



Subclinical Hypothyroidism

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Definition

Subclinical hypothyroidism (SCH) is defined as a serum TSH level above the upper limit of normal despite normal levels of serum Free T4.

Also called as Mild Thyroid Failure

Review Clinical practice. Subclinical hypothyroidism. Cooper DS. N Engl J Med. 2001 Jul 26; 345(4):260-5.

sub·clin·i·cal

- pertaining to an early stage of a disease; having no noticeable clinical symptoms.

Hypothyroidism Stages

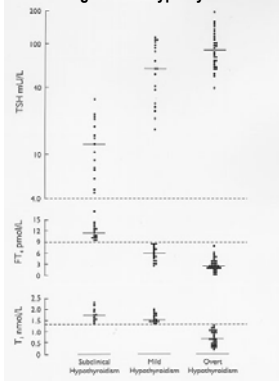
1. Subclinical Hypothyroidism TSH↑ T4→ T3→
2. Mild Hypothyroidism TSH↑↑ T4↓ T3→
3. Overt Hypothyroidism TSH↑↑↑ T4↓↓ T3↓

Table 1. Classification of hypothyroidism according to its clinical manifestations and endocrine biochemical parameters (adapted from ref. 7).

	TRH-TSH stimulus	TSH	T4 (total or free)	T3
Subclinical hypothyroidism				
Stage 1	Hyper-response	Normal	Normal	Normal
Stage 2	Not possible	Increased	Normal	Normal
Clinical hypothyroidism				
Stage 3	Not possible	Increased	Decreased	Normal
Stage 4	Not possible	Increased	Decreased	Decreased

Castillo V, Rodriguez MS, Lalla J. Estimulación con TRH y evaluación de la respuesta de la TSH en perros. Su importancia en el diagnóstico de la enfermedad tiroidea subclínica (hipotiroidismo subclínico y tiroiditis autoinmune eutiroidea). Revista Científica 2001; 11: 35-40.

Individual and median values of thyroid function tests in patients with various grades of hypothyroidism.



Wiersinga WM. Adult hypothyroidism and myxedema coma. In: DeGroot LJ, Jameson JL (eds). *Endocrinology* (5th ed.). Philadelphia, WB Saunders Company, 2004, ch. 107

Epidemiology of thyroid Abs % hypothyroidism in the Wickham survey (#2779 adults for 20 years)

		Women %	Men %	Ratio
Prevalence	Tg antibodies	3	0.9	3.3
	TPO antibodies	10.3	2.7	3.8
	Subclinical hypothyroidism	7.5	2.8	2.7
	Hypothyroidism	1.8	0.1	18
Incidence	Hypothyroidism	0.41/y	0.06/y	6.8

* Tunbridge WMG, Evered DC, Hall R, et al. The spectrum of thyroid disease in the community: the Wickham Survey. *Clin Endocrinol* 1977; 7: 481-493.

* Vanderpump MPJ, Tunbridge WMG, French JM, et al. The incidence of thyroid disorders in the community: a twenty-year follow-up of the Wickham Survey. *Clin Endocrinol* 1995; 43: 55-68.

SCH Epidemiology

- A common Problem 3-8%
- Prevalence increase by age
 - After 6th decade: 10%, F/M=1
- Anti thyroid Abs: 80%
- TSH <10 mIU/L in 80% of patients

Mayo Clin Proc. 2009 January; 84(1): 65-71.
Subclinical Hypothyroidism: An Update for Primary Care Physicians
Yalabik Fatoumeh, MD

Pathogenesis of Hypothyroidism

Cause	Pathogenesis	Goiter	Degree of Hypothyroidism
Hashimoto's thyroiditis	Autoimmune destruction of thyroid	Present early, absent later	Mild to severe
Drug-induced ¹	Blocked hormone formation ²	Present	Mild to moderate
Dyshormonogenesis	Impaired synthesis of T4 due to enzyme deficiency	Present	Mild to severe
Radiation, ¹³¹ I, x-ray, thyroidectomy	Destruction or removal of gland	Absent	Severe
Congenital (cretinism)	Athyresis or ectopic thyroid, iodine deficiency; TSH receptor-blocking antibodies	Absent or present	Severe
Secondary (TSH deficit)	Pituitary or hypothalamic disease	Absent	Mild

SCH Manifestations

Symptoms	<ul style="list-style-type: none"> hypothyroid symptoms impaired well-being and quality of life impaired cognitive functions (working memory) mood disturbances
Signs	<ul style="list-style-type: none"> impaired left ventricle diastolic and systolic function hypertension ↑ systemic vascular resistance ↑ central arterial stiffness impaired endothelium function ↑ carotid intima-media thickness impaired muscle energy metabolism impaired peripheral nerve conduction latency and amplitude impaired stapedial reflex
Biochemistry	<ul style="list-style-type: none"> ↑ serum total and LDL cholesterol ↑ HOMA index (insulin resistance) ↑ serum C-reactive protein ↓ factor VIIa ↑ serum lactate during exercise ↓ serum IGF-1, ↑ serum leptin

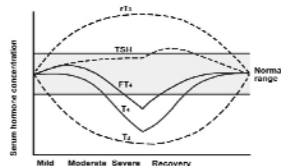
Abnormalities reported in some but not all studies on subclinical hypothyroidism.

