EDITORIAL

Hypothyroidism: detecting and treating early symptoms as the body's energy rheostat is slowly turned down

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Conditions with subtle early symptoms and slowly progressive morbidity present a greater challenge for early diagnosis and treatment in everyday medical practice than the more common, straightforward acute medical problems. Such is the case with early stage hypothyroidism, where non-specific symptoms (e.g. fatigability and constipation) gradually increase but often do not alert an affected individual to schedule a physician visit until the process is in its advanced stages. Even when a physician is consulted early, the complaints may not be sufficiently striking to trigger appropriate testing, and assurance of early diagnosis is far from certain.

In this issue of *J Med Screen*, Abu-Helalah *et al.* [1] provide valuable new information about the association between thyroid-stimulating hormone (TSH) levels and treatable symptomatology among adults with mildly elevated TSH values. The investigators utilized a randomized double-blind crossover design to overcome the obstacle posed by non-specific symptomatology, thereby allowing each study subject to act as her/his own control. Their results raise the possibility that TSH testing might become part of routine medical evaluation in the future and that the term 'subclinical hypothyroidism', commonly used to describe this level of thyroid deficiency, might be abandoned.

Study subjects were recruited from a subset of individuals attending the British United Provident Association (BUPA Wellness) for general health assessment and included women aged 50–79, men aged 65–79 and women with a family history of thyroid disease aged 35–49. TSH testing was performed on everyone in these categories; those with values above 4.0 mU/L were invited to take part in the trial. A second TSH measurement was obtained at the time of randomization, before medication was begun. This repeat testing documented TSH values above 4.5 mU/L in 15 of 56 subjects. Among these 15, 11 reported feeling better during the four months on thyroxine than during the four months on placebo; none felt worse – a highly significant finding. The remaining 41 subjects were treated similarly, but showed no benefit. It is worth noting that the study's crossover design is especially well suited to this type of situation and is considerably more efficient than the standard randomized controlled trial.

Circulating concentrations of TSH (from the pituitary gland) rise in response to reduced thyroxine production by the thyroid gland. The TSH signal is analogous in some respects to the 'canary in the mine' as an early warning system. Unlike the canary, which becomes silent and falls from its perch to signal danger (a categorical response), TSH sings with steadily increasing volume and intensity as thyroid function deteriorates (a continuous, graded response). Raised levels of TSH signal thyroid deficiency before circulating levels of thyroxine, the major hormone produced by the thyroid gland, become lower. It is of interest that the mildly elevated TSH levels in the present study were associated with symptomatology, suggesting that thyroid hormone function or availability at the tissue level was compromised, even while serum thyroxine levels remained within the reference range. As an integral component in the feedback system to maintain thyroid-related homeostasis, TSH is the most sensitive indicator of deficient thyroid function. When used as a primary screening test, as proposed by this study, TSH measurement also has diagnostic overtones. Follow-up measurement of thyroxine (or free thyroxine) is of no additional help in characterizing the level of thyroid function until the later stages of thyroid gland failure.

This study provides evidence that even mild thyroid deficiency is associated with symptomatology and that treatment leads to improved wellbeing. How severe should thyroid-related symptomatology be before help is offered? Some might argue that symptoms associated with mild TSH elevations do not interfere with one's ability to function and do not merit medical intervention. The degree of symptomatology identified in this study, however, is sufficient to interfere with one's daily life. Furthermore, the energy rheostat referred to in this editorial's title will often continue to be adjusted downward, as thyroid deficiency progresses in the absence of diagnosis and treatment. Abu-Helalah and his colleagues provide documentation that early detection offers medical benefit to about 1% of screened individuals and that TSH testing is a reliable strategy. As a next step, the investigators propose pilot programs to learn more about how TSH screening for mild hypothyroidism functions in everyday practice, including acceptability to patients. Given the health benefit, ease and low cost of treatment, and virtual absence of undesirable side-effects, this next step deserves serious consideration.

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REFERENCE

1 Abu-Helalah M, Law MR, Bestwick JP, Monson JP, Wald NJ. A randomized double-blind crossover trial to investigate the efficacy of screening for adult hypothyroidism. *J Med Screen* 2010;**17**:164–169