The Ups and Downs of Thyroid Function

Heather Lochnan, MD, FRCPC

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Disorders of the thyroid are common. The prevalence of thyroid disease is much higher in females and increases with age in both women and men. Biochemical tests are the most reliable indicator of thyroid function. Frequently, screening with thyroid-stimulating hormone (TSH) reveals unsuspected results. Not surprisingly, TSH is one of the most commonly requested blood tests; it is a very sensitive indicator of primary hypothyroidism or hyperthyroidism. When TSH is abnormal, it is helpful to look at levels of free thyroid hormones, *i.e.*, free thyroxine (FT_4) and free triiodothyronine (FT_3). The free hormone levels can be useful to determine the severity of the thyroid disorder and, in many cases, are normal despite the abnormal TSH.

What is hypothyroidism?

The best screening test for hypothyroidism is TSH. In hypothyroidism, the TSH is elevated. (It is important to note that hypothyroidism is not the only cause of elevated TSH [Table 1].) The exception is in pituitary or hypothalamic disorders, where TSH and FT_4 are low. In either of these cases, central hypothyroidism is usually suspected

Penny's case

Penny, 72, is admitted to hospital with pneumonia and possibly mild heart failure. She has features suggestive of hypothyroidism, including a history of recent fatigue, constipation, and impaired memory. Her thyroid-stimulating hormone (TSH) level is < 0.1 mU/L. Her thyroid exam is normal and she has no prior history of thyroid disease, although both her sisters are taking thyroid hormone replacement. Her heart rate is regular, at 80 beats per minute, and there is no clinical evidence of hyperthyroidism. Her past medical history includes a history of coronary artery disease (CAD), for which she had a bypass one year ago.

She responds well to therapy and is sent home after two nights in hospital. Followup tests eight weeks later indicate the TSH remains suppressed, free thyroxine (FT_4) is 20 pmol/L, and free triiodothyronine (FT_3) is 5.0 pmol/L. She has lost 6 kg over the last three months, despite a good appetite.

With her hormone levels in the upper range of normal, what is the likely diagnosis?

Is treatment indicated?

For a followup on Penny, go to page 73.

Table 1
Causes of elevated TSH

- Hypothyroidism
- Subclinical hyperthyroidism
- Thyroid hormone resistance
- TSH-secreting adenoma

TSH: Thyroid-stimulating hormone

Table 2
Causes of suppressed TSH

- Hyperthyroidism
- Subclinical hyperthyroidism
- Excessive thyroid hormone replacement
- Hypothalamic or pituitary dysfunction
- Non-thyroidal illness
- Depression
- Drugs (*e.g.*, glucocorticoids, dopamine)
- Pregnancy (bHCG stimulates the TSH receptor)

bHCG: Beta human chorionic gonadotropin
TSH: Thyroid-stimulating hormone

because of the clinical picture of pituitary dysfunction. Also, in these cases, diagnosis and replacement therapy rely on the levels of FT_4.

In subclinical hypothyroidism, TSH is minimally elevated, but FT_4 and FT_3 levels are in the normal range. The patient may have vague symptoms, such as fatigue, or may feel well. If the TSH is persistently elevated, replacement should be considered, as it may improve some metabolic factors. Normalization of TSH is especially important in women planning a pregnancy, or in those who are pregnant.

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The mainstay of hypothyroidism treatment is replacement with levothyroxine. Dosage adjustments should be made once a steady state is achieved (usually in six to eight weeks). The TSH level can be used as a guide to determine whether treatment is adequate or excessive.

Dr. Lochnan is an associate professor of medicine, University of Ottawa, and a staff physician, division of endocrinology and metabolism, The Ottawa Hospital, Ottawa, Ontario.

What is hyperthyroidism?

Aside from cases of over-replacement with thyroid hormone, the most common cause of hyperthyroidism is Graves' disease. Graves' is an autoimmune disease characterized by the presence of antibodies which stimulate the TSH receptor, leading to overproduction of thyroid hormone and thyrotoxicosis. Graves' disease may also be accompanied by ophthalmopathy or dermopathy. Patients may, but do not always have a goiter.

Hyperthyroidism is characterized by suppressed TSH and elevated FT_4 and FT_3. TSH is an excellent screening test for hyperthyroidism, although this condition is not the only explanation for low TSH levels (Table 2). Only in

A followup on Penny

The picture is consistent with subclinical hyperthyroidism. In light of her age, known CAD, and weight loss, treatment is reasonable. She declines to have a nuclear medicine scan because she says she will not agree to treatment with radioactive iodine. She is started on methimazole, 5 mg per day, with instructions to stop the drug if she develops a rash, fever, sore throat, or jaundice.

