FREE STATE PROVINCIAL GOVERNMENT

Health

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TO ALL HEADS AND INSTITUTIONS OF THE DEPARTMENT OF HEALTH IN THE FREE STATE

PRIMARY HEALTH CARE CIRCULAR 20OF 2001

GUIDELINES ON THE MANAGEMENT OF TUBERCULOSIS PATIENTS WHO NEEDS TO BE HOSPITALISED

Attached please find the policy for implementation as indicated.
This policy replaces any current policy available regarding this matter
Please ensure the circulation of this policy to all role-players in the your area of responsibility.

DIRECTOR PRIMARY HEALTH CARE
DR RC CHAPMAN
DATE: 6 July 2001

Free State Health

TB HOSPITAL POLICY

FACILITATED BY:CM GRIESSEL

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TB Control Programme

A Healthy and Self-reliant Free State Community

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TUBERCULOSIS: A WORLD EMERGENCY

1. THE IMPORTANCE OF TB IN THE WORLD

The World Health Organisation (WHO) declared TB a "Global Emergency" in 1993. It stated that "TB is humanity's greatest killer" because TB kills more adults each year than any other infectious disease, including malaria and all tropical diseases.

The Department of Health is implementing a strategy to fight TB called Directly Observed Treatment, short-course (DOTS), which is recommended by WHO.

The five key elements of the DOTS strategy are:

- Government commitments to a national TB programme as a specific health system activity, integrated into comprehensive primary care, and supported technically at a national level.
- Standardised, directly observed, short-course treatment prioritising sputum smear positive patient.
- Case detection by means of a patient-friendly and clinically efficient service based primary on smear microscopy (Passive case-finding).
- An ensured supply of essential anti-TB drugs.
- Effective monitoring using standardised registers, quarterly reporting and clear definitions of new and retreatment cases and treatment outcomes.

2. HOSPITAL ADMISSION AND DISCHARGE CRITERIA FOR TB PATIENTS

As a rule, most TB patients can be managed as outpatients at a PHC clinic or Community Health centre. TB patients who are critical and who require supervision by a medical officer and nursing staff should be stabilised at the nearest district hospital. In case of a retreatment patient who is admitted to a district hospital the patient **must remain in hospital for the full time when receiving streptomycin or until such time the patient can be transferred to the TB hospital.**
If the patient needs discharged before the completion of the streptomycin treatment the hospital has the responsibility to ensure the patient is able receive treatment on a daily basis on an outpatient basis at the nearest clinic where he lives. Patients from the farms are however need to remain in hospital for the full duration of the streptomycin treatment.

2.1 HOSPITAL ADMISSION CRITERIA

All Multi Drug Resistant (MDR) patients should be admitted to the MDR unit currently at Santoord Hospital.

1. **Pulmonary TB patients** with positive sputum microscopy and with one or more of the following:
   - dyspnoea

- haemoptysis
- fever more than 38°C
- severe emaciation (weight at least 15% less than expected for height)

2. Retreatment Pulmonary TB patients

All retreatment TB patients should be hospitalised for the duration of the daily streptomycin injection (2 months), unless daily outpatient treatment at a clinic can be arranged.

3. Extrapulmonary TB Patients

This includes:

- TB meningitis
- TB pericarditis
- Miliary TB
- TB spine
- TB peritonitis

2.2 HOSPITAL DISCHARGE CRITERIA

Discharge planning should start within two weeks after the patient has been admitted to a hospital. It should include recruitment of a treatment supporter, health education of the patient, communication with the patient's chosen outpatient clinic and with his employers via a social worker.

Clinic Criteria. A patient should not routinely be kept in hospital for a specific period of time. Each patient should be assessed individually and should be discharged as soon as the following apply:

- the patient is medically stable
  - no dyspnoea at rest or on exertion
  - shows adequate weight gain
  - afebrile
  - no haemoptysis
- sputum has become negative for AFB (in cases where DOTS cannot be ensured)
- able to care for himself or if somebody in the family or community will take care of him/her
- willing and able to go to a local clinic or a community supporter for treatment

MEDICINE TO TAKE OUT (TTO)

A supply for **ONE** week should be given on discharge. The patient should be motivated to attend the nearest clinic with a week after discharge.

HIV-infected TB Patients. The decision to discharge a HIV-infected TB patient should be made in the same way as for any other TB patient.

Nutritional Support. No patient should be kept in hospital for nutritional support only. Outpatient nutritional support should be arranged for patient with inadequate access to food at home.

Extrapulmonary TB Patients. These patients should be discharged from hospital when the TB medical officer with the health team has decided that the patient on clinical grounds is fit for discharge.

MDR TB Patients. MDR patients should have THREE negative sputum cultures taken one month apart and be assessed by a MDR specialist prior to discharge.

2.3 CHILDREN WHO SHOULD BE HOSPITALISED

Any child with the following diagnosis:

- TB meningitis
- Miliary TB
- Airway obstruction with an audible wheeze
- Extensive lung disease with cavities
- TB pericarditis
- A severely malnourished child
- TB of Bones and joints

The duration of hospitalisation will depend on the response to treatment.

3. LABORATORY TESTS

To avoid duplication the clinic requesting admission for a TB patient must supply the laboratory results done by them.

The Laboratory is important in the Tuberculosis Control Programme.

- Positive sputum microscopy identifies those patients who are most infectious with the greatest burden of bacilli.
- Microscopy in a laboratory is essential for the definitive diagnosis of *Mycobacterium tuberculosis*.
- Sputum smear microscopy is the most reliable and cost effective way of diagnosing TB.

3.1 SPUTUM SPECIMEN

- A good specimen of sputum is required.
- Saliva is not useful for diagnostic purposes, as it is not a secretion of the lungs.
- Early morning specimens are best.

Day 1

Collect an "on the spot specimen", i.e. at the time you see the patient when the patient presents to the hospital facility for smear.

Day 2

The patient should produce a specimen first thing in the morning
Write clear instructions regarding what investigations are required, e.g.
TB microscopy, or
TB culture if TB culture alone is required, or
TB culture & susceptibility if susceptibility drug tests are required. Susceptibility drug tests are only done on **INH, Rifampicin and Ethambutol** to identify if a patient is a true MDR case.
Susceptibility for **ethambutol** is also requested to determine if the patient is needs to receive cycloserine.

If the patient is a re-treatment case collect one sputum specimen for smear and one for culture and sensitivity.

Date the specimen correctly.

3.2 REGISTER OF SPUTUM SPECIMENS SENT TO THE LABORATORY

Keep a register of the specimens being sent off.

3.3 WHEN TO DO A SPUTUM EXAMINATION

3.3.1 Sputum TB Microscopy

TWO specimens are taken on THREE separate occasions during the course of treatment of patient with PTB.

- Pretreatment
  When PTB is first suspected (pretreatment) send 2 specimens on consecutive days for TB microscopy. In case of a re-treatment patient sputum should also be collected for culture and sensitivity.

- During treatment
  Two sputum samples should be submitted for direct microscopy just before the end of the intensive phase of treatment (2 months for new patients and 3 months for retreatment patients). Treatment must be stopped for a period of 48 hours before the sputum is collected.

It is suggested to take sputum specimens on Monday before treatment is given.

