Abstract. The prevalence of thyroid dysfunction was investigated in a small, rural community located at the coast in Middle Norway. Two hundred persons (114 women and 86 men) of the total 802 persons over 70 years of age in the community were examined regarding thyroid dysfunction. Blood samples were drawn from 197 (113 women and 84 men). In women previously diagnosed hypothyroidism was found in 3.5% and previously diagnosed hyperthyroidism in 0.9%. In men no previously diagnosed thyroid disease was found. Undiagnosed primary hypothyroidism (TT₄ < 70 nmol/l and TSH > 6 mU/l) was found in 1.8% and 1.2% of women and men, respectively. Latent hypothyroidism (TT₄ 70–150 nmol/l and TSH > 6 mU/l) was found in 3.5% and 2.4%, and borderline hypothyroidism (TSH 4.5–6.0 mU/l) in 3.5% and 2.4%, respectively. Undiagnosed hyperthyroidism was not found in women but in 1.2% of men. Antibody to the thyroid microsomal antigen (TMA) ≥ 400 was detected in 17.5% of women and 9.6% of men. Clearly elevated serum thyrotropin (TSH) concentrations or previously diagnosed thyroid disease were found in 21.7% and 37.5% of the TMA positive women and men, respectively.

The epidemiology of thyroid dysfunction in a random elderly population has not been thoroughly elucidated. Most investigations of the aged have been carried out among institutionalized subpopulations.

The laboratory diagnosis of thyroid dysfunction in old age is poorly defined owing to uncertain reference values. Studies of the physiology of the thyroid gland function in the aged have revealed that definite changes take place with advancing age, in spite of relative constancy of the serum concentrations of thyroid hormones (Ingbar 1976; Hertzmann 1981; Burrough & Sheneman 1982).

The prevalence of circulating antibodies to thyroid gland constituents, particularly against microsomal antigen, indicating chronic autoimmune thyroiditis, increases with age (Tunbridge et al. 1977; Bjoro et al. 1984).

Clinical examination of individuals with a biochemical diagnosis of hypothyroidism has rarely been undertaken in previous studies. Many patients have few symptoms and signs of their disease and these may be nonspecific and mistakenly attributed to old age (Bahemuka & Hodkinson 1975).

Although several epidemiological surveys of healthy populations have been carried out, only two of these studies are confined to individuals over 60 years of age. Falkenberg et al. (1983) found manifest hypothyroidism in 0.97% of a Swedish population of 1442 women over the age of 60 years. The Framingham study (Sawin et al. 1985) included 1256 women and 892 men, and clearly elevated serum levels of TSH were found in 5.9% and 2.3%, respectively. The large discrepancies in the prevalence of hypothyroidism in the different studies are not easily explained.
To obtain better knowledge about the prevalence of thyroid dysfunction in the elderly in a rural area of Norway, a study was undertaken in Nærøy primary health care region, a coastal community of 5850 inhabitants in the middle of Norway. Another purpose of the study was to demonstrate a possible correlation between circulating thyroid antibodies and thyroid disease, as well as to define more precise reference values for thyroid hormone serum levels in the elderly.

Subjects and Methods

Subjects

Of a total of 802 persons over 70 years of age in the Nærøy community, 200 randomly selected persons of both sexes were invited to take part in a screening programme during the first months of 1986. The selected group was representative of the elderly population in the community regarding sex ratio (114 women and 86 men) and age stratification.

All participants were personally invited to participate and inquired about their previous medical history, use of drugs, and family history of endocrine disorders. Their medical records kept at the health centre were examined especially with regard to previously known thyroid disease and previous and present use of drugs known to influence thyroid function. All patients showing abnormal biochemical values were clinically examined, especially regarding signs of thyroid disease.

