Tuberculosis in Children and Adolescents

Introduction

The World Health Organization (WHO) estimated that children represented around 12% of the total burden of tuberculosis (TB) globally in 2019 with around 1.2 million TB cases and 230,000 TB-related deaths in children (WHO Global TB Report 2020).

It is difficult to estimate the true burden of TB in children due to difficulties with confirming diagnosis, especially in young children in TB endemic settings, and due to the widespread problem of under-reporting of child TB cases by TB control programs in those settings. In Australia, as in similar low incidence settings, around 4-5% of all TB cases are in children and the incidence rate is highest in overseas-born children compared to Australian-born (indigenous or non-indigenous) children, and in young children (< 5 years) (Teo et al. 2015). In Victoria 12 cases of active TB disease in children (0-15 years-old) were reported in 2020.

The clinical presentation of TB in children differs to that in adults. Following pulmonary infection with *Mycobacterium tuberculosis*, there is an immune response that involves the regional lymph nodes. A positive tuberculin skin test (TST) or interferon gamma release assay (IGRA) is considered an immunological marker of response to infection. The primary complex comprising the site of infection and the involved regional lymph nodes may heal, or complications may develop from enlargement or rupture of the regional lymph nodes or the spread of tubercle bacilli into the bloodstream, giving rise to disseminated disease.

Most children contain the infection resulting in what has commonly been referred to as ‘latent TB infection’, but the risk of developing disease remains lifelong. Some children progress to develop disease, i.e. ‘active TB’, following infection. Progression to TB disease occurs more commonly in children than in adults and the risk is greatest in the first 12 months following infection. Young children (<5 years) are at particular risk of disseminated TB and TB meningitis, which are associated with a poorer outcome than localised disease, and commonly present within 3 months following infection. **Prompt screening and management of children and adolescents who are close contacts of a TB index case is therefore critical.**

The increased likelihood of dissemination also explains why the presentation of extra-pulmonary TB is more common in children than adults. At all ages, however, pulmonary TB is the most common presentation. Adolescents also have greater risk of TB than adults, however the presentation of TB in adolescents is more similar to that of TB in adults.

Risk of Disease Following Primary Infection

In general, for children who have a normal CXR at the time a positive TST is first detected, the lifetime risk of developing active TB disease is between 2 and 10 per cent. However, the risk is higher in young children, children who have been exposed very recently, and children who have malnutrition, immunodeficiency, or poor general health. A meta-analysis of over 130,000 child and adolescent TB contacts

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reported a two-year cumulative risk of progression to TB of 19% (95%CI: 8.4-37.4) in young (<5 years) child contacts with evidence of infection (Martinez et al. 2020).

Data from Victoria found that the four-year disease risk following infection for aged <5 years, 5 to 14 years, and ≥15 years was 56.0%, 27.6%, and 4.7% respectively with virtually all risk accrued in the first 5 months after exposure (Trauer et al. 2016). This very high risk observed is partly due to inclusion of nodal TB as "active". Active TB was detected in 5% of 574 young child contacts evaluated in Victoria in 2016-2019 (Moyo et al. 2021)

These findings underline the importance of early referral and investigation for TB in all people who have been exposed to TB, as well as the prompt initiation of TB preventive therapy (TPT) for eligible child and adolescent contacts without evidence of active disease.

Infectivity

Childhood TB is rarely contagious because:

- Children with active TB usually have a low bacterial load
- Children are less able to generate the tussive forces needed to aerosolise bacilli
- Young children with pulmonary TB rarely have cavitating disease.
- Young children swallow rather than expectorate sputum

Older children (10-14 years) and especially older adolescents (15-19 years) may present with cavitary and/or sputum-positive TB and are commonly infectious.

Diagnosis

In the assessment of a child with possible infection or disease due to TB, a thorough history of TB contact should be sought as well as a history of recent travel to a TB endemic country. In a low incidence setting, a source case with TB is commonly identifiable. This may be a known contact already diagnosed with and treated for TB, or a contact with TB-related symptoms who requires further investigation. Important information of the possible TB source (or index) case includes site of disease, whether bacteriologically confirmed (by smear, culture or PCR), drug susceptibility test results, as well as whether the index case is receiving treatment for TB, when the treatment was commenced, what treatment regimen, and adherence and response to that regimen.

