THE AURUM INSTITUTE

MANAGING TB

IN A NEW ERA OF DIAGNOSTICS

VERSION 3

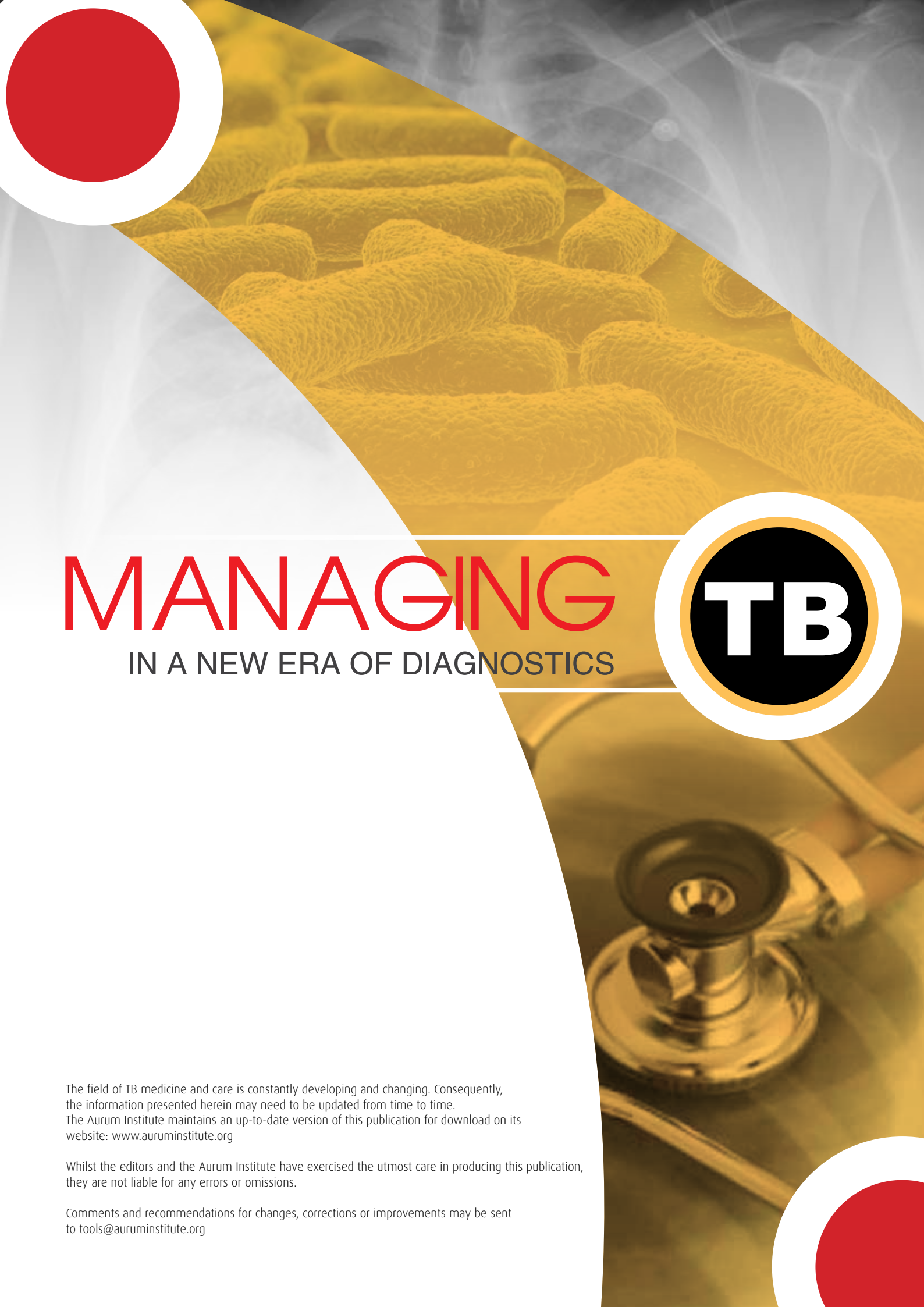
2016

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

CDC

SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

This guide was supported by a Cooperative Agreement Number 3U2GGH000887-02S1 from the Centers for Disease Control and Prevention. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the Centers for Disease Control and Prevention.



MANAGING TB

IN A NEW ERA OF DIAGNOSTICS

The field of TB medicine and care is constantly developing and changing. Consequently, the information presented herein may need to be updated from time to time. The Aurum Institute maintains an up-to-date version of this publication for download on its website: www.auruminstitute.org

Whilst the editors and the Aurum Institute have exercised the utmost care in producing this publication, they are not liable for any errors or omissions.

Comments and recommendations for changes, corrections or improvements may be sent to tools@auruminstitute.org

ACKNOWLEDGEMENTS

EDITORS

DR WAASILA JASSAT

MS LAUREN DE KOCK

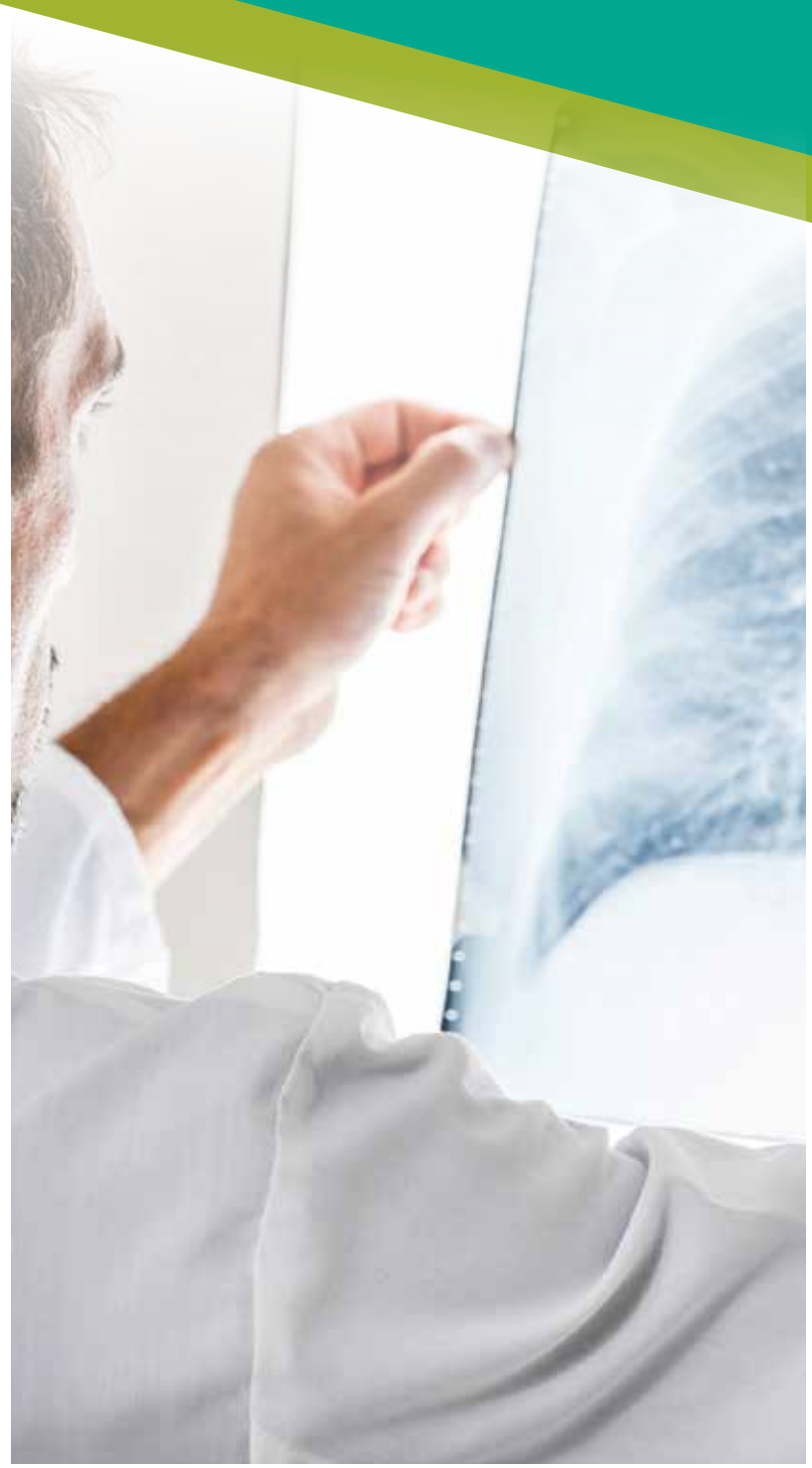
DR LIESL PAGE-SHIPP

DR FRANCESCA CONRADIE

CONTRIBUTORS

Mrs Lindi Bashele
Dr Natalie Beylis
Ms Marieta Booysen
Dr Salome Charalambous
Prof Gavin Churchyard
Mrs Alinah Denge
Dr Linda Erasmus
Mr Piotr Hippner
Ms Prudence Hlabane
Ms Ntombizodwa Hlongoane
Prof Chris Hoffman
Dr Nazir Ismail
Dr Tendesayi Kufa
Ms Bafi Kumalo
Prof Hendrik Koornhof
Mrs Busi Langa
Ms Blantina Mabuela
Ms Nokwazi Madhlala
Ms Cleopatra Maphiri
Mrs Martha Mashele
Mrs Deborah Mashigo
Ms Busisiwe Mashinini
Mrs Thobeka Mathebula
Mrs Harriet Mavuso
Mrs Zodwa Mayane
Dr Kerrigan McCarthy
Mrs Charlene Miller
Ms Salome Moletsane
Dr David Moore
Dr Lindiwe Mvusi
Mr Maanda Netshilindi
Ms Patricia Ntsele
Dr Jasantha Odayar
Mrs Annatjie Peters
Mr Mokete Phungwayo
Dr Elizabeth Prentice
Dr Mamothe Ratshefola
Dr Gary Reubenson
Dr Amashnee Saimen
Ms Martha Sello
Ms Mosala Silinda
Dr Andrew Whitelaw

Designed by:
Aurum Public Relations Department



The content in this toolkit has been developed based on the following Department of Health guidelines:

National Tuberculosis Management Guidelines, 2014
Guidelines for the Management of Tuberculosis in Children, 2013
Management of Drug-Resistant Tuberculosis: Policy Guidelines, 2013
Introduction of New Drugs and Drug Regimens for the Management of Drug-Resistant Tuberculosis in South Africa: Policy Framework, 2015

ABBREVIATIONS

3TC	Lamivudine
ABC	Abacavir
ADA	Adenosine Deaminase
AEFI	Adverse Events Following Immunisation
AFB	Acid-fast Bacilli
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine Aminotransferase
ART	Antiretroviral Therapy
AST	Aspartate Aminotransferase
AZT	Zidovudine
BCG	Bacillus Calmette-Guérin
BDQ	Bedaquiline
CHW	Community Health Worker
CSF	Cerebrospinal Fluid
CXR	Chest X-ray
D4T	Stavudine
DDI	Didanosine
DOT	Directly Observed Therapy
DR-TB	Drug-Resistant Tuberculosis
DST	Drug Susceptibility Testing
E	Ethambutol
EFV	Efavirenz
EPI	Expanded Programme on Immunisation
EPTB	Extra-pulmonary Tuberculosis
FBC	Full Blood Count
FLQ	Fluoroquinolone
FTC	Emtricitabine
GXP	GeneXpert
H	Isoniazid
HB	Haemoglobin
HCT	HIV Counselling and Testing
HCW	Healthcare Worker
HIV	Human Immunodeficiency Virus
ICF	Intensified Case Finding
IGRA	Interferon Gamma Release Assay
INH	Isoniazid
IPT	Isoniazid Preventive Therapy
IRIS	Immune Reconstitution Inflammatory Syndrome
LP	Lumbar Puncture
LPA	Line Probe Assay
LPV/r	Lopinavir/Ritonavir
MDR-TB	Multi-drug Resistant Tuberculosis
MOTT	Mycobacteria Other Than Tuberculosis
MTB	*Mycobacterium Tuberculosis*
NDoH	National Department of Health
NHLS	National Health Laboratory Service
NTM	Non-Tuberculous Mycobacteria
NVP	Nevirapine
OFX	Ofloxacin
PAS	Para-aminosalicylic Acid
PCR	Polymerase Chain Reaction
PHC	Primary Health Care
PMTCT	Prevention of Mother to Child Transmission
PNP	Peripheral Neuropathy
PPD	Purified Protein Derivative
PZA	Pyrazinamide
R	Rifampicin
RIF	Rifampicin
S	Streptomycin
TAT	Turn-around-time
TB	Tuberculosis
TDF	Tenofovir
TST	Tuberculin Skin Test
WHO	World Health Organization
XDR-TB	Extensively Drug-resistant TB
Z	Pyrazinamide
ZN	Ziehl-Neelsen

CONTENTS

THIS ICON INDICATES INFORMATION THAT IS RELEVANT TO CHILDREN

Recording and Reporting

Procedures

Annexures

>>> THIS ICON INDICATES THAT THE SECTION CONTINUES ON THE NEXT PAGE

BACKGROUND 1

TB IN SOUTH AFRICA >>>

2014 Globally

- 9.6 million new cases of TB
- 480,000 cases of MDR-TB
- 1.4 million deaths due to TB
- 12% of new TB cases were co-infected with HIV

THE GLOBAL BURDEN OF TB

- Despite the fact that TB is curable, it is still a major cause of illness and death in South Africa and globally
- TB ranks alongside HIV as a leading cause of death worldwide

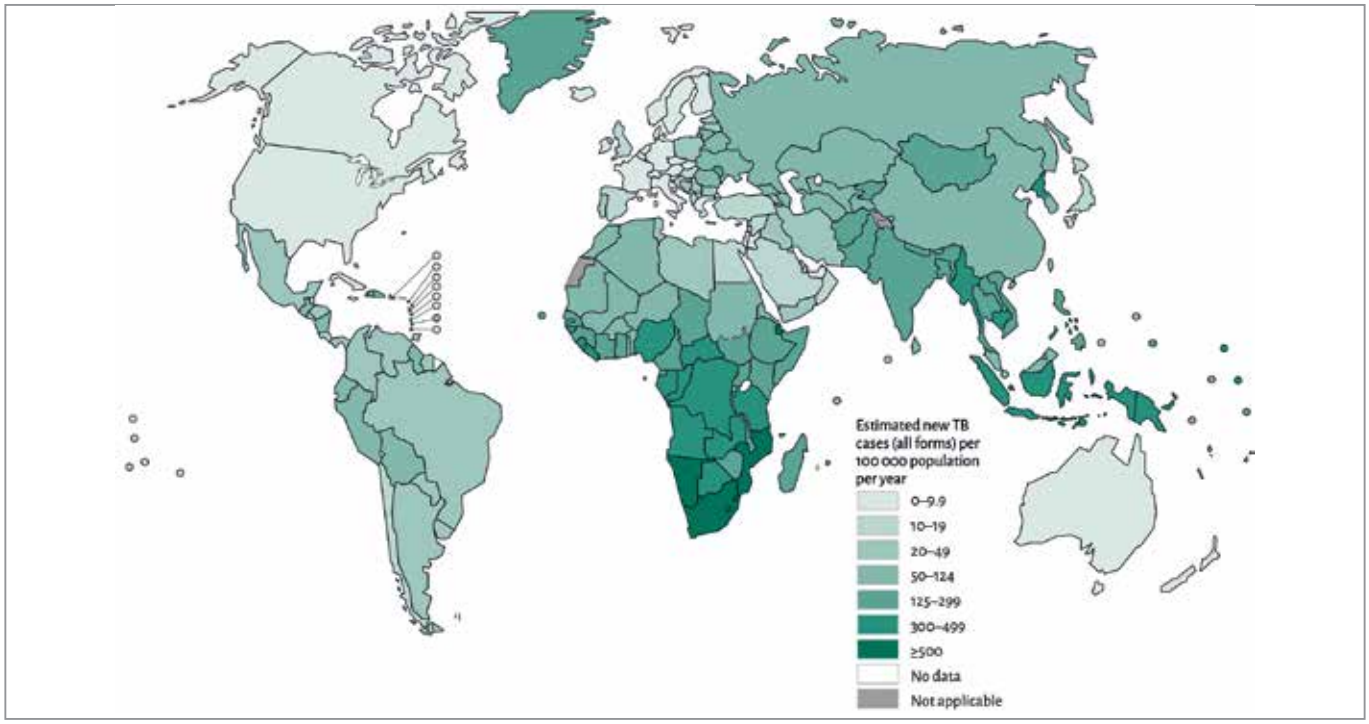
THE SOUTH AFRICAN TB EPIDEMIC

- Numerous factors have converged to create **one of the biggest TB epidemics in the world**
- Drivers of the TB epidemic include:
  - Social conditions including migrant labour, poor health infrastructure
  - Economic conditions including poverty, unemployment
  - Environmental conditions including overcrowded informal settlements
  - The HIV epidemic
  - Inadequate management of TB programme
- New infections have increased by over 400% in the last 15 years
- Currently, South Africa has the **3rd highest number of new TB cases in the world**, after India and China

2014 South Africa

- An estimated 450 000 new cases of TB
- 61% of new TB cases were co-infected with HIV
- In SA 1.8% of new cases and 6.7% of previously treated cases are estimated to have MDR-TB

ESTIMATED TB INCIDENCE RATES, 2014



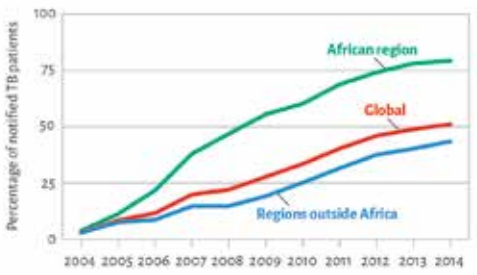
Data Source: Global Tubercolosis Report 2015. WHO, 2015

TB IN SOUTH AFRICA

TB AND HIV CO-INFECTION

- TB and HIV are closely linked
- People living with HIV and infected with TB are 21-34 times more likely to develop TB disease compared to people with TB infection who are not HIV-infected
- In 2014 61% of TB patients in South Africa were co-infected with HIV
- TB is a leading killer of people living with HIV causing 25% of all HIV-related deaths
- TB has also been shown to increase the risk of HIV progression and death, particularly if HIV is untreated

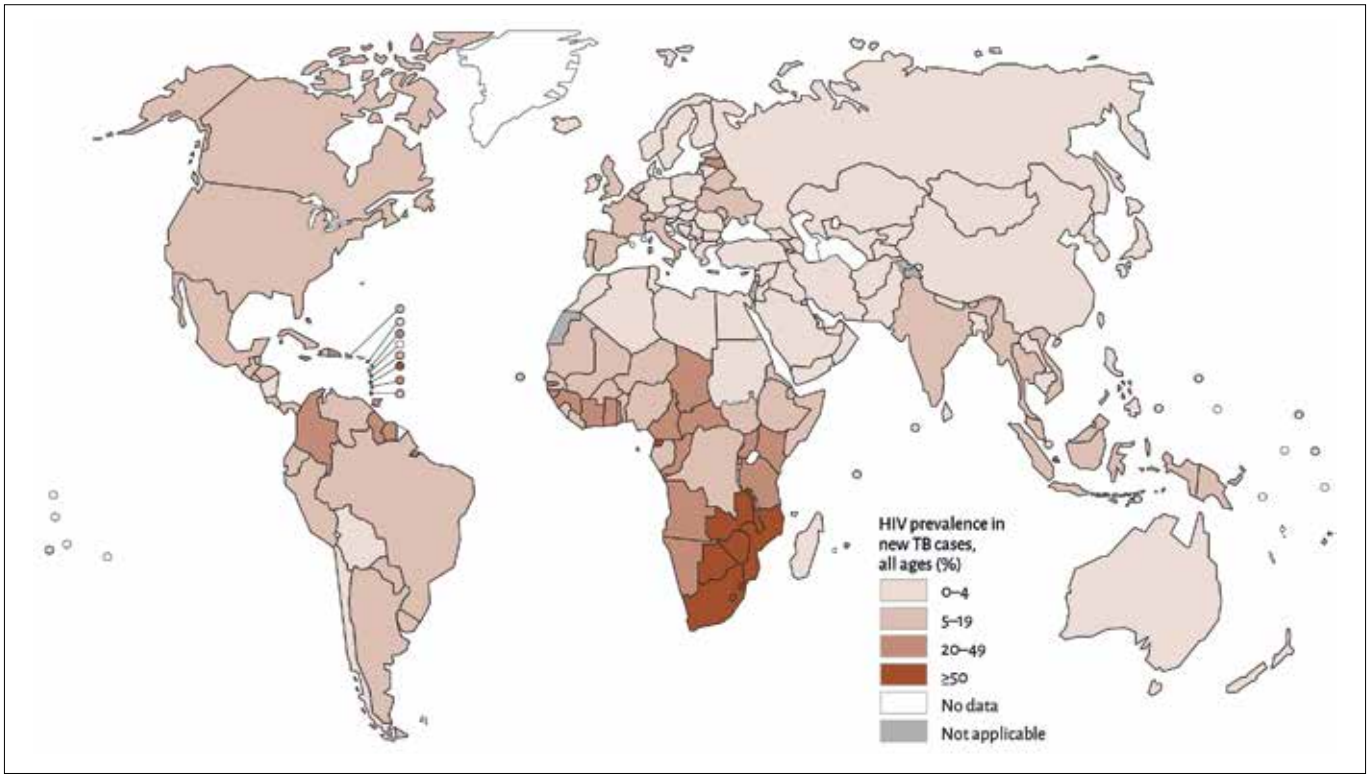
PERECENTAGE OF NOTIFIED TB PATIENTS WITH KNOWN HIV STATUS, 2004 - 2014



TB IN CHILDREN

- For many years, the prevention, diagnosis and treatment of TB among children has been relatively neglected
- The accurate diagnosis of TB in children is somewhat difficult and as a result, the extent of the disease burden in children is often underestimated
- In 2014, there were an estimated 1 million cases and 140 000 deaths due to TB in children globally
- It is estimated that children constitute 15-20% of the total TB disease burden in highly endemic areas
- In 2010, there were about 10 million children orphaned as a result of TB deaths among parents

ESTIMATED HIV PREVALENCE IN NEW AND RELAPSE TB CASES, 2014

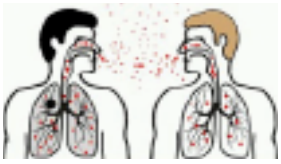


Data Source: Global Tubercolosis Report 2015. WHO, 2015

NATURAL HISTORY OF TB

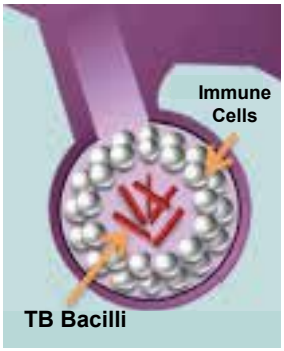
STEP ONE - EXPOSURE

- When someone with pulmonary TB coughs, invisible droplets containing TB bacilli are dispersed into the air
- They remain suspended in the air and fall at a rate of 12mm/hr
- These droplets can then be inhaled by others



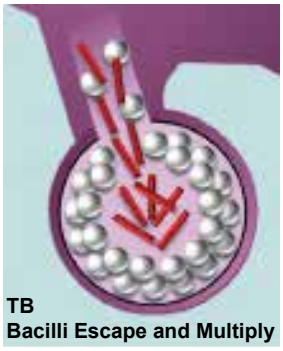
STEP TWO - TB INFECTION

- When inhaled, they reach the alveoli of the lungs and TB infection may occur
- The immune system may gain control of the TB bacilli, potentially resulting in latent infection
- In latent infection some bacilli do not die, but remain dormant
- The patient is asymptomatic
- The immune system has been sensitised to TB and the tuberculin skin test may be positive

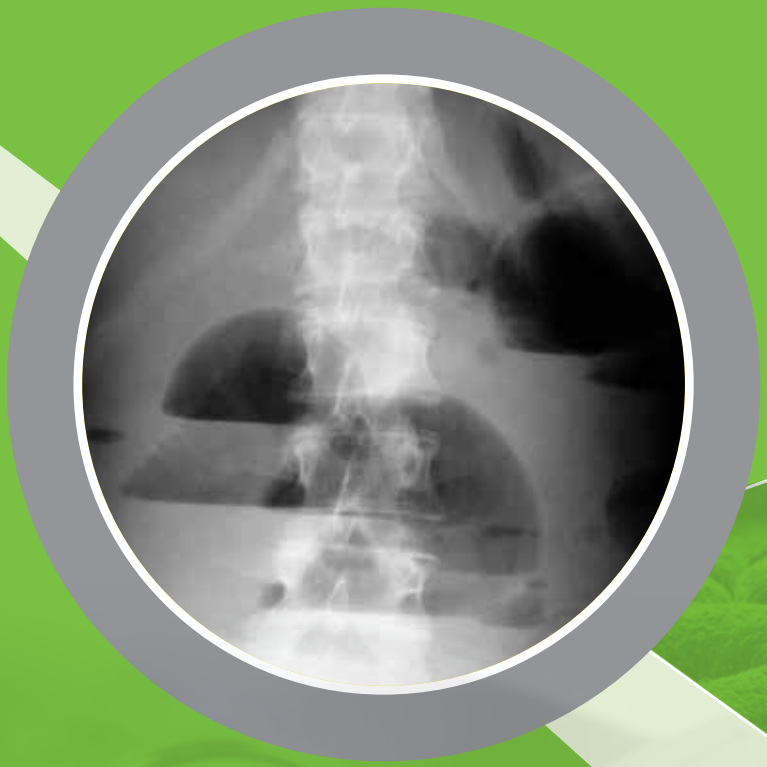


STEP THREE - TB DISEASE

- Latent infection may then progress to TB disease
- This occurs if there is repeated heavy exposure to TB or a weak immune system which could occur in the following instances:
  - HIV infection with falling CD4 count
  - Alcohol abuse
  - Malnutrition
  - The elderly
  - Children <5 years
  - Chronic immunosupressive illnesses such as cancer and diabetes
  - Immuno-suppresive drugs such as corticosteroids and chemotherapy
  - Smoking
- The immune system is no longer able to control the TB bacilli and the TB disease becomes active
- Infection may go directly to disease in some patients; with no intervening latent infection
- The bacilli multiply and cause damage to the lung and/or other parts of the body
- The person develops symptoms such as cough, fever, night sweats, loss of weight



DIAGNOSIS 2



INTENSIFIED CASE FINDING >>>

WHAT IS INTENSIFIED CASE FINDING (ICF)?

ICF refers to the process of actively screening persons for signs and symptoms of TB

WHO SHOULD BE SCREENED FOR TB?

In SA, everyone who presents to a health care facility for any reason, including reasons not related to ill health (i.e. for preventive services, well baby clinic, family planning etc.), should be screened for TB

IS ICF ONLY FOR HIV-INFECTED PATIENTS?

- **No**!
- We need to use every opportunity to ask all patients for TB symptoms at every visit to the Health Care Facility
- This is important for:
  - detecting TB early
  - separating patients with TB symptoms from other patients to improve TB infection control

WHO IS A HIGH PRIORITY FOR ICF?

- Children under 5 years
- The elderly
- HIV-infected persons
- Persons with a TB contact
- Persons with Diabetes
- Persons with Silicosis
- Persons on Steroids > 4 weeks
- Persons receiving chemotherapy for malignancy
- High risk groups such as correctional services inmates, miners, peri-mining community

HOW DO WE IMPLEMENT ICF IN COMMUNITIES?

We need to make every effort to look for persons with TB through:

- Active, community or facility based interventions
- Community outreach events to schools, places of work, or through screening or investigating persons who have had contact with someone with recently diagnosed TB
- TB screening to be conducted in health campaigns
- Community Health Workers (CHWs) employed in Ward Based Outreach Teams (WBOTs) play a significant role in ICF, contact tracing and treatment support during household visits

The aim is to screen every person for TB annually.

WHAT SCREENING TOOL MUST WE USE?

- The tool on the next page can be used for screening all patients entering the clinic (HIV-infected and uninfected)

INTENSIFIED CASE FINDING

TB SCREENING TOOL

TB SYMPTOM SCREENING TOOL FOR ADULTS AND CHILDREN

PATIENT DETAILS

Surname:	First Name:
Physical Address:	Age:
Telephone Number:	Patient folder Number:

MEDICAL HISTORY

Close contact of a person with infectious TB:	Yes	No	Unknown	(Tick √)
Type of index patient:	DS-TB	Rif Resistant TB	MDR-TB or XDR-TB	
Diabetic:	Yes	No	Unknown	
HIV Status:	Positive	Negative	Unknown	

Other: (Specify) _____

TB SYMPTOM SCREEN

1. ADULTS

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more OR of any duration if HIV positive		
Persistent fever of more than two weeks		
Unexplained weight loss >1.5kg in a month		
Drenching night sweats		

2. CHILDREN

Symptoms (Tick √)	Yes	No
Cough of 2 weeks or more which is not improving on treatment		
Persistent fever of more than two weeks		
Documented weight loss/ failure to thrive (check Road to Health Card)		
Fatigue (less playful/ always tired)		

If "Yes" to one or more of these questions, consider TB.
If the patient is coughing, collect sputum specimen and send it for Xpert testing.
If the patient is not coughing but has the other symptoms, clinically assess the patient or refer for further investigation.

Date of last TB test:		
Patient referred for assessment and investigation:	Yes	No
Date of referral:	Facility name:	
Name:	Date:	

CONTACT INVESTIGATION >>>

WHY IS CONTACT INVESTIGATION IMPORTANT?

Close contacts of people with active pulmonary tuberculosis are at increased risk of acquiring infection, developing active disease and spreading it. Timely identification and adequate treatment of those with active pulmonary tuberculosis reduces the risk of exposure of community members. Identification of contacts that are eligible for IPT is important.

WHAT IS THE DEFINITION OF A CONTACT?

- People who share the same air for prolonged periods of time with people who are coughing up the MTB into the air (smear or culture positive PTB)
- This applies not only to households but to hostels, prison cells, boarding schools and homeless shelters.

HOW SHOULD YOU CONDUCT CONTACT INVESTIGATION?

- Interview patient with laboratory confirmed PTB (index patient) promptly after diagnosis
- Estimate the period of infectiousness of the patient (a rough estimate can be made based on the date of onset of cough)
- The following situations should receive priority for contact tracing:
  - index patient is "sputum smear-positive"
  - index patient has MDR-TB/XDR-TB
  - there are children or immune compromised people among household contacts
- Assure the patients that confidentiality regarding other aspects of their disease management will be ensured.
- Compile a list of all contacts including the name, age, residential address during the period of illness of index patient and contact details. This information must be recorded in the Patient Treatment Record.
- Complete the contact notification form. Explain the purpose of the form to the index patient and ask him/her to pass them on to the named contacts.
- The named contacts must present the form to any clinic for screening and testing. The feedback must be provided to the referring facility by completing the bottom section of the form. The interviewer should record in the Patient Treatment Record that contact forms were given to the index case.

WHAT DETERMINES THE RISK OF TRANSMISSION OF INFECTION?

- The infectiousness of the index patient (i.e. person with smear positive PTB)
- Closeness and duration of exposure (i.e. spending at least eight continuous hours with the index patient)
- The environment in which the exposure is suspected to have occurred (i.e. poorly ventilated room)
- In specific settings of presumed increased risk such as outpatient departments, general/TB wards or while conducting sputum inducing procedures, frequent but intense contact of less than 8 hours may be considered to pose similar risk as above.

HOW SHOULD CONTACTS BE ASSESSED DURING A HOME OR CLINIC VISIT?

1) Symptom screening: Contact is screened for TB symptoms (use TB symptom screening tool). If any of the symptoms are present, they should be asked to provide sputum for investigation and a follow up clinic visit should be scheduled.
2) Investigations: If contact is coughing, one sputum specimen must be collected for Xpert testing. Those who are not coughing or cannot produce sputum but are symptomatic must be referred to the clinic/hospital for investigation.
3) Risk factor assessment: The person should be assessed for the risk factors for development of TB disease (e.g. age < 5years, HIV positive, diabetes, malnutrition).
   a. HIV testing must be offered and diabetic screening conducted.
   b. All children less than 5 years must be assessed for nutritional status.
   c. Children under 5 years and HIV positive children should be considered for IPT.
   d. HIV positive contacts of MDR and XDR patients should be followed up every six months for a period of two years.
4) Environmental assessment: An environmental assessment can be done and information provided on how to prevent TB transmission through appropriate environmental interventions.

CONTACT INVESTIGATION

TB CONTACT NOTIFICATION FORM

TB CONTACT NOTIFICATION FORM

Name of Health Facility:	Telephone No.:
Address:	
Name of health care worker completing this form:	
Patient name (index case):	Date of issue:
TB Registration number:	Date of Birth/ Age:

Please note that the person presenting this form has been in close contact with the above patient who has been diagnosed with:

	Xpert positive, smear positive Rifampicin susceptible pulmonary TB
	Xpert positive, culture positive Rifampicin susceptible pulmonary TB
	Xpert positive, Rifampicin resistant pulmonary TB

Please screen this person for TB and perform appropriate tests if indicated.

Signature:	Date:

Please send this slip back to the issuing facility as soon as possible

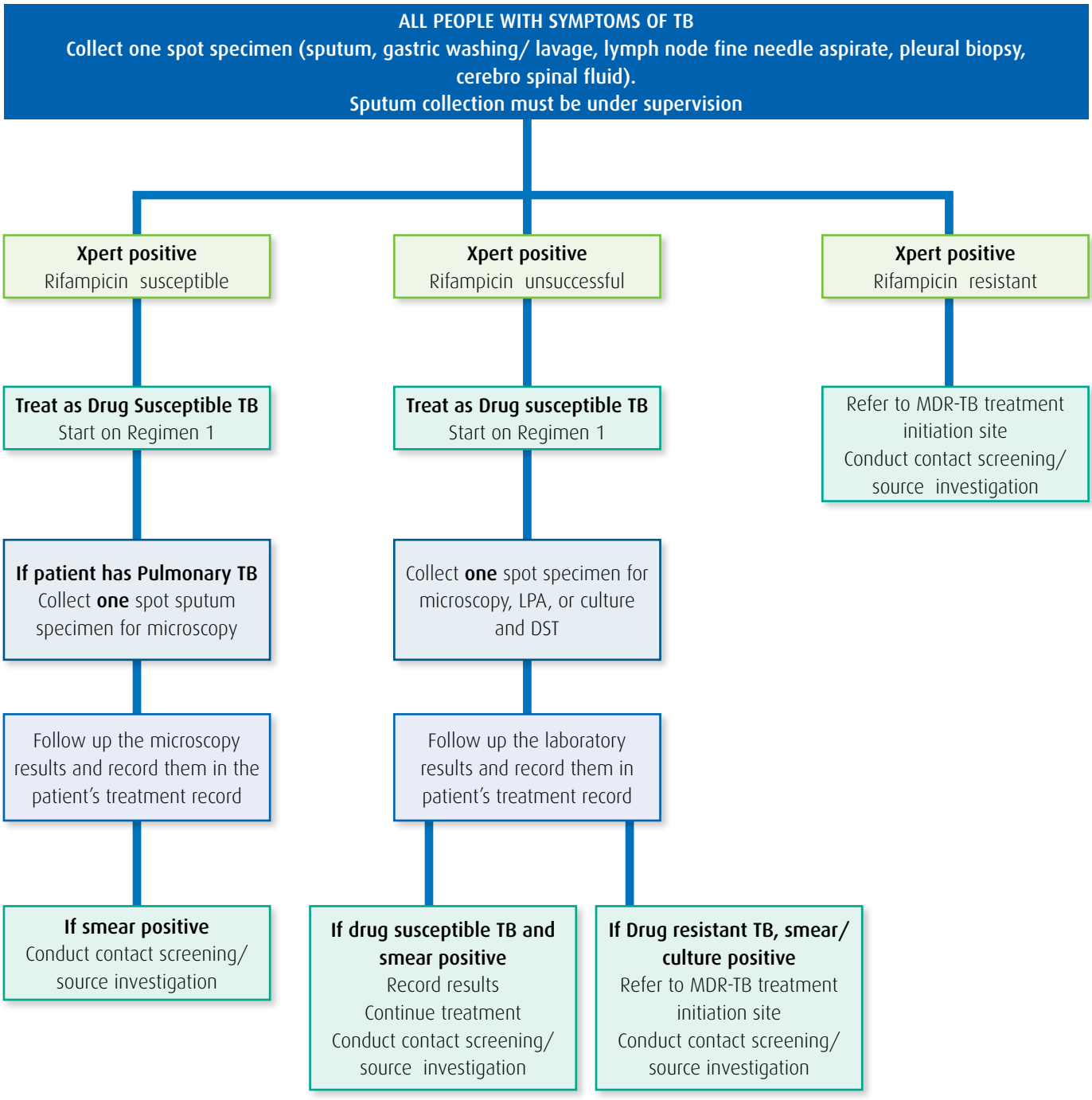
Name of reporting health facility:	Telephone No:
Name of person completing the form:	
Patient name:	Date of reporting:

Screening results	Positive	Negative		
Test conducted	Xpert	Smear	Culture	LPA
Diagnosis	TB	RR-TB	MDR-TB	
Treatment given	Yes	No		
Isoniazid preventive therapy given	Yes	No		

Treatment start date:	Signature:

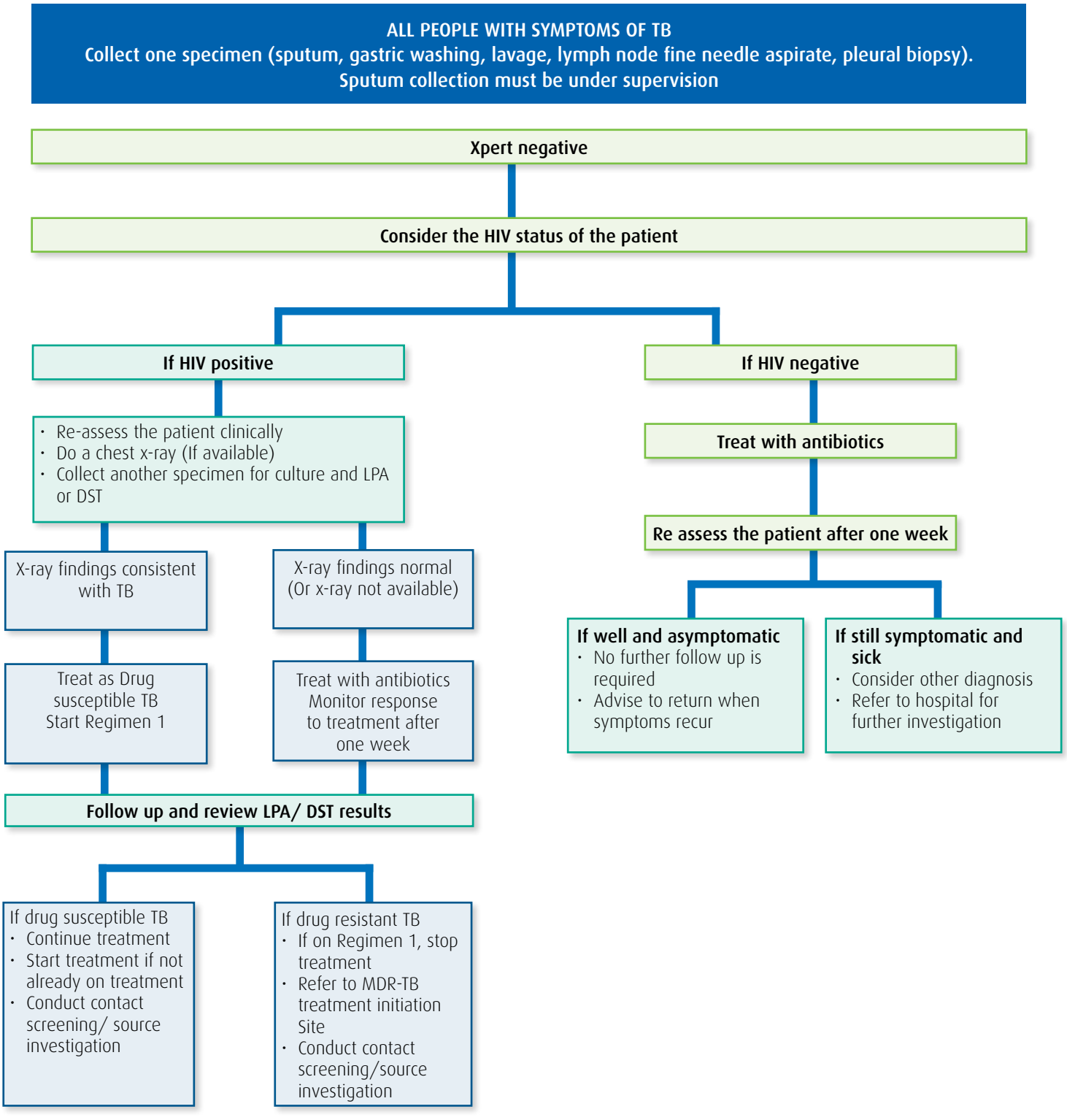
DIAGNOSTIC ALGORITHMS >>>

DIAGNOSIS OF TB USING XPERT MTB/RIF



DIAGNOSTIC ALGORITHMS >>>

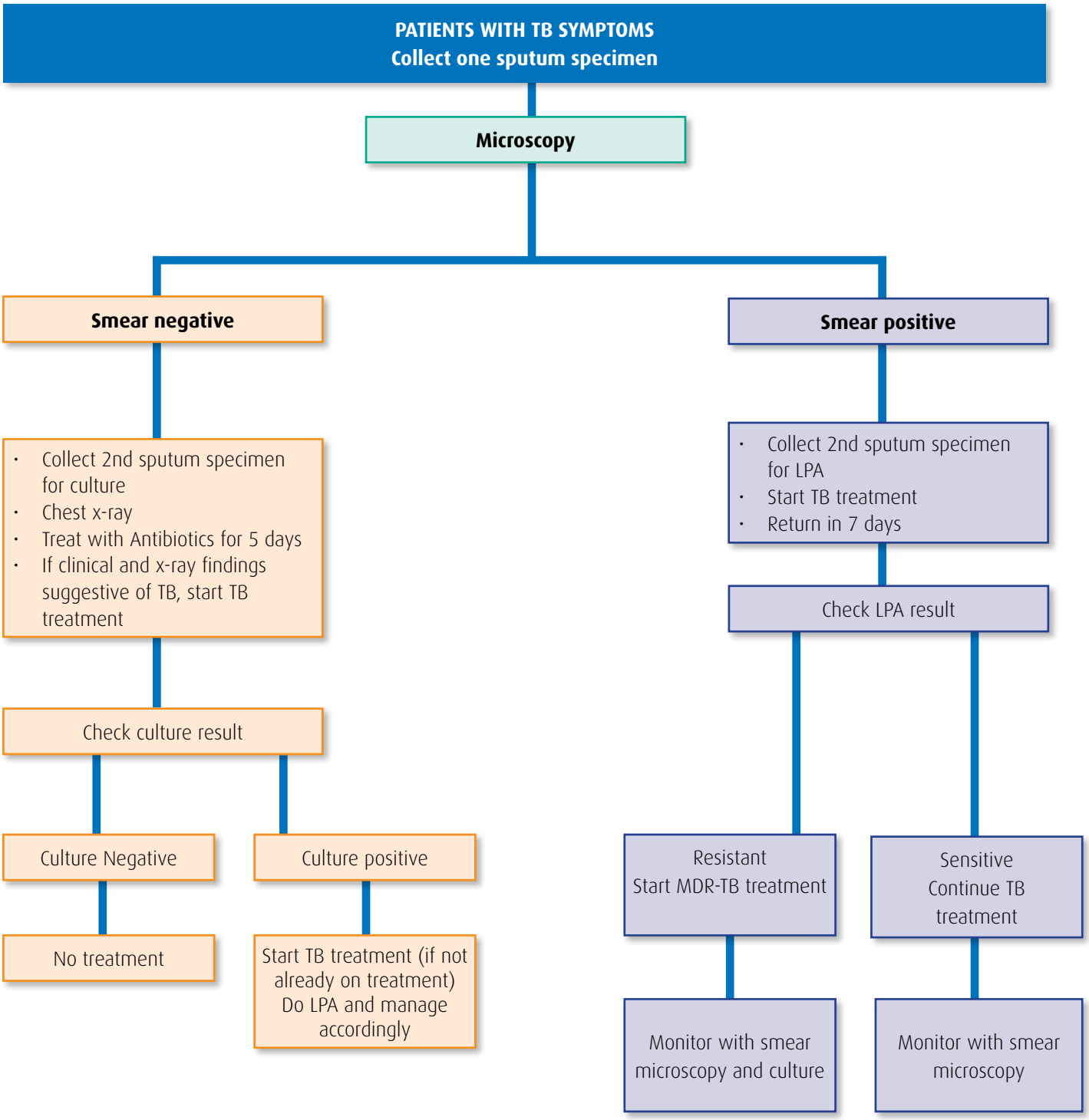
DIAGNOSIS OF TB USING XPERT MTB/RIF



NOTE: If an antibiotic is required the following can be used: amoxycillin 500mg 8 hourly orally for 5 days. If allergic to penicillin use erythromycin 500mg 6 hourly orally for 5 days.