Thyroid function tests

Serum total thyroxine (TT₄), free thyroxine (FT₄), and total triiodothyronine (TT₃) were determined by routine radioimmunoassays (TT₄ and TT₃) and FT₄ by using commercially available kits, Amerlex-M-T₄ and Amerlex-M-free-T₄, respectively, from The Radiochemical Centre, Amersham, England, and TT₃ as described by Haug et al. (1977). Serum TSH was determined by time resolved fluoroimmunoassay (commercially available kit, DELFIA-TSH from LKB-Wallac, Turku, Finland).

The sera were stored at -20°C before being analysed. The laboratory’s normal ranges were: TT₄ 70–150 nmol/l, FT₄ 9.4–25 pmol/l, TT₃ 1.2–2.5 nmol/l, TSH 0.2–4.5 mU/l (hypothyroidism < 0.2 mU/l, primary hypothyroidism > 6.0 mU/l, borderline hypothyroidism 4.6–6.0 mU/l).

Autoantibody test

Autoantibodies to the thyroid microsomal antigen (TMA) and to thyroglobulin (TGA) were detected in passive haemaglutination using commercially available kits (Thymune M and Thymune T, Wellcome Reagents Ltd, Beckenham, England).

Results

The study group

Out of the 114 women and 86 men above 70 years of age invited, 113 women and 84 men participated in the study. Of the three persons not attending, one woman died before the study started and the two men had moved out of the area. Three women on thyroxine-sodium replacement were excluded from the group when evaluating the thyroid function tests. No other persons used drugs which are known to interfere with thyroid function.

Previously diagnosed thyroid disease

Three women had been treated with thyroxine-sodium, two owing to biochemically verified primary hypothyroidism (verified in the medical records), one had secondary hypothyroidism verified with TRH-test. She also received cortisone substitution. Another woman had initially been on replacement with thyroxine-sodium from 1963 to 1967 owing to primary hypothyroidism, but had later developed hyperthyroidism and goitre. After partial thyroidectomy in 1967 she has been euthyroid. Altogether, 4 women (3.5%) had been treated for hypothyroidism and one (0.9%) for hyperthyroidism.

No previous history of thyroid disease was found in men. However, one man was suspected of having had hyperthyroidism in 1981–83 owing to TT₄ values in the upper range of the reference values, but escaped follow-up.

Thyroid antibodies

Twenty-three women (20.2%) and 8 men (9.6%) had TMA values ≥ 100. If we exclude those with the weakest TMA titre (3 women and 2 men had TMA < 400), 20 women (17.5%) and 6 men (7.2%) were still TMA-positive (TMA ≥ 400). Fig. 1 shows that no one had TMA titre larger than 6400, i.e. all had weak or moderate TMA titre. TGA was detected in 16 women (14.0%) and in 7 men (8.4%), and 16 women and 5 men had both TMA and TGA.

Elevated TSH (> 6 mU/l) or previously diagnosed hypothyroidism were found in 5 TMA-positive women and in 3 TMA-positive men (TMA ≥ 400), i.e. 21.7% and 37.5% of the TMA-positive women and men, respectively. The prevalences of elevated TSH (> 6 mU/l) were significantly higher in the TMA group (TMA ≥ 400).
Fig. 1.
TMA titre distribution histogram for (A) women (N = 113) and (B) men (N = 84). TMA-positive subjects having TSH > 6.0 mU/l and TSH 4.6–6.0 mU/l are marked.

Fig. 2.
TMA distribution histogram for (A) women (N = 113) and (B) men (N = 84). Hyperthyroidism TSH < 0.2 mU/l, normal range TSH 0.2–4.5 mU/l (horizontal line), borderline hypothyroidism TSH 4.6–6.0 mU/l (horizontal dotted line), and primary hypothyroidism TSH > 6.0 mU/l. * All values between 4.0 and 4.9 mU/l were between 4.0 and 4.5 mU/l. Subjects having TT4 > 150 nmol/l combined with TSH ≤ 0.1 mU/l, and subjects with TT4 < 70 nmol/l combined with TSH > 6 mU/l are marked.
Three women on thyroxine-sodium, two women and one man with primary hypothyroidism (TT\textsubscript{4} < 70 nmol/l and TSH > 6 mU/l), and one man with clinical and biochemical hyperthyroidism were excluded.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Thyroid function tests (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>TT\textsubscript{4} (nmol/l)</td>
</tr>
<tr>
<td>Women (N = 108)</td>
<td>78.6 ± 5.4</td>
<td>102.1 ± 18.9</td>
</tr>
<tr>
<td>Men (N = 82)</td>
<td>77.1 ± 5.6</td>
<td>96.9 ± 14.4</td>
</tr>
</tbody>
</table>

