1: Introduction and Who Guideline applies to:

This guideline covers referral pathways and management of children with suspected or confirmed Tuberculosis (TB) infection who require admission and/or follow up at University Hospitals of Leicester. The children will be looked after by the Paediatric TB team with occasional involvement of other specialties such as the paediatric orthopaedic, respiratory, general surgery or the ENT surgeons.

*TB treatment should only be started on the advice of a consultant with expertise in managing paediatric TB.*

**Related Documents:**
This guideline should be used in conjunction with Tuberculosis UHL Policy, infection prevention management of patients with tuberculosis B45/2005

**Contents**
- Related Documents ........................................................................................................... 1
- Figure 1: Management of Contacts of Sputum Smear Positive Tuberculosis ............. 2
- 2. Paediatric Tuberculosis................................................................................................. 3
  - 2.1 Background: ........................................................................................................... 3
  - 2.2 Referral Pathways: ................................................................................................. 3
  - 2.3 Isolation and Infection control: ................................................................................ 4
  - 2.4 Screening of children with presumed or suspected TB infection: ...................... 4
  - 2.5 Diagnosis: ............................................................................................................. 5
2.6 HIV infection and immunocompromised children: ........................................... 6
2.7 The neonate: ........................................................................................................ 6
2.8 Indirect Tests for TB: ............................................................................................ 7
2.9 Regime: .................................................................................................................. 8
3. Education and Training .......................................................................................... 9
4. Monitoring Compliance ......................................................................................... 9
5. Supporting References ......................................................................................... 9
6. Key Words: .............................................................................................................. 9
Contact and review details: ...................................................................................... 9
TB NURSING SERVICE - REFERRAL FORM: .......................................................... 10

**Figure 1: Management of Contacts of Sputum Smear Positive Tuberculosis**

This pathway is for the management of children who are close contacts of a smear positive TB. In smear negative cases and extra pulmonary TB, please refer to Paediatric TB clinic (SBRTB).

<table>
<thead>
<tr>
<th>Sputum smear +ve contacts/smear –ve but culture positive within 10 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonates (if well)</td>
</tr>
<tr>
<td>Start isoniazid,</td>
</tr>
<tr>
<td>Pyridoxine + refer to</td>
</tr>
<tr>
<td>Paediatric TB clinic</td>
</tr>
<tr>
<td>At 6 weeks: clinical</td>
</tr>
<tr>
<td>assessment + CXR, mantoux and quantiferon tests</td>
</tr>
<tr>
<td>Negative result</td>
</tr>
<tr>
<td>- May stop treatment</td>
</tr>
<tr>
<td>- Offer BCG</td>
</tr>
</tbody>
</table>

| 1 month– 2 years old                                          |
| Start isoniazid and rifampicin treatment                      |
| At 6 weeks, clinical assessment + mantoux and quantiferon tests |
| Positive result                                               |
| Assess for active disease                                     |
| If no active disease:                                          |
| Neonates: complete 6 months of isoniazid                      |
| Children 1 month – 2 years: complete 3 months of latent TB treatment |

| 2-5 years old                                                 |
| Refer to TB clinic as soon as possible                        |
| Clinical assessment, quantiferon and mantoux tests, +/- CXR   |
| Negative result                                               |
| - review in 6 weeks                                          |
| - Clinical assessment + Mantoux Aand quantiferon +/- CXR      |
| - If negative then, then offer BCG                           |

| 6 –16 years old                                               |
| Refer to TB clinic as soon as possible                        |
| Clinical assessment, quantiferon +/- CXR                      |
| Positive result                                               |
| Assess for active disease                                     |
| If no active disease, start latent TB treatment               |
2. Paediatric Tuberculosis

2.1 Background:

Tuberculosis (TB) is a major global health problem and is one of the top 10 causes of death worldwide. In 2016, 10.4 million people fell ill with TB, and 1.7 million died from the disease (including 0.4 million among people with HIV). Over 95% of TB deaths occur in low- and middle-income countries.\(^{(1)}\)

