

# Thyroid dysfunction in the elderly

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**Objectives.** To determine the prevalence of thyroid dysfunction in institutionalised elderly people in Cape Town and to assess the usefulness of an abnormal thyroid-stimulating hormone (TSH) concentration as a screening test in this group.

**Design.** Cross-sectional survey.

**Setting.** Four old-age homes in Cape Town.

**Subjects.** Old-age home residents aged 60 years and over.

**Outcome measures.** Serum concentrations of TSH, free thyroxine and free tri-iodothyronine.

**Results.** Serum TSH estimations were performed on 658 participants, and were abnormal in 103 (15.6%) — 41 (6.2%) being elevated ( $> 5.0 \mu\text{U/ml}$ ) and 62 (9.4%) being low ( $< 0.4 \mu\text{U/ml}$ ). There were 3 newly diagnosed cases of hyperthyroidism and 7 of hypothyroidism. Subclinical disease was diagnosed in 40 subjects. The overall prevalence of thyroid dysfunction in this population was 11.2%. In 22 (3.4%) this had previously been recognised, while in 50 (7.8%) the dysfunction was newly diagnosed by the current survey. The positive predictive value of a TSH concentration  $> 20 \mu\text{U/ml}$  in predicting hypothyroidism is 67%, while it will predict 100% of cases of subclinical hypothyroidism. A TSH concentration  $< 0.1 \mu\text{U/ml}$  will predict 23% of cases of hyperthyroidism, but 81% of cases of subclinical disease.

**Conclusions.** The prevalence of thyroid dysfunction in institutionalised elderly people in Cape Town is similar to that reported for elderly people in other centres. Thyroid dysfunction had not previously been recognised in approximately two-thirds of the subjects in this study. The serum TSH concentration is a reliable screening test for thyroid dysfunction in the elderly, but is less useful if used to identify biochemical thyroid disease. An elevated TSH concentration is a better predictor of thyroid dysfunction in the elderly than a depressed TSH concentration.

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Thyroid disease may manifest atypically in the elderly, leading to difficulties with clinical diagnosis.<sup>1,2</sup> There are well

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recognised alterations in thyroid physiology which occur during normal ageing.<sup>3,5</sup> Both iodine uptake by the gland and thyroxine ( $T_4$ ) production decrease. As a result of decreased peripheral metabolism, however, serum levels of  $T_4$  remain normal. Diminished 5'-deiodinase activity results in decreased conversion of  $T_4$  to tri-iodothyronine ( $T_3$ ) and slightly lower serum  $T_3$  levels.

Several reports have suggested that thyroid dysfunction is more common in older subjects,<sup>1,4,6</sup> but the exact prevalence has been difficult to determine. The clinical diagnosis of both hypo- and hyperthyroidism may be obscured by the fact that their clinical features are often incorrectly attributed to ageing *per se*. In addition, the lack of uniformity in laboratory techniques has resulted in reported prevalence rates that are not strictly comparable.

The general availability of sensitive thyroid-stimulating hormone (TSH) assays able to measure very low levels has resulted in the use of TSH as a screening test for hyperthyroidism as well as hypothyroidism. Its utility seems to be well established in young subjects, but its value as a marker of thyroid dysfunction in the elderly is unproven.

The present study was undertaken with the following aims: (i) to determine the prevalence of thyroid dysfunction in institutionalised elderly in Cape Town; and (ii) to assess the usefulness of an abnormal TSH concentration as a screening test in this group.

## Subjects and methods

The residents of four old-age homes who were aged 60 years and older were invited to participate in the study. The only exclusions were those residents who refused to take part and those from whom venous blood could not readily be obtained. After written consent had been obtained, questionnaires were completed by trained nursing and medical staff. These contained baseline demographic data as well as health status data, including previous or current medical or thyroid problems and current therapy. Blood was taken for serum TSH estimation. After separation of the serum, it was stored at  $-20^{\circ}\text{C}$ . TSH concentrations were measured with the Gamma-BCT TSH method (Immunodiagnostic Systems, Boldon, Tyne & Wear, UK). The normal range for this laboratory is 0.4 - 4  $\mu\text{U/ml}$ . However, we used 5  $\mu\text{U/ml}$  as the upper limit of normal in this study, in line with a recent published series using the same technique. In patients whose initial TSH concentration fell outside the range 0.4 - 5  $\mu\text{U/ml}$ , a second sample was drawn and the TSH measurement repeated together with estimations of the serum free  $T_4$  ( $FT_4$ ) and free  $T_3$  ( $FT_3$ ) concentrations (Amerlex-M RIA method, Kodak Clinical Diagnostics Ltd, Amersham, UK). The normal range for  $FT_4$  was 6.3 - 22.8  $\text{pmol/l}$ , while that for  $FT_3$  was 3.3 - 8.1  $\text{pmol/l}$ . Subjects with clear biochemical evidence of thyrotoxicosis or hypothyroidism were referred for appropriate treatment. After a further 6 months, TSH,  $FT_4$  and  $FT_3$  estimations were repeated in all who had had an abnormal baseline TSH level.