* Mean and sd of logarithmic transformed values.

(P < 0.01 and P < 0.000001, respectively for women and men, χ\textsuperscript{2} test). Two TMA-positive women and one TMA-positive man had in addition slightly elevated TSH (4.6–6.0 mU/l).

**Thyroid function test**

There were no correlations between increasing age and the values of TT\textsubscript{4}, FT\textsubscript{4}, TT\textsubscript{3} or TSH. No significant differences were found regarding the values of the thyroid function tests between women and men (Mann-Whitney U-test). The mean values, sd and range for TT\textsubscript{4}, FT\textsubscript{4}, TT\textsubscript{3} and TSH in women and men not receiving thyroxine-sodium are presented in Table 1. Two women and one man with primary hypothyroidism and one man with hyperthyroidism are also excluded.

One man and two women had TSH ≤ 0.1 mU/l. Only the man had elevated TT\textsubscript{4}, FT\textsubscript{4} and TT\textsubscript{3}, and he also had clinically manifest hyperthyroidism. Two women had slightly elevated TT\textsubscript{4} with both FT\textsubscript{4} and TT\textsubscript{3} within the reference range.

Fig. 2 demonstrates the TSH values. Six women (5.3%) and 3 men (3.6%) had TSH > 6 mU/l. However, 2 women and one man had also low TT\textsubscript{4} (< 70 nmol/l) indicating primary hypothyroidism. The others (4 women and 2 men) had latent hypothyroidism (TSH > 6 mU/l and 70 < TT\textsubscript{4} < 150 nmol/l). Borderline hypothyroidism (4.5 < TSH < 6.0 mU/l) was found in 4 women and 2 men, 3.5% and 2.4%, respectively, all having TT\textsubscript{4} and FT\textsubscript{4} within the normal ranges (see Table 2).

All patients with abnormal thyroid function tests were examined clinically. None had obvious signs of hypothyroidism. The thyroid gland appeared normal in size and consistency in 34 out of 35 clinically examined. One woman aged 86 with biochemical borderline hypothyroidism had a diffuse symmetrical goitre. However, this patient was both TMA- and TGA-negative. No significant connections were seen regarding previous and present drug intake.

**Discussion**

The prevalence of clearly elevated TSH level (TSH > 6 mU/l) in elderly women and men in our

<table>
<thead>
<tr>
<th>No. (%)</th>
<th>Primary hypothyroidism TSH (mU/l) &gt; 6 and TT\textsubscript{4} (nmol/l) &lt; 70</th>
<th>Latent hypothyroidism TSH (mU/l) &gt; 6 and TT\textsubscript{4} (nmol/l) 70–150</th>
<th>Borderline hypothyroidism TSH (mU/l) 4.6–6.0 and TT\textsubscript{4} (nmol/l) 70–150</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women</td>
<td>2 (1.8%)</td>
<td>4 (3.5%)</td>
<td>4 (3.5%)</td>
</tr>
<tr>
<td>Men</td>
<td>1 (1.2%)</td>
<td>2 (2.4%)</td>
<td>2 (2.4%)</td>
</tr>
</tbody>
</table>
study were 5.3% and 3.6%, respectively, but only one third of these (both women and men) had low serum TT$_4$ as well. These results are, however, in reasonably good agreement with the results of a large screening study in the USA (Savin et al. 1985), and indicate a higher prevalence of hypothyroidism in individuals over 70 years of age than in younger age groups (0.64–1.0%) (Gordin et al. 1972; Tunbridge 1979; Kågedal et al. 1981). None of our participants had obvious clinical manifestations of hypothyroidism. A study from Sweden revealed elevated TSH in 2.2% and manifest hypothyroidism in 0.97% (Falkenberg et al. 1983). The prevalence of hyperthyroidism in our study was low, 0.9% for females and 1.2% for males, compared with the Swedish study (Falkenberg & Kågedal 1985). Environmental, geographic and ethnic factors may partly explain these differences. However, the ethnic differences are presumably less between Swedish and Norwegian than between American and Norwegian populations. The Swedish study was from a goitre region (Højér 1931), and Nærøy, which is a costal community, is not a goitre region. However, urinary iodine excretion has repeatedly been determined in several Norwegian communities in the later years and shows little variation. This also goes for the costal communities not far from Nærøy (Frey et al. 1974; Kapelrud et al. 1987).