DIAGNOSTIC ALGORITHMS

DIAGNOSIS OF TB USING LINE PROBE ASSAY



SYMPTOM SCREENING AND DIAGNOSIS IN CHILDREN >>>

WHICH CHILDREN SHOULD BE ROUTINELY SCREENED FOR TB?

- Children who live in the same household with a person diagnosed with smear and/or culture positive PTB (infectious TB)
- Children with symptoms or signs suggestive of TB
- Children with evidence of TB infection as indicated by a positive TST
- HIV positive children (for both TB symptoms and contacts) at every clinic visit
- Children less than five years
- Children with severe malnutrition

WHY IS IT DIFFICULT TO DIAGNOSE TB IN CHILDREN?

- Bacteriological confirmation of TB infection is often not possible in children due to difficulties with sputum collection and because cavitation is rare
- Never rely solely on sputum microscopy to diagnose pulmonary TB in children, as these tests are very rarely positive because children usually have 'paucibacillary' (few bacilli) disease
- Despite this, bacteriological confirmation should always be sought
- Expectorated sputum samples should be taken in those old enough to produce them
- Gastric washings and induced sputum samples can be done in children unable to produce sputum samples
- Relevant investigations for extra-pulmonary TB must be done if this is suspected

WHAT TOOLS CAN BE USED TO DIAGNOSE TB?

Taking a Detailed History

Physical Examination

Tuberculin Skin Test (TST)

Chest X-ray

Bacteriological Confirmation

SYMPTOM SCREENING AND DIAGNOSIS IN CHILDREN >>>

1. TAKING A DETAILED HISTORY

1.1. When taking a history, what should I ask?

- Explore exposure to a TB contact
  - The source case is usually an adult or adolescent in close contact with the child, either in the same household or in regular contact, who has recently been diagnosed with TB or has symptoms suggestive of TB
- Find out about the possible presence of drug-resistant TB in the contact:
  - Enquire about whether the contact has known drug-resistant TB or is not responding to treatment.
  - This is important because the presence of drug resistance might have implications for the treatment of the child

1.2. Which symptoms suggest TB?

Symptoms are often nonspecific and can overlap with other conditions, especially those that occur in HIV infection.

- The most common symptoms are:
  - Persistent cough or wheeze present for more than 2 weeks, which is not responding to antibiotics
  - Documented loss of weight or failure to thrive for 3 months. This is particularly significant if the child does not respond to nutritional intervention
  - Persistent fever of ≥38°C for more than 2 weeks
  - Fatigue or reduced playfulness

Please note: although 'chronic cough' is an important indicator of Pulmonary TB in children, it is important to remember that up to 40% of culture-confirmed pulmonary TB episodes in children may present in the context of a cough of less than 10 days duration

2. PHYSICAL EXAMINATION

2.1. What should I check for on physical examination?

The following signs are suggestive of TB:

- Failure to thrive
- Gibbus (suggestive of vertebral TB)
- Painless, matted, enlarged cervical lymph nodes (>2x2 cm) with fistula formation
- Meningitis not responding to antibiotics
- Pleural effusion
- Pericardial effusion
- Abdominal distension with ascites
- Painless enlarged lymph nodes without fistula formation
- Painless enlarged joint
- Signs of tuberculin hypersensitivity (phlyctenular conjunctivitis, erythema nodosum)
- Other non-specific signs: night sweats, breathlessness, peripheral oedema, painful limbs and joints

SYMPTOM SCREENING AND DIAGNOSIS IN CHILDREN >>>

3. TST TEST

3.1 What are the criteria for a positive TST result?

Immune status	HIV positive, malnourished, severe illness	Other children (including previous BCG)
Diameter of induration	5 mm or more	10 mm or more

3.2. What do I do if the TST is positive?

If the child is under 5 years of age or is HIV-infected (regardless of age):

- Screen for TB disease and treat if detected.
- If TB disease is excluded, the child should be put on INH preventive therapy (IPT). This should be given whether there is a known contact or not.

3.3. What if the TST is negative?

- A negative test does not necessarily mean that there is no TB infection
- False negative results occur in the following situations:
  - Severe malnutrition
  - HIV infection
  - Disseminated TB e.g. miliary TB or TB meningitis
  - If on immunosuppressive drugs e.g. high-dose steroids
  - Severe viral infections e.g. measles or chicken pox
  - Malignancy or cancer chemotherapy

The procedure for administering TST is discussed in the Procedures Section

4. CHEST X-RAY (CXR)

4.1. Are CXRs useful in children?

- This can be a useful test as children with pulmonary TB will often have suggestive CXR changes
- X-rays should be of good quality and should be read by someone with experience

4.2. What are the most common changes on CXR?

- The most common manifestation is persistent opacification in the lung with hilar and/or paratracheal lymphadenopathy
  - A lateral X-ray helps to identify these signs
- Enlarged lymph nodes can obstruct airways
  - Complete occlusion leads to lobar collapse
  - Partial occlusion can cause a ball-valve effect with segmental or lobar hyperinflation
- Parenchymal disease may be present due to:
  - miliary disease or
  - spread from airway involvement
- Unilateral pleural effusions can occur (usually in children over 5 years of age)

IN HIV-INFECTED CHILDREN THERE IS OVERLAP WITH OTHER CONDITIONS, FOR EXAMPLE LYMPHOCYTIC INTERSTITIAL PNEUMONITIS (LIP), MAKING THE CXR MORE DIFFICULT TO INTERPRET.

SYMPTOM SCREENING AND DIAGNOSIS IN CHILDREN >>>

5. BACTERIOLOGICAL CONFIRMATION

5.1. How is bacteriological confirmation obtained in children?

- Specimens from suspected sites of involvement should always be obtained for Xpert or culture, in order to confirm diagnosis.
- Appropriate samples include sputum obtained through expectoration or sputum induction, gastric aspirates, fine needle aspiration (FNA) or biopsies, for example of lymph nodes
- PTB in young children is usually paucibacillary (few bacilli) and the collection of adequate samples is difficult.

5.2. When is bacteriological confirmation important?

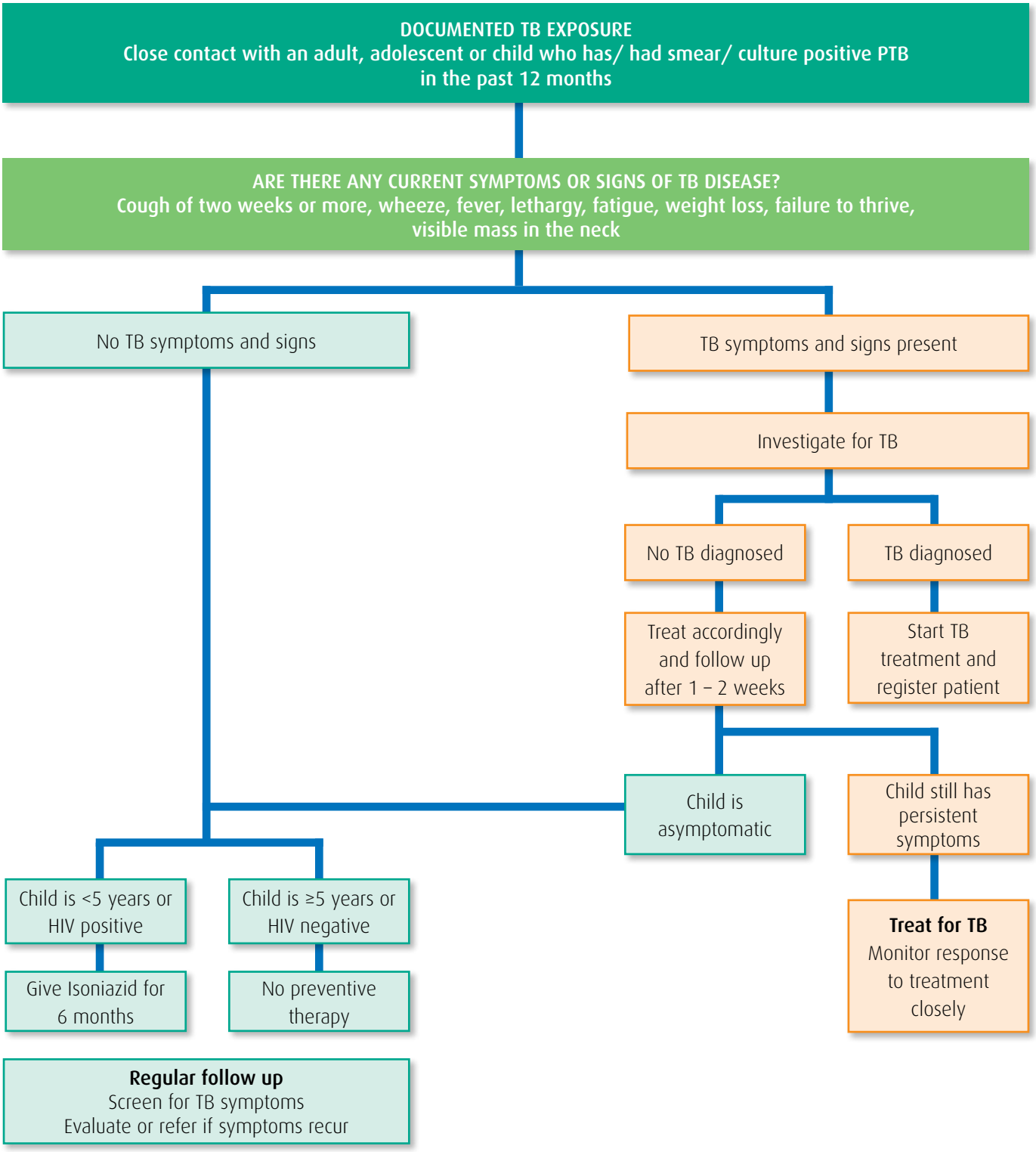
- Bacteriological confirmation is particularly important in the following cases:
  - suspected drug resistance
  - severe or complicated cases
  - if the diagnosis is uncertain

Drug susceptibility testing (DST) of isolates should be done if drug resistance is suspected (e.g. if the source case has drug-resistant TB) and if the child is not responding to treatment.

The process of sample collection is discussed in the Procedures Section

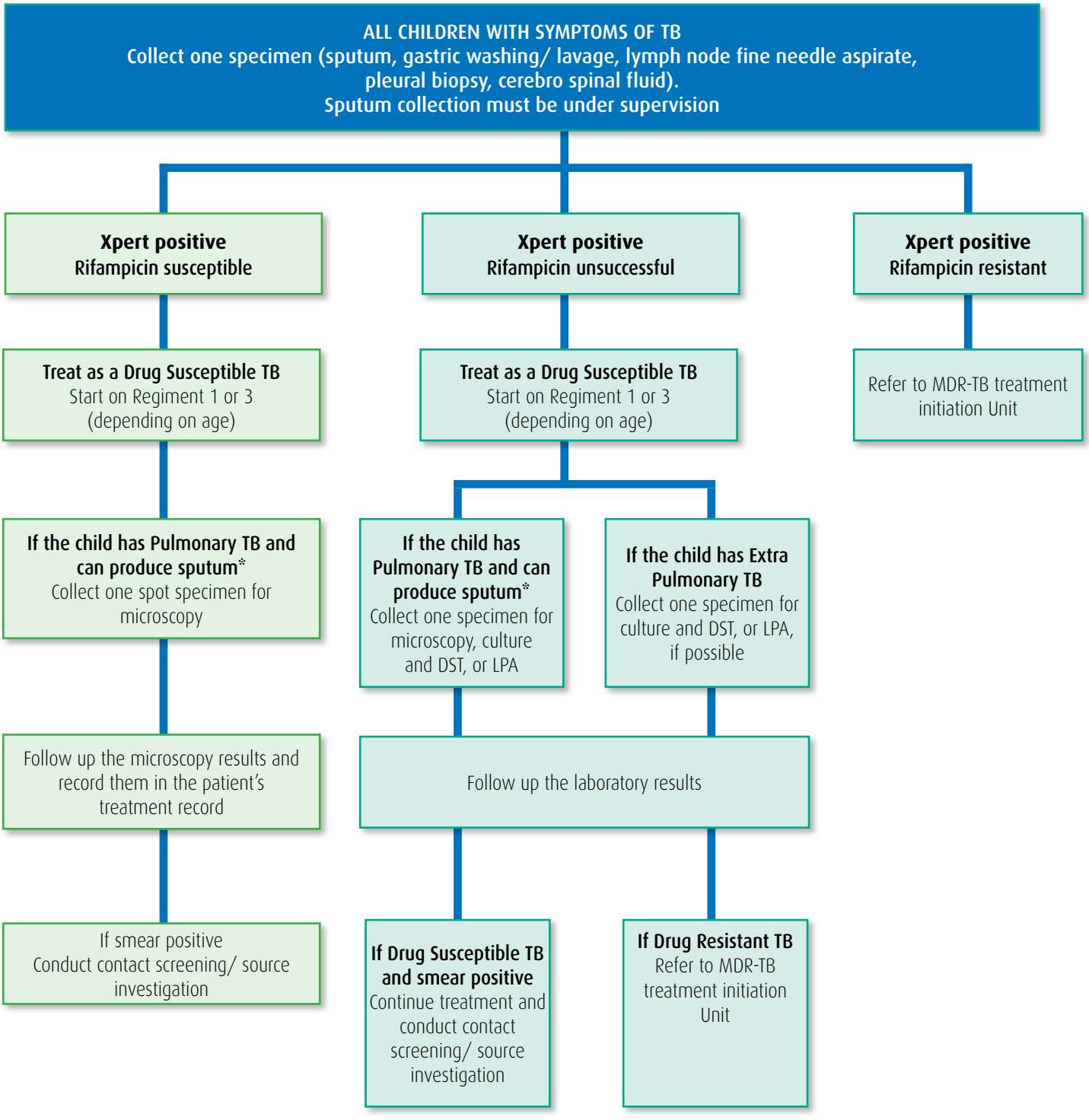
SYMPTOM SCREENING AND DIAGNOSIS IN CHILDREN

TB SCREENING ALGORITHM IN CHILDREN



DIAGNOSTIC ALGORITHMS IN CHILDREN >>>

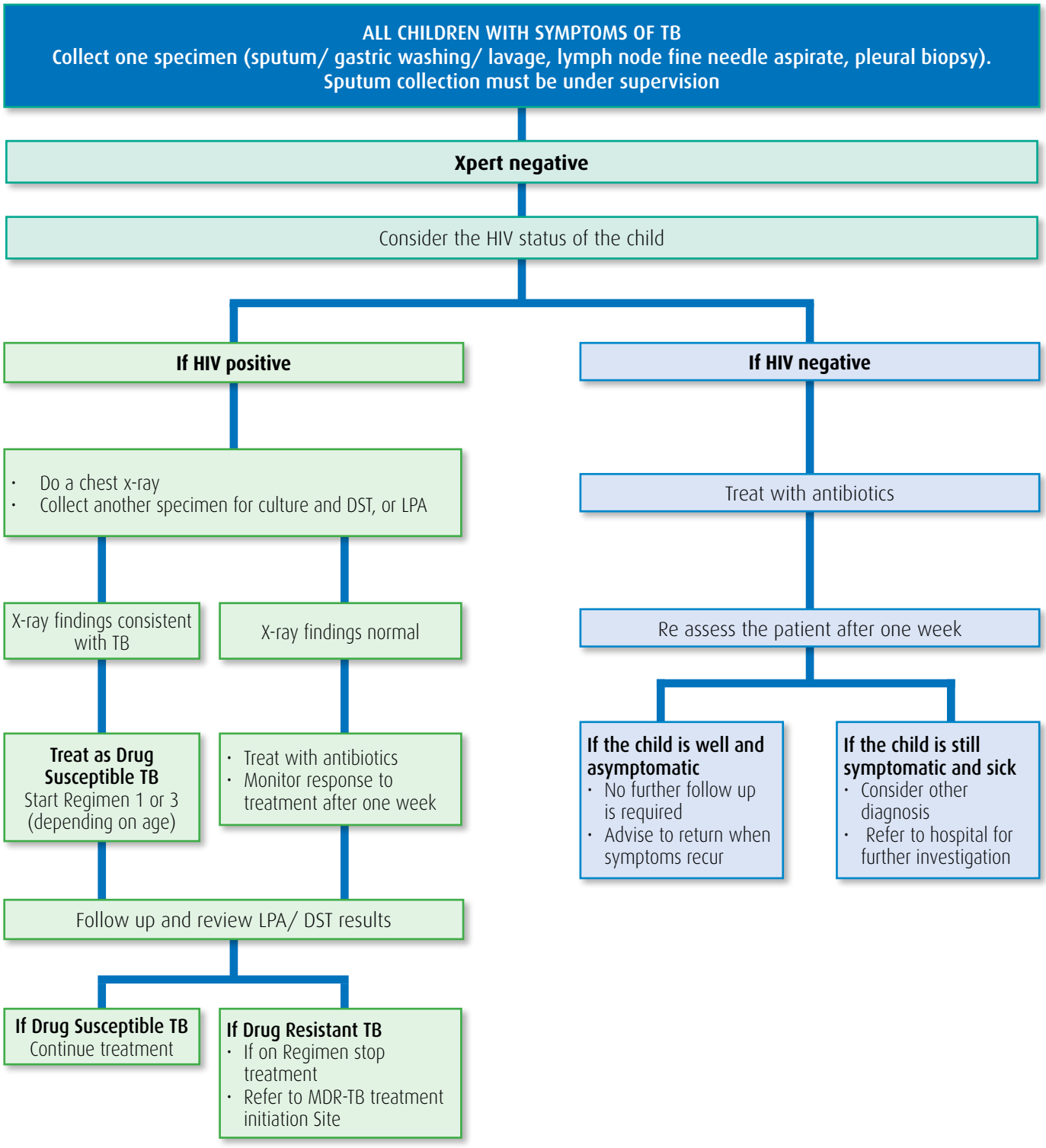
XPERT DIAGNOSTIC ALGORITHMS IN CHILDREN



* Baseline smear microscopy should only be done on children who have pulmonary TB and can produce sputum spontaneously. If the Xpert test failed or unsuccessful - collect another specimen for a repeat Xpert

DIAGNOSTIC ALGORITHMS IN CHILDREN

XPERT DIAGNOSTIC ALGORITHMS IN CHILDREN

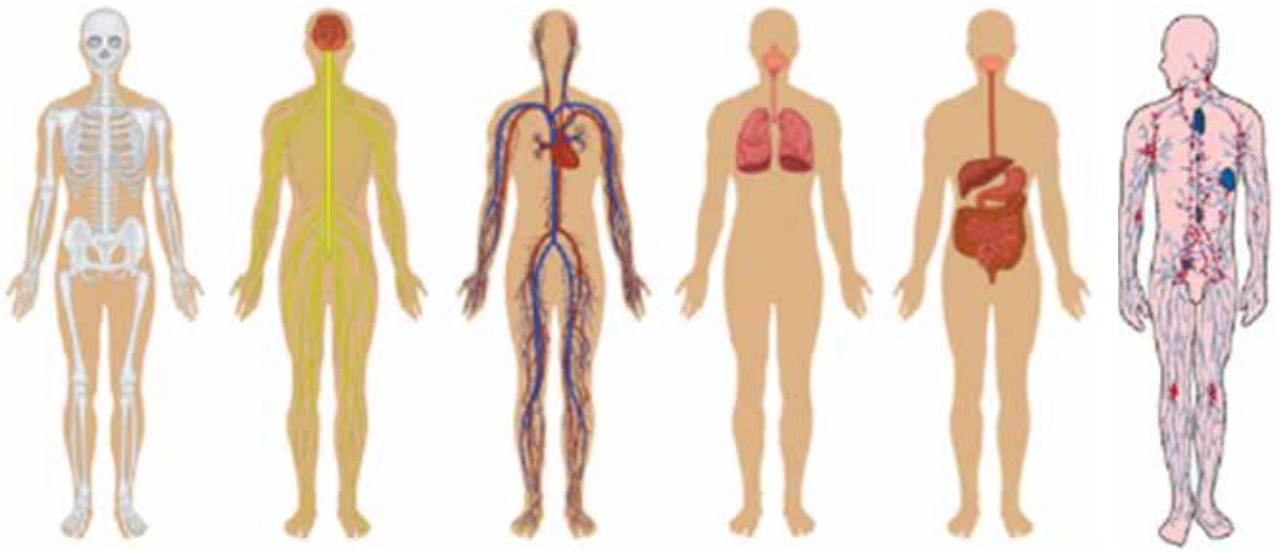


NOTE: In patients with NTM, MTB will not be detected by Xpert, therefore a culture and speciation or LPA must be conducted

EXTRA-PULMONARY TB (EPTB) >>>

- TB occurring in any site other than the lungs
- Caused by TB spreading to other organs through haematological and lympathic dissemination
- EPTB is more common in people living with HIV, particularly with low CD4 counts

WHAT ARE COMMON TYPES OF EPTB?



Skeletal TB including spinal | CNS including Meningitis | TB Pericarditis | Pleural TB | Abdominal TB | TB Lymphadenitis

Disseminated TB may include multiple sites

DIAGNOSIS OF EPTB

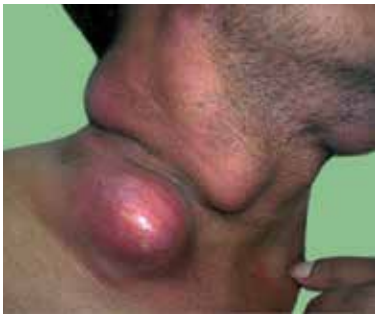
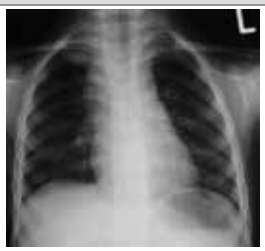
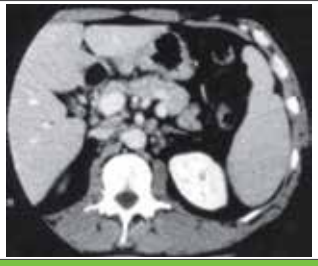
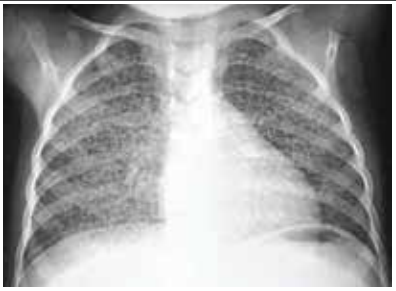
- EPTB diagnosis is difficult and invasive procedures are often required; presumptive TB treatment may be commenced.
- Xpert MTB/RIF may be conducted on gastric washings/ lavages, lymph node fine needle aspirates, cerebrospinal fluid, pleural effusions and biopsies

HOW SHOULD EPTB TREATMENT BE APPROACHED?

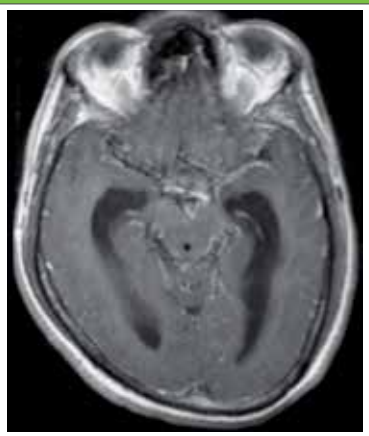
- Six months treatment is as effective in extra-pulmonary as in pulmonary disease
- In some instances of severe or complicated disease (meningitis, TB bones/joints, miliary TB) treatment may need to be extended to nine months
- The intensive phase remains two months and the continuation phase is prolonged to seven months
- Disseminated TB may be fatal and TB treatment should not be delayed, especially in HIV-infected patients
- When disseminated TB or TBM is suspected, commence TB treatment immediately without waiting for bacteriological proof of diagnosis
- Corticosteroids may be used, especially for TB pericarditis and TB meningitis

NB: EPTB OCCURS MORE COMMONLY IN HIV-INFECTED PATIENTS. ALL HIV-INFECTED TB PATIENTS SHOULD BE INITIATED ON ART

EXTRA-PULMONARY TB >>>

1. TB LYMPHADENITIS		
1.1 Peripheral Lymphadenitis	**Signs and Symptoms**	**Diagnosis and Treatment**
	• Large (>2 cm), tender, non-symmetrical, matted, firm to fluctuant, rapidly growing lymph node, may have skin fistula • Needs to be differentiated from persistent generalised lymphadenopathy (PGL) which occurs in HIV: ○ occurs in up to 80% of early HIV infection ○ is typically non-tender, <2 cm in size and symmetrical	• Microscopy if exuding caseous material through a fistula • Fine needle aspirate for Xpert MTB/RIF testing, culture or cytology • If the above-mentioned is negative, do lymph node biopsy – send for histology and TB culture
1.2 Mediastinal Lymphadenitis	**Signs and Symptoms**	**Diagnosis and Treatment**
	• Can compress the airways leading to: ○ wheeze ○ brassy cough	• CXR
1.3 Intra-abdominal Lymphadenitis	**Signs and Symptoms**	**Diagnosis and Treatment**
	• Obstructive symptoms • Tenderness on palpation	• Sonar • CT Scan • Treat empirically unless nodes can be readily aspirated at a tertiary health facility
2. DISSEMINATED (MILIARY) TB	**SIGNS AND SYMPTOMS**	**DIAGNOSIS AND TREATMENT**
	• High fever • General signs and symptoms of TB • May reflect involvement of other organs e.g. pleural effusion, digestive problems, hepatosplenomegaly • Meningeal signs	• CXR: diffuse uniformly distributed small nodules (resembling millet seeds) • FBC may show pancytopenia or anaemia • Liver function tests may be abnormal • Bacteriological confirmation is sometimes possible from sputum (may be negative due to few bacilli), CSF, bone marrow, TB blood culture or urine culture (3 early morning urine TB cultures should be requested) • Abdominal ultrasound may show hepatosplenomegaly • When disseminated TB is suspected, treatment should be commenced immediately without waiting for bacteriological proof of diagnosis

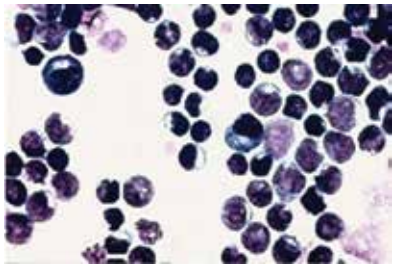
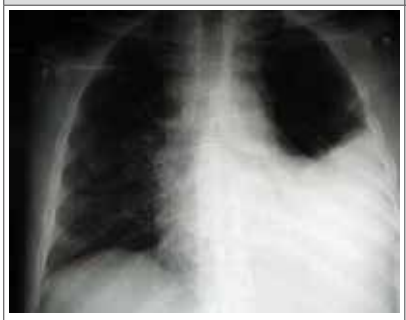
EXTRA-PULMONARY TB >>>

3. TB MENINGITIS	SIGNS AND SYMPTOMS	DIAGNOSIS AND TREATMENT
	• Gradual onset headache • Malaise • Confusion • Decreased level of consciousness • Vomiting • Neck stiffness • Seizures • Positive Kernig's sign	• Do a lumbar puncture ○ Request differential WCC, protein, glucose, ADA, MC&S, Xpert MTB/RIF, TB culture (include tests for cryptococcal meningitis if immunocompromised) • CT brain may be helpful in diagnosing TB meningitis • ART initiation should be delayed for at least one month after starting TB treatment as IRIS may be fatal

DIFFERENTIAL DIAGNOSIS FOR TB MENINGITIS

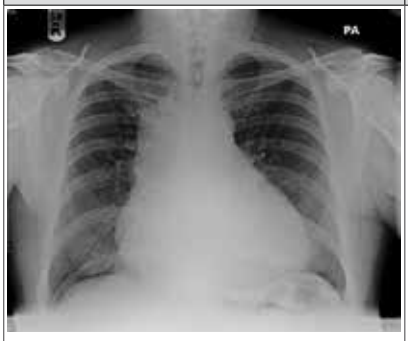
Disease	White Cell Count	Protein	Glucose	Microscopy
Tuberculous meningitis	Elevated lymphocytes (L) > polymorphonucleocytes (PMN)	Increased	Decreased	Presence of AFB (rare)
Bacterial meningitis	Elevated PMN > L (L increases with partial treatment)	Increased	Decreased	Presence of bacteria after gram staining (rare)
Viral meningitis	Elevated L > PMN	Moderately increased	Normal	Negative
Cryptococcal meningitis	Elevated L > PMN	Increased	Decreased	Presence of parasites shown by India ink stain (or cryptococcal antigen test)

EXTRA-PULMONARY TB >>>

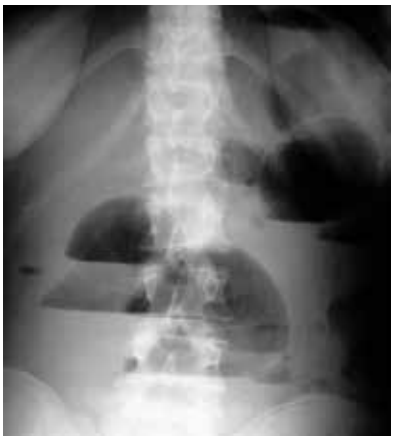
4.TUBERCULOUS SEROUS EFFUSIONS	SIGNS AND SYMPTOMS	DIAGNOSIS AND TREATMENT
	• Dependent on the site • Discussed below	*Generally diagnosis* includes aspiration: • Request the following tests: differential white cell count, total protein, LDH, glucose, ADA, TB microscopy, TB culture • TB produces an exudate: protein content > 30g/l • Biochemical tests not required to diagnose an exudate: ○ if aspirate clots after standing, it is an exudate (failure of aspirate to clot does not exclude TB as it may indicate low protein content as in wasted clients) • Microscopy rarely shows AFBs (fluid forms as an inflammatory reaction to TB lesions in the serous membrane)
4.1. Pleural Effusions	**Signs and Symptoms**	**Diagnosis and Treatment**
	• Acute: ○ non-productive cough ○ chest pain ○ shortness of breath ○ high fever • Chronic weakness in elderly • Systemic TB symptoms • Signs can include: ○ decreased breath sounds ○ decreased movement of chest wall ○ dull percussion of chest ○ friction rub ○ effusion unilateral	• CXR shows unilateral uniform white opacity, often with concave upper border • Pleural aspiration shows: ○ straw coloured exudate ○ protein content >30g/l ○ white cell count is high (1000-2500 per mm^3) with predominantly lymphocytes ○ adenosine deaminase (ADA): >30 IU • AFB not usually seen on microscopy but culture may be positive • Xpert MTB/RIF on pleural biopsies to confirm diagnosis • If aspiration not possible, commence TB treatment unless the CXR suggests a different diagnosis

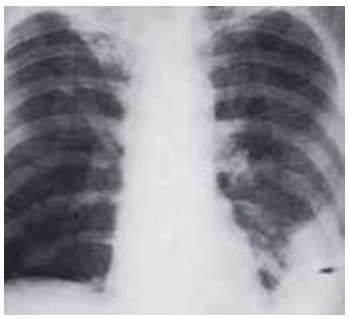
EXTRA-PULMONARY TB >>>

4.2. Pericardial Effusions	Signs and Symptoms	Diagnosis and Treatment

	• Low cardiac output
	  ○ chest pain
	  ○ shortness of breath
	  ○ cough
	  ○ dizziness
	  ○ weakness
	• Right-sided heart failure
	  ○ leg swelling
	  ○ right hypochondrial pain
	  ○ ascites
	• Tachycardia
	• Low blood pressure
	• Raised jugular venous pressure
	• Pulsus paradoxus
	• Impalpable apex beat
	• Distant heart sounds
	• Pericardial friction rub
		• Ultrasound
		• CXR
		  ○ large globular heart
		  ○ clear lung fields
		  ○ bilateral pleural effusions
		• ECG
		  ○ tachycardia
		  ○ flattening of ST and T waves
		  ○ low voltage QRS complexes
		• In cases of suspected cardiac tamponade refer to a specialist for aspiration
		• May be safer for the patient to start presumptive TB treatment than to undergo diagnostic pericardiocentesis
		• Corticosteroids may be added to treatment
		• ART initiation should be delayed for at least one month after starting TB treatment as IRIS may be fatal

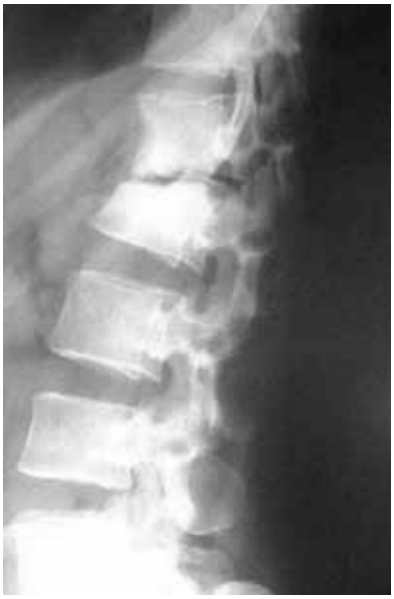
4.3. Peritoneal Tuberculosis	**Signs and Symptoms**	**Diagnosis and Treatment**

	• Systemic TB features
	• Ascites with no signs of portal hypertension
	• May be palpable abdominal masses
	• Bowel obstruction may develop from adhesion of nodules to bowel
		• Always do a diagnostic ascitic tap
		• Ascitic fluid:
		  ○ usually straw coloured (may be turbid or blood-stained) exudate
		  ○ usually >300 white cells/mm^3 with predominating lymphocytes
		• Abdominal ultrasound may show retroperitoneal or mesenteric lymph node enlargement
		• Biopsy from exploratory surgery or laparoscopy in doubtful cases

4.4. Tuberculous Empyema	**Signs and Symptoms**	**Diagnosis and Treatment**
	• Similar to pleural effusion	• Pleural tap reveals thick pus ○ send pus to laboratory for examination for TB, gram stain and bacterial culture • For diagnosed pyopneumothorax, insert a chest drain with underwater seal to remove fluid and air

EXTRA-PULMONARY TB

5. TUBERCULOSIS OF THE SPINE	SIGNS AND SYMPTOMS	DIAGNOSIS AND TREATMENT

	• TB can affect any bone but most commonly affects the vertebral column
	  ○ if severe, may have neurological sequelae
	• Back pain/stiffness
	• May cause referred pain radiating out from original site
	• Localised swelling, sometimes with an obvious lump or abnormal curvature of the spine
	• Cold abscess can develop behind sternocleidomastoid muscle
	• May have weakness or paraplegia
		• X-rays of the spine may show:
		  ○ disc space narrowing
		  ○ erosion of adjacent vertebral bodies
		  ○ wedge-shaped collapse
		  ○ angulation
		• Biopsy of cold abscess for Xpert, microscopy and culture, if possible

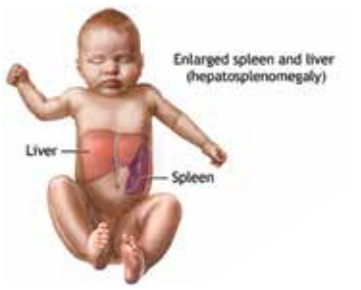
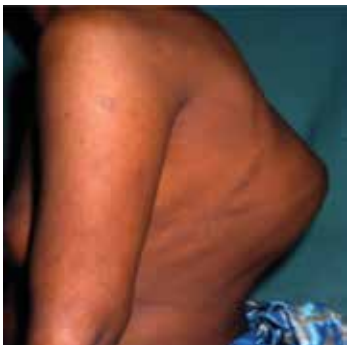
PULMONARY AND EXTRAPULMONARY TB COMMONLY OCCUR TOGETHER
ALWAYS TAKE A SPUTUM SPECIMEN FOR TB TESTING

http://www.meddean.luc.edu/lumen/MedEd/Medicine/PULMONAR/cxrself/list3.htm
http://www.naika.or.jp/im2/43/04/17c.aspx
http://radiographics.highwire.org/content/20/2/449.full
http://www.gpnotebook.co.uk/simplepage.cfm?ID=1174798340
http://radiopaedia.org/cases/pericardial-effusion
http://www.isradiology.org/tropical_diseases/tmcr/chapter8/imaging.htm

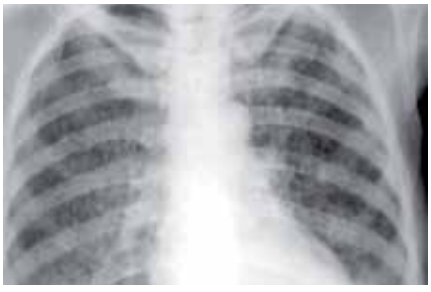
EXTRA-PULMONARY TB IN CHILDREN >>>

WHAT DANGER SIGNS SHOULD PROMPT URGENT REFERRAL TO A HOSPITAL?

1. Severe respiratory distress
2. Severe wheezing not responding to bronchodilators
3. Headache (especially if accompanied by vomiting, possibly indicating raised intracranial pressure), irritability, drowsiness, neck stiffness and convulsions (possible TBM)
4. Hepatosplenomegaly (possible miliary TB)
5. Angulation of the spine – gibbus (possible TB spine)
6. Breathlessness and peripheral oedema (possible TB pericardial effusion)
7. Distended abdomen with/without ascites (possible abdominal TB)

Severe Respiratory Distress	Opisthotonos (Severe Neck Stiffness)	Hepatosplenomegaly
		
Gibbus	**Facial Oedema**	**Ascites**
		

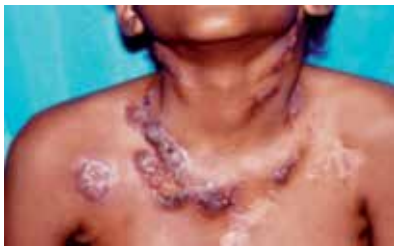
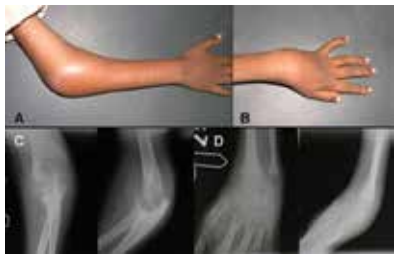
WHICH INDICATIONS FOR REFERRAL CAN BE DETECTED ON CHEST X-RAY?