Approval for the study was obtained from the UCT Ethics and Research Committee, as well as from the Chairman of the Cape Peninsula Organisation for the Aged and from the

doctors involved in providing medical care for these residents. Confidentiality was ensured, and abnormal findings were passed on to each patient's doctor.

## Definitions

'Thyroid dysfunction' encompassed previously diagnosed hyperfunction or hypofunction, previous thyroidectomy (for whatever reason), newly diagnosed thyrotoxicosis or hypothyroidism and subclinical thyroid disease. Those with the sick euthyroid syndrome and the single participant with a transient elevation of  $FT_3$  were not considered to have thyroid dysfunction.

'Hypothyroidism (overt)' was present in patients with previously diagnosed thyroid hypofunction, as well as those in the present study whose initial and subsequent TSH levels were elevated, and who had depression of  $FT_4$ .

'Subclinical hypothyroidism' was present in patients with no overt clinical features of hypothyroidism, but elevated TSH levels and normal  $FT_4$  and  $FT_3$  levels. In this study this included those whose initial and subsequent TSH levels were elevated but who had normal  $FT_4$  levels.

'Thyrotoxicosis (overt)' was characterised by elevated thyroxine levels with depression of the TSH. This includes those in whom both the initial and subsequent TSH levels were depressed, and who had elevation of  $FT_4$ .

'Subclinical hyperthyroidism' was characterised by an absence of clinical features of hyperthyroidism, but low TSH levels with normal  $FT_4$  and  $FT_3$  levels. It included those patients whose initial and repeat TSH levels were depressed but who had normal  $FT_4$  and  $FT_3$  levels. The TSH depression was frequently transient, later returning to normal.

'Sick euthyroid syndrome' entailed depression of the TSH level in individuals who were euthyroid as evidenced by normal  $FT_4$  levels, but who had non-thyroidal illness, stress or physical trauma. For the purposes of this study, the sick euthyroid syndrome was diagnosed in those whose initial TSH was low and who had a depressed  $T_3$  with a normal or low TSH level on repeat estimation.

## Results

There were 658 participants, aged between 60 and 98 years (mean age 77.9 years). Of these, 169 were male (25.7%) and 489 were female (74.3%). The participation rate was high, with 86% of the 776 residents in the 4 old-age homes taking part. The reasons for non-participation were that the resident was too young (< 60 years) or refused consent, or that a blood specimen could not be obtained.

One hundred and three (15.6%) of the initial 658 serum TSH estimations were abnormal (Fig. 1). These included 41 (6.2%) subjects with elevated TSH levels (> 5.0  $\mu\text{U/ml}$ ) and 62 (9.4%) with low TSH levels (< 0.4  $\mu\text{U/ml}$ ). The serum TSH concentration was normal in the remaining 555 (84.3%). TSH estimations were repeated together with measurement of  $FT_4$  and  $FT_3$  concentrations in 85 of the original 103 subjects with abnormal TSH levels, the remaining 18 having died in the interim. The denominator for further calculations was therefore 640.

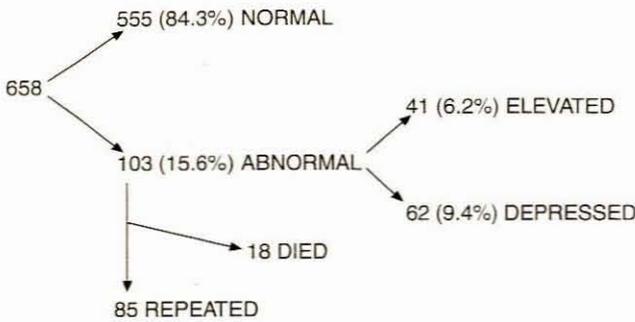


Fig. 1. Initial TSH estimations.