In the UK the incidence of TB was 9.6 \(/10000\) in 2015. Leicester city has one of the highest rates of TB in the UK with an incidence of 38.5/100000.\(^{(2)}\)

*Mycobacterium tuberculosis* (Mtbc) is transmitted through the air and primarily affects the lungs. Tuberculosis is curable and preventable. TB is spread from person to person through the air. When people with pulmonary TB cough, sneeze or spit, they propel the TB germs into the air. A person needs to inhale only a few of these germs to become infected. Most infected individuals remain asymptomatic for a long time (latent infection). The risk of progressing into active disease is around 10% - 15% but is highest in the infant with a risk of invasive disease as high as 50%. The majority of those who become ill develop the active disease within the first two years of exposure.

2.2 Referral Pathways:

1) Outpatient referrals:

- from the TB nursing team,
- Emergency department (ED),
- GP referrals

2) In patient referrals:

- Children who may present to ED will either be admitted to the children’s ward or CICU depending on the clinical need
- Children who seem to be well on initial assessment can then be seen either in outpatient clinic or on the children’s day care unit as appropriate.
- General paediatric or surgical wards,
- Other hospitals in the region

3) Well children that require TB screening investigations, new referrals from primary care, TB nursing team, ED, other hospitals in the region will be referred directly to the Paediatric TB team – this pathway is only for the well children:

   a. Fax: 0116 256 3766
   b. Telephone: 0116 258 3767

4) For urgent referrals please email [TB.RapidAccess@uhl-tr.nhs.uk](mailto:TB.RapidAccess@uhl-tr.nhs.uk)
2.3 Isolation and Infection control:


Staff should wear the masks when in the source isolation room. The patient would only wear a mask when they are being moved through the hospital.

Ensure that all carers/visitors wear a surgical mask for the first 2 weeks of treatment. We generally don’t put household contacts in masks while they are visiting in the cubicle as they are contact screened and have already been exposed. Non household contacts are discouraged from visiting until the patient is deemed to be non-infectious. All adult visitors who have not yet been screened will need to wear surgical masks while in the hospital outside the cubicle until they are screened and cleared.

2.4 Screening of children with presumed or suspected TB infection:

1. Contact with sputum smear positive pulmonary TB OR smear negative but culture positive within 10 days (see flow chart page1)
   - Children < 2 years
     - Children should be seen as soon as possible to start chemoprophylaxis
     - If clinically well then start Isoniazid 10 mg/kg OD and Rifampicin 15 mg/kg once daily
     - Children will be seen in TB clinic 6 weeks later for an assessment and investigations (mantoux and IGRA)
     - If clinically unwell investigate appropriately for TB inc CXR and inform Paediatric TB team
   - All other children (3 – 16 yrs)
     - Refer to TB clinic (SBRTB) Orange Childrens Admin
       OrangeChildrensAdmin@uhl-tr.nhs.uk and email TB nursing team/Dr Bandi as soon as possible
     - Children will be screened with mantoux, IGRA, +/- CXR. If the initial screen is negative then a repeat screen will be arranged in 2-3 months

2. Contact with sputum smear negative pulmonary TB
   - Refer to clinic (SBRTB) OrangeChildrensAdmin@uhl-tr.nhs.uk

3. Contact of extra pulmonary TB
   - Refer to clinic (SBRTB) OrangeChildrensAdmin@uhl-tr.nhs.uk
2.5 Diagnosis:

**Latent Tuberculosis Infection (LTBI):** is when a person is infected with *Mycobacterium Tuberculosis* but do not have any signs of active disease, i.e. they are asymptomatic and their CXRs are normal. However they can develop active disease in the future.

Diagnosis of LTBI is based on a positive Mantoux and /or IGRA (Interferon Gamma Release Assay) with a normal CXR.