Miliary TB

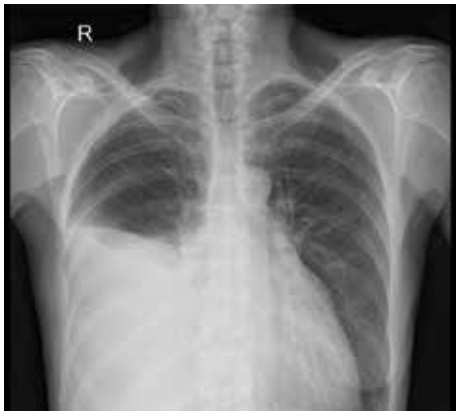
- Widespread fine millet-sized (1-2 mm) lesions (possible miliary TB)
- Extensive parenchymal involvement
- Massive pleural effusion
- Pericardial effusion
- Poor radiological and clinical response to treatment

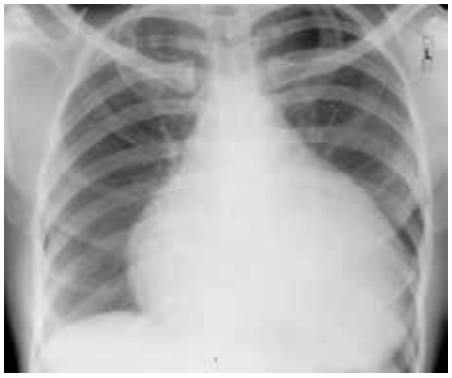
EXTRA-PULMONARY TB IN CHILDREN >>>

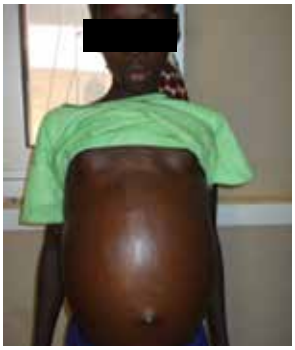
1. PERIPHERAL LYMPHADENITIS	SIGNS AND SYMPTOMS	DIAGNOSIS AND TREATMENT
	• Enlarged cervical nodes • Enlarged lymph nodes ≥14 days • No other cause for lymphadenopathy e.g. lesion on head • No response to antibiotics • Usually painless, firm and matted • Lymph nodes may become fluctuant prior to spontaneous drainage • Sinus formation (scrofula)	• TB microscopy and culture of sinus fluid where possible (although often contaminated with other bacteria) • Fine needle aspiration (FNA): ○ Xpert ○ microscopy, TB culture and DST ○ cytology • Lymph node biopsy
2. BONE AND JOINT DISEASE (OSTEO-ARTICULAR TB)	**SIGNS AND SYMPTOMS**	**DIAGNOSIS AND TREATMENT**
	• Most cases arise in older children • Usually a single large joint • Painful joint(s) • Limp that is frequently misattributed to trauma	• X-ray • Joint aspiration with fluid sent for Xpert, TB microscopy and culture • Synovial biopsy
2.1 SPINAL TB (50% OF ALL OSTEO-ARTICULAR TB)	**SIGNS AND SYMPTOMS**	**DIAGNOSIS AND TREATMENT**
	• Can present acutely as spinal cord compression with lower limb weakness and bladder and bowel neurology ○ needs emergency intervention in order to save neurological function • Can present chronically with backache for a few weeks	• Accurate history • Detailed examination • X-ray • CT Scan • MRI • Biopsy of cold abscess for Xpert, microscopy and culture, if possible

EXTRA-PULMONARY TB IN CHILDREN >>>

3. PLEURAL EFFUSION	SIGNS AND SYMPTOMS	DIAGNOSIS AND TREATMENT

	• Fever
	• Dyspnoea especially if effusion is large
	• Unilateral pleuritic chest pain
	• Decreased breath sounds and stony dullness
	• The child may not be acutely ill, and may have minimal signs
		• CXR
		• Pleural tap:
		  ○ chemistry, including ADA
		  ○ Xpert
		  ○ TB microscopy and culture

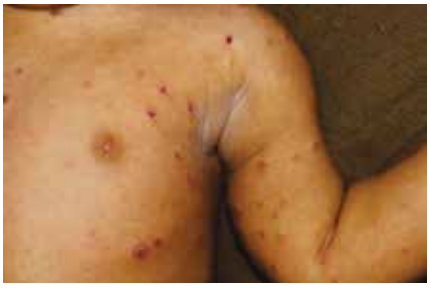
4. PERICARDITIS	**SIGNS AND SYMPTOMS**	**DIAGNOSIS AND TREATMENT**
	• Features of congestive cardiac failure and pericardial constriction (elevated jugular venous pressure, palpable pulsus paradoxus, pericardial friction rub)	• Ultrasound • Pericardial tap invasive, not usually performed
5. ABDOMINAL TB	**SIGNS AND SYMPTOMS**	**DIAGNOSIS AND TREATMENT**

	• Peritonitis
	• Malnutrition with protein-losing enteropathy
	• Abdominal distension with ascites
	• Bowel, biliary or lymphatic obstruction (compression by enlarged intra-abdominal nodes)
		• Abdominal ultrasound
		• Ascitic tap:
		  ○ chemistry, including ADA
		  ○ Xpert
		  ○ TB microscopy and culture

EXTRA-PULMONARY TB IN CHILDREN

6. MENINGITIS	SIGNS AND SYMPTOMS	DIAGNOSIS AND TREATMENT

	• Often have a TB contact
	• Headache
	• Early morning vomiting
	• Irritability, drowsiness, convulsions
	• Weight loss
	• Neck pain and resistance to neck flexion due to meningeal irritation
	• Cranial nerve palsies
	• Altered level of consciousness
	• Sub-acute or acute onset of central nervous system symptoms
	• New onset focal neurology and seizures
	• Hydrocephalus develops as a complication and manifests as:
	  ○ vomiting without diarrhoea
	  ○ early morning headaches
	  ○ irritability
	  ○ deteriorating level of consciousness
	• Always consider TB meningitis in children diagnosed with bacterial or viral meningitis not responding to treatment
		• Lumbar puncture, CSF shows:
		  ○ raised protein and lymphocytes
		  ○ low glucose and chloride
		  ○ gram stain is negative
		  ○ Xpert may be positive
		  ○ usually no AFB, therefore mycobacterial culture is crucial

7. MILIARY TB	**SIGNS AND SYMPTOMS**	**DIAGNOSIS AND TREATMENT**
	• Low-grade fever, weight loss, fatigue and malaise • Cough and respiratory distress • Lymphadenopathy • Hepatosplenomegaly • Tachypnea, cyanosis, and respiratory distress • Other signs - papular lesions on the skin or choroidal tubercles in the retina	• CXR – diffuse, uniformly distributed, small miliary shadows, "millet seed" appearance • FBC – pancytopaenia • LFT – abnormal • Skin biopsy – tubercles on histology • Culture – Isolation of MTB in CSF, bone marrow, sputum

NB: TB MENINGITIS IS A VERY SERIOUS FORM OF TB AND SHOULD NOT BE TREATED AT A PRIMARY HEALTH FACILITY. THESE CHILDREN SHOULD URGENTLY BE REFERRED TO A HOSPITAL FOR MANAGEMENT.

http://www.adi.org.au/picture_gallery.php?id_gallery=7
http://www.solidaritypeacetrust.org/
http://helpfeedthechildren.info/malnutrition/the-preventable-horrors-of-kwashiorkor/
http://en.wikipedia.org/wiki/Pleural_effusion http://www.graphicshunt.com/health/images/constrictive_pericarditis-991.htm
http://www.adi.org.au/picture_gallery.php?id_gallery=7
http://www.manual-of-surgery.com/content/0084-Diseases-of-Lymph-Glands.html
http://jbjs.org/article.aspx?Volume=92&page=436)

OVERVIEW OF TB DIAGNOSTIC TESTS >>>

- Smear microscopy requires ~10 000 TB bacilli per ml of sputum to be detected/positive
- Culture can be positive with only ~10 - 100 TB bacilli per ml of sputum
- GeneXpert requires ~ 130 TB bacilli per ml of sputum for a positive result

Test Description	Specimen for Testing	Strengths	Weaknesses	Effect of HIV on Test
Xpert™ MTB/RIF				
Cartridge-based automated PCR • used on the GeneXpert platform • detects MTB • detects RIF susceptibility	• Sputum • CSF • Aspirates (gastric, pleural, pericardial, lymph node) • Tissue (i.e. pleural biospy)	• Few false negative results (high sensitivity) • Can be located at point of care • Rapid turn-around-time (TAT) (2 hours)	• Does not detect INH resistance • May over-report RIF resistance when MDR is uncommon (low positive predictive value) • Cannot be used for monitoring treatment	• A small reduction in sensitivity because of reduced numbers of AFB
Microscopy				
Visualisation of stained MTB in clinical specimens using: • light or • fluorescent microscopy	• Sputum • Gastric aspirates • Any other clinical specimen	• Very few false positive results (high specificity) • Cheap (±R30/ smear) • Short TAT (24 hours)	• Many false negatives (low sensitivity)	• HIV infection decreases bacillary load in sputum leading to more false negative results (lower sensitivity)
Culture				
Growth of MTB on: • solid or • liquid media	• Any clinical specimen	• Culture is the ***gold standard*** for TB diagnosis • Very few false negatives (high sensitivity)	• Long TAT (2-6 weeks) • Expensive (+/-R700) • High contamination rates (liquid culture)	• No effect
Drug Susceptibility Testing (DST)				
Susceptibility testing for most TB drugs	• Cultured isolate	• Gold standard for drug susceptibility testing-high sensitivity • Accurately detects susceptibility to most TB drugs	• Expensive • Requires sophisticated laboratory	• No effect

OVERVIEW OF TB DIAGNOSTIC TESTS

Test Description	Specimen for Testing	Strengths	Weaknesses	Effect of HIV on Test
Line Probe Assay (LPA)				
PCR-based assays that identify: • DNA specific to MTB • INH and RIF susceptibility • FLQ and aminoglycoside susceptibility	• Smear positive sputum or • Cultured isolate of MTB	• Short TAT • Detects INH and RIF susceptibility • Second-line assay can detect fluoroquinolone and aminoglycoside susceptibility • Does not miss many cases of MDR-TB (high sensitivity)	• Can only be done on smear or culture positive sputum specimen • Not yet approved by the WHO as an initial diagnostic test • Awaiting validation by the NHLS for smear negative TB	• No effect
Tuberculin Skin Testing (TST)				
• PPD is injected into the dermis (skin) and the area of induration is read	• Left inner forearm	• Used to detect the presence of latent tuberculosis infection	• Not useful for diagnosis of active disease in adults • Requires 2 visits • False negatives may occur e.g. due to severe malnutrition, overwhelming infection, HIV	• HIV can lead to anergy, and false negative TST results
Interferon Gamma Release Assay (Quantiferon® - TB Gold Test), (IGRA)				
• Incubation of patient blood with TB antigens and measurement of gamma interferon release from white cells	• Blood	• Used to detect the presence of latent tuberculosis infection	• Not useful for diagnosis of active disease in adults	• IGRA is less likely to give false negative results in HIV-infected persons compared with TST

Other diagnostic tests
- Blood culture
- TB LAM (lateral flow version)
- Histological examination

Adjunctive tests
- CXR
- Ultrasound
- CT scan and MRI
- ESR
- ADA

XPERT MTB/RIF >>>

HOW IS SPUTUM PROCESSED FOR XPERT MTB/RIF?

RECEIVED FROM PATIENT	INACTIVATION	INOCULATION INTO XPERT MTB/RIF CARTRIDGE	INSERTED INTO GENEXPERT MACHINE*
			
	Inactivating agent added to sputum to make up a volume of 2ml, left for 15 mins • kills MTB if present • releases TB DNA	2 ml added to the cartridge	Cartridge inserted into the GeneXpert machine

**Sputum cannot be cultured/used for other tests as organisms are killed and specimen is inaccessible in cartridge*

WHAT ARE THE STRENGTHS OF XPERT MTB/RIF?

- Can be conducted on gastric washings/ lavages, lymph node fine needle aspirates, cerebrospinal fluid and pleural biopsies
- Can detect as few as 130 MTB organisms/ml
- False negative and false positive results uncommon
- TAT of 2 hours
- Detects susceptibility to rifampicin
- Detects MTB and RIF resistance from one specimen at the same time
- Can differentiate MTB from other mycobacteria
- Reduced risk of cross-contamination and human error

WHAT ARE THE WEAKNESSES OF XPERT MTB/RIF?

- Cannot detect INH resistance – therefore it is a screening (not diagnostic) test for MDR-TB
- Cannot be used for monitoring treatment because it does not distinguish between live and dead bacilli. Its use is therefore limited to diagnosis

Why Is Smear Microscopy Done When Xpert MTB/RIF Is Positive?	When Is Sputum Culture and DST Done If Xpert MTB/RIF Is Used As The First-Line TB Test?
• To categorise patient as 'smear positive' or 'smear negative' so that smear conversion can be demonstrated • For monitoring progress on treatment	• When rifampicin resistance is reported • When rifampicin susceptibility is indeterminate • When negative and person remains symptomatic for TB • To confirm MDR-TB and resistance to second line drugs

XPERT MTB/RIF >>>

HOW ARE XPERT MTB/RIF RESULTS INTERPRETED?

MTB Complex not Detected

- Xpert negative for TB
- Negative results could be:
  - correctly negative (client does not have PTB) or
  - false negative - this is uncommon, only about 10% of negative Xpert MTB/RIF results will have a positive culture

MTB Complex Detected/RIF Susceptible

- MTB is present, and susceptible to rifampicin
- Xpert MTB/RIF is sensitive and specific for detection of TB and rifampicin resistance
- This result can be trusted

MTB Complex Detected/RIF Resistant

- MTB present and may be resistant to rifampicin
- Rifampicin resistance may be falsely positive (10%)
- Second sputum specimen must be sent for microscopy, culture and confirmatory DST

MTB Complex Detected/ RIF Indeterminate

- MTB present and rifampicin resistance could not be assessed
- A second sputum must be sent for TB microscopy, culture and DST, or LPA to confirm susceptibility
- Treat the patient as if they have drug sensitive TB

Error

- The test failed
  - caused by problem with the cartridge, e.g. food particles
- Submit a second specimen for Xpert MTB/RIF

Results of Xpert are graded as: Very Low, Low, Medium, High

- Xpert MTB/RIF grading does not correspond with grading for smear microscopy
- All grades indicate significant TB infection and should therefore be treated

XPERT MTB/RIF

HOW ARE XPERT MTB/RIF, MICROSCOPY AND LINE PROBE ASSAY RESULTS REPORTED AND INTERPRETED, AND WHAT ACTION SHOULD BE TAKEN?

What The Lab Report Says:	What Could This Lab Report Mean?	What Should The Clinician Do?
Xpert MTB/RIF: MTB complex detected, rifampicin susceptible **Microscopy:** not done	• Patient has PTB	• TB treatment with first-line TB drugs • Send a second sputum for smear for monitoring purposes
Xpert MTB/RIF: MTB complex not detected **Microscopy:** not done	• Does not rule out TB in a person who is HIV-infected and/or symptomatic	• Offer HIV test • If patient is HIV-infected: send another specimen for smear, culture and DST, or LPA, do CXR, give antibiotics and review after 5 days. If poor response, clinically or on X-ray, commence TB treatment • If patient HIV-uninfected: treat with antibiotics, if poor response, consider another diagnosis and refer
Xpert MTB/RIF: MTB complex not detected **Microscopy:** not done **Culture:** positive for MTB	• Patient has PTB	• Commence TB treatment • This is an uncommon case of a false negative Xpert MTB/RIF result

Xpert MTB/RIF: MTB complex detected, rifampicin resistant
Microscopy: not done
	• Patient has PTB
	• May be rifampicin mono-resistant or MDR-TB
		• Commence MDR-TB treatment (see section on MDR-TB Diagnosis And Management)
		• Send a second sputum for smear microscopy, culture and DST or LPA
		  ○ for monitoring purposes
		  ○ to confirm rifampicin resistance and investigate for resistance to other drugs

Xpert MTB/RIF: MTB complex detected, rifampicin susceptible **Microscopy:** positive for AFB	• Patient has PTB	• Commence TB treatment • Positive smear microscopy means that the patient has 'smear positive TB' • Send sputum after 2 months to document smear conversion
Xpert MTB/RIF: MTB complex detected, rifampicin susceptible **Microscopy:** negative for AFB	• Patient has PTB	• Commence TB treatment • Negative smear microscopy means that the patient has 'smear negative TB' • Send sputum for smear microscopy for monitoring purposes
Xpert MTB/RIF: MTB complex detected, rifampicin resistant **Microscopy:** positive/negative for AFB **LPA:** RIF resistant, INH resistant	• Patient has MDR-TB	• MDR-TB treatment • Send a sputum for culture and DST to establish susceptibility to second-line TB drugs • Record patients details in MDR-TB register
Xpert MTB/RIF: MTB complex detected, rifampicin resistant **Microscopy:** positive/negative for AFB **LPA:** RIF resistant, INH sensitive	• Patient has rifampicin mono-resistant TB	• MDR-TB treatment • Send a sputum for culture and DST to establish susceptibility to second-line TB drugs
Xpert MTB/RIF: MTB complex detected, rifampicin resistant **Microscopy:** positive/negative for AFB **LPA:** RIF sensitive, INH sensitive	• Patient has fully sensitive TB	• Stop MDR-TB treatment if started based on initial Xpert MTB/RIF results • Start first-line TB treatment • Send a sputum for culture and DST

IDENTIFICATION OF DRUG-RESISTANT TB >>>

WHAT IS DRUG-RESISTANT TB (DR-TB)?

- DR-TB is any strain of MTB that is resistant to one or more anti-tuberculosis drugs
- DR-TB is ***always a laboratory diagnosis***
  - clinical failure to respond to TB treatment does not mean that the strain is DR-TB
- INH and RIF susceptibility is initially performed
  - if resistance to INH and/or RIF detected; further DST is performed

WHEN SHOULD DRUG SUSCEPTIBILITY TESTING BE DONE?

- If Xpert MTB/RIF results show the following: MTB detected and rifampicin resistant or rifampicin indeterminate
- Repeat episode of TB
- Known DR-TB contact
- TB acquired in institutions
- Smear positive TB after intensive phase of TB treatment

WHICH DIAGNOSTIC TESTS CAN DETECT DRUG RESISTANCE AND WHAT IS THE MECHANISM OF THESE TESTS?

Diagnostic Modality	Explanation	Additional Tests Required
Xpert™ MTB/RIF	Detects resistance to **RIF** on sputum (smear positive or smear negative) by detecting mutations in the *rpo*B gene	RIF-resistant TB may be mono-resistant or MDR-TB. Request culture and DST. (See algorithm on adjacent page)
MTBDR*plus* Line Probe Assay (LPA)	Detects resistance to **RIF** (*rpo*B mutations) and **INH** (*kat*G and *inh*A mutations) on smear positive sputum, or MTB cultures	If RIF and/or INH resistant, request DST to RIF, INH and remaining first and second-line drugs
MTBDRsl Line Probe Assay (LPA)	Detects resistance to **fluoroquinolones** and **aminoglycosides** on smear positive sputum, or MTB cultures, to exclude XDR or pre XDR-TB	Refer to specialist centre for further management if resistance is detected
Culture and phenotypic DST	• **Gold standard** for the detection of drug resistance • Requires solid media or automated liquid media technology	• Contamination may occur • Use this result to guide patient management

IDENTIFICATION OF DRUG-RESISTANT TB

HOW SHOULD A PATIENT WITH THE FOLLOWING XPERT MTB/RIF RESULTS BE MANAGED?

Result: MTB complex detected / rifampicin resistant

If patient does not return within 48 hrs call and/ or send TB tracer

- Counsel patient that he/she might have DR-TB but that a confirmatory test must be done
- Request a second sputum specimen for microscopy, culture and phenotypic DST
  - to confirm RIF resistance
  - to determine susceptibility to other drugs
- Start MDR-TB treatment within 5 days
- Register and notify the patient
- Screen contacts for TB symptoms and investigate if symptomatic

Obtain result of phenotypic DST

If result shows resistance to RIF and susceptibility to isoniazid:
- Diagnosis is rifampicin mono-resistant TB
- Continue MDR-TB treatment and add isoniazid (see page 52)

If RIF and INH resistance detected:
- Diagnosis confirmed as MDR-TB
- Continue MDR-TB treatment (see page 54-57)

If result indicates RIF and INH susceptibility:
- Diagnosis is fully sensitive TB
- Stop MDR-TB treatment
- Start patient on regimen 1

If INH resistant and RIF susceptible
- Diagnosis is isoniazid mono-resistance
- Treat with regimen 1 (see page 52)

TREATMENT 3

BASELINE ASSESSMENT

CHECKLIST

	HOW SHOULD ADULTS BE ASSESSED BEFORE INITIATING TB TREATMENT?	DONE
1	Establish whether contacts are present and screen contacts: • Symptomatic for TB • Eligible for IPT	✓
2	Record the following: • Weight • Height • Refer for nutritional support if BMI <18.5	✓
3	Ensure that HIV status is known, test for HIV if status unknown	✓
4	Ensure baseline smear is taken for microscopy pre-treatment to monitor the response to treatment	✓
5	Blood tests: • Blood glucose for symptomatic patients • LFTs in patients with history of liver disease or excessive alcohol intake • Serum creatinine in patients with history of renal disease	✓
6	CXR in patents with concomitant lung disease or history of working in mines	✓
7	Family planning: • Do pregnancy test • Assess contraceptive needs • Avoid oral contraceptives • Use injectable/IUCD + condoms	✓
8	Counselling should include: • Adherence to treatment • Possible side effects that should be reported promptly	✓
9	Advice on when to return to work: • Drug-sensitive TB – after 2 weeks • Drug-resistant TB – when culture is negative	✓
10	Address substance abuse	✓
11	Arrange clinic DOT for the first 2 weeks and then arrange for CHW or workplace support	✓

FIRST LINE TB TREATMENT >>>

WHAT ARE THE FIRST-LINE REGIMENS?

- Standardised treatment with fixed dose combination medicines are used for TB treatment.
- The standard treatment regimen for all patients is made up of an intensive phase lasting 2 months and a continuation phase lasting 4 months.
- Due to the introduction of rapid tests (LPA or Xpert MTB/RIF) Regimen 2 has been phased out. There are now three treatment regimens:

Regimen 1: for new and previously treated adults and children >8yrs/>30kg
Regimen 3A for children < 8yrs and < 30kg with uncomplicated TB disease
Regimen 3B: for children < 8yrs and < 30kg with complicated TB disease

WHAT ARE THE DRUGS DOSAGES USED IN ADULTS?

Adult TB Drug Dosages		
Essential TB Drug (abbreviation)	**Dose mg/kg**	**Dose Range mg/kg**
Rifampicin (R)	10	8 – 12
Isoniazid (H)	5	4 – 6
Pyrazinamide (Z)	25	20 – 30
Ethambutol (E)	15	15 – 20
Streptomycin (S)	15	12 – 18

Please note Streptomycin is not included in the first line regimens. It is available by prescription for patients with liver disease as it is a liver-friendly drug.

WHICH FIXED-DOSE COMBINATION TABLETS ARE AVAILABLE FOR ADULTS?

RHZE (150,75,400,275mg)	Intensive Phase
RH (150,75mg)	Continuation Phase
RH (300,150mg)	Continuation Phase

WHAT ARE THE DRUG DOSAGES USED IN CHILDREN?

- This is dependent on the body weight of the child
- Should be adjusted as weight changes during the course of treatment (i.e. at each health visit)

Recommended Doses for First-Line TB Drugs in Children			
Drug	**Dose (mg/kg)**	**Range (mg/kg)**	**Maximum Dosage (mg/day)**
Isoniazid (H)	10	10-15	300
Rifampicin (R)	15	10-20	600
Pyrazinamide (Z)	35	30-40	2000
Ethambutol (E)	20	15-25	1200

FIRST-LINE TB TREATMENT

REGIMEN 1: FOR ADULTS AND CHILDREN OLDER THAN 8 YEARS OR WEIGHING MORE THAN 30KG

REGIMEN 1: FOR ADULTS AND CHILDREN OLDER THAN 8 YEARS OR WEIGHING MORE THAN 30KG			
Pre-treatment Body Weight	Intensive Phase 7 days a week for 2 months	Continuation Phase 7 days a week for 4 months	
	RHZE (150, 75, 400, 275)	RH (150, 75)	RH (300,150)
30-37 kg	2 tabs	2 tabs	
38-54 kg	3 tabs	3 tabs	
55-70 kg	4 tabs		2 tabs
>70 kg	5 tabs		2 tabs

Treatment for Extra pulmonary TB

- Six months treatment is as effective in extra-pulmonary as in pulmonary disease.
- In some instances of severe or complicated disease (meningitis, TB bones/joints, miliary TB) treatment may need to be extended to nine months.
  - 2(RHZE)/ 7(RH)
  - intensive phase remains two months
  - continuation phase is prolonged to seven months
- Steroids recommended in EPTB particularly TB meningitis and pericarditis
  - high dose steroid treatment with Prednisone 1-2 mg for 4 weeks then taper gradually over two weeks

Adjunctive treatment

Pyridoxine is given to prevent peripheral neuropathy, most commonly caused by INH:

- 25mg daily for high risk adult patients started on TB treatment
- High risk: HIV positive, diabetic, malnourished, pregnant, alcohol abuse
- If peripheral neuropathy develops increase to 50-75mg (up to maximum of 200mg) until symptoms subside then reduce to 25 mg daily

TB TREATMENT IN CHILDREN >>>

REGIMEN 3A: FOR UNCOMPLICATED TB WITH LOW BACILLARY LOAD, CHILDREN UP TO 8 YEARS

REGIMEN 3A: FOR CHILDREN <8 YEARS AND <30 KG WITH UNCOMPLICATED TB DISEASE				
Body Weight	Intensive phase (2 months)			Continuation phase (4 months)
	Rifampicin/ Isoniazid 60,60	Pyrazinamide 150mg* or 150mg/3mL	Pyrazinamide 500mg	Rifampicin/ Isoniazid 60,60
2–2.9 kg	½ tablet	1.5 mL	expert advice on dose	½ tablet
3–3.9 kg	¾ tablet	2.5 mL	¼ tablet	¾ tablet
4–5.9 kg	1 tablets	3 mL	¼ tablet	1 tablet
6–7.9 kg	1½ tablets		½ tablet	1½ tablets
8–11.9 kg	2 tablets		½ tablet	2 tablets
12–14.9 kg	3 tablets		1 tablet	3 tablets
15–19.9 kg	3½ tablets		1 tablet	3½ tablets
20–24.9 kg	4½ tablets		1½ tablets	4½ tablets
25–29.9 kg	5 tablets		2 tablets	5 tablets

* For each dose, dissolve 150mg dispersible (1 tablet) in 3mL of water to prepare a concentration of 50mg/mL (150mg/3mL). Only Pyrazinamide 150mg or 500mg tablets may be given at a time depending on availability but NOT both

Children who are malnourished or HIV positive: Pyridoxine 25mg daily may be given for children >5years and 12.5mg for children <5years

UNCOMPLICATED TB IN CHILDREN

- Low bacillary load TB disease
- PTB with minimal lung parenchyma involvement
- Intrathoracic disease (mediastinal/ hilar lymph node involvement)
- TB cervical lymphadenitis
- TB pleural effusion

TB TREATMENT IN CHILDREN >>>

REGIMEN 3B: FOR COMPLICATED TB WITH HIGH BACILLARY LOAD, CHILDREN UP TO 8 YEARS

REGIMEN 3B: FOR CHILDREN < 8 YEARS AND <30KG WITH COMPLICATED TB DISEASE					
Body Weight	Intensive phase 2 months				Continuation phase 4 months***
	Rifampicin, Isoniazid 60,60	Pyrazinamide 150mg* or 150mg/3mL	Pyrazinamide 500mg	Ethambutol 400 mg tablet OR 400mg/8mL** solution	Rifampicin, Isoniazid 60/60
2–2.9 kg	½ tablet	1.5 mL	Expert advice on dose	1 mL	½ tablet
3–3.9 kg	¾ tablet	2.5 mL	¼ tablet	1.5 mL	¾ tablet
4–5.9 kg	1 tablet	3 mL	¼ tablet	2 mL	1 tablet
6–7.9 kg	1½ tablet		½ tablet	3 mL	1½ tablets
8–11.9 kg	2 tablets		½ tablet	½ tablet	2 tablets
12–14.9 kg	3 tablets		1 tablet	¾ tablet	3 tablets
15–19.9 kg	3½ tablets		1 tablet	1 tablet	3½ tablets
20–24.9 kg	4½ tablets		1½ tablet	1 tablet	4½ tablets
25–29.9 kg	5 tablets		2 tablets	1½ tablets	5 tablets

* For each dose, dissolve 150mg dispersible (1 tablet) in 3mL of water to prepare a concentration of 50mg/mL (150mg/3mL). Only Pyrazinamide 150mg or 500mg tablets may be given at a time depending on availability but NOT both

** For each dose, crush 400mg (1 tablet) to a fine powder and dissolve in 8 ml of water to prepare a concentration of 400mg/8mL. Discard unused solution

*** The continuation phase may be prolonged to 7 months in slow responders and children who are HIV positive

Children who are malnourished or HIV positive: Pyridoxine 25mg daily may be given for children >5years and 12.5mg for children <5years

COMPLICATED TB IN CHILDREN

- High bacillary load PTB with extensive parenchymal involvement
- TB Meningitis
- Miliary TB
- TB pericarditis
- Abdominal TB
- Spinal TB
- Osteo-articular TB
- Cavitatory TB

TB TREATMENT IN CHILDREN

HOW IS TB MENINGITIS IN CHILDREN TREATED?

- In children under 8 years, a six month regimen is recommended
- If there are concerns about clinical progress the treatment can be prolonged to 9 months in total
- Consult with a specialist

Drug	Dosage (single daily dose)	Maximum daily dose
Rifampicin	20 mg/kg	600 mg
Isoniazid	20 mg/kg	400 mg
Pyrazinamide	40 mg/kg	2 000 mg
Ethionamide	20 mg/kg	1 000 mg

WHEN SHOULD ORAL STEROIDS BE USED IN CHILDREN?

Oral steroids should be added to the treatment in children with the following forms of TB:

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

The recommended dose is: Prednisone 2 mg/kg orally, daily for 4 weeks (maximum daily dose 60mg). The dose should be tapered to stop over 2 weeks.

HOW SHOULD I MANAGE A CHILD WHO DETERIORATES ON TB TREATMENT?

Ask the following questions:

- Is the drug dosage correct
- Is the caregiver administering the drugs to the child as prescribed
- Is the child taking the drugs as prescribed
- Is the child HIV-infected
- Is the child severely malnourished
- Is there a reason to suspect drug- resistant TB
- Has the child developed IRIS
- Is there another possible diagnosis

MONITORING OF PATIENTS ON TB TREATMENT >>>

HOW OFTEN SHOULD PATIENTS ON TB TREATMENT BE ASSESSED?

- after 2 weeks on treatment
- at least monthly thereafter

HOW SHOULD TB PATIENTS BE ASSESSED AT FOLLOW-UP VISIT?

CHECKLIST

	Checklist
TB symptoms • Refer to doctor if symptoms worsen or do not improve	✓
Weight • Give nutritional support • Adjust dosages based on weight gain • Refer to doctor in the same week if losing weight on treatment	✓
Ask about contacts if symptomatic	✓
Enquire about family planning	✓
Assess adherence • Review patient treatment card (green card) • Conduct pill count	✓
Ask about side effects to medications	✓
Test for HIV if status unknown	✓
Check results of tests done during work-up • Smear microscopy result - register as smear negative or smear positive depending on result • Smear culture result - register as culture negative or culture positive depending on result • Check result of LPA or DST if done	✓
Manage co-morbidities including HIV	✓

HOW SHOULD THE PATIENT ON TB TREATMENT BE MONITORED?

Bacteriological:

- All patients diagnosed with Xpert must have a baseline smear result
- They must be followed up and monitored bacteriologically with sputum smears
- If there is poor response to treatment, drug resistance should be excluded through LPA or culture and DST

Clinical:

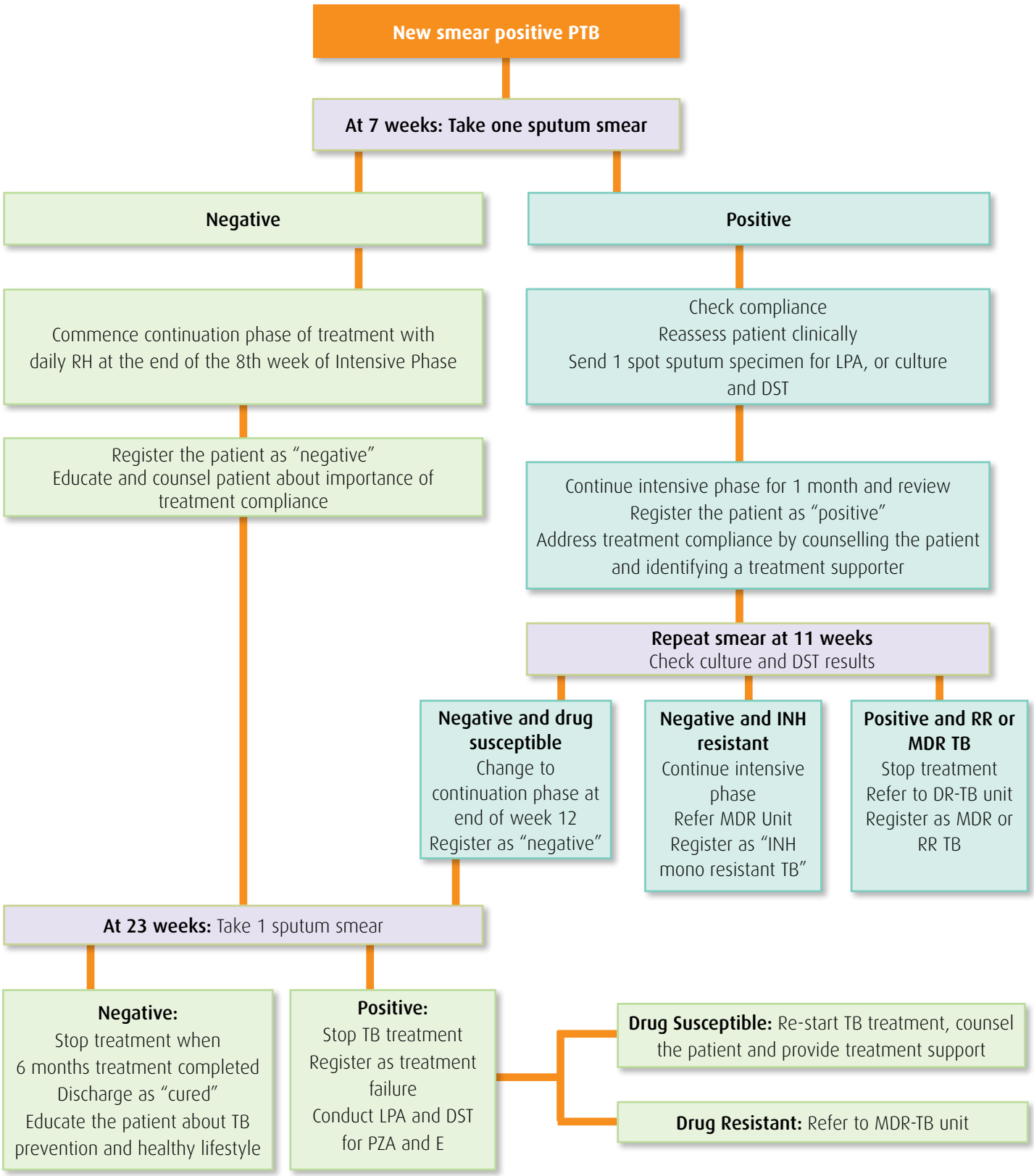
- Those with EPTB or those who were diagnosed on clinical grounds without bacteriological confirmation of TB should be monitored clinically over the duration of treatment.
- Weight is a useful indicator of clinical improvement therefore it should be monitored monthly.
- If there is poor response to treatment, alternative diagnoses and the possibility of drug resistance must be considered.

WHEN SHOULD SPUTUM SPECIMENS BE TAKEN FOR SMEAR MICROSCOPY?

Take 1 spot specimen for smear microscopy at:

- Week 7 – response to treatment
- Week 23 – treatment outcome

MONITORING OF PATIENTS ON TB TREATMENT



MANAGEMENT OF A PATIENT WHO INTERRUPTS TB TREATMENT

- Trace the patient and determine reason for treatment interruption
- Ask about substance abuse, stress and side effects
- Give increased adherence support and educate the client about the risks of poor adherence
- Determine duration of treatment interruption and manage further according to this

Interruption <1 month

- Continue TB treatment
- Extend treatment phase by the number of missed doses

Interruption 1-2 months

- Send 1 spot sputum specimen for Xpert
- Continue TB treatment and review results

Xpert negative Rif sensitive

- Continue until end of treatment (6 months)

Xpert positive Rif sensitive

- Continue TB treatment
- Extend treatment phase by the number of missed doses

Xpert positive Rif resistant

- Stop TB treatment
- Register as RR-TB
- Refer to MDR-TB unit

Interruption ≥2 months

- Send 1 spot sputum specimen for Xpert
- Do not re-start TB treatment until results available

Xpert positive Rif resistant

- Register as RR-TB
- Refer to MDR-TB unit

Xpert positive Rif sensitive

- Register as "Treatment after LTFU"
- Restart Regimen 1

When a patient refuses to continue treatment every effort should be made to convince the patient to continue. When all measures fail and patient insists on stopping treatment, the patient should sign a refusal of hospital treatment (RHT). See Annexures for form

SIDE EFFECTS OF FIRST-LINE TB TREATMENT >>>

WHAT ARE THE MOST COMMON SIDE EFFECTS OF FIRST-LINE TB TREATMENT?

SIDE EFFECTS	DRUG(S) RESPONSIBLE	MANAGEMENT
Minor		
Anorexia nausea, abdominal pains	Rifampicin	Exclude other causes Treat symptomatically Take Rifampicin at least 30 minutes before meals or before going to bed Use antacids at least 2 hours before or after taking treatment
Joint pains	Pyrazinamide	Continue TB drugs. Treat symptomatically (aspirin). If severe, allopurinol may be required for the treatment of gout
Burning sensation in feet	Isoniazid	Pyridoxine 25mg daily
Orange/ red coloured urine	Rifampicin	Warn patients of this possible side-effect before commencing treatment. Reassure if it occurs.
Major		
Skin itching/ rash	Streptomycin, Rifampicin, Isoniazid	See page 47
Jaundice (other causes excluded)	Isoniazid, Rifampicin, Pyrazinamide	See pages 48-49
Deafness (no wax on otoscopy)	Streptomycin	Stop Streptomycin
Dizziness (vertigo, nystagmus)	Streptomycin	Reduce dosage
Peripheral Neuropathy	Isoniazid (also HIV and D4T)	Continue TB drugs. Pyridoxine 50-75 mg daily, can increase to 200mg daily in HIV positive patients
Renal impairment	Streptomycin	Reduce dosage by half
Vomiting, confusion	Isoniazid, Rifampicin, Pyrazinamide	Refer for supportive treatment if severe.
Visual impairment/ loss	Ethambutol	Stop ethambutol immediately and never reintroduce
Generalised purpura and shock	Rifampicin	Stop Rifampicin Administer Vitamin K at birth to infant of mother taking Rifampicin

SIDE EFFECTS OF FIRST-LINE TB TREATMENT >>>

HOW IS SKIN RASH MANAGED?

- Skin rash due to TB drugs usually begins 3-4 weeks after start of TB treatment
  - take a careful history regarding onset of the rash
- Skin reactions are not always related to TB drugs. Consider:
  - other drugs (co-trimoxazole, EFV, NVP)
  - underlying causes (HIV)
  - infectious conditions (varicella zoster virus, coxsackie virus, scabies)

GRADING AND MANAGEMENT OF SKIN RASH

Type of rash	Management
Mild itching rash	1. Give antihistamine 2. Prednisone may be added at 40mg/day and tapered gradually as the rash clears 3. A topical cream may be added
Petechial rash	1. Mainly due to Rifampicin 2. Conduct Platelet count 3. If below normal range (150,000 – 450,000 per microliter), stop Rifampicin and exclude from regimen. 4. Monitor platelet count until it returns to normal
Erythematous rash with fever	1. Stop all drugs 2. Rule out anaphylaxis reaction which can be characterised by any of the following – angioedema, swollen tongue/ throat, flushed face, airway constriction, wheezing, difficulty in breathing, hypotension 3. If treatment cannot be interrupted due to severity of disease, a regimen comprising other drugs the patient has not used can be started (amikacin/ kanamycin/ ofloxacin/ levofloxacin/ cycloserine) 4. If rash improves, the drugs can be re-introduced one by one every 2-3 days starting with Rifampicin which is potent and least likely to cause the rash, followed by Isoniazid, then pyrazinamide and ethambutol. 5. Monitor the signs and symptoms and if rash recurs at any point the last drug added should be stopped.

SIDE EFFECTS OF FIRST-LINE TB TREATMENT >>>

MANAGEMENT OF HEPATITIS

EVALUATION
Does patient have jaundice, severe nausea or vomiting, anorexia, weakness, dark urine, pale stool, right-sided abdominal pain, pruritus?

NO

ROUTINE LABORATORY SURVEILLANCE
- Patients <50 years without co-morbidities: clinical monitoring
- Patients > 50 years and/or with co-morbidities: every 3-6 months
- Patients with a history of hepatitis: every 3 months

YES

Check serum liver tests immediately

AST (SGOT) or ALT (SGPT)
> 3 times normal values

NO

YES

ANTITUBERCULOSIS DRUGS THAT CAN CAUSE HEPATITIS: Z, H, R, Ethio, PAS, E, FQ

EMERGENCY
Possible acute hepatitis: suspend all antituberculosis medications immediately

Rule out other etiologies, Hep-A, -B, -C, other viral infections, alcohol, and non-antituberculosis drugs (e.g., anti-epileptics, acetaminophen, sulfa drugs, erythromycin, etc.)

TREATMENT
- Follow serum liver tests and clinical exam for signs of improvement
- Treat symptoms as needed
- Consider hospitalisation in patients with severe hepatitis
- Follow for clinical improvement
- Normalisation of serum liver tests prior to considering reinitiation of antituberculosis medications

ONCE SYMPTOMATIC IMPROVEMENT AND DOCUMENTED DECREASE IN TRANSAMINASES
- If possible, eliminate the most likely agent from the regimen
- Reinitiate antituberculosis medications, one by one, with serial monitoring of serum liver tests
- Introduce agents most likely to cause hepatitis first
- If possible, replace the hepatotoxic medications with equally efficacious antituberculosis medications

THROUGHOUT DOTS-PLUS TREATMENT
- Follow serum liver tests every 1-2 months thereafter
- Maintain close surveillance for treatment failure and/or resistance amplification, given period of irregular therapy

Refer to guidelines for comprehensive management of drug-induced liver injury.
Conradie F, Meintjies G et al. Consensus statement: Management of drug-induced liver injury in HIV-infected patients treated for TB, 2013

SIDE EFFECTS OF FIRST-LINE TB TREATMENT

REINTRODUCING FIRST-LINE TB DRUGS FOLLOWING DRUG-INDUCED HEPATITIS

1. • Rule out other causes such as excessive alcohol use, other medication the patient might be taking, pre-existing liver disease and viral hepatitis
2. • Stop all medicines the patient is taking - the combination TB treatment (RHZE or RH), cotrimoxazole, ART
3. • Conduct liver function tests, serological testing for Hepatitis A, B and C (for patients who are high risk for hepatitis) and HIV test (if status is not known)
4. • Monitor the clinical symptoms until they resolve
5. • Start Rifampicin 10mg/kg/day (max 600mg/ day)
6. • Repeat ALT on day 3
7. · If normal, add Isoniazid 5mg/kg/day (max 300mg/ day) on day 4 to 6
8. • Repeat ALT on day 7
9. • If normal, add Ethambutol 15mg/kg/day on day 8-10
10. • Check ALT on day 10
11. • If normal consider Pyrazinamide 25mg/kg/day (if patient is in intensive phase of treatment) and continue as per Regimen 1, repeating ALT weekly for a month

TREATMENT FOR PATIENTS WHO CANNOT TOLERATE ONE OF THE FIRST LINE DRUGS

Drug omitted	Intensive phase	Continuation phase
Rifampicin	Isoniazid, Moxifloxacin, Ethambutol, Streptomycin for 2 months*	Isoniazid, Moxifloxacin, Ethambutol for 16 months
Isoniazid	Rifampicin, Moxifloxacin, Ethambutol for 2 months*	Rifampicin, Moxifloxacin, Ethambutol for 10 months
Pyrazinamide	Rifampicin, Isoniazid, Ethambutol for 9 months	

*May consider PZA re-challenge and use during intensive phase particularly if DILI occurred early during intensive phase

- If the patient is severely ill due to TB, and stopping treatment is not an option, a liver friendly regimen comprising Ethambutol, Moxifloxacin and Streptomycin can be started. This can be stopped if the patient is ready to be re challenged with Rifampicin, Isoniazid (or both).
- Reintroduce Cotrimoxazole after TB treatment once liver function tests are acceptable, if they deteriorate consider changing to Dapsone.

MONO- AND POLY-RESISTANT TB >>>

HOW IS RESISTANCE TO TB DRUGS CLASSIFIED?

Mono-resistant TB	Resistance to one first line TB drug other than rifampicin (isoniazid, pyrazinamide or ethambutol)
Rifampicin-resistant TB	Resistance to rifampicin, with or without resistance to other TB medicines. This maybe mono, poly, multi or extensive drug resistance.
Poly-resistant TB	Resistance to two or more first-line drugs (other than INH and RIF)
Multi-drug resistant TB	Resistance to both INH and RIF
Extensive Drug Resistant TB	Resistance to any fluoroquinolone and to at least one of the three second line injectable drugs (capreomycin, kanamycin and amikacin), in addition to multi drug resistance.