TB Infection

Diagnostic tests that indicate TB infection include a positive tuberculin skin test (TST) or interferon-gamma release assay (IGRA). TST and IGRA are both imperfect tests that can yield false positive and false negative results (Tebruegge et al. 2015). Their interpretation and subsequent clinical management depend on the prior probability

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of the test being positive and on the clinical and epidemiological circumstances of the individual.

A missed diagnosis of TB infection has greater implications for children than adults (due to the higher risk of disease, particularly severe disease). As such, interpretation and response to TB testing depends on age, TB contact history (including the infectiousness of the source case and the timing, closeness and duration of contact), and the clinical situation.

Tuberculin skin test (TST)

The TST has been the standard indicator of infection with *M. tuberculosis* for more than a century and remains the preferred diagnostic tool for evidence of infection in children (particularly children <5 years of age), where available. The interpretation of a positive test may be modified by the risk of infection, which is influenced by the contact history, medical history and age of the child. For example, a positive TST in a child or adolescent contact is considered to indicate infection with *M.tuberculosis* even if they have received BCG vaccination (Farhat et al. 2006).

Table 1 lists the classification of the TST reaction as per current CDC USA guidelines. In general, a TST of 10 mm or greater is regarded as positive including in children and adolescents at risk of exposure such as those who were born in TB endemic countries or have been exposed to adults at-risk of TB. However, in those who are close contacts of active TB patients or in immunocompromised individuals, such as a child living with HIV or who is severely malnourished, a TST of 5 mm or more is also regarded as positive.

Table 1. Classification of the Tuberculin Skin Test Reaction

Induration ≥5 mm	Induration ≥10 mm	Induration ≥15 mm
Children aged <5 People living with HIV People with organ transplants Other immunosuppressed people (e.g., patients on prolonged therapy with corticosteroids ≥15 mg per day of prednisone or those taking TNF-a antagonists)	People with a history of close contact with confirmed TB People with chest x-ray findings suggestive of previous TB disease (consider IGRA as supplementary test)	People with no known risk factors for TB

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Interferon-gamma release assay (IGRA)

IGRA, like TST, can be used as an indicator of infection with *M. tuberculosis*. The commonest IGRA in use is the QuantiFERON-TB Gold (QFT®, Qiagen). Most studies show that IGRA and TST have similar sensitivity for the detection of TB infection - although the results for the two tests are not always concordant. Studies suggest that IGRA is less sensitive than the TST in young children. As such, the TST remains the test of choice for asymptomatic children, particularly children <5 years of age. Limited data suggest that IGRA may be useful in individuals at risk of a false-negative TST, e.g. the immunocompromised.

Interpretation of TST and IGRA results in children

Positive TST or IGRA

A positive TST or IGRA indicates infection with mycobacteria **but does not distinguish individuals with infection only (previously known as LTBI) from those with active TB**. Therefore, interpretation of the test is made in the context of contact history, symptoms, signs and radiology according to established guidelines. Recent conversion of either a TST or IGRA from negative to positive is likely to indicate a greater likelihood of progression to active disease. The IGRA is more specific for infection with *M.tuberculosis* than the TST which can be positive following infection with other mycobacteria such as BCG (*M.bovis*) or non-tuberculous mycobacteria (e.g. *M.ulcerans*).

Negative TST or IGRA

Although a positive TST or IGRA indicates infection with *M. tuberculosis*, **a negative test does not rule out either infection with or active disease due to *M.tuberculosis*.** The sensitivity of these tests is around 80% in individuals with bacteriologically confirmed TB but is reduced if immunocompromised, such as due to severe TB disease, HIV co-infection or severe malnutrition. Sensitivity of IGRA is also lower in infants and young children with higher numbers of "indeterminate" results.

Discordant IGRA and TST result

In some children the IGRA and TST results are contradictory or "discordant" – either TST + / IGRA – (more commonly) or TST – / IGRA +. It is safest to assume that a negative IGRA or TST in this situation does not exclude TB infection. **Most experts therefore recommend that a discordant result is regarded as a positive result** when making treatment decisions.

Indeterminate IGRA result

Indeterminate IGRA results are more common in children, especially in infants and young children under 5 years of age. If the result is indeterminate no interpretation can be made and the test should either be repeated or excluded from the process of

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evaluating the diagnosis.

History of BCG

BCG vaccination can cause false positive TST results – however the risk of this is lower than previously thought, especially if BCG was administered in infancy (Farhat et al. 2006). Given the implications of missing TB infection in children, guidelines on the interpretation of TST results no longer account for prior BCG. It is safest to assume that a positive TST indicates TB infection, regardless of BCG status.

