CHAPTER 10

TUBERCULOSIS

10.1 TUBERCULOSIS, PERINATAL

P37.0
*Notifiable condition.

DESCRIPTION

Tuberculosis acquired in the first 3 months of life. Perinatal tuberculosis may be acquired in one of the following ways:

» Transplacental transmission – usually extrapulmonary or disseminated TB.
» Via the passage of swallowed maternal blood or amniotic fluid during delivery – usually extrapulmonary TB.
» Inhalation of the bacilli during the neonatal period – usually pulmonary TB.

DIAGNOSTIC INVESTIGATIONS

» Hepatosplenomegaly, a suggestive chest X-ray, TB exposure via a mother or close contact with another source case.
» Positive smear or culture on any suitable sample, e.g. gastric aspirate in the neonate or tissue histology suggestive of TB.
» Endometrial swabs or sputum samples in the mother positive for *M. tuberculosis*. See section 10.2: Tuberculosis, Pulmonary in children.

GENERAL AND SUPPORTIVE MEASURES

» Have a low threshold for starting presumptive treatment based on clinical assessment.
» Check drug sensitivity of the source. If drug resistant, refer.
» Check HIV status of the mother and, if positive, test the baby with HIV PCR.
» Screen all household contacts.
» Monitor the nutritional status of the neonate closely.
» Do not give BCG vaccine at birth but administer BCG after completing TB treatment or prophylaxis.

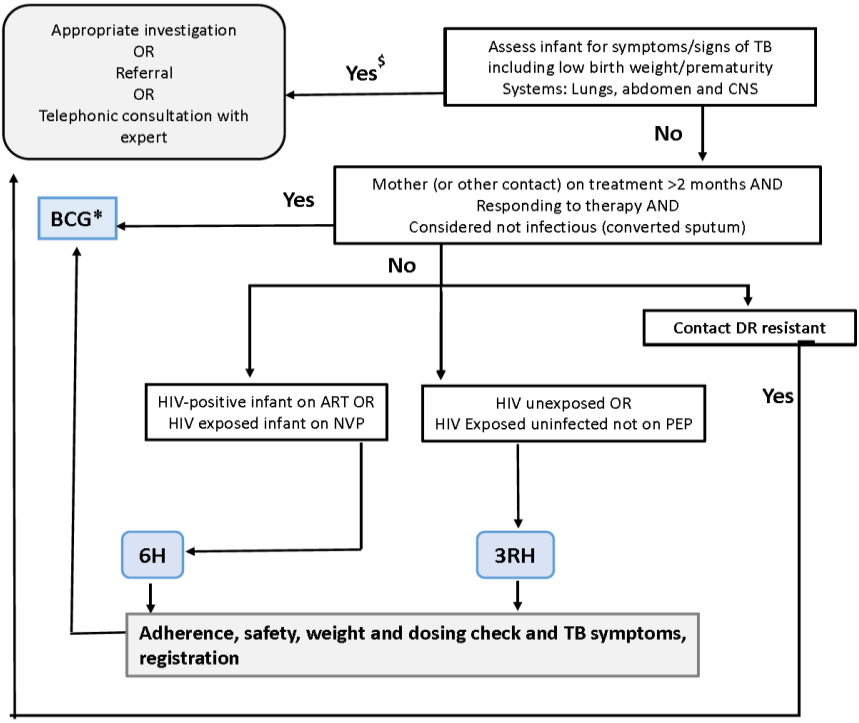
MEDICINE TREATMENT

Treatment for Drug Sensitive (DS) Tuberculosis

Newborn infant of mother with DS tuberculosis with newborn having any signs suggestive of illness:

Intensive Phase	Continuation Phase
• Rifampicin, oral, for 2 months. **PLUS** • Isoniazid, oral, for 2 months. **PLUS** • Pyrazinamide, oral, for 2 months.	• Isoniazid, oral, for 4 months. **PLUS** • Rifampicin, oral, for 4 months.

TB Preventative Therapy (TPT)



$ These infants must be investigated for TB disease – if TB disease is definitely excluded, infants should also return to algorithm for TPT

* BCG to be given in all infants after completion of TB preventive therapy

- ART=antiretroviral therapy; BCG=bacillus Calmette-Guérin; CNS=central nervous system; DST=drug susceptibility testing; INH=isoniazid; PEP=post exposure prophylaxis for HIV, RIF=rifampicin; Rx=treatment; TPT=tuberculosis preventive therapy
- For management of DR TB exposure, refer to next level of care and/or consult, refer to 2019 National DR TB Guidelines

All asymptomatic neonates:

- Rifampicin/Isoniazid, oral, once daily for 3 months (3RH) – HIV-unexposed or HIV-exposed, uninfected, not on NVP.