WHAT TYPES OF RESISTANCE ARE THERE?

RESISTANCE CAN BE DIVIDED INTO 2 MAIN TYPES:	
New Patients (previously called 'primary resistance')	**Previously Treated Patients** (previously called 'acquired resistance')
This is resistance in patients with no history of previous TB treatment **or** patients who have received TB treatment **for less than one month previously**	Resistance in these patients refers to resistance in cultures from patients with one or more previous TB treatment episodes, of more than one month each

WHY IS IT IMPORTANT FOR US TO KNOW ABOUT MONO- AND POLY-RESISTANT TB?

- Mono-and poly-resistant TB may be a step on the way to development of MDR-TB
  - It is very important to manage these patients correctly
- MDR-TB may develop when persons with mono-resistant TB are not receiving a sufficient number and dosage of drugs to which the strain is susceptible

HOW IS MONO- AND POLY-RESISTANT TB TREATED?

- Treatment is complex and expert opinion should be always be sought
- Treatment is individualised according to:
  - drug susceptibility patterns of resistance (whether INH or RIF resistance is present)
  - TB treatment history
  - potential for development of resistance to other drugs

HOW IS MONO- AND POLY-RESISTANT TB MONITORED?

- TB microscopy and TB culture monthly during intensive phase AND continuation phase
- Repeat DST if unsatisfactory clinical progress after 3-4 months of treatment

HOW ARE MONO- AND POLY-RESISTANT PATIENTS RECORDED?

- All mono-and poly-drug resistant patients should be recorded in the DR-TB register (NOT the drug-sensitive register)
- Patients that are mono-drug resistant to rifampicin must be recorded as MDR-TB "not confirmed"

MONO- AND POLY-RESISTANT TB >>>

ALGORITHM FOR THE OUTPATIENT MANAGEMENT OF MONO- AND POLY-RESISTANT TB

RIF or INH resistance confirmed by LPA

1. Counsel patient regarding the implications of drug-resistant TB
2. Start patient on TB treatment regimen according to the table on the following page
3. Notify the patient to authorities
4. Send a further sputum specimen for microscopy, culture and DST
5. Request laboratory to do phenotypic (culture) drug susceptibility testing to first and second-line TB drugs
6. Offer an HIV test and initiate ART and cotrimoxazole if infected

Review the patient's culture and DST results 4 weeks after TB treatment initiation

1. Review laboratory DST results and confirm susceptibility results
2. Adapt TB treatment according to table on the following page
3. Send a sputum specimen for microscopy, culture and DST
4. If no clinical improvement, refer for specialist opinion
5. Manage HIV infection if present

Review the patient and all culture and DST results every 4 weeks until treatment completion

1. Manage drug adverse effects
2. Manage HIV infection if present
3. Repeat TB microscopy and TB culture every month during intensive phase until TB culture conversion.
4. Repeat TB microscopy and culture monthly during continuation phase
5. Repeat DST if unsatisfactory clinical and biological progress after 3-4 months of treatment.

CONFIRMATORY DST OR LPA DONE AT BASELINE MUST NOT DELAY THE INITIATION OF TREATMENT

PATIENTS MUST BE REFERRED TO A HIGHER LEVEL OF CARE OR EXPERT OPINION SOUGHT AT ANY POINT IF DEEMED NECESSARY

MONO- AND POLY-RESISTANT TB

SUGGESTED REGIMENS AND DURATION OF TREATMENT FOR MONO-AND POLY-RESISTANT TB

Drug Resistance Pattern	Suggested Regimen	Minimum Duration of Treatment (months)	Comments
H	• RHZE for the full duration of treatment • In practice it is easier to use fixed drug combinations	• 6 - 9 months based on symptomatic response to treatment, weight gain and sputum culture • A minimum of 6 months treatment after culture conversion is adequate	• Monitor the patient monthly ○ sputum smear microscopy and culture monthly throughout treatment ○ monthly clinical assessment required • Refer to MDR-TB expert if patient is not responding well to treatment
R (± any other 1st line drug other than INH)	• Standardized MDR-TB regimen plus INH	• 18 months treatment after culture conversion required	• These patients will need confirmation of diagnosis if diagnosed through GXP; LPA is a confirmatory diagnosis
Poly-resistant TB cases			• Refer to MDR-TB expert for regimen design based on resistance pattern and history of anti-TB drug use

MDR-TB DIAGNOSIS AND MANAGEMENT >>>

MDR-TB		XDR-TB	
Stands For	**Definition**	**Stands For**	**Definition**
Multi-**D**rug **R**esistant	• Resistance to at least **INH and rifampicin WITH OR WITHOUT** resistance to other drugs	**Ex**tensively **D**rug **R**esistant	• Resistance to INH and rifampicin **AND** • resistance to any of the fluoroquinolones **AND** • any second-line injectable e.g. kanamycin, amikacin or capreomycin

HOW DOES ONE ACQUIRE MDR-TB?

- Get infected with resistant TB bacteria
- Develop resistance if TB is not adequately treated

HOW IS MDR-TB DIAGNOSED?

- Xpert MTB/RIF only detects RIF resistance, it must be confirmed with other tests while MDR-TB treatment is started in the interim
- Culture and DST is required to make a definitive diagnosis of MDR-TB
- LPA which shows resistance to INH and RIF, is a confirmatory diagnosis for MDR-TB
- All strains identified as MDR-TB should routinely undergo second-line DST in order to diagnose or rule out XDR-TB.

IT IS VERY IMPORTANT TO ENSURE THAT THE ORGANISM IDENTIFIED IS MTB AND NOT ANOTHER SPECIES (NTM)

HOW DO WE TREAT CLOSE CONTACTS OF MDR-TB PATIENTS?

- **If symptomatic:**
  - Investigate contacts promptly using Xpert or LPA
  - Symptomatic children should be referred to hospital for evaluation

- **If asymptomatic:**
  - Screen close contacts at six-monthly intervals for up to two years
  - Follow up HIV positive contacts six-monthly
  - Educate contacts about signs and symptoms of TB and inform them that they should present at a health facility immediately if these develop
  - If active MDR-TB develops refer immediately for treatment

NB: M/XDR-TB IS DIFFICULT TO TREAT, ALWAYS REFER IF ANY UNCERTAINTY

MDR-TB DIAGNOSIS AND MANAGEMENT >>>

HOW IS MDR-TB TREATED?

- A standardised MDR-TB treatment regimen should be given 7 days a week
- An individualised regimen must be used in the following patients:
  - have used second line drugs in the past for more than one month
  - LPA or DST show resistance to quinolone and/or the second line injectable
  - contact of an MDR TB patient whose resistance patterns are known
  - all preXDR and XDR TB patients
- Suspected/ unconfirmed DR-TB patients should be isolated
- Educate patient regarding cough hygiene and infection control if at home
- Patients who do not meet criteria to start ambulatory care should be hospitalized for up to eight weeks or until they are confirmed to be non-infectious (smear negative on two consecutive tests)
- Smear positive patients who refuse admission but are willing to receive medication should still be treated.
- An improvement in the patient's medical condition (e.g., weight gain, no fever, no cough, etc.) indicates that s/he is tolerating all MDR-TB drugs and is smear negative
- Patients who meet set criteria can be discharged to the community and continue receiving treatment either from the mobile team or their nearest primary health-care facility.
- HCWs should observe infection control during home visits and patient transport

WHAT ARE THE CRITERIA FOR ADMISSION AND AMBULATORY CARE?

Patients to start in ambulatory care	Patients admitted until TWO negative TB smear microscopy	Patients admitted until TWO negative TB cultures (6 months+)
Essential Criteria • Patient is ambulant, in fair to good general condition (BMI > 18.5) • Patient is low grade transmission risk (smear negative) • Patient refuses admission or beds are unavailable **Additional Criteria** • Stable accommodation • Household treatment support • Good reason for not wanting to be Hospitalised	• Patient with high grade transmission risk (smear positive) • Patients without associated diseases • Patients without extensive resistance pattern	• XDR-TB patients • Very sick MDR-TB patients with extensive resistance patterns, pulmonary cavitations • MDR-TB re-treatments • Severe adverse drug reactions • Other associated diseases • May not have access to decentralised or satellite units – until they achieve TB culture conversion

WHAT ARE THE DRUGS AND DURATION OF TREATMENT FOR MDR TB?

Phase	Duration	Drugs
Intensive phase (injectables and oral drugs)	At least 6 months	5 drugs: Kanamycin/ amikacin; moxifloxacin; ethionamide; terizidone/ cycloserine; pyrazinamide
Continuation phase (oral drugs only)	18 months post culture conversion	4 drugs: Moxifloxacin; ethionamide; terizidone; pyrazinamide

MDR-TB DIAGNOSIS AND MANAGEMENT >>>

THE DURATION OF THE INTENSIVE PHASE WILL BE DETERMINED BY ADDING 4 MONTHS TO THE DATE OF TB CULTURE CONVERSION. INTENSIVE PHASE MUST BE SIX MONTHS OR MORE

Intensive phase: standardised regimen for adults and children 8 years and above		
Patients Weight	**Drug**	**Dosage**
<33 kg	Kanamycin	15-20 mg/kg
	Moxifloxacin	400 mg (children: 7.5 to 10 mg/kg)
	Ethionamide	15-20 mg/kg
	Terizidone	15-20 mg/kg
	Pyrazinamide	30-40 mg/kg
33-50 kg	Kanamycin	500-750 mg
	Moxifloxacin	400 mg
	Ethionamide	500 mg
	Terizidone	750 mg
	Pyrazinamide	1000-1750 mg
51-70 kg	Kanamycin	1000 mg
	Moxifloxacin	400 mg
	Ethionamide	750 mg
	Terizidone	750 mg
	Pyrazinamide	1750-2000 mg
>70 kg	Kanamycin	1000 mg
	Moxifloxacin	400 mg
	Ethionamide	750-1000 mg
	Terizidone	750-1000 mg
	Pyrazinamide	2000-2500 mg

MDR-TB DIAGNOSIS AND MANAGEMENT >>>

THE DURATION OF THE CONTINUATION PHASE WILL BE DETERMINED BY ADDING 18 MONTHS TO THE DATE OF TB CULTURE CONVERSION.

EXTENSION FOR UP TO 24 MONTHS MAY BE INDICATED IN CHRONIC CASES WITH EXTENSIVE PULMONARY DAMAGE.

Continuation Phase: Standardised Regimen for Adults and Children 8 years and above		
Patients Weight	**Drug**	**Dosage**
<33 kg	Moxifloxacin	400 mg
	Ethionamide	15-20 mg/kg
	Terizidone	15-20 mg/kg
	Pyrazinamide	30-40 mg/kg
33-50 kg	Moxifloxacin	400 mg
	Ethionamide	500 mg
	Terizidone	750 mg
	Pyrazinamide	1000-1750 mg
51-70 kg	Moxifloxacin	400 mg
	Ethionamide	750 mg
	Terizidone	750 mg
	Pyrazinamide	1750-2000 mg
>70 kg	Moxifloxacin	400 mg
	Ethionamide	750-1000 mg
	Terizidone	750-1000 mg
	Pyrazinamide	2000-2500 mg

PLEASE NOTE:

- Pyridoxine (Vit B6) 150 mg (maximum 200 mg) to be given daily to patients on terizidone
- Adults who may not tolerate moxifloxacin will be given levofloxacin at the following dosage: 750 mg for patients weighing below 51 kg, and 1000 mg for patients with a weight equal or above 51 kg

MDR-TB DIAGNOSIS AND MANAGEMENT

Standardised MDR-TB Treatment Regimen for Children Younger than 8 Years

Drug	Dosage
Amikacin	15 – 22.5 mg/kg
Levofloxacin	10 – 15 mg /kg daily for children < 8 years
Ethionamide	15 – 20 mg/kg
Terizidone	15 – 20 mg/kg
Pyrazinamide	30 – 40 mg/kg

- **NB: Ethambutol may be given at the dosage of 20 - 25 mg/kg**
- **High-dose INH 15-20mg/kg may be given if no katG mutation**

GIVEN THAT MDR- AND XDR-TB ARE LIFE-THREATENING DISEASES, NO DRUGS ARE ABSOLUTELY CONTRAINDICATED IN CHILDREN

XDR-TB MANAGEMENT >>>

HOW IS XDR-TB TREATED?

New drugs have been introduced for the treatment of XDR TB including Bedaquiline and Linezolid. XDR-TB requires an individualised approach based on the previous history of drug use in a patient and the results of DST. Therefore, treatment of XDR-TB should always be initiated under guidance of the clinical management team and the review committees.

- At least five drugs, pyrazinamide and four drugs to which the organisms are known or presumed to be susceptible, including an injectable agent, should be used in a 6–8 month intensive phase
- At least 3 drugs to which the organisms are known or presumed to be susceptible, should be used in the continuation phase
- Treatment should be given for at least 18–24 months beyond culture conversion

HOW SHOULD YOU CONSTRUCT A REGIMEN FOR PRE-XDR/XDR TB TREATMENT IN ADULTS?

- Go through this list one drug at a time to decide whether or not to include in the treatment regimen.
- Use a minimum of 4 drugs likely to be effective but preferably as many as possible that are tolerated.

First Line Drugs	Guidance	Dosage	Duration
Pyrazinamide	Use in all XDR and pre-XDR cases, unless PZA resistance on culture-based DST or previous drug reaction due to PZA (rash, hepatitis)	30-40 mg /kg/day	24 months
Ethambutol	Consider using in all XDR and pre-XDR cases, unless ethambutol resistance on DST or patient unlikely to tolerate pill burden	15-20 mg /kg/day	24 months
INH high dose	Include in regimen if inhA mutation alone is present, but exclude if katG present Exclude if previous drug reaction due to INH (rash, hepatitis, neurotoxicity)	15mg/kg	24 months
Second Line Drugs	**Guidance**	**Dosage**	**Duration**
Kanamycin	Use only if kanamycin/amikacin susceptible on DST Avoid if severe renal impairment If hearing impairment discuss with expert – its use in such a situation depends on a number of factors	>50kg: 1g/day <50kg: 500-750mg/day Reduce dosing frequency and monitor levels if renal impairment (CrCL<50ml/min)	6-8 months
Levofloxacin	Use in all XDR and pre-XDR (including ofloxacin resistant) cases unless moxifloxacin used instead	>50kg: 1g daily <50kg: 750mg daily	24 months
Moxifloxacin	Use rather than levofloxacin if DST reports moxifloxacin susceptible and ofloxacin resistant (if moxifloxacin resistant or moxifloxacin DST not done use levofloxacin instead) When using with BDQ and/or Cfz monitor QTcF weekly for first month then monthly Avoid if QTcF> 450ms	400mg daily	24 months
Terizidone	Use in all XDR and pre-XDR cases Avoid in those with a history of psychosis	>50kg: 750mg daily <50kg: 500mg daily	24 months
Ethionamide	Use in all XDR and pre-XDR cases Avoid if inhA mutation present	>50kg: 750mg daily <50kg: 500mg daily	24 months

XDR-TB MANAGEMENT

Third Line Drugs	Guidance	Dosage	Duration
Capreomycin	There is 80-90% cross-resistance between aminoglycosides and capreomycin, thus it is now generally not used when there is aminoglycoside resistance. When there is aminoglycoside susceptibility then aminoglycosides are used in instead. If capreomycin DST is available this could be used to direct its use. Some clinicians use it when there is aminoglycoside susceptibility but ototoxicity, but the evidence to support this practice is limited. Avoid if renal impairment	>50kg: 1g/day <50kg: 500-750mg/day	6-8 months
PAS	Use in all XDR and pre-XDR cases	Dose: 4g BD	24 months
Clofazimine	XDR: Use for all patients Pre-XDR: Not used in all patients, but use if patient cannot access or tolerate linezolid, or patient with aminoglycoside susceptible TB cannot tolerate kanamycin When using with BDQ monitor QTcF weekly for first month then monthly	Dose: 100mg daily	24 months
Bedaquiline	Use in all cases of XDR and pre-XDR Avoid if QTcF> 450msec (could start BDQ later if QTcF< 450msec provided no evidence of Rx failure)	400mg daily for 2 weeks, then 200mg daily M, W, F	6 months
Linezolid	Use in all cases of XDR and pre-XDR Avoid if severe anaemia (Hb< 7) or severe peripheral neuropathy (could start linezolid later if anaemia or neuropathy improves provided no evidence of Rx failure). Extension of treatment beyond the indicated 12 months should be reviewed by the clinical advisory committee.	>50kg: Start at 600mg daily. Reduce dose to 300mg if toxicity. Consider transfusion if anaemic. Stop if toxicity life threatening or worsens. <50kg: start at 300mg daily	12 months
Amoxycillin/ Clavulanic acid	Not recommended Exception - unless being used with meropenem in highly drug-resistant cases treated in specialised centres	–	–
Clarithromycin/ azithromycin	Not recommended (lack of clinical evidence)	–	–
Dapsone	Not recommended (lack of clinical evidence)	–	–

XDR-TB MANAGEMENT

HOW IS XDR AND PRE-XDR TB IN CHILDREN TREATED?

Use this guidance in conjunction with the overall (adult) guidance provided.

Drug	Guidance for use in paediatric patients	Paediatric dosage	Duration
Pyrazinamide		30-40 mg /kg/day	24 months
Ethambutol		20-25 mg /kg/day	24 months
Isonaizid		15-20 mg /kg/day	24 months
Amikacin	Amikacin preferred to Kanamycin Not likely helpful if resistant to kanamycin. Not more than 6 months or 4 months after negative culture	15-20mg/kg/day	4 to 6 months
Levofloxacin	Use in all XDR and pre-XDR (including ofloxacin resistant) cases unless moxifloxacin used instead	15-20mg/kg/day	24 months
Moxifloxacin	Limited data in children; limit to children at least 8 years of age.	10mg/kg/day	24 months
Terizidone		15-20mg/kg/day	24 months
Ethionamide		15-20mg/kg/day	24 months
Capreomycin		15-20mg/kg/day	4-6 months
PAS		150-200mg /kg /day in two divided doses	24 months
Clofazimine	Because capsule size (50mg or 100mg – cannot be cut or split) – could give every second day, as has long half-life.	3-5 mg/kg/day Max 100mg/day	24 months
Bedaquiline	Not currently recommended in children.	No dosing or safety studies yet in children	
Linezolid	At recommended doses above, few adverse effects experienced and good outcome even in XDR-TB cases if used in combination with clofazimine and PAS (and other supporting drugs)	10mg/kg twice daily (suspension available) If >10years of age or weight >25kg, give 300mg daily	6-12 months

MONITORING OF DR-TB PATIENTS ON TREATMENT >>>

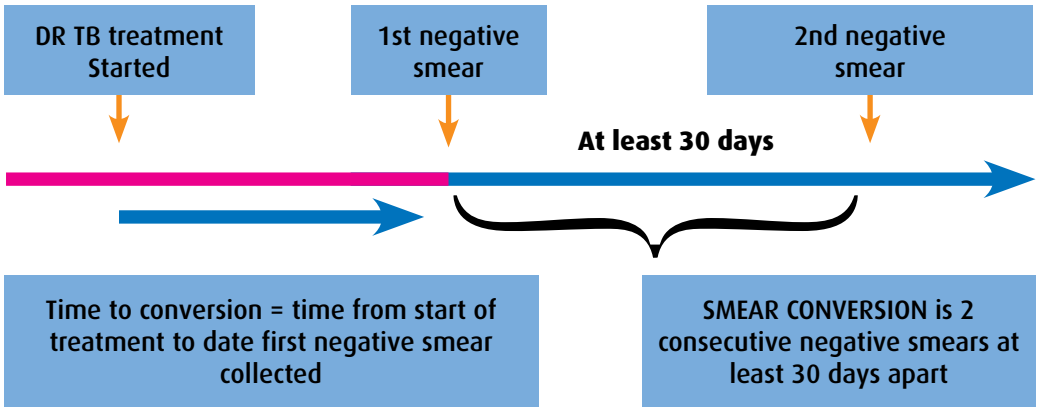
HOW OFTEN MUST DR-TB PATIENTS BE REVIEWED?

- Intensive (injectable) phase → Weekly once clinically stable
- Continuation phase → Monthly

HOW OFTEN MUST SPUTUM BE SENT?

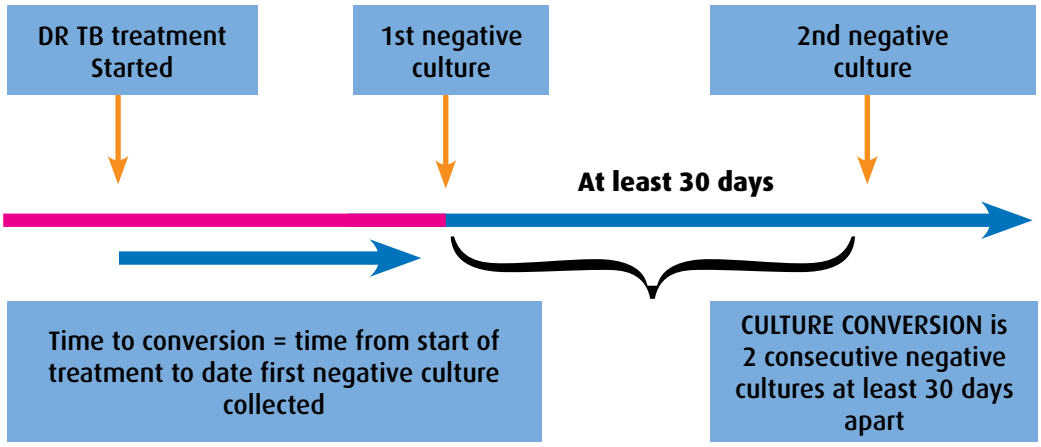
- One sputum specimen should be sent **monthly** for smear microscopy and culture (not DST)
- Only culture can determine if organisms are still viable (alive); culture is therefore required for monitoring progress

WHAT IS SMEAR CONVERSION?



TB SMEAR CONVERSION: DATE OF COLLECTION OF THE FIRST SPUTUM THAT TURNED TB SMEAR NEGATIVE

WHAT IS CULTURE CONVERSION?



TB CULTURE CONVERSION: DATE OF COLLECTION OF THE FIRST SPUTUM THAT TURNED TB CULTURE NEGATIVE

MUST THE PATIENT RECEIVE FOLLOW-UP AFTER BEING CURED?

- Patients with DR-TB must be followed up 6 monthly for at least 2 years after cure
- Assess for signs and symptoms of relapse
- Conduct smear and culture every six months

MONITORING OF DR-TB PATIENTS ON TREATMENT

Clinical and laboratory monitoring	Recommended Frequency
Evaluation by Doctor	• At baseline • Twice to three times per week for stable patients and daily for very sick patients until conversion • Every month or bi-monthly for outpatients in continuation phase
Evaluation by Nurse	• Daily
Sputum Smear and Cultures	• At baseline • Monthly
Weight	• At baseline and weekly during intensive phase • Monthly during continuation phase
Height	• At baseline in adults and children
Body Mass Index (BMI)	• At baseline and then monthly
DST	• At baseline • For patients who remain culture positive at six months
CXR	• At baseline • Every six months (for children every 2 to 3 months in intensive phase) • At treatment completion • When requested by clinician
Serum Creatinine	• At baseline, then monthly during injectable phase
Serum Potassium	• Monthly during injectable phase
Thyroid Stimulating Hormone	• Every six months if receiving ethionamide and /or PAS • Monitor monthly for signs of hypothyroidism • In children every 2 months
Liver Serum Enzymes	• Periodic monitoring (every 1-3 months) ○ In patients receiving pyrazinamide for an extended period ○ For patients at risk of/with symptoms of hepatitis ○ In Children: if symptoms or every six months if on ART
HIV Screening	• At baseline, and repeat if clinically indicated
Pregnancy Test	• At baseline for women of child bearing age and repeat if indicated
Audiometry	• At baseline, monthly during injectable phase and 3 months after completion of the injectable therapy
Eye Test	• At baseline and when indicated
Lung CT-scan	• When indicated

SIDE EFFECTS OF DR-TB TREATMENT >>>

WHAT ARE THE MOST COMMON SIDE EFFECTS OF DR-TB TREATMENT?

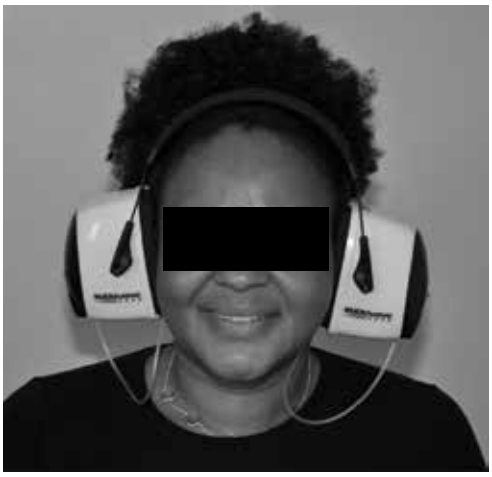
Adverse Effects	Offending Drug	Management
Skin Reactions	• Could be several agents	• Desensitisation, may reintroduce drugs within one or two weeks
Ototoxicity	• Injectable agents	• See next page
Peripheral Neuropathy	• Cycloserine • Terizidone	• Pyridoxine or • amitriptyline
Electrolyte Wasting	• Capreomycin • Amikacin • Kanamycin	• Is reversible once the injectable is suspended • Supplement electrolytes as needed
Psychiatric Symptoms	• Cycloserine • Terizidone • Ethionamide • Quinolones especially in the elderly	• Pyridoxine • Drug substitution for moderate or severe reaction. • Refer to psychiatrist if not improving
Nephrotoxicity	• Aminoglycosides • Capreomycin	• Adjust dosing or discontinue suspected drug • Drug substitution for moderate to severe reaction. • Continue for mild reaction; monitor 2 weekly
Impaired Vision	• Ethambutol	• Avoid in patients with impaired vision except those that have myopia, hyperopia or presbyopia • Stop the drug and refer to ophthalmologist
Hypothyroidism	• PAS • Ethionamide	• Monitor closely • Initiate Thyroxine
Hepatotoxicity	• Bedaquiline • Pyrazinamide • PAS • Ethionamide • INH	• Discontinue BDQ if ALT/AST elevations severe or persist beyond 2 weeks. • Consider re-challenge with BDQ if another drug identified as cause.
Arrhythmia (QT prolongation)	• Bedaquiline • Clofazimine • Moxifloxacin	• Drug withdrawal for moderate and severe. • Consider re-challenge if moderate reaction resolves. • Mild reactions should be monitored.

SIDE EFFECTS OF DR-TB TREATMENT

ARE DR-TB DRUGS SIDE-EFFECTS DIFFICULT TO MANAGE?

- Almost all patients on MDR- and XDR-TB treatment will report adverse effects to second-line drugs
- Drug-drug interactions may also produce adverse effects.
- Since patients are receiving combination treatment, often also taking ARVs, it may be difficult to know which drug is causing the side-effects
- Close monitoring is necessary to ensure that ADRs are recognised and addressed quickly

HOW IS HEARING LOSS MANAGED?



Audiometry

- Baseline audiometry for all patients using any ototoxic drug, even in patients who have pre-existing hearing loss
- Monthly audiometry in Intensive phase
- Audiometry at 3 and 6 months after discontinuation of treatment with ototoxic drug

If a patient on treatment developed hearing loss

- Check that the dosage of the aminoglycoside given is appropriate for weight and age
- Avoid certain diuretics (especially loop diuretics) as ototoxicity is potentiated by these drugs

Management of patient with hearing loss

- Stop the drug and change to another agent e.g. BDQ or LZD
- Refer to audiologist and rehabilitation services as appropriate and available
- Monitor monthly after hearing loss even after the SLD has been stopped
- Patients with hearing loss can benefit from use of hearing aids

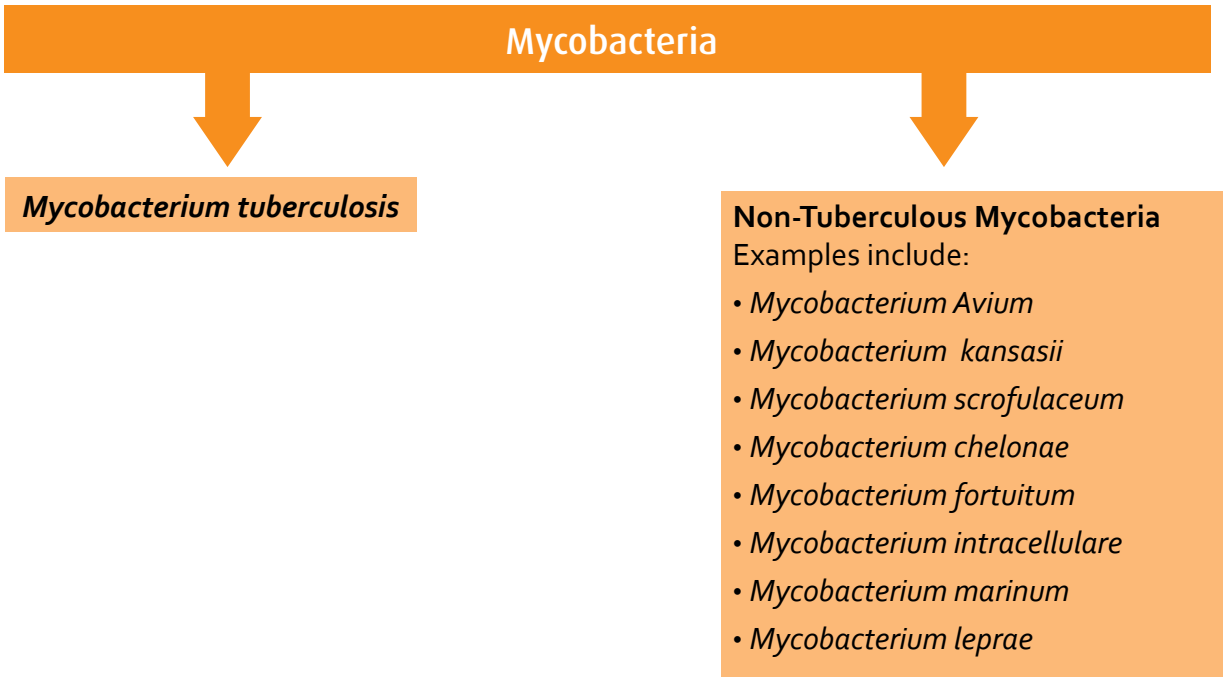
NON-TUBERCULOUS MYCOBACTERIA (NTM) >>>

WHAT DOES NTM STAND FOR?

Non-**T**uberculous **M**ycobacteria - Also called **M**ycobacteria **O**ther **T**han **T**uberculosis **(MOTTs)**

WHAT ARE NON-TUBERCULOUS MYCOBACTERIA?

Mycobacteria are a diverse group of bacteria that include more than 100 different species. *Mycobacterium tuberculosis* is a species within this group. The non-tuberculous mycobacteria also form part of this group.



HOW DOES NTM INFECTION OCCUR?

- NTM live in the soil and water and are found throughout the world.
- NTM are acquired through environmental exposure to water, aerosols, soil, and dust – through inhalation, ingestion, and through breaks in the skin due to injuries, surgical procedures, or IV catheters.
- Unlike *M. tuberculosis*, they are not passed from person-to-person.

WHO IS AT RISK FOR NTM INFECTION?

Anyone can become infected, but the following groups are more at risk for disease:

- people with suppressed immune systems (such as those with HIV/AIDS and transplant recipients)
- people with pre-existing lung damage

IS NTM THE SAME AS TB OR MULTI-DRUG RESISTANT TB (MDR-TB)?

- **No**, it is very important to note that NTM is **different** to TB and MDR-TB
- We can tell the difference by looking at the identification of the organism

NON-TUBERCULOUS MYCOBACTERIA (NTM) >>>

WHAT IS THE DIFFERENCE BETWEEN DRUG-SENSITIVE TB, MDR-TB AND NTM?

	Drug-sensitive TB	MDR-TB	NTM
Smear AFB	Positive or negative	Positive or negative	Positive or negative
Xpert MTB/RIF	MTB detected/RIF resistance not detected	MTB detected / RIF resistance detected	Negative (Xpert detects *mycobacterium tuberculosis* only)
Pulmonary disease	Yes	Yes	Maybe
Extra-pulmonary Disease	Yes	Yes	Maybe
DST	Sensitive to INH and RIF	Resistant to INH and RIF	May be resistant to INH and/ or RIF
Organism Identification	*Mycobacterium Tuberculosis* (MTB)	*Mycobacterium Tuberculosis* (MTB)	Non-tuberculous mycobacterium e.g. *Mycobacterium Avium complex, Mycobacterium intracellulare, Mycobacterium kansasii* etc.
Treatment	Must be treated	Must be treated	Does not always require treatment if asymptomatic

HOW DOES NTM PRESENT?

- **Pulmonary disease –** may mimic TB clinically and/or radiologically
- **Lymphadenitis**
  - more common in children aged 1-5 years
  - typically in the head and neck
  - nodes painless and non-tender
  - little systemic symptoms
- **Infections of the skin, soft tissue and bones** may occur after penetrating trauma, surgery or the insertion of catheters and prostheses
- **Disseminated disease** can present in one of two ways:
  - Clients who are immunosuppressed due to causes other than HIV may present with fever of unknown origin (commonly due to *M. avium*) or with subcutaneous nodules and abscesses that drain spontaneously (due to *M. kansasii*).
  - Severely immunosuppressed HIV-infected patients (CD4 count < 50 cells/mm^3) present with a high temperature, night sweats, weight loss, abdominal pain, and diarrhoea. This is most commonly due to *M. avium* but can also be due to *M. kansasii*.

NON-TUBERCULOUS MYCOBACTERIA (NTM) >>>

HOW IS NTM DIAGNOSED?

- MTB and NTM cannot be differentiated by microscopy (AFBs)
- To diagnose NTM a culture and identification of the species is required
    - NTM is cultured in the same way as MTB and then differentiated using molecular or other tests.
    - Preliminary reports prior to completion of identification tests may indicate "Mycobacterial species" which could mean MTB or NTM
    - When the species is identified on the culture, it will be identified as NTM
    - Sputum, blood and biopsy specimens can be sent for culture and identification

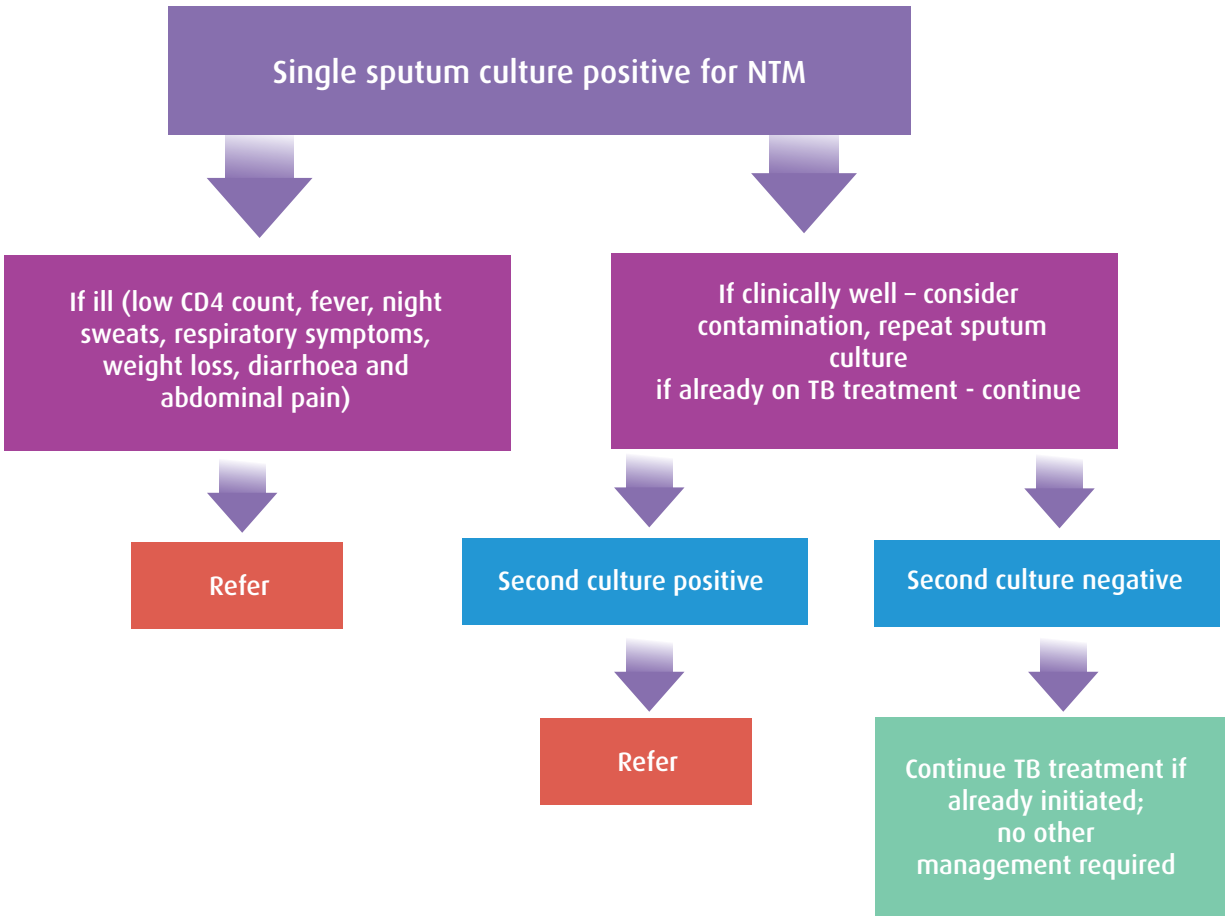
IT IS IMPORTANT TO REMEMBER THAT MOST SMEAR POSITIVE PATIENTS HAVE TB (AND NOT NTM), IF ONLY A SMEAR RESULT IS AVAILABLE, PATIENTS MUST BE TREATED FOR TB

DOES NTM ALWAYS NEED TO BE TREATED?

- No, NTM may be a "coloniser" i.e. we find it in the sputum culture but it does not cause disease
- Clinical and radiological details, specimen type, number of isolates, and specific NTM identified are considered
- In HIV-infected patients, NTM infection may present as an unmasking Immune Reconstitution Inflammatory Syndrome (IRIS) with anaemia, fever and hepatosplenomegaly
- However, if *M.Avium is isolated from blood, bone marrow or lymph node* in an HIV-infected patient, the patient must be treated
- Generally the decision about whether to treat NTM should be made by an expert at a specialised centre

NON-TUBERCULOUS MYCOBACTERIA (NTM)

HOW ARE POSITIVE NTM CULTURES MANAGED?



ALL POSITIVE NTM BLOOD CULTURES MUST BE REFERRED FOR TREATMENT

WHEN IS NTM PROPHYLAXIS GIVEN?

- There is little agreement regarding when prophylaxis should be given
- Patients with proven *M.Avium* infection, must receive treatment until their CD4 count is above 200 cells/mm^3

WHAT DRUGS ARE USED TO TREAT NTM?

- At least 2 (in more severe cases, 3 drugs) should be used for at least one year
- These may include clarithromycin, ethambutol, ciprofloxacin, levofloxacin, moxifloxacin (or rifabutin if it is available)
- An injectable (e.g. amikacin) may be used for ill patients
- HIV-infected clients should receive ART. Azithromycin should replace clarithromycin for patients receiving efavirenz

American Thoracic Society Documents: An Official ATS/IDSA Statement: Diagnosis, Treatment and Prevention of Nontuberculous Mycobacterial Diseases), 2007.
SA Medicines Formulary

IMPORTANT TB DRUG INTERACTIONS >>>

1. ISONIAZID DRUG INTERACTIONS

	Effect of Interaction	Management
Antacids	• Absorption of INH is reduced by concurrent use of aluminium	• These agents should be administered at least 2 hours apart
Carbamazepine	• Serum levels of carbamazepine increase rapidly	• Carbamazepine toxicty can occur • Carbamazepine dosage must be reduced • Must be closely monitored and dose adjusted
Paracetamol	• Potential paracetamol toxicity	• Normal daily analgesic dosages of 4g may not be safe • Warn patients to limit their use of paracetamol
Phenytoin	• Phenytoin levels increased if administered with INH alone • If both rifampicin and INH are given, serum phenytoin levels may decrease in fast acetylators of INH, but may rise in slow acetylators	• Phenytoin toxicity may occur if the dosage of phenytoin is not reduced appropriately.
Theophylline	• Plasma level of theophylline may be increased	• Monitor levels
Warfarin	• Warfarin levels increased	• Dose adjustment may be required

2. RIFAMPICIN DRUG INTERACTIONS

	Effect of interaction	**Management**
Lopinavir/ritonavir	• Ritonavir levels reduced • Increased ALT/AST	• Adjust LPV/r dose • Monitor liver functions • Consider change to rifabutin
Phenytoin	• Phenytoin serum levels reduced • When INH and RIF used with phenytoin, the reduction in level may be less	• Monitor phenytoin levels and increase dose appropriately if used with rifampicin • Monitor closely to adequately adjust dose
Zidovudine	• Clearance of zidovudine increased	• Monitor for reduced response to AZT
Nevirapine	• Nevirapine levels reduced	• Consider alternative
Valproic acid	• Valproate levels may be reduced	• Monitor valproate levels and adjust dose accordingly

IMPORTANT TB DRUG INTERACTIONS >>>

	Effect of interaction	Management
Calcium channel blockers: Nifedipine, Amlodipine, Verapamil	• Calcium channel blocker levels reduced	• Monitor closely and increase calcium channel blocker dose if necessary
Beta-blockers: Carvedilol, Propanolol	• Beta-blocker levels reduced	• Beta-blockers excreted in the liver affected, those excreted unchanged in the urine e.g. atenolol not expected to be affected • Monitor closely and adjust dose as needed
Antifungals: Itraconazole, Ketoconazole	• Antifungal levels markedly reduced • Rifampicin levels can be reduced by concomitant use of ketoconazole	• Antifungal effects reduced • Administer ketoconazole and rifampicin 12 hours apart
Oral contraceptives: Ethinylestradiol, Levonorgestrel, Norgestrel	• Contraceptive effect reduced	• Do not use concomitantly – break through bleeding common, pregnancy may not be prevented • Use oral contraceptive pill containing a higher dose of oestrogen (50mcg) • Use nonhormonal method of contraception while on Rifampicin
Progesterone-only injectable contraceptives: Medroxyprogesterone acetate, Norethisterone enanthate	• Contraceptive effect reduced	• Shorten the interval between injections o 8 weekly Norethisterone enanthate o 10 weekly Medroxyprogesterone acetate • Consider use of barrier contraceptives
Progestin subdermal implants: Implanon	• Contraceptive effect reduced	• Use another method, e.g. intrauterine devices or depot medroxyprogesterone acetate • If already have Implanon inserted should be covered with another non-hormonal contraceptive method (intrauterine devices or condoms) for the duration of TB treatment
Opioids: Morphine, Codeine	• Opioid levels reduced	• Monitor for adequate pain control • Opioid doses may need to be increased, re-evaluate when rifampicin stopped
Other: Glucocorticosteroids, Theophylline, Warfarin, Sulphonyureas, Cyclosporin, Quinine, Digoxin, Cimetidine	• Levels of these drugs may be reduced	• Increased doses may be required

IMPORTANT TB DRUG INTERACTIONS

3. PYRAZINAMIDE DRUG INTERACTIONS

	Effect of interaction	Management
Anti-gout agents: Allopurinol, Probenecid	• Pyrazinamide inhibits urate clearance	• Dose of allopurinol or probenecid may require adjustment
Diuretics, Ethambutol	• Additive increase in serum urate	• Monitor closely

4. ETHAMBUTOL DRUG INTERACTIONS

	Effect of interaction	Management
Pyrazinamide, Diuretics	• Additive potential for increase in serum urate	• Monitor closely

Drug Interactions With Tuberculosis Therapy, Annoesjka Swart and Vanessa Harris, CME, February 2005, Vol. 23, No.2
South African Medicines Formulary, 2012, 10th Edition

SUPPORTING ADHERENCE IN TB PATIENTS >>>

WHY IS ADHERENCE SUPPORT IMPORTANT?

