

Evidence based treatment of sub-clinical hypothyroidism

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hypothyroidism***

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***Should We Treat
Subclinical
Hypothyroidism?***

SUBCLINICAL HYPOTHYROIDISM

- State of elevated TSH level with a normal free T4 level--is referred to as subclinical hypothyroidism
- The term "**subclinical**" may not be strictly correct, since some of these patients may have clinical symptoms, but no better term has been proposed

How Common is Subclinical Hypothyroidism?

- Subclinical hypothyroidism is found in –
 - 6-8% of adult females
 - 3% of adult males
- More prevalent with age specially common among middle-aged women
- One study found 7% of women and 3% of men aged 60-89 years had TSH level greater than 10 mU/l.(Normal range 0.5-4.5mU/l.)*

*Sawin CT, Chopra D, Azizi F, et al;
JAMA. 1979 Jul 20;242(3):247-50. [abstract]

CAUSES OF HYPOTHYROIDISM

- Chronic autoimmune thyroiditis
- Treated Graves' disease
- Radioactive iodine therapy
- Subtotal thyroidectomy
- Antithyroid drugs
- Head and neck surgery
- Radiation therapy to the head, neck or chest area
- Iodine deficiency
- Medications: lithium, iodine, amiodarone
- Idiopathic
- Congenital

Course

- Reversion to normal
 - Episode of silent thyroiditis with a transient hypothyroid phase
 - Laboratory error
- Remains unchanged
- Progression to overt hypothyroidism
 - Occurs ~ **5 percent per year** in patients with detectable antithyroid antibodies
 - Elderly patients, the risk of progression to overt disease ~ **20 percent per year** (with high titers of antithyroid antibodies)

Consideration of these possible outcomes affects the decision about whether to **treat** or to **observe** without treatment

Other causes of elevated serum TSH includes

- Recovery from nonthyroidal illness,
- Assay variability
- Heterophil antibodies
- Central hypothyroidism with biologically inactive TSH
- Thyroid hormone resistance

The most common cause of elevated serum TSH is autoimmune thyroid disease

Associated Changes

- Elevation serum levels of – (but are less marked and less consistent)
 - Triglycerides
 - Total cholesterol
 - Low density lipoprotein (LDL) cholesterol

Elder J, McClelland A, O'Reilly DS, et al.
Ann Clin Biochem 1990;27:110-113

- **An important risk factor for cardiovascular disease**
- Recent studies have shown a significant increase in coronary heart disease and cardiovascular related mortality in people with subclinical hypothyroidism and a TSH concentration >10 mU/l, but no difference in overall mortality

Miura S, Itaka M, Suzuki S, Fukasawa N, et al.
Endocrinol J 1996; 43(6):657-663

- Some studies have shown a decrease in LDL and total cholesterol levels after treatment with L-thyroxine, although others have refuted

Danese MD, Ladenson PW, Meinert CI, et.al.
Clin Endocrinol Metab 2000;85:2993-3001

Pregnancy

- Maternal hypothyroidism has been associated with –
 - **Mental retardation** in their euthyroid children
 - Increased **fetal loss**
- Early screening and treatment should be given in pregnancy with –
 - Goitre
 - High anti-thyroid antibody titre
 - Family history of thyroid disease
 - Symptoms suggestive of hypothyroidism,

Brent GA; Maternal hypothyroidism: recognition and management.; *Thyroid*. 1999;9(7):661-5

What Are the Risks of Not Treating Subclinical Hypothyroidism?

- Elevation of cholesterol and triglycerides leading to atherosclerosis and ischaemic heart disease
- Depression, anxiety, and panic attacks
- Miscarriage
- Fetal developmental delays

Should Doctors Treat Subclinical Hypothyroidism to Help Prevent Heart Disease?

