Harder than just hitting a bulls-eye: treatment for hypothyroidism in children might have more than just one target

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We read with interest the Cannavo et al. article, which evaluates levothyroxine requirements in children with acquired hypothyroidism [1]. While the reported results are interesting, we discuss two areas of the study that may detract from the clinical significance and applicability of their findings.

The authors find that children with central hypothyroidism secondary to pituitary tumor treatment require a higher dose of levothyroxine to achieve euthyroidism in comparison to children with hypothyroidism due to Hashimoto's thyroiditis. In this study, patients with Hashimoto's thyroiditis were diagnosed based on both thyroid ultrasonography characteristics and thyroid antibodies (TPOAbs/TGABs) while patients with central hypothyroidism were not diagnosed in the same manner. While we understand that abnormal findings are not expected in these cases, coexisting thyroid autoimmune disease in children with central nervous system tumors or post-radiotherapy central hypothyroidism (CeH) cannot be excluded and could skew the results of this study.

Furthermore, the use of FT4 values and TSH values to define treatment target dose in CeH and HT groups, respectively, inherently renders these values incomparable. Therefore, the use of differing parameters to form a ROC curve to establish a cutoff value of LT4 dosage is imprecise. In addition, part of the treatment goal was to achieve "clinical euthyroidism," which was not explicitly defined within the study. Clinical hypothyroidism, is known to include an assortment of signs and symptoms that do not have an established direct relationship with LT4 dose or TSH levels. Specifically, in the pediatric population, there are no concrete measures that can definitively attribute slowed growth and development to hypothyroidism rather than organic disorders [2]. Of note, hypothyroidism symptoms may also be

underreported by pediatric patients who lack the capacity to thoroughly communicate them.

Some thyroid hormone responses in central peripheral tissues may actually be a consequence of T3 levels, which the current study does not account for. Studies in adults have suggested that isolated low T3 values might be responsible for hypothyroidism symptoms or metabolic changes [3]. Lastly, it is well known that T3 hormone levels play an important role in the hypothalamic–pituitary–thyroid feedback loop, which should be accounted for when defining treatment goals in patients with hypothyroidism of different etiologies.

Though we understand the conclusions made by Cannavo et al. [1] to be unsubstantiated by the results presented in the article, we readily acknowledge the merit of this research as the framework for future research on this subject.

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Compliance with ethical standards

Conflict of interest M.L.U. is the Medical Advisor of the THANC Foundation.

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