

# Alberta Doctors' Digest

## Seniors' health: Subclinical hypothyroidism

### Case

Your patient, Meredith, is 90 years' old and is experiencing mild fatigue, slight cold intolerance and reduced ability to lose weight. Her symptoms are non-specific. Meredith's laboratory results indicate slightly elevated thyroid stimulating hormone (TSH) levels with a normal free T4. You've diagnosed her with subclinical hypothyroidism. What would your approach be?

### Background

Subclinical hypothyroidism is a common clinical problem best defined as an increase in serum thyroid stimulating hormone (TSH) with normal concomitant circulating free thyroxine levels. The term subclinical hypothyroidism can be confusing as it is purely a laboratory diagnosis and does not take clinical features into account. Subclinical hypothyroidism is commonly encountered in clinical practice with estimates of prevalence ranging from 4-20% depending upon the age and population studied.<sup>1-3</sup> The vast majority of affected patients have mild subclinical hypothyroidism defined as a serum TSH falling between the upper end of the reference range and 10 mU/L. The symptoms of hypothyroidism are notoriously non-specific.<sup>4</sup> Patients with these common non-specific complaints, such as fatigue, cold intolerance or inability to lose weight, may be falsely diagnosed with thyroid disease. This may lead to dissatisfaction with a lack of a sustained response to levothyroxine therapy and a diversion from uncovering the underlying cause of the symptoms.



Subclinical hypothyroidism is a common clinical problem amongst seniors (Photo credit: Josep Curto Turro, Freepik.com)

Studies evaluating the effects of subclinical hypothyroidism may be flawed by using only a single TSH evaluation and including cohorts of older patients for whom higher age-adjusted reference ranges may be more appropriate. A “one size fits all” approach may therefore not be appropriate.<sup>5,6</sup>

Patients, particularly women, may be at an increased risk to develop iatrogenic hyperthyroidism with consequences that increase with age.<sup>7</sup> Furthermore, data from healthy octogenarians and nonagenarians in the United States and the Netherlands suggest that higher TSH levels may correlate with longevity and may instead be “normal for their age.”<sup>8,9</sup> An evaluation of the merits of an age-based TSH reference ranges may need to be considered.

There has been long standing controversy in the literature as to the potential merits and pitfalls of treating subclinical hypothyroidism.<sup>10-12</sup> Some cross-sectional and association studies have purported links to an increased risk of vascular events in subsets of patients with subclinical hypothyroidism.<sup>13-14</sup> However, the best prospective cohort studies and pooled data do not support an association with coronary heart disease events, cardiac mortality or, indeed, total mortality.<sup>15-16</sup> Heterogeneous patient populations in these reports suggest a need to temper definitive conclusions about harm or lack thereof.

Until recently, there has been a paucity of large randomized controlled trials. However in 2017, Stott et al. published a prospective, randomized controlled trial of levothyroxine in older adults in the New England Journal of Medicine.<sup>17</sup> This study randomized 737 patients, mean age 74 (54% female) to either levothyroxine to target a normal TSH or placebo for one year in patients with persistent subclinical hypothyroidism: TSH 4.6-20 mU/L and a normal free T4. The primary endpoints were: hypothyroid symptoms score changes and tiredness quality-of-life score. The results showed no consistent benefit of levothyroxine on any thyroid related symptoms. Furthermore, >60% of patients screened spontaneously normalized their TSH without any treatment at all.

Finally, in October 2018, a systematic review and meta-analysis of studies looking at the association of thyroid hormone therapy with quality of life and thyroid-related symptoms in patients with subclinical hypothyroidism was published.<sup>18</sup> The authors reviewed 3,088 possible publications before identifying 21 appropriate papers for analysis. They concluded that there is no association of levothyroxine treatment with improvements in the quality of life or thyroid-related symptoms and thus cannot support the routine use of thyroid hormone in patients with subclinical hypothyroidism.

#### **Back to the case – my suggested approach**

1. If lab results reveal elevated TSH, ensure free T4 level is normal to confirm subclinical hypothyroidism.
2. Repeat lab testing in two-to-three months to show the patient has *persistent* subclinical hypothyroidism.
3. If TSH levels are between 4 and 10, most patients will not benefit from prescription thyroid medication. Observation is the best strategy.
4. If TSH levels are greater than 10, consider a low dose trial of levothyroxine.

5. If your patient with subclinical hypothyroidism has definite hypothyroid symptoms, their thyroid gland is firm or enlarged or repeated labs indicated TSH levels are rising, consider a six-month trial period of levothyroxine.
6. Monitor closely older patients on levothyroxine to avoid subclinical hyperthyroidism (TSH below the reference range).
7. Do not be afraid to stop levothyroxine if you are not seeing any clinical benefit.

#### Bottom line

1. Subclinical hypothyroidism is common and may spontaneously normalize in ~ 50% of patients.
  2. Healthy, older patients may have a TSH up to 7-8 mU/L.
  3. Subclinical hypothyroidism TSH < 10 mU/L: Uncommonly will progress to overt hypothyroidism; is not associated with adverse cardiovascular effects.
  4. A randomized trial of levothyroxine and a meta-analysis showed *no difference* in symptoms.
  5. Iatrogenic subclinical *hyper*thyroidism is: Easy to achieve, especially in seniors on levothyroxine; associated with a higher risk for atrial fibrillation and cardiovascular endpoints; associated with a higher risk for bone loss and probably fractures.
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#### About Optimized Prescribing with Seniors

A joint communication of the Alberta Medical Association and the College of Physicians & Surgeons of Alberta, these articles are written by physicians for physicians prescribing in the care of older patients.

Is there a specific issue you'd like to see addressed? Do you see a scenario frequently and want to know an ideal, yet practical, approach to management? Uncertain about the "latest and greatest" new drug?

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References available upon request

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