Weight band	Daily Rifampicin/Isoniazid 75/50 mg tablet	
	75/50	If dispersed in 10 mL water
2–2.9 kg	½ tablet	5 mL
3–3.9 kg	¾ tablet	7.5 mL
4–5.9 kg	1 tablet	10 mL
6–7.9 kg	1½ tablets	15 mL

- Isoniazid, oral, 10 mg/kg/dose once daily for 6 months (IPT) – HIV-infected or HIV-exposed, on NVP.

Weight band	Daily Isoniazid (H) 100 mg tablet
2–3.4 kg	¼ tablet
3.5–4.9 kg	½ tablet
5–7.4 kg	¾ tablet

During prophylaxis, monitor the infant for active TB disease (including growth monitoring) and re-evaluate for TB if necessary. Administer BCG vaccine after completing TPT to prevent inactivation of BCG by TB medication.

In severely immunosuppressed patients, the tuberculin reaction test can be negative in the presence of active tuberculosis.

REFERRAL

» Patients not responding to adequate therapy.
» Perinatal TB with a drug resistant (DR) source.

10.2 TUBERCULOSIS, PULMONARY IN CHILDREN

A16.9
*Notifiable condition.

DESCRIPTION

A chronic, granulomatous disease of the lungs caused by *M. tuberculosis*. Most children acquire tuberculosis from infected adults by inhalation.

Malnourished, immunosuppressed (HIV-infected) and children < 3 years of age with pulmonary tuberculosis (PTB) are always regarded as having serious disease.

Complications include:

» enlarged hilar and mediastinal lymphadenopathy with obstruction, e.g. tracheal or bronchial airway compression or occlusion with secondary atelectasis or hyperinflation;

» local spread of infection, e.g. TB bronchopneumonia, pleural effusion or cavitation;
» disseminated disease, e.g. miliary TB, TB meningitis and metastatic extrapulmonary involvement.

DIAGNOSTIC CRITERIA

Any child presenting with symptoms and signs suggestive of pulmonary TB is regarded as a child with TB if there is:
» A chest X-ray suggestive of TB.
AND/OR
» History of exposure to a person with infectious TB.
» Positive Tuberculin Skin Test (TST), e.g. Mantoux.

The diagnosis is supported by a positive rapid TB molecular test (e.g. GeneXpert®) if a specimen can be obtained. Culture, usually on gastric aspirates, induced sputum or other appropriate sample, is a confirmatory test.

» Signs and symptoms include (not an exhaustive list):
  > unexplained weight loss or failure to thrive,
  > lack of energy, child is less playful,
  > unexplained fever for ≥ 2 weeks,
  > chronic, unremitting cough for > 14 days,
  > lymphadenopathy (especially cervical, often matted),
  > hepatosplenomegaly,
  > consolidation and pleural effusion on chest examination.

» The following may be evident on chest X-ray:
  > Direct or indirect evidence of hilar or mediastinal adenopathy with or without parenchymal opacification and/or bronchopneumonia, miliary changes, or pleural effusions.

  Note:
  Miliary pattern on chest X-rays of HIV-infected children may also be suggestive of a diagnosis of lymphoid interstitial pneumonitis (LIP). (The miliary pattern of TB extends into the periphery of the lungs whereas LIP usually does not).

» Exposure to an adult with symptoms of TB or known pulmonary tuberculosis.
» Tuberculin skin test (TST), e.g. Mantoux.
  > A positive TST has an induration of ≥ 10 mm.
  > A TST may be falsely negative in the presence of:
    - malnutrition,
    - immunodeficiency, e.g. HIV,

- immunosuppression, e.g. steroid therapy, cancer chemotherapy,
- following overwhelming viral infection, e.g. measles or post vaccination.

In these circumstances a TST induration of ≥ 5 mm may be regarded as positive. Frequently, the TST will be non-reactive in these cases and a decision not to start TB treatment should not be based on a negative TST test.

» *M. tuberculosis* is suggested by a positive rapid TB molecular test (e.g. GeneXpert®) and confirmed by culture on the following specimens, noting that most children will not have microbiological confirmation of TB:
  > early morning gastric aspirate (empty stomach, no oral food intake for ≥ 4 hours),
  > sputum (older children),
  > induced sputum,
  > stool (if testing is available),
  > CSF,
  > pleural and ascitic fluids,
  > fine needle aspirate biopsies of lymph nodes,
  > ear swabs for tuberculosis culture in chronic otorrhoea.