- At end of treatment
  Two sputum samples should be sent after the completion of 5 months on treatment in new cases, and after 7 months in retreatment cases. (See flow diagram)

3.3.2 Sputum reports

3.3.2.1 Smear results

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

6 Number of bacilli seen on a smear		
No AFB	Per 100 oil immersion fields	0
1-9 AFB	Per 100 oil immersion fields	Scanty
10-99AFB	Per 100 oil immersion fields	1+
1-10 AFB	Per 1 oil immersion field	2++
>10AFB	Per 1 oil immersion field	3+++

TB Culture **indicate if the result is negative or postive.**

3.4 WHAT TO DO WHEN A TB SUSPECT HAS A NEGATIVE TB MICROSCOPY

If the sputum microscopy remains negative the patient may not have TB. You should think of the following possibilities:

	Pointers to the correct diagnosis
Congestive cardiac failure	• Dyspnoea (shortness of breath) • Haemoptysis • Oedema • Enlarged tender liver • CXR showing enlarged heart and pulmonary oedema
Asthma	• Intermittent chest symptoms • Expiratory wheezes • Normal CXR
Chronic obstructive airway disease	• Smoking history • Dyspnoea • Generalised wheezes
Purulent Bronchiectasis	• Large amounts of purulent sputum • Clubbing of fingers
Bronchial carcinoma	• Smoking history • Clubbing of fingers • Haemoptysis

Bacterial pneumonia	• Acute onset • Responds to antibiotic • Bacteria can be identified on microscopy and culture
Lung abscess	• Fluid level seen on chest x-ray • Large amounts of purulent sputum • Halitosis
Pneumocystis carinii	• Dyspnoea prominent • Parasite can be identified on microscopy • Often HIV positive

3.5 TB CULTURE

TB culture is expensive and should not be done routinely

TB culture testing is done:

- to identify patients suspected of having TB who are smear negative, but may be culture positive (in cases of early disease, HIV-associated disease), and
- so that drug susceptibility tests can be done (only possible on cultured organisms).
- For patients, who have two negative smears and initially have had a course of antibiotics but TB is still suspected.
- **On patients who have had TB treatment in the past (interrupters, failures or relapses.**
- **For patients who remain positive at the end of intensive phase of treatment and/or at the end of treatment.**

4. CHEST X-RAYS

Too much reliance on chest X-rays in the diagnosis of PTB results in unnecessary treatment, because the chest X-ray is not a reliable indicator of active PTB disease. An effective Provincial TB Control Programme (PTCP) concentrates on sputum positive patients.

No radiographic picture is absolutely typical of tuberculosis. Many diseases mimic TB on chest X-rays and this may lead to incorrect diagnosis of PTB. X-rays may show lung fibrosis or destruction due to previous TB and this may also lead to unnecessary treatment. Where X-ray facilities are available, a chest X-ray may be helpful but it is not essential for diagnosing TB nor for recording improvement.

Cure can only be established by negative sputum smears at the end of a treatment course.

4.1 INDICATIONS FOR CHEST X-RAY

When the sputum results are positive:

- Suspected complications, e.g. a breathless patient needing specific treatment, e.g. pneumothorax or pleural effusion.
- Frequent or severe haemoptysis (to exclude malignancy, bronchiectasis)
- To help in diagnosing other lung diseases.
- Only one of the two pretreatment smears is positive. (In this case an abnormal chest X-ray is a necessary additional criterion for the diagnosis of PTB).

When the sputum results are negative:

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

Indications for X-ray during and at the end of treatment:

It is only necessary to do X-rays during and at the end of treatment **if** there are **specific** clinical reasons and the progress has not been satisfactory. X-rays **should not** be done routinely on every case at the end of treatment.

4.2 X-RAY PATTERNS

Classical Pattern	**Atypical Patters**
Bilateral upper lobe infiltrates	Interstitial infiltrates (especially lower zones)
Cavitation	No cavitation
Pulmonary fibrosis and shrinkage	No abnormalities

4.3 DIFFERENTIAL DIAGNOSIS OF CHEST X-RAY FINDINGS

X-ray changes are not specific to TB. Here is a short list of other possibilities you should think of when looking at a chest X-ray:

Chest X-ray Finding	**Differential Diagnosis**
Cavitation	Bacterial pneumonia Lung abscess Fungal infections Bronchial carcinoma
Unilateral infiltrations	Pneumonia/bronchial carcinoma
Bilateral infiltrations	Bronchopneumonia Occupational lung disease Connective tissue disorders Sarcoidosis Pulmonary oedema

Mediastinal Lymphadenopathy	Lymphoma Bronchial carcinoma Sarcoidosis

5. TESTS NOT USEFUL IN THE DIAGNOSIS OF TB IN ADULTS

There is no place for "trial of treatment" as a means of diagnosing PTB. If PTB is suspected even with negative sputum smears and culture, the patient should be referred to the TB medical officer for a decision on diagnosis.

In South Africa the tuberculin test (TINE/MONO or Mantoux) should not be used for the routine diagnosis of TB in adults.

PCR (polymerase chain reaction) and ELISA tests are expensive new tests that are not yet useful for the routine diagnosis of TB.

6. AN OVERVIEW OF EXTRAPULMONARY TB

In all cases of extrapulmonary TB smear microscopy investigation should be done to exclude the possibility of PTB.

Type of disease	**Clinical features**	**Diagnosis**	**Differential diagnosis**
Lymph-adenopathy	Common in cervical nodes Matted together May cause chronic sinuses	Aspiration biopsy and histology	PGL (persistent generalised lymphadenopathy) in HIV Carcinoma Sarciodosis
Miliary TB	Sick patient Fever Weight loss Hepatosplenome-galy Tubercles in the choroid of the eye	Chest x-ray Pancytopenia Bacilli in sputum CSF Bone marrow or liver biopsy	AIDS Septicaema Disseminated carcinoma
Type of disease	**Clinical features**	**Diagnosis**	**Differential diagnosis**
Pleural effusion	Chest pain Breathlessness Mediastinal shift Decreased breath sounds Stony dullness on percussion	Chest x-ray Aspiration of straw coloured fluid (raised ADA) Pleural biopsy	Malignancy Post pneumonic effusion Pulmonary embolism
Pericardial effusion	Cardiovascular features Pericardial friction rub	Chest x-ray shows a large globular heart ECG: ST and T	Cardiomyopathy

		wave changes Sonar tape effusion	
Ascites (due to pertoneal TB) ad GIT TB	Weight loss Abdominal mass, ascites Fistulae may develop Diarrhoea	Chest x-ray (to exclude PTB) Ascitic tap Peritoneal biopsy Barium x-ray (in suspected malignancy)	Malignancy Liver disease
TB meningitis	Irritability Fever Weight loss Headache Decreasing consciousness Neck stiffness Fits	CSF microscopic and chemical examination **NB Prompt diagnosis vital!!**	Acute meningitis
TB spine	Back pain Psoas abscess Spinal cord compression	X-ray spine/CT scan Tissue biopsy	Secondary malignancy
TB bone	Chronic osteomyelitis	X-ray Biopsy	Malignancy
Hepatic TB	Hepatomegaly	Ultrasound Biopsy	Hepatoma Amoebic abscess
Renal TB	Frequency Dysuria Haematuria Loin pain Oedema	Sterile pyuria Urine culture for TB IV pyelogram	Bilharzia Carcinoma Nephritis
Adrenal glands	Hypo-adrenalism features: Hypotension, raised urea, low serum sodium	Ultrasound X-ray shows calcifications	Malignancy
Type of disease	**Clinical features**	**Diagnosis**	**Differential diagnosis**
Upper respiratory tract TB	Hoarseness Pain in ear Pain on swallowing	Laryngoscopy Oesophagoscopy	Carcinoma vocal cords Carcinoma of oesophagus
Female genital TB	Infertility Pelvic infection Ectopic pregnancy	Pelvic examination X-rays of genital tract Biopsy, urine for TB culture	Sexually transmitted diseases (STD) Malignancy
Male genital tract	Epididymitis, local pain	Tissue biopsy X-ray kidney Urine for TB culture	STD Malignancy