DIAGNOSIS OF HYPOTHYROIDISM

Stage 1	<p>Is hypothyroidism present?</p> <p>A. Clinical assessment: B. Biochemical assessment: TSH and FT4 assays</p>
Stage 2	<p>If hypothyroidism is present, what is the cause?</p> <p>A. Clinical assessment: history, goiter B. Biochemical assessment: TPO antibodies; sometimes thyroid ultrasound</p>

Differential Diagnosis

- Other causes of elevated TSH
 - Recovery from NTI
 - Assay variability (5-10%)
 - Presence of heterophile Abs
 - Thyroid hormone resistance

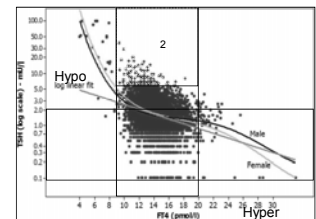


FT4 → and TSH ↑ (Zone 2)

- Common**
- Subclinical hypothyroidism

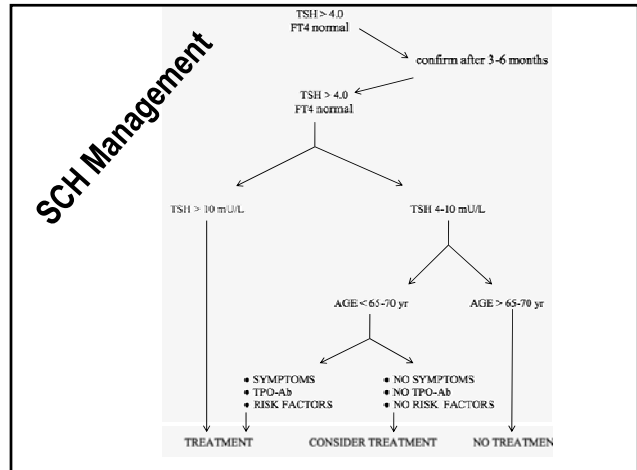
- Rare**
- Heterophile (interfering) antibody
 - Poor compliance with thyroxine
 - Malabsorption of thyroxine
 - Drugs (e.g. amiodarone, sertraline, cholestyramine)
 - NTI recovery phase

- Congenital**
- TSH-receptor defects
 - Resistance to TSH associated with other (unspecified) defects
 - Pendred's syndrome—some cases (associated with sensorineural deafness and goitre)



Natural History of SCH

- Spontaneous return of TSH level 5.5 % after 1 year
- Progression to Overt hypo: 7.8-17.8 %
30 % after 10 years
- Higher TSH = Greater risk
- TPO Abs+ = Greater risk



Factors Favoring Levothyroxine Therapy in Patients With a TSH Level of 5 to 10 mIU/L

Pregnancy or intention of pregnancy
 Goiter
 Therapeutic trial for possible hypothyroid symptoms
 Patient preference
 Childhood and adolescence
 2 TSH levels >8 mIU/L
 Bipolar disorder, depression
 Infertility
 Presence of antithyroid antibodies
 Progressive TSH increase
 Ovulatory dysfunction
 Young age of the patient
 Hyperlipidemia?

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 Yahab Fatourecht, MD


Case Study

A 30-year-old woman presents with fatigue and a weight gain of 9.1 kg in the past 6 months.

- She has a sister who is receiving levothyroxine therapy for hypothyroidism. On examination, a diffuse 35-g thyroid is palpable.
- Laboratory tests are unremarkable except for a serum free thyroxine level of 1.3 ng/dL and a serum TSH level of 7 mIU/L.
- Thyroperoxidase (TPO) antibodies are detected.

Which *one* of the following statements is *least* applicable to this patient?

1. Levothyroxine therapy will result in substantial weight loss
2. Levothyroxine therapy has a 25% chance of improving her quality of life
3. Levothyroxine therapy will reduce the size of the goiter
4. The likelihood of progression to clinical hypothyroidism in 10 years is 50%
5. Therapy is semiurgent if she plans pregnancy



Thank you for your Attention

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