**Active TB:** TB can affect any organ and a high index of suspicion is required to diagnose TB in children.

**Pulmonary TB:**
- Lungs are the most commonly affected organ in TB. Symptoms usually include fever, malaise, cough, loss of appetite and weight loss.
- Examination of the chest may show signs of parenchymal (reduced breath sounds, crackles) and /or pleural involvement (pleural effusion)
- CXR – the most common finding is hilar adenopathy. Other findings include patchy consolidation, pleural effusion, nodular infiltration and less commonly cavitary lesions and miliary TB.
- 3 x spontaneous sputum samples, induced sputum or gastric aspirates (including at least one in the early morning) stained for acid fast bacilli and culture – Culture positivity is around 30-40% and can take up to 40 days.
- Gastric aspirates: is an alternative for children who can’t produce sputum (see below)
- Sputum induction (see below) or BAL are alternatives
- Xpert MTBTIF (GeneXpert) for MTB complex gives rapid information (within few hours) on positive samples and detects the main genetic mutation for rifampicin resistance. This is now used more commonly in the diagnosis of TB.
- Tuberculin skin test (Mantoux) and IGRA are indirect tests to show immunity against M Tb. They do not differentiate between active and latent Tb. A *negative test does not exclude active Tb*.
  - Children aged 5 years and under : do both Mantoux and IGRA
  - Children aged > 5 years: do IGRA

**NB:** *Young children with pulmonary tuberculosis are rarely infectious as cavitary disease is uncommon.*

- **Gastric aspirates:**
  Gastric aspiration usually requires a child to have a nasogastric tube insitu for 3 days. Three early morning consecutive samples should be collected while the child is recumbent and fasted overnight.
A minimum of 5 mls of gastric aspirate is required and placed into a white specimen bottle and sent for AFB and Tb culture.
If no gastric aspirate is obtained, place 5 mls of sterile water down the nasogastric tube, wait for 5 minutes and aspirate back.

- **Induced sputum:**
  An alternative to gastric aspirates is to induce sputum with a hypertonic saline (7% NaCl) nebulisation. This has to be done in a negative pressure environment.
  Options are the
  - Respiratory lab on level 0, Windsor – prior agreement is required from the respiratory physiologist.
  - The other option is Infectious Diseases Unit (IDU) on level 6, Windsor. This has to be pre-arranged with IDU staff and paediatric physiotherapists.

- **Bronchioalveolar lavage (BAL):** this requires a general anaesthetic and is limited by the lack of a dedicated operation theatre in paediatrics. BAL should be sent in children who are ventilated and are suspected to have TB.

**Extra-pulmonary TB:** Tb can affect any organ and diagnosis requires a high index of suspicion.

- Investigations should be tailored according to the site (organ) involved.
- CNS Tb – neuroimaging (CT/MRI), CSF should be sent for AFB, Tb culture and Tb PCR in addition to routine microscopy, chemistry and culture.
- Extra-thoracic lymph node - biopsy material stained for acid fast bacilli and culture.
- Tuberculin skin test (Mantoux) and IGRA are indirect tests to show immunity against M Tb. They do not differentiate between active and latent Tb.
  - Children aged 5 years and under : do both Mantoux and IGRA
  - Children aged > 5 years: do IGRA

**2.6 HIV infection and immunocompromised children:**

Diagnosis is more complicated in immunocompromised patients. Mantoux and IGRA could be negative due to immunosuppression.
If there is history of contact with a smear positive patient, without any clinical/radiological evidence of disease, start chemoprophylaxis. Please refer to TB team as soon as possible.

