

Key advances and remaining challenges in childhood and adolescent tuberculosis

Item Type	Article
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Citation	Marais BJ, Nicol M, Zar HJ. Key advances and remaining challenges in childhood and adolescent tuberculosis. Paediatr Respir Rev. 2020 Nov;36:25-26. doi: 10.1016/j.prrv.2020.07.008
DOI	10.1016/j.prrv.2020.07.008
Publisher	Elsevier
Journal	Paediatric Respiratory Reviews
Rights	Attribution 3.0 United States
Download date	2024-05-27 06:46:19
Item License	http://creativecommons.org/licenses/by/3.0/us/
Link to Item	https://pubmed.ncbi.nlm.nih.gov/32830068/



Editorial to Mini-Symposium: Tuberculosis

Key advances and remaining challenges in childhood and adolescent tuberculosis



Tuberculosis (TB) remains the leading infectious disease killer on the planet. The World Health Organization (WHO) estimates that 1.1 million children (aged < 15 years) developed TB disease in 2018 [1], and TB is now recognized as a top-10 cause of under-5 mortality in settings with poor epidemic control [2]. The recent 'Roadmap towards Ending TB in Children and Adolescents', launched at the United Nations (UN) high-level meeting on TB in 2018, highlights the urgent need and necessary steps required to improve TB prevention and care in these neglected age groups [3].

Reducing ongoing TB transmission within communities, by diagnosing and treating all infectious cases with an effective regimen as early as possible in their disease course, remains a key strategy to protect children. However, active case finding among adults should not divert attention away from TB prevention and care in children, because childhood TB is easily preventable and treatable – even if they are considered to be less infectious. Poor infection control in health care facilities offers an example of how children may come to harm if their best interests are not considered. Since TB is an airborne disease, children are at risk of TB infection wherever they share poorly ventilated airspaces with coughing adults or adolescents. This risk has been well illustrated in a TB outbreak recorded in a multi-bed 'Kangaroo care unit' in South Africa without any cough triage [4]. In these 'Kangaroo care units' vulnerable pre-term babies spend prolonged periods of time in close contact with multiple other mother-infant pairs and visitors who may pose a transmission risk if they are not triaged for symptoms suspicious of TB. The same situation occurs in clinics where babies coming for routine vaccinations or well-baby checks often share a communal waiting room with coughing adults.

In this mini-series we focus on key advances and remaining challenges in childhood TB across a range of different topics. TB preventive therapy (TPT) is an effective measure to prevent disease progression after TB exposure or infection, mainly within the short-term when risk of disease progression is highest, but also to reduce the reservoir of infection from which future disease may arise [5]. Despite universal endorsement and consistent WHO guidance for more than 10 years, TPT provision to young household contacts remains poorly implemented; in 2018 only 349 487 children <5 years received TPT, which is less than 10% of the 4 million target set at the UN high-level meeting on TB for 2023. In high incidence settings TB transmission frequently occurs outside the household and this should be acknowledged [6], but

even if many infections are missed household exposure offers an excellent opportunity for intervention given that TB services are already engaged with the family. In the first paper of this series, Reuter et al. explore what should be done to close this persistent policy-practice gap in 'Preventing Tuberculosis in Children: A Global Health Emergency' [7].

Vulnerable young children represent an important target group for new and better TB vaccines, but much remains to be discovered about bacillus Calmette Guerin (BCG), which was first introduced in the 1920s and is the oldest vaccine in current use. A recent study in macaque monkeys suggest that intravenous administration may provide enhanced protection against disseminated TB compared to traditional intradermal administration [8], prompting careful reassessment of optimal routes of delivery. Other recent studies demonstrated that repeat BCG vaccination may protect interferon-gamma release assay (IGRA)-negative adolescents against TB infection [9], while the novel M72/AS01E subunit vaccine may protect against adult-type TB disease when used as a post-BCG boost [10]. Ritz et al. review these advances in 'BCG and new TB vaccines' [11].

A significant obstacle to understanding the true burden of TB in children, and to early effective treatment, is the poor performance of diagnostic tests for TB disease in children. Nicol et al. review 'Advances in the diagnosis of pulmonary tuberculosis in children' [12], while Pillay et al. consider new developments in 'Chest imaging in paediatric pulmonary TB' [13]. Chest X-ray remains the most widely used diagnostic tool, but there is wide variability in interpretation, especially of key features such as hilar adenopathy. Imaging methods that may provide a more accurate diagnosis include chest ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI), but cost, availability and lack of expertise limit their use. Rapid diagnosis of TB and potential drug resistance is now possible using automated nucleic acid amplification tests such as Xpert Ultra[®] and a variety of specimen collection techniques. However, sensitivity remains sub-optimal and while testing multiple specimens improves the yield the cost is prohibitive and the increase in yield beyond 2–3 high quality specimens is minimal. New urine antigen tests may hold promise for point-of-care diagnosis, but older versions lacked sensitivity and data on the new Fujifilm SILVAMP TB LAM[®] (FujiLAM) test are eagerly awaited. The search for reliable biomarkers in blood or other easily accessible samples delivered promising candidates,

but further validation is required. In the meantime, the search for additional biomarkers, particularly those that could be used to rule-out TB disease, should be prioritized.

Huynh et al provide an overview of TB treatment principles and advances in 'Tuberculosis treatment in children: the changing landscape' [14], and the series concludes with a specific focus on 'TB in adolescents, pregnant women and infants' by Snow et al. [15]. It is well recognised that adolescents require a tailored approach to encourage positive health care engagement with careful consideration of emerging autonomy, reduced perception of vulnerability, sensitivity to social stigma and peer pressure, impacts on participation in education, and mental health issues including harmful substance use [16]. A specific group that is poorly represented in programmatic and research data is pregnant women and major knowledge gaps remain regarding the effect of pregnancy on TB risk, the safety and pharmacokinetics of TB drugs in pregnancy, and the impact of TB disease and treatment on maternal and infant outcomes [17].

Given that children with symptoms and signs suspicious of TB present to maternal and child health (MCH) services, close interaction between the TB programme and MCH services, as well as private paediatric health care providers, is essential to reach affected children. To better serve children and adolescents affected by TB, we need to develop better integrated models of care in order to overcome the silos created by vertical programmes established in most TB endemic countries [18].

Conflict of interests to declare

None.

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