On repeat testing, the TSH level was found to have reverted to normal in 13 participants. In 9 of these it had previously been elevated, while in 4 it had been depressed. The overall prevalence of thyroid dysfunction was 11.2% (72/640) (Table I). In 22 (3.4%) this had been previously recognised, while in 50 (7.8%) the dysfunction was newly identified by the current survey. (It should be noted that some subjects with previously diagnosed thyroid dysfunction had normal TSH levels during this study, while some whose initial TSH was abnormal when surveyed were subsequently shown to be euthyroid.) All but 2 of the 10 subjects with newly recognised overt thyroid disease were women, both men having newly diagnosed hypothyroidism. There were 6 men with subclinical hyperthyroidism.

Table I. Thyroid dysfunction — previously recognised and newly diagnosed

	Previously recognised	Newly diagnosed	Total
Hyperthyroidism	2	3	5
Subclinical hyperthyroidism		25	25
Hypothyroidism	11	7	18
Subclinical hypothyroidism		15	15
Surgery	9		9
Total (%)	22 (3.4)	50 (7.8)	72 (11.2)

The serum TSH concentration was found to be > 5 µU/ml in 41 subjects (Table II). Seven subjects had newly diagnosed hypothyroidism with depressed FT<sub>4</sub> levels and

commenced therapy with thyroxine. A further 2 subjects were previously known to be hypothyroid. One was receiving inadequate replacement and was biochemically hypothyroid, while the other had a normal FT<sub>4</sub> level. Of the 15 patients with subclinical hypothyroidism, 13 survived 1 year and, on retesting, none had progressed to biochemical hypothyroidism.

There were 62 participants with depressed TSH concentrations (< 0.4 µU/ml) of whom 5 were thyrotoxic. This was newly diagnosed in 3, while in the other 2 subjects excess thyroxine replacement was the cause (Table II). Subclinical hyperthyroidism (low TSH but normal FT<sub>4</sub> and FT<sub>3</sub> levels) was noted in 25 subjects. This was transient in 10 as thyroid function normalised on repeat testing.

Table II. Outcome in subjects whose initial TSH level was abnormal

	Initial TSH		Total
	> 5.0	< 0.4	
Died	7	11	18
Normal repeat	9	4	13
Hyperthyroidism: old		1	1
Hyperthyroidism: new		3	3
Subclinical hyperthyroidism		25	25
Hypothyroidism: old	2	2*	4
Hypothyroidism: new	7		7
Subclinical hypothyroidism	15		15
Surgery		3*	3
Sick euthyroid syndrome	1	12	13
Transient T <sub>3</sub> toxicity		1	1
Total	41	62	103

\* These groups each contain 1 subject who was thyrotoxic as a result of excess administered thyroxine, and are added to the 3 with newly diagnosed thyrotoxicosis to give a total of 5 patients found to be hyperthyroid.

The sick euthyroid syndrome was present in 13 subjects. The initial TSH level was depressed in all but 1, in whom it was elevated. This subject later developed depressed TSH and T<sub>3</sub> levels, dying soon thereafter of carcinoma of the lung. Elevation of T<sub>3</sub> was noted in 1 subject, but this was transient. These latter 2 groups were not considered to have thyroid dysfunction.

Many participants were on medications which are known potentially to influence TSH levels (Table III). However, most

Table III. Subjects on medications with the potential to influence TSH levels

	TSH								Total
	Elevated				Depressed				
	Normal	Normal repeat	Hypothyroid	Subclinical hypothyroid	Hyperthyroid	Subclinical hyperthyroid	Sick euthyroid syndrome	Transient T <sub>3</sub> toxicity	
Thyroxine	11		1	1	2	2	1		18
Corticosteroids	8		1		1	1			11
Dopamine	19								19
Dopamine-blocking agents	127	2	4	1		3	3		140
Dopamine competitors	41				1	1	1	1	45
Lithium						1			1
Amiodarone	1								1
									235

of the subjects on these agents had normal TSH concentrations. There were 18 subjects on thyroxine replacement therapy for hypothyroidism (spontaneous or post-thyroidectomy). Corticosteroids (usually prednisone for chronic chest disease) were being taken by 11 subjects. Dopamine preparations were being used for treatment of parkinsonism in 19 subjects, while 140 subjects were receiving dopamine receptor-blocking agents, mostly neuroleptics used for behaviour modification in patients with dementia or chronic schizophrenia. The antihypertensive agents, methyl dopa and reserpine, which are known to compete with or block the action of dopamine, were being used by 45 subjects. Lithium and amiodarone were each being taken by a single participant.

