Tuberculosis in Children

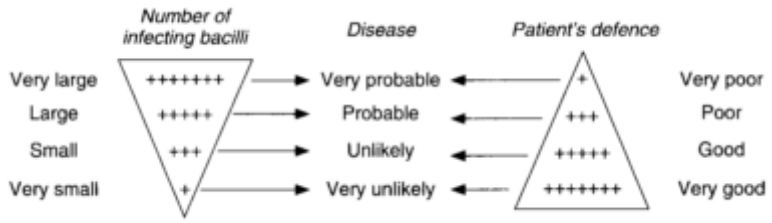
Background

Children who are close contacts of an infectious (usually adult) TB case are at substantial risk of becoming infected with *M. tuberculosis* and developing active TB. Therefore, we have a low threshold for investigating and starting young children on TB treatment. Contacts with positive sputum on direct smear (i.e. TB visible under the microscope) are much more infectious than those positive only on culture. The closer someone is to the patient and the longer the two spend together, the higher the chance that the person in contact with the patient will inhale TB. Children under 5 years of age and ALL HIV infected children who have been in contact with a sputum smear positive (SSP) TB case, should be referred to the TB clinic for investigation and management

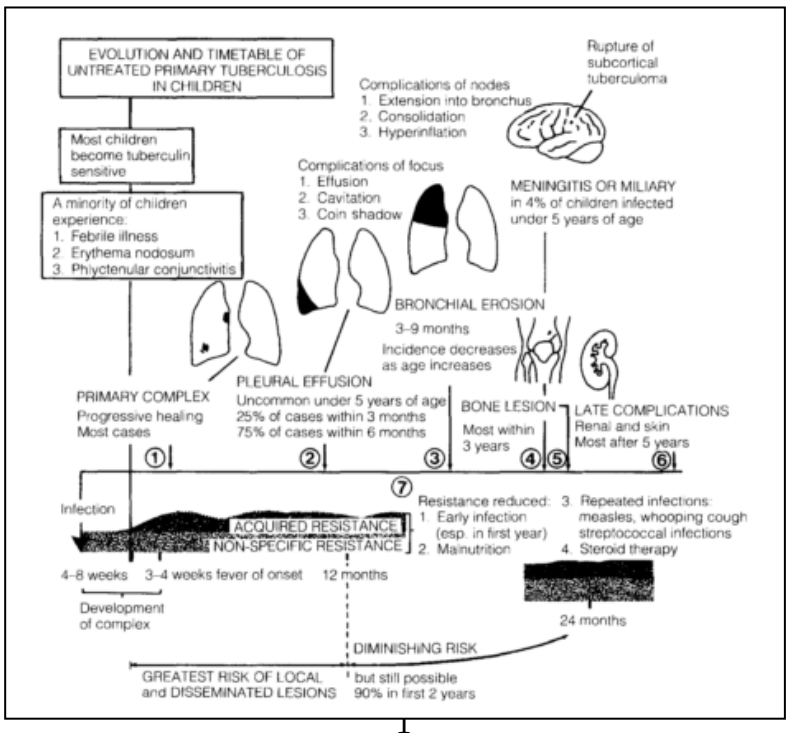
Risk factors:

- Proximity to and duration of exposure to the index case influences the risk of becoming infected.
- HIV-positive status or other causes of immunosuppression including malnutrition reduces resistance to disease.
- Up to 2 years of age, infection is particularly liable to result in the most fatal forms, miliary tuberculosis and tuberculous meningitis

Probability of developing TB



Evolution and timeframe of TB



Initial assessment – all children

To exclude signs and symptoms of active TB disease and to determine if the child needs to be commenced on full treatment, or chemoprophylaxis with INH.

History

- Document who referred and the reason for referral
- Has the child has been treated with recurrent courses of antibiotics?
- Has the child been vaccinated with BCG? Check passport and scar.

Symptoms to ask about: (Note symptoms may be non-specific)

- A chronic cough that is getting worse, especially if it has not responded to antibiotics
- Failed to gain weight or has lost weight for more than 4 weeks (a weight chart is valuable)
- Decrease in energy levels
- Low-grade fever for more than a week without any explanation
- Chronic diarrhoea with large pale stools, which has not responded to treatment for worms or giardiasis
- A headache and irritability, occasional vomiting, child wishes to be left alone and gradually becomes less rousable over 2-3 weeks

Contact History

- Who is the contact? Household member/neighbour?
- **What has been the duration and proximity of contact?** E.g.: Sleeping same room/ same bed?

