CHAPTER 6: TUBERCULOSIS (TB) IN CHILDREN AND ADOLESCENTS

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SUMMARY OF RECOMMENDATIONS

- TB infection (previously called latent TB infection) in children and adolescents is diagnosed when there is a positive immunological test for TB (TST or IGRA) without evidence of TB disease. Tuberculosis Preventative Treatment (TPT) should be administered in children <2 years of age following significant exposure whether or not the immunological test is positive (**window prophylaxis**).
- The preferred TPT regimen in Ireland for children of any age is Rifampicin and Isoniazid for a total of 3 months. Pyridoxine is recommended for infants being breast fed and for children who are malnourished.
- A diagnosis of TB disease in children and adolescents should be made based on clinical symptoms, with appropriate investigations depending on the presumed site of infection. (See Section 6.4.1 for more detail).
- All children under 12 months with suspicion for TB disease should have a lumbar puncture performed as part of their diagnostic work-up.
- Treatment regimens for TB disease should be tailored based on clinical manifestation and results of drug-sensitivity testing, once available (see section 6.4.2 for more detail).
- All children living with HIV should be screened annually for TB and all children with TB disease should have a HIV screen. Children commencing biologic therapy should be screened for TB.

6.1 Introduction

Tuberculosis in children accounts for approximately 12% of the global burden of TB disease, resulting in approximately 1.3 million cases and 166,000 deaths in 2023 (1).Tuberculosis in children is underdiagnosed and undertreated (2). The risk of developing TB disease (TBD) following exposure changes throughout childhood. The greatest risk is in the neonatal period; following exposure up to 50% of newborns develop disease and they have an increased likelihood of extra-pulmonary disease such as meningitis (3). In a large meta-analysis of children with confirmed TB infection, 20% of children under 5-year of age had progressed to disease within 2 years of exposure (4).The risk of progression reduces in school age children and increases again in adolescence (3).

6.2 Clinical Presentation

Clinical manifestations of TB are dependent on the primary site of infection. Pulmonary TB remains the most common presentation in childhood. In young children pulmonary TB is often paucibacillary, rarely cavitating or transmissible and may present with clinical features secondary to lymphadenopathy. Children may have the classical features of fever, night sweats, cough and weight loss but symptoms and signs may be subtle. Children may present with failure to thrive rather than weight loss, and lethargy or reduced playfulness is well described (5). Therefore, it is important to have a high index of suspicion for TB in children living in at risk settings or having spent significant time in countries with a high incidence of TB (>40 cases of TB disease per 100,000 population per year).

The investigation and management of TB disease in children and young people is best undertaken by either a Paediatric Infectious Disease (PID) specialist, a paediatrician with experience and training in TB or by a general paediatrician with advice from a specialist. The PID team in Children's Health Ireland (CHI) is available to discuss appropriate case management for all cases of TB in children.

Children being assessed for TB should have an appropriate history taken to ascertain risk factors and symptoms. A full clinical examination and a chest x-ray should be performed. Further investigations such as abdominal ultrasound and microbiological sampling may also be warranted depending on the exposure risk.

6.3 TB Infection in Children and Adolescents

6.3.1 Diagnosing TB Infection

TB infection (TBI) is diagnosed when a child has a positive immunological test for TB without evidence of TB disease. TBI was previously referred to as “latent TB infection” or LTBI, but, as infection cannot always be considered latent, the term TBI is now preferred. Children with TBI may be identified through contact tracing following exposure to a case of TB disease, or as part of screening programmes for children from high-risk settings, or who are immunosuppressed, for example children living with HIV or those on medications such as TNF blockers.

The immunological tests commonly used in Ireland are the **Tuberculin Skin test (TST)** and **Interferon Gamma Release Assays (IGRA)**. These tests have similar sensitivity and specificity and either can be used at any age and may be used in conjunction when results are difficult to interpret. Recent evidence is reassuring regarding the utility of IGRAs in younger children and the choice between TST or IGRA is a logistical one based upon the local availability and feasibility of either test (6). The interpretation of the TST is described in Appendix I. It can take up to 8 weeks to mount an immunological response so children with a negative test following a recent TB exposure should have repeat testing no sooner than 8-weeks following exposure.

6.3.2 TB Preventative Treatment

TB Preventative Treatment (TPT) is offered to people who are considered to be harbouring TB and to be at risk of developing TB disease in order to reduce that risk. This was previously referred to as LTBI treatment. In the absence of known anti-mycobacterial drug resistance in the contact case, the preferred TPT regimen in Ireland for children of any age is Rifampicin and Isoniazid for a total of 3 months. Pyridoxine is recommended for infants who are being breast-fed and for children who are malnourished and may be considered for all patients on TPT. Rifampicin may be contra-indicated due to drug-drug interactions, particularly with antiretrovirals or antiseizure medication. Isoniazid for 6-9 months is an alternative regimen. If the index case is known to be infected with a drug-resistant strain, the appropriate TPT should be determined following discussion with the PID team at Children’s Health Ireland. Full blood count, renal and liver function tests can be considered for children commencing TPT (often done at time of IGRA). Children should be reviewed monthly but if baseline bloods are normal and the child remains well without signs of hepatotoxicity (jaundice, vomiting, abdominal distension or pain) no blood monitoring is necessary.

6.3.2.1 Window prophylaxis

Children less than 2 years of age with a significant exposure to TB are at greater risk of disease progression, severity and dissemination. In addition to an assessment for TB disease, it is recommended that children less than 2 years receive TPT even if the immunological test is negative This ensures that the exposed child receives appropriate treatment during the window in which an immune response may develop and is known as window prophylaxis. If the immunological test becomes positive when rechecked there is no need to restart TPT as long as there has not been further TB exposure. This strategy may also be employed for children of any age at high risk of progressing to TB disease such as Human Immunodeficiency Virus (HIV) infection or treatment with Tumour Necrosis Factor (TNF) blockers following significant TB exposure. If repeat testing following an appropriate time-period is negative, window prophylaxis can be discontinued.