GENERAL AND SUPPORTIVE MEASURES

» Identify and treat persons considered to be the TB source.
» In case of known contact with a person with DR TB, the child requires referral for appropriate DR TB prophylaxis or treatment.
» Screen all close contacts for symptoms and signs of TB disease.
» Provide TPT to child and high-risk adult contacts (HIV-infected) once TB disease excluded.
» Monitor the nutritional status of the child to assess response to treatment.
» Only symptomatic pleural effusions should be drained via pleural aspiration (in such cases consider adjunctive steroid therapy).
» Ensure household infection control practices.
» Refer for nutrition support.

MEDICINE TREATMENT

Tuberculosis control programme drug regimens (2013) and Circulars

Directly observed therapy (DOT), short-course, using fixed medicine combinations is used to avoid the development of antimicrobial resistance.

Give treatment daily in both the intensive (initial) and the continuation phase.

HIV-infected children with tuberculosis should be treated according to the standard treatment protocol with clinical, radiologic and microbiologic follow-up to determine response to treatment.

	Recommended dose ranges in mg/kg	
	Daily	Max. daily
Isoniazid (H)	10–15	300 mg
Rifampicin (R)	10–20	600 mg
Pyrazinamide (PZA/Z)	30–40	2 g
Ethambutol (EMB/E)	15–25	1200 mg

10.2.1 NON-SEVERE TUBERCULOSIS DISEASE

Indications:
Includes smear-negative pulmonary TB (low bacillary load) or with no more than mild to moderate lymph node enlargement and/or lung field opacification, or simple pleural effusion.

See:
https://theunion.org/sites/default/files/2022-03/The%20Union_Diagnostic%20Atlas%20for%20TB%20in%20Children_2022.pdf

Dosing:
» Adjust treatment dosages to current body weight.
» If calculating dosages, rather give ½ tablet more than ½ tablet less.

Children up to 8 years:

Dosing recommendations for dispersible combinations tablets:

Pre-treatment body weight	2 months intensive phase given daily	2 months continuation phase given daily
	RHZ	RH
	75/50/150 mg dispersible tablet (scored) **OR** 75/50/150 mg per 4 mL solution*	75/50 mg dispersible tablet (scored) **OR** 75/50 mg per 4 mL solution*
2–2.9 kg	½ tablet or 2 mL	½ tablet or 2 mL
3–3.9 kg	¾ tablet or 3 mL	¾ tablet or 3 mL
4–7.9 kg	1 tablet or 4 mL	1 tablet or 4 mL
8–11.9 kg	2 tablets or 8 mL	2 tablets or 8 mL
12–15.9 kg	3 tablets or 12 mL	3 tablets or 12 mL
16–24.9 kg	4 tablets or 16 mL	4 tablets or 16 mL

Note: Children should be taught and encouraged to swallow whole tablets or, if required, fractions of tablets so as to avoid large volumes of liquid medication.
*If oral suspension required, for each dose, disperse 1 x RHZ 75/50/150 mg or 1 x RH 75/50 mg tablet in 4 mL of water, administer required dose, discard unused suspension.

	Intensive phase 2 months			**Continuation phase 2 months**
Weight	**RH**	**PZA**		**RH**
	60/60 mg	Give one of the following:		60/60 mg
		150 mg* **OR** 150 mg/3 mL	500 mg	
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 tablet	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 150 mg dispersible (1 tablet) in 3 mL of water to prepare a concentration of 50 mg/mL (150 mg/3 mL).

LoE I[1]

AND

- Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy:
  - Child < 5 years: 12.5 mg.
  - Child ≥ 5 years: 25 mg.

Children > 8 years of age and adolescent (and > 25 kg):

Pre-treatment body weight	2 months intensive phase given daily	2 months continuation phase given daily	
	RHZE (150, 75, 400, 275)	**RH** (150, 75)	**RH** (300, 150)
25–37.9 kg	2 tablets	2 tablets	
38–54.9 kg	3 tablets	3 tablets	
55–70.9 kg	4 tablets		2 tablets
> 71 kg	5 tablets		2 tablets

AND

- Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy:
  - Child < 5 years: 12.5 mg.
  - Child ≥ 5 years: 25 mg.