Active TB disease

The care of a child suspected of having TB should involve a physician experienced in the management of childhood TB. Diagnosis of TB disease is based on clinical symptoms and signs, chest x-ray, laboratory tests of samples for bacteriological confirmation and drug susceptibility, and other investigations depending on clinical presentation (Table 12.1).

Laboratory samples. The main tests for bacteriological confirmation are smear microscopy, WHO-approved molecular rapid tests such as Xpert, and culture – and for drug susceptibility are Xpert for rifampicin-resistant mutations and phenotypic drug susceptibility testing. Compared to adults, a larger proportion of TB disease in children is not bacteriologically confirmed (around 50%) - classified as “clinically diagnosed” - and this is particularly common in young children. However, **microbiological confirmation and drug susceptibility testing should be sought whenever possible**. Treatment should be started as soon as samples have been obtained.

Imaging. Chest x-ray is usually indicated in children with presumptive TB and a lateral chest x-ray increases the yield for detecting hilar or mediastinal lymphadenopathy. Higher-resolution imaging such as thoracic CT scans or MRI will improve detection of lymphadenopathy, parenchymal changes and cavities. However, CT scan of the chest should not be performed routinely because of the associated radiation dose and MRI is not usually required to diagnose intrathoracic TB. MRI is particularly useful in the diagnosis and management of TB of the central nervous system such as TB meningitis, spinal TB or tuberculoma in the brain. Ultrasound detects effusions due to TB (pleural, abdominal, pericardial) and is also useful for diagnosis of TB involving gastrointestinal tract (usually ileal), intra-abdominal lymph nodes, genitourinary tract, liver or spleen.

Collection of specimens for bacteriological confirmation

Pulmonary:

In younger children when it is not possible to obtain sputum, gastric aspirates should be collected on three consecutive days. About 50 mL of gastric contents should be aspirated via a nasogastric tube early in the morning after the child has fasted for 8 to 10 hours, preferably while the child is still in bed. This is best performed in

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hospital but can be undertaken through some hospital in the home programmes. Smear microscopy, culture and PCR (e.g. Xpert Ultra) should be performed on the aspirate.

If there is radiological evidence of focal disease such as lobar, segmental or subsegmental collapse or clinical evidence of bronchial obstruction a flexible fibreoptic bronchoscopy with broncho-alveolar lavage may be indicated in addition to gastric aspiration. Otherwise, there is no advantage of bronchoscopy over gastric aspiration.

Inhalation of nebulised sterile hypertonic saline (3 to 6%) via an ultrasonic nebuliser can be used to induce sputum in those unable to expectorate sputum. However, the cough produced by this technique may be of sufficient force to aerosolize tubercle bacilli and infect health care workers. For this reason, **nebuliser-induced sputum collection is not the procedure of choice for obtaining respiratory samples in children** (particularly during the COVID-19 pandemic) and should only be performed in areas with high-efficiency particulate air filters and qualified personnel wearing appropriate respiratory protection.

Extrapulmonary:

Table 2 lists approaches to obtaining samples for bacteriological confirmation of the various forms of extrapulmonary TB. Note that the yield from Xpert (Ultra) or culture are much higher than from smear microscopy of extrapulmonary specimens but that the likelihood of bacteriological confirmation is dependent on sample, being high for lymph node TB but very low from TB effusions such as pleural, pericardial or peritoneal effusions. It is not uncommon for a child with extrapulmonary TB to also have pulmonary TB, so **always consider obtaining pulmonary samples as well** (as above).

Table 2: Approach to diagnosis of extra-pulmonary TB

Site of EPTB	Typical clinical presentation	Investigations to consider	Laboratory test
TB adenitis	Asymmetrical, painless, non-tender lymph node enlargement for more than one month +/- discharging sinus Most commonly in neck	Fine needle aspiration +/- biopsy TST usually positive	Xpert and culture (with DST): high yield Histology
Pleural TB	Dullness on percussion and reduced breath sounds	CXR; ultrasound	Xpert and culture: low yield