7. ADDITIONAL FEATURES OF SOME FORMS OF EXTRAPULMONARY TB

7.1 TUBERCULOSIS MENINGITIS

TB Meningitis is a life threatening disease with serious consequences if not treated promptly. Patients may lose their ability to lead independent lives.

Routes of spread of TB to the meninges include the following:

- Blood borne
- From rupture of a cerebral tuberculoma into the subarachnoidal space.

Clinical features:

- There is a gradual onset and progression of headache and decreased consciousness.
- Examination often reveals neck stiffness and a positive Kerning's sign.
- Cranial nerve palsies result from exudates around the base of the brain.
- Tuberculomas and vascular occlusion may cause focal neurological deficits and seizures.
- Obstructive hydrocephalus may develop.
- Spinal meningeal involvement as well as the meningitis itself may cause paraplegia.

Diagnosis:

The diagnosis is made from clinical features and cerebrospinal fluid (CSF) examination. In most cases of clinically suspected TB meningitis, lumbar puncture is safe.

Treatment

- Hospitalisation is always indicated initially.
- Intensive phase of treatment with four drugs for TWO months (Regimen 1)
- Continuation phase for SEVEN months
- Cortisone should be added to the treatment regimen and prescribed by a medical officer.

Differential Diagnosis

The table below shows the differential diagnosis of TB meningitis, with typical CSF abnormal findings. A normal CSF does not exclude disease in HIV-positive patients.

DIFFERENTIAL DIAGNOSIS OF TUBERCULOSIS MENINGITIS				
CSF ABNORMALITIIES				
Disease	**CSF White cells**	**Protein**	**Glucose**	**Microscopy**
Tuberculosis meningitis	Elevated L>PMN (PMN raised initially)	Increased	Decreased	AFB (in some cases)
Cryptococcal* meningitis	Elevated L>PMN	Increased	Decreased	Positive India ink staining
Partially treated bacterial meningitis*	Elevated both PMN and L	Increased	Decreased	Bacteria on Gram stain (rarely)
Viral meningitis	Elevated L>PMN	Increased	Normal (low in mumps or H.simplex)	
Secondary syphilis	Elevated L>PMN	Increased	Normal	
RARE CAUSES				
Late stage trypanosomiasis	Elevated L>PMN	Increased	Decreased	Motile trypanosomes
Tumour (Carcinoma/lymphoma)	Elevated L>PMN	Increased	Decreased	Cytology shows malignant cells
Leptospirosis	Elevated L>PMN	Increased	Decreased	Leptospires
Amoebic meningitis	Elevate L>PMN	Increased	Decreased	Amoebae
NOTE: TB Culture of CSF is important for diagnosis > = greater than PMN = polymorphonuclear leucocytes L = Lymphocytes *common differential diagnosis				

7.2 TUBERCULOSIS LYMPHADENOPATHY

The lymph nodes most commonly involved are the cervical nodes. The usual course of lymph node disease is as follows:

Firm discrete nodes → *Fluctuating nodes, matted together* → *Skin breakdown*
Abscesses → *Chronic sinuses* → *Heal with scarring*

In severe immuno compromised (HIV+) patients, tuberculosis lymphadenopathy may resemble acute pyogenic lymphadenitis. Persistent Generalised Lymphodenopathy (PGL) is a feature of HIV infection that develops in 50% of HIV-positive individuals.

Diagnosis

The possibility should always be suspected in cases of lymphodenopathy. The diagnosis can usually be made from other clinical features of TB. If you suspect TB in a patient with enlarged lymph nodes, refer to a doctor who may need to aspirate. All aspirates must be sent for microscopy and culture. This will be positive for AFB in 70% of cases of TB lymph nodes. Routine biopsy for histology is only done if the diagnosis is still in doubt.

Treatment

TWO months intensive phase, FOUR months continuation phase (Regimen 1).

7.3 MILIARY TUBERCULOSIS

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

Clinical features

The patient presents with systemic features (fever, weight loss etc.). He may have hepatosplenomegaly and tubercles in the choroids of the eyes. Miliary TB is a common cause of terminal illness in HIV-positive patients.

Diagnosis

- Sputum smear microscopy is usually negative.
- Chest X-ray shows diffuse, uniformly distributed, small miliary shadows. "Miliary" means "like small millet seeds."
- Fever present for more than 10 days.
- Blood count may show a pancytopenia
- Liver function tests may be abnormal.
- Confirmation of the diagnosis is sometimes possible from culture of sputum, CSF, bone marrow, or biopsy, i.e. liver, showing typical tubercles on histology.

Treatment
(When a patient has suffered PTB before but is now diagnosed to suffer extra pulmonary TB he/she should receive regimen 1 as it is a new disease

TWO months intensive phase, SEVEN months continuation phase (Regimen 1).

7.4 TUBERCULOUS SEROUS EFFUSIONS

Inflammatory tuberculous effusions may occur in any of the serous cavities of the body, i.e. pleural, pericardial or peritoneal cavities.

They are a common form of TB in HIV-positive patients.

Diagnosis

Patients usually have systemic and local features.

Microscopy of the aspirates from tuberculous serous effusions rarely shows AFB because the fluid forms as an inflammatory reaction to TB lesions in the serous membrane.
The Adenosine Deaminase (ADA) is raised >30U/l (this is a measure of the lymphocyte count). The ESR is also raised.

TB culture, even if available, is of no immediate help. A culture result takes six weeks.

The aspirate is usually an axudate, i.e. the protein content is more than 30g/l.

In populations with a high prevalence of HIV, TB is the commonest cause of an exudative serous effusion.

7.4.1 TUBERCULOUS PLEURAL EFFUSION

Typical clinical features are systemic and local:

- chest pain
- breathlessness
- tracheal and mediastinal shift away from the side of the effusion
- decreased chest movement
- stony dullness

Chest X-ray shows unilateral or bilateral, uniform, white opacity, with a concave upper border.

Diagnosis

A pleural aspiration will show that:

- the fluid is an exudate (protein content is >30g/l)
- it is usually straw coloured, occasionally blood stained
- the white cell count is high with predominantly lymphocytes (1000 – 2500 per mm^3)

- the Adenosine Deaminase (ADA) is raised >30U/l (this is a measure of the lymphocyte count)

If the fluid is bloody, you should exclude carcinoma. If the fluid contains pus, it indicates an empyema.