- TB is a complex disease that has biological, social, economic and cultural effects on the patient
- These factors affect adherence, which in turn affects treatment outcome
- Health care providers should thus take a comprehensive approach and consider the impact of TB on the patient's life as a whole

WHAT ARE THE FACTORS THAT INFLUENCE TREATMENT OUTCOME?

Social And Economic Factors	Health System Factors	Patient Related Factors	Therapy Related Factors
• Extreme poverty • Poor support networks • Unstable living circumstances • Beliefs about TB and its treatment	• Poor health infrastructure • Poorly trained or supervised health care personnel • Poor relationships with patients • Inadequate development of community based support for patients	• Stigma • Depression • Disempowerment • Poor knowledge about TB and the efficacy of treatment	• Complex treatment regimens • Large pill burden • Adverse effects of medication • Long treatment duration

WHO SHOULD DO ADHERENCE COUNSELLING?

- Appropriately trained nurses, lay counsellors or community health workers can do adherence counselling
- When possible a clinic staff member or a health care worker should accompany the patient home to:
  - screen household contacts
  - identify social problems

WHAT SHOULD BE INCLUDED IN ADHERENCE COUNSELLING?

- Information about TB:
  - what it is; how it is transmitted and how to protect those around you from infection
- Discuss medication used to treat TB:
  - when and how to take it; possible side effects and what to do about them
- The importance of:
  - adherence to treatment
  - completing treatment
  - HIV and the need for HIV testing
  - healthy lifestyle
- Identify barriers to treatment and address these
- Develop a clear treatment plan:
  - highlight duration of treatment, dates when sputa are due, when medication will be changed

NO PATIENT SHOULD BE DENIED TREATMENT DUE TO NOT HAVING A TREATMENT SUPPORTER!

SUPPORTING ADHERENCE IN TB PATIENTS >>>

HOW CAN WE APPLY DIRECTLY OBSERVED TREATMENT (DOT) TO FIT PATIENTS' NEEDS?

- DOT means a treatment supporter watches the patient swallowing his/her medication
- DOT allows non-adherence and adverse effects to be picked up at an early stage
- Patients should receive treatment as close to home or work as possible
- DOT may occur at the clinic, workplace or in the community, depending on the patients' needs
- Community DOT is often more accessible and convenient for patients

Always ensure that you have the patients latest contact details, including address, so that he/she can be readily contacted if necessary.

Ensure that treatment taken daily is recorded in order to detect patients lost to follow up timeously

WHAT ARE THE ROLES AND RESPONSIBILITIES OF THE TB TREATMENT SUPPORT TEAM?

TB Patient
• Take their tablets as prescribed
• Report side-effects to the treatment supporter or clinic nurse
• Return to the clinic for scheduled visits
• Bring sputum specimens to the clinic for testing at the required times
• Provide feedback to the team of any problems that they experience
• Inform treatment supporter and clinic staff if they are going away and make plans for taking medication whilst away
• Take responsibility for completing their treatment
Family / Friend:
• Provide emotional support to the patient
• Encourage/remind patient to take their tablets daily
• Supervise treatment on the weekends, or daily if required, and record doses in the patient-held green card
• Remind patient to bring sputum specimens to the clinic for testing at the required times
• Motivate patient to complete the full course of treatment
• Report problems to the clinic

SUPPORTING ADHERENCE IN TB PATIENTS

ROLES AND RESPONSIBILITIES OF THE TB TREATMENT SUPPORT TEAM

Nurse:
• Provide basic information on TB
• Initiate TB treatment and explain how to take the tablets
• Provide daily treatment at the clinic for all patients for a minimum of 2-3 weeks and for those patients receiving Clinic DOT thereafter
• Keep a record of where all patients registered at the facility are receiving DOT
• Complete clinical records: clearly indicate when sputa are due; update records (blue clinic records)
• Update the TB register
• Assess patients on a scheduled basis, monitor response to treatment, encourage treatment completion
• Provide monthly treatment to the patient receiving DOT in the community or worklplace
• Get feedback from treatment supporters on patients receiving community DOT
• Arrange transfer of patients moving to another area
• Arrange tracing of patients who have defaulted treatment
Treatment supporter
• If possible, visit patients commencing treatment at their homes: assess and refer other suspects and contacts to the clinic; identify problems in the household that might affect adherence and report these to the clinic; confirm the patients address
• Meet with patients on a daily basis (including over weekends if possible) and supervise their treatment
• Complete the patient-held green card to record doses taken
• Ensure that patients have collected their monthly medication
• Provide support to TB patients and their families
• Motivate TB patients to complete their treatment
• Remind TB patients to bring their sputa to the clinic for testing at the appropriate times
• Provide regular feedback to the clinic on their patients
• Trace patients who have interrupted treatment
• Create awareness in the community about TB and HIV
Adherence Counsellor
• Provide structured education and counseling to patient
• Prepare patient for completing their TB treatment
• Assist the TB patient in anticipating problems with adherence and planning ways to overcome these
• Offer additional counseling to patients having problems with adherence

TB IN PREGNANCY 4

TREATING TB IN PREGNANCY >>>

WHAT ARE THE RISKS ASSOCIATED WITH TB IN PREGNANCY?

MOTHER

- TB is a major cause of maternal mortality, especially in HIV-infected women

BABY

- Prematurity
- Low birth weight
- Perinatal death
- TB infection and disease, either before or after birth
- Increased risk of HIV transmission to the baby in HIV-infected pregnant women with TB, compared to HIV-infected pregnant women without TB

HOW IS TB DIAGNOSED IN PREGNANCY?

- Use the four TB screening questions in all pregnant women at every visit; which are:
    1. Are you coughing?
    2. Are you losing weight (or not gaining weight adequately)?
    3. Are you sweating at night?
    4. Do you have a fever?
- If any one of these symptoms is present, investigate for TB as per national diagnostic algorithms (see pages 9-10)

WHAT TB TREATMENT CAN BE USED FOR THE MOTHER?

Pregnancy:	Breastfeeding:
First-line TB drugs	All first-line TB drugs are safe
DO NOT USE streptomycin (ototoxic to foetus)	

OFFER HIV TEST TO ALL PREGNANT WOMEN WITH UNKNOWN HIV STATUS

TREATING TB IN PREGNANCY

SAFETY OF SECOND-LINE DRUGS DURING PREGNANCY

Medication	Safety Class	Comments
Ethambutol	B	• Experience in gravid patients suggests safety
Pyrazinamide	C	• Use with caution. Most references suggest it is safe to use
Streptomycin Kanamycin Amikacin Capreomycin	D	• Documented toxicity to developing foetal ear • Risks and benefits must be carefully considered • Avoid use where possible
Fluoroquinolones	C	• Use with caution. • No teratogenic effects seen in humans when used for short periods of time (2-4 weeks) • Associated with permanent damage to cartilage in weight-bearing joints of immature animals • Experience with long-term use in gravid patients is limited, but given bactericidal activity, benefits may outweigh risks
Ethionamide Prothionamide	C	• Avoid use • Teratogenic effects observed in animal studies. • Significantly worsens nausea associated with pregnancy
Cycloserine Terizidone	C	• No significant experience in gravid patients: animal studies have not documented toxicity

A = Safety established using human studies	C = Uncertain safety, no human/animal studies show adverse effects
B = Presumed safety based on animal studies	D = Unsafe, risk may only be justified under clinical circumstances

TREATING TB IN PREGNANCY

HOW SHOULD TB TREATMENT IN AN HIV-INFECTED PREGNANT WOMAN BE APPROACHED?

If already on ART	If not on ART
• Start TB treatment • Continue ART • If on Lopinavir/ritonavir, the dose should be doubled • Monitor for hepatotoxicity • Stop the double dose of LPV/r 2 weeks after completing TB treatment	• Start TB treatment • Start AZT monotherapy • Counsel and monitor for IRIS • Change from AZT monotherapy to lifelong FDC (TDF+FTC+EFV) after about 2 weeks of TB treatment (once stable on treatment)

ARE HIV-INFECTED PREGNANT WOMEN ELIGIBLE FOR IPT?

- Yes, pregnancy is not a contra-indication to IPT
- All HIV-infected pregnant women with a negative TB symptom screen must be considered for IPT
- However ART is the priority and IPT should be started once the patient is stable on ART
- TST should be done to determine duration of IPT:
  - If TST positive - IPT for 36 months
  - If TST negative - IPT for 12 months
  - If TST not done - IPT for 12 months

NOTE: IPT can still be offered even when TST is unavailable

HOW SHOULD MDR-TB IN PREGNANCY BE TREATED?

- The benefits of initiating treatment upon diagnosis outweigh the risks of not starting treatment.
- Refer to a specialist site

Gupta A et al. Maternal tuberculosis: a risk factor for mother-to-child transmission of HIV. J Infect Dis 203(3): 358-63, 2011.
HIV & AIDS Information: HATIP #203, February 14th 2013 – HIV and TB in Practice for Nurses: Pregnancy and HIV

TREATING AN INFANT BORN TO A MOTHER WHO HAS TB >>>

WHICH PREGNANCIES SHOULD I BE CONCERNED ABOUT?

- A mother diagnosed with TB in the last two months of pregnancy
- A mother who has not shown good clinical response to therapy and/or whose smear microscopy has not converted

HOW DO I EXCLUDE TB IN THIS INFANT?

- Do a clinical examination, including an abdominal examination
- Look for the following signs and symptoms:
  - respiratory rate ≥60/min OR difficulty breathing
  - feeding problems OR poor weight gain
  - abdominal distension, enlarged liver OR spleen
  - jaundice
- Post natal examination of the placenta for calcification may also be useful. Where there is placental calcification, endometrial samples should be obtained within 72 hours of delivery and sent for mycobacterial culture and histological examination if possible.

CAN A MOTHER WITH TB STILL BREASTFEED HER INFANT?

- YES
- Maternal TB infection is not an indication to separate mother and child, and is not a contraindication to breastfeeding

ALL MOTHERS, INCLUDING THOSE ON TB TREATMENT AND/OR HIV-INFECTED, SHOULD BE ENCOURAGED TO BREASTFEED

WHAT ARE SOUTH AFRICA'S CURRENT GUIDELINES REGARDING INFANT FEEDING?

South Africa adopts the 2010 WHO Guidelines as follows:

- All mothers can safely breastfeed
- SA supports and promotes exclusive breastfeeding for 6 months irrespective of HIV status, followed by appropriate complementary feeding
- If mother is HIV-uninfected continue breastfeeding for 2 years and beyond
- SA Guidelines recommend that HIV-infected women breastfeed for maximum 12 months

WHAT ARE THE INFANT FEEDING RECOMMENDATIONS FOR HIV-INFECTED MOTHERS?

- Exclusive breastfeeding for 6 months
- Introduction of complementary feeding after 6 months with continued BF for 12 months, AND
  - the mother should be on lifelong ART or
  - the infant should be on daily NVP prophylaxis for 6 weeks or 12 weeks depending on when the mother's HIV test was done

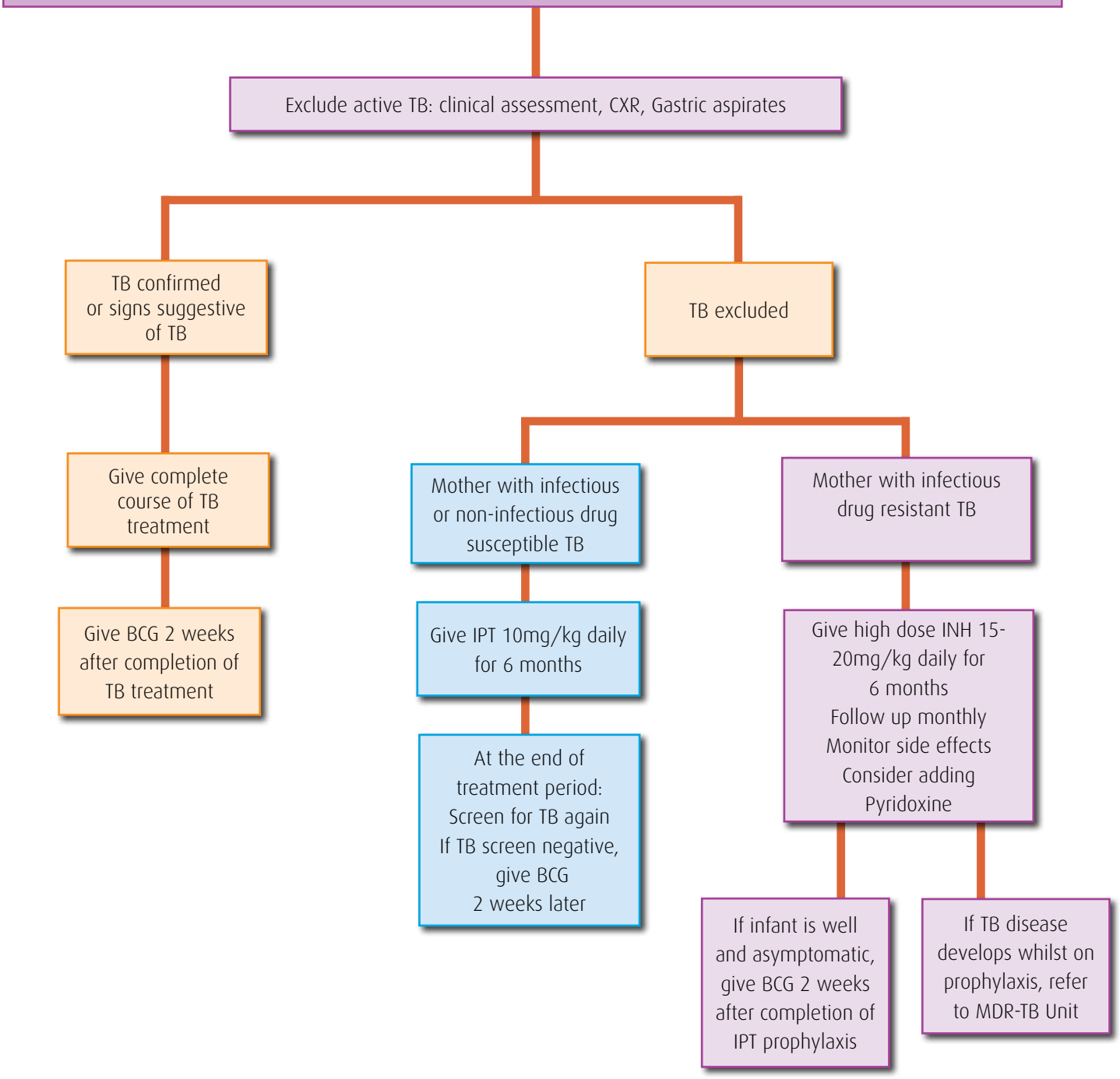
HOW DO I MANAGE AN INFANT BORN TO A MOTHER WITH TB?

- Vitamin K should be administered as part of routine care at birth, especially if the mother is taking rifampicin (to avoid postnatal haemorrhage)

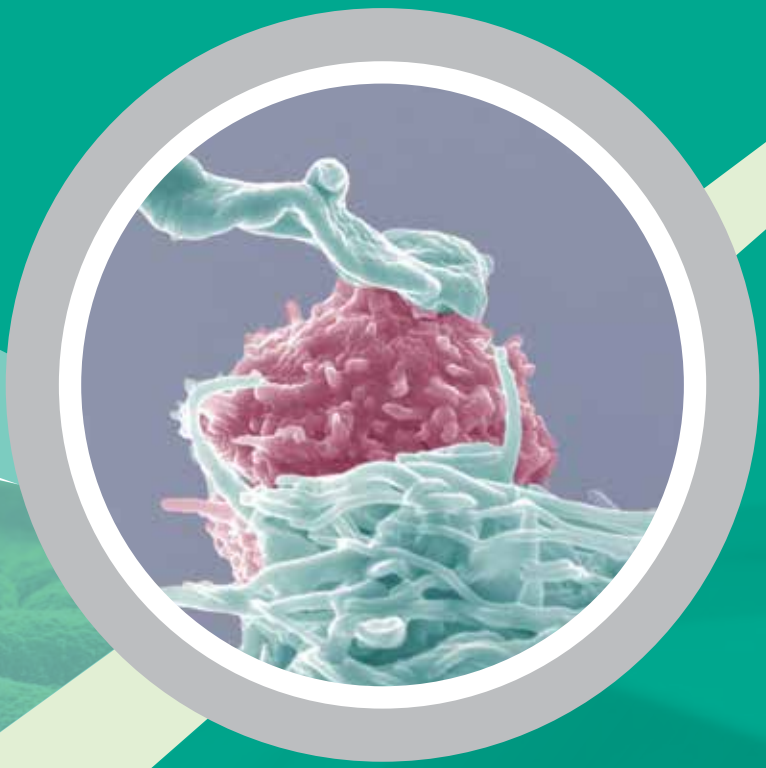
Infant and Young Child Feeding policy, Draft 2nd edition, 2012

TREATING AN INFANT BORN TO A MOTHER WHO HAS TB

- **Assess baby for TB symptoms and do not give BCG to the baby at birth**
- **Make a record in the Road-to-Health Booklet that the child was exposed to TB in utero**
- **All mothers should be encouraged to breastfeed, regardless of TB and/or HIV status**



TB AND HIV 5



TB AND HIV INTEGRATION >>>

WHAT DO WE MEAN BY TB/HIV INTEGRATION?

Both TB and HIV services are provided by the same provider at the same visit, a "**one-stop-shop**"[1]

WHAT IS THE DIFFERENCE BETWEEN INTEGRATION AND COLLABORATION?

- Collaboration: cross referral of patients between TB and HIV services
- Integration: one provider

WHAT DOES TASK SHIFTING MEAN?

- Distribution of tasks among levels of healthcare staff

EXAMPLES OF TB/HIV SERVICE RELATED TASK SHIFTING

Health Care Professional	Traditional Role	Expanded (Task-Shifting) Role to Achieve Integrated TB/HIV Services at PHC Facilities
Doctor	Initiating patient on ART	Managing complicated HIV & TB referred by PHC facility nurse
Professional Nurse	Managing clinically stable patients already initiated on ART	• Prescribing and dispensing ART (Schedule 4) • Managing patients on ART
Counsellor	• Adherence Counselling • HIV Testing	Finger-prick of consenting adults to obtain blood for rapid HIV testing
Administrative staff including security personnel	Data Collection	• Screening for TB symptoms • Help to enforce TB Infection Control measures through education of waiting patients in cough etiquette/hygiene

[1]. National Department of health. A 'hands-on' guide to integration of TB/HIV services including antiretroviral therapy at primary health care facilities in South Africa. 2010
[2]. Legido-Quigley H, Montgomery CM, Khan P, Fakoya A, Getahun H, Grant AD. Integrating tuberculosis and HIV services in low and middle-income countries: a systematic review. Available from www.hsr-symposium.org

TB AND HIV INTEGRATION

WHAT ARE THE KEY TB/HIV INTEGRATION ACTIVITIES?

For People Living With HIV to Reduce the Burden of TB (5Is)

- Intensified Case Finding for TB
- IPT
- Infection control for TB
- Initiate ART early
- Integration of services

For Patients With Presumptive TB And Diagnosed TB to Reduce the Burden of HIV

- Provider Initiated Counselling and Testing
- HIV prevention interventions for HIV negative and HIV positive patients
- For HIV positive TB patients
  - Cotrimoxazole prophylaxis
  - ART

WHAT COMPONENTS OF HIV CARE SHOULD BE PROVIDED TO TB/HIV CO-INFECTED PATIENTS?

- Immunological staging with CD4 counts
- RPR test to screen for syphilis
- Pap smears for all HIV positive women
- Symptomatic screening for STIs at every visit and syndromic management of STIs
- Reproductive healthcare with emphasis on effective contraception use of condoms
- Cotrimoxazole prophylaxis against opportunistic infections
- Diagnosis and management of other opportunistic infections
- Nutritional assessment and provision of nutritional supplements
- Social assessment including:
  - family circumstances and status of caregivers
  - identification of orphans or vulnerable children
  - application for disability grants, child support grants or care dependency grants
- On-going counselling support:
  - assess how patient is dealing with HIV status
  - discuss disclosure and support available to patient
  - emphasize practicing safer sex
  - reinforce good adherence to treatment
  - reassure and encourage patients
- Fast tracking ART initiation
- VL monitoring

ART AND TB TREATMENT >>>

WHY IS THE MANAGEMENT OF TB/HIV CO-INFECTED PATIENTS DIFFICULT?

- Drug interactions - rifampicin interacts with NNRTIs and PIs
- Increased risk of drug toxicity
- Increased pill burden with possible impact on adherence
- Tuberculosis immune reconstitution inflammatory syndrome (TB-IRIS)

WHICH ADULTS ARE ELIGIBLE FOR LIFELONG ART?

- CD4 ≤500 cells/mm^3
- WHO Stage 3 or 4 irrespective of CD4 count
  - Includes pulmonary, extrapulmonary, drug susceptible and drug resistant TB
- All women who are pregnant, breastfeeding or within one year postpartum irrespective of CD4 count
- Hepatitis B Infection

WHAT ARE THE RECOMMENDED ART REGIMENS FOR ADULTS?

	Category	Recommended regimen
1st line:	• Adults • Adolescents ≥ 15 years **AND** ≥ 40kg • All TB co-infection • All HBV co-infection • Women who are pregnant, breastfeeding or within 1 year postpartum	TDF + emitricitabine (FTC) OR lamivudine (3TC) + efavirez (EFV) Provide as fixed dose combination (FDC)
	If EFV contraindicated	TDF + FTC (or 3TC) + NVP*
	If EFV and NVP contraindicated	TDF + FTC (or 3TC) + LPV/r
	If TDF contraindicated	Abacavir (ABC) + 3TC + EFV
	If TDF and EFV contraindicated	ABC + 3TC + NVP
	Adolescents<15 years OR <40kg	ABC + 3TC + EFV
	If on a stavudine (d4T) based regimen: • d4T to be discontinued in all patients • Switch to TDF if virally suppressed and creatinine clearance normal, even if d4T well tolerated • Switch to FDC if regimen compatible • If patient is not virally suppressed, manage as per high viral load (VL)	

	Category	Recommended regimen
2nd line:	Failing on a TDF-based 1st line regimen	AZT + 3TC + LPV/r
	Failing on a d4T -based 1st line regimen	TDF + 3TC (or FTC) and LPV/r
	Dyslipidaemia or diarrhoea associated with LPV/r	Switch LPV/r to ATV/r

*** Avoid NVP if CD4 count ≥ 250 in women or ≥ 400 in men**

ART AND TB TREATMENT >>>

WHICH SIDE EFFECTS ARE SHARED BY TB DRUGS AND ART?

Side Effects	Antiretroviral Treatment	Tuberculosis Treatment
Nausea and Vomiting	Didanosine, zidovudine, protease inhibitors	Pyrazinamide, ethionamide, PAS
Hepatitis	• Nevirapine, efavirenz • Protease inhibitors (especially when dose is increased to overcome rifampicin induction)	Rifampicin, isoniazid, pyrazinamide
Peripheral Neuropathy	Stavudine, didanosine	Isoniazid, ethionamide, terizidone/cycloserine
Neuropsychiatric Side Effects	Efavirenz	Isoniazid, terizidone/cycloserine, quinolones, ethionamide
Renal Toxicity	Tenofovir	Aminoglycosides, capreomycin, rifampicin
Rash	Nevirapine, efavirenz	Rifampicin, isoniazid, pyrazinamide, ethambutol, streptomycin

Note that cotrimoxazole can also cause rash, hepatitis, neutropaenia and other haematological effects

WHICH TB DRUG AND ART COMBINATIONS ARE PROBLEMATIC?

- Rifampicin reduces the levels of PIs and NNRTIs; but does not require dose adjustment for NNRTIs
- Of the NNRTIs, efavirenz (EFV) is preferred to nevirapine; used at standard doses with standard TB treatment

NVP & RIF → Start NVP at 200mg bd in adults i.e. omit lead-in dose

LPV/r & RIF → Increase LPV/r dose as in table on adjacent page

TDF & amikacin or kanamycin or capreomycin → Avoid combination (nephrotoxicity)
AZT can be used in place of TDF
If HB <8 g/dl, use D4T
Can be switched back to TDF on completion of aminoglycoside if creatinine clearance >50ml/min

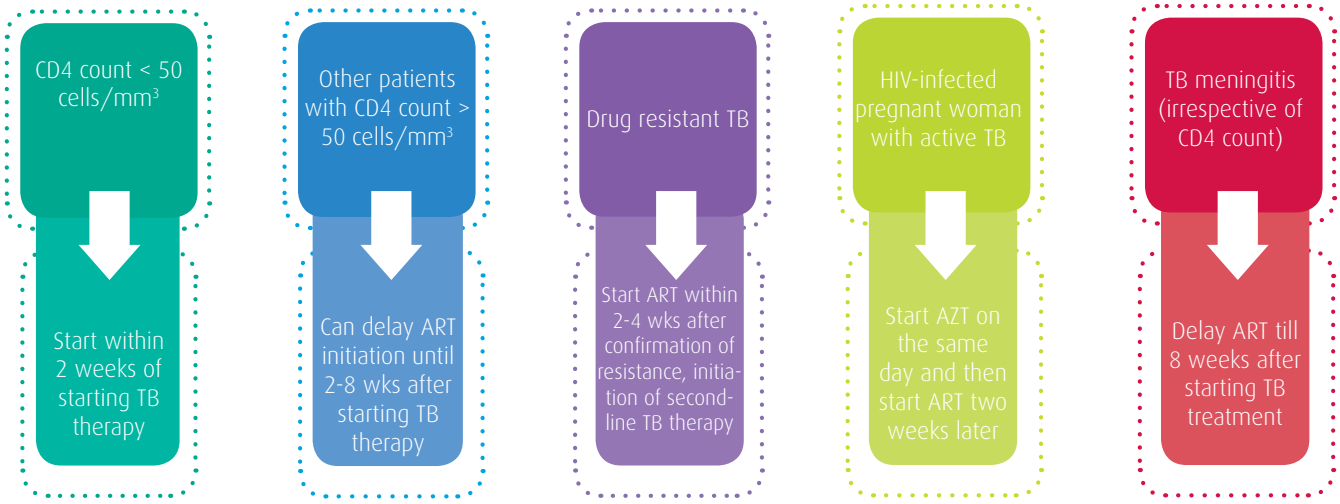
ART AND TB TREATMENT >>>

ANTIRETROVIRAL TREATMENT FOR ADULTS ON CONCOMITANT TB TREATMENT	
If TB develops while on ART	**If TB diagnosed before starting ART**
• **Continue ART throughout TB treatment** • **If on first-line ART regimen** ○ Patient can remain on this regimen ○ Some clinicians advocate switching NVP to EFV, but this is not necessary if the patient is stable on NVP	• **Start TB treatment first** • **All TB patients qualify for ART** ○ Timing of ART initiation depends on CD4 count and clinical status (see below) ○ Avoid NVP if possible ○ If EFV contraindicated, use NVP, starting with 200 mg bd (i.e. omit lead-in dose)
• **If on second-line ART regimen** ○ LPV/r dose should be doubled (from 2 tablets 12 hourly to 4 tablets 12 hourly) while on rifampicin based TB treatment ○ Stop the double dose of LPV/r 2 weeks after completing TB treatment ○ Monitor ALT monthly	

Also remember that all HIV-infected patients who are WHO stage 2, 3 or 4 qualify for cotrimoxazole prophylaxis. This includes all patients with TB. Cotrimoxazole should be stopped when CD4 >350 on two occasions six months apart.

WHEN SHOULD ART BE STARTED IN HIV-INFECTED PATIENTS DIAGNOSED WITH TB?

- All HIV-infected TB patients qualify for life-long ART, regardless of CD4 count
- If an HIV-infected patient is not on ART and is diagnosed with TB, TB treatment must be started first.
- When TB treatment is well tolerated and the patient is stable, ART can be started thereafter as below:



*Low Karnofsky score, low body mass index, low haemoglobin, low albumin, organ system dysfunction, extent of disease

ART AND TB TREATMENT >>>

WHAT ARE THE CRITERIA FOR STARTING ART IN CHILDREN?

Age	Clinical Stage	CD4 Criteria
<5 years	All stages	All CD4 counts
≥ 5 years	WHO Stage 3 or 4	Absolute CD4 count ≤ 500 cells/mm^3

WHAT ARE THE RECOMMENDED ART REGIMENS FOR CHILDREN?

	Clinical Scenario	Recommended Regimen
1st line:	All infants and children under 3 years (or < 10kg)	ABC + 3TC + LPV/r
	Children ≥ 3 years (and ≥ 10kg)∞	ABC + 3TC + EFV
	Currently on d4T-based regimen	• If VL is undetectable, change d4T to ABC • If VL >1000 copies/ml manage as treatment failure • If VL between 50 – 1000 copies/ml consult with expert for advice

	Failed First line PI Based regimen	Recommended Second line regimen
2nd line:	ABC + 3TC + LPV/r	**Consult with expert for advice**
	D4T + 3TC + LPV/r	
	Unboosted PI based regimen	
	Failed First line NNRTI Based regimen	**Recommended Second line regimen***
	ABC + 3TC + EFV (or NVP)	AZT + 3TC + LPV/r
	d4T + 3TC + EFV (or NVP)	AZT + ABC + LPV/r

∞ Children ≥ 3 years and exposed to NVP for 6 weeks or longer (PMTCT) should be initiated on ABC + 3TC + LPV/r

*** Discuss with expert before changing**

ART AND TB TREATMENT

WHEN SHOULD ART BE INITIATED IN CHILDREN WITH TB?

- Since TB is a stage 3 disease, children with TB will need to be started on ART
- If the child is not yet on ART when TB is diagnosed:
  - Initiate ART after 2 weeks of TB treatment if CD4 count <50 cells/mm^3
  - Initiate ART after 8 weeks of TB treatment if CD4 count >50 cells/mm^3 or TB meningitis
- If the child is already on ART when TB is diagnosed:
  - continue with ART and start TB treatment, see below for instances in which treatment should be adjusted

HOW SHOULD THE REGIMENS BE CHANGED IN CHILDREN ON TB TREATMENT AND ART?

- Rifampicin reduces the levels of lopinavir/ritonavir. If on rifampicin and LPV/r:
  - LPV/r dose must be increased by giving additional ritonavir
  - See Antiretroviral Drug Dosing Chart for Children 2013 (next page):
    - Column titled 'ritonavir boosting' indicates the dose of ritonavir that must be given in addition to the standard dose of LPV/r, depending on the weight
  - Alternatively, if ritonavir syrup is not available, the dose of LPV/r can be doubled but this is less effective
- All other antiretrovirals should be continued at standard doses
- TB treatment should be given at standard doses in children on ART

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

ANTIRETROVIRAL DRUG DOSING CHART FOR CHILDREN 2013

Compiled by the Child and Adolescent Committee of the SA HIV Clinicians Society in collaboration with the Department of Health

SOUTHERN AFRICAN HIV CLINICIANS SOCIETY

	Abacavir (ABC)		Lamivudine (3TC)		Efavirenz (EFV)	Lopinavir/ritonavir (LPV/rtv)	Ritonavir boosting (RTV)	Stavudine (d4T)	Didanosine (ddI)	Nevirapine (NVP)	Zidovudine (AZT)	
Target Dose	8mg/kg TWICE daily **OR** **≥10kg:** 16mg/kg ONCE daily		4mg/kg TWICE daily **OR** **≥10kg:** 8mg/kg ONCE daily		By weight band **ONCE** daily	300/75mg/m²/dose LPV/rtv **TWICE** daily	ONLY as booster for LPV/rtv when on Rifampicin **TWICE** daily (0.75xLPV dose bd)	1mg/kg/dose **TWICE** daily	180-240mg/m²/dose **ONCE** daily	160-200 mg/m²/dose **TWICE** daily (after once daily lead-in x 2 wks)	180-240mg/m²/dose **TWICE** daily	**Target Dose**
Available Formulations	Sol 20mg/ml Tabs 60mg (scored dispersible), 300mg (not scored), ABC/3TC 600/300mg		Sol. 10mg/ml Tabs 150mg (scored), 300mg, ABC/3TC 600/300mg		Caps 50,200mg Tabs 50,200, 600mg (not scored)	Sol. 80/20mg/ml Adult Tabs 200/50mg, Paeds Tabs 100/25mg	Sol. 80mg/ml	Sol. 1mg/ml Caps 15,20,30mg	Tabs 25,50,100mg (dispersible in 30ml water) Caps 250mg EC	Sol. 10mg/ml Tabs 200mg (scored)	Sol. 10mg/ml Caps 100mg Tabs 300mg (not scored), AZT/3TC 300/150mg	**Available Formulations**
Wt. (kg)	**Currently available tablet formulations of abacavir (except 60mg), efavirenz, LPV/rtv and AZT must be swallowed whole and NOT chewed, divided or crushed**											**Wt. (kg)**
<3	**Consult with a clinician experienced in paediatric ARV prescribing for neonates (<28 days of age) and infants weighing <3kg**											**<3**
3-3.9	2ml bd		2ml bd		**Avoid using when <10kg or <3 years:** dosing not established	*1ml bd	1ml bd	6ml	Avoid	5ml bd	6ml bd	**3-3.9**
4-4.9												**4-4.9**
5-5.9	3ml bd		3ml bd			*1.5ml bd	1.5ml bd	**7.5mg bd:** open 15mg capsule into 5ml water: give 2.5ml	100mg od: *(2x50mg tabs)*			**5-5.9**
6-6.9									125mg od: *(1x100mg + 1x25mg tabs)*	8ml bd	9ml bd	**6-6.9**
7-7.9	4ml bd		4ml bd					**10mg bd:** open 20mg capsule into 5ml water: give 2.5ml				**7-7.9**
8-8.9											1 cap bd OR 12ml bd	**8-8.9**
9-9.9												**9-9.9**
10-10.9	Choose only one option: 6ml bd OR 2x60mg tabs bd	Choose only one option: 12ml od OR 4x60mg tabs od	Choose only one option: 6ml bd	12ml od	200mg nocte *(1x200mg cap/tab)*	2ml bd	1.5ml bd	**15mg bd:** open 15mg capsule into 5ml water	150mg od: *(1x100mg + 1x50mg tabs)*	10ml bd		**10-10.9**
11-13.9												**11-13.9**
14-16.9	8ml bd OR 2.5x60mg tabs bd	5x60mg tabs od OR 1x300mg tab od OR 15ml od	½ x150mg tab bd OR 8ml bd	1x150mg tab od OR 15ml od	300mg nocte: *(200mg cap/tab + 2x50mg cap/tab)*	Choose one option: -2.5ml bd -100/25mg **paeds tabs:** 2 bd -200/50mg **adult tabs:** 1 bd	2ml bd	**20mg bd:** open 20mg capsule into 5ml water (if the child is unable to swallow a capsule)	175mg od: *(1x100mg + 1x50mg + 1x25mg)*	1 tab am ½ tab pm OR 15ml bd	2 caps am 1 cap pm OR 15ml bd	**14-16.9**
17-19.9												**17-19.9**
20-22.9	10ml bd OR 3x60mg tabs bd	1x300mg tab + 1x60mg tab od	1x150mg tab bd OR 15ml bd	2x150mg tab od OR 1x300mg tab od OR 30ml od		Choose one option: -3ml bd - 100/25mg **paeds tabs:** 2 bd - 200/50mg **adult tabs:** 1 bd	2.5ml bd		200mg od: *(2x100mg tabs)*		2 caps bd OR 20ml bd	**20-22.9**
23-24.9		1x300mg tab + 2x60mg tabs od										**23-24.9**
25-29.9	1x300mg tab bd	2x300mg tabs od OR 1xABC/3TC 600/300mg tab od	1x150mg tab bd	2x150mg tabs od OR 1x300mg tab od OR 1xABC/3TC 600/300mg tab od	400mg nocte: *(2x200mg caps/tabs)*	Choose one option: - 3.5ml bd - 100/25mg **paeds tabs:** 3 bd - #200/50mg **adult tabs:** 1 bd + 100/25mg **paeds tabs:** 1 bd	3ml bd	**30mg bd**	250mg od: *(2x100mg + 1x50mg tab)* OR 1x250mg EC cap od	1 tab bd	1x300mg tab bd OR 1xAZT/3TC 300/150mg tab bd	**25-29.9**
30-34.9						Choose one option: - 4ml bd - 100/25mg **paeds tabs:** 3 bd - #200/50mg **adult tabs:** 1 bd + 100/25mg **paeds tabs:** 1 bd						**30-34.9**
35-39.9						Choose one option: - 5ml bd - 200/50mg **adult tabs:** 2 bd	4ml bd					**35-39.9**
>40					600mg tab nocte							**>40**

od = once a day (usually at night)
bd = twice a day

* Avoid LPV/rtv solution in any full term infant <14 days of age and any premature infant <14 days after their due date of delivery (40 weeks post conception) or obtain expert advice.
# Children 25-34.9kg may also be dosed with LPV/rtv 200/50mg adult tabs: 2 tabs am; 1 tab pm

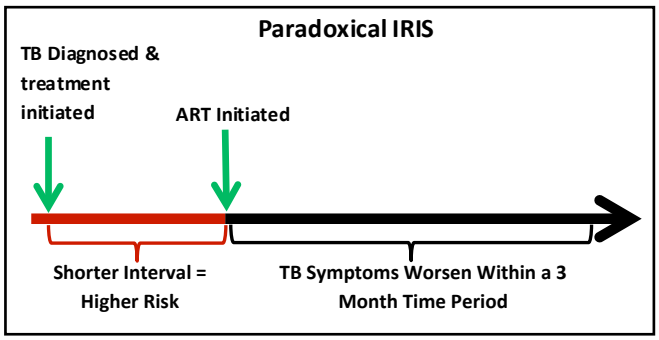
Weight (kg)	3-4.9	5-9.9	10-13.9	14-29.9	≥30
Cotrimoxazole Dose	2.5ml od	5ml od	5ml od	10ml or 1 tab od	2 tabs od
Multivitamin Dose	2.5ml od	2.5ml od	5ml od	5ml od	10ml or 1 tab od

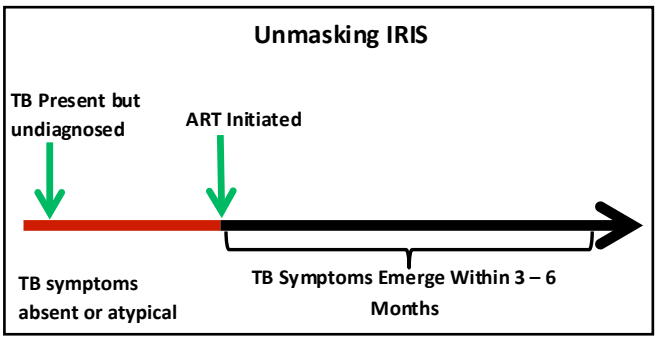
IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME

WHAT IS IMMUNE RECONSTITUTION INFLAMMATORY SYNDROME (IRIS)?

- It refers to a worsening in the clinical status of patients after ART initiation
  - after ART initiation, the immune system begins to recover
  - as a result, inflammatory symptoms and sings worsen in the presence of an opportunistic infection (OI)
- IRIS may occur with a number of opportunistic infections including TB, cryptococcal meningitis, hepatitis B etc.
- May occur in:
  - patients already on treatment for the OI at ART initiation – paradoxical IRIS
  - patients in whom the OI is unrecognised at the time of ART initiation – unmasking IRIS
- It may manifest 1 week to several months after ART initiation
- These patients develop a recurrence/progression of TB symptoms or develop new features of TB in the first few weeks after starting ART
- Common clinical features include:
  - enlarging lymph nodes
  - fevers
  - worsening CXR infiltrates
  - enlarging pleural effusions
- Meningitis or enlarging tuberculomas may be life-threatening

HOW DOES TB IRIS PRESENT?





HOW IS TB IRIS DIAGNOSED?

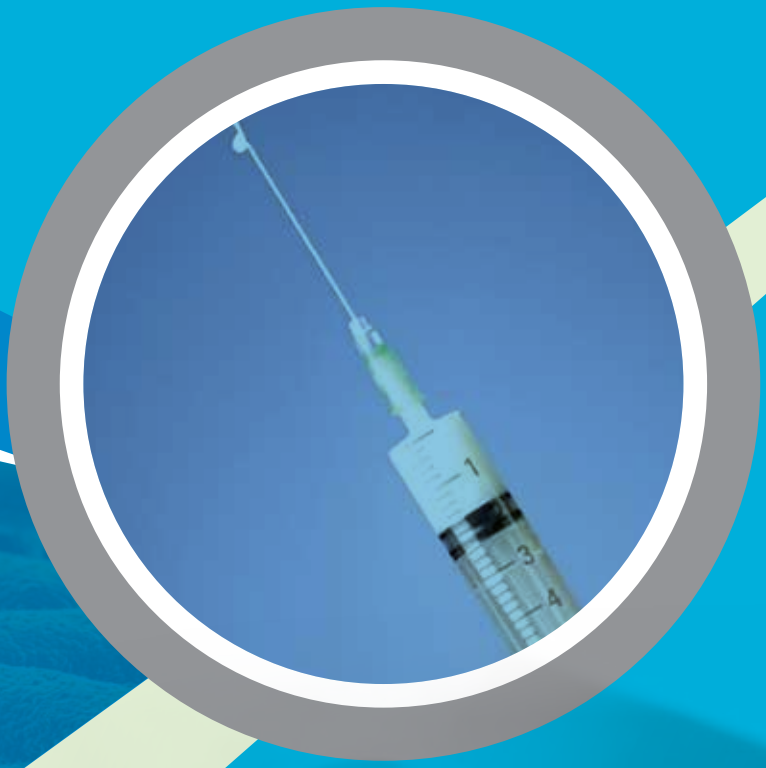
- Diagnosis of exclusion-exclude other possible causes of clinical deterioration including:
  - MDR-TB
  - alternative diagnoses e.g. bacterial pneumonia, Pneumocystis pneumonia, Kaposi's sarcoma etc
  - poor adherence
  - malabsorption
  - drug toxicity

HOW IS IRIS MANAGED?

- Most patients can be managed in an out-patient setting
- Treat underlying OIs
- Anti-inflammatories should be added
- ART should be continued unless IRIS is life-threatening
- If life-threatening IRIS develops, the patient requires urgent referral to hospital
- Corticosteroids may be required in severe reactions

TB-IRIS is infrequently fatal. ART should not be delayed in patients with low CD4 counts to prevent TB-IRIS as the mortality is high when ART is delayed.