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	+/-chest pain	Pleural tap – usually straw-coloured fluid	
TB meningitis	Headache, irritability/abnormal behaviour, vomiting (without diarrhoea), lethargic/reduced level of consciousness, convulsions, neck stiffness, bulging fontanelle, cranial nerve palsies	Lumbar puncture MRI brain CXR for miliary or pulmonary TB	High CSF protein and predominant lymphocytosis Xpert and culture: moderate yield
Miliary TB	Non-specific, lethargic, persistent fever, weight loss, wasted	CXR Lumbar puncture; MRI brain	
Abdominal TB	Abdominal swelling with ascites (usually painless) or abdominal masses	Abdominal ultrasound Ascitic tap	Xpert and culture: low yield
Spinal TB	Back pain Deformity of spine May have lower limb weakness/paralysis/unable to walk	X-ray vertebra MRI spine Biopsy paraspinal abscess	Xpert and culture
Pericardial TB	Cardiac failure Distant heart sounds Apex beat difficult to palpate	CXR Echocardiogram Pericardial tap	Xpert and culture: low yield
TB bone and joint	Swelling end of long bones (usually painless) with limitation of movement Unilateral effusion of usually knee or hip	X-ray and ultrasound bone/joint Joint tap	Xpert and culture: low yield

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Treatment

In Victoria, public health services are mandated to provide all TB-related care to patients without any out-of-pocket costs regardless of Medicare eligibility or residency status, including inpatient and outpatient care, pathology, diagnostics, pharmaceuticals (Victorian Government, 2017).

TB Infection

Treatment of children and adolescents with TB infection and no evidence of TB disease is known as tuberculosis preventive treatment (TPT), and is indicated because:

- it greatly reduces the risk of developing disease in the years immediately after acquiring the infection (Martinez et al. 2020), including of severe disease in young children;
- the lifelong risk of developing TB can be reduced substantially, especially as the risk of re-infection in a low TB-endemic setting is extremely low; and
- TPT is very well tolerated in children and adolescents and serious adverse events are rare

Therefore, **TPT is recommended for otherwise healthy children and young people who have a positive TST or IGRA and no evidence of TB disease**.

TPT is **strongly recommended** in the following risk groups:

- Young children (<5 years) who have been in close contact with a case of bacteriologically confirmed TB irrespective of initial TST. If TST positive, complete TPT course. If TST negative on initial screening, commence TPT and review with repeat TST at three months from break of contact. If break-of-contact TST is negative, TPT may be ceased.
- Older children and adolescents who have been in contact with TB and have evidence of infection
- Children with co-morbidities such as HIV or diabetes at risk of TB infection.
- Children in whom corticosteroid or immunosuppressive therapy (including anti-TNF therapy) is contemplated.

Suitable TPT regimens to treat TB infection

The traditional or usual recommended TPT regimen for the treatment of infection with presumptive drug-susceptible TB has been a minimum of six months (up to nine) of isoniazid 10 (7-15) mg/kg (up to max of 300 mg) once daily (**6H or 9H**). There are now a number of shorter regimens that are also recommended with strong evidence, showing equivalent effectiveness, improved safety and better adherence (WHO guidelines, 2020) - Tables 12.2 and 12.3. These include:

- 3 months of daily isoniazid and rifampicin (3RH) – preferred option for young child contacts (weight < 30kg), if the dispersible fixed-dose combination (FDC) formulation – R75mg/H50mg – is available.

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- 4 months of daily rifampicin (4R) – preferred option for older children and adolescents and increasingly used in adults.
- 3 months of weekly rifapentine and isoniazid (3HP) - Rifapentine is not yet recommended for children < 3 years (awaiting safety and pharmacokinetic data), child-friendly formulation is still under development, and it is not currently available in Victoria

TPT considerations

Rifamycin-containing regimens (i.e. rifampicin or rifapentine) are not suitable for children and adolescents receiving anti-retroviral therapy for HIV co-infection due to drug-drug interactions. **Isoniazid preventive therapy (6-9H) is widely used and very well tolerated in people living with HIV**.

The main potential side-effect of concern for TPT is hepatotoxicity which is usually due to isoniazid and dose-related causing asymptomatic elevations in liver transaminases. More severe isoniazid hepatitis is rare and unrelated to dose (idiosyncratic reaction), typically presenting with abdominal symptoms and varying degrees of liver injury and dysfunction. However, isoniazid-related hepatotoxicity is rare in children and therefore **routine monitoring of liver function is not recommended** if the baseline liver function tests are normal.