General:

- Full systems review
- HIV status?

PM History:

- Is there a history of asthma, wheeze, chronic cough?
- Regular medicines? BCG vaccination?

Examination: Physical findings suggestive of TB in children include:

- Temp, Pulse, RR
- Are they anaemic? Are they clubbed?
- Height, Weight. Are they failing to thrive? Check health passport growth chart
- Lymphadenopathy - check cervical, axillary, epitrochlear & inguinal nodes
- A lymph node abscess which may be affecting or coming through the skin
- One or more soft swellings under the skin; these are not painful; the skin may have broken, leaving an ulcer with sharply cut edges and usually a clean base
- A discharging sinus (wound) near any joint
- Decreased unilateral expansion
- Dullness to percussion of the chest may suggest a TB pleural effusion, usually children > 5years.
- Abnormalities on auscultation - crackles, coarse breath sounds.
- Is there more air entering one side than the other, is there a wheeze on one side Any signs of miliary TB e.g. hepatosplenomegaly?

- A swollen abdomen, especially if a lump is felt and if the lump remains after treatment for worms
- A spinal gibbus,
- Swelling of a joint, a limp on walking; a stiff spine and is unwilling to bend his
- Neck stiffness or cranial nerve palsy

Investigations and Management - See algorithms below

- HIV test
- CXR - Tuberculosis is difficult to diagnose with certainty from a chest X-ray alone.
- Mantoux test if purified protein derivative (PPD) is available.
- Children do not expectorate well but if they can collect sputum/induced sputum for microscopy for AFB (Acid Fast Bacilli), Gene Xpert (and Culture if available)
- Gastric aspirate for microscopy, culture and/or gene Xpert.
  Ideally done in the early morning before breakfast after a night of starving (if a patient on three hourly feeds, do before the next feed). Insert an NGT and aspirate gastric content.
  Collect it into a CSF bottle and send to laboratory.
  Gene Xpert can also be done on other body fluids, sensitivity varies.

CXR – changes compatible with PTB in >70% cases

Chest x-rays need to be of decent quality and interpretation depends on the expertise of the person reading them. CXR changes are often non-specific and may be completely normal in the HIV-infected or malnourished child. **TB disease should not be diagnosed from the CXR alone. The whole clinical picture should be considered.**

The most common x-ray findings suggesting TB in children are:

• Enlarged hilar lymph nodes as evidenced by splaying of the right and left mainstream bronchi) and/or a widened mediastinum due to enlarged lymph nodes (this is the most common x-ray abnormality in children with TB).
• Unilateral infiltration on x-ray may indicate lobar disease.
• Diffuse uniformly distributed small miliary shadows.
• One-sided pleural effusions usually occur in children > 5 years

Mantoux procedure - (depending on the availability of PPD)

- The Mantoux test measures the delayed-type hypersensitivity response to purified protein derivative (PPD)—a mixture of inactivated mycobacterial proteins.
- A positive Mantoux does not indicate active TB disease, it only indicates latent infection with M. tuberculosis (LTBI).
- Intradermal injection of 2 tuberculin units (TU) of PPD RT23. Usually completed on the left forearm.
- The Mantoux test is positive when the diameter of skin induration (swelling, not redness) is ≥ 10 mm (or ≥ 5 mm in an HIV-infected or malnourished child).
- Transverse induration measured 48-72hrs later using a tape measure and the ball-point pen technique.
- Result MUST be documented in mm and not just as ‘positive’ or ‘negative’
- A negative TST does not exclude TB infection or disease

Treatment regimens

- All TB drugs are dispensed by the TB officer Monday to Friday 9-4pm
- Refer all patients requiring treatment and prophylaxis to the TB officer on Ward 3A

The WHO has recently (2010) revised their treatment dosages for first line medicines for paediatric TB. These are as follows:

Rifampicin (R) 15mg/kg/d (10-20mg/kg/d)
Isoniazid (H) 10mg/kg/d (10-15mg/kg/d)
Pyrazinamide (Z) 35mg/kg/d (30-40mg/kg/d)
Ethambutol (E) 20mg/kg/d (15-25mg/kg/d)

We generally use a fixed drug combinations (FDC) to treat TB

It is important to monitor the child's weight at every clinic visit and to adjust drug doses accordingly. Many children rapidly gain weight after initiation of TB treatment.