The positive predictive values of TSH in detecting thyroid dysfunction or overt thyroid disease are shown in Tables IV and V. The TSH appears to be a fairly reliable predictor of thyroid dysfunction, but it is considerably less useful in predicting overt thyroid disease. An elevated TSH level is a far more useful indicator of thyroid dysfunction (including overt thyroid disease) than a depressed one.

**Table IV. Positive predictive value of elevated TSH levels**

Positive predictive value (%) for:	TSH ( $\mu$ U/ml)		
	> 5	> 10	> 20
Predicting hypothyroidism	23.5	41.2	66.7
Predicting thyroid dysfunction	70.6	88.2	100

Positive predictive value =  $\frac{\text{true positive}}{\text{true positive} + \text{false positive}}$ .

**Table V. Positive predictive value of depressed TSH levels**

Positive predictive value (%) for:	TSH ( $\mu$ U/ml)			
	< 0.4	< 0.15	< 0.1	0
Predicting hypothyroidism	9.8	21.7	22.7	26.7
Predicting thyroid dysfunction	62.7	78.3	81.3	80.0

Positive predictive value =  $\frac{\text{true positive}}{\text{true positive} + \text{false positive}}$ .

It was not possible to determine the sensitivity or specificity of TSH as a screening test for thyroid dysfunction since participants with normal TSH values were not assessed further.

## Discussion

This is the first published study of its kind to have been conducted in South Africa. It was undertaken in 4 old-age homes, 2 of which at the time of the study were exclusively for whites while the other 2 were for people of mixed descent. At that time there were no similar facilities for elderly blacks. (Recent changes in the country have meant that admission criteria of old-age homes have changed to include people of all races, although full integration will take some time to achieve.)

The study population comprised residents of old-age homes and not community-dwelling elderly. As a consequence, they were probably more infirm on average

than elderly people living in the community, and therefore more likely to have non-thyroidal illness or to be on medications which could influence their TSH levels.

As a normal serum TSH level excludes hyperthyroidism or hypothyroidism for practical purposes,<sup>5</sup> in this study only those participants with abnormal TSH results were subjected to additional investigations; the remainder were considered to have normal thyroid function.

Our finding that 15.6% of the initial TSH estimations were outside the normal range is similar to the result of 13.8% obtained by Parle *et al.* in their recent study.<sup>6</sup> However, in the latter study all patients on thyroxine therapy were excluded. If those in our study who were on thyroxine are excluded, the overall prevalence of abnormal TSH concentrations is 14.9%.

The 6.2% prevalence of elevated TSH levels in this study is slightly lower than the 7.9% reported by Parle *et al.* and the 10.3% of Sawin *et al.*, both of whom used a TSH level > 5  $\mu$ U/ml as their cut-off value.<sup>6,7</sup>

In this study 7 of the 41 (17.1%) subjects with an increased TSH level were found to be hypothyroid, giving a prevalence of newly diagnosed hypothyroidism of 1.1% (7/640). Parle *et al.* report that 18 of 94 (19.1%) with an elevated TSH level were hypothyroid (1.5% overall), as compared with 2.5% in the Sawin study.<sup>6,7</sup>

Subclinical hypothyroidism was diagnosed in 15 patients, giving a prevalence of 2.4% in subjects not on thyroxine. The prevalence rates in other reported studies have been somewhat higher. Parle *et al.* had a prevalence of 6.1%, while in the study by Sawin *et al.* the figure was 7.1%.<sup>6,7</sup> In the report by the latter group it was not clear how many of the subjects in their study population were on thyroid replacement.

In contrast to the report by Parle *et al.*, in which 17.8% of their patients with subclinical hypothyroidism progressed to hypothyroidism within a year, none of the 13 subjects in this study developed biochemical evidence of overt hypothyroidism when followed up for a similar period.<sup>6</sup> Parle *et al.* noted that progression was more likely in those where the initial TSH level was greater than 10  $\mu$ U/ml and in those with positive antithyroid antibodies. Antithyroid antibodies were not evaluated in the present study.