Two months later, Penny's TSH level is 2.2 mU/L. She feels great and has regained the 6 kg she had lost. She also reports she is sleeping well at night and she believes her thyroid medication has made the difference. Penny's TSH levels will continue to be analyzed every three to six months, depending on the stability of her levels.

unusual cases would TSH be elevated in hyperthyroidism.

A frequent finding is a suppressed TSH with normal FT_4 and FT_3. This finding usually represents subclinical hyperthyroidism, which has the same causes as hyperthyroidism. Patients may not have symptoms, or the symptoms may be subtle (such as insomnia or unexplained weight loss). Subclinical hyperthyroidism is associated with an increased risk of atrial fibrillation. In patients who are frail or elderly, treatment to normalize the TSH should be considered. Treatment options include antithyroid drugs, radioactive iodine, or surgery.

What are other causes of suppressed TSH?

A low TSH can be seen in central hypothyroidism, as discussed above. In these cases FT_4 is usually low. A low TSH is also often seen in individuals with non-thyroidal illness. It is a frequent occurrence in hospitalized patients, but can be seen in those with chronic illness or less severe illnesses. TSH is usually low during chronic illness and may transiently rise during recovery. Also during chronic illness, FT_4 levels may be normal, low, or elevated, and FT_3 levels can be very low. The key to determining whether or not low TSH levels are caused by non-thyroidal illness is to ensure that:

- the patient does not have strong clinical

Frequently Asked Questions

1. When should treatment for hypothyroidism be initiated?

   If the TSH is consistently above normal, treatment should be started.

2. What are features of sick euthyroid syndrome (non-thyroidal illness)?

   Patients with sick euthyroid syndrome have significant illness and do not appear to have hypothyroidism. TSH levels can be low or normal initially and may be elevated in the recovery period. The FT_4 level may be high, normal, or low, and the FT_3 level is usually very low. The biochemical abnormalities normalize as the patient recovers from the non-thyroidal illness.

3. Do all patients with thyroid nodules require a thyroid scan?

   A scan is usually ordered if the TSH is suppressed and there is suspicion that a hot nodule is present. If the TSH is normal and there is a palpable nodule, a fine-needle aspiration biopsy is indicated.

evidence of hypothyroidism,
- the patient has an acute or chronic illness, and
- that repeat testing shows improvement as the patient recovers.

No treatment is indicated in these individuals.

A similar picture can be seen in patients with psychiatric disorders, and is sometimes a side-effect of drugs, such as glucocorticoids or dopamine. In most cases, the thyroid tests normalize over a period of months.

Thyroid nodules, or goiters, are also common occurrences, although thyroid cancer is rare. The presence of a goiter or nodules does not necessarily lead to hypothyroidism or hyperthyroidism; in most cases, the TSH is completely normal. Investigation of a thyroid nodule includes TSH measurement. If the TSH level is low, a functioning nodule is possible, thus, a thyroid scan would be useful. If the TSH is normal or low, the nodule is likely non-functioning; if it is ≥ 1 cm in size, consideration for fine-needle aspiration biopsy is recommended. A nuclear medicine scan is not routinely needed when the TSH is normal. Thyroid ultrasound is a helpful tool to document the size and characteristics of the thyroid gland and nodules as a baseline indicator. Fine-needle aspiration biopsy remains the best tool, short of surgery, to help diagnose malignant thyroid nodules. Dx

Take-home message

What are the typical biochemical signs of hypothyroidism?
- High TSH
- FT_3 and FT_4 may be normal or low

What is the treatment?
- Replacement with levothyroxine, using TSH level as guide for dosage

What are the typical biochemical signs of hyperthyroidism?
- Low TSH
- FT_3 and FT_4 are usually high

What is the treatment?
- TSH can be normalized using antithyroid drugs, radioactive iodine, or surgery.

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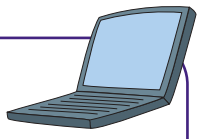

1. Thyroid Disease Manager: *www.thyroidmanager.org*
2. American Association of Clinical Endocrinologists (Clinical guidelines): *www.aace.com/clin/guidelines*
3. Mythyroid.com (Dr. Daniel Drucker, University of Toronto): *www.mythyroid.com*
4. Thyroid Foundation of Canada: *www.thyroid.ca*