**2.7 The neonate**

Congenital TB is extremely rare. Babies most at risk of congenital TB are those born to mothers who sputum smear positive TB, either not on treatment or within the first 2 weeks of treatment. Babies needs to be assessed for active TB quite soon after birth and may need further investigations. Please inform the paediatric TB team as soon as possible.
If the baby is completely well chemoprophylaxis with isoniazid is recommended (see figure 1).
If the mother is known to be TB positive then the placenta should be sent to the microbiology laboratory (sample in universal specimen bottles with NO formalin) and to histology (sample in formalin) as per normal procedure. If the baby is born to a mother with extra-pulmonary TB or with sputum negative TB then the risk of transmission to the baby is small. These babies should be referred to Paediatric TB team. Breastfeeding is not contraindicated (in the first 2 weeks of maternal treatment the mother should wear a mask).

2.8 Indirect Tests for TB:

**The Tuberculin Skin Test (TST, Mantoux test)**

This test assesses the individual’s sensitivity to tuberculin protein. A positive test means the individual is infected but it does not differentiate between an active infection and latent infection. 0.1 ml of PPD [2TU] is injected intradermally on the volar side of the forearm leaving a bleb under the skin (if no bleb, needs to be repeated). The reading is made between 48 and 72 hrs. Any induration (firm swelling of the skin, not erythema) is measured.

<table>
<thead>
<tr>
<th>Induration</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-4 mm</td>
<td>Negative</td>
</tr>
<tr>
<td>&gt; 5mm</td>
<td>Positive</td>
</tr>
</tbody>
</table>

**Positive Mantoux:**

- If the patient is asymptomatic and the CXR is normal chemoprophylaxis (latent TB) is indicated.
- If the patient is symptomatic and/or the CXR is abnormal – investigate for active disease

**IGRA Tests**

In UHL we use QuantiFERON TB Gold plus. The advantages of IGRA are that there is no need for the child to come back for the reading. They are less accurate in younger children (<5 years of age) and hence Mantoux is used in combination in this group.

**Treatment:** All children commenced on TB treatment (active or LTBI) should be referred back to the TB nursing service for follow-up with a completed referral form (Appendix 1).

**Latent TB (Chemoprophylaxis)**

Chemoprophylaxis is used when there is evidence of infection i.e a positive Mantoux +/- IGRA and there are no signs or symptoms of TB with a normal Chest x-ray. There are different regimes available and at UHL we use the following regime:

- 12 week course of Isoniazid and Rifampicin
  - Isoniazid (H) 10mg/kg (maximum dose 300mg)
- Rifampicin (R) 15mg/kg (< 50 kg - maximum dose 450 mg; >50 kg max 600 mg)

- The family should be explained that urine and all body fluids will turn red because of rifampicin; this is not a side effect but is normal.

**Active TB:**

It is imperative that all the diagnostic samples are collected before starting TB treatment. The culture can take up to 6 weeks to be positive; treatment can start before culture results are available.

Baseline LFTs, vitamin D and an HIV test should be done on all patients diagnosed with TB. LFTs should be repeated if the child develops any side effects (abdominal pain, vomiting, skin rashes, and jaundice)

**2.9 Regime:**

Standard TB regime is for a total 6 months (26 weeks). Four drugs are given for the first two months - isoniazid, rifampicin, pyrazinamide, ethambutol* followed by four months of isoniazid and rifampicin. Consider adding pyridoxine, particularly in children who are breast fed or malnourished.

**TB meningitis (CNS TB)** requires a 12 months course, with two months of quadruple therapy (isoniazid, rifampicin, pyrazinamide, and ethambutol) and 10 months of isoniazid and rifampicin

Steroids should be added in CNS TB and pericardial TB: Prednisolone 1–2 mg/kg (max 40 mg) for four weeks with gradual withdrawal over the next 4-8 weeks and over 2-3 weeks for pericardial TB. Steroids are sometimes used in other situations eg. Ureteric TB.

**Drug Dosages:** all once daily

- Isoniazid (H) 10mg/kg (maximum dose 300mg)
- Rifampicin (R) 15mg/kg (< 50 kg - maximum dose 450 mg; >50 kg max 600 mg)
- Pyrazinamide (Z) 35mg/kg (maximum 1.5 grams)
- Ethambutol (E) 20mg/kg (ethambutol can be omitted or stopped if it is known that the isolate is sensitive to all the first line drugs)

In general doses are rounded up to facilitate administration of suitable volumes of liquid or an appropriate strength of tablet.

