The ABCD of target height

Gianluca TORNESE *

Department of Pediatrics, IRCCS Burlo Garofolo Institute for Maternal and Child Health, Trieste, Italy

*Corresponding author: Gianluca Tornese, Department of Pediatrics, IRCCS Burlo Garofolo Institute for Maternal and Child Health, via dell'Istria 65/1, 34137 Trieste, Italy. E-mail: gianluca.tornese@burlo.trieste.it

Short stature is the most common referral in pediatric endocrinology.[1] Since approximately 80 percent of height is determined by genetic factors,[2] the potential size a child will reach as an adult height can be estimated by calculating the target height (TH), a standard procedure for every pediatrician over the last 50 years. The 90% of children's height is known to be within 1.5 SDS (approximately 2 centile lines) of mid-parental height (MPH),[3] and if the estimated final height is outside this range, a variant growth pattern or a pathologic cause should be considered. While Galton introduced the MPH in 1886, which was simply the average of parents' heights,[4] it was Tanner in 1970 who defined an adjustment concerning gender on the MPH in girls, the father's height minus 13 cm is averaged with the mother's height; in boys, the mother's height plus 13 cm is averaged with the father's height.[5] In recent years, several corrections to TH have been proposed: a correction that considers the secular trend (the increase in height over decades),[6] a calculation based directly on the average of the height SDS of parents,[7] a revision that considers assortative mating and the parent/offspring correlation.[8] However, when considering TH – especially during short stature evaluation – it is necessary to remember four key features, easily memorable with the ABCD's rule. "A" is for "amplitude:" TH is based on the assumption of an equal magnitude of polygenic factors derived from both parents. However, if one of the parents is unusually tall or short, the TH will be a poor predictor of attained height since genetics is not just a matter of average:[8] the child will inherit traits relating to stature more from one parent than the other. This matter is essential when examining familial short stature (FSS) as it should be considered when at least one parent has height of ≤-2 SDS, even if their TH was not ≤-2 SDS; otherwise, an inherited monogenic condition in an autosomal-dominant pattern cannot be classified as FSS.[9] On the other hand, in cases of autosomal-recessive genetic abnormalities, while heterozygous parents may have near-normal height, homozygous child may result in severe short stature[10]. "B" is for "betrayal:" a common Latin phrase said that "*mater semper certa est, pater numquam*" (*i.e.*, the mother is always certain, the father is never). It should always be kept in mind that the rate of "paternal discrepancy" (*i.e.*, when children are identified as being biologically different from the man whom they believed to be the father) is not negligible: according to various study, it is estimated from 0.8% in Switzerland to 30% in southern England, with a median of 3.7%.[11] These percentages indicate that, even if calculated correctly, the TH may not consider the father's real genetic contribution to the child's stature. However, If the father's height is unknown, a correction could be applied using only the maternal height.[12] In addition to this, the possibility of heterologous fertilization must be investigated when taking medical history. "C" is for "cheating:" generally, when parents report height, an incorrect measurement is communicated, even higher than 8 cm. In particular, adults with short stature or parents of a children referred for short stature tend to overestimate

their height, making the TH unreliable.[13, 14] This overestimation has its clinical effects as the use of reported rather than measured parental heights could lead to a high rate of inappropriate GH testing (*e.g.*, when considering a child's height <-1.5 SDS compared to TH)[14] and can also interfere in the evaluation or treatment of several other conditions (*e.g.*, FSS and children born SGA without catch-up growth). Therefore, parents should always be directly measured for usable data. "D" is for "descendant:" we must not forget that a child is part of a whole family, other than parents; therefore, information on heights (especially an unusually tall or short stature) of siblings, grandparents, uncles, and aunts should always be collected.[15] Sometimes an autosomal-dominant pattern can be evident over several generations; rarely, a *de-novo* mutation causing short stature can be identified in a parent and his/her child if the grandparents are of average/tall stature. This simple rule can help doctors to use TH properly in clinical practice. In conclusion, although we cannot easily identify "paternal discrepancy," all pediatricians should measure the parents' heights (when possible), ask about the other family members' stature, and remember not to consider TH tout court when one parent is unusually tall or short.

References

1. Bellotto E, Monasta L, Pellegrin MC, Bossini B, Tamaro G, Conte MS, *et al.* Pattern and Features of Pediatric Endocrinology Referrals: A Retrospective Study in a Single Tertiary Center in Italy. Front Pediatr 2020;8:580588.

2. Visscher PM, Medland SE, Ferreira MA, Morley KI, Zhu G, Cornes BK, *et al.* Assumption-free estimation of heritability from genome-wide identity-by-descent sharing between full siblings. PLoS Genet 2006;2:e41.

3. Wright CM, Cheetham TD. The strengths and limitations of parental heights as a predictor of attained height. Arch Dis Child 1999;81:257–60.

4. Galton F. Regression towards mediocrity in hereditary stature. J Anthropol Inst 1886;15:246–63.

5. Tanner JM, Goldstein H, Whitehouse RH. Standards for children's height at ages 2-9 years allowing for heights of parents. Arch Dis Child 1970;45:755–62.

6. Fredriks AM, van Buuren S, Burgmeijer RJ, Meulmeester JF, Beuker RJ, Brugman E, *et al.* Continuing positive secular growth change in The Netherlands 1955-1997. Pediatr Res 2000;47:316–23.

7. Cole TJ. Galton's midparent height revisited. Ann Hum Biol 2000;27:401–5.

8. Hermanussen M, Cole J. The calculation of target height reconsidered. Horm Res 2003;59:180–3.

9. Vasques GA, Jorge AA. Response to Letter to the Editor: "IHH Gene Mutations Causing Short Stature With Nonspecific Skeletal Abnormalities and Response to Growth Hormone Therapy". J Clin Endocrinol Metab 2019;104:5118–9.

10. Ranke MB. Towards a consensus on the definition of idiopathic short stature. Horm Res 1996;45:64–6.

11. Bellis MA, Hughes K, Hughes S, Ashton JR. Measuring paternal discrepancy and its public health consequences. J Epidemiol Community Health 2005;59:749–54.

12. van Dommelen P, Schönbeck Y, van Buuren S. A simple calculation of the target height. Arch Dis Child 2012;97:182.

13. Gunnell D, Berney L, Holland P, Maynard M, Blane D, Frankel S, *et al.* How accurately are height, weight and leg length reported by the elderly, and how closely are they related to measurements recorded in childhood? Int J Epidemiol 2000;29:456–64.

14. Ceconi V, Grigoletto V, Pellegrin MC, Faleschini E, Barbi E, Tornese G. Accuracy and consequences of reported target height. Acta Paediatr 2021;110:1513–5.

15. Nwosu BU, Lee MM. Evaluation of short and tall stature in children. Am Fam Physician 2008;78:597–604.

Conflicts of interest.—The author certifies that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

Authors' contributions.—The author wrote, read and approved the final version of the manuscript.

Acknowledgements.—The author acknowledges Martina Bradaschia for the English revision of the manuscript.