Treatment duration
WHO published guidelines (2010) for the duration of treatment in paediatric TB as follows:

Site	HRZE - duration	HR - duration	Total length
TB meningitis, miliary TB, Osseous – spine, joints	2 months	10 months	12 months
Pulmonary TB, TB lymphadenitis All other types of TB	2 months	4 months	6 months

Prednisolone

- Used in the treatment of TBM and TB pericarditis and occasionally in large pleural effusions that fail to resolve.
- Commence at the start of treatment, treat at 2mg/kg for two weeks and then taper over 2 weeks (1mg/kg for one week and 0.5mg/kg for one week) before stopping.

Pyridoxine:

Pyridoxine (vitamin B6) protects against isoniazid-induced peripheral neuropathy. Pyridoxine is recommended for all children on TB treatment and IPT. The recommended dose is 25 mg/ day until treatment is completed

Follow-up Paediatric TB – review every month for three months and then at 6 months

Isolation procedures

- Pre-pubertal children who are suspected of having TB are of low infection risk to others as children rarely develop cavitary disease.
- Isolate all children > 8 years who are being treated for TB, especially if the child is coughing a lot and has cavities on CXR and/or is SSP.
- Even if the child is not considered a risk due to age, consider if the guardian is an infection risk, are they coughing too? order a CXR for the guardian and refer to the TB officer.

Note: Chemotherapy rapidly reduces infectiousness, usually within 2 weeks, if the bacilli are susceptible. If an inpatient - isolate for 14 days as it takes TB drugs about 10-14 days to sterilise the lungs. If the child is stable discharge as soon as possible. Advise the child/parent to avoid crowded areas (e.g. minibus taxis, crowded wards, the HIV clinic etc.) & to spend time outside in a well-ventilated area.

Enquire if there are other young children at home. If one child has TB then it is likely that others are infected too. Refer any children <5 years of age to the TB clinic for screening

Disseminated tuberculosis is the result of spread of bacilli via the blood stream, which then seeds into the lungs, liver, spleen and brain. The earliest symptoms of disseminated tuberculosis are a loss of energy and activity, weight loss and fever.

Special situations:

1. TB Meningitis

- The most serious complication of TB in childhood, especially in children <2yrs
- Usually, develops 6 -12 months after initial TB infection

Clinical signs and symptoms

- Insidious onset- behaviour change, headache, FTT
- May present with cranial nerve palsy coma, hemiplegia, convulsions

Investigations

- CSF - may be confused with bacterial meningitis
- Low CSF glucose, raised protein, may initially have low cell count with polymorph predominance
- Repeat CSF if no response to Antibiotics – increased protein and cell count

CT brain – basal enhancement with contrast, +/- hydrocephalus

2. Neonates exposed to an SSP Mother

- A sizeable number of mothers reactivate latent TB infection in the third trimester of pregnancy or around the time of delivery/immediate post-partum period.
- Any mother in whom TB is suspected should be sent for a CXR and a minimum of x2 sputum samples collected for AFB microscopy.

The following scenarios are a guide on what to do:

Neonates exposed to a mother with TB – two common scenarios

I. **Mother was diagnosed with TB prior to the third trimester of pregnancy, is taking TB medications with good adherence and is clinically well**:

• Examine the new-born for signs of disease. If the baby is well, no action is required.

• Refer all other household children <5 years of age to the TB clinic for clinical assessment.

II. **Mother is diagnosed with TB in the third trimester of pregnancy or shortly after delivery**,

Examine her baby closely for symptoms and signs of disease – two further possible scenarios'

a. If the baby is well, commence isoniazid (H) prophylaxis at 10 mg/kg/day and continue for 6 months. Do not give BCG vaccine.

Isoniazid dose

Weight band	Dose of Isoniazid
< 2.5 Kg	25 mg (1/4 tablet) every 24 hours
2.5 -5 kg	50 mg (1/2 tablet) every 24 hours
5-10kg	100 mg (1 tablet) every 24 hours

Infants need to be reviewed at 1, 3 and 6 months after commencing isoniazid. Infants' weights must be checked regularly and their isoniazid dosages increased as they grow. Refer all other household children to the TB clinic for clinical assessment and screening. As BCG is a live vaccine, isoniazid will kill the vaccine and prevent an effective immune response from developing. If isoniazid is commenced within 2 weeks of receiving BCG vaccination, the infant will need repeat BCG vaccination following the end of treatment. If no BCG vaccine was given at birth, then vaccinate the baby two weeks after completing isoniazid.

b. The baby is not well and has signs/symptoms suggestive of TB disease, collect gastric aspirates, send for gene Xpert and culture where possible and commence full TB treatment.