<table>
<thead>
<tr>
<th>Standard TB treatment</th>
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<tbody>
<tr>
<td>Intensive phase (first 2 months)</td>
<td>HRZE</td>
</tr>
<tr>
<td>Continuation phase (month 3 – 6)</td>
<td>HR</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CNS TB treatment</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Intensive phase (first 2 months)</td>
<td>HRZE</td>
</tr>
<tr>
<td>Continuation phase (month 3 – 12)</td>
<td>HR</td>
</tr>
</tbody>
</table>
3. Education and Training - None

4. Monitoring Compliance

<table>
<thead>
<tr>
<th>What will be measured to monitor compliance</th>
<th>How will compliance be monitored</th>
<th>Monitoring Lead</th>
<th>Frequency</th>
<th>Reporting arrangements</th>
</tr>
</thead>
<tbody>
<tr>
<td>Screening of TB contacts Management of children with TB</td>
<td>Audit every 2-3 years</td>
<td>S Bandi</td>
<td>2-3 years</td>
<td>Present in departmental audit meetings</td>
</tr>
</tbody>
</table>

5. Supporting References


- NICE Tuberculosis guideline. [https://www.nice.org.uk/guidance/ng33](https://www.nice.org.uk/guidance/ng33)

- Paediatric TB guideline 2015. St George’s Hospital, London.

6. Key Words

TB, Tuberculosis, Paediatric TB.

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs. As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

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**Contact and review details**

<table>
<thead>
<tr>
<th>Guideline Lead (Name and Title)</th>
<th>Executive Lead</th>
</tr>
</thead>
<tbody>
<tr>
<td>S Bandi, Consultant Paediatrician, UHL.</td>
<td>Chief Medical Officer</td>
</tr>
</tbody>
</table>

Details of Changes made during review:

Added - **Bronchioalveolar lavage (BAL):** this requires a general anaesthetic and is limited by the lack of a dedicated operation theatre in paediatrics. **BAL should be sent in children who are ventilated and are suspected to have TB.**
## TB NURSING SERVICE - REFERRAL FORM

### PATIENT DETAILS

<table>
<thead>
<tr>
<th>Hospital Number</th>
<th>Hospital Site</th>
</tr>
</thead>
<tbody>
<tr>
<td>Name / Address</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date of birth</th>
<th>Male / Female</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Telephone Number (Please add mobile number if available):</th>
<th>Occupation</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>GP NAME / ADDRESS</th>
<th>Language Spoken</th>
</tr>
</thead>
</table>

### CONSULTANT

<table>
<thead>
<tr>
<th>WARD / DEPARTMENT</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>ADMISSION DATE</th>
<th>DISCHARGE DATE</th>
</tr>
</thead>
</table>

### SITE OF TUBERCULOSIS

- Pulmonary
- Pleural effusion
- Intra-thoracic lymph node

#### CHEMOPROPHYLAXIS (Latent TB)

- AAFB POSITIVE: YES / NO
- CULTURE POSITIVE: YES / NO
- HIV TESTED: YES / NO

#### DRUG / TREATMENT REGIME ON REFERRAL

(Drug Name / Dose / Frequency / Amount issued)

#### PATIENTS CURRENT WEIGHT in KG:

#### ADDITIONAL INFORMATION / DATE OF NEXT OUTPATIENT APPOINTMENT

<table>
<thead>
<tr>
<th>Signature</th>
<th>Date</th>
</tr>
</thead>
</table>

Name (please print)

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Please return to: TB Nursing Service Glenfield Hospital

Fax (0116) 2583766 Tel (0116) 258 3767

Title: Tuberculosis V.2 Approved by O

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