10.2.2 SEVERE TUBERCULOSIS DISEASE

Indications:

» Includes more serious pulmonary TB, such as smear-positive TB, cavitatory pulmonary TB, bronchopneumonic TB, extensive (multiple lobes involved) pulmonary TB disease, and tuberculous empyema.
» Includes all HIV/TB co-infected cases.
» Includes extrapulmonary TB, e.g. spinal, osteo-articular or abdominal TB.

However:

» Exclude TB meningitis and miliary TB.

Dosing:

» Weigh at each visit and adjust treatment doses to body weight. If calculating dosages, rather give ½ tablet more than ½ tablet less.
» Keep strictly to the correct dose and the duration of treatment.
» The patient should be weighed regularly and the dose adjusted according to the current weight.

Children up to 8 years of age:
Intensive phase:
Standard dose 4-drug therapy daily (RHZE) for 2 months.

Follow with:
Continuation phase:
Standard dose 2-drug therapy daily (Isoniazid + Rifampicin) for 4 to 7 months.

Dosing recommendations for dispersible combinations tablets:

Pre-treatment body weight	2 months intensive phase given daily		4–7*** months continuation phase given daily
	RHZ	E	RH
	75/50/150 mg dispersible tablet (scored) **OR** 75/50/150 mg per 4 mL solution*	400 mg tablet **OR** 400 mg/8 mL solution**	75/50 mg dispersible tablet (scored) **OR** 75/50 mg per 4 mL solution*
2–2.9 kg	½ tablet or 2 mL	1 mL	½ tablet or 2 mL
3–3.9 kg	¾ tablet or 3 mL	1.5 mL	¾ tablet or 3 mL
4–7.9 kg	1 tablet or 4 mL	2.5 mL	1 tablet or 4 mL
8–11.9 kg	2 tablets or 8 mL	½ tablet or 4 mL	2 tablets or 8 mL
12–15.9 kg	3 tablets or 12 mL	¾ tablet or 6 mL	3 tablets or 12 mL
16–24.9 kg	4 tablets or 16 mL	1 tablet or 8 mL	4 tablets or 16 mL

Note: Children should be taught and encouraged to swallow whole tablets or, if required, fractions of tablets so as to avoid large volumes of liquid medication.

*If oral suspension required, for each dose, disperse 1 x RHZ 75/50/150 mg or 1 x RH 75/50 mg tablet in 4 mL of water, administer required dose, discard unused suspension.

**If oral suspension required, for each dose, crush 1 x ethambutol 400 mg tablet to a fine powder, disperse in 8 mL of water to prepare a concentration of 400 mg/8 mL (50 mg/mL), administer required dose as indicated in above chart, discard unused suspension.

***Continuation phase may be prolonged to 7 months in slow responders and children with HIV.

	Intensive phase 2 months				Continuation phase at least 4 months (up to 7 months ***)
Weight	**RH**	**PZA Give one of the following:**		**EMB**	**RH**
	60/60	150 mg* **OR** 150 mg/3 mL	500 mg	400 mg tablet **OR** 400 mg/8 mL** solution	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 tablets		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

Notes:
*For each dose, dissolve 150 mg dispersible (1 tablet) in 3 mL of water to prepare a concentration of 50 mg/mL (150 mg/3 mL).
**For each dose, crush 400 mg (1 tablet) to a fine powder and dissolve in 8 mL of water to prepare a concentration of 400 mg/8 mL. Discard unused solution.
***Continuation phase may be prolonged to 7 months in slow responders and children with HIV.

AND

- Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy:
  - Child < 5 years: 12.5 mg.
  - Child ≥ 5 years: 25 mg.

Children > 8 years and adolescent:

Pre-treatment body weight	2 months intensive phase given daily	4 months continuation phase given daily	
	RHZE (150, 75, 400, 275)	**RH** (150, 75)	**RH** (300, 150)
25–37.9 kg	2 tablets	2 tablets	
38–54.9 kg	3 tablets	3 tablets	
55–70.9 kg	4 tablets		2 tablets
> 71 kg	5 tablets		2 tablets

AND

Pyridoxine, oral, daily for 6 months if HIV-infected, malnourished, or with existing neuropathy:

- Child < 5 years: 12.5 mg.
- Child ≥ 5 years: 25 mg.

Adjust treatment dosages to body weight.
If calculating dosages, rather give ½ tablet more than ½ tablet less.