A closed pleural biopsy can be done by a medical officer with an Abrams needle for histological diagnosis. The yield is about 75% positive for TB. This is the best way to confirm the diagnosis.

Treatment

TWO months intensive phase, FOUR months continuation phase (Regimen 1).

7.4.2 TUBERCULOUS PERICARDIAL EFFUSION

Diagnosis

The diagnosis usually rest on suggestive clinical features and investigations (ECG, chest X-ray):

Cardiovascular signs and symptoms	• Chest pains • Shortness of breath • Cough • Dizziness and weakness • Leg swelling	• Tachycardia • Low blood pressure • Raised jugular venous pressure • Impalpable apex beat, 3rd heart sound • Pericardial friction rib
Chest X-ray	• Large globular heart • Clear lung fields • Pleural effusion	
ECG	• Tachycardia • Flattening of ST and T waves • Low voltage QRS complexes	

Treatment

TWO months intensive phase, FOUR months continuation phase (regimen 1). Corticosteroids can be added. Treatment with steroids and anti-TB drugs without

pericardiocentesis (tap) usually results in satisfactory resolution of tuberculous pericardial effusion. In cases of cardiac tamponade the effusion should be aspirated.

A possible outcome of a TB pericardial effusion is the development of constrictive pericarditis. All patients with pericardial effusion should be referred to a specialist centre.

7.4.3 TUBERCULOS ASCITES (TB PERITONITIS)

Ascites results from peritoneal TB. Routes of spread of TB to the peritoneum include the following:

- From tuberculous mesenteric lymph nodes.
- From intestinal TB.
- Blood borne.

Clinical features

- Patients present with systemic features, ascites and abdominal pain.
- There may be palpable abdominal masses
- Fistulae may develop between bowel, bladder and abdominal wall
- Bowel obstruction may occur

8. CASE DEFINITIONS:

8.1 CASE DEFINITIONS BY SITE AND RESULT OF SPUTUM SMEAR

Smear Positive PTB Case

- There are at least 2 sputum smears positive for AFB's, or
- 1 sputum smear positive for AFB's and chest x-ray abnormalities consistent with active TB culture positive TB, or
- 1 sputum smear or culture positive and clinically ill

Smear Negative PTB Case

- At least 2 sputum smears negative for AFB's
- Chest X-ray abnormalities consistent with active TB. In most cases, the patient will have had treatment with a broad spectrum antibiotic with no response

Extra pulmonary TB

There is clinical and/or histological evidence consistent with active TB.

The following are some of the forms of extra pulmonary TB:

- Pleural effusion (the pleura is outside the lung)
- Hilar adenopathy
- Miliary TB (TB is widespread throughout the body and not limited to the lungs)

8.2 CASE DEFINITIONS BY TREATMENT

New TB Case

Decide whether a patient is a new patient i.e. has never been treated before or has been treated for less than 4 weeks before.

Retreatment TB Case

A retreatment case can be ONE of the following four categories:

- Relapse after previous cure (RC). A sputum smear positive PTB who received treatment and was declared cured (sputum became negative) **AND** has now developed sputum smear positive PTB again.
- Relapse after previously completed treatment (RT), but no proof of sputum conversion to negative.
- Retreatment after treatment failure (RF). A PTB patient who is still sputum smear positive at the end of the treatment period.
- Retreatment after treatment interruption (RI). A TB patient who interrupted the treatment for more than 10 days during the intensive phase of treatment **OR** who interrupted treatment for a total of more than one month during the continuation phase.

9. PRINCIPLES OF TB TREATMENT

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

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

Treat with combination drugs. Combined tablets are the best as they improve patient compliance.

In hospitals, treatment is given for seven days a week. Intermittent therapy (3 times a week), if used, may be given in the continuation phase only.

No trials of therapy should be given. A patient either has TB or should be treated, or does not have TB and should not be treated.

In Summary: Criteria for Starting TB Treatment

- 2 positive sputum smears
- 1 positive sputum smear and an abnormal chest X-ray
- 1 positive sputum smear and one or more positive sputum culture
- 1 positive sputum culture and an abnormal chest X-ray
- Sick patient with 1 positive smear or positive culture.

10. STANDARDISED TB TREATMENT REGIMES

- Directly Observed Therapy (DOTS) is essential during the intensive phase of treatment to ensure that the patient takes every single dose.
- To retain its high potency against TB, rifampicin has to be protected.
- The weight of the patient, when determining the dosage, refers to patient weight BEFORE treatment for ALL REGIMES.
- It should be adjusted accordingly after the intensive phase.

10.1 REGIMES FOR TB TREATMENT
(See Annexure D)

Regimen 1: New Adult TB patient (smear or culture positive and extra pulmonary TB)

A patient who has never been treated before or who has previously been treated for less than 4 weeks. Weights refer to weights before treatment, dosage according to weight. Intensive phase of treatment for 2 months and then continuation phase for 4 months.

Exceptions to duration of treatment for new patients:

Patients with TBM, miliary and bone TB should have 9 months treatment.

Regimen 2: Retreatment Adult TB patients.
(See Annexure D)

A patient who has had a previous course of treatment (failure, relapse or previous interruption). Intensive phase of treatment for 3 months, then continuation phase for 5 months.

10.2 IMPORTANT DRUG INTERACTIONS

Rifampicin reduces the efficacy of oral and injectable contraceptives. The result may be unplanned pregnancies. Therefore it is very important when introducing new patient to treatment to:

- ask about contraception

- explain the problem
- if necessary, after the oral or injectable contraceptive or suggest IUCD.
- Intervals for contraceptives should be changed to:
    - Oral contraceptives – placebo phase to 5 days (red pills)
    - Depo Provera 2 months
    - Nuristirate – 6 weeks

INH increases Phenytoin (Epanuting) and Carbamazepine (Tegretol) levels. Therefore it is important to find out whether patients are on anti-convulsant treatment and to watch for overdose. Tremors, muscle stiffness and other CNS effects may result. If anti-convulsant dosage is already high get medical advice.

Pyridoxine (vitamin B6)

It is unnecessary to give pyridoxine routinely, but the use of alcohol during drug therapy should be discouraged or restricted. However, Pyridoxine should be added for TB patients who are alcohol abusers, pregnant, diabetic, or epileptic and for HIV positive patients. The protective dose is 10 – 25 mg daily. This dose should never be exceeded in pregnancy. The dose for those who have an established peripheral neuropathy is 50mg daily.

11. MANAGEMENT OF TB IN PREGNANCY

A patient with tuberculosis should be advised not to become pregnant while she is on TB treatment. Rifampicin stimulates liver enzymes which may breakdown other drugs more rapidly than normal. Those on the contraceptive pill and on rifampicin should take extra precautions against pregnancy.

If a pregnant patient presents with tuberculosis, all drugs recommended in the standard regimes are safe, with the exception of streptomycin. Give pyridoxine with isoniazid to avoid the small risk of damaging infant's nervous system. Daily dose of pyridoxine should NOT exceed 25mg daily.