The significance of subclinical hypothyroidism is uncertain, other than the possibility of progression to frank hypothyroidism.<sup>4</sup> Although by definition there should be no clinical features of hypothyroidism, symptoms such as fatigue, dry skin, cold intolerance, constipation and muscle cramps have been shown to occur twice as often in patients with subclinical hypothyroidism.<sup>8</sup> Of patients given thyroxine replacement, 50% showed a symptomatic improvement compared with 12% of those on placebo. Improvements in left ventricular function, lipoprotein abnormalities, short-term memory, calculation speed and reaction time have been reported in patients given thyroid hormone.<sup>9-11</sup>

There are concerns that thyroxine therapy in subclinical hypothyroidism may aggravate coexisting coronary artery disease, with worsening of angina, or that it may precipitate cardiac arrhythmias especially atrial fibrillation.<sup>12</sup> It has also been suggested that bone loss may be accelerated, perhaps hastening the development of osteoporosis.<sup>13,14</sup> At present the major benefit of detecting subclinical hypothyroidism is

that it alerts one to the possibility of the later development of overt hypothyroidism.

Depressed serum TSH concentrations were indicative of thyrotoxicosis in only 5 of 62 patients. In 3 this was due to newly diagnosed hyperthyroidism (0.5% of the total study population as opposed to 0.1% in Parle *et al.*'s study<sup>6</sup>). A further 2 were on excess thyroxine replacement, 1 for spontaneous hypothyroidism and 1 following thyroidectomy.

Assays sensitive enough to distinguish between normal and low concentrations of TSH allow the identification of a group of patients with low TSH levels but no clinical manifestations of hyperthyroidism and normal concentrations of FT<sub>4</sub> and FT<sub>3</sub>. These patients are considered to have subclinical hyperthyroidism. Twenty-five participants in this study satisfied these criteria, giving a prevalence of 3.9% (25/640). The prevalence in other studies has ranged from 5.5% to 12.4%. The observation of the frequently transient nature of subclinical hyperthyroidism was clearly demonstrated in 10 subjects (40%) in our study, and in 60.6% elsewhere.<sup>6</sup> Progression to overt hyperthyroidism is not well recognised. This was confirmed in this study where only 1 subject (4%) developed thyrotoxicosis within 1 year.

It is now recognised that subclinical hyperthyroidism is an independent risk factor for the development of atrial fibrillation, those subjects with a TSH level of 0.1 µU/ml or less having a threefold greater chance of developing atrial fibrillation than those whose TSH level is normal.<sup>15</sup>

Subclinical hyperthyroidism may be accompanied by features such as muscular weakness or neuromuscular dysfunction, increase in the pulse rate, premature atrial contractions and an increase in left ventricular mass and contractility.<sup>16,17</sup> Bone loss may be accelerated, with a resultant decrease in bone density.<sup>18</sup>

There were 13 subjects with depressed serum TSH concentrations who were considered biochemically euthyroid, as evidenced by normal FT<sub>4</sub> levels, but who had reduced FT<sub>3</sub> levels. The exact cause of this was not determined. It is known that 5'-deiodinase activity decreases with age, resulting in decreased formation of T<sub>3</sub>, and this may be at least partly responsible for this phenomenon. The sick euthyroid syndrome might have been a cause of decreased T<sub>3</sub> levels in at least some of those with depressed TSH levels, as they all had chronic medical problems, usually hypertension or cardiac failure.<sup>19,20</sup>

Approximately one-third of the subjects in this study were receiving pharmacological agents reported to affect the results of thyroid function tests,<sup>20</sup> but biochemical evidence of thyroid dysfunction was observed in only a small percentage (25/235 = 10.6%) in this study.

The value of the serum TSH concentration as a screening test depends on what one is hoping to achieve. This study demonstrates that the serum TSH concentration predicts thyroid dysfunction 1.5 to 3 times more often than biochemical disease. The utility of a raised TSH concentration is greater than that of a depressed one, as many subjects may have a TSH concentration of 0 and yet be euthyroid. It is also apparent that the cut-off level used has a significant effect on the usefulness of the test. A TSH > 20 µU/ml will correctly predict hypothyroidism 3 times more often than a TSH > 5 µU/ml. Similarly, a TSH of 0 is 3

times more likely to be indicative of hyperthyroidism than a TSH < 0.4 µU/ml.

In conclusion, thyroid dysfunction in this population of elderly people had a prevalence of 11.2%, which had hitherto been unrecognised in two-thirds (7.8%). This study indicates that the TSH is reliable if used as a screening test to predict thyroid dysfunction in elderly persons, but is less valuable when used to predict biochemical thyroid disease. An elevated TSH concentration is a better predictor of thyroid dysfunction than a depressed one.

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