PREVENTION 6



TB PREVENTION BY BCG VACCINE >>>

WHAT DOES BCG STAND FOR?

BACILLUS CALMETTE-GUÉRIN

WHAT IS THE BCG VACCINE AND WHAT DOES IT DO?

- Live attenuated form of *Mycobacterium bovis* (part of *Mycobacterium tuberculosis* complex)
- Routinely given intradermally in the right deltoid region soon after birth
- Part of the South African Expanded Programme on Immunisation (EPI) schedule
- It provides 60-80% protection against disseminated forms of TB, including TB meningitis and miliary TB
- It provides limited and inconsistent immunity against pulmonary TB for not longer than 10 years

BCG IS GIVEN TO ALL NEONATES AT BIRTH EXCEPT SYMPTOMATIC HIV EXPOSED NEONATES.

WHO IS AT RISK OF ADVERSE EVENTS?

- Immunocompromised infants, including HIV-infected

WHAT IS A NORMAL BCG REACTION?

- A red, indurated area 5-15 mm in diameter appears 3-4 weeks after vaccination
- There may be central crusting which later falls off, leaving an ulcer
- Upon healing of the ulcer a 3-7 mm scar is left
- Ulceration and scarring at the site is common and may indicate a better immunological response to the vaccine

WHAT ADVERSE EVENTS CAN OCCUR WITH BCG?

Adverse events related to BCG vaccination are classified according to the site of disease:

Category	Description
Local BCG disease	A local process at the site of vaccination. This includes any of the following: • BCG infection site abscess conforming to EPI definitions: ≥ 10 mm X 10 mm • Severe BCG inoculation site ulceration
Regional disease	Involvement of any regional lymph nodes or other regional lesions beyond the vaccination site: ipsilateral axillary, supraclavicular, cervical and upper arm glands. Lymph node involvement must conform to EPI definition and may include enlargement, suppuration and fistula formation.
Distant disease	Involvement of any site beyond a local or regional ipsilateral process. This includes: BCG confirmed from at least 1 distant site beyond the vaccination site, e.g. pulmonary secretions (gastric aspirate, tracheal aspirate, sputum), cerebrospinal fluid, urine, osteitis (usually right humerus), distant skin lesions
Disseminated disease	BCG confirmed from >1 remote site, as described under distant disease, and/or from at least 1 blood or bone marrow culture.

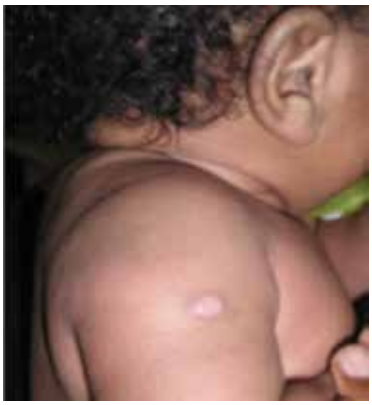
ASK PARENT TO RETURN WITH CHILD IF SIDE EFFECTS OCCUR, E.G. INOCULATION SITE ABSCESS OR ENLARGED RIGHT AXILLARY OR SUPRACLAVICULAR NODES

TB PREVENTION BY BCG VACCINE

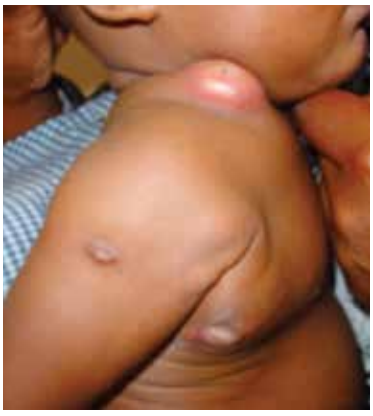
WHAT IS BCG IRIS?

- Occurs in HIV-infected children within 3 months of initiation of antiretrovirals
- Categorisation is the same as for BCG disease, being divided into local, regional, distant or disseminated disease
- It is one of the most common forms of IRIS in infants in South Africa
- Expected to improve slowly with time, but while mortality is low, morbidity is high

THE CHER STUDY SHOWED THAT EARLY INITIATION OF ART BEFORE 12 WEEKS OF AGE AND BEFORE CLINICAL AND IMMUNOLOGICAL DETERIORATION OCCURRED WAS ASSOCIATED WITH A SIGNIFICANTLY REDUCED INCIDENCE OF BCG IRIS



Normal BCG Reaction



Regional BCG Reaction

HOW DO I DIAGNOSE BCG DISEASE?

- *M. bovis* BCG is a member of the MTB complex of organisms
- When it is isolated at a laboratory it will be reported as "MTB complex" and not as "*M. bovis* BCG"
- If clinical suspicion/confirmation of BCG is required, this must be indicated on the laboratory request form so that additional confirmatory testing can be done in the form of a BCG PCR
- It is important to confirm the diagnosis, especially in supraclavicular and cervical lymphadenitis and in disseminated BCG disease, as TB can present in a very similar manner

HOW SHOULD BCG ADVERSE EVENTS BE REPORTED?

- Any suspected BCG related adverse event must be reported as an Adverse Event Following Immunisation (AEFI) to the EPI – See Annexures for AEFI Reporting Template

HOW SHOULD I MANAGE BCG ADVERSE EVENTS?

- Children with local or regional BCG disease can often be safely monitored without using antimycobacterial treatment
- However, HIV-infected children must be monitored closely for the development of disseminated BCG disease
- If suppurative, take a swab and send specimen for TB investigations
- Needle aspiration of purulent material can be considered as a means to relieve symptoms
- May need incision and drainage
- Treat conservatively.
- If TB confirmed (i.e. BCG disease excluded on the basis of a negative BCG PCR result), treat with standard TB regimen
- Start ART in HIV-infected children, if not already initiated
- Monitor closely for drug-drug interactions and side effects

Hesseling, AC, et al. Bacille Calmette-Guérin Vaccine-Induced Disease in HIV-Infected and HIV-Uninfected Children. Clinical Infectious Diseases, 42, 548-58, 2006.
Hesseling, AC, et al. BCG vaccination in HIV-exposed infants – risks and benefits. S Afr Med J. 2009 Feb; 99(2): 88-91
Moore, DP, et al. Childhood tuberculosis guidelines of the southern African Society for Paediatric Infectious Diseases, South Afr J Epidemiol Infect 2009; (24)3 Wilson, D, et al. Handbook of HIV Medicine, 2nd edition. Oxford University Press South Africa: 2008; Violari A, et al. N Engl J Med 2008; 359: 2233-44.

ISONIAZID PREVENTIVE THERAPY (IPT) >>>

HOW DOES IPT WORK?

WHY SHOULD WE OFFER IPT?

- Multiple studies have shown that IPT reduces tuberculosis incidence in HIV-infected patients:
  - by 62% in those with a positive TST
  - by 11% in those with a negative TST[1]
- Although ART reduces the likelihood of developing TB disease, TB incidence amongst HIV-infected patients receiving ART is still 10 times greater than the general South African population[2]

HOW DO WE EXCLUDE ACTIVE TB?

Answering 'no' to the following four questions has been shown to be 98% effective in ruling out active TB disease in high prevalence settings[3]:

- Cough for more than 24 hours?
- Any fever?
- Any weight loss?
- Drenching night sweats?

IS TB THAT OCCURS AFTER IPT MORE LIKELY TO BE INH RESISTANT?

- No
- TB that occurs after starting IPT is not more likely to be INH resistant[4]
- If the patient does have INH mono-resistance, first-line TB treatment is generally effective

NB:

- **POSITIVE TST IS NOT A REQUIREMENT TO INITIATE IPT**
- **PATIENTS ON ART AND HIV-INFECTED PREGNANT WOMEN ARE ELIGIBLE FOR IPT**
- **PATIENTS WITH PREVIOUS TB MAY RECEIVE IPT**
- **IPT MAY BE COMMENCED AND MONITORED BY A NURSE**
- **TST SHOULD BE DONE AS SOON AS POSSIBLE AFTER INITIATING IPT (WHEN TST IS AVAILABLE) AND TREATMENT DURATION CONTINUED ACCORDING TO TABLE ON PAGE 96**

1. Akolo C, Adetifa I, Shepperd S, Volmink J. Treatment of latent tuberculosis infection in HIV infected persons. *Cochrane Database of Systematic Reviews 2010*, Issue 1. Art. No.: CD000171. DOI: 10.1002/14651858.CD000171.pub3
2. Golub JE, Pronyk P, Mohapi L, Thsabangu N, Struthers H, Gray GE, McIntyre JA, Chaisson RE, Martinson NA. Isoniazid preventive therapy, HAART and tuberculosis risk in HIV-infected adults in South Africa: a prospective cohort. AIDS. 2009 Mar 13;23(5):631-6.
3. Getahun H, Kittikraisak W, Heilig C, Corbett EL, Ayles H, Cain K, et al. Standardized Tuberculosis screening algorithm for the prevention and treatment of tuberculosis in people living with HIV in resource constrained settings: a result of a primary meta-analysis. 40th World Conference on Lung Health of the International Union against tuberculosis and Lung disease, Cancun, Mexico, Late Breaker 3-7 December 2009.
4. van Halsema CI, Fielding KL, Chihota VN, et al. Tuberculosis outcomes and drug susceptibility in individuals exposed to isoniazid preventive therapy in a high HIV prevalence setting. AIDS 2010, 24:1051-55.

ISONIAZID PREVENTIVE THERAPY (IPT) >>>

WHICH ADULTS ARE ELIGIBLE FOR IPT?

HIV-infected adults who:

- are not on TB treatment
- are asymptomatic for TB (as above)
- have no active liver disease
- do not consume large amounts of alcohol
  - Large amounts = men >28 units per week / women >21 units per week
- have no history of psychosis, convulsions, neuropathy
- have no adverse reactions to INH
- are incarcerated with the Department of Correctional Services

WHAT DOSE OF IPT SHOULD BE GIVEN TO ADULTS?

- INH 5mg/kg/day (max 300mg/day)
- Pyridoxine 25 mg daily

WHICH CHILDREN ARE ELIGIBLE FOR IPT?

- The following children in close contact with an infectious case of TB
  - All children less than 5 years (including neonates)
  - All HIV-infected children irrespective of age (up to age 15 years)
- If asymptomatic for TB
- And have no contraindications to INH
- Children <2 years who are staying with incarcerated mothers, irrespective of HIV status

WHAT DOSE OF IPT SHOULD BE GIVEN TO CHILDREN?

Weight band (kg)	Daily Isoniazid (INH) 100 mg Tablet
2 - 3.4	¼ tab
3.5 - 4.9	½ tab
5 - 7.4	¾ tab
7.5 –9.9	1 tab
10 – 14.9	1 ½ tabs
15 – 19.9	2 tabs
20 – 29.9	3 tabs

Add Pyridoxine if HIV positive or malnourished

- If < 5 years of age: 12.5mg daily
- If ≥ 5 years of age: 25mg daily

If child unable to swallow tablet, crush and dissolve appropriate fraction of 100mg tablet in water or multi-vitamin syrup

NOTE: THE MAXIMUM DAILY DOSE OF INH MUST NOT EXCEED 300mg

ISONIAZID PREVENTIVE THERAPY (IPT) >>>

IPT DURATION BASED ON TST RESULT

	Pre-ART (CD4 > 500)	On ART
TST unavailable	6 months	12 months
TST negative	no IPT	12 months
TST positive	36 months	36 months

Note: HIV-infected incarcerated patients should receive IPT for the duration of their stay

MANAGEMENT OF ADULTS AND CHILDREN ON IPT

Monthly follow up:

- 'Fast-track' patients through the clinic
- Accurate serial weights
- Monitor for side effects of IPT – **be especially vigilant with elderly or alcohol history**
- TB symptom screen
- Patient education (see adjacent page)

NOTE: MONITORING OF LIVER ENZYMES IS NOT REQUIRED UNLESS INDICATED BY HISTORY OR CLINICAL SIGNS

WHEN SHOULD CONSIDERATION BE GIVEN TO STOPPING IPT?

1. When active TB is suspected

- Investigate for TB, STOP IPT if active TB is diagnosed

2. Hepatotoxicity possibly due to IPT

- Discontinue IPT immediately and refer to hospital

3. Hypersensitivity rash

- If mild, stop INH until rash resolves and then restart INH
- If severe, stop INH and refer urgently
- See page 47 for management of hypersensitivity rash

4. Peripheral neuropathy (PNP) possibly due to IPT

- Assess severity and rate of progression
- If patient has difficulty in walking or complains of excessive pain, stop IPT
- If PNP symptoms are mild, continue IPT. Counsel and treat:
  - Counsel that PNP may be due to HIV infection and/or IPT
  - Counsel patient that PNP resolves after IPT course is completed
  - Increase pyridoxine from 25 mg to 100mg dly
  - For adults, medicate with amitryptiline 25mg nocte if PNP is uncomfortable
  - If on D4T switch to AZT or TDF

National Consolidated Guidelines for the Prevention of Mother to Child Transmission of HIV (PMTCT) and the Management of HIV in Children, Adolescents and Adults. National Department of Health, 2015

ISONIAZID PREVENTIVE THERAPY (IPT) >>>

5. Fits or psychosis

- Stop INH and refer

6. Poor adherence

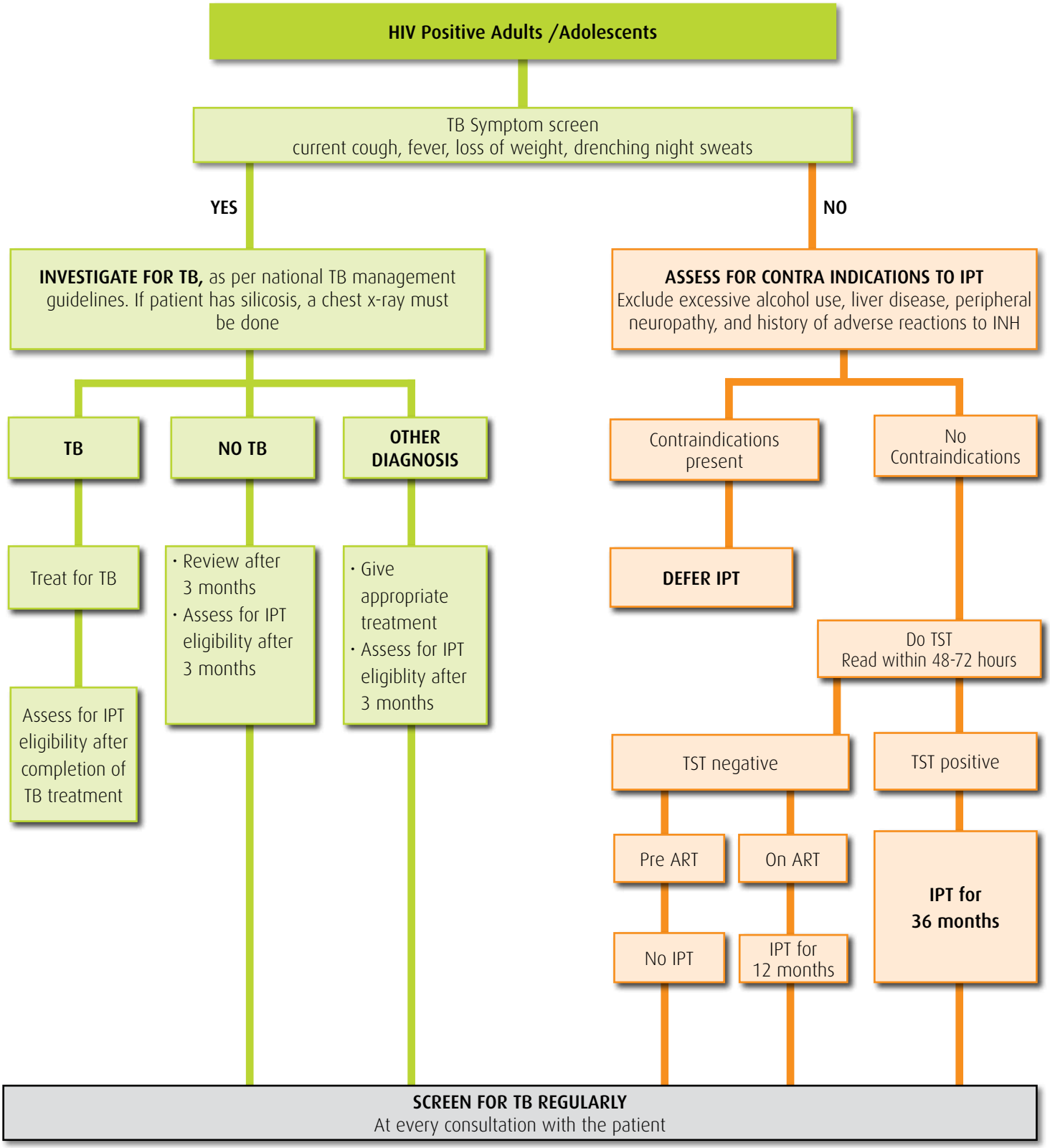
- If a patient interrupts treatment for less than 3 consecutive months:
  - Enquire about the reasons for treatment interruption
  - Address patient concerns
  - Counsel the patient on the importance of adherence
  - Screen for TB
  - Conduct investigations to exclude TB if signs and symptoms of TB are present
  - If asymptomatic and no signs of TB disease, continue on IPT and add missed doses of isoniazid to total duration of IPT.
- If a patient interrupts treatment for more than 3 consecutive months:
  - Stop IPT
  - If the patient returns at any point and commits to restarting IPT, the patient may be reassessed for IPT eligibility and restarted on IPT
- Any treatment interruption for a second time, regardless of duration of interruption:
  - Stop IPT

PATIENT EDUCATION SHOULD INCLUDE:

- Adherence to daily INH and monthly visits
- Minimal alcohol
- Patient should return to clinic immediately if they have:
  - Possible side effects of IPT
    - pain in the right abdomen
    - nausea and vomiting
    - dark urine and pale stools
    - yellow eyes
    - severe rash
    - tingling hands and feet
    - hearing voices or seeing things that are not actually there
  - Symptoms of active TB:
    - cough
    - fever
    - loss of weight
    - night sweats
- Patients **do not** need to take IPT with meals
- If patients see another health care worker it is important that they understand that they are not receiving TB **treatment** but only **taking one drug for TB prevention**
- HIV counselling, including:
  - Prevention – use of condoms
  - Need to stay in care – regular monitoring
  - Need for ART as soon as eligible

ISONIAZID PREVENTIVE THERAPY (IPT)

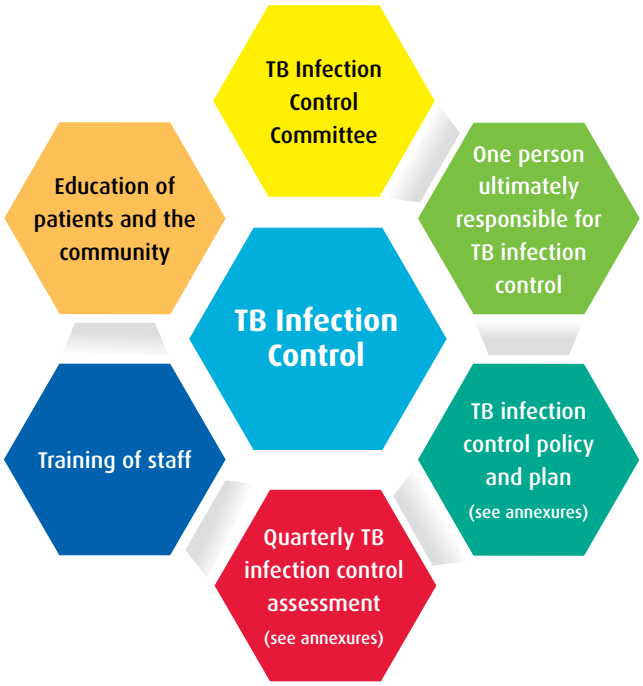
TB SCREENING ALGORITHM FOR IPT IN ADOLESCENTS AND ADULTS



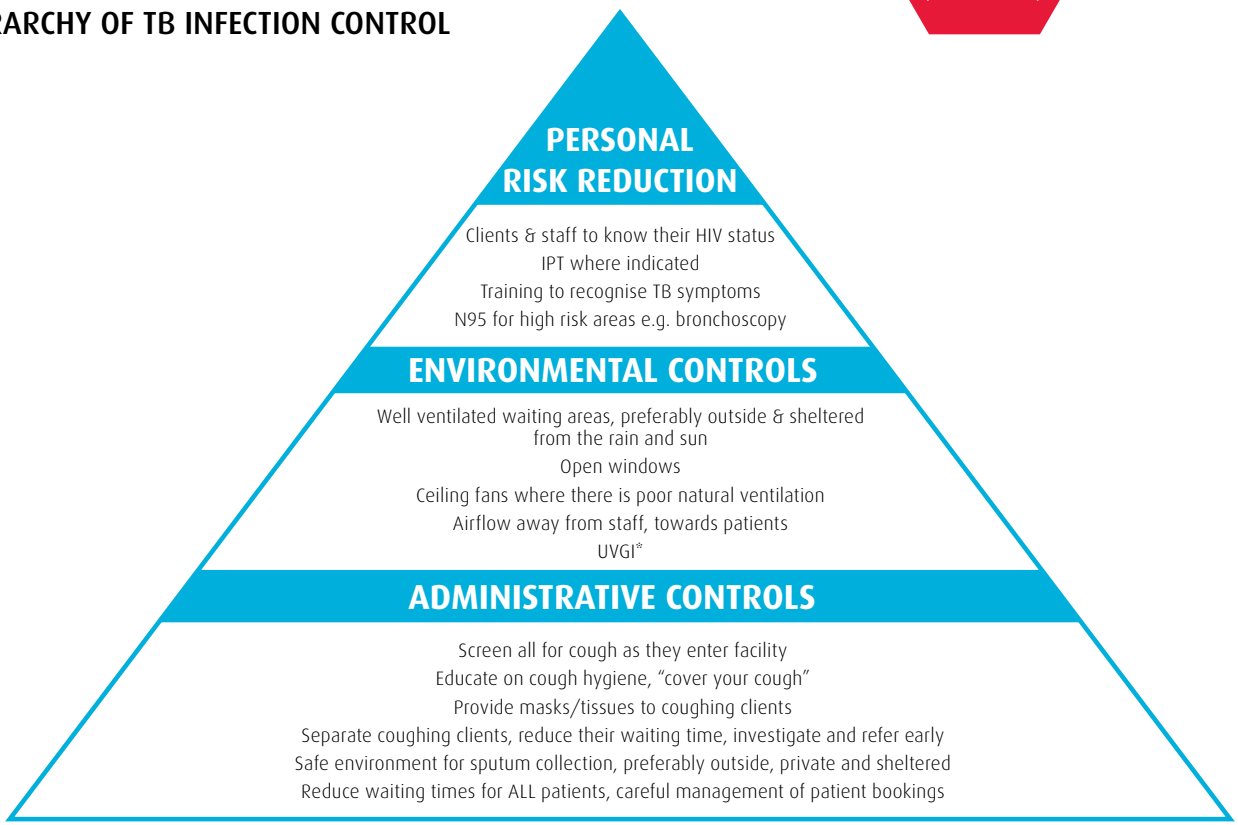
INFECTION CONTROL IN HEALTH CARE FACILITIES

WHY DO WE NEED INFECTION CONTROL?

TB patients may produce infectious droplets when they cough, these are suspended in the air for prolonged periods and may be inhaled leading to possible TB infection and disease



HIERARCHY OF TB INFECTION CONTROL



*UVGI is an additional environmental control but is expensive to install and maintain annually. UVGI is only effective if there is good air flow past the lights. UVGI may give a false sense of security which results in other controls e.g. open windows, cough hygiene not being practised. Skin and eye damage can result from over-exposure.

TB IN HEALTH CARE WORKERS >>>

IS TB A PROBLEM AMONGST HEALTH CARE WORKERS (HCWS)?

- Yes
- Health care workers are at high risk of occupationally-acquired tuberculosis, especially if they are HIV-infected

HOW CAN HCWS PROTECT THEMSELVES?

- They must be aware of the signs and symptoms of TB and present early for testing if they develop any symptoms
- All HCW must know their HIV status and take care of themselves accordingly
- They should be trained on TB upon induction and annually

WHAT ARE EXAMPLES OF SOUTH AFRICAN POLICIES AND ACTS REGARDING TB IN HCWS?

- The Constitution of South Africa in Act 108 of 1996 and its Bill of Rights:
  - "Everyone has the right to an environment that is not harmful to their health and wellbeing"
- Public Service Regulations, Part 6, 2001
  - "Government will work towards the improvement of a working environment...to include employees health"
- Occupational Health and Safety Act
  - Outlines the general duties of employees and employers
- Compensation for Occupational Injuries and Diseases Act (COIDA)
  - Allows for compensation under very specific circumstances

WHAT ARE KEY ASPECTS OF TB PREVENTION AND MANAGEMENT AMONGST HCWS?

1. Ensure adherence to TB infection control principles

- TB Education and training focussing on:
  - TB symptoms
  - Infection control measures
- Promote HIV testing
- Allow priority and private access to HCWs for TB and HIV management:
  - Prevention: offer IPT
  - Diagnosis: HCWs should be evaluated as "high risk TB suspects"
  - Management: ART and appropriate placement of HIV positive staff in low TB risk areas of the facility

2. Administrative management of TB disease amongst HCWs

- Ensure that the HCWs take sick leave until smear microscopy is negative
- Complete administrative procedures for diseased/injured HCWs:
  - Employer's Report of an Occupational Disease
  - First Medical Report in respect of an Occupational Disease
  - Notice of an Occupational Disease and Claim for Compensation
  - The laboratory results demonstrating *Mycobacterium tuberculosis* or NTM
  - Exposure history or an appropriate history
  - Progress Medical Report in respect of an Occupational Disease
  - Medical report detailing the employee's symptoms and clinical features
  - Final Medical Report and lung function tests must be submitted 12 months after completion of TB treatment or when treating medical practitioner considers that no further improvement is anticipated
  - CXR and/or radiology reports where applicable

Government Gazette, Vol. 451, No 24231, January 2003

TB IN HEALTH CARE WORKERS >>>

WHAT PROCESSES SHOULD BE IN PLACE IN ORDER TO PROTECT HCWs IN THE WORK PLACE?

Area:	Implementation:
TB SCREENING	• All staff should receive TB symptom screening at baseline, biannually and on exit
OCCUPATIONAL HIV PREVENTION	• Written and disseminated Post Exposure Prophylaxis policy/guideline • Named person/committee responsible for infection prevention • Refresher training on safe injection techniques • Gloves, soap, running water, sharps bins available • Safe sharps disposal
HIV (SEXUALLY TRANSMITTED) PREVENTION	• Ongoing education on safe sex • Condoms available in both female and male toilets
PROMOTION OF HIV TESTING FOR STAFF	• Written facility policy/ guideline concerning HIV testing of staff • Facilitated access for staff wanting HIV testing
ACCESS TO ART FOR STAFF	• Written facility policy/guideline/directive concerning access to ART for staff • Ongoing education or promotion of benefits of knowing status and getting tested • Facilitated access to free ART for staff
ACCESS TO ART FOR FAMILY OF STAFF	• Written facility policy/guideline/directive concerning access to ART for family of members of staff • Access to HIV diagnosis for family members • Facilitated access to free ART for family of staff
TB INFECTION CONTROL	• Written policy/guideline including TB infection control • Named person/committee responsible for infection control • Refresher training/monitoring of control practices • Education on cough hygiene • TB suspected in anyone with prolonged cough • TB patients or those with presumptive TB should be separated from other patients • TB diagnosed & treated promptly
PREVENTION OF TB IN STAFF	• Written policy/guideline/training material/directive concerning TB as an occupational health risk • Refresher education/training of staff on HIV/TB • Promotion of HIV testing among staff with high exposure to TB patients
MEDICAL SURVEILLANCE PROGRAMME	• Pre-placement screening • Periodic medical assessments 6 monthly Medical history, TB symptom review, TST, Physical assessment, CXR, Other tests, as appropriate • Exit medical examination • Medical leave • Return to work policy • Medical records

TB IN HEALTH CARE WORKERS

WHAT ARE THE 7 STEPS FOR PATIENT MANAGEMENT?

STEP	ACTION	DESCRIPTION
1.	Screening	• Early recognition of patient with suspected or confirmed TB disease • Assign a staff member to screen patient for TB symptoms • Cough of any duration or under investigation & treatment for TB should be separated
2.	Cough hygiene	• Educating patients in cough hygiene covering their noses & mouths (using inner part of the elbow) or provide tissues or face masks • Safe disposal of tissues and masks
3.	Separate	• Separating TB suspects or cases from other patients • Patients to wait in a separate well ventilated waiting area
4.	Fast-track	• Place symptomatic patients at the front of the line for services they are seeking • To reduce the waiting time of exposure to TB
5.	Investigate for TB or refer	• TB diagnostic test should preferably be done on site or via an established link with TB diagnostic & treatment • All suspects should be offered provider-initiated HCT • Contact investigation & management
6.	Treatment	• Appropriate TB treatment should be initiated within 2 days • ART should be initiated in HIV/TB co-infected irrespective of CD4 count
7.	Discharge plan	• The health facility should establish a discharge policy • Linkage with community healthcare workers to conduct IPC home assessment

ALL ABOVE MEASURES REQUIRE A SUPPORTIVE ENVIRONMENT AND SENIOR STAFF AND MANAGEMENT NEED TO MAKE AN EFFORT TO ENSURE EFFECTIVE TRANSLATION OF POLICY INTO PRACTICE

RECORDING AND REPORTING

7

MONITORING AND EVALUATION OF TB PROGRAMME >>>

WHAT IS TB INCIDENCE?

The incidence of TB is defined as the number of new TB cases in one year per 100,000 population

WHAT IS TB PREVALENCE?

The prevalence of TB is defined as the number of TB cases in a population at a given point in time, per 100,000 population

WHAT IS MONITORING?

Monitoring is the routine collection and analysis of information to track progress against set plans and check compliance to established standards. It helps identify trends and patterns, adapt strategies and inform decisions for programme management.

WHAT IS EVALUATION?

Evaluation is the systematic and objective assessment of a programme / policy, its design, its implementation and results. The aim is to determine the relevance and fulfilment of objectives, efficiency, effectiveness, impact and sustainability. An evaluation should provide information that will enable the incorporation of lessons learned into the decision-making process and improve future interventions.

WHAT IS IMPROVEMENT?

Data centred process that identifies root causes of indicators currently not meeting targets and acts upon them by changing processes and systems that are causing the identified outcome.

WHAT IS SURVEILLANCE?

Epidemiologic surveillance is the ongoing systematic collection, recording, analysis, interpretation, and dissemination of data reflecting the current health status of a community or population.

WHY IS MONITORING AND EVALUATION (M&E) IMPORTANT?

- To ensure that each patient with TB symptoms and each TB case receives appropriate management
- For facilities, sub-districts, districts and provinces to monitor their performance
- For NDoH to allocate resources appropriately
- For assessing progress made towards achieving TB control goals

WHICH TOOLS ARE USED FOR MONITORING TB PATIENTS?

- TB Identification Register (GW 20/13)
- Laboratory request form for Sputum Examination
- TB Treatment Record (GW 20/12)
- TB Patient treatment card (GW 20/15)
- Tuberculosis Register (GW 20/11)
- Transfer form (GW20/14)
- TB symptom screening tool
- Notification of Notifiable Medical Conditions Form
- TB Daily Diary
- DR-TB treatment Card (yellow)
- DR-TB Patient Identity Card (green and red)
- DR-TB Patient consent form
- DR-TB Treatment follow-up card (Pink)
- TB sputum request form
- TB patient referral form
- DR-TB Register (Paper based, electronic)

Refer to Annexures for copies of important tools and forms used in TB care.

MONITORING AND EVALUATION OF TB PROGRAMME >>>

HOW SHOULD PATIENTS BE CATEGORISED IN ORDERED TO BE ENTERED IN THE REGISTER?

- **Xpert positive TB:**
  - A positive Xpert result or MTB detected in at least one specimen tested
- **Xpert negative TB:**
  - A negative Xpert result or MTB not detected in at least one specimen tested
- **Smear positive PTB:**
  - A positive Xpert result plus
  - At least 1+ acid-fast bacilli in at least 1 sputum smear examination
- **Smear negative PTB:**
  - A positive Xpert result plus
  - A least one sputum smear microscopy negative for AFBs
- **Culture positive PTB Case:**
  - A positive culture result with or without Xpert result
- **Clinically diagnosed PTB "Smear not Done":**
  Clients started on TB treatment without smear microscopy result
  - CXR abnormalities consistent with active PTB
  - History and clinical picture suggestive of PTB or EPTB
  - Histological and biochemical tests suggestive of TB

CATEGORIES OF NEW/ PREVIOUSLY TREATED

1. **New:** A client who has never had treatment for TB or who has taken anti-TB drugs for less than 4 weeks
2. **Previously Treated:** A client who has taken TB treatment for 4 weeks or more in the past and either relapsed, been lost to follow up or had treatment failure
3. **Other:**
   All cases that do not fit the above definitions such as:
   - those without a clear history of previous TB treatment
   - those with unknown outcomes of previous TB treatment
   - those who have been previously treated but have smear/culture negative PTB and/or EPTB

Categories of previously treated patients:

Category	Definition
Relapse	A client who received treatment and was declared cured or treatment completed at the end of the treatment period and has now developed **sputum smear or culture positive pulmonary TB again**
Retreatment After Failure	A pulmonary TB client who is still **sputum smear or culture positive** at the end of the treatment period.
Retreatment after loss to follow up	A client who completed at least one month of treatment and returns after interrupting treatment for two months or more, and is still **sputum smear or culture positive**

MONITORING AND EVALUATION OF TB PROGRAMME >>>

HOW SHOULD TREATMENT OUTCOMES BE RECORDED?

Outcome	Definition
Cure	Patient whose baseline smear (or culture) was positive at the beginning of the treatment and is smear/ culture negative in the last month of treatment and on at least one previous occasion at least 30 days prior.
Treatment completed	Patient whose baseline smear (or culture) was positive at the beginning and has completed treatment but does not have a negative smear/ culture in the last month of treatment and on at least one previous occasion more than 30 days prior. *The smear examination may not have been done or the results may not be available at the end of treatment.*
Treatment success	Treatment success is a combination of the patients who were cured and those who completed treatment.
Treatment failure	Patient whose baseline smear (or culture) was positive and remains or becomes positive again at 5 months or later during treatment. *This definition excludes those patients who are diagnosed with RR-TB or MDR-TB during treatment.*
Died	Patient who dies for any reason during the course of TB treatment.
Lost to follow up	Patient whose treatment was interrupted for two consecutive months or more during the treatment period.
Transfer out	Patient who was referred to a facility in another district to continue treatment and for whom the treatment outcome is not known.

WHAT HAPPENS TO TB DATA?

- TB data collected at the facility is reported to various levels: sub-district, district, provincial and national
- TB register data is collated electronically at the sub-district level into the electronic TB register (ETR.net) which forms the basis of the M&E system for the TB programme

WHAT ARE KEY ISSUES IN COMPLETING THE TB NOTIFICATION FORMS?

- TB is an infectious disease with major public health significance; therefore a notifiable medical condition
- TB notifications are reported to the South African Disease Notification System which is a passive surveillance system
- Complete and submit a notification form for each newly diagnosed TB case

OBTAIN ACCURATE CONTACT AND ALTERNATE CONTACT DETAILS TO ENSURE FOLLOW-UP IN THE EVENT OF DEFAULT. CONFIRM CONTACT DETAILS AT EACH VISIT

MONITORING AND EVALUATION OF TB PROGRAMME >>>

TB IDENTIFICATION REGISTER

1. All clients with presumptive TB should be entered in the TB identification register.
2. "Specimen Code" = barcode on the laboratory request form. It is important to make sure that each specimen has the correct code-label attached to it. If diagnosed with Xpert the patient will also have smear taken for baseline monitoring. Both barcodes must be affixed into the register:
   - Smear
   - Xpert
3. HIV status must be recorded on the register.
4. The treatment start date needs to be recorded.
   a. If the patient died before treatment started – patient still needs to be registered, but as a "Died before Rx started".
   b. If a patient is lost to follow-up, they are then registered as a "did not start treatment" = Primary loss to follow up
5. Summary for TB Identification Register: At the end of each register is a copy of the summaries that need to be filled in:
   a. at the end of each month to be submitted on DHIS
   b. at the end of each quarter, these totals need to be sent to province as part of the quarterly report

TUBERCULOSIS REGISTER

1. Each register page is followed by three carbonized pages. The set of four must be separated by the thick divider (on the right side of the register) to prevent bleed-through.

2. Use only a BALL-POINT pen to fill in the register. PRESS FIRMLY.
3. No overwriting is allowed as this might not transfer properly to the carbonated papers below.
4. Care should be taken to strike the number where a mistake has been made and the proper number written within the row provided.
5. The facility name is entered at the top left of each set of pages. This must be included in order for the pages to be re-assembled at sub-district-level.

6. As patients are diagnosed, they are entered into the register.
7. The "TB Registration Number" needs to be chronologically numbered – as patients present themselves, e.g. ####/yy
8. A new page is started at the beginning of each new month even if the previous page has space for more patient entries.

Page	Use	Action	Timeframe
Pink Initial	Define case finding cohort	Send to sub-district	Submit to the sub-district for capturing as soon as the page is full and accurately filled. (E.g. Information of ten patients up to the pre-sputum)
Yellow Follow-up 1	Update patient information (smear conversion)	Send to sub-district	Submit to the sub-district for capturing as soon as the page is full and accurately filled. (E.g. Information of ten patients up to the smear conversion at 2/3 months)
Green Follow –up 2	Update patient information (outcome)	Send to sub-district	Submit to the sub-district for capturing as soon as the page is full and accurately filled. (E.g. Information of ten patients)
White	Facility record	Retain in facility	Retain in facility

9. The revised TB Recording and Reporting System depends on the flow of information from several sources:

10. At sub-district level, the TB coordinator (or other designated person responsible for TB) is responsible for re-assembling the submitted registers into facility-specific order and entering the new or updated information into the TB Registration software.
11. Signatures of the facility manager and TB coordinator are required at the bottom of each page submitted.

IPT REGISTER

1. ALL patients initiated on IPT must be entered into this register
2. Each month should start on a new page
3. Each page should have the year and month clearly written at the top of the page.
4. The patient number should consist of a number/mm/yy. Eg, 001/11/2012.
5. The registration date is the date the patient was initiated.

WHAT ARE THE KEY IPT INDICATORS?

- HIV positive client eligible for IPT
- HIV positive client initiated on IPT

MONITORING AND EVALUATION OF TB PROGRAMME

THE 90-90-90 STRATEGY HAS BEEN ADOPTED FOR TB:

- 90% of high risk and vulnerable groups screened for TB
- 90% of prevalent TB diagnosed and treated
- 90% of TB treated successfully

It is important for facilities to understand and review the performance of the TB programme so that they can contribute to achieving these goals. This can be done through cascade analysis at facility level.

HOW TO CONDUCT CASCADE ANALYSIS AT FACILITY LEVEL?

- Facilities must analyse TB programme data on a monthly and quarterly basis.
- This will help to identify gaps in patient management and enable the facility to implement strategies to address them early, thus preventing adverse treatment outcomes.

DATA ELEMENTS	DESCRIPTION
TB DETECTION	
Total PHC Headcount	Total number of patients seen at the facility (OPD in case of hospital)
Number of patients screened for TB symptoms	This includes all patients screened using the symptom screening tool. *Source document: TB symptom screening Book*
Number of patients found to have TB symptoms	Includes all patients with a positive symptom screen (with or without a cough) *Source document: TB symptom screening Book*
Number of patients with TB symptoms tested for TB	Includes all tests conducted (bacteriology, histology, chemistry, x-rays) to confirm TB in the patient. This includes patients who were referred to another facility for further investigation and down referred with a diagnosis of TB *Source document: TB identification register*
Number of patients tested for TB with a positive TB result	Includes all tests conducted (bacteriology, histology, chemistry, x-rays) to confirm TB in the patient. This includes patients who were referred to another facility for further investigation and down referred with a diagnosis of TB *Source document: TB identification register*
Number of patients tested positive for TB started on TB treatment	All TB patients who are started on treatment. This includes patients who were referred to another facility for further investigation and down referred with a diagnosis of TB *Source document: TB register*
CONTINUUM OF CARE (Cohort analysis)	
Number of TB patients successfully completing the intensive phase of treatment	Total number of ALL TB patients who completed intensive phase of treatment at 2 months and changed to continuation phase
Number of TB patients successfully completing treatment	Total number of patients who are cured and those who completed treatment at the end of the continuation phase (6 -9 months)

Refer to the National TB guidelines for a full description of TB programme indicators

PROCEDURES 8

TUBERCULIN SKIN TEST (TST) >>>

HOW DO I ADMINISTER A TST?

WHAT EQUIPMENT IS REQUIRED?

- 2 units (0.1 ml) of tuberculin purified protein derivative PPD-RT23 2 TU
- A tuberculin syringe with a short 27-gauge needle with a short bevel
- Check the expiration date on the vial

WHAT SHOULD I TELL THE PATIENT?

- Explain the procedure to the caregiver or to the patient if age-appropriate
- Explain the need to return in 48-72 hours for TST reading

WHAT DOES THE PROCEDURE ENTAIL?

a) Choose an injection site

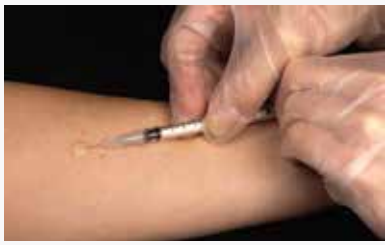
- Place the left forearm on a well-lit surface with the palm facing upwards
- Locate an area midway between the elbow and wrist which is free of any scars or sores

b) Prepare the tuberculin

- Draw up 0.1 ml of tuberculin

c) Inject tuberculin

- Insert the needle slowly with the bevel facing upwards at an angle of 5-15 degrees and inject the tuberculin
- The needle bevel should be visible just below the surface of the skin
- The PPD is injected between layers of skin (intradermally)



Administration of PPD

d) Check injection site

- After the injection is given, a flat wheal of 8-10 mm in diameter should be visible
- If it is not visible the PPD has been injected too deeply and the injection should be repeated at a site at least 5 cm away from the first injection or on the right forearm
- A pen can be used to draw a wide circle around the injection site to indicate the area

e) Record information

- Record the relevant information including the date, time and location of the test

TUBERCULIN SKIN TEST (TST) >>>

HOW DO I READ A TST?

WHAT EQUIPMENT IS REQUIRED?

