Subclinical hypothyroidism in the elderly: a common dilemma

By Professor Gregory Peterson

Subclinical hypothyroidism is relatively prevalent in the general population, especially among women and the elderly; it occurs in more than 15% of elderly women and 10% of elderly men.1,2

Mrs BN, a 71-year-old woman, tells her GP that she lacks energy and ‘just does not feel like herself’. She has no known medical problems. Physical examination is unremarkable. There is no palpable thyroid tissue; reflexes are normal on testing; and her skin, nails, and hair are normal. Laboratory values are unremarkable, except for the following: total thyroxine (T4) 75 nmol/L (normal: 64–160 nmol/L); free thyroxine 15 pmol/L (normal: 10–25 pmol/L) and thyroid-stimulating hormone (TSH) 7.6 mU/L (normal: 0.2–4.0 mU/L).

Mrs BN has subclinical hypothyroidism (also called mild thyroid failure2), diagnosed when peripheral thyroid hormone levels are within the normal reference laboratory range but serum thyroid-stimulating hormone (TSH) levels are mildly elevated. As serum TSH varies over time in healthy subjects, leading to occasional abnormal values, repeat serum TSH along with free thyroxine measurements within 3–4 months is required.1 If elevated serum TSH concentrations are consistent, and free thyroxine values are within the normal range, the diagnosis of subclinical hypothyroidism is confirmed. Of all patients with subclinical hypothyroidism, 80% have a serum TSH of less than 10 mU/L.3

The prevalence of subclinical hypothyroidism is 4% to 10% in the general population, increases with age and is higher in women.1–6 The most common cause of elevated TSH and subclinical hypothyroidism is autoimmune thyroid disease,1–4 and antithyroid antibodies can be detected in 80% of patients with subclinical hypothyroidism. Less common causes include previous thyroid surgery or external radiation therapy, iodine-induced hypothyroidism (from radiocontrast agents, amiodarone, or supplemental potassium iodide), and the use of lithium or antithyroid drugs.5

An underestimated, yet obvious, cause of subclinical hypothyroidism is insufficient thyroxine doses to maintain euthyroidism in patients with clinical hypothyroidism.1 Also, the problem of endemic iodine deficiency, which may cause subclinical hypothyroidism, is still present in some countries and regions with mountainous topographies and significant leaching of iodine from the soils (e.g. Tasmania).

The term ‘subclinical hypothyroidism’ implies that the patient has no symptoms. The term may not be strictly correct, however, since some of these patients have mild clinical symptoms.4 Table 1 lists the main symptoms and signs of hypothyroidism reported in approximately 30% of patients with subclinical hypothyroidism.1 Elderly patients have significantly fewer symptoms of overt hypothyroidism than do younger adults and their complaints are often subtle and vague.1 Many elderly patients with hypothyroidism present with nonspecific symptoms, such as confusion, anorexia, weight loss, falling, incontinence, and decreased mobility.5

There is considerable ongoing controversy regarding the morbidity and clinical significance of subclinical hypothyroidism, and whether these patients should be treated.4,7 It has been suggested that older adults may be more vulnerable to the effects of subclinical hypothyroidism, given age-related changes to the hypothalamic-pituitary-thyroid axis, and there may be an association between thyroid status and cognitive decline and dementia in the elderly.8 Subclinical hypothyroidism has also been linked with depression.1,9,10 In one study, the presence of subclinical hypothyroidism in a patient over the age of 60 increased the risk of developing depression by more than four times.10 In contrast, other studies have found no relationship between subclinical hypothyroidism and cognitive function or depression in the elderly.11–14

The most important implication of subclinical hypothyroidism is the relatively high likelihood of progression to clinical hypothyroidism.2 Approximately 2–5% of patients with subclinical hypothyroidism will progress to overt hypothyroidism annually.1,2,5 The rate of progression is proportional to the baseline serum TSH concentration (a level greater than 10 mU/L predicts a higher rate of progression) and is increased in patients with elevated thyroid autoantibodies.

