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## Updated Pediatric Tuberculosis Guidelines

We read with interest the review article by Khurana, *et al.* [1], published recently in *Indian Pediatrics*. We would like to highlight the recent changes in the management of pediatric tuberculosis (TB) based on Revised National Tuberculosis Control Programme (RNTCP) Updated Pediatric TB Guidelines 2019 and WHO consolidated guidelines on drug resistant tuberculosis treatment 2019 [2].

*Changes in diagnostic algorithm:* As tuberculosis is a paucibacillary disease in children, performance of smear microscopy and culture is poor. Hence, Cartridge based nucleic acid assay (CBNAAT) is the preferred investigation of choice over smear examination (and best yield when ordered based on positive chest X-ray). If CBNAAT is not available, smear microscopy is to be performed.

*Newer classification of drugs:* The drugs for multidrug resistant tuberculosis (MDR-TB) have been recategorized into three groups. Thus, Box 2 of the review article needs revision.

*Changes in treatment approach for previously treated cases:* Previously treated TB includes (recurrence, treatment after loss to follow-up and treatment failure). All these children need to be evaluated for drug-resistant TB. In case they are found to be drug sensitive, they shall be started on the same regimen as for a newly diagnosed case. Category II has been now withdrawn from RNTCP. Streptomycin is now considered as second-line medicine, and should be used only as a substitute for Amikacin, when it is not available or confirmed resistance to it.

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## AUTHORS' REPLY

We agree with the readers about the issues that have been mentioned. As our manuscript was drafted and submitted for publication much before the new revised RNTCP-IAP guidelines were released, these changes could not be incorporated in the review article. Further, we would like to add a few more updates:

1. Presumptive drug-resistant tuberculosis (DRTB) is diagnosed in a patient who needs to be subjected to genotypic (CBNAAT, LPA) or phenotypic (LC-DST) drug sensitivity tests (DSTs) while probable MDR-TB is diagnosed in a patient, who after getting the results of the above tests, cannot be microbiologically confirmed and needs to be started on DRTB regimen based on their clinical and /or radiological deterioration (clinically diagnosed case of MDR TB).
2. Drugs used for second-line Anti-tubercular therapy (ATT) have been re-categorized as group A (Levofloxacin/Moxifloxacin, Bedaquiline and Linezolid), group B (Clofazimine and Cycloserine/Terazodone) and group C (Ethambutol, Delamanid, Pyrazinamide, Amikacin/Streptomycin, Para-amino salicylic acid, Imipenem Cilastin/Meropenem and Ethionamide/Prothionamide). This re-grouping is more relevant to design longer duration standard MDR-TB regimens. Group A drugs are most relevant to design longer duration MDR-TB regimens followed by group B; group C drugs are used only if other cannot be used for some reason [1]. The shorter MDR regimen of 9-12 months with seven second-line ATT drugs has gained acceptance by the WHO as well as RNTCP. The 4-6 months intensive phase consists of Moxifloxacin, Ethambutol, Clofazimine, Pyrazinamide, Kanamycin, high-dose Isoniazid, and Ethionamide. The continuation phase of 5 months consists of former four drugs only. This shorter regimen has been included for pulmonary pediatric MDR-TB patients or those with isolated lymph nodes or pleural effusion.
3. Delamanid may be included in the treatment of MDR/RR-TB patients aged 3 years or more on longer

regimens. ECG monitoring for QTc prolongation should be done at the baseline and then on a monthly basis for children receiving Delaminid [2].

4. Bedaquiline may also be included in longer MDR-TB regimens for patients aged 6–17 years. (need for more data before considering an upgrade of this recommendation to a strong one) [2].
5. Hearing loss can have a permanent impact on the acquisition of language and the ability to learn at school, and therefore should amikacin or streptomycin use be resorted to in children, regular audiometry is recommended [2].

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## Balancing the Covariates in Studies on Enteral Feeding in Preterm Neonates

We congratulate Modi, *et al.* [1] for their work on early aggressive enteral feeding in neonates, published recently in *Indian Pediatrics* [1].

Successful establishment of enteral feeding and prevention of the dreaded complication of necrotizing Enterocolitis (NEC) in very and extreme preterm neonates is dependant on a multitude of factors. Some of the factors that can modify the risk of NEC as well as mortality include the use of maternal antibiotics, extended use of empirical antibiotics in the neonatal period, delayed cord clamping and probiotic use [2,3]. However, the above mentioned parameters fail to find a mention in the baseline characteristics in the present article, thus making it unclear if the covariates were equally balanced amongst the two groups. Though this trial is a randomized controlled trial (RCT), even RCTs are not immune from imbalance in baseline characteristics between the two treatment groups [4]. This imbalance is known to occur more frequently in trials with small sample sizes [4].

In spite of enrolling sick preterm neonates by the investigators, the NEC incidence rate of the subjects in either of the two groups was very low (1.5-3%). The Vermont Oxford Network and the National Institute of Child Health (NICHD) had reported the incidence of NEC to be 7.4% and 7% respectively in their cohort of very low birth weight (VLBW) neonates [5]. The ADEPT (Analysis of prospectively collected data from a randomised feeding trial, the Abnormal Doppler Enteral Prescription) trial, which had enrolled growth restricted

preterm neonates <35 weeks gestation with antenatal doppler abnormalities had reported a NEC incidence rate of 18% in the early feeding group and 15% in the late feeding group [6]. Despite a higher percentage of growth retarded preterm neonates and the use of preterm formula milk as the second choice for enteral feeding in this study, the incidence rates of NEC are significantly lower than that reported from the Western literature. Could the authors dwell upon this unexpected finding of their study?

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