

EDITORIAL

Overuse or Misuse of Thyroid Function Tests in Pediatrics

In a recent assessment of the laboratory work-up of patients referred for pediatric endocrine evaluation in my database, an assessment of thyroid function was performed in 89% of 35,500 patients. In most cases thyroid function tests were performed in order to exclude hypothyroidism. Referrals for growth retardation and obesity were the most frequent; less frequent reasons were slow psychomotor development and constipation. The most disturbing referrals were for 'abnormal thyroid tests' - blood tests were taken for non-obvious reasons. In some of the referrals the main reason was 'unexplained unusual T3'.

It is basic knowledge that decrease in thyroid hormone production decreases the feedback inhibition of TSH, which in turn induces an increase in blood TSH levels. At a later stage, T4 becomes subnormal, and T3 becomes subnormal sometimes much later. I have seen adolescents with Hashimoto goiter with TSH >80 mU/l, FT4 8 nmol/l and a perfectly normal TT3 of 2.3 nmol/l. Although this phenomenon has been known for many years, it is not mentioned in several books of pediatric endocrinology to which an inexperienced physician will go for understanding his patient's blood test results. Lum *et al.*¹ explained in 1984 that the residual functioning thyroid tissue, under super-normal TSH secretion, has a preferential production of T3 over T4. In addition, the efficiency of T4 conversion to T3 in thyroid and skeletal muscle increases with the decrease of T4 production and decrease in its blood levels¹. Consequently, a hypothyroid patient might have perfectly normal T3 in an overt hypothyroid state. The phenomenon of increased efficiency in end product production in a deficiency state is not unique to the thyroid. On the other hand, severe systemic disease and subnormal caloric intake may induce subnormal T3 production. Therefore, the use of TT3 and FT3 in a 'thyroid panel' for the diagnosis of primary hypothyroidism does not contribute information and might be confusing to inexperienced people, especially since this

information is lacking in some of the textbooks.

Thus, for the diagnosis of primary hypothyroidism in a patient without any other disease, TSH and FT4 are sufficient, provided an age-specific reference range of the specific assay procedure is used - a difference of up to 20% may be found between different assay methods.

As in any biological parameter there is a continuum of TSH and FT4 from very low to very high levels, and a gray zone in between. In many cases clinical signs are not helpful in decision making in this gray zone. Obesity complicates the normal range, since an increase in TSH may be found in 15% of obese patients and its interpretation is not yet clear^{2,3}. Patients with elevated TSH and normal FT4 are defined with 'subclinical hypothyroidism' or 'compensated hypothyroidism'. In adults, long-term follow up has demonstrated the development of overt hypothyroidism at a rate of 5-20% per year, especially in autoimmune thyroiditis⁴. In children during the first 2 years of life, there is a common agreement that when in doubt, we treat. Although there is a common agreement that a TRH test is not necessary for the diagnosis of hypothyroidism, in some cases, it may still be helpful in reaching a diagnosis.

Where is the border between pediatric hyperthyrotropinemia that needs thyroid replacement or observation? Is a controlled trial during the first two years of life unethical? The few controlled trials beyond that age are sparse, or on a relatively small number of children⁵⁻⁸. Wasniewska *et al.*⁸ demonstrated that 88% of patients with subclinical hypothyroidism turned out to be euthyroid in the long run. In addition, there are no clinical or laboratory guidelines to predict who will need replacement in the future. Genetic testing might help to reach a diagnosis in a part of this gray zone^{3,8}.

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