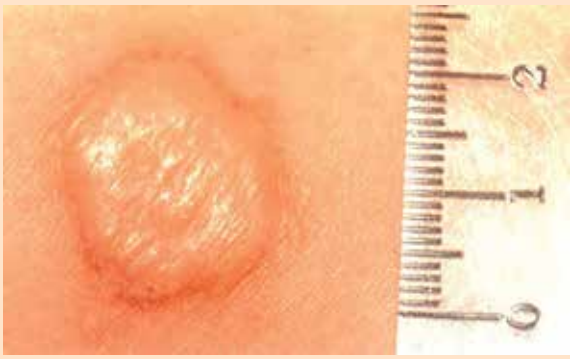
- Pen
- Clear flexible ruler

WHAT DOES THE PROCEDURE ENTAIL?

a) Read the results 48-72 hours after administration of TST

b) Palpate and identify the induration

- Inspect the site under good lighting and identify the induration (not the erythema)
- Palpate the induration by using your fingertips to identify the edges of the induration
- The edges of the induration should be marked with a pen to help measure accurately
  - Draw horizontal lines from the periphery towards the area of induration
  - The raised edges of the area of induration will prevent the pen from drawing onto the indurated area



c) Measure the diameter of the induration

- Use the ruler to measure the widest transverse diameter in millimetres

d) Record the diameter of the induration

- Do not record as positive or negative
- Record the measurement in millimetres

WHAT ARE THE CRITERIA FOR A POSITIVE TST RESULT?

IMMUNE STATUS	HIV-INFECTED / SEVERE MALNUTRITION	HIV-UNINFECTED
DIAMETER OF INDURATION	5 mm or more	10 mm or more

TUBERCULIN SKIN TEST (TST)

HOW IS A POSITIVE TST INTERPRETED?

- A positive test indicates infection with TB, but not necessarily presence or extent of TB disease.
- It shows that the person has at some time been infected with M. tuberculosis or been vaccinated
- In a child under 5 years or an HIV-infected child of any age, a positive skin test indicates recent infection and is a risk factor for progression to disease. In the presence of other features such as a history of a TB contact, signs and symptoms of TB and chest x-ray changes, a positive tuberculin skin test is suggestive of TB disease in children
- In adults, it is used to diagnose latent infection in immunosuppressed patients who would benefit from IPT
- Children under the age of 5 years, HIV-infected children of any age and HIV-infected adults, who have a positive skin test and no symptoms or signs of TB, should be put on TB prophylaxis for six months.

HOW IS A NEGATIVE TST INTERPRETED?

- A negative tuberculin skin test does not exclude TB.
- Various conditions may cause a false negative reaction including:
  - HIV infection
  - severe malnutrition
  - severe viral infections (e.g. measles, chicken pox)
  - cancer
  - immuno-suppressive drugs (e.g. steroids)
  - severe disseminated TB.

SPUTUM COLLECTION IN ADULTS AND OLDER CHILDREN >>>

WHAT EQUIPMENT IS REQUIRED?

- Sterile specimen jar (label with patient details)
- NHLS specimen request form and plastic specimen packet
- Preferably outside in a private well ventilated area, sheltered from rain
  - must ***not*** be done in bathrooms

WHAT SHOULD I TELL THE PATIENT?

- Explain that sputum is required to diagnose TB
- Ask the patient to do the following:
  - Rinse his/her mouth with water
  - Take a deep breath
  - After exhalation, inhale sharply and cough strongly
  - Expectorate sputum into the jar
  - Close the jar tightly
  - Clean the outside of the jar
  - Place the jar in the plastic specimen packet

ALWAYS LABEL SPECIMEN JARS WITH:

- Patient name
- Clinic or hospital name
- Clinic or hospital number
- Date of specimen collection
- Whether it is a
  - pre-treatment specimen
  - follow-up (7 weeks) specimen
  - end-of-treatment (23 weeks) specimen
- Attach NHLS barcode

COMPLETE THE LABORATORY FORM:

- Name of clinic/ hospital
- Patient details
- Name and registration number of person requesting test
- Date, time and type of specimen collected
- Relevant clinical information
- Tick test that is required
  - GeneXpert
  - TB Microscopy
  - TB Culture

See Annexures for sample NHLS request form

WHAT SHOULD I DO ON RECEIPT OF THE SPECIMEN FROM THE PATIENT?

- Label the specimen request form clearly
- Send the specimen to the lab as soon as possible
- Store in fridge if transport not immediately available
- Keep in cold, dark container while being transported

WHAT SAFETY PRECAUTIONS SHOULD I ADHERE TO?

- Do not be near the patient when he/ she coughs
- Wash hands immediately after handling sputum specimen

HOW SHOULD I RECORD THE TEST?

- Record the patient's details in the TB Identification Register, include the NHLS barcode
- Record the NHLS barcode and details of the test in the patients' record

SPUTUM COLLECTION IN ADULTS AND OLDER CHILDREN

PATIENT INFORMATION SHEET

WHY IS A SPUTUM TEST NECESSARY?

Tuberculosis is a very common but treatable sickness of the lungs. When a person has TB, the TB germ can be found in their sputum. Checking your sputum is the best way to find out if you have TB disease.

To ensure that your test is accurate, you must cough up sputum from deep inside your lungs. Sputum from your lungs is usually thick and sticky. Saliva comes from your mouth and is watery and thin. Do not collect saliva.

HOW TO COLLECT A SPUTUM SAMPLE

Your nurse will give you a special plastic cup for collecting your sputum. The nurse will supervise you during the procedure. Follow these steps very carefully:

The cup is very clean. Don't open it until you are ready to use it.	
Rinse your mouth with water. Go outside to an open and well ventilated area to collect sputum. This helps protect other people from TB germs when you cough. Take a very deep breath and hold the air for 5 seconds. Slowly breath out. Take another deep breath and cough hard until some sputum comes up into your mouth.	
Spit the sputum into the plastic cup. Keep doing this until you have about 1 teaspoon of sputum.	
Screw the lid on the cup tightly so it doesn't leak. Wash and dry the outside of the cup. Put the cup into the bag the nurse gave you.	

Contact details of PHC:

Clinic name: .....

Facility manager: .....

Clinic telephone number: .....

Tips: If you cannot cough up sputum, try breathing steam from a hot shower or pan of boiling water first, and then cough.

INDUCED SPUTUM COLLECTION IN ADULTS AND OLDER CHILDREN >>>

- This procedure is used in the diagnosis of TB when patients are unable to expectorate spontaneously
- Hypertonic saline is nebulised in order to irritate the airway, increase and liquefy secretions and induce coughing and expectoration

WHAT EQUIPMENT IS REQUIRED?

- Sterile specimen jars identified with patient's details
- NHLS specimen request form and plastic specimen packet
- Gloves
- Nebulising mask and nebuliser
- Bronchodilater e.g. salbutamol
- Oxygen supply
- N95 mask for HCW
- Hypertonic saline solution 5%
- 19 gauge needle
- 20 ml syringe
- Cup of water

WHAT SHOULD I TELL THE PATIENT?

- The procedure should be fully explained to adults and older children, including the risks and benefits

WHAT DOES THE PROCEDURE ENTAIL?

- The patient should rinse his/her mouth with water prior to starting
- Pre-medicate with salbutamol in patients with asthma or severely impaired lung function
- Load 5-10 ml of 5% hypertonic saline solution into the nebuliser cup
- Instruct the patient to take deep breaths while being nebulised
- Nebulise the patient for approximately 5 minutes
- If the patient does not cough spontaneously, ask him/her to attempt a forced cough
- If necessary, use gentle chest physiotherapy
- Deep cough sputum specimens should be expectorated into the specimen jar
- Saliva should be discarded into a separate container
- Stop the procedure when:
  - The patient has produced 5-10 ml of sputum
  - The patient has been nebulised for 15 minutes
  - The patient feels dyspnoeic, light-headed, nauseous or develops respiratory distress
- Observe the patient at all times during the procedure

INDUCED SPUTUM COLLECTION IN ADULTS AND OLDER CHILDREN

WHAT SAFETY PRECAUTIONS MUST BE ADHERED TO?

FOR THE PATIENT:

- Safe even in young infants, but staff must be adequately trained
- Low-risk procedure, but may be poorly tolerated in children with high supplementary oxygen requirements
- Contra-indications are severe respiratory distress, reduced level of consciousness, severe bronchospam, bleeding tendency (as the procedure may precipitate severe nosebleeds)
- Adverse events include coughing, mild wheezing and nosebleeds
- Children requiring supplemental oxygen should have continuous saturation monitoring during the procedure
- If saturation drops below 88% for longer than one minute, the procedure should be abandoned and the child stabilised before the procedure reattempted

FOR HEALTH CARE WORKER:

- This procedure is high risk when done on a patient with suspected TB – health care workers present should wear N95 masks
- This is an aerosol-generating procedure and should thus be done in an isolation room with adequate infection control

WHAT SHOULD I DO ON RECEIPT OF THE SPECIMEN?

- Ensure the patient's details are recorded on the specimen jar
- Place the NHLS barcode on the specimen
- Label the specimen request form clearly
- Indicate what tests are required (microscopy only, or microscopy, culture and sensitivity, or Xpert MTB/RIF)
- Send the specimen to the lab as soon as possible or store in a fridge if awaiting transport

HOW IS THE TEST RECORDED?

- Record the patient's details in the TB Identification Register
- Record the NHLS barcode and details of the test on the patient's record

INDUCED SPUTUM COLLECTION IN CHILDREN >>>

WHAT EQUIPMENT IS REQUIRED?

- Sterile specimen jar (label with patient details)
- NHLS specimen request form and plastic specimen packet
- Gloves
- Nebulising mask and nebuliser
- Bronchodilator (e.g. salbutamol)
- Oxygen Supply
- Metered dose inhaler (MDI)
- Spacer device and BabyMask (with which to administer the bronchodilator)
- N95 mask for person(s) conducting the procedure
- 5 ml hypertonic (5%) saline
- Mucus extractor with feeding tube catheter (usually 5 to 8 French)
- Wall or portable suction
- Normal saline flush with syringe (5 ml)
- Alcohol or chlorhexidine

WHAT SHOULD I TELL THE PATIENT?

- The procedure must be explained to the parent and the child, if age-appropriate
- The child must be nil per os for at least 3 hours

WHAT DOES THE PROCEDURE ENTAIL?

- It should ideally be performed by two health care professionals: one to collect the specimen, and another to restrain the child
- If the child is medically stable, the caregiver can restrain the child (the caregiver need not wear an N95 mask if he/she resides with the child)
- Because hypertonic saline nebulisation may precipitate wheezing in children, two puffs of a bronchodilator are administered using an MDI, via a spacer device and BabyMask, 5 minutes before giving the nebulisation
- Administer 5 ml hypertonic saline via a nebulising mask, for 10-15 minutes.
- If necessary, gentle chest physiotherapy, using cupped hands, can be performed to loosen secretions
- Older children who are able to expectorate can do so
- If the child is unable to expectorate, collect nasopharyngeal secretions:
  - gently insert a 5 to 8 French feeding tube into the nasopharynx
  - apply suction when the tip of the catheter is in the nasopharynx (this prevents the collection of nasal secretions which may reduce the quality of the specimen)
  - Once an adequate volume (1-2 ml) of sputum has been collected into the mucus extractor chamber, discontinue suctioning and withdraw the feeding tube from the nasopharynx
  - Use 5 ml normal saline to flush residual secretions adhering to the walls of the feeding tube into the mucus extractor chamber. This also helps to optimise the volume of the induced sputum specimen
- Observe the patient at all times during the procedure
- Disinfect and sterilise any equipment (i.e. spacer device, BabyMask) that will be reused
- Discard nebulising mask and used feeding tubes

INDUCED SPUTUM COLLECTION IN CHILDREN

WHAT SAFETY PRECAUTIONS MUST BE ADHERED TO?

FOR THE PATIENT:

- Safe even in young infants, but staff must be adequately trained
- Low-risk procedure, but may be poorly tolerated in children with high supplementary oxygen requirements
- Contra-indications are severe respiratory distress, reduced level of consciousness, severe bronchospam, bleeding tendency (as the procedure may precipitate severe nosebleeds)
- Adverse events include coughing, mild wheezing and nosebleeds
- Children requiring supplemental oxygen should have continuous saturation monitoring during the procedure
- If saturation drops below 88% for longer than one minute, the procedure should be abandoned and the child stabilised before the procedure reattempted

FOR HEALTH CARE WORKER:

- This is an aerosol-generating procedure and should therefore be done in an isolation room with adequate infection control
- Staff members performing the procedure should wear N95 masks

WHAT SHOULD I DO ON RECEIPT OF THE SPECIMEN?

- Record the patient's details on the specimen jar
- Place the barcoded NHLS sticker on the specimen
- Send the specimen to the lab as soon as possible or store in a fridge if awaiting transport

WHICH TESTS SHOULD I REQUEST IN CHILDREN?

- Indicate clearly which tests are required:
  - microscopy, culture and DST or
  - Xpert MTB/RIF
- TB microscopy is usually negative in small children, and should not be relied upon in making a diagnosis of childhood TB

HOW IS THE TEST RECORDED?

- Record the patient's details in the TB Identification Register
- Record the NHLS barcode and details of the test on the patient's record

COLLECTION OF GASTRIC ASPIRATES IN CHILDREN >>>

WHAT EQUIPMENT IS REQUIRED?

- Sterile specimen jar (label with patient details)
- Nasogastric tube (usually 10 French or larger)
- Syringe (5, 10, 20, or 30 ml)
- Litmus paper
- Tape measure
- Normal saline
- Sodium bicarbonate solution (8%)
- Alcohol or chlorhexidine
- NHLS specimen request form and plastic specimen packet

WHAT SHOULD I TELL THE PATIENT?

- Explain the procedure to the child's parents
- Children should be nil per os for 4 hours and infants for 3 hours prior to the procedure.

WHAT DOES THE PROCEDURE ENTAIL?

- **One specimen should be taken on each of 3 three consecutive mornings as soon as the child wakes up**
- Position the child on his/her back or side and have an assistant hold the child
- Measure the distance between the nose and stomach to gauge the distance required to insert the tube into the stomach
- Attach a syringe to the nasogastric tube
- Gently insert the tube through the nose and advance it into the stomach
- Aspirate 2-5 ml of gastric content
- Check the position of the tube:
  - This can be done by testing the aspirated contents with litmus paper
    - Due to their acidity, gastric contents turn blue litmus paper red
  - The tube position can also be checked by pushing 3-5 ml of air into the stomach using the syringe and listening over the stomach with a stethoscope.
- If no fluid is withdrawn during the aspiration, insert 5-10 ml of normal saline and aspirate again
- This can be repeated up to 3 times
- Then withdraw 5-10 ml of gastric contents if possible and transfer the fluid into the specimen jar
- Add an equal volume of sodium bicarbonate solution to the fluid to neutralise the gastric contents and prevent destruction of the mycobacteria if present
- Make sure that the cap of the specimen jar is securely fastened, to prevent leakage of the specimen
- Wipe the specimen jar with alcohol and label it
  - The patient's details, the collection date and time should be written on the container
  - Place the NHLS barcoded sticker on the specimen
- Fill out the lab requisition forms clearly
- The specimens should be transported to the lab as soon as possible
- If the wait for transport is more than 4 hours, keep specimens in a fridge at 4-8°C until transported
- Feed the child normally after the procedure

COLLECTION OF GASTRIC ASPIRATES IN CHILDREN

WHAT SAFETY PRECAUTIONS MUST BE ADHERED TO?

FOR THE PATIENT:

- This is a low-risk procedure, so intensive monitoring of the child is not required
- Children with a low platelet count or bleeding tendency should not undergo this procedure as insertion of a feeding tube may precipitate severe nose bleeds

FOR THE HEALTHCARE WORKER:

- Gastric aspiration is not an aerosol-generating procedure and young children are not highly infectious
- It is therefore considered a low-risk procedure for TB transmission and can be done at the child's bedside or in a routine procedure room

HOW IS THE TEST RECORDED?

- Record the NHLS barcode number on the patient's record
- The patients details and the specimen type must be recorded in the TB Identification Register

FINE NEEDLE ASPIRATION >>>

- Fine needle aspiration is a simple procedure and can be performed safely by trained nurses in out-patient and in resource-limited settings
- It provides material for Xpert, smear microscopy, culture and DST
- Clients with deeper masses should be referred for ultrasound guided FNA

WHAT EQUIPMENT IS REQUIRED?

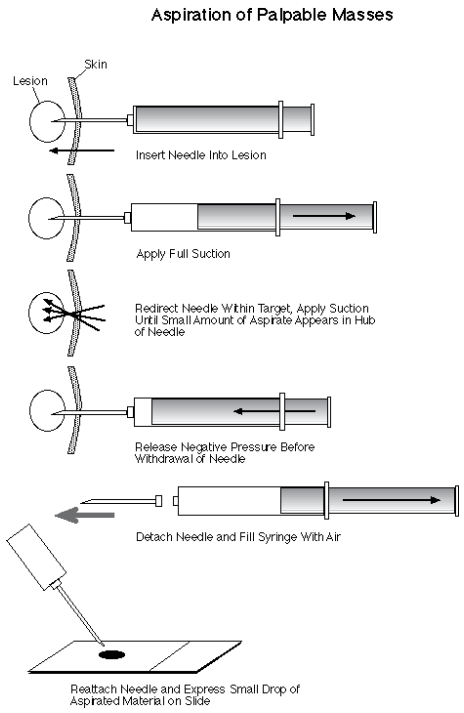
- Liquid culture medium (TB Bactec bottle)
- 22 or 23G cutting needles
- 10 ml disposable plastic syringes
- Alcohol swabs
- NHLS specimen request form and plastic specimen packet
- Gloves
- Glass cytology slides
- Spray fixative or 95% alcohol

WHAT SHOULD I TELL THE PATIENT?

- Explain the procedure
- Warn the patient that pain might be experienced

WHAT DOES THE PROCEDURE ENTAIL?

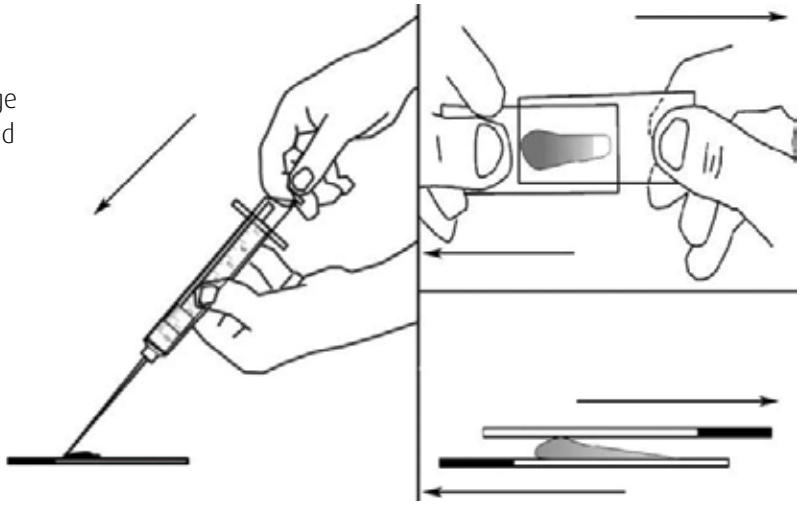
- Identify the best site for aspiration
- Clean the skin and wait for the area to dry
- Immobilise the mass
- Position the needle so as to be able to access the entire mass without passing through muscles e.g. sternocleidomastoid
- Insert the needle firmly and apply constant suction throughout of no more than 1 ml
- Aspirate, moving the needle in a fan-like motion throughout the mass
- When there is material in the hub of the needle, release suction and withdraw the needle
- Ask the assistant to apply pressure to the wound



FINE NEEDLE ASPIRATION >>>

PREPARE THE SLIDE:

- Remove the needle from the syringe
- Pull 10 ml of air into the syringe and reattach the needle
- Use the air to expel the material in the needle onto the slide
- Place the second slide face down on the first; allow the material to spread
- Gently separate the slides
- Fix one slide with alcohol or spray fixative and allow the other to air dry

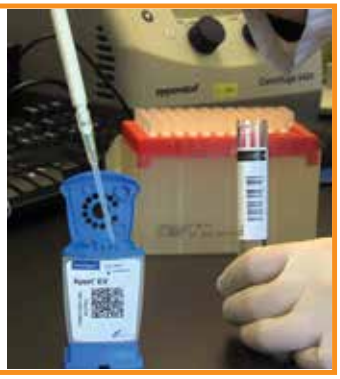


PREPARE THE CULTURE:

- Prepare the TB Bactec bottle before you begin by removing the lid and cleaning the rubber stopper with alcohol
- After preparing the slide, the residual material in the needle may be rinsed directly into TB culture medium
- Withdraw liquid media from the liquid culture bottle into the syringe
- Expel the liquid back into the bottle, thereby using the culture medium to rinse the syringe in a sterile manner
- If TB culture bottle is not available the needle may be rinsed in sterile saline but the yield will not be as good.
- If pus is aspirated from the node, 1 - 2 drops only should be placed in the transport medium. This is to prevent a false positive culture or inactivation of the molecular test due to inhibitors in the pus. Aspirated pus may also be placed in a sterile tube and submitted to the microbiology laboratory.

PREPARE XPERT SPECIMEN:

- The residual material after preparing the slide may be rinsed in the TB transport medium and sent for the Xpert® MTB/ RIF test



FINE NEEDLE ASPIRATION

WHAT SAFETY PRECAUTIONS ARE REQUIRED?

- Observe universal precautions
- Do not recap the needle and dispose of all sharps into a biohazard container

WHAT COMPLICATIONS OCCUR?

- Complications such as haematoma are rare

HOW DO I RECORD THE TEST?

- Record the NHLS barcode number on the patient's record
- The patients details and the specimen type must be recorded in the TB Identification Register

ANNEXURES 8

PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE

NATIONAL HEALTH LABORATORY SERVICE

Practice number 5200296

PRIMARY HEALTH CARE

MARK IF URGENT ☐

NHLS LAB NUMBER BARCODE

AAAA0001P

LOC

CHC / CLINIC / HOSP	
WARD	
eGK APPROV. CODE	
COPY REPORT TO	

SPEC

SPECIMEN	
ANATOMICAL SITE	
COLLECTION DATE	TIME
COLLECTED BY	

PATIENT

PATIENT ID NO	ID / Passport
HOSPITAL NUMBER	
SURNAME	
FIRST NAME	SEX M F
DATE OF BIRTH (D D / M M / Y Y Y Y)	AGE
RACE	TITLE
PATIENT ADDRESS	
PATIENT TEL NO	H: W: C:

CLIN

ICD10 DIAGNOSIS CODES	
Warfarin	Heparin

HCW

CLINICIAN / HCW NAME	
HPCSA / SANC NO	
PRACTICE NO	
CONTACT NO	
EMAIL ADDRESS	
CLINICIAN'S SIGNATURE	

PRIVATE ACCOUNT

AUTHORISATION NO	FEE CLASS
MEDICAL AID	PLAN
MEDICAL AID NO	DEP CODE
MEMBER NAME	
MEMBER ID NO	
MEMBER ADDRESS	
MEMBER TEL NO	
EMPLOYER	
MEMBER'S SIGNATURE	I consent to tests and take responsibility for payment of this account

HAEMATOLOGY

P ☐	Haemoglobin	R16
P ☐	White cell count	R16
P ☐	Platelet count	R19
P ☐	Rhesus factor	R31
P ☐	Direct Coombs	R31

CHEMICAL PATHOLOGY

Y ☐	Potassium	R16
Y ☐	Creatinine	R16
Y ☐	ALT	R16
Y ☐	Total Cholesterol	R41
Y ☐	Triglyceride	R60
P ☐	HbA1c	R77
Y ☐	TSH	R 158

SEROLOGY

Y ☐	Syphilis serology	>R18
Y ☐	Hepatitis B Surface Antibody	R113
Y ☐	Hepatitis A IgM	

MICROBIOLOGY TESTS

- ☐ MC & S
- ☐ Blood culture
- ☐ Fungal microscopy & culture
- ☐ Parasites
- ☐ Cryptococcal antigen
- ☐ Malaria

OTHERTESTS

MUST BE APPROVED BY A SENIOR DOCTOR

For all TB and HIV - specific tests: TURN OVER FORM

UNIPRINT-F VERSION MAY2101

P02A1392

FOR LABORATORY USE ONLY				
Yellow / Red with gel		Purple		Received
Red without gel		Grey		
White (PPT)		Blue		
Blood culture		Black		
Sterile screwtop tube		Green		Labelled
Specimen container		DBS		
Other				

NHLS LAB NUMBER

NHLS LAB NUMBER

LOC - Location detail • HCW - Healthcare Worker • SPEC - Specimen • CLIN - Clinical detail

PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE PLEASE TEAR HERE

NATIONAL HEALTH LABORATORY SERVICE

Practice number 5200296

NATIONAL PRIORITY PROGRAMME

NHLS LAB NUMBER BARCODE

AAAA0001P

TB TESTS

SUSPECTED TB (PRE-TREATMENT):

- ☐ TB GeneXpert R173
- ☐ TB Microscopy R24
- ☐ TB Culture >R96

ON TREATMENT (MONITORING)

- ☐ TB Microscopy R24
- ☐ TB Culture >R96

DRUG SUSCEPTIBILITY TESTING:

- ☐ 1st line / Line probe (rifampicin and isoniazid) R176
- ☐ 2nd line R71

FOLLOW UP (only if smear pos after 7 weeks or treatment interuptions)

- ☐ TB GeneXpert R173

TB DATA COLLECTION - MUST BE COMPLETED

SUSPECTED TB (PRE-TREATMENT): DS: drug sensitive DR: drug resistant

Tick all that apply ✓

- ☐ Suspected **DS-TB** (not on treatment)
- ☐ Suspected **DR-TB** (not on treatment)
- ☐ **Previously treated for DS-TB**
- ☐ Previously treated for **DR-TB**

ON TREATMENT (MONITORING): Number of months on treatment

- ☐ **DS-TB** (on treatment) ☐ 2-3 mnths ☐ 4-7 mnths
- ☐ **DR-TB** (on treatment) ☐ 1-3 mnths ☐ 4-7 mnths ☐ > 7 mnths
- ☐ **DS-TB** failing treatment or persistently smear-positive ☐ 2-3 mnths ☐ 4-7 mnths ☐ > 7 mnths

COMMENTS / OTHER TESTS:

PATIENT'S HIV STATUS:

Pos ☐ Neg ☐ Unknown ☐

HIV - SPECIFIC TESTS

P ☐ HIV serology R50

P ☐ CD4 count (PLG) R60

W P ☐ HIV Viral Load R306

P ☐ DBS ☐ HIV PCR R342

P ☐ HIV Drug Resistance R1872

HIV drug resistance genotype testing **will not be done** if the HIV status, results and treatment questions are not completed.

The DOH has approved HIV drug resistance genotype testing only for certain categories.

HIV DATA COLLECTION - MUST BE COMPLETED

If ordering HIV serology, please supply:

Clinic's HIV rapid result (if available): _____

If ordering CD4 count, please tick one category:

- **A1** ☐ First ever CD4 count
- **A2** ☐ CD4 count taken previously, not yet in ART care
- **A3** ☐ In ART care (please mark current drugs)

If ordering HIV viral load, please tick one categorty:

- **B1** ☐ First ever viral load (paediatric)
- **B2** ☐ Routine monitoring
- **B3** ☐ Other (e.g. illness, virological failure)

If ordering HIV PCR, please answer:

- Has mother received PMTCT? Yes ☐ No ☐
- Has infant received PMTCT? Yes ☐ No ☐
- Infant breastfed in past 6 weeks? Yes ☐ No ☐

If ordering HIVDR, please tick one category and supply results:

- ☐ Baseline testing
- ☐ 1st line failure
- ☐ 2nd line failure
- ☐ 3rd line failure

HIV viral load previous: _____ Date _____

HIV viral load latest: _____ Date _____

Latest CD4 count: _____ Date: _____

Please tick current and previous ARV drugs

According to national ARV guidelines virological failure is defined as 2 consecutive viral loads > 1000 cp/ml at least 2 months apart.

Months on ARV treatment:

- **C1** ☐ Baseline / work-up
- **C2** ☐ 6 months
- **C3** ☐ 12 months
- **C4** ☐ 24 months
- **C5** ☐ 36 months
- **C6** ☐ Other

Currently off ART due to:

- **D1** ☐ Adverse event
- **D2** ☐ Non-adherence
- **D3** ☐ Toxicity
- **D4** ☐ Other

Current ARV drugs:

- ☐ FDC (Fixed dose combination)
- ☐ AZT ☐ 3TC ☐ EFV
- ☐ ABC ☐ ddI ☐ NVP
- ☐ TDF ☐ d4T ☐ LPV/r
- ☐ Other ARVs: _____

Previous ARV drugs:

- ☐ FDC (Fixed dose combination)
- ☐ AZT ☐ 3TC ☐ EFV
- ☐ ABC ☐ ddI ☐ NVP
- ☐ TDF ☐ d4T ☐ LPV/r
- ☐ Other ARVs: _____

P02A1392

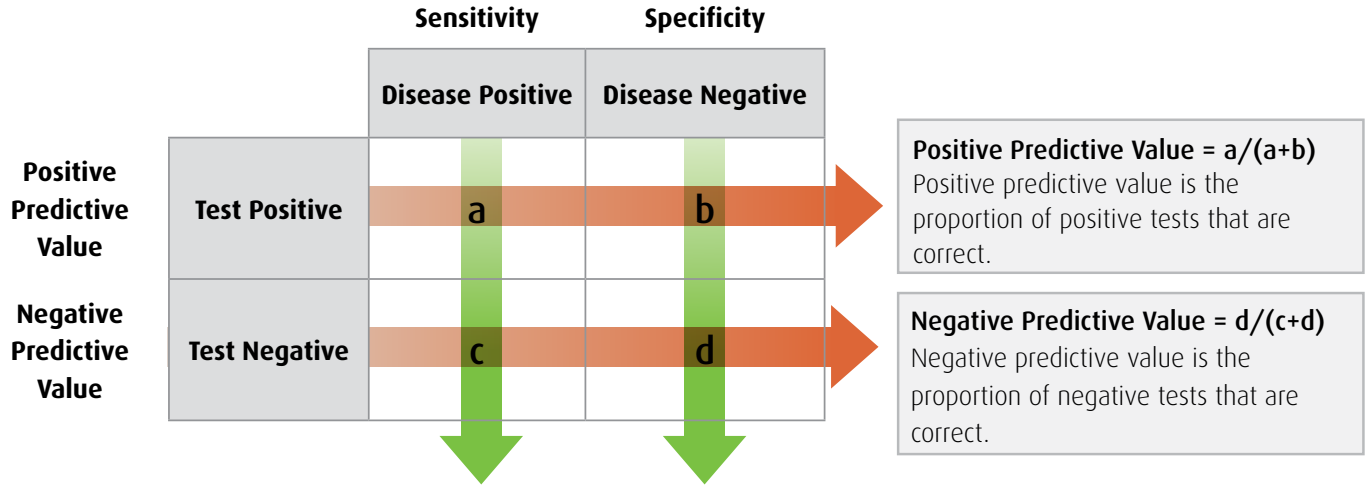
AAAA0001P AAAA0001P AAAA0001P

AAAA0001P AAAA0001P AAAA0001P

COMPARING DIAGNOSTIC TESTS

HOW ARE DIAGNOSTIC TESTS COMPARED?

Diagnostic tests can be compared by evaluating their 'sensitivity' and 'specificity' when compared to the 'gold standard', which is the best available test for the condition. For TB, the gold standard is TB culture.



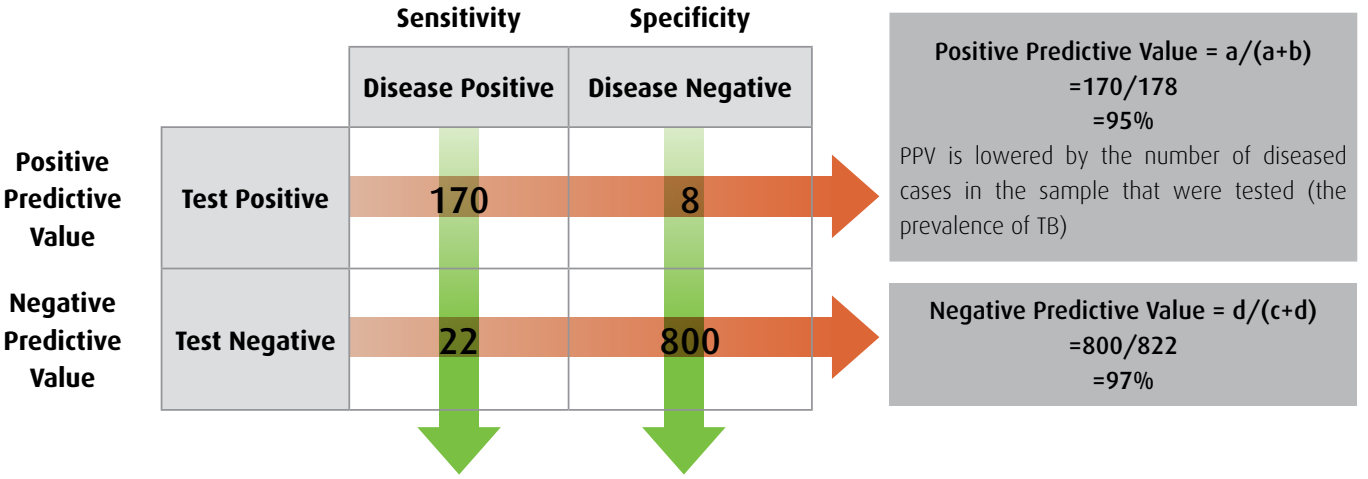
Positive Predictive Value = a/(a+b)
Positive predictive value is the proportion of positive tests that are correct.

Negative Predictive Value = d/(c+d)
Negative predictive value is the proportion of negative tests that are correct.

Sensitivity= a/(a+c)
Sensitivity is the proportion of diseased cases identified by the test. Low sensitivity means that many cases are falsely negative.

Specificity= d/(b+d)
Specificity is the proportion of cases without disease that are identified as being disease-free by the test. Low specificity means that many cases are falsely positive.

FOR EXAMPLE, WHEN PERFORMING XPERT MTB/RIF AND TB CULTURE ON 1000 CONSECUTIVE TB SUSPECTS, THE FOLLOWING RESULTS COULD BE OBTAINED:



Positive Predictive Value = a/(a+b)
=170/178
=95%
PPV is lowered by the number of diseased cases in the sample that were tested (the prevalence of TB)

Negative Predictive Value = d/(c+d)
=800/822
=97%

Sensitivity = a/(a+c)
=170/192
=88%
Sensitivity is lowered by false negative tests (if fewer than 22 were falsely negative, the test would have a higher sensitivity)

Specificity = d/(b+d)
=800/808
=99%
Specificity is lowered by false positive tests (if fewer than 8 were falsely positive, the test would have a higher specificity)

ADVERSE DRUG REACTION REPORT FORM >>>

health
Department: Health
REPUBLIC OF SOUTH AFRICA

NATIONAL PHARMACOVIGLANCE CENTRE (NPC)
TEL: 012 395 9506/ 8099
Fax2email: 086 241 2473
Email: npc@health.gov.za

SUSPECTED ADVERSE DRUG REACTION REPORT HIV/AIDS AND TB TREATMENT PROGRAMME

FACILITY NAME			
SUB-DISTRICT			
DISTRICT		**TEL**	
PROVINCE		**FAX**	

(Please see instructions on back of page. Please send duplicate to NDoH and complete additional information on a separate sheet)

PATIENT DETAILS:

Patient Initials			**Age**		**Date of Birth (dd/mm/yyyy)**	
ID/Reference No			**Gender**	☐ **M** ☐ **F**	**Pregnant**	☐ **Yes** ☐ **No**
Allergy	**Weight (kg)**		**Height (cm)**		**Estimated Gestational Age**	

MEDICINES (AND CONCOMITANT MEDICINES, INCLUDING HERBAL PRODUCTS, IF KNOWN)

Medicine	Suspect drug/ Trade Name	Dose	Interval	Route	Date started	Date stopped	Prescriber (Dr/ Pharm/Nurse)

Key: **1.** AZT **2.** 3TC **3.** TDF **4.** FTC **5.** D4T **6.** ABC 7. DDI **8.** NVP **9.** EFV **10.** ETR **11.** ATV **12.** DRV **13.** RTV **14.** LPV/r **15.** ATV/r 15.R **16.** RAL **17.** TDF+FTC **18.** TDF+FTC+EFV **19.**R **20. 20.** H **21.** Z **22.** E **23.** RH 24. RHZE **25.** Km **26.** Am **27.** Cm **28.** Mfx**29.** Lvx**30.** Gfx**31.** Eto**32.** Trd**33.** Pto**34.** Cs **35.** PAS **36.** Cfx**37.** AZI **38.** Clr**39.** Amx/Clv**40.** MEROPENEM **41.** Lzd**42.** Imipenem**43.** Bedaquiline**44.** Delamanid**45.** PA 824 **46.** High Dose INH

ADVERSE DRUG REACTION

Date of onset of reaction (dd/mm/yyyy) _____ Date Reported (dd/mm/yyyy) _____

Description of reaction or problem (tick all that apply) – Attach additional information if required

☐ Abdominal pain	☐ Dizziness	☐ Hyperpigmentation	☐ Pancreatitis	☐ Unusual fatigue
☐ Abnormal behavior	☐ Enlarged breast/s	☐ Impaired concentration	☐ Persistent muscle pain	☐ Violent behavior
☐ Anxiety	☐ Fat gain	☐ Impotence	☐ Problems with breathing	☐ Vomiting
☐ Back pain	☐ Fat loss	☐ Insomnia/sleep issues	☐ Psychosis/hallucinations	☐ Weight loss
☐ Chills	☐ Fat redistribution	☐ Lactic acidosis	☐ Rash	☐ Other
☐ Confusion	☐ Fever	☐ Loss of appetite	☐ Ringing in the ears	_____
☐ Constipation	☐ Headache	☐ Nausea	☐ Vision changes	
☐ Depression	☐ Hearing loss	☐ Pain/tingling/numbness in	☐ Unusual bleeding	_____
☐ Diarrhoea	☐ Heartburn	☐ extremeties	☐ Unusual bruising	

LABORATORY RESULTS: SELECT ABNORMAL ONE(S) AND WRITE THE VALUES (BL=BASELINE; CUR=CURRENT)

	K+	*Creat*	*eGFR*	*ALT*	*AST*	*HB*	*Platelets*	*CD4*	*Viral Load*	*Lact*	*Other:*
BL											
CUR											

ADVERSE REACTION OUTCOME

Intervention:	*Action Taken:*	*Patient Outcome:*
☐ Patient Counseled	☐ Discontinued suspected drug	☐ Recovering
☐ Referred to expert	☐ Replaced by _____	☐ Died
☐ Additional clinic visit	☐ Decreased dose	☐ Other: _____
☐ Discontinued Suspected drug	☐ Treated with _____	☐ Other: _____
☐ Additional lab request	Other _____	
☐ Hospitalization		
☐ Other:		

RELEVANT CLINICAL HISTORY (ATTACH ADDITIONAL INFORMATION IF REQUIRED)

Date patient initiated ARVs (dd/mm/yyyy)		Initial regimen	Other:	
How long has patient been diagnosed with HIV		Years		Months
How long has patient been on ARV treatment		Years		Months

CONCOMITANT MEDICAL CN(S) (TICK ALL THAT APPLY):

☐ HTN ☐ DM ☐ KS ☐ Hep B ☐ PCP ☐ Esophageal Candidiasis ☐ Oropharyngeal Candidiasis
☐ Cryp Meningitis ☐ Other/s

REPORTED BY:

Name		**Highest Qualification**	
Designated	Doctor Nurse Pharmacist Other	**Email**	
Tel	**Signature**	**Date**	

THIS REPORT IS NOT AN ADMISSION THAT THE SUSPECTED DRUG(S) CAUSED THE ADR

Version 29.0 dated 12-Mar-2015

ADVERSE DRUG REACTION REPORT FORM >>>

ARF

ADVICE ABOUT VOLUNTARY REPORTING

Report adverse experiences with:

- medications (drugs, vaccines and biologicals)
- medical devices (including in-vitro diagnostics)
- traditional and herbal remedies
- **For Adverse Events Following Immunisation (AEFI), please follow the reporting procedure recommended by the Expanded Programme in Immunisation (EPI)**

Please report:

- adverse drug reactions to recently marketed products
- serious reactions and interactions with all products
- adverse drug reactions which are not clearly reflected in the package insert.

Report even if:

- you're not certain the product caused the event
- you don't have all the details

Report Product Quality Problems such as:

- suspected contamination
- questionable stability
- defective components
- poor packaging or labelling
- therapeutic failures

Important numbers:

Investigational Products and Product Quality Problems:

- (012) 326-4344 to fax a report
- (012) 312-0000 to report by phone

Registered Medicines and Traditional and Herbal remedies:

- (021) 448-6181 to fax a report
- (021) 447-1618 to report by phone

Adverse Events Following Immunisation:

- (012) 312 0110 to phone for information
- (012) 321 9882 to fax a report

Confidentiality: Identities of the reporter and patient will remain strictly confidential.

Your support of the Medicine Control Council's adverse drug reaction monitoring programme is much appreciated. Information supplied by you will contribute to the improvement of drug safety and therapy in South Africa.

PLEASE USE ADDRESS PROVIDED BELOW- JUST FOLD IN THIRDS, TAPE and MAIL

Postage will be paid by Addressee
Posgeld sal deur die geadreseerde betaal word

No postage stamp necessary if posted in the Republic of South Africa
Geen posseël nodig nie indien in die Republiek van Suid-Afrika gepos

BUSINESS REPLY SERVICE
BESIGHEIDSANTWOORDDIENS
Free Mail Number:
***Vryposnommer*: BNT 178**

DEPARTMENT OF HEALTH
DEPARTEMENT VAN GESONDHEID
REGISTRAR OF MEDICINES
REGISTRATEUR VAN MEDISYNE
PRIVATE BAG/ *PRIVAATSAK* X828
PRETORIA
0001

ADVERSE DRUG REACTION REPORT FORM

Instructions on filling the ADR Report

A) Patient Details – All fields to be completed

B) Medicines (and Concomitant medicines, including herbal products) – All fields to be completed as per the example below:

Medicine	Suspect drug/ Trade Name	Dose	Interval	Route	Date started	Date stopped	Prescriber (Dr/ Pharm/Nurse)
1	AZT/Retrovir	300mg	BID	PO	16-Oct-2014	NA	Doctor
Paracetamol	Panadol	1g	TDS	PO	16-Oct-2014	19-Oct-2014	Nurse
St John's Wort		2 drops	TDS	PO	16-Sep-2014		Pharmacist
Key: **1**. AZT **2**. 3TC **3**. TDF **4**. FTC **5**. D4T **6**. ABC **7**. DDI **8**. NVP **9**. EFV **10**. ETR **11**. ATV **12**. DRV **13**. RTV **14**. LPV/r **15**. ATV/r 15.R **16**. RAL **17**. TDF+FTC **18**. TDF+FTC+EFV **19**.R 20. **20**. H **21**. Z **22**. E **23**. RH **24**. RHZE **25**. Km **26**. Am **27**. Cm **28**. Mfx**29**. Lvx**30**. Gfx**31**. Eto**32**. Trd**33**. Pto**34**. Cs **35**. PAS **36**. Cfx**37**. AZI **38**. Clr **39**. Amx/Clv**40**. MEROPENEM **41**. Lzd**42**. Imipenem**43**. Bedaquiline**44**. Delamanid**45**. PA 824 **46**. High Dose INH							

In the first column, please insert preferably the accepted abbreviation of the name of the medicine the patient is taking (AZT in the example), in the second column, insert the name of the drug suspected of causing the ADR, preferably its trade name(In this case it is AZT and the Trade name is Retrovir). You should then enter the dose, route of administration, the date started and stopped (where applicable) and the professional category of the prescriber namely, Doctor, pharmacist or nurse. You may also use the numeric key if you prefer e.g. 1 instead of AZT.