Table 6.1: Tuberculosis Preventative Treatment (TPT) for Children and Adolescents of any age

Tuberculosis Preventative Treatment (TPT) For Children and Adolescents of any age	
Preferred Regimen	Rifampicin and Isoniazid x 3 months*
Alternative Regimens	Rifampicin x 4 months* OR Isoniazid x 6-9 months*
*Pyridoxine is recommended for breast feeding infants and for children who are malnourished and can be considered for all.	

6.4 TB Disease in Children and Adolescents

6.4.1 Diagnosing TB Disease

The principles of diagnosing children are similar to adults, and symptoms of cough, weight loss or failure to thrive, fever or night sweats may be suggestive of TB disease. Appropriate

investigations are dependent on the presumed site of infection, for example, lumbar puncture and MRI brain for children with meningitis. All children under 12 months with suspicion for TB disease should have a lumbar puncture performed as part of their diagnostic work-up, even in the absence of symptoms and signs of meningitis. The PID team in CHI is available to discuss appropriate case management for all cases of TB in children.

For the investigation of pulmonary TB, three respiratory samples should be sent. Spontaneously produced, deep cough sputum samples are preferable, but rarely obtained in younger children, otherwise three induced sputum or three early morning gastric aspirates (GA) will suffice.

To collect GA samples, a nasogastric tube should be inserted and left in-situ. Shortly after waking and prior to eating or drinking, 5-10ml of gastric content should be aspirated and sent for investigation.

Specimens should be sent for staining for acid fast bacilli, mycobacterial culture and rapid diagnostic nucleic acid amplification tests for *M. tuberculosis* complex (*M. tuberculosis*, *M. bovis*, and *M. africanum*). Usually only one nucleic acid amplification test is needed per specimen type (for example, spontaneous sputum, induced sputum or gastric aspirate).

Tissue specimens may be required in order to isolate the organism and confirm the diagnosis of nodal or extra-pulmonary TB. The advantages and disadvantages of both biopsy and needle aspiration, with the aim of obtaining adequate material for diagnosis, need to be discussed with the family and patient where appropriate.

6.4.2 Treatment of TB Disease

TB disease in children should be managed by a TB specialist and by paediatric trained nursing staff, where possible. In life threatening disease, treatment should not be withheld while awaiting confirmation of the diagnosis. Treatment regimens should be based on known resistance phenotyping of contacts and regimens may need to be altered as results become available. At baseline children commencing TB treatment should have a full blood count, renal and liver function and HIV antibody sent.

Traditionally, treatment of drug-sensitive pulmonary TB in children includes a 2-month intensive phase followed by a continuation phase of 4 months. More recently, the WHO has recommended a shorter 4-month regimen for children over 3-months of age with non-severe TB based on the Shorter Treatment for Minimal Tuberculosis in Children (SHINE) trial. This includes two months of quadruple therapy with isoniazid (H), rifampicin (R), pyrazinamide (Z)

and ethambutol (E); followed by another two months of dual therapy (HR). Non-severe TB is defined as peripheral lymph node TB, intrathoracic lymph node TB without airway obstruction, uncomplicated TB pleural effusion or paucibacillary, non-cavitary disease confined to one lobe of the lungs and without a miliary pattern.

Longer treatment regimens are recommended for disseminated disease such as TB meningitis (TBM) and osteoarticular disease which should be guided by the PID team in CHI. A shorter 6-month intensive treatment regimen including ethionamide instead of ethambutol is also recognised by the WHO as a treatment option for drug sensitive TBM.

Adjuvant corticosteroid should be offered as part of the treatment for TBM and pericarditis and may be used for other complicated forms of TB.

Children receiving treatment for TB disease should be seen 2- and 4-weeks following initiation of treatment and one to two monthly thereafter. If baseline bloods are normal and the child remains well without signs of hepatotoxicity (jaundice, vomiting, abdominal distension or pain) further blood monitoring is not routinely necessary.

6.5 Public Health Contact Tracing

Children are considered less contagious than adults due to lower likelihood of cavitating disease, primarily swallowing rather than expectorating sputum and have lower cough volumes. In older children and adolescents, cavitating disease is possible resulting in similar contagiousness to adults. Children are more likely to progress to active disease more rapidly, therefore a new diagnosis of TB in a child likely represents a recent transmission event following close contact with an adult with TB disease and Public Health will undertake relevant source investigation as necessary and appropriate (see further information in upcoming Chapter 8: Contact tracing and case-finding.) It is important that family members who are attending with a child with likely TB follow appropriate local isolation precautions until they have also been screened to out rule TB disease.

6.6 BCG

BCG has not been available in Ireland since 2014.* The introduction of a selective BCG immunisation programme is an objective of the national TB strategy "Striving to End Tuberculosis – A Strategy for Ireland 2024 – 2030" (7). The National Immunisation Advisory Committee guidelines outline the groups currently eligible for BCG vaccination under a selective vaccination programme (8).

6.7 Special Populations

All children living with HIV should be screened annually for TB by paediatric services. Children being assessed for TB disease should have a HIV screen sent and consideration should also be given for screening for Hepatitis B and C. Children commencing biologic therapy should be screened for TB.

6.8 Drug-resistant TB

Regimens for treatment of drug-resistant TB disease in children are based on WHO recommendations (9) and should be made in consultation with the PID team in CHI.

* See Appendix I (Report of the National Immunisation Advisory Committee BCG Vaccine Subcommittee) in the Selective Strategy for BCG vaccination for more information.

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