It is difficult to compare our data with the results of many of the other studies, as the participants in those studies have been selected in one way or the other, being either hospitalized or persons attending centres for the elderly, geriatric wards etc. (Lloyd & Goldberg 1961; Bahumeka & Hodkinson 1975; Proteus 1979; Savin et al. 1979; Riniker et al. 1981). Furthermore, there are methodological differences between the studies, especially regarding the TSH assays. We have in our study used a new highly sensitive fluoroimmunoassay for TSH.

The high attendance rate (197 of 200) was probably due to local factors such as a close relationship between the population and the doctors and the fact that the local health centre served the entire population in the community. High attendance rate, a small community, and a stable population are factors which contribute heavily to the reliability of the results.

The significance of slightly elevated TSH levels is not yet clear. Using the same highly sensitive fluoroimmunoassay for TSH Juva et al. (1986), reported that the reference values for elderly women (above 65 years of age) were higher (0.6–8.8 mU/l) than for middle-aged women and men (0.6–3.8 mU/l). However, Kallner et al. (1987) reported no significant differences between women aged 16–50 years of age and women above 50 years of age.

The prevalence of TMA (titre ≥ 400) in this study (women 17.5% and men 7.2%) was significantly higher than in healthy blood donors both for women (10.8%) and men (4.1%), but not significantly higher than in blood donors aged 45 years or more (women 18.0% and men 7.9%) (Bjøro et al. 1984). Interestingly, no one in the Nærøy study had TMA titre > 6,400, which is in contrast to the findings in the blood donors (Bjøro et al. 1984). This may be due to simple change factors, related to the smaller number of individuals studied (197) as compared with the blood donors (1627). One might also speculate that the autoimmune process loses intensity in subjects aged 70 years or more. In agreement with the findings of several other groups (Gordin et al. 1979; Tanner et al. 1982; Lindstedt et al. 1983), thyroid dysfunctions were observed more often in TMA-positive subjects. Also Betterle et al. (1987) recently reported thyroid autoantibodies as good markers of symptomless autoimmune thyroiditis.

The total prevalence of primary and latent hypothyroidism in this study was 5.3% and 3.6% in women and men, respectively. This finding rises the question of screening elderly persons for thyroid dysfunctions by measuring serum levels of TSH and probably also TT$_4$, since mild thyroid dysfunction is not easily recognized clinically. However, we do not know enough about the relationship between biochemical thyroid dysfunction and reduced mental capacity, cognitive dysfunction, and cardiovascular diseases. More knowledge is needed about the implication of slightly elevated TSH, of clearly elevated TSH and normal TT$_4$ and FT$_4$, as well as of the effects of putative treatment.

Acknowledgments

Financial support from Trøndelags Medisinske Selskaps Fond is gratefully acknowledged. We also thank Åsta Bøe Volden, Nils Somby, and Kjersti Helle for skilful technical assistance.
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Received June 9th, 1987.
Accepted October 14th, 1987.

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