VOLUME 05
ISSUE 02

CLINICAL PRACTICE UPDATE IN

ENDOCRINOLOGY & DIABETES

THYROIDROUNDS

LMC

THYROID NODULES

Diane is a well 52-year old woman who's been seeing you reliably for annual physicals throughout her adult life. At this exam, you find a nodule in her left thyroid bed. She has had no neck pain, no compressive symptoms, and is euthyroid. The nodule is solitary, non-tender, mobile, and approximately 2cm in diameter without associated cervical adenopathy. Diane has never had thyroid problems or external radiation and has no family history of thyroid disease.

Which investigations should be performed? What, if any, treatment should be offered?

Thyroid nodules are a common problem encountered in clinical practice. 5% of adults have a palpable thyroid nodule but ultrasound series show prevalence as high as 50%. The majority of thyroid nodules are benign, 5% being malignant. Thyroid cancer overall represents 1% of all cancers and 0.5% of cancer deaths.

Findings that indicate a higher risk of malignancy include a family history of thyroid cancer, a personal history of external radiation, rapid growth of the nodule, associated compressive symptoms, extremes of age, male sex, the presence of a hard, fixed nodule, and cervical adenopathy.

Initial diagnostic work-up includes measurement of the TSH and obtaining an ultrasound (US). A radioactive iodine scan should not be performed routinely, unless the patient also has a suppressed TSH. In that setting, finding a hot nodule on scan is reassuring, as almost all hot nodules are benign. Thyroid US helps in further characterization of the nodule and differentiates solid nodules from cysts, provides additional information on the presence /absence of cervical lymphadenopathy, and often will demonstrate additional thyroid nodules which are not palpable. US findings that increase the likelihood of the nodule being malignant include the presence of hypoechogenicity, calcification, irregular margins, and increased blood flow.

Fine needle aspiration (FNA) is an extremely useful tool in differentiating benign from malignant nodules. It is suggested that all nodules over 10-15 mm in size, and smaller nodules with suspicious US features should be aspirated. FNA sensitivity is only 80 – 90%, therefore multiple biopsies from multiple nodules are recommended.

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The treatment of thyroid nodules depends primarily on the result of the FNA. If the results are suspicious or clearly malignant, surgery is required. If inadequate or a non-diagnostic specimen is obtained, repeat FNA, often done with ultrasound guidance is needed. If the FNA is clearly benign, then options include follow-up with clinical, US and cytological reassessment as needed. Suppressive treatment aimed at keeping the TSH to less than 0.1miU/L does lead to clinically significant reduction in nodule size in about 20% of cases; however, the risks of suppressive therapy include increasing bone resorption, osteoporosis, atrial fibrillation, and possibly increased cardiovascular morbidity. Thus it is suggested that suppressive therapy not be used, particularly in patients with underlying CV disease, reduced bone density and those over the age of 60.

In Diane's case, the TSH was normal and the thyroid US confirmed a 2.5cm single, solid, nodule. FNA was suggestive of a colloid nodule and Diane is being followed clinically, without suppressive treatment, with repeat US planned in 6-12 months.

PEARLS

- Thyroid nodules are common and the majority are benign.
- Most nodules >1 cm in size, and some smaller nodules with suspicious US features, need FNA
- Benign nodules can be followed clinically +/- US without suppressive treatment.

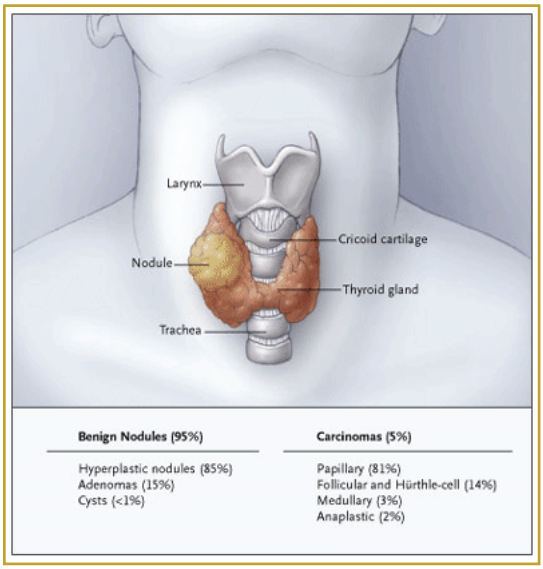
SUBCLINICAL HYPOTHYROIDISM

Susan is a generally well, overweight 53-year old woman, new to your practice. She has non-specific symptoms of fatigue and occasional constipation is found to have a TSH of 12miU/L, fT4 of 15pmol/l. Interestingly, her lipid profile demonstrates an LDL of 3.93mmol/l, HDL 1.02mmol/l, TG 0.88mmol/l.

What additional investigations are necessary? Should she be treated? If not, what follow-up is required?