If any findings suggest active disease, start full anti-TB treatment, according to national guidelines.

- Breastfeed as normal
- Delay BCG vaccination until 2 weeks after treatment is completed.
- If BCG has already been given, repeat 2 weeks after the end of Isoniazid treatment.

3. BCG disease

Bacille Calmette-Guerin (BCG) is a live, attenuated vaccine and is routinely given to neonates in Malawi, in the right deltoid, in the first week of life. The bacilli originally came from a strain of bovine TB grown for many years in the laboratory. BCG stimulates immunity, increasing the body's defences without itself causing damage. Following BCG vaccination, the body's increased defences will control or kill any TB that enter the body. Most trials in infants in poor countries have shown important protection against disseminated tuberculosis and tuberculous meningitis.

- BCG vaccination may be associated with injection-site abscesses, (suppurative) adenitis, and (very rarely) with disseminated disease.
- HIV- infected infants and other immunodeficient infants are at risk of BCG-related complications.
- Any child <2years who presents with right-sided axillary or regional lymph nodes indicates possible BCG disease and immunocompromised.
- These children require further evaluation.

HIV status unknown?
- Send for VCT.

Are they known to be HIV infected?
- Have they recently commenced ART? If so, then this is likely to be **BCG IRIS.**

Management:

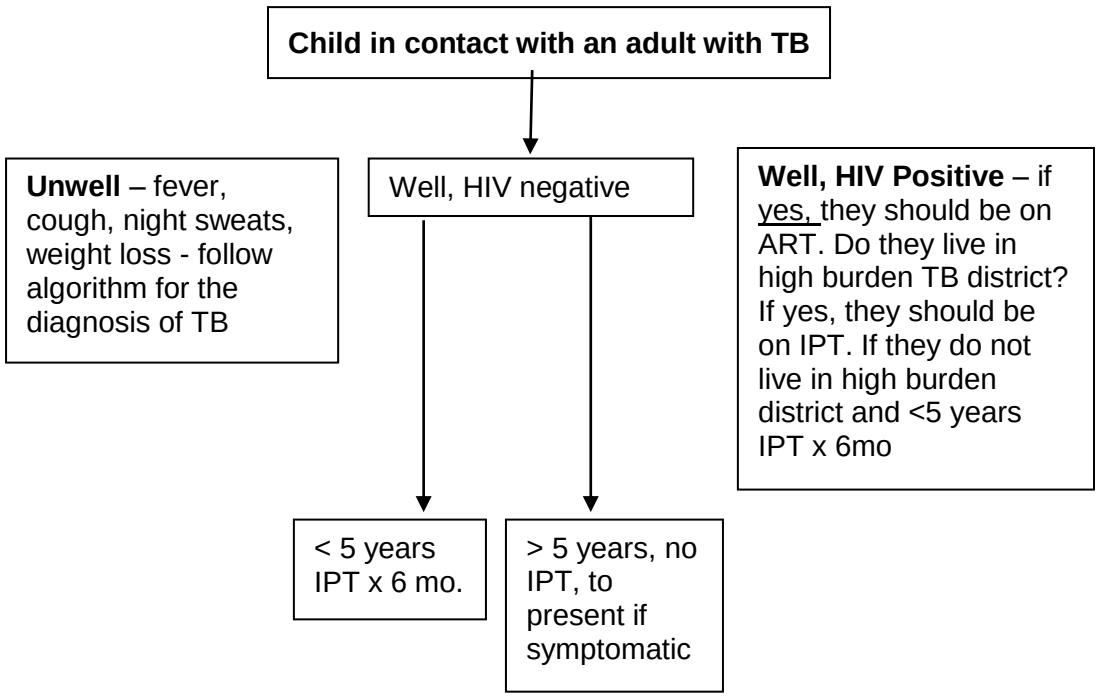
- **HIV-uninfected or exposed** and thriving and with no other signs of disseminated disease - no drug treatment or management is required. Repeated needle aspiration of a large, fluctuant lymph node may be needed until it spontaneously resolves.
- **HIV-infected and otherwise well**, refer the patient to the ART clinic and commence on HAART.
- **HIV-infected and unwell** – febrile, failure to thrive, and/or respiratory signs and symptoms – admit for further investigation and management of possible disseminated BCG disease. These children require four-drug TB treatment with RHZE even though M. Bovis is not sensitive to pyrazinamide since co-infection with *M. tuberculosis* may occur.

