name _____ **Address** _____

_____ **Telephone No.** _____ **Code** _____

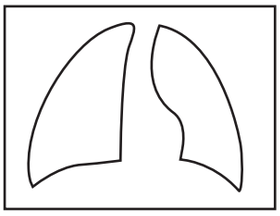
NOTES

Draw in pre- and post-treatment chest X-ray pictures if taken

Pre-treatment

Date taken .....

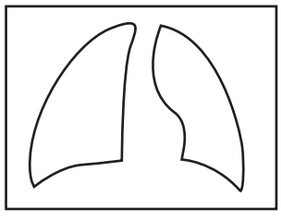
X-ray No .....



Post-treatment

Date taken .....

X-ray No .....



Date	Weight	Notes

PATIENT CONTACTS

Name and Surename		Relationship	Age	Sputum		X-ray		Tuberculin test	
				Date	Result	Date	Result	Date	Result
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
11									
12									
13									
14									
15									

Number of contacts traced cc Number of contacts treated cc

TREATMENT OUTCOME

c**(C)** **Cured;** Patient who is smear-negative at, or one month prior to, completion of treatment and on at least one previous osccasion

c**(TC)** **Treatment completed** without bacteriologic proof of cure

c**(TF)** **Treatment failure**, patient remains, or becomes again smear-positive at 5 months or later during treatment

c**(D)** **Patient died** (any reason)

c**(TI)** **Treatment interrupted** for 2 or more months

c**(TRAN)** **Patient transferred** to another district; treatment outcome unknown

c**(MVD)** Check here if patient **MOVED** to another facility in the **SAME** district

COMMENTS

_____

_____

_____

_____

_____

_____

_____

d d m m y y y y

Discharged by (print name) _____ Date of dischrge cc/cc/cccc

Annexure 7: Tuberculosis suspect register (for suspects age 5 years and older)

A7

TUBERCULOSIS SUSPECT REGISTER (For suspects age 5 years and older)

HEALTH FACILITY: DISTRICT: YEAR

Date	TB Suspect Number	3 Specimen Code	Name and Surname	Age M	Age F	4 Physical Address	5 Date sputum collected	Date results received	6 Results	7 Date Rx started	Observations; Diagnosis
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
		1					1	1	1		
		2					2	2	2		
							Number of suspects with Positive results			No. on Treatment	

1 First sputum
2 Second sputum

3 Barcode on specimen form, eg. AAGX8459

4 Full, detailed adress so that the patient can be located is s/he does not return for the result and the microscopy is positive Neg

5 Date the sputum was collected from the patient

6 Results of sputum-smear examination, eg. Scanty; +; ++; +++;

7 Date treatment started - TB treatment card was opened

GW 20/11

DISTRICT TUBERCULOSIS REGISTER

HEALTH DISTRICT:

REGISTRATION NUMBER ###/yy	REGISTRATION DATE AT THIS FACILITY dd/mm/yyyy	Transfer/ Moved? 1	NAME IN FULL *Upper space* Surname *Lower space* First names	SEX M/F	AGE	RACE 2	ADDRESS IN FULL	PATIENT CATEGORY 3	SITE OF DISEASE 4	THIS COURSE OF TREATMENT START DATE 5 *Upper space* Date *Lower Space* Regimen

1 Transfer/ Moved?

N = No, newly registered
M = Moved in from facility in this district
T = Transferred in from facility in another district

2 Race

1 = African/ Black
2 = Coloured
3 = Indian/ /Asian
4 = WhiteR
5 = Unspecified/ other

3 Patient Category

N = New patient who has never been treated or who has been treated less than four weeks.

RETREATMENT CATEGORIES

C = AFTER CURE: A patient who was previously treated for TB and who was declared cured and is now smear positive.
RAC = AFTER COMPLETION: Retreatment after completion of a previous course without microscopy results.
RF = TREATMENT FAILURE: A patient who, while on treatment, remained or became again smear-positive five months or later after commencing treatment. It is also a patient who was initially smear-negative before treatment and became smear-positive after the 2nd month of treatment.
RI = TREATMENT AFTER INTERRUPTION: A patient whose treatment is interrupted for two or more months and who returns to the health service (smear +ve or -ve).

4 Site of Disease (ICD-10)

A16.2 = TB pulmonary
A16.3 = TB lymph nodes
A16.5 = TB pleura and other respiratory organs
A16.7 = TB primary
A17.0 = TB meningitis
A18.0 = TB of the bone/joints
A18.8 = TB other organs
A19.9 = TB miliary

Followup TB Register

HEALTH FACILTY: _____ QUARTER: _____ YEAR: _____

SPUTUM SMEAR RESULTS (Enter date specimen collected)								CULTURE NON-CONVERTERS & RETREATMENT CASES			TREATMENT STOP DATE	OUTCOME 8	REMARKS (For example, use to note current status, last available information, etc.
Pre-Treatment		End of Intensive Phase (2 months)		End of Intensive Phase (3 months)		End of Treatment 6							
Smear Date(s)	Smear Results	Smear Date(s)	Smear Result(s)	Smear Date(s)	Smear Result(s)	Smear Date(s)	Smear Result(s)	Date(s)	Culture Results	Suscept. Results 7	dd/mm/yyyy		