TB drugs that should NOT be given are the following:

- *Streptomycin* (or related drugs capreomycin, kanamycin) or ofloxacin. All these may cause deafness in the infant.
- *Ethionamide and prothionamide* (drugs used for MDR TB should not be given because they can cause abnormalities of development in the foetus).

12. TREATMENT OF TB IN HIV-POSITIVE PATIENTS

Anti-TB drug treatment is the same for HIV-positive and HIV-negative TB patients.

- **The same drugs are used for the same duration.**
- Thiacetazone should not be used in a HIV-positive patient as it may cause severe skin reactions that may be potentially fatal.

- Take extra care when administering streptomycin injections to prevent possible needlestick injuries and cross infection.
- New patients are treated with Regimen 1.
- Reactivation or re-infection is treated with the retreatment Regimen 2.
- Peridoxine 10 – 25mg to be given daily.

The recurrence of TB in HIV-positive cases after completion of treatment is higher than in HIV-negative cases. The reasons for this are:

- True relapse – reactivation of persistent bacilli not killed by the anti-TB drugs
- Re-infection – due to re-exposure to a NEW source of infection

Non-tuberculous Mycobacteria (NTM) is usually non-pathogenic but in HIV-positive patient may cause disease and should be treated. They can only be identified on culture tests. A HIV-positive patient with NTM on culture should be referred to a specialist

13. MULTIDRUG RESISTANT (MDR) TB

Multidrug resistant (MDR) TB refers to resistance to at least both **INH** and **Rifampicin.** The handling of the above mentioned patients are discussion in the MDR Policy.
Also do test if the patient is resistant to **Ethambutol.** Patients resistant to Ethambutol will be put onto Cycloserine.

14. TUBERCULOSIS IN CHILDREN

14.1 AN APPROACH TO DIAGNOSIS OF PTB IN CHILDREN

It is easy to over diagnose TB in children but it is also easy to miss it. We need to assess carefully all the evidence before making the diagnosis. Bacteriological confirmation of TB in children is usually not possible. Under the age of ten years, children with PTB rarely cough up sputum. They usually swallow their sputum. Gastric aspiration and laryngeal swabs are sometimes used to identify swallowed organisms in the diagnosis of PTB in children.

The diagnosis of TB in children revolves around:

- the clinical features
- tuberculin skin test
- chest X-ray
- history of contact with a sputum positive PTB case

14.2 THE IMPACT OF HIV ON THE DIAGNOSIS OF TB IN CHILDREN

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

- Several HIV-related respiratory diseases, including TB may have similar symptoms.
- Weight loss is a common problem in HIV-positive children.
- The interpretation of the tuberculin skin test is even more unreliable than usual. An immunocompromised child may have a negative tuberculin skin test despite having TB.

The radiological features of TB in HIV positive children with TB are often atypical (see Chapter 11).

Differential diagnosis of PTB in HIV-infected children

- Bacterial pneumonia
- Pneumocystis carinii pneumonia
- Viral pneumonia
- Pulmonary lymphoma
- Fungal lung disease

14.3 A SCORE SYSTEM FOR THE DIAGNOSIS OF TB IN CHILDREN

A score system is one way of trying to improve diagnosis of childhood TB by the careful and systemic collection of diagnostic information.

A score system is there to help you in your clinical judgement.
The table below shows a score chart (adapted from the WHO book HIV/TB) for the diagnosis of childhood TB.

SCORE SHEET FOR TB IN CHILDREN (A score of 7 or more indicates a high likelihood of TB)

Feature	0	1	2	3	4	Score
GENERAL						
Weeks of illness	<2	2-4		>4		
Nutrition (% weight for age)	>80%	60-80%		<60%		
Family history of TB	None	Reported by family		Proved sputum positive		
Tuberculin test				Positive		

Malnutrition				Not improving after 4 weeks		
Unexplained fever and night sweats			No response to treatment			
LOCAL						
				Lymph nodes		
				Joint or bone swelling		
				Abdominal Mass or ascites		
				CNS signs, abnormal CSF		
					Angle deformity of spine	
						TOTAL

Name of child …….
Date: …….. Completed by: ……

(>=more than; <=less than.)

How to apply/read score system

Example: Score the following patient for TB:

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

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

Any score of 7 or more is suggestive of TB!

14.4 SOME FURTHER ISSUES IN CHILDHOOD TB

14.4.1 RESPONSE TO TB TREATMENT

- The child gains weight and the TB symptoms disappear.
- Fever can take two weeks or more to subside.
- A child who is on treatment but does not improve may have some other disease and should be reassessed.
- X-ray changes, especially hilar and mediastinal adenopathy, may remain unchanged for 18 months or longer, despite a satisfactory response to treatment.

14.4.2 A BABY BORN TO A MOTHER WITH ACTIVE PTB

- The baby should have treatment for THREE months starting immediately after birth with INH 5mg per kg per day for 6 months
- BCG immunisation should be done three days after the TB treatment is completed.

14.4.3 A CHILD WITH TB CERVICAL ADENITIS (SWOLLEN GLANDS IN THE NECK)

- Even if the neck glands are hard and matted together children should be treated for six months and not more.
- It might be advisable to add steroid therapy for a few weeks to prevent ulceration and obstruction of the airways.
- Hilar adenopathy can take 2 years to disappear. A six-month course of anti-TB treatment is sufficient.

15. DETECTION AND DIAGNOSTIC TOOLS (INCLUDING SKIN TESTING AND X-RAY)

Tuberculin Skin Test

The basis of the tuberculin skin test is the injection into the skin of PPD (purified protein derivative). This is an extract of tuberculin material.

Principles of Tuberculin skin testing

- It measures the body's reaction to tuberculin protein.
- It is a useful indicator of infection in young children.
- It is easy to perform and interpret (TINE or MONO test are PPD impregnated tools and Mantoux is an intradermal injection).

Methods of the Tuberculin skin test

- *Mantoux Test*

  Inject a known amount of PPD between the layers of skin (intradermally). Ensure that the injection goes into and not under the skin. Measure the reaction to the test at the site of injection 48-72 hours later.

- *TINE/MONO Test*

  The instruments are impregnated with PPD and need only to be pressed into the skin of the forearm. The area of induration is measured 72 hours later.

What does a POSITIVE Tuberculin Skin Test mean?

A positive reaction is only one piece of evidence in favour of the diagnosis.

Positive results of skin test:

Tuberculin Test	Previous BCG	No previous BCG	HIV+
Mantoux	15 mm or more	10 mm or more	4 mm or more
Monotest	8 mm or more	4 mm or more	Uncertain
TINE test	Blistering and confluent swelling	Ring of induration	Uncertain

Chest radiography (X-ray)

X-rays are expensive and usually only available in hospitals. Changes on X-rays are often non-specific. It is undesirable to diagnose TB from X-rays alone. Many diseases can look like TB on X-ray.

The most common X-ray signs in children with TB are:

- A broad medistinum due to enlarged hilar or mediastinal glands. The enlarged hilar glands may compress the airway and cause obstruction on lobar collapse.
- Miliary infiltrations in the lungs
- Pleural effusions that usually occur in children older than six years.