REFERRAL

» Poor response to standard TB treatment.
» Failure to exclude MDR-TB.
» Adverse drug reactions (ADR) requiring single drug combinations.
» MDR or MDR-TB contact.

10.3 MILIARY TB IN CHILDREN

A19.9

DESCRIPTION

Miliary tuberculosis is a potentially fatal form of TB disease due to the spread of the organism in the bloodstream to the lungs, brain and other organs. Patients with miliary TB are assumed to have CNS involvement and are treated accordingly.

MEDICINE TREATMENT

Children < 8 years:
The 75/50 RH and 75/50/150 RHZ formulations are not suitable for achieving the required doses in miliary TB, TBM/CNS TB, so the 60/60 RH formulation should be used for such children.

A 6-month regimen of all 4 of the following medicines:

- Rifampicin, oral, 20 mg/kg as a single daily dose.
  - Maximum dose: 600 mg daily.

PLUS

- Isoniazid, oral, 20 mg/kg as a single daily dose.
  - Maximum dose: 400 mg daily.

PLUS

- Pyrazinamide, oral, 40 mg/kg as a single daily dose.
  - Maximum daily dose: 2000 mg.

PLUS

- Ethionamide, oral, 20 mg/kg as a single daily dose.
  - Maximum daily dose: 1000 mg.

<table>
<tr><th rowspan="2">Body weight</th><th colspan="3">Single phase of treatment, 6–9 months
Once daily; 7 days a week</th></tr>
<tr><th>Rifampicin/ Isoniazid (RH)</th><th>Pyrazinamide (Z)</th><th>Ethionamide (Eto)</th></tr>
<tr><td></td><td>60/60 mg dispersible tablet (scored)</td><td>500 mg tablet (scored) OR 500 mg/8 mL suspension</td><td>250 mg tablet (scored) OR 250 mg/8 mL suspension</td></tr>
<tr><td>< 2</td><td colspan="3">Obtain Expert Advice</td></tr>
<tr><td>2–2.9</td><td>¾ tablet or 3 mL</td><td>1 mL</td><td>1.5 mL</td></tr>
<tr><td>3–3.9</td><td>1 tablet or 4 mL</td><td>2 mL</td><td>2 mL</td></tr>
<tr><td>4–4.9</td><td>1½ tablets or 6 mL</td><td>2.5 mL</td><td>2.5 mL</td></tr>
<tr><td>5–5.9</td><td>1¾ tablets or 7 mL</td><td>3 mL</td><td>3 mL</td></tr>
<tr><td>6–6.9</td><td>2 tablets or 8 mL</td><td rowspan="2">½ tablet or 4 mL</td><td rowspan="2">½ tablet or 4 mL</td></tr>
<tr><td>7–8.9</td><td>2½ tablets or 10 mL</td></tr>
<tr><td>9–9.9</td><td>3 tablets or 12 mL</td><td rowspan="2">¾ tablet or 6 mL</td><td rowspan="2">¾ tablet or 6 mL</td></tr>
<tr><td>10–11.9</td><td>3½ tablets or 14 mL</td></tr>
<tr><td>12–12.9</td><td>4 tablets or 16 mL</td><td rowspan="3">1 tablet or 8 mL</td><td rowspan="2">1 tablet or 8 mL</td></tr>
<tr><td>13–14.9</td><td>4½ tablets or 18 mL</td></tr>
<tr><td>15–16.9</td><td>5 tablets or 20 mL</td><td rowspan="2">1¼ tablet or 10 mL</td></tr>
<tr><td>17–17.9</td><td rowspan="2">5½ tablets or 22 mL</td><td rowspan="2">1¼ tablets or 10 mL</td></tr>
<tr><td>18–19.9</td><td rowspan="2">1½ tablets or 12 mL</td></tr>
<tr><td>20–24.9</td><td>6 tablets or 24 mL</td><td>1½ tablets or 12 mL</td></tr>
</table>

Note: Children should be taught and encouraged to swallow whole tablets or, if required, fractions of tablets so as to avoid large volumes of liquid medication if possible.

*If oral suspension required, for each dose, disperse 1 x HR 60/60 mg tablet in 4 mL of water, administer required dose as indicated in above chart, discard unused suspension.
**If oral suspension is required, crush 1 x 500 mg pyrazinamide tablet to a fine powder, disperse in 8 mL water to prepare a concentration of 500 mg/8 mL (62.5 mg/mL), administer required dose as indicated in above chart, discard unused suspension.
***If oral suspension is required, crush 1 x 250 mg ethionamide tablet to a fine powder, disperse in 8 mL of water to prepare a concentration of 250 mg/8 mL (31.3 mg/mL); administer required dose as indicated in above chart; discard unused suspension.