Prevention

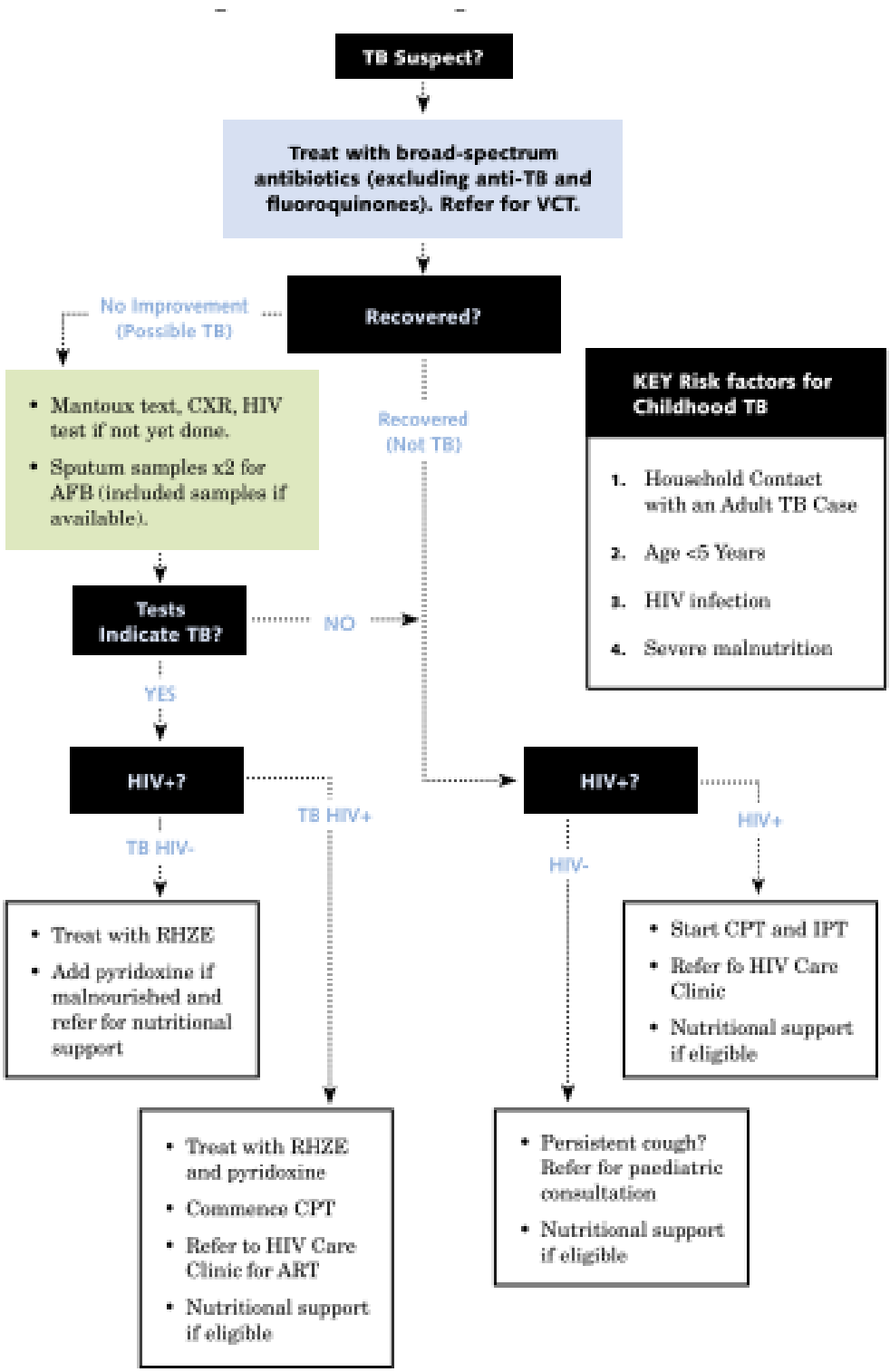
In terms of prevention, your most important priority is to diagnose patients with a direct positive sputum smear and to make sure that they complete a standardised treatment. There is a limit to what can be achieved as economic development and interventions to reduce poverty are the most important, however, the following helps.

- Reduce overcrowding wherever possible (which also reduces other infectious
- respiratory diseases, such as pneumonia in infants).
- Improve ventilation of houses.
- Discourage smoking. Smoking increases the risk of tuberculosis.

ALGORITHM FOR THE MANAGEMENT OF A CHILD EXPOSED TO TB



ALGORITHM FOR THE DIAGNOSIS OF TB IN CHILDREN



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