16. NOTIFICATION AND RE-NOTIFICATION

- **New cases** must be notified on form **GW 17/5** and also telephonically if possible. The **death** of a patient being treated for tuberculosis must be notified using form **GW17/5.** The person who makes the diagnosis should

notify the patient. There is a place on all Patient Cards and Forms for showing whether a patient has been notified. It is there to avoid uncertainty and duplication.

- **Re-notification.** Only patients who have
  a) previously completed a full course of treatment, **and**
  b) have been shown to be smear or culture negative at the end of treatment, **and**
  c) have been shown to be smear or culture positive again should be re-notified.

17. RECORD KEEPING

All standard cards and records from the hospital must be used including the following:

Clinic/Hospital Register (GW 20/11)

The aim of the Tuberculosis register is to improve the management of tuberculosis cases. A TB register should be kept in a hospital where the treatment is given to a TB patient for a period longer than 2 weeks.

Patient treatment card (GW 20/15)

The patient keeps this pocket-sized card for presentation during clinic visits after discharge from the hospital. This card must be kept updated.

Quarterly Report (GW 20/16)

The quarterly case finding report should be completed and forwarded to the District TB Coordinator at the end of each quarter for any patient admitted to receive treatment for the intensive phase.
No outcome reports need to be kept by the hospitals', as patients are discharge before the completion of their treatment.

18. THE HEALTH CARE SETTING

18.1 THE TB WARD AND THE CLINIC

It has become necessary to give attention to the control of transmission of tuberculosis in health care settings, following the nosocomial (hospital) outbreaks of multi-drug resistant tuberculosis in the USA in association with HIV infection.

A joint statement by the WHO Tuberculosis Programme and the IUATLD includes guidelines on the identification and isolation of infectious tuberculosis patients, environmental control and protection of health care workers and others. These

guidelines are applicable to all TB patients and health workers whether or not multi-drug resistant tuberculosis is present.

The initial phase of treatment must be supported through DOTS. This might necessitate hospitalisation of patients. Unless hospital and clinic take certain precautions staff, TB can be transmitted to health workers.

18.2 CORE ELEMENTS OF EFFECTIVE TB PREVENTION

Identification and Treatment of Infectious Tuberculosis Patients

The best way of interrupting the chain of tuberculosis transmission is by rapid diagnosis and treatment of infectious pulmonary TB patients.

The most infectious tuberculosis patients are those with sputum positive pulmonary disease.

Ventilation

Good ventilation is one of the most effective environmental measures to reduce tuberculosis transmission. Tuberculosis wards with doors closed and windows open to the outside are ideal. Exhaust fans are useful for moving air from wards and isolation rooms to the outside.
Difficulty may arise in areas with cold winters when windows are kept closed. In these situations it is important that airflow from tuberculosis wards and isolation rooms are not directed into other parts of the hospital. Fans to the outside may be useful.

Collection of Sputum

Areas where sputum specimens are collected must be well ventilated. Health workers need to take special care that patients do not cough directly onto them (see Chapter5).

Outpatient clinics that screen for suspected tuberculosis cases should also be well ventilated. Sputum specimens should be collected in an area separate from the waiting room, outdoors or in a well-ventilated room.

Laboratories processing sputum specimens from tuberculosis suspects should follow published guidelines to minimise tuberculosis transmission to laboratory workers.

Ultraviolet Light/Direct Sunlight

Some authorities have recommended that ultraviolet lights be installed in areas where tuberculosis transmission is likely to happen, or in wards where TB patients (especially MDR TB patients) are treated. The installation and maintenance is

expensive and requires expert supervision, as it can be potentially harmful if incorrectly installed.

18.3 PROTECTION OF THE HEALTH WORKER

Education and Orientation

Health care workers need to be educated about tuberculosis. Health staff that knows that they are HIV-positive should avoid working with tuberculosis patients.

Infectious PTB patients with uncontrolled coughing who are being transported to other areas of the hospital, e.g. the radiology department, should wear masks, if available. For maximal efficiency masks should be tight fitting and filter particles 1-5 microns, i.e. the size of infectious droplet nuclei. These masks are expensive and probable cannot be used routinely.

Other masks, such as surgical masks, which prevent larger particles from being aerosolised as patients' cough or sneeze, may have some protective effect. Surgical masks, however, do not prevent inhalation of infectious droplet nuclei and cannot be relied on for full protection. They are thus not indicated for staff and visitors.

Health workers should be encouraged to eat well, stay fit, restrict their alcohol consumption and not smoke cigarettes.

Staff Surveillance

ON EMPLOYMENT

On employment, each new employee should complete a standardised questionnaire. This should include questions on:

- BCG immunisation
- Past TB infection
- Previous contact with TB
- Underlying medical conditions which affect immunity

A Chest X-ray as a baseline should be done
No tuberculin test should be done and **no** BCG should be give.

Voluntary HIV counselling and testing should be offered, after explaining the increased risk of TB to an HIV-positive person. HIV-positive staff should be advised to avoid contact with TB patients and should be given responsibilities that limit their exposure to TB patients.

Most importantly, health workers should be instructed to seek care if they develop symptoms of TB.

MONITORING

Serial tuberculin testing is not currently recommended in South Africa because of their high prevalence of TB infection in South Africa. An estimated 60% of adults would have positive tuberculin tests. Additionally more than 90% of children in South Africa are immunised with BCG that makes the interpretation of tuberculin skin test difficult.

The only situation in which tuberculin testing should be considered in a HIV-positive health worker in settings where decisions for provision of TB preventive therapy are based on tuberculin results.

Regular questionnaires on symptoms of TB and regular weighing every six months to detect unexplained weight loss should also be considered.

Annual chest X-ray screening is not recommended.

POST EMPLOYMENT

Tuberculin skin tests may be done on termination of employment. If the test is positive, and the pre-employment test was negative, and if the health worker subsequently gets sick with TB, the worker is eligible for compensation according to the Compensation for Occupational Injuries and Diseases Act.

A chest X-ray may be done to compare with the pre-employment chest X-ray.

19 ORDERING OF TB DRUGS

Each hospital is responsible to budget for TB drugs. TB drugs are ordered on the standard system used in each hospital for the ordering of drugs.