PLUS

- Pyridoxine 25 mg daily for 6 months.

Children ≥ 8 years:
Treatment as per adult guidelines for pulmonary tuberculosis. See Adults Hospital Level STGs and EML, section 16.9: Tuberculosis, pulmonary.

» Treatment duration: 6 to 9 months.

Note:
All cases of miliary TB should have a lumbar puncture (LP) performed. Any abnormal CSF results, or where a LP is not performed, should be treated as a patient with TBM. See section 10.4: Meningitis, tuberculosis (TBM) in children.

10.4 MENINGITIS, TUBERCULOUS (TBM) IN CHILDREN

A17.0
*Notifiable condition.

DESCRIPTION

Tuberculous meningitis is an infection of the meninges caused by *M. tuberculosis*. Early diagnosis and treatment improves the prognosis.

Differentiation from acute bacterial meningitis may be difficult. If in any doubt, treat for both conditions.

Complications may be acute or long term:

» Acute:
- > raised intracranial pressure,
- > cerebral oedema,
- > hemi/quadriplegia,
- > hydrocephalus,
- > brain infarcts,
- > convulsions,
- hyponatraemia due to inappropriate antidiuretic hormone (ADH) secretion or cerebral salt wasting.

Syndrome of inappropriate antidiuretic hormone secretion (SIADH) and cerebral salt wasting both present with hyponatraemia; the former responding to fluid restriction and the latter to fluid replacement, i.e. sodium chloride 0.9%.

SIADH has lower serum uric acid and low urine output. Cerebral salt wasting has a normal serum uric acid and high urine output.

» Long-term neurological sequelae include: mental handicap, blindness and deafness.

DIAGNOSTIC CRITERIA

Clinical

» History of contact with an infectious tuberculosis case.
» Onset may be gradual with vague complaints of drowsiness (or fatigue), vomiting, fever, weight loss, irritability and headache.
» Later symptoms such as convulsions and neurological fall-out may occur.
» Older children may present with behavioural changes.
» Examination may reveal signs of meningeal irritation and raised intracranial pressure, convulsions, cranial nerve palsies, localising signs (such as hemiparesis), altered level of consciousness or coma and choroidal tubercles.
» The degree of involvement is classified into 3 stages. Prognosis relates to the stage of the disease.
  > Stage 1: Non-specific signs, conscious, rational, no focal neurological signs, no hydrocephalus.
  > Stage 2: Signs of meningeal irritation, confusion and/or focal neurological signs.
  > Stage 3: Stupor, delirium, coma and/or neurological signs, i.e. hemiplegia.

Investigations

» CSF findings:
  > May vary depending on the stage.
  > Protein is usually raised.
  > Chloride and glucose are moderately low.
  > Lymphocytes usually predominate.
  > Gram stain is negative and acid-fast bacilli are seldom found.
  > A rapid TB molecular test (e.g. GeneXpert®) should be done on CSF. It is helpful where it is positive, but a negative rapid TB molecular test (e.g. GeneXpert®) does not exclude TBM.
  > A negative result does not exclude TB and CSF cultures must still be done.

  Bacilli may be cultured from the CSF but may take up to 4–6 weeks. If culture is positive, drug susceptibility testing will be done. Always send for culture, do not perform a stain as there is a low diagnostic yield from low concentration of organisms and wastes the CSF sample.
» A TST and chest X-ray must be done, but are often unhelpful.

» If depressed level of consciousness or focal neurological signs are present, a CT scan is useful to determine if safe to LP (do CT first before LP in such cases).
» Electrolytes: check for hyponatraemia.

GENERAL AND SUPPORTIVE MEASURES

» Monitor neurological status on a regular basis. If rapid deterioration in level of consciousness, consider neurosurgical referral for a ventriculoperitoneal shunt (VP shunt).
» Ensure optimal nutrition. Initially naso-gastric feeding is usually needed. Refer for nutrition support.
» Rehabilitative measures: most patients need physiotherapy and occupational therapy.
» Surgical treatment (VP shunt) is needed for a non-communicating hydrocephalus, diagnosed by air-encephalogram.
» Communicating hydrocephalus with severely raised pressure may be managed with medicines once hydration status is stable and/or with serial lumbar puncture with specialist consultation (tertiary hospital care).