The risk of isoniazid-related peripheral neuropathy is negligible in children with TB infection only (i.e. well and not malnourished), and **so prophylactic pyridoxine is not normally recommended with isoniazid-containing TPT regimens in children.**

Isoniazid and/or rifampicin are not recommended as TPT for children who are contacts of TB cases with known resistance to those antibiotics. The use and choice of TPT regimen in child contacts of drug-resistant TB cases who do not have active TB should be considered on an individual basis against perceived risks and benefits, and informed by the drug susceptibility profile of the index case. For an infected young child contact of a case with multidrug-resistant TB, the most commonly used TPT regimen contains a fluoroquinolone such as levofloxacin.

Table 3: Recommended dosages and formulations by weight bands for TPT regimens in children and adolescents

Weight bands	Isoniazid (H) mgs	Isoniazid 100 mg tablet	Rifampicin-isoniazid (RH) (mgs)	FDC RH 75/50mg tablet	Rifampicin (R) (mgs)
4-7kg	50	1/2	75/50	1	-
8-11kg	100	1	150/100	2	-
12-15kg	150	1 1/2	225/150	3	-
16-24 kg	200	2	300/200	4	-
25-30 kg	300	3	300/200	4	-
30 kgs +	300	3	-	-	600

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Table 4: Drug preparations and instructions for preparations currently available in Australia

Drug	Formulation	Comments
Isoniazid	100mg tablet	If an oral liquid formulation is required, disperse tablet(s) in 5mL water and measure the appropriate dose
FDC: rifampicin + isoniazid	75mg/50mg dispersible tablet *	Fully dispersible in water and fruit-flavoured.
FDC: rifampicin + isoniazid + pyrazinamide	75mg/50mg/150mg dispersible tablet *	Fully dispersible in water and fruit-flavoured.
Rifampicin	150mg, 300mg capsule 600mg tablet 20mg/mL syrup	
Pyrazinamide	500mg tablet *	
Ethambutol	100mg, 400mg tablet	If an oral liquid formulation is required, crush tablet(s), mix in 5mL water and measure the appropriate dose
Pyridoxine (Vitamin B6)	25mg tablet	Dose: 25mg (adult); 5mg (child). Crush a 25mg tablet, make up to 5mL with water and give 1 ml.

* requires Special Access Scheme

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Active TB disease

All children with TB disease should be managed in consultation with a paediatrician who is experienced with child TB. Choice of treatment regimen is informed by site and severity of disease, laboratory rapid test result (e.g. Xpert Ultra MTB/RIF), and drug susceptibility profile of the index case (if known). Table 5 lists the current recommended treatment regimens for children with presumptive or confirmed drug-susceptible TB.

Typically, children with non-severe pulmonary or peripheral lymph node TB are treated for six months, including two months of initial 'intensive' treatment phase with isoniazid (H), rifampicin (R), and pyrazinamide (Z), followed by a minimum of four months of continuation therapy with isoniazid and rifampicin, i.e. **2RHZ/4RH**. Outcomes with this regimen are excellent in children with non-severe disease.

Ethambutol (E) is currently recommended by WHO to be added to the intensive phase of treatment for: adolescents with TB (as per adult guidelines); children living with HIV irrespective of severity; and all children with severe forms of TB, including those with sputum-positive pulmonary TB or disseminated TB, i.e. **2RHZE/4RH**. The role of ethambutol is primarily to prevent the emergence and transmission of drug-resistant TB. Therefore, when a more potent fourth drug is required, as with isoniazid mono-resistant TB, it is currently recommended to add a fluoroquinolone to replace isoniazid.

Six months of treatment is highly effective for most forms of TB in children (Table 5). A more prolonged course using standard dosages but with an extended continuation phase, i.e. **2RHZE/10RH**, is currently recommended by WHO (2014) for CNS, bone (including spinal) and joint TB. However for CNS TB, the penetration into cerebrospinal fluid of rifampicin and ethambutol is poor at current dosages. An alternative regimen that can be considered is a six-month regimen of daily treatment with four drugs, with increased dosage of rifampicin and replacement of ethambutol with a fourth drug with far better penetration and safety such as a fluoroquinolone (Seddon et al, 2019). Irrespective of treatment regimen, management of these severe, disseminated forms of TB often require multi-disciplinary specialist input as even with an effective treatment response, sequelae are common.

Corticosteroids are routinely indicated in CNS and pericardial TB, or may be used to reduce mass of TB lesion such as when causing large airway obstruction or spinal cord compression.