- Treating subclinical hypothyroidism can improve a number of heart disease risk factors, as well as certain quality of life measurements

The Journal of Clinical Endocrinology & Metabolism. May 2007

Effects of Therapy

- The possible advantages of treating subclinical hypothyroidism generally fall into three categories –
 - Progression to overt hypothyroidism, with its attendant morbidity, would be prevented by thyroxine therapy.
 - Thyroxine therapy may improve the serum lipid profile and thereby potentially decrease the risk of death from cardiovascular causes.
 - Treatment may reverse the symptoms of mild hypothyroidism, including psychiatric and cognitive abnormalities.

Effects of Therapy

- In women with ovulatory dysfunction, thyroxine therapy may restore fertility

Lincoln SR, Ke RW, Kutteh WH.
J Reprod Med 1999;44:455-7

- Although difficulty in losing weight is often attributed to subclinical hypothyroidism, body weight is unlikely to decrease with thyroxine therapy

Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC.
Ann Intern Med 1984;101:18-24

Effect on CVS

- Myocardial contractility has been shown to improve in patients with subclinical hypothyroidism, treated with L-thyroxine, compared to those on placebo

Cooper DS, Halpern R, Wood LC, Levin AA, Ridgway EC.
Ann Intern Med 1984;101:18-24

Arguments Against Treatment

- Treatment expense and the likelihood that some, or even most, patients will not benefit

Adlin, V. Subclinical hypothyroidism: deciding when to treat. Am Fam Phys [online] 1998 February 15 [cited 2001 Feb 2]

- There is a danger of overtreatment, which could cause iatrogenic hyperthyroidism and ultimately lead to more serious abnormalities (e.g. osteopenia and atrial fibrillation)

Marqusee E, Haden ST, Utiger RD. Endocrinol Metab Clin North Am 1998;27:37-49)

- In one study, overtreatment were found in 21 % of patients

Canaris GJ, Manowitz NR, Mayor GM, Ridgway EC. Arch Intern Med 2000;160:526-34

Clinical Approach Until More Evidence Is Available

- **Mayo Clinic** physicians generally follow these guidelines:
 - TSH levels between 5 and 10 mIU/L should be treated selectively
 - Thyroxine replacement therapy should be reserved for
 - Goiter
 - Women who are anticipating pregnancy or are pregnant
 - Depression or bipolar disorder
 - Subclinical hypothyroidism associated with autoimmune thyroiditis of children and adolescents should be treated