MEDICINE TREATMENT

Differentiation from acute bacterial meningitis may be difficult.
If in doubt, treat for both conditions.

Anti-tuberculosis treatment

» Requires therapy with a combination of 4 drugs as a special regimen.
» All treatment should be directly observed therapy.
» Single drugs may form part of the regimen to provide the total daily required dose for each medicine by supplementing the combination to give the necessary therapeutic dose per kilogram.

A 6-month regimen of all 4 of the following drugs:

- Rifampicin, oral, 20 mg/kg as a single daily dose.
  - Maximum daily dose: 600 mg.

PLUS

- Isoniazid, oral, 20 mg/kg as a single daily dose.
  - Maximum daily dose: 400 mg.

PLUS

- Pyrazinamide, oral, 40 mg/kg as a single daily dose.
  - Maximum daily dose: 2000 mg.

PLUS

- Ethionamide, oral, 20 mg/kg as a single daily dose.
  - Maximum daily dose: 1000 mg.

The 75/50 RH and 75/50/150 RHZ formulations are not suitable for achieving the required doses in disseminated TB & TBM, so the 60/60 RH formulation should be used for such children.

Body weight (kg)	Single phase of treatment, 6–9 months Once daily; 7 days a week		
	Rifampicin/Isoniazid (RH)*	**Pyrazinamide (Z)**	**Ethionamide (Eto)**
	60/60 mg dispersible tablet (scored)	500 mg tablet (scored) **OR** 500 mg/8 mL suspension**	250 mg tablet (scored) **OR** 250 mg/8 mL suspension***
< 2	**Obtain Expert Advice**		
2–2.9	¾ tablet or 3 mL	1 mL	1.5 mL
3–3.9	1 tablet or 4 mL	2 mL	2 mL
4–4.9	1½ tablets or 6 mL	2.5 mL	2.5 mL
5–5.9	1¾ tablets or 7 mL	3 mL	3 mL
6–6.9	2 tablets or 8 mL	½ tablet or 4 mL	½ tablet or 4 mL
7–8.9	2½ tablets or 10 mL		
9–9.9	3 tablets or 12 mL	¾ tablet or 6 mL	¾ tablet or 6 mL
10–11.9	3½ tablets or 14 mL		
12–12.9	4 tablets or 16 mL	1 tablet or 8 mL	1 tablet or 8 mL
13–14.9	4½ tablets or 18 mL		
15–16.9	5 tablets or 20 mL		1¼ tablets or 10 mL
17–17.9	5½ tablets or 22 mL	1¼ tablets or 10 mL	
18–19.9			1½ tablets or 12 mL
20–24.9	6 tablets or 24 mL	1½ tablets or 12 mL	

Note: Children should be taught and encouraged to swallow whole tablets or, if required, fractions of tablets so as to avoid large volumes of liquid medication if possible.

*If oral suspension required, for each dose, disperse 1 x RH 60/60 mg tablet in 4 mL of water, administer required dose as indicated in above chart, discard unused suspension.

**If oral suspension is required, crush 1 x 500 mg pyrazinamide tablet to a fine powder, disperse in 8 mL water to prepare a concentration of 500 mg/8 mL (62.5 mg/mL), administer required dose as indicated in above chart, discard unused suspension.

***If oral suspension is required, crush 1 x 250 mg ethionamide tablet to a fine powder, disperse in 8 mL of water to prepare a concentration of 250 mg/8 mL (31.3 mg/mL); administer required dose as indicated in above chart; discard unused suspension.

Consider prolonging treatment for another 3 months if there are concerns about ongoing disease. Consult with a specialist.

In case of suspected/confirmed multidrug-resistant TBM, refer immediately for admission and treatment.

Steroid therapy:

- Prednisone, oral, 2 mg/kg as a single daily dose for 4 weeks.
  - Maximum daily dose: 60 mg.
  - Taper to stop over further 2 weeks.

Hydrocephalus

Avoid low sodium IV fluids in these patients, i.e. < 60 mmol/L.

To differentiate communicating from non-communicating hydrocephalus an air-encephalogram is usually required. Communicating hydrocephalus is more common in this condition.

In children with a sudden deterioration of level of consciousness and other comatose children with TBM, inform the neurosurgeon before doing the air-encephalogram so that shunt surgery can immediately be done if the hydrocephalus is non-communicating. Air-encephalogram procedure: do a lumbar puncture, inject 5 mL of air with a syringe and do an immediate lateral X-ray of the skull. Air in the lateral ventricles on skull X-ray indicates communicating hydrocephalus; air at the base of the brain (not in lateral ventricles), indicates non-communicating hydrocephalus.