The possibility that subclinical hypothyroidism is a cardiovascular risk factor has also been a subject of much debate.1,4,15–17 It has been suggested that women over 50 years of age with TSH levels greater than 10 mU/L and who smoke have the highest risk for cardiovascular complications.18 Intuitively, subclinical hypothyroidism may worsen many

Table 1. Symptoms/signs reported in patients with elevated serum TSH only (subclinical hypothyroidism)

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<thead>
<tr>
<th>Symptom</th>
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<td>Depression</td>
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<td>Anxiety</td>
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<td>Lack of energy</td>
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<td>Poor memory</td>
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<td>Constipation</td>
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<td>Hoarse voice</td>
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<td>Weight gain</td>
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<td>Cold intolerance</td>
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<td>Dry skin</td>
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risk factors for cardiovascular disease, including hypertension, abnormal endothelial function, and elevated low-density lipoprotein cholesterol concentrations. However, a 12-year study of 3,233 community-dwelling participants aged 65 years and older found no significant difference in the risk of coronary heart disease, cerebrovascular disease, cardiovascular death, or all-cause death between euthyroid patients and those with subclinical or overt hypothyroidism. The management of subclinical hypothyroidism remains controversial. Although there is evidence that thyroxine may improve lipid profiles, cognitive function, and left ventricular function, there is no evidence that this will decrease morbidity or mortality in patients with subclinical hypothyroidism. Large-scale randomised studies are clearly needed for evidence-based recommendations regarding the management of subclinical hypothyroidism. A Cochrane review of 14 randomised clinical trials, which were only of six to 14 months duration and enrolled a total of only 350 patients with subclinical hypothyroidism, concluded that thyroxine therapy for subclinical hypothyroidism does not result in improved survival or decreased cardiovascular morbidity. Only four studies reported adverse events of therapy, with no statistically significant differences between groups. Currently, the consensus view appears to be that thyroxine therapy be routinely used in patients with a persistent serum TSH of more than 10 mU/L, with individualised therapy for those with a TSH of less than 10 mU/L. Hypercholesterolaemia may also be a factor that favours early treatment of subclinical hypothyroidism, because meta-analysis suggests that treatment produces a small but statistically significant decrease in serum cholesterol. A decision to begin treatment should be individualised. In asymptomatic older people, with slightly elevated TSH (<10 mU/L) and without antithyroid antibodies, there is probably no need to treat, but continued monitoring of the TSH is advised.

Mild TSH elevation (in the range 4 to 10 mU/L) in the absence of symptoms does not require immediate treatment, but follow-up every six to 12 months is appropriate. A clear trend towards hypothyroidism (i.e. a progressive rise in TSH) or symptoms that could be attributed to hypothyroidism are indications for treatment. Persistent clear TSH excess (more than 10 mU/L) is generally accepted as an indication to commence treatment, because of a high risk of progression to frank hypothyroidism. In patients with serum TSH >10 mU/L, there is a high likelihood of progression to overt hypothyroidism. These patients are also more likely to have hypercholesterolaemia and atherosclerosis. They should be treated with thyroxine, even if they are asymptomatic. For patients with TSH levels between 4.5 and 10 mU/L, a trial of thyroxine is reasonable if symptoms of early hypothyroidism (e.g. fatigue, depression) are present. The decision to commence therapy for subclinical hypothyroidism cannot be taken lightly. It needs to be acknowledged that therapy with thyroxine is not without risks, especially in older individuals. The elderly are at increased risk of cardiovascular effects; thyroxine may aggravate angina or precipitate myocardial infarction. If the patient has coronary artery disease, it would be reasonable to delay treatment, at least until there is evidence that the hypothyroidism is getting worse. If a decision to commence thyroxine is made, the starting dose in the elderly should be low (25 to 50 micrograms/day) and increased gradually with the objective of returning the TSH level to normal without inappropriately elevating the serum thyroxine concentration. Further reinforcement of the importance of keeping the dosage of thyroxine as low as possible in older patients came in a very recent Canadian study of 213,000 patients aged 70 years or older prescribed thyroxine and followed for up to 6 years. More than 10% experienced a fracture over the mean 3.8 years of follow-up, 88% of whom were women. Use of thyroxine was associated with a significantly higher risk of fracture (adjusted odds ratio 1.88, 95% confidence interval 1.71 to 2.05), despite adjustment for numerous risk factors. Among current users, high and medium doses (>93 micrograms/day and 44–93 micrograms/day) were associated with a significantly increased risk of fracture compared with low doses (<44 micrograms/day): 3.45 (3.27 to 3.65) and 2.62 (2.50 to 2.76), respectively. It was concluded that ongoing monitoring of thyroxine dose is important to avoid overtreatment in older patients. Patients with subclinical hypothyroidism should have annual measurement of serum TSH and free thyroxine to assess progress of the condition if untreated or to adjust the thyroxine dosage if treated. To return to our case, a trial of thyroxine in Mrs BN is reasonable, given her TSH level and the presence of symptoms of early hypothyroidism.

References