5 Regimen

1 = New adult patients
Initial intensive Phase: 2 HRZE
Continuation Phase: 4 HR
2 = Retreatment adult patients
Initial intensive phase: 2 HRZES
Third Month: 1 HRZE
Continuation phase:
3 = New pediatric patients
Initial intensive Phase: 2 RHZ
Continuation Phase: 4 HR

6 Discharge

New cases:
End of six months, request sputum investigation at 5 months

Retreatment cases:
End of 8 months, request sputum investigations at 7 months.

7 Susceptibilitie

SAD = Sensitive to all drugs

H = Resistant to INH
HR = Resistant to INH,
HRE = Resistant to INH,

etc….

8 Outcome

C = Cure; Patient who is smear-negative at, or 1 month prior to completion of treatment and on at least one previous occasion
RIFC = Patient who completed treatment without bacteriologic proof of cure.
TF = Treatment failure; patient remains or becomes again smear-positive at 5 months or later during treatment.
D = Patient who died for any reason during treatment.
I = Treatment was interrupted for 2 or more months.
TRAN = Patient who has been transferred to another district & for whom the treatment outcome is not known.
(MVD = Moved to another facility in the same district)

A Annexure 9: Referral form

PATIENT REFERRAL FORM
(This form should be accompanied by a duplicate of the patient's Clinic/Hospital Card GW 20/12)

Patient Surname _____ Full Names _____

Register number cccc/cc (y y) Sex c Age (in year) cc

Referral to _____ Facility Address _____ Telephone number _____	Referral from _____ Facility Address _____ Telephone number _____
Home address (New) _____ Telephone number _____	Home address (Previous) _____ Telephone number _____

Work address _____ Nearest relative address _____

Transferred/Moved? c (d d m m y y)

R = Referring, has not been registered
N = Newly registered
M = Moved in from facility in this district
T = Transferred in from facility in another district

Registration date cc/cc/cc
Treatment start date cc/cc/cc

Patient Category? ☐

N New Patient
RC Retreatment after cure
RAC Retreatment after completion
RF Retreatment after failure
RI Retreatment after interruption

Regimen ☐

1 = New adult
2 = Retreatment adult
3 = Children

ICD-10 Code ☐

Sputum Bacterionlogy

Pre Treatment		End of Intensive Phase (2/3 months)	
~~Smear~~ Date(s)	~~Smear~~ Result(s)	~~Smear~~ Date(s)	~~Smear~~ Result(s)

Was patient notified? C Y/N

d d m m y y
Referral Date cc/cc/cc

OTHER INFORMATION (for example, basis of dx if smear negative, TTO, etc.)

_____

_____

_____

(Tear at perforation)

ACKNOWLEDGEMENT OF REFERRAL (to be completed within one mont after receiving referral)

From: (Facility) Register number (As referred) (y y) cccc/cc

(Facility address)

We have received the referral form and treatment card of (insert patiet name) _____

The patient has C has not C been seen in our facility to continue his/her treatment

Name: _____ Signature: _____

Date: (d d m m y y) cc/cc/cc

Annexure 10: Quarterly report on sputum conversion

A10

Sub-District:		
Facility:	Patients registered in Q……. Year…….	Date of completion of report ……/……/…….
Name of person completing report:		

New and relapse cases

Case categories	Pulmonary			Extra-pulmonary		Total
	Smear +	Smear -				
		< 15 yrs	>15 yrs	< 15 yrs	>15yrs	
New						
Relapses						

Other cases

Treatment after failure	Treatment after default	Other

New smear positive cases by sex and age group

	Age group in years							
Sex	0-14	15-24	25-34	35-44	45-54	55-64	>65	Total
F								
M								

A11 Annexure 11: Quarterly report on treatment outcomes

Sub-District:		
Facility:	Patients registered in Q……. Year…….	Date of completion of report ……/……/…….
Name of person completing report:		

Patient categories	**Number of smear positive patients registered**	**Smear conversion**						**Smear not done at 2/ 3 months**
		After 2 months		**After 3 months**		**Total**		
		N	%	N	%	N	%	
New cases								
Relapses								
Treatment after failure								
Treatment after default								

Annexure 12: Quarterly report on TB case finding

A12

Sub-District:		
Facility:	Patients registered in Q……. Year…….	Date of completion of report ……/……/…….
Name of person completing report:		

Case categories number		**Total number of pulmonary TB patients registered during quarter**	**Treatment outcomes**						**Total evaluated for outcomes**
			Cure	**Treatment completed**	**Died**	**Treatment failure**	**Default**	**Transfer out (and outcome not known)**	
New	Smear +								
	Smear -								
Re-treatment	Relapses								
	Treatment after failure								
	Treatment after default								