Communicating hydrocephalus

If dehydrated, rehydrate with sodium chloride 0.9%, IV.

Start diuretics as soon as the patient is well hydrated and serum electrolytes are within the normal range:

- Acetazolamide, oral, 20 mg/kg/dose 8 hourly.
  - Maximum daily dose: 1000 mg.
  - Monitor for metabolic acidosis and serum potassium derangements.

PLUS

- Furosemide, oral, 0.3 mg/kg/dose 8 hourly for the first month of treatment.
  - Taper slowly over 2 weeks if the intracranial pressure has normalised, as indicated by clinical response or resolution of hydrocephalus on follow-up scan.
  - Do not restrict fluids once on diuretics.

Sudden deterioration of level of consciousness:

- Mannitol, IV, 250 mg/kg administered over 30–60 minutes.

REFERRAL

» TBM not responding to adequate therapy.
» TBM with complications.
» Suspicion of non-communicating hydrocephalus.
» Suspected drug-resistant TB (contact with drug-resistant TB case).

10.5 TB PREVENTIVE THERAPY (TPT) FOR TB EXPOSURE/INFECTION

Screen all children in close contact with an infectious pulmonary TB case for TB disease. Screening includes clinical history and examination with appropriate investigations of children with suspected TB disease. Give full anti-tuberculosis treatment if the diagnosis of TB disease is confirmed or suspected.

Indications for TB Preventive Therapy (TPT):

» All asymptomatic children and adolescents, i.e. clinically well, normal chest X-ray irrespective of TST, in close contact with an infectious pulmonary TB case should receive TPT.

» Previous TPT or treatment does not protect the child against subsequent TB exposure/infection. If there is a new exposure to an infectious pulmonary TB case after completion of a course of TPT, it can be given again. TPT should be repeated after each episode of documented TB exposure. In cases of a new exposure to an infectious source case while the child is on TPT, the duration of TPT should continue for at least as long as the source case remains infectious.

Preventive therapy in case of a drug-susceptible TB contact:

- Isoniazid, oral, 10 mg/kg daily for 6 months.

Preventive therapy in case of a drug-resistant TB contact:

Isoniazid monoresistance (rifampicin susceptible):

- Rifampicin, oral, 15 mg/kg daily for 4 months.

Rifampicin monoresistance (isoniazid susceptible):

- Isoniazid, oral, 10 mg/kg daily for 6 months.

MDR-TB with second line sensitivity:

- Levofloxacin 15–20 mg/kg daily for 6 months (maximum dose: 1000mg)

AND/OR

- Isoniazid, oral, 15–20 mg/kg daily for 6 months (maximum dose: 600mg)

Refer case or discuss with specialist if simplification of prophylaxis regimen is required.

Also see the National Department of Health Clinical Reference Guide: **Management of Rifampicin-Resistant Tuberculosis**, 2019[2] for further guidance.

XDR-TB:

- Close follow-up for two years.
- Ensure household infection control practices are observed.
- Refer all cases.

10.6 TREATMENT OF CHILDREN WHO WERE PREVIOUSLY SUCCESSFULLY TREATED FOR TB (RETREATMENT)

A child who was previously successfully treated for pulmonary TB is at increased risk for re-infection with TB. It is imperative to exclude drug-resistant TB by carrying out a sputum rapid TB molecular test (e.g. GeneXpert®) plus culture with drug susceptibility testing (DST), and also determine DST of any known TB source case. If the above does not indicate resistant TB, treat as drug susceptible TB (high bacillary load) with close monitoring of response. Consider an extension of the duration of the continuation phase of therapy in these retreatment cases.

REFERRAL

» Poor clinical response to TB retreatment.

10.7 DRUG RESISTANT TB (DR-TB)

U84.3

See the National Department of Health Clinical Reference Guide: **Management of Rifampicin-Resistant Tuberculosis**, 2019.[2]

References

[1] Turkova A, Wills GH, Wobudeya E, Chabala C, Palmer A, Kinikar S. Shorter Treatment of Nonsevere Tuberculosis in African and Indian Children. NEJM. 2022, 386 (10): 911-922.

[2] National Department of Health. Management of Rifampicin-Resistant Tuberculosis. November 2019. https://www.health.gov.za/wp-content/uploads/2020/11/management-of-rifampicin-resistant-tb-booklet-1219-v6.pdf