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UP DATE 28 MAY 2001

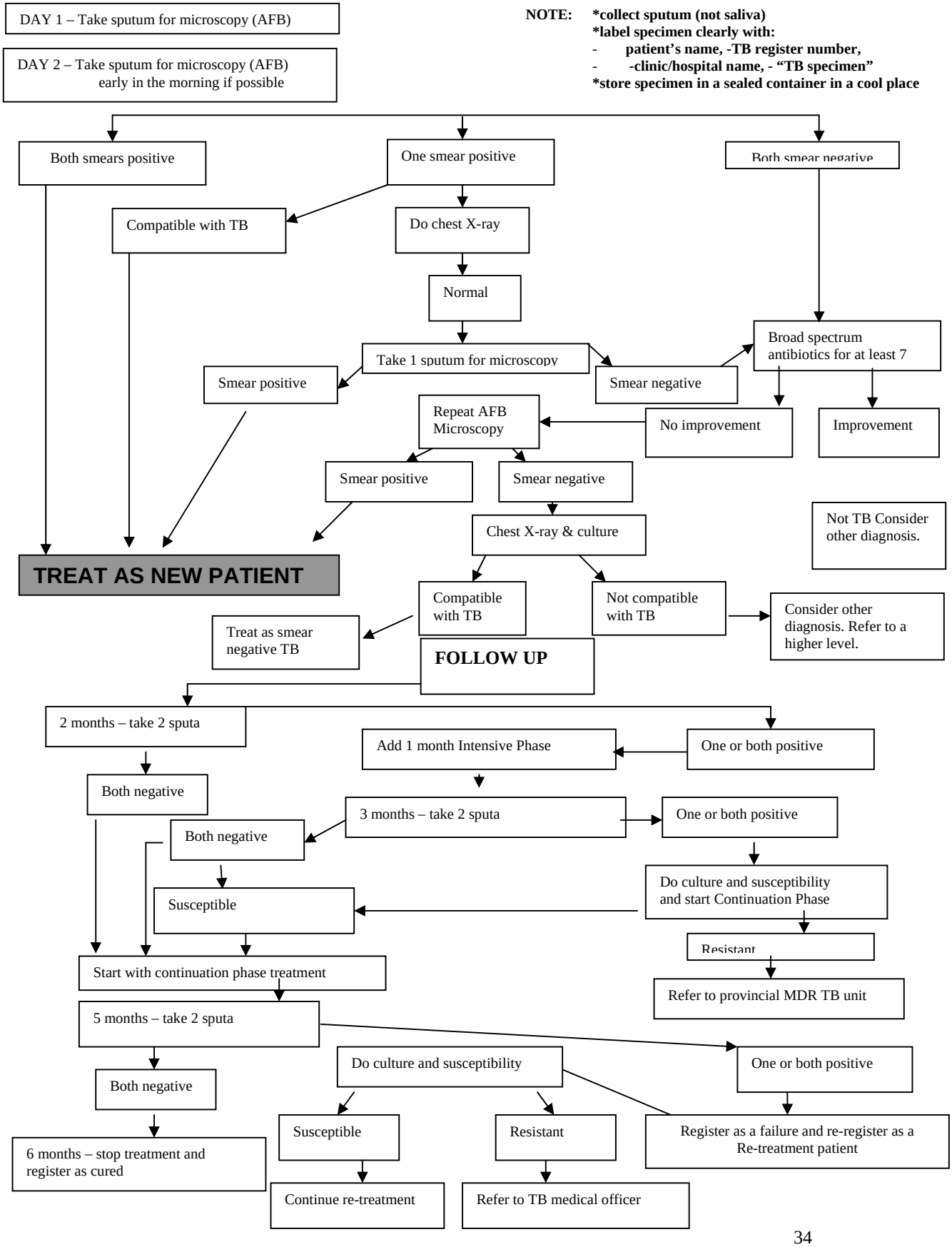
REFERENCE

The South African Tuberculosis Control Programme Practical Guidelines 1999. Department of Health.

The South African Tuberculosis Control Programme Practical Guidelines 2000 Department of Health.

Tuberculosis: A training manual for Health Care Workers. Department of Health. First edition 1998

