

# INCIDENTALLY ELEVATED THYROTROPIN IN OTHERWISE PROPERLY TREATED HYPOTHYROID PATIENTS DOES NOT REQUIRE HIGHER LEVOTHYROXINE DOSE

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**SUMMARY** – In 20 properly treated hypothyroid patients with normal thyrotropin (TSH) values during previous observation, TSH was incidentally mildly/moderately elevated (4.5–8.0 mIU/L; normal values 0.4–4.0) on the last follow up. However, they were continuously treated with the same levothyroxine (LT4) dose (mean: 95 µg) and six months later all TSH values normalized. The authors suggest that the physicians, in response to incidentally increased TSH value in otherwise properly treated hypothyroid patients, refrain from prompt increasing the LT4 dose unless TSH values are persistently elevated or/and progressing.

**Key words:** *Hypothyroidism – therapy; Thyrotropin*

## Introduction

Treatment of hypothyroidism, although apparently simple, poses challenges and complexities<sup>1,2</sup>, and the search for optimal replacement therapy is still going on. Serum thyrotropin (TSH) is considered to be the most reliable assay for proper treatment follow up, however, it has some limitations<sup>3,4</sup>. The normal values of TSH, especially in the upper range, are a matter of dispute<sup>5</sup>. It has been proposed that the upper limit of the normal range should be reduced to 2.5 mIU/L (usually 4–4.5 mIU/L)<sup>6</sup>, which is supported by some<sup>7,8</sup>, but opposed by others<sup>9,10</sup>. This proposal has also been challenged by the finding that mildly increased TSH in elderly people did not lead to impaired cognition<sup>11</sup>, and could be a proper adaptation phenomenon even associated with longevity<sup>12</sup>. Differences between nar-

rower intra-individual and wider inter-individual distributions of thyroxine (T4)<sup>13</sup> and TSH<sup>14</sup> could explain the origin of the earliest phase of thyroid failure and certainly confirm that the distinction between normal thyroid function and mild, subclinical hypothyroidism is merely arbitrary<sup>13</sup>.

In our large series of hypothyroid patients treated with levothyroxine (LT4) for several years, long enough to perform necessary modifications of therapy, 75% had normal TSH, while in others, mildly or moderately increased TSH was overwhelmingly dominant<sup>15</sup>.

In this study, we were especially focused on hypothyroid patients, otherwise properly treated for several years, with an incidentally increased TSH value.

## Subjects and Methods

The study included 20 middle-aged (average 52 years) hypothyroid patients treated with LT4 for several (mean 2.8) years and examined between July 2011 and June 2012. This group accounted for about 10% of

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the total number of hypothyroid patients treated by one of the authors (M.S.) in that period. They were properly treated with normal TSH value, except for a single mildly/moderately increased value on the last follow up. Serum values of T4 and triiodothyronine (T3) were normal.

## Results

Twenty hypothyroid patients, previously properly treated, showed increased serum TSH (4.5-8.0 mIU/L; normal values: 0.4-4.0- value 1) on the last follow up. They were continuously treated with the same LT4 dose (mean 95.0 µg) and six months later TSH values (value 2) unexceptionally normalized (Fig. 1).

## Discussion

We demonstrated that the incidentally elevated TSH in previously properly treated hypothyroid patients normalized without increasing the LT4 dose. Obviously, a *vice versa* situation is as possible. This supports our previous statement that in the majority

of hypothyroid patients with mildly or moderately elevated TSH, the LT4 dose could remain unchanged<sup>15</sup>.

Proper compliance in these patients was carefully tested by a short questionnaire and direct physician-patient communication. Furthermore, there was no reason to suspect suddenly occurring LT4 absorption problems. We believe that, rather than flaws in the adherence to LT4, or malabsorption, intra-individual variations in TSH suppressibility could be responsible. These variations are wider in hypothyroid patients, even if properly treated, than in healthy subjects, reflecting impairment in the TSH-thyroid hormone feedback control in hypothyroidism (unpublished data). The results point to the limitations of TSH alone being an adequate measure for thyroid hormone-controlled homeostasis in hypothyroid patients treated with LT4 and confirm the growing need of personalized replacement therapy<sup>14,16</sup>.

We advise that the physicians, facing an incidentally increased TSH value, refrain from promptly increasing LT4 dose, unless TSH values are persistently elevated or/and progressing. Such an aggressive increase in LT4 dose could result in over-suppressed, or, at least, low normal TSH, which have been both reported to be associated with atrial fibrillation in the elderly<sup>17,18</sup>.

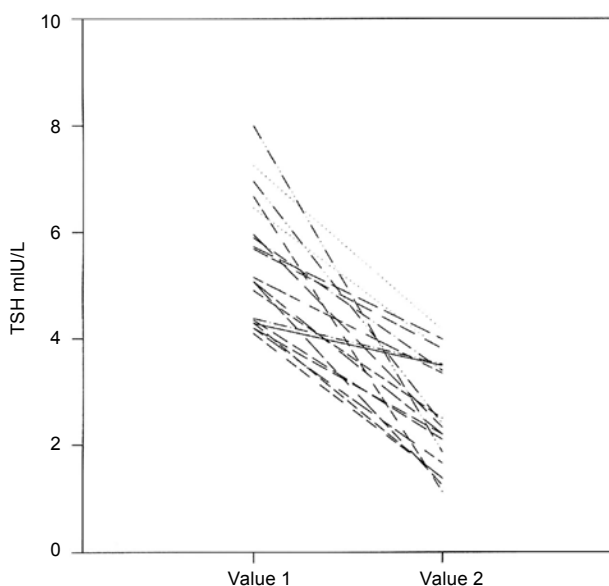


Fig. 1. Incidentally increased thyrotropin (TSH) values (value 1) in otherwise properly treated hypothyroid patients normalized 6 months later (value 2) with the same levothyroxine dose ( $p < 0.001$ ; paired *t*-test).

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#### Sažetak

### INCIDENTNO POVIŠENA VRIJEDNOST TIREOTROPINA U INAČE DOBRO LIJEČENIH HIPOTIREOIDNIH BOLESNIKA NE ZAHTIJEVA POVIŠENJE DOZE LEVOTIROKSINA

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Kod 20 hipotireoidnih bolesnika koji su prethodno dobro liječeni uz uredne vrijednosti tireotropina (TSH) na posljednjoj kontroli nađena je blago do umjereno povišena vrijednost TSH (4,5-8,0 mIU/L: n.v. 0,4-4,0). Ipak je nastavljeno liječenje istom dozom levotiroksina (LT4), u prosjeku 95 µg, a nakon 6 mjeseci vrijednosti TSH su se normalizirale. Autori preporučuju da se liječnik suočen s incidentno povišenom vrijednošću TSH u inače dobro liječenih hipotireoidnih bolesnika suzdrži od povišenja doze LT4 ako vrijednost TSH nije trajno povišena i/ili u progresiji.

Ključne riječi: *Hipotireoza – terapija; Tirotropin*