



March 24, 2017

World TB Day: Children with MDR-TB should not be left behind

Tuberculosis (TB) is a serious infectious disease that, although treatable, can be fatal. TB remains a common disease and an important cause of morbidity and mortality in Europe. It has the second highest burden of disease of all infectious diseases in Europe [1]. In 2014, the average annual reporting rate in EU/EAA countries (excluding Italy and Liechtenstein) was 12.8 per 100 000 population. In one out of six of these countries, rates were above 20 per 100 000 population (Bulgaria, Latvia, Lithuania, Romania and Portugal). Importantly, in Latvia, Lithuania and Estonia, multidrug-resistant tuberculosis (MDR-TB) was most prevalent.

In Europe, children younger than 18 years account for a substantial portion of patients with TB [2]. Children with TB have excellent outcomes if diagnosed and treated early [3,4]. Unfortunately, treatment of TB in children is hampered by limited data for safety, dosing and drug-drug interactions and scarcity of child-friendly drug formulations [5]. Especially for the management of children with MDR-TB, children younger than 5 years of age [7-9] and for preventive treatment [10], there is a prudent need for more effective and safe child-friendly drugs with simpler regimens.

Specifically, treatment options for MDR-TB in children are lacking behind those for adults. Children with MDR-TB have not benefited from therapeutic advances due to the use of new and repurposed drugs in adults with MDR-TB [11]. Clinical guidance is lacking on the use of these drugs and regimens in children and adolescents, in part because of exclusion of children from most drug trials for TB [12]. As a result, current recommendations are based on extrapolations from adult recommendations and expert opinion [13]. However, children can be included in studies at the early phases of drug development and should be an integral part of the clinical development plan, rather than studied after regulatory approval in adults is obtained [14].

The WHO *End TB Strategy* aims to reduce TB deaths by 90%, to cut new cases by 80% between 2015 and 2030, and to ensure that no TB-affected family faces catastrophic costs due to TB. Elimination of TB can only be achieved by means of strong collaboration within and across governments, and between partners from the communities, researchers, the private and the public sector.

All children, our world's future, have the right to live in a safe environment where they can grow up and achieve their potential [15]. The European Academy of Paediatrics (EAP) strongly advocates a structured and accountable paediatric training programme focusing on new and old infectious diseases for all doctors providing first-line care to children in the community and at the hospital. The EAP also urges EU politicians and national governments to support studies with

the aim to increase efficacy and safety of TB treatment in children.

TB is a preventable and treatable illness with excellent treatment outcomes, if diagnosed and treated early. Therefore, no child should die from TB.

On behalf of the European Academy of Paediatrics representing 32 countries,

Hans Jürgen Dornbusch (Austria)
Adamos Hadjipanayis (Cyprus)
Karoly Illy (Netherlands)
Jean-Christophe Mercier (France)
Robert Ross-Russel (United Kingdom)
Lenneke Schrier (Netherlands)
Tom Stiris (Norway)
Stefano del Torso (Italy)
Arunas Valiulis (Lithuania)
Jernej Završnik (Slovenia)

References:

1. European Centre for Disease Prevention and Control. Burden of Communicable Diseases in Europe 2015 (unpublished study).
2. European Centre for Disease Prevention and Control. Annual Epidemiological Report 2016 – Tuberculosis. [Internet]. Stockholm: ECDC; 2016. Available from: <http://ecdc.europa.eu/en/healthtopics/Tuberculosis/Pages/Annual-epidemiological-report-2016.aspx>
3. Perez-Velez CM, Marias BJ. Tuberculosis in children. *N Engl J Med* 2012;367(4):348-61.
4. Jenkins HE, Yuen CM, Rodriquez CA, Nathavitharana RR, McLaughlin MM, Donald P, Marais B, Becerra MC. Mortality in children with tuberculosis: a systematic review and meta-analysis. *Lancet Infect Dis* 2017;17:285-95.
5. Brigden G, Furin J, Van Gulik C, Marais B. Getting it right for children: improving tuberculosis treatment access and new treatment options. *Expert Rev. Anti Infect. Ther.* 2015;13(4):451-61.
6. Dooley KE, Mitnick CD, DeGroot AM, et al. Old drugs, new purpose: retooling existing drugs for optimised treatment of resistant tuberculosis. *Clin Infect Dis* 2012;55:572-81.
7. Russell GK, Merle CS, Cooke GS, et al. Towards the WHO target of zero childhood tuberculosis deaths: an analysis of mortality in 13 locations in Africa and Asia. *Int J Tuberc Lung Dis* 2013;17:1518-23.
8. Drobac PC, Shin SS, Huamani P, et al. Risk factors for in-hospital mortality among children with tuberculosis: the 25-year experience in Peru. *Pediatrics* 2012;130:e373-79.
9. Vanden Driessche K, Persson A, Marais BJ, Fink PJ, Urdahl KB. Immune vulnerability of infants to tuberculosis. *Clin Dev Immunol* 2013;2013:781320.
10. Seddon JA, Hesselting AC, Finlayson, et al. Preventive therapy for child contacts of multidrug-resistant tuberculosis: a prospective cohort study. *Clin Infect Dis* 2013;57:1676-84.
11. Harausz P, Garcia-Prats AJ, Seddon JA, et al. New/repurposed drugs for pediatric multidrug resistant tuberculosis: practice-based recommendations. *Am J Respir Crit Care Med.* 2016 Nov 17. [Epub ahead of print]
12. Becerra MC, Swaminathan S. Commentary: a targets framework: dismantling the invisibility trap for children with drug-resistant tuberculosis. *J Public Health Policy* 2014;35(4):425-54.
13. World Health Organisation. Guidelines for the programmatic management of drug-resistant TB, 2011. Update. WHO, Geneva; 2011.
14. Nachman S, Ahmed A, Amanullag A, et al. Towards early inclusion of children in tuberculosis drugs trials: a consensus statement. *Lancet Infect Dis* 2015;15:711-20.
15. Ferrara P, Amato M, Hadjipanayis A, del Torso S, Stiris T. The rights of children arriving in Europe. *Lancet* 2015;386(10007):1939-40.