Any patient diagnosed with TB should have a Department of Health notification completed within five days of diagnosis. (Latent) TB infection is not currently a notifiable condition.

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Table 5: Recommend treatment regimens for new cases of TB in children (WHO, 2014)

TB diagnostic category	Suggested treatment		Considerations
	Initial phase	Continuation phase	
Smear-negative pulmonary TB Intrathoracic lymph node TB Tuberculous peripheral lymphadenitis Other extrapulmonary TB (other than tuberculous meningitis/ osteoarticular TB)	2 HRZ	4 HR	
Extensive pulmonary disease, including miliary TB Smear-positive pulmonary TB Severe extrapulmonary TB (other than tuberculous meningitis/osteoarticular TB) Children living with HIV, irrespective of severity	2 HRZE	4 HR	Consider steroids for pericardial TB *
CNS, bone, or joint TB	2 HRZE	10 HR	Consider steroids for CNS TB *
Multi-drug resistant TB	Individualised regimens. Seek specialist advice for when there is presumptive or confirmed MDR-TB in child or index case.		
*1-2mg/kg prednisolone (maximum 40mg) or 0.3-0.5mg/kg dexamethasone, with gradual withdrawal starting 2-3 weeks after initiation			

Strategies to Improve Adherence

- Involve the Victorian Tuberculosis Program public health nurse consultants
- Effective education with particular attention to the rationale for the long duration of treatment required
- Strategies to enhance adherence to treatment (see DOT chapter) are generally relevant to treatment in children. Provide family integrated treatment support as much as possible.
- Support management of any adverse events

- Ensure that there are no out-of-pocket costs for TB drugs, and that clinic access (transport) for follow-up is feasible, or consider telehealth.
- Wherever possible, liquid preparations should be used. Fixed-dose dispersible formulations of RHZ and RH have high acceptability with children, parents and health workers in many settings.
- Social support, school attendance and support.
- Reduce stigma and misunderstandings in community such as regarding transmission risks of disease v infection, in children and once treated.

References

False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria?
Farhat M, Greenaway C, Pai M, Menzies D.
Int J Tuberc Lung Dis 2006; 10: 1192-204

The risk of tuberculosis in children after close exposure: a systematic review and individual-participant meta-analysis.
Martinez L, Cords O, Horsburgh CR, Andrews JR; Pediatric TB Contact Studies Consortium.
Lancet 2020; 395: 973-984

Tuberculosis contact tracing for young children: an Australian cascade of care review.
Moyo N, Tay EL, Nolan A, Graham HR, Graham SM, Denholm JT.
Public Health Action 2021; 11(2): 91–96. doi: 10.5588/pha.20.0086

Tuberculosis in children.
Perez-Velez CM, Marais BJ.
N Engl J Med 2012; 367: 348-61

The current global situation for tuberculous meningitis: epidemiology, diagnostics, treatment and outcomes.
Seddon JA, Tugume L, Solomons R, Prasad K, Bahr NC; Tuberculous Meningitis International Research Consortium. Wellcome Open Res. 2019; 4: 167

Diagnostic Tests for Childhood Tuberculosis: Past Imperfect, Present Tense and Future Perfect?
Tebruegge M, Ritz N, Curtis N, Shingadia D.
Pediatr Infect Dis J. 2015 Sep;34(9):1014-9.

The epidemiology of tuberculosis in children in Australia, 2003-2012.
Teo SS, Tay E, Douglas P, Krause VL, Graham SM.
Med J Aust 2015; 203: 440.

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Risk of Active Tuberculosis in the Five Years Following Infection . . . 15%?
Trauer JM, Moyo N, Tay EL, Dale K, Ragonnet R, McBryde ES, Denholm JT.
Chest. 2016 Feb;149(2):516-25

WHO Global tuberculosis report 2020.
World Health Organization, 2020

Guidance for national tuberculosis programmes on the management of tuberculosis in children
World Health Organization, 2014 (update in preparation, 2021)

WHO consolidated guidelines on tuberculosis – tuberculosis preventive treatment.
World Health Organization, 2020.

WHO consolidated guidelines on tuberculosis – drug-resistant tuberculosis treatment.
World Health Organization, 2020.

Hospital provision of tuberculosis services

Victorian State Government Department of Health, Hospital circular 02/2017.
https://www2.health.vic.gov.au/about/news-and-events/hospitalcirculars/circ0217

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