C) Adverse Drug Reaction – Please complete the date of onset of the ADR and please tick ADRs presented in the form as appropriate. If they do not appear on the list, please complete in the section labelled other. Please provide as much detail as possible.

D) Laboratory Results – Please select the abnormal laboratory results and write the value. (BL = Basline; Cur = Current). If they are not among the ones listed, there is a section provided for other lab results. Please complete in as much detail as possible.

E) Adverse Drug Reaction Outcome – Please complete the Intervention, action taken and patient outcome in all fields. A section is provided in cases where interventions, actions and outcomes other than those provided occur.

F) Relevant Clinical History – Please complete all fields in this section

G) Concomitant Medical Conditions – Please complete all fields in this section. If they are not among the ones listed, there is a section provided for other lab results. Please complete in as much detail as possible.

H) Reported by – Please complete all fields. Your contact details may be required in case of follow up to clarify information

Abbreviations

AZT = Zidovudine	**DRV** = darunavir	**RAL** = raltegravir	**Km** = Kanamycin	**Cm** = Capreomycin	**RTV**=ritonavir/r=ritonavir,low dose
3TC = lamivudine	**ETR** = etravirine	**SQV** = saquinavir	**Lzd** = Linezolid	**Mfx** = Moxofloxacin	**LPV/r** = lopinavir/ritonavir
ABC = Abacavir	**FPV** = fosamprenavir	**TDF** = Tenofovir	**TRD** = Terizidone	**LFX** = Levofloxacin	**PAS**=*para*-aminosalicylic acid
APV = amprenavir	**FTC** = Emtricitabine	**TPV** = tipranavir	**Pto** = Protionamide	**Gfx** = Gatifloxacin	**PAS**=Para-Aminosalicylic Acid
ATV = atazanavir	**IDV** = indinavir	**R** = Rifampicin	**Cs** = cycloserine	**Eto** = Ethionamide	**Amx/Clv** =Amoxicillin/Clavulanic Acid
d4T = stavudine	**MVC** = maraviroc	**H** = Isoniazid	**Cfx** = Ciprofloxacin	**EFV** = efavirenz	**PA824**=Experimental Nitroimidazole drug
ddC = zalcitabine	**NFV** = nelfinavir	**E** = Ethambutol	**AZI** = Azithromycin	**ENF** = enfuvirtide	
ddI = didanosine	**NVP** = Nevirapine	**Z** = Pyrazinamide	**Clr** = Clarithromycin		
DLV = delavirdine					

GUIDELINES FOR ADVERSE DRUG REACTION REPORTING >>>

National Pharmacovigilance Programme

The Medicines Control Council (MCC) has a responsibility to ensure the safety, efficacy and quality of all medicines used by the South African public. The National Pharmacovigilance Programme is coordinated by the MCC and has two dedicated Units responsible for the monitoring of the safety of medicines. The National Adverse Drug Event Monitoring Centre (NADEMC) in Cape Town monitors the safety of all registered medicines in South Africa. In addition, a focused surveillance unit at MEDUNSA is responsible for monitoring the safety of antiretroviral medicines and complementary medicines. The unit at MEDUNSA is also responsible for monitoring the safety of unregistered medicines used during clinical trials.

What is Pharmacovigilance?

Pharmacovigilance is defined as the science and activities concerned with the detection, assessment, understanding and prevention of adverse reactions to medicines (i.e. adverse drug reactions or ADRs). The ultimate goal of this activity is to improve the safe and rational use of medicines, thereby improving patient care and public health.

What is an Adverse Drug Reaction (ADR)?

MCC defines an Adverse Drug Reaction (ADR) or adverse reaction as a response to a medicine which is noxious and unintended, including lack of efficacy, and which occurs at any dosage and can also result from overdose, misuse or abuse of a medicine.

Who should report Adverse Drug Reactions?

All HCWs, including doctors, dentists, pharmacists, nurses and other health professionals are encouraged to report all suspected adverse reactions to medicines (including vaccines, X-ray contrast media, traditional and herbal remedies), especially when the reaction is not in the package insert, potentially serious or clinically significant.

What happens to a report?

All ADR reports are entered into a national ADR database. Each report is evaluated to assess the causal relationship between the event and the medicine. A well-completed adverse drug reaction/ product quality form submitted could result in any of the following:

- Additional investigations into the use of the medicine in South Africa
- Educational initiatives to improve the safe use of the medicine
- Appropriate package insert changes to include the potential for the reaction
- Changes in the scheduling or manufacture of the medicine to make it safer

The purpose of ADR reporting is to reduce the risks associated with the use of medicines and to ultimately improve patient care.

Will reporting have any negative consequences on the health worker or the patient?

An adverse drug reaction report does not constitute an admission of liability or that the health professional contributed to the event in any way. The outcome of a report, together with any important or relevant information relating to the reaction, will be sent back to the reporter as appropriate. The details of a report are stored in a confidential database. The names of the reporter or any other health professionals named on a report and the patient will be removed before any details about a specific adverse drug reaction are used or communicated to others. The information is only meant to improve the understanding of the medicines used in the country.

GUIDELINES FOR ADVERSE DRUG REACTION REPORTING

Is the event possibly an ADR?

The following factors should be considered when an adverse drug reaction is suspected:

1. What exactly is the nature of the reaction? (describe the reaction as clearly as possible and where possible provide an accurate diagnosis)
2. Did the reaction occur within a reasonable time relationship to starting treatment with the suspected medicine? (some reactions occur immediately after administration of a medicine while others take time to develop)
3. Is the reaction known to occur with the particular medicine as stated in the package insert or other reference? (If the reaction is not documented in the package insert, it does not mean that the reaction cannot occur with that particular medicine)
4. Did the patient recover when the suspected medicine was stopped? (some reactions can cause permanent damage, but most reactions are reversible if the medication is stopped)
5. Did the patient take the medicine again after the reaction abated (i.e., rechallenge). If so, did the same reaction occur again? (In most situations it is not possible or ethical to rechallenge the patient with the same medicine. If such information is available or if such a rechallenge is necessary, recurrence of the event it is a strong indicator that the medicine is may be responsible
6. Can this reaction be explained by other causes (e.g. underlying disease/s; other medicine/s; toxins or foods)? (It is essential that the patient is thoroughly investigated to decide what the actual cause of any new medical problem is. A medicine-related cause should be considered when other causes do not explain the patient's condition)

What types of reactions should be reported?

The following adverse drug reactions should be reported:

- All ADRs to newly marketed drugs or new drugs added to the EDL
- All serious reactions and interactions
- ADRs that are not clearly stated in the package insert.
- All adverse reactions or poisonings to traditional or herbal remedies

Report even if you are not certain the medicine caused the event.

What product quality problems should be reported?

The following product quality problems should be reported:

- Suspected contamination
- Questionable stability
- Defective components
- Poor packaging or labelling
- Therapeutic failures

How can ADRs be prevented from occurring?

Some ADRs are unavoidable and cannot be prevented. However, most ADRs can be prevented by following the basic principles of rational use of medicines

How are adverse drug reactions reported?

An Adverse Drug Reaction/Product Quality Report Form is enclosed in this book and should be completed in as much detail as possible before returning it by fax or post to any of the addresses provided below. Additional forms can be obtained by contacting the MCC at these addresses.

Report forms may also be accessed via the following website: http://www.mccza.com

1. The Registrar of Medicines
Medicines Control Council, Department of Health, Private Bag X828
Pretoria, 0001
Tel: (021) 312 0295; Fax: (021) 3123106

2. The National Adverse Drug Event Monitoring Centre (NADEMC)
C/o Division of Pharmacology, University of Cape Town, Observatory, 7925
Tel: (021) 447 1618; Fax: (021) 448 6181

3. MEDUNSA Pharmacovigilance Unit
Fax (012) 521 4335

Page 1 of 2

Case Investigation Form
ADVERSE EVENTS FOLLOWING IMMUNISATION (AEFI)

INSTRUCTIONS: This form should be completed in full for each AEFI case

Official use only: **EPIDNUMBER:** Received on 19

IDENTIFICATION OF PATIENT

Surname of patients: _____

First names of patient: _____

Names of father/mother: _____

Sex Male Fem Date of birth ____ /____ /19____ Age ____ months____ yrs

Res.address / Contact information Clinic/ Hospital name _____

_____ Town: _____

_____ District _____

_____ Province _____

REPORT / INVESTIGATION

Reported by: _____ Tel no: _____

Date district notified: ___ /___/ 19___ Date case investigation ___/___ /19 ___

HISTORY OF IMMUNISATION

Date of immunisation ___ /___/ 19___ Date of onset of event: ___/___/ 19 ___

Place of immunisation _____ Name of vaccination _____

VACCINES GIVEN TO PATIENT				MANUFACTURES	BATCH No./ LOT No.	DOSE No.
BCG	Yes	No	Unk			
OPV	Yes	No	Unk			
DTP	Yes	No	Unk			
Hib	Yes	No	Unk			
Hepatitis B	Yes	No	Unk			
Measles	Yes	No	Unk			
DT	Yes	No	Unk			
TT	Yes	No	Unk			
Other	Yes	No	Unk			

Specify vaccine

TRIGGER EVENT

Local reactions		**Systemic reactions**	
	Severe local reaction (swelling extended more than 5cm from the injection site or redness and swelling for more than 3 days)		**Severe local reaction** (thought to be related to immunisation)
	Lymphadenitis		**Encephalopathy within 7 days**
	Injection site abscess		**Collapse/ shock-like state within 48 hours**
Mark the trigger event with an X in the box in front of it			**Fever of more than 40.5ºC within 48 hours**
			Seizures within 3 days
			All deaths (thoughts to be related to immunisations)

DETAILS OF EVENT (Symptoms at time or onset)

Case Investigation Form
ADVERSE EVENTS FOLLOWING IMMUNISATION (AEFI)

Official use only: **EPIDNUMBER:**

RESPONSE TO THIS EVENT

Treated at OPD	Yes	No	Unk	Admission date: ____ /___/19 ____
Admitted to hospital for treatment	Yes	No	Unk	Hosp. No. _____
Name of hospital: _____				
Event explained to parent/guardian?	Yes	No	Unk	Interview date: ____ /___/19 ____
Vaccinator guidance/ retraining given?	Yes	No	Unk	Interview date: ____ /___/19 ____

HISTORY OF PREVIOUS REACTIONS TO IMMUNISATION AND / OR TREATMENT

Has this child had any previous reaction after immunisation?	Yes	No	Unk
Was a history of any allergies in this child obtained?	Yes	No	Unk
Was any information given prior to immunisation?	Yes	No	Unk
Was the health status of the child assessed before immunisation?	Yes	No	Unk
Were any other AEFIs reported from this clinic in the last 30 days?	Yes	No	Unk

FINAL CLASSIFICATION
(By provincial EPI coordinator in cooperation with national office)

Programme Error		Coincidental	
Faulty vaccine		Unknown	

Give a brief reason for the classification: _____

_____

_____

Date of final classification: ____ /___/19 ____

INVESTIGATOR; Name _____ Tel: _____

Position and facility district Fax:

An AEFI should be reported within 24 hours of the event and the case investigation done within 36 hours. Please keep the district and provincial EPI coordinators informed about your progress and anyproblems. Send a copy of this from to the Provincial EPI Coordinator.

In addition, please complete an EVENT DESCRIPTION REPORT (EDR) on a separate page where you describe step by step the development of the adverse event and its consequenses and the actions taken in the treatment and investigation.

THANK YOU FOR YOUR RAPID RESPONSE

SAMPLE INFECTION PREVENTION AND CONTROL PLAN >>>

A. The plan will include, but not be limited to, the following policy areas:

1. Screening patients to identify persons with symptoms of TB disease or who report being under investigation or treatment for TB disease.
2. Providing face masks or tissues to persons with symptoms of TB disease or who report being under investigation or treatment for TB disease, and providing waste containers for disposal of tissues and masks.
3. Placing patients with presumptive TB and cases in a separate waiting area.
4. Triaging patients with presumptive TB and cases to the front of the line to expedite their receipt of services in the facility.
5. Referring patients with presumptive TB to TB diagnostic services and confirming that TB cases are adhering to treatment.
6. Using and maintaining environmental control measures.
7. Educating staff periodically on signs and symptoms of TB disease, specific risks for TB for HIV-infected persons, and the need for diagnostic investigation for those with signs or symptoms of TB.
8. Training and educating staff on TB, TB control, and the TB infection prevention and control plan.
9. Monitoring the TB infection and control plan's implementation.

B. The facility will implement each policy by following the procedure(s) that accompany it.

POLICY AND PROCEDURES

Purpose: Early identification, separation, receipt of services, and referral of patients with TB disease is essential in preventing spread of TB.

Lead: _____ has the responsibility for overseeing the implementation of these policies and its procedures, and reports to (District health executive committee, etc).

POLICY 1: SCREENING PATIENTS TO IDENTIFY PERSONS WITH SYMPTOMS OR RECENT HISTORY OF TB DISEASE

Procedures:

(i) Before patients enter an enclosed part of the facility, a designated staff person should ask each adult and any child capable of coughing forcefully (usually age 14 or older) about symptoms or recent history of TB. The questioning should occur before patients wait in line for long periods to register or obtain services.

(ii) Many combinations of symptoms have been recommended as sensitive and specific for TB. A simple screen is:
"Do you have a cough?" If patient answers" yes," ask
"For how long have you been coughing?"
An adult who has coughed for two weeks or more may be considered a patient with presumptive TB.
To determine whether a patient may be under investigation or a diagnosed case of TB, who may still be infectious, ask - "Are you being investigated or treated for TB?"
If the answer to either is "yes," the screen classifies the patient as a patient with presumptive TB or a TB case, and he should be managed as described in the procedures under policies 2 – 5 below.

(iii) As patients who are not identified as a patient with presumptive TB or a TB case on the initial symptoms screen enter an examination room with the clinical officer, nurse, or counsellor, they should again be asked the simple screening questions. Those patients who report a cough of two or more weeks or who are being investigated or treated for TB should be managed as follows in the procedures under policies 2 – 5 below. Staff seeing patients in examination rooms should report patients they find to be patients with presumptive TB or a TB case to the infection control officer in a timely manner so that factors contributing to the potential exposure (e.g. an emergency or short staffing interfering with the designated person screening all patients) can be documented and corrected.

POLICY 2: INSTRUCTIONS ON COUGH HYGIENE

Procedures:

(i) Patients who are found to have presumptive TB or TB cases should immediately be informed about the importance of cough hygiene and be handed tissues (or pieces of cloth) and instructed to cover their mouths and noses when they cough. Alternatively, patients should be given a facemask and asked to wear it while in the facility. Patients should also be instructed to dispose of used tissues or masks in identified no-touch receptacles and not on the ground or on the benches.

When tissues, cloths or facemasks are not available, clients should be instructed to lift their arm up and cover their nose and mouth with the inner surface of the arm or forearm when they cough or sneeze. M. tuberculosis cannot be spread from the hands, but other serious lung infections can.

(ii) No-touch receptacles for disposal of used tissues and masks should be available in the waiting areas.

POLICY 3: PLACING TB SUSPECTS AND CASES IN A SEPARATE WAITING AREA

Procedures

(i) A staff person should direct or escort the patient to a separate waiting area. This special waiting area should have the highest natural ventilation possible. Patients should be assured of their place in the line for registration and/or services.

POLICY 4: TRIAGING TB SUSPECTS AND CASES TO THE HEAD OF THE LINE TO RECEIVE SERVICES IN THE FACILITY

Procedures

(i) Patients with presumptive TB and cases should be moved to the head of the line for whatever services they want or need.e.g. VCT, medication refills, or medical investigation. This reduces the duration of potential exposure while they wait in the facility and may be an incentive to disclose information during screening.

SAMPLE INFECTION PREVENTION AND CONTROL PLAN >>>

POLICY 5: REFERRING TB SUSPECTS TO TB DIAGNOSTIC SERVICES

Procedures

(i) _____ is the designated staff person to counsel patients about obtaining TB diagnostic services.

(ii) Patients will be referred to _____ (a TB diagnostic centre with which the health care facility has a previously negotiated agreement).

(iii) Patients should be given a card with the name, location, and operating hours of the TB diagnostic centre. The card should also have the name of the referring facility on it, with date of referral marked. These cards can be collected at the TB centre and used as an anonymous check on number of referrals that successfully obtain TB services.

POLICY 6: USING AND MAINTAINING ENVIRONMENTAL CONTROL MEASURES

Procedures

(i) _____ is the designated staff person to check on environmental control measures and maintain a log of monitoring and maintenance.

(ii) Windows and doors should be checked on a daily basis to assure they are in proper position (open or closed as called for in the plan). Generally, all windows and doors should be open when natural ventilation is the primary environmental control to allow for the free, unencumbered movement of air (e.g. across room, from window to door or vice versa). Generally, all windows and doors should be closed when using mechanical ventilation to ensure air movement in a controlled manner (air from supply vent and from slots either under or in door toward the exhaust vent).

(iii) Fans should be checked on a monthly basis to assure they are clean, are pulling (or pushing) the correct amount of air, and are pulling (or pushing) air in the correct direction.

POLICY 7: PROVIDING CONFIDENTIAL TB AND HIV SERVICES TO HEALTH CARE WORKERS AND STAFF

Procedures

(i) Health care workers and all other staff working at the facility should be educated about the signs and symptoms of TB and encouraged to seek investigations promptly if they develop symptoms and signs suggestive of TB.

(ii) Health care workers and other staff should be informed about the special specific risks for TB for HIV-infected persons (see section on Training of staff).

(iii) Health care workers and staff should be encouraged to undergo HIV testing, and given information on relevant HIV care resources.

(iv) Staff training should include reduction of stigma of TB and HIV.

National TB Infection Control Guidelines, NDOH, June 2007

SAMPLE INFECTION PREVENTION AND CONTROL PLAN

(v) _____ is responsible for determining when staff who develop TB disease may return to work.

(vi) Staff who develop TB disease may return to work when determined to be no longer infectious after:

a. Having completed at least two weeks of standard anti-TB therapy;
b. Exhibiting clinical improvement;
c. Having continued medical supervision and monitoring of treatment until cured; and
d. Where possible, having had three consecutive negative sputum smears obtained on three different days with at least one morning specimen. (Note: Frequent evaluation of sputum smear status may not be done routinely in resource-limited settings.)

POLICY 8: TRAINING OF STAFF ON ALL ASPECTS OF TB AND THE TB INFECTION PREVENTION AND CONTROL PLAN

Procedures

(i) _____ is the designated staff person to provide training to new staff as they are employed and to maintain a log indicating who has had initial training.

(ii) _____ is the designated staff person to provide annual training to all staff and to maintain a log indicating who has attended training. This may be incorporated into a broader training topic or it could be stand-alone TB infection control training.

POLICY 9: MONITORING THE TB INFECTION PREVENTION AND CONTROL PLAN'S IMPLEMENTATION

Procedures

(i) Determine the frequency of the infection prevention and control plan evaluation.

a. During initiation of procedures, monitoring and evaluation should be done frequently, perhaps monthly or bi-monthly.
b. When procedures are running well, less frequent evaluation will be necessary – at a minimum, annually.

(ii) Evaluate the screening process.

a. Were patients with significant cough missed when entering the facility and only detected at a later time or in the examination room?
b. What correctable factors were associated with these potential exposures?

(iii) Evaluate the success of referrals to the TB diagnostic centre.

a. Did referred patients access care?
b. Did referred patients have TB disease?
c. What changes in screening or referral process should be made, if any?

(iv) Evaluate the training process.

a. Did all new staff receive training on TB infection prevention and control during their induction?
b. Did all staff receive annual re-training on TB infection control?

(v) Revise the infection prevention and control plan to reflect changes in staff responsibilities, policies, and procedures.

(vi) Develop a plan for correcting inappropriate practices or failure to adhere to institutional policies.

a. Identify incentives to participate fully and adhere to policies.
b. Identify corrective actions if policies are not followed.

INFECTION CONTROL RISK ASSESSMENT >>>

PHC RISK ASSESSMENT TOOL

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

TUBERCULOSIS INFECTION PREVENTION AND CONTROL RISK ASSESSMENT FORM FOR CLINICS AND COMMUNITY HEALTH CENTERS

FACILITY DATA SHEET

Facility Identification

Facility Name:	
Facility Type:	

Physical Address

Building Name:			
Street Number:		Street Name:	
Suburb:			
Town/City:			

Location

Province:	
District:	
Local Authority:	

Information Source / Lead facility representative

Name:	
Designation:	
Contact Numbers:	
Email Address:	

Data Control

Lead Assessors Name:	
Designation:	
Contact Numbers:	
Email:	
Assessment Date:	

INFECTION CONTROL RISK ASSESSMENT >>>

ADMINISTRATIVE CONTROLS

Section 1: Facility Staff Details

Facility Staff Complement	

Section 2: Facility Patient Access / Occupancy Data

Patient Visits *per* Quarter (Number of Patients):				Year:			
First Quarter		Second Quarter		Third Quarter		Fourth Quarter	
Total visits (all):		Total visits (all):		Total visits (all):		Total visits (all):	
No: screened		No: screened		No: screened		No: screened	
No: TB suspects		No: TB suspects		No: TB suspects		No: TB suspects	
New Susceptible TB		New Susceptible TB		New Susceptible TB		New Susceptible TB	
Total SusceptibleTB		Total SusceptibleTB		Total Susceptible TB		Total SusceptibleTB	
New Drug Resistant TB		New Drug Resistant TB		New Drug Resistant TB		New Drug Resistant TB	
Total Drug Resistant -TB		Total Drug Resistant -TB		Total Drug Resistant -TB		Total Drug Resistant -TB	

Section 3: Staff Screening for TB

3.1. Is there a TB screening programme in place for facility staff?	Yes	No
3.2. Are base-line chest X-rays undertaken for facility staff?	Yes	No
3.3. Is sputum collected for all identified facility staff?	Yes	No
3.4 Is completing a screening questionnaire part of the program?	Yes	No
3.5. How frequently are the facility staff screened?	Every	Months

Section 4: TB among Staff

4.1.1. How many staff members have been diagnosed with TB in the past 12 months?		
4.1.2. How many staff members have been diagnosed with TB in the past 3 years?		
4.1.3 Did you submit occupational illness report(s) to the compensation commission?	Yes	No
4.1.4. Have you investigated the case(s) of occupational illness & took corrective actions?	Yes	No
4.1.5. Do you have access to occupational health services and advice?	Yes	No
4.1.6. Are you aware of support services available to help you with staff health matters?	Yes	No

Section 5: Management of Infection Control (IC) Program

5.1. TB Infection Control Policy

5.1.1. Is there a facility-specific infection control policy for airborne infections?	Yes	No
5.1.2. Do (all) staff have access to the infection control policy?	Yes	No
5.1.3 Are the HCWs being routinely trained on TB IC practices and requirements?	Yes	No
5.1.4. Is there someone appointed in writing to be in-charge of infection control?	Yes	No
5.1.5. Is there a functional infection control committee?	Yes	No
5.1.6. Are the infection control committee members appointed in writing?	Yes	No

5.2. Is the IC Policy supported by an IC Plan that allows implementation of the following?

5.2.1. Screening of all patients arriving at the hospital?	Yes	No
5.2.2. Separation of patients with suspected or confirmed TB disease?	Yes	No
5.2.3. Fast-tracking of patients with suspected or confirmed TB disease?	Yes	No
5.2.4. Appointment of person(s) to assist in triaging & fast-tracking suspects?	Yes	No
5.2.5. Provision of surgical masks to patients?	Yes	No
5.2.6. Health education and cough etiquette?	Yes	No
5.2.7. Inclusion of respiratory protection programme?	Yes	No
5.2.8. Inclusion of an open window policy (If not relying fully on mechanical ventilation)?	Yes	No
5.2.9. Appointment of open window marshals with access to “open window registers”?	Yes	No
5.2.10. Integration of TB screening with HCT and TB/HIV in general?	Yes	No
5.2.11. Conducting a TB risk assessment frequently or updating one for the hospital?	Yes	No
5.2.12. If yes, when was the last assessment undertaken?	Date	

Comments:

Section 6: Turn-Around Times (Average number of days it takes for the following)

6.1. Collection of patient sputum until laboratory test results are returned to the facility?		Days
6.2. Time between receipt of tests until initiation of anti-tuberculosis treatment?		Days
6.3. Time taken by laboratory to provide outcome of culture results		Days

Comments:

Section 7: Additional Comments

Section 8: Summary of Recommendations

INFECTION CONTROL RISK ASSESSMENT >>>

ENVIRONMENTAL CONTROLS

Section 1: Sputum Collection

1.1. Where is sputum collection undertaken? (Tick all that apply)	
1.2. An inside room or other (toilet, consulting room, ward etc.)	
1.3. Designated, purpose made outside area for sputum induction	
1.4. No designated area (outside etc.) – Just an open space	
1.5. Local exhaust ventilation booth	

Comments:

Section 2: Natural Ventilation

2.1. If facility relies on natural ventilation, are the spaces open directly to the outside?	Yes	No
2.2. If naturally ventilated, are all openable windows always open?	Yes	No
2.3. Does the facility have “open window stickers and register”?	Yes	No

Comments:

Section 3: Mechanical Ventilation (Where applicable)

3.1. Are air changes per hour measured in this facility or unit?	Yes	No
3.2. Are any of the air changes per hour measured below 12 ACH?	Yes	No
3.3. Are ventilation systems regularly checked, maintained&maintenance logbook kept?	Yes	No
3.4. Are these results readily available?	Yes	No

Comments:

Section 4: Air Disinfecting Systems by Upper Room UVGI(Where applicable)

4.1. Were the UVGI units installed using an electrical engineer? (if by supplier state No).	Yes	No
4.2. Were the UVGI units validated for operation by an independent authority?	Yes	No
4.3. Are the UVGI units regularly checked and maintained?	Yes	No
4.4. Are each of the UVGI unit performance results recorded in maintenance logs?	Yes	No
4.5. Has the staff been trained to ensure safe operation of the UVGI Units?	Yes	No

Section 5: Additional Comments

Section 6: Summary of Recommendations

INFECTION CONTROL RISK ASSESSMENT

PERSONAL PROTECTION EQUIPMENT

Section 1: Respiratory Protection Program (RPP)

1.1. Does the facility has a respiratory protection program (RPP)	Yes	No
1.2. Are respirators used in this setting for all health-care workers who may be at risk?	Yes	No

1.3. If YES, specify manufacturer, model and specific application below.

Manufacturer:	
Class: (NIOSH - N95 or CEN-FFP2)	
Serial Number (e.g. TC number for NIOSH approved respirators)	
Describe the practice and method of respirator donning, use and storing:	

1.4. Is respiratory-protection training conducted for HCWs?	Yes	No
1.5. If YES, is it conducted every six months?	Yes	No
1.6. After direct observation of selected staff, can they perform *fit-checking*?	Yes	No
1.7. Have the relevant health-care workers undergone *fit-testing* for respirator use?	Yes	No

Comments:

Section 2: Summary of Recommendations

SUMMARY OF TUBERCULOSIS ICD CODES >>>

(A15-A19)

Includes:

- Infections due to Mycobacterium tuberculosis and Mycobacterium bovis

Excludes:

- Congenital tuberculosis **(P37.0)**
- Human immunodeficieny [HIV] disease resulting in tuberculosis **(B20.0)**
- Pneumoconiosis associated with tuberculosis **(J65)**
- Sequelae of tuberculosis **(B90)**
- Silicotuberculosis **(J65)**

A15 Respiratory tuberculosis, bacteriologically and histologically confirmed

A15.0 Tuberculosis of lung, confirmed by sputum microscopy with or without culture
A15.1 Tuberculosis of lung, confirmed by culture only
A15.2 Tuberculosis of lung, confirmed histologically
A15.3 Tuberculosis of lung, confirmed by unspecified means
A15.4 Tuberculosis of intrathoracic lymph nodes, confirmed bacteriologically and histologically
A15.5 Tuberculosis of larynx, trachea and bronchus, confirmed bacteriologically and histologically
A15.6 Tuberculous pleurisy, confirmed bacteriologically and histologically
A15.7 Primary respiratory tuberculosis, confirmed bacteriologically and histologically
A15.8 Other respiratory tuberculosis, confirmed bacteriologically and histologically
A15.9 Respiratory tuberculosis unspecified, confirmed bacteriologically and histologically

A16 Respiratory tuberculosis, not confirmed bacteriologically or histologically

A16.0 Tuberculosis of lung, bacteriologically and histologically negative
A16.1 Tuberculosis of lung, bacteriological and histological examination not done
A16.2 Tuberculosis of lung, without mention of bacteriological or histological confirmation
A16.3 Tuberculosis of intrathoracic lymph nodes, without mention of bacteriological or histological confirmation
A16.4 Tuberculosis of larynx, trachea and bronchus, without mention of bacteriological or histological confirmation
A16.5 Tuberculous pleurisy, without mention of bacteriological or histological confirmation
A16.7 Primary respiratory tuberculosis without mention of bacteriological or histological confirmation
A16.8 Other respiratory tuberculosis, without mention of bacteriological or histological confirmation
A16.9 Respiratory tuberculosis unspecified, without mention of bacteriological or histological confirmation

SUMMARY OF TUBERCULOSIS ICD10 CODES

A17+ Tuberculosis of nervous system

A17.0+ Tuberculous meningitis (G01)

A17.1+ Meningeal tuberculoma (G07)

A17.8 +Other tuberculosis of nervous system

A17.9 +Tuberculosis of nervous system, unspecified (G99.8)

A18 Tuberculosis of other organs

A18.0 Tuberculosis of bones and joints

A18.1 Tuberculosis of genitourinary system

A18.2 Tuberculous peripheral lymphadenopathy

A18.3 Tuberculosis of intestines, peritoneum and mesenteric glands

A18.4 Tuberculosis of skin and subcutaneous tissue

A18.5 Tuberculosis of eye

A18.6 Tuberculosis of ear

A18.7 Tuberculosis of adrenal glands

A18.8 Tuberculosis of other specified organs

A19 Miliary tuberculosis

A19.0 Acute miliary tuberculosis of a single specified site

A19.1 Acute miliary tuberculosis of multiple sites

A19.2 Acute miliary tuberculosis, unspecified

A19.8 Other miliary tuberculosis

A19.9 Miliary tuberculosis, unspecified

WHO CLINICAL STAGING IN ADULTS

STAGE 1

- Asymptomatic
- Persistent generalized lymphadenopathy

STAGE 2

- Moderate unexplained weight loss (<10% of presumed or measured body weight)
- Recurrent upper respiratory tract infections: sinusitis, tonsillitis, otitis media, pharyngitis
- Minor mucocutaneous manifestations
- Seborrhoeic dermatitis
- Prurigo (chronic itchy skin)
- Fungal nail infections
- Recurrent oral ulceration
- Angular cheilitis
- Papular pruritic eruptions
- Herpes zoster (shingles) <5 years

STAGE 3

- Unexplained severe weight loss (>10% of presumed or measured body weight)
- Unexplained chronic diarrhoea for >1 month
- Unexplained persistent fever (>37.6°C, intermittent or constant, for >1 month)
- Persistent oral candidiasis
- Oral hairy leukoplakia
- Pulmonary tuberculosis (current)
- Severe bacterial infections (such as pneumonia, empyema, pyomyositis, bone or joint infection, meningitis or bacteraemia)
- Acute necrotising ulcerative stomatitis, gingivitis or periodontitis
- Unexplained anaemia (<8 g/dL), neutropaenia (<0.5 × 10^9/L) or chronic thrombocytopaenia (<50 x 10^9/L)

STAGE 4

- HIV wasting syndrome
- Pneumocystis (jirovecii) pneumonia
- Recurrent severe bacterial pneumonia
- Chronic herpes simplex infection (orolabial, genital or anorectal for >1 month or visceral at any site)
- Oesophageal candidiasis (or candidiasis of trachea, bronchi or lungs)
- Extrapulmonary tuberculosis
- Kaposi's sarcoma
- Cytomegalovirus infection (retinitis or infection of other organs)
- Central nervous system toxoplasmosis
- HIV encephalopathy
- Extra-pulmonary cryptococcosis including meningitis
- Disseminated non-tuberculous mycobacterial infection
- Progressive multifocal leukoencephalopathy
- Chronic cryptosporidiosis (with diarrhoea)
- Chronic isosporiasis
- Disseminated mycosis (coccidiomycosis or extrapulmonary histoplasmosis)
- Recurrent non-typhoidal salmonella bacteraemia
- Lymphoma (cerebral or B-cell non-Hodgkin) or other solid HIV-associated tumours
- Invasive cervical carcinoma
- Atypical disseminated leishmaniasis
- Symptomatic HIV-associated nephropathy or symptomatic HIV-associated cardiomyopathy

WHO CLINICAL STAGING IN CHILDREN

STAGE 1

- Asymptomatic
- Persistent generalized lymphadenopathy

STAGE 2

- Unexplained persistent hepatosplenomegaly
- Papular pruritic eruptions
- Extensive wart virus infection
- Extensive molluscum contagiosum
- Recurrent oral ulcerations
- Unexplained persistent parotid enlargement
- Lineal gingival erythema
- Herpes zoster
- Recurrent or chronic upper respiratory tract infections (otitis media, otorrhoea, sinusitis, tonsillitis)
- Fungal nail infections

STAGE 3

- Unexplained moderate malnutrition not adequately responding to standard therapy
- Unexplained persistent diarrhea (14 days or more)
- Unexplained persistent fever (above 37.5 °C, intermittent or constant, for longer than one month)
- Persistent oral Candidiasis (after first 6 weeks of life)
- Oral hairy leukoplakia
- Acute necrotizing ulcerative gingivitis/ periodontitis
- Lymph node TB
- Pulmonary TB
- Severe recurrent bacterial pneumonia
- Symptomatic lymphoid interstitial pneumonitis
- Chronic HIV-associated lung disease including bronchiectasis
- Unexplained anaemia (<8.0 g/dl), neutropenia (<0.5×10^9/L) or chronic thrombocytopenia (<50 × 10^9/L)

STAGE 4

- Unexplained severe wasting, stunting or severe malnutrition not responding to standard therapy
- Pneumocystis pneumonia
- Recurrent severe bacterial infections (e.g. empyema, pyomyositis, bone or joint infection, meningitis, but excluding pneumonia)
- Chronic herpes simplex infection; (orolabial or cutaneous of more than one month's duration, or visceral at any site)
- Extrapulmonary TB
- Kaposi sarcoma
- Oesophageal candidiasis (or candiadisis of trachea, bronchi or lungs)
- Central nervous system toxoplasmosis (after the neonatal period)
- HIV encephalopathy
- Cytomegalovirus (CMV) infection; retinitis or CMV infection affecting another organ, with onset at age more than 1 month
- Extrapulmonary cryptococcosis including meningitis
- Disseminated endemic mycosis (extrapulmonary histoplasmosis, coccidioidomycosis, penicilliosis)
- Chronic cryptosporidiosis (with diarrhoea)
- Chronic isosporiasis
- Disseminated non-tuberculous mycobacterial infection
- Cerebral or B cell non-Hodgkin lymphoma
- Progressive multifocal leukoencephalopathy
- HIV-associated cardiomyopathy or nephropathy

CONSENT FORM FOR DR-TB PATIENTS

Undertaking by patient

I, ... (name patient) of (residential physical address) .....
....
.....

Understand the nature of my disease and treatment as explained by the doctor/ nurse, hereby give an undertaking that.

1. I will follow the prescribed and agreed treatment regimen and to conscientiously comply with the instructions given to improve my health and protect that of others
2. I agree to be hospitalised for the duration to be determined by my doctor if hospitalisation is deemed necessary to facilitate administration of the treatment and clinical monitoring
3. I will inform the doctor/ nurseof any difficulties or problems in following treatment, or if any part of the treatment is not clearly understood
4. I will provide the sputum specimen required for testing to monitor clinical progress
5. I will provide the blood specimen required for monitoring adverse events caused by the drugs
6. I will undergo audiometric tests required to monitor adverse events.
7. I will adhere to cough hygiene practises at all times to prevent spreading the infection to others
8. I will show consideration and respect for the rights of other patients and health-care providers during my stay in the hospital

I understand that if I wilfully interrupt my treatment the following measures could apply:

1. My treatment could be stopped.
2. Any form of social support I may be getting will be stopped

Name ..... Signature Patient: .....
Date: .....

Undertaking by health care worker

I..... (name)

Undertake to:

1. Explain fully to you the nature of your disease and explain the treatment plan to you (including any side effects you might experience)
2. Provide you with regular clinical progress reports whilst on treatment
3. Ensure confidentiality of your medical condition at all times
4. Address your complaints or concerns to the best of my ability
5. Address any socio-economic problems you may encounter whilst in hospital as far as reasonably possible

Name: ..... Signature: .....
Date: .....
Witness: ..... Date: .....
Witness ..... Date: .....

GUIDELINES FOR REFERRAL OF DR-TB PATIENTS FOR REVIEW

Any patient diagnosed with DR-TB, must follow a process of documentation, education/awareness and evaluation of conditions for good treatment adherence, before starting on a suitable treatment regimen. This involves the patient and possibly their families, provided that the patient is adequately informed of the process and is in agreement with it. Only when these requirements/ criteria are fulfilled, should the patient be started on DR treatment.

All patients who are, chronic defaulters, non-converters, have more extensive resistance, treatment failures must be referred to the PRC for a decision to continue or stop treatment.

The committee will consider each case and make recommendations to the hospital on the management and records of all decisions taken by the committee must be kept safely for medicolegal purposes as well as monitoring compliance with those recommendations.

The province must coordinate the meetings based on cases submitted for review and set dates for submission for next scheduled meeting of the committee.

All paperwork must be completed at the referring institution by delegated nurse, doctor. This will include:

- The MDR-MRB application form
- The MDR form
- The contract signed by patient and relevant HCWs on initiation of treatment

The MDR-TB co-ordinator of the MDR-TB Centre will check submission and accept for review only if paperwork is complete and the basic requirements for the review have been met.

The referring institution will be notified of meeting date and patient will be requested to attend the review meeting, wherever this is possible.

The Review Board will peruse the submission, interview the patient where possible, discuss the case, and make recommendations.

The referring facility will be informed of the Review Board's decision and within 10 working days.

STANDARD ADMISSION/ DISCHARGE/ REFUSAL OF HOSPITAL TREATMENT FORM

HOSPITAL ..... Ward .....

....Gender M F Age .....

Patient

Patients' No. [ ]

Classification .....

ADDRESS

.....

Doctor

Phone .....

ADMISSION

Admitted by ..... Date ..... Time .....

Provisional diagnosis .....

Doctor's signature (if available) .....

DISCHARGE

Date of discharge .....Time .....

Final diagnosis .....

Doctor's signature .....

REFUSED HOSPITAL TREATMENT

I, the undersigned, leave the ..... Hospital on my own responsibility and against the advice of the attending doctor.

Witnesses: 1 ..... Signature of patient .....

2 ..... Date ..... Time .....

I, the undersigned, take the patient ..... out of the ..... Hospital on my own responsibility and against the advise of the attending doctor.

Witnesses: 1 ..... Signature .....

2 .....

Date ..... Time ..... Capacity .....

For particulars of treatment use from TPH 3 (a).

PASS-OUT CONSENT FORM FOR DR-TB PATIENTS

I,.....(Name patient) of (residential physical address)
.....
.....understand the conditions of the pass out as explained to me by the doctor/nurse and hereby give an undertaking to abide by these conditions. During this period, I will be resident at the following address
.....
.....

I will take precautions to prevent spreading the infection to people I come into close contact with, and will continue to take my medication as explained.

I will report back at the hospital on the ..... day of the ..... month ....., as agreed upon and understand that during this time the hospital cannot take responsibility for my well-being. If I experience any problems during this period I will inform my local clinic or the hospital as soon as possible.

Name of Patient: ..... Signature: .....

Date: .....

Name of Nurse/ Doctor: ..... Signature: .....

Date: .....

Witness 1: ..... Date:.....

Witness 2: ..... Date:.....

health
Department:
Health
REPUBLIC OF SOUTH AFRICA

TB SYMPTOM SCREENING SUMMARY

Page Number:

Sub District: Facility: Month:

Date	Head Count			Total Screened for TB	Number of people screened for TB symptoms				Number of people identified with TB symptoms		Number of people referred for assessment and investigation	
	Total	< 5yrs	≥ 5yrs		HIV positive	Diabetic	Contacts	Other	< 5yrs	≥ 5yrs	< 5yrs	≥ 5yrs
Total												

health
Department of Health
REPUBLIC OF SOUTH AFRICA

SUMMARY FOR TB DETECTION

GW 20/13
2013

Page Number:

District: | Sub-District: | Facility:

Year: _____		Head Count			Number of people screened for TB symptoms					Number of people identified with TB symptoms		Number of people ≥ 5 yrs with TB symptoms whose sputum was tested	Number of people ≥ 5 yrs with a positive test result		Number of people ≥ 5 yrs with a positive test result for Rif susceptibleTB			Number of people ≥ 5yrs with a positive test result for Rif resistant TB			Number of people started on TB treatment		Number of child contacts < 5yrs with a negative test result started on IPT	Number of specimens sent to lab for testing (Xpert and microscopy)	Number of results (Xpert and microscopy) received within 48hrs (2 days)
		Total	< 5yrs	≥ 5yrs	HIV positive	Diabetic	Contacts	Other	Total	< 5yrs	≥ 5yrs		Rif Susceptible TB	Rif resistant TB	Started on treatment	Died before starting treatment	Lost to follow-up	Started on treatment	Died before starting treatment	Lost to follow-up	< 5 yrs	≥ 5yrs			
Quarter 1	January																									
	February																									
	March																									
	Total																									
	%																									
Quarter 2	April																									
	May																									
	June																									
	Total																									
	%																									
Quarter 3	July																									
	August																									
	September																									
	Total																									
	%																									
Quarter 4	October																									
	November																									
	December																									
	Total																									
	%																									

Compiled By:

Name: Signature: Date:

Approved by:

Name: Signature: Date:

NOTES

NOTES

NOTES

NOTES

NOTES

NOTES

MANAGING TB
In a New Era of Diagnostics

The Aurum Institute, Aurum House | The Ridge | 29 Queens Road | Parktown | Johannesburg | 2193
Postnet Suite 300 | Private Bag X30500 | Houghton | 2041 | South Africa
Telephone: (010) 590-1300 | E-mail: info@auruminstitute.org | www.auruminstitute.org

ISBN 978-0-9946566-3-6

Share - You are free to copy, distribute and transmit this work
Attribution – You must acknowledge the copyright holder and fully reference this work
Non-commercial – You may not use this work for commercial purposes
No Derivative Works – You may not alter, transform or build upon this work