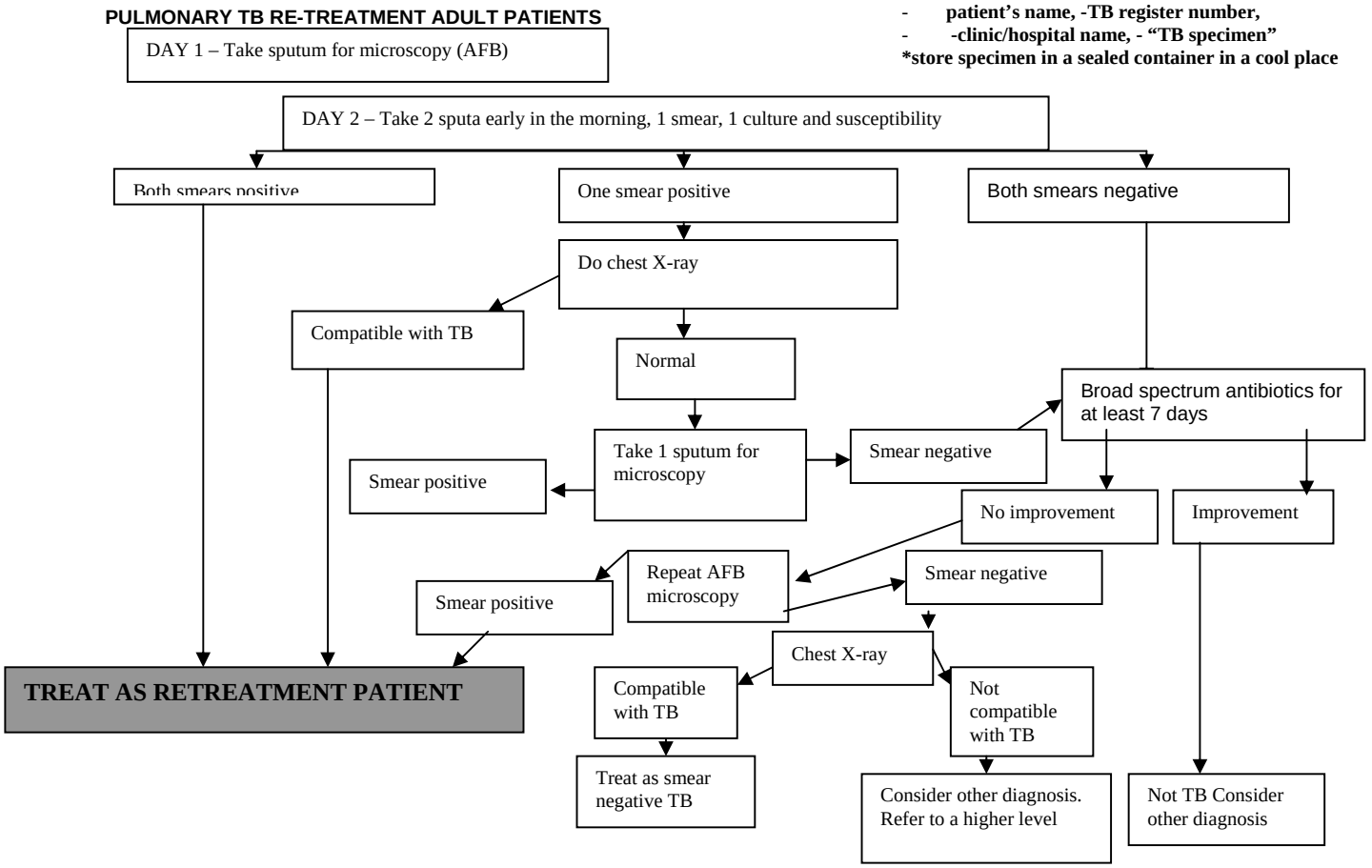
PULMONARY TB–NEW ADULT PATIENTS – DIAGNOSIS **ANNEXURE A**

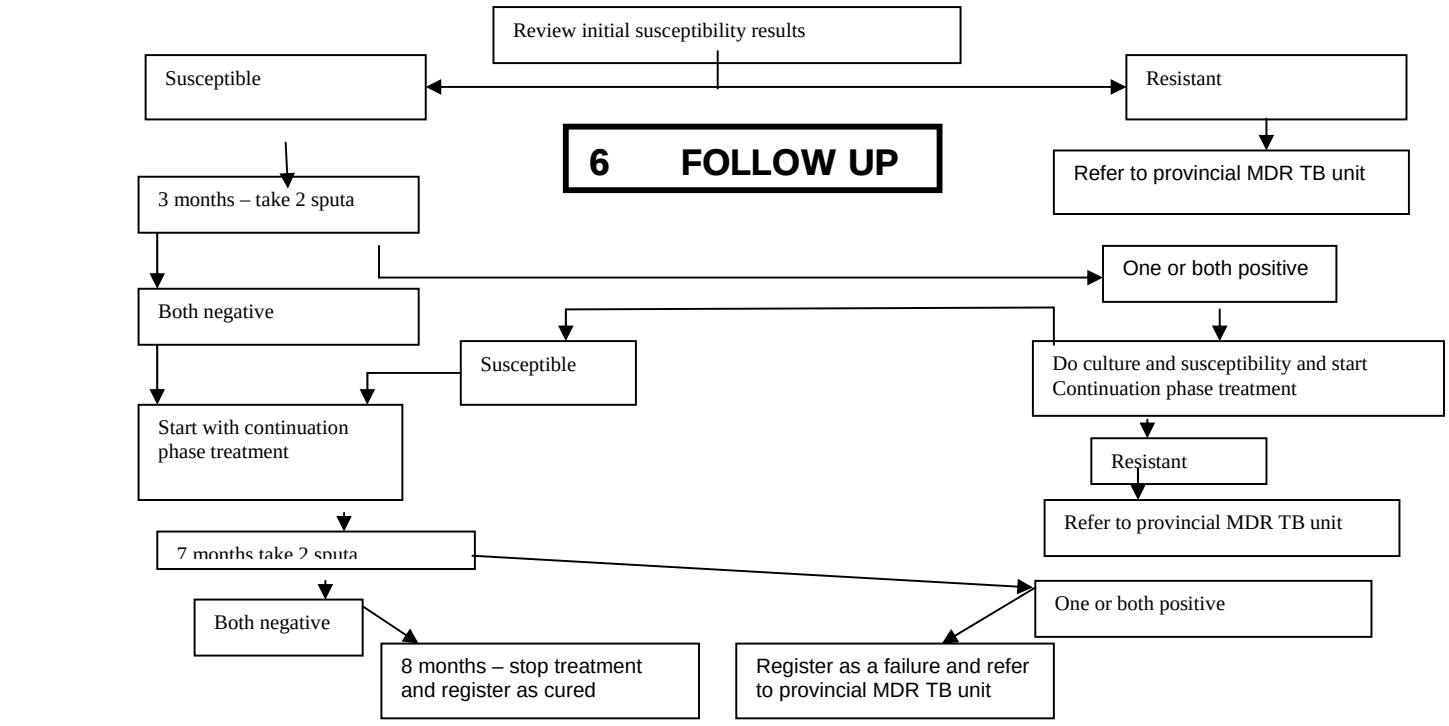


NOTE: ***collect sputum (not saliva)**
***label specimen clearly with:**
- **patient's name, -TB register number,**
- **-clinic/hospital name, - "TB specimen"**

***store specimen in a sealed container in a cool place**

PULMONARY TB RE-TREATMENT ADULT PATIENTS





ANNEXURE C

TREATMENT OF PULMONARY TB AND EXTRA PULMONARY TB PATIENTS

INITIATION OF TREATMENT

(REGIMEN 1) NEW ADULT PATIENTS

New smear positive and other serious pulmonary and extra pulmonary tuberculosis.

2 MONTHS INITIAL PHASE (treatment given 5 times a week)	**PATIENT UNDER 50 KG**	**PATIENTS OVER 50 KG**
Combination tablet RHZE 120/60/300/200mg*	4 tabs	5 tabs
4 MONTHS CONTINUATION PHASE (treatment given 5 times a week)	**PATIENT UNDER 50 KG**	**PATIENTS OVER 50 KG**
Combination tablet RH 150/100 mg	3 tabs	
Combination tablet RH 300/150 mg		2 tabs

R - rifampicin
H - isoniazid (INH)
Z - pyrazinamide.
E – ethambutol
S – streptomycin
***Ethambutol 225 mg in combination is also acceptable.**

ANNEXURE D

(REGIMEN 2) RETREATMENT ADULT PATIENTS
(smear positive retreatment cases (failure, relapse and return after interruption)

2 MONTHS INITIAL PHASE (treatment given 5 times a week)	**PATIENT UNDER 50 KG**	**PATIENTS OVER 50 KG**
Combination tablet RHZE 120/60/300/200mg*	4 tabs	5 tabs
Streptomycin	750 mg	1000 mg
3 RD MONTH (five times a week)	**PATIENT UNDER 50 KG**	**PATIENTS OVER 50 KG**
RHZE	4 tabs	5 tabs
5 MONTHS CONTINUATION PHASE (treatment given 5 times a week)	**PATIENT UNDER 50 KG**	**PATIENTS OVER 50 KG**
Combination tablet RH 150/100 mg	3 tabs	
E 400 mg	2 tabs	
Combination tablet RH 300/150 mg		2 tabs
E 4oo mg		3 tabs

Note
Streptomycin should be reduced to 150mg per day to those older than 45 years and not be given to those over 65 years. It should <u>not</u> be given during pregnancy.
***Ethambutol 225 mg in combination is also acceptable.**

Rifampicin reduces the efficacy of oral and injectable contraceptives. It is very important when introducing new patients to treatment to:
*** Ask about contraception**
*** Explain the problem**
*** If necessary, aIter the oral and injectable contraceptive or suggest and IUCD.**
Ask patients about other durgs they may be taking and check that there is no cross reaction.

ANNEXURE E

(REGIMEN 3) CHILDREN WITH TUBERCULOSIS

PRETREATMENT Body weight	**2 MONTHS INITIAL PHASE (treatment given 5 times a week)** RHZ 60/30/150 mg	**4 MONTHS CONTINUATION PHASE (treatment given 5 times a week)** RH 60/30 mg
3 – 4 kg	½ tab	½ tab
5 – 7 kg	1 tab	1 tab
8 – 9 kg	1½ tab	1½ tab
10 – 14 kg	2 tabs	2 tabs
15 – 19 kg	3 tabs	3 tabs
20 - 24 kg	4 tabs	4 tabs
25 – 29 kg	5 tabs	5 tabs
30 – 35 KG	6 tabs	6 tabs

R – rifampicin
H – isoniazid
Z - pyrazinamide

All children with severe forms oaf tuberculosis (TB-bone, meningitis, spine, peritonitis, military TB) should be referred to hospital for management. Guidelines for management of such cases are different and longer.

CHEMOPROPHYLAXIS

Active case-finding is recommended for all children under the age of 5 years. Such children in close household contact with smear positive case of pulmonary TB or who are tuberculin skin test positive should be given prophylaxis. The correct regimen to give as prophylaxis to a well child under 5 years is **5mg isoniazid per kg for 6 months.**

Routine chemoprophylaxis of those older than 5 years is not recommended.

Ethambutol should not be given to children under 8 years of age.

Note
Refer to weights before treatment for all regimens