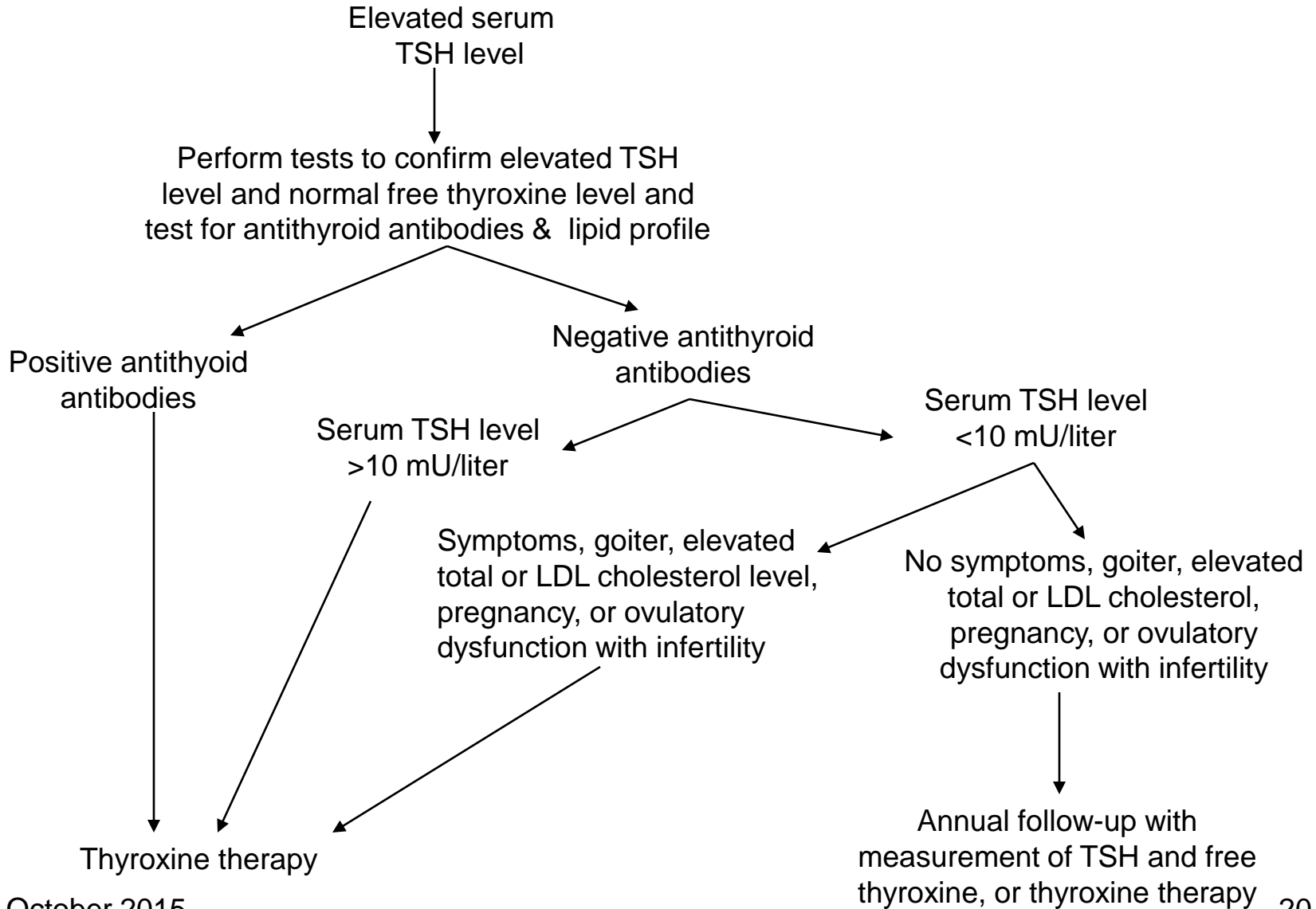
Clinical Approach Until More Evidence Is Available

- Mayo data show that patients with serum TSH levels higher than 8 mIU/L have a high likelihood of progression to TSH above 10 mIU/L in 4 years and may be considered for thyroxine replacement therapy
- Improvement in serum lipid levels with thyroxine replacement therapy is more likely for patients who have baseline TSH levels higher than 10 mIU/L
- If hyperlipidemia is encountered in a patient with a serum TSH between 5 and 10 mIU/L, specific lipid-directed therapy or lifestyle changes are needed

Clinical Approach Until More Evidence Is Available

- Following factors should also be considered before starting treatment –
 - Patient preference
 - Clinical circumstance
 - Age
 - Presence of symptoms of hypothyroidism
 - Thyroperoxidase antibody positivity
 - Level of and progression of TSH over time

ALGORITHM FOR THE MANAGEMENT OF SUBCLINICAL HYPOTHYROIDISM.



Thyroxine Therapy

- **Dosing** –
 - Young start at 50 mcg once daily
 - Elderly and/or young with associated CVS disease, starting dose at 12.5 to 25mcg once daily
- **Goals for treatment** are –
 - A fall in LDL cholesterol, or
 - Symptomatic improvement, or
 - TSH normalising to < 4.0 (aim to lower TSH to mid-normal – 3 mU/L)
- **Monitoring** –
 - At 6-8 week intervals initially
 - Once the correct dose has been established, monitoring can be done at 6-12 months intervals

Relative Contraindications – osteoporosis

Thank you