An elevated TSH with normal fT4 and fT3 levels defines the entity of subclinical hypothyroidism (SCH). About 20% of women over the age of 60 have SCH and most have few, if any, symptoms or signs. For Susan, it becomes important to exclude prior thyroid disease or surgery or neck radiation, thyroxin use, and family history of thyroid disease. Repeat levels should be drawn in 2-12 weeks to exclude transient forms of hypothyroidism. Measurement of thyroid antibodies is controversial; however, patients with positive antibodies may progress to overt hypothyroidism at a higher rate than those who are antibody negative (4.5%/year vs. 2.5%/year). There is no need to perform a thyroid ultrasound or a radioactive iodine scan routinely.

Treatment of subclinical hypothyroidism is controversial and depends on the degree of TSH elevation, presence of symptoms and the risk of progression to overt hypothyroidism. Treatment does not alter the natural course of the disease, but may prevent the onset of symptoms or their metabolic side effects.



In patients with TSH levels between 5-10 miU/L, there is no evidence that treatment improves quality of life or clinical outcomes. There is some evidence that treatment may improve cardiac contractility; however, the evidence of impact of treatment on clinical cardiac endpoints is not available. There is no compelling evidence that the lipid profile is significantly abnormal in such patients and there are no randomized clinical trials showing the benefit of treatment on lipid profile. Thus, unless the patient is planning a pregnancy, in which case she should be treated; there is no compelling evidence for or against treatment of this degree of hypothyroidism. However, clinicians will often treat patients with mild TSH elevations if they have at least one of the following: elevated anti-TPO antibodies; goiter; infertility; sign or symptoms.

If the TSH however is greater than 10miU/L, there is suggestive evidence to support treatment. Potential benefits include improvement in lipid profile (5% reduction in total cholesterol and LDL level) and cardiac function. A recent study did demonstrate improvement in fatigue when patients with subclinical hypothyroidism were treated. Furthermore, observational studies show an increased risk of CHF and CHD in patients with subclinical hypothyroidism.

Susan's TSH exceeded 10miU/L and some "soft" symptoms were present. If the TSH remains abnormal on repeat testing, treatment could be initiated to see if there is improvement in fatigue and dyslipidemia; however deferring treatment in a reluctant patient is also reasonable.

PEARLS

- Subclinical hypothyroidism is associated with an elevated TSH and normal fT4/fT3 levels.
- Most asymptomatic patients with TSH <10miU/L do not require treatment.
- Patients with TSH >10 miU/L may benefit from treatment in prevention of symptoms and goiter.

SUBCLINICAL HYPOTHYROIDISM

Joanna is a 77-year old woman well-known to you, with a background of coronary artery disease and osteoporosis. At this exam, you have found a TSH of 0.09miU/l, fT4 of 14pmol/l and fT3 of 4.0pmol/l). She feels well apart from occasional mild stable angina. Examination reveals that she is in sinus rhythm, thyroid is palpably normal, and she is euthyroid clinically.

What additional investigations are needed? What treatment, if any, should be recommended?

A TSH below the lower limit of the reference range, with normal fT4 and fT3 levels, defines the entity of subclinical hyperthyroidism. It is much less common than subclinical hypothyroidism, with a prevalence between 2-3%. The most common cause of subclinical hyperthyroidism is iatrogenic due to thyroxine therapy for hypothyroidism. Other common causes of subclinical hyperthyroidism are the same as those for full hyperthyroidism: Graves' disease, autonomously functioning thyroid nodules, iodine exposure such as with amiodarone, and thyroiditis; however, the hyperthyroidism due to thyroiditis is mostly transient.

A low TSH level should be repeated as it will often normalize on repeat measurement. fT3 levels become particularly important in patients with a low TSH, to exclude the possibility of isolated T3 hyperthyroidism. In these cases, fT4 levels may be normal.

Examination should follow signs and symptoms of hyperthyroidism, cardiovascular risk factors, increased fracture risk, and atrial fibrillation. Thyroid antibodies can be obtained to aid in the determination of the cause of hyperthyroidism. Finally, a thyroid uptake and scan will provide information as to whether the hyperthyroidism may be due to an identifiable cause such as Graves' disease, toxic nodule(s), or thyroiditis. There is no need to obtain an ultrasound routinely.

The natural history of subclinical hyperthyroidism in young asymptomatic patients, is benign, particularly if the TSH is between 0.1-0.5miU/L. Annual risk of progression to overt hyperthyroidism is 1-2%. Treatment is therefore not routinely recommended due to the risks associated with available anti-thyroid drugs, and of permanent hypothyroidism with radioactive iodine therapy. However, in older patients, particularly if the TSH <0.1miU/L, subclinical hyperthyroidism has been associated with higher rates of atrial fibrillation, osteoporosis and increased cardiovascular mortality and treatment is usually recommended, on empiric grounds.

Joanna's investigations were consistent with an early toxic multinodular goiter. Given the age, degree of TSH suppression, osteoporosis, and underlying CAD etc, it would be advisable to treat her subclinical hyperthyroidism.

PEARLS

- Subclinical hyperthyroidism is much less common than hypothyroidism.
- Most patients are asymptomatic and do not progress to overt hyperthyroidism.
- Risks of treatment outweigh their benefits in most patients however, patients with reduced bone density or increased cardiovascular risk may benefit from treatment.

Supported by educational grants from members of the pharmaceutical industry.