Subclinical hypothyroidism: diagnosis and treatment in adults

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BACKGROUND
Subclinical hypothyroidism (also denoted asymptomatic hypothyroidism or latent hypothyroidism), in analogy with overt hypothyroidism, is often thought to cause a variety of clinical signs. This gives rise to the widespread prescription of biological and therapeutic substances, often with no clear justification.

AIMS
- To clarify the concept of subclinical hypothyroidism and its relationship with the clinical or biological signs which are commonly attributed to it.
- To assess the benefits of screening.
- To rationalise the prescription of tests to measure TSH (thyroid stimulating hormone) and free thyroxine (FT4) levels.
- To assess the usefulness of treating subclinical hypothyroidism and the indications of treatment.

HEALTHCARE PROFESSIONALS CONCERNED
First-line physicians (in particular general practitioners, endocrinologists, gynaecologists and obstetricians), midwives, and laboratory analysts.

DEFINITION
Subclinical hypothyroidism is defined by a TSH level > 4 mU per L, confirmed by a second test one month later, with FT4 levels in the normal range.

PREVALENCE
- Prevalence in France among the general population: males 1.9%, females 3.3%.
- Sub-population where prevalence is higher: individuals aged over 60, who have a history of thyroid problems, or who are taking medication (amiodarone, lithium, interferon) putting them at risk.
PROGRESSION TO OVERT HYPOTHYROIDISM
- Patients do not necessarily progress to overt hypothyroidism:
  - Return to normal ~ 1/3 of cases, stabilisation ~ 1/3, overt hypothyroidism ~ 1/3;
  - annual incidence of clinical hypothyroidism: females 4/1,000, males < 1/1,000.
- Key predictive factors for developing overt hypothyroidism:
  - high initial TSH (> 10 mU per L)
  - antithyroperoxidase antibody (anti-TPO)
  - age > 60 years
  - past history of thyroid problems, treatment by certain drugs (amiodarone, lithium, interferon)

REPERCUSSIONS OF SUBCLINICAL HYPOTHYROIDISM
- Clinical repercussions: irregular, non-specific, and non-discriminatory.
  If TSH > 10 mU per L:
    - increased cardiovascular risk;
    - repercussions on neuropsychological condition and quality of life.
- Biological repercussions: Impaired lipid profile (increase in total cholesterol and LDL cholesterol)
  - partially reversible after replacement therapy;
  - not significant if TSH < 10 mU per L.

SCREENING
- No screening advocated in the general population.
- Targeted screening for individuals at risk of developing overt hypothyroidism, i.e. in women over 60 years old who also present risk factors.

TREATMENT INDICATIONS
The aim of thyroxine treatment is to prevent progression to overt hypothyroidism. Treatment does not significantly improve clinical signs or quality of life. The expected benefit depends on the initial TSH level, the clinical, biological and therapeutic context, and the risk of the patient developing overt hypothyroidism.

Thyroxine treatment is recommended for TSH levels >10 mU per L or in the presence of anti-TPO antibodies.

Treatment consists in stepwise levothyroxine replacement therapy in order to restore normal TSH levels. It must be reconsidered if the patient has coronary artery disease.

SPECIAL CASE OF PREGNANT WOMEN
It is thought that subclinical hypothyroidism might be associated with a greater risk of retroplacental haematoma, prematurity, and neonatal respiratory distress.

Targeted screening (simultaneous assay of TSH, FT4 and anti-TPO antibodies) is indicated where clear signs are present, i.e. where the patient or a relative has a history of thyroid problems, past history of dysthyroidism, thyroid surgery, possible elevated antithyroid antibodies, or auto-immune disease.

In patients with TSH levels > 3 mU per L, TSH and anti-TPO must be measured once a month.

Treatment is warranted when TSH is over 4 mU per L, with the aim of bringing the level down to < 2.5 mU per L.
Diagnostic and treatment strategy for suspected subclinical hypothyroidism

No systematic measurement of TSH

Non-pregnant adult
Identify high-risk subjects

clear clinical signs, goitre, hypercholesterolaemia, history of thyroid problems, thyroid auto-immunity, cervical irradiation, high-risk drug treatment (amiodarone, lithium, interferon, other cytokines, etc.)

Measure TSH only in high-risk subjects

TSH < 4 mU/L
STOP!

TSH > 4 mU/L
Check after one month: TSH + FT4

TSH > 4 mU/L + normal FT4

Measure anti-TPO antibodies if they are likely to affect treatment

Look for confounding factors if TSH is very high

Treatment

TSH < 10 mU/L
no anti-TPO antibodies: Check TSH after 6 months, then once a year if it has not returned to normal

TSH < 10 mU/L
+ anti-TPO antibodies++, very clear clinical or biological signs, high cardiovascular risk: consider thyroxine treatment

TSH > 10 mU/L
Administer thyroxine
Target: TSH within normal range

Pregnant woman
Identify high-risk women

clear signs, personal or family history of thyroid problems, auto-immunity

Measure TSH only in high-risk women

TSH < 3 mU/L
STOP!

TSH > 3 mU/L

Measure TSH + FT4 + anti-TPO antibodies

TSH between 3 and 4 mU/L
normal FT4

Monitor monthly

TSH between 3 and 4 mU/L
and positive anti-TPO antibodies

Monitor monthly

TSH > 4 mU/L

normal FT4: Subclinical hypothyroidism

Monitor monthly Treatment?

Replacement therapy
Target: normal TSH < 2.5 mU/L

The full guidelines and supporting document (in French) can be found at www.has-sante.fr